

# What do Somali Nurses Know About Esophageal Cancer? A Cross-Sectional Study

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## Abstract

**BACKGROUND/AIMS:** Esophageal cancer (EC) is increasing in Somalia. To be a knowledgeable nurse, it is essential to create awareness in the public and individuals regarding screening. This study aimed to assess the knowledge of EC among Somali nurses.

**MATERIALS AND METHODS:** A cross-sectional study was conducted among Somali nurses to elicit information regarding their knowledge of EC at Banadir Government Hospital in Mogadishu, Somalia. Data were collected using a self-designed questionnaire.

**RESULTS:** The Somali nurses' mean age was 25.15±1.4 years. 47.6% had visited a doctor 1-2 times within the prior year, 60.5% were not willing to be screened for EC, and 80.3% were willing to receive further education on this issue. Barrett's esophagus (70.1%), reflux (70.1%), alcohol use (85.0%), smoking (68.0%), and gender (68.7%) were most commonly known as being the risk factors for EC, while the least known risk factors were race, obesity, non-steroid anti-inflammatory drugs, diet, the presence of *FOXF1* and *BARX1* genes and low socioeconomic status. The nurses' knowledge rates about risk factors, diagnosis/symptoms, and treatment were found to be moderate. Visiting a doctor within the past year was a significant predictor for having correct knowledge regarding the diagnosis, symptoms and treatment of the Somali nurses who participated in this study ( $p<0.005$ ).

**CONCLUSION:** We found that Somali nurses' knowledge was moderate. Knowledge may be raised among Somali nurses by establishing continuous education programs regarding ECs.

**Keywords:** Esophageal cancer, Somali nurses, knowledge

## INTRODUCTION

Esophageal cancer (EC) is the eighth most common type of cancer and the sixth leading cause of death around the world. It has an aggressive nature and a low survival rate, and changeability based on geographic location.<sup>1-3</sup> Most EC cases are diagnosed in less developed countries. It is estimated that about 600,000 people were diagnosed with EC in 2018, including 3.2% of all cancer diagnoses.<sup>4</sup> Its prevalence is higher in

males in all regions<sup>5</sup> and EC is responsible for the second-highest rate of cancer-related deaths in South Africa.<sup>6</sup>

Somalia is located in the East African region. Unfortunately, Somalia is a vulnerable country due to conflicts, war, and political issues, all of which have destroyed the health system. In Somalia, mortality is frequently due to obstetric, nutritional problems, infectious diseases, and cancer. No literature demonstrates the real cancer data in Somalia.

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The population-based EC incidence is unknown, however, the first retrospective study focused on the distribution of cancer patients in Mogadishu, Somalia indicated that the five most common cancers in all cases were esophagus, non-Hodgkin lymphoma, liver, breast, and skin. Four hundred three cancer cases were diagnosed between 2016 and 2017. One study revealed that EC is one of the most common cancers (21.7%) for both genders in new cancer cases between 2017 and 2020 in Somalia.<sup>7</sup> Notably, incidence rates are on the rise and causative factors include lifestyle, dietary changes, and environmental events. It was noted that environmental risk factors have an impact on this population.<sup>8</sup> In Somalia, alcohol consumption is prohibited on religious terms and there is no alcohol production or sales. It was stated that the considerable increase in the nitrogenous ingredients in those foods cooked over coal fires was an important factor for EC. Furthermore, extremely hot brass and tea consumption habits and chewing the Khat plant are also very widespread in Somalia.<sup>9</sup> Studies have showed that there was a higher incidence of EC among khat plant users in some African countries.<sup>10,11</sup> Additionally, EC affects physical and mental health, as well as the quality of life.<sup>12</sup>

Cancer screening is essential for early detection and effective treatment processes. Delayed cancer detection and screening difficulties facing Somalia are exacerbated by an absence of healthcare professionals. With no active or effective formal educational institutions during the war between 1991 and 2012, there was little to no training for a generation of healthcare providers.<sup>13,14</sup> Since the installation of the government in 2012, Somalia has prioritized developing its health professional workforce.<sup>15</sup> Nurses go abroad to get postgraduate education. According to our knowledge, Türkiye is one of the countries where Somalian nurses choose postgraduate education. In all aspects of the fight against cancer, the government is aware of nurses' contribution as being a crucial part of a team. Nurses are responsible for providing health promotion, evaluating risk, and caring for people receiving cancer treatment. Adequately knowledgeable nurses can play instrumental roles in cancer control and can create awareness. Nurses should address cancer risks including smoking, obesity, nutrition, and environmental factors.<sup>16</sup> Nurses knowledgeable about EC may effectively create awareness in the society. To the best of our knowledge, there has been a lack of studies which have focused on evaluating Somalian nurses' knowledge levels of EC. Therefore, we aimed to evaluate Somalian nurses' knowledge levels regarding EC risk factors, its diagnosis, screening, and treatment.

## MATERIALS AND METHODS

### Study Design and Setting

This prospective cross-sectional study was conducted in Banadir Government Hospital in Mogadishu, Somalia from February to September, 2020. The Banadir Teaching Hospital which was built as part of a Chinese project in 1977 is the largest in Mogadishu, Somalia.

### Sample Population

The total number of Somalian nurses who were working in Mogadishu Banadir Government Hospital was 160. All were invited to participate, and of those, 147 (respond rate: 99.8%) gave verbal consent and participated in this study. The inclusion criteria were being licensed nurses in a permanent position, being aged between 18 to 65, and being willing to participate in this study.

### Study Tools

Data were collected using a self-designed questionnaire which was prepared by the researchers in line with the literature.<sup>3,4,17-21</sup> It was designed in English and its content was checked by three academicians. The questionnaire consists of two parts with a total of 41 items. Part 1, which has 16 items, was used to assess sociodemographic data (e.g., age, gender, educational level, working state, marital status, alcohol use, and nutritional habits). Part 2, which consists of 25 items, was used to evaluate the nurses knowledge regarding EC risk factors (14 items), diagnosis and screening methods (7 items), and treatment (4 items). This survey's Cronbach  $\alpha$ -value was found to be 0.698, 0.706, and 0.646, respectively. A pilot study was carried out on three nurses in order to evaluate the reliability of this questionnaire, and these nurses were excluded from the sample. All selected nurses were invited to join the study after being told the aims of the study, and their confidentiality was ensured. Data were collected in the hospital. Filling out the questionnaire took approximately fifteen minutes.

### Data Processes and Scoring Systems

In scoring for all the questions about EC, 1 was given for correct answers, and 0 to those who gave wrong answers or had no idea. As the answers to the questions were 1 point for "true" and 0 for "false", internal consistency was calculated by the Kuder-Richardson method (KR-20).<sup>22</sup> In this study, the number of correct answers was divided by the number of questions, their percentages were calculated and a knowledge index was obtained. The number of correct responses when multiplied by four yielded the total score, which ranged from 0-100. Scores of  $\leq 50$ , 51-70, and  $\geq 70$  were rated as *poor*, *moderate*, or *good* respectively.<sup>23-25</sup>

### Ethical Consideration

Permission was obtained from the Karabük University Ethics Committee (no: 77192405099-E50699) and written approval was also obtained from the Mogadishu Banadir Government Hospital (approval number: 27105693-806.01.03-1697). We explained the aims of this study and received informed written consent from each nurse. This study conformed to the principles of the Declaration of Helsinki.

### Statistical Analysis

The SPSS (IBM) for Windows 20.0 program was used. The distribution of the sociodemographic characteristics and the nurses' knowledge rates of EC were evaluated by descriptive statistics. Linear regression was used to evaluate some factors related to the nurses' correct knowledge rates. A p-value less than 0.05 was statistically significant.

## RESULTS

### Sociodemographic Characteristics, Health Checks and Screening of the Somalian Nurses

Table 1 shows the sociodemographic distribution of the Somalian nurses. The nurses' mean age was  $25.15 \pm 1.4$  years. 50.3% of nurses were male, 51.0% were married, 57.1% had a master's degree education, 46.3% had 0-1 years of work experience and 27.8% worked in internal clinics.

Table 2 shows Somalian nurses' health checks and EC screening. Of the study population, 47.6% had visited a doctor 1-2 times within the previous year, 40.8% had had a health check within the prior two years,

**Table 1. Socio-demographic characteristics of the Somalian nurses (n=147)**

Characteristics	Number (%)
<b>Age groups</b>	
18-29	84 (57.1)
30-40	47 (32.0)
≥41	16 (10.9)
Mean age ± SD	25.15±1.4
<b>Gender</b>	
Female	73 (49.7)
Male	74 (50.3)
<b>Marital status</b>	
Single	72 (49.0)
Married	75 (51.0)
<b>Education</b>	
Associate degree	22 (15.0)
Undergraduate	41 (27.9)
Master's degree	84 (57.1)
<b>Work experience</b>	
0-5 years	68 (46.3)
6-10 years	40 (27.2)
11-15 years	27 (18.4)
≥15 years	12 (8.2)
<b>Clinic</b>	
Internal medicine	40 (27.8)
Surgery	33 (22.9)
Intensive care unit	30 (20.8)
Operating theatre	21 (14.6)
Emergency	20 (13.9)

SD: Standard deviation.

**Table 2. Somalian nurses' health checks, and esophageal cancer screening (n=147)**

Characteristics	Number (%)
<b>Visiting a doctor within the previous year</b>	
I never went	38 (25.9)
1-2 times	70 (47.6)
3-4 times	39 (26.5)
<b>Health check status</b>	
within the previous year	58 (39.5)
more than two years previously	60 (40.8)
Do not remember	29 (19.7)
Existence of EC in first-degree relatives (yes)	38 (25.9)
Willingness to have screening for esophageal cancer (yes)	58 (39.5)
<b>Barriers to screening for esophageal cancer</b>	
I did not find it necessary	57 (38.7)
Nobody suggested	38 (25.9)
Fear of cancer diagnosis	38 (25.9)
Fear of the screening procedures	14 (0.5)
Willingness to receive training (yes)	118 (80.3)

EC: Esophageal cancer.

25.9% had a family history of cancer, 39.5% were willing to be screened for EC, and 80.3% were willing to receive training on EC.

**Somalian Nurse's Answers Regarding Esophageal Cancer and Predictors of Their Knowledge**

Table 3 shows the Somalian nurses' answers to questions about EC. The most commonly known risk factors were gender (68.7%), age (63.2%),

**Table 3. Somalian nurses' answers about esophageal cancer**

Items	Yes		No		No idea	
	n	%	n	%	n	%
<b>Risk factors</b>						
1. Women are at lower risk than men.	101	68.7	33	22.4	13	8.8
2. Being over 55 years of age increases the cancer risk.	93	63.2	47	32	7	4.8
3. The susceptibility is higher in white than in black people.	71	48.3	45	30.6	31	21.1
4. Barrett's esophagus increases EC cancer.	103	70.1	30	20.4	14	9.5
5. Reflux complaints are more common in EC.	103	70.1	37	25.1	7	4.8
6. Obesity is a risk factor.	45	30.6	81	55.1	21	14.3
7. Alcohol use is a risk factor.	125	85.0	18	12.2	4	2.8
8. Smoking increases the EC risk.	100	68.0	38	25.9	9	6.1
9. A diet rich in fiber, fruits, and vegetables decrease EC risk.	79	53.7	44	29.9	24	16.4
10. Low socioeconomic status is not a risk factor.	83	56.5	48	32.7	16	10.8
11. <i>FOXF1</i> and <i>BARX1</i> genes increase the risk.	51	34.7	42	28.6	54	36.7
12. The use of proton pump inhibitors and aspirin reduces the risk.	69	46.9	41	27.9	37	25.2
13. Statins reduce the risk.	71	48.3	51	34.7	25	17
14. Excessive intake of non-steroidal anti-inflammatory drugs increases the risk of EC.	49	33.3	74	50.3	24	16.4
<b>Diagnosis/symptoms</b>						
15. Endoscopy is a diagnostic method but it has little importance.	98	66.7	43	29.3	6	4.0
16. The biopsy method is the certain diagnosis method.	110	74.8	30	20.4	7	4.8
17. Other diagnostic methods are MR, CT, PET CT, and endoscopic ultrasound.	105	71.4	25	17	17	11.6
18. Common symptoms are dysphagia, reflux, chest inflammation, or pressure sensation.	99	67.3	31	21.1	17	11.6
19. Weight loss and indigestion may be symptoms.	123	83.7	16	10.9	8	5.4
20. Cough and hoarseness may be other symptoms.	66	44.9	70	47.6	11	7.5
21. One of the late symptoms may be hematemesis.	86	58.5	33	22.4	28	19.1
<b>Treatment</b>						
22. Neoadjuvant treatment method is used after surgery.	79	53.7	46	31.3	22	15
23. Surgery is a major treatment.	93	63.3	44	29.9	10	6.8
24. Radiotherapy is used with neoadjuvant treatment.	88	59.8	37	25.2	22	15

EC: Esophageal cancer, MR: Magnetic resonance, CT: Computed tomography, PET: Positron emission tomography.

Barrett's esophagus (70.1%), reflux (70.1%), alcohol use (85.0%), and smoking (68.0%). The least known risk factors were race, obesity, non-steroidal anti-inflammatory drugs, diet, *FOX1* and *BARX1* genes, and sociological status. The nurses' most commonly known symptoms/diagnosis were unexplained weight loss and indigestion, dysphagia, reflux, and chest inflammation, while for screening, it was biopsy (74.8%), magnetic resonance (MR), computed tomography (CT), positron emission tomography (PET)/CT, and endoscopic ultrasound (71.4%) and endoscopy (66.7%). The nurses' most commonly known treatment of EC was surgery (63.3%).

Table 4 shows the Somalian nurses' correct knowledge rates of EC risk factors, diagnosis/screening, and treatment. The nurses' correct knowledge rates of risk factors, diagnosis/screening, and treatment were found to be moderate (range=51 to 70) (respectively; 55.53±17.75; 66.76±24.35; 62.75±27.03).

Table 5 shows that the frequency of visiting a doctor in the prior year was a significant predictor for knowledge of diagnosis/screening and treatment among the nurses.

**DISCUSSION**

This present study aimed to identify EC risk factors, diagnosis, screening and treatment knowledge, and associated factors among Somalian nurses. The important findings of this study were that Somali nurses have a moderate level of knowledge about EC and frequent visits to the doctor for health check-ups increased their correct diagnosis, symptom, and treatment knowledge rates. Previous studies have reported risk factors for many cancers, including EC, are gender, increasing age, smoking, alcohol use, low fruit and vegetable intake, inadequate or low fiber diets, and cancer in first-degree relatives.<sup>26-28</sup> Most Somali nurses have sufficient knowledge about these major risk factors. It is known that being male and over 55 age poses more risk for EC.<sup>7</sup> In addition, a meta-analysis reported that alcohol consumption and smoking increase the risk of developing cancer in a dose-dependent manner.<sup>26</sup> Many Somali nurses agreed with this knowledge.

When considering the habits of Somali nurses' health checks, and EC screening, it was found that about half of them had been for a health check-up 1-2 times within the prior year. In addition, a quarter of the nurses have EC in a first-degree relative. Nurses need to have regular health checks for EC, which is known to have a high genetic predisposition. However, more than half of the nurses were not willing to be screened for EC and a significant portion (38.7%) considered EC screenings unnecessary. The most important reason for this may be that they may not have had a desire for screening because they had regular health checks. In addition, the nurses were willing to receive training on EC. In this context, it can be said that this working group takes care of and are well aware of their own health.

	Mean ± SD	Median (min.-max.)
Risk factors	55.53±17.75	50 (0-100)
Diagnosis and symptoms	66.76±24.35	71.42 (0-100)
Treatment	62.75±27.03	75 (0-100)
Total correct knowledge rate	59.83±17.70	60 (0-100)

SD: Standard deviation, min.: Minimum, max. Maximum.

Barrett's esophagus is one of the most important risks for EC. In patients with Barrett's esophagus, a multicenter study showed an increased risk of dysplasia by 3.3% per year of age.<sup>3,21</sup> Also, other studies have shown Barrett's EC is usually diagnosed on routine screening, and its prevalence is higher in males around the world.<sup>5,28</sup> In the present

Predictors of risk factors correct rate	R=0.312 R <sup>2</sup> =0.097	F=1.767	Sig. F=0.089	
	B	95% CI	SE	p-value
Age	-1.327	-6.407-3.753	2.500	0.606
Gender (male)	0.488	-5.494-6.470	3.025	0.872
Marital status	4.283	-2.467-11.034	3.414	0.212
Education	0.531	-3.832-4.893	2.206	0.810
Work experience	-5.090	-11.193-1.013	3.085	0.101
Working clinics	1.353	-1.608-4.315	1.497	0.368
Visiting doctor within the previous year	2.732	-2.821-8.284	2.807	0.332
Predictors of diagnosis and symptoms correct rate	R=0.396 R <sup>2</sup> =0.157	F=3.146	Sig. F=0.003	
Age	-6.164	-12.803-0.474	3.357	0.069
Gender (male)	2.037	-5.780-9.857	3.953	0.607
Marital status	8.198	-0.625-17.020	4.461	0.068
Education	3.895	-1.806-9.596	2.883	0.179
Work experience	0.561	-4.168-5.290	2.391	0.815
Working clinics	1.917	-0.914-4.747	1.431	0.183
Visiting doctor in the past year	-8.581	-13.991--3.170	2.736	0.002
Predictors of treatment correct rate	R=0.348 R <sup>2</sup> =0.121	F=2.318	Sig. F=0.023	
Age	-2.967	-10.316-4.381	3.716	0.426
Gender (male)	1.774	-6.879-10.427	4.375	0.686
Marital status	5.946	-3.819-15.711	4.938	0.231
Education	1.550	-4.760-7.860	3.191	0.628
Work experience	-1.169	-6.403-4.065	2.647	0.659
Working clinics	0.930	-2.202-4.063	1.584	0.558
Frequency of visiting doctor within the previous year	-9.784	15.773- 3.796	3.028	0.002
Presence of EC in first-degree relatives	4.791	-5.184-14.767	50.044	0.344
Predictors of total knowledge score	R=0.360 R <sup>2</sup> =0.130	F=2.511	Sig. F=0.014	
Age	-2.944	-7.837-1.946	2.474	0.236
Gender (male)	1.127	-4.634-6.889	2.913	0.699
Marital status	5.645	-0.857-12.148	3.288	0.088
Education	1.636	-2.566-5.837	2.124	0.443
Work experience	-0.065	-3.550-3.420	1.762	0.941
Working clinics	0.333	-1.753-2.419	1.055	0.752
Visiting doctor within the previous year	-6.007	-9.994- 2.019	2.016	0.003
Presence of EC in first-degree relatives	6.116	-0.526-12.758	3.359	0.071

Sig.: Significant, CI: Confidence interval, B: Coefficient; SE: Standard error.

study, many Somalian nurses agreed that Barrett's esophageal disease is the leading cause of EC. This shows the nurses are familiar with the common causes of EC.

Susceptibility genes for EC are starting to be discovered, which may help in the determination of high-risk groups needing more preventive measures.<sup>26</sup> The literature has reported that three genes (*CRTC1*, *FOXP1*, and *BARX1*) play a role in the development of EC and Barrett's esophagus.<sup>29</sup> Although the information about these genes is limited, the fact that a significant number of the nurses (34.8%) know about these genes can be attributed to their encountering EC cases and having detailed information.

Low socioeconomic status is important in the development of EC due to its effect on nutrition and lifestyle. In addition, reflux is the most important risk factor for the development of Barrett's Esophagus and EC.<sup>26</sup> The relationship between EC and low socioeconomic status and long-term reflux complaints was answered correctly by most nurses.

Early diagnosis is important in cancer prevention. For this reason, regular doctor check-ups are important for these screenings, and cancer awareness should be increased with training in the community.<sup>17</sup> Gastroesophageal cancer guidelines offer suggestions for reflux and/or Barrett's esophagus during screening and surveillance of patients.<sup>30</sup> The nurses agreed that, based on their knowledge of diagnosis and screening, endoscopy plays a minor role in the diagnosis of cancer. Additionally, the nurses thought that the definitive diagnostic method is a biopsy of the esophagus. There is no standard or routine screening test for EC and endoscopy is not a recommended screening method for the entire population.<sup>31</sup> However, for the diagnosis of EC, flexible endoscopy with biopsy is the primary method. MR, CT, PET/CT, and endoscopic ultrasound are other diagnostic methods used in EC.<sup>32</sup> It was seen that the nurses had the desired knowledge levels on this subject.

It is also important to determine patient anamnesis in the diagnosis of this disease. Our study indicates most nurses agreed on the common symptoms of EC including dysphagia, reflux, chest pain or sensation, weight loss, indigestion, cough, and hoarseness. Additionally, many Somalian nurses knew hematemesis to be one of the late symptoms of EC. In a study conducted in Iran, it was found that more than one alarming symptom (such as weight loss, dysphagia, GI bleeding, or persistent vomiting) is important in the diagnosis of two-thirds of cancers.<sup>33</sup> In this study, the nurses knew most of the alarm symptoms required for the diagnosis of EC.

Survival in cancer also depends on the successful management of treatment.<sup>26</sup> In a study conducted in Canada, it was reported that neoadjuvant, adjuvant chemotherapy, and esophagectomy surgical treatment are frequently applied for the treatment of EC.<sup>34</sup> In this study, regarding the management and treatment of EC, most Somali nurses were aware of the treatment of EC such as neoadjuvant chemotherapy, surgery, or radiotherapy.

Somalian nurses' correct knowledge rates of risk factors, diagnosis/screening, and treatment were found to be *moderate*. Additionally, it was promising that most of them were willing to receive further education on this issue. This result may be attributed to the high incidence of EC (27%) in the population meaning that nurses encounter EC frequently.<sup>8</sup> However, we have not found any research other than our study which compares the knowledge levels of nurses on EC.

The frequency of nurses' visits to doctors within the previous year was found to be associated with the correct diagnosis, symptom, and treatment knowledge rates of EC. Regular doctor visits may have led to an increase in the knowledge of nurses on the mentioned subjects. The fact that almost half of these frequent doctor visits were made with the aim of check-ups shows the importance that nurses give to their health. In the literature, there is a study examining the cancer screening behaviors of nurses and midwives.<sup>35</sup> Unfortunately, there was no comparable data for nurses' EC screening in that study.

### Study Limitations

This current study has several limitations. Firstly, the COVID-19 pandemic occurred between the starting and ending dates of this study, and in Somalia, the Mogadishu hospital was a pandemic hospital where all clinics were converted into COVID-19 services. Correspondingly, difficulties were experienced when reaching nurses due to virus risks. The hard work of Somalian nurses during the outbreak and the psychological issues caused by COVID-19 may have affected the nurses' responses. Results may depend on information given by participants and may be open to bias. The extent of truthful responses or confirming the participants' claims is not fully known in a descriptive study and so their responses must be taken at face value. Additionally, comparing knowledge about EC among different populations is challenging. There is a lack of studies evaluating EC knowledge in different populations. This may limit the discussion of this study data. Additionally, there is also a lack of standardized, validated questionnaires to compare results from different populations. The strength of this study is that, as far as we know, this current study is the first descriptive study which evaluates nurses' knowledge about EC in Somalia. However, the data were obtained from participants in Mogadishu, Somalia, so this cannot be generalized to other regions of the country or the world.

### CONCLUSION

In this present study, The Somalian nurses had *moderate* knowledge. Considering the increasing incidence of EC around the world, we strongly suggest planning educational programs for nurses regarding increasing their knowledge of EC, including its risk factors, diagnosis, screening, and treatment modalities. The presence of nurses who have adequate knowledge about EC cancer in Somalian society will undoubtedly lead to patients receiving earlier diagnosis, and more successful treatment processes. Future studies are needed to compare the knowledge of Somalian nurses with nurses from different communities regarding EC.

### MAIN POINTS

- Esophageal cancer (EC) is increasing in Somalia. EC screening and awareness are essential for early detection and effective treatment.
- Adequately knowledgeable nurses can play many vital roles in the early detection of EC and screening awareness.
- There are limited studies which have focused on evaluating Somalian nurses' knowledge levels of esophageal cancer.

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## ETHICS

**Ethics Committee Approval:** Permission was obtained from the Karabük University Ethics Committee (no: 77192405099-E50699) and written approval was also obtained from the Mogadishu Banadir Government Hospital (approval number: 27105693-806.01.03-1697).

**Informed Consent:** We explained the aims of this study and received informed written consent from each nurse.

**Peer-review:** Externally peer-reviewed.

## Authorship Contributions

Surgical and Medical Practices: Z.S.N., Concept: Z.S.N., I.I.A., A.B.Ç., Design: Z.S.N., I.I.A., A.B.Ç., Data Collection and/or Processing: Z.S.N., Analysis and/or Interpretation: I.I.A., A.B.Ç., Literature Search: Z.S.N., I.I.A., A.B.Ç., Writing: I.I.A., A.B.Ç.

## DISCLOSURES

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

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