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Sleep quality in patients with chronic spontaneous urticaria

Kronik spontan ürtikerli hastalarda uyku kalitesi

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Abstract

Background and Design: Chronic urticaria is characterized by the occurrence of hives (wheals) and/or angioedema for 6 weeks or more.
Materials and Methods: This was a cross-sectional study. All participants were asked to complete the Epworth Sleepiness Scale (ESS), Pittsburgh Sleep Quality Index (PSQI), and Insomnia Severity Index (ISI). Patients with chronic spontaneous urticaria (CSU) completed the Urticaria Activity Score 7 (UAS-7) and Chronic Urticaria Quality of Life Questionnaire.
Results: The study included 88 patients with CSU (26 men and 62 women) and 88 healthy controls (26 men and 62 women). The mean global PSQI score was 7.27±4.54 in the patient group and 4.97±2.82 in the control group (p<0.001). The mean ISI score was significantly higher in the patient group than in the control group (p=0.001). The mean ESS score did not differ between the patient and control groups (p=0.262).
Conclusion: In this study, we found that more people in the patient group experienced poor sleep quality and insomnia compared with the control group. In the patient group, female sex, presence of CSU for more than 5 years, and presence of angioedema were associated with poor sleep quality. Patients with severe disease (high UAS-7 scores) had worse sleep quality. The erythrocyte sedimentation rate was found to be correlated with sleep disturbance.
Keywords: Chronic spontaneous urticaria, sleep, quality of life, Pittsburg Sleep Quality Index, Insomnia Severity Index, Epworth Sleepiness Scale, Chronic Urticaria Quality of Life Questionnaire

Öz

Amaç: Kronik ürtiker, 6 hafta veya daha uzun süre kurdeşen (kabarcıklar) ve/veya anjiyoödem oluşumu ile karakterizedir.
Gereç ve Yöntem: Çalışmamız kesitsel bir olgu kontrol çalışmasıdır. Bütün katılımcılara Epworth Uykusuzluk Ölçeği (ESS), Pittsburg Uyku Kalitesi Ölçeği (PSQI), Uykusuzluk Şiddeti Ölçeği (ISI) uygulanmıştır. Kronik spontan ürtikeri (CSU) olan hasta gurubuna Ürtiker Aktivite Skoru 7 (UAS-7) ve Kronik Ürtiker Yaşam Kalitesi Anketi uygulanmıştır.
Bulgular: Çalışmaya 88 hasta (26 erkek ve 62 kadın) ve 88 (26 erkek ve 62 kadın) sağlıklı kontrol grubu alınmıştır. Ortalama PSQI skoru hasta grubu için 7,27±4,54 iken, kontrol grubu için 4,97±2,82 idi (p<0,001). Kronik ürtiker hastalarının ISI ortalaması anlamlı olarak yüksek idi (p<0,001). Ortalama ESS skorları hasta ve kontrol grubunda farklı değildi (p=0,262).
Sonuç: CSU'lu hasta grubunda bozulmuş uyku kalitesi ve uykusuzluk daha fazlaydı. Hasta grubunda kadın cinsiyet, beş yıldan uzun hastalık süresi, anjiyoödem varlığı kötü uyku kalitesi ile ilişkili bulundu. Daha şiddetli hastalığa sahip olanlarda (yüksek UAS7 skoru) uyku kalitesi daha kötüydü. ESR düzeyleri de uyku düzensizliği ile bağlantılı bulundu.
Anahtar Kelimeler: Kronik spontan ürtiker, uyku, yaşam kalitesi, Pittsburg Uyku Kalitesi Ölçeği, Uykusuzluk Şiddeti Ölçeği, Epworth Uykusuzluk Ölçeği, Kronik Ürtiker Yaşam Kalitesi Ölçeği

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Introduction

Chronic urticaria (CU) is a common disorder affecting the skin and mucosal tissues, which is characterized by the occurrence of hives (wheals) and/or angioedema for more than 6 weeks. CU is further classified into the following two subgroups, depending on whether the skin lesions appear spontaneously or are elicited by a specific trigger: chronic spontaneous urticaria [CSU; previously called chronic idiopathic urticaria (CIU)] and chronic inducible urticaria[1-5].

The overall lifetime prevalence of CSU ranges between 0.02% and 5%. The disease is more common in female individuals than in male individuals[2,6,7]. The course and duration of CSU are unpredictable, and patients with CSU are at risk of developing psychiatric comorbidities, sexual dysfunction, and sleep disorders[8].

Sleep is very important for the appropriate functioning of the human body[9]. People spend about one-third of their lives sleeping[10]. Skin conditions can affect the sleep process in many aspects, including body temperature, thermoregulation, pH, barrier function, and transepidermal water loss. It has been shown that chronic skin dermatoses affect sleep quality, with symptoms of itching, pain, and odor[9-11].

Both CSU and sleep disturbances (SD) can adversely affect the quality of life of patients and can result in excessive daytime sleepiness, fatigue, psychiatric complications, decreased cognition, and decreased performance at work or school. In addition, the economic burden of CU is even more than that of many other diseases, including acne, psoriasis, atopic dermatitis, intermittent asthma, perennial rhinitis, and severe coronary artery disease requiring bypass grafting[12,13].

The association between SD and CU is bidirectional. While some studies have shown that patients with CSU have a high risk of insomnia, other studies have reported that patients with sleep disorders have an increased risk of CSU[14-16].

Besides CSU, SD has been evaluated in many chronic skin disorders, including psoriasis, acne, hidradenitis suppurativa, atopic dermatitis, vitiligo, prurigo nodularis, and lichen planus, in both adults, and children[17-19].

The present study aimed to assess the quality of life and sleep of patients with CSU. Although SD in patients with CSU has been studied in some previous studies, to our knowledge, this is the most detailed study evaluating SD and the factors affecting the quality of life and sleep of patients with CSU.

Materials and Methods

This cross-sectional case-control study was conducted in our dermatology department between September 2020 and January 2021. Written informed consent was obtained from the patients and controls after providing an explanation of the aims of the study under the Declaration of Helsinki. Ordu University Clinical Research Ethics Committee approval was obtained prior to the study (approval number: 248, date: 10.12.2020). We recruited healthy controls from the hospital staff. Healthy controls were examined to rule out any dermatological or systemic diseases that could impair their sleep quality. Individuals' baseline demographic data, including sex, age, education level, occupation, marital status, disease duration, presence of angioedema, triggering factors, smoking status, alcohol consumption status, past or current therapies, any known previous medical diseases, and drug treatment, were recorded. Serum C-reactive protein (CRP) levels, erythrocyte sedimentation rate (ESR), immunoglobulin E (IgE) levels, and eosinophil, and basophil counts were obtained retrospectively from hospital records.

Patients over the age of 18 years with a confirmed clinical diagnosis of CSU, who voluntarily agreed to participate in the study, were included. Patients with any known psychiatric disease and those with any disease or medication that can affect sleep quality were excluded from the study. In addition, patients on omalizumab treatment, and pregnant patients were excluded from the study. All participants were asked to complete the Epworth Sleepiness Scale (ESS), Pittsburgh Sleep Quality Index (PSQI), and Insomnia Severity Index (ISI). Moreover, patients with CSU completed the Urticaria Activity Score 7 (UAS-7) and the Chronic Urticaria Quality of Life Questionnaire (CU-Q2oL).

The UAS-7 is a tool to assess urticaria severity, and it is recommended by the EAACI/GA2LEN/EDF guidelines. The UAS-7 estimates hive number (range: 0-3) and itch intensity (range: 0-3) separately, and the final score is obtained by summing these two scores. Patients are asked to record their scores for 7 consecutive days to obtain the total UAS-7 score (range: 0-42)[20].

The CU-Q2oL is a disease-specific, health-related quality of life assessment tool developed for CU. It comprises 23 questions in the following six subscales: itching, swelling, impact on life activities, sleep problems, limits, and looks. The scores of the subscales are transferred to a 0-100 scale for comparisons between subscales. Higher scores indicate more impairment in the quality of life[21]. Kocatürk et al.[22] validated the Turkish version of the CU-Q2oL.

The ESS is a tool used to assess daytime sleepiness. It comprises eight questions, which patients are asked to rate on a scale of 0-3. Higher scores indicate greater daytime somnolence, and a score of 10 or greater indicates sleepiness[23].

The PSQI is a self-rated questionnaire that is used to evaluate sleep quality and disturbances over 4 weeks. It comprises 14 questions rated on a scale of 0-3. It is divided into seven components, including subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleep medication, and daytime dysfunction. The total score ranges from 0 to 21 points, and a score of ≥5 indicates poor sleep quality[24]. Agargun et al.[25] validated the Turkish version of the PSQI.

The ISI is a validated questionnaire that was developed to evaluate the quality of sleep in order to assess the extent of insomnia during the previous 2 weeks. The total score ranges from 0 to 28. A score of 7 is considered normal, 8-14 is considered to indicate subclinical insomnia, 15-21 is considered to indicate clinical insomnia, and 22-28 is considered to indicate severe insomnia[26]. Boysan et al.[27] translated and validated the Turkish version of the ISI.

Statistical Analysis

Statistical analyses were performed using IBM SPSS 22 (IBM Corp, Armonk, NY, USA). Categorical parameters are expressed as numbers and percentages, and continuous parameters are expressed as mean and standard deviation (SD). Data distribution was assessed using the Kolmogorov-Smirnov/Shapiro-Wilk test. For continuous variables, the Mann-Whitney U test was used. Pearson's chi-square test or Fisher's exact chi-square test was used for evaluating categorical variables.

Pearson's correlation test was used to examine the relationship between scale scores. A p-value of <0.05 was considered statistically significant, and the confidence interval was set at 95%.

The sensitivity, specificity, and cut-off values of the ISI, ESS, and PSQI were calculated between the patient and control groups using receiver operating characteristic (ROC) curve analysis.

The success of the scale scores in distinguishing between controls and patients was evaluated by ROC analysis. The ISI had statistically significant sensitivity of 59.1% and specificity of 56.8%, and it was successful in identifying the disease with a score of 8.5 or above [area under the curve (AUC): 0.615]. Since the ESS did not yield statistically significant results, it did not have the power to discriminate between patients and controls. The PSQI showed the best results among the scales. It had statistically significant sensitivity of 48.9% and specificity of 73.9%, and it was successful in identifying the disease with a score of 6.5 or above (AUC: 0.644).

Based on these data, the ISI, and PSQI have a decision-support system for distinguishing patients from controls.

Results

The study included 88 patients with CSU (26 men and 62 women) and 88 healthy controls (26 men and 62 women). The mean age of the patients was 39.57±12.41 years (range: 18-77 years), and the mean age of the controls was 39.57±12.47 years (range: 20-75 years). We observed no significant differences between the groups in age (p=0.99) or sex (p=1). The control group had a better level of education than the patient group (p<0.05). Marital status did not differ between the patient and control groups (p>0.05). Moreover, 35.5% of the individuals in the patient group and 64.5% of the individuals in the control group had an occupation (p<0.05). The levels of smoking and alcohol consumption were similar in the two groups (p>0.05). The ratios of people with any known systemic disease and individuals who were on any medical treatment were not different between the patient and control groups (p=0.86 and p=0.85, respectively). The incidences of reported thyroid diseases and asthma were similar in the two groups (p=0.27 and p=1, respectively).

In the patient group, the mean disease duration was 49.01 months (range: 2-48 months). Among the patients, 75 (85.2%) had the disease for less than 5 years, 29 (33%) had the disease for less than 1 year, and 55 (62.5%) had angioedema.

Thirty-two patients with CSU described at least one triggering factor. Stress was the most prevalent trigger, and it was noted in almost half of the patients (52.3%). IgE levels were normal in 29.5% of patients with CSU and 5 times or higher than normal in 20.5% of patients. The mean UAS-7 score was 31.14 (SD: 9.12; range: 10-42). The UAS-7 score distribution was as follows: score 7-15, 6 patients (6.8%); score 16-27, 25 patients (28.4%), and score 28-42, 57 patients (64.8%).

Only two patients did not complete the CU-Q2oL; the rest of the questionnaires were fully completed by the respondents.

The mean global PSQI score was 7.27±4.54 in the patient group and 4.97±2.82 in the control group, indicating that more people experienced poor sleep quality in the patient group than in the control group (p<0.001). The PSQI component scores are shown in Table 1. Moreover, 57% of patients were identified as poor sleepers (PSQI >5), compared with 42% of controls (p=0.023). When we analyzed PSQI components separately, patients had worse scores than controls in all components, except sleep duration (Table 1).

Patients with CSU had significantly higher ISI scores (10.8±7.37) compared with controls (7.82±4.29; p=0.001) (Table 1). When we looked at the ISI, we found that 51.1% of controls and 55.1% of patients had some level of insomnia (ISI score >7). There were 12 patients (13.6%) in the patient group with severe insomnia, whereas no individuals had severe insomnia among controls. The number of patients experiencing insomnia was not significantly different between the patient and control groups (p=0.225).

The mean ESS scores were 5.95±5.57 in the patient group and 5.14±3.92 in the control group, indicating that the mean ESS score did not differ between patients and controls (p=0.262) (Table 1). Twelve individuals (13.6%) in the control group and twenty-one patients (23.9%) in the patient group had ESS scores >10, indicating daytime sleepiness (p=0.082).

In patients with CSU, female sex was found to be associated with abnormal PSQI scores (p=0.018) and abnormal ISI scores (p=0.011). However, the abnormal ESS scores were similar between the two sexes. Insomnia and poor sleep were more prominent in females with CSU than in females without CSU (p=0.001 and p=0.001 for ISI and PSQI, respectively). Education level, working status, and marital status

Table 1. Comparison of the mean ISI score, ESS score, and PSQI total, and component scores between patients and controls

Variable	Controls (n=88)	Patients (n=88)	p-value
	Mean ± SD	Mean ± SD	
ISI score	7.82±4.3	10.8±7.4	0.001
ESS score	5.14±3.9	5.96±5.58	0.262
PSQI total score	4.97±2.8	7.27±4.5	<0.0001
PSQI Comp-1	1.13±0.6	1.51±0.8	0.001
PSQI Comp-2	1.3±1.0	1.7±1.2	0.016
PSQI Comp-3	0.60±0.9	0.9±1.0	0.074
PSQI Comp-4	0.17±0.5	0.6±0.9	<0.0001
PSQI Comp-5	1.15±0.5	1.41±0.7	0.004
PSQI Comp-6	0.06±0.3	0.25±0.8	0.042
PSQI Comp-7	0.59±0.7	1.0±1.0	0.005

The Mann-Whitney U test was used, and p<0.05 was considered significant. ESS: Epworth Sleepiness Scale; ISI: Insomnia Severity Index; PSQI: Pittsburgh Sleep Quality Index

were not associated with poor sleep scores and insomnia in patients with CSU. Patients with a disease duration of ≥5 years had worse PSQI scores, but their ISI, and ESS scores were similar between the two groups. Patients with CSU having angioedema had poor sleep according to the PSQI scores (p=0.044), but the ISI, and ESS scores were not different. Among patients with CSU, smoking, and alcohol status, chronic disease, medication use, and a history of asthma or thyroid diseases did not affect the sleep status. UAS-7 scores were not associated with insomnia or daytime sleepiness in patients with CSU, but UAS-7 scores were higher in patients with a poor sleep status (PSQI >5) (p=0.035). Factors affecting PSQI scores were analyzed, and serum eosinophils, basophils, IgE levels, and CRP levels were not different between CSU patients with and without poor sleep. ESR levels were higher in patients with CSU experiencing poor sleep and patients with insomnia (p=0.01 and p=0.016, respectively).

The mean total CU-Q2oL score was 60.24±18.61 (minimum: 29; maximum: 113). The mean sleep parameter score of the CU-Q2oL was 60.95±20.62. The sleep parameter of the CU-Q2oL was correlated with the ESS, ISI, and PSQI (r=0.286, r=0.614, and r=736, respectively). Patients with angioedema had worse CU-Q2oL scores (p=0.016), but angioedema did not affect the sleep parameter of the CU-Q2oL. Disease duration and serum IgE levels did not affect the total CU-Q2oL score and the sleep parameter of the CU-Q2OL.

Patients with abnormal PSQI and ISI scores had worse CU-Q2oL scores (p<0.001 and p<0.001, respectively). CU-Q2oL scores were not associated with abnormal ESS results. Female patients had worse sleep quality than male patients, according to the results of the sleep parameter of the CU-Q2oL (p=0.021).

The UAS-7 was found to be correlated with the total PSQI score and the CU-Q2oL (Pearson correlations were 0.211 and 0.264, respectively), but it was not correlated with the ISI and ESS (p=0.385 and p=0.879, respectively) (Table 2).

ROC analyses of the ISI, ESS, and PSQI are shown in Table 3 and Figure 1.

Discussion

Sleep is critical for mental and physical well-being, as well as quality of life[10,28,29]. Sleep disturbances, including insomnia, fatigue, and drowsiness, are defined as some of the major problems in patients with urticaria[30-35].

In this study, we found that more people in the patient group experienced poor sleep quality (PSQI >5) than the control group. Similar to our results, in a number of studies, the authors detected poor sleep quality in patients with psoriasis, atopic dermatitis, and urticaria[11,36-39]. Similarly, patients with psoriasis who had pruritus experienced more sleep disturbances and an impaired quality of life[19]. In another study, the authors reported that patients with both urticaria and psoriasis had a higher prevalence of sleep disorders and anxiety[29]. In the Release study, more than half of the patients with CU experienced SD because of itch[40]. Dias et al.[32] found that patients with CU aged between 41 and 60 years were adversely affected in their professional lives because of impairments in sleep and mental states. In this study, we found that patients with CSU experiencing poor sleep and insomnia had worse CU-QoL scores.

In this study, insomnia was more frequently reported in the patient group than in the control group. Insomnia has been examined in other dermatological diseases, and researchers have reported that they found more people with psoriasis affected by insomnia compared with

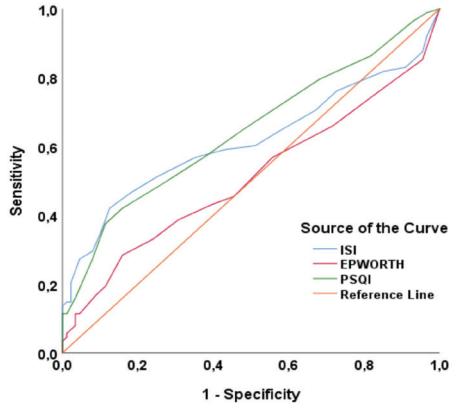

Figure 1. ROC analysis for distinguishing patients from the control group using scales

ROC: Receiver operating characteristic, ISI: Insomnia Severity Index, PSQI: Pittsburgh Sleep Quality Index

Table 2. Correlation between the UAS-7 and the ESS, PSQI, ISI, and CU-Q2oL

Parameter	Statistics	ESS	PSQI	ISI	CU-Q2oL
UAS-7	Pearson correlation (r)	-0.016	0.211*	0.094	0.264*
	p-value (two-tailed)	0.879	0.048	0.385	0.013

*Correlation is significant at the 0.05 level (two-tailed). **Correlation is significant at the 0.01 level (two-tailed). CU-Q2oL: Chronic Urticaria Quality of Life Questionnaire; ESS: Epworth Sleepiness Scale; ISI: Insomnia Severity Index; PSQI: Pittsburgh Sleep Quality Index; UAS-7: Urticaria Activity Score 7

Table 3. ROC analysis for distinguishing patients from controls using assessment scales

Scale	AUC	Standard error	p-value	Asymptotic 95% CI		Sensitivity, (%)	Specificity, (%)	Cut-off value
				Lower bound	Upper bound			
ISI	0.615	0.044	0.009	0.529	0.700	59.1	56.8	8.5
ESS	0.508	0.044	0.847	0.422	0.595	45.5	54.5	4.5
PSQI	0.644	0.042	0.001	0.562	0.725	48.9	73.9	6.5

P<0.05 was considered significant. ROC: Receiver operating characteristic curve, AUC: Area under the curve, CI: Confidence interval, ISI: Insomnia Severity Index, ESS: Epworth Sleepiness Scale, PSQI: Pittsburgh Sleep Quality Index

controls[11,38,39]. Mann et al.[41] evaluated insomnia in patients with atopic dermatitis and urticaria. They measured the ISI score before and after disease flares and found increased ISI scores during flares. Moreover, the ISI scores significantly decreased after treatment. They measured the quality of life with the dermatology life quality index and found a correlation between quality of life and the ISI score. In this study, quality of life was measured with the CU-Q2oL, and we found a correlation between CU-Q2oL scores and ISI scores. On the other hand, the authors failed to show a correlation between UAS-7 and ISI scores, in line with our study findings. They argued that the UCT and UAS-7 instruments are not sufficient to provide information about insomnia[41].

In this study, although more people experienced daytime sleepiness in the patient group, the mean ESS score was not different between the patient and control groups. Similar to our findings, a previous study revealed that the mean ESS score was not different between patients with psoriasis and controls[39]. In their case-control study, Alatas et al.[18] investigated the risk of obstructive sleep apnea syndrome in patients with CIU. They found that there was no difference between the urticaria and control groups in terms of the ESS and PSQI scores[18].

In this study, the majority of patients with CSU were female, in line with the findings in the literature. The mean age of individuals in the control group was slightly less than that of individuals form Germany and Japan, while it was higher than that of individuals from China and Nepal[34,40,42].

In our study, 62.5% of patients with CSU had angioedema, which is similar to the findings in previous studies[30]. In their cross-sectional study that included 390 adults, Choi et al.[34] found that 39% of patients had angioedema. Similar to the findings in our study, the authors reported lower CU-Q2oL scores in patients with CSU having angioedema[34].

Although our data revealed that the disease duration and total IgE levels did not affect CU-Q2oL scores, it has been reported that the total IgE level was one of the factors that significantly predicted CU-Q2oL impairment[34]. Ograczyk-Piotrowska et al.[17] studied stress, itch, and quality of life in female patients with CU, and they reported that sleep disturbances were seen in 39% of patients. In our study, stress was found to be the most common trigger. There was also a positive correlation among urticaria severity, insomnia, and poor sleep quality. In agreement with our findings, a previous report discovered a link between disease severity and the apnea hypoxia index[18].

In the patient group, female patients experienced more sleep disturbances and insomnia than male patients, which is similar to the findings in previous studies[43,44]. Among patients who had CSU for more than 5 years, the presence of angioedema was associated with poor sleep. Patients with a more severe disease (higher UAS-7 scores) had worse sleep quality. ESR levels were found to be correlated with sleep disturbances. In a previous study, the authors reported that patients with more severe CU had higher impairments in quality of life scores[34,43]. The authors discovered that people who had a longer disease duration had more sleep disturbances[43].

In their prospective, cross-sectional study, Heng et al.[44] aimed to determine the quality of life of adults with CU. In their study, the majority of patients were female, and the mean age was similar to that of our patient population. The disease duration was more than 2 years, which is in line with our experience of disease duration of about 4 years. Their study showed that the quality of life of patients with CU was negatively affected. Moreover, sleep problems and daytime sleepiness because of poor night sleep were expressed as the most affected areas. Furthermore, female patients with CU had more sleep problems than males. However, in contrast to our findings, disease duration had no effect on the quality of life and sleep status of the patients[44].

Study Limitations

The study had some limitations. First, the study had a relatively small sample size. Second, sleep quality was assessed with only questionnaires. We were not able to use a validated instrument to evaluate sleep and sleep quality. Third, this was a single-center study, and thus, the results cannot be generalized to the overall population. Fourth, this study had a cross-sectional design, and thus, we were not able to find the exact causality between SD and CSU. On the other hand, the strength of this study was that sleep quality was assessed with four different sleep quality questionnaires, and its effect on quality of life was also assessed.

Conclusion

It is well known that the quality of life of patients with CSU is severely impaired. Moreover, sleep disturbances have a detrimental effect on quality of life. Sleep disturbances were found to be more prevalent in patients with CSU than in controls, resulting in the worsening of quality of life in patients with CSU. Female sex, disease duration, presence of angioedema, disease severity, and high ESR were identified as factors that affect sleep quality in patients with CSU. Sleep disturbances affecting quality of life, which are commonly observed in patients with CSU, should be taken into account when evaluating patients.

Ethics

Ethics Committee Approval: Ordu University Clinical Research Ethics Committee approval was obtained prior to the study (approval number: 248, date: 10.12.2020).

Informed Consent: Written informed consent was obtained from the patients and controls after providing an explanation of the aims of the study under the Declaration of Helsinki.

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Authorship Contributions

Surgical and Medical Practices: F.E., S.Ö., Concept: F.E., S.Ö., Design: F.E., S.Ö., Data Collection or Processing: F.E., S.Ö., Analysis or Interpretation: F.E., S.Ö., Literature Search: F.E., S.Ö., Writing: F.E., S.Ö.

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