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Editorial

Editöryal

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Evaluation of the Orthopedic Traumas in the Earliest Days of the 2023 Kahramanmaraş Earthquakes

2023 Kahramanmaraş Depremlerinin İlk Günlerindeki Ortopedik Travmaların Değerlendirilmesi

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ABSTRACT

In this editorial article, we endeavor to describe our experiences concerning earthquake victims with orthopedic injuries in a secondary hospital in one of the epicenters in the immediate post-quake period.

ÖZET

Bu editöryal yazıda, depremin hemen sonrasında depremin merkez üslerinden biri olan ikinci basamak bir hastanede deprem mağdurlarında gözlemlediğimiz ortopedik yaralanmalar ile ilgili deneyimlerimizi paylaşmaya çalışacağız.

Key Words: Kahramanmaras earthquakes, Musculoskeletal injury, Orthopeadic trauma. Disaster Organisiation. Experience

Anahtar Kelimeler: Kahramanmaraş depremleri, Kas-iskelet yaralanması, Ortopedik travma, Afet organizasyonu, Deneyim

Two devastating earthquakes (magnitudes of 7.7 and 7.6), whose epicenters were in the Pazarcık and Elbistan districts of Kahramanmaraş in Türkiye, struck on 6 February 2023. According to the World Health Organization, the affected regions of Türkiye and Syria are home to approximately 23 million people, 1.4 million of them children. According to official figures, at least 50,783 people in Türkiye and 8,476 in Syria lost their lives due to these quakes, while more than 122,000 were injured. In addition, more than half a million buildings were damaged, including homes, hospitals, schools, and public buildings, and some two million people were forced to migrate due. According to official records, the earthquakes centered in Kahramanmaraş resulted in the greatest loss of life and material damage of all quakes in the history of the Turkish Republic [1-5]. The country's ancient cities, the place where I was born and raised, and we ourselves were all devastated.

Many injuries among earthquake survivors are orthopedic, so orthopedic surgeons play a crucial role in providing care for victims. Earthquake injuries can range from simple soft tissue damage to closed or open fractures, compartment or crush syndrome, spinal and pelvic fractures, and even life-threatening polytrauma. These injuries may require simple splints or debridement, fasciotomy, amputation, or complex surgical treatment of fractures. The basic functions of the orthopedist are to save life and limb through rapid diagnosis and treatment while identifying emergency situations, with the application of damage-control orthopedic surgery principles and a multidisciplinary approach.

Understanding the epidemiology and treatment of orthopedic injuries following an earthquake is essential for planning effective interventions [6-8]. However, such activity in an earthquake is highly problematic. In addition, the fact that volunteer health workers who take over the relevant departments in hospitals all come from different schools and systems, and differences among institutions in terms of branch units and job descriptions, can result in difficulties

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among the workers themselves and in communications with coordinating centers [5]. In this editorial article, we endeavor to describe our experiences concerning earthquake victims with orthopedic injuries in a secondary hospital in one of the epicenters in the immediate post-quake period.

The moment we heard of the devastating scale of the disaster, we immediately went to Elbistan, the epicenter of the second quake, as a group of volunteer physicians and other health personnel. We immediately began working with orthopedists, other physicians, and other health and administrative personnel working in the health institution in Elbistan. We once established a system of the organization together with Orthopedist Colleagues who arrived subsequently. The collaboration and coordination that quickly developed among the orthopedists arriving at the hospital on a volunteer basis and those on the permanent staff included the following components:

- The most senior orthopedist in terms of age and experience coordinated the emergency unit, ward, intensive care, and operating room teams. As the head of this new, spontaneously established clinic, he also organized the working arrangements of the other orthopedic specialists.
- The hospital's resources were rapidly reviewed through meetings with the hospital management. The requisite communication groups were established with specialists from other branches and auxiliary health personnel, particularly emergency medicine, intensive care, anesthesia, and nephrology specialists.
- The cases evaluated with the team in the emergency department were reviewed on the operating table, and rapid decisions concerning debridement, fasciotomy, amputation, or external/internal fixation were taken with mini-councils at the bedside. Surgical interventions were also performed with the same rapidity.
- Collaboration was established with multiple teams and anesthesia specialists simultaneously in the operating room. Cases were again evaluated at the bedside. Decisions regarding amputation/limb salvage, especially in pediatric cases, were based on the opinions of three or more physicians.
- Postoperative patients were followed up in intensive care or on the ward. The patients were again re-evaluated at periodic visits. General status, extremities, wound care, and all treatments were reviewed. Use was made of drugs, equipment, hemodialysis, and all available means.
- Since materials ran out on the first day, contact was made with implant firms in the region, and efforts were made to obtain as much orthopedic equipment as possible. A national implant provider, which originated in Gaziantep (*Zimed® Medical*), went the extra mile and exhibited the highest level of generosity to ensure that the requisite orthopedic implants were obtained.
- The allocation of wards to patients with orthopedic injuries was carried out in a coordinated manner. Less busy physicians were charged with the medical management and the clinical follow-ups of these patients. Orthopedic teams worked in the specified units on a rotating basis. Groups were established over social networks for group communications. At the same time, the treatment of almost 200 patients was organized over four floors.
- In order to reduce density in the clinic that resulted from referrals based on the hospital's bed capacity, patients who received first aid and emergency treatment and whose conditions permitted this were transferred to hospitals in surrounding provinces in coordination between the hospital management and the 112 emergency service.
- Once their acute conditions had subsided, patients were followed-up in a out-patient clinic. In the event that further surgical intervention was required, patients were either re-admitted or transferred to other centers. Patients were transferred as much as possible to ensure that only emergency and chronic patients were treated.

Based on our experiences, the main principles of the treatment of orthopedic injuries at the time of the earthquake involved the following:

- Life-threatening conditions were treated with the debridement of salvageable and amputation of non-salvageable limbs.
- Limb salvage in case of open fractures was performed with extensive debridement, limb shortening if required, external fixation with local coverage, and broad antibiotic coverage, followed by second and third debridement procedures.
- A significant proportion of closed fractures were treated conservatively, accepting some degree of displacement and deformity.
- Some procedures, such as first-day debridement and fasciotomy in a few cases, were carried out in the emergency department due to the high intensity in the operating room. Surgical procedures with internal and/or external implants were carried out under maximal sterile conditions under anesthesia in the current active operating rooms.
- Some cases of compartment syndrome were regarded as chronic. However, in many cases, compartment syndrome also entailed crush syndrome and frostbite findings. Priority fasciotomy and debridement were applied to the greatest extent possible in these cases. Hemodialysis facilities were employed as much as possible before deciding on amputation, particularly in pediatric or young patients with crush syndrome.

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- Whether or not soft tissues were infected and/or devitalized was carefully re-evaluated during the intraoperative period. Muscular contractility and color were also checked (4C rule). Amputations, particularly in children and the young, were performed on a limited basis, and only in case of totally devitalized limbs.
- Whether the patient was a child, young, or elderly, upper or lower extremity involvement, other accompanying injuries, and general vital functions were considered during the decision to amputate.
- Closed fractures requiring surgery, including those of the pelvis and acetabulum, were successfully treated with internal fixation wherever possible.

Turkish orthopedists worked with enormous self-sacrifice in the field and hospitals where patients were transferred during the Kahramanmaraş-centered earthquakes. They immediately hastened to the field after the quakes in the light of both institutional and personal initiatives. They worked untiringly, despite encountering major difficulties in terms of transport, in the field, and subsequently. They described their problems and experiences on the 'Türk-ortopod' mail group, online discussion groups, and regional and national scientific assemblies. An extensive earthquake session was held at the Bone Joint 2023 Congress (Antalya,3-6 May 2023). Other important activities were organized by the Turkish Society of Orthopaedics and Trauma (TOTBİD), the Turkish Association of Orthopedics and Traumatology (TOTDER), The Association of Bone and Joint Surgery (KECD), the Turkish Society for Surgery of the Hand and Upper Extremity (TEÜECD), and others.

Various problems experienced in and outside the hospital after previous earthquakes in Turkey had previously been reported. The transportation to the region of health and rescue teams, communications between the field, in the hospital, and between hospitals, triage, and patient record problems, physical shortages, increased presentations to the emergency department among patients who were not victims of the quakes, and problems with patient transportation and referral were all described. The importance of organization, coordination, education, and preparation was also emphasized [8-11]. All-round readiness for earthquakes is essential to reduce loss of life to a minimum and maximize early recovery [3-5,12].

Despite their devastating nature, the earthquakes we experienced also serve as an essential learning tool for all of us. We must develop more beneficial and appropriate approaches by combining our work and knowledge in a spirit of solidarity. We must transform our personal experiences into events that allow ourselves and our profession to grow. We can only learn from each other. As orthopedic trauma surgeons, it is incumbent upon us to transfer such valuable knowledge and experience to scientific publications. If the demographic characteristics, clinical outcomes, and injuries of presenting victims are known, it may be useful to report these for the purpose of developing policies aimed at preparedness for future earthquakes, response, recovery, and reducing losses caused by natural disasters. An effective disaster assistance program, using a good communication and organization strategy may also be useful in minimizing the damage caused by earthquakes [3,4,12-15].

In conclusion, I once again extend my sincere thanks and admiration to my orthopedic and traumatology colleagues working in the field and hospitals where the victims were transferred following the Kahramanmaraş-based earthquakes. I think it is of the greatest importance for our colleagues to share and report their experiences. Finally, I extend my deepest condolences to our colleagues and fellow citizens who lost their lives in these quakes.

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Figure 1. The orthopaedic surgeons who worked in the Elbistan State Hospital during the Kahramanmaraş earthquakes. The photo belongs to 4th day of the earthquake.

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Research Article

Araştırma

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Predictors Of Variceal Rebleeding In Liver Cirrhosis

Sirotik Varis Kanamalarında Tekrar Kanama Belirleyicileri

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ABSTRACT

Aim: Cirrhotic patients with acute variceal bleeding are characterized by a high mortality and rebleeding rate. The aim of this study was to explore predictors of rebleeding in cirrhotic patients.

Methods: Cirrhotic patients who were admitted to the hospital were retrospectively analyzed. Rebleeding was defined as a new onset of hematemesis, hematochezia or melena after endoscopic therapy, and a period of stable vital signs and hemoglobin. Medical records as laboratory data include hemoglobin and platelet level, prothrombin time, creatinine, bilirubin, albumin level, vital signs, need of blood transfusions, comorbidities, medications, clinical findings as presence of ascites and hepatic encephalopathy, and endoscopic findings of varices were recorded and entered a computer-based database. Child-Pugh grade was also calculated and recorded.

Results: 20 patients (21%) with recurrent hemorrhage after control of the variceal bleeding during the six-week follow-up period were included in this study. The level of albumin and hemoglobin in the rebleeding group were significantly lower than those in non-rebleeding group. The mean level of albumin was 2.45 mg/dL (vs. 3.05 mg/dL, p=0.01) and hemoglobin was 7.96 g/dL (vs. 9.92 g/dL, p=0.001). Ascites was seen to be significantly higher in the rebleeding group (50% vs. 14%, p=0.002). After multivariate regression analysis, we found that lower hemoglobin level and Child-Pugh grade were the only independent significant predictors for variceal rebleeding.

Conclusion: Since factors such as the Child-Pugh grade, hypoalbuminemia and presence of ascites are associated with portal hypertension and hepatic failure, we found that lower hemoglobin level and Child-Pugh grade were the only independent significant predictors for variceal rebleeding.

Key Words: Varice, Hemorrhage, Mortality.

ÖZET

Amaç: Sirotik varis kanamaları yüksek mortalite ve tekrar kanama oranları ile karakterizedir. Bu çalışmada tekrar kanama belirleyicilerinin saptanması amaçlanmıştır.

Yöntem: Hastaneye başvuran siroz hastaları retrospektif olarak değerlendirilmiştir. Endoskopik müdahale ve vital bulguların stabil hale gelmesi sonrasında yeni gelişen hematemez, melena, hematokezya bulguları ve hemoglobin düzeyinde düşme görülmesi tekrar kanama olarak tanımlanmıştır. Hastaların hemoglobin ve trombosit düzeyi, protrombin zamanı, kreatinin, bilirubin, albümin düzeyi, vital bulguları, kan transfüzyonu ihtiyacı durumu, komorbiditeleri, ilaçları, asit varlığı ve hepatik ensefalopati varlığı gibi klinik bulguları ve varislerin endoskopik bulguları bilgisayar tabanlı bir veritabanına kaydedilmiştir. Child-Pugh evresi de kaydedilmiştir.

Bulgular: Varis kanamalarının kontrolünden sonraki altı haftalık dönemlerinde tekrarlayan kanaması olan 20 hasta (%21) saptanmıştır. Tekrar kanaması olan grupta albümin ve hemoglobin düzeyi, tekrar kanamayan gruba göre anlamlı derecede düşüktü. Albümin seviyesi (2.45 & 3,05 mg/dl, p=0.01) ve hemoglobin 7.96 & 9.92 g/dl'ydi, p=0.001). Tekrar kanaması olan grupta asit sıklığı, tekrar kanamayan gruba göre anlamlı olarak daha yüksekti (%50 & %14, p=0,002). Çok değişkenli regresyon analizden sonra, düşük hemoglobin seviyesi ve Child-Pugh evresinin varislerde tekrar kanama için tek bağımsız anlamlı risk faktörleri olduğu saptanmıştır.

Sonuç: Child-Pugh evresi, hipoalbüminemi ve asit varlığı gibi faktörler portal hipertansiyon ve karaciğer yetmezliği ile ilişkili olduğundan, düşük hemoglobin düzeyi ve Child-Pugh evresinin tekrarlayan varis kanaması için tek bağımsız anlamlı risk faktörleri olduğu saptanmıştır.

Anahtar Kelimeler: Varis, Kanama, Mortalite

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Introduction

Variceal bleeding is a frequent and severe complication observed in cirrhosis [1]. Cirrhotic patients with acute variceal bleeding are characterized by a high mortality and rebleeding rate [2]. Although there are new therapeutic options, variceal rebleeding still occurs in a high rate, with some studies showing 50% rebleeding rate [1]. This high rate of variceal rebleeding is associated with increased morbidity, length of hospital stay and mortality in cirrhotic patients [3]. In a study by Habib et al., over 60 years of age, renal failure, alcoholic cirrhosis, thrombocytopenia, hemoglobin lower than 8 g/dL at presentation, presence of ascites and encephalopathy, were found to be related with rebleeding [4]. The aim of this study was to explore predictors of rebleeding in cirrhotic patients.

Materials and Methods

Study Design and Data Collection

Cirrhotic patients who were admitted to Osmangazi University Hospital in Eskisehir due to variceal bleeding between 2013 and 2017, were retrospectively analyzed. Ethic approval was obtained from the Ethics Committee of Medicine Faculty with the decision date 13.02.2017 and number 6. The inclusion criterion was history of variceal bleeding with cirrhotic etiology. The exclusion criteria included non-cirrhotic etiology and patients with incomplete clinical data. Rebleeding was defined as a new onset of hematemesis, hematochezia or melena after endoscopic therapy, a period of stable vital signs and hemoglobin. Medical records as laboratory data include hemoglobin and platelet level, prothrombin time, creatinine, bilirubin, albumin level, vital signs, need of blood transfusions, comorbidities, medications, clinical findings as presence of ascites and hepatic encephalopathy, as well as endoscopic findings of varices, were recorded and entered a computer-based database. Child-Pugh grade was also calculated and recorded.

Statistical Analysis

Statistical analysis was performed with the IBM SPSS, version 21 (IBM, NY, USA). Normality test was performed with the Shapiro-Wilk test. Variables were compared using the Kruskal-Wallis test for continuous variables and the chi-square test for categorical variables. Univariate logistic regression analysis was done first for each predictor to identify the significant predictor and then, the most independent significant predictors were evaluated using the multivariable logistic regression analysis by entering all the previously identified significant predictors simultaneously, with a stepwise backward strategy. A P value below 0.05 was considered statistically significant and a 95% confidence interval were calculated for measures of association.

Results

A total of 134 patients with cirrhosis and variceal bleeding were enrolled in this study, in which 38 patients whose clinical data was incomplete were excluded. Of the remaining 96 patients, 20 (21%) with recurrent hemorrhage after control of the variceal bleeding during the six-week follow-up period, were assigned to the rebleeding group. Table 1 of our results shows the participants' demographic criteria, the different clinical presentations of variceal bleeding, laboratory and other parameters related with liver dysfunction and the endoscopic variceal signs.

There were no significant differences between two groups (rebleeding & non-rebleeding group) in mean age (59 vs. 58 years, p=0.87), gender (female %) (40% vs. 36.8%, p=0.79), bilirubin level (3.1 vs. 1.7, p=0.07), platelet count (148 vs. 132×10^9/L, p=0.58) and endoscopic findings (p=0.22). The level of albumin and hemoglobin in the rebleeding group were significantly lower than those in the nonrebleeding group. The level of albumin was 2.45 mg/dl (vs. 3.05 mg/dl, p=0.01) and hemoglobin were 7.96 g/dl (vs. 9.92 g/dl, p=0.001). The frequency of ascites in the rebleeding group were significantly higher than those in the non-rebleeding groups (50% vs. 14%, p=0.002).

In the logistic regression analysis model, two variables were positively correlated with rebleeding: Child-Pugh grade C (OR=2.587, 95% CI 1.197–5.594) (compared with Child-Pugh grade A-B) and presence of ascites (OR=5.333, 95%CI 1.826 -15.574). The albumin level (OR=0.224, 95% CI 0.091-0.554) and hemoglobin level (OR=0.676, 95% CI 0.517–0.808) were negatively correlated with rebleeding of the cirrhotic inpatients. After multivariate analysis, we found that a lower hemoglobin level and the Child-Pugh grade were the only independent significant predictors for variceal rebleeding. This data is shown in Table 2.

Discussion

Cirrhosis is associated with high morbidity and mortality due to complications such as hepatic insufficiency and portal hypertension, and such as ascites, hepatic encephalopathy and variceal bleeding and survival is shortened when decompensation develops [5]. Approximately one third of cirrhotic patients with esophageal varices will eventually bleed, and one third of these may die as a result of a variceal hemorrhage [6].

Rebleeding is an important cause of poor prognosis and mortality in variceal bleeding. Therefore, it is important to determine the patients with high risk of rebleeding

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Table 1. Demographic criteria, endoscopic characteristics and laboratory parameters.

		Total n=96		Rebleeding n=20		No rebleeding n=76		Sig.
Demographic criteria								
Age (years)	Mean (SD)	58	(14)	59	(13)	58	(15)	0.87
Sex (Female)	Count (%)	36	(37.5)	8	40%	28	36.8%	0.79
Clinical presentation								
Hematemesis	Count (%)	84	87.5%	20	100%	64	84.2%	0.014
Melena	Count (%)	50	52.1%	11	55%	39	51.3%	0.769
Syncope	Count (%)	10	10.4%	4	20%	6	7.8%	0.142
Liver function test								
Serum albumin mg/dl	Mean (SD)	2.92	(0.69)	2.45	(0.58)	3.05	(0.66)	0.001
Serum bilirubin mg/dl	Mean (SD)	1.99	(2.74)	3.1	(4.4)	1.70	(2.0)	0.07
Prothrombine time(INR)	Median (25-75)	1.40	(1.28-1.60)	1.54	(1.32-1.87)	1.35	(1.27-1.57)	0.46
Child- Pugh Grade								
Grade A	Count (%)	45	46.9%	7	35%	38	46.9%	
Grade B	Count (%)	42	43.8%	7	35%	35	43.8%	
Grade C	Count (%)	9	9.4%	6	30%	3	9.4%	0.002
Presence of ascites	Count (%)	22	23%	10	50%	12	16%	0.002
Presence of Encephalopathy	Count (%)	3	3%	1	5%	2	2.6%	0.594
Other parameters								
Hemoglobin (g/dL)	Mean (SD)	9.51	(2.38)	7.96	(1.7)	9.92	(2.3)	0.001
Platelets (×103/mm3)	Mean (SD)	135	(112)	148	(107)	132	(114)	0.58
Serum creatinine (mg/dL)	Median (25-75)	0.85	(0.60-1.16)	0.9	(0.52-1.45)	0.82	(0.6-1.09)	0.78
Endoscopic signs								
Variceal Form								
F1	Count (%)	11	11.5%	1	5%	10	13.2%	
F2	Count (%)	36	37.5%	10	50%	26	34.2%	
F3	Count (%)	48	50%	9	45%	39	51.6%	0.226
Red Color(RC) Sign								
RC +	Count (%)	75	78.1%	14	70%	61	80.2%	
RC–	Count (%)	20	20.8%	6	30%	14	18.5%	0.52

and the factors associated with it in order to decrease the rate of rebreeding and mortality [7]. The rates of rebleeding in the first six-week period were 17% in the study of Krige et al., as well as 28.8% in the Al Freah et al. and 10.7% in the Hobolth et al. studies [8-10]. In the latter, the rate of rebleeding had decreased from 22.2% to 10.7% between the 1980s and 2000s, although this decrease did not reach a statistical significance. The rate of vasoactive drug use was significantly higher in the 2000s [10]. In comparison, the rate of rebleeding in our study was 20%. In previous studies, rate of rebleeding was found to be associated with vasoactive drug use [10], MELD score [11], serum creatinine, albumin and necessity for blood transfusion [7]. However, other studies did not find such an association with the MELD score [7,9] and blood transfusion [9,11]. Child-Pugh score and presence of ascites were not found to be associated with rebleeding in these studies. In our study, the Child-Pugh grade, presence of ascites, lower average hemoglobin and lower average serum albumin at presentation, were found to be associated with rebleeding. However, after the multivariate analysis, only the lower average hemoglobin at presentation and the Child-Pugh grade were independently associated with rebleeding.

Table 2. Univariate logistic regression analysis for the evaluated predictors

	Constant	B	SE	Wald	Sig.	EXP(B)	%95 CI Lower	Upper
Demographic criteria								
Age (years)	-1.499	0.003	0.017	0.026	0.87	1.000	0.969	1.037
Sex	-1.119	-0.134	0.515	0.067	0.79	0.875	0.319	2.399
Liver functions								
Serum albumin mg/dl	2.76	-1.49	0.461	10.49	0.001	0.224	0.091	0.554
Serum bilirubin mg/dl	-1.658	0.146	0.082	3.154	0.076	1.157	0.985	1.358
Prothrombine time (INR)	-1.717	0.241	0.337	0.512	0.474	1.273	0.657	2.466
Child-Pugh Grade	-2.986	0.951	0.393	5.837	0.016	2.587	1.197	5.594
Presence of ascites	-1.856	1.674	0.547	9.373	0.002	5.333	1.826	15.574
Presence of Encephalopathy	-1.360	0.666	1.251	0.284	0.594	1.947	0.168	22.630
Other laboratory parameters								
Serum creatinine mg/dl	-1.230	-0.103	0.368	0.079	0.779	0.902	0.439	1.854
Platelets($x10^3/mm^3$)	-1.488	0.001	0.001	0.307	0.58	1.0	1.0	1.0
Hemoglobin g/dl	2.16	-0.391	0.127	3.43	0.02	0.676	0.517	0.808
Endoscopic parameters								
Variceal form	-6.424	1.347	1.113	1.465	0.226	3.846	0.434	34.064
Red Color Sign	-0.847	-0.641	0.571	1.261	0.261	0.527	0.172	1.612

Limitations

Our study had two limitations, namely that most of our patient populations had Child-Pugh grade A and B, whereas a small group was Child-Pugh grade C. In addition, our study was done retrospectively and had a small patient population. There is now a need for additional studies with large patient cohorts.

Conclusion

Since factors such as Child-Pugh score, hypoalbuminemia and presence of ascites are associated with portal hypertension and hepatic failure, we tried searching other laboratory parameters that may be associated with rebleeding. After univariate and multivariate analysis of other laboratory criteria for our participants, we found that lower hemoglobin level and Child-Pugh grade were the only independent significant predictors for variceal rebleeding.

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Research Article

Araştırma

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Comparison Of The Effectiveness And Complications Of Transobturator Tape and Transvaginal Tape Methods In The Treatment Of Stress Urinary Incontinence

Stres Üriner İnkontinans Tedavisinde Transobturator Teyp ve Transvajinal Teyp Yöntemlerinin Etkinliğinin ve Komplikasyonlarının Karşılaştırılması

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ABSTRACT

Aim: Comparison of the effectiveness and complications of transobturator tape and transvaginal tape methods in the treatment of stress urinary incontinence.

Method: Clinical records of 106 patients who underwent surgery in Istanbul Kanuni Sultan Suleyman Training and Research Hospital due to stress urinary incontinence between January 2015 and December 2016 were retrospectively analyzed. Trans obturator tape (TOT) was classified as Group 1, and transvaginal tape (TVT) was classified as Group 2. The urogenital distress inventory-6 (UDI-6) and the incontinence impact questionnaire-7 (IIQ-7) were used to determine the severity of preoperative and postoperative incontinence and objectively compare the quality of life in all patients.

Results: There was a significant difference between the two groups in terms of mean age, menopausal status, complications, and duration of surgery ($p<0.05$). In both groups, there was a significant improvement in postoperative UDI-6 and IIQ-7 tests evaluating the negative effects of urinary incontinence on daily life.

Conclusion: A significant improvement was observed in UDI-6 and IIQ-7 scores after TOT and TVT operations. There is no significant difference between TOT and TVT methods in terms of efficacy and success in the treatment of stress urinary incontinence.

Key Words: Transobturator tape, Trans vaginal tape, Stress urinary incontinence, UDI-6, IIQ-7

ÖZET

Amaç: Stres üriner inkontinans tedavisinde transobturator teyp ve transvajinal teyp yöntemlerinin etkinlik ve komplikasyonlarının karşılaştırılması.

Yöntem: Ocak 2015-Aralık 2016 tarihleri arasında İstanbul Kanuni Sultan Süleyman Eğitim Eğitim ve Araştırma Hastanesinde stres üriner inkontinans (SUI) nedeniyle opere edilen 106 hastanın klinik kayıtları retrospektif incelendi. Transobturator teyp (TOT) Grup 1 ve gerilimsiz trans vajinal teyp (TVT) Grup 2 olarak sınıflandırıldı. Hastalarda preoperatif ve postoperatif inkontinans şiddetini ve operasyon başarı düzeylerini değerlendirmek için Q tip test, pet test, rezidü idrar ölçümü, stres testi ve yaşam kalitesini karşılaştırmak için ürogenital distres envanteri-6 (UDI-6) ve inkontinans etki anketi-7 (IIQ-7) kullanıldı.

Bulgular: İki grup arasında ortalama yaş, menopoz durumu, inkontinans süresi, eş zamanlı yapılan cerrahiler, mesane perforasyonu ve ameliyat süresi açısından anlamlı fark saptandı ($p<0.05$). Her iki grupta inkontinansın günlük yaşama olumsuz etkilerini değerlendiren postoperatif UDI-6 ve IIQ-7 testlerinde anlamlı düzelme saptandı.

Sonuç: TOT ve TVT ameliyatlarından sonra UDI-6 ve IIQ-7 skorlarında belirgin düzelme gözlendi. Stres üriner inkontinans tedavisinde etkinlik ve başarı açısından TOT ve TVT yöntemleri arasında anlamlı bir fark yoktur.

Anahtar Kelimeler: Transobturator teyp, Transvajinal teyp, Stres üriner inkontinans, UDI-6, IIQ-7

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Introduction

Stress and mixed urinary incontinence, the most frequent types of incontinence in women, have become significant public health problems affecting the quality of life. Stress urinary incontinence (SUI) is the uncontrollable urine leakage in women caused by actions that increase intraabdominal pressure, such as vomiting, breathlessness, laughing, and carrying heavy loads. Urinary incontinence occurs when the intravesical pressure exceeds the urethral closure pressure without detrusor contraction [1,2]. It is due to urethral hypermobility and pelvic floor muscle or sphincter insufficiency. After the loss of urethral support in the bladder neck was described as the main mechanism in the pathophysiology of stress urinary incontinence, tension-free vaginal tape (TVT) surgery, which provides hammock-like support to the ureterovesical junction, was described by Ulmsten and Petros in 1995 [3]. Although the short-term success rate of this surgery is quite high, different techniques were developed to prevent vital complications that may occur with the blind passage of the needle or trocar from the retropubic region, and the trans obturator tape (TOT) technique was recommended in 2001 [4]. The trocar or needle does not pass through the retropubic area in the trans-obturator tape technique. The trans-obturator tape method is reliable, effective, and easy to apply [5].

Although these methods were compared in literature, objective quality-of-life tests were used in very few studies before and after the operation. Incontinence impact questionnaire-7 (IIQ-7) and Urogenital distress inventory-6 (UDI-6) were used to determine incontinence severity preoperatively and postoperatively in all patients [6].

In this study, we aim to compare the effectiveness and complications of these methods by using quality-of-life tests in patients who underwent trans obturator tape and transvaginal tape operations due to stress urinary incontinence.

Material and Methods

Clinical records of 106 patients who underwent surgery in Istanbul Kanuni Sultan Suleyman Training and Research Hospital due to stress urinary incontinence between January 2015 and December 2016 were retrospectively analyzed. Patients who underwent TOT were assigned to Group 1 and TVT to Group 2. UDI-6 and the IIQ-7 tests were used to assess the severity of preoperative and postoperative incontinence and compare the patient's quality of life. Age, parity, body mass index (BMI), menopausal status, duration of operation, residual volume after micturition, additional vaginal surgery, intraoperative and postoperative hematoma, reoperation, postoperative urinary retention, de-novo urge incontinence, pelvic pain, and complications were recorded. All patients were subjected to detailed physical, urogynecological, and neurological examinations and evaluated in terms of complete urinalysis, urine culture, voiding diary, urinary ultrasound, and post-void remnant urine measurements conducted before and after the operation. A Q-tip test with 200 ml of urine stored in the bladder in the lithotomy position was performed to detect vesicourethral mobility. Bladder neck mobility was evaluated as positive when the change of angle in the straining and resting states of the cotton swab, the tip of which was placed in the internal urethral meatus, was above 30 degrees. The provocative stress test was performed while on the lithotomy table and standing with a full bladder. A urodynamic test confirmed the diagnosis in undiagnosed patients with mixed urinary incontinence. The patients who were diagnosed with urinary infections were given antibiotics.

Inclusion criteria: Female patients who did not plan to give birth in their future life between the ages of 35-75 with stress incontinence complaints, without urinary tract infection or neurological disease, not prone to bleeding, who had involuntary urinary leakage by coughing and sneezing, vesicourethral mobility more than 30 degrees, stress incontinence and whose residual urine was less than 100 milliliters were included in the study.

Exclusion criteria: Patients with urge incontinence, overactive bladder, urinary tract infection, chronic cystitis, who were prone to bleeding, planning birth, had a history of anti-incontinence surgery, and missing file information were excluded from the study.

For prophylactic treatment, 2 gr cefazolin sodium was administered intravenously approximately one hour before and six hours after the operation. All operations were performed with Obtryx™ (Boston Scientific, Natick, MA, USA) brand kit.

Surgical Technique: TOT operations were carried out under spinal anesthesia. The dorsal lithotomy position was used to prepare the patient, and the operation was performed with a classic technique [7]. TVT operations were carried out under spinal anesthesia. The dorsal lithotomy position was used to prepare the patients, and the operation was performed with a classic technique.

Cystoscopy was applied to all patients who underwent TVT. Complications that occurred during the operation were recorded and treated. Post-void residual urine was measured. Catheterization persisted for 6-8 hours in patients with more than 100 ml of remnant urine. Patients with less than 100 ml of remnant urine were discharged with oral antibiotics. [8].

After the operation, patients with a negative postoperative stress test, residual urine amount less than 100cc, and

full continence were considered as "complete recovery"; those with a positive postoperative stress test but did not describe incontinence were considered as "partial recovery". Patients evaluated as "full recovery" and "partial recovery" were accepted as successful, while patients with positive postoperative stress tests and incontinence continued as "failure".

Postoperative cases were followed up for six months, and urogynecological examinations were performed. In addition, the patients were reevaluated with quality-of-life tests (UDI-6 and IIQ-7), examination findings, neurological evaluation, residual urine measurement, Q-tip test, and pads. These scales used to report patients' urinary incontinence symptoms and to obtain concrete evidence of the effects of urinary incontinence on patients' lives [9].

Ethics approval: This study was conducted according to the 2013 revision of the Declaration of Helsinki and was approved by the Ethics Committee of Istanbul Kanuni Sultan Süleyman Training and Research Hospital (KAEK 2021.12.321). The requirement for patient consent for participation and publication was waived owing to the retrospective nature of the study. Written informed consent for treatment was obtained from all patients.

Statistical analysis: The data was analyzed using the Statistical Package for Social Sciences (SPSS Inc, Chicago, Illinois, USA) for Windows 24.0 package program. Mean and standard deviation values were used as descriptive statistics. In addition, an independent t-test was used to compare two groups of continuous data and chi-square analysis was utilized to compare two groups of categorical data; p-values less than 0.05 were considered statistically significant in the study.

Results

106 patients who underwent TOT and TVT operations for stress urinary incontinence in a tertiary hospital between January 1, 2015, and December 31, 2016 were included in this retrospective study. 56 patients underwent TOT, and 50 patients underwent TVT. Table 1 shows the analysis of patient characteristics according to the group. The mean age was 53.32±10.8 years in the TOT group, and 47.18±7 years in the TVT group (p=0.01). There was a statistically significant difference between the two groups in terms of mean age, menopausal status, and duration of incontinence but not in terms of mean parity, body mass index, incontinence type or smoking. The difference in simultaneous operations between the TOT and TVT groups was significant (p=0.03). Colporrhaphy anterior (CA) was more common in the TVT group. Vaginal hysterectomy with colporrhaphy anterior/posterior and sacrospinous fixation (SSF) were more common in the TOT group.

Table 2 shows the recovery rates, quality-of-life tests, and clinical test results (preoperative and postoperative sixth-month follow-up). The levels of operational success in the TOT and TVT groups were not different. In the TOT group, 47 (83.92%) patients recovered completely, 8 (14.28%) recovered partially, and 1 (1.78%) patient did not recover

Table 1. Characteristics of patients

	TOT	TVT	p-value
Age, years (mean ±SD)	53,32 ±10,8	47,18 ± 7	0,01*
Parity, n (mean ±SD)	3,74 ±2,09	3,74 ±2,06	0,99
BMI, kg/m^2 (mean ±SD)	25,04 ±2,17	25,96 ±2,36	0,13
Duration of incontinence, years (mean±SD)	6,22 ±4,21	4,16 ±2,61	0,01*
Smoking status			
Smoker, n (%)	16 (32%)	22 (44%)	0.08
Non-smoker, n (%)	34 (68,0%)	28 (56%)	
Menopausal status			
Postmenopausal, n (%)	15 (30,0%)	28 (56,0%)	0.02*
Premenopausal, n (%)	35 (70%)	22 (44,0%)	
Incontinence type			
Stress urinary incontinence, n (%)	8 (14,3%)	7 (14,0%)	0.09
Mix urinary incontinence, n (%)	48 (85,7%)	43 (86,0%)	

TOT: transobturator tape, and TVT: transvaginal tape.
Independent t-test was used to compare the two groups of continuous variables.
Chi-square test was used to compare these two groups of categorical variables.
*Statistically significant, p<0.05.

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Table 2. Recovery rates and, quality-of-life tests and clinical test results

		TOT n (%)		TVT n (%)		p-value
Full recovery		47 (%83.92)		41 (%82)		0.86*
Partial recovery		8(%14,28)		8(%16)		
Failure		1(%1.78)		1 (%2)		
	Preoperative	Postoperative 6th month	P value	Preoperative	Postoperative 6th month	P value
	TOT X±SD	TOT X±SD		TVT X±SD	TVT X±SD.	
UDI-6	13,62±1,77	3,22±1,53	0.02*	14,21±1,42	3,40±1,50	0,01**
IIQ-7	12,68±2,79	3,03±1,73	0.02*	12,40±1,88	3,28±1,85	0,02**
Q Tip Test	48,9±10,18	41,9±10,18	NS	44,8±6,34	40,8±6,34	NS
Pad Test	1,3±1,1	0,3±0,6	0.02*	1,4±1,2	0,4±0,30	0,01**
Residue Urine	58,5±29,8	15.1±0,16	0.02*	54,1±20,2	6,8±0,78	0,01**
Stress Test (+)	56(100)	9 (16,07)	0.03*	50(100)	9(18)	0,03*

TOT: Transobturator tape, TVT: Transvaginal tape
TOT: Transobturator tape, TVT: Trans vaginal tape, SD: standard deviation, NS: not significant
IIQ-7: İncontinence impact questionnaire, UDI-6: Urinary distress inventory,
*Chi-square test was used to compare two groups of categorical data
**Independent t-test was performed to compare two groups of continuous data
Statistically significant, p<0.05.

(p=0.86). In the TVT group, 41 (82%) patients recovered completely, 8 (16%) recovered partially, and 2 (2%) patients failed (p=0.86). In both groups, there was a significant improvement in postoperative UDI-6 and IIQ-7 tests, which investigated the negative effects of urinary incontinence on daily life (p=0.01 and p=0.02, respectively). After micturition, the amount of postoperative residual urine was 15.1±0.16 ml in the TOT group and 6.8±0.78 ml in the TVT group, which were statically significant (p= 0.01). Table 3 shows the complications, length of hospital stays, and duration of operations. The TOT group had 9 (16.07%) complications, while the TVT group had 11 (22%). Furthermore, 1 (1.78%) patient in the TOT group had a bladder perforation, 2 (3.57%) had mesh erosion, 1 (1.78%) had a vaginal perforation, and 1 (1.78%) had bleeding more than 200 ml. De novo urge incontinence was found in 2 patients (3.57%), perineal pain in 1 (1.78%), and dyspareunia in 1 (1.78%). Bladder perforation occurred in 5 (10%) of the TVT patients, mesh erosion occurred in 2 (4%) patients, de novo urge incontinence occurred in 2 (4%) patients, more than 200 milliliters of bleeding occurred in 1 (2%) patient and urinary retention occurred in 1 (2%) patient. Patients in the TVT group had longer operation times than those in the TOT group (48.2±25.83 vs. 44.60±19.74, p=0.01*). There was no significant difference in the length of hospital stay between the TOT and TVT groups, which were 2.2±1.3 and 2.3±1.3 days, respectively. In terms of bladder perforation and operation times, there was a significant difference between the TOT and TVT groups (p=0.02* and p= 0.01*, respectively).

Discussion

A significant decrease was observed in UDI-6 and IIQ-7 tests after TOT and TVT operations. The stress test and pad test results were significantly decreased in both postoperative periods compared to the preoperative period. The risk of complications, especially bladder perforation, was higher in TVT than in the TOT. TVT had a longer operation time than the TOT procedure.

Mid-urethral sling methods are the most commonly used to treat stress urinary incontinence since they are simple to use, have a shorter learning curve, have fewer complications, and provide long-term success [10]. IIQ-7 and UDI-6 were used as quality-of-life tests in our clinic. Urinary symptoms were questioned with UDI-6 and daily activities such as physical activity, travel, social relationships, and mental health status with IIQ-7. The operational success rates were not different in TOT and TVT groups. While 83.94% were fully recovered, 16.04% were partially recovered, 1.78% did not recover in the TOT group, 82% were fully recovered, 16% were partially recovered, and 2% did not recover in the TVT group. Although the TVT offers long-term success, there is a risk of serious vascular, bowel, and bladder injury due to the blind passage of the needle through the retropubic area due to surgery. In TOT procedure, the needle is safer because it does not pass through the retropubic space. The success rates of TOT and TVT vary between 84% and 95% [11, 12]. Since the surgical success rates in mid-urethral sling surgeries are based on the definition of success and follow-up times, success

Table 3. Operation time, hospital stay, and complications

	TOT	TVT	
	n (%)	n (%)	p-value
Bladder perforation	1(%1,78)	5(%10)	0,02*
Mesh erosion	2(%3,57)	2(%4)	NS
Vaginal perforation	1(%1,78)	0(%0)	NS
Perineal pain	1(%1,78)	0(%0)	NS
De novo urgency	2(%3,57)	2(%4)	NS
Bleeding	1(%1,78)	1(%2)	NS
Dyspareunia	1(%3,57)	0(%0)	NS
Urinary retention	0(%0)	1 (%2)	NS
Operation time (min)	44,60±19,74	48,2±25,83	0,01*
Hospital stay (d)	2,2±1,3	2,3±1,3	NS

min: minute, d: day, NS: not significant, n: number, %: percentage
* Statistically significant, p<0.05.

rates vary between 64% and 100% [13]. Treatment is considered unsuccessful if persistence and recurrence occur after stress incontinence surgery. The persistence of urinary incontinence after surgery is defined as persistence. On the other hand, recurrence is defined as a patient who has benefited from surgery becoming incontinent again [14]. Six-week cut-off between surgery and the onset of symptoms was used to differentiate recurrence and persistence [15].

The necessity of performing urodynamic studies before SUI surgery is controversial [16]. In our study, urodynamic testing was performed only in an undiagnosed group of patients with mixed urinary incontinence to confirm the diagnosis. Mesh erosion is a serious side effect of mid-urethral surgery. This rate varies between 3.8% and 15% in the literature [17]. In our study, mesh erosion was observed in 2 (3.57%) patients in the TOT group and 2 (4%) patients in the TVT group. The overall mesh complication rate was 3.77%, and the eroded mesh parts were resected.

Bleeding is an important complication seen in TOT and TVT operations. It is due to venous plexus injury during urethrovaginal dissection or blind interventions in the retropubic area. Major vessel injury, bleeding, and hematoma formation are complications that may be encountered more frequently in TVT. It usually stops with pressure and hemostasis. However, bleeding due to damage to the corona mortis vessel during TVT may disrupt the patients' hemodynamics and may require abdominal surgery [18]. In our study, two hemorrhages, one (1.78%) in the TOT group and one (2%) in the TVT group, were stopped with conservative approaches without additional surgical intervention.

Bladder perforation is rare during TOT operation. The incidence of bladder perforation was reported as 0-4.2% for TOT and 0.2-32.6% for TVT [19,20]. Bladder perforation was observed in 2.7% of 2795 multicenter TVT operations [21]. In our study, bladder perforation occurred in 1 (2%) patient after TOT surgery and 5 (10%) patients after TVT surgery. The bladder was sutured vaginally with 3/0 polyglactin as an intraoperative double layer. De novo urge-type incontinence is observed between 3-26% after mid-urethral sling operations [22]. The most important reason is that the mesh is tighter than normal, causing urethral obstruction, and anticholinergic drugs are effective in its treatment. In our study, de nova urge incontinence was observed in 4 (3.77%) patients in both groups. Dyspareunia was observed between 4.5% and 24% after mid-urethral sling [23]. In our study, dyspareunia was observed in 1 (1.78%) patient in the TOT group. In the literature, the average operation time for the TOT operation is 20-25 minutes [24]. In our study, TVT operations took longer time than TOT operations. This may be because all patients undergoing TVT had cystoscopies.

Limitations: Since the project was at a training and research hospital, the operations were performed by different surgeons and specialists. The study covers six months postoperatively. Longer follow-up periods are needed to assess the efficacy and safety of mid-sling operations. Another limitation of our study was the lack of randomization.

Conclusion: UDI-6 and IIQ-7 test scores were significantly lower after TOT and TVT procedures. Following TOT and TVT procedures, the patient's quality of life improved dramatically. Regarding efficacy and success in treating stress

urinary incontinence, there was no difference between TOT and TVT methods. UDI6 and IIQ-7 questionnaires can be used to evaluate the results of TOT and TVT methods. The TOT and TVT sling procedures were safe and effective in treating stress urinary continence, with no serious side effects. The TVT method was more likely to result in bladder perforation than the TOT method. The TVT operation took longer than the TOT operation.

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Research Article

Araştırma

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Comparison of Three Different Color Doppler Techniques for the Assessment of Blooming in Venous Flow during Pregnancy

Gebelikte Venöz Akımda Blooming Artefaktının Değerlendirilmesi için Üç Farklı Renkli Doppler Tekniğinin Karşılaştırılması

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ABSTRACT

Aim: Blooming is an important color Doppler artifact for the assessment of small or slow-flow blood vessels during pregnancy. The degree of blooming varies depending on the color Doppler technique used. The purpose of our study is to compare doppler techniques related to the flowering artifact so that the imaging method closest to the actual size of small vessels can be selected.

Method: A total of 100 pregnant women were included in this study. The diameter of the intrahepatic umbilical vein was measured using three different color Doppler techniques: conventional color Doppler (CCD), power Doppler (PWD), and advanced dynamic flow (ADF). Blooming was assessed by comparing the diameter of the vessel in B-mode and in color Doppler mode.

Results: The diameter of the intrahepatic umbilical vein measured by ADF was smaller than that measured by CCD and PWD, indicating less blooming. The difference in diameter was statistically significant ($p < 0.05$).

Conclusion: ADF is a superior color Doppler technique for the assessment of blooming in venous flow during pregnancy, as it results in less blooming compared to CCD and PWD. This finding has important implications for the accurate assessment of small or slow-flow blood vessels during pregnancy.

Key Words: Color doppler ultrasonography, Artefacts, Pregnancy, Fetal ultrasonography, Vascularity

ÖZET

Amaç: Blooming, gebelik sırasında küçük veya yavaş akan kan damarlarının değerlendirilmesi için önemli bir renkli Doppler artefaktıdır. Çiçeklenme derecesi kullanılan renkli Doppler tekniğine göre değişir. Çalışmamızın amacı, küçük damarların gerçek boyutuna en yakın görüntüleme yönteminin seçilebilmesi için çiçeklenme artefaktı ile ilgili doppler tekniklerini karşılaştırmaktır.

Yöntem: Bu çalışmaya toplam 100 gebe dahil edildi. İntrahepatik göbek damarının çapı, üç farklı renkli Doppler tekniği kullanılarak ölçüldü: geleneksel renkli Doppler (CCD), güçlü Doppler (PWD) ve ileri dinamik akış (ADF). Blooming, damar çapının B modunda ve renkli Doppler modunda karşılaştırılmasıyla değerlendirildi.

Bulgular: ADF ile ölçülen intrahepatik umbilikal venin çapı, CCD ve PWD ile ölçülenden daha küçüktü, bu da daha az çiçeklenmeyi gösteriyor. Çaptaki fark istatistiksel olarak anlamlıydı ($p < 0.05$).

Sonuç: ADF, CCD ve PWD'ye kıyasla daha az çiçeklenme ile sonuçlandığı için gebelik sırasında venöz akışta çiçeklenmenin değerlendirilmesi için üstün bir renkli Doppler tekniğidir. Bu bulgunun hamilelik sırasında küçük veya yavaş akan kan damarlarının doğru değerlendirilmesi için önemli etkileri vardır.

Anahtar Kelimeler: Renkli doppler ultrasonografi, Artefaktlar, Gebelik, Fetal ultrasonografi, Vaskülarite

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Introduction

Blooming is a common color Doppler artifact that occurs when the color extends beyond the boundaries of a vessel, making it appear larger than its actual size [1,2]. This lack of lateral discrimination can lead to exaggerated or false positive vascular colorization, which can be a significant limitation for the visualization of vascular territories [1].

Advanced dynamic flow (ADF) uses a wide-band Doppler technique, while conventional color Doppler (CCD) employs narrow-band frequency transmission [3]. Power Doppler (PWD) is a variation of color flow imaging that displays intensity based on the sum of all Doppler shift frequencies, rather than on the mean Doppler shift as in color flow imaging [4].

In CCD and PWD, spatial resolution is low, and blood vessels may appear thicker than their actual size due to blooming, which can cause overlapping and difficulty in differentiating slow-flow blood vessels in the vicinity of a particular area in the fetus. In contrast, ADF with the wide-band Doppler technique can provide refined imaging of tiny vessels [5].

The aim of this study is to investigate and compare the blooming artifact in ADF, CCD, and PWD techniques. The results of this study may help to identify the best color Doppler technique for visualizing small or slow-flow blood vessels during fetal ultrasound examinations.

Material and Methods

Patients; Our study was conducted over a period of 2 months and included 100 patients who were referred to the Radiology Department of Antalya Training and Research Hospital for obstetric ultrasonography (US). The mean age of the individuals was 28.23 years (range: 18 to 43 years), with an average height of 1.62 meters (range: 1.50 to 1.75 meters) and an average weight of 62 kg (range: 45 to 118 kg). The average body mass index was 26.37 kg/m2 (range: 18.73 to 38.53 kg/m2). The mean gestational age based on the last menstrual period was 27 weeks (range: 15 weeks and 5 days to 40 weeks and 6 days), while the mean ultrasonographic gestational age was 27 weeks (range: 15 weeks and 4 days to 40 weeks). Measurements of the diameter of intrahepatic umbilical veins were obtained from all 100 fetuses by the same radiologist using a Toshiba diagnostic ultrasound system, Applio TUS-A500 (Toshiba Medical Systems Europe, Zoetermeer, Netherlands). Our study was approved by the institutional review board with the data usage permission numbered 24.03.2016/ 76/20, and written informed consent was obtained from all patients after a detailed explanation of the procedures they may undergo.

*Radiological Examination***:** In this study, the Twin-view Mode in Toshiba US systems was used to display monochrome and color images simultaneously in real-time. This mode allows for the simultaneous assessment and comparison of structural information in B-mode and hemodynamics in CCD or PWD. Intrahepatic umbilical veins were displayed longitudinally in Twin-view mode with B & CCD, B & ADF, and B & PWD modes in frozen magnified images for each of the three types of Doppler techniques. The vertical diameters of the veins were measured in the Doppler side and then in the B-mode next to the Doppler side at the same screen. This process was repeated for all three types of Doppler techniques by switching them consecutively. All of the Doppler US techniques' preset parameters were identical and had been created before the study started. The parameters were set as follows: dynamic range (DR) 70, dynamic frequency (DF) 3.0, color gains (CG) 30, color PRF 5, 9, and color filter (F) 4. The diameter of the vein was measured from the inner to the inner side of the vessels in the B-mode side and each colorized lateral side of the vessels in all of the Doppler modes (Figures 1, 2, 3). The diameters in each color Doppler technique minus the diameter of the grey-scale B-mode were calculated as the difference and named "delta."

Statistical Analyses: Continuous variables were summarized as average and standard deviations and categorical data were analyzed for frequency and percentage. Repeated Measures ANOVA and Bonferroni Post hoc tests were used for comparing techniques by diameter measurements. Intraclass correlation coefficients (ICC) were determined for checking the consistency of the calculated techniques. Statistical analyses were performed for multiple comparisons of the Doppler techniques for all parameters with SPSS v.22 and the level of statistical significance was set as 0.05.

Results

The study included 100 patients with a mean age of 28.23 years, a mean height of 1.62 m, and a mean weight of 62.62 kg. The patients had a mean gestational age of 27 weeks, with a range of 15 weeks 4 days to 40 weeks. The diameter measurements of the intrahepatic umbilical veins were obtained using three different Doppler techniques: ADF, CCD, and PWD.

The results of the study showed that there were significant differences in the diameter measurements obtained by the three techniques. The ADF technique produced smaller diameter measurements (4.660 mm ± 1.448) compared to CCD (6.984 mm ± 1.883) and PWD (6.857 mm ± 2.259). When comparing the delta values of the techniques with the B mode, ADF had significantly smaller delta values compared to CCD and PWD. CCD and PWD had similar

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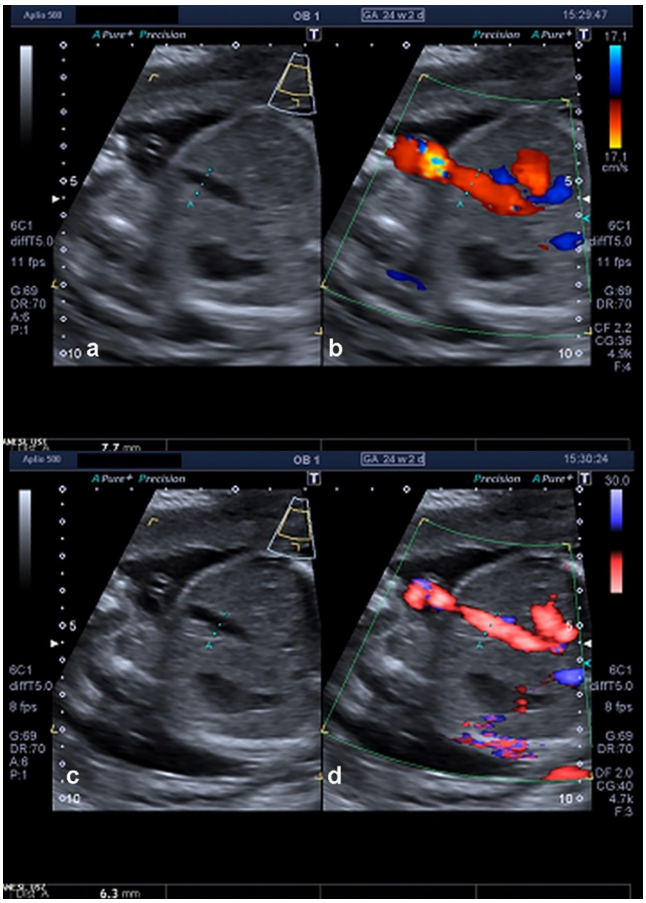

Figure 1. (a) Twin-view with CCD technique image of vessel diameter measurement from B mode side. (b) Twin-view with CCD technique image of vessel diameter measurement from CCD Doppler side. (c) Twin-view with ADF technique image of vessel diameter measurement from B mode side. (d) Twin-view with ADF technique image of vessel diameter measurement from ADF Doppler side.

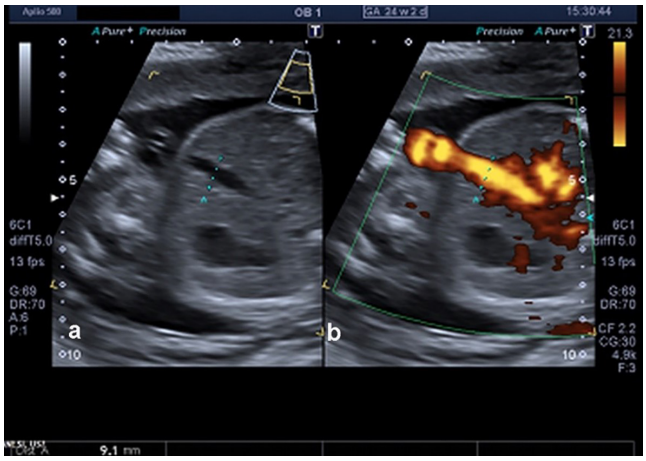

Figure 2. (a) Twin-view with PWD technique image of vessel diameter measurement from B mode side. (b) Twin-view with PWD technique image of vessel diameter measurement from PWD Doppler side.

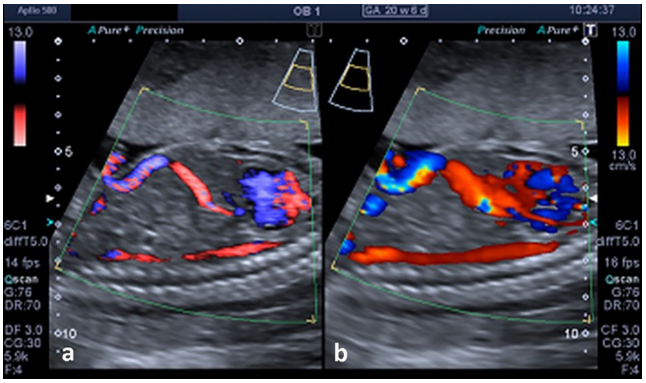

Figure 3. Imaging of the umbilical vein and the ductus venosus with (a) ADF and (b) CCD technique in a 14 weeks 5 days pregnant patient.

delta values (Table 1). This suggests that CCD and PWD techniques overestimate the diameter measurements due to blooming artefacts, while ADF technique measures the diameters closer to the gray-scale.

The study also found that the consistency of the color Doppler technique and gray-scale was highest with ADF, followed by PWD and CCD. The differences between CCD and PWD were not statistically significant, and both techniques overestimated the diameters similarly due to the similar blooming effects.

Intraclass correlation coefficients (ICC) were calculated to check the consistency of the techniques, and the results showed that ADF had the highest ICC value (0.964), followed by PWD (0.947) and CCD (0.882). These values indicate good consistency among the measurements obtained by the different techniques (Table 2 and Table 3).

Table 1. Comparisons of B mode and the Doppler techniques

	Mean	Std. Deviation	N
Delta CCD	2,371	1,253	99
Delta ADF	0,091	0,619	99
Delta PWD	2,134	1,414	99

CCD: Conventional Color Doppler, ADF: Advanced Dynamic Flow, PWD: Power Doppler

Table 2. Consistency of the Doppler techniques

	Intraclass Correlation[b]	95% Confidence Interval	
		Lower Bound	Upper Bound
Single Measures	0,786[a]	0,716	0,843

All color Doppler techniques' consistency was well (ICC= 0,786 and 95 % GA=0,716-0,843).

Table 3. Consistency of the Doppler techniques in gray-scale mode

	Intraclass Correlation[b]	95% Confidence Interval	
		Lower Bound	Upper Bound
Single Measures	0,921[a]	0,891	0,943

All color Doppler techniques' consistency in gray-scale was quite well (ICC=0,921 and 95 % GA=0,891 – 0,943).

Overall, the study suggests that ADF technique may provide more accurate diameter measurements of the intrahepatic umbilical veins compared to CCD and PWD techniques, due to less blooming artefacts.

Discussion

The techniques of Doppler ultrasound have been available to clinicians for nearly 40 years [4]. CCD and PWD are used to guide the mapping of the vascular tree in the body, including fetal parts. Users of Doppler ultrasound techniques must be aware of the complicated aspects of flow in the body [2]. The pulse Doppler (PD) sampling gate is placed in the vascular bed with the guidance of CCD or sometimes with PWD. However, both techniques have limitations such as blooming and color scatters off the vessel wall.

ADF was announced in April 2001 with Toshiba's Applio diagnostic ultrasound systems. Even though ADF has been available for more than a decade, its efficacy and capabilities in fetal Doppler examinations are not well understood amongst Doppler ultrasound examiners. The aim is to objectively compare ADF, CCD, and PWD techniques, independent of the manufacturer of Toshiba Medical.

CCD imaging uses a long burst pulse, which means it employs narrow-band frequency transmission. In contrast, ADF uses a short pulse, which is similar to B-mode imaging, and wide-band transmission. This is the fundamental principle of wide-band Doppler technology (Figure 1) [5].

Blooming is particularly important in the case of the tiny or slow-flow blood vessels of the fetus. Blooming can increase false vascularity and also lead to incorrect sampling in PD. Lowering the Doppler gain can reduce the blooming artifact, but this may also result in the loss of flow information. Conversely, raising the gain can overestimate the vessel diameter or over-colorize the tissue or mass in terms of vascularity.

The potential for misdiagnosis due to blooming artefacts is particularly concerning in inexperienced hands, as it can lead to prolonged examination times and unsatisfactory color guiding for visualizing small vessels such as the ductus venosus and middle cerebral artery in fetuses. In some cases, accurate vascular colorization is crucial for correct placement of a PD sampling gate and to obtain reproducible measurements, especially when investigating structures like the ductus venosus in fetuses between 11 and 14 weeks. Blooming can also prevent the depiction of vascular borders in close proximity to other structures, such as the ductus venosus, middle cerebral artery in the circle of Willis, and fetal renal arteries. This can be especially problematic in spectral pulsed Doppler techniques, leading to misinterpretation of findings and decreased diagnostic accuracy. [6].

The study aimed to compare the blooming effects and accuracy of vessel diameter measurement between ADF, CCD, and PWD techniques in Doppler ultrasound examinations using the intrahepatic umbilical vein. The study did not aim to establish normal reference values for the diameter of the intrahepatic umbilical vein.

The results of the study suggest that ADF is a more effective technique than CCD and PWD in terms of reducing blooming and improving visualization of the actual lumen of vessels. This improved visualization can lead to better accuracy in determining vessel diameter, as well as easier visualization of small vessels and improved placement of PD sampling gates. Overall, the study supports the use of ADF as a preferred technique in PD examinations. The improved visualization of the lumen enables easier detection of small vessels, accurate placement of the sampling gate, and clearer spectral analysis [7].

The usefulness of the ADF Doppler technique with regard to less blooming for evaluating fetal vasculature, which was statistically proven, has not been reported previously to the best of our knowledge.

Despite the apparent advantages of ADF for vascular mapping, it has not been widely used in Doppler US examinations worldwide. In an incomprehensible manner, ADF applications have not been well studied in the medical literature, as can be seen by the limited number of references available on the topic.

There are some limitations to using the ADF technique, such as the inability to detect turbulences as well as CCD can. However, this limitation can be overcome by adjusting the color encoding preset according to the user's preference or by combining both techniques. For instance, the ADF can be used initially for accurate vascular mapping, followed by CCD to determine turbulence in the ductus venosus for sampling gate placement before spectral analysis.

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The decreased blooming artefact in vascular mapping in fetuses has several benefits. Firstly, it allows for easier visualization of the ductus venosus even by inexperienced sonographers, thereby reducing the number of unsuccessful examinations and the need for supervised training. Maiz et al. [8,9] found that at least 80 exams are needed for successful ductus venosus examination under supervised training, which can potentially be reduced with the use of ADF technique. Secondly, the reduced blooming artefact decreases contamination from neighboring vessels in spectral analysis, potentially leading to more reproducible and reliable spectral waveforms for accurate diagnosis. Finally, congenital vascular variations or displaced vessels due to intrauterine malformations, such as diaphragmatic hernia, can be more easily visualized and assessed with ADF Doppler technique.

Conclusion: The ADF Doppler technique is a promising tool for evaluating fetal vasculature with less blooming and higher resolution compared to CCD and PWD techniques. Its benefits include easier visualization of small vessels, correct sampling gate placement, clearer spectral analysis, and less contamination from neighboring vessels in spectral analysis. However, the technique's limitations include decreased ability to detect turbulence and limited availability in current clinical practice. Further research is needed to define the potential applications of ADF not only in prenatal examinations but also in adults.

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Acta Medica Alanya

Research Article

Araştırma

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Depression, Anxiety and Pain Catastrophizing in Migraine Patients

Migren Hastalarında Depresyon, Anksiyete ve Ağrıyı Felaketleştirme

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ABSTRACT

Aim: In this study, we aimed to evaluate the relationship between anxiety, depression, and pain catastrophizing in individuals with and without migraine.

Method: Data of the study was collected using the socio-demographic data form, Beck Depression Scale (BDI), Beck Anxiety Scale (BAI), Pain Catastrophizing Scale (PCS), Migraine Disability Assessment Scale (MIDAS), and Visual Analogue Scale (VAS).

Results: Of the 183 patients, 80 were migraine patients and 103 were the control group. The BDI, BAI, and PCS scores were found to be higher in the migraine patients compared to the control group. The migraine patients were found to have "moderate" depression, "mild" anxiety, and "moderate" disability. There was a positive correlation between BDI, BAI, PCS, MIDAS, and VAS scores in the migraine patients. According to the total BDI and BAI scores of the migraine patients, the PCS total score and the PCS subscales "helplessness", " magnification", and "rumination" scores were higher in the patients with depression or anxiety.

Conclusions: It was found that the migraine patients had "moderate" depression and "mild" anxiety, and their pain catastrophizing level increased with increasing depression and anxiety severity.

Key Words: Migraine, Depression, Anxiety, Pain Catastrophizing.

ÖZET

Amaç: Bu çalışmada migreni olan ve olmayan bireylerde anksiyete, depresyon ve ağrıyı felaketleştirme arasındaki ilişkiyi değerlendirmeyi amaçladık.

Yöntem: Araştırmanın verileri sosyodemografik veri formu, Beck Depresyon Ölçeği (BDÖ), Beck Anksiyete Ölçeği (BAÖ), Ağrıyı Felaketleştirme Ölçeği (AFÖ), Migren Yetersizliği Değerlendirme Ölçeği (MIDAS) ve Görsel Analog Ölçeği (VAS).

Bulgular: 183 hastanın 80'i migren hastası ve 103'ü kontrol grubuydu. Migren hastalarında BDI, BAI ve AFÖ puanları kontrol grubuna göre daha yüksek bulundu. Migren hastalarının "orta" depresyon, "hafif" anksiyete ve "orta" yeti yitimine sahip oldukları bulundu. Migren hastalarında BDÖ, BAÖ, AFÖ, MIDAS ve VAS skorları arasında pozitif korelasyon vardı. Migren hastalarının toplam BDÖ ve BAÖ puanlarına göre, depresyon ya da anksiyetesi olan hastalarda AFÖ toplam puanı ve AFÖ alt ölçekleri "çaresizlik", "büyütme" ve "ruminasyon" puanları daha yüksekti.

Sonuç: Migren hastalarının "orta" depresyon ve "hafif" anksiyeteye sahip oldukları ve artan depresyon ve anksiyete şiddeti ile ağrıyı felaketleştirme düzeylerinin arttığı bulundu.

Anahtar Kelimeler: Migren, Depresyon, Anksiyete, Ağrıyı Felaketleştirme

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Introduction

Migraine, a chronic disease usually characterized by pulsatile headache attacks on one side of the cranium, can begin at any age, and its frequency tends to decrease in older ages [1]. It is one of the causes of headache affecting up to 11% of the adult population worldwide [2]. Migraine negatively affects the quality of life, social functionality, and working life. Its pathophysiology has not been fully elucidated yet [3]. Migraine diagnosis criteria were determined by the International Headache Society (IHS) [4]. It is basically divided into two groups: migraine with and without aura [5].

The degree of disability in migraine is important in determining the treatment [6]. Migraine may be associated with some psychiatric disorders. Depression is 2-4 times more common in migraine patients than in general population [7]. Concomitant depression and anxiety make the migraine treatment difficult [8]. Similar biological pathways and neurotransmitters play a role in the development of depression and pain [9]. These findings are supported by the previous studies investigating the analgesic effects of tricyclic antidepressants and serotonin-noradrenaline reuptake inhibitors [10]. Symptoms of depression, which are quite common in the course of chronic pain, make it difficult for the patient to comply with the treatment [11].

Catastrophizing is the tendency to evaluate one's situation or physical complaint with the fear that it will get worse each time [12]. Pain catastrophizing may increase with depression and anxiety in patients with migraine. This situation is evaluated by the pain catastrophizing scale (PCS) [13]. Catastrophizing pain has been associated with various diseases, chronic pain, deterioration of quality of life, increased degree of disability, and more healthcare use [14]. In individuals with migraine, pain catastrophizing has been associated with poor response to treatment and decreased health-related quality of life [15].

In this study, we aimed to compare the levels of anxiety, depression, and pain catastrophizing between individuals with and without migraine.

Materials And Methods

*Patients;*183 individuals, 80 migraine patients who were previously diagnosed with migraine according to IHS diagnostic criteria and 103 non-migraine individuals (control group), were included in the study. Migraine Disability Assessment (MIDAS), Visual Analogue Scale (VAS), Beck Depression Inventory (BDI), Beck Anxiety Inventory (BAI), and PCS were filled and evaluated with a questionnaire prepared previously by the researchers.

The socio-demographic data form includes the following information: age, gender, history of psychiatric and chronic disease, migraine type, and duration of the disease. *MIDAS* evaluates the disability associated with migraine and consists of 7 questions [16]. In VAS, pain severity is scored between 0 (no pain) and 10 points (worst pain imaginable) [17]. BDI is used to assess depression level. In BDI, the scores within the range of 0-9 refer to "no depression", 10-16 to "mild depression", 17-23 to "moderate depression", 24 or more to "severe depression" [18, 19]. BAI is a self-assessment scale developed to determine the frequency of anxiety symptoms experienced by individuals. In BAI, the scores within the range of 0-7 points refer to minimal anxiety symptoms, 8-15 points to mild, 16-25 points to moderate, and 26-63 points to severe [12].

PCS was developed to determine the catastrophic thoughts or feelings of patients regarding pain. The higher the total score, the higher the level of catastrophizing. PCS is used to assess the patient's feelings and thoughts about pain. The scores for each item are added to determine the subscale scores [20].

Inclusion and exclusion criteria; Migraine patients with cognitive functions sufficient to answer the questions and the control group were included in the study. Individuals with cognitive impairment preventing them from answering the questions, those who did not answer the questionnaire completely, and those with missing sociodemographic data were excluded from the study (Figure 1).

Ethical approval; was taken from the local ethics committee for this study (Approval No: 2020/295).

Statistical Analysis; IBM SPSS software package (v.22.0) was used. Based on the distribution of data in the comparison between groups, One-way ANOVA test was used for normally distributed values in non-categorical data, and Mann-Whitney U test for non-parametric data. Categorical data were compared using the Chi-square test. Pearson Correlation analysis was used to analyze the relationship between scale scores. The statistical significance was set at $p < 0.05$.

Results

Of the 183 patients participating in the study, 80 were the migraine patients and 103 were in the control group. The mean age of the migraine patients was 38.7 ± 13.5 years and 88.8% (n = 71) of them were women. The mean age of the control group was 39.0 ± 9.9 years and 86.4% (n = 89) of them were women, so the control group consisted of the individuals of similar age and gender to the migraine patients ($p > 0.05$, all). Majority of the migraine patients

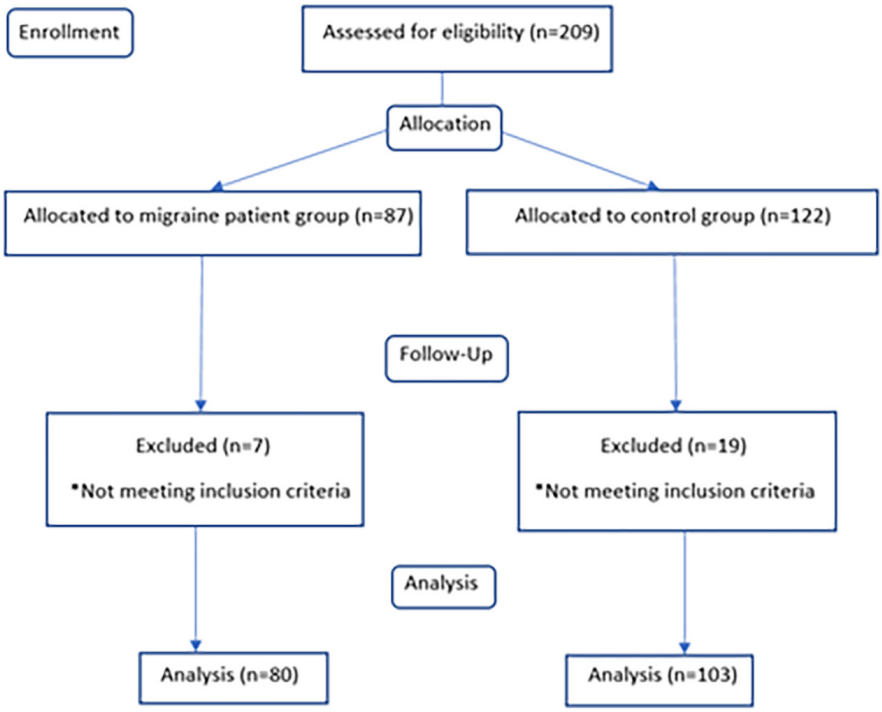

Figure 1. Flow diagram of the study The scale was applied to 209 people. 87 of these individuals were from the migraine group and 122 from the control group. 7 individuals from the migraine group and 19 individuals from the control group were excluded because they did not meet the inclusion criteria. As a result, the data of 80 migraine patients and 103 control groups were analyzed.

were diagnosed with non-aura migraine (72.5%). The mean disease duration of the migraine patients was 10.25 ± 8.15 years (Table 1).

When the BDI, BAI, and PCS scores of the migraine patients and the control group were compared, it was observed that the BDI, BAI, PCS scores were higher in the migraine patients compared to the control group ($p < 0.001$, all). The migraine patients were found to have "moderate" depression according to BDI score, "mild" anxiety according to BAI score, "moderate" disability according to MIDAS score (Table 2).

When the migraine patients were divided into the migraine subgroups, that is, those with and without aura; it was found that age, duration of illness, and test results were higher in the patients with migraine without aura compared to those with aura, but the difference was not statistically significant (Table 3).Correlation analysis was carried out between BDI, BAI, PCS, MIDAS, VAS scores and disease duration in migraine patients. There was a positive correlation between the scores for BAI and BDI, PCS and BDI, MIDAS and BDI, VAS and BDI, PCS and BAI, MIDAS and BAI, BAI and VAS, PCS and MIDAS, PCS and VAS, and MIDAS and VAS. There was no correlation between the disease duration and the scales ($p > 0.05$, all) (Table 4).

The PCS subscale scores of the patients with and without depression were evaluated in terms of their total BDI scores, and those of the patients with and without anxiety in terms of their BAI total scores. The PCS total score ($p = 0.003$) and the scores for the PCS subscales "helplessness" ($p = 0.001$), "magnification" ($p = 0.048$), and "rumination" ($p = 0.016$) were found to be significantly higher in the migraine patients with depression than in those without. Likewise, the PCS total score ($p < 0.001$) and the scores for the PCS subscales "helplessness" ($p < 0.001$), "magnification" ($p = 0.009$), and "rumination" ($p = 0.001$) scores were found to be higher in the migraine patients with anxiety than in those without. This shows that the level of pain catastrophizing increases with depression and anxiety (Table 5).

Discussion

Migraine is more common in women than men due to some genetic and hormonal reasons [21]. In our study, the majority of migraine patients (88.8%) were women. In the study by Atalar et al., it was shown that, in women, the migraine attacks was more frequent, their duration was longer, and the severity of pain was higher, and they were

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Table 1. Sociodemographic and clinical characteristics of migraine patients and control groups

Variables	All participiants (*n* = 183)	Migrain patients (*n* =80)	Control groups (*n* = 103)	***p***
Age (year), (mean ± sd)	38.91 ± 11.65	38.78 ± 13.57	39.01 ± 9.98	0.709
Gender, *n* (%)				0.635
Female	160 (87.4)	71 (88.8)	89 (86.4)	
Male	23 (12.6)	9 (11.2)	14 (13.6)	
Chronic disease history, *n* (%)				0.122
Yes	27 (14.8)	7 (8.7)	20 (19.4)	
No	156 (85.2)	73 (91.3)	83 (80.6)	
Psychiatric history, *n* (%)				0.068
Yes	8 (4.4)	6 (7.5)	2 (1.9)	
No	175 (95.6)	74 (92.5)	101 (98.1)	
Duration of migraine disease (year), (mean ± sd)	-	10.25 ± 8.15	-	-
Migraine Type, *n* (%)	-		-	-
Aura Migraine		22 (27.5)		
Non-Aura Migraine		58 (72.5)		

p, chi square test; *n*, number; sd, standard deviation.

Table 2. Comparison of BDI, BAI, PCS, MIDAS and VAS scores of migraine patients and control group

Scales	Migrain Patients (mean ± sd)	Control Groups (mean ± sd)	*p*
BDI	17.56 ± 9.69	5.26 ± 4.08	<0.001
BAI	15.38 ± 9.10	3.90 ± 1.78	<0.001
PCS	22.38 ± 12.30	10.70 ± 12.73	<0.001
MIDAS	12.14 ± 5.12	-	-
VAS	6.26 ± 1.68	-	-

p, independent sample T-test; sd, standard deviation; BDI, Beck Depression Inventory; BAI, Beck Anxiety Inventory; PCS, Pain Catastrophizing Scale; MIDAS, Migraine Disability Assesment Scale; VAS, Visual Analogue Scale.

Table 3. Comparison of migraine groups with and without aura in terms of age, disease duration and test results

Variables	Aura Migraine (mean ± sd)	Non-Aura Migraine (mean ± sd)	*p*
BDI	15.82 ± 7.99	18.22 ± 10.24	0.324
BAI	13.09 ± 8.76	16.24 ± 9.15	0.169
PCS	18.55 ± 11.78	23.83 ± 12.28	0.087
MIDAS	10.32 ± 1.28	12.34 ± 4.20	0.421
VAS	5.86 ± 1.46	6.10 ± 1.65	0.092
Age	37.50 ± 9.09	39.27 ± 14.96	0.605
Duration of illness	13.13 ± 8.54	9.15 ± 7.79	0.051

p, independent sample T-test; sd, standard deviation; BDI, Beck Depression Inventory; BAI, Beck Anxiety Inventory; PCS, Pain Catastrophizing Scale; MIDAS, Migraine Disability Assesment Scale; VAS, Visual Analogue Scale.

Table 4. Correlation analysis between BDI, BAI, PCS, MIDAS, VAS scores and duration of illness in migrain patients

Variables		BDI	BAI	PCS	MIDAS	VAS
BDI	*r*	-	0.750	0.347	0.315	0.276
	95% CI	-	0.584,0.870	0.126,0.569	0.065,0.522	0.046,0.477
	p	-	<0.001	0.002	0.004	0.013
BAI	*r*	0.750	-	0.453	0.540	0.556
	95% CI	0.584,0.870	-	0.264,0.630	0.329,0.721	0.360,0.713
	p	<0.001	-	<0.001	<0.001	<0.001
PCS	*r*	0.347	0.453	-	0.372	0.387
	95% CI	0.126,0.569	0.264,0.630	-	0.152,0.574	0.171,0.582
	p	0.002	<0.001	-	0.001	<0.001
MIDAS	*r*	0.315	0.540	0.372	-	0.726
	95% CI	0.065,0.522	0.329,0.721	0.152,0.574	-	0.606,0.828
	p	0.004	<0.001	0.001	-	<0.001
VAS	*r*	0.276	0.556	0.387	0.726	-
	95% CI	0.046,0.477	0.360,0.713	0.171,0.582	0.606,0.828	-
	p	0.013	<0.001	<0.001	<0.001	-
Duration of illness	*r*	-0.029	-0.049	-0.081	-0.117	-0.062
	95% CI	-0.227,0.181	-0.251,0.175	-0.029,0.797	-0.330,0.099	-0.314,0.168
	p	0.797	0.668	0.473	0.300	0.586

p value, Pearson Partial Correlation Test; *r*, Correlation Coefficient; CI, Confidence Interval; sd, standard deviation; BDI, Beck Depression Inventory; BAI, Beck Anxiety Inventory; PCS, Pain Catastrophizing Scale; MIDAS, Migraine Disability Assesment Scale; VAS, Visual Analogue Scale.

Table 5. PCS subscale scores according to the presence of depression or anxiety in migraine patients

PCS Subscales	No Depression (BDI) (mean ± sd)	Depression (BDI) (mean ± sd)	*p*
Helplessness	7.55 ± 6.41	12.60 ± 4.24	0.001
Magnification	5.35 ± 3.03	6.72 ± 2.31	0.048
Rumination	6.84 ± 3.99	9.04 ± 3.02	0.016
Total	19.65 ± 12.88	28.36 ± 8.41	0.003
	No Anxiety (BAI) (mean ± sd)	Anxiety (BAI) (mean ± sd)	*p*
Helplessness	7.45 ± 6.09	13.04 ± 4.86	<0.001
Magnification	5.23 ± 2.87	7.04 ± 2.54	0.009
Rumination	6.63 ± 3.62	9.63 ± 3.57	0.001
Total	19.23 ± 11.95	29.71 ± 9.92	<0.001

p, independent sample T-test; sd, standard deviation; BDI, Beck Depression Inventory; BAI, Beck Anxiety Inventory; PCS, Pain Catastrophizing Scale.

more susceptible to the environmental and hormonal factors [22].

Non-Aura Migraine accounts for approximately 80-90% of all migraine cases [4]. Also, in the present study, the patients with Non-Aura Migraine constituted the majority (72.5%). Although age, duration of illness, and test results were higher in the patients with migraine with aura compared to the patients diagnosed with Non-Aura Migraine, the difference was not statistically significant (Table 1). While some studies assert that there are no differences in the levels of anxiety and depression symptom between patients with migraine with and without aura [7], some other studies assert that the psychiatric disorders are more common in those with aura than in those without aura [23].

In our study, the BDI, BAI, PCS scores were found to be higher in the migraine patients compared to the control group. The levels of depression, anxiety, and pain catastro-

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phizing were higher in the migraine group than in the normal population. The migraine patients were found to have "moderate" depression, "mild" anxiety, and "moderate" disability according to MIDAS (Table 2). It can be thought that migraine patients are depressed due to having a chronic disease for a long time. In the study by Kutlu et al., it was asserted that as the level of depression increased, the quality of life decreased significantly in all areas [24]. The psychiatric disorders such as depression, anxiety disorder, bipolar disorder, and phobia thought are common in individuals with migraine. Juang et al. reported that 78% of the patients with migraine and 64% of the patients with tension headache had psychiatric disorders [25]. In the study by Breslau et al., it was found that major depression and migraine increased the frequency of each other, and this relationship was not found to exist in other headaches [26]. In the study by Selekler et al., major depression and dysthymic disorders were found to be more common in the patients with migraine and tension-type headache than those with secondary headache [27]. In the similar previous studies, the levels of depressive symptom and anxiety severity were found to be higher in the migraine group compared to the control group [28, 29].

No relationship was found between the duration of the disease and the levels of depressive symptoms in our study. Although there are some studies with similar results to ours [7], there are also some other studies reporting a relationship between disease duration and depressive symptom levels [30]. Since anxiety and depression can negatively affect the quality of life in patients with migraine, physical and psychosocial symptoms that may lead to anxiety and depression should be well recognized and evaluated, and appropriate treatment modalities should be developed for patients. According to the study by Gürsoy et al., the medication to be used in prophylactic treatment should be selected according to its efficacy and side effect profile, and the patient's comorbid diseases should also be considered [31]. Antidepressant use may be preferred if the patient with migraine has a mood disorder. According to the study by Tassorelli et al., major depression and anxiety are common in migraine patients, and psychiatric comorbidities and allodynia are the risk factors for progression to chronic migraine [4].

Pain catastrophizing is the tendency to feel increased pain, whether real or imaginary. This inability to distract the focus of attention from pain causes an increase in pain perception and sensitivity. In our study, PCS scores, which show the emotional and cognitive attitudes of individuals towards their pain, were found to be higher in the migraine patients compared to the control group (Table 2). In the study by Bond et al., it was observed that the duration of attack and pain sensitivity were higher in the patients with migraine. They asserted that when treating headache, it was necessary to address the pain catastrophizing and mood disorders [15]. Pires et al. reported that those with migraine exhibited different psychological characteristics than those without migraine, and the levels of anxiety and pain catastrophizing were higher in the migraineurs [32]. In our study, according to the total BDI scores of migraine patients, the PCS total score and the scores for PCS subscales were statistically significantly higher in the patients with depression and anxiety than those without ($p < 0.05$, all). Thus, in our study, it was found that the overall level of pain catastrophizing and the levels of PCS subscales were higher in the patients with depression or anxiety. The subscales "helplessness" (inability to cope with pain effectively), "magnification" (discontent created by focusing excessively on the negative consequences of pain), and "rumination" (inability to inhibit thoughts about pain) reflect the cognitive content of psychopathologies such as anxiety and depression accompanying headache and migraine (Table 5). It was shown in previous studies that the scores for the subscales of PCS were higher in those with migraine and tension-type headache than in the control group [8]. A positive correlation was observed between BDI, BAI, PCS, MIDAS, and VAS scores in migraine patients, in our study ($p < 0.05$, all) (Table 4). This indicates that pain catastrophizing increases with depression and anxiety. In our study, it was found that as the degree of pain and migraine disability increased, the levels of depression, anxiety, and pain catastrophizing also increased, and vice versa. In migraine patients, psychosocial approach also plays an important role in breaking this vicious circle in addition to medical treatment, and incorporation of psychosocial approach into treatment can increase its effectiveness. If these problems are not expressed by patients or questioned by clinicians, it can be difficult to treat migraine.

One of the limitations of our study is that it is single-centered. Future studies should be carried out in multiple centers with more participants. The strength of our study lies in that it is a prospective study and includes the comparison of the symptom levels of anxiety, depression, and pain catastrophizing between normal individuals and migraine patients, and between migraine patients with and without aura, and the evaluation of these levels together with MIDAS and disease duration.

Conclusion In this study, it was observed that the levels of depressive symptoms, anxiety, and pain catastrophizing were significantly higher in the migraine patients compared to the control group. It was found that the migraine patients generally had "moderate" depression and "mild" anxiety. It was found that as the severity of anxiety and depression increased in the migraine patients; their levels of pain catastrophizing, helplessness, magnification, and rumination also increased. In migraine patients, in addi-

tion to medical treatments, psychiatric approaches should be incorporated into the treatment for patients who are indicated after psychosocial evaluations.

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Research Article

Araştırma

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Comparison Of Diaphragm Thickness Values In Cases of Adenotonsillectomy Before And After The Operation

Adenotonsillektomi Olgularında Ameliyat Öncesi ve Sonrası Diyafram Kalınlık Değerlerinin Karşılaştırılması

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ABSTRACT

Aim: Measurement of the thickness of the diaphragm is a parameter that can be used to decide before separation from mechanical ventilation and extubation. In these cases where intubated and extubated at the end of the operation, it is planned to examine the ratio of the aperture muscle thickness to each other in the last inspirium and exprium before extubation. Determining the current ratio may be meaningful for determining the extubation time.

Material and Method: In the study, 60 patients, who were in the physical state of ASA I and II, 3-12 age range, and who were scheduled for elective adenotonsillectomy operation were included. Age, gender, body mass index (BMI), and operation time data of patients were recorded. Before and after the procedure, inspiratory and expirtuar diaphragm thicknesses were measured by ultrasonography. In addition, the ratio of the last inspirium and the diaphragm muscle thicknesses in the last expiration were also calculated.

Results: There was no significant difference between the pre-operation values and the end of the operation in the diaphragm thickness measurements. The incidence of laryngospasm was 1.5 %.

Conclusion: Diaphragm thickness measurements with ultrasound have many benefits but further studies are needed.

Key Words: Diaphragm, Ultrasound, Pediatric, Anesthesia

ÖZET

Amaç: Diyaframın kalınlığının ölçülmesi, mekanik ventilasyon ve ekstübasyon ayrılmadan önce karar vermek için kullanılabilecek bir parametredir. Ameliyat sonunda entübe edilen ve ekstübe edilen bu olgularda ekstübasyon öncesi son inspirum ve son ekspiryumda diyafram kas kalınlığının birbirine oranının incelenmesi planlanmıştır. Bu oranın belirlenmesinin ekstübasyon süresinin belirlenmesinde anlamlı olabileceği düşünülmektedir.

Gereç ve Yöntem: Çalışmaya elektif adenotonsillektomi operasyonu planlanan 3-12 yaş aralığında fiziksel durumu ASA I ve II olan 60 hasta dahil edildi. Hastaların yaş, cinsiyet, vücut kitle indeksi (VKİ) ve operasyon süresi verileri kaydedildi. Ameliyat öncesi ve sonrası ultrasonografi ile inspiratuar ve ekspiratuar diyafram kalınlıkları ölçüldü. Son inspiryum ve son ekspirasyondaki diyafram kası kalınlıklarının oranı hesaplandı.

Bulgular: Diyafram kalınlık ölçümlerinde ameliyat öncesi değerler ile ameliyat sonu değerleri arasında anlamlı fark yoktu. Laringospazm insidansı %1.5 idi.

Sonuç: Ultrason ile diyafram kalınlığı ölçümlerinin birçok faydası vardır ancak daha ileri çalışmalara ihtiyaç vardır.

Anahtar Kelimeler: Diyafram, Ultrason, Pediatrik, Anestezi

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Introduction

When determining whether a patient can be successfully extubated, timing is critical [1]. Weaning of mechanical ventilation too early can induce an increase in cardiovascular and respiratory stress, CO2 retention, and hypoxemia [1-3]. Extubation timing is even more important, especially in child cases. Child cases are more prone to laryngospasm and hypoxemia[2, 3]. Due to the reality of those, determining the fact that the patient is completely saved from the effect of the neuro-muscular blocker agent [4].

The use of ultrasonography (US) in the operating room tends to increase recently and, US is a kind of assessment device which can be used to appraise the thickness of the diaphragm [5, 6]. Appraisement of the thickness of the diaphragm is a parameter that can be used to separate from mechanical ventilation and pre-extubation [5, 7]. Appraisement of the thickness of the diaphragm with US is a non-invasive, easily accessible method and may guide the patient in anesthesia in terms of extubation timing [4, 6]. Adeno-tonsillectomy operations are one of the frequently applied operations in children [8-10]. In these cases where intubated and extubated at the end of intervention, it is thought that an objective parameter could be obtained for extubation timing by examining the ratio of the diaphragm muscle thickness to each other in the last inspirum and last exprium before extubation. It is planned that the determination of this ratio may be meaningful for the determination of the extubation time.

Material and Methods

With the approval of the Ethics Committee and the approval of the volunteers with written forms, 60 patients, who were in the physical state of ASA I and II, 3-12 age range, and who were scheduled for elective adenotonsillectomy operation were included. Age, gender, body mass index (BMI), and operation time data of patients were written down. Before and after the operation, inspiratory and expritуar diaphragm thicknesses were measured by ultrasonography. The ratio of the last inspirium and the diaphragm muscle thicknesses in the last expiration were calculated the consensus of the extubation criterion was examined.

Patients with a physical defect to prevent US examination, the children of the parents who do not know Turkish literacy and did not agree to participate in the study were excluded. Before and at the end of operation, inspiratory and expritуar diaphragm thicknesses were measured by ultrasonography. Patients who underwent adenotonsillectomy operations involved in the study were measured in a 45-degree head-up position while measurements were performed. Right hemi-diaphragm, 8th and 10th intercostal gaps midaxillary between the diaphragm and rib cage is displayed by ultrasonography from the area where the cage was settled, and the last exprium and the last inspirium muscle thickness were recorded. The ratio of the last inspirium and the last exposure of the last exposure was measured by measuring muscle thicknesses. Induction of anesthesia was performed with 2-4 mg/kg of propofol, rocuronium 0.6 mg/kg and 1 mcg/kg fentanyl. It was maintained with 2% sevofluran and 60% nitrogen oxide in oxygen. Extubation was determined by the anesthesist, including the study, considering awake extubation criteria. In the initiation and continuity of anesthesia, cases other than the above-mentioned induction and maintenance regulations were excluded. In the study, anesthesia induction and maintenance were not involved.

Results

Sixty patients undergoing adenotonsillectomy were enrolled from September 2018 to October 2019 in the study (Table 1). During this period, three eligible patients were excluded: 3 refused informed consent. When we look at the demographic values, for the gender of the patients, there was a statistic difference within the patients ($p<0.001$). About the age, There was a statistic difference within the patients ($p<0.001$). When we consider BMI statistically, There was a statistic difference within the patients ($p<0.001$).

The operation time was recorded. When we consider operation time statistically, There was a statistic difference within the patients ($p<0.001$). The SPO2 values were recorded as a preoperative and preextubation period. When we consider the SPO2 values with correlation test statistically, There was a correlation within the patients in preoperative and preextubation period. ($p=0.016$, $R=0.311$).

Table 1. Characteristics of Patients Undergoing Adeno-tonsillectomy

Characteristics	**n/mean**
Sex, Male:Female	30/30
Age (years)	7.41
Body mass index (kg/m2)	16.35
Operation time (min)	51.05

Table 2. Sonographic Variables PreOT(preoperative time) and PreET(preextubation time)(mean)

Sonography	PreOT (preoperative time)	PreET (preextubation time)
DIA (deep, cm)	0.52	0.50
DEA (deep, cm)	0.50	0.47

Sonographic Data

The perioperative DIA (diaphragmatic inspiratory Amplitude) and DEA (diaphragmatic expiratory Amplitude) values during breathing before and after adenotonsillectomy were summarized in Table 2. After adenotonsillectomy, DIA and DEA values determined a eloquent degree of decrease from their preoperative values on PreOT(preoperative time) and PreET(preextubation time) when we considered the values with correlation test ($P < 0.001$). (Table 2, Fig. 1A and 1B).

When we considered the spasm and DIA and DEA with a correlation test, there was no correlation within the patients. The results of the spasm were showed in table 3.

Discussion

In medical interventions, many efforts are made to reduce complications. Each clinical discipline is a tremendous effort to prevent complications related to itself. Especially in child cases, complications can develop much faster, measures must be kept at the highest level. In particular, anesthetists may encounter many complications in surgical procedures involving the supraglottic airway [4, 11-13]. The safe intubation of the patient is a part of the anesthesia physician until safe transfer after the operation is followed by vital data during the operation and after being extubated. Extubation timing is also a critical detail. Although there are methods that provide numerical data, such as neuromuscular monitoring (NMT), Bi-Spectral Index (BIS), and Near Infra-Red Spectroscopy (NIRS), complications can be encountered [2, 3, 10, 14]. There are also question marks about NMT monitoring in pediatric cases such as dosing the current. Additionally, most NMT monitor apparatus are designed for adult sizes. The difficulties related to the implementation of NMT in child cases pushed the anesthetists to different searches [14]. The way that assessment of diaphragm and aperture via US, is one of the results of these inquisitorials [2, 3]. Non-invasive and easy to apply (even when the patient is awake) is the advantage. However, disadvantages such as access to the device and physician experience are also available. According to the results of our study, there is no statistically significant difference between the diaphragmic thicknesses measured during the extubation times of physicians and pre-operation values. In addition, the fact that laryngospasm has been observed in only one case (1.5%). Laryngospasm incidence has been reported from %4 to % 16 [15] in different studies. However, in our study laryngospasm incidence was lower. That data could not have been correlated with other studies. Because in our study, just muscle contraction has been confirmed by US guidance and it is not expected to have a lower incidence.

Table 3. The Pearson correlation test values (R) about spasm with PreOT(preoperative time) and PreET(preextubation time)(mean)

Spasm	PreOT (preoperative time)	PreET (preextubation time)
DIA (deep, R) / *P*	-0.43/0.743	-0.45/0.731
DEA (deep, R) / *P*	0.13/0.923	-0.61/0.642

In our study, it is a result that has in prospect to be a considerable distinction between the pre-operation and the end of the intervention in the assessment of US and diaphragm thickness. Accordingly, the evidence of the methods that the muscle thickness has reached pre-operation values with the measurements made is evidence that the method may be useful, but considering the limitations of the study, our evidence is weak. Because NMT has not been used, an objective process cannot be followed for extubation timing.

Limitations: Being not tracked of complications in Postoperative 24 hours period, and not applying NMT and standardized postoperative analgesia, represent the limitations of the present study.

Conclusion: According to our data, there was no significant difference between the pre-operation values and the end of the operation in the diaphragm thickness measurements. The incidence of laryngospasm was 1.5 %. these data showed that diaphragm thickness measurements with ultrasound have many benefits but further studies are needed with larger study groups to confirm that data and to widen its correlation.

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Evaluation of Thyroid Fine Needle Aspiration Biopsy Results: A Single Center Experience

Tiroid İnce İğne Aspirasyon Biyopsi Sonuçlarının Değerlendirilmesi: Tek Merkez Deneyimi

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ABSTRACT

Aim: It was aimed to examine the results of thyroid fine needle aspiration (FNA) biopsy performed in our clinic and to investigate its effectiveness.

Methods: In this study, the results of 101 patients who underwent thyroid FNAB in Tarsus State Hospital endocrinology clinic between December 2021 and July 2022 were retrospectively analyzed.

Results: Ultrasonographic features of thyroid nodules were classified according to EU-TIRADS, 51(50.5%) were in EU-TIRADS-3, 31 (30.7%) were in EU-TIRADS-4, 19(18.8%) were in EU-TIRADS-5. When we categorize cytology results according to Bethesda classification, 23 (22.8%) Bethesda I, 48 (47.5%) Bethesda II, 16 (15.8%) Bethesda III, 4(4%) Bethesda IV,10(9.9%) detected as Bethesda VI. Bethesda II was found in the EU-TIRADS-3 category with the highest frequency, while Bethesda VI was found in the EU-TIRADS-5 category with the highest frequency. The mean nodule diameter was found to be 20.48± 9.73mm.

Conclusion: Ultrasonographic findings of the nodules correlated with cytology results. The EU-TIRADS categorization has a good concordance with the Bethesda system. The coordinated use of the two classifications helps the clinician to avoid the risk of unnecessary invasive procedures.

Key Words: Biopsy, Thyroid Nodule, Ultrasonography

ÖZET

Amaç: Kliniğimizde yapılan tiroid ince iğne aspirasyon biyopsi (İİAB) sonuçlarımızı inceleyip etkinliğini araştırmak amaçlandı.

Yöntem: Bu çalışmada Aralık 2021 -Temmuz 2022 tarihleri arasında Tarsus Devlet Hastanesi Endokrinoloji Kliniğinde tiroid İİAB yapılan 101 hastanın sonuçları retrospektif olarak incelendi.

Bulgular: Tiroid nodüllerinin ultrasonografik özelikleri EU-TIRADS'a göre sınıflandırıldığında 51(50.5%)'i EU-TIRADS-3, 31 (30.7%)'i EU-TIRADS-4, 19(18.8%)'u EU-TIRADS-5 kategorisindeydi. Sitoloji sonuçlarını Bethesda sınıflamasına göre kategorize ettiğimizde ise 23 (22.8%)'ü Bethesda I, 48 (47.5%)'i Bethesda II, 16(15.8%)'sı Bethesda III, 4(4%)'ü Bethesda IV, 10(9.9%)'si Bethesda VI olarak tespit edildi. Bethesda II en yüksek frekans ile EU-TIRADS-3 kategoride saptanırken Bethesda VI ise en yüksek frekans ile EU-TIRADS-5 kategoride yer aldı. Ortalama nodul çapı 20.48± 9.73 mm olarak bulundu.

Sonuç: Nodüllerin ultrasonografik bulguları sitoloji sonuçları ile korelasyon göstermiştir. EU-TIRADS sınıflandırması, Bethesda sistemi ile iyi bir uyum içindedir. İki sınıflamanın koordineli kullanılması, klinisyene gereksiz invaziv prosedür riskinden kaçınmak için yardımcı olmaktadır.

Anahtar Kelimeler: Biyopsi, Tiroid nodülü, Ultrasonografi

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Introduction

Thyroid nodules are a common clinical problem, and epidemiological studies have shown that the prevalence rate of palpable nodules in iodine-deficient areas is 5% in women and 1% in men [1,2]. These are intrathyroidal lesions that can be radiologically separated from the thyroid parenchyma and have been detected incidentally on ultrasonography (USG) at a rate of up to 68% in healthy people [3,4]. Most nodules are cytologically benign and do not require treatment, but some nodules may cause compression symptoms and cosmetic complaints. These nodules may cause overt or subclinical hyperthyroidism by gaining autonomy [4-6]. USG-guided fine-needle aspiration biopsy (FNAB) is a widely used and accepted method in the investigation of thyroid nodules [7]. The clinical significance of thyroid nodules is due to the fact that 7–15% of nodules are associated with thyroid cancer, and this is related to age, sex, radiation exposure, and family history [5,8]. In this single-center study, we present the FNAB results of thyroid nodules examined in our hospital.

Materials and Methods

The study protocol was approved by the institutional Ethics Committee of Cukurova University (Date: 22/07/2022, No: 124/57).

In this study, the results of 101 patients who underwent thyroid FNAB in the endocrinology clinic of Tarsus State Hospital between December 2021 and July 2022 were retrospectively analyzed.

FNAB procedure was performed in endocrinology clinic with high frequency (7-13 mHz) linear probe USG (Aplio 300, Toshiba, Tokyo, Japan). All procedure performed by the single endocrinologist and all specimens evaluated by the same pathologist. FNAB procedure was performed using 22 gauge needle tip and 10-20 cc injectors. During aspiration, negative pressure was applied by sonographically monitoring that the tip of the needle was inside the nodule.

Information including demographic data of the patients, USG findings and cytology results were recorded. Nodule morphologies were categorized according to the findings in the USG results. All Cytology results of thyroid biopsies were classified according to the "Bethesda thyroid cytopathology reporting system" 2017 guidelines [9]. These cytological results were compared with the USG findings.

All of the 101 nodules were scored according to the European Thyroid Association Guidelines for Ultrasound Malignancy Risk Stratification of Thyroid Nodules in Adults (EU-TIRADS) [10].

Statistical Analysis

A frequency analysis was performed for the categorical variables (sex, FNAB results, and USG characteristics), and descriptive statistics were performed for the numerical variables (age, diameter, thyroid-stimulating hormone [TSH] level, and thyroxine [T4] level). The suitability of the numerical variables to the normal distribution was evaluated using the Kolmogorov-Smirnov test. Among all variables, only age showed a normal distribution. The relationship between EU-TIRADS categori and FNAB results was evaluated with Chi-Square analysis, and the relationship between nodule diameter and FNAB results was evaluated with Kruskal-Wallis H test. The relationship between TSH and T4 levels and US character was evaluated with Kruskal-Wallis H test, and the relationship between TSH and T4 levels and nodule diameter was evaluated with Pearson Correlation analysis. Significance level was accepted as $p<0.05$. All evaluations were made in SPSS 28.0 program.

Results

In this study we included 84 (83.2%) female and 17 male (16.8%) patients. The patients' mean age was 49.3 ± 11.5 years. When the patients' thyroid functions were examined, the mean TSH level was found to be 2.13 ± 1.85 mIU / L (0.35–5.5), and the free T4 level was 1.09 ± 0.18 ng/dl (0.89–1.76). The mean nodule diameter was 20.48 ± 9.73 mm.

Using the EU-TIRADS, all of the nodules were categorized on the basis of the USG features described in ETA guidelines (Table 1). When we categorized the cytology results according to the Bethesda classification, 23 (22.8%) were Bethesda I; 48 (47.5%), Bethesda II; 16 (15.8%), Bethesda III; 4 (4%), Bethesda IV; and 10 (9.9%), Bethesda VI (Table 1).

Statistically significant difference was found between the nodule characteristics detected on USG and the FNAB cytology results ($p = 0.017$). Cytologically Bethesda VI nodules were more frequently detected among the nodules with category EU-TIRADS 4-5.

The FNAB cytology results showed no statistically significant correlation with age, sex, and thyroid function (Table 2). While nodule diameter and TSH level showed a significant negative correlation ($r = –0.263$), neither of the two showed a significant correlation with the FNAB results.

Discussion

Thyroid nodules alone do not cause a serious problem unless they cause an obstructive pressure or cosmet-

Table 1. EU-TIRADS categories and cytology results

Nodule character	Bethesda I	Bethesda II	Bethesda III	Bethesda IV	Bethesda VI	Total
EU-TIRADS-3	12	31	6	1	1	51(50.5%)
EU-TIRADS-4	8	13	5	1	4	31(30.7%)
EU-TIRADS-5	3	4	5	2	5	19 (18.8%)
Total	23(22.8%)	48(47.5%)	16(15.8%)	4(4%)	10(9.9%)	101(100%)

Table 2. Comparison of FNAB cytology results with other parameters

	Age (years)	Sex	TSH (mIU/L)	Free T4 (ng/dL)	Nodule diameter (mm)
FNAB Cytology (p-value)	0.269	0.833	0.059	0.52	0.467

ic discomfort. The main concern with thyroid nodules is whether they are suspected of malignancy or cause thyroid dysfunction. Most thyroid nodules are benign, and thyroid cancer develops in 5% to 15% of thyroid nodules. The incidence of thyroid cancer depends on age, sex, radiation exposure, and family history [11). Many studies have shown that thyroid nodules are more prevalent in women than in men [12,13]. In our study, the prevalence of thyroid nodules was higher in the female population, consistent with the reports in the literature.

In our study malignancy rate was found to be 9.9% in nodules, which was in line with the studies conducted around the world and in our country. [14-17] and malignancy rate was found to be statistically significantly higher among EU-TIRADS-5 category. Highest concordance was found among both the low risk (EU-TIRADS 3 and Bethesda II) and the higher risk categories (EU-TIRADS 5 and Bethesda IV-VI) in this study, which is consistent with the previously described in literature [28]. The American Thyroid Association (ATA) has associated thyroid nodules with a high risk of malignancy if they are hypoechoic, have irregular and unclear infiltrative borders, present with microcalcifications, show no halo, and have a height greater than the transverse size. The ATA recommends a FNAB for nodules which have these features and more than 1 cm in size [4]. Studies have shown that hypo echogenicity has high sensitivity and specificity in predicting malignancy [18,19]. However, it should be kept in mind that some benign nodules may have a hypoechogenic appearance [20]. The malignancy rate was found to be higher in hypoechoic, irregularly circumscribed nodules in our study. A direct relationship was reported between nodule size and cancer risk [21]. In our study, all of the patients except one with malignant results had the nodule larger than 1 cm.

In our study, the rate of nondiagnostic cytology was slightly higher than that reported in the literature [22,23]. Considering that FNAB was performed for the first time in our center, factors such as cytologist experience and equipment adequacy undoubtedly had a significant impact on the adequacy of the procedure.

We found that the FNAB results in our study were not statistically significantly correlated with age and sex. Although we cannot associate cytology with age and sex, we know that both are risk factors of thyroid cancer [24-26]. Thyroid cancer is more common in women than in men, although the cause cannot be fully understood. This is mainly attributed to estrogen, and studies have shown that estrogen levels may be associated with the risk of thyroid cancer [24,27]. Similarly, age is a risk factor of thyroid cancer and is a main component of important thyroid cancer staging systems [26].

Conclusion

FNAB is an easy-to-apply method with high specificity in the diagnosis of thyroid nodules. In determining the necessity of surgery in the thyroid nodules management, the result of a FNAB performed under USG guidance is of great diagnostic value to clinicians. The coordinated use of EU-TIRADS category and Bethesda helps the physician to avoid the risk of unnecessary invasive operations. Our results are similar to those reported in the literature and clearly demonstrate that the rate of proficiency in performing the procedure will improve with increasing experience. Performing the procedure with USG affects both the diagnostic accuracy and adequacy. Considering that the hospital where the procedure was initially performed is a second care hospital and that more than a hundred

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biopsy procedures were performed in a short time by the single endocrinologist, this study reveals that the biopsy procedure to be performed to diagnose thyroid cancer is easily accessible even in limited working conditions. Thus, this study may encourage clinicians working under similar conditions to perform the procedure.

Limitations

The first among the limitations of the study is that only the first biopsy results were incorporated in the study. Parcipiants were scheduled to undergo repeat biopsies for Bethasda I and Bethasda III results, but the results could not be included because these procedures did not occur within the planned this study period. The second limitation is that the histopathology results of the patients who were referred surgery for Bethasda IV and Bethasda VI could not be included in the study because there was no experience of thyroid surgery in our center. Study was conducted in a one district of Turkey, and it may not reflect the country's thyroid nodule epidemiology.

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Ethics Committee Approval: Prior to the study, approval was obtained from the Çukurova University Faculty of Medicine Non-Invasive Clinical Research Ethics Committee. (Date: 22/07/2022, No: 124/57).

ORCID and Author contribution: B.K. (0000-0002-4011-4622): *Concept and Design, Data collection, İnterpretation of results ,Critical Review.* Final approval.

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Research Article

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The Impact of the COVID-19 Pandemic on Children with Cerebral Palsy

COVID-19 Pandemisinin Serebral Palsili Çocuklar Üzerindeki Etkisi

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ABSTRACT

Aim: The purpose of this study was to examine the sustainability of the treatment of children with cerebral palsy during the pandemic, the physical and psychosocial impact of the pandemic on children, and the fear of COVID-19 among parents.

Method: The authors' questionnaire and the COVID-19 Fear Scale were completed by 350 parents who were reachable and willing to participate in the study.

Results: According to the information given, we can conclude that 46 (21.9%) of 210 children who received education could not participate in online education. In addition, 123 (63.4%) of 194 children who received individual education and 108 (78.8%) of 137 children who received physiotherapy could not continue. According to family reports, 26.3% of children had worse physical development, 21.1% had worse sleep quality, 11.7% had worse linguistic skills, and 39.1% of children had higher levels of anxiety than before the pandemic. The mean COVID-19 Fear Scale score of the parents who stated that their child's physical development was worse compared to before the pandemic (18.23±5.63) was higher than that of the parents who stated that there was no change in their child's physical development (16.91±5.26) (p=0.031). The mean COVID-19 Fear Scale score of the parents who stated that their child's anxiety was higher than before the pandemic (18.02±5.49) was higher than the parents who stated that there was no change in their child's anxiety (16.81±5.28) (p=0.04).

Conclusion: During the pandemic period, rehabilitation of children with cerebral palsy was interrupted and children were affected physically and psychosocially. Family-centered approaches and telerehabilitation opportunities should be studied for future periods.

Key Words: COVID-19, Pandemic, Cerebral palsy, Quarantine, Parent, Fear

ÖZET

Amaç: Bu çalışmada amacımız pandemi döneminde serebral palsili çocukların tedavilerinin sürdürülebilirliğini, çocukların fiziksel ve psikososyal etkilenimlerini ve ebeveynlerin COVİD- 19 korkusunu araştırmaktır.

Yöntem: Ulaşılabilen ve ankete katılmayı kabul eden 350 ebeveyne yazarlar tarafından oluşturulan anket formu ve COVİD-19 Korku Ölçeği dolduruldu.

Bulgular: Eğitim alan 210 çocuktan 46'sı (%21,9) pandemide uzaktan eğitime katılamamıştı. Bireysel eğitim alan 194 çocuktan 123'ü (%63,4) ve fizyoterapi alan 137 çocuktan 108'i (%78,8) devam edememişti. Ailelerin beyanlarına göre çocukların %26,3'ünün fiziksel durumu, %21,1'inin uyku kalitesi, %11,7'sinin dilsel becerileri daha kötüydü.Pandemi öncesine göre kaygı düzeyleri çocukların %39,1'inde daha yüksekti.Pandemi öncesine göre çocuğunun fiziksel durumunun daha kötü olduğunu ifade eden ebeveynlerin COVİD Korku Ölçeği puanı ortalaması (18,23±5,63), pandemi öncesine göre çocuğunun fiziksel durumunda değişiklik olmadığını belirten ebeveynlerden (16,91±5,26) daha yüksekti (p=0,031). Pandemi öncesine göre çocuğunun kaygı seviyesinin daha yüksek olduğunu ifade eden ebeveynlerin COVİD Korku Ölçeği puanı ortalaması (18,02±5,49), pandemi öncesine göre çocuğunun kaygı durumunda değişiklik olmadığını belirten ebeveynlerden (16,81±5,28) daha yüksekti (p=0,04)

Sonuç: Pandemi döneminde serebral palsili çocukların rehabilitasyonu kesintiye uğramış ve çocuklar fiziksel ve psikososyal açıdan etkilenmiştir. Gelecek dönemler için aile merkezli yaklaşımlar ve telerehabilitasyon olanakları üzerine çalışmalar yapılmalıdır.

Anahtar Kelimeler: COVID-19, Pandemik, Serebral palsi, Karantina, Ebeveyn, Korku

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Introduction

The COVID-19 pandemic has significantly impacted global life due to the SARS-CoV-2 virus [1]. Although every child was affected by the pandemic, children with special needs were at greater risk during this period. Due to quarantine, the closure of individual education centers, and a decline in family social support systems, it was predicted that this special population would be disproportionately affected by the COVID-19 pandemic. In the majority of countries, Cerebral Palsy (CP) is the most prevalent cause of childhood-onset and lifelong physical disability, affecting 1 in 500 newborns with an estimated prevalence of 17 million [2]. The term CP refers to a collection of lasting movement and posture impairments, which limit an individual's activities due to non-progressive damage to the brain during fetal development or infancy. Along with motor disorders, individuals with CP often experience difficulties with sensory and perception, cognitive function, communication and behavior, epilepsy, and secondary musculoskeletal disorders [3]. Due to their special needs, many children with CP receive lifelong individualized education and rehabilitation. Social isolation, economic challenges, treatment disruptions, and other factors can lead to physical, mental, behavioral, and psychosocial changes in children with CP. These factors may worsen their functional abilities and potentially lead to complications [4].

Varengue R et al. stated that 81% of children with physical disabilities were adversely affected by quarantine. They also reported that behavioral problems were more common and parental stress was higher in these children compared to children without disabilities during the pandemic period [5]. The systematic review, which aimed to analyze the results of studies examining how the COVID-19 pandemic has affected people with physical disabilities, concluded that there was insufficient early research on the impact of COVID-19 on this population [6].

The purpose of this study was to examine the sustainability of the treatment of children with CP during the pandemic period, as well as the physical and psychosocial effects of the disease on children from the parent's perspective. We aimed to compare the affect status of children according to their ambulation levels. We also aimed to compare the fear levels of parents of affected and unaffected children.

Material and Methods

The parents of children with CP younger than 18 years of age who were admitted to our hospital in the last 5 years were contacted through the phone numbers in our hospital registration system and asked whether they wanted to participate in the survey after being informed about the study. The questionnaire form created by the authors and the COVID-19 Fear Scale were filled in to the parents who could be reached and agreed to participate in the survey.

Children's age, gender, place of residence, parents' occupation, loss of job and/or income during the pandemic and whether the child has a history of COVID-19 infection were queried as demographic information.

The authors created a two-part questionnaire form based on their clinical observations of children with CP, which was subsequently utilized in their research. In the first part of the questionnaire, children's medication use, school and/or special education attendance, cognitive education, online education, physiotherapy, orthotic use, and whether they were able to continue during the pandemic period, and home exercise frequency before and after the pandemic were asked. The questions were closed-ended, yes/no, or multiple-choice in nature. Also Gross Motor Function Classification System (GMFCS) were queried.

GMFCS is a standard classification used to quantify the "severity of movement disability" in children with cerebral palsy. Children classified as Level I in the Gross Motor Function Classification System (GMFCS) can perform age-appropriate activities, but may experience some difficulty with speed, balance, and coordination. On the other hand, children classified as Level V typically have difficulty controlling their head and trunk posture in most positions, and struggle with voluntary movement [7]. Morris et al. revised the GMFCS Family Report Questionnaire for parents and caregivers in 2004 [8]. It was determined that the Turkish version was reliable, valid, and consistent [9].

In the second section of the questionnaire, changes in physical and linguistic development, sleep quality, and anxiety levels among children relative to the pre-pandemic period were examined. This section's questions were answered the same or worse. Furthermore, the study also assessed parents' fear of COVID-19 by utilizing a COVID-19 Fear Scale that comprised of 7 questions. Ahorsu et al. developed the components of this scale by extensively reviewing existing fear scales, consulting with experts, and gathering feedback from study participants. The COVID-19 Fear Scale is comprised of seven items rated on a five-point Likert scale (1 = Strongly disagree; 5 = Strongly agree), and is characterized by a single-factor structure. The internal consistency of the scale was determined to be 0.82, and its test-retest reliability was found to be 0.72. A high score on the scale suggests a greater fear of COVID-19. Additionally, the Turkish version of the scale has been shown to be both reliable and valid [10,11].

Ethics approval: The present study obtained ethical approval from the Clinical Research Ethics Committee (Protocol 2021/206, dated 02.04.2021) and the Ministry of Health, following review by the local ethics committee of Afyonkarahisar Health Sciences University

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*Statistical analysis:*The statistical analysis was conducted using SPSS Statistics 20.0 software (SPSS Inc., Chicago, IL). Descriptive statistics, such as arithmetic mean, median, standard deviation, and percentage distributions, were used to evaluate the data. The normality of the distribution was assessed based on the skewness and kurtosis values, with values less than 1 or greater than -1 considered acceptable. The Independent Groups T-Test was utilized when comparing the means of two independent groups, while the Chi-square test was used to compare the percentage distributions of categorical data between groups. A p-value of less than 0.05 was considered statistically significant.

Results

The parents of 379 of 584 children diagnosed with CP admitted to our hospital in the last 5 years were contacted by telephone between 15.04.2021 and 15.05.2021, and 350 parents who agreed to participate in the study completed the questionnaire.

The mean age of the children was 9.66±3.96 years (2-18). 52% of the children were male and 48% were female. Demographic informations, GMFCS levels, medication, assistive device/orthotic use, education and cognitive education, physiotherapy and COVID histories are given in Table 1.

Of the 173 children who used medication, 2 (1.2%) could not obtain their medication. Among 205 children using assistive devices/orthotics, 10 (4.8%) could not obtain them during the pandemic. Of the 210 children who received an education, 46 (21.9%) could not participate in online education during the pandemic. Of 194 children who received individual education, 123 (63.4%) could not continue during the pandemic. Of 137 children who received physiotherapy, 108 (78.8%) could not continue physiotherapy.

While the frequency of home exercise was 1.68±1.1 per week before the pandemic, it was 1.84±1.21 during the pandemic period (p<0.001). While the frequency of going out was 5.99±1.48 per week before the pandemic, it decreased to 2.62±2 during the pandemic (p<0.001).

According to the statements of the families, 67.1% of the children were in the same physical development as before the pandemic, while 26.3% were worse. In 69.4% of cases, their sleep quality remained unchanged, whereas, in 21.1% of cases, it deteriorated. In 84.3% of cases, their linguistic abilities were the same, and in 11.7% of cases, they were worse. In 58.6% of cases, anxiety levels remained unchanged, while in 39.1% of cases, they increased.

When the status of children according to GMFCS levels were analyzed there was no significant difference in the frequency of worsening physical development, sleep quality, linguistic development or anxiety levels (respectively p=0.078, p=0.113, p=0.130, p=0.374) between the groups (Table 2).

The mean COVID-19 Fear Scale score of the parents was 17.28±5.4. The mean COVID-19 Fear Scale score of the parents who stated that their child's physical development was worse compared to before the pandemic (18.23±5.63) was higher than that of the parents who stated that there was no change in their child's physical development compared to before the pandemic (16.91±5.26) (p=0.031). Parents who reported their child's anxiety level as higher than before the COVID-19 pandemic had a higher mean score on the COVID-19 Fear Scale (18.02 ± 5.49) compared to parents who reported no change in their child's anxiety level before the pandemic (16.81±5.28) (p=0.04) (Table 3).

Discussion

Despite its importance in controlling the pandemic and protecting at-risk groups, social isolation can have a biopsychosocial impact on the lives of children with CP. Due to strict isolation measures in some countries, Panda and Sharawat reported that children with epilepsy and neuromuscular diseases may be deprived of medication [12]. We aimed to examine the sustainability of the treatment of children with CP during the pandemic period and we detected that a small number of children (1.2%) were unable to obtain medication due to pandemic conditions. But we also detected that the rate of children who could not continue physiotherapy was 78.8%, similar to Bıyık et al [13]. Cankurtaran et al. found that in their study, 12.8% of the children with CP had dropped out of physical therapy sessions [14]. We think that this difference in the results is due to the fact that our study was conducted in the early stages of the pandemic when social restrictions were intense.

When we look at the studies carried out in the world outside our country, in surveys conducted by reaching 101 caregivers in India, 25.7% of children had never received any therapy sessions and 23.7% had received online sessions during the pandemic period [15]. In France, 76% of children were home-schooled, while 22% received ongoing medical care, 48% physiotherapy, and 27% occupational therapy. More than 60% of children received therapy from their parents [16]. We also found that the frequency of home exercise increased during the pandemic period. This situation shows the efforts of families to continue physiotherapy at home, as seen in the findings of other studies.

Bıyık et al. reported increased anxiety, pain sensation and sleep problems in at least one out of four children with CP during the pandemic [13]. In our study, 21.1% of children reported worse sleep quality and 39.1% reported

Table 1. Demographic Informations, GMFCS levels, medication, assistive device/orthotic use, education, individual education, physiotherapy and COVID history

Age (Mean±SD) (min-max)		9.66±3.96 (2-18)	
		n=350	%
Gender	Male/Female	182/168	(52%) /(48 %)
GMFCS	GMFCS 1	99	28.3 %
	GMFCS 2	70	20 %
	GMFCS 3	48	13.7 %
	GMFCS 4	10	2.9 %
	GMFCS 5	123	35.1 %
Place of residence	Town center	172	49.1 %
	Town	71	20.3 %
	Rural	107	30.6 %
Mother's Job	Housewife	316	90.3%
	Employee	9	2.6 %
	Officer	16	4.6 %
	Other	9	2.6 %
Father's Job	Employee	102	29.1 %
	Officer	72	20.6 %
	Self-employment	154	44 %
	Not working	22	6.3 %
Medication	Antispastic	62	17.71 %
	Antiepileptic	106	30.29 %
	Other	18	5.14 %
	None	176	50.29 %
Assistive device/orthotic use	Yes	208	59.4 %
	No	142	40.6 %
Education	Yes	210	60 %
	No	140	40 %
Cognitive Education	Yes	194	55.4%
	No	156	44.6 %
Physiotherapy	Yes	137	39.1 %
	No	213	60.8 %
Loss of income in the pandemic	Yes	153	43.7 %
	No	197	56.3 %
COVID positive history	Yes	18	5.1 %
	No	332	94.9%

Mean±SD:Mean ±Standart Deviation, min-max:Minimum-Maximum, n: number of patients,
GMFCS: Gross Motor Function Classification System

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Table 2. Changes in physical and linguistic development, sleep quality, and anxiety levels among children relative to the pre-pandemic period according to GMFCS groups.

	Child's Condition During the Pandemic compared to pre-pandemic		
Physical development	**The same n/(%)**	**Worse n/(%)**	**p**
GMFCS I, II, III n=217	167/77	50/23	0.078
GMFCS IV,V n=133	91/68.4	42/31.6	
Sleep quality	**The same n/(%)**	**Worse n/(%)**	**p**
GMFCS I, II, III n=217	177/81.6	40/18.4	0.113
GMFCS IV,V n=133	99/74.4	34/25.6	
Linguistic development	**The same n/(%)**	**Worse n/(%)**	**p**
GMFCS I, II, III n=217	196/90.3	21/9.7	0.130
GMFCS IV,V n=133	113/85	20/15	
Anxiety levels	**The same n/(%)**	**Worse n/(%)**	**p**
GMFCS I, II, III n=217	136/62.7	81/37.3	0.374
GMFCS IV,V n=133	77/57.9	56/42.1	

GMFCS: Gross Motor Function Classification System, n: number of patients, p: Significance level of data between groups

Table 3. Comparisons of COVID-19 Fear Scale scores according to frequency of changes in physical development, sleeping quality, linguistic development and anxiety levels during the pandemic compared to pre-pandemic

		COVID-19 Fear Scale Mean±SD	**p**
Physical development	The same n=258	16.91±5.26	
	Worse n=92	18.23±5.63	**0.031**
Sleep quality	The same n=276	17.14±5.33	
	Worse n=74	17.79±5.61	0.359
Linguistic development	The same n=309	17.11±5.39	
	Worse n=41	18.56±5.28	0.107
Anxiety levels	The same n=213	16.81±5.28	
	Worse n=137	18.02±5.49	**0.04**

Mean±SD:Mean ±Standart Deviation, n: number of patients, p: Significance level of data between groups

higher anxiety. In a study in the UK, the rate of children whose mental health was negatively affected was up to 90% [17]. In France, quarantine was reported to have negative effects on morale, behaviour, and social interactions. [16]. Sutter et al. reported that more than 40% of children experienced decreased physical activity and mobility and increased stress in their study. In our study, 26.3% of parents reported that their children's physical development was worse. In another study conducted in our country in which 110 children were evaluated, the functional independence scales of the children were significantly worse. [18]. Bıyık et al. found that in their study, more than half of the children had reduced physical activity levels [13]. All these results reveal that children with CP have been greatly affected by the pandemic.

The results of limited studies examining the effects of the pandemic on children with CP based on their mo-

bilization levels suggest that physical and psychological effects may be more prevalent in children who are unable to mobilize or who have more severe clinic. In the study by Bıyık et al. the number of body parts with increased muscle tone, the number of restricted joints, and changes in activity and participation levels were higher in children with GMFCS levels IV and V compared to children with GMFCS levels I, II and III [13]. According to the results of your study, there was no significant difference in the frequency of worsening physical development, sleep quality, linguistic development, or anxiety levels between the GMFCS groups. Bıyık et al. investigated children with objective evaluations but in our study these results were the parent's subjective assessments. For this reason, this difference in results may be due to the evaluation method.

During the pandemic, the anxiety levels of caregivers were found to be high [5,19,20,21]. Cacioppo et al. conducted a study where they found that the primary concern of parents was rehabilitation (72%), and their primary challenge was the mental burden (50%) [16]. According to Sutter et al.'s study, participants who reported a decrease in the number of therapies also reported a decrease in the child's mobility, and an increase in caregiver stress [19]. The parent's level of anxiety may affect the home-based continuation of the rehabilitation process. A statistically significant difference was found in the trait anxiety levels of caregivers who exercised their child at home compared to those who did not [20]. Because parents' anxiety and fears of COVID may affect their approach to their children and thus their situation in this period we also evaluated parents' fear of COVID. The mean COVID-19 Fear Scale score was 17.28±5.4, like the study by Cankurtaran et al [14]. The COVID fear level of parents who stated that their child's physical development and anxiety level were worse than before the pandemic was higher than the parents who stated that there was no change in their child's physical development and anxiety level before the pandemic. These results suggest that the physical and psychological effects on children may be parallel to the parents' fear of COVID. This situation of parents with high fear and anxiety may be reflected in their children and may have negatively affected the exercise and education process that should continue at home.

Limitations: In our study, the condition of the children was evaluated with questions directed to the families. The fact that children were not evaluated with objective scales is one of the limitations of our study.

Conclusion: During the pandemic period, rehabilitation of children with CP was interrupted and children were affected physically and psychosocially. Parents' fear levels and child influence may be related. Therefore, further studies on family-centered approaches and telerehabilitation opportunities are needed in the future.

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Acta Medica Alanya

Research Article

Araştırma

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Have the Online Patient Information Materials on Biceps Tendon Disorders Adequate, Quality and Readability?

Biseps Tendon Bozukluklarına İlişkin Çevrimiçi Hasta Bilgilendirme Materyalleri Yeterli, Kaliteli ve Okunabilir mi?

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ABSTRACT

Aim: The study aimed to analyze the quality, adequacy and readability of websites created for patients with shoulder complaints associated with biceps tendon disorders.

Methods: The terms 'shoulder injury', 'biceps tendinitis' and 'biceps tendon rupture' were searched in the most used search engines in United States (Google, Yahoo, and Bing). One hundred forty seven websites designed to inform patients were included in the study. The quality, popularity, adequacy and reliability were meausured.

Results: Flesch reading ease scores of websites with content creation by health professionals were significantly lower than those without; in contrast, Flesch-Kincaid grade level (FKGL) and Koleman-Liau index scores were significantly higher ($p<0.05$). Global Quality Score and originality scores were greater in website created by health professionals ($p<0.05$). The Gunning Fog, FKGL, Simple Measure of Gobbledygook, Automated readability index and Linear write formula scores were lower for websites with the HON code than those without the HON code. Also orginality score and Alexa Popularity Rank (APR) scores were lower in websites with HONcode than without HON code ($p<0.05$).

Conclusion: Websites with HON code and prepared by healthcare professionals can provide sufficient and quality information to patients with biceps tendon disorders. The web content available for biceps tendon disorders is above the recommended reading level. Health professionals should be encouraged to increase the readability of the content.

Key Words: Health literacy, Musculoskeletal Disorder, Pain, Patient education, Patient information, Shoulder.

ÖZET

Amaç: Çalışma, biseps tendon bozuklukları ile ilişkili omuz şikayetleri olan hastalar için oluşturulan web sitelerinin kalite, yeterlilik ve okunabilirliğini incelemeyi amaçlamıştır.

Yöntem: Amerika Birleşik Devletleri'nde en çok kullanılan arama motorlarında (Google, Yahoo ve Bing) 'omuz yaralanması', 'biseps tendiniti' ve 'biseps tendon rüptürü' terimleri arandı. Hastaları bilgilendirmek için tasarlanmış 147 web sitesi çalışmaya dahil edildi. Kalite, popülerlik, yeterlilik ve güvenilirlik ölçüldü.

Bulgular: Sağlık profesyonelleri tarafından içerik oluşturulan web sitelerinin Flesch okuma kolaylığı puanları, oluşturmayanlara göre önemli ölçüde düşüktü; aksine, Flesch-Kincaid sınıf düzeyi (FKGL) ve Koleman-Liau endeksi skorları anlamlı olarak daha yüksekti ($p<0.05$). Sağlık profesyonelleri tarafından oluşturulan web sitesinde global kalite puanları ve özgünlük puanları daha yüksekti ($p<0.05$). Gunning Fog, FKGL, Gobbledygook'un Basit Ölçüsü, Otomatik okunabilirlik endeksi ve doğrusal yazma formülü puanları, HON koduna sahip web sitelerinin HON kodu olmayanlara göre daha düşüktü. Ayrıca özgünlük puanı ve APR puanları, HONcode'lu web sitelerinde HONcode'suz web sitelerine göre daha düşüktü ($p<0.05$).

Sonuç: Sağlık profesyonelleri tarafından hazırlanan HON kodlu web siteleri biseps tendon bozukluğu olan hastalara yeterli ve kaliteli bilgi sağlayabilir. Biseps tendon bozuklukları için mevcut olan web içeriği, önerilen okuma seviyesinin üzerindedir. Sağlık profesyonelleri içeriğin okunabilirliğini artırmaya teşvik edilmelidir.

Anahtar Kelimeler: Sağlık okuryazarlığı, Kas-iskelet sistemi bozukluğu, Ağrı, Hasta eğitimi, Hasta bilgilendirme, Omuz.

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Introduction

Health literacy is terminologically defined as "the degree to which individuals can obtain, process, and understand basic health information and services in order to make appropriate health decisions"[1]. Lower health literacy has generally been found to be associated with higher complication rates, more hospitalizations, higher health care expenditures, and poor health care [2].

Advances in information technologies have changed health literacy habits and sources of information. Today, patients use social media, websites, etc. internet-based platforms more in order to have information about any health-related issue [3]. However, it is reported that most of the content on websites claiming to provide health information is not written by health professionals and is not supervised by any governing body or is not bound by any ethical regulation [4]. It is also reported that the quality of websites contents is questionable. For these reasons, the internet can also be a source of inaccurate or inadequate health information [5].

Inaccurate or inadequate information has a negative impact on people's ability to make decisions about health problems. Patients may ignore their serious medical problems or suffer permanent harm because of inaccurate or inadequate health information [6]. The reason for inaccurate or inadequate health information may be that the referenced source does not have sufficient content, its quality is not at the desired level and its readability is low [7].

There are studies investigating the quality and readability of internet content related to different branches of medicine [8]. In addition, the quality and readability of internet content related to different orthopedic diseases such as ankle problems, clavicle fractures, carpometacarpal joint arthritis, hip dysplasia, subacromial impigment were examined [9-11]. However, to the best of our knowledge, there is no study investigating the quality and readability of internet content related to biceps tendonitis and biceps rupture. Therefore the present study aimed to analyze the quality, adequacy and readability of websites created for patients with shoulder complaints associated with biceps tendon disorders.

Material And Methods

Data were scanned on December 16, 2020, using the three preferred search engines in the United States, consisting of Google, Yahoo, and Bing, for diagnosis of 3 common orthopedic conditions, including shoulder injury, biceps tendinitis, and biceps tendon rupture, that were included in the ''Patient Information Materials" section of the uptodate website. All three search engines captured the top 25 websites that contained text for all three patient terms, and only one of the recurring websites was included in the study. Networks that targeted physicians or health professionals, were not in English, contained only videos and newspaper news, presentations at conferences or academic training, and were restricted by subscriptions or fees were excluded. A total of 147 websites were evaluated for quality, adequacy and readability by 3 orthopedist. This type of study no ethics review and approval are required.

Quality: The webpages were reviewed for quality. The educational value for each website was rated using a 5-point global score modified from that of Singh et al. and recorded as Global Quality Score (GQS). These two scoring systems provide nonspecific assessment of the health-related websites [12]. The websites studied were also evaluated as those with and without "Health on the Net Foundation (HON)" code. Websites that meet the criteria for this code are allowed to include a logo on their site showing that it complies with the code. Websites that meet the 8 criteria set by HON are allowed to include a logo on their site showing that it complies with the code. The criteria required to obtain the HON logo are: authority, complementarily, confidentiality, attribution, justifiability, transparency of authorship, financial disclosure, and advertising policy [13].

Popularity: The popularity and visibility of websites were evaluated with "Alexa Popularity Rank". The Alexa Popularity Rank is indicated that how often a website is frequented relative to all other sites on the web over the past 3 months [14].

Adequacy: It was assessed whether the content of the websites studied included a disease definition, the importance, symptoms, signs and treatment of the disease, and the mechanism of the disease occurrence. These six items were identified as the most highlighted six basic contents in texts disseminated for the diseases investigated in our study on the websites of the recognized academic association such as AAOS (American Academy of Orthopedic Surgeons), EFORT(European Federation of National Associations of Orthopedics and Traumatology) and SICOT (International Society of Orthopedic Surgery and Traumatology). Prior to analysis, text from each website was copied into a word processing document and converted to the same font (Times New Roman), text size, and monospaced [15]. Website identifiers, links, sponsors, advertisements, videos, unnecessary images, and author names were removed prior to evaluation to allow for blind scoring.

Readability: All text from the articles was copied and pasted into separate Microsoft Word documents (Microsoft). Authors, advertisements, links, images, copyright notices, disclaimers, acknowledgments, citations, and videos, were excluded. The degree of readability was evalu-

ated using FRES (Flesch reading ease), Gunning Fog, FKGL (Flesch-Kincaid grade level), CLI (Koleman-Liau index), SMOG (Simple Measure of Gobbledygook), ARI (Automated readability index), and LWF (Linear write formula), which are recommended and most commonly used by AAOS for readability [15, 16]. To analyze the readability of this online health information released to patients, used the index scores whic are reported by '' National Institutes of Health, US National Library of Medicine, and Medicare and Medicaid Centers ''[17].

Statistical Analysis: Research data were uploaded to the computer and analyzed using "SPSS (Statistical Package for Social Sciences) for Windows 22.0 (SPSS Inc, Chicago, IL)." Descriptive statistics were presented as median (interquartile range), frequency distribution, and percentage. The data of websites with content prepared by healthcare professionals and websites with content prepared by people other than healthcare professionals were compared. Also the data of the websites with and without HON-code were grouped and compared. The chi-square test and Fisher's Exact Test were used to assess associations between categorical variables. Suitability of variables for normal distribution was assessed using visual (histogram and probability plots) and analytical methods (Kolmogorov-Smirnov test/ Shapiro Wilk test). For variables that did not fit the normal distribution, the Mann-Whitney U test was applied to reveal statistical significance between two independent groups, while the Kruskal Wallis test was performed between three independent groups. The relationship between variables was assessed using Spearman correlation test. The correlation coefficient was interpreted as at "weak level" between 0-0.25, "medium level" between 0.26-0.50, "strong level" between 0.51-0.75 and at "very strong level" between 0.76-1.00. The statistical significance level was taken as $p<0.05$.

Results

The GQS median and APR median were 5 (IQR: 2 - 5) and 69821 (IQR: 5781 - 712202), respectively; furthermore, the APR score was below 25000 for 33.3% of the websites, between 25000 and 250000 for 31.3%, and above 25000 for 35.4%. Of the 147 websites studied, 78.2% had content created by health professionals and 29.3% had a HON code. While 42.9% of the websites studied cited a reference as the content source, 74.1% were enriched with illustrations and images (Table 1).

In assessing the adequacy of the content of the websites studied, 94.6%, 89.1%, 83.0%, 83.0%, 76.2%, and finally 75.5% of the websites included the importance, symptoms, treatment, signs of the disease, and mechanism of the disease occurrence, respectively.

Table 1. Parameters evaluating the quality of websites included in the research

Quality	
Global Quality Score (GQS), median (IQR)	5 (2 - 5)
Alexa Popularity Rank (APR), median (IQR)	69821 (5781 - 712202)
APR groups, n (%)	
<25000	49 (33.3)
25000-250000	46 (31.3)
>250000	52 (35.4)
Characteristics by the source of upload, n (%)	
Health professionals	115 (78.2)
Non-health professionals	32 (21.8)
HON Code, n (%)	
Yes	43 (29.3)
No	104 (70.7)
Originality, n (%)	
Citing reference	63 (42.9)
Not citing reference at all	84 (57.1)
Illustrations and images, n (%)	
Yes	109 (74.1)
No	38 (25.9)

n: number of sites; %: Column percentage; IQR: Interquartile range (25% - 75%)

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The median FRES score of the websites included in the study was 47.8 (IQR: 39.2 - 54.6), the median Gunning FOG score was 12.5 (IQR: 11 - 14), the median FKGL score was 11.0 (IQR: 9.7 - 12.8), CLI median 12 (IQR: 10 - 13), SMOG median 9.9 (IQR: 8.9 - 11.3), ARI median 11.0 (IQR: 9.5 - 13.0) and LWF median was 11.9 (IQR: 9.3 - 14.1).

FRES scores of websites with content creation by health professionals were significantly lower than those without; in contrast, FKGL and CLI scores were significantly higher ($p<0.05$). GQS scores and originality scores were greater in website created by health professionals. In addition, the percentage of websites with reference citations and addressing the importance, symptoms, treatment, signs and mechanism of the disease was significantly higher in websites with content creation by health professionals than in those without ($p<0.05$) (Table 2).

The Gunning FOG, FKGL, SMOG, ARI and LWF scores were lower for websites with the HON code than those without the HON code. Also orginality score and APR scores were lower in websites with HONcode than without HON code ($p<0.05$). Other quality and readibility scores were similar ($p>0.05$) (Table 3).

Discussion

The present study aimed to analyze the quality, adequacy and readability of websites created for patients with shoulder complaints associated with biceps tendon injuries. Websites with and without the HON code had similar adequacy in the content they presented about the disease. Websites without HON code were more original and preferred than websites with HON code. However, the readability of websites with HON code was better than those without HON code. Websites prepared by health professionals offer adequate and quality content about the disease compared to those not prepared by health

Table 2. Distribution of the readability, quality and adequacy of information parameters on websites studied according to the status of uploading content by health professionals

	Characteristics according to the source of upload		
Health Professionals (n = 115)	**Non-health Professionals** (n = 32)		**p**
Readability, median (IQR)			
FRES	46.8 (35.9 - 52.5)	54.0 (45.2 - 60.1)	0.002[a]**
Gunning Fog	12.5 (11.0 - 14.1)	12.6 (10.9 - 13.8)	0.683[a]
FKGL	11.2 (9.9 - 12.9)	10.3 (8.8 - 12.1)	0.019[a]*
CLI	12.0 (11.0 - 13.0)	11.0 (10.0 - 12.0)	0.015a*
SMOG	10.1 (9.0 - 11.6)	9.6 (8.4 - 10.5)	0.058[a]
ARI	11.3 (9.7 - 13.4)	10.7 (9.0 - 12.2)	0.120[a]
LWF	12.0 (9.4 - 14.6)	11.0 (8.6 - 13.2)	0.149[a]
Quality			
GQS, median (IQR)	5 (4 - 6)	2 (1 - 3)	<0.001[a]**
APR, median (IQR)	66943 (7169 - 664215)	157777.5 (450 - 994832.5)	0.996[a]
HON code, n (%)	35 (30.4)	8 (25.0)	0.550[b]
Originality, n (%)	58 (50.4)	5 (15.6)	<0.001[b]**
Illustrations and images, n (%)	83 (72.2)	26 (81.3)	0.300[b]
Adequacy of information, n (%)			
Definition of the disease	109 (94.8)	30 (93.8)	0.685[c]
Importance of the disease	107 (93.0)	24 (75.0)	0.008[c]**
Symptoms of the disease	102 (88.7)	20 (62.5)	<0.001[b]**
Treatment of the disease	104 (90.4)	18 (56.3)	<0.001[b]**
Signs of the disease	99 (86.1)	13 (40.6)	<0.001[b]**
Mechanism of the disease occurrence	97 (84.3)	14 (43.8)	<0.001[b]**

n: Number of websites ; %: Column percentage; IQR: Interquartile range (25%-75%); [a]Mann-Whitney U Test; [b]Pearson Chi-squared test ; [c]Fisher's Exact Test; *p<0.05; **p<0.01, FRES: Flesch reading ease, FKGL: Flesch-Kincaid grade level, CLI: Koleman-Liau index, SMOG: Simple Measure of Gobbledygook, ARI: Automated readability index, LWF: Linear write formula, GQS: Global Quality Score, APR: Alexa Popularity Rank

Table 3. Distribution of the readability, quality and adequacy of information parameters on the websites included in the study according to quality and accreditation status

	HON Code		p
	Yes (n = 43)	No (n = 104)	
Readability, median (IQR)			
FRES	48.8 (44.5 - 57.8)	47.2 (34.1 - 54.5)	0.078[a]
Gunning Fog	11.7 (10.5 - 13.4)	12.8 (11.3 - 14.4)	**0.018[a]***
FKGL	10.4 (9.3 - 12.0)	11.3 (9.9 - 13.6)	**0.024[a]***
CLI	11 (11 - 12)	12 (10 - 13)	0.506
SMOG	9.4 (8.5 - 10.8)	10.1 (9.1 - 11.7)	**0.020[a]***
ARI	10.0 (9.1 - 12.3)	11.5 (9.7 - 13.4)	**0.029[a]***
LWF	10.7 (8.2 - 13.8)	12.3 (10.7 - 14.9)	**0.007[a]****
Quality			
GQS, median (IQR)	5 (2 - 5)	4 (3 - 5)	0.850[a]
APR, median (IQR)	5634 (423 - 29939)	164927.5 (32260.0 - 1070407.2)	<0.001[a]**
Uploading content by health professional n (%)	35 (81.4)	80 (76.9)	0.550[b]
Originality, n (%)	25 (58.1)	38 (36.5)	0.016[b]*
Illustration and images, n (%)	31 (72.1)	78 (75.0)	0.714[b]
Adequacy of information, n (%)			
Definition of the disease	41 (95.3)	98 (94.2)	1.000[c]
Importance of the disease	37 (86.0)	94 (90.4)	0.561[c]
Symptoms of the disease	38 (88.4)	84 (80.8)	0.264[b]
Treatment of the disease	37 (86.0)	85 (81.7)	0.526[c]
Signs of the disease	33 (76.7)	79 (76.0)	0.919[b]
Mechanism of the disease occurrence	33 (76.7)	78 (75.0)	0.823[b]

n: Number of websites ; %: Column percentage; IQR: Interquartile range (25%-75%); [a]Mann-Whitney U Test; [b]Pearson Chi-squared test ; [c]Fisher's Exact Test; *p<0.05; **p<0.01, FRES: Flesch reading ease, FKGL: Flesch-Kincaid grade level, CLI: Koleman-Liau index, SMOG: Simple Measure of Gobbledygook, ARI: Automated readability index, LWF: Linear write formula, GQS: Global Quality Score, APR: Alexa Popularity Rank

professionals. However, the readability of the content presented by health professionals was lower than those not prepared by health professionals.

The quality and readability of online materials related to diseases about different medical fields were investigated. Most of these studies reported that online patient education materials were insufficient in terms of quality and were above the reading level of the society [8]. As in other fields of medicine, there are online contents prepared for orthopeic diseases, but the quantity of these contents is not sufficient [18, 19].

Online patient education materials prepared for orthopedic diseases provide advantages in terms of time and cost compared to other education tools. However, there are serious problems with the adequacy and quality of online content [20]. In their review, Cassidy JT et al reported that the quality of the websites prepared for information on orthopedic diseases is poor [21]. A study of 10 common orthopaedic sports diagnoses, such as reconstruction of the anterior cruciate ligament, medial collateral ligament tear, posterior cruciate ligament tear, rotator cuff tear, meniscal tear, labral tear, tennis elbow, acromioclavicular joint separation, patellofemoral syndrome, and osteochondral defects revealed that the quality of information was generally higher for website with HON code than witout HON code. Garcia GH et al reported that web content accessed for shoulder instability often contains false information [18]. According to the results of the current study, the rate of websites with HON code about the importance, symptoms, signs and injury mechanism of biceps tendon pathologies is higher than those without HON code. According to the current study results; the number of websites with HON code giving adequte information about the importance, symptoms, signs and mechanism of injury of biceps tendon pathologies was higher than those without HON code. Therefore, it can be said that websites

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with HON code provide adequate information about biceps tendon pathologies compared to those without HON code. However, as a result of the study, it was seen that websites without HON code have more original content and have higher popularity. Also in the results of study; it has been seen that the websites prepared by health professionals offer more adequate and higher quality content for biceps tendon disorders than those prepared by non health professional.

Only 12% of general patient informative texts are prepared below the 8th grade level recommended for society [22]. This is also a problem for online content that concerns the orthopedic patient population. Although online content prepared for orthopedic diseases is useful for young, highly educated and internet-savvy patients, it is not suitable for the entire orthopedic patient population [20]. One of the reasons for this is the low readability of the contents of the websites prepared to inform orthopedic patients [23]. Kiapour AM et al reported that online content available for femoroacetebular impigment syndrome was prepared above the recommended level [24]. Akinleye SD et al reported that the online content available for patients with arthroscopic injuries exceeded the average reading ability of adults [25]. According to the current study results, the readability of sites with HON code was higher than the recommended level for the general public, but better than those without HON code. However, another remarkable result of the study was that the readability of websites with content prepared by health professionals was lower than those prepared by non health professional.

The result of the current study that has not been emphasized in the literature before; the content of the websites accessed as a result of the online search for bicep tendon disorders is variable. Websites with HON code and/or prepared by healthcare professionals are more successful in presenting sufficient and quality information to patients. However, the readability of websites prepared by healthcare professionals for biceps tendon disorders is low. With these results, it can be thought that the study will contribute to the literature.

There were some limitations in our study. The first is that non-sponsored websites or websites that do not want to pay fees refuse to obtain a HON code certificate because it has become chargeable in recent years, whereas HON Code can be purchased upfront as a free foundation service. Although the FKGL rating system is well formulated, descriptive audio/visual data (video, sound recording, etc.), in addition to photo and illustration, which do not accompany the rating but support the written text, can increase text comprehension. The number of syllables in words and words in sentences affects computation in this formula and the FRES formula. Besides, although comprehension in this formula can be calculated as good, abbreviations of medical terms that the patient may not understand can also be misleading (e.g., lupus and physis).

Conclusion: Websites with HON code and prepared by healthcare professionals can provide sufficient and quality information to patients with biceps tendon disorders. The web content available for biceps tendon disorders is above the recommended reading level for patients. Health professionals should be encouraged to increase the readability of the content.

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Ethics Committee Approval: Publicly available YouTube videos were used in this study. No ethics review and approval are required for this type of study.

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Research Article

Araştırma

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Disc Herniations with Spontaneous Regression

Spontan Regresyon Gösteren Disk Herniasyonları

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ABSTRACT

Aim: Vertebral disc hernias are a common clinical condition. There are reported cases of recovery without surgery. However, no collective study has yet been conducted to reveal spontaneously regressing disc hernias statistically significant. Our aim is to determine the cases of spontaneous regression disc herniation and to reveal statistically significant and to reveal the chance of spontaneous regression without surgery.

Methods: For this purpose, a retrospective cohort was made from the files of 2,700 patients who came to our clinic during a period of 4.5 years. Surgical indication was determined in 341 patients and 323 patients were operated on. Physical and drug therapy as well as rest were recommended to 18 patients. These 18 patients who did not receive surgical treatment, it was determined that the disc hernias had spontaneous regression. Incidence, relative risk (RR), attributable risk (AR), and rate of protection were calculated. Comparison of the means in the SPSS and Chi-square test.

Results: The most spontaneously regressed disc herniation was determined as L5S1 level. In those treated surgically, surgical intervention as a positive factor was found to provide complete recovery in 94% of patients. Surgery indication determined that 94.42% of those who had surgery were indicated and those who did not undergo surgery and went to spontaneous regression, represented 5.57%. Spontaneous regression of disc hernias without surgery was found to be statistically significant ($p<0.05$).

Conclusion: It is important to consider the possibility of spontaneous regression before surgical treatment in disc herniations. In disc herniation, time should be allocated for the body's inflammatory response to heal.

Key Words: Disc herniation, Spontaneous regression, Cohort, Retrospective

ÖZET

Amaç: Vertebral disk hernileri sık görülen bir klinik durumdur. Cerrahiye gitmeden iyileşen vakalar vardır. Spontan regresyon gösteren disk hernilerini istatistiksel olarak anlamlı şekilde ortaya koyan bir toplu çalışma yapılmamıştır. Amacımız, cerrahi endikasyona rağmen, spontan regresyon gösteren disk hernisi vakalarını belirleyip istatistiksel olarak anlamlı şekilde ortaya koymaktır.

Yöntemler: Bu amaçla, 4,5 yıldır beyin cerrahisine gelen 2700 hastanın dosyalarından retrospektif kohort yapıldı. 341 hastaya cerrahi endikasyon kondu. 323 hasta opere edildi. Cerrahi endikasyona rağmen ameliyat olmayan 18 hastaya fizik tedavi, ilaç tedavisi, istirahat önerildi. 18 hastanın kontrol MRG sonuçlarına göre disk hernilerinin spontan gerilediği belirlendi. İnsidans, rölatif risk (RR), atfedilen risk (AR) ve korunabilirlik hızı hesaplandı. Demografik değerler için SPSS'de ortalamaların karşılaştırılması kullanıldı. Ki-kare testi yapıldı. $P<0,05$ istatistiki olarak anlamlı kabul edildi.

Bulgular: Disk herrnisi spontan regresyon gösterenlerin yaş ortalaması 46,4 idi. Yaş olarak iki grupta istatistiki olarak anlamlı bir fark yoktu ($P>0,05$). En fazla spontan regresyon Lumbal 5 Sakral 1'de görüldü. 4,5 yıl için vertebral disk hernisi insidansı % 12.62 bulundu. Rölatif risk, 1.06 bulundu. Cerrahi uygulananlarda, pozitif etken olarak cerrahi girişimin % 94 hastada tam iyileşme olduğu belirlendi. Negatif etken olarak, cerrahi endikasyon olduğu halde cerrahi yapılmayan, istirahat, medikal ve fizik tedavi uygulananlarda tam iyileşme %100'dü. Cerrahi endikasyonu olup, cerrahi yapılanlar %94,42, cerrahisiz spontan regresyona gidenler %5,57 bulundu. Cerrahi gitmeyenlerin tüm hastalar içindeki yüzdesi % 0,66 idi. Disk hernilerinde, cerrahisiz spontan regresyon düşünülmesi istatistiki olarak anlamlı bulundu ($p<0,05$).

Sonuç: Uygun klinik takipteki disk hernilerinde cerrahi tedaviden önce spontan regresyon ihtimalinin göz önünde bulundurulmalı, vücudun iyileşme yönünde inflamatuar yanıtına zaman verilmelidir.

Anahtar Kelimeler: Disk herniasyonu, Spontan regresyon, Kohort, Retrospektif

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Introduction

The first report of spontaneous regression of lumbar disc herniation was made in 1984 [1]. Many case reports continued to be published afterwards. Today, although spontaneous regression in disc herniation is a well-known and frequently reported phenomenon, the exact healing mechanism has not been fully explained [2-13]. Patients were evaluated together with clinical and radiological findings, and recovery was demonstrated according to clinical and radiological findings. Studies to date have definitively demonstrated that there is spontaneous regression in disc hernias. However, it has not yet been revealed whether spontaneous regression can be an alternative to the surgical approach in disc hernias, nor the statistically significant value of the definitive recovery chance, when surgical treatment is not chosen despite the surgical indication. Ultimately, opting for spontaneous regression has not been established as a definitive evidence-based treatment. Analytical examination on this subject has not been done yet. In the simplest instances, when the spontaneous regression case reports of disc herniation are examined, the recovery times determined by clinical and imaging methods can vary from two to twenty-four months. In retrospective and prospective epidemiological studies on spontaneous regression of disc hernias, the causality criteria of strength of the relationship, consistency of the relationship, temporality of the relationship, biological acceptability of the relationship and compatibility with all information (biologic plurality and coherence) has not been set. In this sense, the advantages and disadvantages of disc herniation in the choice between surgical treatment and recovery, or spontaneous regression and recovery, have not been scientifically revealed. In our study, a statistically significant advantage of spontaneous regression over surgical intervention was shown, in disc herniation.

Material and Methods

For our purpose, a retrospective cohort was constituted from the files of 2,700 patients who came to our neurosurgery clinic during a period of 4.5 years. It was observed that surgical indication was ascertained with the diagnosis of vertebral disc herniation in 341 patients, according to the clinical conditions of the patients determined by basic physical examination and magnetic resonance imaging (MRI) methods. 323 patients were operated. Physical therapy, drug therapy or rest were recommended to eighteen patients who did not have surgery for various reasons, although the decision for surgical indication was provided. Spontaneous regression of disc hernias was observed according to the control physical examination and control MRI results of these eighteen patients who did not receive surgical treatment (Table 1).

Statistical analysis

Incidence, relative risk (RR), attributable risk (AR) and rate of protection were calculated. Comparison of the means in the SPSS program was used for demographic values. The Chi-square test was performed; $P<0.05$ was considered statistically significant.

Results

2,700 patients were equally split between males (50%) and females (50%) in gender. When comparing the two groups' ages, there was no statistically significant difference ($P>0.05$). Patients who experienced spontaneous disc herniation regression on average were 46.4 years old (Table 1, graph 1). The most spontaneously regressed disc herniation was determined as right lumbar 5 sacral 1 level and left lumbar 5 sacral 1 level. In addition, it was observed that one cervical and one thoracal disc hernia went into spontaneous regression (Table 1, graph 1-2, figure 1). The incidence of vertebral disc hernia for 4.5 years was 12.62%. The relative risk was determined as 1.06. In terms of the relationship between relative risk surgical treatment and spontaneous regression, the two treatment approaches were nearly of equal value in terms of ultimately complete recovery. In those treated surgically, surgical intervention as a positive factor was found to provide complete recovery in 94% of patients. As a negative factor, complete recovery was found to be 100% in patients who did not undergo surgery for various reasons although surgery was indicated, and were given rest, medical treatment or physical therapy. The attributed risk was 6%. In other words, while there was a 6% risk of non-healing in patients who went to surgery, there was no risk of no recovery in patients who went into spontaneous regression. In the absence of surgery for herniated disc, the recovery rate was close to 100%. Surgery indication was found in 12,62% of all patients. It was found that 94.42% of those who had surgery were indicated and those who did not undergo surgery and went to spontaneous regression were 5.57%. The percentage of non-surgical patients among all patients was 0.66%. Considering spontaneous regression in disc hernias without surgery was found to be statistically significant ($p<0.05$) (Table 2).

Discussions

Lumbar and cervical disc herniation is one of the most typical spinal diseases. Although thoracic hernias are rare, the surgery in these cases is challenging. One of the most important factors affecting the outcome in disc surgery is the selection of the appropriate patient [1-3]. Only 1 to 2% of all patients with lumbar discopathy refer to surgeons. Cauda syndrome is seen in approximately

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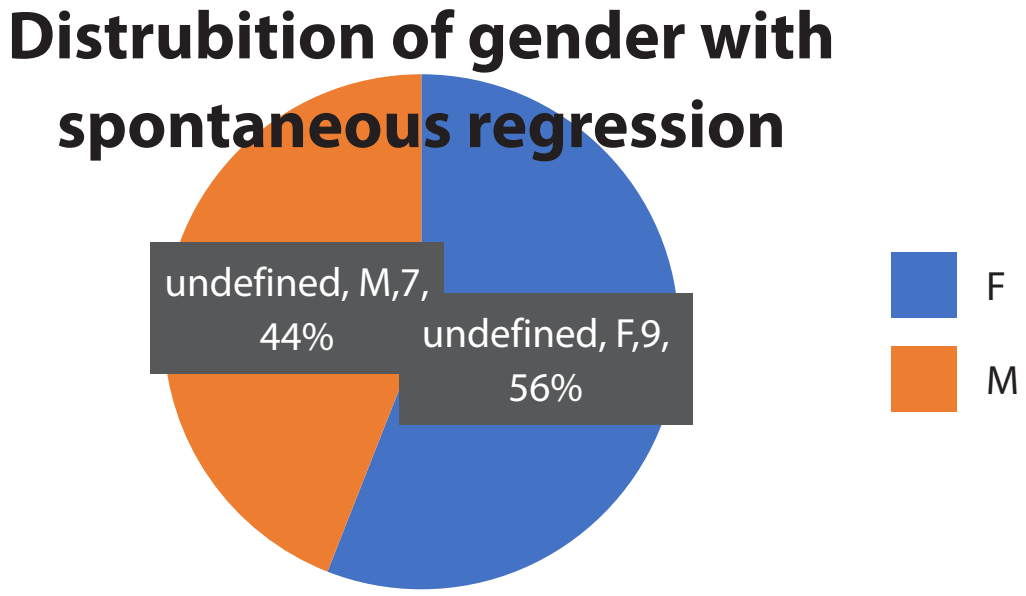
Table 1. In neurosurgery, patients with regression of disc herniation without surgery, although two thousand patients were screened within two years and had surgery indications.

sex	age	level of disk hernia	type of hernia	neurologic deficit	laseq test	physical therapy	resting	medical therapy	time for regression in hernia
m	60	R L4-5	protrusion	+	35	+	+	+	3 months
m	51	L L5-S1	extrude	_	10	_	+	+	2 months
f	53	R L5-S1	p/e	-	70	_	+	+	2,5 months
f	30	R L4-5	p/e	-	45	_	+	+	3 months
m	51	R L5-S1	extrude	-	55	_	+	+	15 months
f	37	L L5-S1	protrusion	mild neurologic deficit	60	+	+	+	12 months
f	52	R L4-5	protrusion	_	25	+	+	+	5 months
f	49	L L2-3/R L5-S1	extrude	_	65	_	+	+	2 months
m	70	R L5-S1	protrusion	_	45	+	+	+	6 months
m	39	L L4-5	extrude	_	35	+	+	+	3 months
f	36	L L4-5	extrude	_	10	_	+	+	6 months
f	36	L L5-S1	extrude	_	25	+	+	+	1 months
f	36	R L5-S1	protrusion	_	40	_	+	+	4 months
f	46	R L4-5	extrude	_	70	_	+	+	6 months
f	25	L L5-S1	extrude	_	35	_	+	+	18 months
f	71	L L5-S1	extrude	_	55	_	+	+	6 months
m	46	R TH12- L1	protrusion	_		_	+	+	8 months
m	48	L C5-6	protrusion	_		+	+	+	24 months

m; MALE, f; FEMALE, R; RIGHT, L; LEFT, L5; LUMBAL 5 VERTEBRAE, S; SACRAL VERTEBRAE, C; CERVICAL VERTEBRAE, TH; THORACAL VERTEBRAE, +; present, -; absent, p/e; protrusion/extrude



m; MALE, f; FEMALE

Graph 1. Distribution of gender with spontaneous remission

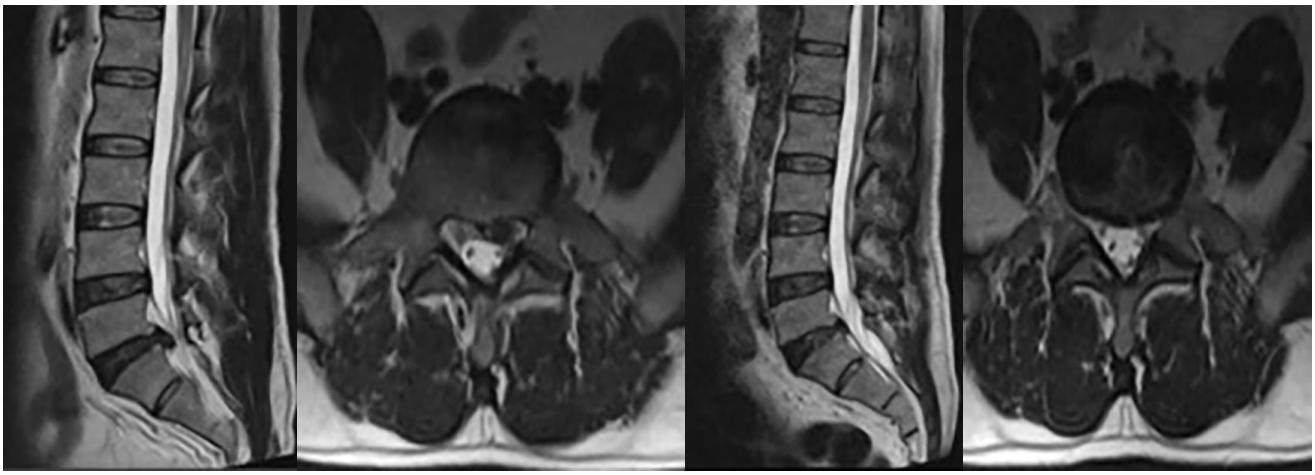
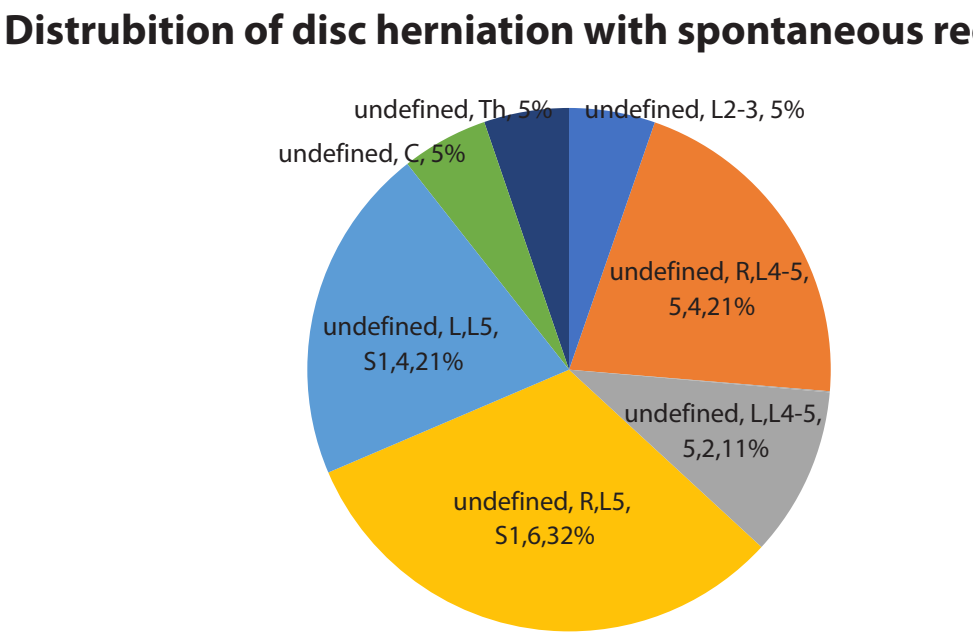


Figure 1. T2-weighted MRI showed caudal migration of the herniated nucleus pulposus and complete spontaneous regression of the herniated nucleus pulposus at the L5S1 level (her complaints were resolved 12 weeks later)

Table 2. A retrospective cohort was made from the files of 2700 patients who came to our neurosurgery clinic for 4.5 years.

Incidence of vertebral disc herniation for 4.5 years	12.62 %
Those who have a surgical indication and undergo surgery	94.47 %
Those who did not undergo surgery and went to spontaneous regression	5.57 %
Relative risk (RR)	1.06
Recovery from surgery	94 %
Recovery from spontaneous regression	100 %
Attributed risk (AR)	6 %
Recovery rate without surgery for disc herniation	100 %
Spontaneous regression of disc hernias without surgery was found to be statistically significant	P<0.05



R; RIGHT, L; LEFT, L5; LUMBAL 5 VERTEBRAE, S; SACRAL VERTEBRAE, C; CERVICAL VERTEBRAE, TH; THORACAL VERTEBRAE

Graph 2. Distribution of disc herniation with spontaneous regression

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0.0004% of all patients with low back pain [4]. Especially in the majority of patients with lumbar disc herniation, there is a chance to regress in the clinic and return to their daily lives with medical treatment, without the need for a surgical intervention [5], and it improves by 85% in approximately six weeks [3]. This can be seen in cervical disc herniation, specifically in soft discs. With many medical and physical therapy programs performed today, there are studies in which full recovery is achieved even in extruded discs. When we look at the literature, there are many previous and recently published studies on the spontaneous regression of herniated nucleus pulposus, primarily in the lumbar region, cervical region and thoracic region [1,6-10]. In the literature on spontaneous regression, three hypotheses are accepted to a greater extent. The first of these is retraction of the disc into the intervertebral space, the second is the shrinkage of the sequestered part due to dehydration, whereas the third and most widely accepted is regression due to inflammatory and phagocytic processes [11,12]. It has been suggested by in vitro studies that vascular endothelial growth factor (VEGF) is produced in the surgically removed disc material, VEGF increases when macrophages are added, and in another study, matrix metalloproteinases (MMP) released from macrophages are effective in disc resorption [10,11]. It is thought that vascularization plays a serious role in disc resorption [12].

Ninety percent of patients with lumbar disc herniation can recover without surgery. The painful phase of recovery can be made tolerable by using pain relievers such as muscle relaxants, short-term steroids, and bed rest [4,14-15]. A manuscript on the partial or complete regression of lumbar disc herniation has been published, where the L4-5 area is the most commonly affected, regression occurs more quickly in younger patients and the rate of recovery is greatest between the ages of 41 and 50 [14]. Another finding is that discs that are protruding or detached regress quickly: if large and sequestered discs are located laterally by craniocaudal migration, they tend to regress more readily than smaller and protruding discs [15–18]. Numerous uncertain factors contribute to the causes of spontaneous disc herniation. Age of the patient, dehydration of the nucleus pulposus, hematoma resorption, revascularization, HNP, PLL, cartilage and annulus fibrosus, are some of these factors [19]. In disc herniation, macrophages, B lymphocytes, and CD 68 (+) are observed. On the first day, TNF-alpha and IL-1 are synthesized, and MCP-1 is produced on the third day [4].

The question of whether or not spontaneous regression in disc herniation can be considered as an alternative to surgical intervention should be the main topic of discussion. Surgical intervention in disc herniation may pose a risk for recurrence, postoperative fibrosis as well as serious complications, such as nerve injury and dural injury. In cauda equina syndrome and disc herniation that impairs quality of life surgical intervention may be considered. However, since spontaneous regression due to macrophage phagocytosis is common in cases of sequestered disc herniation, a chance for spontaneous regression may be considered by saving time with medical treatment.

As stated above, spontaneous regression brings many advantages over surgical treatment and it is a method that should be considered for patients, in light of the available information. However, in our study, the fact that the number of patients undergoing surgery for disc herniation was approximately fifteen times higher than the number of patients left to spontaneous regression, is statistically debatable. Cases for study samples in studies conducted at present have been selected from clinics in the hospital. This may result in the "Berkson error", which is well known in epidemiology. In our study, the sample group was selected from patients admitted to the hospital, allowing for potential bias. Therefore, it ensues that future studies should include samples from the whole population.

Limitations This study had limitations, including a single-center design, a shorter study period and a smaller sample size. The principal limitation of this study was the retrospective design.

Conclusions

When the literature is investigated, the presence of spontaneous regression in disc herniation is highlighted with all its features. In our study, we examined regression disc herniation from another angle and concluded that the possibility of spontaneous regression should not be ruled out before surgical treatment.

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Research Article

Araştırma

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Effect of Subthalamic Nucleus Deep Brain Stimulation Treatment on Non-motor Symptoms and Sleep Quality in Parkinson's Disease Patients

Parkinson Hastalarında Subtalamik Çekirdek Derin Beyin Stimülasyonu Tedavisinin Non-motor Semptomlara ve Uyku Kalitesine Etkisi

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ABSTRACT

Aim: To evaluate the effect of subthalamic nucleus deep brain stimulation (STN-DBS) on non-motor symptoms (NMS), sleep quality, and excessive daytime sleepiness in patients with Parkinson's Disease (PD).

Method: Sixteen PD patients, who had undergone bilateral STN-DBS surgery were enrolled. The patients were assessed at the baseline and 12 months after surgery using the Unified Parkinson's Disease Rating Scale (UPDRS), Parkinson's Disease Questionnaire (PDQ-39), Beck Depression Inventory-II (BDI), Hospital Anxiety and Depression Scale (HADS), Pittsburgh Sleep Quality Index (PSQI), Epworth Sleepiness Scale (ESS), and Non-Motor Symptom Questionnaire (NMS-Quest).

Results: There were significant improvements in the levodopa-equivalent daily dose, UPDRS-part-II, UPDRS-part-III, and UPDRS-part-IV at 12 months post-DBS surgery. The NMS-Quest total score at baseline was correlated with the disease duration of the patients (p=0.005 R:0.66). The PSQI score at baseline was significantly associated with a high total UPDRS and HADS score (p=0.03, p=0.004 respectively). There were no significant differences in terms of NMS-Quest total and subdomains thereof and PSQI total score and subdomains thereof, UPDRS-part I, BDI-II and HADS scores between baseline and 12 months post-DBS surgery (p>0.05 for all of them).

Conclusion: STN-DBS surgery did not change subjective sleep quality, excessive daytime sleepiness, and NMS although it improved motor symptoms, motor fluctuations, and the health-related quality of life.

Key Words: Subthalamic nucleus deep brain stimulation (STN-DBS), Sleep quality, Non-motor symptoms

ÖZET

Amaç: Parkinson Hastalığı (PH) olan hastalarda subtalamik nukleus derin beyin stimülasyonunun (STN-DBS) non- motor semptomlar (NMS), uyku kalitesi ve gündüz aşırı uykululuk üzerine etkisini değerlendirmek.

Yöntem: Bilateral STN-DBS cerrahisi geçirmiş 16 PH hastası çalışmaya alındı. Hastalar ameliyat öncesi ve ameliyattan 12 ay sonra Birleşik Parkinson Hastalığı Derecelendirme Ölçeği (BPHDÖ), Parkinson Hastalığı Anketi (PDQ-39), Beck Depresyon Envanteri-II (BDI), Hastane Anksiyete ve Depresyon Ölçeği (HADS), Pittsburgh Uyku Kalitesi İndeksi (PSQI), Epworth Uykululuk Ölçeği (ESS) ve Non-motor Semptom Anketi (NMS-Quest) kullanılarak değerlendirildi.

Bulgular: DBS ameliyatından 12 ay sonra levodopa eşdeğeri günlük dozunda, BPHDÖ-bölüm-II, BPHDÖ-bölüm-III ve BPHDÖ-bölüm-IV'te anlamlı iyileşmeler oldu. Başlangıçtaki NMS-Quest toplam puanı, hastaların hastalık süresi ile koreleydi (p=0,005 R:0,66). Başlangıçtaki PSQI skoru, yüksek BPHDÖ toplam skor ve HADS skoru ile anlamlı şekilde ilişkiliydi (sırasıyla p=0.03, p=0.004). Başlangıçtaki ve DBS cerrahisinden 12 ay sonraki NMS-Quest toplam ve alt alanları, PSQI toplam puanı ve alt alanları, BPHDÖ-bölüm-I, BDI-II ve HADS puanları arasında anlamlı fark yoktu (p>0,05 tümü için).

Sonuç: STN-DBS cerrahisi motor semptomları, motor dalgalanmaları ve sağlıkla ilişkili yaşam kalitesini iyileştirmesine rağmen gündüz aşırı uykululuk halini, subjektif uyku kalitesini ve NMS'yi değiştirmedi.

Anahtar Kelimeler: Subtalamik nukleus derin beyin stimülasyonu (STN-DBS), Uyku kalitesi, Non- semptomlar

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Introduction

Parkinson's Disease (PD) is a chronic, progressive neurodegenerative disorder, characterized by both motor symptoms and non-motor symptoms (NMS). The PD diagnosis is based on the presence of motor symptoms, including bradykinesia, rigidity, and tremor. Main NMS consist of cognitive dysfunction, psychiatric symptoms, sleep disturbances, fatigue, autonomic dysfunction, olfactory dysfunction, gastrointestinal dysfunction, and pain. NMS are very common in PD patients. Also, NMS have a more negative effect on health-related quality of life compared with motor symptoms, even in the early stages of PD (1). Sleep disorders are common NMS and have a prominent negative effect on the quality of life in PD patients. Multiple sleep disorders, such as sleep fragmentation, insomnia, REM sleep behavior disorder, excessive daytime sleepiness (EDS), periodic limb movements during sleep, and restless legs syndrome, may be seen in PD patients (2).

Subthalamic nucleus deep brain stimulation (STN-DBS) is an effective treatment, especially in PD patients with motor complications despite the best medical therapies. STN-DBS treatment effectively improves motor symptoms and quality of Life (QoL) and decreases the need for dopaminergic drugs (3). However, in the literature, there are fewer studies on the effects of STN-DBS surgery on NMS than its effects on motor symptoms. Moreover, limited available data on the effects of STN-DBS surgery on NMS, is still controversial. Some authors have reported that the total NMS burden was mitigated post-STN-DBS surgery (4-6). In contrast, some NMS such as cognitive performance, depression, suicidal attempts, impulsivity, mania, and apathy might have been worsened after STN-DBS surgery (7, 8). In addition, data on the effects of STN-DBS surgery on sleep quality and EDS, is also still contradictory. A previous study has reported improvements both in subjective sleep quality and objective sleep parameters after DBS surgery (9). Some studies have found an improvement in subjective sleep quality despite no change or deterioration in objective sleep parameters post-DBS surgery (10, 11). Although most studies have reported no changes in EDS (12-14), a few studies have demonstrated an improvement in EDS after STN-DBS surgery (15, 16). We aimed to investigate the effect of STN-DBS on NMS total and subdomains, the subjective sleep quality, and the EDS of the patients.

Material and Method

This retrospective study was approved by the University of Akdeniz Ethics Committee (KAEK-672). Sixteen advanced-stage PD patients, who had undergone bilateral STN-DBS surgery at Akdeniz University, were enrolled in this study. The indication criteria for STN-DBS surgery were the presence of a conclusive diagnosis of idiopathic PD, troublesome motor complications, including motor fluctuations or dyskinesia despite the best medical treatment and motor response to dopaminergic drugs, and the absence of uncontrolled psychiatric diseases and dementia. All surgeries were performed by the same neurosurgeon (T.U.). All patients were routinely followed by the same neurologist (N.Ş.E) during the pre-operative and post-operative periods. A week post-surgery, stimulation was turned on. During follow-ups, the stimulation settings were adjusted to provide a maximum decline in motor symptoms while avoiding the negative effects of stimulation. Informed consent forms for data collection were signed by all the patients during the visits.

Demographic information, such as sex, age, and disease duration, was collected from an electronic medical database. The patients' dopaminergic drug doses were evaluated using levodopa-equivalent daily dose (LEDD). The patients' clinical stages were assessed by a modified Hoehn and Yahr scale and the Unified Parkinson's Disease Rating Scale (UPDRS) at the baseline and follow-up visit 12 months post-DBS-surgery. UPDRS includes four parts, Part I assesses "non-motor experiences of daily life," Part II assesses "motor experiences of daily life, and Part IV assesses "motor fluctuations". Part III related to motor examination was tested under two conditions; medication-ON (Med-ON) and medication-OFF (Med-OFF) condition. Med-ON was considered as at least an hour after taking their usual levodopa dose and Med-OFF was considered as at least 12 hours without taking dopaminergic medications. At follow-up visits 12 months post-DBS surgery, the UPDRS part III was performed both under Med-ON and Med-OFF conditions when stimulation was on. The health-related quality of life of the patients was assessed with the Parkinson's Disease Questionnaire (PDQ-39), consisting of 39 items and measures "quality of life" in eight domains; mobility, stigma, activity living, communication, emotional well-being, social support, cognition, and pain. The total score ranges from 0 to 100 and a higher score indicates a poorer health-related quality of life.

The cognitive performance of the patients was performed with Mini-Mental State Examination (MMSE) scale. Montreal Cognitive Assessment (MoCA) was also used to evaluate the cognitive performance of patients. The total MoCA score ranges from 0 to 30 and a higher score shows a better cognitive function. The patients' mood was assessed with Beck Depression Inventory-II (BDI) and Hospital Anxiety and Depression Scale (HADS). BDI-II is a self-report psychometric scale, aiming to evaluate depressive symptoms. Higher global BDI-II scores indicate more severe depressive symptoms. HADS is a self-assessment scale to determine the level of depression and anxiety in a hospital medical outpatient clinic setting. It consists of 14 items, half of which are related to anxiety. Higher total HADS score shows more anxiety and depressive symptoms.

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The sleep quality of the patients was evaluated with the Pittsburgh Sleep Quality Index (PSQI) scale. It is a reliable scale that evaluates sleep quality over a 1-month term. It consists of 19 questions, including seven domains following subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medication and daytime dysfunction. A higher total PSQI score indicates poorer sleep quality. A PSQI total score of greater than 5 is accepted as poor sleep quality. The Epworth Sleepiness Scale (ESS) was used to evaluate EDS in the patients. The ESS requires people to rate their likelihood of falling asleep in 8 different real-life situations over the past month. The total ESS score is the sum of scores for the 8 items and ranges from 0 to 24. A higher ESS score represents greater daytime sleepiness. The ESS scores greater than 10 represent excessive daytime sleepiness.

The non-Motor Symptom Questionnaire (NMS-Quest) is a self-administered 30-item questionnaire, featuring responses as "yes," or "no," to each item with the aim of screening for the presence a wide of spectrum of NMS. A "Yes," answer indicates that the patient had experienced the problem during the previous month. NMS-Quest consists of nine different domains (gastrointestinal, urinary, sexual function, cardiovascular/falls, sleep/fatigue, mood, perceptual problems/hallucinations, attention/memory and miscellaneous symptoms including unexplained pain, olfaction, weight changes and excessive sweating). A total NMS-Quest score and an NMS-Quest subdomain score are calculated by summing 'Yes' answers indicating '1' point. An NMS-Quest total score of under 10 represents mild NMS, an NMS-Quest total score of 10 to 20 represents moderate NMS and an NMS-Quest total score of greater than 20 represents severe NMS.

Statistical Analysis: Descriptive statistics were presented as frequency, percentage, mean±standard deviation, and median (interquartile range, IQR), where appropriate. Shapiro-Wilk test, histogram and Q-Q graphics were used for evaluation of normality of distribution. Fisher's exact test was used to analyze relationships between categorical variables. For the comparison of continuous variables, Student's t-test was used when variables showed normal distribution, whereas the Mann-Whitney U test was used in the contrary case. Spearman correlation analysis was applied to determine relationships between ordinal variables or those not conforming to normal distribution. Pearson correlation test was applied to continuous variables with normal distribution. Correlation coefficients were interpreted as 0.00-0.50 = a weak correlation, 0.50 -0.70 = a moderate correlation and 0.70 – 1.00 = a strong correlation. Statistical analyses were performed by using the SPSS version 21.0 package program for Windows. P values <0.05 were accepted to show statistical significance.

Results

The pre-operative and post-operative clinical assessment results of 16 patients were analyzed in this study. Twelve patients (75%) were male. The mean age of the patients at the time of surgery was 53.5±3.6 years. The mean age of patients at the time of PD diagnosis was 42.8±3.4years. The patients had undergone DBS surgery following a mean duration of 10.4±1.4 years after PD diagnosis.

A significant decrease was seen in LEDD at 12 months post-DBS surgery (p<0.001). 12 months after DBS surgery, significant improvements were seen in terms of UPDRS-part-II, UPDRS-part-III (both med-ON and med-OFF conditions), UPDRS-part-IV, Hoehn-Yahr staging (med-OFF condition) (p<0.05 for all of them). A significant decrease was seen in PDQ-39 following DBS surgery (p=0.01). Baseline and one year post-DBS surgery scores for UPDRS-part I, BDI-II, HADS, MMSE and MoCA were not significantly different (p>0.05 for all of them). ***Table 1*** shows the clinical characteristics, mood, cognitive performance and health-related quality of life of the patients during the pre-operative period and at 12-months post-surgery follow-up.

Mean NMS-Quest total scores were 8.9±4.6 and 8.06±5.2 for baseline and after 12-months follow-up, respectively. The NMS-Quest total score at baseline was correlated with the disease duration of the patients (p=0.005; R:0.66) but not with the age, LEDD, and clinical stage of the patients (p>0.005 for all of them). There was no significant difference in the NMS-Quest total score and subdomain score at baseline and 12 months post-DBS surgery (p>0.05 for all of them). At baseline, 8 patients had mild NMS and 8 patients had moderate NMS. At 12 months follow-up post-DBS surgery, 9 patients had mild NMS and 7 patients had moderate NMS. ***Table 2*** summarizes the patients' total and subdomain scores of NMS-Quest at baseline and at 12-months follow-up post-surgery.

The mean total PSQI score was 8.06±5.2 and 6.5±4.8 at the baseline and at 12-months after surgery, respectively. Total PSQI score at the baseline was not correlated with the age, disease duration, LEDD or BDI-II score of the patients (p>0.005 for all of them). PDQI score at the baseline significantly increased with a high total UPDRS and HADS score (p=0.03, p=0.004 respectively). There were no significant differences between baseline scores and 12-months post-surgery follow-up scores for PSQI total and subdomain (p>0.05 for all of them). Nine (56.2%) patients with PSQI scores, greater than 5, had poor sleep quality prior to DBS surgery. At 12 months- follow-up after DBS-surgery, subjective sleep quality improved in 3 of 9 patients with poor sleep quality, yet two patients developed a new-onset poor sleep quality.

The mean total ESS scores at baseline and follow-up visit at 12 month post-surgery were 6.3±3.6 and 5.1±5.6, respec-

Table 1. Clinical characteristics, cognitive performance, and health-related quality of life of the patients during the pre-operative period and at follow-up 12 months post-surgery.

	Baseline mean±sd	**12-Month follow-up mean±sd**	**p**
LEDD (mg)	1697±588	1048±372	***<0.001***
UPDRS-part I	9.8±5.7	9.8±6.7	1
UPDRS-part-II	19.3±8.2	11.8±7.7	***0.01***
UPDRS-part-III (med-ON)	30.1±7.5	25.3±6.1	***0.047***
UPDRS-part-III (med-OFF)	65.8±16	43.5±15	***<0.001***
UPDRS-part-IV	11.4±3.5	4±4.2	***<0.001***
Hoehn-Yahr (med-ON)	2.4±0.3	2.5±0.4	0.3
Hoehn-Yahr (med-OFF)	3.8±0.8	2.9±0.8	**0.001**
PDQ39	42.6±21	26.5±21	***0.01***
MMSE	27.1±2.3	27.9±2.3	0.17
MoCA	21.5±4	22±4.8	0.5
BDI-II	12.4±6.4	12.1±9.5	0.9
HADS	12.5±6.9	10.5±7.5	0.1

LEDD: levodopa-equivalent daily dose, UPDRS: Unified Parkinson's Disease Rating Scale, PDQ-39: Parkinson's Disease Questionnaire, MMSE: Mini-Mental State Examination, MoCA: Montreal Cognitive, BDI-II; Beck Depression Inventory-II, HADS; Hospital Anxiety and Depression Scale

Table 2. The patients' total and subdomain scores of NMS-Quest, during the pre-operative period and at 12-month follow-up post-surgery.

	Baseline mean±sd (min-max)	**12-Month follow-up mean±sd (min-max)**	**p**
NMS-Quest total score	8.9±4.6 (2-15)	8.06±5.2 (0-15)	0.5
Gastrointestinal	1.6±1.5 (0-5)	1.5±1.3 (0-4)	0.9
Urinary	1.5±0.6 (1-2)	1.2±0.85 (0-2)	0.96
Sexual function	0.81±0.83(0-2)	0.75±0.93 (0-2)	0.77
Cardiovascular/falls	0.5±0.51 (0-1)	0.56±0.72 (0-2)	0.75
Sleep/fatigue	1.6±1.4 (0-3)	1.6±1.3 (0-5)	1
Mood	0.56±0.8 (0-1)	0.5±0.73 (0-1)	0.75
Perceptual problems/ hallucinations	0.12 ±0.34 (0-1)	0.6±0.25 (0-O)	0.33
Attention/memory	0.81±0.91 (0-2)	0.56±0.72 (0-2)	0.38
Miscellaneous symptoms	1.3±0.9 (0-2)	1.1±1.04 (0-3)	0.66

NMS-Quest; non-Motor Symptom Questionnaire

tively. The baseline ESS score was not correlated with the patients' age, disease duration, LEDD, BDI-II, HADS, or total UPDRS scores (p>0.05 for all of them). There were no significant differences between ESS total score at baseline and at follow-up visits 12 months post-DBS surgery (p=0.45). EDS had been observed in 2 patients prior to DBS surgery. At follow-up visits 12 months post-surgery, EDS improved in one patient, yet 3 patients developed new-onset EDS. Table 3 summarizes the patients' PSQI total, subdomain, and ESS scores at baseline and 12 months after surgery.

Discussion

The present study evaluated the effect of STN-DBS treatment on sleep quality and non-motor symptoms in PD patients. The present study demonstrated that STN-DBS

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Table 3. The patients' PSQI total and subdomain scores and ESS scores during the pre-operative period and 12-month follow-up post-surgery.

	Baseline mean±sd	12-Month follow-up mean±sd	p
PSQI total score	8.06±5.2	6.5±4.8	0.2
Subjective sleep quality	1.4±0.9	1.25±0.9	0.5
Sleep latency	1.5±1.1	1.3±1.2	0.5
Sleep duration	1.3±1.1	0.93±1.06	0.1
Habitual sleep efficiency	0.81±1.2	0.62±1.02	0.3
Sleep disturbances	1.75±0.6	1.37±0.8	0.1
Use of sleeping medication	0.37±1.02	0.12±0.5	0.4
Daytime dysfunction	1.06±0.77	0.87±1.02	0.4
ESS total score	6.3±3.6	5.1±5.6	0.45

PSQI: Pittsburgh Sleep Quality Index, ESS: Epworth Sleepiness Scale

improved motor symptoms, levodopa-induced motor complications, and health-related quality of life as indicated in previous studies (3, 8).

In this study, NMS was found to be correlated only with the disease duration. We found that NMS, as assessed with UPDRS Part-I, total NMS-Quest and subdomain scores, were not improved with STN-DBS surgery. In the literature, there are conflicting results on the effects of STN-DBS surgery on NMS. A previous study, assessing NMS with NMS-Quest, has found an improvement in total NMS burden at 12 months post-surgery, which was in correlation with improvements in health-related quality of life (4). A 36-month follow-up study has demonstrated that STN-DBS surgery significantly improved total NMS burden and specific NMS, such as sleep/fatigue, urinary symptoms, olfactory functions and pain (5). A recent meta-analysis reported that bilateral STN-DBS therapy significantly reduced total NMS and subdomain scores, including sleep, miscellaneous, urinary, sexual and attention/memory (6). A study has reported that STN-DBS improved some of the NMS domains, such as sleep disturbance, yet worsened cognitive performance, such as verbal fluency and executive function (8). Also, other neuropsychiatric symptoms, such as depression, suicidal attempts, impulsivity, mania and apathy may worsen following STN-DBS surgery (7). In the present study, depression and anxiety symptoms did not change following STN-DBS surgery.

Poor sleep quality was very common in our patients both before and after DBS surgery. We found an association between anxiety symptoms and sleep quality in patients. Also, there was an association between poor sleep quality and high total UPDRS scores. However, despite a significant improvement in total UPDRS scores, STN-DBS treatment did not change PSQI total and subdomain scores. In the literature, there are different results for the effect of STN-DBS therapy on sleep quality. A previous study has found that subjective and objective sleep clinical outcomes improved 6 months after DBS surgery in PD patients (9). Most studies have shown an improvement of the total PSQI score subsequent to STN-DBS surgery (17-19). In contrast, Torun, et al., have shown no significant changes in the total PSQI scores, despite an improvement in the subscore of PSQI, including subjective sleep latency and sleep duration at 3 months post-STN-DBS (20). A meta-analysis, including 30 studies, has demonstrated that in the 6-month follow-up period, STN-DBS treatment improved subjective sleep quality, but did not change most PSG parameters, including sleep efficiency and sleep architecture (10). It has been reported that the improvement in subjective sleep quality could be explained by the improvement in nocturnal mobility, particularly in the early periods after surgery (21). Previous studies have reported a significant association between subjective sleep quality and mood, particularly depression (11, 12). Dulski, et al., have reported that the reason for the improvement in subjective sleep quality despite the worsening of objective sleep parameters at 6 months post-STN-DBS surgery, could be explained by the improvement in mood. They have also shown that at 12 months post-DBS surgery, in parallel to mood deterioration, all subjective sleep quality measures and other non-motor symptoms (especially cardiovascular, gastrointestinal, fatigue and sexual symptoms) were worse than 6 month follow-up visits (11). Therefore, it has been considered that the change in mood due to the placebo effect of the surgery could have a direct effect on subjective sleep quality (21). In this study, no changes in both mood and subjective sleep quality were observed at 12 months post-DBS surgery.

The present study found no correlation between the ESS score at baseline and the age, disease duration, and clinical characteristics of the patients. We showed that total ESS score did not significantly change post-DBS surgery. Also, we observed that EDS worsened in three patients and improved in only one patient post-DBS surgery. In the literature, there are a few studies demonstrating an improvement in the EDS following STN-DBS surgery (15, 16, 22). In contrast, most studies have shown that STN-DBS treatment did not change total ESS scores, despite reductions in dopaminergic drugs as in our study (11-14, 23, 24). Moreover, previous studies have reported no correlation between reduction in dopaminergic medication and changes in ESS scores post-DBS surgery (13, 14). A recent meta analyze including 30 studies also reported that the improvement in excessive daytime sleepiness in the patients did not persist for one year after DBS surgery (10). Multiple factors, including advanced stage, comorbid sleep disorder, the use of anti-Parkinson medication and neurodegeneration of the regions such as the hypothalamus and various brainstem nuclei, responsible for sleep-wake regulation, may have a contribution in EDS in PD patients. We think that the presence of new-onset EDS in our population at 12-month follow-up, could be related to the progression of the disease.

Limitations: This study had several limitations. A major limitation is the small number of patients. The other important limitation is that it was impossible to evaluate the patients' sleep parameters with objective parameters such as PSG. Also, NMS subdomains could not be assessed with objective measures. We did not investigate the effect of STN-DBS surgery on NMS during early post-operative period. The progression of the disease during the 12 months post-surgery may affect the results. Despite these limitations, this study demonstrated, in contrast with most previous studies in the literature, that STN-DBS treatment did not improve NMS, EDS, and sleep quality.

Conclusion: In conclusion, despite improvements in motor symptoms, motor fluctuations and the health-related quality of life, STN-DBS treatment had no beneficial long-term effect on subjective sleep quality, EDS and NMS.

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Research Article

Araştırma

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Factors Associated with Unresponsiveness to Treatment in Patients with Non-Hodgkin Lymphoma: 10 Years of Experience From A Single Center

Non-Hodgkin Lenfoma Hastalarında Tedaviye Yanıtsızlık ile İlişkili Faktörler: Tek Merkezden 10 Yıllık Deneyim

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ABSTRACT

Aim: To investigate factors associated with response to treatment in non-Hodgkin lymphoma (NHL) patients receiving chemo(radio)therapy, and secondarily, to identify parameters influencing mortality.

Methods: This was a retrospective single center study carried out between January 2013 and December 2022. A total of 245 patients newly diagnosed with NHL who were treated in our department were included. Clinicodemographic features, NHL characteristics, treatments and follow-up data were retrieved from the hospital database and charts. Patients were grouped as responders (RT) and non-responders (NRT) to treatment, as well as deceased (DP) and survivors (SP). Factors associated with response to treatment and mortality were determined by univariate and multivariable analysis.

Results: Age was similar in the RT (56.2 ± 14.5) and NRT (59.5 ± 13.7) groups; however, male sex was significantly more frequent in the RT group (58.1% vs. 35.71%; p = 0.042). Multiple logistic regression revealed that female sex, low performance status, frailty, high lymphocyte level, extranodal involvement, mantle cell lymphoma, thrombocytopenia during treatment, and cardiac complications during treatment were independently associated with no response to treatment. With respect to groups based on mortality, the DP group was significantly younger compared to the SP group (50.8 ± 11.7 vs. 57.1 ± 14.6; p = 0.048), while sex distribution was similar (males comprised 54.7% of the DP and 63.6% of SP group). Multiple regression showed that extranodal involvement, thrombosis during treatment, and secondary malignancy were independently associated with mortality.

Conclusion: Considering these characteristics when making treatment decisions and throughout the follow-up period may improve survival and reduce mortality in NHL.

Key Words: Non-Hodgkin lymphoma, Response to treatment, Mortality, Extranodal involvement

ÖZET

Amaç: Kemo(radyo)terapi alan non-Hodgkin lenfoma (NHL) hastalarında tedaviye yanıtla ilişkili faktörleri araştırmak ve ikincil olarak mortaliteyi etkileyen parametreleri belirlemek.

Yöntemler: Bu çalışma Ocak 2013-Aralık 2022 tarihleri arasında retrospektif tek merkezli olarak gerçekleştirilmiştir. Bölümümüzde tedavi gören yeni NHL tanısı almış toplam 245 hasta çalışmaya dahil edilmiştir. Klinikodemografik özellikler, NHL özellikleri, tedavi ve takip verileri hastane veri tabanından ve kayıtlarından elde edilmiştir. Hastalar tedaviye yanıt verenler (RT) ve yanıt vermeyenler (NRT) ile ölenler (DP) ve hayatta kalanlar (SP) olarak gruplandırılmıştır. Tedaviye yanıt ve mortalite ile ilişkili faktörler, tek değişkenli ve çok değişkenli analizlerle belirlenmiştir.

Bulgular: RT (56,2 ± 14,5) ve NRT (59,5 ± 13,7) gruplarında yaş benzerdi; ancak erkek cinsiyet RT grubunda anlamlı olarak daha sıktı (%58.1'e karşı %35.71; p = 0.042). Çoklu lojistik regresyon, kadın cinsiyet, düşük performans durumu, kırılganlık, yüksek lenfosit düzeyi, ekstranodal tutulum, mantle hücreli lenfoma, tedavi sırasında trombositopeni ve tedavi sırasında kardiyak komplikasyonların tedaviye yanıtsızlıkla bağımsız olarak ilişkili olduğunu ortaya koydu. Mortaliteye dayalı gruplara göre, DP grubu SP grubuna kıyasla anlamlı düzeyde daha gençti (50,8 ± 11,7'ye karşı 57,1 ± 14,6; p = 0,048), cinsiyet dağılımı benzerdi (erkekler DP'nin %54,7'sini ve SP'nin %63,6'sını oluşturuyordu). Çoklu regresyon, ekstranodal tutulum, tedavi sırasında tromboz ve sekonder malignitenin mortalite ile bağımsız olarak ilişkili olduğunu gösterdi.

Sonuç: NHL'de tedavi kararı verilirken ve takip süresince bu özelliklerin göz önünde bulundurulması sağkalımı artırabilir ve mortaliteyi azaltabilir.

Anahtar Kelimeler: Non-Hodgkin lenfoma, Tedaviye yanıt, Mortalite, Ekstranodal tutulum

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Introduction

Non-Hodgkin lymphoma (NHL) accounts for about 90% of all lymphomas [1]. It is the 11th most widely diagnosed cancer and 11th most common cause of cancer-related deaths in the world [2]. It is a neoplasm of the lymphoid tissues originating from B and T cell precursors and their mature forms [3]. Approximately 85-90% of NHLs are derived from B cells, while the remaining lymphomas are derived from T cells or natural killer cells [1].

NHLs demonstrate a wide spectrum of pathological characteristics, ranging from the most indolent to the most aggressive malignancies [1]. Various scoring systems have been developed to predict prognosis and make management-related decisions in patients with NHL, such as the International Prognostic Index (IPI) [4], revised-IPI (R-IPI) [5], biological marker-adjusted IPI (B-IPI) [6], the National Comprehensive Cancer Network IPI (NCCN-IPI) [7], and several specialized IPI scores for different NHL subtypes [8,9]. In addition, many independent risk factors have been identified to predict high-risk patients [10-12].

Despite advances in therapies, chemotherapy- and/or radiotherapy-resistant cases and subjects with relapse still represent a considerable proportion of the population with NHL [1]. Similar to all cancers, there is a direct relationship between survival in NHL and appropriate treatment decisions. Response to administered treatment is established as one of the most important prognostic markers associated with NHL-related survival times and mortality rates [1,13]. Therefore, for the optimal management of the disease, it is very important to define high-risk patients not responding to the treatment, before starting treatment. However, there are shortcomings in the availability of prognostic systems with sufficient accuracy to predict treatment-refractory patients. New studies and prognostic markers are needed to identify high-risk patients who are unlikely to respond to treatment [11]. While there are plenty of studies investigating prognostic factors associated with mortality and survival in NHL patients, the number of studies investigating prognostic factors in the context of treatment response is rather low [14,15]. Moreover, existing studies have investigated a limited number of factors [14,15].

Therefore, we aimed to investigate factors related to treatment response in NHL patients receiving chemo(radio) therapy and, as a secondary aim, to identify factors associated with mortality.

Material And Methods

Study design, setting and ethical issues

This was a retrospective single center study carried out at the Hematology Department of Kartal Dr. Lütfi Kırdar City Hospital, Istanbul, Turkey. The protocol for this study was approved by the local ethics committee (date: 22.02.2023, no: 2023/514/244/2). All procedures were performed according to the ethical standards laid down in the Declaration of Helsinki in its latest revision. The requirement for informed consent was waived because of the retrospective study design.

Study participants, inclusion and exclusion criteria

A total of 245 patients newly diagnosed with NHL who received treatment in our department between January 2013 and December 2022 were included in the study. Patients younger than 18 years of age, those whose treatment had not been completed, patients who did not receive treatment for NHL at our center, those undergoing surgical treatment, patients who dropped out of follow-up, those with missing relevant data, and patients who died of causes unrelated to NHL were excluded from the study.

Data collection

Patients' information at initial diagnosis, including age, sex, comorbidity status, smoking status, performance status, presence of B symptoms, blood group, tumor stage and pathology information (NHL type, extranodal involvement, lymph node involvement), R-IPI scores, laboratory results [lactate dehydrogenase (LDH), white blood cell (WBC), lymphocyte and platelet count, hemoglobin, aspartate aminotransferase (AST), alanine aminotransferase (ALT) and C- reactive protein (CRP) levels)] and frailty status were recorded. Also, treatment information and data concerning the period during or after treatment, including interim controls, response to treatment, infection and febrile neutropenia status, anemia, thrombocytopenia and neutropenia status, treatment- or disease-related complications (respiratory, liver, cardiac, renal, gastrointestinal tract, neurologic, psychiatric, dermatologic, musculoskeletal, endocrinologic complications and side effects and thrombosis and severe bleeding), secondary malignancy information, follow-up information, and survival-death information were retrieved from the hospital database and patient charts.

Biochemical and pathological analyses

The blood results studied during the diagnosis process were included in the study. All measurements were made in the Clinical Chemistry Department of Kartal Dr. Lütfi Kırdar City Hospital via use of routine calibrated standard measuring devices according to the manufacturer's recommendations and international standards. Pathological analyses were performed in the Pathology Department of our hospital in accordance with the up-to-date guidelines.

Radiologic imaging

All imaging methods required for cancer diagnosis, nodal and extranodal involvement, response to treatment, secondary tumor diagnosis and complications were performed in our hospital's Radiology and Nuclear Medicine Departments in accordance with international standards using calibrated devices. Imaging with [18F] fluorodeoxyglucose (^{18}F-FDG)-positron emission tomography (PET) / computed tomography (CT) was performed according to the method described previously [11].

Non-Hodgkin lymphoma diagnosis and management

The diagnosis, treatment and follow-up of NHL patients throughout the 10-year study period were performed according to the most up-to-date guidelines from the European Society for Medical Oncology (ESMO) (http://www.esmo.org), National Comprehensive Cancer Network (NCCN), USA, Clinical Practice Guidelines (https://www.nccn.org), and The National Institute for Health and Care Excellence (NICE) (https://www.nice.org.uk). Clinical staging was made according to the Ann Arbor classification system [16].

Instruments and definitions

Performance status (PS) was evaluated by the Eastern Cooperative Oncology Group (ECOG) criteria [17].

The presence of B symptoms was defined as the presence of at least one of the following symptoms; unexplained fever, night sweats, and weight loss (10% in the last six months) [18].

Frailty was assessed using the FRAIL scale, a frailty tool based on 5 components (Fatigue, Resistance (inability to climb stairs), Ambulation (inability to walk a certain distance), Illnesses, and Loss of weight) recommended by The International Association of Nutrition and Aging Task Force. FRAIL scale scores range from 0–5 (i.e., 1 point for each component; 0=best to 5=worst) and the presence of frailty was defined as having 3–5 point [19].

The presence and localization of conglomerate lymph node mass (LNM) and extranodal involvement were detected by PET-CT or CT. An LNM of 7 cm or larger in radiological imaging was defined as conglomerate LNM.

The R-IPI classification was applied as previously described [5]. Briefly, the presence of 5 risk factors (age 60 years, stage III/IV disease, high LDH level, ECOG-PS ≥ 2, more than one extranodal site of disease) was investigated. The absence of any of these factors was classified as "very good", presence of 1 or 2 of them as "good", and presence of more than 2 as "poor" [5]. High LDH was defined as an LDH value of >214 U/L [20].

Responses to treatment were evaluated both in the middle (interim response) and at the end (final response) of the treatment according to the International Workshop Criteria [21] using PET/CT scans. In the interim response, grouping was done as follows: patients with stable disease or progressive disease were defined as "no response", while the other two groups were defined as "complete response" or "partial response" as appropriate, based on the definitions by the International Workshop Criteria. In the final response, the grouping was done as follows: patients with stable disease or progressive disease were defined as "non-responders (NRT)", and patients with complete or partial response were defined as "responders (RT)", again based on the International Workshop Criteria definitions [1]. Patients were also grouped according to their final status as deceased (DP) and survivors (SP).

According to the infection status during or after the treatment, the patients were grouped as no infection (no), infection not requiring treatment (mild), presence of infection requiring treatment but not requiring hospitalization (moderate), and infection requiring hospitalization (severe).

The patients were divided into 5 groups according to their anemia status during or after the treatment as absence of anemia [defined as hemoglobin levels (Hb) ≥12 g/dL [22]], 9.5 ≤ Hb <12, 8.0 ≤ Hb <9.5, 7.0 ≤ Hb <8.0, Hb <7.

Thrombocytopenia status was examined in five groups, during or after the treatment as follows: absence of thrombocytopenia [defined as absolute platelet count (APC) of ≥150000 /μL [23]], 100000 ≤ APC <150000, 50000 ≤ APC < 100000, 30000 ≤ APC < 50000, APC < 30000. Thrombocytopenia management was performed according to the recommendations by the American Society of Clinical Oncology (ASCO) [24,25].

The patients were divided into 5 groups according to their neutropenia status during or after the treatment: absence of neutropenia [defined as the absolute neutrophil count (ANC) of ≥2000 /μL], 1500 ≤ ANC <2000, 1000 ≤ ANC <1500 , 500 ≤ ANC < 1000, ANC < 500 [26]. Febrile neutropenia was defined as the combination of chemotherapy-induced neutropenia (defined as absolute neutrophil count <500 cells/μL or <1000 cells/μL with predicted decrease to <500 cells/μL) and fever (defined as single oral temperature ≥38.3 °C or ≥38.0 °C sustained over a one-hour period) [27]. Management was carried out in accordance with the recommendations of the ASCO and Infectious Diseases Society of America clinical practice guidelines [28,29].

Follow-up time (months) was calculated as the time between the date of diagnosis and the current date or date of death.

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Statistical analysis

The statistical analysis of the data was performed using IBM SPSS for Windows, Version 25.0 (IBM Corp., Armonk, NY, USA). The normality of variables was determined by assessing Histogram and Q-Q plots. Continuous variables were reported as either mean ± standard deviation or median (1st quartile - 3rd quartile) based on their normality, and categorical variables were presented as frequency (percentage). Depending on the normality of the distribution, Student's t-test or Mann Whitney U test was used to compare continuous variables, while categorical variables were compared using the chi-square test, Fisher's exact test, or Fisher-Freeman-Halton test. Logistic regression analysis using the forward conditional method was used to identify significant factors associated with treatment response and mortality, with the initial model including variables that were statistically significant in univariate analyses. The level of statistical significance was set at $p<0.05$.

Results

The rate of non-response to first line treatment was 11.4%. The mean age of the RT group was 56.19 ± 14.49 years, while the NRT group had a mean age of 59.50 ± 13.70 years (p = 0.254). Males represented 58.06% of the RT and 35.71% of the NRT group, and the difference in sex distribution significant (p = 0.042). The percentage of patients with diabetes (p = 0.036), an ECOG-PS of 3 (p = 0.003) and stage IV NHL (p = 0.005) was significantly higher in the NRT group. Hemoglobin level (p<0.001) and follow-up time (p<0.001) of the NRT group were significantly lower than RT. The percentages of patients with frailty (p<0.001), high LDH (p<0.001), extranodal involvement (p = 0.001), conglomerate LNM (p = 0.026), 'poor' R-IPI (p = 0.001), mantle cell lymphoma (p = 0.026), non-response at interim control (p<0.001), severe infection (p<0.001), febrile neutropenia (p<0.001), Hb <8 g/dL (p<0.001) were significantly higher in the NRT group compared to the RT group. Additionally, respiratory (p = 0.034) and cardiac (p = 0.026) complications were more common in NRT, and LDH (p<0.001) and lymphocyte (p = 0.001) levels were significantly higher in NRT (Table 1, Table 2).

The secondary malignancies that occurred were as follows: 1 lung cancer along with stomach cancer, 1 ureter cancer, 1 colon cancer along with bladder cancer and renal cell cancer, 2 malignant melanomas, 1 papillary thyroid cancer, 1 multiple myeloma, 1 colon cancer, 1 bladder cancer, 1 lung cancer, and 1 acute lymphocytic leukemia.

Multiple logistic regression analysis revealed that female sex (OR: 3.388, 95% CI: 1.060 - 10.827, p=0.039), low ECOG-PS score at diagnosis (OR: 1.898, 95% CI: 1.127 - 3.196, p=0.016), frailty at diagnosis (OR: 52.269, 95% CI: 4.096 - 667.070, p=0.002), high lymphocyte level at diagnosis (OR: 3.714, 95% CI: 1.736 - 7.948, p=0.001), extranodal involvement at diagnosis (OR: 5.010, 95% CI: 1.274 - 19.703, p=0.021), mantle cell lymphoma (OR: 7.391, 95% CI: 1.685 - 32.431, p=0.008), thrombocytopenia during treatment (OR: 1.682, 95% CI: 1.104 - 2.564, p=0.016) and cardiac complications during treatment (OR: 13.166, 95% CI: 1.348 - 128.597, p=0.027) were independently associated with non-response to treatment. Other variables included in the analysis, diabetes mellitus at diagnosis (p=0.094), stage at diagnosis (p=0.092), LDH level at diagnosis (p=0.314), hemoglobin level at diagnosis (p=0.179), conglomerate LNM (≥7 cm) at diagnosis (p=0.446), R-IPI at diagnosis (p=0.145), infection during treatment (p=0.880), febrile neutropenia during treatment (p=0.267), anemia during treatment (p=0.898) and respiratory complications during treatment (p=0.985) were found to be non-significant (Table 3).

Analyses concerning mortality showed an overall mortality rate of 8.97%. The mean age of the DP group was 50.77 ± 11.71 years, while it was 57.14 ± 14.55 years in the SP group (p = 0.048). Males represented 54.71% of the DP and 63.64% of the SP group (p = 0.563). Percentage of patients with B symptoms (p = 0.040), extranodal involvement (p = 0.005), thrombosis (p = 0.049) and secondary malignancy (p = 0.001) were significantly higher in DP compared to SP. As expected, median follow-up time of DP was significantly shorter compared to the SP group (p<0.001) (Table 4, Table 5).

Multiple logistic regression analysis revealed that extranodal involvement at diagnosis (OR: 5.534, 95% CI: 1.853 - 16.528, p=0.002), thrombosis during treatment (OR: 6.037, 95% CI: 1.291 - 28.228, p=0.022) and secondary malignancy (OR: 15.322, 95% CI: 3.915 - 59.969, p<0.001) were independently associated with mortality. Other variables included in the analysis age (p=0.058) and B symptoms at diagnosis (p=0.056) were found to be non-significant (Table 6).

Discussion

The main findings of this study demonstrate that female sex and initial findings of ECOG-PS, frailty and lymphocyte count, and the presence of extranodal involvement, mantle cell lymphoma, thrombocytopenia and cardiac complications during treatment were independent risk factors associated with non-response to treatment. Also, extranodal involvement, thrombosis during treatment and secondary malignancy were identified as independent risk factors for mortality.

Response to treatment is one of the most important prognostic markers associated with NHL-related survival times

Table 1. Summary of basic variables with regard to response to treatment

		Response to treatment		
	Total (n=245)	Yes (n=217)	No (n=28)	p
Age	56.57 ± 14.41	56.19 ± 14.49	59.50 ± 13.70	0.254
Sex				
Male	136 (55.51%)	126 (58.06%)	10 (35.71%)	**0.042**
Female	109 (44.49%)	91 (41.94%)	18 (64.29%)	
Smoking	79 (32.24%)	71 (32.72%)	8 (28.57%)	0.820
Comorbidities				
Diabetes mellitus	54 (22.04%)	43 (19.82%)	11 (39.29%)	**0.036**
Hypertension	72 (29.39%)	64 (29.49%)	8 (28.57%)	1.000
Coronary artery disease	33 (13.47%)	30 (13.82%)	3 (10.71%)	1.000
Respiratory diseases	24 (9.80%)	21 (9.68%)	3 (10.71%)	0.744
Chronic renal failure	6 (2.45%)	5 (2.30%)	1 (3.57%)	0.521
Other	15 (6.12%)	15 (6.91%)	0 (0.00%)	0.230
B symptoms	100 (40.82%)	92 (42.40%)	8 (28.57%)	0.232
ECOG performance score				
0	129 (52.65%)	120 (55.30%)	9 (32.14%)	
1	70 (28.57%)	63 (29.03%)	7 (25.00%)	
2	20 (8.16%)	17 (7.83%)	3 (10.71%)	**0.003**
3	24 (9.80%)	16 (7.37%)	8 (28.57%)	
4	2 (0.82%)	1 (0.46%)	1 (3.57%)	
Stage				
Stage I	11 (4.49%)	11 (5.07%)	0 (0.00%)	
Stage II	36 (14.69%)	36 (16.59%)	0 (0.00%)	**0.005**
Stage III	41 (16.73%)	39 (17.97%)	2 (7.14%)	
Stage IV	157 (64.08%)	131 (60.37%)	26 (92.86%)	
Blood group, ABO				
A	155 (63.27%)	138 (63.59%)	17 (60.71%)	
B	12 (4.90%)	11 (5.07%)	1 (3.57%)	0.939
AB	15 (6.12%)	13 (5.99%)	2 (7.14%)	
O	63 (25.71%)	55 (25.35%)	8 (28.57%)	
Blood group, Rh				
Rh(-)	20 (8.16%)	15 (6.91%)	5 (17.86%)	0.062
Rh(+)	225 (91.84%)	202 (93.09%)	23 (82.14%)	
Frailty	156 (63.67%)	129 (59.45%)	27 (96.43%)	**<0.001**
LDH, U/L	245 (190 - 298)	220 (187 - 285)	296.5 (266.5 - 322)	**<0.001**
High LDH (>214)	140 (57.14%)	112 (51.61%)	28 (100.00%)	**<0.001**
WBC, 10^3/uL	5.90 (4.41 - 7.32)	5.96 (4.45 - 7.33)	5.25 (4.15 - 6.78)	0.082
Lymphocyte, 10^3/µL	2.80 (2.43 - 3.30)	2.80 (2.24 - 3.20)	3.17 (2.85 - 3.68)	**0.001**
Hemoglobin, g/dL	13.0 (12.0 - 14.1)	13.2 (12.2 - 14.2)	12 (10.7 - 12.7)	**<0.001**
Platelet, 10^3/µL	209 (162 - 250)	206 (158 - 248)	209.5 (181 - 259)	0.194
AST, U/L	22 (17 - 26)	22 (17 - 26)	18 (12 - 26)	0.094
ALT, U/L	17 (14 - 24)	17 (14 - 25)	15.5 (11 - 21.5)	0.053

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Table 1. Summary of basic variables with regard to response to treatment *(continued)*

CRP, mg/L	10.46 (5.82 - 13.74)	10.14 (4.86 - 13.98)	11.27 (9.77 - 12.56)	0.136
Extranodal involvement	27 (11.02%)	18 (8.29%)	9 (32.14%)	**0.001**
Gastric	10 (4.08%)	7 (3.23%)	3 (10.71%)	
Liver	4 (1.63%)	3 (1.38%)	1 (3.57%)	
Spleen	11 (4.49%)	6 (2.76%)	5 (17.86%)	
Esophagus	1 (0.41%)	1 (0.46%)	0 (0.00%)	
Breast	1 (0.41%)	1 (0.46%)	0 (0.00%)	
Conglomerate LNM (≥7 cm)	22 (8.98%)	16 (7.37%)	6 (21.43%)	**0.026**
R-IPI				
Very good	61 (24.90%)	61 (28.11%)	0 (0.00%)	
Good	135 (55.10%)	118 (54.38%)	17 (60.71%)	**0.001**
Poor	49 (20.00%)	38 (17.51%)	11 (39.29%)	
Diagnosis				
Diffuse large B-cell lymphoma	174 (71.02%)	157 (72.35%)	17 (60.71%)	
Mantle cell lymphoma	27 (11.02%)	18 (8.29%)	9 (32.14%)	
Follicular lymphoma	35 (14.29%)	33 (15.21%)	2 (7.14%)	
Burkitt lymphoma	1 (0.41%)	1 (0.46%)	0 (0.00%)	**0.026**
Double-hit/triple-hit lymphoma	3 (1.22%)	3 (1.38%)	0 (0.00%)	
T-cell lymphoma	5 (2.04%)	5 (2.30%)	0 (0.00%)	
Treatment				
CHOP +/- R	213 (86.94%)	188 (86.64%)	25 (89.29%)	
R-BENDA	1 (0.41%)	1 (0.46%)	0 (0.00%)	
R-PRED	0 (0.00%)	0 (0.00%)	0 (0.00%)	
DA-EPOCH +/- R	25 (10.20%)	23 (10.60%)	2 (7.14%)	0.559
R-LEN	1 (0.41%)	1 (0.46%)	0 (0.00%)	
CHOEP	2 (0.82%)	2 (0.92%)	0 (0.00%)	
CHOP +/- R & DA-EPOCH +/- R	2 (0.82%)	1 (0.46%)	1 (3.57%)	
R-PRED & DA-EPOCH +/- R	1 (0.41%)	1 (0.46%)	0 (0.00%)	

Data are given as mean ± standard deviation or median (1st quartile - 3rd quartile) for continuous variables according to normality of distribution and as frequency (percentage) for categorical variables.
Abbreviations; ALT: Alanine aminotransferase, AST: Aspartate aminotransferase, CHOP +/- R: Cyclophosphamide, doxorubicin, vincristine, and prednisone +/- radiotherapy, CHOEP: Cyclophosphamide, doxorubicin, vincristine, etoposide and prednisone, CRP: C-reactive protein, DA-EPOCH +/- R: Dose-adjusted EPOCH +/- radiotherapy, ECOG: The Eastern Cooperative Oncology Group, LDH: Lactate dehydrogenase, LNM: Lymph node mass, R-BENDA: Bendamustine plus rituximab, R-IPI: Revised International Prognostic Index, R-LEN: Lenalidomide plus rituximab, R-PRED: Prednisone plus rituximab, WBC: White blood cell

Table 2. Summary of follow-up characteristics with regard to response to treatment

		Response to treatment		
	Total (n=245)	Yes (n=217)	No (n=28)	p
Interim control				
No response	13 (5.31%)	4 (1.84%)	9 (32.14%)	
Partial response	84 (34.29%)	65 (29.95%)	19 (67.86%)	**<0.001**
Complete response	148 (60.41%)	148 (68.20%)	0 (0.00%)	
Infection				
No	114 (46.53%)	107 (49.31%)	7 (25.00%)	
Mild	60 (24.49%)	56 (25.81%)	4 (14.29%)	**<0.001**
Moderate (Outpatient)	44 (17.96%)	39 (17.97%)	5 (17.86%)	
Severe (Inpatient)	27 (11.02%)	15 (6.91%)	12 (42.86%)	
Febrile neutropenia	62 (25.31%)	46 (21.20%)	16 (57.14%)	**<0.001**
Anemia				
No	68 (27.76%)	64 (29.49%)	4 (14.29%)	
9.5 < Hb <12 g/dL	116 (47.35%)	108 (49.77%)	8 (28.57%)	
8.0 ≤ Hb ≤ 9.5 g/dL	39 (15.92%)	34 (15.67%)	5 (17.86%)	**<0.001**
7.0 ≤ Hb < 8.0 g/dL	15 (6.12%)	9 (4.15%)	6 (21.43%)	
Hb <7 g/dL	7 (2.86%)	2 (0.92%)	5 (17.86%)	
Thrombocytopenia				
No	186 (75.92%)	176 (81.11%)	10 (35.71%)	
APC > 100000 /µL	29 (11.84%)	24 (11.06%)	5 (17.86%)	
50000 ≤ APC < 100000 /µL	14 (5.71%)	10 (4.61%)	4 (14.29%)	**<0.001**
30000 ≤ APC < 50000 /µL	10 (4.08%)	5 (2.30%)	5 (17.86%)	
APC < 30000 /µL	6 (2.45%)	2 (0.92%)	4 (14.29%)	
Neutropenia				
No	87 (35.51%)	81 (37.33%)	6 (21.43%)	
1500 ≤ ANC < 2000 /µL	28 (11.43%)	27 (12.44%)	1 (3.57%)	
1000 ≤ ANC < 1500 /µL	22 (8.98%)	19 (8.76%)	3 (10.71%)	0.108
500 ≤ ANC < 1000 /µL	34 (13.88%)	30 (13.82%)	4 (14.29%)	
ANC <500 /µL	74 (30.20%)	60 (27.65%)	14 (50.00%)	
Respiratory complications	68 (27.76%)	55 (25.35%)	13 (46.43%)	**0.034**
Liver complications	13 (5.31%)	11 (5.07%)	2 (7.14%)	0.649
Cardiac complications	11 (4.49%)	7 (3.23%)	4 (14.29%)	**0.026**
Renal complications	8 (3.27%)	5 (2.3%)	3 (10.71%)	0.051
Thrombosis	10 (4.08%)	9 (4.15%)	1 (3.57%)	1.000
Severe bleeding	8 (3.27%)	8 (3.69%)	0 (0.00%)	0.602
Gingiva	5 (2.04%)	5 (2.30%)	0 (0.00%)	
Epistaxis	2 (0.82%)	2 (0.92%)	0 (0.00%)	
Hemorrhoid	1 (0.41%)	1 (0.46%)	0 (0.00%)	
GIS side effect[1]	79 (32.24%)	71 (32.72%)	8 (28.57%)	0.820
Nausea/Vomiting	38 (15.51%)	32 (14.75%)	6 (21.43%)	

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Table 2. Summary of follow-up characteristics with regard to response to treatment *(continued)*

Constipation	30 (12.24%)	29 (13.36%)	1 (3.57%)	
Diarrhea	11 (4.49%)	8 (3.69%)	3 (10.71%)	
Oral aphthae/Mucositis	10 (4.08%)	10 (4.61%)	0 (0.00%)	
Gastritis/Dyspepsia	6 (2.45%)	6 (2.76%)	0 (0.00%)	
Dysphagia/Odynophagia	4 (1.63%)	4 (1.84%)	0 (0.00%)	
Neurologic side effect(1)	65 (26.53%)	62 (28.57%)	3 (10.71%)	0.074
Neuropathy/Paresthesia	60 (24.49%)	57 (26.27%)	3 (10.71%)	
Vertigo	6 (2.45%)	6 (2.76%)	0 (0.00%)	
Headache	3 (1.22%)	3 (1.38%)	0 (0.00%)	
Psychiatric side effect(1)	10 (4.08%)	9 (4.15%)	1 (3.57%)	1.000
Insomnia	7 (2.86%)	6 (2.76%)	1 (3.57%)	
Anxiety	3 (1.22%)	3 (1.38%)	0 (0.00%)	
Amnesia	1 (0.41%)	1 (0.46%)	0 (0.00%)	
Dermatologic side effect(1)	27 (11.02%)	25 (11.52%)	2 (7.14%)	0.749
Dermatitis/Urticaria	12 (4.90%)	12 (5.53%)	0 (0.00%)	
Acne	2 (0.82%)	2 (0.92%)	0 (0.00%)	
Zoster	8 (3.27%)	6 (2.76%)	2 (7.14%)	
Cellulitis	3 (1.22%)	3 (1.38%)	0 (0.00%)	
Nail pathology	4 (1.63%)	4 (1.84%)	0 (0.00%)	
Musculoskeletal side effect	3 (1.22%)	3 (1.38%)	0 (0.00%)	1.000
Endocrinologic side effect	3 (1.22%)	3 (1.38%)	0 (0.00%)	1.000
Hypertension	1 (0.41%)	1 (0.46%)	0 (0.00%)	
Diabetes mellitus	1 (0.41%)	1 (0.46%)	0 (0.00%)	
Osteoporosis	1 (0.41%)	1 (0.46%)	0 (0.00%)	
Seconder malignancy	11 (4.49%)	10 (4.61%)	1 (3.57%)	1.000
Follow-up time, months	51 (25 - 82)	60 (31 - 87)	15 (9.5 - 37)	**<0.001**
Final status				
Alive	223 (91.02%)	200 (92.17%)	23 (82.14%)	0.149
Deceased	22 (8.98%)	17 (7.83%)	5 (17.86%)	

Data are given as mean ± standard deviation or median (1st quartile - 3rd quartile) for continuous variables according to normality of distribution and as frequency (percentage) for categorical variables.
(1) Patients may have more than one of the followings.
Abbreviations; ANC: Absolute neutrophil count, APC: Absolute platelet count, GIS: Gastrointestinal system, Hb: Hemoglobin

Table 3. Significant factors independently associated with non-response to treatment, multiple logistic regression analysis

	β coefficient	Standard error	p	Exp(β)	95% CI for Exp(β)	
Sex, Female	1.220	0.593	0.039	3.388	1.060	10.827
ECOG performance score	0.641	0.266	0.016	1.898	1.127	3.196
Frailty	3.956	1.299	0.002	52.269	4.096	667.070
Lymphocyte, 10^3/uL	1.312	0.388	0.001	3.714	1.736	7.948
Extranodal involvement	1.611	0.699	0.021	5.010	1.274	19.703
Diagnosis, Mantle cell lymphoma	2.000	0.754	0.008	7.391	1.685	32.431
Thrombocytopenia	0.520	0.215	0.016	1.682	1.104	2.564
Cardiac complications	2.578	1.163	0.027	13.166	1.348	128.597
Constant	-12.080	2.289	<0.001			

Nagelkerke R^2=0.574
Abbreviations; CI: Confidence Interval, ECOG: The Eastern Cooperative Oncology Group

Table 4. Summary of basic variables with regard to mortality

	Final status		
	Alive (n=223)	Deceased (n=22)	p
Age, years	57.14 ± 14.55	50.77 ± 11.71	**0.048**
Sex			
Male	122 (54.71%)	14 (63.64%)	0.563
Female	101 (45.29%)	8 (36.36%)	
Smoking	72 (32.29%)	7 (31.82%)	1.000
Comorbidities			
Diabetes mellitus	48 (21.52%)	6 (27.27%)	0.590
Hypertension	69 (30.94%)	3 (13.64%)	0.146
Coronary artery disease	32 (14.35%)	1 (4.55%)	0.326
Respiratory diseases	22 (9.87%)	2 (9.09%)	1.000
Chronic renal failure	6 (2.69%)	0 (0.00%)	1.000
Other	15 (6.73%)	0 (0.00%)	0.374
B symptoms	86 (38.57%)	14 (63.64%)	**0.040**
ECOG performance score			
0	117 (52.47%)	12 (54.55%)	0.908
1	64 (28.70%)	6 (27.27%)	
2	19 (8.52%)	1 (4.55%)	
3	21 (9.42%)	3 (13.64%)	
4	2 (0.90%)	0 (0.00%)	
Stage			
Stage I	11 (4.93%)	0 (0.00%)	0.190
Stage II	34 (15.25%)	2 (9.09%)	
Stage III	40 (17.94%)	1 (4.55%)	
Stage IV	138 (61.88%)	19 (86.36%)	
Blood group, ABO			

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Table 4. Summary of basic variables with regard to mortality *(continued)*

A	142 (63.68%)	13 (59.09%)	0.620
B	12 (5.38%)	0 (0.00%)	
AB	14 (6.28%)	1 (4.55%)	
O	55 (24.66%)	8 (36.36%)	
Blood group, Rh			
Rh(-)	18 (8.07%)	2 (9.09%)	0.697
Rh(+)	205 (91.93%)	20 (90.91%)	
Frailty	142 (63.68%)	14 (63.64%)	1.000
LDH, U/L	245 (190 - 298)	236.5 (187 - 308)	0.981
High LDH (>214)	127 (56.95%)	13 (59.09%)	1.000
WBC, 10^3/uL	5.90 (4.39 - 7.32)	6.14 (5.33 - 7.33)	0.516
Lymphocyte, 10^3/ µL	2.80 (2.41 - 3.25)	2.86 (2.65 - 3.46)	0.149
Hemoglobin, g/dL	13.0 (12.0 - 14.1)	13.05 (10.8 - 14.1)	0.490
Platelet, 10^3/ µL	206 (158 - 248)	236 (175 - 299)	0.184
AST, U/L	22 (17 - 26)	18.5 (16 - 25)	0.082
ALT, U/L	17 (14 - 24)	16.5 (14 - 25)	0.727
CRP, mg/L	10.62 (5.82 - 13.90)	9.59 (5.74 - 12.18)	0.281
Extranodal involvement	20 (8.97%)	7 (31.82%)	**0.005**
Gastric	7 (3.14%)	3 (13.64%)	
Liver	3 (1.35%)	1 (4.55%)	
Spleen	8 (3.59%)	3 (13.64%)	
Esophagus	1 (0.45%)	0 (0.00%)	
Breast	1 (0.45%)	0 (0.00%)	
Conglomerate LNM (≥7 cm)	21 (9.42%)	1 (4.55%)	0.703
R-IPI			
Very good	59 (26.46%)	2 (9.09%)	0.155
Good	119 (53.36%)	16 (72.73%)	
Poor	45 (20.18%)	4 (18.18%)	
Diagnosis			
Diffuse large B-cell lymphoma	158 (70.85%)	16 (72.73%)	0.526
Mantle cell lymphoma	24 (10.76%)	3 (13.64%)	
Follicular lymphoma	33 (14.8%)	2 (9.09%)	
Burkitt lymphoma	1 (0.45%)	0 (0.00%)	
Double-hit/triple-hit lymphoma	2 (0.90%)	1 (4.55%)	
T-cell lymphoma	5 (2.24%)	0 (0.00%)	
Treatment			
CHOP +/- R	196 (87.89%)	17 (77.27%)	0.410
R-BENDA	1 (0.45%)	0 (0.00%)	
R-PRED	0 (0.00%)	0 (0.00%)	
DA-EPOCH +/- R	20 (8.97%)	5 (22.73%)	
R-LEN	1 (0.45%)	0 (0.00%)	
CHOEP	2 (0.90%)	0 (0.00%)	
CHOP +/- R & DA-EPOCH +/- R	2 (0.90%)	0 (0.00%)	
R-PRED & DA-EPOCH +/- R	1 (0.45%)	0 (0.00%)	

Table 4. Summary of basic variables with regard to mortality *(continued)*

Interim control			
No response	11 (4.93%)	2 (9.09%)	
Partial response	75 (33.63%)	9 (40.91%)	0.334
Complete response	137 (61.43%)	11 (50.00%)	

Data are given as mean ± standard deviation or median (1st quartile - 3rd quartile) for continuous variables according to normality of distribution and as frequency (percentage) for categorical variables.

Abbreviations; ALT: Alanine aminotransferase, AST: Aspartate aminotransferase, CHOP +/- R: Cyclophosphamide, doxorubicin, vincristine, and prednisone +/- radiotherapy, CHOEP: Cyclophosphamide, doxorubicin, vincristine, etoposide and prednisone, CRP: C-reactive protein, DA-EPOCH +/- R: Dose-adjusted EPOCH +/- radiotherapy, ECOG: The Eastern Cooperative Oncology Group, LDH: Lactate dehydrogenase, LNM: Lymph node mass, R-BENDA: Bendamustine plus rituximab, R-IPI: Revised International Prognostic Index, R-LEN: Lenalidomide plus rituximab, R-PRED: Prednisone plus rituximab, WBC: White blood cell

Table 5. Summary of follow-up characteristics with regard to mortality

	Final status		
	Alive (n=223)	Deceased (n=22)	p
Infection			
No	101 (45.29%)	13 (59.09%)	
Mild	57 (25.56%)	3 (13.64%)	0.110
Moderate (Outpatient)	38 (17.04%)	6 (27.27%)	
Severe (Inpatient)	27 (12.11%)	0 (0.00%)	
Febrile neutropenia	58 (26.01%)	4 (18.18%)	0.583
Anemia			
No	65 (29.15%)	3 (13.64%)	
9.5 < Hb <12 g/dL	105 (47.09%)	11 (50.00%)	
8.0 ≤ Hb ≤ 9.5 g/dL	34 (15.25%)	5 (22.73%)	0.166
7.0 ≤ Hb < 8.0 g/dL	14 (6.28%)	1 (4.55%)	
Hb <7 g/dL	5 (2.24%)	2 (9.09%)	
Thrombocytopenia			
No	171 (76.68%)	15 (68.18%)	
APC > 100000 /µL	25 (11.21%)	4 (18.18%)	
50000 ≤ APC < 100000 /µL	13 (5.83%)	1 (4.55%)	0.532
30000 ≤ APC < 50000 /µL	9 (4.04%)	1 (4.55%)	
APC < 30000 /µL	5 (2.24%)	1 (4.55%)	
Neutropenia			
No	79 (35.43%)	8 (36.36%)	
1500 ≤ ANC < 2000 /µL	24 (10.76%)	4 (18.18%)	
1000 ≤ ANC < 1500 /µL	20 (8.97%)	2 (9.09%)	0.832
500 ≤ ANC < 1000 /µL	32 (14.35%)	2 (9.09%)	
ANC <500 /µL	68 (30.49%)	6 (27.27%)	
Respiratory complications	63 (28.25%)	5 (22.73%)	0.762
Liver complications	13 (5.83%)	0 (0.00%)	0.614
Cardiac complications	10 (4.48%)	1 (4.55%)	1.000
Renal complications	8 (3.59%)	0 (0.00%)	1.000
Thrombosis	7 (3.14%)	3 (13.64%)	**0.049**
Severe bleeding	7 (3.14%)	1 (4.55%)	0.534

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Table 5. Summary of follow-up characteristics with regard to mortality *(continued)*

Gingiva	4 (1.79%)	1 (4.55%)	
Epistaxis	2 (0.90%)	0 (0.00%)	
Hemorrhoid	1 (0.45%)	0 (0.00%)	
GIS side effect(1)	71 (31.84%)	8 (36.36%)	0.846
Nausea/Vomiting	35 (15.70%)	3 (13.64%)	
Constipation	27 (12.11%)	3 (13.64%)	
Diarrhea	10 (4.48%)	1 (4.55%)	
Oral aphthae/Mucositis	8 (3.59%)	2 (9.09%)	
Gastritis/Dyspepsia	6 (2.69%)	0 (0.00%)	
Dysphagia/Odynophagia	2 (0.90%)	2 (9.09%)	
Neurologic side effect(1)	58 (26.01%)	7 (31.82%)	0.737
Neuropathy/Paresthesia	55 (24.66%)	5 (22.73%)	
Vertigo	4 (1.79%)	2 (9.09%)	
Headache	2 (0.90%)	1 (4.55%)	
Psychiatric side effect(1)	8 (3.59%)	2 (9.09%)	0.223
Insomnia	6 (2.69%)	1 (4.55%)	
Anxiety	2 (0.90%)	1 (4.55%)	
Amnesia	1 (0.45%)	0 (0.00%)	
Dermatologic side effect(1)	26 (11.66%)	1 (4.55%)	0.483
Dermatitis/Urticaria	11 (4.93%)	1 (4.55%)	
Acne	2 (0.90%)	0 (0.00%)	
Zoster	8 (3.59%)	0 (0.00%)	
Cellulitis	3 (1.35%)	0 (0.00%)	
Nail pathology	4 (1.79%)	0 (0.00%)	
Musculoskeletal side effect	3 (1.35%)	0 (0.00%)	1.000
Endocrinologic side effect	2 (0.9%)	1 (4.55%)	0.247
Hypertension	1 (0.45%)	0 (0.00%)	
Diabetes mellitus	0 (0.00%)	1 (4.55%)	
Osteoporosis	1 (0.45%)	0 (0.00%)	
Seconder malignancy	6 (2.69%)	5 (22.73%)	**0.001**
Follow-up time, months	60 (29 - 88)	16.5 (11 - 37)	**<0.001**
Response to treatment			
Yes	200 (89.69%)	17 (77.27%)	0.149
No	23 (10.31%)	5 (22.73%)	

Data are given as mean ± standard deviation or median (1st quartile - 3rd quartile) for continuous variables according to normality of distribution and as frequency (percentage) for categorical variables.
(1) Patients may have more than one of the following.
Abbreviations; ANC: Absolute neutrophil count, APC: Absolute platelet count, GIS: Gastrointestinal system, Hb: Hemoglobin

Table 6. Significant factors independently associated with mortality, multiple logistic regression analysis

	β coefficient	Standard error	p	Exp(β)	95% CI for Exp(β)	
Extranodal involvement	1.711	0.558	**0.002**	5.534	1.853	16.528
Thrombosis	1.798	0.787	**0.022**	6.037	1.291	28.228
Seconder malignancy	2.729	0.696	**<0.001**	15.322	3.915	59.969
Constant	-3.052	0.332	<0.001			

Nagelkerke R^2=0.207
Abbreviations; CI: Confidence Interval.

and mortality rates [1]. Patients with primary resistant or recurrent aggressive lymphomas have poor prognosis. Over 50% of patients with diffuse large B-cell lymphoma relapse within two years of diagnosis [15]. Therefore, predicting patients who will not respond to chemo(radio) therapy will allow the application of different or additional treatment strategies for these patients, and thus, will make significant contributions to the improvement of mortality rates and survival times in NHL. Our results showed that female sex, low ECOG-PS score, presence of frailty and high lymphocyte count (at baseline), and the presence of extranodal involvement, mantle cell lymphoma, thrombocytopenia and cardiac complications (during treatment) were poor prognostic factors independently associated with unresponsiveness to treatment. In one study, advanced disease was shown to be a risk factor for recurrent or resistant disease in patients with gastrointestinal NHL (GISNHL) [14]. Provencio et al. reported that C-MYC mRNA positivity in pretreatment samples was a significant predictor of poor progression-free survival and absence of complete response to first-line treatment [15]. In another study, patients with relapsed or refractory NHL with low or low-intermediate IPI score had higher overall response rate to the salvage chemotherapy than patients with high or high-intermediate IPI score –although the difference was not significant. Also, older patients (over 60 years) had significantly lower overall response rate than younger patients [30]. A significant relationship between pretreatment albumin level and survival has been suggested, but such a relationship was not found between pretreatment albumin level and response to treatment [31]. Another important issue is when to start treatment after diagnosis and to determine the patients who need urgent treatment. Drawing attention to this issue, Olszewski et al., in their comprehensive retrospective study of patients with aggressive lymphoma, reported that the time elapsing between diagnosis and treatment may be a significant factor which cannot be identified by standard prognostic assessments [32]. We believe that the risk factors identified in this study should be considered in future studies in order to assess their validity. Also, it may be possible to suggest that patients with these risk factors should be followed more carefully in terms of response to treatment.

NHL-related mortality has an important share in cancer-related deaths. Death from NHL itself, from NHL treatment, and from second primary tumors are all relevant problems today, and the assessment of these features is a major challenge. Conventional factors, such as Ann Arbor stages and extranodal involvement, as well as other factors in IPI scores are still important predictors of clinical outcome [33]. Considering the length of the study period, we also aimed to investigate risk factors associated with NHL-related mortality as a secondary analysis. The only factors independently associated with mortality were extranodal involvement, thrombosis development during treatment, and secondary malignancies. In a study involving patients with primary pulmonary lymphoma (PPL), 78.9% of whom were NHL, it was found that older age (>60 years), elevated LDH and β2-microglobulin levels, clinical stage (II2E disease or higher), and nonsurgical treatment were associated with poor prognosis, but age was the only independent prognostic factor for PPL [10]. Multivariable analysis from one study revealed that bone marrow involvement (defined on ^{18}F-FDG PET/CT), IPI, metabolic tumor volume and elevated LDH were independent predictors for progression free survival. Furthermore, the same study reported that bone marrow involvement, SUVmax value and metabolic tumor volume were independent predictors of overall survival [11]. In another study, it was shown that high LDH levels, poor PS, advanced staging, and malignant pathological type were independent predictors of survival outcomes [12]. Shannon et al. showed that female sex, gastric localization, follicular or mantle cell histology, and radiation therapy were associated with improved survival in patients with primary GISNHL [34]. Wang and colleagues reported that increased pretreatment CRP and higher NCCN-IPI scores were independent predictors for overall survival and progression-free survival. In this study, age (>60 years), extranodal involvement ≥2, higher LDH concentration or higher IPI scores were not associated with survival in multivariable analysis [33]. In a review, the following were identified as clinically significant prognostic markers for pediatric B-cell NHL: central nervous system involvement at diagnosis, elevated LDH, cytogenetic factors, stage, and poor response after pre-phase chemotherapy [35]. Jiang and colleagues reported that age (>60

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years), male sex, and ≥3 involved nodal sites were independent prognostic factors associated with survival in NHL patients with multiple primary malignant tumors [36]. The most important reason for this diversity of risk factors in the literature is probably the differences in patient characteristics. Additionally, the majority of studies investigated risk factors in a specific region or specific type of NHL. In this context, the inclusion of patients with all NHL subtypes and regions in our study may make the results more comprehensive. Nonetheless, considering the results of this study and the large variations in the literature, it is evident that there is a need for new comprehensive studies that include patients with all NHL subtypes.

Although NHL usually involves lymph nodes, it also may occur in any tissue [11]. About half of the patients develop extranodal lymphoma (secondary extranodal disease); whereas, between 10 and 35% of patients have primary extranodal lymphoma at the time of diagnosis [3]. It is very important to demonstrate the presence of extra-lymphatic involvement which can affect therapeutic decision-making [37]. One of the most striking results in the present study is possibly the identification of extranodal involvement as an independent risk factor for both treatment response and mortality. In the present study, extranodal involvement was determined in 11.02% of patients. Given this high rate and its established negative impact on NHL prognosis, the importance of developing treatment protocols specific to the management of patients with extranodal involvement becomes apparent. On the other hand, the most common location of primary extranodal disease is reported as the gastrointestinal tract [3]. In our study, the most common extranodal disease was found in the spleen (4.49%), followed by the gastrointestinal system (4.08%). The reason for this difference may be that many researchers consider spleen as nodal disease [3].

Some limitations of the study should be noted. Firstly, this is a retrospective and single-center study spanning 10 years, throughout which definitions, classifications, management and options for treatment have evolved. This not only limits the assessment of newer data / markers of interest, but also leads to potential bias. Despite being a limitation in and of itself, it is important to mention that the most current guidelines were used for the treatment each patient; thus, this was an unavoidable limitation. Consequently, in relation with aforementioned concerns and the low number of cases with mortality, we did not perform detailed survival analyses. Secondly, due to the difficulties in accessing data and insufficient data, the distinction between treatment-related mortality and NHL-related mortality could not be made, and therefore, these results could not be presented. Thirdly, prognostic factors associated with response to treatment and/or mortality may vary depending on the localization of the tumor, its type, and the treatment protocol applied (both initial and salvage therapy). However, these were not analyzed due to the difficulties in obtaining reliable data. Finally, the short follow-up period of some patients may have affected mortality rates, thereby impacting mortality-related findings.

In conclusion, in patients with NHL, we found that female sex, low performance status, frailty, high lymphocyte count (all analyzed at baseline) and extranodal involvement, mantle cell lymphoma, thrombocytopenia and cardiac complications (at follow-up) were independently associated with non-response to treatment. Extranodal involvement, thrombosis at follow-up, and secondary malignancy were independent risk factors for mortality. Considering these characteristics when making treatment decisions and throughout the follow-up period may have a positive impact on survival and mortality in patients with NHL.

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Ethics Committee Approval: The protocol for this study was approved by the local ethics committee (Kartal Dr. Lütfi Kırdar City Hospital, Clinical Research Ethics Committee; date: 22.02.2023, no: 2023/514/244/2). All procedures were performed according to the ethical standards laid down in the Declaration of Helsinki in its latest revision.

ORCID and Author contribution: Y.İ. (0000-0003-2952-2286): Literature survey, design, planning, data collection, intellectual review of the results, writing, approving the final manuscript.

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Attitudes of Healthcare Professionals Working in Different Fields Towards Organ Transplantation in the Hospital Sample and the Factors Affecting These Attitudes

Hastane Örnekleminde Farklı Alanlarda Görevli Sağlık Çalışanlarının Organ Nakline İlişkin Tutumları ve Bunu Etkileyen Faktörler

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ABSTRACT

Aim: Turkish society has profound distrust and hesitation against the concept of brain death and related cadaveric organ donation. In this study, the attitudes of health workers about organ transplantation from cadavers were investigated. The effects of race, religiosity and political conservatism parameters on the attitudes of the research group were also explored.

Methods: A total of 491 participants between the ages of 18-70 who are hospital employees in different fields were included in this study. An Organ Donation Attitude Scale (ODAS) was applied to the participants, which evaluates organ donation from cadavers explicitly, and the relationships between the emerging trend and the demographic characteristics of the participants, their education, the task they are responsible in the hospital, ethnicity and sectarian origins, religiosity and political conservatism characteristics were evaluated.

Results: ODAS scores of our sample group did not show a significant relationship in age, gender, ethnic origin and sect. There was a negative relationship between cadaveric organ transplantation and religiousness and a positive relationship with liberal political views. On the other hand, there was a significant difference in the attitude toward organ transplantation regarding education levels, position in the hospital, and the geographical region where the person came from.

Conclusion: Higher education and liberal worldview has a positive effect on organ donation attitude from cadaver. On the other hand, there is a negative relationship between religiosity and the approach to organ donation from cadaver.

Key Words: Organ donation, Brain Death, Attitude, Education

ÖZET

Amaç: Türk toplumunda beyin ölümü ve buna bağlı kadavradan organ bağışı kavramına karşı ciddi bir güvensizlik ve tereddüt bulunmaktadır. Bu tereddüt için şimdiye kadar eğitim eksikliği en önemli sorun olarak vurgulanmıştır. Çalışmamızda bu konuda en iyi eğitim düzeyine sahip olduğu düşünülen sağlık çalışanlarının kadavradan organ nakli konusundaki tutumlarını araştırdık. Ayrıca ırk, dindarlık ve politik muhafazakârlık parametrelerinin araştırma grubunun tutumları üzerindeki etkilerini değerlendirdik.

Yöntemler: Bu çalışmaya farklı alanlarda hastane çalışanı olan 18-70 yaş arası toplam 491 katılımcı dahil edilmiştir. Katılımcılara özellikle kadavradan organ bağışını değerlendiren bir Organ Bağışı Tutum Ölçeği (OBTÖ) uygulanmış ve burada ortaya çıkan eğilim ile katılımcıların demografik özellikleri, eğitimi, hastanede aldıkları görev, etnik ve mezhepsel kökenleri, dindarlık ve politik muhafazakârlık özellikleri arasındaki ilişkiler değerlendirilmiştir.

Bulgular: Örneklem grubumuzun Organ Bağışı Tutum Ölçeği (OBTÖ) puanları yaş, cinsiyet, etnik köken ve mezhep açısından anlamlı bir ilişki göstermemiştir. Buna karşın eğitim, hastanede yapılan görev, kişinin geldiği coğrafi bölge bakımından organ nakli tutumu hakkında anlamlı farklılık izlenmiştir. Ayrıca kadavradan organ nakline olumlu yaklaşım ile dindarlık düzeyi negatif ve liberal yöndeki politik tutum arasında pozitif yönde bir korelasyon izlenmiştir.

Sonuç: Yüksek öğrenim ve liberal dünya görüşü kadavradan organ bağışı tutumu üzerinde olumlu bir etkiye sahiptir. Buna karşın dindarlık ile kadavradan organ bağışına yaklaşımda negatif bir ilişki söz konusudur. Ancak ülkemizdeki kadavradan organ nakline yönelik tutum sadece eğitim ile açıklanmayacak şekilde komplekstir. Ülkemiz için kültürel dini ve diğer farklı sosyal yönlerin kavramsal incelenmesi gereklidir.

Anahtar Kelimeler: Organ bağışı, Beyin Ölümü, Tutum, Eğitim

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Introduction

Organ transplantation can be completed in two forms, cadaver and living. The High Council of Religious Affairs in Turkey decided that organ donation is allowed in Islam, and the first fatwa that targeted organ donation and transplantation in Turkey was issued in 1980. In addition, brain death, the basis of organ transplantation from cadavers, is recognized as legal death in our country regarding medical interventions or organ transplants along with civil and criminal law. Despite the previously mentioned mindset of legal and official religious authorities on this issue, reaching the desired level of organ donation has not been possible, especially from cadavers in our country. According to the International Registry of Organ Donations and Transplants (IRODaT -UOBTK 2022), organ donation from cadavers for 2021 per million population is 40.8 in Spain, 41.6 in the United States, 24.7 in France, 26, while it is 11.5 in Iran, it is only 3.6 in our country [1]. From another perspective, as of July 2019, there are a total of 489,593 organ donors in Turkey, and only 8 out of every 1,000 people over the age of 18 are organ donors who have given consent [2].

The results of a study on Turkish society confirm this situation in the attitude plan as well. According to the results of this research, only 0.7% (n=22) of 3000 people stated that they donated their organs, and 88.3% (n=2629) did not want to donate [3]. This situation also coincides with Muslims who live in Western countries showing the same reluctance to accept brain death and organ donation from cadavers [4]. Demirkıran and his colleagues aimed to reveal religious and cultural aspects of organ donation in their study on the general population. As a result, they stated that religious reasons were especially compelling. The study revealed that fewer participants approved of organ donation than expected, and the problem might be related to education [5]. Studies on organ donation in Turkey especially emphasize the lack of awareness and education among the population [5, 6, 7].

In this study, the main aim was to evaluate the attitudes of employees who work in various fields in the hospital, who can represent different education levels and social layers, such as doctors, nurses, pharmacists, technicians and other health personnel, patient caregivers and administrative personnel, and who are expected to be more knowledgeable about the subject than the general population, towards organ transplantation. The study also aims to evaluate the possible effects of gender, age, ethnic and sectarian origin, religiosity and political conservatism parameters on attitudes.

Material and Methods

A total of 491 healthcare professionals, aged between 18-70 years, working in different positions in two private hospitals belonging to the same group in the province of İstanbul, who gave informed consent, were included in the study. The study was approved by the İstanbul Medipol University Local Ethics Committee (Ethics Report No: 10840098-772.02-E.44287).

After obtaining informed consent, participants were first asked to answer questions regarding demographic characteristics, education, hospital position, ethnic and sectarian origin, and definitions of religiosity and conservatism. They were then asked to answer questions assessing their practical and theoretical knowledge about brain death. Finally, Rumsey and colleagues' Organ Donation Attitude Scale (ODAS) was applied to evaluate the attitudes of the participants towards organ donation. [8].

The attitude was defined as the dependent variable in this study. The research was conducted on 491 healthcare workers selected using the purposive sampling model. The distribution of personal characteristics of the sample group is given in Table 1. In the research, personal information (gender, age, education, occupation (the position he assumed at the hospital), geographical region of origin, ethnicity, and sect) was recorded. In addition, participants were asked how they defined themselves on a scale of 10 in terms of religiosity and political conservatism (Not religious (1) / Very religious (10) and again Conservative (1) / Liberal (10). Participants' theoretical (training) and practical (organ donor recognition) knowledge about organ donation was determined by a four-question survey.

ODAS responses, which measure participants' attitudes towards organ donation from cadavers, were evaluated on a 5-point Likert scale (No, I strongly disagree, I do not agree, I am not sure, I am not sure, I agree, Yes, I strongly agree). The scale consists of 20 questions in total. The score range is between 20 and 100, while questions 2,13,14,16 do not support organ donation, questions numbered 4,5,6,7,10,11,15,17,18,19,20 support organ donation, and questions 1,3,8,9 neutral. High scores indicate a positive attitude towards organ donation [8].

Statistical analysis

Descriptive statistics (frequency and percentages) were calculated for the demographic and other descriptive characteristics of the participants. The age ranges of the participants were divided into four groups 17-25, 26-35, 36-45 and 46+. Their education is divided into primary education, high school, associate degree, university and higher. The geographical region where the participants originate; is divided into Mediterranean/Aegean and Marmara, Black Sea, Central Anatolia, and East and Southeast Anatolia. It is organized into 4 groups in terms of their duties in the hospital: 1) Technician/nurse/midwife/pharmacist, 2) doctor, 3) Service

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personnel and 4) Administrative personnel. Statistics were made by classifying them into four groups Turkish, Kurdish, Arab and others in terms of ethnic origin and Hanafi, Alevi, Shafi and others for the sect.

The internal consistency of the ODAS scale was calculated with Cronbach's alpha. Independent groups t-test and/or one-way analysis of variance (ANOVA) was applied to examine the differentiation status of the responses of our sample group to the attitude statements about organ donation from cadavers with ODAS according to gender, age, education status, and working status in the hospital. Least Significant Differences (LSD) analysis was performed to identify the sources of differences for the variables that showed significance. Finally, Pearson correlation analysis was used to determine the relationships between religiosity and political conservatism. IBM-SPSS 25.0 program was used in the analysis, and the significance was checked at the lowest $p < .05$ level.

Results

The characteristics of our sample group, gender, classified age, education, hospitalization, ethnicity, sect and self-definition of religiosity and political conservatism (n= 491) are shown in Table 1.

The table shows that 73.3% of the sample group is female,and 26.7% is male. 48.1% of the group is in the age range of 17-25, 26.1% in the age range of 26-35, 15.6% in the 36-45 age range, and 10.1% in the age range of 46 and over. 6.4% of the group has a primary education, 14.7% high school, 31.5% associate degree, and 47.4% a university or higher education. In terms of geographical origin, 67.6% of our sample is Marmara, Aegean and Mediterranean; 13.3% are from the Black Sea, 8.7% are from Central Anatolia, and 10.5% are from the East and Southeast regions. 39.5% of our sample work in the hospital as technicians, nurses, midwives and pharmacists, 18.7% as doctors, 10.0% as service personnel, and 31.8% as administrative personnel. Regarding ethnicity, 89.6% of our sample is Turkish, 7.7% is Kurdish, 1.7% is Arab, and 1.1% is from other ethnic origins. In terms of the sect, 84.1% stated that they belonged to Hanafi, 2.8% to Alevi, 5.9% to Shafi and 7.2% to other sectarian groups. When asked how the participants describe themselves in terms of religiosity and political conservatism, the sample group's religiosity means = 6.56, standard deviation =2.03 in scoring between 1-10 points; political conservatism mean = 5.42, standard deviation = 1.94. On the other hand, when the data were classified into three groups, 6.4% of the group stated that they were not religious, 38.6% were slightly religious, 55.0% were religious; 14.8% defined themselves as politically conservative, 60.9% neither conservative nor liberal, and 24.3% liberal.

Table 1. All characteristics and frequencies of the sample group

Groups		
Gender		
Woman	360	73.3
Male	131	26.7
Age (Group)		
17-25	234	48.1
26-35	127	26.1
36-45	76	15.6
46+	49	10.1
Education		
Primary education	31	6.4
High school	71	14.7
associate degree	152	31.5
University and above	229	47.4
Area		
Marmara, Aegean and Mediterranean	265	67.6
Black Sea	52	13.3
Middle anatolia	34	8.7
East and Southeast	41	10.5
Job		
Technician and Nurse, Midwife and Pharmacist	186	39.5
Doctor	88	18.7
Service staff	47	10.0
Administrative Staff	150	31.8
Ethnicity		
Turkish	420	89.6
Kurd	36	7.7
Arabic	8	1.7
Other	5	1.1
Sect		
Hanafi	387	84.1
Alevi	13	2.8
Shafi	27	5.9
Other	33	7.2
Piety		
Not Religious	31	6.4
Slightly Religious	186	38.6
Religious	265	55.0
Political Conservatism		
Conservative	71	14.8
Neither conservative nor liberal	293	60.9
Liberal	117	24.3

The rate of receiving training on organ donation from the participants is 43.5%, and the rate of knowing someone who donates an organ is 42.5%.

For ODAS, which can be scored between 20-100 points, the mean of the sample group was = 76.86, the standard deviation =11.78; the lowest score was calculated as 27, and the highest score was calculated as 100. On the other hand, the Cronbach alpha internal consistency coefficient of the scale was calculated as .86.

As shown in Table 2, independent groups t-test was performed to examine the differentiation status of the sample group's ODAS scores according to gender. As a result of the analysis, the difference between the mean of the gender groups for ODAS scores was not found significant (t=1.05; p>.05). Similarly, a one-way ANOVA was performed to examine the differentiation of ODAS scores according to ethnicity and sect. No significant difference was found as a result of the analysis (F=.28; p>.05) and (F=1.53; p>.05), respectively. However, as seen in Table 2, the differentiation of the ODAS scores of the sample group according to the education level is significant and has a high effect size. The difference between the one-way ANOVA and the means of the training groups was significant (F=11.73; p<.001). As a result of the LSD analysis carried out to determine the sources of the differences, the average of associate degree graduates and university and higher graduates is compared to the average of primary school graduates; The average of associate degree graduates and university and higher graduates was found to be significantly higher than the average of high school graduates. Similarly, a one-way ANOVA was performed to examine the job variable of

Table 2. Organ Donation Attitude Scale (ODAS) and t-Test for Gender

Point	Group	n	$\bar{x}$	ss	t	Sd	p	$Cohens\ d$
ODAS	Woman	360	77.18	10,852	1.054	489	.292	-
	Male	131	75.90	14,275				

Organ Donation Attitude Scale (ODAS) and ANOVA for Education, Region, Occupation, Ethnicity, Sect

Point	Group	n	$\bar{x}$	ss	F	p	LSD	
ODAS	primary education (1)	31	69.84	10,178	11,726	.000	3,4>1 3,4>2	.07
	High School (2)	71	72.03	13,319				
	Associate Degree (3)	152	76.78	9,987				
	University + (4)	229	79.36	11,894				
ODAS	Mar., Aegean, Mediterranean (1)	265	78.50	12,296	2,721	.044	1>2	.02
	Black Sea (2)	52	74.04	13,500				
	Central Anatolia (3)	34	75.63	12,836				
	East, Southeast(4)	41	75.15	9,324				
ODAS	Technician/technician and Nurse, Midwife and Pharmacist (1)	186	77.59	11,085	15,416	.000	2>1,3,4 1.4>3	.09
	Doctor (2)	88	82.66	12,843				
	Service Personnel (3)	47	69.51	9,321				
	Administrative Staff (4)	150	75.49	11,026				
ODAS	Turkish (1)	420	76.87	12,157	.284	.837	-	-
	Kurdish (2)	36	76.25	9,639				
	Arab (3)	8	79.17	10,667				
	Other (4)	5	80.50	11,061				
ODAS	Hanafi (1)	387	76.76	11,884	1,533	.205	-	-
	flame (2)	13	80.06	19,494				
	Shafi (3)	27	74.77	8,358				
	Other (4)	33	80.37	11,049				

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the participants in the hospital. As a result of the analysis, the difference between the averages of the occupational groups for ODAS scores was found to be significant with a high effect size (F=15.42; p<.001). As a result of the LSD analysis carried out to determine the sources of the differences, the average of the doctor group is compared to the average of the technician, nurse, midwife and pharmacist group, service personnel and administrative personnel; It was determined that the average of the technician, nurse, midwife and pharmacist group and administrative personnel group was significantly higher than the average of the service personnel group. Another significant relationship is related to our experimental group's geographical region of origin. According to the one-way ANOVA results, the difference between the means of the regional groups for ODAS scores was significant and had a moderate effect size (F=11.73; p<.001). As a result of the LSD analysis carried out to determine the sources of the differences, it was found that the Marmara, Aegean and Mediterranean groups and their averages were significantly higher than the Black Sea average.

As can be seen in Table 3, Pearson correlation was used to determine the relationships between ODAS scores and age, perception of religiosity, and political conservatism. As a result of the analysis, while the relationship between ODAS scores and the age variable was not found significant (r=-.008; p>.05), religiosity and political conservatism scores were significantly related. While the negative view towards organ donation increases as they define themselves more religiously, the positive view increases as they describe themselves as more liberal as a political view.

Discussion

The main reason for selecting the hospital staff as a sample group for our research was to form a group with practical and theoretical experience and knowledge about brain death and organ donation compared to the general population.This group also includes many different educational and social strata that can represent the population of Turkey. In the sample group, there are health professionals such as doctors, technicians, nurses, and pharmacists, a relatively educated but non-professional segment such as administrative personnel, and a segment with a low level of education such as caregivers and cleaning personnel.

Table 3. Relationships between ODAS Scores and Age, Perception of Religiosity, Political Conservatism

Variables	OBTO Scores		
	n	***r***	***p***
Age	486	-.008	.863
Religiosity	482	-.141	.002
Political Conservatism	481	.150	.001

When we look at the literature, it is seen that the level of knowledge of the general population about organ transplantation in our country needs to be increased. Akbulut and his colleagues' study on attitudes, awareness and knowledge levels about organ donation in a general population of 3000 people reported the proportion of those with direct knowledge about organ transplantation as 1.5%. From the population, only 33.9% of the participants thought they had sufficient knowledge about organ donation [3]. According to Akbulut et al., in another research, religious officials were selected as a sample group. 33.5% of religious officials reported receiving information about the subject from in-service training symposiums. However, only 17.9% said they think they have sufficient knowledge about organ donation [9]. Again, in the organ transplant attitude study conducted on the general population in the form of an internet survey, it was reported that 87.7% of the participants did not have any personal experience with organ donation. The source of information of the sample group was mostly the internet and the media [5]. Furthermore, a better knowledge level is observed in samples similar to our sample. In an organ transplant attitude and knowledge research conducted on a university hospital staff, when it was questioned whether the participants had sufficient knowledge about organ donation, 50.2% answered "yes" [7]. The rate of our participants receiving theoretical training on organ donation is 43.5%, and the rate of knowing someone who donates an organ is has 42.5%.

Previous studies in Turkish society reveal the reluctance to organ transplantation from cadavers and the relationship of this situation with education. Demirkıran et al. evaluated a general population of 317 people and reported that only 39.4% of those surveyed would donate their organs [5]. The study showed that educational status influenced the percentage of donor donors. In the survey completed by Hot et al., 24% of nurses stated that they did not accept brain death as actual death [10]. In another study, in a sample of 200 nurses working in the hospital, 58% of the nurses stated that they could donate their organs, and 54% stated that they could donate their relatives' organs in case of brain death [11]. In a sample of 735 people from the medical faculty hospital, 44.4% (n=326) of the participants were asked "yes", 24.8% (n=182) "no" and 30.9% (n=227) replied, "I have no idea" [7].

At this point, we observe that the behavior of filling out an organ donation card is much rarer than the attitude expressed. In the research conducted by Cillimlioğlu, it was determined that only 10.3% of all participants had an organ donation card. Education is also critical here, with most donation card holders being medical students (53.9%) [7]. Again, in a study conducted on 277 intensive

care nurses, 52.71% of the nurses stated that they were considering organ donation, while only 20.22% filled out an organ donation card [12].

The differentiation of the ODAS scores of the sample group according to the education level is significant and has a high effect size. It has been seen that a high level of education is the most determining factor for a positive attitude. Another determinant is the duties of the employees in the hospital. The doctors display the highest positive attitude, and the service personnel exhibits the lowest positive attitude. We can say that at least one level of education lies behind this situation. These findings are compatible with other examples published in our country. Among the health professionals, 58.9% of the residents and 48.1% of the medical faculty students stated the intention of their organ donation [7]. In a sample of 307 people, including health personnel working in the hospital, it has been reported that as the education level increases, the percentage of intention to define brain death as an actual death and to donate their own or a relative's organs when brain death occurs [13]. Religious beliefs and worldviews are other crucial factors in a person's decision to donate organs. Although it is recognized as religious values affect attitudes towards organ donation, people of the same religion may have different opinions on this issue. While some participants who think positively about organ donation associate it with their religious beliefs, others who oppose it base it on their beliefs. [5] However, the situation may be different for different cultural frameworks. Alhawari et al. investigated how religious and sectarian beliefs affect attitudes towards brain death and organ donation in their study with the participation of 1306 people from Germany. According to the results, it has been seen that members of the same religion and belief share similar positions. Significant differences emerged between religious people belonging to different religions and those without religious affiliation. According to the research results, especially the concept of brain death was rejected by Muslims, Buddhists, and Hindus.Jews, Protestants, and non-religious people agreed that a person with brain death was irreversibly dead. It has also been noted that Sunni Muslims, Hindus and Buddhists mostly reject organ donation after brain death [14]. On the other hand, as in Turkey, religious authorities in many Muslim countries accept brain death and support organ donation [5]. Despite the numerous rules supporting organ donation, Muslims have no consensus on whether organ donation is in line with Islam [15]. According to the data provided by Demirkıran et al., 36.5% of the 301 Muslim participants approach organ donation positively, while 6.3% are negative and associate it with religious reasons. These participants stated that they would never donate and thought that organ donation was inappropriate according to their religion [5]. According to the findings of this study, there is an inverse relationship between people's self-identification as more religious and their positive attitude towards organ donation. However, it is seen that religious thinking and perception can also change over time. In a recent study, the rate of those who found organ donation compatible with their religious beliefs was reported as 84% [16]. In an organ donation attitude study conducted in Burdur, 58.0% of the participants stated that organ donation is rewarding (sevap) when they evaluate organ donation from a religious point of view [2]. Among the reasons for not donating organs in our country, the factor of religious belief, which was 26% in 1990, decelerated to 13% in 2000. However, on the other hand, the proportion of those who did not give reasons for a negative attitude increased from 23% to 40% [7]. This situation may still indicate a negative religious mindset that is not expressed or does not want to be expressed. It seems that Turkish religious officials are also confused about this issue. Only 4 out of 550 religious officials (0.7%) who participated in educational seminars on the subject have donated organs before. After attending the seminars, only 32 of them (5.9%) volunteered to donate. However, 83.3% of the religious officials who participated in the study said Islam allows organ donation and transplantation [17]. A similar attitude is also observed in the general society. Although 84% of the respondents in the study of Kececioglu et al said that organ donation is by the Islamic faith, and 77% said that they are in favor of organ donation and transplantation, 86% still said that they would not donate [18] The same attidute has been reported in American muslims [19].

According to other findings in this study, the positive attitude towards organ donation increases as the liberal trend increases from the point of view of political conservatism. Although this finding seems to be in harmony with the mentioned characteristics of the negative approach to organ transplantation from cadavers in our country due to the decrease in the tendency to higher education and religiosity, in our opinion, the formulation of the problem may not be so simple and distinct. Apart from education, the data of this study suggest that there is no such clear polarization among our participants. The average religiosity of our participants was x =6.56 out of 10, while the average political conservatism was x =5.42. In other words, in general, our sample describes itself as both religious and closer to liberal (6.4% not being religious at all and 14.8% being conservative). As some authors have stated, the main problem here is that the concept of brain death, the fundamental concept in organ transplantation from a cadaver, has not been discussed sufficiently at a conceptual level within our own cultural and religious framework [20, 21, 22, 23, 24].

Limitations: The limitations of our study; Due to the nature of the survey method, informed consent must be

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obtained before the survey, so people with a negative attitude towards organ transplantation may have been less willing to participate. The survey method may have affected our findings. Again, since the sample group of our study was composed only of İstanbul and cultural influences are critical in organ donation acceptance, our findings may indicate a slightly different result from the whole of Turkey.

Conclusion; Organ donation from brain-dead people is a procedure that works well despite some problematic areas that are still being discussed in Western societies. The situation seems to be more complicated for Turkey and the Islamic community. Although medically and legally supported and recognized and even imposed by religious discourse, there are probably many different points of resistance where brain death is not widely accepted in society [25]. This study observed that while education and liberal worldview positively affected the attitude to organ transplantation from a cadaver, religious belief had a negative effect. However, in our opinion, the problem requires a much broader perspective from a conceptual point of view. Fifty years after the introduction of brain death, the basic concept of organ transplantation from a cadaver, the subject's essence, has not yet been conceptually sufficiently discussed within our cultural framework.

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The Validation and Verification of the Nottingham Clavicle Score in the Turkish Population

Nottingham Klavikula Skorunun Türk Populasyonunda Geçerliliği ve Doğrulanması

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ABSTRACT

Aim: The aim of this study was to evaluate the validation and verification of the Nottingham Clavicle Score (NCS) in the Turkish population.

Methods: Sixty-eight patients (12 females, 56 males; mean age: 37.1±13.3 years) who underwent surgery due to clavicle fracture or acromioclavicular separation were included in the study. The Turkish version of the NCS (NCS-Tr) was designed in accordance with the stages recommended by Beaton et al. Each patient completed the NCS-Tr twice at 7 to 10-day intervals to evaluate the test-retest reliability based on the interrater correlation coefficient, and Cronbach's alpha was evaluated for internal consistency. Additionally, the Oxford Shoulder Score (OSS), Disabilities of the Arm, Shoulder, and Hand (DASH), Constant-Murley Score (CMS), and Short Form-36 (SF-36) Health Survey tests were completed by each participant to assess the correlation with the NCS-Tr.

Results: The main score of the NCS-Tr was 79.71 ± 20.37. The other mean scores of CMS, OSS, and DASH were 84.14 ± 21.47, 38.34 ± 12.43, and 17.84 ± 22.47 respectively. The translation and adaptation of the NCS-Tr for a Turkish context required no major cultural adaptation. Internal consistency was high (Cronbach's alpha: 0.933). Test-retest reproducibility was excellent (q=0.941, p<0.001).

Conclusion: The NCS-Tr is a valid, reliable, shoulder-specific scale in the assessment of patient-reported outcome measures for the functional assessment of Turkish patients undergoing surgery due to clavicle fractures or acromioclavicular joint separation.

Key Words: Patient-reported outcome measures, Clavicle fracture, Acromioclavicular separation, Turkish validation

ÖZET

Amaç: Bu çalışmanın amacı Nottingham Klavikula Skorunun (NCS) geçerliliğini ve doğrulamasını Türk popülasyonunda değerlendirmektir.

Yöntemler: Çalışmaya klavikula kırığı veya akramioklaviküler ayrışma nedeniyle ameliyat edilen 68 hasta (12 kadın, 56 erkek; ort. yaş: 37.1±13.3) dahil edildi. NCS'nin Türkçe versiyonu (NCS-Tr), Beaton ve arkadaşları tarafından önerilen aşamalara uygun olarak tasarlanmıştır. Her hasta, ölçekler arası korelasyon katsayısına dayalı test-tekrar test güvenilirliğini değerlendirmek için NCS-Tr'yi 7 ila 10 günlük aralıklarla iki kez tamamladı ve iç tutarlılık için Cronbach alfa değerlendirildi. Ayrıca NCS-Tr ile korelasyonu değerlendirmek için Oxford Omuz Skoru (OSS), Kol, Omuz ve El Disabilities (DASH), Constant-Murley Skoru (CMS) ve Short Form-36 (SF-36) Sağlık Anketi testleri her katılımcı tarafından doldurduldu. NCS-Tr ile korelasyonu değerlendirin.

Bulgular: NCS-Tr ana puanı 79.71 ± 20.37 idi. Diğer ortalama CMS, OSS ve DASH puanları sırasıyla 84,14 ± 21,47, 38,34 ± 12,43 ve 17,84 ± 22,47 idi. NCS-Tr'nin Türkçe bağlamına çevrilmesi ve uyarlanması büyük bir kültürel uyarlama gerektirmedi. İç tutarlılık yüksekti (Cronbach alfa: 0.933). Test-tekrar test tekrarlanabilirliği mükemmeldi (q=0.941, p<0.001).

Sonuç: NCS-Tr, klavikula kırığı veya akromioklaviküler eklem ayrışması nedeniyle ameliyat olan Türk hastaların fonksiyonel değerlendirmesi için hasta tarafından bildirilen sonuç ölçütlerinin değerlendirilmesinde geçerli, güvenilir, omuza özgü bir ölçektir.

Anahtar Kelimeler: Hasta tarafından bildirilen sonuç ölçütleri, Klavikula kırığı, Akromiyoklaviküler ayrılma, Türkçe doğrulama

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Introduction

Identifying of patients and follow-up of outcomes are essential for the management of musculoskeletal disorders. In particular, the patient-reported outcome measures (PROMs) are designed to collect measurement data with standardization tools. Scoring systems (PROMs) have been established to standardize the treatment and outcomes of patients. The main goal is to obtain common results of different cases by giving the consensus of clinicians who are experts in scoring systems [1,2]. In this way, the results of different operations performed in different regions can be standardized and global results can be obtained. To illustrate, shoulder and clavicle is a complex region consisting of more than one muscle and tendon junction [3]. Therefore, more than one PROMs are defined for this area. These classifications have been defined separately for shoulder and accompanied functional or anatomical zones [3-5].

Clavicle fractures are frequent disorders that can affect quality of life and disrupt daily working performance of individuals. Different clinical presentations of this area are sourced by both-sided joint formation with the sternum and acromion. Therefore, varying clinical approaches have been described. Differences in localizations of both fractures may cause different treatment outcomes [3].

The main scoring systems for shoulder pathologies can be listed as the Oxford Shoulder Score (OSS), Constant-Murley Score (CMS), Disabilities of the Arm, Shoulder, and Hand (DASH) Questionnaire, and Nottingham Clavicle Score (NCS) [3-6]. Although all these scoring systems are defined for the shoulder joint, the NCS is specific for injuries to the clavicle, acromioclavicular joint (ACJ), and sternoclavicular injuries to the clavicle. The OSS is a patient-reported questionnaire consisting of 12 items [4]. The CMS is one of the best-known scores in the evaluation of results after rotator cuff surgery [5]. The DASH is the other scoring system to evaluate the results of shoulder and hand [6]. To standardize regional differences, these surveys should be validated according to ethnic and regional characteristics. Although the NCS is a frequently used scoring system in clavicle injuries, its validation studies have been carried out in European countries. However, there are fewer studies on its validation in Asia and non-European countries [3].

In the present study, we hypothesized that the NCS questionnaire was a valid and reliable tool for the assessment of outcomes in Turkish population. We, therefore, aimed to perform a cross-cultural adaptation of the NCS questionnaire and to investigate whether it was a valid and reliable instrument for assessing the outcomes of clavicular fractures, and ACJ disorders among Turkish population.

Patients and Method

Translation procedure

Before translation and adaptation of the NCS, permission was obtained from the main developer of the original version of the scoring system [3]. The translation and cross-cultural adaptation were made according to previously described guidance by Beaton et al. [7]. The original (English) form of the NCS was translated into Turkish by two native Turkish speakers (one translator was an expert working as an orthopedic surgeon, and the second translator was a professional English translator working at a university who was not a health specialist and was unaware of the study design and concept). Both translations were combined and a single Turkish questionnaire was produced. The final format of the questionnaire was approved by another independent specialist (Appendix 1). No cultural adaptation or designation changes were required during the translation process. The comprehensibility of the latest version of the scoring system was checked by testing 10 patients with a shoulder disorder and 10 healthy individuals, and the test committee, then, agreed on the compatibility of English and Turkish versions of the NCS.

Study design and study population

Patients who underwent surgery between April 2017 and December 2021 due to clavicle fractures or ACJ separation were screened. All patients were called back to the hospital for follow-up and asked to complete the NCS-Tr and other standard PROMs for the shoulder (DASH, CMS, OSS, Short Form-36 [SF 36]). Patients who did not attend the follow-up or did not give consent to participate in the study and who had mental or social problems that could prevent the completion of the questionnaire were excluded from the study. Inclusion criteria were as follows: age 18 years or older, patients undergoing surgery for clavicle fractures or ACJ separation, those giving consent to participate in both the test and re-test assessments, and being a native Turkish speaker. Finally, of 150 patients eligible for the study, a total of 68 who met the inclusion criteria were recruited. The indicated questionnaires (DASH, CMS, OSS, SF-36, NCS-Tr) were completed in full by all participants and clinical examinations were performed by the study investigators.

PROM data collections and outcome tools

NCS: The questionnaire consists of 10 items with five selection points in each. Each question has five categories of response, corresponding to a score ranging from 2 to 10.

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The scoring ranges from 20 (greater difficulty) to 100 (the lowest difficulty) points, which evaluates the functional scales of the participants. The shoulder pain, pain in bed during sleep, pain during daily activities, and pain during sports activities and recreation are assessed in Items 1 to 4. The overhead strength and lifting capacity of heavy objects is assessed in Items 5 and 6. Cosmetic satisfaction is evaluated in Item 7, and movement of the shoulder and clicking in the shoulder are evaluated in Item 8. Tingling and numbness in the arm and neck were evaluated in Item 9 and heavy or dragging sensations were evaluated in Item 10. The scores are interpreted as excellent (80-100), good (60-79), fair (40-59), or poor (<40) (3).

DASH: The questionnaire is used to evaluate arm, shoulder, and hand disabilities through 30 items. In these items, disability is classified on a 1 to 5 scale. These scales are scored between 0 (no disability) and 100 (severe disability) for testing the degree of strength in performing a variety of daily physical activities. Additionally, the last five items include the severity of pain, aggravated pain with activity, tingling, weakness, and stiffness. Social, work, and sleep problems are also evaluated using this questionnaire. The cultural validity and reliability studies of the DASH were carried out in the Turkish population by Düger et al. [8].

SF-36 Health Survey: This 36-item questionnaire is used to evaluate self-reported quality of life of patients. Subscales include physical functions, social problems, emotional limitations, mental health, vitality, and bodily pain. The scores range between 0 (poor) and 100 (good health) for providing information about well-being. The cultural validity and reliability studies of the SF-36 in the Turkish population were conducted by Demiral et al. [9].

OSS: This questionnaire consists of 12 items which evaluate shoulder functions. All items have five subscales that are scored between 0 (worst) to 48 (best). Pain and quality of life can be evaluated using this questionnaire. The cultural validity and reliability studies of the OSS in the Turkish population were conducted by Tuğay et al. [10].

CMS: This is a 100-point scale which is used to evaluate the severity of pain, activities of daily living, and working in different positions. The scores range from 80-100: excellent, 65-79: good, 51-64: moderate, and to 0-50: poor. The cultural validity and reliability studies of the scale in the Turkish population were conducted by Çelik et al. [11].

Statistical Analysis

According to the G-Power t test, a sample size of 48 was calculated as 95% confidence, 95% power, 5% margin of error and large effect size. The research sample consisted of 68 patients who agreed to participate in the study.

Statistical analysis was performed using the SPSS 25.0 software (IBM Corp., Armonk, NY, USA). Continuous data were expressed in mean ± standard deviation (SD), while categorical data were expressed in number and frequency. The internal consistency of the NCS-Tr was evaluated using Cronbach's alpha (α) coefficient. When the α level is greater or equal to 0.70, reliability is considered acceptable. The effect of each item on reliability, corrected item-total correlations and Cronbach's alpha levels, if any items were deleted, was examined. Intra-class correlation (ICC) coefficients and 95% confidence intervals (CIs) were calculated to investigate test-retest reliability for the NCS-Tr. If the ICC level was greater than 0.75, the test-retest reliability was considered excellent. The construct validity of the NCS-Tr was performed using the Pearson correlation analysis. The degrees of association between the NCS-Tr and other validated instruments (*i.e.*, OSS, DASH, CMS, and SF-36) were calculated using the Pearson moment-product coefficients of correlation. A p value of <0.05 was considered statistically significant.

Results

The cultural adaptation process and translation of the NCS-Tr were completed as described above, and no problems were encountered at this stage.

A total of 68 patients completed the PROM scales. Clavicle fractures were detected in 56 (82.4%) patients and ACJ separation was detected in 12 (17.6%) patients. The right shoulder was the most commonly affected side (n=36/52.9%). There were 56 (82.4%) male patients and the mean age of all patients was 37.1±13.3 years. Demographic and clinical data of the patients are summarized in Table 1.

The mean NCS-Tr score was 76.8 ±19.8. The mean scores of CMS, OSS, and DASH were 86.6±16.2, 39.4±10.8, and 18.3±22.6, respectively. The mean scores of the SF-36 subscales were as follows: physical functioning 84.5±20.4, role functioning/physical 73.5±37.6, role functioning/emotional 77.0±37.4, energy/fatigue 74.0±26.5, emotional well-being 76.5±26.2, social functioning 80.7±23.4, pain 75.8±, and general health 80.5±22.7. In terms of discriminant validity, the NCS-Tr showed the least concordance with the role emotional/physical domain, although it was compatible with the mental subgroups, pain, and general health of the SF-36. The mean scores and range values of the PROMs are presented in Table 2.

The test-retest reliability of each item in NCS-Tr was evaluated and the maximum value was detected in Item 3 with an ICC of 0.823 (CI: 0.933-0.974) and the lowest value was detected in Item 10 with an ICC of 0.517 (CI: 0.647-0.864). The ICC values for each item are given in Table 3.

Table 1. Demographic and clinical characteristics of patients

		n=68
Age (years)		37.1±13.3
Age range (years)		18-61
Sex	Male	56 (82.4%)
	Female	12 (17.6%)
Side	Left	32 (47.1%)
	Right	36 (52.9%)
Diagnosis	Clavicula Fracture	56 (82.4%)
	Acromioclavicular Joint Speration	12 (17.6%)

Table 2. Descriptive statistics for all assessment tools

		Mean	SD	Min	Max
NCS		76.8	19.8	26.0	100.0
OSS		39.4	10.8	6.0	48.0
DASH		18.3	22.6	0.0	83.3
CMS		86.6	16.2	39.0	100.0
SF-36	Physical functioning	84.5	20.4	15.0	100.0
	Role functioning/physical	73.5	37.6	0.0	100.0
	Role functioning/emotional	77.0	37.4	0.0	100.0
	Energy/fatigue	74.0	26.5	0.0	100.0
	Emotional well-being	76.5	26.2	0.0	100.0
	Social functioning	80.7	23.4	12.5	100.0
	Pain	75.8	29.0	0.0	100.0
	General health	80.5	22.7	15.0	100.0

NCS: Nottingham Clavicle Score, OSS: Oxford Shoulder Score, DASH: Disabilities of the Arm, Shoulder and Hand Questionnaire, CMS: Constant-Murley Score, SF-36: Short Form-36 Health Survey, SD: Standard Deviation, Min: Minimum, Max: Maximum.

Table 3. Internal consistency of the Nottingham Clavicle Score

	Mean±SD	Corrected Item-Total Correlation	Cronbach's Alpha if Item Deleted
Item 1	7.0±3.0	0.809	0.912
Item 2	7.2±2.9	0.765	0.915
Item 3	7.9±2.3	0.823	0.913
Item 4	7.2±2.8	0.734	0.917
Item 5	7.3±2.8	0.808	0.912
Item 6	7.2±2.7	0.871	0.908
Item 7	7.6±2.6	0.596	0.924
Item 8	8.4±2.4	0.509	0.928
Item 9	7.9±2.3	0.711	0.918
Item 10	9.0±1.6	0.517	0.927

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Considering the relationship between the total scores obtained in the NCS-Tr examination and other scales, there was a statistically significant, negative, and strong correlation between the mean DASH score and the NCS-Tr score. The mean CMS and OSS physical function, energy, pain, and health scores had statistically significant, positive, and strong correlations with the NCS-Tr score. Also, bodily pain, physical functioning, physical role functioning and vitality in the SF-36 had statistically significant, positive, and moderate correlations with the NCS-Tr score. The correlation of the NCS-Tr score with the other PROMs is summarized in Table 4. The translation and adaptation of the NCS-Tr for a Turkish context required no major cultural adaptation. Internal consistency was high (Cronbach's α=0.933). Test-retest reproducibility was excellent (q=0.941, p<0.001).

In Table 2, descriptive statistics of the scores given for each question item are shown. The NCS scale consists of 10 items and the mean score obtained by the participants from the NCS-Tr was 76.8±19.8, and the current scores of the participants ranged from 26 to 100.

The Cronbach's alpha (internal consistency) coefficient of the NCS-Tr was found to be 0.925. As a result of the reliability analysis, the corrected item-total scale correlation coefficients ranged from 0.509 to 0.871. According to the current results, the existing items performed at the desired level, as all of the adjusted item-total scale correlation coefficients were higher than 0.35. Similarly, even if any of the related question items were deleted, there was no significant change in the Cronbach's alpha internal consistency coefficients.

Test-retest reliability of NCS-Tr was evaluated by calculating the ICC. Accordingly, the ICC value was 0.921 (95% CI: 0.876 - 0.951), and test-retest reliability was found to be at very high levels statistically (p<0.001).

In Table 4, the results of the correlation analysis with other scales whose validity and reliability were conducted, are shown to examine the structural validity of the NCS-Tr. Accordingly, a statistically significant and very high correlation was found between the NCS-Tr and OSS (r=0.867 and p<0.001). There was a statistically significant and highly inverse correlation between the NCS-Tr and DASH (r=-0.898 and p<0.001). A statistically significant and same-directional very high correlation was also found between the NCS-Tr and CMS (r=0.892 and p<0.001). Finally, there were statistically significant, same-directional, and high correlations between all components of the SF-36 and NCS-Tr (p<0.001).

Discussion

In the present study, we performed a cross-cultural adaptation of the NCS questionnaire and investigated its validity and reliability in Turkish populations to assess the outcomes of clavicular fractures, and ACJ disorders. Our study results showed that the NCS-Tr was a avalid and reliable tool for this patient population. The translation and adaptation of the NCS-Tr into Turkish were found to be applicable and did not require significant revision. The Item 10 of the English version is a pattern sentence, and it was translated into Turkish with the integrity of the meaning rather than a literal translation. Therefore, although a significant correlation was found, the lowest ICC was detected for the Item 10 compared to the other questions. The other question types were translated as close to the original as possible. Our study results support that Turkish-speaking individuals are easily able to understand and answer the NCS-Tr in clinical practice. Moreover, the completion of the NCS-Tr is satisfactory compared to previously validated PROMs.

Table 4. Degrees of associations between Nottingham Clavicle Scores and other assessment tools

		Coefficient of correlation	p-value †
OSS		0.867	**<0.001**
DASH		-0.898	**<0.001**
CMS		0.892	**<0.001**
SF-36	Physical functioning	0.685	**<0.001**
	Role functioning/physical	0.758	**<0.001**
	Role functioning/emotional	0.618	**<0.001**
	Energy/fatigue	0.754	**<0.001**
	Emotional well-being	0.664	**<0.001**
	Social functioning	0.595	**<0.001**
	Pain	0.843	**<0.001**
	General health	0.838	**<0.001**

OSS: Oxford Shoulder Score, DASH: Disabilities of the Arm, Shoulder and Hand Questionnaire, CMS: Constant-Murley Score, SF-36: Short Form-36 Health Survey. † Pearson correlation analysis.

In the literature, there are many shoulder PROMs for the identification of symptoms of patients. This is because various shoulder disorders present with different clinical outcomes. Although there are many different scoring systems, relatively more specific scoring, such as the Western Ontario Shoulder Instability Index (WOSI) and Oxford Shoulder Instability Score (OSIS) are used in shoulder instabilities [12,13]. The CMS, OSS, DASH, the Simple Shoulder Test (SST), and American Shoulder and Elbow Surgeons (ASES) scores are used in rotator cuff pathologies [6,14]. Although different scoring systems have been described for the same anatomic region, each scale system reflects different specific pathologies.

To date, the Turkish validation and verification studies of many shoulder scoring systems have been conducted [6,12-14]. The validation of PROMs is important in revealing ethnicity differences and the applicability of scores in different cultures [6]. The intercultural adaptation of the OSS in Turkish was conducted by Tuğay et al. [10]. Other shoulder scores that have been validated in Turkish are the modified CMS and DASH [8,11]. The Turkish versions of these scores have been shown to be utilized reliably in the Turkish population.

The NCS was designed more specifically for injuries to the clavicular and ACJ and sternoclavicular joint. However, there is no study on the validation of the NCS in the Turkish population. Charles et al. [3] described the NCS by comparing the OSS, CMS, and Imatani scoring systems. In this first described version, a high Cronbach's alpha value was found postoperatively (0.87). Cronbach's alpha values higher than 0.70 are considered significant [15]. The Italian version of the NCS was validated and verified by Vascellari et al. [16]. They indicated that the most difficult adaptation or translation for the Italian NCS was found in Item 10, which was attributed to the fact that "dragging sensation" was not a clearly described Italian phrase. The authors used the SF-36, DASH, and OSS scores for the validation of the Italian NCS. Finally, they found a strong correlation with the DASH and OSS scores, a high-to-moderate correlation with bodily pain, physical functioning, physical role functioning, and vitality in the SF-36, and a high ICC was obtained for the NCS (0.86). Similarly, in our study, Item 10 was interpreted with semantic integrity and it was translated into Turkish with the integrity of meaning rather than a literal translation. We compared the NCS-Tr with DASH, CMS, SF-36, and OSS scores and observed highly significant correlations with all PROMs. A high Cronbach's alpha score (0.933) was determined for the NCS-Tr in our validation study.

Study Limitations: The main limitation to this study is its relatively small sample size. Therefore, the results of this study should be cautiously interpreted. Another limitation is the lack of evaluation of responsiveness, which can be identified as the ability of PROMs to assess time-dependent changes in the measurement process. Further well-designed large-scale studies are warranted to draw more reliable conclusions on these issues.

Conclusion: In conclusion, our study results show that the Turkish version of the NCS is valid, reliable, consistent, and comparable to the English version, and can be used as an instrument to assess the functional limitations of patients with injuries of the clavicle and ACJ.

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Appendix 1. Turkish Translation of NCS (NCS-Tr)

"Bir CC BY lisansı altında [3]'den değiştirilmiştir, [Prof W Angus Wallace] izniyle basılmıştır, orijinal telif hakkı [2017]."

Nottingham Klavikula Skoru (Köprücük kemiği, Akromioklavikular veya Sternoklavikular eklem (A/K & S/K eklem) yaralanmaları içindir.)

Aşağıdaki sorular son iki ay boyunca köprücük kemiğiniz/omzunuzun çevresinde hissettiğiniz ağrı düzeyi ve zorluklar ile ilişkilidir.

1. Genelde Omuzunuz/Köprücük kemiğinizdeki ağrıyı nasıl tarif edersiniz?
    a. Hiç
    b. Çok hafif
    c. Hafif
    d. Orta
    e. Ciddi

2. Geceleri yatakta Omuzunuz/Köprücük kemiğinizdeki ağrı nedeniyle ne sıklıkla sorun yaşıyorsunuz?
    a. Hiçbir gece
    b. Sadece bir veya iki gece
    c. Bazı geceler
    d. Çoğu geceler
    e. Her gece

3. Omuzunuz/Köprücük kemiğinizdeki ağrı günlük işlerinizi ne kadar etkiledi? (ev işleri ve araba sürmek dahil)
    a. Hiç
    b. Çok az
    c. Orta
    d. Büyük oranda
    e. Tamamen

4. Spor aktiviteler veya hobiler sırasında Omuzunuz/Köprücük kemiğinizde ne sıklıkla ağrınız oluyor?
    a. Hiçbir zaman
    b. Ara sıra
    c. Bazı zaman
    d. Çoğunlukla
    e. Her zaman

5. Ağır objeleri kaldırabilme açısından Omuzunuz/Köprücük kemiğinizde ne kadar problem yaşıyorsunuz?
    a. Hiçbir zaman
    b. Ara sıra
    c. Bazı günler
    d. Çoğu günler
    e. Her gün

6. Baş üstü aktiviteler sırasında Omuzunuz/Köprücük kemiğinizde yorgunluk veya güçsüzlük hissi oluyor mu?
    a. Hiçbir zaman
    b. Ara sıra
    c. Bazı zaman
    d. Çoğunlukla
    e. Her zaman

7. Köprücük kemiğinizin dış görünüşünden memnun musunuz?

   a. Tamamen mutlu
   b. Çok mutlu
   c. Orta derecede mutlu
   d. Çok az mutlu
   e. Hiç mutlu değil

8. Köprücük kemiğiniz bölgesinde size sorun yaşatan veya sizi endişelendiren herhangi bir hareket veya tıkırtı hisseder misiniz?

   a. Hiçbir zaman
   b. Ara sıra
   c. Bazı zaman
   d. Çoğunlukla
   e. Her zaman

9. Boynunuza veya kolunuza doğru yayılan herhangi bir karıncalanma veya uyuşukluk yaşıyor musunuz?

   a. Hiçbir zaman
   b. Ara sıra
   c. Bazı zaman
   d. Çoğunlukla
   e. Her zaman

10. Daha önce hiç kolunuzda ağırlık veya çekilme hissi yaşadınız mı?

    a. Hiçbir zaman
    b. Ara sıra
    c. Bazı zaman
    d. Çoğunlukla
    e. Her zaman

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Research Article

Araştırma

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Comparison of Two Methods in the Peripheral Nerve Block Application Used in Foot Surgery: USG-Guided and Anatomical Landmark-Guided

Ayak Cerrahisinde Kullanılan Periferal Sinir Blok Uygulamasında İki Metodun Karşılaştırılması: USG Yardımlı ve Anatomic Landmark Yardımlı

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ABSTRACT

Aim: Ankle peripheral nerve block is applied by two methods. These are peripheral block that is performed using USG-assisted and anatomical landmarks that do not require the use of Ultrasonography (USG). In our study, we aimed to compare these two methods applied in foot surgeries retrospectively.

Methods: Peripheral block patients performed with the USG-guided (group 1) were 20, anatomical landmarks- guided (group 2) were 20. In both groups, 40 cc of anesthetic mixture was used (bupivacaine + lidocaine). The recorded information of the patients were as follows: Block application time (BAT), surgery readiness time (SRT), duration of surgery (DoS), duration of block anesthesia (DBA) and intraoperative-postoperative Visual Analogue Scale (VAS). The results of the VAS applied to the patients postoperatively were obtained. Patients were contacted by phone and asked if they were satisfied with the anesthesia.

Results: The BAT and DBA values of the patients in Group 1 were high. SRT and VAS 6 values of the patients in group 2 were high. No significant difference was found between the groups in other parameters. No additional dose of anesthetic was needed in group 1 during the intraoperative period. In group 2, local additional dose was administered to 3 patients.

Conclusion: Peripheral block preparation USG-guided takes a long time. However, it is more comfortable during surgery. The USG-guided peripheral nerve block is more advantageous when considering the possibility of prolonging the duration of surgery for any reason and early postoperative pain control after surgery.

Key Words: Anesthesia, Ankle, Peripheral nerve block, Ultrasonography

ÖZET

Amaç: Ayak bileği periferik sinir bloğu iki yöntemle uygulanır. Bunlar; USG yardımlı periferik blok ve USG kullanımına ihityaç duymayan anatomik landmark'lar kullanılarak yapılan periferik bloktur. Biz de çalışmamızda ayak ameliyatlarında uygulanan bu iki yöntemi retrospektif olarak karşılaştırmayı amaçladık.

Yöntem: 2017 yılından itibaren ayak bileği periferik blok ile ameliyat edilen hastaların bilgilerine ulaşıldı. USG yardımıyla yapılan periferik blok hastaları (grup 1) 20 kişi, USG kullanılmadan, anatomik landmarklara göre yapılan periferik blok hastaları (grup 2) 20 kişiydi. Her iki grupta 40 cc'lik karışım kullanıldı (bupivakain+lidocain). Hastaların kayıt altına alınan bilgileri şunlardı: demografik bulgular, blok uygulanma süresi (BUS), operasyona hazır olma süresi (OHOS), operasyon süresi (OS), blok anestezi süresi (BAS) ve intraoperatif-postoperatif VAS skoru. Ameliyat sonrası hastalara uygulanan vizüel analog skalası (VAS) sonuçlarına ulaşıldı. Hastalara telefonla ulaşılıp anesteziden memnun olup olmadıkları soruldu.

Bulgular: Grup 1'deki hastaların BUS ve BAS değerleri yüksekti. Grup 2'deki hastaların OHOS ve VAS 6 değerleri yüksekti. Diğer parametrelerde gruplar arasında anlamlı bir farklılığa rastlanılmadı. İntraoperatif dönemde grup 1'de ek doz anestezik maddeye ihtiyaç olmamıştır. Grup 2'de ise 3 hastada intraoperatif hafif ağrı hissetmeleri üzerine lokal ek doz uygulanmıştır.

Sonuç: USG kullanılarak uygulanan periferik blok hazırlığı uzun sürmektedir. Anestezistlerin tecrübesi arttıkça bu sürenin kısalacağı kanaatindeyiz. Ancak cerrahi sırasında daha konforludur. Ameliyat süresinin herhangi bir sebepten uzama ihtimali ve postoperatif erken dönem ağrı kontrolü göz önüne alınınca USG eşliğinde yapılan periferik blok daha avantajlıdır.

Anahtar Kelimeler: Anastezi, Ayak bileği, Periferal sinir bloğu, Ultrasonografi

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Introduction

Nowadays, regional anesthesia applications have become popular in lower extremity surgeries. Both economic reasons and complication rates of general anesthesia have been effective in this popularization [1,2]. Moreover, it is of great importance to shorten the length of hospital stay of patients. Chelly et al. revealed that the length of hospital stay depended on the type of anesthesia applied and postoperative pain control [3]. Accordingly, anesthesia is on the agenda as much as the surgeon needs. In other words, general anesthesia is replaced by spinal anesthesia and central/peripheral blocks in lower extremity surgeries. Peripheral nerve blocks influence only the distal of the block area. This reduces the risk of complications [4]. Since peripheral blocks are infiltration blocks, the mixing of the anesthetic agent into the blood occurs slowly. In this respect, the risk of complications is expected to be low [5]. In the literature, it is observed that cardiovascular complications of peripheral blocks are less compared to general and spinal anesthesia [6]. Hallux valgus, hallux rigidus, neuroma excision, Freiberg's disease, and middle-distal foot amputations constitute a significant part of foot surgery. These surgeries can be carried out comfortably with ankle block. This block type is mostly applied under Ultrasonography (USG) guidance. In our clinic, peripheral block at the ankle level is performed both under USG guidance and using anatomical landmarks without the need for USG. In the literature review, there are many studies comparing peripheral block methods among themselves and to spinal anesthesia [7,8]. However, studies comparing ankle block techniques with USG and without the need for USG have generally been conducted on a single nerve [9,10]. There are review studies evaluating all nerves, and these studies were carried out a long time ago [11]. Considering the development of USG devices and anesthesiologists to the present time, we needed to conduct this study. In this study, we aimed to compare the USG-guided ankle block and ankle block without USG guidance in foot surgeries performed in the operating room of our hospital. We think that this study can show that ankle nerve block can be easily applied by orthopedists.

Materials and Methods

The study was initiated after permission from the ethics committee of our hospital was obtained. (Date: 08/08/2022 No:2053) Patients operated on the middle and distal foot region were screened as of January 2017. Patients over the age of eighteen and those administered ankle block anesthesia were included in the study. Patients who underwent amputation due to diabetic foot wounds and trauma patients were excluded from the study. Patients who underwent ankle block with USG guide were called GROUP 1, and patients who underwent ankle block without using USG guide were called GROUP 2. Assuming that the medium effect size (effect size=0.30) is considered as a difference, the alpha significance level was calculated as 0.05 % 95% power, 12 in Group 1 and 14 in Group 2, a total of 26 patients. 20 patients in group 2 were reached. The number of patients in group 1 was higher. Therefore, 20 patients were selected by drawing lots. Fourty patients were reached and evaluated retrospectively.. The anesthesia methods administered to the patients were evaluated. 20 patients were administered USG-guided ankle peripheral block anesthesia (Group 1) and 20 patients were administered ankle anesthesia without USG guidance (Group 2). The patients' files were examined retrospectively. Demographic findings (age, sex, anesthesia risk group) of the patients were recorded. Block application time (BAT), surgery readiness time (SRT), and duration of surgery (DoS) were obtained from the records. The results of the visual analog scale (VAS) applied to the patients following the surgery were obtained. On the VAS, "no pain" was considered as "0," and "unbearable pain" was considered as "10." The first time the patients were administered analgesics was recorded from the ward observation records. The time between the start of the surgery and the time the first analgesic was administered was accepted as the duration of block anesthesia (DBA). The presence of complications due to anesthesia was evaluated. The patients were contacted by phone and asked whether they were satisfied with the anesthesia.

Prior to block anesthesia, 0.02 mg/kg midazolam Intravenous (IV) premedication was administered to all patients. To be used in both groups, a 40 ml mixture of Marcaine® 0.05% (bupivacaine) and Aritmal® 2% (lidocaine), each mixed in equal amounts, was prepared.

In Group 1, the patients were placed in the supine position. A pillow was put under the heel, and the whole ankle was accessible. The area was stained sterile, and the procedure was initiated with a USG probe wrapped with a sterile glove. The anesthetic mixture was administered to the tibial nerve (8-10 ml), superficial peroneal nerve (5-7 ml), deep peroneal nerve (3-5 ml), saphenous nerve (2 ml), and sural nerve (2-3 ml), respectively.

In Group 2, a pillow was put under the heel of the patient in the supine position. Anatomical indicators were marked. Disinfection was done, and the procedure was initiated. The lateral malleolus-end was palpated for the superficial peroneal nerve block. Eight to ten cm proximal to this point, 5-7 ml of the anesthetic mixture was administered subcutaneously at the anterior of the fibula. The deep peroneal nerve runs laterally to the anterior tibial artery at the ankle level. If the artery could not be palpated, the anterior tibial tendon was found 4-5 cm proximal to the distal joint sur-

face of the tibia. The insertion was made in a depth of 1-1.5 cm just lateral to this tendon. First, aspiration was made to ensure that the needle was not in the vein. 3-5 ml of the anesthetic mixture was injected. The medial malleolus-end was palpated for the saphenous nerve block. This point was found to be 3-5 cm proximal, and the needle tip was advanced toward the anterior. After aspiration, 2 ml of the anesthetic mixture was injected. For the sural nerve, 5 cm proximal to the lateral malleolus-end was marked. At this level, the peroneus longus tendon, running in the posterior of the fibula, was found. 2-3 ml of the anesthetic mixture was injected subcutaneously between the peroneus longus tendon and the Achilles tendon. Finally, the tibial nerve block was started. The posteromedial edge of the tibia was palpated 5 cm proximal to the medial malleolus-end. At this level, the flexor digitorum longus tendon and posterior tibial tendons were palpated. The needle inserted between these tendons and the Achilles tendon was guided to the inferior at a 60-degree angle. After aspiration, 8-10 ml of the anesthetic mixture was injected [12].

Pain control was carried out in the patients in both groups. When it was decided that anesthesia was adequate, an elastic bandage (15 cm) was tightly wrapped from around the tip of the toe to the ankle level. The bandage was untied starting from the tip of the toe. The tourniquet was provided by leaving the bandage at the ankle level. The surgical area was prepared with Batticon, and the surgery was initiated. If there were areas where the patient felt pain during the surgery, local infiltration anesthesia was administered using one ml of CITANEST® 2% (prilocaine) until anesthesia was achieved. Patients who required local anesthetic agents were recorded.

Statistical Analysis

The SPSS (Statistical Package for the Social Sciences) 25.0 package program was used in the statistical analysis of the data. Categorical measurements were summarized as number and percentage, while continuous measurements were summarized as mean and standard deviation values (when necessary, median and minimum-maximum values). Chi-square and Fisher's exact test were used in the analysis of categorical statements. The Shapiro-Wilk test was used to identify whether the parameters in the study were normally distributed. The Mann-Whitney U test was conducted to examine differences between the parameters that were not normally distributed. In all tests, the statistical significance level was accepted as 0.05.

Results

The demographic data were the same between the two groups. The BAT min. and DBA ($p<0.001$; $p<0.001$, respectively) findings of the patients in Group 1 were higher than those of the patients in Group 2, and their SRT min. and VAS 6 ($p<0.001$; $p=0.024$, respectively) findings were lower than those of the patients in Group 2, which were found to be significant ($p<0.05$). There was no significant difference between the groups in terms of DoS min., Anesthesia satisfaction, VAS intraoperative, and VAS 12-24 parameters ($p>0.05$) Table 1.

No additional dose of the anesthetic agent was needed in Group 1 in the intraoperative period. In Group 2, an additional local dose was administered to 3 patients since they felt mild intraoperative pain (2 patients VAS 2, 1 patient VAS 3). Two of these three patients felt pain in the tibial nerve, and one in the deep peroneal nerve sensory area. There was no neurological deficit in the examination of the patients on the first postoperative day.

Discussion

In recent years, there has been a considerable increase in studies on peripheral block anesthesia. In parallel, we see that its use in anesthesia routine has increased. The primary reason for this seems to be avoiding the complications of general anesthesia and spinal anesthesia, particularly in lower extremity surgeries. On the other hand, peripheral blocks also have important secondary and tertiary advantages.

The most important secondary advantage of peripheral nerve blocks appears to be postoperative analgesia. There are numerous studies indicating this effectiveness [13,14].

Even peripheral block methods with infusion catheters have been described to prolong the block effect time for postoperative pain control [15].

This situation suggests that the postoperative analgesic effect even takes precedence over the anesthetic effect. The absence of postoperative pain not only increases patient's comfort and satisfaction but also facilitates rehabilitation, increasing surgical success.

Chelly et al. demonstrated that the length of hospital stay was related to postoperative pain control and anesthesia type in orthopedic surgeries [3]. From this perspective, the tertiary advantage of peripheral nerve blocks emerges. They not only reduce the costs of drugs and personnel but also shorten the length of hospital stay.

Neurotransmitters and USG are the most commonly used procedures to determine nerve localization in peripheral nerve blocks. A study conducted by Gürkan et al. in 2014 reported that the most common procedure to determine the location of the nerve in peripheral nerve blocks was using a neurotransmitter, but USG was also becoming widespread [16]. Nowadays, USG is extensively used in ar-

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Table 1. Demographic data and efficacy comparison between groups

	Group 1	**Group 2**	**p[a]**
	n(%)	**n(%)**	
Sex			
Female	8 (40)	14 (70)	0.054
Male	12(60)	6 (30)	
Hospitalization	15 (75.0)	14 (70)	0.838
ASA			
1	16 (80)	15 (75)	0.793
2	4 (20)	5(25)	
Complication	-	3 (21.4)	0.088
	Group 1	**Group 2**	**p[b]**
	Mean±sd	**Mean±sd**	
Age	46±5.6	41.0±4.0	0.279
BAT min.	16.4±0.8	5.1±0.2	**<0.001****
SRT min.	15.4±0.9	21.6±0.9	**<0.001****
DoS min.	49.8±2.1	50.4±2.2	0.935
DBA min.	213.3±3.9	148.2±4.9	**<0.001****
Satisfaction with anesthesia	90.0±0.2	89±0.2	0.801
VAS intraoperative	0.0±0.0	0.5±0.3	0.095
VAS 6	2.1±0.2	2.9±0.2	**0.024***
VAS 12	4.7±0.3	4.5±0.3	0.690
VAS 24	1.58±0.2	1.64±0.7	0.887

* p<0.05, **p<0.001, a: Chi-square and Fisher's exact, b: Mann-Whitney U test

eas where the nerves such as the ankle block are close to the surface. One of the reasons for this is that the USG experience of anesthesiologists has increased considerably.

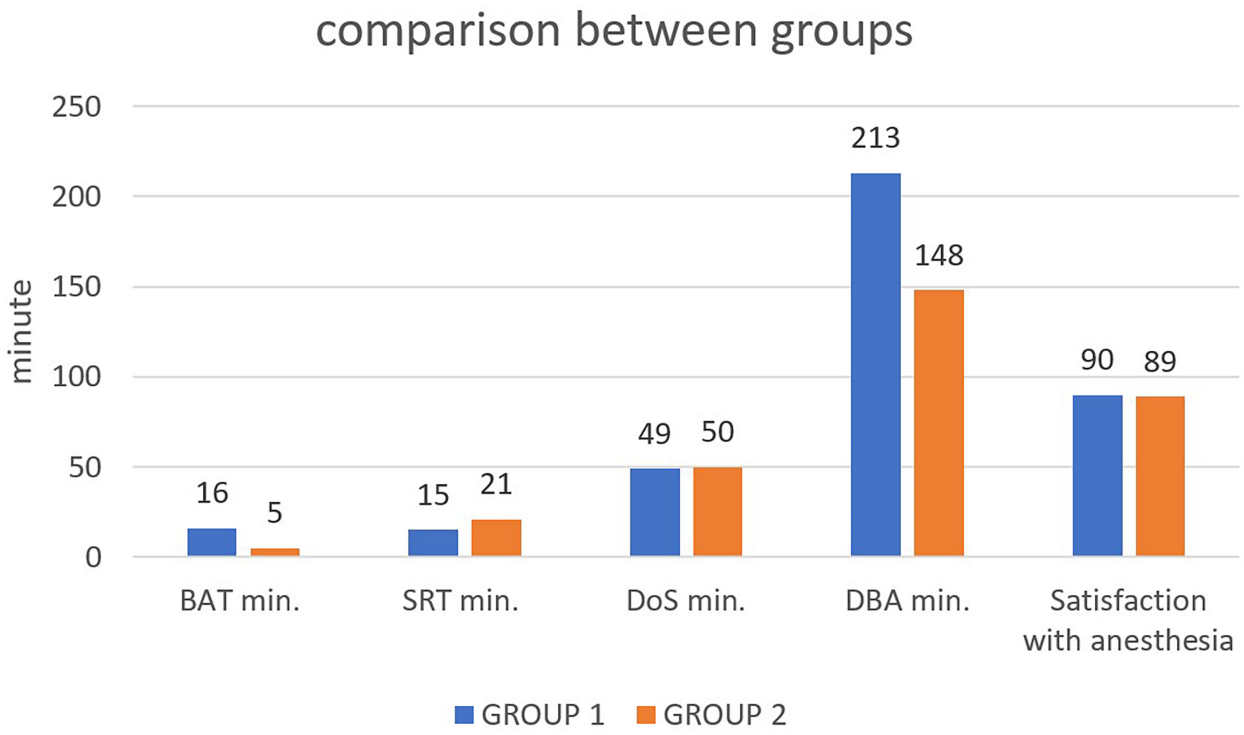
In our study, we tried to reveal whether the use of USG, which is common in ankle-level peripheral nerve block, contributed to the block. We reached striking results in our study, particularly focusing on surgical interventions applied to the metatarsi and phalanges. While the duration of the procedure was significantly longer in Group 1, it was observed that the surgery readiness time after the procedure was significantly longer in Group 2 (Graphic 1). We attribute this situation to finding the nerve via USG exactly in Group 1 and the administration of the anesthetic agent to its immediate surroundings. We see that the administration and readiness time in Group 1 is consistent with the literature [17].

The intergroup difference in the duration of anesthesia did not cause any intraoperative difference in the VAS score. This results from the fact that the surgery times were less than 60 minutes. However, we see that the anesthesia duration of 213 minutes in Group 1 and 148 minutes in Group 2 caused a significant difference in the early postoperative period. This difference resulted in the fact that the VAS score checked at the 6th hour was significantly lower in Group 1. This result suggested that some of the anesthetic agent used in Group 2 did not reach the target area. No significant difference was observed in the VAS scores checked at the 12th and 24th hours when the effect of the anesthesia was over in both groups (Graphic 2).

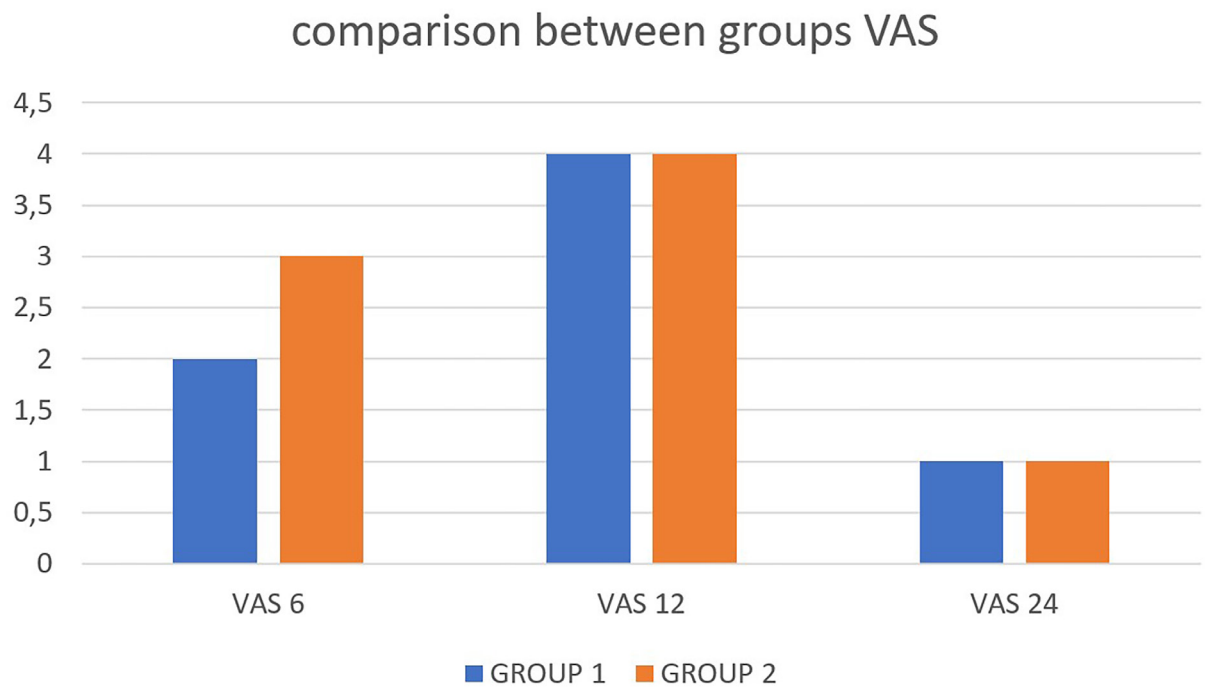
We observe that neither the additional intraoperative dose nor the difference in the 6th-hour VAS score affected the patient satisfaction score.

There are ankle block studies conducted on patients with diabetic foot wounds [17]. However, the results may have been affected since this group might have diabetic neuropathy. Therefore, patients who underwent amputation due to diabetes were excluded from our study.

Compared to spinal anesthesia, the biggest disadvantage of peripheral blocks is shown as the length of administration time and surgery readiness time in the literature [17]. Spinal anesthesia must be applied on the operating table due to the risk of complications at the time of its administration. In block anesthesia, on the other hand, the patient to whom anesthesia is administered in another area can



Graphic 1. Degrees of associations between Nottingham Clavicle Scores and other assessment tools



Graphic 2. Comparison between groups VAS

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be brought to the operation room at the appropriate time. Hence, the disadvantage of time loss can be eliminated.

It is a fact that the complications of peripheral blocks are extremely low [6]. Although there is a risk of the drug entering systemic circulation, this risk can be avoided through aspiration before the drug is injected. This is particularly important at the tibial nerve block stage due to its proximity to the artery. In terms of the location of the tibial nerve, it is recommended to find the tibialis posterior artery. However, most of the time, it cannot be palpated clearly [18]. In our study, additional intraoperative doses were required to be injected into the tibial nerve in two patients in Group 2. By clearly localizing the nerve via USG, it was ensured that no additional dose was required for any patient in Group 1.

Peripheral blocks are usually thought to be safe. [13,19]. However, although rare, there are large-scale studies in which complications were encountered in peripheral block anesthesia administered in foot-ankle surgery. In these studies, smoking and the level of the procedure came to the forefront as risk factors. It has been stated that the complication rate decreases as the procedure level approaches the distal [20]. In our study, we did not face any short-term or long-term anesthesia complications.

In both groups, the ankle tourniquet was well tolerated by the patients, which is consistent with the literature [21]. There are studies reporting that peripheral nerve block can be used safely even in pediatric patients [22].

In both groups, there were patients who were discharged on the day of surgery. There was also no significant proportional difference in the day of hospitalization. However, this situation is a significant advantage of peripheral block compared to other anesthesia techniques.

The authors are aware of the study's limitations. The low number of patients and the non-prospective design of the study are its limitations. Collaborating with other centers focusing on feet, such as our clinic, and turning it into a multicenter study will increase the study's reliability.

The only disadvantage in Group 1 seems to be the duration of administration. We are of the opinion that this period will be shortened with an increase in the experience of anesthesiologists.

We believe that the importance of peripheral nerve block will increase over time. It is known that nerve block application gives successful results in chronic pain [23]. These studies show that the usage areas will also increase.

Conclusion: The common opinion of this team of authors, including surgeons and anesthesiologists, is that more importance should be attached to peripheral blocks in the training of anesthesiologist assistants. In clinics where USG devices cannot be accessed, block application can be performed using anatomical landmarks. However, USG-guided peripheral block is more advantageous when the possibility of prolonging the duration of surgery for any reason and early postoperative pain control are considered.

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