ORIGINAL RESEARCH

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Evaluation of Smoking Status of Cancer Patients Admitted to the Nuclear Medicine Department According to the Demographic Characteristics and Cancer Type

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ABSTRACT Objective: Cigarette smoking is one of the primary causes of cancer. Tobacco exposure affects many parameters such as prognosis, response to treatment, and quality of life after a cancer diagnosis. We aimed to assess the association between smoking status with demographical and clinical characteristics of patients with malignancy who were referred to the Nuclear Medicine Department. **Material and Methods:** A total of 440 (59.8% males; median age 62 years) patients diagnosed with malignancy who applied to the nuclear medicine department between December 2018 and May 2019 were assessed. The smoking behavior of patients was examined according to cancer diagnosis, age, gender, and education level. The factors that may affect quitting smoking after the cancer diagnosis were evaluated. **Results:** Thirty-eight percent of patients were never smoked, 51.4% were former smokers, and 10.7% were current smokers. Smoking history in men and women was present at the rate of 87.8% and 23.7%, respectively. Breast and gynecological cancers were more common in never-smoker females ($p<0.001$). The lung cancer rate was higher in men who smoked ($p<0.05$), gastrointestinal system cancer was higher in never-smoker men ($p<0.05$). Age, male gender, education status that high school and above, and a lung cancer diagnosis were found to be significantly higher in patients with a smoking history ($p<0.05$). Those who were <65 years old and had a smoking history of >30 pack-years had a risk for continuing smoking ($p<0.05$). **Conclusion:** Young age and more cigarette pack-years are factors that negatively affect quitting smoking. Smoking status is associated with the type of cancer in both genders.

Keywords: Cigarette smoking; neoplasm; smoking cessation

Smoking is still the most important cause of morbidity and mortality in Turkey and the world. Smoking is a severe problem in cancer patients and should be handled effectively. Studies have reported that cancer-specific mortality increases in cancer patients who continue smoking and that quitting smoking at any stage after diagnosis is beneficial in treatment outcomes, quality of life, and general survival of patients with cancer.[1-5]

Smoking cessation campaigns in special groups such as those of cancer patients and strategies developed in this patient group are essential for decreasing cancer- related deaths. The diagnosis of cancer is the most significant source of stress in these patients. Many studies have shown that the possibility of smoking cessation increases after the diagnosis of cancer.[6,7]

Continuing to smoke reduces the effectiveness of cancer treatments, increases the probability of relapse, and negatively affects overall survival.[8,9] Quitting smoking is known to improve prognosis and reduce toxicity secondary to treatments. Despite this, approximately 15-18% of cancer survivors continue to smoke.[10,11] Patients with a low level of education, younger age, living alone, and limited access to healthcare services were observed to be at a high risk of smoking after cancer diagnosis.[12-15]

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Patients who continue to smoke after a cancer diagnosis have poor prognosis than those who have never smoked.[16] In a meta-analysis on patients with lung cancer, the 5-year survival rates of small and non-small cell lung cancer patients who quit smoking at the time of diagnosis and who continued smoking were 63% and 70%, while the rates of those who continue to smoke were 29% and 33%, respectively.[17]

The prevalence of cancer types differs according to gender; in addition to biological and physiological differences regarding gender, smoking status also impacts this difference. Regarding lung cancer, the male gender is known to be a risk factor. A recent study evaluating the survival effectors in Turkey showed that the male gender has a 2.41- f old increased risk of having shorter survival rates than females.[18] Therefore, the comparisons in our study were made and presented not only in total but also according to gender.

Few studies have been published on the smoking status of patients diagnosed with cancer and the factors affecting smoking cessation after diagnosis. Our study aimed to assess the effect of age, gender, education level, pack-year, cancer type, and cancer diagnosis on smoking cessation in patients with malignancy referred to the nuclear medicine department.

MATERIAL AND METHODS

STUDY DESIGN AND THE SAMPLE

A total of 440 patients with a cancer diagnosis were included in this cross-sectional study, retrospectively. All cancer patients aged more than 18 years, including hematological malignancies applied to the nuclear medicine department for 18F- fluorodeoxyglucose positron emission tomography/computed tomography (18F-FDG PET/CT) scanning, were included in this study.

Patients under the age of 18 years, patients without biopsy-proven cancer, and who apply for PET/CT scanning for metabolic characterization and guiding biopsy, patients who had PET/CT scans for reasons other than malignancy, such as fever or vasculitis of unknown cause, and those whose mental level made them incapable of answering questions on their own were excluded from the study.

The patients' smoking history was retrospectively analyzed from the patient files and PET/CT anamnesis forms available in the hospital electronic system. Whether the patients smoked, the age of starting smoking, how many packets a day they smoked, and the current smoking status, when the patients quit smoking (before or after the cancer diagnosis), were individually questioned. Also, the education levels of the patients were noted.

Smoking status terminations were classified as following: current smoker: an adult who has smoked 100 cigarettes in his or her lifetime and currently smokes cigarettes; former smoker: an adult who has smoked at least 100 cigarettes in his or her lifetime but who had quit smoking at the time of interview; quitters before cancer diagnosis: an adult who quitted at least one year ago; quitter after cancer diagnosis: an adult who quit smoking after the cancer diagnosis until the interview; never smoker: an adult who has never smoked or smoked less than 100 cigarettes in his or her lifetime.

Cancer diagnosis, age of diagnosis, history of pack- years, and education levels were obtained from existing PET/CT patient forms. PET/CT scans of the patients were performed in a standard oncological PET/CT procedure.

This study was carried out in Recep Tayyip Erdoğan University Department of Nuclear Medicine between December 2018 and May 2019. The study was started after obtaining permission from the Recep Tayyip Erdoğan University, Faculty of Medicine Non-Invasive Clinical Research Ethics Committee dated 17.07.2019 (no: 2019/131). This study was carried out following the principles of the Declaration of Helsinki.

STATISTICAL ANALYSIS

Statistical analysis was performed using the statistical package SPSS 22.0. To confirm whether the quantitative variables were normally distributed or not was checked by the Kolmogorov-Smirnov test. Mann-Whitney U test was used to compare two independent groups, and descriptive statistics for the groups were given as median (25^{th}-75^{th} percentile). Descriptive statistics were presented as mean±standard deviation. Independence between qualitative

variables was determined by chi-square independence analysis, and descriptive statistics were given as frequency (percentage). The effects of independent variables on smoking cessation were determined by univariate and multivariate logistic regression analyses. In the regression anal ysis, the pack-year variable of smokers was split into two categories according to the cut-off value determined by the receiver operating characteristic analysis. Also, posthoc Bonferroni tests were performed to determine the factors providing significance in multiple groups considering the type of cancer. Values of $p<0.05$ were considered statistically significant.

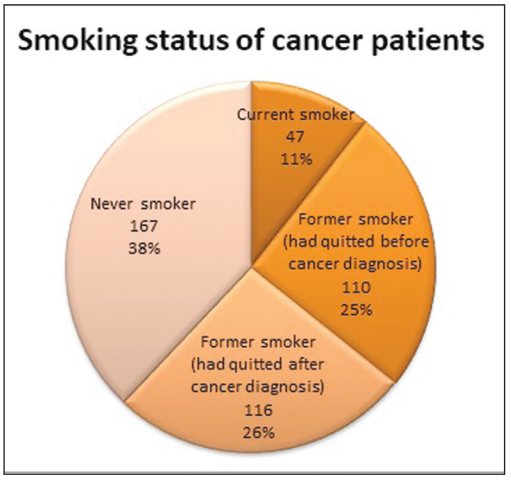

FIGURE 1: Smoking status of cancer patients in the study population.

RESULTS

The median age of 440 patients with a cancer diagnosis applied to the nuclear medicine department was 62 (IQR: 53.0-70.0, range 21-98). A majority of the patients were men (59.8%). Considering the education level of patients, a majority of the patients (69.1%) were primary school graduates.

In the patient cohort, 38% had never smoked, 11% were active smokers, and the remaining were former smokers. On examining the smoking cessation behavior of ex- smokers before or after the cancer diagnosis, the rate of those who quit smoking before cancer diagnosis was 25.9%. At the same time, those who quit after cancer diag nosis were 26.4%. The smoking status of all patients is shown in Figure 1.

Sixty-two percent of patients were found to have a smoking history (mean 42.94±25.46 pack-year, minimum- maximum=5-150). While this rate is 87.8% (46.26±25.85 pack-year, minimum-maximum=5-150) in males, it was 23.7% for females (24.67±12.21 packs-year, minimum-maximum=5-54).

The lung, breast, and gastrointestinal system (GIS) cancers were the most common types of cancer in our study.

Lung, GIS, and hematological cancers were in the top three in men, while breast, gynecological, and GIS cancers were the three most common cancer types in women (Figure 2). A significant difference was observed between genders considering the cancer types. Lung and GIS cancers were more common in men than women, while breast and gynecological cancers were more common in women than in men ($p<0.05$).

In the entire sample, the mean age, the proportion of females, the proportion of those with high school and above education, and the proportion of those diagnosed with lung cancer in the non- smoker group were significantly lower than the participants with a history of smoking ($p<0.05$). When the patients with smoking history were analyzed according to age, gender, education level, and cancer type, the average age of active smokers was found to be lower than former smokers ($p<0.001$). The demographic data of the patients are presented in Table 1.

Although the mean age of those who continued smoking after cancer diagnosis was lower than that of those who quit smoking, the difference was not statistically significant ($p=0.08$). No statistical differences were found in clinical and demographic data in patients with continuing and quit smoking after a cancer diagnosis. Demographic characteristics of patients who quit or continued smoking after a cancer diagnosis are mentioned in Table 2.

According to univariate and multivariate logistic regression analysis, age and pack-year variables were observed to significantly affect quitting smoking. In univariate and multivariate analyses, the risk of continuing smoking after the cancer diagnosis in patients of 65 years and younger was higher than those older than 65 years ($p<0.05$). Again, the risk of continuing

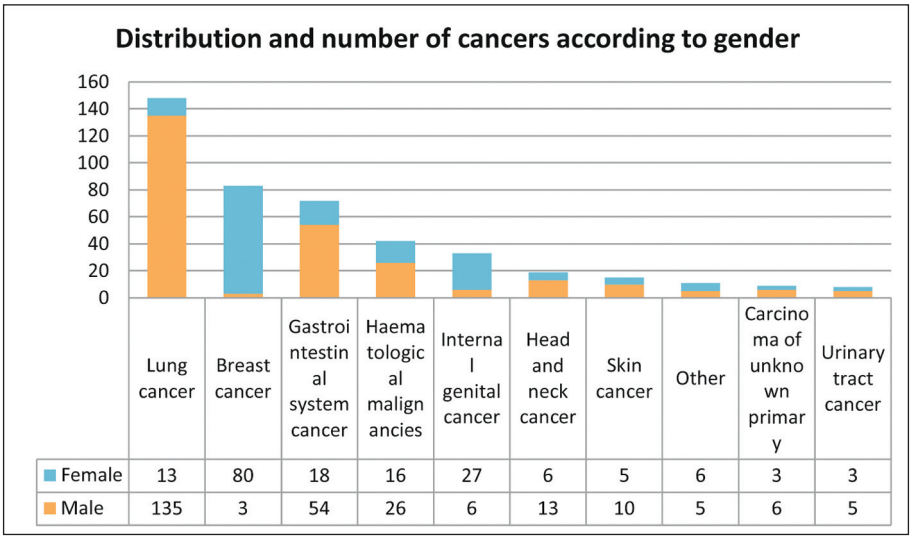

FIGURE 2: Gender-based distribution and number of cancers.

TABLE 1: Patient characteristics according to their smoking status.

	All patients (n=440, 100%)			Smokers (n=273, 62%)		
	Smoker (current or former)	Never smoker		Former smoker	Current smoker	
Variables	**(n=273, 62%)**	**(n=167, 38%)**	**p value**	**(n=226, 82.8%)**	**(n=47, 17.2%)**	**p value**
Age	63.0 (55.0-70.0)	59.0 (48.0-69.0)	0.007	65.0 (56.8-71.0)	54.0 (50.0-63.0)	<0.001
Gender			<0.001			0.573
Female	42 (23.7)	135 (76.3)		33 (78.6)	9 (21.4)	
Male	231 (87.8)	32 (12.2)		193 (83.5)	38 (16.5)	
Education			0.042			0.577
< High school	220 (59.9)	147 (40.1)		184 (83.6)	36 (16.4)	
≥ High school	53 (72.6)	20 (27.4)		43 (79.2)	11 (20.8)	
Type of cancer			<0.001			0.978
Other types	137 (46.9)	155 (53.1)		114 (83.2)	23 (16.8)	
Lung cancer	136 (91.9)	12 (8.1)		112 (82.4)	24 (17.6)	

TABLE 2: Characteristics of patients who quit or continued smoking after cancer diagnosis.

Variables	Former smokers quit after cancer diagnosis (n=116)	Current smokers (n=47)	p value
Age	59.7±11.5	56.3±10.7	0.08
Gender			
Female	15 (62.5)	9 (37.5)	0.31
Male	101 (72.7)	38 (27.3)	
Education			
< High school	92 (71.9)	36 (28.1)	0.7
≥ High school	24 (68.6)	11 (31.4)	
Type of cancer			
Other types	54 (70.1)	23 (29.9)	0.78
Lung cancer	62 (72.1)	24 (27.9)	
Pack-year	50.2±26.9	46.3±22.2	0.37

smoking after cancer diagno sis in patients with a history of smoking more than 30 packs per year was observed to be higher than those who smoked 30 packs or less ($p<0.05$). The results of univariate and multivariate logistic regression analyses are presented in Table 3.

According to smoking status, smokers were in the majority diagnosed cancers of the lung, urinary system, and head and neck. In contrast, non-smokers were in the majority in breast and gynecological cancers (Figure 3). Thus, the differences in cancer types according to smoking history were significant ($p<0.001$). In smokers, lung cancer and uri nary tract cancer were more common while in non-smokers, breast and gynecological cancers were more common.

TABLE 3: Factors associated with quitting smoking in the study population.

	Univariate analysis		Multivariate analysis	
Patient characteristics	**OR (95% CI)**	**p value**	**OR (95% CI)**	**p value**
Age		0.004		0.001
>65	1.00		1.00	
≤65	2.891 (1.402-5.963)		3.510 (1.639-7.517)	
Education		0.448		0.551
High school and above	1.00		1.00	
Less than high school	0.747 (0.352-1.588)		0.766 (0.320-1.838)	
Type of cancer		0.851		0.983
Other types	1.00		1.00	
Lung cancer	1.062 (0.566-1.991)		1.008 (0.487-2.088)	
Gender		0,433		0.214
Female	1.00		1.00	
Male	0.722 (0.320-1.631)		0.529 (0.194-1.443)	
Pack-years		0.043		0.003
≤30	1.00		1.00	
>30	2.077 (1.024-4.212)		3.788 (1.573-9.125)	

OR: Odds ratio; CI: Confidence interval.

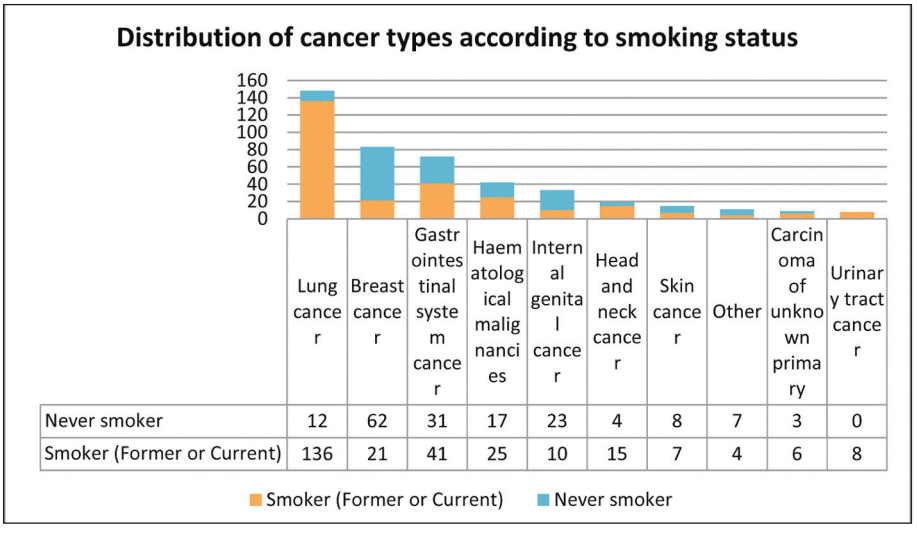

FIGURE 3: Patient distribution of cancer types according to smoking status.

The distribution of cancer types according to the smoking status of both genders is mentioned in Table 4. A significant difference was observed in men in terms of cancer types according to smoking history (p=0.001). The rates of lung and GIS cancers were higher in men with a smoking history. The rate of breast and gynecological cancers were higher in women who never smoked. A significant difference between cancer types was observed according to smoking history in women (p=0.001). We found that in patients with a smoking history, the rate of lung, head, and neck, and urinary system cancers are common.

Considering age, patients with lung cancer were older than those with breast, hematological cancers, and gynecological cancers (p<0.05). When cancer types were examined considering the cigarette pack-year status accounting for only the patients with a smoking history, patients with lung cancer had a higher pack-year smoking history compared to those with breast and gynecological cancers (p<0.05). On the other hand, patients with breast cancer had less pack-year smoking compared to those with cancers of the head and neck and the urinary system (p<0.05).

DISCUSSION

This study examined the distribution of the types of cancer diagnosis by gender and smoking status of patients with cancer who applied to a nuclear medicine clinic. The results showed that 38% of patients diagnosed with cancer never smoked, 25.9% quit smoking before cancer diagnosis, 26.4% quit smoking after the cancer diagnosis, and 10.7% were active smokers. In another study by Shin et al., the rate of patients who quit smoking after a cancer diagnosis was 76.1%, and that of active smokers was 23.9%.[19] In this study, we found that 52.3% of patients quit smoking, and 10.7% of all patients are still active smokers after a cancer diagnosis. The difference between the earlier study and ours is that although Shin et al. included only smoking patients, 38% of our patient group had no smoking history. These differences may be because the patient sample included in the study had different smoking situations.[19] One research group included non-smoking patients similar to the sample group in our study, and the smoking status of cancer patients was similar to that in our study. In this study, the patient group who never smoked was 34.9%, the patient group who still smoked was 8.4%, while those who stopped smoking comprised the largest group (50.9%), similar to that in our study.[20]

When examined according to demographic and clinical characteristics, the mean age, proportion of females, proportion of patients with education until high school and above, and the proportion of those diagnosed with lung cancer in the non-smoker group were significantly lower than those with a history of smoking. The median age of active smokers was lower than that of former smokers. When the factors

TABLE 4: Distribution of cancers according to smoking status for each gender.

	Male		Female	
	Smoker (current or former)	Never smoker	Smoker (current or former)	Never smoker
Cancer type	n (%)	n (%)	n (%)	n (%)
Lung cancer	130 (56.3)	5 (15.6)	6 (14.3)	7 (5.2)
Breast cancer	2 (0.9)	1(3.1)	19 (45.2)	61 (45.2)
Gastrointestinal system cancer	40 (17.3)	14 (43.8)	1 (2.4)	17 (12.6)
Haematological system malignancies	22 (9.5)	4 (12.5)	3 (7.1)	13 (9.6)
Gynecological cancer	4 (1.7)	2 (6.3)	6 (14.3)	21 (15.6)
Head and neck cancer	11 (4.8)	2 (6.3)	4 (9.5)	2 (1.5)
Skin cancer	7 (3.0)	3 (9.4)	0 (0.0)	5 (3.7)
Other	4 (1.7)	1 (3.1)	0 (0.0)	6 (4.4)
Carcinoma of unknown primary	6 (2.6)	0 (0.0)	0 (0.0)	3 (2.2)
Urinary tract cancer	5 (2.2)	0 (0.0)	3 (7.1)	0 (0.0)
Total number	231	32	42	135

associated with smoking cessation after cancer diagnosis were examined, being over 65 years of age had a positive effect on smoking cessation, while being a smoker over 30 pack-year negatively influenced smoking cessation. In a study, when age and smoking cessation status after the diagnosis of cancer were examined, similar to that in our study, the rate of continuing smoking after the diagnosis of cancer was found to be significantly high in young people (<40 years) compared to the elderly (>60 years).[21] In another study, when the age of patients who continued to smoke and those who quit smoking after cancer diagnosis was evaluated, no statistically significant difference was found.[18] These varying results may be caused by the fact that the cut-off age values, based on the deter mination of age groups in statistical evaluation, are taken differently or by taking different numbers of patients in the specified age groups. Similar to our study, in this study too, no difference was found between cancer diagnoses in smoking status. Concurrent with the results of an earlier study, we found no difference between education level with smoking status.[19]

When assessments were performed according to cancer types, the most common were cancers of thelung, breast, and GIS. Lung cancer and GIS cancer were higher in men, and breast and gynecological cancer, in women. In a large-scale prospective cohort study, breast cancer was the most commonly diagnosed in women and prostate can cer in men.[22] In our study, while breast cancer was the most commonly diagnosed in women, lung cancer was the most common in men. The findings of our study were different from an earlier published study may be because we included only patients who applied to the nuclear medicine unit for PET/CT examination; for example, the lack of 18F- FDG PET/CT examination in the evaluation of prostate adenocarcinoma, which is the most common type of cancer in men, can be an alternative explanation. For this reason, we think that the most common type of cancer in men in our study sample is lung cancer and not prostate cancer.

Cancers associated with smoking have been listed as oral cavity, larynx, pharynx, esophagus, lung, trachea, stomach, kidney and renal pelvis, pancreas, liver, bladder, cervix, colon, rectum, and acute myeloid leukemia.[8] Likewise, we observed here that patients with lung cancer had more pack-year smoking history than those with breast and gynecological cancer. On the other hand, those with breast cancer had less pack-year smoking history than those with cancers of the head, neck, and urinary system. When we examined the distribution of cancer types according to smoking status, smokers were in the majority of the patients with lung, urinary system, and head and neck cancers. In contrast, non-smokers were presented in the majority in breast and gynecological cancers.

Similarly, lung, urinary system, and head and neck cancers are reported as smoking-related cancers.[8] In our study, in men, lung cancer was found at a higher rate in smokers, and GIS cancer was found at a higher rate in non- smokers. Among the GIS cancers included in our study, a single type of cancer such as that of the esophagus or rectum was not included. All GIS cancers subtypes, such as those of the liver and pancreas, were combined in a single group under GIS cancers. Therefore, the results may be different in studies published earlier. In women, cancers of the lung, head, and neck urinary system were found to be higher in smokers.

In addition, we observed that the patients diagnosed with lung cancer were older than those with breast, hematological cancers, and gynecological cancers. The older age of patients with lung cancer, which is most strongly associated with smoking, suggests that it can be an indirect indicator of the cumulative carcinogenic effect of smoking. On the other hand, in our study compared to the patients with lung cancer especially in patients with breast and gynecological cancers, both exposure to cigarettes and the level of exposure in pack-year were significantly lower than.

STRENGTHS AND LIMITATIONS OF THIS STUDY

Our cross-sectional study gives a comprehensive overview of cancer patients referred to the Nuclear Medicine Department. The present smoking situation of patients was reported accurately by face-to-face interviewing, and comparisons were made according

to cancer types for all samples and also for both genders. However, the other clinical characteristics that are very well known to affect the prognosis of cancer patients were not recorded, such as Eastern Cooperative Oncology Group performance status, symptoms, comorbidities, making it difficult to suggest an association between continuing or quitting smoking after a cancer diagnosis. Further studies are needed to evaluate this gap by considering more confounding factors with a prospective design.

CONCLUSION

In conclusion, our study showed that 62% of the patients diagnosed with cancer had been exposed to tobacco, and 10.7% of the sample continued to smoke. Considering that continuing to smoke after the diagnosis of cancer negatively affects the treatment response and prognosis, prevention of tobacco exposure and guidance in treating tobacco addiction in the clinical follow-up as well as management of these patients will contribute to the course of the disease.

Source of Finance

During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that pro vides or produces medical instruments and materials which may negatively affect the evaluation process of this study.

Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: *Sibel Göksel, Dilek Karadoğan;* ***Design:*** *Sibel Göksel;* ***Control/Supervision:*** *Sibel Göksel;* ***Data Collection and/or Processing:*** *Sibel Göksel;* ***Analysis and/or Interpretation:*** *Sibel Göksel, Dilek Karadoğan;* ***Literature Review:*** *Sibel Göksel, Dilek Karadoğan;* ***Writing the Article:*** *Sibel Göksel, Dilek Karadoğan;* ***Critical Review:*** *Sibel Göksel, Dilek Karadoğan;* ***References and Fundings:*** *Sibel Göksel, Dilek Karadoğan;* ***Materials:*** *Sibel Göksel.*

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