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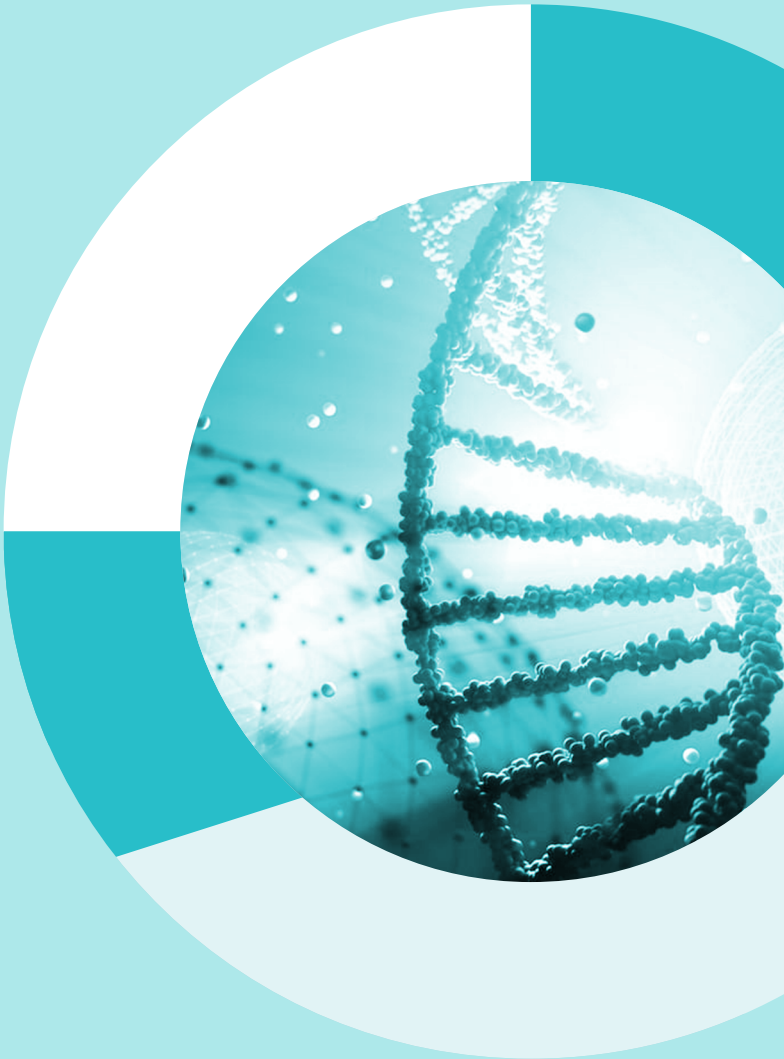

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Case Report	1200	200	15	No tables	4 or total of 8 images
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When a drug, product, hardware, or software program is mentioned within the main text, product information, including the name of the product, the producer of the product, and city and the country of the company (including the state if in USA), should be provided in parentheses in the following format: "Discovery St PET/CT scanner (General Electric, Milwaukee, WI, USA)"

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Books with a Single Author: Sweetman SC. Martindale the complete drug reference. 34th ed. London: Pharmaceutical Press; 2005.

Editor(s) as Author: Huizing EH, de Groot JAM, editors. Functional reconstructive nasal surgery. Stuttgart-New York: Thieme; 2003.

Conference Proceedings: Bengisson S. Sothemin BG. Enforcement of data protection, privacy and security in medical informatics. In: Lun KC, Degoulet P, Piemme TE, Rienhoff O, editors. MEDINFO 92.

Proceedings of the 7th World Congress on Medical Informatics; 1992 Sept 6-10; Geneva, Switzerland. Amsterdam: North-Holland; 1992. pp.1561-5.

Scientific or Technical Report: Cusick M, Chew EY, Hoogwerf B, Agrón E, Wu L, Lindley A, et al. Early Treatment Diabetic Retinopathy Study Research Group. Risk factors for renal replacement therapy in the Early Treatment Diabetic Retinopathy Study (ETDRS), Early Treatment Diabetic Retinopathy Study Kidney Int: 2004. Report No: 26.

Thesis: Yılmaz B. Ankara Üniversitesindeki öğrencilerin beslenme durumları, fiziksel aktiviteleri ve beden kitle indeksleri kan lipidleri arasındaki ilişkiler. H.Ü. Sağlık Bilimleri Enstitüsü, Doktora Tezi. 2007.

Manuscripts Accepted for Publication, Not Published Yet: Slots J. The microflora of black stain on human primary teeth. Scand J Dent Res. 1974.

Epub Ahead of Print Articles: Cai L, Yeh BM, Westphalen AC, Roberts JP, Wang ZJ. Adult living donor liver imaging. Diagn Interv Radiol. 2016 Feb 24. doi: 10.5152/dir.2016.15323. [Epub ahead of print].

Manuscripts Published in Electronic Format: Morse SS. Factors in the emergence of infectious diseases. Emerg Infect Dis (serial online) 1995 Jan-Mar (cited 1996 June 5): 1(1): (24 screens). Available from: URL: http:/ www.cdc.gov/ncidodIElD/cid.htm.

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EDITORIAL

Dear Colleagues,

I hope you are doing well. I know that we are going through wars, crimes, fires, floods, COVID-19 and other new infectious diseases and economic crises, but life continues and we must do our best. I am sorry for those who lost their lives to these tragic and painful events.

As a Cyprus Journal of Medical Sciences, we are trying to publish as many articles as we can within the scope of our journal, which we think they will contribute to the literature. We are also trying to be a bridge with other countries in the sense of sharing data, knowledge and experiences in North Cyprus.

We changed our submission fee policy and now we only demand APC charge of 100 US dollars. We will not request an APC charge from the members of the Cyprus Turkish Medical Association since they already pay a monthly membership fee.

We are sorry for the delayed publication of some articles but we are doing our best and trying to be fair. Sometimes because of current subjects and authors personal situations, we must publish some articles earlier.

We are welcome to original and review articles of specially current topics from worldwide. We would be delighted and helpful to academic medical doctors from Europe, North and South America, middle east and other parts of the world, who want to work as associate editors voluntarily. Our priority will be in those fields of, Internal Medicine, Immunology, Hematology and Oncology, Neurology, Neurosurgery, Dermatology, Urology and Pharmacology. We would also be welcome to our colleagues who want to work as referees. We will wait on your application.

I wish you all a successful, healthy and happy features and I send you my best regards.

Dr. Sonuç Büyük
Editor-in-Chief

LETTER TO EDITOR

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A Rare Complication of a Rare Disease; Spontaneous Bladder Perforation in a Case of Emphysematous Cystitis

İbrahim Topçu, Fatih Oğuz

Department of Urology, İnönü University Faculty of Medicine, Malatya, Turkey

Dear Editor,

Emphysematous cystitis (EC) is a rare variant of a urinary tract infection and it usually occurs in diabetes, neurogenic bladder and urinary stasis due to bladder outlet obstruction[1]. This infection is commonly caused by *Escherichia coli* or other bacteria such as *Klebsiella, Proteus, Clostridium, Pseudomonas* etc.[2,3]. Spontaneous bladder rupture is also a rarely seen situation and it was defined as: "*if the bladder ruptures without external stimulation, it is spontaneous and deserves to be reported as such*" by Sisk and Wear[4] in 1929. Computed tomography (CT) is recommended for both the diagnosis and classification of this disease. EC, especially when diagnosed late, may cause bladder rupture. We hereby present a patient with spontaneous bladder perforation due to EC.

Sixty-seven-year-old male patient presented with acute abdominal pain to the emergency room. The patient had a history of Alzheimer's disease, but no history of diabetes mellitus or any operation. In addition to an inability to urinate for a long time, he had a history of intermittent hematuria for the prior two months.

After examining the patient, acute abdomen was detected and we called for emergency surgery to be performed. When the pre-operative blood and imaging tests were examined, his creatinine value was found to be 7.34 mg/dL and his hemogram value was normal. The patient's CT imaging revealed intraperitoneal diffuse fluid, and perforation of the bladder from the right-anterolateral wall. There was also common mural gas in the bladder wall (Figure 1). Spontaneous bladder perforation was considered. We performed the operation and saw that the right-lateral, dome and posterior wall of the bladder were necrotic and disordered, and that the trigone and both ureters were normal (Figure 2). Partial cystectomy was performed. Meropenem treatment was initiated. During post-operative follow-up, the patient's creatinine levels significantly decreased to within the normal levels in 3 days and his hematuria improved. After 14 days of treatment, his general condition improved and the Foley catheter was removed. His pathology report also confirmed EC.

EC is a rarely seen disease characterized by the presence of gas within the bladder wall and also possibly in the lumen[5]. Spontaneous rupture of the bladder wall is rare, especially due to EC. In this case, acute abdomen due to spontaneous bladder rupture caused by EC was detected and treated by surgery and broad-spectrum antibiotics. We suggest that if the disease causes peritoneal related bladder rupture, emergency exploration should be performed and intravenous antibiotic therapy should be initiated.

Keywords: Emphysematous cystits, bladder perforation, acute abdomen

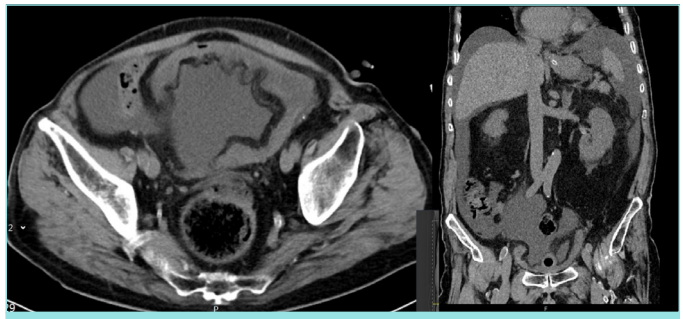

Figure 1. Computed tomography images of the bladder rupture and intra-abdominal fluid.

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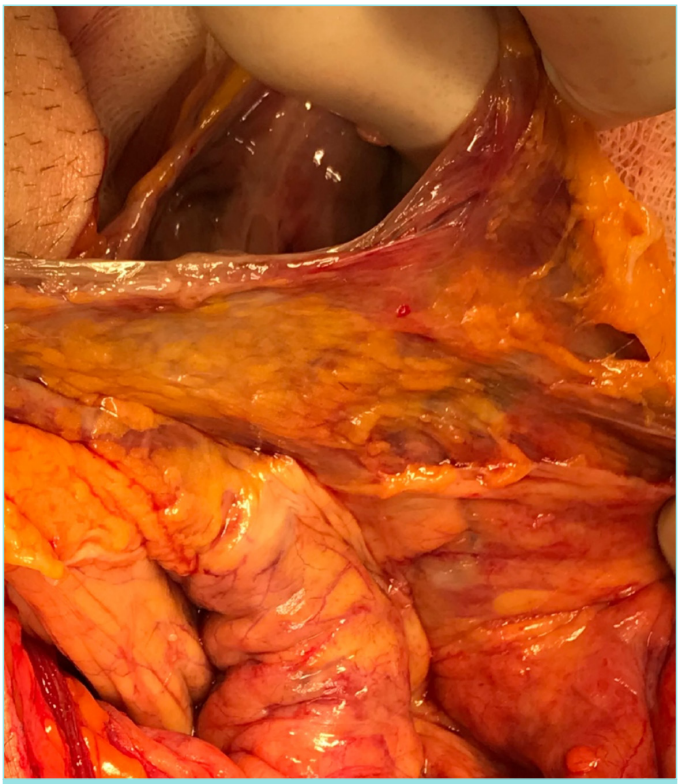

Figure 2. Bladder wall necrosis.

ETHICS

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REVIEW

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Intraoral Repair of Dental Restorations with Resin Composite

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Abstract

Dental restorations suffer deterioration and degradation over time due to undesirable conditions; accordingly, their clinical life is reduced. The complete removal of defective dental restoration can lead to progressive cavity enlargement with unnecessary sound tooth tissue removal and weakening of the remaining dental tissue, which can lead to complicated treatment procedures, loss of vitality of the tooth, and result in an economic disadvantage. The repair approach, which provides the advantage of preserving a sound tooth structure by keeping tissue loss to a minimum level, has become an alternative to the replacement process. Today, there is not a clear consensus on selecting the appropriate treatment method from between the repair or replacement procedures. This review aims to provide information about the procedures to be applied when the repair approach is to be carried out, surface treatment methods and some of the results of studies on this subject which were carried out within the last 5 years.

Keywords: Composite resin, dental restoration repair, ceramics, CAD/CAM, surface treatment

INTRODUCTION

One of the most important principles of modern dentistry is minimally invasive interventions. Dentists should be cautious during the removal process in order to prevent unnecessary loss of sound tooth tissue.[1] Although their durability has been increased with improvements developed in recent years, dental restorations suffer deterioration and degradation due to undesirable conditions in the oral environment over time.[2,3] Localized secondary caries, localized defects, and defective restorations are amongst the most commonly encountered clinical observations in dental practice.[3]

For defective restorations, there are 4 options which can be carried out which were clearly defined in 2004 by Setcos et al.[4] In the presence of minor defects such as superficial staining which do not cause clinical disadvantages, only monitoring without treatment can be chosen. Refurbishment is the process done without damage to the tooth surface such as; recontouring the surface, removal of discoloration, removal of overhangs, sealing of small gaps, and pores without adding new restorative material (except bonding or glaze).[5] Repair is the treatment of localized defects that are clinically unsatisfactory by partially removing the defective part and adding new restorative material. Replacement is the process including the complete removal and rebuilding of defective restoration. While removing the restorative material, the portions that might appear to be clinically acceptable can also be removed. This application also can lead to a loss of dental tissues.[5,6]

Renovation of existing restorations is one of the most common clinical applications in dental practice. Studies have shown that almost half of the restorations performed in dental practice are replacements of restorations rather than new restorations. The complete removal of defective dental restoration approach can lead to progressive cavity enlargement with unnecessary sound tooth tissue removal. This can cause an acceleration in the restoration cycle accompanied by complicating the treatment process and even loss of tooth vitality.[3]

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Further disadvantages of replacements of restorations are that they are an expensive and time-consuming method.[7]

Repair of the restoration approach, which provides the advantages of preserving the sound tooth structure by keeping material loss to a minimum level, and reducing microbial adhesion to the damaged areas, is a viable alternative to the replacement process.[8,9]

Advances in adhesive technology, an integral part of the minimally invasive treatment approach, enable intraoral repair of defective indirect and direct restorations using composite resins so as to extend the longevity of the restoration.[3]

Advantages of repair instead of replacement of a restoration can be summarized as follows;[8,10]

- Preservation of dental remnant and reduction of tooth tissue loss

- Reduction of the risk of pulp damage

- No anaesthesia is needed unless the area to be repaired is large

- Reduction of the risk of iatrogenic damage

- Shortened treatment time

- Reduction of the cost of treatment

- Extension of the life cycle of restoration

- Protection against mercury vapours which may harm patients and dentists during the removal of amalgam restoration.

The results of the meta-analysis of Kanzow et al.[11] published in 2018 showed that although the repair process was taught in most schools, repair of partial defective restorations was preferred by only about two thirds of dentists. In Turkey, it was reported that the demographic differences of Turkish practitioners and the differences of the cases might affect the decision for repair or replacement. It was stated in that study that younger dentists preferred repair procedures more, but this difference with the older ones was not significant.[2] It is obvious that the repair approach, which causes less tooth tissue loss, should be preferred more in suitable indications. Additionally, to the best of our knowledge, there is no clear consensus on the best surface treatment method that should be used in the repair treatment protocol. Therefore, this review aims to provide information about the procedures to be applied when the repair approach is to be carried out and to present the surface treatment methods and results of many studies on this subject which were carried out within the previous 5 years.

Surface treatment methods: The prerequisites for repair protocols are applying the ideal surface treatment method for the existing restoration, and selecting an appropriate adhesive and restorative material.[7] Removing the superficial layer to expose a clean and high-energy surface and increasing the bonding area by creating irregularities are the two main purposes of surface treating the pre-existing adhesive restorations.[12] Surface treatment methods in the repair protocol investigated in the literature are; surface grinding with burs,[13] laser irradiation, surface etching with phosphoric acid and hydrofluoric acid and air abrasion with alumina particles as mechanical procedures, silane applications, and the use of adhesives as chemical procedures[7,13] and additionally tribochemical silica coating as both a mechanical and chemical procedure.[13] The purpose of these procedures is to increase the surface energy of the existing restorative material to be repaired and provide better wettability by the adhesive agents. There have been many investigations about the materials and techniques in the literature[9,12-14] but there is no clear consensus on a universal technique that should be used in repair protocols since there is a great variability in composition among different brands of resin composites.[7]

Air abrasion/sandblasting with Al_2O_3: Sandblasting is a surface roughening method based on direct sandblasting of the surface by an intraoral device that cleans the surface, increases the surface area used for bonding, and provides micromechanical retention by applying aluminium oxide particles to the restoration surface with a certain pressure.[15] Resin composite, amalgam, ceramic, or metal materials are abraded from a distance of approximately 10 mm for about 10 seconds by 30 to 50 µm aluminium oxide particles.[7]

Tribochemical silica-coating: Silica-coating or tribochemical surface conditioning provides micromechanical retention with aluminium oxide particles coated with a silicone-dioxide layer. The tribochemical silica-coating process strengthens the adhesion to the surface of silica-free material. This reinforcement is accomplished by bonding the silane coupling agent to the silica-coated layer formed on the substrate material.[7] The basic principle of the tribochemical silica-coating procedure is that mechanical energy causes chemical and physicochemical changes in the substance throughout the application.[16] Thus, the tribochemical coating can be used to increase both mechanical and chemical bonding. The CoJET (3M ESPE, Seefald, Germany) device is used in dentistry for this purpose.[13]

Bur abrasion: This method is based on the simple roughening of the restoration surface with diamond burs that are commercially available with different grit sizes. After the surface is abraded using diamond burs, macro mechanical retention is achieved through holes and undercuts.[17] It is claimed to be advantageous since it is an easy procedure to be applied and does not require additional equipment or chemical substances allowing it to be cost-effective. In one study, the effect of surface roughness and repair bond strength of three different grit sizes (medium, fine, extra-fine) were evaluated and all types of burs with different grit sizes increased the repair bond strength when compared to an untreated control group. Additionally, it was found that the difference among the grit-sizes affected the repair bond strength. Medium-grit-sized diamond bur showed the lowest repair bond strength while fine grit size achieved the highest repair bond strength.[17] Tınaztepe et al.[18] compared the shear bond strength values of three pre-treatment groups; diamond bur grinding, silica coating, and no treatment, for the repair of CAD/CAM resin nanoceramics with composite repair materials. After each surface pre-treatment group, they applied 4 different conditioning methods. The conditioning methods were as follows; Adper scotchbond multipurpose adhesive (3M ESPE, St. Paul, MN, USA), Scotchbond universal (3M ESPE), Ultradent silane (Ultradent, USA) + Adper scotchbond multipurpose adhesive (3M ESPE, St. Paul, MN, USA) and no conditioning. At the end of the study, they concluded that surface treatment followed by diamond bur grinding followed by silane and adhesive application is superior to the silica coating, and no treatment groups.[18]

Surface etching: Surface etching procedures are usually carried out with phosphoric or hydrofluoric acid in restorative dentistry. Etching with 30-40% phosphoric acid is used for both enamel and dentin tissue. Thus, the smear layer is completely removed; micro-porosity is obtained on the surface, and the bonding capacity increases.[19] Although phosphoric acid is effective in enamel and dentin, it has no direct effect on the surface characteristics of composite resins, ceramics, and metals.

Unlike phosphoric acid, hydrofluoric acid dissolves glass particles and exposes the crystalline matrix in ceramic causing increased surface roughness.[7,20] Enhanced wettability and surface energy are also provided by this process leading to increased bond strength. In cases of resin composite, the effect of hydrofluoric acid is highly dependent on the filler particle composition. Phosphoric acid with 37% concentration is not as adequately effective in removing silica as hydrofluoric acid. 4-10% concentration is recommended to obtain better bond strength for hydrofluoric acid.[20]

Laser irradiation: The application of laser irradiation on enamel surface leads to an irregular and rough shape with the effect of micro-explosions. The surface roughness that is realized is different from acid roughening. After the traditional method, a structure with boundaries of prisms is formed, while after laser irradiation different structural shapes with different sizes and depths are formed.[21] Er:Cr:YSGG (erbium, chromium: yttrium, scandium, gallium, garnet), Er:YAG (erbium: yttrium, aluminium, garnet), neodmium: yttrium, aluminium, garnet (Nd:YAG) and CO_2 (carbon dioxide) lasers are the types of lasers generally used for this procedure. It can be concluded from the studies in the literature that the type of laser used and the substrate material to be repaired are the two most important factors determining the efficiency of this surface treatment method.[16]

Silane coupling agent application: Silane coupling agents are important mediators for combining two dissimilar materials.[16] Silane is a primer with two functional groups, the silanol and the organofunctional groups increase the bond strength between organic and inorganic matrices.[7,14,16,22] The silanol group of silane bonds to the silica and/or alumina particles of the surface-treated substrate material[7,14] and the organofunctional group attaches to the methacrylate of the adhesive system.[14]

Adhesive agents: Adhesive systems have become more important with the repair approach. The content and application method of the adhesive system used for repair affects the success of the repair.[23] The adhesive systems can be divided into two: namely "*etch & rinse*" and "*self-etch adhesive*" systems according to their interaction with the dental substrate. *Etch & rinse* systems, which contain separate etching and rinsing, are classified as 3-step or 2-step depending on the combination of primer and adhesive resin separately or in a single bottle respectively.[24] Unlike *etch & rinse* systems, *self-etch* systems do not require separate etching and rinsing steps thanks to the monomers they contain. Thus, less application time and technical sensitivity as well as lower sensitivity in post-operative make these systems more user-friendly.[25] *Self-etch* adhesive systems are classified as "one-step" or "two-step" according to the number of clinical application steps.[24]

Universal systems can be used for bonding to both dental tissues and restoration materials thanks to the special monomers they contain. The most widely used is 10-Methacryloyloxydecyl dihydrogen phosphate (MDP) functional monomer, which apart from mechanical bonding, provides chemical bonding to restoration materials such as zirconia, while providing mechanical bonding as well as forming insoluble calcium salts in dental tissues. The compatibility of universal adhesives with resin-based systems has the advantage that they can be used in the cementation of indirect restorations. It is also stated that it can be used as a primer in zirconia, precious-nonprecious metal alloys, composite resins, and various silica-based ceramics. In this way, universal adhesives make it possible to bond to these surfaces without the need for separate agents.[26] In addition to being able to be used for adhesion of indirect restorations, universal adhesives can also be used to repair these restorations, and surface roughening is recommended by using burs or air-abrasion before adhesive application in order to increase bond strength. Some manufacturers have added silanes to universal adhesives to simplify the bonding protocol of glass-matrix ceramic restorations. Since bonding is adversely affected due to changes in the content added to the silane, a separate silane application before universal adhesive is recommended for optimal adhesion.[27]

The literature was searched electronically via the PubMed database using the keywords "repair, bond strength, composite resin, surface treatment" as MeSH terms. Original research articles published in English between 2015 to February 2020 were deemed eligible for inclusion. The titles and abstracts of all articles available as full text were carefully reviewed to eliminate those articles that were not within the scope of this review. If the focus of the article could not be determined exactly from the title and abstract, the full text of the article was examined. The surface treatment methods, materials and conclusions of the studies selected in accordance with the specified criteria for resin composites and ceramics, and CAD/CAM materials are indicated in Table 1 and Table 2 respectively.[1,9,13,14,20,22,28-50]

CONCLUSION

For composite repair, air abrasion and diamond burs can both be effectively used for surface roughening, however, the advantages such as ease of availability, lower cost, and reduced risk of damage to the patient make surface roughening with diamond burs preferable. After roughening, the debris on the surface should be removed with phosphoric acid and thus the surface energy should be increased. Micro-hybrid composite resins seem beneficial to be used as the repair material.

In the repair of ceramic restorations, after surface roughening with burs, it is recommended to use hydrofluoric acid if the ceramic material contains silica, and to apply tribochemical silica-coating to the surface if the ceramic does not contain silica. In the next step, by applying silane, both surface wettability and adaptation of the adhesive resin to the surface can be increased. The content of the composite resin as a repair material does not make a significant difference.

In the repair procedure, the application of an adhesive resin step seems to have a positive effect on the bond strength. Universal adhesives in adhesive systems stand out with their special functional monomers which can provide chemical bonding to some materials, for their ease of use and also due to the property that they can be applied as a thinner layer than other systems.

MAIN POINTS

- Repair of restorative materials, which are currently the preferred procedures in terms of minimally invasive approaches, should be performed with surface roughening procedures.
- In cases of composite repair, surface treatment with air abrasion or diamond burs can be effective. However, advantages such as ease of availability, lower cost, and reduced risk of damage to the patient make surface roughening with diamond burs preferable.
- In the repair of ceramic materials, the silica content of the material is important for the surface treatment to be preferred.
- Applications of adhesive resin systems have a beneficial effect on the repair of aesthetic restorative materials.

Table 1. Surface treatment methods used and conclusions of the studies on resin composites

Publication	Substrate	Repair Material	Surface Treatments	Adhesive	Silane	Conclusion
Kaneko et al.[28]	SRC, MRC	SRC, MRC	Al_2O_3	TE	+	Al_2O_3 + adhesive + silane application increased tensile repair bond strength of MRC. It showed higher repair ability than SRC.
Gupta et al.[20]	Nanofill RC	Nanofill RC	H_3PO_4, HF	TE	-	HF application was found to provide more effective shear bond strength than H_3PO_4.
Consani et al.[29]	MRC, SRC	MRC	Al_2O_3	TE	+	Higher tensile bond strength values were observed in MRC samples and greater percentage of adhesive failures in SRC samples.
Wendler et al.[1]	Nano-hybrid RC	Nano-hybrid RC	H_3PO_4, Bur abrasion, Al_2O_3, Tribochemical silica coating	UA, TE	-	Application of bonding system plays a key role in achieving reliable repair tensile bond strengths. Importance of surface treatment method plays a secondary role in bond strength.
Ahmadizenouz et al.[30]	Nanofilled-RC	Nanofilled-RC	H_3PO_4, HF, Laser irradiation, Bur abrasion, Al_2O_3	TE	+	All surface treatment methods showed similar and optimal repair bond strengths.
Arami et al.[31]	Giomer	Giomer	Laser irradiation, Bur abrasion, Al_2O_3	SE	-	The highest repair bond strength was observed in air abrasion group followed by laser and bur groups respectively.
Souza et al.[22]	Micro-hybrid RC	Micro-hybrid RC	HF, Al_2O_3	UA	+	Sandblasting with Al_2O_3 followed by application of a silane layer produced high micro-tensile bond strength after aging procedure up to 1 year.
de Jesus Tavares et al.[32]	Nanofill RC	Microhybrid, nanofilled bulk-fill RC	H_3PO_4, Bur abrasion	TE	-	The micro-shear bond strength of the RC repairs varies in accordance with the type of RC utilized, and roughening the surface is needed to increase the bond strength of these materials.
Kiomarsi et al.[33]	Microhybrid RC	Microhybrid RC	H_3PO_4, Laser irradiation, Bur abrasion	TE	+	Bur abrasion was found to be more effective than laser.
Kiomarsi et al.[34]	Microhybrid RC	Microhybrid RC	H_3PO_4, Bur abrasion	TE, UA	+	Surface preparation of aged RC by bur and application of UA can improve the repair bond strength of RC. Application of silane without adhesive was found to be unsuccessful in providing adequate bond strength. UA showed higher bond strength than TE.
Ghavam et al.[35]	Microhybrid nanohybrid RC, Giomer	Microhybrid nanohybrid RC, Giomer	H_3PO_4, Laser irradiation	TE	-	Laser irradiation + etching was found to increase the micro-tensile bond strength in all groups but giomer groups had a reduction in bond strength.
Altinci et al.[36]	Nanohybrid, Hybrid, Nanofill RC	Nanohybrid, Hybrid, Nanofill RC	Bur abrasion, Tribochemical silica coating	UA	+	UA application is a reliable method for composite repair. Sandblasting and silane application slightly increased the repair strength for all substrate types.
Kouros et al.[37]	Nanofilled RC, MBC, SRC	Nanofilled RC, MBC, SRC	H_3PO_4, Bur abrasion, Al_2O_3	SBA, TE	-	The most critical factor in repairing procedure is selecting the repairing material. Silorane was not a good option for repairing an aged RC.
Ayar et al.[38]	Bulk-fill RC, Conventional posterior RC	Bulk-fill RC, Conventional posterior RC	H_3PO_4, HF	TE	-	The combined application of HF acid etching and adhesive application was found to provide the effective shear bond repair strength.

Table 1. Continued

Publication	Substrate	Repair Material	Surface Treatments	Adhesive	Silane	Conclusion
Sismanoglu[13]	Nanofill RC	Self-adhering flowable RC	H_3PO_4, Al_2O_3, Tribochemical silica coating	UA	-	Acid etching followed by universal adhesive application obtained acceptable micro-tensile repair performance with flowable RC.
de Medeiros et al.[14]	Bulkfill RC, conventional RC	Micro-hybrid RC	H_3PO_4, Bur abrasion	TE, UA	+	Similar micro-tensile bond strength values among different adhesion protocols were observed. Comparable bond strength values are presented between repairs of bulk fill composites and conventional composites.
Kanzow et al.[39]	Conventional RC, Amalgam	Conventional RC	Bur abrasion, Al_2O_3, Tribochemical silica coating	TE, UA	-	Amalgam restorations may be repaired using RC, but the shear bond strength was lower than that obtained with RC. Amalgam repair with RC was suggested to be done with silica coating and application of a silane-containing adhesive.
Eren et al.[40]	Nanohybrid RC	Nanohybrid RC, Self-adhering flowable RC	H_3PO_4, Laser irradiation, Bur abrasion, Al_2O_3, Tribochemical silica coating	SE	+	Bur abrasion, silica coating and air abrasion with Al_2O_3 showed reliable shear bond strengths while laser abrasion was not recommended.

RC: resin composite, H_3PO_4: phosphoric acid etching, HF: hydrofluoric acid etching, Al_2O_3: aluminum oxide, MRC: methacrylate-based resin composite, SRC: silorane-based resin composite, SE: self-etch, TE: total-etch, UA: universal adhesive, SBA: silorane-based adhesive, Ni: nickel, Cr: chromium.

Table 2. Surface treatment methods used and conclusions of the studies on ceramic and CAD/CAM materials

Publication	Substrate	Repair Material	Surface Treatments	Adhesive	Silane	Conclusion
Neis et al.[41]	Feldspathic ceramic, leucite-reinforced glass-ceramic, lithium disilicate-reinforced glass ceramic	Nanofilled RC	H_3PO_4, HF, Bur abrasion, Tribochemical silica coating	TE	+	Effective surface treatment method varies depending on the type of ceramic. Suitable matches were: Feldspathic and leucite-reinforced ceramics-bur abrasion, lithium disilicate-reinforced ceramic- HF etching, leucite-reinforced ceramic -tribochemical silica-coating.
Wiegand et al.[42]	Polymer-based CAD/CAM material, MRC	MRC	Bur abrasion, Al_2O_3, Tribochemical silica coating	TE	+	Surface pre-treatment especially tribochemical silica coating was recommended for CAD/CAM polymers. Repair bond strength of CAD/CAM polymers was found to be weaker than RC.
Sadeghi et al.[43]	Feldspatic Porcelain	Micro-hybrid RC	HF,Laser irradiation	SE	+	Pre-treatment with HF acid was found to provide more effective shear bond strength than laser irradiation.
Yoo et al.[44]	Feldspatic porcelain, Ni-Cr metal alloy	Micro-hybrid RC	HF, Bur abrasion, Al_2O_3, Tribochemical silica coating	SE, TE	+	Al_2O_3 blasting application was suggested for repairing a fracture with exposed area of porcelain. Tribochemical silica coating was recommended if the fracture extended to the metal surface.
Duzyol et al.[45]	Lithium disilicate CAD/CAM, feldspar ceramic CAD/CAM, nanoceramic resin CAD/CAM	Nano-hybrid RC	HF, Bur abrasion, Al_2O_3, Tribochemical silica coating	UA	+	Lithium disilicate CAD/CAM materials require an etching procedure for repair. Surface treatments did not increase repair micro-tensile bond strength of feldspar ceramic CAD/CAM material while they reduced the bond strength of the nanoceramic resin group.
Subaşı and Alp.[46]	Aged-non-aged nanoceramic CAD/CAM	Nano-hybrid RC	Al_2O_3, Tribochemical silica coating	UA	-	For aged nanoceramic CAD/CAM restorations, Al_2O_3 blasting is recommended as a surface treatment method.

Table 2. Continued

Publication	Substrate	Repair Material	Surface Treatments	Adhesive	Silane	Conclusion
Tatar and Ural.[47]	Polymer infiltrated ceramic, nanoceramic CAD/CAM	Micro-hybrid RC	HF, Tribochemical silica coating	-	+	Each surface treatment increased shear-bond strength but air-abrasion with silica coating was found to be the best choice.
Atatol and Ergun.[48]	Lithium disilicate glass ceramic CAD/CAM, Yttrium-stabilized zirconium oxide ceramic CAD/CAM, Zirconia-reinforced lithium silicate glass ceramic CAD/ CAM	Nanofilled RC	HF, Laser irradiation, Al_2O_3	UA	+	Only Al_2O_3 blasting and HF etching provided satisfactory repair bond strengths for each CAD/CAM ceramic tested.
Silva et al.[9]	Hybrid ceramic CAD/CAM	Nanofilled RC	HF, Bur abrasion, Al_2O_3, Tribochemical silica coating	UA	+	Grinding with silicon carbide paper followed by the application of a universal adhesive system is the best option for repairing fractures of the hybrid ceramic CAD/CAM material
Arpa et al.[49]	Nanoceramic CAD/CAM block	Nanofilled RC	H_3PO_4, Al_2O_3, Tribochemical silica coating	UA, TE	+	Air-abrasion with Al_2O_3 or tribochemical silica coating followed by UA application is recommended.
Verissimo et al.[50]	Nanoceramic resin CAD/CAM, Hybric ceramic CAD/CAM, Glass ceramic CAD/CAM	Nanofill RC	HF, Bur abrasion, Al_2O_3, Tribochemical silica coating	UA, TE	+	In situ aging procedure reduced the repair shear bond strength of nanoceramic resin and polymer-infiltrated hybrid ceramic CAD/CAM materials. The best repair protocol for each restorative material differed, with bur-roughening+UA for nanoceramic CAD/CAM and acid etching+silanization recommended for hybrid ceramic and glass ceramic CAD/CAM.

RC: resin composite, H_3PO_4: phosphoric acid etching, HF: hydrofluoric acid etching, Al_2O_3: aluminum oxide, MRC: methacrylate-based resin composite, SRC: silorane-based resin composite, SE: self-etch; TE: total-etch, UA: universal adhesive, SBA: silorane-based adhesive, Ni: nickel, Cr: chromium.

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ORIGINAL ARTICLE

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Magnitude of Antibody Response and Risk Factors for Reduced Immunogenicity after Two Doses of an Inactivated Whole-Virion COVID-19 Vaccine (CoronaVac®)

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Abstract

BACKGROUND/AIMS: CoronaVac® is an inactivated whole-virion Coronavirus disease-2019 vaccine and represents the very first tool in the protective armamentarium in North Cyprus. The aim of this study was to determine the magnitude of anti-severe acute respiratory syndrome-coronavirus 2 spike (S) total immunoglobulin response and the risk factors for reduced immunogenicity post-vaccination.

MATERIALS AND METHODS: Four hundred and twenty-six adults from the general population of North Cyprus were enrolled in this study from the 20th of March 2021 to the 10th of August 2021. The participants involved were actively immunized (with two doses of CoronaVac® at an interval of four weeks).

RESULTS: After the second dose of CoronaVac®, anti-S antibodies were detected in 76% of the participants. Seropositivity was slightly higher among women (77%) than men (75%). Although, intriguingly, seropositivity was found to be highest in both women and men above 65 years, the magnitude of antibody response was moderately negatively correlated with age (r=-0.26), and antibody titers and age were significantly associated ($p<0.001$). Similarly, mean antibody titers for the three age groups studied (18-45, 46-65, >65 years) were significantly different from each other ($p<0.001$), and the magnitude of antibody response decreased as age increased.

CONCLUSION: No statistically significant relationship between self-reported chronic disease status and antibody response to CoronaVac® was found. Quantitation of anti-S antibodies may help facilitate longitudinal monitoring of the humoral response, which can be useful in deciding the dose of CoronaVac® in groups over 65 years of age. This may also help measure the effectiveness of CoronaVac®-based mass vaccination campaigns in yielding collective protection.

Keywords: Antibody titers, CoronaVac, COVID-19, SARS-CoV-2, seropositivity

INTRODUCTION

A previously unheard-of coronavirus crossed the species barrier and emerged as severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2), a novel virus to which humans had no immunity, in Wuhan (Hubei Province, China) in December, 2019. The virus was identified as the causative agent of atypical pneumonia, now called Coronavirus disease-2019 (COVID-19). In spite of containment efforts initiated by public health authorities in China, SARS-CoV-2 rapidly spread across the globe, currently affecting the Americas, Europe, South-East Asia, the Eastern Mediterranean, the Western Pacific, and Africa. COVID-19 was declared a pandemic by the World Health Organization (WHO) on the 11th of March, 2020. As of the 15th of November, 2021, SARS-CoV-2 had

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infected over 250 million people worldwide, with over 5 million deaths reported.[1]

Physicians and scientists around the world have been racing to develop vaccines for COVID-19 since the pandemic began. Acquiring immunity through vaccination is important to the community and, in particular, to those people at increased risk of severe COVID-19, including healthcare professionals, the elderly, and those with underlying chronic conditions. To date, several different types of potential COVID-19 vaccines have been developed, such as inactivated or weakened virus vaccines, viral vector vaccines, RNA and DNA vaccines, and protein-based vaccines. Some of them (e.g. DNA and protein-based vaccines) still await to be listed for WHO emergency use listing. As of November 10th, 2021, over 7 billion vaccine doses had been administered worldwide.[1]

In the fight against the COVID-19 pandemic, Turkey's Pharmaceuticals and Medical Devices Agency gave emergency use approval for the use of an inactivated whole-virion COVID-19 vaccine, called CoronaVac® (produced by the Beijing-based pharmaceutical company Sinovac), on the 13th of January, 2020. The first phase of vaccination started on the 14th of January, 2020 with healthcare workers. The same vaccine was included shortly afterward in the national mass vaccination program of the general population of North Cyprus, which is the subject of this report. The WHO validated CoronaVac® for emergency use on the 1st of June, 2021, giving other countries the assurance that it meets international standards for safety, efficacy, and manufacturing.[2]

The efficacy of CoronaVac® against symptomatic SARS-CoV-2 infection and severe COVID-19 (in which hospitalization is required) and its safety among volunteers aged 18-59 was demonstrated in a double-blind, randomized, placebo-controlled phase 3 clinical trial in Turkey.[3] Outside the scarce number of trials, there are limited data on post-vaccine antibody responses in other groups such as older (>65 years) adults. Also, parameters which predict the risk of low or no antibody titers to inactivated SARS-CoV-2 are yet to be defined explicitly. In the present study, we aimed to determine the magnitude of anti-spike total immunoglobulin response and risk factors for reduced immunogenicity post-vaccination in 426 adults from the general population of North Cyprus.

MATERIALS AND METHODS

Type of research: This study was a retrospective one which involved participants who were actively immunized with two doses of CoronaVac® at an interval of four weeks.

Study Design and Population

The study period comprised of nearly 21 weeks from the 20th of March 2021 to the 10th of August 2021, with test carried out at the Erduran Lab in Kyrenia. During this time, the predominant circulating SARS-CoV-2 lineages in North Cyprus were wild-type and the alpha variant of concern (B.1.1.7). The participants involved were actively immunized (with two doses of CoronaVac® at an interval of four weeks), they were both male and female adults (≥18 years of age) who were interested in confirming their own vaccination success based on the detection of anti-spike antibodies. Those participants who had previously had COVID-19 were excluded from this study. Chronic conditions present in the participants were recorded based on their self-reported information.

Ethical considerations: This study was conducted with Cyprus Science University, Ethics Committee's approval (approval number: 2021.12.002). All participants gave their oral consent to participate in this study, which was conducted in accordance with the Declaration of Helsinki.

Vaccine

CoronaVac® is manufactured by Sinovac Life Sciences. Its production cycle involves inoculating SARS-CoV-2 (CZ02 strain) onto African green monkey kidney cells (Vero cells), cultivation, harvest, inactivation, concentration, purification, and aluminum hydroxide adsorption. Each vial contains a single dose of 0.5 mL which is composed of inactivated SARS-CoV-2 (CZ02 strain) at 600 SU (active ingredient), aluminum hydroxide at 0.225 mg (adjuvant), and excipients (phosphate at 0.0025 mmol, sodium chloride at 4.5 mg, and water for injection). The vaccination of the participants was performed in authorized hospitals with the recommended dosing interval of four weeks between the first and second doses, which were administered into the deltoid muscle.

Sample Collection

Blood samples were collected from the participants within 14 to 28 days after the administration of the second dose of CoronaVac®. Participants underwent blood sampling with standard venipuncture at a single center. Serum separator tubes with separating gel and clot activator were used for the blood collection.

Analysis of Samples

The Elecsys® anti-SARS-CoV-2 S immunoassay (Roche) running on a cobas® e801 modular analyzer (Roche) was used for the analysis of the samples collected. Elecsys® anti-SARS-CoV-2 S is a relatively fast (testing time: 18 minutes) one-step double-antigen sandwich assay for the *in vitro* quantitative determination of total antibodies (including IgG) directed against the SARS-CoV-2 spike (S) protein receptor-binding domain in human serum and plasma. The linear quantification range of the assay is between 0.4 U/mL and 250 U/mL, and the manufacturer's stated threshold cut-off for reactivity or positivity is 0.8 U/mL. The clinical sensitivity of the assay is reported to be 98.8%, and its clinical specificity is nearly 100%. (sensitivity estimations are based on a sampling date of ≥14 days after diagnosis with real-time quantitative PCR).

Statistical Analysis

All statistical analyses were carried out by R packages (available at https://www.r-project.org) and functions, ANOVA (analysis of variance), Student's t-test (t-test), cor.test (correlation test), cor (correlation coefficient), wilcox.test (Wilcoxon test), glm (..., family='binomial') (logistic regression). In group comparisons, One-Way analysis of variance (ANOVA) or independent samples t-tests were used for continuous variables and χ^2-test was used for qualitative variables. In all evaluations, $p<0.05$ was considered statistically significant.

RESULTS

Table 1 shows the descriptive statistics of the patients in terms of frequency and percentage values for the different age groups. A total of 426 patients were enrolled at the beginning of this study. The mean age (± standard deviation) of the participants was 57.7 (±16.7) years, and their median age was 61 years old. The minimum age was 18 years, and the maximum age was 91 years old. The cohort had a slightly greater representation from male individuals, with 55% male and 45% female. The age distribution was as follows: 18-45 years old, 113 (27%); 46-65 years old, 159 (37%); 65 years old and above, 154 (36%) (Table 1).

Table 1. The demographic characteristics of the patients according to their age groups

Patients (%)			
Age (years)	**Female (%)**	**Male (%)**	**Total (%)**
Age (mean ± SD)	55.9 (±16.6)	59.1 (±16.6)	57.7 (±16.7)
18-45 years	57 (30)	56 (24)	113 (27)
46-65 years	73 (38)	86 (36)	159 (37)
>65 years	60 (32)	94 (40)	154 (36)
Total	190 (45)	236 (55)	426 (100)

SD: Standard deviation

Table 2 shows the quantitative assessment of anti-SARS-CoV-2 S total immunoglobulin seropositivity in the patients 14-28 days after the second dose of the CoronaVac® vaccination. Between 14-28 days, anti-S antibody levels were detectable in 324 out of 426 patients. Seropositivity was slightly higher among females (147/190 or 77.4%) than among males (177/236 or 75.0%), though this difference was not statistically significant. In addition, seropositivity was found to be highest in both women and men above 65 years old (81.7% and 81.9%, respectively). Among patients between 46 and 65 years, anti-S antibodies in females and males were 74% and 75.6%, respectively, and among those between the ages 18-45, it was 77.2% in females and 62.5% in males. There was no statistically significant difference between the age groups of both genders in terms of anti-S antibody seropositivity.

Linear correlation between age and anti-S immunoglobulin levels was -0.26 ($p<0.001$) and 95% confidence interval (-0.36, -0.15). Therefore, there seems to be a low-to-moderate negative correlation between age and antibody levels. Figure 1 shows the linear regression plot of anti-S total immunoglobulin and age. As can be seen from this plot, the association between the two variables is highly significant ($p<0.001$).

Table 3 shows logistic regression results with age for different threshold values for the anti-S total immunoglobulin in binary categories, namely (Ig <251, Ig >251), (Ig <201, Ig >201), (Ig <151, Ig >151), (Ig <101, Ig >101) and (Ig <51, Ig >51). Therefore, the logistic regression results for Ig <201, with Ig >201 as the dependent variable, and age as independent variable are significantly associated ($p=2.537614e-05$). Therefore, we can say that the mean age of the patients in the groups with titers <201 versus titers >201 is the most statistically significant ($p<0.001$).

Pearson's χ^2-test for the three immunoglobulin levels <150, 150-250, >250 for the three age groups (18-45, 46-65, >65 years) was statistically significant ($\chi^2=46.4$ with 4 df; $p<0.001$). Therefore, χ^2-test of independence shows that the three titer groups are independent from the three age groups (Table 4). One-Way analysis of variance (ANOVA) results comparing the three age groups (18-45, 46-65, >65 years) for

Table 2. Quantitative assessment of anti-SARS-CoV-2 S total immunoglobulin seropositivity in patients 14-28 days after their second dose of vaccination with CoronaVac®

Characteristics of patients (n=324)			Anti-S antibodies			
Age by group	**Gender**	**COVID-19 history**	**Antibody state (%)**	**Median**	**Minimum**	**Maximum**
18-45 years, (n=113)	Male	Positive	33	207.65	35	>250
		Negative	2	0	0	0
		Male total	**35 (62.5)**	207.65	35	>250
	Female	Positive	43	250	28	>250
		Negative	1	0	0	0
		Female total	**44 (77.2)**	250	28	>250
		Total	79 (69.9)			
46-65 years, (n=159)	Male	Positive	62	93	15	>250
		Negative	3	0	0	0
		Male total	**65 (75.6)**	92	1	>250
	Female	Positive	52	174	21	>250
		Negative	2	0	0	0
		Female total	**54 (74.0)**	174	21	>250
		Total	119 (74.8)			
>65 years, (n=154)	Male	Positive	72	142.10	35	>250
		Negative	5	0.4	0	0
		Male total	**77 (81.9)**	137.65	0	>250
	Female	Positive	48	183.4	16	>250
		Negative	1	0	0	0
		Female total	**49 (81.7)**	183.4	16	>250
		Total	126 (81.8)			

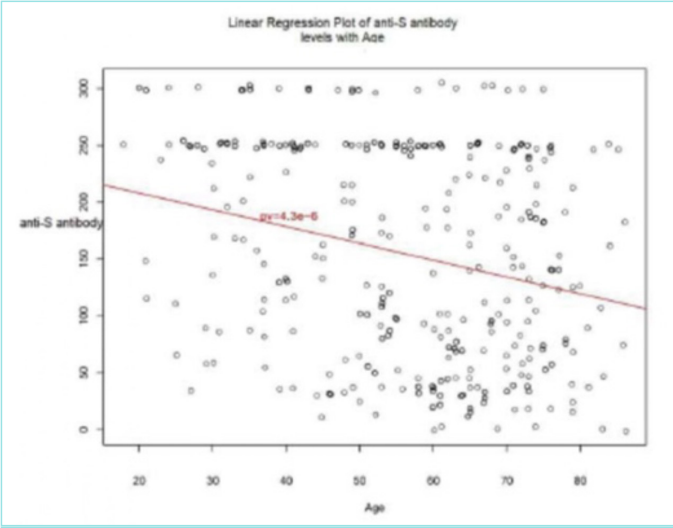

Figure 1. Linear regression plot of anti-S total immunoglobulin and age

anti-S total immunoglobulin levels gives a statistically significant result ($p<0.001$). Therefore, differences in mean immunoglobulin levels for the three age groups are statistically significant. Overall, our findings clearly indicate that as the age increases, immunoglobulin levels decrease.

Table 5 shows the percentage of patients with and without comorbidities. Table 6 shows the additional diseases which the patients had; 6.7% had diabetes mellitus, 15.4% had both diabetes mellitus and hypertension, 41.2% had hypertension, 0.5% had chronic obstructive pulmonary disease, 0.5% had coronary heart disease, 0.5% had rheumatoid arthritis, and 35.2% were not specified. There was no statistically significant relationship between their self-reported chronic disease status and their antibody response to CoronaVac®.

DISCUSSION

The available evidence in the relevant scientific literature suggests that SARS-CoV-2 induces a typical antibody-mediated (humoral) immune response pattern, where IgM is the first antibody to appear, followed closely by IgA (which peaks at two to three weeks post-symptom onset and declines over the following weeks) and finally by IgG which remains elevated for several months post-symptom onset.[4] Therefore, there is a logical need for serological assays which can assess the humoral immunity conferred by infection with SARS-CoV-2 or by vaccination with the currently available COVID-19 vaccines. Neutralization assays, which give information as to whether the detected antibodies can neutralize SARS-CoV-2 and offer potential protection upon subsequent exposure, involve the live authentic virus produced in cell cultures and thus necessitate all procedures to be conducted in a Biosafety Level 3 facility.[5] On the other hand, traditional antibody assays, which measure the reactivity of antibodies in human serum or plasma with virus-specified antigens, can be performed in a standard diagnostic laboratory in a timely and high-throughput manner.

Table 3. Logistic regression results with IgG as dependent and age as independent factors

Threshold IgG	p-value
51	0.004
101	0.0004
151	0.0007
201	**2.537614e-05**
251	0.004

IgG: Immunoglobulin G

From a public health perspective, anti-SARS-CoV-2 antibody assays are indispensable tools for assessing the fraction of people affected by COVID-19 as well as for identifying those who are still at risk of an infection with SARS-CoV-2. In addition, vaccinated people who are interested in confirming their own vaccination protection status also bring increasingly insistent demands for anti-SARS-CoV-2 antibody assays. The SARS-CoV-2 spike (S) protein is highly conserved among all human coronaviruses and participates directly in receptor (angiotensin-converting enzyme 2) recognition, viral attachment, and the entry into host cells. Due to its crucial functions and role in the life cycle of SARS-CoV-2, S protein represents one of the most important targets for both unconventional (modern) vaccine development and therapeutic intervention.[6] Here, we used a commercially available anti-SARS-CoV-2 S total antibody assay to evaluate the immunogenicity of the conventional vaccine CoronaVac®. We note that the threshold cut-off for seropositivity provided by the manufacturer should be considered of diagnostic value only, since it may not always be indicative of absolute protection against SARS-CoV-2 infection.

We showed that CoronaVac® induced robust humoral response only in 76% of patients (324 out of 426), with the resulting antibody titers decreasing with older age in males and females. This could be linked to immunosenescence which leads to an impaired adaptive immune response to vaccinations. Not only the human antibody repertoire, but also the human T-cell receptor repertoire is known to diminish among the elderly, along with a decrease in the relative numbers of naive T-cells and an increase in the relative numbers of memory T-cells in the same age group.[7] Also, we observed lower CoronaVac® immunogenicity in males than in females, albeit falling short of the accepted statistical significance threshold. Indeed, it has been established that, regardless of age, females develop greater antibody responses to vaccinations compared to males, possibly owing to their relatively high basal immunoglobulin levels as well as B-cell numbers.[8]

Table 4. Pearson's χ^2-test results

		Immunoglobulin levels			
		<150	**150-250**	**>250**	
Age groups	18-45 years	42	16	56	114
	46-65 years	99	22	38	159
	>65 years	107	27	20	154
Total		248	65	114	427

Table 5. Additional comorbidities
No additional chronic disease (n=232) (54%)
Additional chronic disease (n=194) (46%)

Table 6. Clinical characteristics of comorbidities						
Additional chronic disease	**DM**	**DM and HT**	**HT**	**COPD**	**CHD**	**RA**
	(n=13)	(n=30)	(n=80)	(n=1)	(n=1)	(n=1)
	6.7%	15.4%	41.2%	0.5%	0.5%	0.5%
DM: diabetes mellitus, HT: hypertension; COPD: chronic obstructive pulmonary disease, CHD: coronary heart disease, RA: rheumatoid arthritis						

As with many other infectious diseases which can be prevented by vaccination, the globally spread SARS-CoV-2 infection may also be controlled by vaccinating a sufficient proportion of the world's population with available and accessible COVID-19 vaccines to achieve herd, or community, immunity. CoronaVac® is an inactive whole-virion COVID-19 vaccine. Inactivated vaccines differ from live attenuated ones in that they are unable to revert to a more virulent phenotype or interfere with each other when combined. CoronaVac® can be kept refrigerated, which facilitates its successful deployment in developing countries. Furthermore, it is available in single-dose vials, which promotes ease of administration and minimizes wastage. Although our findings reveal the presence of non-responders at a ratio of 24%, double-blind, randomized, placebo-controlled phase 2 clinical trials performed by Sinovac Life Sciences demonstrate that receiving a third (booster) dose of CoronaVac® at six months post-vaccination leads to a more than 20-fold increase in quantitative neutralizing antibody response in healthy adults aged 18-59[9] and a more than 30-fold increase in quantitative neutralizing antibody response in older adults.[10]

Study Limitations

One limitation of this study was that it overlooked the presence of truly neutralizing antibodies. The lack of assessment of T-cell responses against CoronaVac® was another limitation of the present study. It could also be instructive to test each subject by means of real-time quantitative PCR prior to the antibody assay since nasopharyngeal-swab PCR positivity, which indicates active SARS-CoV-2 infection, begins to overlap with IgM and IgG seroconversion from the second week of symptom onset.[11]

CONCLUSION

A commercially available anti-SARS-CoV-2 S total antibody assay was used to evaluate the immunogenicity of the conventional vaccine CoronaVac®. It is noted that the threshold cut-off for seropositivity provided by the manufacturer should be considered of diagnostic value only, since it may not always be indicative of absolute protection against SARS-CoV-2 infection. CoronaVac® induced robust humoral response was seen in only 76% of the patients (324 out of 426), with the resulting antibody titers decreasing with older age in males and females, which may be linked to immunosenescence which leads to an impaired adaptive immune response to vaccinations. Lower CoronaVac® immunogenicity in males than in females was also observed, albeit falling short of the accepted statistical significance threshold.

MAIN POINTS

- We used a commercially available anti-SARS-CoV-2 S total antibody assay to evaluate the immunogenicity of the conventional vaccine CoronaVac®. We note that the threshold cut-off for seropositivity provided by the manufacturer should be considered of diagnostic value only, since it may not always be indicative of absolute protection against SARS-CoV-2 infection.
- We showed that CoronaVac® induced robust humoral response in only 76% of the patients (324 out of 426), with the resulting antibody titers decreasing with older age in males and females which could be linked to immunosenescence which leads to an impaired adaptive immune response to vaccinations.
- We observed lower CoronaVac® immunogenicity in males than in females, albeit falling short of the accepted statistical significance threshold.

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ETHICS

Ethics Committee Approval: This study was conducted with Cyprus Science University, Ethics Committee's approval (approval number: 2021.12.002).

Informed Consent: All participants gave their oral consent to participate in this study.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: E.B., Concept: E.B., Design: E.B., A.Ü., Data Collection and/or Processing: E.B., A.Ü., Analysis and/or Interpretation: A.Ü., Literature Search: E.B., A.Ü., Writing: E.B., A.Ü.

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ORIGINAL ARTICLE

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An Assessment of the 100 Most Frequently Cited Articles Regarding Extracorporeal Membrane Oxygenation in the Literature

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Abstract

BACKGROUND/AIMS: The aim of this study was to evaluate the most common 100 publications related to extra-corporeal membrane oxygenation (ECMO) in the literature.

MATERIALS AND METHODS: Our study was conducted using the advanced mode of the Web of Science (WOS) search engine of the institute for scientific information. "TS=Extracorporeal" or "TI=Extracorporeal" terms were used for the search. The search was made on 09/09/2018 and the 100 most cited publications were identified. The total number of citations of each publication, the number of annual citations, the researchers, and the catalog data of the journals were determined using WOS and PubMed.

RESULTS: From September 1975 to 2018, there were a total of 33,007 publications in the WOS search engine. Among the top 100 most cited studies, the highest number of citations was 1,212, and the lowest was 105. The total number of citations was 213.83±157.53. The annual average number of citations of the studies ranged between 121.20 and 3.29, and the mean number of studies was 17.60±16.20.

CONCLUSION: Our study is the first study to evaluate and analyze the first 100 studies related to ECMO in the literature. We found an increase in the number of publications on ECMO over the last five years.

Keywords: Extracorporeal membrane oxygenation, citation, first 100, index, ECMO

INTRODUCTION

In current era, several studies have been conducted by different international or national institutes and surgical disciplines in order to determine the most cited articles for various medical areas.[1-4] When a scientific paper gives a reference to another scientific paper, it is identified as "cited". The scientific articles which have been a resource of the study or strengthen the findings of the study are accepted as cited if they are referred to in any part of another scientific paper. The impact factor of the article is evaluated according to its frequency of citation. The more cited articles and the journals with a higher impact factor accepted as more qualified.[5,6]

The first bibliographic study was written by Garfield et al.[7] regarding the 100 citation classics from the Journal of the American Medical Association and published in the Journal of the American Medical Association (JAMA). Since then, numerous articles have been examined and presented as "the most cited articles" in specific journals.[7-13]

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Myocardial damage may require the use of intra-aortic balloon pump or extra-corporeal membrane oxygenation (ECMO). ECMO is one of the most important and widely used auxiliary devices that provides support to the lung or heart in reversible conditions of cardiac or respiratory failure. ECMO is the preferred life saving device in cases where heart/lung machines (CPB) cannot be applied. Current articles on ECMO indications, follow-up, complications, positive contributions to transplantation or recovery are frequently encountered in the literature.

According to our research, there has been no recent study in the literature examining the number of citations of international articles related to ECMO. This study will be the first to identify the 100 most cited articles on ECMO. In this study, we aimed to examine the most cited internationally related articles about ECMO via the institute for scientific information (ISI) and the Web of Science (WOS) search engines.

MATERIALS AND METHODS

This study was conducted following Dokuz Eylül University Faculty of Medicine Non-Interventional Research Ethics Committee approval with the number 6264-GOA 2018/25-24 and then performed using the advanced mode of the WOS search engines. Consequently, there was no need for patient consent for the study information. The "SU=ECMO" word was searched for and articles published between September 1975 and 2008 were included. The search was made on 15/10/2018. Consequently, the 130 most cited articles pertaining to BAV which had been published in international journals were identified, and thus a list was created. The first authors in each article were reviewed for whether they took part in another article in the same list. The overall and annual citation count and information about the authors, articles and journals were determined via WOS and PubMed. Thereafter, letters to the editor and case reports were excluded from this study.

Statistical Analysis

Statistical analyzes were carried out using the SPSS (Statistical Package for Social Sciences, Chicago, IL, USA) 20.0 software. Categorical data were presented in absolute (n) and relative (%) frequencies. All hemodynamic data were expressed as the mean value ± standard deviation. In the comparison of the groups, Kruskal-Wallis and Mann-Whitney U tests were utilized. A p-value of <0.05 was considered as statistically significant in all statistical tests.

RESULTS

In the literature analysis from September 1975 to 2018, there were 33,007 publications in the WOS search engine with the search keywords "TS=Extracorporeal" or "TI=Extracorporeal". The highest number of citations in the first 100 most cited studies was 1,212, while the lowest was 105. The mean total number of citations of the 100 most cited studies was 213.83±157.53. The annual mean number of citations of the studies ranged between 121.20 and 3.29 and the mean number of studies was 17.60±16.20.

The most cited study was conducted by Peek et al.[14] Lancet trial, published in 2009, titled "Efficacy and economic assessment of conventional ventilatory support versus extracorporeal membrane oxygenation for severe adult respiratory failure (CESAR): A multicentre randomised controlled trial". The first three topics of the 100 most referenced studies in the area of ECMO were acute respiratory distress syndrome (ARDS) (25%), CPR (17%) and neonatal respiratory distress syndrome (YD-RDS) with peritoneopericardial diaphragmatic hernia (YD PPDH) (13%). The study with the highest number of citations was published in the Annals of Thoracic Surgery (9%), followed by Critical Care Medicine (9%), the Journal of Thoracic and Cardiovascular Surgery (7%), Pediatrics (7%), the Lancet (7%), and JAMA (7%).

All of the 100 most cited articles in the field of ECMO were in the SCI index. When the distribution of the studies by country was examined, the first three countries were determined to be the United States (57%), Germany (7%) and France (7%). It was determined that 28% of the studies were from the European countries and 72% from countries outside the European continent. No significant relationship was found between the continent of the author and the total and annual citations or between the continent of the journal and the number of total and annual citations ($p>0.05$) (Table 1, 2).

When the 100 most cited studies were evaluated, it was found that the mean number of annual citations of the studies published between 2005-2009 and after 2010 was significantly higher than the other periods ($p<0.001$). In the evaluation made according to the authors' country, there was no significant difference in terms of the total number of citations and the mean number of annual citations (Table 3, 4).

When evaluated according to the types of the most cited 100 study, the total number of citations of and prospective clinical studies and case series was higher than other studies ($p<0.001$). In addition, meta-analyses, prospective studies and compilations were found to be higher than the other studies ($p=0.019$) In our study, it was determined that the annual mean number of citations of ECMO applications in adults was higher than the study of pediatric and adult ECMO subjects ($p=0.001$).

There was a significant difference between the mean and total number of citations in the evaluation made by the department. It was found that the total number of citations ($p=0.010$) was higher in those studies which were evaluated as pediatrics, anesthesia and other branches in the other branches. It was determined that the mean number of annual citations of the studies ($p=0.001$) involving intensive care and cardiology branches were higher than those of other branches.

According to the journals, the mean number of citations ($p=0.002$) and the number of annual citations average of the studies ($p=0.011$) published in the Lancet, NEJM and JAMA journals were significantly higher than other journals. It was determined that the total number of citations of ARDS and YD PPHT studies were higher and the number of annual mean citations was higher in ARDS-related studies.

DISCUSSION

The aim of this study was to investigate the most cited articles of ECMO through the WOS search engine of the ISI. The mean number of annual citations of the 100 most cited studies was significantly higher than the other studies and the number of citation articles was higher than prospective clinical studies. In addition, the total number of cited cases, and the average number of annual citations of prospective studies and review studies were higher than other studies. The mean number of annual citations was higher in those studies related to practices. Also, there was a significant difference between the mean and total number of citations in the evaluation made according to the department and results of the studies. It was determined that the mean number of annual citations was higher in those articles related with ARDS and YD PPHT.

Table 1. Distribution of first-name authors of the 100 most cited articles in the field of ECMO

Author name	Frequency	Percent
Kinsella JP.	4	4
Bartlett RH.	4	4
Gattinoni L.	3	3
Combes A.	3	3
Clark RH.	2	1
Delnido PJ.	2	2
Duncan BW.	2	2
Finer NN.	2	2
Kagawa E.	2	2
Peek GJ.	2	2
Schmidt M.	2	2
Thiagarajan RR.	2	2
Hoopes CW.	1	1
Abrams D.	1	1
Aharon AS	1	1
Aigner C.	1	1
Arnold JH.	1	1
Barbaro RP.	1	1
Beck R.	1	1
Bennett CC.	1	1
Bermudez CA.	1	1
Biarent D.	1	1
Bisdas T.	1	1
Brodie D.	1	1
Brogan TV.	1	1
Chen JS.	1	1
Chen Y.	1	1
Cheng R.	1	1
Clement KC.	1	1
Conrad SA.	1	1
Dalton HJ.	1	1
Davidson D.	1	1
Davies A.	1	1
Doll N.	1	1
Field D.	1	1
Fuehner T.	1	1
Glass P.	1	1
Haines NM.	1	1
Harrison MR.	1	1
Hemmila MR.	1	1
Hirschl RB.	1	1
Ko WJ.	1	1
Kolla S.	1	1
Kolovos NS.	1	1
Krafft P.	1	1
Le Guen M.	1	1
Lewandowski K.	1	1
MacLaren G.	1	1
Maekawa K.	1	1
Magliocca JF.	1	1
Marasco SF.	1	1
Mason DP.	1	1
Massetti M.	1	1
Morris AH.	1	1
Morris, MC	1	1
Noah MA.	1	1
Orourke PP.	1	1
Paden ML.	1	1
Pagani FD.	1	1
Patroniti N.	1	1
Peura JL.	1	1
Pham T.	1	1
Rastan AJ.	1	1
Roberts JD.	1	1
Sakamoto T.	1	1
Schumacher RE.	1	1
Sheu J.	1	1
Shin TG	1	1
Smedira NG.	1	1
Stolar CJH.	1	1
Stork E.	1	1
Stub D.	1	1
Suchyta MR.	1	1
Towne BH.	1	1
Turner DA.	1	1
Walpoth BH.	1	1
Walsh-Sukys MC.	1	1
Wang J.	1	1
Werdan K	1	1
Zabrocki LA.	1	1
Zangrillo A.	1	1
Zwischenberger JB.	1	1
Total	100	100

ECMO: extra-corporeal membrane oxygenation.

The use of ECMO is being tried in more and more extensive indications with the spread of the ECMO team. The current guidelines include bridging treatments under ECMO support. Original research articles on ECMO have been increasing in number with experience. In this study, reviewing the most cited internationally cited articles related to ECMO through the ISI and the WOS search engine provided an up-to-date perspective to see the differences between these articles according to their authors, countries and institutions.

The first oxygenator-like device was developed by Von Frey and Gruber in 1885, while Gibbon developed the first film/bubble oxygenation heart-lung machine and Clowes et al. continued to develop membrane

Table 2. The distribution of the institutions of the first-named authors of the 100 articles most cited in the field of ECMO

Hospital name	Frequency	Percent (%)
Michigan University	11	11
Pierre-Marie Curie University	5	5
Pittsburgh University	4	4
Washington University Child Hospital	4	4
Boston Child Hospital	4	4
Gottingen University	3	3
Colorado University	3	3
LDS Hospital	2	2
Hannover Medical School	2	2
Emory University	2	2
Royal Alexandra University	2	2
Leipzig University	2	2
Harvard Medical School	2	2
Glenfield Hospital	2	2
Vienna University	2	2
Duke University	2	2
National Singapore University Hospital	1	1
Case Western Reserve University	1	1
Hiroshima Asa Hospital	1	1
Long Island Jewish Medical Center	1	1
Milano Bicocca University	1	1
National Taiwan University Hospital	1	1
Vanderbilt University Medical Center	1	1
Alfred Hospital	1	1
American Cardiology Council	1	1
Arkansas University	1	1
St. Paul Hospital	1	1
Bern University	1	1
Brussels Child Hospital	1	1
Caen Fransa University Hospital	1	1
California University	1	1
Cedars-Sinai Heart Institute	1	1
Chang Gung Memorial Hospital	1	1
Cleveland Cardiovascular Surgery Institute	1	1
Cleveland Clinic	1	1
Columbia University	1	1
Dijon Child Hospital	1	1
ECMO Trial Group	1	1
Extracorporeal Cardiopulmonary Resuscitation Japanese Scientific Research Group	1	1
Epworth Hospital	1	1
Galveson University	1	1
Heartlink ECMO Center	1	1
Hiroshima City Hospital	1	1
Humboldt University	1	1
Kentucky University	1	1
Leicester University	1	1
Louisiana University	1	1
Martin-Luther University	1	1
Monash University	1	1
New York Columbia University	1	1
Pekin Anzhen Hospital	1	1
Penn State Hershey Child Hospital	1	1
Philadelphia Child Hospital	1	1
REVA University	1	1
San Raffaele Science Institute	1	1
Sapporo University Medical School	1	1
Sungkyunkwan University Medical School	1	1
Taiwan University	1	1
Utah University	1	1
Far East Memorial Hospital	1	1
Wisconsin University Medical School	1	1
Yale University Medical School	1	1
Total	100	100

ECMO: extra-corporeal membrane oxygenation.

oxygenators.[15-17] The first successful neonatal ECMO was performed in 1975. A large number of scientific research articles have been published in order to increase the success rate of ECMO applications and to reduce morbidity. In study based on 827 ECMO cases in newborns, it was observed that leukocyte reduced blood use, and decreased complications related to transfusion in ECMO.[17] In neonatal ECMO cases, complications related to transfusion were found to be reduced by 41% with concentrated platelet replacement.[18] In a study with newborns, it was found that high prime volume was a significant risk factor in postoperative ECMO support in 64 cases with low birth weight (below 2.5 kg).[19]

It is important to evaluate the scientific effectiveness of articles with the number of citations and annual mean citations of scientific articles on ECMO. We aimed to capture a scientific point of view by reviewing and interpreting the first 100 publications on ECMO. As a result of the increase in interventional procedures in the cardiovascular field with technology, the number of bibliographic publications has increased in the current literature.

Kolkailah et al.[20] published a bibliographic study on human heart transplantations with half a century of experience. In that study, it was found that 85% of the researchers were male, and they could not find a significant relationship between the journal's primary index and the number of annual journal editions. Usman et al.[21] examined the first 100 publications on heart valve diseases and found an increase in the number of publications with catheter-based methods in recent years. We found that interventional procedures made with the support of ECMO in recent years have also increased in terms of their publication and citation index over the last 5 years. Researchers can carry out more work on this issue.

Lai et al.[22] performed bibliographic research on aortic dissection and reported results on the development of aortic dissection surgical techniques. Liao et al.[23] pointed out an increase in treatment with

Table 3. Number-article year-authors-citation number-citation average					
1	Efficacy and Economic Assessment of Conventional Ventilatory Support Versus Extracorporeal Membrane Oxygenation for Severe Adult Respiratory Failure (CESAR): A Multicentre Randomised Controlled Trial. Lancet; 374(9698):1351-63.	2009	Peek, Mugford M, Tiruvoipati R, et al.	1212	121.20
2	Extracorporeal Membrane Oxygenation for 2009 Influenza A(H1N1) Acute Respiratory Distress Syndrome. JAMA; 302(17):1888-95.	2009	Davies A, Jones D, Bailey M, et al.	783	78.30
3	Randomized Clinical-Trial of Pressure-Controlled Inverse Ratio Ventilation and Extracorporeal CO2 Removal for Adult-Respiratory-Distress-Syndrome. American Journal of Respiratory and Critical Care Medicine; 149(2):295-305.	1994	Morris A, Wallace C, Menlove R, et al.	579	23.16
4	Low-Dose Inhalational Nitric-Oxide in Persistent Pulmonary-Hypertension of the Newborn. Lancet; 340(8823):819-20.	1992	Kinsella J, Neish J, Shaffer E, et al.	571	21.15
5	Extracorporeal-Circulation in Neonatal Respiratory-Failure - A Prospective Randomized Study. Pediatrics; 76(4):479-87.	1985	Barlett R, Roloff D, Cornell R, et al.	498	14.65
6	Inhaled Nitric Oxide and Persistent Pulmonary Hypertension of the Newborn. New England Journal of Medicine; 336(9):605-610.	1997	Roberts J, Fineman J, Morin F, et al.	483	21.95
7	Low-Frequency Positive-Pressure Ventilation with Extracorporeal CO2 Removal in Severe Acute Respiratory-Failure. JAMA; 256(7):881-86.	1986	Gattinoni L, Pesenti A, Mascheroni D, et al.	472	14.30
8	Cardiopulmonary Resuscitation with Assisted Extracorporeal Life-Support Versus Conventional Cardiopulmonary Resuscitation in Adults with In-Hospital Cardiac Arrest: An Observational Study and Propensity Analysis. Lancet; 372(9638):554-61.	2008	Chen Y, Lin J, Yu, Hsi Y, et al.	465	42.27
9	Inhaled Nitric Oxide in Full-Term and Nearly Full-Term İnfants with Hypoxic Respiratory Failure. New England Journal of Medicine; 336(9):597-604.	1997	Stork E, Gorjanc E, Verter J, et al.	463	21.05
10	Low-Dose Nitric Oxide Therapy for Persistent Pulmonary Hypertension of the Newborn. New England Journal of Medicine; 342(7):469-74.	2000	Clark R, Kueser T, Walker M, et al.	392	20.63
11	UK Collaborative Randomised Trial of Neonatal Extracorporeal Membrane Oxygenation. Lancet; 348(9020):75-82.	1996	Field D, Davis C, Elbourne D, et al.	375	1.30
12	Referral to an Extracorporeal Membrane Oxygenation Center and Mortality Among Patients with Severe 2009 Influenza A(H1N1). JAMA; 306(15):1659-68.	2011	Noah M, Peek G, Finney S, et al.	349	43.63
13	Extracorporeal Membrane Oxygenation for ARDS in Adults. New England Journal of Medicine; 365(20):1905-14.	2011	Brodie D, Bacchetta M, et al.	340	42.50
14	Extracorporeal Membrane-Oxygenation and Conventional Medical Therapy in Neonates with Persistent Pulmonary-Hypertension of the Newborn - A Prospective Randomized Study. Pediatrics; 84(6):957-63.	1989	Orourke P, Crone R, Vacanti J, et al.	340	11.33
15	Extracorporeal Life Support Organization Registry Report 2012. Asaio Journal; 59(3):202-10.	2013	Paden M, Conrad S, Rycus P, et al.	318	53.00
16	Extracorporeal Membrane-Oxygenation (Ecmo) in Neonatal Respiratory-Failure - 100 Cases. Annals of Surgery; 204(3):236-45.	1986	Barlett R, Gazzaniga A, Toomasian J, et al.	276	8.36
17	Randomized, Multicenter Trial of Inhaled Nitric Oxide and High-Frequency Oscillatory Ventilation in Severe, Persistent Pulmonary Hypertension of The Newborn. Journal of Pediatrics; 131(1):55-62.	1997	Kinsella J, Truog W, Walsh W, et al.	272	12.36
18	Outcomes and Long-Term Quality-of-Life of Patients Supported by Extyacorpoyeal Membrane Oxygenation for Refractory Caydiogenic Shock. Crit Care Med; 36(5):1404-11.	2008	Combes A, Leprince P, Luyt C, et al.	264	24.00
19	Persistent Pulmonary Hypertension of the Newborn in the Era Before Nitric Oxide: Practice Variation and Outcomes. Pediatrics; 105(1):14-20.	2000	Walsh-Sukys M, Tyson J, Wright L, et al.	260	13,68
20	A Prospective-Study of the Outcome for Fetuses with Diaphragmatic-Hernia. JAMA; 271(5):382-384.	1994	Harrison M, Adzick N, Estes J, et al.	255	10.20
21	Extracorporeal Life Support for Severe Acute Respiratory Distress Syndrome in Adults. Ann Surg; 240(4):595-605.	2004	Hemmila M, Rowe S, Boules T, et al.	254	16.93
22	Clinical-Responses to Prolonged Treatment of Persistent Pulmonary-Hypertension of the Newborn with Low-Doses of Inhaled Nitric-Oxide. Journal of Pediatrics. 123(1):103-108.	1993	Kinsella J, Neish S, İvy D, et al.	253	9.75
23	Extracorporeal Membrane Oxygenation in Adults with Severe Respiratory Failure: A Multi-Center Database. Intensive Care Med; 35(12):2105-14.	2009	Brogan T, Thiagarajan R, Rycus, P, et al.	241	24.10
24	Extracorporeal Membrane-Oxygenation for Newborn Respiratory-Failure - 45 Cases. Surgery; 92(2):425-33.	1982	Barlett R, Andrews R, Toomasian J, et al.	239	6.46
25	Outcome of Survivors of Accidental Deep Hypothermia and Circulatory Arrest Treated with Extracorporeal Blood Warming. N Engl J Med; 337(21):1500-5.	1997	Walpoth B, WalpothAslan B, Mattle H, et al.	232	10.55
26	Lung Structure and Function in Different Stages of Severe Adult-Respiratory-Distress-Syndrome. JAMA; 271(22):1772-79.	1994	Gattioni L, Bombino M, Pelosi P, et al.	229	9.16

Table 3. Continued

27	Extracorporeal Membrane Oxygenation in Awake Patients as Bridge to Lung Transplantation. Am J Respir Crit Care Med; 185(7):763-8.	2012	Fuehner T, Kuehn, C, Hadem J, et al.	221	36.83
28	Extracorporeal Life Support - The University of Michigan Experience. JAMA; 283(7):904-8.	2000	Bartlett R, Roloff D, Custer J, et al.	216	11.37
29	Extracorporeal Membrane Oxygenation for Pandemic İnfluenza A(H1N1)-Induced Acute Respiratory Distress Syndrome A Cohort Study and Propensity-Matched Analysis. American Journal of Respiratory and Critical Care Medicine; 187(3):276-85.	2013	Pham T, Combes A, et al.	208	34.67
30	Initial Experience with Partial Liquid Ventilation in Adult Patients with the Acute Respiratory Distress Syndrome. JAMA; 275(5):383-9.	1996	Hirschl R, Pranikoff, T, Wise C, et al.	200	8.70
31	Early and Late Outcomes of 517 Consecutive Adult Patients Treated with Extracorporeal Membrane Oxygenation for Refractory Postcardiotomy Cardiogenic Shock. J Thorac Cardiovasc Surg; 139(2):302-11.	2010	Rastan A, Dege, A, Mohr M, et al.	195	21.67
32	Extracorporeal Life Support Registry Report 2004. ASAİO J; 51(1):4-10.	2005	Conrad S, Rycus P, Dalton H, et al.	195	13.93
33	Inhaled Nitric Oxide for The Early Treatment of Persistent Pulmonary Hypertension of the Term Newborn: A Randomized, Double-Masked, Placebo-Controlled, Dose-Response, Multicenter Study. Pediatrics; 101(3):325-34.	1998	Davidson D, Barefield E, Kattwinkel J, et al.	195	9.29
34	Treatment of Acute Respiratory-Failure with Low-Frequency Positive-Pressure Ventilation and Extracorporeal Removal of Co2. Lancet; 2(8189):292-4.	1980	Gattinoni L, Pesenti A, Rossi G, et al.	190	4.87
35	Inhaled Nitric Oxide and Hypoxic Respiratory Failure in İnfants with Congenital Diaphragmatic Hernia. Pediatrics; 99(6):838-45.	1997	Finer N, Solimano A, Germain F, et al.	190	4.87
36	Inhaled Nitric-Oxide in Infants Referred for Extracorporeal Membrane-Oxygenation - Dose-Response. Journal of Pediatrics; 124(2):302-8.	1994	Finer N, Etches P, Kamstra B, et al.	189	7.56
37	Contemporary Extracorporeal Membrane Oxygenation for Adult Respiratory Failure: Life Support in the New Era. Intensive Care Medicine; 38(2):210-20.	2012	MacLaren G, Combes A, Bartlett, R, et al.	188	26.86
38	The PRESERVE Mortality Risk Score and Analysis of Long-Term Outcomes after Extracorporeal Membrane Oxygenation for Severe Acute Respiratory Distress Syndrome. Intensive Care Medicine; 39(10):1704-13.	2013	Schmidt M, Zogheib E, Roze H, et al.	186	31.00
39	Refractory Cardiac Arrest Treated with Mechanical CPR, Hypothermia, ECMO and Early Reperfusion (The CHEER Trial). Resusciation; 86:88-94.	2015	Stub D, Bernard S, Pellegrino V, et al.	186	46.50
40	European Resuscitation Council Guidelines for Resuscitation 2010 Section 6 Paediatric Life Support. Resuscitation; 81(10):1364-88.	2010	Biarent D, Bingham R, Eich C, et al.	185	20.56
41	Complications of Extracorporeal Membrane Oxygenation for Treatment of Cardiogenic Shock and Cardiac Arrest: A Meta-Analysis of 1,866 Adult Patients. Annal of Thpracic Surgery; 97(2):610-6.	2014	Cheng R, Hachamovitch R, Kittleson M, et al.	185	37.00
42	Extracorporeal Membrane Oxygenation to Aid Cardiopulmonary Resuscitation in Infants and Children. Circulation; 116(15):1693-700.	2007	Thiagarajan R, Laussen, P, Rycus T, et al.	184	15.33
43	Extracorporeal Life Support for 100 Adult Patients with Severe Respiratory Failure. Annals of Surgery; 226(4):544-64.	1997	Kolla S, Awad S, Rich P, et al.	180	8.18
44	The Acute Respiratory Distress Syndrome: Definitions, Severity and Clinical Outcome - An Analysis of 101 Clinical Investigations. Intensive Care Medicine; 22(6):519-29.	1996	Krafft P, Fridrich P, Pernerstorfer T, et al.	180	7.83
45	High Survival Rate in 122 ARDS Patients Managed According to A Clinical Algorithm Including Extracorporeal Membrane Oxygenation. Intensive Care Medicine; 23(8):819-35.	1997	Lewandowski K, Rossaint R, Pappert D, et al.	177	8.05
46	Clinical-Experience with 202 Adults Receiving Extracorporeal Membrane Oxygenation for Cardiac Failure: Survival at Five Years. Journal of Thoracic and Cardiovascular Surgery; 122(1):92-102.	2001	Smedira NG, Moazami N, Golding CM, et al.	175	9.72
47	Single-Institution Experience with Interhospital Extracorporeal Membrane Oxygenation Transport: A Descriptive Study. Pediatric Critical Care Medicine; 11(4):509-13.	2010	Clement KC, Fiser RT, Fiser WP, et al.	171	19.00
48	Extracorporeal Cardiopulmonary Resuscitation in Patients with In-hospital Cardiac Arrest: A Comparison with Conventional Cardiopulmonary Resuscitation. Crit Care Med; 39(1):1-7.	2011	Shin TG, Choi JH, Joo IK, et al.	171	21.88
49	Back from Irreversibility: Extracorporeal Life Support for Prolonged Cardiac Arrest. Annals of Thoracic Surgery; 79(1):178-84.	2005	Massetti, M, Tasle M, Le Page O, et al.	169	12.07
50	The Italian ECMO Network Experience During the 2009 Influenza A(H1N1) Pandemic: Preparation for Severe Respiratory Emergency Outbreaks. Intensive Care Medicine; 37(99):1447-57.	2011	Patroniti N, Zangrillo A, Pappalardo, F, et al.	166	20.75

Table 3. Continued

51	Extracorporeal Membrane-Oxygenation and Neonatal Respiratory-Failure - Experience from the Extracorporeal Life-Support Organization. Journal of Pediatric Surgery; 26(5):563-71.	1991	Stolar C, Snedecor S, Barlett R, et al.	164	5.86
52	Review of ECMO (Extra Corporeal Membrane Oxygenation) Support in Critically ill Adult Patients. Heart Lung and Circulation; 17:S41-7.	2008	Marasco SF, Lukas G, McDonald M, et al.	163	14.82
53	Inhaled Nitric Oxide in Premature Neonates with Severe Hypoxaemic Respiratory Failure: A Randomised Controlled Trial. Lancet; 354(9184):1061-5.	1999	Kinsella J, Walsh W, Bose C, et al.	163	8.15
54	Five-Year Results of 219 Consecutive Patients Treated with Extracorporeal Membrane Oxygenation for Refractory Postoperative Cardiogenic Shock. Annals of Thoracic Surgery; 77(1):151-7.	2004	Doll N, Kiaii B, Borger, M, et al.	162	10.80
55	Early Extracorporeal Membrane Oxygenator-Assisted Primary Percutaneous Coronary Intervention Improved 30-Day Clinical Outcomes in Patients with ST-Segment Elevation Myocardial Infarction Complicated with Profound Cardiogenic Shock. Critical Care Medicine; 38(9):1810-17.	2010	Sheu J, Tsai T, Lee F, et al.	161	17.89
56	Position Paper for The Organization of Extracorporeal Membrane Oxygenation Programs for Acute Respiratory Failure in Adult Patients. American Journal of Respiratory and Critical Care Medicine; 190(5):488-96.	2014	Combes A, Brodie D, Bartlett, R, et al.	159	31.80
57	Predicting Survival After Extracorporeal Membrane Oxygenation for Severe Acute Respiratory Failure: The Respiratory Extracorporeal Membrane Oxygenation Survival Prediction (RESP) Score. American Journal of Respiratory and Critical Care Medicine; 189(11): 1374-82.	2014	Schmidt M, Bailey M, Sheldrake J, et al.	156	31.20
58	Extracorporeal Membrane Oxygenation to Support Cardiopulmonary Resuscitation in Adults. Annals of Thoracic Surgery; 87(3):778-85.	2009	Thiagarajan R, Brogan T, Scheurer M, et al.	153	15,30
59	Extracorporeal Membrane Oxygenation Support for Adult Postcardiotomy Cardiogenic Shock. Annals of Thoracic Surgery; 73(2):538-45.	2002	Ko W, Lin C, Chen R, et al.	146	8.59
60	Mechanical Circulatory Support for The Treatment of Children with Acute Fulminant Myocarditis. Journal of Thoracic and Cardiovascular; 122(3):440-8.	2001	Duncan B, Bohn D, Atz A, et al.	146	8.11
61	Extracorporeal Cardiopulmonary Resuscitation Versus Conventional Cardiopulmonary Resuscitation in Adults with Out-of-Hospital Cardiac Arrest: A Prospective Observational Study. Resuscitation; 85(6):762-8.	2014	Sakamoto T, Morimura N, Nagao K, et al.	146	29.20
62	A Meta-Analysis of Complications and Mortality of Extracorporeal Membrane Oxygenation. Critical Care and Resuscitation; 15(3):172-8.	2013	Zangrillo A, Landoni G, Biondi-Zoccai G, et al.	145	24.17
63	Prospective, Randomized Comparison of High-Frequency Oscillation and Conventional Ventilation in Candidates for Extracorporeal Membrane-Oxygenation. Journal of Pediatrics; 124(3):447-54.	1994	Clark R, Yoder B, Sell M, et al.	144	5.76
64	Mechanical Circulatory Support in Cardiogenic Shock. European Heart Journal; 35(3):156.	2014	Werdan K, Gielen, S, Ebelt H, et al.	143	28.60
65	Use of Rapid-Deployment Extracorporeal Membrane Oxygenation for the Resuscitation of Pediatric Patients with Heart Disease After Cardiac Arrest. Journal of Thoracic and Cardiovascular Surgery; 116(2):305-11.	1998	Duncan B, İbrahim A, Hraska V, et al.	142	6.76
66	Tolerance and Dependence in Neonates Sedated with Fentanyl During Extracorporeal Membrane-Oxygenation. Anesthesiology; 73(6):1136-40.	1990	Arnold J, Truog R, Orav E, et al.	136	4.69
67	Extracorporeal Support for Organ Donation after Cardiac Death Effectively Expands the Donor Pool. Journal of Trauma-Injury Infection and Critical Care; 58(6):1095-101.	2005	Magliocca J, Magee J, Rowe S, et al.	133	9.50
68	Extracorporeal Life Support Following Out-of-Hospital Refractory Cardiac Arrest. Critical Care; 15(1):R29.	2011	Le Guen M, Nicolas-Robin A, Carreira S, et al.	133	16.63
69	Vascular Complications in Patients Undergoing Femoral Cannulation for Extracorporeal Membrane Oxygenation Support. Annals of Thoracic Surgery; 92(2):626-31.	2011	Bisdas T, Beutel G, Warnecke G, et al.	131	16.38
70	Extracorporeal Membrane Oxygenation in Children after Repair of Congenital Cardiac Lesions. Annals of Thoracic Surgery; 72(6):2095-101.	2001	Aharon A, Drinkwater D, Churchwell K, et al.	131	7.28
71	Extracorporeal Membrane Oxygenation for Adult Respiratory Failure. Chest; 112(3):759-64.	1997	Peek GJ, Moore HM, Moore N, et al.	130	5.20
72	Recommendations for the Use of Mechanical Circulatory Support: Device Strategies and Patient Selection, a Scientific Statement from the American Heart Association. Circulation; 126(22):2648-67.	2012	Peura J, Colvin-Adams M, Francis G, et al.	127	18.14
73	Outcome of Pediatric Patients Treated with Extracorporeal Life Support after Cardiac Surgery Annals of Thorasic Surgery; 76(5):1435-41.	2003	Kolovos N, Bratton S, Moler F, et al.	127	7.94

Table 3. Continued

74	Extracorporeal Membrane Oxygenation for Pediatric Respiratory Failure: Survival and Predictors of Mortality. Critical Care; 39(2):364-70.	2011	Zabrocki L, Brogan T, Statler K, et al.	124	15.50
75	Risk Factors for Mortality in 137 Pediatric Cardiac Intensive Care Unit Patients Managed with Extracorporeal Membrane Oxygenation. Critical Care Medicine; 32(4):1061-9.	2004	Morris MC, İttenbach, RF, Godinez Rİ, et al.	124	8.27
76	Extracorporeal Life Support to Left Ventricular Assist Device Bridge to Heart Transplant - A Strategy to Optimize Survival and Resource Utilization. Circulation; 100(19):206-10.	1999	Pagani F, Lynch W, Swaniker F, et al.	123,00	6.15
77	Extracorporeal Cardiopulmonary Resuscitation for Patients with Out-of-Hospital Cardiac Arrest of Cardiac Origin: A Propensity-Matched Study and Predictor Analysis. Critical Care Medicine; 41(5):1186-96.	2013	Maekawa K, Tanno K, Hase M, et al.	123	20.50
78	Extracorporeal Membrane Oxygenation in Cardiopulmonary Disease in Adults. Journal of American College of Cardiology; 63(25):2769-78.	2014	Abrams D, Combes A, Brodie D, et al.	122	24.40
79	Association of Hospital-Level Volume of Extracorporeal Membrane Oxygenation Cases and Mortality Analysis of the Extracorporeal Life Support Organization Registry. American Journal of Respiratory and Critical Care Medicine; 191(8):894-901.	2015	Barbaro R, Odetola F, Kidwell K, et al.	121	30.25
80	Morbidity for Survivors of Extracorporeal Membrane-Oxygenation - Neurodevelopmental Outcome at 1 Year of Age. Pediatrics; 83(1):72-8.	1989	Glass P, Miller M, Short B, et al.	121	4.03
81	Should We Emergently Revascularize Occluded Coronaries for Cardiac Arrest? Rapid-Response Extracorporeal Membrane Oxygenation and Intra-Arrest Percutaneous Coronary Intervention. Circulation; 126(13):1605.	2012	Kagawa E, Dote K, Kato M, et al.	121	17.29
82	UK Collaborative Randomised Trial of Neonatal Extracorporeal Membrane Oxygenation: Follow-Up to Age 4 Years. Lancet; 357(9262):1094-6.	2001	Bennett C, Johnson A, Field D, et al.	121	6.72
83	Criteria for Extracorporeal Membrane-Oxygenation in a Population of Infants with Persistent Pulmonary-Hypertension of the Newborn. Journal of Pediatric Surgery; 21(4):297-302.	1986	Becal.k P, Anderson K, Pearson G, et al.	119	3.64
84	Institutional Experience with Extracorporeal Membrane Oxygenation in Lung Transplantation. European Journal of Cardio-Thoracic Surgery; 31(3):468-73.	2007	Aigner C, Wisser W, Taghavi S, et al.	118	9.83
85	Right-Sided Brain-Lesions in Infants Following Extracorporeal Membrane-Oxygenation. Pediatyrics; 82(2):155-61.	1988	Schumacher R, Barks J, Johnsgton M, et al.	117	3.77
86	Extracorporeal Membrane Oxygenation for Respiratory Failure in Adults. Current Opinion in Critical Care; 8(1):99-104.	2012	Combes A, Bacchetta M, Brodie D, et al.	116	16.57
87	Extracorporeal Life Support Registry Report 2008: Neonatal and Pediatric Cardiac Cases. Asaio Journal; 55(1);111-6.	2009	Haines N, Rycus P, Zwischenberger J, et al.	116	11.60
88	Extracorporeal Membrane-Oxygenator Rescue in Children During Cardiac-Arrest after Cardiac-Surgery. Circulation; 86(5):300-4.	1992	Delnido P, Dalton H, Thompson A, et al.	115	4.26
89	Increased Survival of ARDS Patients with Severe Hypoxemia (ECMO Criteria). Chest; 99(4):951-5.	1991	Succhyta M, Clemmer T, Orme J, et al.	115	4.11
90	Should Lung Transplantation be Performed for Patients on Mechanical Respiratory Support? The US Experience. Journal of Thoracic and Cardiovascular Surgery; 139(3):765-73.	2010	Mason D, Thuita L, Nowicki E, et al.	114	12.67
91	Extracorporeal Membrane-Oxygenation Support as a Bridge to Pediatric Heart-Transplantation. Circulation; 90(5):66-9.	1994	Delnido P, Armitage J, Fricker F, et al.	113	4.52
92	Outcome of Veno-Arterial Extracorporeal Membrane Oxygenation for Patients Undergoing Valvular Surgery. PLoS One; 8(5):639-24.	2013	Wang J, Han J, Jia Y, et al.	113	18.83
93	Long-Term Follow-Up of Infants and Children Treated with Extracorporeal Membrane-Oxygenation (ECMO) - A Preliminary-Report. Journal of Pediatric Surgery; 20(4):4114.	1985	Towne B, Lott İ, Hicks D, et al.	112	3.29
94	Active Rehabilitation and Physical Therapy During Extracorporeal Membrane Oxygenation while Awaiting Lung Transplantation: A Practical Approach. Critical Care Medicine; 39(12):2593-8.	2011	Turner D, Cheifetz İ, Rehder K, et al.	111	13.88
95	Extracorporeal Membrane-Oxygenation for Cardiac Rescue in Children with Severe Myocardial Dysfunction. Critical Care Medicine; 21(7):1020-8.	1993	Dalton H, Siewers R, Fuhrman B, et al.	111	4,27
96	Initial Experience with Single Cannulation for Venovenous Extracorporeal Oxygenation in Adults. Annals of Thoracic Surgery; 90(3):991-5.	2010	Bermudez C, Rocha R, Sappington P, et al.	110	12.22
97	Complications of Neonatal Extracorporeal Membrane-Oxygenation - Collective Experience from the Extracorporeal Life-Support Organization. Journal of Thoracic and Cardiovascular Surgery; 107(3):838-49.	1993	Zwischhenberger J, Nguyen T, Upp J, et al.	107	4.28

Table 3. Continued					
98	Extracorporeal Membrane Oxygenation as a Bridge to Pulmonary Transplantation. Journal of Thoracic and Cardiovascular Surgery; 145(3):862-8.	2013	Hoopes C, Kukreja J, Golden J, et al.	107	17.83
99	Analysis of the Outcome for Patients Experiencing Myocardial Infarction and Cardiopulmonary Resuscitation Refractory to Conventional Therapies Necessitating Extracorporeal Life Support Rescue. Critical Care Medicine; 34(4):950-7.	2006	Chen J, Ko W, Yu H, et al.	106	8.15
100	Assessment of Outcomes and Differences Between In- And Out-of-Hospital Cardiac Arrest Patients Treated with Cardiopulmonary Resuscitation Using Extracorporeal Life Support. Resuscitation; 81(8):968-73.	2010	Kagawa E, Inoue I, Kawagoe T, et al.	105	11.67

preventive measures by looking at the first 100 citationed research studies on coronary heart disease. In recent years, Shuaib et al.[24] reported a decrease in the number of publications in the field of cardiology, because there has been a shift to the cardiovascular field and the guidelines support this. In our publication, we made a similar comment by looking at the publication citation number increase in recent years in interventional procedures, and we linked this to the team's work together with the heart team and pointed out an increase in hybrid operations.

Pennell et al.[25] found an increase in the number of studies performed in the last 5 years when they examined cardiovascular magnetic resonance. They attributed this to an increase in the number of patients in the cardiovascular field and the widespread use of imaging methods. Oh and Galis[26] reported bibliographic studies on hypertension and emphasized that there has been an increase in the number of citations in parallel with developments in technology. Friedmacher et al.[27] found that the scientometric analysis of congenital diaphragmatic hernias has increased in recent years with technological developments. ECMO shows the positive effect of congenital diaphragmatic hernia treatment on bridging support on surveillance. In order to develop renewable multidisciplinary therapies, citation index evaluation studies have been emphasized as they have global value.

For the expansion of ECMO cost effectiveness and cardiopulmonary resuscitation with ECMO support, Kilchemmann et al.[28] suggested that bibliometric evaluation should be performed at repeated times in ECMO. Eldredge et al.[29] and Bautista-Rodriguez et al.[30] stated in their studies that further research is needed especially for the success of pediatric ECMO applications. Senst and Diaz[31] reported that the use of ECMO has become widespread after looking at recent publications.

Bacon et al.[32] reviewed current publications on ECMO and presented a review of the positive results of ECMO support in stage II bidirectional Glenn and stage III Fontan procedures in single ventricular patients. Iantorno et al.[33] performed a review of the current literature on the emergency valve-in-valve transcatheter aortic valve replacement of acute aortic regurgitation and cardiogenic shock in the use of preoperative veno-arterial ECMO. They emphasized that case series have been introduced in recent years.

Patroniti et al.[34] reported that the best strategy for mechanical ventilation and respiratory monitoring in ECMO patient monitoring has not been defined by the current literature review. They also presented a compilation of ARDS-ECMO and the conclusion that more publications on ECMO are needed. Cohen et al.[35] evaluated the invasive procedures of emergency treatment in 6 countries up to 2006. They pointed out the importance of digital recordings and the storage of data. They also stated that publications should be evaluated bibliographically with PubMed and other search engines at certain intervals. Loomba and Anderson[36] compiled bibliometric studies and demonstrated the weakness or strength of publications in pediatric cardiology.

The most cited study was conducted by Peek et al.[14] (CESAR-2009): A multi-center randomized controlled trial, published in the journal Lancet. They recommended the transfer of adult patients with severe but potentially reversible respiratory failure with a Murray score of 3.0 or less than pH 7.20 in the optimal conventional treatment to a center with ECMO to significantly improve survival without serious problems. Interestingly, in their study, they found a life quality increase of 0.03 in 6 months follow-up in patients with ECMO.[14]

The ECMO team and E-CPR should be continuously trained. Sepsis and renal failure still negatively affect outcomes. Adjusting the fluid volume balance with high flow; cytokine levels and reducing inflammation response can help weaning. The current issues relating to ECMO should be continuously monitored and interpreted. Questions to be taken into consideration in the decision of ECMO application indication include these; "Is the problem life-threatening?" and "Can the disease be reversed?" The most important parameters for improving ECMO results are timing, management of the system, experience and experience of the team. ECMO support can be life-saving in the treatment of temporary cardiopulmonary insufficiency. In the minds of clinicians dealing with critically ill patients, an alternative to ECMO should be included.

Study Limitations

Similar to all bibliometric studies, this study has many limitations. First, ISI and PubMed, WOS were used to search for the most cited articles. It is known that the number of citations varies between databases. The studies were evaluated on the basis of the number of citations and the mean number of annual citations, but were not ranked accordingly. Additionally, although the number of citations and the mean annual citation rate are traditional parameters in the scientific evaluation of an article, its contribution to science cannot be assessed only by these measures.

CONCLUSION

Bibliographic studies are important as they allow for the following of the citation variances of elite publications according to years, study types, study areas and journals in determining the topics of most interest and citation. In the analysis of the elite articles related to ECMO, it was determined that those studies published after 2005, those studies relating to prospective studies, those studies relating to adult ECMO applications, and the references of those studies related to ARDS and Yd PPHT were at a higher rate.

Table 4. Distribution of the 100 most cited articles in the field of ECMO

	Subgroup	n	Total number of citations (mean ± SD)	Number of citations per year (mean ± SD)	Total citations p-value	Year citations p-value
Year	1990≥	11	235.90±145.24	7.17±4.34	0.432	**<0.001**
	1990-1994	13	228.46±162.46	8.80±6.32		
	1995-1999	16	226.81±114.71	10.22±5.19		
	2000-2004	13	209.84±108.52	13.34±9.57		
	2005-2009	21	241.28±263.54	26.86±26.25		
	>2010	26	169.00±69.93	25.61±11.40		
Author's continents	European	28	228.96±210.31	21.68±22.19	0.456	0.144
	Non-European	72	207.94±132.89	16.02±13.02		
Author's country	USA	57	206.43±119.70	13.30±9.80	0.935	0.091
	France	7	176.42±49.41	23.82±8.90		
	Germany	7	213.71±117.75	17.11±11.55		
	England	6	388.66±418.94	36.20±43.93		
	Taiwan	3	239.0±196.74	19.67±19.57		
	Italy	3	172.66±53.31	16.80±6.62		
	Japan	3	124.00±20.66	19.38±8.95		
	Belgium	3	165.00±43.58	15.44±9.83		
	Australia	3	367.33±359.99	41.44±32.95		
	China	2	137.00±33.94	21.88±0.66		
	Switzerland	2	175±80.61	10.19±0.50		
	Austria	1	180	7.83		
	Canada	1	186.00	46.50		
	Singapore	1	188	26.86		
	Korea	1	171.00	21.88		
Type of publication	Retrospective	47	161.63±102.08	13.97±13.04	**<0.001**	**0.019**
	Prospective clinical	16	284.00±267.55	22.99±28.25		
	Retrospective clinical	14	213.83±157.53	19.92±10.95		
	Review	12	166.58±56.28	22.87±11.57		
	Case series	7	247.42±54.01	13.28±12.94		
	Meta-analysis	3	170.00±21.79	23.00±14.62		
	Guideline	1	185.00	20.56		
Type	Adult	54	219.01±185.43	22.28±19.32	0.637	**<0.001**
	Pediatric	39	217.38±125.45	11.04±8.97		
	Adult ± pediatric	7	154.00±39.48	18.08±6.77		
Branches	Non-surgery	68	222.88±135.08	18.56±13.76	0.405	0.393
	Surgery	32	194.59±198.13	15.57±20.55		
Department	Cardiovascular	45	182.33±216.75	16.01±22.40	0.010	0.001
	Pediatric	24	240.54±122.85	12.36±10.41		
	Intensive care	12	207.33±185.22	25.47±18.61		
	Anesthesia	8	244.00±153.53	11.36±7.32		
	General surgery	7	238.42±136.75	12.19±17.60		
	Cardiology	5	165.80±28.63	26.28±14.53		
	Pediatric intensive care	4	135.25±33.62	14.16±5.72		
	Other	15	238.20±136.75	17.60±16.20		
Diseases	ARDS	25	288.84±246.44	25.53±25.94	**<0.001**	**0.016**
	CPR	17	178.35±85.98	18.73±11.75		
	YD RDS	13	215.61±115.65	10.54±6.06		
	Yd PPHT	13	287.61±148.43	12.08±6.91		
	Total	11	153.81±58.34	23.27±13.83		
	Post-op	8	137.12±20.90	11.48±5.25		
	Tx-lung	5	134.20±48.68	18.20±10.79		
	Tx-heart	3	123.00±10.00	6.72±2.53		
	Other	5	151.80±59.31	10.13±4.68		

Table 4. Continued

	Subgroup	n	Total number of citations (mean ± SD)	Number of citations per year (mean ± SD)	Total citations p-value	Year citations p-value
Journals	Annals of Thoracic Surgery	9	146.00±23.61	14.17±9.11	0.002	0.011
	Critical Care Medicine	9	143.88±50.34	6.85±11.57		
	Journal of Thoracic and Cardiovascular Surgery	7	140.85±34.49	11.57±6.24		
	Pediatrics	7	245.85±135.73	8.80±4.62		
	The Lancet	7	442.42±378.36	41.57±26.09		
	JAMA	7	357.71±210.58	25.09±26.53		
	Intensive Care Medicine	6	189.75±26.32	19.76±9.75		
	American Journal of Respiratory and Critical Care Medicine	6	240.66±169.75	31.31±4.68		
	Circulation	6	130.50±26.71	10.94±6.63		
	New England Journal of Medicine	5	382.00±101.39	23.33±11.67		
	Resuscitation	4	155.50±38.47	26.98±14.85		
	Journal of Pediatrics	4	214.50±58.90	8.85±2.84		
	Journal of Pediatric Surgery	3	131.66±28.21	4.26±1.39		
	Annals of Surgery	3	236.66±50.29	11.15±5.00		
	Asaio Journal	3	209.66±101.79	26.17±23.25		
	Chest	2	122.50±10.60	4.65±0.77		
	Critical Care	1	133.00	16.63		
	Anesthesiology	1	136.00	4.69		
	Critical Care and Resuscitation	1	145.00	24.17		
	Current Opinion in Critical Care	1	116.00	16.57		
	European Heart Journal	1	143.00	28.60		
	European Journal of Cardio-Thoracic Surgery	1	118.00	9.83		
	Heart Lung and Circulation	1	163.00	14.82		
	Journal of the American College of Cardiology	1	122.00	24.40		
	Journal of Trauma-Injury Infection and Critical Care	1	133.00	9.50		
	Pediatric Critical Care Medicine	1	171.00	19.00		
	PLoS One	1	113.00	18.83		
	Surgery	1	239	6.46		
Country	USA	84	201.92±118.94	15.92±12.40	**0.384**	**0.280**
	England	9	374.77±354.11	29.54±36.33		
	Scotland	4	155.50±38.47	26.98±14.85		
	Germany	1	118.00	9.83		
	Australia	2	154.00±12.72	19.49±6.61		
Continent	Non-European	86	200.81±117.76	16.01±12.29	0.544	0.110
	European	14	293.78±300.51	27.40±29.84		

ECMO: extra-corporeal membrane oxygenation, SD: standard deviation, ARDS: acute respiratory distress syndrome, USA: United States of America.

MAIN POINTS

- Our study is the first study to evaluate and analyze the first 100 studies related to ECMO in the literature.
- In the literature analysis from September 1975 to 2018, among the top 100 most cited studies, the highest number of citations was 1,212, and the lowest was 105.
- When the 100 most cited studies were evaluated, it was found that the mean number of annual citations of the studies published between 2005-2009 and after 2010 was significantly higher than other periods ($p<0.001$).
- The first three topics of the 100 most referenced studies in the area of ECMO were ARDS (25%), CPR (17%) and neonatal respiratory distress syndrome with peritoneopericardial diaphragmatic hernia (13%).
- All of the 100 most cited articles in the field of ECMO were in the SCI index. When the distribution of the studies by country was examined, the first three countries were determined to be the United States (57%), Germany (7%) and France (7%).

ETHICS

Ethics Committee Approval: This study was conducted following Dokuz Eylül University Faculty of Medicine Non-Interventional Research Ethics Committee approval with the number 6264-GOA 2018/25-24 and then performed using the advanced mode of the WOS search engines.

Informed Consent: There was no need for patient consent for the study information.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: S.B., T.G., S.B., Ç.B., G.A., V.H., Design: S.B., T.G., S.B., Ç.B., G.A., V.H., Supervision: S.B., T.G., S.B., Ç.B., G.A., V.H., Data Collection and/or Processing: S.B., T.G., S.B., Ç.B., G.A., V.H., Analysis and/or Interpretation: S.B., T.G., S.B., Ç.B., G.A., V.H., Literature Search: S.B., T.G., S.B., Ç.B., G.A., V.H., Writing: S.B., T.G., S.B., Ç.B., G.A., V.H., Critical Review: S.B., T.G., S.B., Ç.B., G.A., V.H.

DISCLOSURES

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ORIGINAL ARTICLE

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Preliminary Study of the Effects of Neuroeducational Methods on the 20th Percentile Telomere Length Dynamics

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Abstract

BACKGROUND/AIMS: Telomeres are nucleotide repeats that cap the end of each chromosome arm and ensure the stability of the genome. The telomere length is amongst the most dependable markers of senescence at the cellular level. It is known that telomeres become shorter with each cell division; accordingly, telomere loss correlates with the process of aging *in vivo*. This research aimed to investigate the effect of neuroeducational methods on 20th telomere length shortening.

MATERIALS AND METHODS: Twenty healthy women participated in this study, and ten of them attended regular neuroeducational sessions. We were searching for the impact of lifestyle on cellular aging by measuring the value of the 20th percentile of telomeres before and after the neuroeducational sessions.

RESULTS: The median of the 20th percentile value in the experimental group was 5.8 kb before the study and 5.6 kb after the study ($p<0.05$). The median of the 20th percentile value in the control group was 6.4 kb before the study and 5.7 kb after the study ($p<0.001$).

CONCLUSION: The findings show that neuroeducational methods relieve stress and make telomere shortening slower, as we were expecting.

Keywords: Telomere shortening, neuroeducation, 20th percentile

INTRODUCTION

Aging is a physiological process that involves finite changes at the genetic and epigenetic levels.[1] On the genetic level, the most important drivers tend to be epigenetic dysregulation, DNA damage, mitochondrial dysfunction, and telomere damage, which can cause stable, irreversible growth of cells.[2] In recent studies, telomeres have been intensively studied, and their reliability in indicating biological aging on the cellular level is significant.[3] Telomeres are caps (highly conserved tandems of nucleotide repeats) that include proximal double-stranded and distal single-stranded regions that, in complex with shelterin proteins, afford protection at the chromosomal ends to maintain genomic solidity.[4] If there is no compensatory elongating mechanism, telomeres get shorter with every cell division. Telomerase can elongate telomeres *de novo* during cell severance, but after birth, most telomerases are silenced in somatic cells, and telomeres then undergo oxidative stress and age-dependent incremental attrition.[5] Short or dysfunctional telomeres are recognized as DNA double-stranded breaks, triggering cells to undergo replicative senescence.[4]

The telomere 20th percentile is the shortest quintile of telomeres, indicating a telomere length below 20%, while usually the median

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telomere length represents the 50th percentile in the distribution of cell telomere lengths. The telomere 20th percentile more precisely represents the impact of telomeres on the general health state. This is important because the latest research shows that short telomeres cause the aging processes and the collateral effects of aging.[6] It is known that short telomeres trigger permanent and harmful damage to the cell, in this way provoking precocious biological aging, unless they are repaired by telomerase.[7] Furthermore, there are telomere-based therapies, for example, TA-65 (natural telomerase activator product), that have provided apparent positive immune remodeling and beneficial effects on metabolic, bone, and cardiovascular health, although they have failed to prolong life.[8] In this context, not only pharmaceutical preparations but also lifestyle and emotional state are being intensively examined, and some studies have contributed to demonstrating that this can prolong telomere lengths. A theory was put forward and some clinical trials were conducted to prove the impact of lifestyle on telomere length.[9] Oxidative stress is one of the most important triggers that interfere with the normal functioning of the body. It can arise due to the accumulation of reactive oxygen species (ROS), a phenomenon that increases with age and is accompanied by a reduction in protective mechanisms; this eventually causes a wide range of DNA lesions, leading to mutations and disruption in the epigenetic state of the cell.[10]

As suggested, telomeres can be restored by physical activity, which is one of the main ways to relieve stress.[2] One of the first studies that explored the correlation between regular exercise and telomere length in humans was directed by Cherkas et al. In a cross-sectional survey of 2,401 white men and women, they showed that lymphocyte telomere length (LTL) was positively associated with higher physical activity levels.[1] However, an inactive lifestyle, particularly stress, can potentially lead to oxidative stress through chronic activation of the autonomic and neuroendocrine stress responses; also, it was proven that oxidative stress shortens telomeres in cells cultured *in vitro*.[11] Recently, the emerging field of "neuroeducation", also frequently referred to as "mind, brain, and education" or "educational neuroscience", has been developing. It is known that on a psychological level, some art and mindfulness, and stress management techniques can help people to maintain their emotional stability. However, it is still questionable if those techniques can protect against telomere shortening or if they can be useful on a biological level. This field is also considered the scientifically substantiated art of teaching which embraces many overlapping tenets of brain-based teaching and learning and cognitive neuroscience.[12] Alberto Olivero wrote that "education has the task to shape the brain", and neuroeducation is centered on the neural plasticity feature of the brain that produces neurons and countless connections under the influence of experience.[13] Different methods can be used in neuroeducation activity programs, such as meditation, art therapy, visualization, language codes, yoga, and mindfulness therapy, all of which have the same purpose: to help the human being to handle stress and to protect them from harmful effects. Several study-based articles suggest mechanisms by which various therapies reduce the cortisol level, which is an indicator of stress levels.[13,14]

MATERIALS AND METHODS

Study Design

To assess the neuroeducational methods' influence on telomere shortening, we used a paired-sample, prospective, randomized study. The Institute for Personality Development "Rafaelis" designed and managed this study; the participants' medical histories were gathered, blood samples were taken at the InMedica Clinic (Vilnius), and genetic tests were performed at the Life Length laboratory (Madrid). This study is a continuation of a previous one in which we analyzed the length of telomeres.[15]

The research lasted for six months and involved 20 healthy women aged 20 to 59 years.

We included only women in this study so that the cohort would be more homogenous because studies show that there are differences in telomere length between genders.[16]

For four continuous months, 50% of the participants (10 women) attended regular neuroeducational sessions (20 hours per month) in which various methods were applied (theoretical and neuroeducational). The neuroeducational methods we used in our research were copyrighted works created by Marija Mendele-Leliugienė (Institute for Personality Development "Rafaelis"). Altogether, 57 different neuroeducational methods and their varied algorithms were used in this research. Participants who were in the study group participated in intense (20 hours/month; 80 hours in total) neuroeducational classes, including art therapy, stress management techniques, visualization, and meditation, as described in the methodological book.[17] The main neuroeducational methods were divided into groups:

1) Exercises/tests: These are additional components of education that are specifically designed to achieve the desired educational goal. Exercises are designed for relaxation, concentration, emotional recognition, control, and release.

2) Visualizations: The seven visualizations were meant to be the main motivational keys that could help a person go through their thinking process, sometimes even resulting in mindset/attitude permanent changes, helping to understand, comprehend, assimilate and realize the importance of emotions management, and enabling a person to take full responsibility for their decisions.

3) Verbal codes: Verbal codes are phrases used for self-awareness/self-perception, self-integration, perception of reality, mindset, and behavioral correction. Applying verbal codes enables a person to forgive themselves and others and motivates a person to choose how to live.

4) Art therapy methods: To create unique conditions for the participant to remember the feelings, emotions, and inner states which then are used as the main source of self-regulation.

Another 10 women participated as a control group.

Measurement of Telomere Length

The median telomere length was measured at the life length laboratory in Spain. In this study, we used high-throughput (HT) quantitative fluorescence *in situ* hybridization (Q-FISH). We chose this technique because of its ability to analyze cells, unlike other techniques such as TRF and polymerase chain reaction-substantiated assays where the substrate is DNA. This Q-FISH method is adapted for cells fixed in interphase. The HT technique is automatized and not labor-intensive, which makes it suitable for use in large studies.

Following the methodology of Serapinas and colleagues (2020), the counts of defrosted cells at 37 °C were checked, and after that,

control and sample lymphocyte lines were cultured in black-walled clear-bottom 384 plates. Methanol/acetic acid (3/1, vol/vol) was used to complete cell fixation. Telomeres were hybridized *in situ* with a fluorescent peptide nucleic acid (PNA) probe (binds to sequence Alexa488-OOCCCTAACCCTAACCCTAA, Panagene). Following this, the cells were washed, and a fluorescent stain (DAPI) was added to improve the contrast of the DNA. To accomplish the imaging of the cells and telomeres, a 40×0.95 NA water immersion objective was used. Signals from DAPI were distinguished by UV wavelength, and those from Alexa488 were distinguished by 488 nm wavelength. The images were analyzed using the High Content Screening Opera System (Perkin Elmer, USA) on Acapella software, Version 1.8 (Perkin Elmer). Further interpretation of telomere length was carried out using life length's proprietary program.

Statistical Analysis

Statistical analysis was conducted on all of the gathered data using the SPSS (Statistical Package for the Social Sciences) software (version 27.0. Armonk, NY, IBM Corp). To compare 20th percentile value changes between the first and second measurements in both groups, a non-parametric paired Wilcoxon test was performed. The Mann-Whitney U test was used to compare the variation in the 20th percentile of telomeres between the control and experimental groups. Spearman's correlation test was used to assess the correlation between two variables.

The study was reviewed and approved by the Bioethics Center of the Lithuanian University of Health Sciences; the approval number is BEC-MF-863.3.

RESULTS

This study included an analysis of women of different ages. Q-FISH was performed on all participants before and after the study. Figure 1 shows the Q-FISH of our randomly selected participants.

The participants' average biological age was 42.6 years (minimum: 21.6 years, maximum: 59.8 years). 40.05 years was the average chronological age (minimum: 20.7 years, maximum: 59.3 years). There was a statistically significant difference between their biological and chronological ages ($p<0.05$). Before the study, the median telomere length was 10.8 kb (minimum: 9.4 kb, maximum: 12 kb), and the population percentage was 40.5% (minimum: 1%, maximum: 81%). However, there was no statistically significant difference between the experimental and control groups in the demographic data (Table 1).

Changes in the Value of the 20th Percentile

The experimental group's median 20th percentile value was 5.8 kb (minimum: 4.9 kb, maximum: 7.1 kb) prior to the research and 5.6 kb (minimum: 4.6 kb, maximum: 6.5 kb) after the research ($p<0.05$). The control group's median 20th percentile value was 6.4 kb (minimum: 4.9 kb, maximum: 7.4 kb) prior to the research and 5.7 kb (minimum: 4.6 kb, maximum: 6.3 kb) after the research. The change in the control group's 20th percentile value was statistically significant ($p<0.001$) (Figure 2).

The mean difference of the 20th percentile of telomeres between the first and second measurements in both groups was 0.52 kb (minimum: -0.50 kb, maximum: 1.20 kb).

Measurement of the 20th percentile value in both groups showed that in the experimental group, the 20th percentile decreased in 8 of the 10 participants. However, in the control group, the value of the 20th percentile decreased in all 10 participants.

The Influence of Daily Habits on the 20th Percentile

Every participant (n=20) was asked about their daily lifestyle and habits. We analyzed three aspects of lifestyle: Stress from daily life, physical activity, and smoking. The surveys were created based on self-reports from the participants: If the person was suffering extreme stress daily, life was described as stressful. Respondents were classified as physically

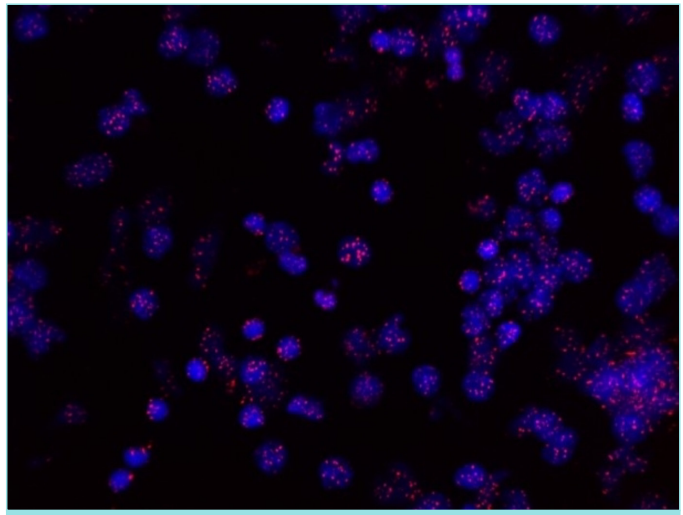

Figure 1. Telomere visualization with quantitative fluorescence *in situ* hybridization.

Table 1. Demographic data of experimental and control groups

Parameter	Experimental group (n=10)	Control group (n=10)	p-value
Biological age in years (mean ± SD)	44.90±8.17	42.93±12.11	>0.05
Chronological age in years (mean ± SD)	41.00±7.88	42.02±11.90	>0.05
BMI (mean ± SD)	22.36±2.65	21.97±3.30	>0.05
Physical activity (number of women)	5	4	>0.05
Smoking status (number of women)	2	4	>0.05
Daily life stress (number of women)	5	8	>0.05
Value of the 20th percentile (kb) before the research (median ± SD)	5.97±0.72	6.34±0.74	>0.05
Value of the 20th percentile (kb) after the research (median ± SD)	5.60±0.73	5.67±0.53	>0.05

SD: standard deviation, BMI: body mass index

Table 2. The impact of lifestyle on the 20th percentile (kb)

Factor	Yes			No			p-value
	Median	Min.	Max.	Median	Min.	Max.	
Smoking	6.35	5.6	7.4	6.0	4.9	7.3	>0.05
Tense life	6.4	4.9	7.4	6.5	4.9	7.1	>0.05
Physical activity	5.8	4.9	7.4	6.3	4.9	7.3	>0.05

Min.: minimum, Max. maximum.

active if they participated in sports or other forms of physical activity for a minimum of 60 minutes each day. We observed that for participants whose lives were more stressful (n=13), the median 20th percentile value at the initial blood sampling was 6.2 kb (minimum: 4.9 kb, maximum: 7.4 kb), while for those whose lives were less stressful (n=7), it was 6.5 kb (minimum: 4.9 kb, maximum: 7.1 kb). There was no statistically significant difference between these groups (p>0.05). Smoking women (n=6) had a median 20th percentile value of 6.35 kb (minimum: 5.6 kb, maximum: 7.4 kb), while non-smokers (n=14) had a value of 6 kb (minimum: 4.9 kb, maximum: 7.3 kb). This difference, however, was not statistically significant (p>0.05). Physically active women (n=9) had a median 20th percentile value of 5.8 kb (minimum: 4.9 kb, maximum: 7.4 kb), while physically inactive women (n=11) had a median 20th percentile value of 6.3 kb (minimum: 4.9 kb, maximum: 7.3 kb). Also, there was no statistically significant difference between the two groups (p>0.05) (Table 2).

All the participants were asked about their sleep routine, and their answers regarding their average sleep duration were divided into three groups: 6, 7, and 8 hours of sleep duration. The median 20th percentile value for those whose slept 6 hours (n=6) was 5.65 kb (minimum: 4.9 kb, maximum: 7.1 kb); for women who slept 7 hours (n=10), it was 6.4 kb (minimum: 4.9 kb, maximum: 7.4 kb); and for participants who slept 8 hours (n=4), it was 6.4 kb (minimum: 5.5 kb, maximum: 7 kb). However, we did not find a statistically significant correlation between the average sleep duration and the 20th percentile value (p>0.05).

No statistically significant correlation between the 20th percentile value and body mass index (BMI) or alcohol consumption was found (Figure 3).

DISCUSSION

Our findings were unique because for the first time in our preliminary study, we analyzed 20th telomere length shortening with regards to psychological factors. 20th telomere analysis is more accurate than general mean length analysis because it more precisely represents body aging and physiological events.[18]

With the outcomes of this study, we aim to contribute to the discussion on the importance of neuroeducational methods to longevity regarding the mechanism of telomere shortening. The main finding of this study was that the value of the 20th percentile of telomere shortening in the control group was statistically significant (p<0.001). Furthermore, in the experimental group, the value of the 20th percentile telomere shortening was also statistically significant (p<0.05). These findings revealed that telomere shortening in the experimental group was less prevalent than in the control group. Nevertheless, because of the low number of participants and the very short period between measurements, these pilot study results should be considered with caution.

Other studies provided similar findings on the 20th percentile of telomere shortening in a control group, and their results echoed those in our study. In research conducted in 2016 in Spain, the impact of dietary supplement TA-65 on 20th percentile telomere length was analyzed. The difference in the value of the 20th percentile of telomere length between the low-dose TA-65 group and the placebo group was statistically significant.[19] It is important to maintain a balance in telomerase activity because excessive telomere elongation can also disrupt chromosomal stability.[20]

There are many genetic and environmental factors related to telomere shortening, and one of the most mentioned in the literature is oxidative

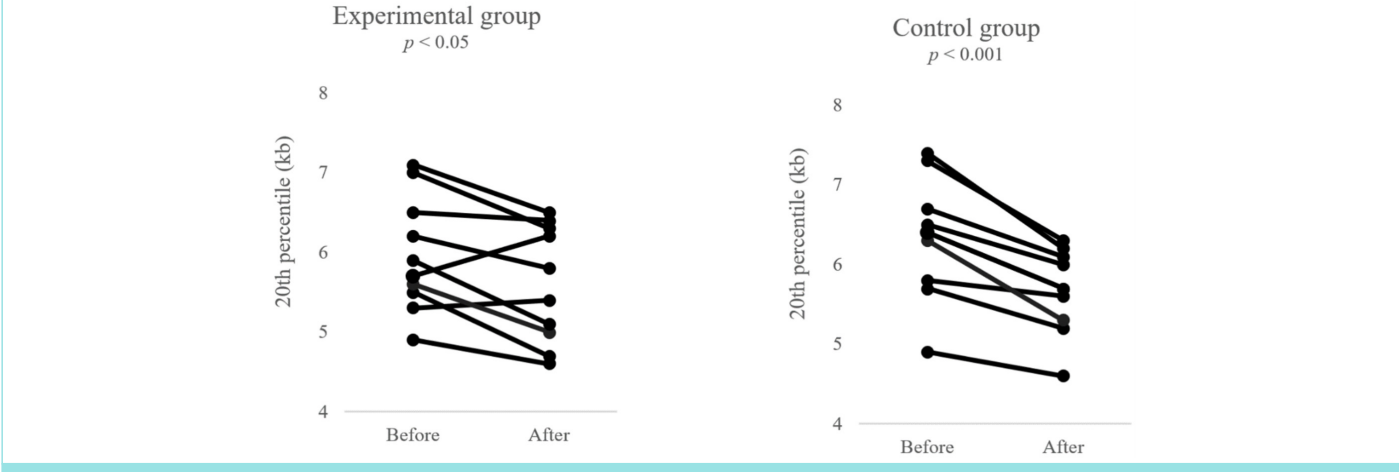

Figure 2. Comparison of 20th percentile values before and after the study using the paired t-test in the experimental group (p<0.05) and control group (p<0.001).

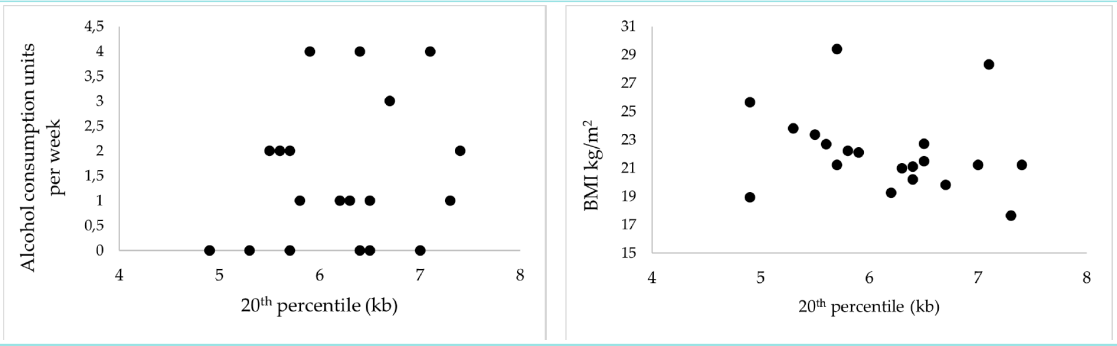

Figure 3. Associations between the 20th percentile and alcohol consumption (left) and BMI (right).
BMI: body mass index.

stress.[21] This is a consequence of an imbalance in the production of ROS and the defense of cellular antioxidants. ROS levels are known to be higher in areas of chronic inflammation and are common in chronic inflammatory illnesses.[22] Several studies have demonstrated that oxidative stress is linked to increased telomere shortening in the majority of degenerative and inflammatory illnesses.[23] That is why it is important to find ways to relieve stress. Studies show that meditation through stress reduction mechanisms can reduce levels of the stress hormone cortisol and reduce levels of ROS, as well as stimulate anti-inflammatory cytokines, endorphins, and neurotrophins.[24] Mindfulness meditation practices were examined in a study with medical students by measuring their serum cortisol levels. The study population consisted of 30 medical students and their cortisol levels were higher before the mindfulness meditation than after the meditation practice.[25]

Environmental stresses, smoking, heavy alcohol consumption, and air pollution can cause metabolic changes on a cellular level and can lead to oxidative stress and telomere shortening.[26,27] Neuroeducational methods are often mentioned in other studies as an opportunity to decelerate chronic disease development.[28] The finnish geriatric intervention study to prevent cognitive impairment and disability (FINGER) is the biggest clinical trial on this topic, focusing on the impact of a multi-domain lifestyle interventions on changes in LTL; unfortunately, over the course of two years, there was no significant difference in LTL between the intervention and control groups. However, LTL maintenance was directly associated with an improvement in lifestyle among FINGER participants.[9] The same results were visible in our research: Participants who attended neuroeducational activities were seen to have fewer changes in the 20th percentile of telomere length, while in the control group, telomeres were more shortened. In another study, LTL was significantly longer in middle-aged US women who were healthy, practiced a healthy lifestyle, and conformed to five low-risk factors for a healthier lifestyle (non-smoking, engaging in regular moderate to intense physical activity, maintaining optimal body weight, eating a healthy diet, and consuming alcohol in moderation).[29] Even though these factors are usually referred to as risky for telomere shortening, in our study, alcohol, smoking, BMI, and physical activity had no statistically significant effect on the value of the 20th percentile of telomere length. It can be hypothesized that neuroeducation activities can protect from telomeres shortening even when high-risk factors are experienced. However, this could not be tested in this study because of the small number of participants. Therefore, this is a preliminary study and because of its small sample size, there is a need for further larger studies to confirm the findings.

CONCLUSION

This study's findings showed that shortening of the 20th percentile of telomere length, which is most important to somatic health, was slower in those participating in the neuroeducational methods program. The mechanism for this is still not clear, but neuroeducation may influence some pathways involved in stress-related mechanisms. However, more studies have to be conducted to confirm the advantages of a neuroeducational methods program concerning telomere length.

MAIN POINTS

- The shortening of the 20th percentile of telomere length was slower in the neuroeducational group than in the control group.
- Neuroeducational exercises might help to slow the 20th percentile of telomere length shortening due to unknown mechanisms but further studies are needed.
- There was a statistically significant difference between the biological and chronological ages of participants.

ETHICS

Ethics Committee Approval: The study was reviewed and approved by the Bioethics Center of the Lithuanian University of Health Sciences; the approval number is BEC-MF-863.3.

Informed Consent: Informed consent was obtained from all subjects involved in the study.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Concept: D.S., R.P.V., M.M.L., Design: D.S., M.M.L., Supervision: D.S., M.M.L., Fundings: M.M.L., Materials: D.S., A.S., G.P., Data Collection and/or Processing: D.S., Analysis and/or Interpretation: D.S., A.S., G.P., Literature Search: R.P.V., A.S., G.P., Writing: A.V., R.P.V., A.S., G.P.

DISCLOSURES

Conflict of Interest: No conflict of interest was declared by the authors.

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ORIGINAL ARTICLE

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Magnetic Resonance Imaging Findings of Intracranial Dural Metastases

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Abstract

BACKGROUND/AIMS: To evaluate the magnetic resonance imaging (MRI) findings of intracranial dural metastases (IDM) due to various cancers.

MATERIALS AND METHODS: Fifty-six male and thirty female patients (total: 86) aged 2-94 years (mean: 58.10±16.32 years) diagnosed with IDM between April 2010 and May 2020 were included in this retrospective study. Dural tumoral involvement patterns [focal, multifocal, diffuse linear, diffuse linear and nodular (mixed)], bone involvements (focal, diffuse, none), tumoral involvement areas (dural; bone and dural; parenchymal and dural; bone, dural, and parenchymal), locations (supratentorial, infratentorial), leptomeningeal involvement and the presence of perineural spread were evaluated in these cases.

RESULTS: IDM were most commonly observed in head and neck cancers (23.3%), lung cancer (17.4%), and breast cancer (15.1%). Focal pattern was observed in 55.8% of the dural tumoral involvements while 16.3% were multifocal, 16.3% diffuse linear and 11.6% mixed pattern. Fifty-seven percent of the cases involved had bone and dural area involvement, whereas 24.4% had parenchymal and dural involvement, 13.9% bone, dural and parenchymal combined involvement, and 4.7% only had dural involvement. Supratentorial involvement alone was seen in 39.5% and infratentorial involvement alone was observed in 7% of the cases, while 53.5% of the cases had both supratentorial and infratentorial involvement. In 38.3% of the cases found to have dural metastasis, cerebral parenchyma invasion was observed. Leptomeningeal involvement was observed in 41.9% of the cases whereas 9.3% had perineural spread.

CONCLUSION: IDM are more commonly observed in the male gender and in head and neck, lung and breast cancers. IDM are more commonly accompanied by bone or parenchymal involvement, while isolated dural metastases are less frequently observed.

Keywords: Dural metastasis, intracranial metastasis, leptomeningeal metastasis, magnetic resonance imaging, perineural spread

INTRODUCTION

Intracranial dural metastases (IDM) can develop due to direct extension from the metastasis of the adjacent skull as well as due to hematogenic extension from distant regions.[1] Dural metastases more frequently develop in breast, prostate, lung cancers and multiple myelomas while in pediatric patients, they develop due to neuroblastoma and sarcoma. Sinonasal or nasopharyngeal cancers, on the other hand, can lead to direct invasion of the dura from an adjacent primary tumor sites or to dural infiltration through perineural spread. In clinical trials, the frequency of IDM due to malignant neoplasms were reported to be approximately 4%.[2] Contrast-enhanced magnetic resonance imaging (MRI) is the method of choice for detecting IDM due to its high resolution and multiplanar nature.[3] On MRI, dural metastases are typically characterized by linear or nodular type thickening and contrast involvement in dura mater.[4] In this retrospective study, the radiological

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imaging findings of IDM in patients who had undergone contrast-enhanced brain MRI due to various cancers in the previous ten-year period were evaluated.

MATERIALS AND METHODS

Radiological reports from April 2010 to May 2020 in the Picture Archiving and Communication System (PACS) of our hospital were searched using the phrase "dural metastasis", and 107 patients with dural metastasis were identified. Twenty-one patients for whom contrast-enhanced brain MRIs were not carried out or whose images were not of sufficient quality to perform radiological evaluation, and those patients with trauma or surgical history were excluded. Thus, a total of 86 patients were included. Fifty-six of them (65.1%) were male and 30 (34.9%) were female. Their mean age was 58.10±16.32 years (range: 2-94).

MRI examinations up to 2017 were carried out using an 8-channel 1.5 T MRI machine (GE Signa Excite HD; GE Healthcare, Milwaukee, WI, United States, 2005), and a 16-channel 1.5 T MRI machine (GE Signa Explorer SV 25; GE Healthcare, Milwaukee, WI, United States, 2016) was used after 2017. All radiological examinations were evaluated by two experienced neuroradiologists (E.G. with more than 10 years of experience and M.B. with more than five years of experience). Dura matter tumoral involvement patterns were evaluated in four groups: focal when there were one or two foci; multifocal when there were three or more foci; diffuse linear when there was common linear involvement; or mixed pattern when there was diffuse involvement along with nodular foci. Tumoral of bone involvements were of three types: focal, diffuse or no bone involvement. Dural and adjacent structures involvements were evaluated in four groups: only dura, bone and dura, parenchyma and dura, and bone, dura and parenchyma combined involvement. Involvements of dural metastases in supratentorial, infratentorial and both supratentional and infratentorial localizations were evaluated. In addition, leptomeningeal and parenchymal involvement and the presence of perineal spread were also evaluated in our cases. The presence of subdural effusion associated with metastases was determined.

The ethics committee approval was received for this study from institutional ethics committee (no: 15- KAEK-155). Informed consent is not necessary due to the retrospective nature of this study.

Statistical Analysis

Descriptive data are given as mean ± standard deviation, while categorical data are expressed as n (%). Analyses were performed using SPSS software (IBM SPSS Statistics 22, SPSS Inc., an IBM Co., Armonk, NY, United States).

RESULTS

IDM were more commonly detected in head and neck cancers (23.3%), lung (17.4%), breast (15.1%) and prostate (11.6%) cancers. Of all head and neck cancers, nasopharyngeal cancers are most frequently caused by metastases. In two cases in the pediatric group, the cause of metastasis was neuroblastoma. Primary cancer types, numbers and percentages of intracranial dural metastasis cases are given in Table 1.

Dural tumoral involvement patterns were of a focal type (Figure 1a) in 48 cases, multifocal (Figure 1b) in 14 cases, diffuse linear (Figure 1c) in 14 cases and mixed (Figure 1d) in 10 cases. No bone tumoral involvement was observed in 25 cases while 34 cases had focal and 24 cases had diffuse bone involvement. Isolated dural involvement (Figure 2a) was observed in only four cases. Bone and dural involvement (Figure 2b) areas were observed in 49 cases, parenchyma and dura (Figure 2c) in 21 cases, and bone, dural and parenchyma (Figure 3a) combined in 12 cases. Forty-six cases had both supratentorial and infratentorial dural involvement (Figure 3a) while supratentorial involvement alone was observed in 34 cases and infratentorial involvement alone was observed in six cases. The cerebral parenchyma was invaded in 38.3% of dural metastasis cases. Leptomeningeal tumoral infiltration was found in 36 cases and perineural spread (Figure 3b) was observed in eight cases. Tumors causing perineural spread were in the head and neck cancers group, and they developed from squamous cell cancer (SCC) in five cases and from adenoid cystic cancer (ACC) in three cases. Bone and dural tumoral involvement patterns, tentorial localizations, leptomeningeal infiltration and perineural spread numbers and percentages in cases who were found to have intracranial dural metastasis are given in Table 2. Subdural effusion associated with dural metastasis was seen in two cases.

DISCUSSION

Dura mater (pachymeninx) forming the outer meningeal layer in the central nervous system is in two layers in the cerebral convexity. These are the outer layer, rich in vascular structures which is periosteum of inner tabula of skull, and the inner layer which is the true meningeal dura mater.[5] After intravenous contrast matter administration, contrast enhancement is observed in the periosteum of the skull bones and in the real meningeal layer. This contrast enhancement could extend to falx cerebri, falx cerebelli, tentorium cerebelli and dural structures in cavernous sinuses.[6]

Table 1. Primary cancer types, numbers and percentages of cases found to have intracranial dural metastases

Primary cancer type	n	%
Head and neck cancer	20	23.3
- Nasopharyngeal cancer	11	12.8
- Sinonasal cancer	7	8.1
- Oral cancer	1	1.2
- Orbital cancer	1	1.2
Lung cancer	15	17.4
Breast cancer	13	15.1
Prostate cancer	10	11.6
Others	11	12.8
- Malignant mesothelioma	2	2.3
- Neuroblastoma	2	2.3
- Non-Hodgkin lymphoma	1	1.2
- Multiple myeloma	1	1.2
- Chronic myeloid leukemia	1	1.2
- Acute myeloid leukemia	1	1.2
- Thyroid follicular cancer	1	1.2
- Hepatocellular cancer	1	1.2
- Adrenocortical cancer	1	1.2
Skin cancer	8	9.3
Glial tumor	5	5.8
Gastrointestinal cancer	4	4.7

Table 2. Bone and dural tumoral involvement patterns, tentorial localizations, leptomeningeal infiltration and perineural spread numbers and percentages in cases found to have intracranial dural metastases

Anatomical involvement of dural metastases		n	%
Dural involvement pattern	Focal	48	55.8
	Multifocal	14	16.3
	Diffuse linear	14	16.3
	Mixed (diffuse linear and nodular)	10	11.6
Bone involvement pattern	Focal	34	39.5
	Diffuse	27	31.4
	None	25	29.1
Involvement area	Bone and dural	49	57.0
	Parenchymal and dural	21	24.4
	Bone, dural, and parenchymal	12	13.9
	Dural	4	4.7
Tentorial location	Supratentorial and infratentorial	46	53.5
	Supratentorial	34	39.5
	Infratentorial	6	7.0
Leptomeningeal infiltration	-	36	41.9
Perineural spread	-	8	9.3

Laigle-Donadey et al.[4] studied 198 dural metastasis cases published in the literature during the 1904-2003 period, and found that the average age of the patients was 59 years (range: 4 months to 84 years). Nayak et al.[7] reported that 61% of cases with intracranial dural metastasis were female gender and that their mean age was 59 years. In the present study, the mean age of the cases with intracranial dural metastasis was 58.1 years, which was in accordance with the literature reports. However, unlike what has been reported in the literature, the frequency of IDM was higher in the male gender (65.1%) in our study. Tumors causing intracranial dural metastasis listed in the literature by their frequency were prostate (19.5%), breast (16.5%) and lung (11.0%) cancers.[4] In the present study, however, the tumors most commonly causing IDM were head and neck cancers (23.3%), followed by lung (17.4%) and breast cancers (15.1%). The higher frequency of dural metastases originating from head and neck cancers and in the male gender in the present study could be related to the genetic and environmental factors affecting the study population as well as to the number of patients.

The radiological diagnosis of dural metastases are based on contrast-enhanced computed tomography (CT) and MRI. Non-contrast-enhanced CT of the brain is often the first imaging method in patients presenting with neurological symptoms. CT imaging has the advantages of being able to detect metastatic lesions and also to reveal bone involvement. Although less reliable than MRI for the assessment of the extent of intracranial lesions, CT scan is a useful method to show lytic bone lesions. However, CT scan does not clearly show extension and degrees of dural invasion of bone metastases.[3,4] MRI is the best imaging modality to accurately identify dural metastases extending along bone structures.[4,8] Careful evaluation of T2-weighted, T1-weighted and contrast-enhanced images is crucial in detecting dural metastases. On T1-weighted MRI, normal dura mater and the inner table of bone is uniformly hypointense. After gadolinium-based contrast matter administration, normal dura mater shows a thin, linear and discontinuous enhancement.[9] MRI findings suggesting dural metastasis are contrast-enhancing in dura mater and thickening which shows a linear continuity which can sometimes be nodular and signal enhancement on T2-weighted images.[2] The lack of blood-brain barrier in dura mater explain intense contrast-enhancing on MRI.[7] The diagnostic feature of dural metastases is the presence of a signal gap between the dural mass and dislocated brain. This gap might contain cerebrospinal fluid or subdural vessels with varying signal intensities depending upon the sequence used.[2] On contrast-enhanced MRI studies in the literature, the radiological appearances of dural metastases were discussed, and classified as simply localized thickening or nodular mass, classical lenticular or biconvex shape, diffuse dural thickening or diffuse involvement with nodular areas.[1,4,7,10] Although dural metastases can be single or multiple, dural tail finding can be observed in contrast-enhanced examinations.[7] Nayak et al.[7] observed single metastasis in 56% of their cases and multiple metastases in 16%, while 25% of their cases had diffuse involvement and 3% had diffuse and nodular dural involvement. In addition, they found brain parenchymal invasion in 34% and subdural effusion in 2% of their cases, and only 11% of them had infratentorial lesions. Similarly, invasion of brain parenchyma was reported in about one third of the cases with dural metastasis.[11] Similar to the literature, focal and multifocal involvement patterns were observed in 55.8% and 16.3% of the cases, respectively, in the present study. Mixed pattern frequency (11.6%) was higher while diffuse linear involvement frequency (16.3%) was lower compared to the literature. In addition, supratentorial localization, parenchymal invasion and subdural effusion frequencies were similar to the ones reported in the literature. Nayak et al.[7] reported a skull metastasis frequency of 70% in cases with dural metastasis, which was very similar to the present study (70.9%).

In cases with known cancer, leptomeningeal metastasis frequency was reported to be in a wide range of 5-70%.[12] MRI findings of leptomeningeal metastases are thin, diffuse leptomeningeal contrast-enhancement which follows gyri and sulci or multiple nodular lesions in the subarachnoid space.[12,13] About half of the cases in the present study had leptomeningeal metastasis, and this frequency was in line with reports in the literature.

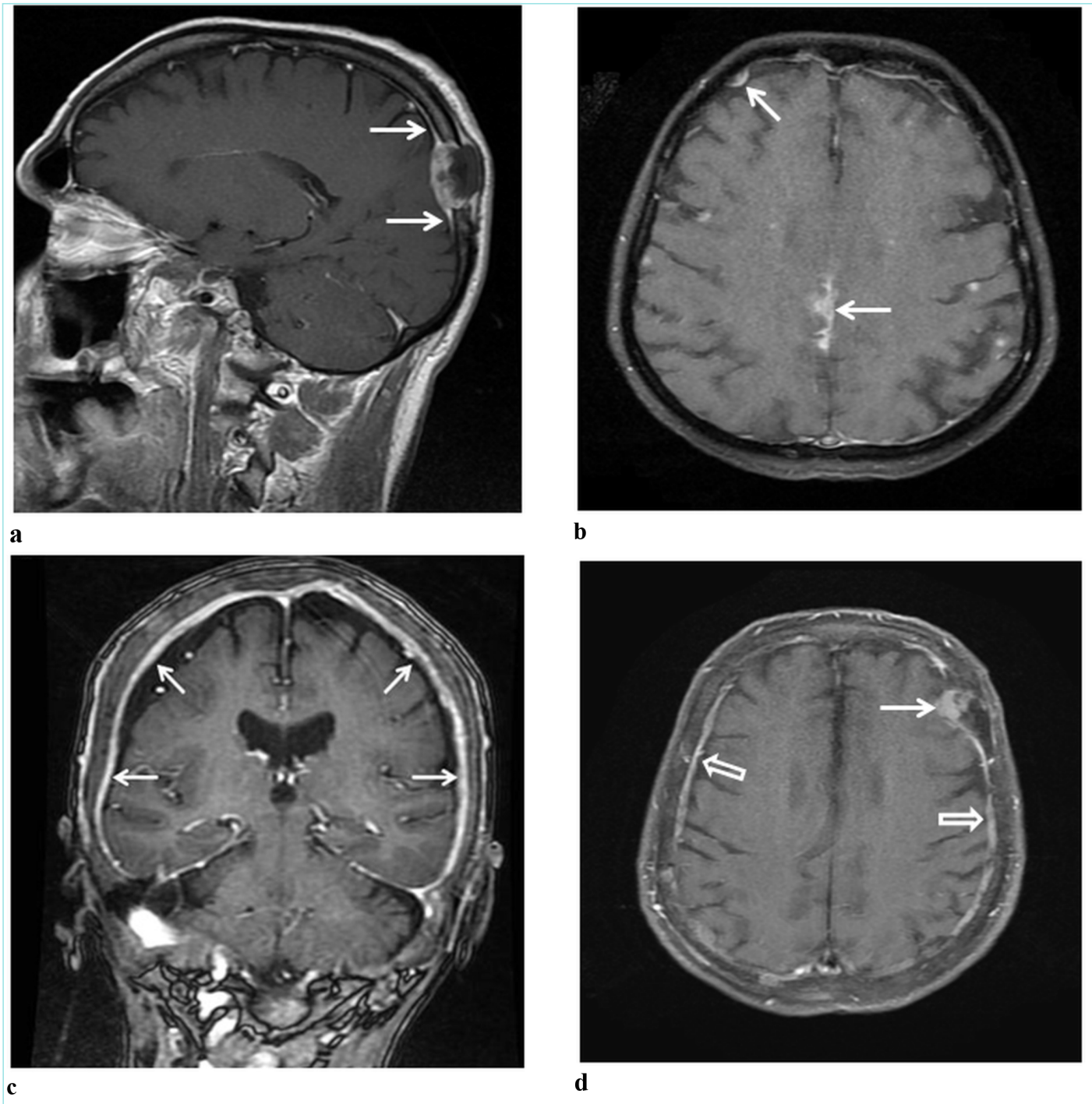

Figure 1. On contrast-enhanced T1-weighted magnetic resonance imaging, **a)** focal metastasis involving left occipital bone and adjacent dura and dural tail (white arrows) are shown. **b)** Multifocal cortical metastases are shown in right frontal and falcine dura and in cerebral parenchyma. **c)** Diffuse linear thickening and contrast-enhancing (arrows) due to tumoral involvement in dura are shown. **d)** Diffuse (open arrows) and nodular type (white arrows) dural thickening and enhancement with diffuse calvarial involvement are observed.

Intracranial invasion through extra-cranial neoplasms are mostly associated with sinonasal or nasopharyngeal malign neoplasms. Neoplastic extension mechanisms are a direct infiltration of the periosteum-bone-dura composite layer or perineurial spread.[2] MRI findings of dural invasion in nasopharynx cancer or sinonasal malign tumors are dural thickening and nodular dural contrast-enhancement.[14] Perineural spread refers to the extension of tumor cells along with the nerve sheath. Perineural spread can also be observed in infections, granulomatous diseases and benign tumors. Among the head and neck cancers, perineural spread is most commonly observed in SCC cases since SCCs constitute most malignancies in the head and neck areas. The frequency of perineural spread in SCCs ranges from 2

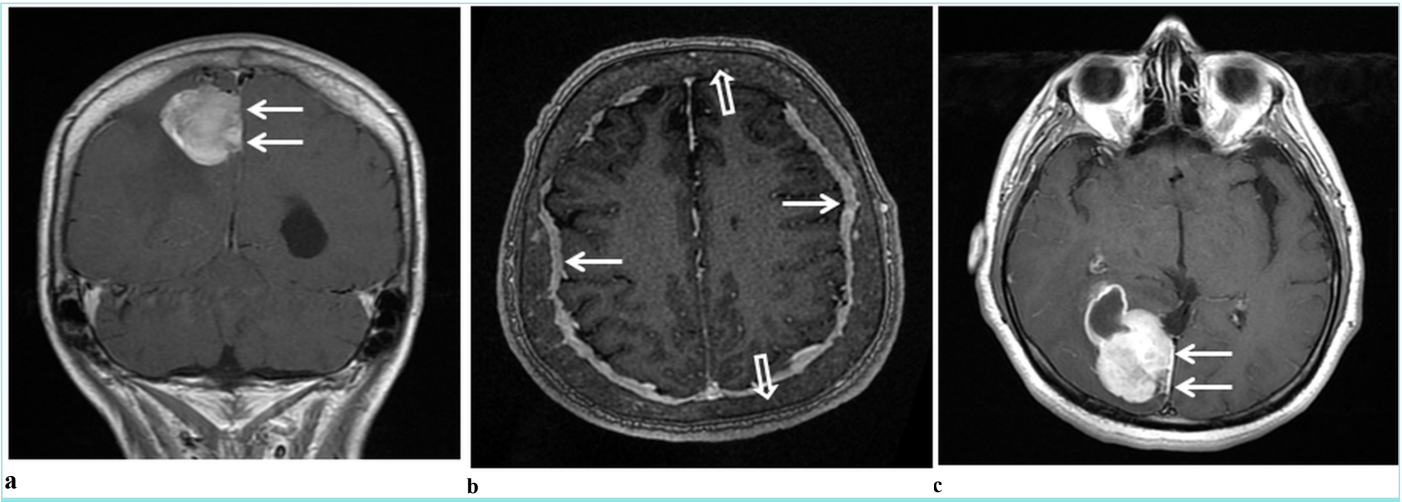

Figure 2. On contrast-enhanced T1-weighted magnetic resonance imaging, **a)** The dura-based mass reveals mildly heterogeneous and intense enhancement (arrows) direct dural involvement due to thyroid follicular cancer. **b)** Bone and dural involvement due to acute myeloid leukemia contrast-enhancing and thickening, nodular and linear in places, of mixed pattern dural involvement are shown. **c)** Pleomorphic xhantoastrocytoma which caused focal metastasis (white arrows) from parenchyma to falcine dura is shown.

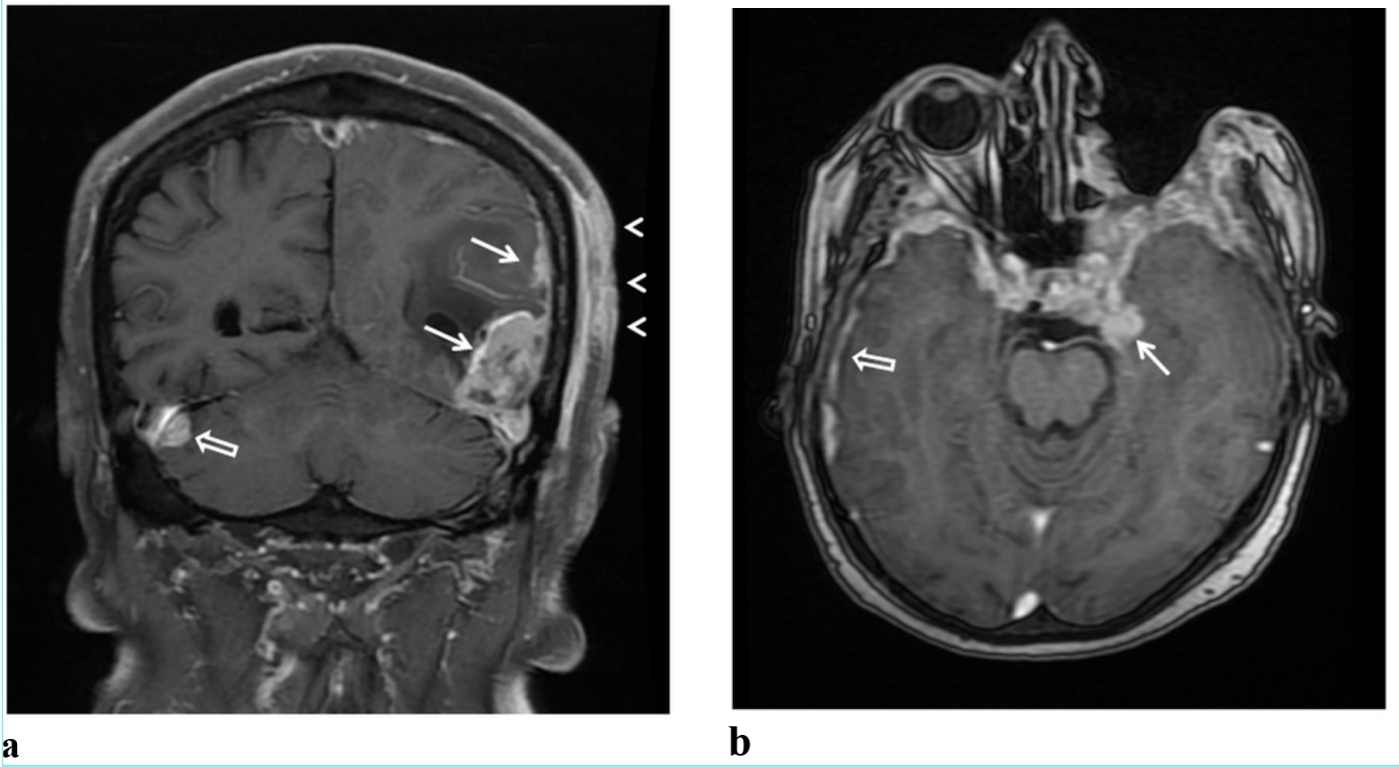

Figure 3. On contrast-enhanced T1-weighted magnetic resonance imaging, **a)** The patient with skin cancer (arrow heads) in addition bone, dural and parenchymal involvement, diffuse linear and nodular dural metastasis in both infratentorial (open arrows) and supratentorial locations (white arrows) are observed. **b)** The patient with adenoid cystic cancer, mixed pattern dural metastases which had both linear (open arrow) and nodular (white arrows) character and which developed from an adjacent tumor site and perineural spread are shown.

to 30%. Despite their very high perineural spread capabilities, ACCs are responsible for less perineural spreads than SCCs since they are rarely observed.[15] In the present study, both bone and dura were involved in all cases with head and neck cancers, and parenchymal involvement was also present in one case. In addition, eight cases were found to have perineural spread, the primary malignancy was head and neck tumors, and SCC was responsible for two-thirds of the cases.

In the differential diagnosis of dural metastases, in addition to neoplasia such as meningiomas and lymphomas, non-neoplastic lesions such as subdural hematoma, intracranial hypotension, sarcoidosis (especially

in the form of granulomatous meningitis), empyema and tuberculosis osteomyelitis should be considered.[2,16-18] While meningioma generally shows a signal intensity similar to that of the cortex on both T2 and T1-weighted sequences, most metastases are slightly hyperintense on T2-weighted MRI and slightly hypointense on T1-weighted MRI.[2] When the dural lesion is single and has a dural tail character, it may not be differentiated radiologically from meningioma. The presence of calvarium metastasis and bone erosion in these cases does not help in the differential diagnosis from meningioma. Diffuse dural involvement can also make diagnosis difficult. Diffuse dural involvement can depend on the dural invasion of the cancers, but it can also be the reactive response of dura to calvarium metastasis. Infectious-inflammatory etiologies can also lead to this appearance.[7] Non-Hodgkin lymphoma should be suspected in the differential diagnosis in soft tissue involvement associated with bone resorption and epidural mass observed in human immunodeficiency virus-positive patients. In patients with osteomyelitis, on the other hand, lytic bone lesions and soft tissue mass are generally observed.[2] When big in size, dural metastases can indent into the cerebral cortex, resulting to vasogenic edema. Dural metastases can sometimes be associated with spontaneous hemorrhages which can hide the underlying lesions, and, though rarely, they can also be associated with parenchymal hemorrhages.[11] Three mechanisms have been suggested to explain the association between dural metastasis and subdural hematoma: hemorrhagic effusion due to dural metastasis, dural venous occlusion due to neoplastic invasion or angiodesmoplastic response of dura against neoplastic cell invasion.[19] In these cases, hemorrhage was assumed to occur into subdural neomembrane, which is an abnormally areolar dural layer with abundant vascularization.[20] Intracranial hypotension, another entity which should be considered in the differential diagnosis of dural metastases, on the other hand, bilateral, diffuse, non-nodular meningeal contrast-enhancement, congestion in venous sinuses and congestion in posterior fossa are observed.[18]

The present study has some limitations. First, the study was only a retrospective screening-based on PACS search using the phrase “dural metastasis”, therefore the search is based on radiological reports, and not based on reviewing the images of the patients with primary malignancy. Second, in most of the cases with known primary tumor, dural involvements in the imaging studies were accepted as dural metastasis without histopathologic diagnosis. Third, while dura was not examined in detail during autopsy, dural thickening and enhancement were accepted as dural metastasis in some cases based only on the radiological imaging findings.

CONCLUSION

IDM are more frequently observed in the male gender and especially in head and neck, lung and brain cancers. Dural metastases frequently have both supratentorial and infratentorial localizations, while only infratentorial localization is rare. Dural metastases are generally accompanied by bone and parenchymal involvements, whereas isolated dural metastases are less frequently observed. The dural tumoral involvement pattern is mostly focal, but multifocal, diffuse linear or mixed type dural metastases can also be observed.

MAIN POINTS

- IDM are more frequently observed in the male gender and in head and neck cancers.
- Dural metastases mostly have supratentorial and infratentorial localizations combined, and isolated infratentorial localization is less frequent.
- Isolated dural metastases are rare, and dural metastases are more frequently accompanied by metastatic involvement of adjacent structures (calvarium and parenchyma).
- Dural metastases mostly have the appearance of focal pattern and less frequently mixed pattern (diffuse linear and nodular).
- Contrast-enhanced MRI is the best method for imaging dural metastases.

ETHICS

Ethics Committee Approval: The ethics committee approval was received for this study from institutional ethics committee (approval number: 15- KAEK-155).

Informed Consent: Informed consent is not necessary due to the retrospective nature of this study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: E.G., Design: E.G., M.B., Supervision: E.G., L.A., Resources: L.A., Materials: M.B., Data Collection and/or Processing: M.B., B.A., Analysis and/or Interpretation: E.G., M.B., Literature Search: L.A., Writing: E.G., M.B., L.A., Critical Review: E.G., B.A.

DISCLOSURES

Conflict of Interest: The authors have no conflicts of interest to declare.

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ORIGINAL ARTICLE

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Mechanical Heart Valve Surgery Patients' Experience with Warfarin: A Qualitative Study

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Abstract

BACKGROUND/AIMS: This study examined mechanical heart valve surgery (HVS) patients' experiences with warfarin. Although warfarin therapy is of vital importance for heart valve patients, the lack of therapeutic international normalized ratio (INR) levels in long-term anticoagulant therapy can cause various complications.

MATERIALS AND METHODS: This qualitative study was carried out as phenomenological. The sample included 12 first time HVS patients who received anticoagulant treatment for at least three months after discharge. Codes were put together for the purpose of this study and classified. Themes were created.

RESULTS: The mean age of the patients was 50.83±12.91 years, and 66.7% (n=8) of them were male. Their mean exposure time to warfarin was 70.50±49.93 months. Content analysis identified four main themes: "difficulties, facilitators, dependence and the impact of side effects from warfarin". Even those patients who had been using warfarin for many years still suffered from different problems. A lack of knowledge and information about warfarin use still exists. Some patients considered using warfarin as a part of their life, considering it to be more manageable when they agreed to use warfarin, and some said that they continue using warfarin with the support of their relatives and health professionals. Since this study was carried out in the Aegean region, patients had difficulties in limiting greens. The patients mentioned their dependence on the hospital because they had no INR measuring instruments. Some patients explained that they feared the side effects of the drugs, and avoided using other medications.

CONCLUSION: HVS patients had problems adhering to warfarin after discharge. They need follow-up and guidance from nurses.

Keywords: Heart valve diseases, adherence, outpatients, surgical procedures, warfarin

INTRODUCTION

The prevalence of heart valve diseases (HVD) is high both in Turkey and in the world. The prevalence of moderate or severe HVD, corrected by age, was found to be 2.5% in a U.S. study (n=11,911).[1] HVD caused by rheumatic or calcific causes may develop into multiple valvular diseases. HVD are generally progressive and surgical treatment is required in cases of severe insufficiency or stenosis.[2,3] It is important for patients to cope with further difficulties despite successful surgery. One of these difficulties in care after mechanical heart valve replacement surgery (MHVRS) is the patients' temporary or permanent use of anticoagulant medication. The age limitation range was increased from 50 to 50-65 years in 2017, which will increase the number of patients who undergo heart valve surgery (HVS) and receive anticoagulant treatment.[3]

Anticoagulation is very important to prevent valve-related complications in patients with mechanical prosthetic valves. It is assessed using the international normalized ratio (INR) test.[3,4] Although the target INR

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value varies according to the valve type, it is between 2.5-3.5 in the mitral valve, and 2.0-3.5 in the aortic valve. If the therapeutic INR level is high in the patient, while the risk of thrombosis is high, the high INR value may cause various bleeding in the patient. Warfarin is used as an anticoagulant after heart valve prosthesis surgery in Turkey. Therefore, one of the most important points after MHVRS is warfarin adherence. Adherence can be defined as a positive reaction to stimulation.[5,6] Factors that increase the patient's adherence to warfarin are: knowing the reason and importance of using this drug, taking the drug at the same time every day, taking the drug at the recommended dose, continuing their check-ups at least once every four weeks, continuing their check-ups in the same hospital/polyclinic, considering food-drug interactions when eating, checking the INR level within 3-7 days after using a new drug, being aware of the symptoms of complications, and being aware of the methods to avoid complications. The effectiveness of the education given to patients about warfarin at discharge should be evaluated.[7,8]

There are some deficiencies in evaluating warfarin adherence in the healthcare system in Turkey. There is no training program for warfarin and the health records of patients cannot be collected on a single system and records may vary from hospital to hospital. This situation also causes difficulties in INR monitoring. When the literature was analyzed, it was seen that the warfarin-related experiences of those patients with HVS were mostly examined by quantitative research. In one study (n=200), it was determined that 56% of the patients were unaware of potential drug interactions, 58% were not informed about side effects, and 12% were hospitalized due to side effects.[9] In another study conducted in Kenya (n=147), the warfarin adherence of the patients was evaluated via the Morisky Medication Adherence Scale, and it was found that adherence was better in women, older age groups and those patients who had undergone HVS.[10] In the Warfarin TR study conducted by Çelik et al.[12], it was determined that the awareness of the Turkish society about warfarin was low, the therapeutic range varied according to the region and the most bleeding was seen in the Aegean region. In other studies conducted in our country, it was seen that the level of awareness and the knowledge levels of the patients about the use of warfarin was low.[11-14] In these studies, patients using warfarin for reasons such as atrial fibrillation and thromboembolism constitute the sample of patients with valvular diseases. With the study we conducted on the warfarin use of MHVRS patients, we thought that understanding the perspectives, opinions and experiences of the patients would be useful in patient education, preventing warfarin-related complications and increasing their adherence to treatment. For these reasons, in our qualitative study, we examined the experiences of those patients with mechanical valve prosthesis regarding warfarin after discharge.

MATERIALS AND METHODS

This study was written using the Consolidated Criteria for Reporting Qualitative Research, which provides guidance in reporting qualitative research.[15] This qualitative and phenomenological study used purposeful sampling. The data were collected in the cardiovascular surgery outpatient unit in a university hospital between June and October, 2017. In the hospital outpatient unit where the study was carried out, no nurses worked. During discharge, education about warfarin therapy was provided by nurses. When they come to the polyclinic, their information needs about warfarin are provided by the physicians.

The sampling criteria were as followed:

- Undergoing HVS for the first time,

- Receiving a mechanical heart valve prosthesis,

- At least three months having passed since surgery,

- Over 18 years old,

- Having no psychiatric diagnoses,

- Having no hearing loss.

These patients came to their polyclinic check-ups to have INR tests done. After giving blood for INR, the patients wait in the outpatient clinic until the test result are ready. Patients meeting the sampling criteria were interviewed while waiting. A total of 15 patients were approached: one declined to participate in the study, two patients left, saying that they had to go 15-20 minutes after the start of the interview, and the study was completed with 12 participants. The sample size was determined following the repetition and saturation of the data.[16,17]

Data Collection

The data were collected using a socio-demographic characteristics form, a semi-structured interview form and a tape recorder. The researcher asked the main interview question, "What is it like to use warfarin?" and these sub-questions in the semi-structured interviews:

- How does warfarin use affect your life?

- What are your difficulties with using warfarin?

- What are the factors that ease the use of warfarin?

This study was conducted by two female academic researchers, E.A.K. and Ö.B. (Ph.D. candidate and associate professor). The researchers had participated in courses related to qualitative research and had qualitative research experience. They also had conducted studies on cardiovascular surgery nursing. In this study, the interviews were conducted by E.A.K. Two academic nurses gave their expert opinions regarding the questions on the semi-structured interview. The data were collected during face-to-face and in-depth interviews which were conducted in a quiet, comfortable room, in the same outpatient clinic of the hospital. The interviews lasted for 35 to 45 minutes. During the interviews, the researcher took notes of her observations and the patients' statements. The notes taken during the interview were confirmed by the patients. The tape recording was transcribed. There was no relationship established prior to the study commencement. Repeated interviews were not conducted with the same patient.

Statistical Analysis

The data were analyzed using content analysis. All the expressions were written by listening to the audio records of the patients. The expressions associated with the patients' experience with warfarin use were combined to create codes. Similar codes were combined and categorized. The codes were put together for the purpose of the study and classified by the authors. Themes were created.[16] Data saturation was discussed and analyzed by two researchers. Their differences were discussed, and the data were organized and finalized. Transcripts were not returned to the participants for comment or correction. No software was used to manage the data. The participants did not provide feedback on the data.

Validity and Reliability

The principles of plausibility, transmissibility, consistency and verifiability were used to confirm the validity and reliability of the study.[16,17] Expert review and long-term interaction ensured plausibility. The findings were presented without generalizing to ensure transmissibility. The same researcher collected the data using the collection forms and a tape recorder for consistency. The researchers reviewed all the data collection tools, voice recordings, raw data, and codes and themes generated during the analysis, which were all preserved to be further examined if necessary.[18,19]

Ethical Considerations

Permission was taken from the hospital where the study was conducted (Dokuz Eylül University Hospital) and the Dokuz Eylül University Ethics Committee for Non-invasive Clinical Studies (approval number: 2016/24-03, date: 08.09.2016). Before the interview, the researcher introduced herself and the purpose of the research was explained and written and verbal informed consent was obtained from the patients. The study data and the notes taken were kept by the researchers.

RESULTS

The mean age of the patients (n=12) was 50.83±12.91 years, and 66.7% (n=8) of them were male. Their mean time being on warfarin treatment was 70.50±49.93 months.

Four main themes and twelve sub-themes were identified in the interviews (Table 1). The socio-demographic characteristics of the patients and the duration of warfarin use are given at the end of the examples of the patients' expressions.

Theme 1: Difficulties

Patients have difficulties in using warfarin. Five sub-themes of this theme were determined.

Subtheme 1.1. Irregular INR Levels

The patients said that they had irregular INR levels, difficulties in organizing the therapeutic range of warfarin.

Table 1. Themes and sub-themes regarding warfarin use

Main Theme	Subthemes
1. Difficulties	Irregular INR levels
	Forgetting to take warfarin
	Limitations on greenery consumption
	Self-reducing warfarin dosage
	Avoidance of using other medications
2. Facilitators	Acceptance
	Support of family and health professionals
3. Dependence	Requirement of frequent follow-ups
	Problems of measuring INR levels in different hospitals
4. Impact of side effects from warfarin	Bleeding and prevention behaviors
	Itchiness
	Fear

INR: international normalized ratio.

"My INR level increased to over 5 about five months ago. I nearly had a brain hemorrhage. I felt nauseous and dizzy. My warfarin dosage was reduced" (24, male, 42 months).

"We realized just as it was about to clot. I ate plenty of vegetables since my INR level was high, and this caused it to fall. Only Allah and I know what I have been going through for almost 7 or 8 months" (47, male, 108 months).

Subtheme 1.2. Forgetting to Take Warfarin

Some of the patients said that they forgot whether they had taken their warfarin daily or doubted whether they had taken it.

"It took a while to get used to warfarin. I would forget to take warfarin. I had some difficulties with taking warfarin every day. But I got used to it after a while" (24, male, 42 months).

"I take a full dose of warfarin for two days, and a half for one day. I forget which day I took a full or a half dose. I wonder what I took this day. With age you get memory problems. What if I took my warfarin, forgot that I did and take it again?" (56, female, 60 months).

Subtheme 1.3. Limitations on Greenery Consumption

Among patients who restrict what they eat because of drug-nutrient interactions, some said they never consume green vegetables.

"When you eat greens, the effect of the blood thinner is reduced. More warfarin was needed. I thought that even though we didn't drink blood thinners, when we ate greens, our blood was diluted. But it wasn't so" (56, female, 60 months).

"We should not consume much greenery. There's too much vitamin K in parsley. Harmful to us. A month after my blood was taken. I can eat them a little bit for more than 15 days. I reduce the greens. I've put myself in such an order" (52, female, 96 months).

"I eat a small bowl of salad and vegetables, but not every day. If a pastry has vegetables in it, I do not eat that either" (41, female, 18 months).

"I did not change anything. They explained that certain foods are not allowed, but I did not pay attention" (24, male, 42 months).

Subtheme 1.4. Self-reducing Warfarin Dose

The patients said that they had reduced the dosage of the warfarin on their own or did not take it from time to time.

"I have not taken my warfarin since last week. I experienced tingling. I stop taking warfarin when I feel like my INR level has increased. You can tell when your INR level is high" (47, male, 108 months).

"If I have gingival bleeding or bleeding elsewhere, I take half of my blood thinner" (56, female, 60 months)

"I reduced the dosage of my warfarin myself. I did not realize its importance. I had a brain embolism, and I really suffered from it" (52, male, 240 months).

Subtheme 1.5. Avoided Using Other Medications

"Since we cannot use medications, I do not kiss anybody in winter because I fear it will be quite difficult for me to heal. I do not use

medication when I get the flu. Doctors do not give antibiotics" (52, male, 96 months).

"I take painkillers when I have too much pain. I do not consult the doctor. I take them when I am quite sick" (45, male, 38 months).

"I do not take medications by myself. I do not even take painkillers" (66, male, 24 months).

Theme 2: Facilitators

Some patients considered using warfarin as a part of their life. They found it more manageable when they agreed to use warfarin, and some said that they continue using warfarin with the support of their relatives and health professionals.

Subtheme 2.1. Acceptance

"They said I will use warfarin for the rest of my life. I have accepted it. It prevents blood clotting. If blood clotting occurs, blood does not flow to the heart and brain. That's why I must take my warfarin" (66, male, 24 months).

"Of course it affects my life, but I do not feel uncomfortable with it because it is good for me. I am obliged to take warfarin and go to check-ups. I am aware of that" (71, male, 72 months).

"Life becomes easier when you psychologically accept the disease. I do not question why or how I use it" (39, male, 180 months).

Subtheme 2.2. Support of Family and Health Professionals

"My husband and daughter helped me a lot. They showed me how much I can eat. They gave me a diet book that says we should not eat heavy food. The dietitian plans my diet in accordance with it" (52, female, 96 months).

"I use the brochure that the doctor gave me. I ask my doctor about things I wonder about at check-ups. My partner helps me" (45, male, 38 months).

Theme 3: Dependence

The patients mentioned their dependence at the hospital because they had no INR measuring instruments.

Subtheme 3.1. Requirement of Frequent Follow-ups

The patients emphasized that going to check-ups every month was time consuming and tiring.

"I will have a tooth removed. I came back to the cardiovascular surgeon. It takes quite a time for us to inject. You cannot have a tooth removed without antibiotics. Taking warfarin, check-ups. Going to the doctor's and coming back. You need check-ups" (71, male, 72 months).

"You have to come to the doctor's every month. Coming and going is a waste of time. I am getting tired. While waiting for the results, I get bored" (66, male, 24 months).

Subtheme 3.2. The Problem of Measuring the INR Level in Different Hospitals

The results of tests done at different health centers and differences with the hospital where they went for check-ups caused the patients to lose trust in the healthcare system.

"I go to my check-ups in another hospital. They did not let me leave the hospital a few times because my INR level was high. I realized that I have nothing wrong, nothing is high. My INR level was 12 or 13 at that time. A value of 12 causes me to have cerebral bleeding. I did not eat anything, and they did nothing. I do not trust them after that" (47, male, 108 months).

"Sometimes when I do not come here, I get check-ups at another hospital. My blood value was much better here. My bleeding returned to normal, but when I got check-ups there, and my warfarin dose was increased, I encountered problems" (41, female, 18 months).

Theme 4: Impact of the Side Effects from Warfarin

Patients explained that they experienced bleeding and itching associated with the use of warfarin. They said that physicians warned them about bleeding, and they feared the side effects of the drugs, and avoided using other medications.

Subtheme 4.1. Bleeding and Prevention Behaviors

Bleeding was the most common problem for patients. Patients stated that the bleeding was so severe that they sometimes referred to emergency services. The types of bleeding that the patients expressed were menstrual bleeding, nasal bleeding and ecchymosis. Patients stated that they were paying attention to the warnings of doctors to protect themselves from bumping into things and falling.

"I had so much nasal bleeding right after surgery, a total of 10 or 15 hours per day. I went to the emergency room lots of times. Sometimes, my arms were black and blue. I once cut my wrist while I was doing technical work, and the bleeding did not stop. I do not do any risky work" (39, male, 180 months).

"When I bump into something, my skin turns black and blue. I take care not to cut my hands while cooking. When I cut myself, the bleeding does not stop. I get bruises because warfarin dilutes the blood. I take care not to bump into sharp objects. We made no special arrangements at home" (41, female, 18 months).

"I use gloves when I work. I use steel-toed shoes, boots so as not to hurt my feet because warfarin dilutes the blood. It immediately causes bleeding when I brush my teeth a little bit too hard" (45, male, 38 months).

Subtheme 4.2. Itchiness

"If severe itching occurs on specific parts of the body while using warfarin, its use should immediately be stopped. If it is not discomforting and there is no itching, then it means that the INR level is quite low. When you estimate the itchiness, you keep your INR around 2.5. I do it like that" (62, male, 96 months).

"I do not know if the reason is my INR level being high or what, but one time I had itching on my body. I had it one week earlier, too. I still have itching. I had it a few times. My back and my entire body itch" (45, male, 38 months).

Subtheme 4.3. Fear

Some patients experienced fear from time to time due to the side effects of warfarin.

"I know how important warfarin is. If I do not use warfarin, my heart valve may develop a clot and it may affect blood flow. I had surgery for gynecology. I had HVS before. I wasn't so scared before heart surgery. Warfarin was discontinued for surgery. What if a clot is formed or I can't wake up? What if my heart doesn't work? I was so scared. I was very affected by the discontinuation of the drug" (52, female, 96 months).

"It did not affect me in the first few months after surgery, but in the last three or four months of taking warfarin, I was hospitalized two or three times. My menstruation did not stop for a month. I lost consciousness the last time I went to the emergency room. After this event, I'm very afraid to go out alone. My husband is afraid for me. He keeps calling frequently. I'm worried something's gonna happen" (41, female, 18 months).

"In the beginning, I was afraid of the risk of paralysis. You adapt with time. You are obliged to" (39, male, 180 months).

"Warfarin may cause bleeding. Stomach bleeding, nosebleeds, gum bleeding... If you don't use it, that can cause clots. You're scared you're affected. If you take less or more, you die" (52, male, 96 months).

DISCUSSION

The investigation of the experience of warfarin use in patients with mechanical heart valves is very important to facilitate training and follow-up. Although warfarin has been used for many years, patients still lack information. We aimed to investigate patients' experiences with warfarin in our study. We thought that understanding what patients experience would enhance their care regarding their treatment process and drug use.

This study found that patients had difficulties with warfarin usage. Some patients had irregular INR levels or had forgotten to take their warfarin. One of the patients who participated in this study stated that he was trying to reduce his high level of INR by eating excessive greens. These problems were thought to be caused by a lack of knowledge about warfarin.[20] A relevant study conducted in Turkey found that 114 patients had low levels of knowledge about warfarin treatment and difficulties adjusting to their warfarin treatment.[14] Another study specified the rate of reaching the desired INR levels of patients (n=57) who came to an internal medicine polyclinic to be 52.6%.[21] A study conducted in Jordan found that 22% of patients (n=331) had knowledge about warfarin-medication interactions, and 37% had knowledge about warfarin-food interactions.[22] The patient in our study who forgot to take warfarin or pay attention to nutrition despite having received education may have failed to accept the disease because he was young. A systematic study of cardiac failure patients determined that medication maladjustment is a significant risk factor, especially for younger patients.[23]

Patients were thought to have knowledge about warfarin-related food selection. One patient stated that he did not pay sufficient attention to the limitations on nutrition, although he had been informed. A few patients were extremely attentive in choosing green foods. The literature indicates that vitamin K affects coagulation.[24,25] Therefore, patients must limit their consumption of foods containing vitamin K, and their daily rate of vitamin K should be constant.[26] There were differences in reaching the therapeutic range in our country according to regions.[11] The consumption of greenery has an important place in the nutrition in Aegean culture. Since this study was conducted in the Aegean region, it was thought that the participants in this study had difficulty in limiting their intake of greens.

It was found that two patients in this study occasionally reduced their own doses of warfarin, and one patient discontinued the use of warfarin without medical advice. It is very important to take warfarin at the dose recommended by the physician in order to maintain a therapeutic INR level. A similar study also found that the rate of patients who were aware of the interaction of medication and food was 55% and that the INR levels of those patients with more awareness were higher.[12] Self-dose reduction or skipping of the medication by the patients may be explained by their low awareness levels on this issue.

Another point that the patients emphasized was the interaction of warfarin and other medications. As warfarin interacts with other drugs, the patients were anxious about taking other drugs. One patient stated that he avoided hugging and kissing other people because of the fear of falling ill, while two other patients even refrained from taking painkillers. Patients should only take other medication after consulting a doctor.[7,8] This is not maintained by all patients and it may be due to their inability to reach a physician easily and the lack of a dedicated anticoagulant clinic or nurse for these patients. Also, the patients' unwillingness to interact with other people because they are afraid of drug use can affect their interpersonal relationships.

Some patients said acceptance of warfarin use was facilitated by the support of their family and health professionals. Acceptance is an indicator of adherence to treatment. As the patients said, individuals must accept the disease and its effects on their lives in order to manage their chronic disease.[27,28] Both the support of family members and the professional support of the medical staff ease patients' acceptance to the disease and help them manage it better.[29]

Another theme identified in this study was dependence. One patient stated that when their INR level was outside of the therapeutic range, it was necessary to go to the polyclinic more frequently and another patient stated that the frequency of follow-up before and after tooth extraction increased. One patient mentioned that it often took a lot of time to come and go to the hospital. Patients may feel uncomfortable with going for constant clinical check-ups. A similar study (n=183) conducted in China found that 40% of patients said that they felt uncomfortable with waiting in anticoagulant clinics.[30] Another sub-theme was the problem of measuring their INR levels in different hospitals. Two patients had problems with visiting different health centers. Patients did not have their own measurement instruments. As a consequence, patients had to go to a polyclinic at least once a month. Different doctors interpreting the results may result in changes in warfarin dosages. Therefore, patients may suffer unwanted side effects, including bleeding. At the same time, hospitals do not have a standard protocol for warfarin dosages. All these factors are thought to cause problems because of the dependency on hospitals.

The last theme detected in our study was the impact of the side effects from warfarin. This study found that patients had bleeding caused by warfarin and fears about it. A few patients mentioned precautions to prevent bleeding. A similar study examining warfarin complications found that the most common hemorrhagic complications were nasal bleeding (n=9, 31%), dermal complications (n=7, 24%) and re-hospitalizations (n=7, 24%).[31] Another relevant study stated that the increase in INR values was found to be associated with the risk of bleeding.[32] The patients' lack of knowledge about warfarin may have caused the occurrence of bleeding. Some patients reported itchiness as emphasized in the literature.[33]

Some of the patients said that they feared paralysis and death because they were unable to determine warfarin dosages. One patient emphasized the fear of clot formation after warfarin discontinuation before gynecological surgery. A patient stated that she had applied to the emergency department because of non-stop menstruation and that she was worried about going out alone. Patients should be allowed to express their fears and express themselves. Precautions need to be taken so that the prevention of side effects is effective.

We think our study will guide other studies in the future. In this study, with or without chronic disease, we worked with patients of different ages. It was important to understand the drug use experiences of this patient group. We could make the sample of our study more specific in a later study. In future studies, the patient experiences can be examined by studying the experiences of a targeted group, with patients having chronic illnesses and using multiple drugs, or patients using only warfarin without chronic disease. In addition, based on our research results, experimental studies can be conducted with MHVRS patients in order to increase the level of awareness and drug adherence.

CONCLUSION

A lack of knowledge and information about warfarin usage still exists. Patients had problems with adherence to warfarin usage and their check-ups. This study was carried out in the Aegean region where the consumption of greenery has an important place in the local nutrition. Therefore, it was thought that the participants had difficulty in limiting their intake of greens. There are some deficiencies in evaluating anticoagulant treatment adherence in the healthcare system in Turkey. The use of personal INR measuring devices could help improve patient comfort while reducing fear and loss of time due to outpatient check-ups.

MAIN POINTS

- The investigation of the experience of warfarin use in patients with mechanical heart valves is very important in order to design training and follow-ups. In our study, it was seen that patients who have been using these drugs for a long time still have information needs.
- The importance that patients attach to drug usage may vary depending on situations such as their eating styles, habits and their perception of their disease. After discharge, patients should be allowed to express their feelings and personalized nursing interventions should be provided.
- There is a need for experimental studies in order to improve the usage of warfarin in patients.

ETHICS

Ethics Committee Approval: Permission was taken from the hospital where the study was conducted (Dokuz Eylül University Hospital) and the Dokuz Eylül University Ethics Committee for Non-invasive Clinical Studies (approval number: 2016/24-03, date: 08.09.2016).

Informed Consent: It was obtained.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: E.A.K., Ö.B., Design: E.A.K., Ö.B., Data Collection and/or Processing: E.A.K., Ö.B., Analysis and/or Interpretation: E.A.K., Ö.B., Literature Search: E.A.K., Ö.B., Writing: E.A.K., Ö.B., Critical Review: E.A.K., Ö.B.

DISCLOSURES

Conflict of Interest: No conflict of interest was declared by the authors.

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ORIGINAL ARTICLE

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Determination of the Technology Use Status and Attitudes Towards Technology of Patients with Type 2 Diabetes

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Abstract

BACKGROUND/AIMS: The aim of this study was to determine the technology use status and attitudes of those patients with type 2 diabetes towards technology.

MATERIALS AND METHODS: The the Strengthening the Reporting of Observational Studies in Epidemiology checklist was used in this descriptive study. This research was carried out on 250 patients diagnosed with type 2 diabetes at a university hospital. The Personal Information form, questions to determine technology use status and the Attitudes Toward Technology Scale were used as the research tools.

RESULTS: According to the results of this study, the patients had a mean age 58.49±1.03 years and included predominately patients who were female (66%), married (93.2%), housewives (48.4%), and who had only completed their primary education (45.6%). It was determined that 34.8% of them used the internet to access health-related information, 43.7% used the internet to learn about their disease and 33.5% used the internet to find out about treatment methods. Among those patients who used the internet to access health-information, 83.9% wanted to receive education and consultation via distance learning tools, and 40.2% did not know whether education and consultation via distance learning tools could solve health problems. The mean score of the Attitude Toward Technology Scale was 47.73±1.11. There was a statistically significant difference between the attitude towards technology scores and age, educational status, occupational status, employment status, and those who used the internet to access health-related information ($p<0.05$).

CONCLUSION: Patients with type 2 diabetes have positive attitudes towards technology. Patients with type 2 diabetes who are younger, have higher education, those who are retired, self-employed or unemployed, and those who use the internet to access health-related information have better attitudes towards technology use. Most patients wanted to receive distance learning tools. Especially when the Coronavirus disease-19 pandemic conditions were present, the use of remote education tools are specifically important. It is recommended to plan individual nursing interventions and use interactive training methods remotely in patients with type 2 diabetes.

Keywords: Nursing, technology, attitude, type 2 diabetes

INTRODUCTION

Diabetes mellitus is a complex, chronic illness requiring continuous medical care with multifactorial risk-reduction strategies beyond glycemic control.[1] According to the International Diabetes Federation, the number of patients throughout the world with diabetes was 425 million in 2017, and it is estimated that this figure may reach 629 million by 2045. In the world, diabetes accounts for 14.5% of the causes of death of individuals in the age group of 20-79.[2] According to the results of the Turkish Diabetes Epidemiology Study-I and II, the prevalence of diabetes increased from 7.2% to 13.7% in the Turkish adult population within the 12-years between 1998-2010.[3] Type 2 diabetes is

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associated with insulin resistance and has a greater prevalence in adult and elderly patients.[4] It is emphasized that it is required for patients with diabetes to manage their diseases through diabetes education in order for the patients to have a healthy and productive life and for complications to be prevented or delayed.[5] Despite the development of versatile diabetes management programs in most developed countries, many patients remain at increased risk of developing macrovascular and microvascular complications.[6]

Continuous development of tele-medical technologies opens up new opportunities to reach patients suffering from diabetes. Moreover, it has the potential to provide better, uninterrupted medical care, which could result in improved treatment outcomes.[7] The development of such technology allows patients to have continuous access to health-related information. The utilization of technology in diabetes will allow us to extend access to professional care and integrate diabetes surveillance into the patient's total healthcare.[8] The study results of Ramasamy et al.[9] showed that the majority of individuals had access to one or more types of technology for communication. Also, several experimental studies have revealed that remote information access approaches have come up with positive results in blood glucose control and have decreased diabetes complications in long-term follow-ups.[8,10,11]

Access to the required information may be restricted due to reasons such as the individual's health status, living conditions, distance from the health center, and their work conditions. Information technologies such as mobile phones and the internet are used in the remote management of individuals for purposes such as sharing information online, providing distance education, and helping to improve health care outcomes.[11] The use of technology by diabetic patients was seen to be very low in the study by Cerna and Maresova.[12] As a result of the study conducted by Mengiste et al.[13] the internet was used in order to search for general information about diabetes among patients with diabetes at a rate of 41.6%. We believe that positive attitudes towards technology and the appropriate use of technology by diabetics with access to technology-based information can significantly improve treatment outcomes, especially during the Coronavirus disease-2019 (COVID-19) pandemic, when personal contact with healthcare professionals is limited. The aim of this study was to determine the technology use status and attitudes towards technology of those patients with type 2 diabetes.

MATERIALS AND METHODS

Study Design

This descriptive study was conducted and reported according to the Strengthening the Reporting of Observational Studies in Epidemiology checklist (Appendix Supplementary 1).

Participants and Data Collection

This study was performed in the department of endocrinology and metabolic diseases at a university hospital in the Mediterranean region in Turkey between January and June 2017. The inclusion criteria were a) being diagnosed with type 2 diabetes at least six months prior to the start of the research, b) being aged 18 years or older, c) the absence of any mental or any other psychiatric disorder according to their medical records, d) being able to speak, read, and write in Turkish, and e) consent to participate in this research. The number of patients with type 2 diabetes who apply to the hospital in an average year is 710. Based on this number, the sample of the study calculated with a confidence level of 95% and 5% error in the Sample Size Calculator Program was 250. During the data collection phase, 17 patients could not be included in this study because they were in the outpatient clinic and the questions in the measurement tools could not be completed. Data collection was continued until we reached 250 patients with type 2 diabetes who met the sampling criteria and agreed to participate in this study. The results include data from 250 patients with type 2 diabetes.

Data Collection Tools

The research data were collected using the Personal Information form, questions to determine their technology use status and the Attitude Towards Technology Scale.

Personal Information Form

The Personal Information form was used to collect the socio-demographic and disease information of the participants. It was created by the researchers after a literature review.[6,10,14] The Personal Information form had eight questions, namely: Age, gender, marital status, education, occupational status, employment status, duration of illness, and the condition of having a chronic disease apart from diabetes.

Questions to Determine Technology Use Status

These questions were prepared by the researchers in line with the literature in order to determine the technology use status of those patients with type 2 diabetes.[15,16] There are six questions in this section, namely: Whether they used the internet to access health-related information, the purpose to use the internet for health, whether they wanted to receive education and consultation about their disease and its treatment period via the internet at their home, the usefulness of talking about/trying to solve their problems with healthcare professionals via e-mail, using the internet in the previous month to get information about their disease and its treatment procedure, and the application of the information which they obtained from healthcare websites.

Attitudes Toward Technology Scale

The Attitudes Toward Technology Scale was developed by Aydin and Karaa[17] in 2013. It examines attitudes toward technology generally. The scale is a one-dimensional scale with 17 items, of which 15 are positive and 2 are negative. In this scale, the five-point Likert-type negative items are scored in the reverse. The scale's score range is 17 to 85. It can be stated that the positive attitude towards technology increases as the score increases. The reported Cronbach's alpha coefficient for this scale was 0.87.[17] In our study, we calculated the Cronbach's alpha coefficient to be 0.91 (α=0.87).

Ethical Considerations

This study was approved by the Ethics Committee for Clinical Research of the Medical Faculty in the Akdeniz University (approval number: 671.AKD, date: 14.12.2016). Written permission was obtained from the Department of Endocrinology and Metabolic Disease in the Akdeniz University Hospital (date: 31.01.2017). Permission was taken to use the Attitudes Towards Technology Scale from Aydin and Karaa[17] via e-mail. Written and verbal consent was obtained from all participants in this study. The objective of the study was explained to the participants.

Statistical Analysis

Statistical analyses were carried out using the IBM SPSS statistical program (v. 22.0; IBM Corporation, Armonk, NY, USA) with a significance level of $p<0.05$. The data were evaluated using frequency distribution, Kruskal-Wallis, and the Mann-Whitney U test as there was no normal distribution. The reliability of the scale was tested with the Cronbach's alpha coefficient.

RESULTS

Socio-demographic and Disease Characteristics

It was found that the mean age of the patients taking part in this study was 58.49±1.03 years, the duration of their illness was 9.54±7.05 years, 43.2% of them were older than 60 years, 66% were female, 93.2% were married, 45.6% were only primary school graduates, 48.4% were housewives, 87.6% were unemployed, the disease duration of 38% was between 5 and 10 years, and 20.8% had a chronic disease apart from diabetes such as heart failure, hypertension, or kidney failure (Table 1).

Findings Related to Technology Use Status

When the technology use status of the patients with type 2 diabetes were examined, it was reported that 34.8% of them used the internet to access health-related information, 43.7% used the internet to learn about their disease and 33.5% used the internet to find out about treatment methods. According to the statements of those patients who used the internet to access health-information, 83.9% wanted to receive education and consultation about their disease and its treatment period via the internet at their home, 40.2% did not know whether talking about/trying to solve their problems with healthcare professionals via e-mail would be useful, 65.5% had used the internet once or more within the previous month to get information about their disease and its treatment procedures and only 26.4% of the participants had actually applied the information that they had obtained from healthcare websites (Table 2).

Findings Related to Attitudes Toward Technology Scale

In the present study, it was found that the mean score of the Attitude Toward Technology Scale was 47.73±1.11. When the mean scores of the patients with type 2 diabetes in the Attitudes Toward Technology Scale were compared in terms of their descriptive characteristics, there were statistically significant differences between their age ($p=0.001$), educational status ($p=0.001$), occupational status ($p=0.001$), employment status ($p=0.004$), and whether they used the internet in order to access health-related information ($p=0.001$) (Table 3).

DISCUSSION

Education and technology are two basic elements playing an important role in making human life more effective. Using technology in education is a significant opportunity to help meet our needs. When considering the importance of diabetes education, the education prepared appropriately for the needs, as an alternative to the usual education, is crucial and patients must be able to access this information easily for their self-efficacy.[15,18] For this reason, this descriptive study was conducted in order to determine the technology use status and attitudes towards the technology of patients with type 2 diabetes.

The study showed that 34.8% of the participants used the internet in order to access health information. This result was thought to be associated with the fact that more than half of the patients were aged 60 or younger. Quartuccio et al.[19] found in their study that the internet use frequency of those patients with diabetes aged between 50-60 years was 27%. A cohort study in 2012 and 2017 showed the use of the internet to search for health information increased over time.[20] That result supports the results of the present study. In another previous study, more than half of the participants trusted and relied on the internet for seeking health information.[9]

As the internet becomes a more popular health information source, individuals with chronic diseases meet their information needs via the internet.[14] When the aims of internet use were examined based on the results of the present study, it was found that nearly half of the patients

Table 1. Demographic and medical characteristics of patients with type 2 diabetes (n=250)

	Mean ± SD	Range
Age (years)	58.49±1.03	19-88
Duration of illness (year)	9.54±7.05	1-25
	n	**%**
Age		
<50	44	17.6
50-60	98	39.2
>60	108	43.2
Gender		
Female	165	66.0
Male	85	34.0
Marital status		
Married	233	93.2
Single	17	6.8
Educational status		
Illiterate	17	6.8
Primary	114	45.6
Secondary	23	9.2
High school	46	18.4
University	50	20.0
Occupational status		
Housewife	121	48.4
Retired	93	37.2
Public servant	25	10.0
Self-employed	11	4.4
Employment status		
Unemployed	219	87.6
Employed	31	12.4
Duration of the illness		
<5 year	73	29.2
5-10 year	95	38.0
>10 year	82	32.8
The condition of having a chronic disease apart from diabetes		
Yes	52	20.8
No	198	79.2

SD: standard deviation.

Table 2. Technology use status of patients with type 2 diabetes (n=250)

	n	%
Used the internet to access health-related information		
Yes	87	34.8
No	163	65.2
Purpose of using the internet for health (n=167)*		
Learn about the disease	73	43.7
Find out about treatment methods	56	33.5
To obtain preliminary information about the symptoms of the disease before going for an examination	14	8.4
Getting information about hospital and doctor selection	13	7.8
Alternative medicine (acupuncture, spa, medicinal plants, etc.)	6	3.6
Receiving prescription or over-the-counter medication information	5	2.9
Wanted to receive education and consultation about their disease and its treatment period via the internet at their home (n=87)*		
Yes	73	83.9
No	14	16.1
The usefulness of talking about/trying to solve the problems with healthcare professionals via e-mail (n=87)*		
Do not know	35	40.2
Could be possible	8	9.3
Undecided	29	33.3
Helpful	14	16.1
Not helpful	1	1.1
Using the internet in the previous month to access information about their disease and its treatment procedure (n=87)*		
Zero/did not use	30	34.5
Once or more	57	65.5
The application status of the information obtained from healthcare websites (n=87)*		
Yes	23	26.4
No	64	73.6

*Percentages were calculated on the value of "n".

used the internet to learn about their disease and one-third of them used the internet to find out about treatment methods. Also, in this study, the vast majority of patients with diabetes who used the internet to access health-related information wanted to receive education and consultation about their disease and its treatment procedure via the internet at home. Dobson and Hall[16] found that 77% of their participants intended to use an internet application to manage their diabetes in the future, and 58% intended to use a mobile application. In our research findings, although the mean age of the participants was high, almost half of them used the internet to learn about the disease, and one-third of them used the internet to find out about health information and treatment options. These findings indicate that patients with type 2 diabetes want to receive disease-related education and counseling at distance. Technology-related needs and technology use behaviors are expected to increase rapidly, especially for chronic diseases such as diabetes, due to the pandemic experienced all over the world. Today, because of the pandemic situation in the world, we recommend that patients with type 2 diabetes should be encouraged in their use of technology. Considering that patients with diabetes especially have disease and treatment-related information needs, it seems appropriate to consider disease and treatment-related information as a priority in education programs which can be planned online for these patients.

Table 3. Comparison of descriptive characteristics and the attitude toward technology scale in patients with type 2 diabetes (n=250)

Variable	Attitudes Toward Technology Scale (mean ± standard deviation)	Z-, KW-, and p-values
Age		
<50	53.7±1.65	KW: 23.124 p=0.000
50-60	48.4±1.11	
>60	44.6±0.97	
Educational status		
Illiterate	30.7±1.31	KW: 63.187 p=0.000
Primary	43.2±0.83	
Secondary	51.9±1.82	
High school	51.0±1.71	
University	55.5±1.58	
Occupational status		
Housewife	45.1±0.81	KW: 20.394 p=0.000
Retired	56.3±4.40	
Public servant	52.1±3.17	
Self-employed	54.5±3.06	
Employment status		
Unemployed	53.7±2.63	Z: -2.886 p=0.004
Employed	46.8±0.69	
Used the internet to access health-related information		
Yes	59.4±0.83	Z: 15.298 p=0.000
No	50.2±4.37	

The results of this study show that when patients with type 2 diabetes are evaluated according to the score they get from the scale, their attitude towards technology is low. This is thought to be due to the high average age of the patients. Similar to our study, the use of technology by diabetic patients was very low in the study of Cerna and Maresova.[12] In a systematic review, technology-assisted education efforts appear to possess both positive and negative aspects as perceived by those patients with diabetes. This review demonstrates that technology platforms should be user-friendly, intuitive to use, and cater to older persons who may not be so technologically savvy.[21]

When the mean scores of the patients with type 2 diabetes for the Attitude Toward Technology Scale were compared with their socio-demographic data in our study, it was found that younger and well-educated participants had more positive attitudes and intentions toward using technology in their treatment than older participants. Similar to our study results, it is seen that younger patients and well-educated patients have better attitudes towards technology use according to the study conducted by Zhang et al.[22] In a few studies examining the technology use of patients with diabetes, it was stated that young patients use technology more.[10,20,23] In line with these findings, it may be asserted that as the educational level increases, the attitude towards technology use becomes more positive.

Appendix Supplementary 1. STROBE Statement-Checklist of items that should be included in reports of cross-sectional studies			
	Item no	**Recommendation**	**Page no**
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	1
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	1
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	2-3
Objectives	3	State specific objectives, including any prespecified hypotheses	3
Methods			
Study design	4	Present key elements of study design early in the paper	3
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	3
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants	3-4
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	4
Data sources/measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	4-5
Bias	9	Describe any efforts to address potential sources of bias	
Study size	10	Explain how the study size was arrived at	3
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	4
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	5
		(b) Describe any methods used to examine subgroups and interactions	5
		(c) Explain how missing data were addressed	5
		(d) If applicable, describe analytical methods taking account of sampling strategy	5
		(e) Describe any sensitivity analyses	
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study-eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	5
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	5, Table 1
		(b) Indicate number of participants with missing data for each variable of interest	
Outcome data	15*	Report numbers of outcome events or summary measures	5-6
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	3
		(b) Report category boundaries when continuous variables were categorized	5
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done-eg analyses of subgroups and interactions, and sensitivity analyses	5
Discussion			
Key results	18	Summarise key results with reference to study objectives	6-9
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	9
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	6-8
Generalisability	21	Discuss the generalisability (external validity) of the study results	8-9
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	Title page

*Give information separately for exposed and unexposed groups. STROBE: Strengthening the Reporting of Observational Studies in Epidemiology.
An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

According to our study results, it was found that the employed participants internet attitudes were better than those who did not work. Also, when the comparison was made based on the occupation, the difference between the technology attitude means scores of the self-employed patients, public servants, and those patients who were retired and housewives were found to be significant. Based on the data of the Household Information Technology Usage Survey in Turkey, it was reported that internet usage rates of the fee-earners, salary-earners, or casual workers were 89.7%, the internet usage rates of the unpaid family workers were 46.8%, and internet usage rates of retirees were 48.5%.[24] Based on these results, it can be asserted that those in the employed group are younger and they have a higher educational level and for this reason, they have better attitudes towards technology.

In this study, the use of the internet to access health-related information and the Attitude Toward Technology Scale mean scores were compared. It was found that those who used the internet to access health-related information had better attitudes towards technology. As a result of the study conducted by Mengiste et al.[13], the internet was one of the major sources of diabetes information and the internet was used in order to search for general information about diabetes at a rate of 41.6%. These results suggested that internet use is preferred for health, but there is a need for reliable education sources. In pandemics and similar problems which are seen in the world today or that may be seen in the future, it is important to be prepared for remote treatment and care management of diabetic patients, to determine the technology-related needs of these patients, and to make improvements and innovations in line with these needs.

Study Limitations

There are several limitations of the current research. The results of this single-center study may be generalized only for the sample of the study. Secondly, the patients' levels of attitudes towards technology being based on their expressions is considered as another limitation of this study.

CONCLUSION

In this study, it was found that patients with type 2 diabetes had positive attitudes towards technology. Their attitudes towards technology differed based on their age, education, occupational status, employment status, and whether they used the internet to access health-related information. Patients with type 2 diabetes who are younger, have higher education levels, those who are retired, self-employed or unemployed, and those who use the internet to access health-related information have better attitudes towards technology use. While some patients would like to receive education and consultation via distance learning tools, on the other hand, others did not know whether education and consultation via distance learning tools could solve their health problems. It may be recommended that nurses should provide current distance learning tools and encourage patients to use distance learning tools for health management. It is recommended to plan individual nursing interventions via technological tools and use interactive training methods remotely in those patients with type 2 diabetes. Due to reduced hospital admissions from COVID-19, the use of remote education tools are especially important.

MAIN POINTS

- According to the results of this study, those patients with type 2 diabetes had positive attitudes towards technology.
- Type 2 diabetes patient's attitudes towards technology differed based on their age, educational status, occupational status and employment status.
- It is necessary to increase the use of technology in chronic disease management, and to support the education of patients with type 2 diabetes remotely with technology.

ETHICS

Ethics Committee Approval: This study was approved by the Ethics Committee for Clinical Research of the Medical Faculty in the Akdeniz University (approval number: 671.AKD, date: 14.12.2016).

Informed Consent: Written and verbal consent was obtained from all participants in this study.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Concept: N.T., F.Ç., H.B., Design: N.T., F.Ç., H.B., Data Collection and/or Processing: N.T., F.Ç., H.B., Analysis and/or Interpretation: N.T., F.Ç., H.B., Literature Search: N.T., F.Ç., H.B., Writing: N.T., F.Ç., H.B., Critical Review: N.T., F.Ç., H.B.

DISCLOSURES

Conflict of Interest: No conflict of interest was declared by the authors.

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ORIGINAL ARTICLE

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Determination of Awareness of University Students about Cancer Risk Factors

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Abstract

BACKGROUND/AIMS: Cancer, a significant health and societal problem, takes first place among causes of death and frequency of cases. The aim of this study was to determine the knowledge and awareness levels regarding the risk factors of cancer for university students studying in various departments of medical sciences.

MATERIALS and METHODS: This study was designed as descriptive cross-sectional feature. This study was conducted at a thematic health university. The knowledge and thoughts of students about cancer risk factors were determined through questionnaires created by the researchers. In this study, students were given questionnaires investigating their socio-demographic parameters and testing their knowledge and attitudes about the risk factors of cancer. In evaluating their state of knowledge, each student was asked to state their opinion on whether a factor is a cancer risk as being "a probable factor", "not a probable factor" or "I don't know". The findings were analyzed taking into account their percentage distributions.

RESULTS: The average age of the participant students was 20.4±2.18 years and their ages ranged from 17 and 30 years. 74.8% of the sample students were female and 25.8% of them were male. In the families of one-fourth of the sample students (24.2%), the existence of cancer cases was present.

CONCLUSION: When the students of Medical Sciences graduate from university and begin their professions, they are thought to be guides in the maintenance and development of health care. It is important to increase the awareness of health professionals regarding cancer and its risk factors in the early stages of their student life. Universities are advised to include cancer and the risk factors of cancer in their curriculum.

Keywords: Cancer, risk factors, awareness, university students

INTRODUCTION

Cancer, which has a high mortality rate, occurs by the uncontrolled division of cells. Cancer is spread to the surrounding tissues and organs from the organ of origin.[1,2] It was determined to be the second highest cause of death after cardiovascular system diseases in the world and also in Turkey.[3] The number of deaths from cancer exceeds 8 million per year worldwide. The cause of 13% of all deaths is cancer.[4,5] 14 million new cancer cases and 8.2 million deaths from cancer were reported in the study which the International Cancer Research Committee published in 2012.[5,6] Cancer incidences vary according to age and gender in Turkey. Cancer incidences were 0.246 percent in males, 0.173 in females, and 0.210 in the total population in 2014 according to the 2015 cancer report of Turkey statistical yearbook.

According to the 2014 data, the most common type of cancers in Turkey are lung, breast, thyroid, colorectal and uterus, respectively.[7] Cancer risk

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factors can be classified as behavioral, biological, environmental and genetic risk factors.[8]

Major risk factors are advanced age, cigarette consumption, alcohol consumption, radiation, ultraviolet sun rays, chemicals, some hormones, insufficient or unbalanced nutrition, a lack of physical activity and obesity.[9] The cause of one third of cancer mortalities are excess body mass index, low consumption of fruit and vegetables, insufficient physical activity, and tobacco consumption.[10] The use of tobacco and its products, which is the world's largest public health threat, causes 6 million deaths each year. According to the 2014 data in Turkey, 14.8 million people use tobacco.[8] Habits are conditioned behaviors which occur when internal and external actions take place in the same way. As a result of research, 30 percent of cancer deaths can be prevented. Prevention can occur by behavioral change in individuals in those populations at risk.

Health workers should be role models for the maintenance of health and for the achievement of positive behaviors in cancer prevention in the future.[11] Awareness means having knowledge or a perception of a situation or phenomenon. It was found that students do not increase their healthy behavior habits; they do not integrate these habits into their lives even when they have the proper knowledge and awareness.[12] The hypothesis that most of the students studying at a thematic health university would know cancer risk factors correctly and change their health behavior accordingly was tested in this study. This study was performed for the purpose of determining the awareness levels regarding cancer risk factors of university students studying in health related departments.

MATERIALS AND METHODS

This study was designed as a descriptive cross-sectional one. The data of this research was obtained from the students in all departments of the thematic university which only has health related departments. The sample number of this research was calculated using the sample formulation formula in certain groups. According to this analysis, the sample size was 393 (universe=957) with 99% reliability. 454 students who willingly participated in this research were included in order to increase reliability further in the universe of 957 people. 22.24% percent of all 957 students were studying medicine, 25.55% percent were nurses, 29.07% were nutrition dietetics and the rest were studying in the physical therapy and rehabilitation departments.

Data Collection

An introductory information form investigating information about the students and an information and awareness form for cancer risk factors were used to collect the data. The Information awareness form for cancer risk factors was created by the researcher using the literature. The cancer risk factors awareness form contains 50 questions with questions regarding topics such as being overweight, alcohol and cigarette consumption, and exercise in order to measure the awareness levels of the participating students regarding cancer risk factors. The students were asked to choose between "possible factor", "not possible factor" and "I do not know" options and their awareness level was measured. The introductory information form was developed by the researchers. The introductory information form contains 20 questions covering information about the personal characteristics of participating students.[13-16] Applications for cancer prevention were written in a table after scanning various scientific resources. There are 20 options in this table such as, periodic check-ups, lung scans, breast scans, PAP smear tests, or testing for blood cells in the stool. The students were asked to answer based on "what should be done", and "what are you doing". Their awareness levels were measured with a prepared form.

Ethics committee approval for this study was received from the Ethics Committee of the Clinical Research Institute of Sanko University with the decision number 01 prior to starting the survey on 02.03.2017. Verbal informed consent was obtained from the students who participated in this study.

Statistical Analysis

The Statistical Package for Social Sciences (SPSS) program was used in the data analysis. The confidence interval was accepted as 95%. Alpha values less than 0.05 were considered significant. Descriptive statistics such as number, percentage, mean standard deviation were used in the data analysis. Independent sample t-test, Pearson correlation analysis, One-Way ANOVA and post hoc test least significant difference analysis were carried out.

RESULTS

As shown in Table 1, the average age of the students participating in this study was 20.4 years, ranging from 17 to 30 years. When the education status of the students was examined, it was determined that 68.5% of them had graduated from Anatolian high schools. It was determined that 94.9% of the students did not work in any job and 43.5% of the students were working in health related fields. 15.4% of the students stated that they used cigarettes and 17% used alcohol. 10.4% of the students had a chronic disease. When the students were asked about going to a state health facility (health institution) for medical reasons, more than half of them (69.6%) remarked that they went to the hospital when they were sick, 3.7% of them had never gone, 7.7% of them went annually, 5.5% of them went when they remembered, and 3.5% of them tried to cure themselves. It was determined that almost one quarter of the students had a family history of cancer.

It was seen that 15.4% of the students used cigarettes, and 17% of then used alcohol. It was seen that the amounts of alcohol use were minimum 1 unit (9.9%) and maximum 40 units (0.2%), with an average of 2 units (3.5%). It was seen that daily smoking amounts were minimum 1 (0.9%) and max 40 (0.2) with an average of 6 cigarettes (0.7%).The number of students exercising was minimum 1 time (11.2%), maximum 35 times (0.2%) and an average of 4 times (5.7%) per week. The duration of exercise was minimum: 10 minutes (0.4%), maximum: 180 minutes (0.4%) with an average of 60 minutes (56.6%) daily. It was detected that 70.9% of the students were normal weight, 17.4% of them were overweight, and 0.2% of them were obese. The majority of the students (91.1%) stated that vegetables and fruits were the main nutrients to reduce the risk of cancer, while 8.9% said that they increased the risk: 69% said that protein and fat rich foods reduced the risk of cancer, while 31% said that they increased the risk; 18.7% said that red meat reduced the risk, while 81.3% said it increased the risk; 10.6% said that acidic drinks reduced the risk, while 89.4% said that they increased the risk; 58.9% said that white meat reduced the risk, while 11% said that it increased the risk; 20.3% said that processed meat reduced the risk, while 79.7% said that it increased the risk; 78.6% said that grain reduced the risk, while 21.4% said that it increased the risk; and finally, 21.4% said that caffeine-containing drinks reduced the risk, while 78.9% said that they increased the risk of cancer.

Table 1. Socio-demographic and health related descriptive characteristics of students-1 (n=454)										
	Nursing		Nutrition and dietetics		Physical therapy and rehabilitation		Medical faculty		Total	
Descriptive characteristics	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Age: Minimum-maximum average 17-30. (20.48±1.45)										
Aged 20 age or under	69	27.9	75	30.4	46	18.6	57	23.1	247	54.4
Aged 21 age or above	47	22.7	57	27.5	59	28.5	44	21.3	207	45.6
Gender										
Female	86	25.5	118	35.0	74	22.0	59	17.5	337	74.2
Male	30	25.6	14	12.0	31	26.5	42	35.9	117	25.8
Marital status										
Single	116	25.8	128	28.4	105	23.3	101	22.4	450	99.1
Married	0	0.0	4	100.0	0	0.0	0	0.0	4	0.9
Education status										
Health vocational high school	4	36.4	6	54.5	0	0.0	1	9.1	11	2.4
Anatolian high school	60	19.3	93	29.9	89	28.6	69	22.2	311	68.5
Normal high school	43	67.2	10	15.6	7	10.9	4	6.3	64	14.1
Vocational high school	3	37.5	5	62.5	0	0.0	0	0.0	8	1.8
Associate degree	0	0.0	1	50.0	0	0.0	1	0.0	2	0.4
License	2	33.3	4	66.7	0	0.0	0	0.0	6	1.3
Other (science, imam hatip, open education high school)	4	7.7	13	25.0	9	17.3	26	50.0	52	11.5
Working status										
Yes	7	30.4	9	39.1	5	21.7	2	8.7	23	5.1
No	109	25.3	123	28.5	100	23.2	99	23.0	431	94.9
Working field (n=23)										
About health	1	10.0	5	50.0	3	30.0	1	10.0	10	43.5
Non-health	6	46.2	4	30.8	2	15.4	1	7.7	13	56.5
Income rate										
Income = expense	74	23.7	99	31.7	72	23.1	67	21.5	312	68.7
Income < expense	33	32.7	21	20.8	28	27.7	19	18.8	101	22.2
Income > expense	9	22.0	12	29.3	5	12.2	15	36.6	41	9.0
Social security										
Yes	103	25.2	113	27.6	96	23.5	97	23.7	409	90.1
No	13	28.9	19	42.2	9	20.0	4	8.9	45	9.9

When students were asked about the most common type of cancer, the most commonly given types of cancer respectively were lung (17.1%), breast (15.8%), colon (11.2%). Skin (7.4%), cervix (6.4%), blood (6.3%), stomach (6%), pancreas (6%), liver (5.7%), lymph (4%), and larynx (4%). Approximately half of the students stated that the reason for self-breast examination was early diagnosis, a small portion of them stated that it was to check, while the others stated that they did not know. Examining the status of the students regarding their knowledge of cancer risk groups, the most commonly given cancer risk groups were genetic (22.6%), malnutrition (21.5%), age (19.9%), stress (6.1%) and gender (65.5%).

Table 2 shows the distribution of answers for necessary/unnecessary procedures for the prevention of cancer according to the gender of the students. When the table is examined, it can be understood that the majority of women did not consider options such as skipping meals, consuming 5 portions or above of vegetable and fruits, consuming bread and cereals every day, frequently consuming caloric and fatty foods, frequently using salt in meals, the consumption of meat and animal products, or using sugar with drinks; which should not be done in cancer prevention. When the difference between the distributions of options by gender were evaluated via chi-square analysis, it was found that there was a significant difference in only the distribution of the "do not know" option. It was noted that men marked the option "I do not know" more than women. When asked whether there were carrying out self-applications and what they should be, it was seen that the majority of the students did not perform the applications in all options. When we evaluated the distribution of options by gender regarding whether they were carrying out their own applications, it was seen that tomography, self-breast examination and 3 main meals with 2 snacks were chosen more by women, and the skipping meal option was chosen more by men.

Table 2. Socio-demographic and health related descriptive characteristics of students-2 (n=454)

	Nursing		Nutrition and dietetics		Physical therapy and rehabilitation		Medical faculty		Total	
Descriptive characteristics	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Place of residence										
City	84	22.8	112	30.4	83	22.6	89	24.2	368	81.1
County	21	31.1	18	26.9	19	28.4	9	13.4	67	14.8
Village-town	11	57.9	2	10.5	3	15.8	3	15.8	19	4.2
Smoking status										
Non-smoker	94	26.0	109	30.2	80	22.2	78	21.6	361	79.5
Smoker	18	25.7	16	22.9	20	28.6	16	22.9	70	15.4
Quit	4	17.4	7	30.4	5	21.7	7	30.4	23	5.1
Alcohol using status										
Non-user	102	28.5	105	29.3	78	21.8	73	20.4	358	78.9
User	9	11.7	22	28.6	20	26.0	26	33.8	77	17.0
Quit	5	26.3	5	26.3	7	36.8	2	10.5	19	4.2
Chronic disease										
No	7	14.9	14	29.8	12	25.5	14	29.8	47	10.4
Yes	109	26.8	118	29.0	93	22.9	87	21.4	407	89.6
Family history of cancer										
No	22	20.0	34	30.9	29	26.4	25	22.7	110	24.2
Yes	94	27.3	98	28.5	76	22.1	76	22.1	344	75.8

Consecutively, Tables 3-7 above show the distribution of the answers of the students about their knowledge of the risk factors of cancer according to their departments. When the distribution of the options according to their departments was examined it was found that the distribution of the majority of the options differed significantly. When the tables are examined, there are significant differences in terms of knowing risk factors such as, age of sexual intercourse, spicy foods, no prior births, alcohol consumption, being overweight, low fiber high fatty foods, advanced age, UV sunlight, gender, meat not being properly stored, being female, being over 50 years of age, vitamin A, C, E, beta carotene, selenium, calcium and fish oil ($p<0.05$). The results of the advanced analysis showing the source of the differences are given in the table.

DISCUSSION

Cigarette consumption is unquestionable first in terms of cancer risk. Cigarettes also increase the rate of chronic bronchitis and heart disease/crisis. Smoking increases the mortality rate by 3 times. Half of those acquainted with this bad habit at an early age have lost their lives due to smoking. The other half of them have lost their lives due to cancer which is caused by smoking in the last 7-8 years of their lives. The earlier smoking is stopped before cancer occurs, the less the effect of this risk. As a result of research, it was stated that in addition to cigarette smoking, cigar smoking, and chewing or the absorption of tobacco increased the formation of esophageal, oral cavity, larynx and pharyngeal cancer.[17]

According to the World Health Organization (WHO), smoking is one of the first six factors which threaten human health and it is the cause of one in every 10 deaths. This ratio started to decrease with the public awareness in developed countries.[18] The habits of smoking among young people aged 17-24 is indicated to be at a rate of 21.7% according to the 2009 statistical data on Turkey.[19] The smoking rate is 21.7% in Turkey. This ratio is composed of 52% of men and 17.3% of women. Turkey ranks in the top ten in terms of smoking rates. The rate of smoking among university students varies between 14-48%.[20-22] In our study, it was determined that 15.4% of the students still smoked, 5% had quit smoking and 79.5% had never smoked. 20.5% of all students were found to have a history of smoking. As for the results of studies related to alcohol use in situations, Turkish college students stated that it varied from 4%, 8-80% of this rate. In our study, it was determined that 17% of the students still used alcohol, 4.2% had quit and 78.9% had never used alcohol. 21.2% of all students had a history of alcohol use. The results of our study on alcohol use and the proportion of students who continue to use alcohol were found to be lower than some previous studies. The fact that the alcohol usage rate of the students who participated in our study was low could be related to the fact that there were no places selling alcohol in the university, the lack of easy access to alcohol and the fact that the university was a health university.

The incidence of cancer between the ages 20-39 is 13.8/100,000, while for these aged between 40-64 years, it is 114.4/100,000 due to changes in hormones caused by age and decreased immune system resistance [Data according to the Turkish Ministry of Health War Policy against Cancer and Cancer Data (1995-1999-2002)].

The mean age of the students who participated in our study was 20.48±1.45 years and their ages ranged from 17-30 years. It was observed that the students who participated in this study are included in the lower risk groups mentioned in the literature in terms of cancer risk. Our study is similar to the literature studies. Kurtuncu et al.[23] reported a mean age of 21.01±3.63 years, İlhan et al.[16] reported 21.26±1.94 years.

Table 3. Distribution of students' responses to cancer prevention according to gender (n=454)

Necessary/non-procedures in cancer prevention	What/what should be done?									Are you doing this?								
	Female (n=337)				Male (n=117)				X^2-p (0.)	Female (n=337)				Male (n=117)				X^2-P
	N		UN		N		UN			N		UN		N		UN		
	n	%	n	%	n	%	n	%		n	%	n	%	n	%	n	%	
1. Check-ups at certain periods	259	76.9	78	23.1	96	82.1	21	17.9	1.48-0.224	85	25.2	252	74.8	27	23.1	90	76.9	0.22-0.643
2. Pulmonary film	259	76.9	78	23.1	89	76.1	28	23.9	0.03-0.86	68	20.2	269	79.8	24	20.5	93	79.5	0.01-0.938
3. Breast film grind	272	80.7	65	19.3	90	76.9	27	23.1	0.77-0.380	69	20.5	268	79.5	17	14.5	100	85.5	1.10-0.157
4. Having tomography	237	70.3	100	29.7	84	71.8	33	28.2	0.09-0.76	73	21.7	264	78.3	15	12.8	102	87.2	**4.34-0.037**
5. Self-breast examination	255	75.7	82	24.3	80	68.4	37	31.6	2.39-0.122	137	40.7	200	59.3	23	19.7	94	80.3	**16.77-0.001**
6. Having a sample from the cervix	243	72.1	94	27.9	83	70.9	34	29.1	0.06-0.809	64	19.0	273	81.0	19	16.2	98	83.8	0.44-0.507
7. Searching for blood cells in feces	216	64.1	121	35.9	79	67.5	38	32.5	0.45-0.503	62	18.4	275	81.6	16	13.7	101	86.3	1.36-0.243
8. 3 main and 2 snacks per day	220	65.3	117	34.7	70	59.8	47	40.2	1.12-0.290	131	38.9	206	61.1	29	24.8	88	75.2	**7.55-0.006**
9. Skipping meals	**63**	**18.7**	**274**	**81.3**	**23**	**19.7**	**94**	**80.3**	0.05-0.819	67	19.9	270	80.1	25	21.4	92	78.6	**7.55-0.006**
10. 5 servings or more of vegetables/fruits.	**147**	**43.6**	**190**	**56.4**	**44**	**37.6**	**73**	**62.4**	1.29-0.256	75	22.3	262	77.7	17	14.5	100	85.5	3.21-0.073
11. Bread and other cereals every day	**152**	**45.1**	**185**	**54.9**	**49**	**41.9**	**68**	**58.1**	0.37-0.545	108	32.0	229	68.0	33	28.2	84	71.8	0.60-0.439
12. Consuming 2-3 liters of water per day	250	74.2	87	25.8	83	70.9	34	29.1	0.47-0.494	161	47.8	176	52.2	44	37.6	73	62.4	3.63-0.057
13. Frequent intake of fatty and calorie foods	**59**	**17.5**	**278**	**82.5**	**26**	**22.2**	**91**	**77.8**	1.27-0.260	46	13.6	291	86.4	21	17.9	96	82.1	1.28-0.259
14. Frequent intake of meat and animal products	**118**	**35.0**	**219**	**65.0**	**48**	**41.0**	**69**	**59.0**	1.35-0.245	80	23.7	257	76.3	27	23.1	90	76.9	0.02-0.884
15. Using salt in meals	**55**	**16.3**	**282**	**83.7**	**26**	**22.2**	**91**	**77.8**	2.0630.151	55	16.3	282	83.7	28	23.9	89	76.1	3.37-0.056
16. Using sugar in beverages	**56**	**16.6**	**281**	**83.4**	**27**	**23.1**	**90**	**76.9**	2.43-0.119	61	18.1	276	81.9	22	18.8	95	81.2	0.03-0.865
17. Regular PST between ages of 30-65	217	64.4	120	35.6	65	55.6	52	44.4	2.88-0.090	15	4.5	322	95.5	2	1.7	115	98.3	1.81-0.178
18. Making BSE after each bath	177	52.5	160	47.5	55	47.0	62	53.0	1.06-0.304	70	20.8	267	79.2	17	14.5	100	85.5	2.18-0.139
19. Observing I-wart changes	229	68.0	108	32.0	77	65.8	40	34.2	0.18-0.670	113	33.5	224	66.5	33	28.2	84	71.8	1.13-0.288
20. I don't know	36	10.7	301	89.3	23	19.7	94	80.3	**6.19-0.013**	20	5.9	317	94.1	5	4.3	112	95.7	0.46-0.497

N: necessary, UN: unnecessary, PST: Pap Smear test.

Table 4. Distribution of students' responses to cancer risk factors-1

Cancer with or without risk factor	Nursing (n=116)						Physical therapy and rehabilitation (n=105)						X^2-p
	Possible factor		Non-possible factor		Do not known		Possible factor		Non-possible factor		Do not known		
	n	%	n	%	n	%	n	%	n	%	n	%	
1. Being overweight	103[a]	88.8	4[a]	3.4	9[a]	7.8	81[a]	77.1	9[b]	8.6	15[b]	14.3	**12.84-0.046**
Alcohol use	112[a]	96.6	2[a]	1.7	2[a]	1.7	93[a]	88.6	5[b]	4.8	7[b]	6.7	**14.41-0.025**
3. Smoking use	112[a]	96.63	2[a]	1.7	2[a]	1.7	97[a]	92.4	3[a]	2.9	5[a]	4.8	10.42-0.108
4. Exercise	5[a]	4.3	107[a]	92.2	4[a]	3.4	5[a]	4.8	94[a]	89.5	6[a]	5.7	9.59-0.143
5. Vit. A, C, E, β-carotene. Se, Ca, and fish oil	12[a]	10.3	86[a]	74.1	18[a]	15.5	6[a]	5.7	83[a]	79.0	16[a]	15.2	**16.72-0.010**
6. Low fiber and high fat	88[a]	75.9	15[a]	12.9	13[a]	11.2	74[a]	70.5	14[a]	13.3	17[a]	16.2	14.60-0.024
7. Sedentary life	92[a]	79.3	11[a]	9.5	13[a]	11.2	84[a]	80.0	10[a]	9.5	11[a]	10.5	3.01-0.808
8. Change in intestinal habit.	83[a]	71.6	12[a]	10.3	21[a]	18.1	58[a]	55.2	10[a,b]	9.5	37[b]	35.2	9.37-0.154
9. Advanced age	96[a]	82.8	11[a]	9.5	9[a]	7.8	71	67.6	11[a,b]	10.5	23[b]	21.9	**28.94-0.001**
10. First degree relative having cancer	98[a]	84.5	9[a]	7.8	9[a]	7.8	84[a]	80.0	9[a]	8.6	12[a]	11.4	10.58-0.102
11. Environmental pollution	104[a]	89.7	6[a]	5.2	6[a]	5.2	86[a]	81.9	7[a,b]	6.7	12[b]	11.4	11.23-0.81
12. Unbalanced or unhealthy nutrition	105[a]	90.5	7[a]	6.0	4[a]	3.4	94[a]	89.5	5[a]	4.8	6[a]	5.7	5.65-0.464
13. Poor body	101[a]	87.1	8a	6.9	7[a]	6.0	86[a]	81.9	10[a]	9.5	9[a]	8.6	2.90-0.821
14. Solar UV rays	104[a]	89.7	4[a]	3.4	8[a]	6.9	74[a]	70.5	12[b]	11.4	19[b]	18.1	**29.15-0.001**
15. Base stations	100[a]	86.2	4[a]	3.4	12[a]	10.3	90[a]	85.7	4[a]	3.8	11[a]	10.5	3.71-0.715
16. Noise	61[a]	52.6	29[a]	25.0	26[a]	22.4	55[a]	52.4	22[a]	21.0	28[a]	26.7	6.23-0.398
17. Use of birth control pills	75[a]	64.7	14[a]	12.1	27[a]	23.3	53[a]	50.5	12a,b	11.4	40[b]	38.1	10.09-0.121
18. Genetic factors	104[a]	89.7	6[a]	5.2	6[a]	5.2	90[a]	85.7	6[a]	5.7	9[a]	8.6	7.02-0.319
19. Being stressed for a long time period	107[a]	92.2	5[a]	4.3	4[a]	3.4	89[a]	84.8	6[a,b]	5.7	10[b]	9.5	9.92-0.128
20. Gender	66[a]	56.9	30[a]	25.9	20[a]	17.2	45	42.9	32[a]	30.5	28[a]	26.7	**25.18-0.001**
21. Depression/anxiety	99[a]	85.3	9[a]	7.8	8[a]	6.9	88[a]	83.8	6[a]	5.7	11[a]	10.5	4.55-0.603
22. Consumption of plenty of fruit and vegetables	13[a]	11.2	98[a]	84.5	5[a]	4.3	10[a,b]	9.5	84[b]	80.0	11[a]	10.5	12.18-0.058
23. Poor quality products	104[a]	89.7	7[a]	6.0	5[a]	4.3	88[a]	83.8	8[a]	7.6	9[a]	8.6	11.57-0.072
24. Ignoring health checks	95[a]	81.9	11[a]	9.5	10[a]	8.6	86[a]	81.9	6[a]	5.7	13[a]	12.4	7.92-0.244
25. Industrialization	105[a]	90.5	2[a]	1.7	9[a]	7.8	89[a]	84.8	5[a]	4.8	11[a]	10.5	6.77-0.343

[a]: post-hoc analysis result = 0.05 indifferent, [b]: post-hoc analysis result = 0.05 show significant difference, Se: selenium, Ca: calcium.

Table 5. Distribution of students' responses to cancer risk factors-2

Cancer with or without risk factor	Nursing (n=116)						Physical therapy and rehabilitation (n=105)						X^2-P
	Possible factor		Non-possible factor		Do not known		Possible factor		Non-possible factor		Do not known		
	n	%	n	%	n	%	n	%	n	%	n	%	
26. Viruses	101[a]	87.1	7[a]	6.0	8[a]	6.9	94[a]	89.5	1[a]	1.0	10[a]	9.5	6.896-0.331
27. Age at starting sexual intercourse	85[a]	73.3	7[b]	6.0	24[b]	20.7	51[a]	48.6	18[a]	17.1	36[a]	34.3	**28.242-0.001**
28. Working conditions	91[a]	78.4	9[a]	7.8	16[a]	13.8	80[a]	76.2	9[a]	8.6	16[a]	15.2	11.224-0.082
29. Air pollution	106[a]	91.4	3[a]	2.6	7[a]	6.0	90[a]	85.7	5[a]	4.8	10[a]	9.5	9.195-0.163
30. Very hot or cold nutrition	82[a]	70.7	12[b]	10.3	22[a,b]	19.0	55[a]	52.4	21[a]	20.0	29[a]	27.6	12.555-0.051
31. Spices/spicy foods	85[a]	73.3	9[b]	7.8	22[a,b]	19.0	47[a]	44.8	25[b]	23.8	33[b]	31.4	**27.201-0.001**
32. Caffeine-containing foods	102[a]	87.9	5[a]	4.3	9[a]	7.8	77[a]	73.3	10[a]	9.5	18[a]	17.1	12.183-0.058
33. Smoked foods	86[a]	74.1	10[a]	8.6	20[a]	17.2	68[a]	64.8	9[a]	8.6	28[a]	26.7	6.397-0.380
34. Meat not stored properly	86[a]	74.1	14[a]	12.1	16[a]	13.8	81[a]	77.1	12[a]	11.4	12[a]	11.4	**16.348-0.012**
35. Chronic diseases	102[a]	87.9	3[a]	2.6	11[a]	9.5	83[a]	79.0	4[a]	3.8	18[a]	17.1	7.105-0.311
36. Cosmetics	102[a]	87.9	6[a]	5.2	8[a]	6.9	93[a]	88.6	1[a]	1.0	11[a]	10.6	8.533-0.202
37. Food additives	110[a]	94.8	3[a]	2.6	3[a]	2.6	96[a]	91.4	3[a]	2.9	6[a]	5.7	5.012-0542
38. Pesticides	102[a]	87.9	6[a]	5.2	8[a]	6.9	91[a]	86.7	3[a]	2.9	11[a]	10.5	4.277-0.639
39. Substance abuse	112[a]	96.6	2[a]	1.7	2[a]	1.7	97[a]	92.4	2[a]	1.9	6[a]	5.7	4.071-0.667
40. Radiation	111[a]	95.7	2[a]	1.7	3[a]	2.6	94[a]	89.5	2[a,b]	1.9	9[b]	8.6	11.980-0.062
41. Difficult living conditions	99[a]	85.3	8[a]	6.9	9[a]	7.8	92[a]	87.6	2[a]	1.9	11[a]	10.5	6.709-0.349
42. Fate	34[a]	29.3	49[b]	42.2	33[b]	28.4	44[a]	41.9	29[a]	27.6	32[a]	30.5	**40.473-0.001**
43. Being a woman	50[a]	43.1	47[a]	40.5	19[a]	16.4	36[a]	34.3	33[a]	31.4	36[b]	34.3	**26.975-0.001**
44. Never having given birth	60[a]	51.7	37[b]	31.9	19[b]	16.4	25[a]	23.8	35[a]	33.3	45[b]	42.9	**46.645-0.001**
45. Having hepatitis	92[a]	79.3	10[a,b]	8.6	14[b]	12.1	71[a]	67.6	6[a]	5.7	28[a]	26.7	10.694-0.098
46. Smoking hookahs	102[a]	87.9	6[a]	5.2	8[a]	6.9	89[a]	84.8	5[a]	4.8	11[a]	10.5	5.945-0.429
47. Starting the day without breakfast	51[a]	44.0	41[a]	35.3	24[a]	20.7	56[a]	53.3	24[a]	22.9	25[a]	23.8	5.503-0.481
48. Consuming 2-3 liters of water per day	13[a]	11.2	97[a]	83.6	6[a]	5.2	9[a]	8.6	84[a]	80.0	12[a]	11.4	6.774-0.342
49. Consuming fatty or calorific foods	101[a]	87.1	7[a]	6.0	8[a]	6.9	83[a]	79.0	10[a]	9.5	12[a]	11.4	7.233-0.300
50. Being over 50	88[a]	75.9	9[a]	7.8	19[a]	16.4	63[a]	60.0	12[a,b]	11.4	30[b]	28.6	**18.863-0.004**

[a]: post-hoc analysis result = 0.05 indifferent, [b]: post-hoc analysis result = 0.05 show significant difference.

Table 6. Distribution of students' responses according to departments cancer risk factors-3

Cancer with or without risk factor	Medical faculty (n=101)						Nutrition and dietetic (n=132)						X^2-p
	Possible factor		Non-possible factor		Do not known		Possible factor		Non-possible factor		Do not known		
	n	%	n	%	n	%	n	%	n	%	n	%	
1. Being overweight	94[a]	93.1	2[a]	2.0	5[a]	5.0	116[a]	88.8	6[a]	4.5	10[a]	7.6	**12.842-0.046**
2. Alcohol use	98[a]	97.0	1[a]	1.0	2[a]	2.0	129[a]	97.7	0[a]	0.0	3[a]	2.3	**14.409-0.025**
3. Smoking use	100[a]	99.0	0[a]	0.0	1[a]	1.0	130[a]	98.5	0[a]	0.0	2[a]	1.5	10.416-0.108
4. Exercise	1[a]	1.0	99[a]	98.0	1[a]	1.0	1[a]	0.8	126[a]	95.5	5[a]	3.8	9.585-0.143
5. Vit. A. C. E. β-carotene, selenium, calcium and fish oil	3[a]	3.0	93[a]	92.1	5[a]	5.0	9[a]	6.8	114[a]	86.4	9[a]	6.8	**16.715-0.010**
6.Low fiber and high fat	90[a]	89.1	6[b]	5.9	5[a,b]	5.0	98[a]	74.2	22[a]	16.7	12[a]	9.1	**14.599-0.024**
7.Sedentary life	86[a]	85.1	6[a]	5.9	9[a]	8.9	103[a]	78.0	16[a]	12.1	13[a]	9.8	3.007-0.808
8. Change in intestinal habit.	66[a]	65.3	12[a]	11.9	23[a]	22.8	85[a]	64.4	13[a]	9.8	34[a]	25.8	9.368-0.154
9. Advanced age	93[a]	92.1	2[b]	2.0	6[b]	5.9	90[a]	68.2	16[a,b]	12.1	26[b]	19.7	**28.937-0.001**
10. First degree relative cancer	96[a]	95.0	2[a]	2.0	3[a]	3.0	112[a]	84.8	9[a]	6.8	11[a]	8.3	10.582-0.102
11. Environmental pollution	96[a]	95.0	2[a]	2.0	3[a]	3.0	121[a]	91.7	4[a]	3.0	7[a]	5.3	11.233-0.81
12. Unbalanced and unhealthy nutrition	96[a]	95.0	1[a]	1.0	4[a]	4.0	123[a]	93.2	6[a]	4.5	3[a]	2.3	5.647-0.464
13. Poor body	86[a]	85.1	6[a]	5.9	9[a]	8.9	116[a]	87.9	9[a]	6.8	7[a]	5.3	2.900-0.821
14. Solar UV rays	96[a]	95.0	2[a]	2.0	3[b]	3.0	105[a]	79.5	14[a]	10.6	13[a]	9.8	**29.147-0.001**
15. Base stations	93[a]	92.1	2[a]	2.0	6[a]	5.9	120[a]	90.9	4[a]	3.0	8[a]	6.1	3.713-0.715
16.Noise	47[a]	46.5	33[a]	32.7	21[a]	20.8	65[a]	50.0	42[a]	31.8	24[a]	18.2	6.228-0.398
17. Use of birth control pills	62[a]	61.4	17[a]	16.8	22[a]	21.8	74[a]	56.1	21[a]	15.9	37[a]	28.0	10.086-0.121
18. Genetic factors	95[a]	94.1	3[a]	3.0	3[a]	3.0	122[a]	92.4	2[a]	1.5	8[a]	6.1	7.015-0.319
19. Stress for a long time	97[a]	96.0	2[a]	2.0	2[a]	2.0	122[a]	92.4[a]	4[a]	3.0	6[a]	4.5	9.920-0.128
20. Gender	68[a]	67.3	24[a,b]	23.8	9[b]	8.9	52[a]	39.4	45[b]	34.1	35[b]	26.5	**25.180-0.001**
21. Depression/anxiety	90[a]	89.1	7[a]	6.9	4[a]	4.0	117[a]	88.6	6[a]	4.5	9[a]	6.8	4.550-0.603
22. Consume plenty of fruit and vegetables	14[a]	13.9	85[a]	84.2	2[a]	2.0	8[a]	6.1	118[a]	89.4	6[a]	4.5	12.181-0.058
23. Poor quality products	84[a]	83.2	12[a]	11.9	5[a]	5.0	124[a]	93.9	4[a]	3.0	4[a]	3.0	11.569-0.072
24. Ignoring health checks	84[a]	83.2	11[a]	10.9	6[a]	5.9	117[a]	88.6	9[a]	6.8	6[a]	4.5	7.917-0.244
25. Industrialization	95[a]	94.1	1[a]	1.0	5[a]	5.0	114[a]	86.4	6[a]	4.5	12[a]	9.1	6.770-0.343

[a]: post-hoc analysis result = 0.05 indifferent, [b]: post-hoc analysis result = 0.05 show significant difference.

Table 7. Distribution of students' responses according to departments cancer risk factors-4

Cancer with or without risk factor	Medical faculty (n=101)						Nutrition And Dietetic (n=132)						X^2-p
	Possible factor		Non-possible factor		Do not known		Possible factor		Non-possible factor		Do not known		
	n	%	n	%	n	%	n	%	n	%	n	%	
26. Viruses	86[a]	85.1	8[a]	7.9	7[a]	6.9	116[a]	87.9	5[a]	3.8	11[a]	8.3	6.896-0.331
27. Age at starting sexual intercourse	67[a]	66.3	18[a]	17.8	16[b]	15.8	67[a]	50.8	17[a,b]	12.9	48[b]	36.4	**28.242-0.001**
28. Working conditions	91[a]	90.1	4[a]	4.0	6[a]	5.9	115[a]	87.1	4[a]	3.0	13[a]	9.8	11.224-0.082
29. Air pollution	96[a]	95.0	3[a]	3.0	2[a]	2.0	125[a]	94.7	2[a]	1.5	5[a]	3.8	9.195-0.163
30. Very hot cold nutrition	64[a]	63.4	20[a]	19.8	17[a]	16.8	72[a]	54.5	25[a]	18.9	35[a]	27.6	12.555-0.051
31. Spicy. spicy foods	62[a,b]	61.4	25[b]	24.8	14[a]	13.9	77[a]	58.3	22[a]	16.7	33[a]	25.0	**27.201-0.001**
32. Caffeine-containing foods	77[a]	76.2	13[a]	12.9	11[a]	10.9	102[a]	77.3	9[a]	6.8	21[a]	15.9	12.183-0.058
33. Smoked foods	79[a]	78.2	4[a]	4.0	18[a]	17.8	95[a]	72.0	9[a]	6.8	28[a]	21.2	6.397-0.380
34. Meat not stored properly	93[a]	92.1	5[b]	5.0	3[b]	3.0	100[a]	75.8	21[a]	15.9	11[a]	8.3	**16.348-0.012**
35. Chronic diseases	84[a]	83.2	7[a]	6.9	10[a]	9.9	109[a]	82.6	4[a]	3.0	19[a]	14.4	7.105-0.311
36. Cosmetics	92[a]	91.1	3[a]	3.0	6[a]	5.9	117[a]	88.6	1[a]	0.8	14[a]	10.6	8.533-0.202
37. Food additives	96[a]	95.0	2[a]	2.0	3[a]	3.0	122[a]	92.4	1[a]	0.8	9[a]	6.8	5.012-0542
38. Pesticides	93[a]	92.1	2[a]	2.0	6[a]	5.9	120[a]	90.9	3[a]	2.3	9[a]	6.8	4.277-0.639
39. Substance use	124[a]	93.9	1[a]	0.8	7[a]	5.3	97[a]	92.4	2[a]	1.9	6[a]	5.7	4.071-0.667
40. Radiation	100[a]	99.0	0[a]	0.0	1[a]	1.0	127[a]	96.2	1[a]	0.8	4[a]	3.0	11.980-0.062
41. Difficult living conditions	93[a]	92.1	3[a]	3.0	5[a]	5.0	118[a]	89.4	4[a]	3.0	10[a]	7.6	6.709-0.349
42. Fate	53[a]	52.5	32[a]	31.7	16[a]	15.8	87[a]	65.9	23[b]	17.4	22[b]	16.7	**40.473-0.001**
43. Being a woman	61[a]	60.4	29[b]	28.7	11[b]	10.9	52[a]	39.4	46[a]	34.8	34[a]	25.8	**26.975-0.001**
44. Never have given birth	52[a]	51.5	34[a,b]	33.7	15[b]	14.9	33[a]	25.0	57[b]	43.2	42[b]	31.8	**46.645-0.001**
45. Being hepatitis	67[a]	66.3	11[a]	10.9	23[a]	22.8	90[a]	68.2	9[a]	6.8	33[a]	25.0	10.694-0.098
46. The habit of hookah	93[a]	92.1	2[a]	2.0	6[a]	5.9	117[a]	88.6	2[a]	1.5	13[a]	9.8	5.945-0.429
47. Starting the day without breakfast	49[a]	48.5	28[a]	27.7	24[a]	23.8	71[a]	53.8	34[a]	25.8	27[a]	20.5	5.503-0.481
48. Consume 2-3 liters of water per day	8[a]	7.9	89[a]	88.1	4[a]	4.0	11[a]	8.3	108[a]	81.8	13[a]	9.8	6.774-0.342
49. Consume fatty and calorie foods	88[a]	87.1	7[a]	6.9	6[a]	5.9	111[a]	84.1	5[a]	3.8	16[a]	12.1	7.233-0.300
50. Being over 50	85[a]	84.2	6[a,b]	5.9	10[b]	9.9	87[a]	65.9	17[a,b]	12.9	28[b]	21.2	**18.863-0.004**

[a]: post-hoc analysis result = 0.05 indifferent.", [b]: post-hoc analysis result = 0.05 show significant difference.

Breast cancer is the most common type of cancer and cause of death in women. Urbanization and westernization increase breast cancer incidence.[24] 25% of women are diagnosed with cancer including breast cancer.[25] In our study, it was determined that students knew that self-breast examination should be carried out after each bath but only 19.2% of them applied it. 35.2% of the students applied self-breast examination but not after each bath. In the study conducted by İlhan et al.[16] in order to determine the behaviors of university students studying in health related departments regarding the early diagnosis of breast cancer, it was found that 53.3% of the students performed regularly self-breast examination. There is a difference between our results and theirs. The reason for this difference may be the fact that there was only a female population in the study by Ilhan, and in our study, there was a majority male population. In our study, while 79.7% of the students thought that mammography should be carried out in cancer prevention, 18.9% of the students had mammography at least one. 71% of women had mammography at least once in a study conducted by Karadag et al.[13] in a city in the southeastern region.

In this study, significant differences were observed in the percentage of making self-breast examination in women who had received education compared to the ones who had not received education on this issue. The reason for this could be that the students had been educated in health departments and had more awareness. When the distribution of the answers of the students about cancer risk factors was examined, 83.5% of the students knew that constant sun exposure, 96.7% knew smoking and 95.2% accepted alcohol as a risk.

Kolutek and Karataş[26] determined the cancer risk factors and early diagnosis of symptoms of individuals. According to their study, 83.5% of the individuals considered constant sun exposure, 52.7% of them considered smoking and 19.4% considered alcohol as a risk. While there was no significant difference between sun exposure being seen as a risk to increase cancer development among students, there were significance differences for smoking and alcohol use.

The types of cancer that students know most are evaluated separately according to the departments. Nursing students stated that the most commonly known form of cancer is the larynx (33.9%), nutrition and dietetics students stated lymph cancer (41.3%), physical therapy and rehabilitation students stated blood cancer (21. 6%) and medical faculty students stated pancreatic cancer (33.3%).

The answers of the students to the question of what the word "cancer" means to you were also examined on the basis of their departments. Nursing students highlighted a deterioration of body image due to a deterioration in the quality of life (75%), nutrition and dietetics students emphasized a difficult period, sadness, stress, and despair (53.4%), physical therapy and rehabilitation students mentioned death, the worst disease, irreversible and untreatable (26.6%) and medical faculty students responded by talking about uncontrolled cell divisions, tumors, metastasis and malign tumors (48.1%).

The distribution of the answers given by the students regarding cancer prevention according to their departments and genders was not discussed because no data was found in the literature.

When the differences between the distribution of the options according to gender was evaluated by chi-square analysis, it was found that only the "do not know" option showed a significant difference. It was determined that men marked the option "do not know" more than women. When asked whether they carry out applications which they say are necessary, it could be seen that the majority of the students did not carry out the application. When the distributions of options according to gender were evaluated in terms of whether they were carrying out the applications themselves, it was observed that having tomography, self-breast examinations and 3 meals with 2 snacks daily were more chosen by women; and skipping meals was chosen more frequently by men.

There are significant differences between the distribution of the options such as periodic check-ups, lung scans, breast scans, tomography, self-breast examination, PAP smear testing, skipping meals, 5 serving or above of fruits and vegetables daily, consumption of bread and cereals, drinking 2-3 liters of water, frequent calorific and fatty foods intake, consumption of meat and animal products, the use of salt with meals, sugar usage with beverages, and being aged between 30-65 years of age. Many of the students correctly stated the cancer risk factors. Between 20% and 25% of the students studying at the health university stated that "they did not know" for questions regarding noise, the use of oral contraceptive, gender, smoked foods, being female, weight, having previously given birth, hepatitis and starting the day with no breakfast. 82.8%-93.8% of students gave the answers "It is not a possible risk factor" to those options which are not cancer risk factors such as drinking 2-3 liters of water, exercise, vitamins A, C, and E, beta carotene, selenium, calcium and fish oil consumption.

Students do not consider exercise, consuming plenty of fruit and vegetables and consuming 2-3 liters of water in a day as a risk factors. The majority of the students (88.1-96.7%) considered options such as, alcohol and cigarette usage, environmental pollutants, an unbalanced diet or malnutrition, genetic factors, base stations, poor quality products, air pollution, industrialization, radiation, cosmetics, foods additives, substance abuse, pesticides, difficult life conditions, and smoking water pipes/hookahs as cancer risk factors. When the distribution of the answers given by the students regarding the knowledge of risk factors of cancer was examined, it was found that the distribution of the majority of the options differed significantly.

CONCLUSION

Based on the results of this research, it was determined that the majority of the students knew about cancer risk factors but many of them did not take any action. It is advised that planning of interventions to create behavioral changes especially in terms of cancer prevention and early diagnosis, by conducting training on these subjects which highlight the responsibility of the individual be carried out. Because of the primary responsibility for protection from cancer is given to the media; as the information resources of the students are mostly health personnel, referring to the guide that has the largest and the most current information, to teach and spread the applications that are known to be effective in early diagnosis such as self-breast examination which a small percentage of students applied despite general student awareness. Planning informative training activities on cancer risk factors is needed due to the fact that the students marked the options "I do not know" option for many risk factors. It is important to increase the awareness of health professionals regarding cancer and its risk factors in the early stages of their student life. Universities are advised to include cancer and the risk factors of cancer in their curriculums. It is very important for students who will become healthcare professionals to know about

cancer risk factors in order to increase their health as well as the health of the society they will provide care for. Another issue is to evaluate whether information is reflected in behavior. Identifying the current situation in this specified area can provide professionals with valuable data.

MAIN POINTS

- It was determined that the students participating in this study did not perform any applications although they knew the cancer risk factors and those practices which are known to be effective in early diagnosis such as breast self-examination.
- In order to improve this situation, initiatives aiming at creating behavioral change especially for cancer prevention and early diagnosis should be planned.
- It should be ensured that these practices, which have an important effect on the early diagnosis and treatment of cancer, are taught and expanded.

ETHICS

Ethics Committee Approval: Ethics committee approval for this study was received from the Ethics Committee of the Clinical Research Institute of Sanko University with the decision number 01 prior to starting the survey on 02.03.2017.

Informed Consent: Verbal informed consent was obtained from the students who participated in this study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: N.P., Design: N.P., M.K., Data Collection and/or Processing: N.P., Analysis and/or Interpretation: M.K., Literature Search: M.K., Writing: M.K., Critical Review: M.K.

DISCLOSURES

Conflict of Interest: No conflict of interest was declared by the authors.

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ORIGINAL ARTICLE

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Determining the Knowledge Level of Students on Food Additives

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Abstract

BACKGROUND/AIMS: Food additives are substances which are not consumed as a food alone, having no nutritious value, and they are not used as a characteristic component of any food. This study aimed to determine the knowledge level of students on food additives.

MATERIALS AND METHODS: This descriptive study was carried out between the 20th and the 30th of May 2019. 363 voluntary students at the Faculty of Nursing and Dentistry participated in this study. They were asked questions on their knowledge about packaged processed foods, whether they have information on the nature of additives, their sources on obtaining information related to additives, and for what purpose additives are used.

RESULTS: 38.9% of the students stated that they consumed packaged processed food every day, 41.6% for nourishment, and 43.5% due to its pleasant taste. 23.4% of the students indicated that they consumed all types of packaged food, 55.9% of them cared about the brand when buying it and 63.4% of them were affected by the taste and smell while buying these food items. In addition, 47.7% of the students stated that they did not care about food ingredients when buying packaged processed food and 46% of them did not have any information on the additive content of packaged processed food.

CONCLUSION: It is considered that the knowledge level of students on food additives is insufficient, and thus, they should be informed. Governments and universities should alleviate food safety-related fears on time and appropriately, and ensure the food safety of consumers by explaining the necessary information in a timely and understandable way.

Keywords: Food additives, nutrition, food, student

INTRODUCTION

Food additives are substances which are not consumed as a food alone having no nutritious value and they are not used as a characteristic component of any food. They or their by-products are expected to become an ingredient of that food directly or indirectly as a result of being added to food during the production, handling, processing, preparation, packaging, transportation or storage in line with a technological purpose.[1-3]

The number and types of additives used in prepared foods have increased rapidly in parallel with rapid developments in the food industry and prepared food production.[2] Additives are chemical compounds without any nutritional value bringing the appearance and taste of foods in line with the demands by society, being put into foods during production in order to prevent adulteration and to allow for storage for a longer time. The benefits of these chemical substances when they are put in food are as follows:[3-6]

- allow food to have a longer life,

- make foods have better tastes, flavours and smells,

- correct their shapes and colours,

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- allow foods to have a better appearance.

- protect their quality and stiffness,

- prevent the formation of microorganisms causing disease,

- help to protect nutritional and biological values.

However, when these chemical substances are consumed particularly on a regular basis and excessively, the following results may occur:

- can spoil the natural flavour of the food,

- nutritional elements are at risk of being lost,

- if their shelf lives are not adhered to, they have the risk of poisoning the food.

Today, there are more than 10,000 additives approved by the U.S. Food and Drug Administration (FDA) for the purposes of preserving, packaging and changing tastes, appearances, tissues or nutrition in food. Increasing scientific evidence has shown that of the synthetic chemicals used as a food additive, the ones put into food directly for various reasons during processing and the ones used later in order to extend the shelf-life have negative effects on human health, especially children.[1,7] While some of these substances allowed by responsible organisations do not cause any problems regarding health, some may lead to serious dangers if they are consumed continuously.[8] Many effects such as food allergies, food intolerance, cancer, multiple sclerosis, attention deficit hyperactivity disorder, brain damage, nausea, and heart disease were reported in a review article examining studies on the effects of food additives and preservatives on human health.[9] For example; artificial colouring agents or sodium benzoate preservatives (or both of them) cause an increase in hyperactivity in the whole population and in children in 3, 8/9 years old.[10]

In the event that the food with additives is consumed excessively, a person may develop diseases such as skin rash, asthma, obesity, metabolic syndrome, liver function impairment, and even cancer.[4,5] The substances added in order to increase the nutritional value of prepared food or for fraudulent purposes are not included in this group.[3]

The size of this threat is increasing, especially for children.[6,7] Considering the above-mentioned reasons, we aimed to investigate the knowledge of our students and to create an awareness in society and among our students regarding these substances which are not natural and are added with commercial goals in mind. The goal of this study was to determine the knowledge of students on food additives. Students studying in health-related departments have social responsibilities. They are guides for society in the protection and promotion of health. This research was carried out in order to determine the knowledge level and awareness of students at Near East University Faculty of Nursing and Dentistry about the use of additives in processed food.

This study aimed to determine the knowledge level of students on food additives.

MATERIALS AND METHODS

This study, which was designed as a descriptive study, was carried out with the students of a nursing and dentistry faculty in Turkish Republic of Northern Cyprus in the spring semester of the 2018-2019 academic year. The sample of the research was determined to include the universe and an attempt was made to reach all 490 senior students registered to the Nursing and Dentistry faculties in that semester. A total of 363 students who agreed to participate in this research and completed the questionnaires were included in the study. Approximately 74% of the universe was reached.

The students were asked questions on their knowledge about packaged processed food, whether they had any information on the nature of additives, their sources of obtaining information related to additives, and for what purposes additives are used.

Demographic information was obtained in the first part of a questionnaire form, created by searching the related literature,[2-10] and in the second part, students were asked about their packaged food consumption and what additives were, the purpose of putting additives into food and thus, it was attempted to determine their knowledge levels. In the third part, they were asked about the intended use of additives in the mixture forming the prepared food, and it was investigated to what extent they had correct information on additives.

Ethical Considerations

Ethics committee approval was received for this study from the Near East University Ethics Review Board (appoval number: 2019-68-815). The purpose and method of this research and questionnaires were explained to the students, and their consent was obtained after notifying them that their participation in the research was voluntary. Permission was obtained from the related faculties.

Statistical Analysis

21.0 version of the Statistical Package for the Social Sciences (IBM Corp.; Armonk, NY, USA) package program was used for the statistical analysis of the responses obtained from the data collection forms. Descriptive statistics, such as percentage and frequency, were used in order to interpret the results.

RESULTS

A total of 363 students participated in this study. 47.4% of them were enrolled at the faculty of nursing, and 52.6% of them studied at the faculty of dentistry. 51.5% of these students were female and 48.5% male with an age average of 23±2.05 years.

38.9% of the students indicated that they consumed packaged processed food every day, and 40.2% sometimes. 41.6% consumed packaged processed food for nourishment, 43.5% for its good taste. 23.4% of the students stated that they consumed all packaged products, 26.7% of them consumed chocolate the most, 55.9% of them paid attention to the brand of the packaged processed food when buying it and 63.4% of them were affected by the taste and smell of this food while buying it (Table 1).

While 47.7% of the students stated that they did not pay attention to the content of the packaged processed food when buying it, 46% of them indicated that they had no information on the additive content of the prepared packaged food. Furthermore, 56.2% of the students specified that they used the internet as a source of information regarding packaged processed foods and their additives. 80% of the students stated that food additives are put into prepared packaged food so that it could have a longer shelf-life, 62% said that food additives enhanced

Table 1. Responses of students on packaged food consumption (n=363)

Questions on packaged food consumption		Number (n)	Percent (%)
How often do you consume packaged processed food?	Several times a day	17	4.7
	Very rare	28	7.7
	Once a week	31	8.5
	Everyday	141	38.9
	Sometimes	146	40.2
For what purpose do you consume packaged processed food in general?	No idea	23	6.3
	For fun	31	8.6
	For nourishment	151	41.6
	For its good taste	158	43.5
What is the type of packaged processed food you consume the most?*	Biscuits	52	14.3
	Chips and similar products	63	17.4
	Fast food	79	21.8
	All products	85	23.4
	Chocolate	97	26.7
What do you pay attention to when buying packaged processed food?*	Package	24	6.6
	Advertisement	28	7.7
	Friends' advice	59	16.3
	Nutritional value	73	20.1
	Brand	203	55.9
What affects you the most while buying packaged prepared meals?*	Its advertisement	4	1.1
	Its nutritional value	39	10.7
	Its package	45	12.4
	Its brand	53	14.6
	Its taste, smell	230	63.4

*multiple options can be selected.

the risk of poison to the food if their shelf-lives were not adhered to, and finally, 83.5% of them indicated that in the case that food with additives are consumed excessively, this may lead to obesity/metabolic syndrome (Table 2).

Most of the students responded that they did not know anything on the intended use of food additives. While some of the students indicated that sodium nitrite (29.8%) and sodium benzoate (20.9%) are used for preservative purposes, the rest expressed that aspartame (32.8%), caramel (52.9%) and fructose syrup (63.7%) are used for flavouring purposes. 41.6% of students specified that caramel is used as a flavour enhancer while the rate for Epsom salt was 22.9% and it was 23.7% for fructose syrup. Additionally, 15.7% of the students indicated that beta carotene is used as a colouring agent, and 23.1% of them stated that niacin is used for vitamin purpose (Table 3).

DISCUSSION

The concern regarding food additives has increased much in the last two decades due to studies revealing endocrine system disorders and other negative health effects.[10,11] In this regard, this study was conducted in order to determine the knowledge levels of our students on food additives. Of the 363 students who participated in this study, 47.4% of them were enrolled in the faculty of nursing, 52.6% of them studied in the faculty of dentistry. 51.5% of these students were female and 48.5% were male with an age average of 23±2.05 years.

Related to their responses on packaged food consumption, 38.9% of the students stated that they consumed packaged processed food every day and 40.2% sometimes. 41.6% stated that they consumed packaged processed foods for nourishment, and 43.5% for its pleasant taste. 23.4% of the students indicated that they consumed all types of packaged food, 26.7% of them consumed chocolate the most, 55.9% of them cared about the brands when buying it and 63.4% of them were affected by the taste and smell while buying these foods (Table 1).

Studies found that the most commonly consumed processed foods were packaged cakes, cookies and chocolate, packaged milk and dairy products, chicken and chicken products, whereas the least commonly consumed processed foods were canned goods, salami, and sausage.[2,12,13] Gökçe et al.'s[13] studies demonstrated that almost half of students consumed processed foods daily, 32.8% consumed them 2-3 times a week, 11.2% consumed them once a week, while 1.4% never consumed processed foods.

In responses to the questions on the ingredients and additives in the second section, 47.7% of the students stated that they did not pay attention to ingredients when buying packaged processed food and 46% of them did not have any information on the additive contents of packaged processed food (Table 2). Our results showed a great similarity to prior studies.[12,14-17]

Research carried out on 488 consumers in 2013 investigated the criteria which consumers cared about related to the food additives

Table 2. Responses of students on packaged food additives (n=363)

Questions about food additives		Number (n)	Percent (%)
Do you pay attention to the content of packaged processed food when buying?	Yes	190	52.3
Do you have information about the additive content of packaged processed food?	Yes	196	54.0
What information source do you generally use about packaged processed foods and additives?*	Newspaper	8	2.2
	Advertisements	32	8.8
	TV	38	10.5
	Other	46	12.7
	Friend circle	58	16.0
	Internet	204	56.2
What do you think are the reasons for putting food additives into packaged processed food?*	Increase nutritional value	30	8.3
	Help to protect nutritional and biological values	68	18.8
	Prevent the formation of microorganisms causing diseases	112	30.9
	Contribute food to protect their quality and strength	126	34.7
	Make their appearances better	170	46.9
	correct their shapes and colours	170	46.9
	Allow them to have better tastes, flavours and smells	231	63.6
	Allow food to have a longer life	289	80.0
What happens when additives, which are chemical substances, are used excessively?*	Nothing	33	9.1
	Natural tastes of food may spoil	155	42.7
	There is a risk of losing nutritional elements	177	48.8
	If their shelf-lives are not adhered to, they increase the risk of poison for food	225	62.0
What can food with additives cause when consumed excessively?*	Asthma	48	13.2
	Skin rashes	99	27.3
	Liver function impairments	202	55.6
	Cancer risk	231	63.6
	Obesity, metabolic syndrome	303	83.5

*multiple options can be selected.

Table 3. Responses of students on intended use of food additives (n=363)

Additive/classification*	Preservative		Flavouring		Flavour enhancer		Colouring agent		Vitamin	
	n	%	n	%	n	%	n	%	n	%
Aspartame	72	19.8	119	32.8	17	4.7	11	3.0	1	0.3
Sodium nitrite	108	29.8	18	4.9	19	5.2	9	2.5	3	0.8
Caramel	7	1.9	192	52.9	151	41.6	26	7.1	1	0.3
MSG (epsom salt)	56	15.4	58	16.0	83	22.9	13	3.6	6	1.7
Fructose syrup	4	1.1	231	63.7	86	23.7	23	6.3	7	1.9
Niacin	34	9.4	17	4.8	11	3.0	21	5.8	84	23.1
Beta carotene	34	9.4	12	3.3	16	4.4	57	15.7	47	12.9
E120 carmine	45	12.4	15	4.1	13	3.6	16	4.4	42	11.6
Sodium benzoate	76	20.9	20	5.5	12	3.3	13	3.6	9	2.5

*multiple options can be selected.

used in prepared and semi-prepared food. It was found that most of the subjects (72.4%) did not know the definition of food additives completely but more than half of them (57.5%) were informed about some food additives. It was revealed that of the subjects, the older ones had a more negative opinion, had more awareness and attempted to take precautions against food additives.[12]

56.2% of the students in this study indicated that they used the internet as a source of information about packaged processed foods

and additives (Table 2). We are of the opinion that this source is not sufficient for correct information due to information pollution in numerous advertisements. 80% of students expressed the opinion that food additives are put into prepared packaged food so that they have a longer shelf-life, 62% said that food additives add to the risk of poison for the food if their shelf-lives are not adhered to, and finally, 83.5% of them indicated that in cases where food with additives are consumed excessively, this may lead to obesity/metabolic syndrome (Table 2). Our students were found to have sufficient knowledge on obesity since it is a common issue with different sources, and they had sufficient knowledge on the shelf-life of food which differs from other studies.[15,17]

In one study conducted with students in different educational institutions, it was found that medical students had a significantly higher knowledge level (92.2%) on food additives compared to engineering students (80.4%). In addition, it was seen that students' daily consumption of food with additives was quite high despite having a high knowledge level on food additives. This showed that more research and effective responses are required in order to turn knowledge into action.[13]

The responses received in the last section questioning additives and their intended uses were highly challenging. Most of the students responded that they did not know anything on the intended use of food additives. While very few of the students indicated that sodium nitrite and sodium benzoate are used for preservative purposes, the rest stated that aspartame, caramel and fructose syrup are used for flavouring purposes. 41.6% of the students specified that caramel is used as a flavour enhancer while the rate of Epsom salt was 22.9% and it was 23.7% for fructose syrup. Additionally, 15.7% of the students indicated that beta carotene is used as a colouring agent, and 23.1% of them stated that niacin is used for vitamin purposes (Table 3). It was seen that the responses on the intended uses of additives excluding caramel, aspartame and fructose syrup were insufficient.

Consumer awareness and safety perception were investigated by a survey of 430 subjects by MiShim et al.[14] It was found that their subjects were very concerned about preservatives, colouring agents and flavourings in food, but more than two-thirds of them had insufficient knowledge on food additives. It was concluded that this lack of knowledge originates from difficulties regarding the subject of food additives, inadequate education and insufficient public relations.[14] Kim et al.[15] reached similar conclusions in their study carried out with 360 secondary school students. They found that few of them examined additives in prepared foods and nearly all of them had insufficient knowledge on additives.[15] In another study conducted with 2,782 subjects, the knowledge of consumers on additives before education intervention was assessed. The questionnaire performed before the intervention revealed that many of the consumers did not have the correct information on food additives and they were concerned in this respect. It was seen that food additive safety awareness was raised from 33.1% to 78.6% following this process.[16] It was found in a face-to-face interview made with consumers in Mauritius University that 65% of the subjects never read food labels regarding additives.[17] The conclusions of that study and the approaches of our students who had insufficient knowledge on the intended use of food additives have many similarities.

It is clearly seen that the knowledge levels of consumers on food additives in our country is insufficient, which is in line with prior studies. Consumers should be informed adequately on these additives, some of which are quite dangerous. In this regard, all state institutions, especially universities, have a significant duty. It is crucial that the awareness of consumers be raised. They should be informed about food additives in the light of the huge number of studies conducted in this field.[16,18,19]

CONCLUSION

It is considered that the knowledge levels of students on food additives is insufficient, and thus, they should be informed.

MAIN POINTS

- Governments and universities should alleviate food safety-related fears on time and appropriately and ensure the food safety of consumers by explaining the necessary information in a timely and understandable way.

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ETHICS

Ethics Committee Approval: Ethics committee approval was received for this study from the Near East University Ethics Review Board (appoval number: 2019-68-815).

Informed Consent: Their consent was obtained after notifying them that their participation in the research was voluntary

Peer-review: Externally peer-reviewed.

Authors' Contributions

Concept: T.Y., Ü.D.Y, Design: T.Y., Ü.D.Y., Supervision T.Y., Resource: T.Y., Ü.D.Y., Data collection and/or processing: T.Y., Ü.D.Y., Analysis and/or Interpretation: T.Y., Literature review: T.Y., Writing: T.Y., Ü.D.Y., Critical Reviews: T.Y.

DISCLOSURES

Conflict of Interest: The authors have no conflicts of interest to declare.

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ORIGINAL ARTICLE

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Traditional and Local Food Knowledge on the Island of Cyprus

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Abstract

BACKGROUND/AIMS: Cyprus is a multi-cultural island in the Mediterranean Sea. In addition to the Cypriots (native islanders), foreigners live in this country because of its location and lifestyle. Nowadays, immigration and emigration rates have increased for this island. At the same time, local production is limited and traditional food production, such as Commandaria, halloumi, olive oil etc., supports the economy. In addition, numerous natural and traditional consumable herbs grow in the local vegetation. This study aimed to determine the traditional and local food knowledge in Cyprus as a Mediterranean Food Model.

MATERIALS AND METHODS: The researchers designed an online questionnaire in five languages using Google Forms. Each questionnaire included a Nutritional Memory Catalog which was developed with a number of traditional and local food photos which were generally speaking not easy to recognize. All data was collected online due to the Coronavirus pandemic conditions.

RESULTS: Only voluntary adults (≥19 years) took part in this study. Cypriots (85.6%) and latecomers (14.4%) who had come this island later but had a duration of residence of more than ten years participated voluntarily (n=917). According to the results, traditional and local foods had a recognition rate of between 67.3% and 99.9%. Most of the traditional and local foods, such as vegetables, meat products etc., had a high recognition rate (≥99.0%). However, natural consumable herbs which grow in the mountains had the lowest recognition rate (<68.8%).

CONCLUSION: In conclusion, as with so many new trends in food and human behavior, there is a need to highlight traditional and local food consumption and increase awareness for healthy Mediterranean herbs.

Keywords: Traditional foods, Cyprus, Mediterranean region

INTRODUCTION

The Mediterranean region has gained a certain interest for healthy living, not only because of its climate and location but also due to its healthy nutrition and lifestyle. Providing a unique strategical basis, Cyprus is a candidate to study a large spectrum of features in the scope of nutrition and dietetics. This island is literally in the center of Mediterranean Sea where Cypriots, the native islanders, live.[1]

Cyprus has hosted different civilizations during its history. Thus, the island possesses multi-cultural traces.[2] Due to its location and lifestyle, it also includes multicultural background- foreigners who choose to live on Cyprus.[1] Local food production, such as citrus, grapes, strawberries, olives, vegetables etc., has an important role in the economy of the island while other food items are limited in their production.[3,4] There are several traditional local products. Halloumi is a traditional cheese of Cyprus and it has different types such as old, fresh and dried. Paphos red wine (*Commandaria)* is a traditional red wine which supports the economy.[5,6] Wild asparagus (*Asparagus acutifolius*), artichoke (*Cynara scolymus*), Molehiya (*Corchorus olitorius),* coriander (*Coriandrum sativum*) and taro (*Colocasia esculanta*) are important seasonal traditional foods.[7,8] At the same time, many natural and traditional consumable herbs, such as common mallow (*Malva sylvestris*), wild

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artichoke (*Cynara cardunculus*), tagarninas (*Scolymus hispanicus*) etc., grow in the local vegetation.[9,10] In addition, there are many traditional desserts and pickles which are made from the local and traditional foods/products.[11]

From the broader scope of planet health, traditional foods are very important for food security and local food consumption has important effects in many dimensions.[12,13] In addition, traditional food consumption is important for the economy and for the transfer of cultural heritage to future generations.[14] Furthermore, there are numerous studies showing the beneficial effects of the traditional and local foods of Cyprus on health.[15-17]

As seen elsewhere, immigration and emigration rates have increased to and from the island of Cyprus. This can cause cultural traces to be erased or altered.[18] From this point of view, the current study aimed to determine the traditional and local food knowledge of adults, both native islanders or latecomers who have lived on this island for more than ten years, and it also paves the way for the recording of the island's social nutritional memory.

MATERIALS AND METHODS

Place and Time of Study, Sample Selection

This study was conducted on the island of Cyprus between November 2020 and March 2021. The sample size had initially been estimated to be a minimum of 386 adults (95.0% confidence interval, 5.0% confidence level) according to general population (nearly 1.3 million). Due to concerted social calls, the data was collected within five months and with a total population of 917 adults (≥19 years old) who participated voluntarily in this study. Only Cypriots and latecomers who had come to this island later and who had a duration of residency of more than ten years could participate. Living in a country for a long time brings about an adaptation to its nutritional and lifestyle habits regardless of one's original culture.[19,20] This study had a local ethical compliance (approval number: NEU/2020/85-1198) and the volunteers participated with online consent in accordance.

Data Collection

Data was collected with a questionnaire and by using the Nutritional Memory Catalog which were all developed by the researchers. This was an online research due to the Coronavirus pandemic. The researchers designed an online questionnaire in Turkish, Greek, English, German and Russian using Google Forms. Each questionnaire included the Nutritional Memory Catalog showing some traditional and local foods which may not have been otherwise possible to recognize without their pictures. The questionnaire included two parts, namely the participants' general backgrounds and their traditional and local food knowledge. There were 63 traditional and local foods covered in the questionnaire (Table 1).

Nutritional Memory Catalog

The researchers reviewed numerous traditional and local foods photos which were not easy to recognize. When possible, they took photos of certain food items. In addition, the rest of the food types were placed in the catalog by referring to the source. The names of all foods were made available in five different languages (Turkish/Greek/German/Russian/English) in this catalog.

The current catalog includes 11 groups and 63 foods in order to determine traditional and local Cyprus foods knowledge.

Statistical Analysis

Statistical Package of the Social Science program-version 24.0 (SPPS Inc., Chicago) was used to analyze the data. Descriptive statistics were used to determine the frequencies (n) and percentages (%) of the qualitative data.

RESULTS

The spectrum of local food items is rather wide and it could potentially dissolve as global items overtake. In order to make our efforts stable for the long term, we have created a novel catalog with high resolution photos, Latin botanical counterparts as well as local names in available forms (mostly binomial), and further plotted them across their available and relative locations on the island map (Figure 1). This figure was developed by a team of professional graphic designers and researchers to introduce these traditional and local food items to the outside world properly. This effort was carried out in parallel to the present article. The relevant food items were prepared under similar conditions to enable easier comprehension for a non-expert eye. The numbers represent the names of the food items and respectively match with items in Table 1. To be more specific, items of the Nutritional Memory Catalog numbered 23, 36, 37, 46 and 53 were placed according to their exact geographical production locations. As such, other traditional food productions are not limited to a specific location and are mapped in a broader sense (Figure 1).

There were 917 participants in the current study. 85.6% were native islanders and the rest of the participants (14.4%) had lived on this island for more than 10 years. According to Table 1, traditional and local foods had a recognition rate of between 67.3% and 99.9%. Celery stalk (*Apium graveolens*), Cyprus muffin, "Çakısdez" (green olive), olive bread, wild asparagus (*Asparagus acutifolius*), pickled capari (*Capparis spinosa*) leaves, Zivania, "Seftali kebab", coriander (*Coriandrum sativum*), carob (*Ceratonia siliqua*), *Cyprus pastrami*, Cyprus pita, walnut jam, fresh halloumi, taro (*Colocasia esculanta*), "Pasedembo" (pumpkin seeds), old halloumi, artichoke (*Cynara scolynus*), "Garavolli" (snail), Indian fig

Figure 1. The map of the island of Cyprus and the locations of some traditional/local foods in accordance with the Nutritional Memory Catalog.

Table 1. Participants' local and traditional food recognition rates (n=917)

Food	Recognition rate		Food	Recognition rate		Food	Recognition rate	
	n	%		n	%		n	%
Fresh halloumi[1]	912	99.5	Wild spinach *(Spinacia oleracea)*	865	94.3	Pickled capari seeds *(Capari; Capparis spinosa)*[27]	907	98.9
Old halloumi	911	99.3	Louvana *(Lathyrus ochrus)*[13]	836	91.2	Pickled Mangolla *(Eryngium creticum)*[28]	858	93.6
Dried halloumi	865	94.3	Gavcar mushroom *(Pleurotus fuscus var. ferulae)*[14]	903	98.5	Taro *(Colocasia esculanta)*[29]	912	99.5
Fresh curd[2]	848	92.5	Celery stalk *(Apium graveolens)*[15]	916	99.9	Bullez *(Colocasia esculantasya)*	833	90.8
Dried curd	858	93.6	Zucchini *(Cucurbita pepo)*[16]	873	95.2	Cyprus tarhana[30]●	904	98.6
Seftali kebab[3]□	914	99.7	Zucchini *blossom*[17]	905	98.7	Pirohu *(Cyprus ravioli)*[31]	903	98.5
Tsamarela[4]■	904	98.6	Purslane *(Portulaca oleracea)*[18]	844	92.0	Cyprus pita[32]	913	99.6
Cyprus pastrami[5]	913	99.6	Lapsana *(Sinapis alba)*[19]	839	91.5	Cyprus muffin[33]	916	99.9
Dusky spinefoot (*Siganus luridus*)[6]	900	98.1	Wild asparagus *(Asparagus acutifolius)*[20]	915	99.8	Olive bread[34]	915	99.8
Garavolli (*Snail*)[7]	910	99.2	Gavulya *(Notobasis syriaca)*[21]	631	68.8	Chickpea bread[35]	896	97.7
Coriander *(Coriandrum sativum)*[8]	914	99.7	Hawthorn *(Crataegus azarolus)*[22]	902	98.4	Hackberry rusks[36]	891	97.2
Kohlrabi *(Brassica oleracea gongylodes)*[9]	905	98.7	Carob *(Ceratonia siliqua)*[23]	914	99.7	Limassol dessert (Cone dessert)[37]	848	92.5
Common mallow *(Malva sylvestris)*[10]	904	98.6	Gonnara *(Zizyphus lotus)*[24]	845	92.1	Tavern/crop dessert[38]◘	859	93.7
Tagarninas *(Scolymus hispanicus)*[11]	790	86.2	Jujube *(Ziziphus jujuba)*[25]	846	92.3	Şambali[39]○	901	98.3
Hostes *(Cynara cornigera)*[12]	869	94.8	Indian fig *(Opuntia ficus-indica)*[26]	910	99.1	Gollifa[40]☼ *(Cyprus Ashura)*	909	99.1
Molehiya *(Corchorus olitorius*[41]	878	95.7	Pomelo *(Citrus maxima)*[46]	892	97.3	*Samsi*[49]▲	886	96.6
Bladder campion *(Silene vulgaris)*[42]	843	91.9	Unripe almond *(Amygdalus communis)*	915	99.8	*Gullirikya*[50]▼	796	86.8
Yellow star-thistle *(Centaurea hyalolepis)*[43]	617	67.3	Cyprus thyme *(Thymus capitatus)*	897	97.8	*Walnut jam*[51]	913	99.6
Artichoke *(Cynara scolymus)*[44]	910	99.2	Çakısdez *(Green olive)*[47]◊	916	99.9	*Hawtorn jam*	891	97.2
Wild artichoke *(Cynara cardunculus)*[45]	814	88.8	Pasedembo *(Pumpkin seeds)*[48]	912	99.5	*Pumpkin jam*[52]	908	99.0
Wild leek *(Allium ampeloprasum var. porrum)*	855	93.2	Pickled wild asparagus	900	98.1	Paphos red wine *(Commandaria)*[53]	894	97.5
Cinnara/Cinares (leaves of *Cynara cardunculus* plant)	625	68.2	Pickled capari leaves	915	99.8	*Zivania*[54]	914	99.7

□: grilled spicy meatballs wrapped in lamb/sheep abdominal fat, ■: sun-dried spicy meat, ◊: green olive which served with olive oil, garlic, sumac and coriander seed, ●: a soup made with bulgur, yoghurt and halloumi, ◘: a dessert made with curd and cream, served with honey, molasses, walnuts and pomegranates, ○: a sherbet dessert made with semolina, ☼: a dessert which is mixture of wheat, anise, pomegranate, raisin, almond, sesame and made for the New Year celebration, ▲: a fried dessert which made with almonds and cinnamon placed in the dough, ▼: dough boiled in molasses.

(Opuntia ficus-indica), "Gollifa" (*Cyprus Ashura*) and pumpkin jam were the most well-known traditional/local food items with a recognition rate of ≥99.0%.

On the other hand, yellow star-thistle (*Centaurea hyalolepis*), "Cinnara/Cinares" (leaves of Cynara cardunculus plant) and "Gavulya" (*Notobasis syriaca*), which are all natural indigenous herbs, were the least recognized food items (recognition rates from 67.3% to 68.8%).

DISCUSSION

Nutrition is commonly based on plants and local foods in the Mediterranean region. Most of the Mediterranean countries give enough importance to local production.[21] Cyprus is a Mediterranean island and the recognition rates of the local and traditional food items were quite high (up to 99.0%). The vegetation of Cyprus is very suitable for natural consumable herb growth.[10] However, the least recognized three food items were found to be natural indigenous herbs, namely, yellow star-thistle (*Centaurea hyalolepis*), Cınnara/Cinares (leaves of *Cynara cardunculus* tree) and Gavulya (*Notobasis syriaca*). *Centaurea hyalolepis* is an herb that has an important role on human health in terms of anti-cancer, anti-inflammatory and so on.[22] *Cynara cardunculus* is a flower head which is known as wild artichoke. It is a common part of some traditional Mediterranean dishes. The leaves of this plant are consumable.[23] Table 1 shows that 88.8% of the participants consumed *Cynara cardunculus* and 68.2% consumed the leaves of this plant. Another natural herb which has been shown to have an anti-inflammatory role on rats is *Notobasis syriaca*. Humans

have consumed it for more than 20 thousand years.[24] Furthermore, we have reported common recognition rates for common mallow (*Malva sylvestris*), tagarninas (*Scolymus hispanicus*), wild spinach (*Spinacia oleracea*), gavcar mushroom (*Pleurotus fuscus var. ferulae*), bladder campion (*Silene vulgaris*), Lapsana (*Sinapis alba*) and wild leek (*Allium ampeloprasum var. porrum*) (recognition rates are between 98.6% and 86.2%) (Table 1).

Hadjichambis et al.[25] designed a study about natural plants in seven Mediterranean countries. According to their results, Cypriots know different plants and different parts of the natural herbs distinctive from other Mediterranean regions. In addition, they use natural foods to make pickles and jam. According to Table 1, pickled capari (*Capparis spinosa*) leaves (99.8%), walnut (99.6%) and pumpkin jams (99.0%) were found to be the most recognized food items in the presented study.

Pickled *Cappariss spinosa* seeds, pickled Mangolla (*Eryngium creticum*) and pickled wild asparagus (*Asparagus acutifolius*) had high recognition rate (98.9-93.6%). Pickled vegetables and natural herbs show prebiotic effects on human health and their antioxidant capacities remain a long time after fermentation. Thus, they may show beneficial effects on human health with balanced consumption.[26]

The land of Cyprus is suitable for citrus production.[27] Islanders commonly recognized (97.3%) Pomelo (*Citrus maxima*) (Table 1). In addition, the main source of the public economy is vegetable and fruit production on the island so having a substantial knowledge about them is important.[3] There is production of celery stalks, zucchini (*Cucurbita pepo*), zucchini blossoms, purslane (*Portulaca oleraceace*), louvana (*Lathyrus ochrus*), Indian figs (*Opuntia ficus-indica*), unripe almonds, Molehiya (*Corchorus olitorius*), artichoke (*Cynara scolymus*) in Cyprus (recognition rates of 99.9% to 91.2%).

According to our results, Cyprus thyme (*Thymus capitatus*) had a 97.8% recognition rate. It is a spice which grows naturally in the Cyprus mountains.[28] *Opintia ficus-indica* is specific to the Mediterranean region. It includes a high number of anti-oxidants and can play an important role in the prevention of diseases.[29] Cypriots showed a recognition rate of 99.1% (Table 1). At the same time, they generally knew Gonnara (*Zizyphus lotus*) (92.1%). *Zizyphus lotus* grows generally in arid and semiarid countries such as Greece, Cyprus, Spain etc. It is part of the angiosperm *Rhamnaceae* family.[30]

Halloumi is known as Cypriot cheese. There is wide production, marketing and serving of halloumi on the island.[31] It has three types, namely, fresh, old and dried.[5] Recognition rates of them were 99.5%, 99.3% and 94.3%, respectively (Table 1). Paphos red wine (*Commandaria*) and Zivania are also produced in Cyprus. They are characteristic of Cyprus and have importance to the economy of the island.[6,32] According to the present study, participants recognized Zivania (99.7%) more than Paphos red wine (97.5%).

Paphos red wine and Zivania are both fermented alcoholic beverages. Fermented beverages play important roles on human's gut microbiota and health.[33] At the same time, red wine is a good source of resveratrol which is a beneficial phenolic compound.[34]

Although Cyprus is an island in the Mediterranean Sea, Cypriots displayed a preference for red meat compared to fish consumption.[35] In the current study, participants recognized Seftali kebab (99.7%), Cyprus pastrami (99.6%) and Tsamarela (98.6%) more than *Siganus lirudus* (98.1%) which is known as dusky spinefoot (Table 1).

Cyprus tarhana is a fermented dried soup which has probiotic effects. It is made with yoghurt, bulgur and halloumi.[36] Most of the participants recognized it (98.6%) (Table 1). Fermented foods which have probiotic contents may show positive effects on human gut microbiota.[37]

Pita is the most common bakery product in Cyprus culture. Nearly 500,000 pieces/day of Cyprus pita production is reported.[38] Participants recognized it with a rate of 99.6%. In addition, the population knew about Cyprus ravioli, Cyprus muffin, olive bread, chickpea bread and hackberry rusks which are some of the traditional bakery products of Cyprus (recognition rates of 99.9% to 97.2%).

Taro (*Colocasia esculanta*) is a tuber similar to a potato. Cyprus plays an important role in taro production all around world along with the United States of America and Canada.[39] The recognition rate of taro was found to be 99.5% in this study.

There are many traditional Cyprus desserts which are served in local restaurants and/or made at home.[11] According to Table 1, participants commonly recognized them (99.1-86.8%). High simple carbohydrate intake is related with many chronic diseases such as obesity, diabetes mellitus etc. so people should avoid the regular consumption of them.[40]

Study Limitations

The present study was initiated in 2020, which is known as the year of the Corona pandemic. All data were collected with online questionnaires and the Nutritional Memory Catalog. However, the Coronavirus disease-2019 pandemic led to a number of limitations while reaching out to more participants.

The current study was the first research which aimed to determine adults' traditional and local food item knowledge on the island of Cyprus. It has an important role in recording the islanders' data. In addition, the researchers developed the Nutritional Memory Catalog which includes some traditional and local Cyprus food items. Generally, the recognition rates of these food items were found to be more than 90.0%. On the other hand, natural indigenous herbs with health benefits were among the least recognized foods.

CONCLUSION

The modern world is seeking its early roots as human interactions with the planet are increasingly troublesome. This area is open for new research to address planet health, human health, food security, and cultural heritage. Thus, with so many new trends in food and human behavior, there is a need to highlight traditional/local food consumption and increase awareness of healthy Mediterranean herbs.

MAIN POINTS

- The current study is the first aiming to determine comprehensive traditional and local food knowledge on the island of Cyprus. It sheds light on these points as a Mediterranean Food Model:
- The recognition rate of traditional and local foods was found to be between 67.3% and 99.9%. The most recognized foods were vegetables, meat products etc. (recognition rates of ≥99.0%).
- Natural consumable herbs, which grow in the mountains, had the lowest recognition rates (<68.8%).

- There are photos of these traditional and local food items in this manuscript in order to introduce them to the world as a novel approach.

ETHICS

Ethics Committee Approval: This study had a local ethical compliance (approval number: NEU/2020/85-1198).

Informed Consent: The volunteers participated with online consent in accordance.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: T.D., A.O., Design: T.D., A.O., Supervision: T.D., A.O., Materials: T.D., A.O., Data Collection and/or Processing: T.D., A.O., Analysis and/or Interpretation: T.D., A.O., Literature Search: T.D., A.O., Writing: T.D., A.O., Critical Review: A.O.

DISCLOSURES

Conflict of Interest: No conflict of interest was declared by the authors.

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ORIGINAL ARTICLE

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Determining the Genetic Knowledge Levels of Oncology and Chemotherapy Nurses

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Abstract

BACKGROUND/AIMS: Genetics has a primary role in providing nurses with the ability to know their patients in every respect including preventive and therapeutic care, to diagnose symptoms of existing diseases, and to determine treatment processes and genetic diseases which may occur in future generations. This study was conducted to determine the genetic knowledge levels of oncology and chemotherapy nurses.

MATERIALS AND METHODS: The sample of this study was composed of 101 nurses who were working in oncology and chemotherapy units. This descriptive study was conducted between September 2018 and March 2019. The "Socio-demographic and Nurses' Characteristics About Genetics Data form" and "Genetic Knowledge test" were used as the data collection tools in this study.

RESULTS: The mean score obtained by the nurses from their answers to those questions relating to the contents about the genetic concepts was 5.01±2.75; the mean score they obtained from their answers to those questions about general genetic information was 7.43±1.88; and the total genetic knowledge mean score was 12.43±3.78. No effect of the characteristics of the nurses relating to genetic science on their genetic knowledge levels was determined ($p>0.05$).

CONCLUSION: It was observed that the genetic knowledge levels of the nurses working in the oncology and chemotherapy units were moderate. However, the nurses cared about developments in genetics and they were ready to provide the correct, appropriate and up-to-date genetic and genomic information, resources, services and/or technologies to their patients.

Keywords: Genetics, genetic science, oncology nursing, chemotherapy nursing

INTRODUCTION

The increase in genetic diseases, high rates of consanguineous marriages in Turkey compared to western countries, and the early diagnosis of genetic diseases with genome and molecular studies have increased the importance of medical genetic information.[1,2] Unlike many nursing fields, genetics is important at every stage of life and thus, it should be addressed in all patient groups ranging from newborns to geriatric care.[3] In different countries, the genetic counseling role of nurses is determined via associations and consensus. In contrast, some countries, such as Turkey, Hungary, and Germany, have no genetics nurses or counselors.[4] It is thought that this lack of genetic nursing or counseling increases the importance for nurses to have a full basic genetic knowledge regarding the fields they work in.

Advancements in genetics and especially in oncology, gastroenterology, pediatric and prenatal care fields have led to an increased demand for genetics and genetic healthcare and they have enabled nurses to develop both skill and information competencies about genetics in order to support clinical practices.[3]

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Nurses need to know the internal and external factors causing cancer, correctly comprehend the principles underlying human genetics, and integrate them into cancer genetics.[5] Individuals and families are informed and advised about their risks for passing on or inheriting diseases, their genetic and familial risk estimates, their individualized risk management, preventive measures, and their treatment options by including genetics and genomics in the care given by oncology nursing.[6]

Integrating this information into clinical nursing practices by nurses will enhance patient care quality.[5,7] In order to carry out the best practices for prevention, early diagnosis and/or care of genetic diseases, all nurses should receive education on genetics.[8] This study aimed to reveal whether nurses have adequate genetic knowledge levels or not. Thus, in the light of this information, it will be possible to make arrangements for in-service training to be planned for oncology and chemotherapy nurses. This study was conducted to determine the genetic knowledge levels of nurses working in oncology and chemotherapy units in private and public hospitals.

MATERIALS AND METHODS

Type of study: This was a descriptive study.

Population-sample: The population of this study was comprised of all the nurses working in the oncology and chemotherapy units of four private hospitals and one state hospital between September 2018 and March 2019. All the nurses working in the aforementioned services were determined as the population. By reaching the whole population, all the nurses, who agreed to participate in the study and who met the inclusion criteria, were included in this study (n=101). No sampling calculation was used to determine the sample size.

This study was conducted at inpatient clinics where patients were suffering from an oncologic disease and required long-term treatment. In addition, those patients with suspected tumor are also hospitalized in these services for follow-up during their diagnosis processes. Chemotherapy units where patients receive chemotherapy with one-day hospitalization and are discharged after the treatment were also included in this study.

Inclusion Criteria of the Study

*Working in the specified services for at least 3 months,

* Agreeing to participate in this study.

* Being 18 years old or over.

Exclusion Criteria

* Changing the service area between the dates of the study.

* Being on leave between the dates of the study.

Data collection method: The data were collected via face-to-face interviews. The nurses completed the surveys themselves. It took approximately ten minutes for each nurse to complete the surveys.

Data collection tools: In this study, the "Socio-demographic and Nurses' characteristics about Genetics Data form" and the "Genetic Knowledge test" were used as the data collection tools.

1. Socio-demographic and Nurses' Characteristics Regarding Their Genetics Data Form

In this form prepared by the researchers upon a literature review, there are a total of 15 questions including data about the socio-demographic and genetics characteristics of the nurses working in the oncology and chemotherapy units of the specified hospitals.

2. Genetic Knowledge Test

This test which was developed by the researchers in order to determine the competencies of nurses about genetic diseases comprises 20 questions about genetic concepts and genetic knowledge (Appendix 1). It was aimed to prepare questions based on the National Nursing Core Curriculum in order to examine the basic genetic knowledge of the nurses. For these questions, expert opinions were taken from 10 experts including seven faculty members from the nursing department, two faculty members from the molecular biology and genetics and one faculty member from the department of medical biology. The questions were sent to the experts in tables with tabs such as "Question Appropriate", "Question Not Appropriate", and "Your Suggestion" added to each questions. The questions were finalized in line with the feedback received from the experts.

There are 10 open-ended questions investigating the definitions of genetic concepts in the knowledge test. In the part questioning genetic information, there are 10 questions with True/False answer options. The highest score the participant can obtain from both parts is 10 and the lowest score is 0. Therefore, the highest score of the overall Genetic Knowledge Test is 20 and the lowest score is 0.

Ethical considerations: In order to conduct this study, written ethics committee approval with number: 2018/14/2 was obtained from the Ethics Committee of Acıbadem University. After informing the participants about the study subject, their verbal and written consent was obtained.

Statistical Analysis

SPSS 22.0 software was used to assess the data. Descriptive data were given as number, percentage, and mean. The data were analyzed using the Kruskal-Wallis test, the Mann-Whitney U test and Student's t-test.

RESULTS

The average age of the nurses participating in this study was 27.49±6.37 years. The average duration of the professional experience of the nurses was 6.15±6.79 years and their duration of working in their current services was 2.96±3.01 years. When examining the demographic characteristics of the nurses; 78.2% of the nurses were women and 66.3% of them were single. When examining the educational background of the nurses, 56.4% of the nurses had a bachelor's degree (Table 1).

The mean score obtained by the nurses from their answers to the questions about genetic concepts was 5.01±2.75, their mean score from their answers to the questions about their general genetic information was 7.43±1.88; and their total genetic knowledge mean score was 12.43±3.78.

The negative correlations of the nurses' professional experience duration and their cancer patients experience duration with their genetic knowledge score was not found to be statistically significant ($p>0.05$) (Table 2).

Table 1. Socio-demographic characteristics of the nurses (n=101)		
Gender	**n**	**%**
Female	79	78.2
Male	22	21.8
Marital status		
Married	33	32.7
Single	67	66.3
Educational status		
Health vocational high school	20	19.8
Associate	10	9.9
Undergraduate	57	56.4
Graduate	14	13.9
Position		
Responsible nurse	28	27.7
Intensive care service nurse	73	72.3
Working unit		
Oncology service	55	54.5
Chemotherapy	42	41.6
Internal medicine	4	4.0

Table 2. Correlation between the nurses' professional experience duration and their duration of experience with cancer patients and their genetic knowledge scores	
	Genetic knowledge scores, r/p
Duration of professional experience	-0.122/0.224
Duration of experience with cancer patients	-0.076/0.453
Pearson correlation analysis (r) was performed.	

When examining the genetics-related characteristics of the nurses, 27 (27.7%) participants stated that they had received training on genetics and genetic diseases before.

Twenty-one (20.8%) of those who had received this training received it while at school, 14 (13.9%) from in-service training, 15 (14.9%) from books and journals, 12 (11.9%) from seminars/courses/conferences, and 10 (9.9%) from the Internet. Six (5.9%) of the nurses obtained their knowledge about genetics from the media and television and 4 (4%) obtained it from their friends. The associations between the nurses' genetics-related characteristics and their genetic knowledge status were also analyzed. There was no statistically significant difference between the nurses' status of previously receiving any training on genetics/genetic diseases and their genetic knowledge level (x^2=0.054, p=0.973). There was no statistically significant difference between their level of caring about advancements in genetics and their genetic knowledge level (x^2=5,839, p=0.054). There was no statistically significant difference between the nurses' level of being aware of their own values and attitudes relating to genetics which may affect the care given to an individual and their genetic knowledge level (U=5.839, p=0.777). There was no statistically significant difference between the nurses' status of patients to make informed decision making about the genetics, volunteer in actions and defend autonomy rights and their genetic knowledge level (U=-1,465, p=0.143). There was no statistically significant difference between the nurses' status of all individuals to identify issues which may affect/prevent the rights of autonomy, making informed/enlightened decisions about genetics and volunteering in their actions and their genetic knowledge level (U=-0.473, p=0.632). There was no statistically significant difference between the nurses' level of providing accurate, suitable and up-to-date genetic and genomic information, resources, services and/or technologies to the patients in order to facilitate and support their decision making processes and their genetic knowledge levels (U=-0.473, p=0.632). There was no statistically significant difference between their level of providing accurate, suitable and up-to-date genetic and genomic information, resources, services and/or technologies to the individuals to facilitate and support their decision making process and their genetic knowledge levels (t=-0.444, p=0.658) There was no statistically significant difference between nurses' defining ethnic, social, cultural, religious, legal, financial and social issues relating to genomic information and technologies and their genetic knowledge levels (t=-0.625, p=0.533). There was no statistically significant difference between the effect of the nurses' characteristics about genetics and their genetic knowledge levels (p>0.05) (Table 3).

DISCUSSION

Rapid discoveries in genetics and genomics significantly affect all aspects of health care and help in the discovery of new treatments especially for cancer patients or in creating individualized treatment and care opportunities for people at high risk of cancer.[9] In this study, the genetic knowledge levels of nurses working in oncology and chemotherapy units were evaluated.

It was determined that the genetic knowledge level mean score of the nurses was 12.43±3.78. Considering that the highest score of the genetic knowledge test is 20, it can be asserted that the nurses' basic genetic knowledge levels were moderate. In other studies investigating nurses' opinions about their roles in genetic fields, it was determined that the nurses' knowledge about basic genetic information was insufficient and they needed training in this field.[10,11] Seven et al.[3] determined that nurses did not have sufficient knowledge about genetics and did not use it in their clinical practice. However, in the same study, it was reported that nurses were ready to learn more about genetics and that genetics should be integrated primarily into nursing education. Similar to the literature, it was determined in the present study that the genetic knowledge level of the nurses was not sufficient.

In the present study, 64.4% of the nurses had not previously received any training about genetics and genetic diseases. 20.8% of those who had received such training reported that they received the training during their professional education. Turaçlar et al.[12] determined that 97.1% of nursing and midwifery students received their genetic knowledge during their undergraduate education and they received 64.4% of this information from the child health and diseases course and 61.7% from the obstetrics and gynecology course during this education. Terzioğlu and Dinç[10] reported that 23.3% of the nurses in their study stated that they had received information about genetics during their professional education but this information was insufficient (Terzioğlu and Dinç[10]). Vural et al.[13] conducted their study with nursing students, and determined that most of the students had "very low" levels of knowledge about genetics but they had a high level of knowledge in terms of awareness about genetic abnormalities and diseases (lung, colon cancer, thalassemia etc.). A great majority of the students (93.9%) stated that they wanted to receive more training about genetic diseases and genetic counseling and this information was limited in their basic nursing education program.[13] Similarly, low genetic knowledge of oncology and chemotherapy nurses after graduation may be due to the

Table 3. Associations between the nurses' and genetics characteristics and genetic knowledge level (n=101)				
		Genetic knowledge levels total scores		
	n (%)	X ± SD	Statistics value	p
Status of receiving any previous training on genetics and genetic diseases				
Yes	28 (27.7)	12.57±3.40	0.973	0.054[1]
No	65 (64.4)	12.42±4.16		
I do not remember	8 (7.9)	12.00±.92		
Status of caring about the advancements in genetics				
Yes	77 (76.2)	12.95±3.92	5.839	0.054[1]
No	10 (9.9)	11.00±1.63		
I have no idea	14 (13.9)	10.57±3.34		
Status of being aware of their own values and attitudes related to genetics which may affect the care given to an individual				
Yes	82 (81.2)	12.49±3.76	-0.282	0.777[2]
No	19 (18.8)	12.1579±3.96		
Status of patients to make informed decision making about genetics, volunteer in actions and defend autonomy rights				
Yes	100 (99)	12.48±3.76	-1.465	0.143[2]
No	1 (1)	7.00		
Status of all individuals to identify issues that may affect/prevent the rights of autonomy, making informed/enlightened decisions about genetics, and volunteering in their actions				
Yes	72 (71.3)	12.53±3.63	-0.473	0.632[2]
No	29 (28.8)	12.17±4.18		
Status of providing accurate, suitable and current genetic and genomic information, resources, services and/or technologies to the individuals to facilitate and support their decision-making process				
Yes	68 (67.3)	12.31±3.83	-0.444	0.658[3]
No	33 (32.7)	12.67±3.71		
Defining ethnic, social, cultural, religious, legal, financial and social issues related to genomic information and technologies				
Yes	56 (55.4)	12.21±3.87	-0.625	0.533[3]
No	45 (44.6)	12.69±3.69		

[1]Kruskall-Wallis, [2]Mann-Whitney U test, [3]t-test, SD: standard deviation.

Appendix 1. Match the following concepts related to genetic with their definitions				
Genetic knowledge test				
Genetic concepts				**TERMS**
1) What is the structure that carries the hereditary characters of living individuals and transfers them from generation to generation?				
2) What are the areas where the genes are located on the chromosomes called?				
3) What is the genetic disorder causing down syndrome?				
4) What cell division creates gametes?				
5) What is the genetic material the child inherits only from the mother?				
6) What is the chromosomal abnormality which is also known as "Turner Syndrome"?				
7) What are the genes with the potential of causing cancer when mutated despite having important biological functions in healthy individuals called?				
8) What are the genes with the potential of causing cancer when mutated but prevent cancer formation in cells in healthy individuals called?				
9) What is the condition which may cause a nucleotide change in the DNA?				
10) What is the name of the procedure in which an individual or species is/are ranged on the basis of their number, size and shape after their chromosomes are paired as identical chromosomes?				
a. Trisomy 21	**b. Meiosis**	**c. Genome**	**d. Monosomy X**	**e. Tumor suppressor gene**
f. Mutation	**g. Locus**	**h. Karyotyping**	**j. Mitochondrial DNA**	**k. Proto-oncogen**

Specify the following knowledge related to genetic diseases as "true" or "false"		
Genetic knowledge	**True**	**False**
1) After completing the human genome project, the meaning of the associations between genetics and diseases has been explained.		
2) Some viral infections may cause cancer.		
3) Cancer is basically a multifactorial disease.		
4) Unless an individual has a genetic disease in their family, neither she/he nor her/his descendants will develop any genetic disease.		
5) Characterized by alpha or beta-globin deficiency; "Thalassemia" is a genetic disease.		
6) There is no repair mechanism in cells to prevent the development of permanent mutations caused by DNA damage.		
7) There is a direct correlation between HPV and cervical cancer.		
8) Mitochondrial DNA is passed on from father to son.		
9) Autosomal inherited genetic diseases are independent of gender.		
10) There is a correlation between the *BRCA1* or *BRCA2* gene mutation and hereditary breast or ovary cancer.		
HPV: human papilloma virus.		

fact that genetics is mostly included as a sub-subject in their courses rather than as a separate course integrated in the undergraduate curriculum.

In previous studies, it has been reported that nurses did not have information about delivering genetic-based healthcare service and they did not use it in the clinic.[14-16] A systematic review reported that the genetic and genomic knowledge of nurses was not sufficient to deliver suitable genetic healthcare services, for example, to determine if a condition may be genetic, to understand and explain genetic diseases and its risks to a family or to direct families to specialized services. In a study conducted with nursing students, student nurses stated that preparing a person for a genetic test, taking the medical history of a person, counseling a family before genetic tests, and providing psychological support to the family were their nursing roles and responsibilities. They stated that their levels of dealing with genetic test results, conducting research on genetic test and the counseling process under the roles and responsibilities of nurses were at a very low rate.[16] This may show that the roles and responsibilities of the nurses regarding the use of genetic information have been misplaced in the undergraduate education system and thus, nurses could not improve themselves sufficiently in this field. In the present study, it was thought that the nurses' knowledge levels had no correlation with their duration of experience in providing care to cancer patients or their total duration of professional experience since the nurses have insufficient genetic knowledge and do not use their knowledge about genetics in their clinical practices sufficiently.

CONCLUSION

Consequently, it was observed that the genetic knowledge levels of those nurses working in oncology and chemotherapy units were moderate. However, two important results obtained in this study were that most of nurses working in oncology and chemotherapy units cared about developments in genetics and they are ready to provide accurate, appropriate and up-to-date genetic and genomic information, resources, services, and/or technologies to individuals in order to support and facilitate the decision making of their patients. Therefore, education programs which will increase the knowledge levels of oncology and chemotherapy nurses should be organized and nurses should be supported institutionally. In addition, genetics can be recommended to be included in nursing undergraduate programs in order to improve nurses' roles and responsibilities about genetics.

MAIN POINTS

- The nurses' knowledge about basic genetic information was insufficient and they need education in this field
- The nurses' knowledge levels had no correlation with their duration of experience in providing care to cancer patients or the total duration of their professional experience
- There was no difference between the genetic information levels with respect to the characteristics of the nurses related to genetic science.

ETHICS

Ethics Committee Approval: In order to conduct this study, written ethics committee approval with number: 2018/14/2 was obtained from the Ethics Committee of Acıbadem University.

Informed Consent: Written informed consent was obtained from the nurses who participated in this study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: V.K., Design: V.K., D.Y., M.Y., Supervision: V.K., D.Y., Fundings: V.K., D.Y., M.Y., Data Collection and/or Processing: V.K., D.Y., Analysis and/or Interpretation: V.K., Literature Search: V.K., D.Y., M.Y., Writing: V.K., D.Y., Critical Review: V.K., D.Y., M.Y.

DISCLOSURES

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The Relationship between the Use of Complementary and Alternative Medicine in Cardiovascular Diseases with Self-Care Ability and Life Quality

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Abstract

BACKGROUND/AIMS: Cardiovascular diseases are one of the leading global causes of morbidity and mortality. Lifestyle changes are critical for the prevention of cardiovascular diseases and improving self-care levels during treatment. This study aimed to explore the relationship between the use of complementary and alternative medicine (CAM) and the quality of life and self-care ability in individuals with cardiovascular disease.

MATERIALS AND METHODS: The study population in this cross-sectional and correlational research consisted of cardiovascular patients hospitalized in a public hospital between 1st April and 30th June 2018. One hundred and six patients agreeing to participate in this study were selected for sampling. A Patient Information Form, the Exercise of Self-Care Scale, and the World Health Organization Quality of Life Scale-Short Form were employed as the data collection tools.

RESULTS: The mean age of the patients in this study was 62.83±1.40 years, 59.4% were women, and 34.0% had coronary heart disease. The patients' mean self-care score was 101.18±22.31, and their mean quality of life score was 28.61±9.50. Age, education, diagnosis and duration of disease, constipation, and CAM use were found to affect their quality of life ($p<0.005$). A positive correlation was determined between CAM use and self-care ability.

CONCLUSION: The use of CAM in individuals with cardiovascular disease has a positive effect on self-care ability and enhances their quality of life.

Keywords: CAM, cardiovascular, quality of life, self-care

INTRODUCTION

Despite significant advances in modern medicine, complementary and alternative medicine (CAM) is still widely used. The general reported prevalence of CAM worldwide is 9.8-76.0%[1] and 46.2% in Turkey, which is higher than in many other countries.[2]

The use of CAM has recently gained more attention in cardiovascular diseases, the leading global cause of deaths among non-infectious chronic diseases.[3] The literature cites that individuals with cardiovascular disease often use CAM, particularly herbal products, and mind-body therapies.[4-6] It has been also reported that CAM is used for overcoming anxiety and losing weight in cardiovascular diseases.[6]

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In addition to the use of CAM, self-care, which is defined as the individuals' fulfilling their responsibility to protect and improve their health, is reported to be a significant parameter in achieving the positive management of cardiovascular diseases and compliance with treatment, and thus in raising the quality of life.[7,8] Self-care is affected by several factors and is a determinant of quality of life.

Nurses are now required to take part in widely used complementary therapies. Parallel to this, there have been changes in the roles and responsibilities of nurses, and nurses are expected to develop nursing practices regarding the use of complementary and alternative approaches, determine effective methods, and use complementary therapies for healthy/sick individuals in a reliable and appropriate manner.[9]

Recent studies have shown that studies on self-care strength and quality of life are most focused on cancer[10,11], while in chronic diseases, they indicate the relationship between CAM use and self-care related to diabetes, migraines, asthma, and self-care.[12,13] It is stated that cancer patients most benefit from methods such as vitamin and mineral mixtures, herbal therapy, and meditation[14], whereas people with chronic diseases use dietary supplements, mind-body practices, and herbal therapy as a complementary treatment method in addition to their medication.[15-17] It has been emphasized in the relevant literature that there are only a limited number of research results specific to cardiovascular diseases. Although it is noted that methods such as herbal therapy, supplemental food intake, etc. are being applied, there exists no study on their effects on self-care and quality of life.

The purpose of this study was to determine the effects of CAM use in cardiovascular diseases on the self-care levels and the quality of life of individuals.

Research Questions

1. What is the rate of use of CAM in cardiovascular diseases?

2. What is the relationship between the patients' use of CAM and their self-care levels?

3. What is the relationship between the patients' use of CAM and their quality of life?

4. Is there a significant difference in the self-care levels and quality of life in individuals with cardiovascular disease?

MATERIALS AND METHODS

Type of Research

The research was designed as a descriptive, cross-sectional and correlational study.

Research Population and Sampling

The research population consisted of individuals hospitalized in the internal diseases and cardiology clinics of a public hospital in Turkey between April and June, 2018. No sampling was performed; the entire population was included in the study. All voluntary patients (n=189) who were conscious and over 18 years old and who had at least one cardiovascular disease were included in this study at the specified clinics at the time of the study. This study was completed with 106 patients who filled out the questionnaires.

Data Collection Tools and Data Collection Process

Data collection tools were the Patient Introduction Form, The World Health Organization Quality of Life Scale-Short Form, and the Exercise of Self-Care Scale. The data were collected by the researchers from hospitalized patients using a face-to-face interview technique at the clinic.

Patient Information Form

Developed by the researchers, this form consists of two parts. The first part includes questions investigating the patients' socio-demographic characteristics (sex, age, marital status, education, and smoking status), and the second part investigates CAM use and the methods employed.[1,4,7-11]

The World Health Organization Quality of Life Scale-short Form (WHOQOL-BREF)

The reliability and validity of the Turkish-language version of this scale, developed by the WHO Quality of Life Group (1996) to assess how individuals perceive their own quality of life, were investigated by Fidaner et al.[18] The Cronbach's alpha of the scale was 0.85. It consists of four domains (physical, psychological, social relationships, and environmental) and 26 questions. When the Turkish version is employed (a 27th question is a national one). The environmental domain score is described as environment-TR. Scores range between four (4) and twenty (20), with higher scores indicating a higher quality of life. The scale's Cronbach alpha value in this study was 0.814.

The Exercise of Self-Care Scale

The Exercise of Self-Care Scale (ESCA) is a five-point Likert-type scale used to evaluate an individual's performance of self-care activities. The scale was developed by Kearney and Fleischer in 1979[19], the Cronbach's alpha of this scale was 0.92 and its Turkish-language reliability and validity were investigated by Nahcivan.[20] ESCA consists of 35 items, each scored between zero (0) and four (4). Eight items (3, 6, 9, 13, 19, 22, 26, and 31) are reverse scored. The total possible scores range between 35 and 140 with higher scores indicating a higher self-care ability. The scale's Cronbach alpha value in this study was found to be 0.916.

Ethics

Approval for this research was granted by the Gümüşhane University Non-Interventional Clinical Research Ethical Committee (approval number: 2018/3). Written permission was obtained from the institution where the study was performed, and informed consent was received from the patients in line with the principle of voluntary participation. This study was conducted in accordance with the principles of the Declaration of Helsinki.

Statistical Analysis

For the statistical analysis of the data, the statistical package for social sciences (SPSS) 23 program was used. Continuous variables are expressed as median values (25th-75th percentiles) and categorical variables as numbers (percentages). Non-normally distributed variables were compared between the groups using the Mann-Whitney U test, the Kruskal-Wallis test, and Spearman's correlation analysis.

RESULTS

The analysis of the patients' demographic characteristics revealed that the mean age of participants was 62.83±1.40 years (min: 60, max: 96),

59.4% were women, 83% were married, 46.2% were literate, 49.1% were housewives, and 73.6% smoked. Thirty-four percent of the participants had coronary heart disease, 68.8% had had chronic diseases for more than 10 years, and 32.1% experienced constipation. The rate of CAM use among individuals with cardiovascular disease was 38.7% (Table 1).

The Exercise of Self-Care Scale and Quality of Life scores according to various socio-demographic characteristics are shown in Table 2. The comparison of the mean quality of life scores in terms of the patients' education levels revealed a significantly higher mean score among 'literate' patients (p=0.000). A significant difference was observed in the mean self-care and quality of life scores, with hypertensive patients recording significantly higher self-care (p=0.008) and quality of life scale (p=0.001) scores than those patients with other diseases. The mean quality of life score of those patients who reported experiencing constipation was significantly higher than that of those patients without constipation (p=0.005). Patients using CAM recorded a significantly higher mean quality of life score than those patients not using CAM (p=0.005). No statistically significant difference was determined between the patients' CAM use and Exercise of Self-Care Scale scores (p>0.05). A significant relationship was found between age and the quality of life mean scores, with quality of life rising with age (p=0.000). Quality of life scores also increased in line with disease duration (p=0.001) (Table 2).

The patients' mean self-care and quality of life scores were 101.18±22.31 and 28.61±9.50, respectively. A significant positive weak correlation was observed between CAM use and the patients' self-care (r=0.249 p=0.014) and quality of life (r=0.213 p=0.021) (Table 3).

DISCUSSION

Individual self-care is important in the management of cardiovascular diseases, and CAM use, which may have an impact on the quality of life, is becoming more widespread day by day. The purpose of the present study was to determine the relationship between CAM use and self-care and quality of life among individuals with cardiovascular disease.

Scientific advances have led to an improved understanding of the pathophysiology of numerous diseases, thus leading to evidence-based applications. However, CAM continues to be widely used, both by itself and in addition to modern treatment. A moderate level of CAM use (38.7%) was determined among cardiac patients in the present study, and its use was higher among men than women. In terms of CAM use among individuals with heart disease in the literature, one in three patients with myocardial infarction were reported to use CAM,[21] while Bahall reported that 56.2% of their patients used CAM,[22] Greenfield et al.[23] reported a rate of 31.7%, and Krasuski et al.[24] a rate of 54%, which shows that CAM use is widespread across the world.

Most patients (61.3%) in this study did not discontinue the treatment recommended by physicians, which reveals a high confidence in modern medicine and also that CAM is not fully trusted.[25] In addition, the cardiac conditions shown in Table 1 may require the use of anticoagulants such as aspirin, heparin, warfarin, and clopidogrel which can react with several herbal products widely employed by patients. However, the likelihood of plant-plant and plant-drug interactions and herbal toxicity may be overlooked by patients who regard natural products as "safe".[26]

No statistically significant difference was found between the patients' education levels and self-care. Several previous studies have reported that patients' education levels and their receiving education about

Table 1. Distribution of participants' socio-demographic characteristics (n=106)

Descriptive information	n	%
Age (mean ± SD)	**(62.83±1.40) (min: 60, max: 96)**	
Sex		
Female	63	59.4
Male	43	40.6
Marital status		
Married	88	83
Single	18	27
Education		
Literate only	49	46.2
Elementary school	35	33.0
Middle school	9	8.3
High school	8	7.5
University	5	4.5
Occupation		
Retired	27	25.5
Clerical	4	3.8
Self-employed	19	17.9
Housewife	52	49.1
Not working	2	1.9
Smoking status		
Smoker	7	6.6
Non-smoker	78	73.6
Quit smoking	21	19.8
Type of cardiovascular disease		
Hypertension	27	25.5
Coronary artery disease	36	34.0
Chronic heart failure	11	10.4
Other**	32	30.1
Duration of disease		
10 years or less	73	68.8
11-20 years	13	12.4
21-30 years	17	16.0
30 years or more	3	2.8
Constipation		
Yes	34	32.1
No	72	67.9
CAM use		
Yes	41	38.7
No	65	61.3
Continuing to use treatment recommended by a physician		
Yes	65	61.3
No	41	38.7

SD: standard deviation, CAM: complementary and alternative medicine, min.: minimum, max.: maximum.

Table 2. Patients mean Exercise of Self-Care and Quality of Life Scale scores by various socio-demographic characteristics (n=106)

Socio-demographic characteristic	Exercise of self-care scale	Quality of life scale
Education	Median (25^{th}-75^{th} percentile)	Median (25^{th}-75^{th} percentile)
	93 (80.5-113)	30 (24-38)
Literate only[a]	115 (93-126)	28 (27-34) a>b=c=d=e
Elementary school[b]	103 (92-120)	24 (21-29)
Middle school[c]	103 (92.5-117.5)	24.5 (21-28.2)
High school[d]	99 (92.5-123)	20.5 (19-24.2)
University	p=2,237[a]	**p=0.001**
Diagnosis	122 (89-133)	31 (28-37)
Hypertension[a]	100 (89-113)	25 (22-29.7)
Coronary heart disease[b]	83 (67.5-91.2)	29 (25-38) a>b=c=d
Chronic heart failure[c]	95 (90-103)	23 (21-27.5)
Other [d]	**p=0.008**	**p=0.001**
Constipation	97 (89-113)	25 (21-29.7)
Yes	99 (89-121)	29 (23.7-40.5)
No	**p=0.766**	**p=0.028**
CAM use	98 (87.0-121.0)	29 (23.0-32.2)
Yes	92 (90.7-124.0)	25 (21.0-28.0)
No	**p=0.035**	**p=0.005**
Age	r=-0.074	r=0.521
	p=0.468	**p=0.001**
Duration of disease	r=0.164	r=0.353
	p=0.130	**p=0.001**

CAM: complementary and alternative medicine.

Table 3. Patients' CAM use, mean self-care and quality of life scores, and relationships between them

			CAM use	Quality of life	Self-care level
Variable	**Mean ± SD**	**Median (min.-max)**	**r**	**r**	**r**
(1) CAM use	-	-	**1**		
(2) Quality of life	28.61±9.50	26.00±9.50 (17-67)	0.213*	1	
(3) Self-care level	101.18±22.31	98.0±22.31 (46-139)	0.249*	-0.013	1

SD: standard deviation, r: Pearson correlation coefficient, *: p<0.05, min.: minimum, max.: maximum, CAM: complementary and alternative medicine.

their diseases affects their learning needs and improves their self-care behaviors.[27-29] A significant correlation was observed in the present study between the patients' education levels and their quality of life scores. This was found to derive from the literate group. While some studies have reported that a low level of education is associated with a poorer quality of life[30], other studies have reported that those patients who have received higher education have low quality of life values.[31,32] These discrepancies may be attributed to differences in sampling and age groups, and to different tools being used to measure quality of life. In addition, individuals with high levels of education may also have higher self-expectations but may have reported lower quality of life since they are unable to meet those expectations because of their diseases.

It is stated in the literature that chronic disease is one of the strongest determinants of health-related quality of life. Annaç[33] showed that the quality of life of cardiovascular patients is generally low. Snarska et al.[34] argue that patients with hypertension have determined their quality of life at a good or medium level in the physical, psychological, social, and environmental domains. Cardiovascular diseases are more exposed to physical and psychological symptoms and have inadequate coping mechanisms.

Although it is not a disease, constipation is an important societal health problem interpreted differently by individuals.[35] No statistically significant relationship was observed in the present study between constipation status and self-care levels. However, a significant relationship was determined between the patients' experiencing constipation and their quality of life, with those patients experiencing constipation have a significantly poorer quality of life. Previous studies have also reported that constipation adversely impacts individuals' quality of life.[36-38]

No significant relationship was observed between the patients' ages and their self-care levels, which contradicts with the results of previous studies investigating the relationship between age and self-care. Some studies report that self-care improves with age[39,40], and others argue that it decreases with age[26], still others report no significant relationship as in the present study.[29,30] However, a positive correlation was observed in this study between age and quality of life scores. Hickey et al.[41] indicated that elderly individuals scored lower on their quality-of-life scale physical domain, but better on the mental domain and that the elderly exhibited better satisfaction and coping skills. In their systematic review, Baert et al.[42] reported a positive correlation between age and

quality of life. Various studies have shown that although their physical health worsens, individuals' quality of life can remain high on condition that their scores on other domains and enjoyment also remain high.[42,43] It may be concluded that quality of life increases with increased life expectancy, on condition that this is accompanied by a reasonable level of mental and physical health and increasing socialization.

Patients endeavor to ameliorate their symptoms, improve their quality of life and self-care levels, and potentially treat their diseases. Greene reported that patients experienced greater strength, increased hope, and psychological support following CAM use.[34] Votova and Wister[44] showed that self-care attitudes and spirituality were important predictors of CAM use. Kristoffersen et al.[45] showed that people use CAM in response to a perceived risk of developing CHD, and to prevent disease and to maintain their health. Findings concerning CAM use for the enhancement of quality of life in cardiovascular diseases have generally been positive.[21,44-48] Some degree of improvement in the quality of life has been reported six months after hospitalization in patients admitted due to acute coronary syndrome.[19] Consistent with the previous literature, patients using CAM exhibited greater self-care and a better quality of life.

In this study, the use of CAM was found to increase the quality of life and the self-care ability of the patients. In the literature, some studies have shown that CAM is widely used to reduce the adverse effects of many diseases such as cardiovascular diseases and to increase the quality of life.[49-51] The importance of CAM use in cardiovascular diseases, especially in individuals at risk, has been reported.[52] In another study on the use of CAM for the prevention and treatment of cardiovascular diseases, including hypertension, hyperlipidemia, coronary artery disease, heart failure, and arrhythmias, it was reported that the use of CAM significantly improves the quality of life.[53] At the same time, some sources emphasize that when the appropriate CAM method is applied, tolerance to the disease, quality of life, and self-care ability increase.[54-56] Our findings are consistent with the literature.

Study Limitations

The main identified limitation of this study is that it was carried out with hospitalized patients with a diagnosis of cardiovascular disease in internal medicine and cardiology services between April and June, 2018 in a public hospital; therefore, it cannot be generalized to all patients diagnosed with cardiovascular disease.

CONCLUSION

Patients with cardiac problems such as chronic heart failure, angina, and hypertension are reported to use CAM. Since existing evidence-based studies regarding CAM use have not yet produced definite conclusions, further scientific research on this subject is required. In addition to prescription cardiovascular medications, health care professionals should therefore educate patients about the possible dangers of other drugs, vitamins, and herbal supplements which they may use without the knowledge of a physician or a prescription.

It is recommended that healthcare professionals have knowledge about the use and benefits of CAM. Also, that the CAM methods used in diseases are questioned in terms of medical history of the patients so that these methods are determined to enhance the self-care ability and quality of life in patients with different diagnoses.

ETHICS

Ethics Committee Approval: Approval for this research was granted by the Gümüşhane University Non-Interventional Clinical Research Ethical Committee (approval number: 2018/3).

Informed Consent: Written permission was obtained from the institution where the study was performed, and informed consent was received from the patients in line with the principle of voluntary participation.

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Author Contributions

Design: N.K., S.U., Data Collection and/or Data Processing: N.K., A.A.S., S.U., Analysis and/or Interpretation: N.K., Literature Search: N.K., S.U., A.A.S., Writing of the Article: N.K., S.U., A.A.S.

DISCLOSURES

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Working Conditions and Quality of Life of Cancer Survivors: A Cross-Sectional Study

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Abstract

BACKGROUND/AIMS: Work ability, which is based on the self-report of individuals while they work, is the strongest predictor of cancer survivors' (CS) return to work. This study aimed to investigate the working conditions and quality of life (QoL) of individuals with cancer who survived after receiving cancer treatment.

MATERIALS AND METHODS: The sample of this cross-sectional and correlational survey type study consisted of 262 CSs. Data were collected using the Socio-Demographic and Health Information Questionnaire, the SF-36 Health-Related Quality of Life (HRQoL) and the Work Ability Index (WAI).

RESULTS: Of the 262 CSs who participated in this study, 21.4% were employed. The mean score obtained from the WAI by the employed CSs was 33.20. The mean scores the employed CSs obtained from the physical functioning and role physical subscales of the SF-36 HRQoL were higher than those of the unemployed CSs ($p<0.05$). There was a correlation between the mean score of the employed CSs obtained from the overall WAI and the mean scores they obtained from all the sub-dimensions of the SF-36 QoL scale ($p=0.01$). The strongest correlation was found between the WAI and the Social Functioning subscale of the HRQoL (SF-36).

CONCLUSION: The QoL of the employed CSs was better than that of the unemployed CSs and there was a correlation between their work ability and QoL.

Keywords: Cancer survivors, return to work, quality of life

INTRODUCTION

Cancer, which leaves deep scars on the physical, psychological, spiritual, economic and social conditions of individuals, is one of the most common diseases of modern life.[1] Working-age individuals (aged 15-64 years) represent around 40% of all newly diagnosed cancer patients in Europe.[2] Despite the increase in the number of new diagnoses, thanks to early diagnosis and effective treatment strategies, the rate of cancer survival is increasing day by day. According to the International Agency for Research on Cancer, there were 18 million new cancer cases worldwide in 2018, and 43.8 million cancer patients who had been diagnosed within the previous 5 years were still alive.[1] Thanks to the increase in life expectancy, working age, and survival rates in cancer patients, the labor force participation rates have also increased for people with chronic illnesses such as cancer.[3] Approximately 50% of those newly diagnosed with cancer and more than one third of cancer

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survivors (CSs) were in their working age.[4] The risk of unemployment within 10 years after a cancer diagnosis is 1.31 times higher in all patients diagnosed with cancer, 2.71 times higher in those individuals diagnosed as having a brain tumor, and 1.66 times higher in those individuals diagnosed with lymphoma.[5]

The rate of return to work (RTW) after cancer treatment is affected by disease-related factors (type and degree of cancer, type and duration of treatment, relapse status, presence of sequelae), CS-related factors (age, sex, physical activity status, income status, participation in family's income etc.) and job-related factors (laws of the country regarding work life, social security, retirement age, wages, re-employment, working hours, activity required by the job, difficulty of work).[6-8] RTW rates in CSs range from 39% to 77%.[3] It is known that RTW rates are higher in those people diagnosed with breast, colon and prostate cancers,[9] and that many individuals with breast cancer continue to work after their diagnosis.[10]

Work ability, which is based on the self-report of individuals while they work,[11] is the strongest predictor of CSs' RTW[12]. Problems related to cancer and its treatment may continue after the treatment is completed and traces of these problems can be observed throughout the survivor's life. CSs face many physical difficulties (e.g. fatigue)[13], and symptoms of neurocognitive disorder,[9] cognitive (e.g. brain fog) and psychological side effects (e.g. depressive symptoms).[6,7] The sequelae of cancer treatments also adversely affect individuals.[6] Widespread views and social image that the prognosis of cancer is poor may negatively affect work ability as well. There are several studies on RTW and the work ability of individuals with cancer. Most of these studies were conducted in Nordic and western countries.[6,9,10,14-16] However, the results on samples from different countries are of great importance because they indicate work ability and RTW levels of individuals with cancer, and also because business culture, work values and working conditions differ from country to country. For example, the working hours which are officially eight hours in Turkey are longer than in Nordic countries.[16] In some countries such as Japan, employers do not have a legal obligation to hire individuals with disabilities such as CSs.[17] In Turkey, according to the labor act number 4,857, 3% of employees in the private sector and 4% of employees in the public sector should be people with disabilities. CSs who are considered to be up to forty percent disabled are among these people with disabilities.[18] Our search for studies investigating the employment status, quality of life (QoL) and work ability of cancer patients demonstrated a gap in the Turkish literature. The purpose of the authors in this cross-sectional study was to investigate the working conditions and QoL of individuals who were diagnosed with cancer and who received cancer treatment. In this context, the research questions are as follows: 1) What is the employment rate and RTW rate among CSs? 2) What is the level of the QoL of employed and unemployed CSs? 3) Is there a relationship between the work abilities and the QoL of employed CS?

MATERIALS AND METHODS

Design

The present study had a cross-sectional and correlational design. This study was conducted with individuals who were admitted to the outpatient clinic of the medical oncology clinic of a training and research hospital and who met the inclusion criteria (n=262). During the six-month data collection process (November 2018-April 2019), CSs who were selected using a non-probability sampling method were interviewed.

The inclusion criteria of the study were as follows: being in the 18-65 age group, having been diagnosed with cancer after the age of 18, knowing that they were diagnosed with cancer, not having active cancer treatment, having no cancer treatment-related complications, having no hearing or vision impairment or mental problems which might interfere with their participation in the study, and volunteering to participate in the study. Of the cancer patients, those who met the inclusion criteria gave their written consent. Data were collected in the outpatient clinic room using a face-to-face interview method between 8.30 a.m. and 4.30 p.m. on weekdays. During the six-month data collection process, 262 individuals were interviewed. As some individuals were interviewed more than once during the data collection process, a post hoc analysis was performed in the G*power 3.1 program (effect size 0.20, α=0.05). After the power of the study was determined to be 94%, the data collection process was terminated.[19]

The ethics committee permission of the study was obtained from the İzmir Katip Çelebi University Non-Interventional Clinical Research Ethics Committee (approval number: 2018/10). Written consent was obtained from cancer patients participating in this study.

Instruments

1. Socio-demographic and health information questionnaire: This questionnaire includes 10 items questioning the participants' socio-demographic characteristics, cancer type, treatment type, employment status, and working conditions if the person is employed.[6,10,12,14,15]

2. SF-36 health-related quality of life: The HRQoL developed by Ware and Sherbourne[20] in 1992 is a self-assessment form comprising 36 items. It was adapted to Turkish by Pınar.[21] It has eight subscales: Physical functioning (10 items), social functioning (2 items), role limitations caused by physical health problems (4 items), role limitations caused by emotional problems (3 items), emotional well-being (5 items), vitality (energy and fatigue) (4 items), bodily pain (2 items), and general health perceptions (5 items). An additional single item assesses changes in perceived health. The items in the form investigate the person's health-related quality of life (HRQoL) during the past four weeks. The HRQoL can be rated by taking into account each subscale separately or under two subgroups; namely the physical and the mental subscales. As the score obtained from the form increases, so does their QoL. The Cronbach's alpha value of the original scale was 0.92. It was 0.93 in the present study. This form was administered to all the participants.

3. Work ability index: This index, developed in the early 1980s, has been adapted to more than 30 languages and is used to assess an employee's health, mental and social abilities, and their compliance with the physical and mental requirements of the work done.[11] The WAI consists of seven items. The minimum and maximum possible scores to be obtained from the index are 7 and 49 respectively. The higher the score is, the better the individual's work ability is. Those scores ranging between 7 and 27 indicate poor work ability, between 28 and 36 indicate moderate work ability, between 37 and 43 indicate good work ability and between 44 and 49 indicate excellent work ability.[13] In the Turkish adaptation study of the WAI, the Cronbach's alpha value was calculated to be 0.72.[22] In the present study, it was 0.71. The index was filled in by those currently employed.

Statistical Analysis

The Statistical Product and Services Solutions (SPSS) for Windows 22.0 (SPSS, Inc., Chicago, IL) was used to analyze the data collected. There was no missing data because the data were collected by the researchers through face-to-face interviews. In the analysis of the data, descriptive statistics such as numbers, percentage distribution, arithmetic mean, standard deviation and median were used. As the scale scores were not normally distributed, the Mann-Whitney U test was used to compare two groups, and the Kruskal-Wallis test was used to compare three groups. Spearman's correlation coefficient was used to compare scale scores. The chi-square test was used to compare the categorical data of the employed and unemployed participants. The statistical significance level was set at $p<0.05$ at the 95% confidence interval.

RESULTS

The mean age of the participating CSs was 50.87±9.53 years (employed ones: 44.82±8.78; unemployed ones: 52.51±9.06) (minimum: 20, maximum: 64). The mean age of the employed participants was lower than that of the unemployed participants ($p<0.05$). Their median years of education was eight years (minimum-maximum: 0-15). Of them, male participants, those with a higher education level, those who underwent only surgical operations, those who had no chronic disease comorbid with cancer, and those diagnosed with testicular cancer had longer working lives than the other participants ($p<0.05$). The employment rate was lowest among those CSs diagnosed with colon and breast cancer, and those having undergone all the three treatment types ($p<0.05$). There was no correlation between the participating CSs' employment status and their marital status or perceived income level ($p>0.05$) (Table 1).

Currently, of the participants, 21.4% (n=56) were employed and 78.6% (n=206) were not. However, before they were diagnosed with cancer, 81.5% (n=212) of them did not work, but 18.5% (n=50) of them were employed (Table 2). Of the employed participants, the most popular sector was the private sector (41.1%) and 60.7% were full time workers. Of the employed participants, 46.4% were away from work for up to 180 days (6 months) and 37.5% for more than 12 months. When the participants were asked "Do you think your illness has prevented you from working?", 76.8% of them stated various reasons. Seven of the CSs had problems at work due to their health. The problems that they had were as follows: not being able to do heavy work (n=4) and not getting a leave of absence from work (n=3) (Table 1). The mean score of the Work Ability Index was 33.20±8.42, and 44.6% of CSs had a good level of work ability (Figure 1).

Of the participants, those who were employed obtained higher scores from the Physical Functioning and Role Limitations Caused by Physical Health Problems sub-dimensions of the SF-36 HRQoL than those who were not employed ($p<0.05$). As for the other sub-dimension scores, there were no differences between the employed and unemployed CSs ($p>0.05$) (Table 3). There was a moderate positive correlation between the mean scores that the employed CSs obtained from the overall WAI and all the sub-dimensions of the SF-36 HRQoL scale ($p=0.01$) (Figure 2, 3). While the strongest correlation was found between the overall WAI and the Social Functioning sub-dimension of the SF-36 HRQoL scale ($r=0.54$, $p=0.01$), the weakest relationship was seen between the overall WAI and the General Health Perceptions sub-dimension of the SF-36 HRQoL scale ($r=0.38$, $p=0.01$).

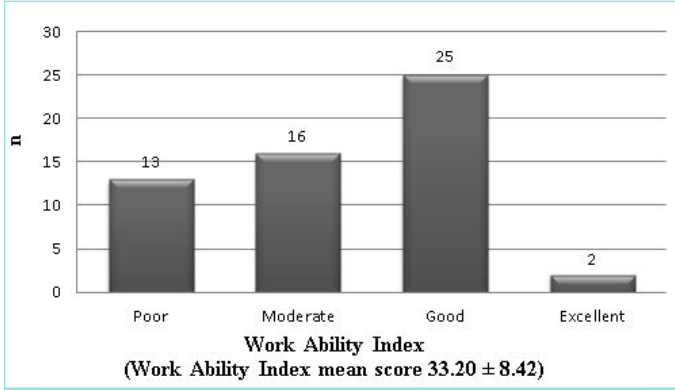

Figure 1. The work ability of employed cancer patients according to the Work Ability Index (n=56).

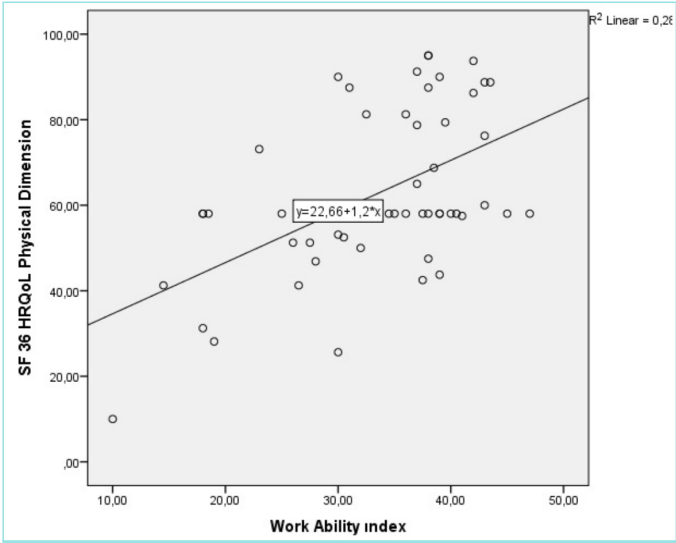

Figure 2. Correlation between Work Ability Index and SF-36 health-related quality of life scale (physical dimension).

HRQoL: Health-related quality of life.

DISCUSSION

In the current study, the results reflect the work conditions and QoL of CSs living in a developing country. In addition, the results of this study can be a source for those planning to carry out training and adaptation programs for CSs in work life.

Considering the high number of people who have cancer and those who have recovered from cancer today, the absence of these people in work life affects both the country's economy and the CSs' lives. Returning to work is a sign of a re-transition to a routine life. CSs need an income to live on and health insurance for their health expenditures. Therefore, the employment of CSs will be beneficial for both the individual and the development of the country[23,24]. In the present study, the rate of the employed CSs did not decrease after cancer treatment; conversely, it slightly increased by 12% (Table 2). The employed CSs were at a younger age (Table 1). In Turkey, since 2003, the retirement age has been 60 for women and 65 for men.[18] Since the retirement age has increased, young CSs have to continue to work. In addition, more than one third of the CSs had their own businesses, which positively affected them

Table 1. Comparisons between participants currently employed or unemployed			
Characteristics	**Employed (n=56)**	**Unemployed (n=206)**	**p[a]**
	n (%)	**n (%)**	
Sex			
Female	34 (60.7)	159 (77.2)	χ^2=6.157
Male	22 (39.3)	47 (22.8)	p=0.013
Marital status			
Married	40 (71.4)	153 (74.3)	p>0.05
Single/divorced/widow/widower/living separately	16 (28.6)	53 (25.7)	
Educational level			
Illiterate[†]	-	16 (7.8)	
Primary education	23 (41.1)	132 (64.1)	χ^2=15.325
High school	21 (37.5)	40 (19.4)	p=0.001
University and above	12 (21.4)	18 (8.7)	
Perceived income level			
Income less than expenses	20 (35.7)	109 (52.9)	
Income equal to expenses	29 (51.8)	79 (38.3)	p>0.05
Income more than expenses	7 (12.5)	18 (8.7)	
Cancer type			
Breast	26 (46.4)	112 (54.4)	
Column	5 (8.9)	30 (14.6)	
Testicular/kidney	6 (10.7)	6 (2.9)	χ^2=12.82
Ovarian/uterine/cervix	4 (7.1)	10 (4.9)	p=0.005
Lung, nasopharynx	2 (3.6)	6 (2.9)	
Stomach/pancreas/liver/esophagus	2 (3.6)	24 (11.7)	
Others[†††]	15 (26.8)	24 (11.7)	
Treatment type			
Chemotherapy	4 (7.1)	11 (5.3)	
Surgery	12 (21.4)	14 (6.8)	χ^2=12.015
Surgery + chemotherapy, or surgery + radiation therapy	17 (30.4)	62 (30.1)	p=0.007
Surgery + chemotherapy + radiation therapy	23 (41.1)	119 (57.8)	
The presence of a chronic disease comorbid with cancer			
No	40 (71.4)	97 (47.1)	χ^2=8.973
Yes	16 (28.6)	109 (52.9)	p=0.003
Type of the chronic disease comorbid with cancer (n=126)[††]			
Hypertension	2 (12.5)	21 (19.3)	
Diabetes	3 (18.8)	22 (20.2)	
Hypertension and diabetes	-	21 (19.3)	-
Others	11 (68.8)	43 (39.5)	
Age	**X ± SD**	**X ± SD**	t=-5,669
	44.82±8.78 (21-61)	52.51±9.06 (20-64)	p=0.001

[a]chi-square test, [†]not included in the analysis because there were no illiterate individuals in the employed CSs, [††]test statistics were not performed due to the insufficient number of the participants in categories, [†††]brain, lymph, thyroid, cell tumors, melanoma, soft tissue sarcoma and cancer whose primary site cannot be determined, SD: standard deviation.

to RTW (Table 2). In the literature, there have been studies indicating that CSs who worked before the diagnosis continued to work after treatment. In these studies, the rate of the CSs who continued working after treatment varied over a wide range (from 11.3% to 95.1%).[6,9,10,15,25-27] As in other studies, in the present study, the rate of RTW was high. These differences in working rates are probably due to the fact that working conditions and business cultures vary from country to country. In the current study, that the number of CSs who worked before and after the diagnosis was low is a reflection of Turkey's socio-cultural and economic conditions. The unemployment rate in Turkey (13% in 2019) is relatively lower than that in Spain (13.9%) and Greece (17%) but higher than those in the other OECD countries and the USA.[28] Moreover,

Table 2. Characteristics of the participants currently employed (n=56)	
Characteristics	**n (%)**
Did you work before you were diagnosed with cancer?	
Yes	46 (82.1)
No	10 (17.9)
Do you currently work?	
Yes	56 (21.4)
No	206 (78.6)
What sector are you currently employed in?	
Private sector	23 (41.1)
Public sector	13 (23.2)
Self-employment (food, livestock, agriculture)	20 (35.7)
Type of current employment	
Part-time	2 (3.6)
Full-time	34 (60.7)
Shift	8 (14.3)
Self-employed	12 (21.4)
Duration of being away from work after being diagnosed with cancer	
1-180 days	26 (46.4)
181-360 days	7 (12.5)
>361 days	21 (37.5)
No days	2 (3.6)
Do you think your illness has prevented you from working?	
No	13 (23.2)
I am able continue working but I have some complaints	10 (17.9)
Sometimes I have to slow down and change my work schedule	5 (8.9)
I often slow down my work rate	11 (19.6)
I usually can work part-time	5 (8.9)
I cannot work at full performance	12 (21.4)
Are you having problems at work due to your health?	
No	49 (87.5)
Yes (having to do heavy work, not getting a leave of absence from work)	7(12.5)
Do you think there have been any changes in your employer's or colleagues' attitudes or behaviors towards you due to your illness?	
No	53 (94.6)
Yes (unfavorable approaches)	3 (5.4)

according to data released by the Turkish Statistical Institute (TurkStat) in 2019, the labor force participation rate which is 52.9% on average (34.7% in women; 72.4% in men) has ranged between 50.5 and 53.2% over the last five years.[29] These rates are lower than the employment rates in the other OECD countries (68.3%). Similar to this study, as the education level increases, so does the labor force participation rate in other studies.[30] Another finding in the present study is that the number of women working before or after their diagnosis is low. Among OECD countries, the country where the women's labor force participation rate is the lowest is Turkey.[28] As the largest proportion of people only have primary level education in Turkey, women either do not work or work in jobs which require no skills. Therefore, women mostly prefer to be a homemaker due to the effects of the traditional structure of Turkish culture. The fact that the majority of the CSs in the present study were both women and were only primary school graduates may explain the

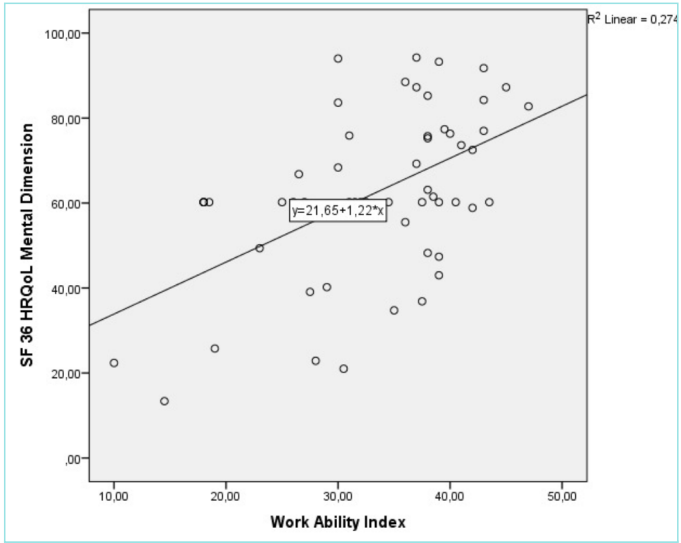

Figure 3. Correlation between Work Ability Index and SF-36 health-related quality of life scale (mental dimension).

HRQoL: Health-related quality of life.

low number of employed CSs in our sample (Table 1). In addition, since 2012, all Turkish citizens have been able to benefit from health services within the scope of general health insurance.[31] This health insurance system reduces the need for people to work. All of the aforementioned economic and social conditions affect the labor force participation rate. The employment rate in the province where this study was performed was similar to that in Turkey overall.[32] Therefore, the data on employment rates obtained in the present study reflect the sample of Turkey.

Many factors affect CSs' RTW.[6,9,24] The first one of these factors is the type of cancer and its treatment. In the present study, confirming previous studies,[6,9,10] the rate of RTW was higher in those CSs diagnosed with breast cancer (Table 1). The employment rate is higher among those who are younger and have a higher education level.[6,10] As indicated in Cheung et al.'s[10] study, the presence of a chronic disease accompanying the cancer diagnosis is a condition that prevents the person from working. One out of nine employed CSs reported that they had problems such as doing heavy work and not getting a leave of absence from work (Table 2). These problems may negatively affect the rate of job retention of individuals in the long term,[24] and lead to disability retirement. Supporting CSs on this journey brings about social benefits in terms of the economy and work efficiency. Therefore, multi-dimensional approaches such as workplace cancer management, legislative disabilities acts, and reducing physical problems should be adopted.[33]

Due to the long-term side effects of cancer treatment, CSs' QoL becomes a crucial issue[14,34,35]. The QOL of the employed CSs in the present study is high in terms of physical functioning and physical roles. The reason for this may be their lower average age, fewer chronic diseases, and higher education levels. The number of studies comparing the QOL of employed and unemployed CSs is limited.[10] At this point, it is recommended that in the future, comparative studies which may reveal the QOL status of employed and unemployed CSs should be conducted.

Work ability is a strong predictor of an individual's RTW and ability to continue at work.[11,12] In CSs with different cancer types,[36,37] the mean

Table 3. The mean scores the employed and unemployed participants obtained from the SF-36 health-related quality of life scale

Sub-dimensions of the SF-36 health-related quality of life scale	Employed participants	Unemployed participants	p[a]
	Median (1st and 3rd quartiles)	Median (1st and 3rd quartiles)	MWU: 3513.50 p=0.048
Physical functioning	60.00 (51.3-80)	59.59 (40-80)	MWU: 4081.00 p=0.042
Role limitation - physical	45.55 (0-100)	25.00 (0-100)	p>0.05
Bodily pain	77.50 (55-100)	76.25 (45-100)	p>0.05
General health perceptions	60.00 (50-70)	59.04 (45-75)	p>0.05
Vitality (energy and fatigue)	50.07 (30-63.8)	50.00 (33.8-65)	p>0.05
Social functioning	75.00 (50-100)	75.00 (50-100)	p>0.05
Role limitation - emotional	59.95 (8.33-100)	53.22 (0-100)	p>0.05
Mental health	66.46 (53-76)	64.91 (52-76)	p>0.05
Physical dimension	58.04 (52.7-79.2)	58.03 (41.1-70.8)	p>0.05
Mental dimension	60.21 (56.3-76.2)	60.21 (45.2-73.9)	MWU: 3513.50 p=0.048

[a]Mann-Whitney U test.

scores obtained from the WAI by employed CSs indicate a good level of work ability. However, only a fifth of the individuals reported that their disease did not interfere with their working. Regardless of work ability, which is evaluated subjectively, the individuals' emphasis regarding disability is related to work responsibilities and work arrangements. Therefore, support for employed CSs in these areas comes to the fore. Work ability is associated with global health, physical functioning and role functioning.[25] The analysis of the relationship between work ability and QOL demonstrated that the work ability levels of CSs were good and were associated with all the sub-dimensions of the SF-36 Health-Related QOL scale which is consistent with the result of the research conducted with ovarian CSs.[34] This relationship is the strongest in the social dimension. These results show that working life has a positive effect on CSs. Considering the fact that the rate of CSs is increasing day by day, carrying out individual and corporate initiatives aimed at improving their QOL gains importance. At this point, healthcare teams should follow up CSs, employers, corporate executives, and the government which sets the legal dimensions of this issue.

Study Limitations

One of the limitations of the present study is that the sample size of the employed CSs was small. The hospital where the present study was conducted is a state-owned hospital. This hospital has a capacity of 1,200 beds and provides health service in all departments, which slows down the achievement of work and prolongs the duration of waiting times in the hospital. Therefore, individuals working and diagnosed with cancer prefer private hospitals for various reasons (fast hospital procedures, early RTW and thus not losing their job, etc). Costs of most of the cancer treatments in private hospitals are covered by the social security system. Therefore, in the present study, the number of CSs who worked before they were diagnosed with cancer was low because most of them were either homemakers or retirees. It is recommended that this should be considered when our findings are interpreted. In addition, due to the design and objective of this study, no information regarding work-related characteristics (i.e. job requirements, workload, pressure of competition, work responsibilities, work arrangements, job satisfaction and financial pressures) were investigated.

Another limitation was that the QOL of the CSs was not fully reflected as no specific instrument was developed to measure QOL among Turkish CSs. Finally, the number of studies on CSs' work ability and QOL is limited. Therefore, we could not sufficiently compare our findings on this issue with those of other studies. The results of this study may serve as a baseline for future studies to verify our findings.

CONCLUSION

In conclusion, while existing studies present results obtained in developed countries, the current study presents results obtained in a developing country, where the incidence of both cancer cases and CSs is increasing. Clearly, younger CSs are an integral part of the workforce. Given the findings of the present study, it is important to assess the work-related needs of employed CSs and the impact on their QOL.

In Turkey where the present study was conducted, no programs are available for RTW. Although the rate of employed CSs is still low, as the rate of CSs increases, so does the rate of CSs who should work. Therefore, it is essential to start and accomplish multi-faceted approaches covering not only the employed CSs but also their colleagues, healthcare professionals, occupational health practitioners and policymakers. It is also necessary both for oncology nursing managers and for occupational health nurses to plan RTW programs concerning these patients in order to facilitate their RTW. Any such initiatives which are likely to improve the QOL of CSs may be provided with better support.

MAIN POINTS

- The rate of RTW after cancer treatment is affected by disease-related factors, CS-related factors and job-related factors.
- Work ability is a strong predictor of CSs' RTW and ability to stay at work
- The QOL of the employed CSs in the present study is high in terms of physical functioning and physical roles.

ETHICS

Ethics Committee Approval: The ethics committee permission of the study was obtained from the İzmir Katip Çelebi University Non-

Interventional Clinical Research Ethics Committee (approval number: 2018/10).

Informed Consent: Written consent was obtained from cancer patients participating in this study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: M.Y., Design: M.Y., Supervision: M.Y., A.A., Materials: G.D., Data Collection and/or Processing: G.U., F.E.A., G.D., Analysis and/or Interpretation: G.U., F.E.A., Literature Search: G.U., Writing: M.Y., G.U., Critical Review: M.Y., A.A.

DISCLOSURES

Conflict of Interest: No conflict of interest was declared by the authors.

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ORIGINAL ARTICLE

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Pressure Injuries in the Emergency Department: Prevalence and Healthcare Professionals' Knowledge Levels-A Pilot Study

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Abstract

BACKGROUND/AIMS: Patients in emergency departments (EDs) are a risk group in terms of pressure injuries.

MATERIALS AND METHODS: We conducted this descriptive study to determine both the prevalence of pressure injuries (PIs) in EDs and the level of knowledge of healthcare professionals working there regarding PIs. This study was a pilot study. The point prevalence study in the ED was conducted on 17.12.2018 with 23 patients who were being treated in the ED for more than 2 hours and who voluntarily participated in this study. A questionnaire to determine the level of knowledge of health professionals working in the ED was carried out with 16 physicians and 17 nurses working in the ED between 17-23 December, 2018. The data of this study were collected using The Demographic Questionnaire, Pressure Injuries Knowledge form, and Pressure Injuries Assessment form.

RESULTS: The prevalence of PIs in the patients followed up within the scope of this study was 17.4%; 85.71% of them were hospital-acquired injuries; 57.14% of them were stage 1; and 71.4% of them were related to medical devices. The mean knowledge test score of the participating physicians and nurses was 54.18±13.08. The mean knowledge test scores of the physicians and nurses who had received training on PIs were found to be higher than those who had not received training, and the difference was statistically significant ($p<0.05$).

CONCLUSION: Healthcare professionals need to evaluate patients holistically, take precautions to avoid PIs, evaluate patients in terms of the risk of developing PIs, and provide treatment and care. Therefore, training about PIs should be given to healthcare professionals working in emergency departments.

Keywords: Emergency department, pressure injury, prevalence, healthcare professionals

INTRODUCTION

Pressure injuries (PIs), one of the quality indicators of healthcare departments, remain a common health problem today.[1,2] PIs increase healthcare costs, mortality, morbidity, and the hospitalization period, and also negatively affect the quality of life of patients and their families.[3-7] According to data from the Joint Commission Center for Transforming Healthcare, more than 2.5 million patients in acute care units in the USA are exposed to PIs each year, and 60,000 people die from PI-related complications. The estimated cost of treating stage 4 PIs in the USA is up to $70,000, and the total cost of PI treatment is $11 billion annually.[3] PIs are frequently seen in care areas, with a prevalence

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of 4% to 40%, while they are seen in emergency departments (EDs) with a prevalence of 12.8% to 19.6%.[8,9] Although there are no studies on the prevalence of PIs in EDs in Turkey, the prevalence of PIs in hospitals overall was 9.5% according to studies conducted in different clinical areas.[10]

EDs are accessible at any hour, have high patient numbers, and are special places that differ from other units as a result of the unique problems they face, how they function, and the need for making quick and correct decisions.[11] Although the duration of stays in EDs varies, it ranges from 6.5-15.4 hours on average in the literature.[9,12] The follow-up periods of patients are prolonged, especially in elderly patients and patients with chronic diseases and also those with bad general health statuses.[8,12,13] The fact that the physical environment of an ED often does not have the necessary infrastructure to handle high patient densities and there is a greater number of patients with severe diseases means that patients can be monitored on stretchers for lengthy periods of time and it limits the quality of care provided and decreases efficiency.[14] The high risk of critically ill emergency patients developing PIs is thus a critical problem. For example, traumatic injuries can lead directly to tissue damage, loss of sensation, and impairment of tissue perfusion, which are known risk factors for the development of PIs, due to prolonged immobilization, hypovolemic shock and impaired tissue nutrition.[15] In trauma patients, monitoring and oxygen masks are frequently used, while plasters, splints, and traction may be employed to stabilize spinal injuries or to fix broken bones. In addition to pressure and frictional forces, the skin beneath these medical devices is also affected by moisture and heat, and thus the risk of developing PIs due to the use of these devices increases.[16]

Although PIs are a preventable health problem, preventive measures are not always implemented effectively, and PIs continue to be prevalent in hospitals.[17,18] It is the responsibility of healthcare professionals to identify those patients who are at risk of PIs and to prevent them.[1,2] It is thus necessary to increase the awareness of healthcare professionals about how to diagnose and prevent PIs and to use evidence-based practices. Healthcare professionals need training in the prevention and treatment of PIs.[19] In studies, it has been found that training provided on PIs can improve the assessment and diagnostic skills of emergency healthcare personnel.[8,20,21]

This study was carried out to determine the prevalence of PIs in an ED and the level of knowledge of health personnel about PIs. It is our hope that this study will contribute to a reduction of both PIs in EDs and the incidence of complications due to PIs, as well as to the literature on this topic.

MATERIALS AND METHODS

Study Design

This descriptive study was conducted as a pilot study to determine the prevalence of PIs in an ED and the level of knowledge of healthcare professionals in this department regarding PIs. In this study, the prevalence of PIs in the ED was determined by the point prevalence method.

Study Sample

The study was conducted between 17-23 December 2018 in the adult ED in the largest state university hospital in Ankara, the capital of Turkey.

Inclusion criteria for the study;

- Participants who voluntarily agreed to participate in the study (health workers and patients),

- Since it was stated that the risk of PIs increased in patients who were followed up on for more than 2 hours in the emergency room[22], patients who stayed in the emergency room for 2 hours or more were included in this study.

This study was conducted between 17-23 December, 2018 in the adult ED of the largest state university hospital in Ankara, the capital of Turkey. The sample consisted of the physicians (n=38) and nurses (n=22) working in the ED between 17-23 December, 2018 and the patients hospitalized in this department on 17.12.2018.

The point prevalence study in the ED was conducted on 17.12.2018 with 23 patients who voluntarily participated in this study. The questionnaire to determine the level of knowledge of health professionals working in the ED was conducted with 16 physicians and 17 nurses who voluntarily participated in this study. The participation rate was 100% for patients, 77.2% for nurses, and 42.1% for physicians.

Data Collection Tools

The data were collected using the Demographic Questionnaire, PIs Knowledge Form, and PIs Assessment Form, which were created by the researchers in line with the current literature.[1,8,21,23-26]

In the Demographic Questionnaire, there were 10 questions about the basic characteristics of the physicians and nurses, such as age, gender, education level, total years of employment, years of employment in the ED, whether or not they had received training about PIs, etc.

The PIs Knowledge Form consisted of 25 multiple-choice questions with illustrations. Each question had five possible answers. The form was intended to evaluate the knowledge levels of physicians and nurses about diagnosis, evaluation, categorization of the stages of PIs, prevention, treatment, and care of PIs. Before the application, the questions were evaluated by five experts in the fields of PIs, emergency nursing, and surgical nursing, and any necessary corrections were made.

The PIs Assessment Form included 37 closed-ended questions to assess the patients' characteristics, nutritional status, laboratory findings, position, mobilization, stretcher characteristics, PIs, and the Braden Pressure Injury Risk Assessment Scale. The Braden Pressure Injury Risk Assessment Scale (Braden Scale) is a widely used scale in the assessment of PIs in Turkey and around the world.[27] In categorizing the PIs, the current stages of PIs proposed by the National Pressure Injury Advisory (2016) were used.[28]

Data Collection

The scope of this study required the objective evaluation and categorizing of PIs. Before the study, the nurses who would conduct the prevalence study were trained by the Wound Ostomy Continence Nurses Association on the prevention, categorizing and evaluation of PIs. The prevalence study for PIs was carried out simultaneously by two nurses, one of whom was an internal observer (the emergency room head nurse), and the other of whom was an external observer (researcher), on 17.12.2018. Patients who stayed in the ED for more than

2 hours and who voluntarily agreed to participate in this study were evaluated for PIs; the PIs Assessment Form was applied by the internal observer nurse and the external observer nurse. The prevalence study took an average of 4 hours, and the administration of the assessment form took an average of 10 minutes for each patient. The Demographic Questionnaire and the PIs Knowledge Form were then administered to 33 healthcare professionals who were working in the ED during the week of the study and who agreed to participate. The administration of these forms took an average of 10-15 minutes.

Statistical Analysis

The data analysis was carried out using the Statistical Package for the Social Sciences (SPSS) version 22.0 (IBM SPSS Corp.; Armonk, NY, USA). Each multiple-choice questions on the PIs Knowledge Form was scored out of 4, for a total score of 100. The descriptive statistics of the variables examined within the scope of this study are shown as frequency, percentage, mean and standard deviation. The Shapiro-Wilk test was used to test the fitness to the normal distribution in the groups in order to compare the knowledge test scores of the groups. While parametric tests were used for the groups in which there was a normal distribution, nonparametric tests were used for those groups where the data did not fit a normal distribution. In this context, the Mann-Whitney U Test and the Kruskal-Wallis H test were used to evaluate the knowledge test scores according to the participants' characteristics. $p<0.05$ was accepted as statistically significant. Those patients who were in the ED were checked for PIs on the specified date.

Ethical Considerations

Ethical committee permission from Yıldırım Beyazıt University Ethical Committee (nr: 240/date: 2018) and official permission from the institution were obtained in order to conduct this research. The verbal and written consent of all the nurses, physicians, and patients who voluntarily agreed to participate in this study was obtained. The informed consent of two intubated patients who were followed up in the resuscitation department was obtained from their relatives. The principles of the Declaration of Helsinki were followed during this study. All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee.

RESULTS

The mean age of the patients was 59.56±17 years. Of the patients, 73.9% (n=17) were male. Of the patients who had been admitted to the ED, 43.5% (n=10) were due to respiratory system problems, 21.7% (n=5) of them were due to neurological disorders, 17.4% (n=4) of them were due to gastrointestinal disorders, and 65.2% (n=15) of them were due to chronic disease. The general condition of the skin of 78.3% (n=18) of the patients was normal, 65.2% (n=15) were able to move independently, 8.7% (n=2) were completely dependent and 13.0% of the patients were only fed with liquid intravenously (Table 1).

While 30.4% (n=7) of the patients had been evaluated within the previous 24 hours, only 13% (n=3) of them were evaluated for the risk of PI within the previous 24 hours. The stretcher head angle of 87% of the patients (n=20) was higher than 30 degrees (Table 1). Of the patients, 4.3% (n=1) had PIs during their hospitalization in the ED; and 17.4% of them had PIs at the time of evaluation. The mean Braden score of the patients was 19.56±4.33 (Table 1).

In this study, the prevalence of PIs in the patients was 17.4% (n=4). Of the detected PIs, 85.71% (n=6) were hospital acquired. Of the wounds, 57.14% (n=4) were stage 1, 28.57% (n=2) of the wounds were stage 2 and 14.29% (n=1) were suspected deep tissue damage. 71.4% (n=5) of the wounds were in the ear; 14.29% (n=1) of them were in the neck; and one of them was in the coccyx. 71.4% (n=5) of the wounds were related to medical devices. While 60% (n=3) of the medical devices causing PIs were oxygen masks, 40% (n=2) of the PIs were related to surgical masks (Table 2). The mean age of the patients with PIs was 61.25±15.69 years and two (50%) of the patients were male. All of the patients with PIs had a chronic disease, and all had been admitted to the ED with respiratory system disorders (n=4). Three (75%) of the patients with PIs had normal skin. Three (75%) of the patients were able to independently move. While skin evaluation had been performed in only one (25%) of the

Table 1. Characteristics of the patients in the emergency department (n=23)

Characteristics		Mean	SD
Age (24-84 years)		59.56	17.60
Braden score (8-23)		19.56	4.33
		n	%
Gender	Male	17	73.9
	Female	6	26.1
Diagnosis	Neurological disorders	5	21.7
	Fluid/electrolyte imbalance	2	8.7
	Respiratory system disorders	10	43.5
	Gastrointestinal system disorders	4	17.4
	Cardiological disorders	2	8.7
Chronic disease	Yes	15	65.2
	No	8	34.8
General state of the skin	Normal	18	78.3
	Dry	5	21.7
Nutrition method	Oral feeding	18	78.3
	IV. liquid feeding	3	13.0
	IV. liquid and oral feeding	2	8.7
Mobilization status	Independently mobile	15	65.2
	Able to sit/lie	6	26.1
	Completely dependent	2	8.7
Status of having a skin assessment within the previous 24 hours	Yes	7	30.4
	No	16	69.6
Status of having a risk assessment within the previous 24 hours	Yes	3	13.0
	No	20	87.0
Position of stretcher head (angle)	0-30 °	3	13.0
	>30 °	20	87.0
Status of having pis at the time of the hospitalization in the Emergency department	Yes	1	4.3
	No	22	95.7
Status of having PIs at the time of assessment	Yes	4	17.4
	No	19	82.6

SD: standard deviation, PIs: pressure injuries.

patients with PIs within the previous 24 hours, none (n=4) of them had a risk assessment within the previous 24 hours. The stretcher head angle of three (75%) of the patients with PIs was higher than 30 degrees. Two PIs were detected in three (75%) of the patients, and three (75%) of the patients were fed orally (Table 3).

The mean age of the healthcare professionals in the ED included in this study was 28.51±3.65 years; the mean total years of employment was 3.33±3.09 years; and the mean years of employment in the ED was 2.14±1.68 years. Of the employees, 45.5% (n=15) were female. 48.5% (n=16) of the employees were physicians, and 51.5% (n=17) of them were nurses. Of the healthcare professionals, 75.8% (n=25) had an experience of working with a patient with PIs; and 42.2% (n=14) of them had received training on PIs (Table 4).

The mean score of the physicians and nurses was 15.27±5.42 on the sub-dimension of the diagnosis and evaluation of PIs; their mean score on the sub-dimension of categorizing the stage of the PI was 18.18±5.92; their mean score on the treatment and care sub-dimension was 4.36±3.21; their mean score on the prevention sub-dimension was 16.36±4.83; and finally their mean score on the whole scale was 54.18±13.08 out of 100 (Table 5).

No statistically significant correlation was found between the mean knowledge test scores of the physicians and nurses and their age, total years of employment, and their duration of working in the ED (p>0.05). The mean knowledge test scores of the healthcare professionals did not differ statistically significantly according to their education levels and their status of having previously worked with PIs (p>0.05). However, their mean knowledge test scores were statistically significantly different according to whether they had received training on PIs (U=65.50, p=0.013): the mean score of the physicians and nurses who had previously received training on PIs was 60.28±13.53 and this was significantly higher than the mean score of those who had not received training (49.68±11.02) (Table 6).

Table 2. Pressure injury characteristics of the patients

Pressure injury characteristics		n	%
Pressure injury prevalence		4	17.4
Place of PI development	Non-hospital PI	1	14.29
	Hospital acquired PI	6	85.71
	Total	7	100.0
Stage	Stage 1	4	57.14
	Stage 2	2	28.57
	Suspected deep tissue injury	1	14.29
	Total	7	100.0
Body area	Ear	5	71.4
	Neck	1	14.29
	Coccyx	1	14.29
	Total	7	100.0
Pressure injury/medical device relation	Yes	5	71.4
	No	2	29.6
	Total	7	100.0
Medical device causing PIs	Oxygen mask	3	60.0
	Surgical mask	2	40.0
	Total	5	100.0

PI: pressure injuries.

DISCUSSION

This study, which was conducted to determine the prevalence of PIs in the ED and the level of knowledge of healthcare professionals about PIs, was a pilot study. Despite the small sample size, the point prevalence of ED PIs was 17.4% in this study. In addition, medical device-related PIs due to oxygen masks were often detected in patients. No study has been found on the prevalence of PIs in specifically regarding EDs in Turkey. This study is important in that it is the first study specific to an ED. At the same time, considering that ED PI studies are limited in the literature, the results of this study will contribute to the literature.

EDs are places where treatment and care are given to many people of different age groups and different diseases. Patients are extensively evaluated and monitored, usually on stretchers[14,20] until their acute condition resolves[20]. During follow-up, PIs can develop due to an

Table 3. Characteristics of the patients with pressure injuries

Characteristics		Mean	SD
Age (years) (n=4) (48-84)		61.25	15.69
Braden score (n=4) (8-21)		17.00	6.05
		n	%
Gender	Male	2	50.0
	Female	2	50.0
	Total	4	100.0
Diagnosis	Respiratory system disorders	4	100.0
Chronic disease	Yes	4	100.0
General state of the skin	Normal	3	75.0
	Dry	1	25.0
	Total	4	100.0
Mobilization status	Independently mobile	3	75.0
	Completely dependent	1	25.0
	Total	4	100.0
Status of having a skin assessment within the previous 24 hours	Yes	1	25.0
	No	3	75.0
	Total	4	100.0
Status of having a risk assessment within the previous 24 hours	No	4	100.0
Position of stretcher head (angle)	30	1	25.0
	>30	3	75.0
	Total	4	100.0
Number of PIs	1 PI	1	25.0
	2 PIs	3	75.0
	Total	4	100.0
Nutrition method	Oral feeding	3	75.0
	IV fluid feeding	1	25.0
	Total	4	100.0

SD: standard deviation, PIs: pressure injuries.

inability to move for reasons that may include obesity, the narrowness of the stretcher, the presence of an oxygen mask/cannula, etc., or as a result of lying in the same position for a long period of time.[29] Immobilization, which is frequently applied in life-threatening situations, prevents ambulation.[8] Measures such as raising the armrests of the stretcher to ensure patient safety, and applications such as intravenous treatments, fluids, catheters, intubation, etc., can limit patient mobility. All of these result in an increased risk that patients in EDs will develop PIs. Dugaret et al.[8] emphasized that there is a risk of PIs in patients in EDs. Denby and Rowlands[22] emphasized that 99.2% of patients in EDs were followed up for more than 2 hours, and they were at risk in terms of the development of PIs due to their comorbidity and critical conditions. In this study, it was observed that the patients had chronic diseases which posed a risk for the development of PIs and that patients frequently applied to the ED due to respiratory system diseases.

Table 4. Socio-demographic characteristics of the physicians and nurses in the emergency department

Socio-demographic characteristics		Mean	SD
Age (years) (n=31) (23-37)		28.51	3.65
Total years of employment (n=33) (min.: 1; max.: 14 years)		3.33	3.09
Years of employment in the emergency department (n=33) (1-6 years)		2.14	1.68
		n	%
Gender	Female	15	45.5
	Male	18	54.5
	Total	33	100.0
Profession	Physician	16	48.5
	Nurse	17	51.5
	Total	33	100.0
Education level	Bachelor's	17	51.5
	Master's	13	39.4
	PhD	3	9.1
	Total	33	100.0
Status of previously working with a patient with PIs	Yes	25	75.8
	No	8	24.2
	Total	33	100.0
Status of receiving training about PIs	Yes	14	42.4
	No	19	57.6
	Total	33	100.0

SD: standard deviation, PIs: pressure injuries, min.: minimum, max.: maximum.

Table 5. Distribution of PI knowledge scores of the emergency healthcare professionals according to question groups

Knowledge test sub-dimensions	Score interval	Knowledge test score	
		Mean	SD
Diagnosis and evaluation of PIs[1-3,12,13,20,21]	0-28 Points	15.27	5.42
Categorization of stages[4-6,16,23-25]	0-28 Points	18.18	5.92
Treatment and care[14,15,17,19]	0-16 Points	4.36	3.21
Prevention[7-11,18,22]	0-28 Points	16.36	4.83
Total score	0-100 Points	54.18	13.08

SD: standard deviation.

In this context, emergency healthcare professionals need to evaluate the risk that patients will develop PIs after they have been admitted to the department.

In the current study, four patients had PIs, and the prevalence of PIs was 17.4% (Table 2). Fulbrook et al.[29] conducted a study on patients who arrived at EDs via ambulance and found that the prevalence of PIs was 5.2% during admission. This rate increased during follow-up and rose to 7.8% during hospitalization. Pham et al.[9] determined that the prevalence of hospital-acquired PIs was 19.6% in elderly patients admitted to the ED. Dugaret et al.[8] evaluated the prevalence and incidence of PIs with a 15-day follow-up in the ED and found that the prevalence of PIs was 12.8% when patients were admitted and 19.1% when they were discharged. The prevalence rates in these studies are similar to the prevalence rate in the current study. Although the prevalence of PIs at the time of admission was not evaluated in this study, we believe that the prevalence of PIs probably increased in parallel with the risk factors of the patients and their length of stay in the ED.

When the stages of PIs are examined, in the prevalence studies of Fulbrook et al.[29], six of the 14 (42.9%) PIs found were stage 1; 14.3% of them were stage 2; 14.3% of them were stage 3; and 35.7% of the injuries had formed in the ears. Pham et al.[9] conducted a study on elderly patients and determined that 9.0% of PIs in the ED were stage 1; 9.9% of them were stage 2; and 0.6% of them were stage 3. Denby and Rowlands[22] found that 61.6% of the PIs that developed in patients in an ED were stage 1; 38.4% of them were stage 2; and they most commonly formed in the sacrum (42.4%), coccyx (30%) and heels (14.4%). In the study of Dugaret et al.[8], the regions where PIs developed most frequently were the heels (42.4-46.1%), sacrum (48.7-49.3%), and hip (5.2-7.8%). In the current study, seven (57.14%) PIs were stage 1 and 28.57% of them were stage 2; the majority of them (71.4%) were found to have developed due to the use of medical devices such as a nasal cannulas or masks, and were localized in the ear (71.4%) (Table 2). Patients who are admitted to an ED must receive medical interventions as soon as possible,[20] and during medical interventions, tools such as catheters, oxygen cannulas/masks, intubation ties, etc. are often used. It has been emphasized that the PIs found in EDs are often in the earliest stages and that they are associated with the use of medical devices.[22,29] These data reveal that healthcare professionals working in EDs should take precautions to protect patients from PIs, and especially from medical device-related PIs.

Although the hospital stay of the patients is shorter compared to inpatient and intensive care units, the risk of developing PIs is higher due to the patients' profiles and characteristics, and the equipment and treatment used in the EDs.[8,22] Healthcare professionals in EDs consider resolving the acute problems affecting their patients' lives as their top priority and focus on this.[20,21] This situation may cause them to ignore PIs. Padula and Pronovost[20] stated that healthcare professionals focus little on the preventing PIs during the immediate follow-up, and they mostly monitor acute problems since the priority in the emergency room is to address the patients' acute problems.

Healthcare professionals working in these departments should evaluate patients holistically, take measures to prevent possible problems such as PIs while solving existing problems, evaluate the patients' risks of PIs, and provide treatment and care for PIs.[15,21,30] It has been recommended in the clinical guidelines that patients in EDs should be evaluated for PI risk within the first eight hours, and that other healthcare professionals

Table 6. Distribution of PI knowledge scores of the emergency healthcare professionals according to socio-demographic characteristics

Socio-demographic characteristics		r*		p		
Age (years) (n=31)		0.083		0.659		
Total years of employment (n=33)		-0.163		0.365		
Years of employment in the emergency department (n=33)		0.082		0.649		
		n	Mean	SD	H/U	p
Education level	Bachelor's	17	58.35	12.96	3.963[H]	0.138
	Master's	13	49.23	12.47		
	PhD	3	52.00	12.00		
Status of previously working with a patient with PIs	Yes	25	56.00	13.61	63.50[U]	0.123
	No	8	48.50	9.89		
Status of receiving training about PIs	Yes	14	60.28	13.53	65.50[U]	0.013
	No	19	49.68	11.02		

*pearson correlation co-efficient, H: Kruskal-Wallis H test, U: Mann-Whitney U test, SD: standard deviation.

should be informed about PIs in patients when they are transferred to different units (intensive care units, wards, etc.) or sent home after follow-up.[20,29]

Healthcare professionals should have sufficient knowledge about the diagnosis, risk assessment, categorization of stages, prevention, treatment, and care of PIs.[8,21] We determined that the mean score of the healthcare professionals in EDs for the PI knowledge form was 54.18±13.08 out of 100, and the most well-known subjects were categorization of stages, prevention, definition and evaluation, treatment and care, respectively. However, the total score was lower than expected (Table 5). There are many studies relating to the knowledge of nurses and nursing students about PIs.[31,32] However, the number of studies on healthcare professionals working in EDs in terms of their level of knowledge of PIs is quite limited, and they have generally determined that the knowledge of healthcare professionals is at a moderate or lower level.[21,31,33] Rafiei et al.[33] found that nurses working with trauma patients in the ED had the greatest knowledge about the characteristics of wounds (77.3%), while they had the lowest knowledge (57%) about the onset of PIs. Ham et al.[21] conducted a single-group pre-post-test intervention study on nurses and physicians in an ED and they emphasized that training improved their ability to define and categorize stages of PIs. The healthcare professionals in the current study did not have the desired knowledge levels regarding PIs, and therefore their knowledge should be improved by training.

The prevalence of PIs is considered to be a quality indicator for healthcare institutions, and a patient outcome affected by nursing care.[34,35] In this context, the training given to healthcare professionals in EDs is very important in reducing the prevalence of PIs.[21] In the current study, the fact that the total knowledge scores of the healthcare professionals who had received training on PIs were significantly higher supports this finding (Table 6). It has been recommended that periodically repeated training programs on the diagnosis, categorization of stages, prevention, treatment, and care of PIs be provided.[8,21,31,33]

Study Limitations

This study has some limitations. First, this study was conducted in the ED of a state university hospital, and therefore the data represents a single center. This was accepted as a limitation. Secondly, this study was the first pilot study conducted in the ED and it was descriptive. In this study, all of the patients who stayed in the ED for more than 2 hours constituted the sample of the study. Therefore, the age range of the patients included in the sample was wide and it was determined that those patients who developed PIs were 50 years or older. In the future, it is recommended to conduct in-depth studies investigating the PIs risk factors specific to patient groups and the ED.

CONCLUSION

PIs are a serious problem which occur after patients have been hospitalized in EDs and they tend to increase during follow-up.[8,9,29] The intensive follow-up period and the critical status of patients in EDs further increase the risk of developing PIs.[8] As the primary goal of emergency healthcare professionals is to solve the acute problems of their patients, PIs remain only a background concern from the moment the patient enters the ambulance. In this study, the prevalence of PIs shows the need to place more emphasis on this problem. The moderate level of knowledge of emergency healthcare professionals regarding PIs can be considered to affect their prevalence. The prevalence of PIs is one of the quality indicators and nursing care-responsive patient outcomes.[34,35] Healthcare institutions should organize training programs and comprehensively evaluate the measures they are taking for the prevention, treatment, and care of PIs in all care areas and clinics.

MAIN POINTS

- Patients in EDs form a risk group for PIs.
- The risk of PIs remains in the background as the primary aim of emergency room staff is to solve the patients' acute problems.
- Emergency health staff have a moderate knowledge of PIs.
- The prevalence of PIs in the ED is a reflection of the knowledge and practices of healthcare professionals working in these units.

ETHICS

Ethics Committee Approval: Ethical committee permission from Yıldırım Beyazıt University Ethical Committee (approval number: 240, date: 2018) and official permission from the institution were obtained in order to conduct this research.

Informed Consent: The verbal and written consent of all the nurses, physicians, and patients who voluntarily agreed to participate in this study was obtained.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: G.Y., Design: G.Y., D.A., S.G., H.B., Z.G.B., A.D., Supervision: G.Y., S.G., H.B., Z.G.B., A.D., Data Collection and/or Processing: G.Y., Analysis and/or Interpretation: G.Y., D.A., S.G., H.B., Literature Search: G.Y., Writing: G.Y., D.A., S.G., Critical Review: G.Y., H.B., Z.G.B., A.D.

DISCLOSURES

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ORIGINAL ARTICLE

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A Retrospective Analysis of Anaesthesia Management for Geriatric Patients in the Non-Operating Room

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Abstract

BACKGROUND/AIMS:In the present study, we aimed to analyse typically used anaesthesia methods and associated complications in geriatric patients.

MATERIALS AND METHODS: We included 3,012 outpatients who received anaesthesia. The patients' data were obtained from anaesthesia records and analysed retrospectively. Anaesthesia methods (sedation, spinal anaesthesia, general anaesthesia, combined spinal-epidural anaesthesia or monitored anaesthesia care); descriptive statistics (age, weight, operation time, gender, American Society of Anesthesiologists (ASA) classification, drug intake and operation type); and complications (desaturation, injection pain, nausea/vomiting, aspiration, hypotension, bradycardia and perforation) were analysed.

RESULTS: The mean age of the patients who developed intra- and post-operative complications was 73.35±5.88 years. The mean anaesthesia time was 69.98±55.44 min. Hypotension and gender showed significant association. Hypotension was observed in 29 (1.7%) male and 7 (0.5%) female patients. The ASA classification and bradycardia showed significant association; sedation and general anaesthesia were significantly associated with complications.

CONCLUSION: No major complication, morbidity or mortality was observed in any geriatric patient who received anaesthesia outside the operating room. Comorbidities should be detected with appropriate physical, laboratory and radiological examinations and appropriately treated prior to the anaesthesia application. Moreover, the anaesthesia method must be determined based on the results of these examinations and the characteristics of the procedure.

Keywords: Geriatric patients, anaesthesia, complications, sedation

INTRODUCTION

The elderly population (>65 years) has tripled over the past 50 years and it is estimated to increase three-fold over the next 50 years, reaching approximately 72.1 million. In the United States, the number of people >65 years of age is expected to increase nearly two-fold by 2050. A similar trend has been reported in Europe, with the elderly population expected to account for 30% of the total population by 2060.[1,2] Recently, outpatient anaesthesia practices for diagnosis and treatment have been implemented in different fields such as endovascular intervention, the placement of automatic implantable cardioverter-defibrillator (AICD), as well as for cerebral and other embolization.[3] Due to advances in technology and pharmacological procedures, more complicated and invasive interventions are being increasingly used to manage extremely ill patients, in addition to non-invasive interventions for the diagnosis and treatment of outpatients receiving anaesthesia; this has led to an

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increased incidence of specific problems and potential complications.[4] The most common complications are serious hemodynamic instability and respiratory complications.[5] In particular, risks and complications associated with anaesthesia increase in geriatric patients [age, comorbid diseases and American Society of Anesthesiologists (ASA) classification]; therefore, such cases warrant more attention and more thorough anaesthesia implementation.[3,4] The incidence of most major complications was higher for all examined outcomes in the OR population.

In addition, non-invasive surgical alternatives force anaesthesiologists to work in units other than operating rooms to reduce health care costs.[3] Therefore, attempts should be made to achieve basic standards for appropriate monitoring and equipment to be used in performing practices outside operating rooms in order not to undermine patient safety.[3,4]

Physiologically, ageing can alter the pharmacokinetics and pharmacodynamics of anaesthetics. Thus, anaesthesiologists should take into account all age-related changes in organ systems as cardiovascular, pulmonary and central nervous system functions are significant determinants of the outcomes of surgical interventions performed under general and local anaesthesia.[3] Additionally, elderly patients have decreased homeostatic reserves, which can compromise their ability to cope with stress and inflammatory processes during the perioperative period. Therefore, anaesthetic methods and drugs should be individualised with consideration to age-related physiological changes.[4]

The aim of this study was to analyse some typically used outpatient anaesthesia methods and related complications in geriatric patients at our hospital.

MATERIALS AND METHODS

The study was approved (approval number: 602-GOA) by the non-interventional ethics Committee of our university. Geriatric patients who were diagnosed and treated during a 9-year period (2003-2011) and who received outpatient anaesthesia were included. Patient data regarding anaesthesia methods were retrieved from their anaesthesia records. Descriptive data, including age, weight, operation time, gender, ASA classification, anaesthetics and complications [desaturation (SpO_2 <90), injection pain, nausea/vomiting, aspiration, hypotension (systolic artery pressure <90 mmHg or diastolic artery pressure <60 mmHg), bradycardia (<50/min) and perforation], were retrospectively analysed.

Statistical Analysis

The Statistical Package of Social Sciences 15 (SPSS 15.0, Chicago, IL, USA) was used for the data analysis. Statistically significant differences between demographic characteristics and other continuous variables were estimated using Student's t-test. Statistically significant differences between groups and categorical variables were estimated using the chi-square test. The Mann-Whitney U test was used for subgroup analyses of data with non-normal distribution $p<0.05$ was considered significant.

RESULTS

Among 16,045 patients who received outpatient anaesthesia in our hospital for diagnosis or treatment, 3,012 (18.7%) patients were included as their data were available. The patients' demographic characteristics were significantly different (Table 1). Overall, 29 types of interventions were performed on these 3,012 patients. The intervention types and the anaesthetics used are shown in Tables 2 and 3, respectively.

The overall rate of complications was 18.5%. Rates of bradycardia, hypotension, desaturation, injection pain, arrhythmia, tachycardia, aspiration and nausea/vomiting were 14%, 3%, 1.9%, 1.7%, 1.6%, 0.3%, 0.1% and 0.1%, respectively. The distribution of the incidence of complications according to ASA classifications was examined (Table 4). ASA class III and IV patients showed significantly higher rates of complications than ASA class I and II patients ($p<0.007$). When the complications were individually evaluated, ASA class III and IV patients more frequently developed bradycardia, hypotension and arrhythmia (Table 4). A list of the frequently used drugs during anaesthesia management is shown in Table 5.

The total number of patients admitted into clinics was 195. Sixty-six patients had stents inserted due to carotid artery stenosis, 53 patients had endovascular intervention, 34 patients had automatic AICD inserted and 26 patients had cerebral or other embolization (aneurysm, AVM and others). All these patients were admitted into the clinic for 1 day as routine procedure. Here, the specific difference relates to 16 patients with electroconvulsive therapy (ECT). These patients who had ECT applied were psychiatry clinic patients. This patient group had 8 or 10 sessions with ECT administered 3 days per week, so the duration of their admission was as long as their treatment duration.

DISCUSSION

According to the World Health Organization, the ageing of the world population has led to an increase in the rates of cancer, diabetes, cardiovascular diseases, chronic lung diseases and mental disorders, particularly dementia. Comprehensive studies are required to prevent these diseases.[6]

Table 1. Patient demographics (n=3,012)

Features	Range	Average
Age (year)	65-99	75.89±6.06
65-74	1,913	
75-80	744	
>81	355	
Weight (kg)	35-125	71.66±10.01
Duration of anaesthesia (min)	15-480	47.96±34.65
Sex	**Number of patients (n)**	**Percent (%)**
Female (%)	1,300	43.2
Male (%)	1,712	56.8
ASA classifications	**Number of patients (n)**	**Percent (%)**
ASA I	30	1.0
ASA II	2,179	72.3
ASA III	691	22.9
ASA IV	112	3.7
Interventions	**Number of patients (n)**	**Percent (%)**
Elective	2,974	98.7
Emergency	38	1.3

ASA: American Society of Anesthesiologists

Table 2. Distribution of outpatient diagnoses and treatment interventions

Intervention	Number of patients (n)	Percent (%)
Colonoscopy	923	30.6
Endoscopy-colonoscopy	721	23.9
Endoscopic retrograde cholangiopancreatography (ERCP)	487	16.2
Gastroscopy	224	7.4
Endoscopic ultrasonography (EUS)	143	4.7
Percutaneous endoscopic gastrostomy opening	93	3.1
Placing a stent due to carotid artery stenosis	66	2.2
Computed tomography	57	1.9
Endovascular intervention (abdominal and/or thoracic aortic aneurysm)	53	1.8
Double balloon	49	1.6
Prostate biopsy	37	1.2
Placing automatic implantable cardioverter-defibrillator	34	1.1
Cerebral and other embolisation (aneurysm, AVM and others)	26	0.9
Bronchoscopy	20	0.7
Magnetic resonance imaging	18	0.6
Electroconvulsive therapy	16	0.5
Orthopaedic interventions	10	0.3
Hydatid cyst aspiration	9	0.3
Brachytherapy	9	0.3
Pace-maker placement	4	0.1
Cardiac catheterisation with and without electrophysiological examination	2	0.1
Radiotherapy and brachytherapy due to various reasons	2	0.1
Bone marrow biopsy	2	0.1
ERCP + EUS	2	0.1
Liver biopsy	1	0.0
Renal biopsy	1	0.0
Operations for aches	1	0.0
Catheterisation	1	0.0
Double-J catheterisation	1	0.0
Total	3,012	100

Statistically significant differences between hypotension and male gender were noted in this study. This may be explained by excessive cardiovascular practices employed in females, such as endovascular interventions for abdominal aorta and/or thoracic aortic aneurysms; stent placement for carotid artery stenosis; cerebral and other embolisations for aneurysms or arteriovenous malformation; pacemaker placement; AICD placement and cardiac cauterisation with or without electrophysiological examination. Therefore, more cardiovascular interventions may be required in male geriatric patients than in female patients, which may, in turn, lead to more complications.

Emergency interventions for geriatric cases were presumed to be effective when complications occurred. However, we noted that except for nausea/vomiting, no complications related to emergency interventions occurred. Therefore, geriatric patients receiving general anaesthesia have a lower frequency and less severity of post-operative pain and nausea/vomiting than younger patients.[7]

Decreased vocal cord sensitivity against stimuli in elderly patients increases the risk of aspiring stomach content and the possibility for pulmonary complications.[8] In the present study, nausea/vomiting and aspiration occurred in 2 patients each, which is consistent with previous reports. Interestingly, hypotension was observed only in those geriatric patients who received combined spinal-epidural anaesthesia. In contrast, bradycardia and hypotension were observed in those geriatric patients who received spinal anaesthesia. We speculate that these complications occurred because of the high rates of cardiovascular diseases in geriatric patients who frequently undergo interventions for abdominal aorta and/or thoracic aortic aneurysms and stent placements.

Table 3. Anaesthesia management for geriatric patients

Anaesthesia types	Number of patients (n)	Percent (%)
Sedoanalgesia	2,950	97.9
Spinal anaesthesia + sedation	12	0.4
Combined spinal-epidural anaesthesia + sedation	6	0.2
Spinal anaesthesia without sedation	21	0.7
General anaesthesia	21	0.7
Monitored anaesthesia care without sedation	2	0.1
Total	3,012	100

Table 4. Distribution of complications according to the ASA classifications of patients

Complications	ASA I and II, n (%)*	ASA III and IV, n (%)*	p-value
Desaturation	18 (0.8)	9 (1.1)	0.431
Injection pain	21 (1.0)	6 (0.7)	0.600
Bradycardia	125 (5.7)	67 (8.3)	0.008
Aspiration	2 (0.1)	0 (0)	-
Nausea/vomiting	1 (0.0)	1 (0.1)	0.462**
Hypotension	18 (0.8)	18 (2.2)	0.001
Tachycardia	2 (0.1)	2 (0.2)	0.290**
Arrhythmia	4 (0.2)	11 (1.4)	0.000**
Total complications	171 (7.7)	87 (10.8)	0.007

*Column percent, **Fisher's exact test, ASA: American Society of Anesthesiologists

Table 5. Frequently used drugs

Drugs	Number of patients (n)	Percent (%)
Midazolam	2,947	97.8
Flumazenil	2,491	82.7
Propofol	2,660	88.3
Etomidate	230	7.6
Lidocaine	135	4.5
Ketamine	47	1.6
Bupivacaine	37	1.2
Sevoflurane	15	0.5
Thiopental	12	0.4
İsoflurane	7	0.2

Careful titration to produce desirable effects of anaesthetics helps to prevent the extension of effect duration and other undesirable side effects.[9] Short-acting anaesthetics, such as propofol, desfluran, remifentanil, mivacurium, atracurium and cisatracurium, that do not greatly depend on circulation and lung function may be useful.[10] In this study, midazolam-ketamine (25 mg), only after premedication with midasolam propofol-fentanil/remifentanil, etomidate-remifentanil/fentanyl and ketamine-fentanyl combinations, was used for sedation depending on the patient characteristics and interventions to be carried out.

In interventions where general anaesthesia was implemented, thiopental and etomidate for induction and sevoflurane and isoflurane for maintenance as inhalation agents were used. Since many of these cases were outpatients, flumazenil was used in a majority (82%) of these cases who received midazolam for antagonisation.

Owing to recent advances in anaesthesia procedures as well as surgical and monitoring modalities, the ambulatory setting offers numerous potential advantages for elderly patients undergoing elective surgery.[3,8] The most common procedures for elderly outpatients can be performed with minimally invasive approaches and safely managed in ambulatory settings. However, age is independently associated with an increased rate of unanticipated hospital admissions within 30 days of ambulatory surgery.[7,11]

Age and a multitude of comorbidities during the implementation of outpatient anaesthesia increase the risks associated with interventions.[9] Generally, geriatric patients fall under ASA classes III and IV, which is important information when implementing anaesthesia. Our thorough search of the literature yielded no studies regarding the implementation of outpatient anaesthesia in geriatric patients. The complication rate increases with increasing ASA classification.[5,12] Moreover, more geriatric patients in this study were ASA class II. Of note, the bradycardia rate significantly increased in geriatric patients in relation to comorbidities (chronic renal failure, carotid artery stenosis and pacemaker placements).

Study Limitations

This study has a few limitations: We included geriatric patients with comorbid diseases. We have ASA classes of these patients who were included in this study. However, there were no results of the comorbidities in the geriatric patients. There were no records of the years of experience of the anaesthesiologists who managed the anaesthesia. Another limitation of this study was that we did not find any information regarding the admission day to the hospital or the re-planned hospital admission rates.

CONCLUSION

The ambulatory setting offers potential advantages for elderly patients undergoing elective surgery owing to advances in both surgical and anaesthetic modalities, which in turn can result in a more rapid recovery, fewer complications, greater patient satisfaction and lower medical care cost. In this study, we presented our experiences with anaesthesia in geriatric patients. No major complication, morbidity or mortality was observed in any geriatric patient who underwent outpatient anaesthesia. Outpatient anaesthesia was implemented through various methods, and we observed increased rates of routine anaesthesia practices in this group for both diagnosis and treatment. Therefore, before implementing outpatient anaesthesia, it is crucial to evaluate pre-anaesthetics administered to the patients, to know the patients' psychological and anatomical characteristics, to know the features of the best anaesthesia method and to inform the patients and their relatives.

ETHICS

Ethics Committee Approval: The study was approved (decision no: 602-GOA) by the non-interventional ethics Committee of our university.

Informed Consent: Patient data regarding anaesthesia methods were retrieved from their anaesthesia records.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: O.D., Design: O.D., Supervision: L.İ., Data Collection and/or Processing: S.B., Ş.Ö., Analysis and/or Interpretation: S.B., Ş.Ö., Literature Search: S.B., Ş.Ö., E.A., Writing: O.D., Critical Review: L.İ.

DISCLOSURES

Conflict of Interest: No conflict of interest was declared by the authors.

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Neuroendocrine Tumors Presenting with Liver Metastasis, is it Necessary to Find the Primary Site for a Better Outcome?

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Abstract

BACKGROUND/AIMS: Neuroendocrine tumors (NET) presenting with multiple liver metastasis are a heterogeneous group of tumors and their prognosis differs greatly from each other according to their differentiation, grade, and possibly to their primary site of origin.

MATERIALS AND METHODS: Seven patients diagnosed with NET who presented with multiple liver metastases between October 2014 and November 2018 were included in this retrospective study. The patients' details, their tumor characteristics, the local and systemic treatments administered, the response evaluation and their survival data were collected from the hospital files and analyzed.

RESULTS: The median age of the 7 patients was 50 (range: 27-64) years. Carcinoid syndrome was present in two patients. The histopathology of all the patients were consistent with well-differentiated NET. As an initial treatment, one patient underwent right hepatectomy. All patients received somatostatin analog for a median of 20.7 months (range: 6-48 months) as an initial systemic treatment. One patient received radionuclide therapy and palliative radiotherapy for bone metastasis, one patient received trans arterial chemo embolization to the liver and one patient received capecitabine and temozolamide treatment after progression to somatostatin analog treatment. The median progression free survival and median overall survival (follow-up) was 15 months (range: 6-48 months) and 17 months (range: 8-48 months) respectively. All patients were still alive at the end of this study.

CONCLUSION: Primary unknown well-differentiated NETs presenting with liver metastasis have different clinical and survival characteristics than primary known metastatic NETs. Treating these patients as the same disease may not be appropriate.

Keywords: Neuroendocrine tumor, liver metastasis, prognosis

INTRODUCTION

Neuroendocrine tumors (NETs) constitute less than 5% of all cancers of unknown primary sites.[1] NETs of unknown primary site are seen 10 to 13% of all NETs.[2,3] Their prognosis differs greatly from each other according to their differentiation, grade, and possibly to their primary site of origin. Survival is lower in unknown primary NETs compared to patients with liver metastasis whose primary of NETs is known so it may be important to find the primary site.[4]

The distant metastasis rates are around 40 to 45% in small intestine, colon and pancreas, 15% in stomach, 6% in rectum and 3% in appendix primaries. The five-year-survival rate is lower with distant metastatic

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NETs including the liver (about 30 to 60%).[5] Clinical symptoms may help to detect the primary site of NETs. Carcinoid syndrome is present in 17% of cases and this suggests a small intestinal primary.[6] Immunohistochemistry (IHC) is used to find the primary site of liver metastatic NETs. Thyroid transcription factor 1 (TTF-1) is positive in poorly differentiated neuroendocrine carcinomas (NECs) and some well-differentiated NETs of lung origin but caudal-type homeobox-2 (CD-X2) is positive in well-differentiated NETs of intestinal origin.[6] Mesenteric masses also indicate a primary located in the small intestine. Pancreatic primaries are usually larger than both small and large bowel primary tumors (7.5 cm vs. 1.7 cm and 3.8 cm respectively).[7]

Resection of the primary tumor, locoregional lymph node, and liver metastasis prolongs survival and improves the quality of life in NETs.[8] Somatostatin analogue therapy is beneficial mostly in all functional NETs and small intestinal grade G1 and G2 primaries. Everolimus and sunitinib are approved for pancreatic NETs.[9] Pancreatic NET are also sensitive to chemotherapy such as temozolamide alone or in combination with capecitabine.[9] For patients with advanced poorly differentiated NECs, the prognosis is poor and determining the primary site may not alter the treatment which is usually platinum based chemotherapies but treatment for patients with metastatic well-differentiated NETs depends on the primary site.[10]

The aim of this study was to answer the question of whether the primary site is important for the management of well-differentiated liver metastatic NETs whose primary site is not known after routine screening. For this, we have retrospectively analyzed seven unknown primary NET cases.

MATERIALS AND METHODS

Seven patients diagnosed with NET who presented with multiple liver metastases between October 2014 and November 2018 were included in this retrospective study. The patients' characteristics, the pathological characteristics of their tumors, the local and systemic treatments administered, their response evaluations and survival data were collected from the hospital files and analyzed. NET was defined as well-differentiated if the Ki-67 index was equal to or below 20%. Well-differentiated, low-grade (G1) tumors have a mitotic count of less than 2/2 mm^2 [10 high-power field (HPF)] and/or a Ki-67 index of less than 3% while well-differentiated, intermediate-G2 tumors usually have a mitotic count of 2 to 20/2 mm^2 (10 HPF) and/or a Ki-67 index of 3% to 20%.[11] Progression free survival (PFS) was calculated as the time in months from the date of diagnosis to either the date of progression or the date of last follow-up for those patients without progression. Overall survival (OS) was calculated as the time in months from the date of diagnosis to the date of death or the last follow-up date.

The protocol for this retrospective study was compatible with the local ethical guidelines.

The study protocol was approved by the Ethics Committee of Sakarya University Training and Research Hospital and was conducted in accordance with the principles of the Declaration of Helsinki (approval number: 714522473/050.01.04/464).

Statistical Analysis

Statistical analysis was performed by SPSS 15.0 software, (SPSS Inc, Chicago, Illinois, USA). Data are expressed as median, mean and proportion. Survival analysis was estimated using the Kaplan-Meier method. Significance was defined as $p<0.05$.

RESULTS

Five of the patients were men and two were women. The median age of the 7 patients was 50 (range: 27-64) years. Abdominal pain was the leading symptom. Carcinoid syndrome was present in two patients. There was no sign of multiple endocrine neoplasia. One only patient was resectable. Basal serum chromogranin A (CgA) and urine 5-hydroxyindoleacetic acid (5HIAA) were elevated in four and three patients respectively (Table 1). The histopathology of all the patients were consistent with well-differentiated NET. IHC staining showed CgA and synaptophysin positivity in all cases. According to the mitotic count and Ki-67 index, four tumors were G2 and three tumors were G1. Three tumors were also positive for CD-X2 but TTF-1 was negative in all cases (Table 2). As an initial treatment, one patient underwent right hepatectomy. All patients received somatostatin analogue for a median of 20.7 months (range: 6-48 months) as an initial systemic treatment. One patient received radionuclide therapy and palliative radiotherapy for bone metastasis, one patient received trans-arterial chemo-embolization to the liver and one patient received capecitabine and temozolamide treatment after progression of somatostatin analog treatment. Median PFS and median OS (follow up) were 15 months (range: 6-48 months) and 17 months (range: 8-48 months) respectively. All patients were still alive at the end of this study (Table 3).

DISCUSSION

In addition to routine computed tomography (CT), magnetic resonance imaging, somatostatin receptor scintigraphy (SRS, Octreoscan), upper and lower endoscopies, endoscopic ultrasound (EUS), and capsule endoscopy may be needed in order to find small primaries.[7] We did

Table 1. Characteristics of patients with primary unknown neuroendocrine tumor presenting with liver involvement

Patient no	Age	Gender	Symptom	Co-morbidity	Resectable	CgA	5HIAA	Carcinoid syndrome
1	27	M	Gastric pain	None	No	High	High	Yes
2	64	M	Dyspnea	CAD	No	N	N	No
3	50	F	Abd. pain	DM, HT, COPD	No	High	N/A	No
4	50	M	RUQ pain	None	Yes	N	N	No
5	64	M	None	GI bleeding	No	High	High	No
6	54	F	Abd. pain	HT	No	N	N	No
7	39	M	Abd. pain	Appendectomy	No	High	High	Yes

G: gender, M: male, F: female, Abd: abdominal, RUQ: right upper quadrant, CAD: coronary artery disease, DM: diabetes mellitus, COPD: chronic obstructive lung disease, GI: gastrointestinal, HT: hypertension, CgA: serum cromogranin A, 5HIAA: urine 5- hydroxyindoleacetic acid, N: normal, N/A: not available.

Table 2. Pathological characteristics of patients with primary unknown well-differentiated neuroendocrine tumors presenting with liver metastasis

Patient no	Pathology	Diff.	Tumor grade	Mitotic count*	Ki-67 index	CgA	Synaptophysin	CD-X2	TTF-1
1	NET	Well	G2	>2	10	+	+	+	-
2	NET	Well	G1	<2	1	+	+	-	-
3	NET	Well	G2	>2	4	+	+	-	-
4	NET	Well	G2	>2	11	+	+	-	-
5	NET	Well	G2	>2	3	+	+	-	-
6	NET	Well	G1	<2	1	+	+	+	-
7	NET	Well	G1	<2	1	+	+	+	-

Diff: differentiation, NET: neuroendocrine tumor, CgA: chromogranin A, CD-X2: caudal-type homeobox, intestine-specific transcription factor, TTF-1: thyroid transcription factor 1, *mitotic count: counted in 10 high power fields, at 400x magnification evaluated in area of highest mitotic density. Cut-offs PER American Joint Commission on Cancer Stating Manual, 7th edition.

Table 3. Treatment characteristics of patients with primary unknown neuroendocrine tumor presenting with liver metastasis

Patient no	Initial Tx	Somatostatin analogue Tx	Dose (mg)	Somatostatin time (m)	Response	Secondary Tx	PFS (m)	OS* (m)
1	Palliative Rt (bone)	Octreotide LAR	10-30	48	Stable*	Radionuclide Tx (2 times)	48	48
2	-	Octreotide LAR	20	39	Stable	-	39	39
3	-	Octreotide LAR	30	6	Progression	Capecitabine-temozolamide (4 m)	6	17
4	Right hepatectomy	Octreotide LAR	30	15	Stable	-	15	15
5	TACE (liver)	Octreotide LAR	30	12	Stable	-	12	12
6	-	Octreotide LAR	30	17	Stable	-	17	17
7	-	Lanreotide	90	8	Stable	-	8	8

Tx: treatment, Rt: radiotherapy, TACE: transarterial chemo-embolisation, LAR: long acting release, M: month, PFS: progression free survival, OS: overall survival, *After 15 months' treatment with octreotide LAR, there was a progression of liver lesions, and patient one received radionuclide treatment 2 times in two months interval, then the disease remained stable with octreotide LAR 30 mg treatment until now. *All patients are alive at the end of the study.

not find the primary sites in our 7 liver metastatic NETs after routine workup. We did not use either EUS or capsule endoscopy because of the unavailability of these procedures in our hospital. Identification of the primary site may influence the surgical management of resectable metastatic NETs.[10] There was only one resectable liver metastasis in our primary unknown cases. If the primary site was the small intestine, the primary tumor would be so small that it would be extremely hard to find the primary site. However, this small primary NET can metastasize to regional lymph nodes causing mesenteric fibrosis and can be detected as multiple liver metastasis, which is not suitable for metastasectomy. In this case, resection of the primary intestinal tumors and regional lymph nodes or fibrosis is accepted as unresectable but stable liver metastasis.[10] This knowledge would have been beneficial in our cases if we had found the primaries of our cases to be in the small intestine.

When their primary cannot be found, well-differentiated tumors usually present with unresectable liver metastasis.[6] The presence of mesenteric mass, CD-X2 positivity and the presence of carcinoid syndrome may be the clues of intestinal primary and TTF-1 positivity may be positive in poorly-differentiated NECs and some well-differentiated NETs of lung origin.[6] In our primary unknown NET cases, they all presented as multiple liver metastasis. Our cases were all well-differentiated NETs. Four of them were G2 and three of them were G1 disease. Patients no: 1, 6 and 7 had CD-X2 positivity and patients no: 1 and 7 had carcinoid syndrome. There was no TTF-1 positivity in our cases. Treatment for well-differentiated NETs depends on the primary site. Pancreatic NETs are more sensitive to chemotherapy than other NETs from other sites. Everolimus and sunitinib are approved for those patients with advanced pancreatic NETs. Octreotide acetate improves the outcomes for those patients with advanced midgut (lower jejunum, ileum, cecum and appendix) NETs. We used octreotid acetate or lanreotide in all primary unknown cases. All patients responded to octreotid acetate or lanreotid treatment except for patient no: 3. Further treatment with capecitabine and temozolamide was also not effective in patient no: 3. The median duration of octreotid acetate treatment was 20.7 months (range: 6-48 months). This may show that our cases were sensitive to octreotid acetate similar to a midgut tumor.

Is it appropriate to treat primary unknown well-differentiated NETs as if they are a single entity? There are some clues that these tumors are different from each other. Gene expression analysis of C-type lectin domain family 13 member A (CD302) and peptidylprolyl isomerase domain and WD repeat containing 1 (PPWD1) in NET metastasis correctly identifies the primary in the ileum or in the pancreas in 80% of cases.[12] Even by using sensitive somatostatin receptor positron emission tomography/CT, the primary of one third of NET patients could not be determined.[13] Genetic signatures of primary and liver metastasis may explain the survival difference and somatostatin receptor agonist response as seen in our cases. Alternative lengthening of telomeres was also found to be a useful biomarker in patients with NET liver metastasis. This marker is positive in pancreatic origin in 56% of pancreatic NETs and positive only in 4% in gastrointestinal carcinoid tumors ($p<0.001$).[14,15] This may explain the treatment response differences of pancreatic and intestinal NETs to certain chemotherapies and targeted therapies such as everolimus and sunitinib. We did not use everolimus or sunitinib in our patients. Since patient no: 3 was not sensitive to somatostatin analogue, we tried capecitabine and temozolamide but she did not respond to chemotherapy at all. We have speculated that

patient no: 3 would not respond to everolimus or sunitinib as her tumor was not symptomatic. These targeted drugs are also approved for use in pancreatic functioning tumors. We managed all unknown primary cases like those with metastatic non-pancreatic well-differentiated tumors. We could control the carcinoid symptoms with somatostatin analogue treatment in patients no: 1 and 7. After treatment of somatostatin analogue, the high levels of CgA in the serum and 5-HIAA in the urine also decreased to normal levels in patients 3 and 5. In these patients, there was no overt carcinoid syndrome signs.

Depending on the patient's clinic and metastasis extend, local therapies may be used such as resection of the metastasis, hepatic arterial embolization or radionuclide therapies if the metastasis are somatostatin receptor positive in SRS. Curative resection is associated with better survival in all series and survival rates of 60 to 80% can be achieved in liver metastasis. In well-differentiated unresectable liver metastatic NETs, liver transplantation is a valid option in selected patients. The 5-year-survival and disease specific survival rates are 52% and 30% respectively. Although post-operative mortality is still high.[16] New surgical methods and liver parenchymal preserving surgical and radionuclide treatments may give better results in the future. In our patient no: 1, we achieved 4-year-survival in this multiple liver and bone metastatic patient with radionuclide therapy and somatostatin analogue treatment.

Study Limitations

This study was conducted on patients in a single university hospital, and this was accepted as a limitation. The limitations of this study include its small sample size and recruitment from a single center. Since NETs are one of the rare cancers, the number of cases in our study is low. This is another limitation.

CONCLUSION

Primary unknown well-differentiated NETs presenting with liver metastasis have different clinical and survival characteristics than primary known metastatic NETs. Treating these patients as if they are the same disease may not be appropriate. Well-designed prospective randomized studies about unknown primary NETs are needed.

MAIN POINTS

- Primary unknown well-differentiated NETs presenting with liver metastasis have different clinical and survival characteristics than primary known metastatic NETs. Treating these patients as if they are the same disease may not be appropriate.
- Gene expression analysis may guide us to identify the primary origin, the survival difference and somatostatin receptor agonist response.
- Depending on the patient's clinic and metastasis extend, local therapies may be used, such as resection of the metastasis, hepatic arterial embolization or radionuclide therapies.
- New surgical methods and liver parenchymal preserving surgical and radionuclide treatments may give better results in the future.

ETHICS

Ethics Committee Approval: The study protocol was approved by the Ethics Committee of Sakarya University Training and Research Hospital and was conducted in accordance with the principles of the Declaration of Helsinki (approval number: 714522473/050.01.04/464).

Informed Consent: Retrospective study.

Peer-review: Internally peer-reviewed.

Authorship Contributions

Concept: A.D., Design: A.D., Materials: H.C., C.V., Data Collection and/or Processing: H.C., C.V., Analysis and/or Interpretation: A.D., H.C., C.V., Literature Search: A.D., H.C., C.V., Writing: A.D., Critical Review: A.D., C.V.

DISCLOSURES

Conflict of Interest: No conflict of interest was declared by the authors.

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ORIGINAL ARTICLE

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The Effects of Preeclampsia on Breastfeeding Self-Efficacy and Postpartum Depression

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Abstract

BACKGROUND/AIMS: The aim of this study was to determine the effects of preeclampsia on breastfeeding self-efficacy and postpartum depression.

MATERIALS AND METHODS: This descriptive and cross-sectional study was conducted between January 2018 and May 2019 in a research and training hospital in İzmir, Turkey. Those mothers who complied with the acceptance criteria, who gave birth via caesarean section and who had preeclampsia (n=73) were accepted into this study. Data were collected using the Personal Identity Form, the Edinburgh Postpartum Depression Scale and the Breastfeeding Self-Efficacy Scale (BSES) in two follow-ups. The first follow-up was conducted in the patient room via a face-to-face interview with the mothers 24 hours after the birth. The second follow-up was conducted by telephone in the second month after the birth. Descriptive statistics, non-parametric tests and correlation analysis were used in the data evaluation.

RESULTS: The depression risk of the preeclamptic mothers was 16.4% in the 24th hour after birth, while it was 9.6% in the second month. A positive strong correlation was found between the BSES score averages of the mothers at the 24th hour and the second month after the birth.

CONCLUSION: According to the results found in this study, the self-efficacy of preeclamptic mothers was low and although the postpartum depression risks of the preeclamptic mothers were lower in their second month, this risk was still present.

Keywords: Preeclampsia, breastfeeding, self-efficacy, postpartum depression

INTRODUCTION

Preeclampsia, which is one of the pathologic processes of pregnancy, is observed in 3-10% of all pregnancies and it is one the most important factors for maternal and prenatal mortality and morbidity.[1] It causes negative results such as an increase in preeclampsia maternal and prenatal morbidity and mortality, intrauterine growth retardation, ablation placenta, caesarean birth, preterm birth and maternal-fetal death.[2,3] Beside these negative effects on maternal fetal health through the pregnancy period, preeclampsia also affects the medical conditions of both the mother and the newborn in the postpartum period. The health risks of hypertension, diabetes mellitus and cardiovascular increase for those mothers who have hypertensive disorder in their pregnancy.[4] Anxiety and affective disorder probability, as well as prenatal and postnatal depression frequencies are higher in preeclamptic women.[3] In addition, hypertensive disorders through pregnancy can lead to negative breastfeeding results by causing variations in the structure of the breast milk and disrupting prolactin levels. Preeclampsia has the risk of hypogalactia (the decreased or deficient secretion of milk) and agalactia (the failure of the secretion of milk from any cause other than the normal ending of the lactation period). Additionally, problems arise in starting breastfeeding and in its duration due to factors such as being apart from the newborn and a decrease in mother-newborn interaction as a result of maternal or fetal complications.[5,6]

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Postpartum maternal health and maternal functionality affects future pregnancy results, the development of maternal chronic disorders and the health of the newborn.[7] To protect and improve mother and newborn health, it is important to determine, support and give information regarding the needs of mothers on breastfeeding anxiety and life style arrangements, and newborn care, as well as the physical and emotional symptoms in the postpartum period. Preeclampsia, which is known to be one of the pregnancy risk types, might cause mothers to be more inclined to depression in pregnancy and the postpartum period. Depression might become severe in the postpartum period so as to effect breastfeeding negatively. Studies on postpartum depression levels and the breastfeeding self-efficacy of preeclamptic mothers are very limited in the literature.[5,8]

Health professionals should pay attention to mothers who have preeclampsia in the postpartum as well as in the antepartum period. They should determine their nursing requirements, have an awareness of any potential problems, make diagnoses in the early stages and plan appropriate interventions. The aim of this study was to analyze the effects of preeclampsia on postpartum depression and breastfeeding self-efficacy.

MATERIALS AND METHODS

This descriptive study was conducted between January 2018 and May 2019 in the maternity clinic of a training and research hospital in İzmir, Turkey.

Population-sample: This study was conducted with preeclamptic mothers who gave birth by cesarean section and who were appropriate for the inclusion criteria. In the hospital where this study was conducted, preeclamptic mothers were followed up in intensive care units for a minimum of 24 hours after surgery, so breastfeeding was not efficient through this period. During this period, the newborn was given to an attendant and followed up in clinics. Newborn formula was given according to a pediatric doctor's instructions. Breastfeeding was only able to be initiated after the mother's exit from the intensive care unit.

The sampling size was determined by prior power analysis GPower 3.1 software. The sampling size was determined to be 71 and the effect size (d) was determined to be 0.31 by using the Edinburgh Postpartum Depression Scale (EPDS). The sample set of the study was built up by using a purposive sampling method with 73 preeclamptic mothers who were appropriate for the inclusion criteria. Those mothers who were older than 18 years, had caesarean surgery, did not have any other complication except for preeclampsia, were willing to attend the study, and did not have any complications in the postpartum period were accepted into this study.

Data collection: The Personal Identification Form, the EPDS and the Breastfeeding Self-Efficacy Scale (BSES) were used to collect the data in this study. The Personal Identification form was prepared by the researchers with respect to the literature.[3,4,8] There were 22 questions which collected data about the socio-demographic and obstetric characteristics and breastfeeding situations of the mothers. The EPDS was developed by Cox et al.[9] to investigate depression risks in women in the postpartum period. EPDS is a Likert type personal evaluation scale with 10 questions. The total scoring can vary between 0-30. The cut-off scores of the scale are 12 and below or 13 and above[9] and in this study, participants who had scores of 13 or above were accepted as being in the risk group. Engindeniz et al.[10] conducted the Turkish validity and reliability studies. The Cronbach's alpha value was determined to be 0.79 in Engindeniz et al.[10] study and it was determined to be 0.76 in Aydin et al.'s study. In this study, it was determined to be 0.91. The BSES was developed by Dennis and Faux[11] to evaluate how mothers feel regarding their self-efficacy about breastfeeding. The scale has 14 items and is a five-point Likert type scale, with a minimum score of 14 and a maximum score of 70. There is no cut-off point but higher scores show higher self-efficacy levels. Dennis and Faux[11] determined the Cronbach's alpha score to be 0.94, Alus Tokat and Okumus[12], who conducted the Turkish validity reliability study, found it to be 0.86. In this study, the Cronbach's alpha score was found to be 0.88.

The data were collected by the researcher in a research and training hospital in İzmir by conducting two follow-ups with the mothers in the sample set. The first follow-up was conducted with the mothers when they had completed their first 24 hours after giving birth and the second follow-up was conducted in the second month after birth. The Personal Identification Form, EPDS and BSES were given to the mothers in the first follow-up and the EPDS and BSES were used in the second follow-up.

Ethical considerations: Ethics committee approval was received for this study from the Ethics Committee of University of Health Sciences Turkey, İzmir Tepecik Training and Research Hospital (approval number: IRB: 23, date: 10.01.2018). The content of this study was explained and written consent was obtained from the participants.

Statistical Analysis

IBM SPSS 22.0 (IBM Corp., Armonk, NY, USA) statistical software was used in the analysis of the data collected in this study. The socio demographic characteristics of the mothers in the sample set are given as arithmetic mean, number and percentage distribution. Normal distribution convenience analysis was made to analyze the EPDS and BSES mean scores according to the socio-demographic characteristics of the mothers. In addition, non-parametric tests, Mann-Whitney U, Kruskal-Wallis and Wilcoxon tests were used. Correlation analysis was used to analyze the relationship between the 24th hour and 2nd month depression and breastfeeding self-efficacy of the preeclamptic mothers. $P<0.05$ was taken to be the significance level in all statistical analysis.

RESULTS

The mean age of the preeclamptic mothers was 30.63±6.54 years, 32.9% of the mothers were having their first pregnancy (Table 1). In this study, 54.8% of the mothers declared that they had received information about breastfeeding during their pregnancy, 81.6% had breastfed their previous baby. The ratio of starting breastfeeding in the first hour was 16.4%, and 69.9% of the mothers started breastfeeding within the first day. Nothing except mother's milk was given to 78.1% of the newborns in the first 24 hours. All preeclamptic mothers were breastfeeding in their second month after giving birth and 43.8% of the newborns were being fed formula together with breastfeeding. In this study, 71.2% of mothers declared that they were feeding their babies once every 1-3 hours, and 41.1% of the mothers were planning to go on feeding for up to three years (Table 2).

The depression risk of the preeclamptic mothers who participated in this study was found to be 16.4% at the 24th hour and 9.6% at the second month. No statistical difference was found between the means

of the EPDS total scores of the mothers in the 24th hour and the second month (z=-0.336; p=0.737). The mean of the BSES total scores of the preeclamptic mothers increased in the second month compared to their 24th hour score, the difference between them was statistically significant (z=-7,188; p=0.000) (Table 3).

No correlation was found between the means of the EPDS and BSES total scores of the preeclamptic mothers in the postpartum 24th hour and the second month in this study. However, a positive strong correlation was found between the mean of the BSES total scores in the 24th hour and the second month (r=0.714; p=0.000) (Table 4).

DISCUSSION

Preeclampsia had a relationship with some complications such as preterm and low birth weight newborns. These negative complications might cause negative feelings and stress which might enhance the mothers' risks of postpartum depression. Preeclampsia is a serious issue and it may lead to maternal depression in the postpartum period.[5-8] In this study, the depression risk of the preeclamptic mothers was found to be 16.4% in the 24th hour and 9.6% in the second month. In many studies conducted in different countries, it was found that the depression rate was higher in postpartum period for preeclamptic mothers compared to healthy mothers, and this rate ranged between 6.8% and 39.8%.[13-17] Meltzer-Brody et al.[16] conducted a study in Denmark to determine the predictive factors which cause postpartum depression and postpartum psychosis. In their study, it was found that postpartum depression risk was 1.84 times higher for hypertensive mothers and 1.45 times higher for preeclamptic mothers.[16] In the study, no other complications arose for the preeclamptic mothers and both the mothers and their newborn did not have any problems in the postpartum period, or indications relating to hypertension downfall. All these result in decrease of risk perception that preeclampsia caused/might cause, so depression risk decreased in the second month of preeclamptic mothers.

In this study, it was found that the breastfeeding self-efficacy of the preeclamptic mothers was higher in the second month compared to their 24th hour. However, it was found in the literature that the breastfeeding self-efficacy of eclamptic mothers was lower compared to healthy mothers.[18-20] Self-efficacy perception is decisive on a person's participation in activities or avoidance of activities. Dennis defined breastfeeding self-efficacy perception as the "efficacy perception of the mother for breastfeeding".[14] It was found in the literature that mothers

Table 1. Socio-demographic characteristics of mothers (n=73)

Variables	Mean ± SD[a]	
Mean age (year) (min.-max.)	30.63±6.54 (18-46)	
	Number (n)	Percentage (%)
Education status		
Literate	15	20.5
Primary school	24	32.9
Secondary school or higher	34	46.6
Employment status		
Working	6	8.2
Not working	67	91.8
Family type		
Nuclear	55	75.3
Extended	18	24.7
Number of pregnancy		
First	24	32.9
Second	13	17.8
Third	12	16.4
>4	24	32.9
Planned pregnancy or not		
Planned	54	74.0
Unplanned	19	26.0
Gestational week		
Term (>37th week)	50	68.5
Preterm (<37th week)	23	31.5
Sex of newborn		
Girl	40	54.8
Boy	33	45.2
	Mean ± SD[a]	
Mean of newborn weight (gram) (min.-max.)	2,951.31±517.03 (1,900-4,130)	
Mean of baby weight in the second month (gram) (min.-max.)	4,726.42±677.98 (3,520-6,800)	

SD[a]: standard deviation, min.: minimum, max.: maximum.

Table 2. Breastfeeding conditions of mothers (n=73)

Variables	Number (n)	Percentage (%)
Had training on breastfeeding		
Yes	40	54.8
No	33	45.2
Breastfed her previous baby (n=49)		
Yes	40	81.6
No	9	18.4
Presence of social support		
Yes	54	74.0
No	19	26.0
The first time breastfeeding		
In the first hour	12	16.4
In the first day	51	69.9
In the second day	10	13.7
Formula feeding within 24 hours		
Yes	57	78.1
No	16	21.9
Formula feeding within 2 months		
Yes	32	43.8
No	41	56.2
Feeding frequency in the 2nd month		
Whenever the baby cries	17	23.3
Once in 1-3 hours	52	71.2
Once in 4-6 hours	4	5.5
How long will breastfeeding be continued?		
Until the baby wants to stop	17	23.3
Up to one year	3	4.1
Up to two years	23	31.5
Up to three years	30	41.1

Table 3. The mean of EPDS and BSES total scores of mothers in the postpartum 24th hour and second month

Variables	Postpartum 24th hour (mean ± SD[a])	Second month (mean ± SD[a])	z/p
EPDS[b] total score	5.90±5.04	5.32±4.40	-0.336 0.737
	Number (%)	**Number (%)**	
Depression risk			
Yes	12 (16.4)	7 (9.6)	-
No	61 (83.6)	66 (90.4)	-
	Mean ± SD[a]	**Mean ± SD[a]**	
BSES[c] total score	52.42±8.61	62.12±4.85	-7,188 0.000

EPDS[b]: Edinburgh Postpartum Depression Scale, BSES[c]: Breastfeeding Self-Efficacy Scale: SD[a]: standard deviation.

Table 4. The relationship between the mean of EPDS and BSES total scores of preeclamptic mothers in postpartum 24th hour and 2nd month

Variables	Second month EPDS[a] total score	Postpartum 24th hour BSES[b] total score	Second month BSES total score
Postpartum 24th hour EPDS total score	r=0.142 p=0.232	r=0.055 p=0.644	r=-0.041 p=0.731
Second month EPDS total score	-	r=0.135 p=0.255	r=-0.043 p=0.718
Postpartum 24th hour BSES total score	-	-	r=0.714 p=0.000

EPDS[a]: Edinburgh Postpartum Depression Scale, BSES[b]: Breastfeeding Self-efficacy Scale.

who had lower breastfeeding self-efficacy completed their breastfeeding in a much shorter time than recommended. On the other hand, those mothers who had higher breastfeeding self-efficacy had less problems in starting and continuing breastfeeding.[21,22] Strapasson et al.[21] conducted a study to analyze the effects of gestational hypertension on the feeding of a newborn in his/her first six months and it was found in their study that the breastfeeding period of gestational hypertension mothers was shorter compared to normotensive mothers and their rate was higher in giving other formulas in place of mother's milk. In the study of Leeners et al.[22], which was conducted to analyze the breastfeeding of those mothers who had hypertensive diseases in their pregnancy, it was found that 76.1% of preeclampsia mothers had breastfeeding intentions, 43% continued breastfeeding into their first month and 39.9% continued into their third month. In the literature, for studies which were conducted with preeclamptic mothers, it was stated that the most important factor affecting breastfeeding was premature birth and intensive care admission. In this study, the fact that most of newborns were born term and their birth weight means were within the normal limits may have affected the breastfeeding self-efficacy. In addition, it is thought that the fact that the majority of the mothers had been trained with regards to breastfeeding, received support during breastfeeding, and that all of them wanted to continue breastfeeding are other factors affecting breastfeeding self-efficacy.

In this study, no correlation was found between the 24th hour and second month depression risks and breastfeeding self-efficacy of the preeclamptic mothers. No other research was found in the literature which analyzed the correlation between breastfeeding self-efficacy and the postpartum depression of preeclamptic mothers. Küçükoğlu et al.[23] conducted research on postpartum depression and the breastfeeding self-efficacy of mothers (n=110) whose babies were inpatients in newborn clinics and no correlation was found between self-efficacy and postpartum depression. Haga et al.[24] found in their study which was conducted in the postpartum period that postpartum depression levels were less for mothers who had higher breastfeeding self-efficacy. In the cross sectional study by Zubaran and Foresti[18] which was conducted in Brazil to analyze the correlation between breastfeeding self-efficacy and postpartum depression of healthy mothers, it was found that there was a negative correlation between postpartum depression levels and breastfeeding self-efficacy. In another study conducted by Aslan and Ege[25] with healthy mothers, no correlation was found between breastfeeding self-efficacy and postnatal depression.

Postpartum maternal health affects future pregnancy outcomes, maternal chronic disease development and infant health. Early identification and intervention with respect to the mothers' needs for information and support regarding their physical and emotional symptoms, baby care, breastfeeding anxieties and lifestyle arrangements are important for the protection and development of women's and children's health. Preeclampsia, which is known to be one of the risky pregnancies, may cause mothers to become more prone to depression and affect breastfeeding outcomes during the postpartum period. Healthcare professionals should determine the care needs of mothers with preeclampsia in the antepartum period as well as in the postpartum period, be aware of the problems which may arise and be able to quickly diagnose and plan appropriate interventions.

Study Limitations

This study was a cross-sectional survey design and its results cannot be generalized to all preeclamptic mothers.

CONCLUSION

This study is conducted to analyze the effects of preeclampsia on breastfeeding self-efficacy and postpartum depression. Health professionals should evaluate the postpartum depression levels in mothers with appropriate measuring instruments and advise the ones at risk, and they should evaluate the breastfeeding self-efficacy of the mothers before they are discharged from hospital. More researches should be conducted on the breastfeeding self-efficacy of mothers who have been diagnosed with postpartum depression with wider sample sets.

MAIN POINTS

- The depression risks of preeclamptic mothers who participated in this study were found to be 16.4% at the 24th hour and 9.6% in the second month.
- The mean of the BSES total scores of the preeclamptic mothers increased in the second month compared to their 24th hour score, and the difference between them was statistically significant
- A positive strong correlation was found between the mean of the BSES total scores in the 24th hour and the second month.

ETHICS

Ethics Committee Approval: Ethics committee approval was received for this study from the Ethics Committee of University of Health Sciences Turkey, İzmir Tepecik Training and Research Hospital (approval number: IRB: 23, date: 10.01.2018).

Informed Consent: The content of this study was explained and written consent was obtained from the participants.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: T.Ö., N.E.C., Design: T.Ö., N.E.C., Supervision: T.Ö., N.E.C., Data Collection and/or Processing: T.Ö., N.E.C., Analysis and/or Interpretation: T.Ö., N.E.C., Literature Search: T.Ö., N.E.C., Writing: T.Ö., N.E.C., Critical Review: T.Ö., N.E.C.

DISCLOSURES

Conflict of Interest: No conflict of interest was declared by the authors.

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ORIGINAL ARTICLE

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Knowledge on Medical Waste Management Among Health Care Personnel: A Report from Turkey

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Abstract

BACKGROUND/AIMS: The amount of medical waste from hospitals and other health institutions is on the rise which leads to more significant risks for healthcare personnel. This risk can be decreased primarily by increasing health care personnel's knowledge and awareness of this issue. The aim of this study was to determine the level of knowledge among healthcare personnel on medical waste management (MWM) and whether it differs with socio-demographic characteristics, or across different occupational groups, and hospital units.

MATERIALS AND METHODS: This study was conducted on 412 healthcare personnel [98 doctors, 206 nurses and midwives, 56 auxiliary health staff (AHS), and 52 other staff]. A questionnaire consisting of 15 questions was used in order to measure knowledge on MWM. MWM knowledge was evaluated as inadequate (≤5 correct answers), moderate (6-10 correct answers) or adequate (≥11 correct answers).

RESULTS: The average score on the MWM questionnaire was 68.38±15.73% in all participant. The distribution of participants in the MWM knowledge groups of adequate, moderate, inadequate was 48.5%, 47.9%, and 3.6%, respectively. Nurses, AHS and other staff had higher MWM knowledge scores than doctors (71.62±14.51%, 69.88±16.13%, 69.36±16.66% and 60.20±14.75%, respectively, $p<0.01$). Laboratory staff had higher MWM scores than all other professional groups ($p<0.01$). High-school and associate degree graduates had higher MWM scores ($p<0.05$) than master and PhD graduates.

CONCLUSION: Despite a moderate-adequate level of MWM knowledge among healthcare personnel, there is still a lack of knowledge on critical topics. Increasing the knowledge and awareness on MWM needs to be a primary concern for all health personnel, and especially for doctors.

Keywords: Health risks, healthcare workers, knowledge, medical waste management

INTRODUCTION

Medical waste is defined as waste produced during medical procedures in healthcare facilities, research centers, and laboratories, and waste from small or dispersed resources during household medical care. They are categorized into hazardous waste (including infectious, pathologic, pharmaceutic, cytotoxic, chemical, and radioactive wastes) or general waste (including biologic, chemical, radioactive or non-hazardous wastes).[1] Medical waste encompasses harmful viruses such as human immunodeficiency virus and hepatitis B or C, which can potentially affect patients, health workers, and/or the general population, and resistant microorganisms from health institutions that can spread to the environment.[2] Medical waste and their side products can give rise to piercing and cutting injuries; exposure to toxic pharmaceutical products such as antibiotics, cytotoxic drugs, mercury, and dioxin among others during transportation and disposal of medical waste; possible chemical burns during disinfection, sterilization or waste treatment processes; air pollution due to particles occurring during the disposal of medical

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waste; and burns due to medical waste disposal and radiation.[3,4] According to the World Health Organization, 85% of waste generated during health processes is general, non-hazardous waste, and the remaining 15% is infectious, toxic or radioactive hazardous waste.[5] In addition to doctors, nurses, midwives, auxiliary health personnel, and laboratory technicians, all individuals who are exposed to medical and other waste are potentially at risk.[6] Risk can be reduced through regular education of health personnel, thereby increasing their knowledge and awareness on medical waste management (MWM).[7,8]

The basis for this study is the current lack of studies on MWM knowledge levels, as determined after a search in the PubMed database using the keywords "*medical waste management*, *healthcare workers*, *knowledge*, and *Turkey*". The purpose of this work was to determine the MWM knowledge levels of healthcare personnel working in a training and research hospital, and whether the level of knowledge changed with respect to demographic characteristics, occupational groups, education levels, and work units.

MATERIALS AND METHODS

A single center, prospective, descriptive study was conducted on 412 health personnel aged 18 years or above, between February 15th, 2019, and March 15th, 2019 in İstanbul. The written consent of the participants and approval of the İstanbul Medeniyet University, Göztepe Training and Research Hospital Local Ethics Committee were obtained for this study. This study complied with the principles of the Helsinki Declaration.

Sample size: The probability of type 1 error (α) was accepted as 0.05 (95% confidence level), the value of z was found to be 1.96. Standard deviation (SD) values obtained for the MWM knowledge levels of the participants were combined and the SD of the population was estimated to be 10, the margin of error was accepted as 1 unit. According to these calculations, it was found appropriate to include a total of 412 participants to determine a population average with a 95% confidence level with a 1-unit margin of error, also taking into consideration the possibility of 10% data loss.

Inclusion criteria: Health staff aged 18 years or above who agreed to provide written consent to participate in this study.

Exclusion criteria: Health workers who contributed to the design and execution of the study, hospital MWM unit managers, MWM staff and MWM field personnel, and staff involved in the preparation of MWM hospital education programs.

Primary endpoint of this study: Determining the levels of MWM knowledge among health personnel, and investigating whether the level of knowledge differed according to their occupational groups, demographic characteristics, education levels, and work units.

Study design: Participants who gave written consent were randomly included in the study and were categorized according to their occupational groups [doctors, nurses and midwives, auxiliary health staff (AHS), and other staff (administration, data entry, and security personnel)], and also according to their work units [internal medical sciences, surgical medical sciences, intensive care units, laboratories, emergency services and other units (administration and polyclinics)], and according to their educational status (primary/high school; associate degree, bachelor's, and master's degrees; and doctoral graduates). Operating room personnel were not included in this study because face-to-face surveys were not possible for this group.

Survey: Before this study was carried out, the survey was validated by an expert in terms of content and relation to the topic. A dry run was conducted to assure a high acceptance level. A pre-test was administered to 20 health personnel who did not participate in the final study. The survey was carried out by appointment at the participants' own working units during working hours and conducted in a face-to-face method. No time limitation was enforced so that the participants could complete the questions comfortably. Correct answers were provided to the participants after the survey was completed if requested. The three-part survey was conducted by the authors of this article. The questions and participant answers are given in Table 1. The first part consisted of questions on the age and sex, occupational groups, work units, and educational status of the participants. In the second part, five questions relating to MWM training and the general thoughts of the participants were asked. In the third part of the survey, 15 test questions with single correct answers were asked, measuring their knowledge on MWM. These questions were prepared in accordance with the "*Medical Waste Control Regulation*"[9] published by the Ministry of Environment and Urbanization (25.01.2017) in the Official Gazette (number: 29959). The points for correct answers to these 15 MWM questions were calculated and the results were normalized to a scale in the range of 0-100 for statistical purposes. No correct answers were adjusted 0 points, all correct answers to these 15 questions were adjusted to 100 points and an MWM knowledge score was calculated. These scores were then compared according to the demographic characteristics, occupational groups, work units, and educational status of the participants. Additionally, according to the distribution of the correct answers, MWM knowledge levels were classified as inadequate (≤5 correct answers), moderate (6-10 correct answers), or adequate (≥11 correct answers).

Statistical Analysis

The NCSS (Number Cruncher Statistical System) 2007 (Kaysville, Utah, USA) program was used. Descriptive statistical methods (mean, SD, median, frequency, ratio, minimum, maximum) were used to evaluate the study data. The normal distribution of quantitative data was tested using the Kolmogorov-Smirnov and Shapiro-Wilk test and graphical evaluations. Student's t-test was used to compare two groups of quantitative data with normal distribution. The Bonferroni test was used for double comparisons and One-Way analysis of variance was used in triple or more group comparisons with normal distribution. Pearson's chi-square test and the Fisher-Freeman-Halton exact test were used to compare qualitative data. Pearson's correlation analysis was used to evaluate the relationships between variables with normal distribution. Significance was evaluated as $p<0.05$.

Results

A total of 412 participants (127 males, 285 females) participated in the survey. The mean age of the participants was 32.73±8.9 years. Ninety-eight of the participants (23.8%) were doctors, 206 (50%) were nurses and midwives, 56 (13.6%) were AHS, and 52 (12.6%) were other staff. According to their educational status, 8.7% of the participants were primary school graduates, 15.8% were high school graduates, 9% were associate graduates, 39.1% were bachelor graduates, 22.3% master graduates (18.7% of them were medical doctors, 3.6% were other healthcare professionals) and 5.1% were PhD graduates (all medical

Table 1. Questions, correct answers and participant answers of questionnaire

Questions	Options	Answers, n (%)
1. Who is responsible for waste management in the hospital?	a. Chief doctor	4 (1)
	b. Director of administrative and financial services	2 (0.5)
	c. Director of health care services	14 (3.4)
	d. Director of support and quality services	100 (24.3)
	e. ***Environment and Waste Unit Supervisor***	***292 (70.9)***
2. Which of the following does not describe medical waste?	a. Dangerous	60 (14.6)
	b. Bloody	6 (1.5)
	c. Infectious	11 (2.7)
	d. Sick	117 (28.4)
	e. ***Private waste***	***218 (52.9)***
3. Which of these symbols indicates medical waste?	a.	43 (10.4)
	b.	12 (2.9)
	c.	***352 (85.4)***
	d.	2 (0.5)
	e.	3 (0.7)
4. Which color is the bag of hazardous waste?	a. Red	141 (34.2)
	b. Blue	3 (0.7)
	c. Orange	28 (6.8)
	d. Black	7 (1.7)
	e. ***Yellow***	***233 (56.6)***
5. Which color is the domestic waste bag?	a. Red	0 (0)
	b. Blue	45 (10.9)
	c. Orange	2 (0.5)
	d. Gray	40 (9.7)
	e. ***Black***	***325 (78.9)***
6. Which color is the recycling waste bag?	a. Red	3 (0.7)
	b. ***Blue***	***377 (91.5)***
	c. Orange	11 (2.7)
	d. Gray	8 81.9)
	e. Black	13 (3.2)
7. Which color is the medical waste bag?	a. ***Red***	***394 (95.6)***
	b. Blue	1 (0.2)
	c. Yellow	14 (3.4)
	d. Gray	1 (0.2)
	e. Black	2 (0.5)
8. Which color do the medical waste personnel wear?	a. Red	40 (9.7)
	b. Blue	1 (0.2)
	c. ***Orange***	***336 (86.4)***
	d. Yellow	13 (3.2)
	e. Black	2 (0.5)
9. Where is the place for temporary waste storage in our hospital?	a. Pathology building	13 (3.2)
	b. Infectious diseases clinic	36 (8.7)
	c. Medical consumable storehouse	46 (11.2)
	d. ***Side area of technical services***	***306 (74.3)***
	e. Central emergency service	11 (2.7)
10. Which organization is responsible for medical and hazardous waste disposal?	a. Ministry of health	58 (14.1)
	b. Ministry of environment and urbanization	176 (42.7)
	c. Ministry of transportation	0 (0)
	d. Ministry of finance	1 (0.2)
	e. ***İSTAÇ İstanbul Metropolitan Municipality***	***177 (43.0)***
11. Which is the right bucket color for disposal of Chemotherapeutic drugs?	a. Red	74 (18.0)
	b. Green	64 (15.5)
	c. ***Yellow***	***226 (54.9)***
	d. Orange	45 (10.9)
	e. Blue	3 (0.7)
12. In which box are the intravenous catheter waste products disposed?	a. ***Medical waste***	***300 (72.8)***
	b. Domestic waste	2 (0.5)
	c. Recycling waste	4 (1.0)
	d. Dangerous waste	102 (24.8)
	e. Pathologic waste	4 (1.0)
13. Which is the correct bucket for glass waste disposal?	a. Medical waste	18 (4.4)
	b. Domestic waste	10 (2.4)
	c. ***Recycling waste***	***231 (56.1)***
	d. Dangerous waste	147 (35.7)
	e. Pathologic waste	6 (1.5)
14. Which of the buckets is for diapers?	a. Medical waste	85 (20.6)
	b. ***Domestic waste***	***310 (75.2)***
	c. Recycling waste	7 (1.7)
	d. Dangerous waste	6 (1.5)
	e. Pathologic waste	4 (1.0)
15. Which of the correct choice for cleaning supply package waste?	a. Medical waste	23 (5.6)
	b. Domestic waste	129 (31.3)
	c. Recycling waste	119 (28.9)
	d. ***Dangerous waste***	***129 (31.3)***
	e. Pathologic waste	12 (2.9)

Correct answers are marked in bold and italic.

doctors). Some 34.2% of the participants worked in internal medical sciences, 25% worked in surgical medical sciences, 8.5% worked in intensive care units, 6.6% worked in laboratories, 12.6% worked in emergency services, and 13.1% worked in other units.

The results of the survey evaluating MWM training status and general considerations are presented in Table 2. The majority (79.6%) stated that they had received training in MWM, 63.3% thought that the education they had received was adequate and sufficiently frequent, 88.1% stated that medical waste was collected regularly, and 74% thought that waste was appropriately separated. The percentage of participants who stated that they were exposed to very low, low, moderate, high or excessive risk during the collection and transportation of medical waste was 14.1%, 18.9%, 36.2%, 26.4%, and 4.4%, respectively. The ratios of MWM-trained nurses, AHS, and other staff was higher than that of doctors (p=0.001). The ratio of MWM-trained nurses was higher than all other staff (p=0.001). The percentage of participants who stated that their MWM training was adequate and sufficiently frequent was higher in nurses, AHS, and other staff when compared to doctors, and also higher in nurses and AHS compared to other staff (p=0.001). The ratio of doctors,

nurses, and AHS who thought that they were exposed to numerous risks during collection and transportation of waste was higher than that of the other personnel (p=0.009). There were more individuals among the doctors, AHS, and other staff with a lack of waste collection knowledge compared with the nurses (p=0.001). The rate of reporting regular waste collection was higher in hospital units with a higher proportion of nurses than in other units with a higher proportion of doctors and AHS (p=0.001).

The average number of correct answers to the questions on MWM was 10.26±2.36, and the average level of knowledge in percentages was 68.38±15.73%. The rates of participants with adequate, moderate, and inadequate MWM knowledge were 48.5%, 47.9%, and 3.6%, respectively. Women had better MWM knowledge than men (69.59±15.37% vs. 65.67±16.22%, p=0.019). There was a statistically significant weak positive correlation between age and MWM knowledge (r=0.128; p=0.009).

The MWM knowledge levels of the nurses, AHS, and other personnel were higher than those of doctors (71.62±14.51%, 69.88±16.13%, 69.36±16.66% vs. 60.20±14.75%, p=0.001, p=0.001, p=0.003, respectively) (Table 3).

The MWM knowledge levels of high school graduates were higher than those of staff with master's and doctoral degrees (p=0.049; p=0.024, respectively). The MWM knowledge of associate graduates was better than master's and PhD graduates (p=0.034, p=0.016, respectively) (Table 4). There was no statistically difference between medical doctors and other healthcare professionals in the master's graduates group in terms of MWM knowledge scores (p=0.006).

The MWM knowledge of laboratory workers was higher than medical ward, intensive care unit, and emergency department staff (p=0.002; p=0.004; p=0.001). Personnel working in the surgical wards and other units had higher knowledge levels than those in the emergency department (p=0.015; p=0.036, respectively) (Table 5).

The participants who had had MWM training had higher MWM knowledge levels than those without previous training (69.88±15.32% vs. 62.54±16.03%, p=0.001).

DISCUSSION

This study shows that the MWM knowledge of healthcare personnel can be ascertained as moderate-to-adequate, and doctors' MWM knowledge levels and MWM training statuses are lower than those of nurses, AHS, and other staff. Also, the level of MWM knowledge is higher among laboratory staff and in high school and associate degree graduates compared to the others.

The amount of medical waste from hospitals and other health institutions in our country is on the rise, which leads to more significant

Table 2. The results of the survey evaluating medical waste management training status and general considerations according to occupational groups

		Occupational groups				p
		Doctors, (n=98)	Nurses, (n=206)	AHS, (n=56)	Others, (n=52)	
		n (%)	n (%)	n (%)	n (%)	
MWM training status	Yes	53 (54.1)	190 (92.2)	47 (83.9)	38 (73.1)	**0.001**
	No	45 (45.9)	16 (7.8)	9 (16.1)	14 (26.9)	-
Considerations about sufficiency and frequency of received MWM training	Yes	35 (35.7)	154 (74.8)	43 (76.8)	29 (55.8)	**0.001**
	No	63 (64.3)	52 (25.2)	13 (23.2)	23 (44.2)	-
Considerations about risk of exposure during waste collection and transportation	Very Low	9 (9.2)	24 (11.7)	11 (19.6)	14 (26.9)	**0.009**
	Low	22 (22.4)	38 (18.4)	10 (17.9)	8 (15.4)	-
	Moderate	39 (39.8)	69 (33.5)	20 (35.7)	21 (40.4)	-
	High	24 (24.5)	68 (33.0)	13 (23.2)	4 (7.7)	-
	Excessive	4 (4.1)	7 (3.4)	2 (3.6)	5 (9.6)	-
Status of frequent waste collection in the assigned unit	Yes	82 (83.7)	191 (92.7)	44 (78.6)	46 (88.5)	**0.001**
	No	2 (2.0)	14 (6.8)	5 (8.9)	3 (5.8)	-
	No Idea	14 (14.3)	1 (0.5)	7 (12.5)	3 (5.8)	-
Status of waste sorting	Yes	71 (72.4)	154 (74.8)	41 (73.2)	39 (75.0)	0.973
	No	27 (27.6)	52 (25.2)	15 (26.8)	13 (25.0)	-

MWM: medical waste management, AHS: auxiliary health staff.

Table 3. Levels of medical waste management knowledge according to occupational groups

		MWM knowledge level (%)			p	Paired comparison
		n	Min.-max. (median)	Mean ± SD		
Duty	[1]Doctor	98	13.3-93.3 (60)	60.20±14.75	**0.001**	p_{1-2}: 0.001 p_{1-3}: 0.001 p_{1-4}: 0.003
	[2]Nurse	206	26.7-100 (73.3)	71.62±14.51		
	[3]AHS	56	33.3-100 (73.3)	69.88±16.13		
	[4]Others	52	20-100 (73.3)	69.36±16.66		

MWM: medical waste management, AHS: auxiliary health staff, min.: minimum, max.: maximum, SD: standard deviation.

Table 4. Levels of medical waste management knowledge according to educational status

		MWM knowledge level (%)			p	Paired comparison
		n	Min-max (median)	Mean ± SD		
Education status	[1]Primary school	36	33.3-93.3 (73.3)	69.26±16.89	**0.028**	p_{2-5}: 0.049 p_{2-6}: 0.024 p_{3-5}: 0.034 p_{3-6}: 0.016
	[2]High school	65	26.7-100 (73.3)	70.77±15.44		
	[3]Associate	37	20-100 (73.3)	72.25±15.91		
	[4]Bachelor's	161	13.3-100 (73.3)	68.65±16.10		
	[5]Master's	92	33.3-93.3 (66.7)	65.80±14.60		
	[6]PhD	21	40-93.3 (60)	61.90±14.01		

MWM: medical waste management, min: minimum, max: maximum, SD: standard deviation.

Table 5. Levels of medical waste management knowledge according to work unit

		MWM knowledge level point (%)			p	Paired comparison
		n	Min-max (median)	Mean ± SD		
Unit	[1]Medical wards	141	20-100 (66.7)	66.71±15.73	***0.001***	p_{1-4}: *0.002* p_{2-5}: *0.015* p_{3-4}: *0.004* p_{4-5}: *0.001* p_{5-6}: *0.036*
	[2]Surgical wards	103	13.3-93.3 (73.3)	70.81±15.48		
	[3]ICU	35	33.3-86.7 (60)	64.57±13.60		
	[4]Laboratory	27	53.3-100 (80)	79.01±13.92		
	[5]Emergency services	52	33.3-93.3 (60)	62.18±14.51		
	[6]Others	54	26.7-100 (73.3)	71.23±15.96		

MWM: medical waste management, ICU: intensive care unit, min: minimum, max: maximum, SD: standard deviation.

risks for health personnel.[10,11] This risk can be decreased primarily by training those health personnel at regular risk of exposure to medical waste and increasing their knowledge and awareness.[12] Our finding that participants with previous MWM training had higher scores than those with no training supports this idea.

There is a lack of literature on the MWM knowledge levels of health personnel in Turkey. A study evaluating MWM knowledge of health personnel in a public hospital in central Sakarya revealed that 69.6% of the health personnel had received training on medical waste. These MWM-trained personnel stated that there was an institutional waste plan (66.9%), that there were special storage areas for medical waste (73.5%), that there were trained personnel assigned to the collection and disposal of medical waste (72.6%), and that waste was classified according to color codes (81.5%).[13]

Studies evaluating MWM knowledge, awareness, positive attitudes and practices are conducted more often in developing countries; however, MWM knowledge scores are generally low. In a study by Deress et al.[14], MWM knowledge, attitudes, and practices of health personnel in Northwest Ethiopia were evaluated. Participants with sufficient knowledge made up 56%, positive attitudes were at a rate of 66.2%, and sufficient practical scores were 77.4%. Moreover, most of the participants had no previous biomedical waste management training.[14] A study by Dehghani and Rahmatinia[15] evaluating biomedical waste management knowledge, attitudes, and practices in Iran showed that general knowledge on MWM was low, activity levels were moderate, and there was no relationship between gender, occupation, or educational levels on knowledge. Only differences in practice were observed.[15] The study conducted by Sarker et al.[16] on the knowledge, practice, and potential barriers of MWM of health personnel in Bangladesh found that one-third of nurses and doctors and two-thirds of cleaning staff had insufficient knowledge. Moreover, 44% of doctors and 56% of cleaning staff had bad practices.[16] A study conducted by Hakim et al.[17] in a university hospital evaluating MWM knowledge, attitude, and practices of health personnel demonstrated that, in terms of waste disposal and hospital policies, management personnel had more knowledge than doctors and nurses; however, in terms of special disposal, they knew less. Furthermore, more nurses had sufficient practical scores than doctors (84% vs. 67.3%).[17] Njiru et al.[18] conducted a study on biomedical waste management awareness and practices of health personnel in a national hospital. The total awareness level was 60%, and among doctors, nurses, and auxiliary personnel, it was 51%, 65%, and 55%, respectively. In practice, general awareness was found to be high; however, doctors had lower scores than the other personnel.[18]

The "*Medical Waste Control Regulation*" published by the Environment and Urbanization Ministry in Turkey aims to provide administrative, technical, legal principles, policies, and programs for the collection, storage, recycling, transportation, and disposal of medical waste produced by health institutions without harming the population or the environment.[9] Compliance with this regulation across the country is high.[19] Our finding that MWM knowledge among health personnel is moderate-adequate might stem from obedience to the national policies and the positive effects of MWM training. Furthermore, the 80% of MWM-trained participants and their higher MWM scores compared with the untrained personnel supports this idea. Information from our hospital's research and development unit shows that personnel are informed on MWM through different communication methods, such as training being offered twice annually to all personnel, and units having one training session every month. Similar to results from other studies, the significantly low scores among doctors on our MWM test is another surprising and thought-provoking finding. The percentage of doctors who received MWM training was significantly lower than among nurses, AHS, and other personnel. This might be a result of an indifference among doctors towards MWM training, which in turn would negatively affect their knowledge levels. This is supported by data from the research and development unit of our hospital showing a low number of MWM-trained doctors.

The reason that MWM knowledge levels were higher in women could be because half of the participants were nurses and midwives, who also received the highest scores. In a study that included 540 nurses from a tertiary hospital in Eastern Turkey, Calikoglu and Aras[20]. reported that nurses had adequate knowledge on medical waste; mean scores of 17.6/20 would equate to 88.2% in our survey. This finding supports the idea that nurses have higher levels of MWM knowledge, similar to the results of our study.

Moreover, compared with master's and PhD graduates, high school and associate graduates had higher MWM scores. Master's and PhD graduates include mainly doctors, whereas high school and associate graduates include mainly nurses, midwives, AHS, and other staff. Therefore, the higher MWM knowledge levels of nurses, midwives, AHS, and other staff compared with doctors is paralleled by the higher knowledge levels of high school and associate graduates. The greater MWM knowledge of laboratory unit personnel is a result of their direct involvement with MWM. The low MWM knowledge level in the emergency service personnel group, which is at increased risk of exposure to medical waste, is another interesting finding of this study.

An intriguing result of our study is the high number of incorrect answers to questions about the disposal of chemotherapeutic drugs, hazardous waste materials, and glass waste. Emphasizing these topics in MWM training will help decrease health risks in connection to medical waste.

Study Limitations

The questions were prepared in accordance with the Medical Waste Control Regulation published by the Ministry of Environment and Urbanization as there is no national, validated reference survey on MWM.[9] A face-to-face survey of the operating room personnel was not possible. Moreover, this study was conducted in only one hospital, making generalizations of the findings problematic.

CONCLUSION

Despite the moderate-adequate level of MWM knowledge among health personnel, there is still a lack of knowledge on critical topics. MWM knowledge levels were higher in women healthcare workers (the vast majority of nurses and midwives), those working in laboratory units, and high school and associate degree graduates. The low level of MWM knowledge among doctors compared to other healthcare professionals might be a result of an indifference among doctors towards MWM training, which in turn would negatively affect their knowledge levels. Increasing the knowledge and awareness of MWM needs to be a primary concern, for all health personnel, especially for doctors. For this purpose, regular monitoring and training are required at all levels.

ETHICS

Ethics Committee Approval: The approval of the İstanbul Medeniyet University, Göztepe Training and Research Hospital Local Ethics Committee were obtained for this study.

Informed Consent: The written consent of the participants obtained for this study.

Peer-review: Internally peer-reviewed

Authorship Contributions

Concept: G.U., M.U., Design: G.U., M.U., Supervision: S.S., A.G., Fundings: F.Ö., A.G., G.U., Materials: G.U., Data Collection and/or Processing: G.U., S.S., Analysis and/or Interpretation: A.G., F.Ö., Literature Search: M.U., Writing: M.U., F.Ö., Critical Review: M.U., S.S.

DISCLOSURES

Conflict of Interest: No conflict of interest was declared by the authors.

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ORIGINAL ARTICLE

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Determination of Nurses' Perceptions of Nursing Diagnoses

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Abstract

BACKGROUND/AIMS: A nursing care plan is of great importance in detecting and evaluating a patient's health problems. The most important part of the care plan is making an accurate nursing diagnosis. As this is the first step, the perceptions of nurses about the process of making a correct diagnosis affects all care outcomes. In this respect, it is very important to measure nurses' perceptions of nursing diagnoses using systematic and standardized material.

MATERIALS AND METHODS: This descriptive study was conducted using the quantitative research method. It was conducted in a university hospital between the 16th of October and the 20th of November 2017. The sample of the study consisted of 56 nurses who agreed to participate in this study. The data were collected using a questionnaire including socio-demographic data and the "Perceptions of Nursing Diagnoses Survey". The data used were obtained using a face-to-face interview method. The SPSS 17 package program was used in the analysis.

RESULTS: The majority of the nurses (80.4%) participating in this study were women. 83.9% of them were language graduates, 50% had been employed for an average of one to four years, and 92.9% were clinical nurses. The mean score for the "definition and promotion of a career in nursing" sub-scale of the "Perception of Nursing Diagnoses Survey" (2.10±0.75) was the lowest, indicating that the nurses had the most positive perception of this aspect. The highest mean score was found in the sub-scale of "clearly determining the patient's condition" (3.10±0.65) and it was seen that nurses were inadequate in this area.

CONCLUSION: The Perception of Nursing Diagnoses Survey was used to examine all aspects of the nurses' perceptions of nursing diagnoses, which are one of the basic foundations of the practice of nursing. It was found that nurses had negative perceptions regarding the capacity of the nursing diagnosis to clearly define or understand the patient's condition.

Keywords: Nursing diagnosis, perception, nursing

INTRODUCTION

The nursing process is a systematic method of managing care. It has an important place in ensuring that nurses use a common language and that there is continuity of care. The nursing process is a scientific way of thinking which nurses are expected to internalize in order to have sufficient knowledge and skills when starting their professional lives.[1-3] A nursing diagnosis is an indispensable element of this process. According to NANDA, it is a clinical decision made by a nurse about the reactions of an individual, family or community to existing or potential health problems/life processes. These decisions allow for individualized holistic care by addressing the patient's problems, identifying possible risks, and maintaining and improving their health.[4-13] Nursing diagnoses also have an important place in both theoretical knowledge and nursing practices and they contribute to their development.[2-11] They make it easier for nurses to choose the interventions which they are authorized to carry out, and outline the goals to be achieved.[1,4,5]

Although the importance of nursing diagnoses is undeniable, there are significant problems in making and applying them. In order to be able to apply these diagnoses, sufficient knowledge is required, and their importance should be well understood. Nurses' differing

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perceptions of nursing diagnoses and their contribution to practice may adversely affect their usage.[1-25] The use of common terminology and universally accepted methods of planning patient care may also be affected. According to data obtained from Akın-Korhan et al.'s[1] "Nursing Diagnosis Perception Scale" validity/reliability study, nurses scored badly in the following areas: "clearly determining the patient's condition" (2.90±0.57); "ease of use" (2.75±0.50) and "conceptual direction" (2.73±0.59). In the study completed by Avşar et al.[4], when asked whether they experienced difficulties when making a diagnosis, 23% of nurses said "Yes", 29.4% said "No", and 53.1% said "Sometimes".

Having a positive perception of the use of the nursing diagnosis makes it easier to identify a patient's problems, plan patient care, and increase its quality. In this respect, it is important to create guidelines for the appropriate use of nursing diagnoses.[13-17] The benefits of these guidelines include improving nurses' critical thinking and diagnostic competence, and being able to evaluate the relationship between interventions and patient outcomes.[19-28]

The number of studies regarding nursing diagnoses is increasing. However, studies about the perception of nursing diagnoses are mostly conducted with students, rather than fully-qualified nurses. Some studies have stated that students are better at making diagnoses (when there is a limited number of diagnoses to be made). This has been explained as being due to them being in a period of continuing education.[27-29] The results of this study will thus be beneficial in terms of the quality of care provided and will contribute to the literature about nursing. In this respect, the aim of the study was to determine how nursing diagnoses are perceived by nurses and the factors affecting this.

MATERIALS AND METHODS

This study was conducted as a descriptive study in order to determine nurses' perceptions of nursing diagnoses. This study took place in a university hospital. It was completed with patients in a private hospital which had two private intensive care units and four inpatient service units with a capacity of 100 beds. The patients were distributed among the nurses. In order to obtain data, each patient was monitored using a daily nurse observation form. Nurses use the care plan for diagnosis, implementation of treatment and evaluation. This care plan is commonly used for diagnoses (infection risks, risk of falling, etc.).

It was planned that all the nurses from the intensive care units and the inpatient service unit would take part in this study (89 nurses). However, the final sample of the study consisted of 56 (62.9%) nurses who agreed to participate in the study, and who were not on leave or on report at the time of this study.

The Introductory Characteristics Form and the Perceptions of Nursing Diagnosis Survey were used to collect the data. The Introductory Characteristics Form was prepared by the researcher in consultation with the literature.[6-24] The Introductory Characteristics Form collected information such as the nurses' age, gender, educational status, position at the hospital etc. Some of this socio-demographic data, e.g. year of graduation, years of employment etc., is thought to affect the perception of diagnosis. The data collected was analyzed with regard to its effect on making diagnoses. The Perceptions of Nursing Diagnosis Survey was developed by Olsen, Frost and Orth in 1991. The original Cronbach's alpha value of this scale was 0.94 and the Cronbach's alpha values of the sub-scales ranged from 0.79 to 0.92. The validity and reliability study of the Turkish version was conducted by Akın-Korhan et al.[1] and its Cronbach's alpha value was found to be 0.84. The survey includes four sub-domains that assess the ease of use of nursing diagnoses, perceptions about the benefits to the profession, and the care process. In this scale, there are 9 items in the sub-domain which evaluates perceptions about the effect of the diagnoses on the definition and promotion of a career in nursing, 8 items in the sub-domain which evaluates perceptions about how diagnoses facilitate understanding of the patient's situation, 8 items in the sub-domain which evaluates perceptions about the ease of use of diagnoses, and 5 items related to the conceptual aspect of diagnoses. The scale is a 5-point Likert-type scale, and each item is scored from 5 "strongly agree" to 1 "strongly disagree". The total scale score is calculated by dividing the total score by the number of items. Lower scores indicate that nurses have a more positive perception of nursing diagnoses.

In the present study, the Cronbach's alpha value was 0.81 for the whole scale, while it was 0.75, 0.65, 0.78 and 0.68 for the sub-scale of "definition and promotion of a career in nursing", "clearly defining the patient's condition", "ease of use", and "conceptual aspects", respectively.

The Introductory Characteristics Form was applied to 10 nurses initially, and then the rest of the sample was included. The data were collected face-to-face over the course of three months during the nurses' afternoon shifts, although they also worked night shifts. The SPSS 17 program was used to analyze the data. The data were analyzed in terms of number, percentage frequency, standard deviation, average and vet testing.

Ethical Considerations

In order to conduct this research, written permission was obtained from the University Ethics Committee (approval number: 459, date: 26.10.2017) and the Hospital's Chief Physician. In addition, written consent was obtained from the nurses who volunteered to participate in this study.

RESULTS

As can be seen in Table 1, the mean age of the participants was 35± and 80.4% of them were women. More than one third of them stated that they were living in Northern Cyprus and 67.9% of them were single. 83.9% stated that they had a bachelor's degree, 50% of them stated that they had been employed in the profession between one and four years, and 51.8% of them stated that they had worked in the clinic for between one to four years. Almost all of the nurses who participated in our study (92.9%) were working as clinical nurses. 83.9% of them worked in shifts, and 62.2% worked more than 40 hours per week; in other words they were working longer than the legal number of working hours. The nurses stated that they worked with an average of four nurses in each shift and provided care for five patients in that time.

As seen in Table 2, 78.6% of the nurses participating in this study stated that they had received information about nursing diagnoses. 64.9% of them had received this information during their formal education, while 14.3% had received information during in-service training. 88.7% of the participants stated that they had sufficient information about nursing diagnoses, and 87.5% of them stated that these diagnoses should be used in patient care. However, only 55.4% stated that they provided care using nursing diagnoses. 42.8% of nurses stated that they would like to receive more education about nursing diagnoses.

Table 1. Distribution of the data on the socio-demographic characteristics of the nurses

Socio-demographic characteristics, (n=56)	Number	%
Gender		
Female	45	80.4
Male	11	19.4
Place of residence		
Turkish Republic	18	32.1
Turkish Republic of Northern Cyprus	22	39.3
TR + TRNC	14	25
Other	2	3.6
Marital status		
Married	18	32.1
Single	38	67.9
Educational status		
High school degree (vocational school of health)	2	3.6
Associate's degree	4	7.1
Bachelor's degree	47	83.9
Postgraduate degree	3	5.4
Working years in the profession		
0-11 months	16	28.6
1-4 years	28	50
5-20 years	12	21.4
Working years in the clinic		
0-11 months	17	30.4
1-4 years	29	51.8
5-20 years	9	17.8
Status		
Chief nurse	4	7.1
Clinic nurse	52	92.9
Shift		
Daytime	9	16.1
Night	47	83.9
Working hours		
40 hours a week	35	62.2
40 hours or over a week	21	37.8
Number of nurses working together in the shift		
1-4	48	85.7
5+	8	14.3
Number of patients receiving care during the shift		
1-5	29	51.8
6+	27	48.2

As seen in Table 3, the mean score of the nurses for the Perceptions of Nursing Diagnoses Survey ranged from a minimum of 1.10 to a maximum of 4.55, and their average score was 2.23±0.40. The mean score of the nurses for the "definition and promotion of a career in nursing" sub-scale was 2.10±0.75, their mean score for the "clearly defining the patient's condition" sub-scale was 3.10±0.62, their mean score for the "ease of use" sub-scale was 2.25±0.53, and their mean score for the "conceptual aspects" sub-scale was 2.85±0.58.

Table 2. Distribution of the data related to the nursing diagnoses of the nurses

Socio-demographic characteristics, (n=56)	Number	%
Sufficient knowledge status for nursing diagnoses		
Yes	48	88.7
No	8	14.3
Status of receiving information/training on nursing diagnosis		
Yes	44	78.6
No	12	21.4
The resource of nursing diagnoses training		
In service	8	14.3
VSOH-AD-BD	33	64.9
Congress	1	1.8
Other	2	3.6
No information or training received	12	21.4
Willingness to receive further training regarding nursing diagnoses		
Yes	24	42.8
No	32	57.2
Status of using nursing diagnoses in clinics		
Yes	31	55.4
No	10	17.9
Partially	15	26.8
Status of using ND by receiving training		
Yes	39	69.6
No	7	12.5
Partially	10	17.9
Status of having ideas on using nursing diagnoses in patient care		
Yes	49	87.5
No	2	3.6
Partially	5	8.9

VSOH-AD-BD: Vocational school of health or Associate's degree Bachelor degree and over.

Table 4 compares some of the characteristics of the nurses and the average scores for the sub-scale of the Perceptions of Nursing Diagnosis Survey. The mean score for the survey was 2.30±0.45 for male nurses, while the mean score for the "definition and promotion of a career in nursing profession" was higher for males (2.13±0.65). The female nurses' scores were higher for the other three areas ("clearly defining the patient's condition": 3.55±0.71; "ease of use": 2.42±0.50; and "conceptual aspects": 2.92±0.65). However, these differences in results were not found to be statistically significant. When marital status is taken into consideration, the results for nurses who were married, the scores for the whole survey (3.10±0.42) and for "conceptual aspects" (3.5±0.35) were found to be higher. For single nurses, the scores were higher for the "definition and promotion of a career in nursing" (3.2±0.32), "clearly defining the patient's condition" (3.1±0.57), and "ease of use" (5.2±0.28) sub-scales. Those nurses who had a bachelor's degree or below had scores of 3.5±0.25 for the whole survey, and 4.2±0.52 for the "ease of use" sub-scale, while the scores for those with a bachelor's degree or above the were 3.5±0.26 for the "definition and promotion of a career in nursing"; 4.6±0.32 for the "clearly defining the patient's condition"; and 3.2±0.42 for the "conceptual aspects" sub-scales. These results were calculated to have a higher average. The scores for those

Table 3. Mean scores of the nurses on the sub-scales of perceptions of nursing diagnoses survey

Scale and sub-scales	Min.	Max.	Mean	SD
Perceptions of nursing diagnoses survey	1.10	4.55	2.23	0.40
Definition and promotion of the nursing profession sub-scale	1.13	5.00	2.10	0.75
Clearly defining the patient's condition sub-scale	1.18	4.80	3.10	0.62
Ease of use sub-scale	1.15	4.42	2.25	0.53
Conceptual aspect sub-scale	1.00	4.35	2.85	0.58

Min.: minimum, Max.: maximum, SD: standard deviation.

Table 4. The mean scores of the nurses on the perceptions of nursing diagnoses survey and its Sub-scales according to their introductory characteristics

Introductory characteristics	Perceptions of nursing diagnoses		The definition and promotion of the nursing profession		Clearly defining the patient's condition		Ease of use		Conceptual aspect		p
	X	SD	X	SD	X	SD	X	SD	X	SD	
Gender											
Female	2.30	0.45	2.13	0.65	3.55	0.71	2.42	0.50	2.92	0.65	0.262
Male	2.46	0.47	2.42	0.70	3.45	0.68	2.36	0.47	2.76	0.55	
t	0.367		0.003		1,066		0.904		0.016		-
Marital status											
Married	3.10	0.42	2.54	0.36	2.5	0.65	4.1	0.36	3.5	0.35	0.1
Single	2.91	0.33	3.2	0.25	3.1	0.57	5.2	0.28	2.8	0.42	
t	0.457		1,267		0.192		0.106		3,095		-
Educational status											
Vocational school of health or associate's degree	3.5	0.25	2.3	0.34	3.4	0.25	4.2	0.52	2.8	0.54	0.301
Bachelor degree and over	2.1	0.41	3.5	0.26	4.6	0.32	2.8	0.45	3.2	0.42	
t	0.537		2,578		1,301		0.234		0.765		-
Working years in the profession											
<5 years	3.3	0.27	3.5	0.21	3.5	0.25	2.5	0.28	3.2	0.27	0.065
≥5 years	4.7	0.31	4.2	0.32	4.2	0.31	3.8	0.32	4.1	0.31	
t	0.752		2,289		0.030		1.,544		0.407		-
Working years in clinic											
<5 years	3.2	0.26	2.4	0.23	2.6	0.24	3.5	0.29	3.8	0.25	0.542
≥5 years	4.1	0.32	3.1	0.25	3.6	0.35	4.7	0.31	4.7	0.51	
t	0.345		1,129		0.154		0.170		1,493		-
Status in clinic											
Chief nurse	3.5	0.28	3.3	0.26	2.5	0.28	3.4	0.25	3.2	0.27	0.421
Clinic nurse	4.7	0.41	3.6	0.31	3.8	0.32	4.6	0.32	4.1	0.31	
t	0.356		0.013		0.678		1,686		0.016		-

who had been in the nursing profession and had worked at a clinic for five years or more also had a higher average overall.

DISCUSSION

This research examined the perceptions of nurses working in a university hospital regarding nursing diagnoses. Nurses' perceptions of nursing diagnoses, how they interpret data and their individual knowledge may vary. Assessing these differences using a standardized scale provides both objectivity and makes them easier to interpret. The ability to make a nursing diagnosis and plan interventions suitable for that diagnosis are provided through systematic nursing education. Nurses are also supported through in-service training when they start their professional life.[8-26]

The average score of the nurses participating in this study for "the definition and promotion of a career in the nursing profession" sub-scale was the lowest, indicating a more positive perception. The reason for this is thought to be that the nurses had been working for five years on average. It is also thought that periodic in-service training had an

effect in the institution where this study was conducted. In the validity and reliability study of Akın-Korhan et al.[1], the lowest average score was obtained in this field, and the nurses were found to have a positive perception of their profession. In the study conducted by Karaca and Aslan[17], it was reported that students regard the nursing care process more positively. In addition, they reported that the increasing workload of nurses as they started their professional life had a negative effect on their ability to use and diagnose care.[15-17-30] Axelson et al.[7] in their study on Swedish nurses' ability to make accurate nursing diagnosis reported that the nurses' stealing process has advantages such as saving time and being systematic. Contrary to this situation, they stated that they were insufficient in diagnosis as in our study. Çınar Yücel et al.[10] reported in their study that the nursing students had a highly positive perception of the nursing profession, and this supports the results of our study.

In this study, the highest average score was determined in the "clearly defining the patient's condition" sub-scale. The increase in the average score obtained from the scale indicates that there was a more negative perception. In the study by Collins[9] on the effect of continuous education on nurses, nurses are reported to be inadequate in making a diagnosis before training. In a study conducted by Uysal et al.[29], the nursing students were reported to prefer medical diagnoses to nursing diagnoses. There are clearly difficulties in using nursing diagnoses in practice and during education, and more systematic and concrete thinking is required in this area. Working nurses avoid focusing on the medical diagnosis of patients.[16-28] Ogunfowokan et al.[23] in their study of leading nurses for the NANDA-1 guide stated that students had sufficient knowledge in making and using diagnosis but their knowledge was insufficient for correct diagnosis skills. In the study conducted by Erika et al.[14] about Minnesotan nurses' perceptions of nursing diagnoses, they stated that nurses were confused about diagnoses and had a negative perception. Nursing diagnoses and medical diagnoses are different from each other. A medical diagnosis aims to help the patient using a standard treatment that does not change from one patient to another. A nursing diagnosis varies from one patient to another and enables an individual to achieve complete well-being.[5-21,22]

Although the "conceptual aspect" and "ease of use" of the scale had moderate average scores, the average scores for "clearly defining the patient's condition" were better. A nurse's ability to learn the nursing process requires a conceptual understanding. In their study of nurses working in a hospital in Nigeria aimed at perceiving the nursing process, Edet et al.[12] stated that nurses had positive perceptions towards the nursing process as they did in our study, and they were beneficial for many uses. In this respect, supporting nurses who use "concept maps" makes the nursing process easier to understand. Concept maps are tools that provide meaningful learning and can be used to help retain information in the long-term memory. They also play a role in facilitating remembering by ensuring that information is stored in a certain order.[18-20]

CONCLUSION

The Perception of Nursing Diagnosis Survey was used to examine the basic foundation of the nursing profession, namely nursing diagnosis. It was found that nurses had a negative perception of nursing diagnoses in terms of whether they helped to clearly understand the patient's condition. The number of people in our sample was low, and it is thought that studying larger groups may well lead to different results. It is also necessary to examine why nurses are unable to adequately carry out the care process. It is recommended that the factors that affect the care process be investigated in different types of in-depth studies (e.g., phenomenological studies). This will be useful for in-service training regarding the nursing process both during nursing education and in the professional life. Most studies on the perception of nursing diagnoses in the literature have been carried out with students, and it is recommended that the focus be placed on fully-qualified nurses.

ETHICS

Ethics Committee Approval: In order to conduct this research, written permission was obtained from the University Ethics Committee (approval number: 459, date: 26.10.2017) and the Hospital's Chief Physician.

Informed Consent: In addition, written consent was obtained from the nurses who volunteered to participate in this study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: E.B., H.B., Design: E.B., H.B., Supervision: E.B., H.B., Data Collection and/or Processing: E.B., H.B., Analysis and/or Interpretation: E.B., H.B., Literature Search: E.B., H.B., Writing: E.B., H.B., Critical Review: E.B., H.B.

DISCLOSURES

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CASE REPORT

CYPRUS
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A Rare Case: Variation in the Third Part of the Axillary Artery

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Abstract

Axillary artery branching pattern variations are commonly observed during routine dissections. These variations have great importance due to the wide range of therapeutic and diagnostic procedures carried out in the axillary region. Therefore, neurovascular abnormalities should be well-known before surgeries involving the axillary region in order to prevent complications. This case report presents a common trunk at the third part of the axillary artery which gives rise to the deep brachial artery.

Keywords: Axillary artery, common trunk, deep brachial artery, variation

INTRODUCTION

Anatomy knowledge of the axillary region is of great importance to neurosurgeons, orthopedic, plastic, and cardiovascular surgeons as well to radiologists. Although variations in the axillary region are observed commonly, they are not well defined. The axillary artery is one of the structures located in this region and it requires to be studied well before any procedures are planned.

Classically, the subclavian artery in the neck continues as the axillary artery at the outer border of the first rib and passes through the axilla. It consists of three parts and has six branches. The first part lies between the superior border of the pectoralis minor muscle and the first rib. It gives rise to a single branch, the superior thoracic artery, which supplies the pectoral muscles. The second part gives rise to two arteries; the thoraco-acromial and lateral thoracic arteries, and it is located posterior to the pectoralis minor muscle. These two arteries provide blood supply to the pectoral muscles, the skin around that region, and the axillary lymph nodes. Finally, the third part lies inferior to the pectoralis minor muscle and it has three branches. The first and the largest artery which arises from the third part is the subscapular artery, supplying the skin and the muscles of the shoulder and the thoracic wall. The other two arteries arising from the third part are the posterior and the anterior humeral circumflex arteries. The surgical neck of the humerus is wrapped with these two arteries which supply the shoulder joint. The axillary artery continues its course and becomes the brachial artery right after exiting the axilla, at the inferior border of the teres major muscle. The deep brachial artery is the largest branch of the brachial artery, and it arises below the inferior border of the teres major muscle.[1,2]

CASE PRESENTATION

During a routine dissection for educational purposes, a variation was noticed in the branching pattern of the third part of the axillary artery. The variation was observed on the left axillary region of a male cadaver aged 63 years. To view the axillary artery clearly, the skin and the fascia were removed, and the pectoralis major muscle was retracted. Median and musculocutaneous nerves were detected and pulled away with clamps in order to view all of the branches of the axillary artery. The branching pattern of the first and the second parts of the axillary artery were observed to be normal. A common trunk was observed just below the subscapular artery at the third part of the axillary artery. This common trunk had branches to the anterior and posterior humeral circumflex arteries, the brachial artery, and the deep brachial artery

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(Figure 1). Further branching patterns and the course of the deep brachial artery were noted as regular, and no additional abnormalities were detected.

DISCUSSION

Variations located in the axillary region, especially the axillary artery branching pattern, are frequently observed either during cadaveric dissections or clinical cases. A study conducted with 40 cadavers showed that the variant pattern of the axillary artery was 63% in males and 58% in women.[3] Variations similar to our case have been reported; the common trunk at the third part of the axillary artery provided branches to the anterior and posterior circumflex humeral, the ulnar collateral arteries, and the deep brachial artery at the same time.[4] Another interesting case of axillary artery variation was published in which the medial and lateral roots of the median nerve sandwiched the abnormal common trunk.[5] An unusual variation at the third part of the axillary artery was published in 2017, where a common trunk gave branches to the lateral thoracic artery and continued as the posterior circumflex humeral artery.[6]

Knowledge of the axillary artery branching pattern is vital for surgeons while treating axillary artery thrombosis, attending to axillary region traumas, or cannulating the axillary artery.[7] The right axillary artery can be used for cannulation as another option to femoral artery cannulation, especially in patients suffering from iliofemoral arterial occlusion.[8] Axillary lymph node dissection is commonly performed as a part of the surgical treatment of breast cancer patients, and this procedure is also used to determine the stage and the management of breast cancer. Any variation in the course of the vessels located in the axillary region must be well identified when planning this procedure.[9] Radiological and surgical reviewing of the region can prevent complications which can occur during procedures scheduled in the axillary region. Therefore, anatomical knowledge of any variations of this region are vital for surgeons and radiologists.

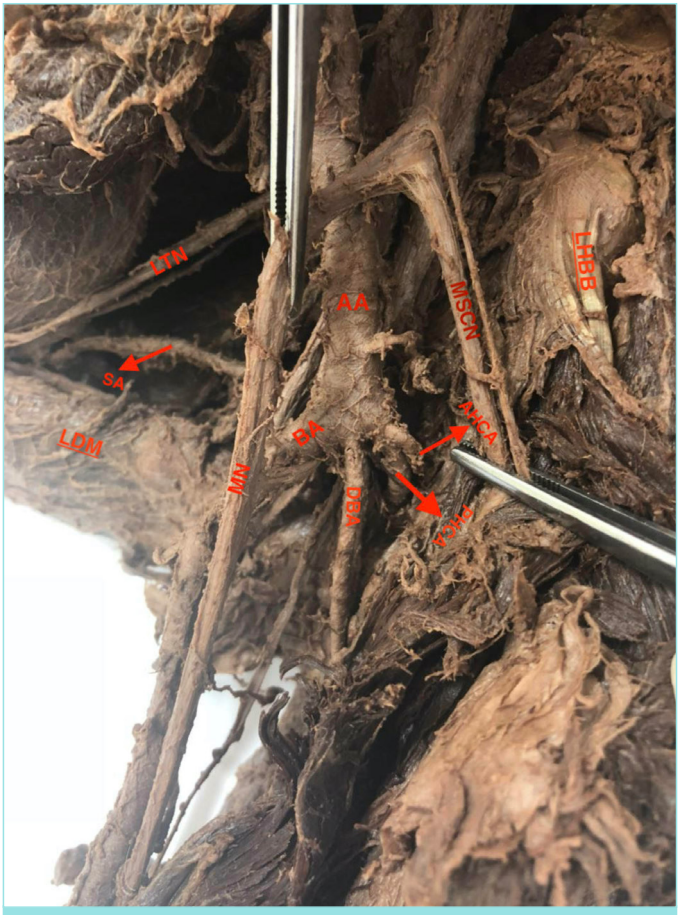

Figure 1. High bifurcation of brachial artery

BA: brachial artery, DBA: deep brachial artery, PHCA: posterior humeral circumflex artery, AHCA: anterior humeral circumflex artery, LTN: long thorasic nerve, MSCN: musculocutenous nerve, MN: median nerve

MAIN POINT

- Arterial variations in the axillary region is of great importance when preparing for a surgical procedure towards the region.
- A variation has been observed in the third part of the artery, presented with a common trunk that gave branches to anterior and posterior humeral circumflex arteries, brachial artery, and deep brachial artery.

ETHICS

Informed Consent: This study was conducted on a cadaver that was donated by consent to be used in medical studies and education.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: B.Ç.Ö., Design: S.Ü.Ş., Literature Search: U.V., Writing: B.Ç.Ö., Critical Review: U.V., A.Y.

DISCLOSURES

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CASE REPORT

CYPRUS
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A Rare Diagnosis of Abdominal Pain

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Abstract

Abdominal pain is a very common complaint among patients presenting to the emergency department. Many different reasons can cause abdominal pain; therefore, the differential diagnosis list can be quite long. In differential diagnosis, anamnesis, examination findings, laboratory tests, and radiological imaging methods are helpful. This article presents the findings of a 79-year-old male patient who presented to an emergency room with nausea and vomiting and increased right upper quadrant pain for three days. Based on his physical examinations and laboratory test results, the only positive finding was rebound tenderness in the right upper abdominal quadrant. Computed tomography sections showed a 3x1 cm diverticular filling extending from the antrum to the perigastric region's superomedial part. Edema, increased wall thickness, and enhancement were observed in the walls of the diverticulum. As a result of all these findings, the diagnosis was considered to be gastric diverticulitis (GD). Gastric diverticulum is the rarest diverticulum in the gastrointestinal tract. GDs are often asymptomatic and are rarely symptomatic, depending on their size. Physical examinations and laboratory tests in diagnosing GD are non-specific; however, radiological imaging methods play an essential role. Additionally, GD can be diagnosed via endoscopic procedures.

Keywords: Gastric diverticulitis, computed tomography, abdominal pain

INTRODUCTION

One of the most frequent complaints among patients who visit the emergency room is abdominal pain. Abdominal pain can occur due to a variety of causes. Therefore, the list of differential diagnoses is extensive. In this article, we aimed to present an infrequent cause of abdominal pain with computed tomography (CT) findings.

CASE PRESENTATION

Questions

A 79-year-old male patient was admitted to the emergency department with the chief complaints of nausea, vomiting, and increased right upper quadrant pain for three days. The patient had a history of indapamide treatment for hypertension for about 15 years. On physical examination, his vitals were stable. Bowel sounds were normoactive, and there was no palpable abdominal mass. The only positive finding was rebound tenderness in the right upper abdominal quadrant. Laboratory tests were normal, including complete blood count and liver and kidney function tests.

As a result of physical examinations and laboratory results, the patient was further evaluated with radiologic examinations. Initially, supine and erect direct abdominal graphics, and afterwards, abdominal ultrasonography examinations were performed. In these examinations, there was no significant finding. After these evaluations, the patient underwent contrast-enhanced abdominal CT. CT images showed diffusely increased wall thickness at the gastric antrum. Additionally, medial contour irregularity and increased gastric wall enhancement at the level of the antrum were observed. Significant heterogeneity and increased density were observed in the perigastric fat tissue plan around the antrum (Figure 1a, b).

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CT sections showed a 3 cm by 1 cm diverticular filling excess extending from the antrum to the superomedial part of the perigastric region (Figure 2a, b). Edema, increased wall thickness, and enhancement were observed in the walls of the diverticulum (Figure 3a). Furthermore, in perigastric fat plans around the diverticulum, heterogeneity and increased density values due to inflammation were determined (Figure 3b). As a result of all these findings, the diagnosis was considered as gastric diverticulitis (GD). Non-steroidal anti-inflammatory and anti-acid drugs were used in the treatment of GD. After treatment with the appropriate dose and duration, abdominal pain and other complaints disappeared. The patient was discharged with a gastroenterology outpatient clinic follow-up recommendation. In the gastroenterology outpatient clinic, follow-up esophagogastroduodenoscopy was applied. The diverticulum was also proved by endoscopy (Figure 4).

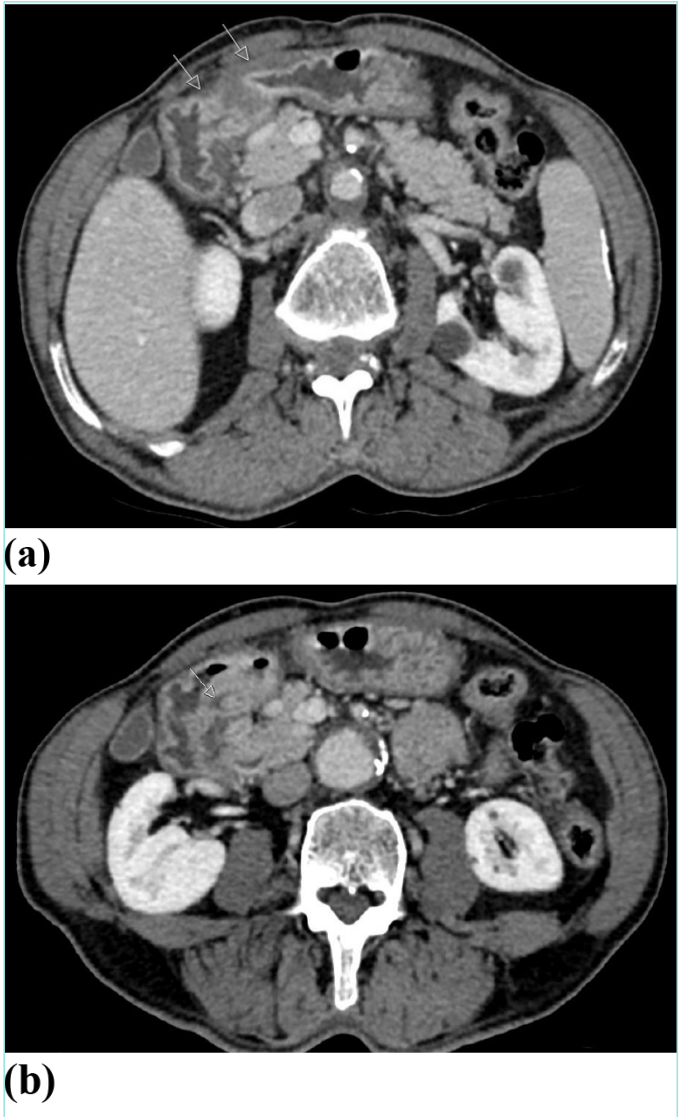

Figure 1. Axial contrast-enhanced abdomen computed tomography revealed diffusely increased wall thickness at the gastric antrum, significant heterogeneity and increased density in perigastric fat tissue plan (a), medial contour irregularity, and increased enhancement of gastric wall at the level of the antrum (b)

DISCUSSION

Gastric diverticulum is the rarest diverticulum in the gastrointestinal tract.[1] There are limited numbers of GD cases reported in the literature. GDs are often asymptomatic and are rarely symptomatic, depending on their size. The most common symptoms are epigastric pain, nausea, vomiting, and dyspeptic complaints, as in our case.[2]

In diagnosing GD, physical examinations and laboratory tests are nonspecific. However, radiological imaging methods play an important role. Among all imaging modalities, sectional methods, including abdominal CT and magnetic resonance imaging, are the most important diagnostic modalities.[3] Additionally, GD can be diagnosed via endoscopic procedures.[4]

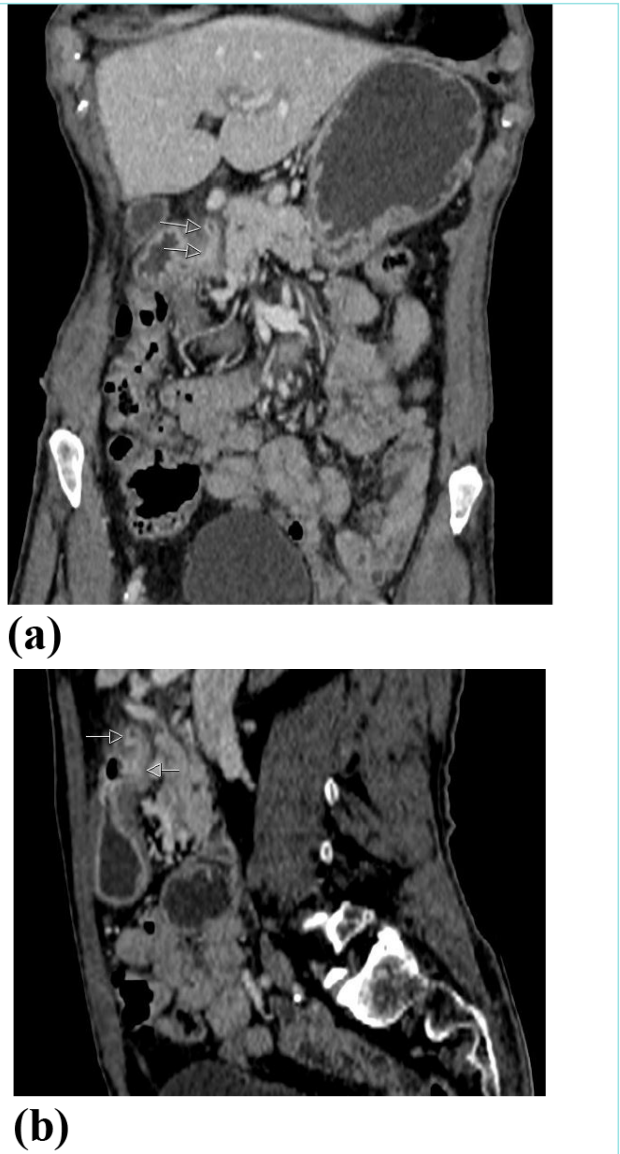

Figure 2. Coronal (a) and sagittal (b) reformatted contrast abdomen computed tomography sections showed a 3x1 cm diverticular filling excess (white arrows) extending from the antrum to the superomedial part of the perigastric region

(a)

(b)

Figure 3. In axial (a, b), contrast-enhanced abdomen computed tomography sections, edema, increased wall thickness, and enhancement were observed in the walls of the diverticulum (a). In perigastric fat plans around the diverticulum, heterogeneity and increased density values due to inflammation were determined (b).

In the treatment of GD, the primary method is a conservative approach and anti-acid treatment. In cases of response failure to medical therapy, diverticular haemorrhage or diverticulum perforation may occur. In these cases, surgical options, primarily laparoscopic methods, should be considered in the treatment.

In conclusion, although gastric diverticulum is one of the rarest and asymptomatic pathologies of the gastrointestinal tract, it may be symptomatic when GD occurs. GD should be considered in the differential diagnoses of those patients presenting with sudden onset upper quadrant pain.

MAIN POINTS

- Many different reasons can cause abdominal pain, and therefore, the differential diagnosis list can be quite long.
- Gastric diverticulum is the rarest diverticulum in the gastrointestinal tract.

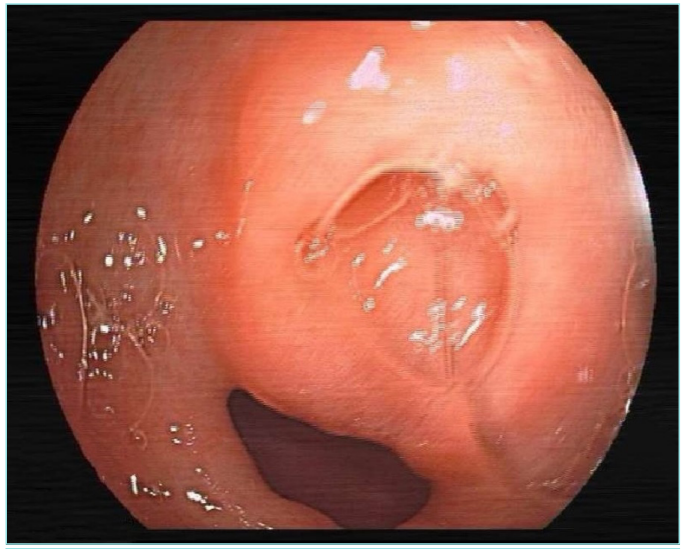

Figure 4. Follow-up esophagogastroduodenoscopy showed the antral diverticulum also

- Gastric diverticulitis is often asymptomatic and is rarely symptomatic, depending on its size. Epigastric pain, nausea, vomiting, and dyspeptic complaints are the most common symptoms.
- Among all imaging modalities, sectional methods, including abdominal CT and magnetic resonance imaging, are the most important diagnostic modalities.

ETHICS

Informed Consent: It was obtained.

Peer-review: Internally peer-reviewed.

Authorship Contributions

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CASE REPORT

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A Very Rare Lesion of the Nipple with Preliminary Diagnosis of Malignancy: Verruciform Xanthoma

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Abstract

Verruciform xanthoma (VX), a significantly rare benign skin lesion, is often confused with other malignant and benign lesions due to its macroscopic clinical appearance. A 35-year-old female patient was admitted to the general surgery clinic with a VX lesion on her nipple. The lesion was subject to excision due to suspected malignancy. As far as we are aware, this is the only case in which VX was found on the nipple of a patient. Multiple skin lesions with similar macroscopic appearances were accompanied by a clinical history of lactation, mastitis and breast lesion. We aimed to discuss this unique case due to its rarity, aetiology and clinical location history in light of the literature.

Keywords: The nipple, verruciform xanthoma, Papet's disease, verruca vulgaris, skin malignancies

INTRODUCTION

Verruciform xanthoma (VX) is a benign, rare tumour of unknown aetiology usually found in the oral mucosa.[1-3] Most of the extra-oral lesions are located in the genital area.[3] It is mentioned in the literature as occurring in mucosal areas, such as the oesophagus, larynx, glottis, nose and lips and the extremities, such as the hands, feet and legs.[2,4] A single case with a breast location was described as a lesion of cystic structure on the retro-areolar region of the breast of one patient.[4] As for the aetiology, immunological factors, long-term local irritation and viral agents have been suspected, but no definitive cause has been identified.[2,3,5] The microscopic appearance of VX is typical and diagnostic. Excision is the most appropriate method for its diagnosis and treatment. In haematoxylin sections of the dermis, hypertrophic epidermis, irregular acanthosis in rete ridges and lipid-rich macrophages (xanthomas) are typical.

CASE PRESENTATION

A 35-year-old woman, who had given birth eight months previous to her clinical admission and was still breastfeeding, applied to the general surgery polyclinic with complaints of pain, tenderness and swelling in the upper external quadrant of her right breast. No ultra-sonographic findings were detected in either breast. The case was diagnosed with a breast infection due to lactation, and drug treatment was given. After four months, the patient was admitted to the polyclinic with a mass in her right breast. Additionally, a papillomatous lesion of about 3 mm in diameter was detected on the nipple. According to the information provided on the pathology requisition form, the papillomatous lesion on the nipple was excised with suspicion of Papet's disease, nipple adenoma, and skin malignancies. On macroscopic examination, skin with an irregular surface measuring 0.6x0.5x0.3 cm was observed. In haematoxylin sections, verrucous hyperplasia of epidermis, acanthosis, occasionally parakeratosis and neutrophil leukocyte infiltration were observed in some areas (Figure 1). Many foamy cytoplasmic cells which occasionally entered the epidermis and completely filled the papillary dermis and elevated capillary vessels were observed (Figure 2). P-16 and human papillomavirus were also administered immunohistochemically. No staining was observed in either marker. Accordingly, the case was diagnosed as VX. Three months after this diagnosis, the patient was admitted to the dermatology polyclinic with papillomatosis lesions

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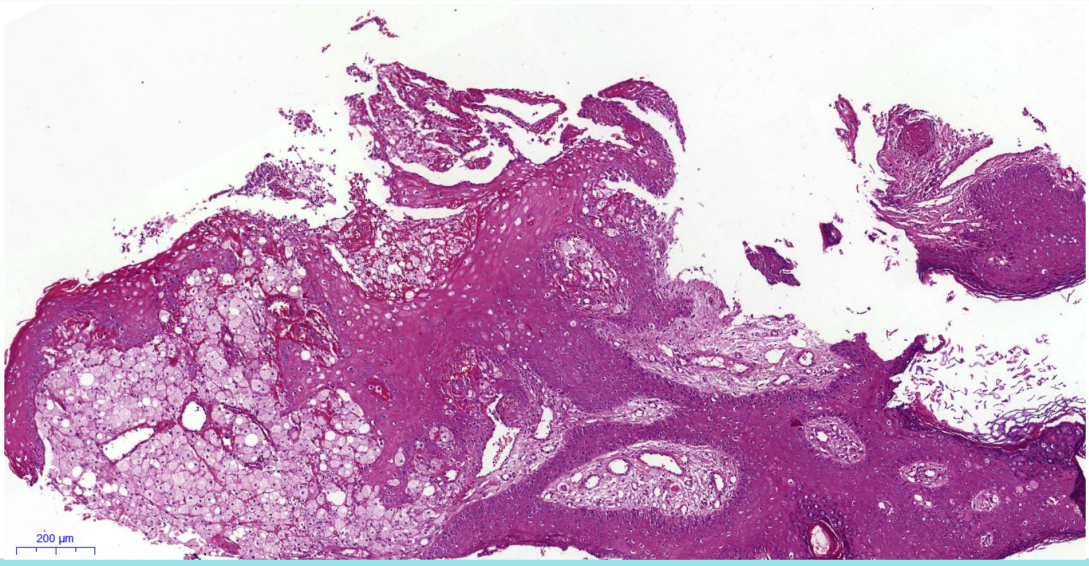

Figure 1. Verrucous hyperplasia of epidermis (H&E)

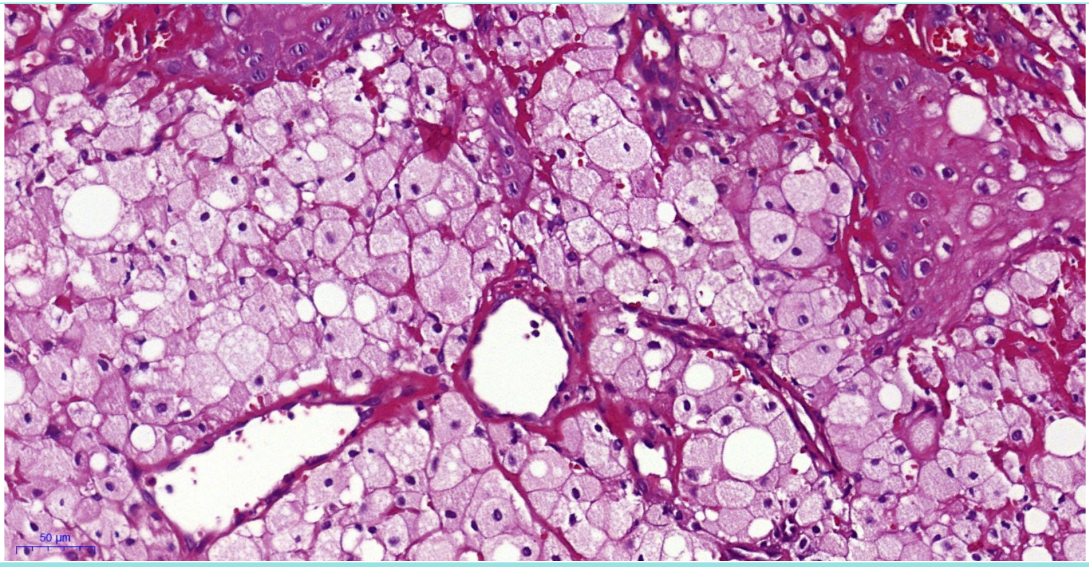

Figure 2. Lipid-rich macrophages (xanthomas) (H&E)

in the abdomen, midline of the back, lumbar region and neck. These skin lesions started about three months prior to her admission, and their numbers were increasing. In the derma-pathology polyclinic, cryotherapy was applied with the preliminary diagnosis of seborrheic keratosis and verruca vulgaris. Unfortunately, the pathology of these lesions could not be evaluated, as no samples were sent to the laboratory for examination. Informed consent was obtained.

DISCUSSION

Chronic irritation may be emphasized as one of the factors of VX aetiology.[2-5] In our case, the patient was lactating, which exposed her nipple to chronic irritation. Also, four months prior to the appearance of the lesion, mastitis developed secondarily to lactation. Chronic trauma and infection are considered triggering factors in the development of this lesion. No other cases of VX located on the nipples of patients were revealed by a literature review. Our case is the first reported VX case located on the nipple of a patient. Although some similarities exist between our case and a case reported in 2014, the morphological patterns and locations of the lesions are different.[4] The lesion reported in 2014 was defined as a cystic VX of the breast originating from the squamous epithelium of the lactiferous ducts in the retro-areolar region,[4] and both cases had a history of mastitis. However, the VX in our case was located on the nipple.

In both cases, chronic inflammation predisposition to VX is suggested by the presence of a mastitis history, but in our case, due to lactation, the nipple was also exposed to continuous irritation. In our case, all brown-coloured papillomatous lesions in the clinical history had the same onset. However, the lesion on the nipple was surgically removed due to suspicion of malignant lesions of the breast and skin (Paget's disease, nipple adenoma, Bowen's disease, squamous cell carcinoma

etc.). The lesions at other locations were examined in the dermatology clinic three months after the excision of the nipple. In the dermatology polyclinic, cryotherapy was applied to 20 other papillomatous lesions, but no samples were taken for pathological evaluation. Although we did not have pathological specimens of the other lesions, the lesions on the breast and other locations were concurrent and had the same macroscopic appearance. VX can be macroscopically confused with verruca vulgaris, condyloma acuminatum, seborrheic keratosis, squamous cell carcinoma, verrucous carcinoma, or Bowen's disease and biopsy materials may be sent with these preliminary clinical diagnoses.[5,6] It is reported that VX can be diagnosed only by histopathological examination, and excision is sufficient as treatment.[2] Therefore, in our case, cryotherapy was considered the appropriate treatment. However, due to the absence of histopathological findings of the other lesions, we only claim that the other lesions might have been VX. There are skin lesions and syndromes observed with VX in the literature, but we could not find a case of verruca vulgaris or seborrheic keratosis skin lesions coexisting with VX.[6-8]

In the studied case, chronic trauma and inflammation are considered triggering mechanisms or critical causes of VX aetiology.[2-5] VX on the nipple was observed for the first time, and malignancy was suspected based on its macroscopic appearance. We recommend considering VX in such lesions of the nipple and obtaining a biopsy for differential diagnosis. If the pathology of the other concurrent skin lesions could have been examined, more detailed and precise answers could have been obtained to some of the questions about VX. Nevertheless, in this case, the positive side was that excision or cryotherapy was sufficient for VX treatment. In our case, no other skin lesions developed during a 5-year clinical follow-up.

MAIN POINTS

- This is the first VX case reported on the nipple in the literature.
- Due to its macroscopic appearance, VX can be mistaken for nipple malignancies by clinicians.
- Microscopic appearance is typical and diagnostic.

ETHICS

Informed Consent: It was obtained.

Peer-review: Internally peer-reviewed.

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Concept: S.E., Design: S.E., Fundings: A.H.K., Materials: S.E., A.H.K., Data Collection and/or Processing: S.E., A.H.K., Analysis and/or Interpretation: S.E., Literature Search: S.E., Writing: S.E.

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