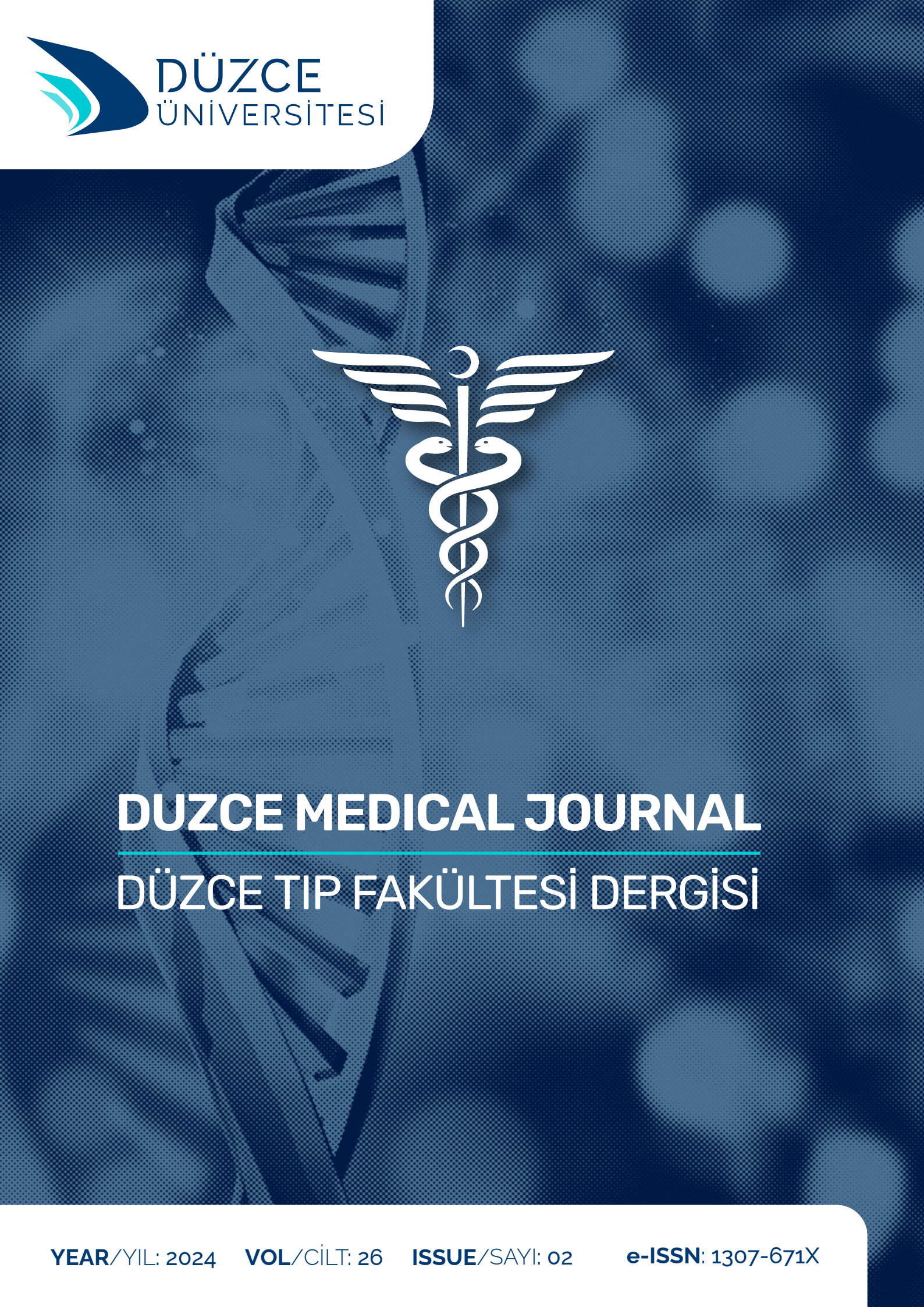

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Diagnosis and Treatment Approaches in Vaginal Agenesis

Vajinal Agenizde Tanı ve Tedavi Yaklaşımları

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ABSTRACT

The development of the female genital system is a complex process that depends on a series of events involving cellular differentiation, migration, fusion, and recanalization. Failure of any of these processes results in congenital anomalies. Developmental anomalies can occur at various stages, resulting in conditions that impact both the urinary and reproductive systems. In younger patients, such malformations can significantly affect their overall health and quality of life, including aspects such as fertility, sexual function, and psychological well-being. The psychosexual effects of vaginal agenesis should not be overlooked, and clinical care primarily involves comprehensive counseling and support through open communication with the patient. For adult patients, treatment for vaginal agenesis typically starts with therapeutic counseling and education, with non-invasive vaginal dilation being recommended as the first-line approach, or surgery if necessary. Consequently, managing these issues often requires a multidisciplinary approach, engaging specialists such as urologists, gynecologists, endocrinologists, and geneticists, among others. Early detection and timely intervention can greatly enhance the outlook for individuals with these conditions. Besides considering the patient's expectations, the surgeon's experience plays a crucial role in selecting the appropriate surgical technique. This is because the success of the initial surgery is critical to the effectiveness of any subsequent procedures if required. In this review, the evaluation and treatment of vaginal agenesis, which constitutes an important part of congenital anomalies of the vagina, were discussed.
Keywords: Müllerian canal; vaginal agenesis; vaginoplasty.

ÖZ

Kadın genital sisteminin gelişimi, hücresel farklılaşma, göç, füzyon ve yeniden kanalizasyonu içeren bir dizi olaya bağlı olan karmaşık bir süreçtir. Bu süreçlerden herhangi birinin başarısızlığı doğumsal anomalilerle sonuçlanır. Gelişimsel anomaliler çeşitli aşamalarda ortaya çıkabilir ve hem üriner hem de üreme sistemlerini etkileyen durumlarla sonuçlanabilir. Genç hastalarda, bu tür malformasyonlar doğurganlık, cinsel işlev ve psikolojik refah gibi hususlar da dahil olmak üzere genel sağlıklarını ve yaşam kalitelerini önemli ölçüde etkileyebilir. Vajinal agenezinin psikoseksüel etkileri göz ardı edilmemelidir ve klinik bakım öncelikle hastayla açık iletişim yoluyla kapsamlı danışmanlık ve desteği içerir. Yetişkin hastalar için vajinal agenezi tedavisi tipik olarak terapötik danışmanlık ve eğitimle başlar, ilk basamak yaklaşım olarak invazif olmayan vajinal dilatasyon veya gerekirse cerrahi önerilir. Sonuç olarak, bu sorunların yönetimi genellikle ürologlar, jinekologlar, endokrinologlar ve genetikçiler gibi uzmanları içeren multidisipliner bir yaklaşım gerektirir. Erken teşhis ve zamanında müdahale, bu durumlara sahip bireylerin görünümünü büyük ölçüde iyileştirebilir. Hastanın beklentilerini göz önünde bulundurmanın yanı sıra, cerrahın deneyimi de uygun cerrahi tekniğin seçilmesinde çok önemli bir rol oynar. Bunun nedeni, ilk ameliyatın başarısının, gerekirse sonraki prosedürlerin etkinliği açısından kritik olmasıdır. Bu derlemede, vajinanın konjenital anomalilerinin önemli bir bölümünü oluşturan vajinal agenezinin değerlendirilmesi ve tedavisi tartışılmıştır.
Anahtar kelimeler: Müllerian kanal; vajinal agenezi; vajinoplasti.

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INTRODUCTION

Vaginal agenesis is a complex condition affecting the female genital system. Sometimes this condition is an isolated vaginal agenesis and sometimes it is part of a complex disorder of sexual development. To understand why this disorder occurs, it is necessary to understand the embryology of the female genital system.

Sexual development in the female direction is independent of the gonadal or endocrine system. Since the female fetus lacks Müllerian inhibitory factor (MIF), the paramesonephric ducts continue to develop and the caudal part of the duct fuses with the opposite side to form the uterine horns, corpus uteri, and uterine cervix. It is in contact with the uterovaginal canal and the urogenital sinus, which are formed at the end of the 2nd intrauterine month. Afterwards, these parts form the lower part of the vagina which will ensure the continuity of the uterovaginal canal (1).

Genetic factors play an important role in the etiology of vaginal agenesis. However, genetic factors alone are insufficient to explain all cases of vaginal agenesis. In addition to genetics, defective MIF release, estrogen receptor disorders at the caudal end of the paramesonephric duct, exposure to teratogenic agents, mesenchymal induction defects or genetic loss in cytoplasmic receptor proteins of androgenic target cells as in androgen insensitivity syndrome may disrupt normal vaginal canal development (2).

This review aimed to discuss the evaluation and treatment of vaginal agenesis, which constitutes an important part of congenital anomalies of the vagina.

EVALUATION OF VAGINAL AGENESIS CASES

In these patients, basic initial evaluation should be performed in two aspects. The first one is laboratory evaluation including testosterone, follicle stimulating hormone (FSH), and karyotype analysis and the second one is radiological evaluation. Radiological evaluation can be performed with transabdominal, translabial, or transrectal two-dimensional and three-dimensional ultrasound in order to evaluate the internal genital structures. Magnetic resonance imaging (MRI) should be used in addition to radiological evaluation. This allows visualization of rudimentary Müllerian structures, which may be present in most patients with Müllerian agenesis. In addition, MRI can also assess the presence of endometrial activity in the Müllerian structures. Since the evaluation of rudimentary Müllerian structures may be difficult with ultrasound, especially before puberty, MRI is preferred in this age group (3).

In addition, it should be kept in mind that urinary system and skeletal system anomalies may accompany genital system anomalies in these patients (4). In many studies, anomalies including kidney and collecting system, horseshoe kidney, pelvic kidney, renal agenesis, or ureter duplication have been found in approximately one-third of the patients. Therefore, urinary system ultrasonography should be included in the initial evaluation of patients. In addition, scoliosis, hemivertebra, and other vertebral arch disorders involving the skeletal system are encountered more frequently in this group compared to the normal population and X-ray spine radiography may be used in the evaluation (5,6).

PSYCHOSOCIAL COUNSELLING AND SUPPORT

The psychological effects of vaginal agenesis are often underestimated. Many patients with this condition experience intense anxiety and depression. The basis of this is the questioning of their female identity and the feeling of not being able to have children, which they are worried about in their future lives. At the same time, patients sometimes have difficulty in sharing their current situation with their family, friends, or partners. Considering all these factors, appropriate psychological counseling should be offered to these patients. In addition, contact with other patient groups with a similar diagnosis may also be useful (7).

TREATMENT OPTIONS IN PATIENTS WITH VAGINAL AGENESIS

Historically, surgical neovagination in patients with vaginal agenesis was first performed by Hippocrates who lived between 460 and 377 BC (8). However, surgeons did not show much interest in such patients in the following period. In 1898, Abbe succeeded in creating a neovagina long enough to have intercourse with a vaginal mould after surgically opening the perineum in two women (9). In the first half of the 20th century, many surgical and non-surgical methods were described to create neovagina (10).

The aim of treatment of vaginal agenesis is to treat anatomical abnormalities. The methods to be applied for this purpose are passive vaginal elongation or surgical creation of neovagina. In this section, passive methods and surgical techniques will be discussed.

Vaginal Elongation

Passive vaginal elongation with a dilatator should be the first-line treatment option because it can be performed safely and simply under patient control, and it has a lower complication risk and lower cost compared to surgery. The prerequisite for the success of vaginal dilatation is the patient's emotional maturity and willingness to apply this method. Initiation of dilatation at an early age, lack of sufficient knowledge about the diagnosis and anatomical differences of the patients, insufficient understanding of how the dilatation process works, and sociocultural reasons decrease the success of the method.

The dilatation procedure should be performed in an environment adapted to the patient, in which he/she feels comfortable and in which monitoring is possible. Initially, the patient should be thoroughly familiarized with the external genitalia with a mirror so that she can recognize her own clitoris, urethra, and distal vagina. In this way, she learns how to place the dilator in the appropriate location at the appropriate angle. Increasingly larger dilators are inserted into the distal vagina and advanced towards the apex. The application should be between 10 and 30 minutes three times a day. Patients using dilators are evaluated every two weeks to assess the extent of progress. Pain or bleeding may occur during dilatation, patients should be informed about this and encouraged to continue dilatation, lubricants can be used if necessary, or softer dilators can be tried. With passive vaginal dilatation, there is no limit to the vaginal length to be achieved before sexual intercourse. The fact that patients can have vaginal intercourse in a comfortable and functional way is considered as a success (11).

Laparoscopic Vecchietti Vaginoplasty

In this operation, an elliptical body called "olive" is placed at the apex of the distal vagina to provide rapid vaginal elongation. The ropes hanging on the sides of the olive at the vaginal apex are passed through the laparoscopically created vesicorectal and retroperitoneal space in the anterior abdominal wall and fixed to the traction device on the abdominal wall. A vaginal length of 9-10 cm is obtained in approximately one week by daily traction of 1-1.5 cm. Afterward, the olive in the vagina and the traction device on the anterior abdominal wall are removed. Afterward, the patient continues passive vaginal dilatation with a suitable dilator for one month. Sexual intercourse can start one month after the use of the dilator. If there is no sexual intercourse, the patient should continue passive dilatation (12-14). The most common problems encountered are postoperative pain, fever, and urinary tract infections. Rarely, cases of urethral necrosis due to the pressure of the olive have been reported in the literature. At the end of the operation, anatomical success is achieved in 98% of the patients and the average vaginal length is 9.5 cm. Functional sexual intercourse requires 12-16 weeks. In some patients, granulation may develop in the newly formed vaginal tissue and this condition is treated with silver nitrate (15).

Davydov Vaginoplasty

In Davydov vaginoplasty, the vesicorectal space is dissected vaginally to the level of the pelvic peritoneum, then the pelvic peritoneum is mobilized laparoscopically and the free peritoneum is fixed to the introitus with sutures. The proximal side of the peritoneal cavity is sutured and closed, thus creating a neovagene. Afterward, a mould is placed in the neovagina formed with peritoneum for one week. The patient is not mobilized during this period. After the mould is removed, the use of a dilator or regular sexual intercourse is essential. After a successful operation, a vagina length of 7-8 cm can be obtained. Up to 10% of patients experience dyspareunia or dissatisfaction with sexual intercourse. Other rare complications include rectal perforation, rectoneovaginal fistula, bladder injury, and neovaginal prolapse requiring sacrocolpopexy and pelvic adhesions (14,16,17).

Abbe-McIndoe Vaginoplasty

In Abbe-McIndoe vaginoplasty, the vesicorectal space is vaginally dissected to the level of the pelvic peritoneum, usually about 10 cm in length. A full-thickness skin graft, usually from the buttocks or thighs, is placed on a mould that is inserted into the previously dissected vesicorectal. The mould is left in place for one week and then removed in the operating theatre and the condition of the graft is assessed. Patients should then continue passive dilatation and regular sexual intercourse for 6 months. The reported anatomical success of Abbe-McIndoe vaginoplasty is around 80-90%. Pain and cosmetic problems may occur especially in the area where the skin graft is taken. In patients with such concerns, synthetic grafts that will provide neovaginal epithelialization or buccal mucosa can be used instead of skin grafts (18-21).

Intestinal Vaginoplasty

In intestinal vaginoplasty, which is usually performed by pediatric surgeons and urologists, the sigmoid is most commonly used to create a neovagina. The sigmoid colon, which is approximately 10-12 cm long, is mobilized with care to preserve blood flow. The proximal part of the sigmoid colon neovagina is fixed inside the abdomen to prevent prolapse, and the distal part is sutured introitus. There is no need for dilatation after the operation. If there is no regular sexual activity, stenosis may occur in the introitus, but most of these can be opened with dilatation. If neovagina prolapse occurs, sacrospinous fixation can be performed (22).

CONCLUSION

Absolutely, understanding genitourinary embryology is crucial for diagnosing and treating genital malformations. The development of the genitourinary system is a complex process that involves the differentiation of structures from the mesoderm and the interaction of various signaling pathways. Anomalies can arise at different stages of development, leading to a range of conditions that may affect both the urinary and reproductive systems. In young patients, these malformations can have significant implications for their health and quality of life, including issues related to fertility, sexual function, and psychosocial well-being. Therefore, a multidisciplinary approach is often necessary for management, involving urologists, gynecologists, endocrinologists, and geneticists, among others. Referral to specialized centers that have experience in managing complex genital malformations is essential. These centers can provide comprehensive care, including advanced imaging, surgical interventions, and long-term follow-up, ensuring that patients receive the best possible outcomes. Early diagnosis and intervention can significantly improve the prognosis for individuals with these conditions. In addition to the patient's expectations, surgical experience is extremely important in the choice of surgical method. Because the success of the first operation is decisive in the success of subsequent operations if necessary. Whether the patients used passive methods or surgical vaginoplasty, as a result, they had a similar length of a neovagina, and the female sexual function scale scores were similar between the groups. Among the surgical methods, the need for lubricant use during intercourse was seen more in patients who underwent Abbe-McIndoe vaginoplasty compared to other methods.

Ethics Committee Approval: Since our study was a review, ethics committee approval was not required.

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Evaluation of Incidental Proliferative Non-Proliferative Lesions Detected in Mammoplasty Specimens Performed for Aesthetic Purposes

Estetik Amacı ile Yapılan Mammoplasti Spesmenlerinde Saptanan İnsidental Proliferatif Non-Proliferatif Lezyonların Değerlendirilmesi

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ABSTRACT

Aim: Reduction mammoplasty (RM) operations are frequently performed for breast reduction and asymmetry correction. Evaluation of these materials is important in patients at high risk of developing invasive breast carcinoma (IBC) to detect precancerous lesions or lesions that may accompany cancer. This study aimed to evaluate the histopathologic and clinical features of proliferative and non-proliferative lesions in RM materials.
Material and Methods: In this study, 214 cases (402 specimens) of RM operated for aesthetic purposes (except gynecomastia) at Eskişehir Osmangazi University Hospital between the years 2020 and 2023 were included. The age of cases, location and bilaterality of the lesions, and proliferative and non-proliferative lesions were evaluated.
Results: The mean age of RM cases was 38.5±10.9 years. The most common lesion was apocrine metaplasia in RM materials. Proliferative and non-proliferative lesions were found bilaterally in 24.8% (n=53) of all RM cases. The most common bilaterality was intraductal papilloma and the most common unilateral lesion was ductal ectasia. 0.2% (n=1) case of ductal carcinoma in situ and 0.9% (n=4) cases of lobular carcinoma in situ was found.
Conclusion: Detection of high-risk lesions is important for appropriate clinical follow-up. In this study, high-risk proliferative lesions were found considerably in RM cases. Patients with high-risk proliferative lesions should be followed up more closely in terms of cancer risk in the future. In addition, it is crucial to perform a careful macroscopic examination in mammoplasty operations performed for aesthetic purposes to avoid missing these lesions.
Keywords: Breast carcinoma in situ; breast neoplasms; mammoplasty.

ÖZ

Amaç: Redüksiyon mammoplasti (RM) operasyonları sıklıkla meme küçültme ve asimetri düzeltilmesi için yapılmaktadır. İnvaziv meme karsinomu (İMK) gelişme riski yüksek hastalarda bu materyallerin değerlendirmesi prekanseröz lezyonların ya da kansere eşlik edebilecek lezyonların saptanması açısından önemlidir. Bu çalışmada RM materyallerinde görülen proliferatif ve non-proliferatif lezyonların histopatolojik ve klinik özelliklerinin değerlendirilmesi amaçlanmıştır.
Gereç ve Yöntemler: Bu çalışmaya 2020 ve 2023 yılları arasında Eskişehir Osmangazi Üniversitesi hastanesinde estetik amaçlı (jinekomasti hariç) olarak opere edilmiş olan, 214 RM olgusu (402 örnek) dahil edildi. Olguların yaşları, lezyonların lokalizasyonu ve bilateralitesi ve proliferatif ve non-proliferatif lezyonlar değerlendirildi.
Bulgular: RM olgularının yaş ortalaması 38,5±10,9 yıl idi. RM materyallerinde en sık rastlanan lezyon apokrin metaplazi idi. Tüm RM olgularının %24,8 (n=53)'inde proliferatif ve non-proliferatif lezyonlar bilateral olarak saptandı. En çok bilateralite gösteren lezyon intraduktal papillom, çoğunlukla unilateral olan lezyon ise duktal ektazi idi. %0,2 (n=1) duktal karsinoma in situ olgusu ve %0,9 (n=4) lobüler karsinoma in situ olgusu saptandı.
Sonuç: Yüksek riskli lezyonların tespiti uygun klinik takip için önemlidir. Bu çalışmada RM olgularında önemli oranda yüksek riskli proliferatif lezyonlar saptanmıştır. Yüksek riskli proliferatif lezyon saptanan hastaların gelecekte kanser riski açısından daha sıkı takip edilmesi gerekmektedir. Ayrıca estetik amaçlı yapılan mamoplasti operasyonlarında bu lezyonların gözden kaçırılmaması amacı ile makroskopik incelemenin dikkatli yapılması büyük önem taşımaktadır.
Anahtar kelimeler: Duktal karsinoma in situ; meme neoplazileri; mammoplasti.

INTRODUCTION

Reduction mammoplasty (RM) operations are frequently performed for breast reduction and asymmetry correction. Evaluating these materials is important in patients at high risk of developing invasive breast carcinoma (IBC) to detect precancerous lesions or lesions associated with cancer (1). RM, the seventh most common reconstructive surgical procedure in the United States, is one of the most common procedures performed by plastic surgeons. Performed more than 100,000 times per year, RM accounts for more than 40% of plastic surgery breast procedures (2). Previous studies have compared the incidence of occult malignancy (3,4) or atypical lesions (5) in resection specimens between groups undergoing breast reduction for symptomatic macromastia and breast asymmetry after breast cancer surgery. It is known in the literature that the risk of IBC is seen in patients with proliferative lesions. Previous studies have found that the relative risk of proliferative lesions with atypia increases compared to proliferative lesions without atypia (6).

This study aimed to analyze the interrelationships and clinical follow-up of proliferative and non-proliferative lesions seen in RM materials.

MATERIAL AND METHODS

This study has 214 RM cases (402 specimens) operated on at Eskişehir Osmangazi University Hospital between 2020 and 2023. Age distribution of the cases and bilaterality of the lesions were evaluated. For the clinical and molecular follow-up of the operated patients, help was received from the relevant clinician and hospital database. All cases who underwent mammoplasty for aesthetic purposes in the study center were included in the study, and male mammoplasty cases operated due to gynecomastia were not included in the study.

After the materials were received in formalin from the clinic, they were cut into 1-2 cm thick sections and left to formalin fixation for 20-22 hours. When any lesion was noticed after fixation, lesion-directed sampling was performed. Otherwise, a random tissue sampling was performed. At least three samples per breast were taken from each resected breast specimen. Additional samples are routinely taken when precancerous lesions are detected incidentally. After the tissue processing steps, tissue was embedded in paraffin, and 4-5 micrometer-thick sections were taken and stained with hematoxylin and eosin. Paraffin-embedded, hematoxylin-eosin-stained slides were prospectively reviewed by one breast pathologist, and detailed findings were recorded on a data form.

Age, weight of breast tissue, location (right/left), and bilaterality of lesions were recorded. Proliferative and non-proliferative lesions detected in all breasts were recorded. Cystic changes, ductal ectasia, apocrine metaplasia, columnar cell change, and usual ductal epithelial hyperplasia were recorded as non-proliferative lesions. Florid epithelial hyperplasia, fibroadenoma, sclerosing adenosis, intraductal papilloma, radial scar, atypical lobular hyperplasia, atypical ductal hyperplasia, lobular carcinoma in situ (LCIS), and ductal carcinoma in situ (DCIS) were recorded as proliferative lesions. The cases were divided into two groups: over 30 years old and over 40 years old. Then, it was evaluated whether proliferative and non-proliferative lesions showed a significant increase over the age of 30 or 40. Among all lesions, lesions that were more frequently seen together with other lesions were evaluated. Also, since DCIS and LCIS cases are the highest-risk preneoplastic lesions, their relationship with other lesions and age groups was evaluated. Reoperations of patients at high risk of developing cancer (LCIS, DCIS) were recorded.

Statistical Analysis

The normal distribution assumption was evaluated with the Shapiro-Wilk test. Continuous data were reported as mean±standard deviation, and categorical data were as a percentage (%). The Pearson chi-square or Fisher's exact test evaluated the differences between groups regarding these parameters and clinical and pathological variables. The data analysis was done with SPSS v.16.0, and $p<0.05$ was accepted as a statistical significance level.

RESULTS

Of the 214 operations performed, 191 (89.3%) were symptomatic mammoplasty, 3 (1.4%) were implant revision, 5 (2.3%) were for correction of breast asymmetry, and 15 (7%) were contralateral breast reduction after IBC. There were 402 breast specimens evaluated in total.

The distribution of non-proliferative lesions was as follows; cystic changes were detected in 40 (9.9%), ductal ectasia in 20 (4.9%), apocrine metaplasia (Figure 1) in 89 (22.1%), columnar cell changes in 26 (6.4%), and usual epithelial hyperplasia in 25 (6.2%) materials. As proliferative lesions; florid epithelial hyperplasia (Figure 2) was detected in 6 (1.4%), fibroadenoma in 27 (6.7%), sclerosing adenosis (Figure 3) in 25 (6.2%), and intraductal papilloma (Figure 4) in 7 (1.7%) materials. Radial scar, atypia ductal hyperplasia, atypia lobular hyperplasia, and IBC were not detected. 1 (0.2%) case of DCIS (Figure 5) and 4 (0.9%) cases of LCIS (Figure 6) were found in RM specimens. The mean weight of the materials was 867.9 (range, 6-6356) grams. This was not found related to detecting any other lesion.

The mean age of the patients was 38.5±10.9 years. The mean age of patients with lesions was 42.2±2.5 years, and 35.9±12.0 years without lesions. While the patients with columnar cell changes in the lesions were the oldest, fibroadenoma patients were the youngest (Table 1).

Table 1. Mean ages of the patients by lesions

Lesions	**Age** (years)
Non-Proliferative Lesions	
Cystic changes	40.3±7.9
Ductal ectasia	41.9±11.5
Apocrine metaplasia	41.9±8.3
Columnar cell change	45.9±6.9
Usual epithelial hyperplasia	43.0±9.3
Proliferative Lesions	
Florid epithelial hyperplasia	41.0±8.8
Fibroadenoma	37.7±9.5
Sclerosing adenosis	42.1±6.8
Intraductal papilloma	44.6±5.6
DCIS	40
LCIS	45.0±4.2

DCIS: ductal carcinoma in situ, LCIS: lobular carcinoma in situ

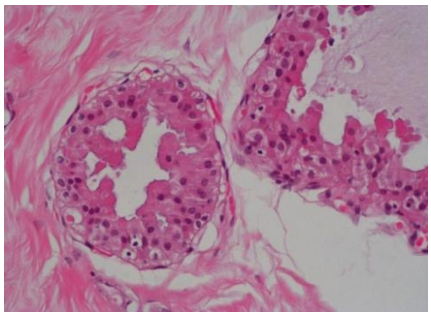

Figure 1.
Apocrine metaplasia (H&E x400)

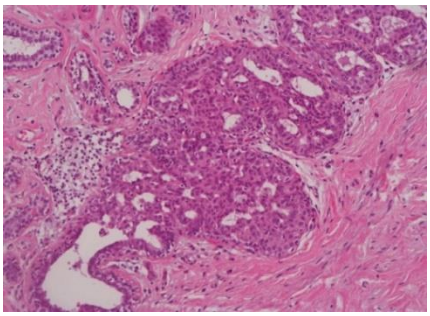

Figure 2.
Florid epithelial hyperplasia (H&E x100)

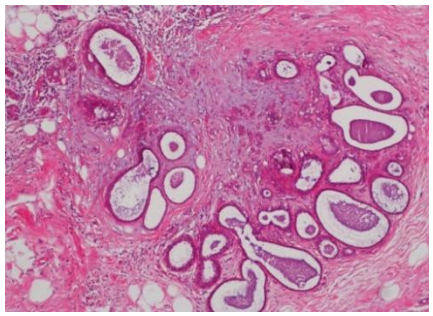

Figure 3.
Sclerosing adenosis (H&E x40)

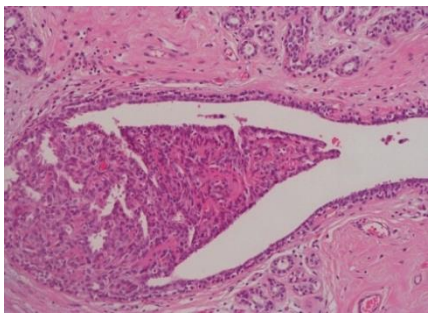

Figure 4.
Intraductal papilloma (H&E x100)

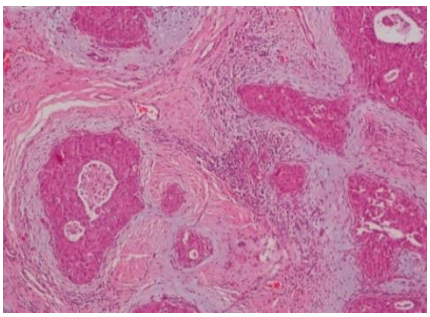

Figure 5.
Ductal carcinoma in situ (H&E x40)

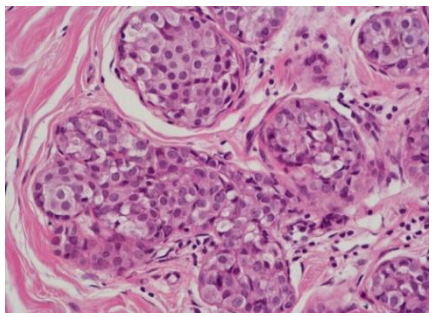

Figure 6.
Lobular carcinoma in situ (H&E x400)

In breast cancer screening studies, imaging screening is recommended due to the increased incidence of cancer in women over the age of 40. Based on this, we investigated whether there was a statistically significant increase in proliferative lesions that increase the risk of cancer in cases over 40 years of age, compared to the cases under 40 years of age (7). Additionally, in cases with a family history or known BRCA mutation, breast cancer screening should be started earlier due to the high risk. For this reason, we also investigated whether the frequency of proliferative lesions increased in patients over 30 years of age compared to the cases under 30 years of age (8,9). In patients aged 30 years and older, a significantly higher frequency of both proliferative ($p=0.016$) and non-proliferative ($p<0.001$) lesions was found. In patients aged 40 years and older, no association was found with proliferative lesions (Table 2). In these patients, the frequency of detection of non-proliferative lesions was found to be statistically significant.

Proliferative and non-proliferative lesions were found to coexist statistically significantly more frequently with columnar cell change (Table 3).

Some lesions were mainly observed bilaterally. Among the proliferative lesions, intraductal papilloma was the most common bilateral lesion, while among the non-proliferative lesions, apocrine metaplasia was the most common bilateral lesion. The most common unilateral lesion was ductal ectasia. Whether the lesions were on the right or left side did not show a significant result.

Additionally, the prevalence of DCIS and LCIS in cases over 30 and 40 years of age was evaluated (Table 4). It was also evaluated whether the co-occurrence of DCIS and LCIS with non-proliferative and proliferative lesions was statistically significant. Accordingly, the co-occurrence of LCIS cases in proliferative and non-proliferative lesions was found to be statistically significant ($p=0.003$, and $p=0.027$, respectively). 2 of these cases had subcutaneous mastectomy. Diffuse LCIS was reported in these two specimens. These patients are followed up with magnetic resonance imaging (MRI) every six months. No metastasis, recurrence, or IBC development has been observed so far. Three patients refused subcutaneous mastectomy. They are followed up with MRI every six months.

Table 2. Relationship of age groups with PL and NPL

	Age (years)		**p**
	<30 (n=47)	**≥30 (n=167)**	
PL, n (%)	5 (10.6)	46 (27.5)	**0.016**
NPL, n (%)	7 (14.9)	81 (48.5)	**<0.001**

	Age (years)		**p**
	<40 (n=112)	**≥40 (n=102)**	
PL, n (%)	23 (20.5)	28 (27.5)	0.236
NPL, n (%)	36 (32.1)	52 (51.0)	**0.005**

PL: proliferative lesion, NPL: non-proliferative lesion

Table 3. Relationship of columnar cell change with PL and NPL

	Columnar Cell Change		**p**
	Negative (n=195)	**Positive (n=19)**	
PL, n (%)	42 (21.5)	9 (47.4)	**0.021**
NPL, n (%)	71 (36.4)	17 (89.5)	**<0.001**

PL: proliferative lesion, NPL: non-proliferative lesion

Table 4. Relationship of age groups, PL, and NPL with DCIS and LCIS

	Age (years)		p
	<30 (n=47)	≥30 (n=167)	
DCIS, n (%)	0 (0.0)	1 (0.6)	>0.999
LCIS, n (%)	0 (0.0)	4 (2.4)	0.578

	Age (years)		p
	<40 (n=112)	≥40 (n=102)	
DCIS, n (%)	0 (0.0)	1 (1.0)	0.477
LCIS, n (%)	0 (0.0)	4 (3.9)	**0.050**

	Proliferative Lesion		p
	Negative (n=163)	Positive (n=51)	
DCIS, n (%)	0 (0.0)	1 (2.0)	0.238
LCIS, n (%)	0 (0.0)	4 (7.8)	**0.003**

	Non-Proliferative Lesion		p
	Negative (n=126)	Positive (n=88)	
DCIS, n (%)	0 (0.0)	1 (1.1)	0.411
LCIS, n (%)	0 (0.0)	4 (4.5)	**0.027**

PL: proliferative lesion, NPL: non-proliferative lesion, DCIS: ductal carcinoma in situ, LCIS: lobular carcinoma in situ

DISCUSSION

Detection of precancerous and high-risk lesions is essential for appropriate clinical follow-up. RM materials usually contain lesions with benign proliferation (10). According to the data in this study, the associations of proliferative and non-proliferative lesions have increased significantly in patients aged 30 years and over who underwent RM surgery. Atypical lesions are known to carry a higher risk of developing IBC. The literature reports that high-risk proliferative lesions are detected more frequently in cases of IBC (10). In our cases, the lesions that increased the relative risk of developing IBC were relatively numerous. We think that early diagnosis and treatment of these incidental lesions is important. In a study by Nergiz et al. (11), patients with lesions at high risk of IBC were followed clinically, and IBC developed in 2 of them. In the same study, the age group of 40 years was used, and proliferative lesions over 40 years of age were found to be significant in contrast to the present study. Non-proliferative lesions in patients over 40 years of age were significant. In a study conducted by Kakagai et al. (12) on current specimens without follow-up, 3 (1%) cases of occult breast cancer were found in 314 RM cases. We found 1 (0.2%) case of DCIS and 4 (0.9%) cases of LCIS in RM specimens. This rate is similar to the literature (13). A more recent study found 0.7% (n=1) of DCIS in 288 patients (14). Especially when DCIS and LCIS, which are precursor lesions of IBC, are detected, reoperation is recommended. Three of five carcinoma in situ cases in this study were reoperated. In 1 reoperated case, a unilateral lesion was seen on the RM specimen, but bilateral LCIS was detected on subcutaneous mastectomy. All our carcinoma in situ cases are followed up with an MRI every six months. BRCA testing and breast MRI are sometimes indicated for patients perceived to be at higher risk, including patients with a strong family history of breast cancer (15). We wonder whether these incidental precursor lesions are associated with BRCA mutation. We think that the relationship between BRCA status and carcinoma in situ may be important in the future. None of our patients received genetic counseling. We also believe that specimen sampling may vary depending on BRCA1 or BRCA2 status. We agree with the literature on this issue (16). Recent publications on this subject show a correlation between increased proliferative lesions and atypical hyperplasia in patients with familial history (17). In our study, there was no increase in proliferative lesions and atypical hyperplasia with age. Columnar cell changes are believed to represent the same genetic alterations as low-grade breast neoplasia. But so far, it has been found that it does not increase the risk of developing IBC more than proliferative lesions (18). In cases in this study, its association with proliferative and non-proliferative lesions was found to be significant. It is particularly noteworthy that it is seen together with DCIS and LCIS. Additionally, it was observed that the significance level of columnar cell change increased with increasing age. In this respect, we think that the relative risk assessment of columnar cell changes can be updated in light of other studies in the literature. We think that the English literature does not sufficiently cover columnar cell change. However, many studies have documented lesions with significant association with columnar cell change in this research.

The limitation of this study is that the cases were evaluated retrospectively. We think prospective studies are needed, especially in correlation with preoperative radiology.

CONCLUSION

Patients over the age of 30 years should be approached more carefully histopathologically, macroscopically, and intraoperatively. RM specimens are important materials for early diagnosis and treatment of patients. In light of the parameters found significant in this study, macroscopic sampling should be performed more carefully. It should be known that patients over 40 years of age with RM may be at risk for proliferative and non-proliferative lesions. When lesions such as fibroadenoma, sclerosing adenosis, and intraductal papilloma are encountered, additional sampling can be performed in terms of accompanying lesions that increase the risk of IBC. Sensitivity to these issues in macroscopy guidelines will significantly affect the prognosis of patients with a possible IBC case.

Ethics Committee Approval: The study was approved by the Non-Invasive Clinical Research Ethics Committee of Eskişehir Osmangazi University (16.05.2023, 21).

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An Evaluation of the Reliability and Quality of Information in Labiaplasty Videos Shared on YouTube

Youtube'da Paylaşılan Labioplasti Videolarındaki Bilgilerin Güvenilirliğinin ve Kalitesinin Değerlendirilmesi

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ABSTRACT

Aim: The objective of this study was to evaluate the reliability and quality of videos on YouTube about labiaplasty procedures.
Material and Methods: A search was carried out on YouTube using the search terms 'labiaplasty' and 'labia minora reduction'. The first 100 videos for each keyword were evaluated and 42 videos were analyzed. The distribution of video types was examined. The videos were scored by a five-member committee using the global quality scale (GQS) and modified DISCERN (mDISCERN) scales. Videos uploaded by physicians and academicians were classified as professional, and patients, commercial entities, and allied health personnel were classified as non-professional groups.
Results: The mean mDISCERN score of all videos was 2.29±0.65, while the mean GQS score was 2.75±0.67. When professional and non-professional groups were compared, the mDISCERN and GQS scores were significantly higher in the professional group (p=0.017 and p=0.010, respectively). When surgical technique videos and videos providing information about the disease or surgery were compared, there was a significant difference in video power index (VPI), viewing rate, and number of comments (p=0.001, p=0.001, and p=0.003, respectively), while there was no significant difference in terms of mDISCERN and GQS scores. Weak negative correlations were observed between the mDISCERN score and VPI (r_s=-0.326, p=0.037), between the GQS score and viewing rate (r_s=-0.392, p=0.010), and between the GQS score and VPI (r_s=-0.382, p=0.014).
Conclusion: YouTube is not a reliable source of information about labiaplasty. Low-quality videos receive more engagement. Obstetrics and gynecology associations should produce content on YouTube about this subject.
Keywords: Genitalia; female; social media; video recording.

ÖZ

Amaç: Bu çalışmanın amacı YouTube'da yer alan labioplasti prosedürlerine ilişkin videoları güvenilirlik ve kalite açısından değerlendirmektir.
Gereç ve Yöntemler: Youtube'da "labiaplasty" ve "labia minora reduction" arama terimleri ile bir arama yapıldı. Her bir anahtar kelime için ilk 100 video incelendi ve 42 video analiz edildi. Video türlerinin dağılımı incelendi. Videolar beş kişilik bir komite tarafından küresel kalite ölçeği (global quality scale, GQS) ve modifiye DISCERN (mDISCERN) ölçekleri kullanılarak puanlandı. Hekimler ve akademisyenler tarafından yüklenen videolar profesyoneller grubu, hastalar, ticari kuruluşlar ve yardımcı sağlık personelleri tarafından yüklenenler ise non-profesyoneller grubu olacak şekilde sınıflandırıldı.
Bulgular: Tüm videoların mDISCERN puan ortalaması 2,29±0,65, GQS puan ortalaması 2,75±0,67 idi. Profesyonel ve non-profesyonel grupları karşılaştırıldığında mDISCERN ve GQS puanı profesyonel grupta anlamlı olarak daha yüksekti (sırasıyla p=0,017 ve p=0,010). Cerrahi teknik videoları ile hastalık veya cerrahi hakkında bilgi veren videolar karşılaştırıldığında, mDISCERN ve GQS puanları bakımından anlamlı bir farklılık yokken video güç indeksi (video power index, VPI), görüntülenme oranı ve yorum sayıları açısından anlamlı farklılık mevcuttu (sırasıyla p=0,001, p=0,001 ve p=0,003). mDISCERN puanı ile VPI arasında (r_s=-0,326; p=0,037), GQS puanı ile izlenme oranı arasında (r_s=-0,392; p=0,010) ve GQS puanı ile VPI arasında (r_s=-0,382; p=0,014) zayıf negatif korelasyonlar gözlendi.
Sonuç: YouTube labioplasti ile ilgili güvenilir bir bilgi kaynağı değildir. Düşük kaliteli videolar daha fazla etkileşim içindedir. Obstetri ve jinekoloji dernekleri bu konu hakkında Youtube'da içerik üretmelidirler.
Anahtar kelimeler: Üreme organları; kadın; sosyal medya; video kayıt.

INTRODUCTION

Female genital cosmetic surgeries (FGCSs) have become more popular in recent years. FGCSs, especially labiaplasty, seem to have a positive effect on women's self-esteem (1). Labiaplasty is the most common FGCS. For example, the rate of labiaplasty in the United States increased by about 42% between 2017 and 2021 (2).

Because it is generally easy to access, the internet has become a common and frequently preferred platform for searching for health information in recent years. Women thinking about FGCSs use the internet as an important source of information when making decisions (3). In recent years, labiaplasty has been preferred more than vaginoplasty, platelet therapy, and clitoral hood reduction (2).

Previously, a study was conducted in which YouTube videos about FGCSs were evaluated (4). However, we could not find any research evaluating YouTube videos about the most common procedure; labiaplasty. Therefore, the purpose of our study was to evaluate videos about labiaplasty procedures on YouTube in terms of their content, accuracy, reliability, and quality.

MATERIAL AND METHODS

Data Collection

A search was performed on https://www.youtube.com/ on January 10, 2023, with the keywords 'labiaplasty' and 'labia minora reduction'. The browser's search history and all cookies had been deleted, and no personal Google or YouTube account had been logged into before searching.

The videos were listed by relevance, which is the current default option on YouTube. Several studies about search engine user behavior have demonstrated that most users click on a search result on the first page of results, and 90% of search engine users click on a result within the first three pages of results (5). However, currently, YouTube's search engine displays results in the form of an infinite scrolling list, not as pages. Therefore, to conduct the most reliable statistical analysis, the first 100 videos for each keyword were analyzed.

Videos uploaded on YouTube in English that were related to the subject and between 1-10 minutes were included. Since videos under 10 minutes would be more effective, we took the duration of the videos 1 to 10 minutes (6). If the videos were not related to the subject (n=17), not in English (n=9), repetitive (n=45), low image quality (n=6), under 60 seconds, or over 10 minutes (n=49), they were excluded from the study, as were advertisements (n=32). A total of 158 videos were excluded and 42 videos were evaluated in the final analysis.

Video Analysis

For each video, the type of image (real/animated), number of views, number of likes and dislikes, number of comments, time since upload, and duration were recorded. The view ratio (number of views/days), like ratio (likes × 100/[likes + dislikes]), and video power index (VPI; like ratio × view ratio/100) were calculated.

The primary purposes of the videos were categorized into three groups: 1) concerning surgical techniques, 2) providing information about the disease or surgery, and 3) sharing personal experiences. The videos were further classified into five basic groups by the type of uploader: 1) academic or institution, 2) physician, 3) patient, 4) commercial entity, and 5) allied health professional.

A committee of five people was established to analyze the videos. Each participant rated the videos based on the modified DISCERN (mDISCERN) and global quality score (GQS) scales.

DISCERN Scale

The DISCERN scale is a scoring tool used to assess the reliability of health information on treatment options for consumers. In this study, we used the mDISCERN tool, which was created by Charnock et al. (7) and shortened by Singh et al. (8). The scale consists of five questions evaluated on a 5-point Likert scale between 0 and 5. Higher scores represent greater reliability. One point indicates very poor quality, two points for poor quality and limited use, three points for medium quality, four points for good quality, and five points for very good quality.

Global Quality Score (GQS)

The GQS scale was introduced by Bernard et al. (9) to measure the quality of a video's content based on the usefulness of the information offered in the video. This scale consists of five questions that evaluate the quality, flow, and ease of use of information provided in a video on a 5-point Likert scale. Higher scores represent higher quality. One point indicates very poor quality, two points for poor quality and limited use, three points for medium quality, four points for good quality, and five points for very good quality.

Ethical Considerations

Approval from an ethics committee was not required, as this was an observational study performed using data collected from publicly available YouTube videos.

Statistical Analysis

We performed statistical analysis using IBM SPSS Statistics for Windows, v.25.0 (IBM, Armonk, New York, USA). The continuous variables were investigated using visual methods (histograms, probability plots) and analytical methods (Shapiro-Wilk test) to determine whether they were normally distributed. Data were presented as median, interquartile range (IQR), minimum, and maximum for continuous data, and as numbers and percentages for categorical data. The Mann-Whitney U test was used when comparing continuous variables between the two groups because the variables did not fit a normal distribution. The relationships between the median mDISCERN and GQS scores, VPI index, video view rate, and number of comments were investigated using Spearman's correlation test. Two-sided p values <0.05 were considered statistically significant.

RESULTS

Of the videos, 40 (95.2%) were real. Most of the videos were uploaded by physicians (n=36, 85.7%). The most common (n=25, 59.5%) video content was information about the disease or surgery (Table 1). Physicians and academy groups were classified as professionals; patients, commercial entities, and allied health personnel were classified as non-professionals.

The median duration of the videos was 246 seconds, the number of views was 23999, the time since upload was 1240 days, the view ratio was 20.7, the number of likes was 116.5, the number of dislikes was 13.5, the like ratio was 93.8, the VPI was 19.5, and the number of comments was 6.5 (Table 2).

Table 1. Distribution of video types

	n (%)
Image Type	
Real	40 (95.2)
Animation	2 (4.8)
Uploaders	
Academic or institution	2 (4.8)
Physician	36 (85.7)
Patient	2 (4.8)
Commercial entity	1 (2.4)
Allied health professional	1 (2.4)
Video Content	
Surgical technique	15 (35.7)
Information about the disease or surgery	25 (59.5)
Personal experiences	2 (4.8)

According to the mDISCERN median scores, 1 (2.4%) video was good, 15 (35.7%) videos were medium quality, 15 (35.7%) videos were poor quality, and 11 (26.2%) videos were very poor quality. According to the GQS median scores, 5 (11.9%) videos were good, 20 (47.6%) videos were medium quality, 11 (26.2%) videos were poor quality, and 6 (14.3%) videos were very poor quality. There were no videos ranked as very good quality on both scales. The median of all videos' mDISCERN scores was 2.2, while the median GQS score was 2.8. The mean of all videos' mDISCERN scores was 2.29±0.65, while the mean GQS score was 2.75±0.67 (Table 3).

When uploaders as professionals and non-professionals were compared, both the mDISCERN and GQS scores were significantly higher in the professional group (p=0.017 and p=0.010, respectively). For professionals, the median mDISCERN score was 2.4 (range, 1.4-3.8), while the median GQS score was 2.9 (range, 1.4-4.2). There was no significant difference in view ratio, VPI, and number of comments between professional and non-professional uploaders (Table 4). When surgical technique videos were compared with videos that provide information on the disease or surgery, there was no significant difference in mDISCERN and GQS scores, but there was a significant difference in view ratio, VPI, and number of comments in favor of surgical technique videos (p=0.001, p=0.001, and p=0.003, respectively, Table 5).

A correlation analysis was performed for mDISCERN and GQS scores with view ratio, VPI, and number of comments. While there was no significant correlation for the mDISCERN score with view ratio, and number of comments, a weak negative correlation was observed with the VPI (r_s=-0.326, p=0.037). While weak negative correlations were also observed between the GQS score and

Table 2. Descriptive statistics by video type

	Mean±SD	Median	IQR	Min-Max
Duration (sec)	257.17±128.71	246	161-345	78-549
Number of views	1456916.45±4300833.26	23999	8612-399777	404-20939879
Time since upload (day)	1548.07±1700.55	1240	634-1676	150-10225
View ratio	932.88±3005.75	20.7	13.1-264.5	0.7-14746.4
Number of likes	5198.12±22175.42	116.5	43-1750	0-143000
Number of dislikes	1155.69±5062.96	13.5	0-138	0-32000
Like ratio	91.34±8.71	93.8	85.9-100	69.9-100
VPI	753.99±2335.20	19.5	11.2-286.8	0.7-12049.9
NOC	401.95±1768.09	6.5	0-74	0-11292

VPI: video power index, NOC: number of comments, SD: standard deviation, IQR: interquartile range (25^{th}-75^{th} percentile)

Table 3. Descriptive statistics of mDISCERN and GQS scores of the videos

	Mean±SD	Median	IQR	Min-Max
DISCERN	2.29±0.65	2.2	1.8-2.8	0.8-3.8
GQS	2.75±0.67	2.8	2.2-3.2	1.4-4.2

GQS: global quality score, SD: standard deviation, IQR: interquartile range (25^{th}-75^{th} percentile)

Table 4. Comparison between professionals and non-professionals

	Professionals				Non-Professionals				p
	Mean±SD	Median	IQR	Min-Max	Mean±SD	Median	IQR	Min-Max	
DISCERN	2.38±0.61	2.4	1.8-2.9	1.4-3.8	1.50±0.50	1.6	0.8-2	0.8-2.0	**0.017**
GQS	2.84±0.65	2.9	2.4-3.3	1.4-4.2	1.95±0.25	2.0	1.7-2.2	1.6-2.2	**0.010**
View ratio	973.24±3148.33	20.1	13.1-264.5	0.7-14746.4	549.50±1003.88	71.6	6.4-1570.5	1.6-2053.2	0.830
VPI	787.92±2448.35	18.6	11.2-286.8	0.7-12049.9	440.16±794.07	64.9	6.4-1249.2	1.6-1629.2	0.792
NOC	441.26±1856.66	73.5	0.8-7.5	0-11292	28.50±56.33	0.5	0-85	0-113	0.270

GQS: global quality score, VPI: video power index, NOC: number of comments, SD: standard deviation, IQR: interquartile range (25^{th}-75^{th} percentile)

Table 5. Comparison of surgical technique videos and videos that provide information on diseases or surgery

	Surgical Technique				Information about the Disease or Surgery				p
	Mean±SD	Median	IQR	Min-Max	Mean±SD	Median	IQR	Min-Max	
DISCERN	2.17±0.54	2.0	1.8-2.8	1.4-3.0	2.36±0.70	2.4	1.8-3.0	0.8-3.8	0.329
GQS	2.61±0.58	2.6	2.2-3.2	1.4-3.6	2.83±0.73	3.0	2.2-3.4	1.4-4.2	0.310
View ratio	1387.77±3334.60	191.6	70.1-1243.3	15.4-13164.4	680.17±2841.42	16.8	6.0-32.3	0.7-14746.4	**0.001**
VPI	1125.32±2404.70	185.5	53.2-1165.1	14.7-9195.7	561.45±2320.65	13.7	5.6-27.9	0.7-12049.9	**0.001**
NOC	327.87±636.92	46	8-382	0-2363	443.11±2169.41	1	0-21	0-11292	**0.003**

GQS: global quality score, VPI: video power index, NOC: number of comments, SD: standard deviation, IQR: interquartile range (25^{th}-75^{th} percentile)

view ratio (r_s=-0.392, p=0.010), and VPI (r_s=-0.382, p=0.014), there was not a significant correlation between the GQS score and the number of comments (Table 6).

Table 6. Correlation of mDISCERN and GQS scores with view ratio, VPI, and NOC

	View ratio		VPI		NOC	
	r	p	r	p	r	p
DISCERN	-0.295	0.058	-0.326	**0.037**	-0.229	0.145
GQS	-0.392	**0.010**	-0.382	**0.014**	-0.189	0.145

GQS: Global quality score, VPI: Video power index, NOC: Number of comment

DISCUSSION

This study determined that the quality and reliability of labiaplasty videos on YouTube are low. In particular, the quality of videos shared by non-physicians is very low. A statistical comparison could not be made since videos uploaded by patients, commercial entities, and allied health personnel were very few in number. For this reason, academics and physicians were grouped as professionals and others as non-professionals.

Health videos shared on YouTube are generally average or below average. In a systematic evaluation of the quality of health information on YouTube, Osman et al. (10) found that the mean mDISCERN score of videos reviewed was 2.36, while the mean GQS score was 2.68. Similar values were found in this study (mDISCERN: 2.29, GQS: 2.75). In a study evaluating the quality of FGCS videos by Erdoğan (4) found that the videos were of average quality. This shows that the present study is consistent with the broader literature.

Health information videos on YouTube come from various sources, such as doctors, academic institutions, patients, and advertisers. In studies evaluating YouTube videos, there is a remarkable number of videos uploaded by patients. In a study by Lee et al. (11), 37% of videos were shared by patients, while 48% were uploaded by physicians and academics. In the study of Andan et al. (12), 30% of the video uploaders were physicians, while 70% were non-physicians. In the present study, very few videos were uploaded by parties other than physicians and academic institutions (non-professionals: 9.6%). Most women do not prefer talking about private health matters, even with doctors (13). Therefore, not sharing their own experiences with labiaplasty on a video platform like YouTube is understandable. In addition, for liposuction, which has gained popularity in recent years, the vast majority of videos (83.1%) are uploaded by healthcare providers (2,14). Commercial concerns, such as labiaplasty and liposuction, may have pushed physicians to share more on these subjects.

Many studies evaluating the quality of health-related YouTube videos, especially the quality of videos uploaded by non-doctors, have found them to be poor or moderate in quality, and they have been reported to have misleading and harmful content (11,12,15). When mDISCERN scores were compared between doctors and non-physicians in Erdogan's (4) study, no difference was detected, and the video quality was moderate. In the present study, a significant difference was observed when comparing mDISCERN and GQS scores between professional and non-professional uploaders. However, it should not be ignored that the videos in the professional group were of low quality. It has been reported in some studies that videos uploaded by patients and other users are watched and liked more (11,12,15). The time elapsed since a video was uploaded affects its rates of likes and views, therefore, we decided that it would be more appropriate to evaluate VPI and view ratio in this study. These factors were found to be similar in the two groups.

Most women get information about their sexual organs through the media (16,17). In Sharp et al.'s (16) research, 78.6% of participants reported that their first inquiry into labiaplasty occurred through the media. Almost all participants (92.9%) drew attention to the importance of searching for information about labiaplasty in detail before committing to surgery. A Dutch study found that women who used the internet to learn about labiaplasty considered the procedure more acceptable (18). In the present study, when videos about surgical techniques were compared with videos that provide information about the disease, view ratio, VPI, and the number of comments were found significantly higher. The internet can be made a stronger reference point for those considering genital modification surgery, as many women are reluctant to discuss their genital concerns with their healthcare professional (3). That two groups had similar mDISCERN and GQS scores but different view ratio and VPIs might be because patients considering a surgical procedure have more interest in these videos.

In this study, a weak negative correlation was observed between mDISCERN score and VPI. Likewise, between GQS score and view ratio and VPI, a weak negative correlation was observed. This shows that videos of poor

quality attract more interaction than higher-quality videos. Similarly, in studies evaluating information about sleeve gastrectomy and prostate cancer on YouTube, negative correlations were identified (19,20).

The strength of this study is that the videos were reviewed by a five-person commission. In previous studies, they were generally evaluated by two people. Moreover, as far as we know, this is the first study evaluating YouTube videos about labiaplasty.

The primary limitation of the present study is that only English videos were analyzed. Another major limitation was that we were taking snapshots of information on YouTube, which has a dynamic structure in that the contents are constantly updated. A further limitation is that we only scored videos on YouTube; content from other health-related websites was excluded from the study.

CONCLUSION

It was determined that videos on YouTube about labiaplasty have generally poor quality. Most of the videos included in this study were uploaded by physicians, which is remarkable. YouTube is not a reliable information source with up-to-date data about labiaplasty. However, healthcare providers must accept that patients use the internet, particularly the video content provider YouTube, as a source of medical and health information. The American College of Obstetricians and Gynecologists (ACOG), the Royal College of Obstetricians and Gynecologists (RCOG), etc. organizations should provide up-to-date content on YouTube similar to the "Patient" section on their official websites.

Ethics Committee Approval: Since our study was not an experimental study including human or animal subjects, ethics committee approval was not required.

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Use of NHS PREDICT Tool and Prognostic Factors for Survival in Patients with Breast Cancer

Meme Kanserli Hastalarda Hayatta Kalma için NHS PREDICT Aracının Kullanımı ve Prognostik Faktörler

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ABSTRACT

Aim: The PREDICT tool is used to estimate survival in breast cancer patients according to the types of treatment given. This study aimed to assess the accuracy of the PREDICT tool and identify the prognostic factors for survival in patients with breast cancer.
Material and Methods: A retrospective study was performed based on data collected from the Hospital Sultanah Nur Zahirah, Terengganu, Malaysia. All female patients diagnosed with stage I to IV breast cancer were identified from the year 2011 to 2017.
Results: Based on data from 355 eligible patients, the predicted and observed 5-year overall survival rates were 75.8% and 75.2%, respectively. The model performed fairly well, with the area under the curve (AUC) of 0.747 (95% confidence interval (CI): 0.69-0.81) in the predicted 5-year overall survival. Among the 585 patients diagnosed with stage I to IV breast cancer, stage at the presentation (stage III hazard ratio (HR): 5.80, 95% CI: 1.69-19.94, p=0.005, stage IV HR: 10.61, 95% CI: 3.09-36.49, p<0.001), without surgical treatment (HR: 2.29, 95% CI: 1.73-3.00, p<0.001), without radiotherapy (HR: 1.92, 95% CI: 1.41-2.62, p<0.001), and without neoadjuvant chemotherapy (HR: 0.63, 95% CI: 0.47-0.86, p=0.003) were associated with death in breast cancer patients.
Conclusion: The PREDICT tool accurately estimated the 5-year overall survival in the study center. It might serve as a useful prognostication tool during consultation. Late stages of the disease, patients without surgical treatment, and patients without radiotherapy were associated with a higher risk of death in breast cancer.
Keywords: PREDICT; breast cancer; 5-year overall survival.

ÖZ

Amaç: PREDICT aracı, meme kanseri hastalarında verilen tedavi türlerine göre sağkalımı tahmin etmek için kullanılır. Bu çalışmanın amacı, PREDICT aracının doğruluğunu değerlendirmek ve meme kanserli hastalarda sağkalım için prognostik faktörleri belirlemektir.
Gereç ve Yöntemler: Malezya'nın Terengganu şehrindeki Sultanah Nur Zahirah Hastanesi'nden toplanan verilere dayalı olarak geriye dönük bir çalışma yapıldı. 2011 ve 2017 yılları arasında evre I ila IV meme kanseri tanısı alan tüm kadın hastalar belirlendi.
Bulgular: Uygun 355 hastadan elde edilen verilere dayanarak, öngörülen ve gözlemlenen 5 yıllık genel sağkalım oranları sırasıyla %75,8 ve %75,2 idi. Model, öngörülen 5 yıllık genel sağkalımda 0,747 (%95 GA: 0,69-0,81) eğri altında kalan alan (area under the curve, AUC) ile oldukça iyi performans gösterdi. Evre I ila IV meme kanseri tanısı alan 585 hasta arasında, başvuru anındaki evre (evre III hazard oranı (hazard ratio, HR): 5,80, %95 GA: 1,69-19,94, p=0,005, evre IV HR: 10,61, %95 GA: 3,09-36,49, p<0,001), cerrahi tedavi olmaması (HR: 2,29, %95 GA: 1,73-3,00, p<0,001), radyoterapi olmaması (HR: 1,92, %95 GA: 1,41-2,62, p<0,001) ve neoadjuvan kemoterapi olmaması (HR: 0,63, %95 GA: 0,47-0,86, p=0,003) meme kanseri hastalarında ölümle ilişkiliydi.
Sonuç: PREDICT aracı çalışma merkezindeki 5 yıllık genel sağkalımı doğru bir şekilde tahmin etti. Konsültasyon sırasında yararlı bir prognoz aracı olarak hizmet edebilir. Hastalığın ileri evreleri, cerrahi tedavi uygulanmayan hastalar ve radyoterapi uygulanmayan hastalar meme kanserinde daha yüksek ölüm riskiyle ilişkilidir.
Anahtar kelimeler: PREDICT; meme kanseri; 5 yıllık genel sağkalım.

INTRODUCTION

Breast cancer remains the most common cancer among women in Malaysia. According to the National Cancer Registry (NCR), breast cancer constituted 19% of all the cancers registered in Malaysia, with an age-standardized rate (ASR) of 34.1 per 100,000 population from 2012 to 2016. Compared with the ASR of other Asian countries such as Beijing (24.6), Hiroshima (36.6), Chennai (23.9), and Seoul (20.8), the ASR of Malaysia is still higher. The incidence of breast cancer in Malaysia also showed variation between different ethnicities. It is highest among Chinese, followed by Indian and Malay, with ASR of 59.9, 54.2, and 34.9, respectively (1).

Patients in Malaysia tend to delay seeking treatment and present at a later stage of the disease. This contributed to the low survival rate of patients with breast cancer in Malaysia (2). The 5-year overall survival rate was 49.0% among all breast cancer patients diagnosed from January 2000 to December 2005 (3). The 5-year overall survival rates were 82.5% in stages 0 to II, and 30.2% in patients with stage III and IV diseases, respectively (4).

Low survival may be related to delay. Two types of delays have been described in breast cancer, namely patient delay and provider delay (5). Patient delay is defined as the period when the patient discovers the symptoms to first contact with a physician, and provider delay is defined as the initial contact with a physician for definitive treatment for breast cancer. Delay in presentation is associated with a lower education level and lack of knowledge (6).

In order to improve patients' adherence to treatment, we need to provide objective data for patient references, such as the survival rate if they receive treatment. Multiple online prognostic tools, such as Adjuvant! Online, CancerMath.net, and PREDICT have been used. However, all of these prognostic tools are developed and validated in the Western population. PREDICT is an online free prognostication tool developed in the United Kingdom (UK). Using the tool required the clinician to key in the required data such as age, tumor size, lymph node number, tumor grading, estrogen receptor (ER), and human epidermal growth factor receptor 2 (HER2) status. However, it does not consider patient comorbidity. The tool will then generate the predicted 5- and 10-year overall survival rates based on different types of treatment given. Therefore, it will guide the clinician in choosing the best treatment modality to provide the best survival rate for the patients.

PREDICT predicts overall survival reliably in most Dutch breast cancer patients (7). The Cambridge Breast Unit uses the tools to guide the need for adjuvant chemotherapy. If the improvement in survival is more than five percent with chemotherapy, adjuvant chemotherapy is recommended. As with PREDICT, studies conducted among Asian patients showed that it was accurate in most subgroups. However, it overestimates predicting survival in patients younger than 40 years old (8). Besides this study, PREDICT also accurately estimated the 5- and 10-year overall survival in Japanese populations (9). Therefore, in this study, it was aimed to assess the accuracy of the PREDICT prognostic tool in the Malaysian population, especially for patients from East Coast Malaysia, Kuala Terengganu. It will help in consultation towards the best treatment options.

MATERIAL AND METHODS

This is a retrospective study based on the breast cancer database of the Hospital Sultanah Nur Zahirah (HSNZ), a tertiary medical center in Kuala Terengganu, Terengganu, Malaysia. Inclusion criteria for this study included all adult female patients aged more than 18 years old with stage I to IV breast cancer diagnosed in HSNZ with follow-up for at least 5 years. Patients who defaulted follow-up after treatment and patients with incomplete data were excluded from the study.

For comparison of the observed and predicted 5-year overall survival rates, a dataset comprised of 355 patients from stage I to III breast cancer who underwent surgical intervention in the form of mastectomy or breast-conserving surgery with axillary clearance was analyzed. Data from 585 patients who had been diagnosed with stage I to IV breast cancer from the year 2011 to 2017 were included for analysis of prognostic factors for survival in patients with breast cancer.

The sample size for the first objective was calculated using the sample size calculator by Wan Nor Arifin available at https://wnarifin.github.io/ssc/sssnsp.html. The required sample size was calculated using parameters such as the expected sensitivity as 0.98, the expected specificity as 0.91, and the prevalence of the disease as 0.20 with a significance level (α) of 0.05, and a precision of 10%. The final targeted sample size was determined by considering a 10% drop-out rate. For the second objective, which is to determine the factors affecting the 5-year survival rate in patients with breast cancer, the sample size was calculated using the PS: Power and Sample Size Calculation v.3.1.6 based on parameter estimates obtained from Nordin et al. (10), with the significance level (α) of 0.05, and the power of the study (1-β) of 80%. The final targeted sample size was determined by considering a 20% drop-out rate. The estimated sample size for this study was 504 samples.

Data from patients diagnosed with stage I to IV breast cancer between the years 2011 to 2017 in the HSNZ were extracted from electronic medical records, the hospital information system. The patients' medical records were reviewed and followed up for more than five years. If the patient is still present for follow-up after five years, the 5-year overall survival outcome was classified as alive for a patient who defaulted or lost follow-up within five years. Their identification data was submitted to the Jabatan Pendaftaran Negara (JPN) for mortality data matching service. For those patients who passed away within five years, the outcome was classified as dead. Their date of death was recorded, and the time of survival was recorded in months. Patients diagnosed with stage I to III breast cancer and who underwent operation were selected. Their predicted 5-year overall survival rates were calculated using PREDICT and expressed in percentages.

All required information was entered into the data collection form to avoid bias. Variables required for the study included patient demographics, age at diagnosis, menopausal status, hormonal status (ER and HER2 status), tumor size (cm) and grade, lymph node involvement, stage at diagnosis, hormonal therapy, surgical treatment, radiotherapy, chemotherapy regime, duration from symptoms to a hospital visit and duration from a hospital visit to definitive treatment.

The study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki (6th revision, 2008) as reflected in a priori approval by the Human Research Ethics Committee, Universiti Sains Malaysia in Kelantan, Malaysia (13.02.2022, USM/JEPeM/21090640) and the Medical Research & Ethics Committee, Ministry of Health Malaysia (19.08.2021, NMRR-21-1560-59266 (IIR)).

Statistical Analysis

The data were descriptively analyzed in mean and standard deviation or median and interquartile range for continuous data. For categorical data, frequency and percentage were used. Kaplan-Meier analysis was used to analyze the observed 5-year overall survival. The predicted 5-year survival was obtained from PREDICT. The survival probabilities were used to compare the observed and predicted 5-year overall survival. A chi-square goodness-of-fit test was performed to assess the accuracy of PREDICT. Receiver-operating characteristic (ROC) curve analysis was performed to test the sensitivity and specificity of the PREDICT tool. The value of the area under the curve (AUC) was recorded. Survival analysis was performed using the Cox proportional hazards regression model to identify the important prognostic factors of death. The model was presented as crude hazard ratio (HR), 95% confidence interval (CI), Wald statistics, and p-value. Data analyses were performed using IBM SPSS Statistics for Windows, v.26.0 (IBM Corp., Armonk, NY, USA). The limit of significance was set at 0.05.

RESULTS

Patient Demographics and Clinical Characteristics

A total of 585 patients included who had been diagnosed with stage I to IV breast cancer from the year 2011 to 2017. Of all patients, 556 (95.0%) were Malays, and 29 (5.0%) were non-Malays, including Chinese and Indian patients. This is consistent with the demographic data of the Terengganu, Malaysia population where more than 90% of the population is Malay. The mean age at diagnosis was 50.4±12.1 years and the mean tumor size was 5.3±3.3 cm. ER and HER2 status were expressed in 397 (67.9%) and 116 (19.8%) patients, respectively, and 294 (50.3%) of the tumors are grade 2 tumors. While 356 (60.8%) patients presented with late-stage disease (stage III and IV, 28.7% and 32.1%, respectively), 229 (39.2%) of the patients presented with early disease (stage I and II, 5.6% and 33.5%, respectively). The mean duration from symptoms to the first visit was 9.7 months. Most patients came to the hospital visit because of breast lumps (86.7%, n=507). Other reasons included breast ulcer (2.7%, n=16), presence of axillary nodes (1.2%, n=7), breast pain (0.9%, n=5), and nipple discharge (0.9%, n=5). Only 21 (3.6%) patients came because of a positive screening mammogram. From this study, 126 (21.5%) patients received neoadjuvant chemotherapy, mainly for locally advanced diseases. Of all patients, 334 (57.1%) patients received hormonal therapy, in which most patients received tamoxifen. However, only 39.5% (n=132) of these 334 patients complied and completed hormonal therapy for at least five years. Among the 116 patients with HER2-positive breast cancer, only 18.1% (n=21) of them received trastuzumab as part of their treatment. The 5-year overall survival rate according to staging was 90.9% (stage I), 80.6% (stage II), 52.4% (stage III), and 17.6% (stage IV).

Predictive Accuracy of PREDICT Tool

The distribution of the predicted 5-year overall survival as estimated by PREDICT in the study group, excluding patients with stage IV diseases and patients who did not undergo surgical treatment was shown in Figure 1. It included 355 patients from stage I to III breast cancer who underwent surgical intervention in the form of mastectomy or breast-conserving surgery with axillary clearance.

The results of the observed and predicted 5-year overall survival were shown in Table 1. PREDICT accurately predicted the 5-year overall survival in most subgroups, as most of the results showed no significant differences between the observed and predicted 5-year overall survival. In the subgroup of tumor size 2 to 5 cm (p=0.006), ER-positive patients (p<0.001), and patients who underwent neoadjuvant chemotherapy (p=0.001) showed significant differences. PREDICT seems to overestimate the 5-year overall survival of these subgroups with a difference of 7.5% compared to the predicted value. The most significant difference observed in patients who received neoadjuvant chemotherapy as PREDICT overestimated the 5-year overall survival with a difference of 15.2%. The ROC analysis of PREDICT showed that the online prognostication tool discrimination performance was fairly good, with an AUC of 0.747 (95% CI: 0.69-0.81) in predicting 5-year overall survival (Figure 2).

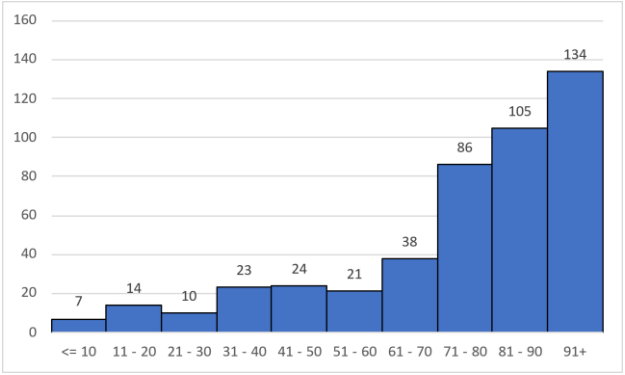

Figure 1. Distribution of the predicted 5-year overall survival using PREDICT

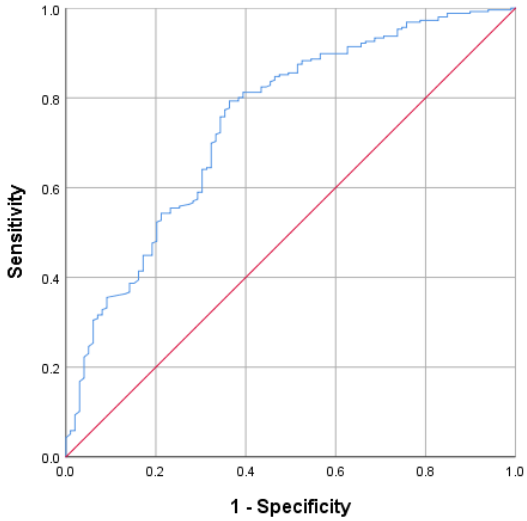

Figure 2. Discriminatory performance of 5-year overall survival by PREDICT

Table 1. Comparison of the observed and predicted 5-year overall survival rates in patients stage I to III (n=355)

	n (%)	Observed (95% CI)	PREDICT score*	Difference+	p#
Age					
<40 years	60 (16.9)	66.1 (66.1-67.8)	69.7	3.6	0.260
40-64.9 years	265 (74.6)	78.2 (77.4-78.5)	78.2	0	0.180
≥65 years	30 (8.5)	72.4 (72.4-72.4)	70.3	-2.1	0.690
Ethnicity					
Malay	330 (93.0)	74.7 (74.1-75.6)	75.3	0.6	0.075
Non-Malay	25 (7.0)	88.0 (88.0-88.0)	85.4	-2.6	0.585
Menopausal status					
Pre-menopause	180 (55.0)	75.2 (75.2-75.9)	76.6	1.4	0.053
Menopause	147 (45.0)	74.7 (73.6-74.7)	75.5	0.8	0.443
Tumor size					
<2 cm	29 (8.2)	86.2 (86.2-86.2)	90.8	4.6	0.542
2-5 cm	228 (64.2)	78.8 (78.8-79.7)	81.5	2.7	**0.006**
>5 cm	98 (27.6)	63.3 (63.3-64.3)	59.0	-4.3	0.538
Lymph nodes involvement					
Yes	202 (56.9)	67.8 (65.8-67.8)	67.0	-0.8	0.052
No	153 (43.1)	89.3 (89.3-89.3)	88.0	-1.3	0.802
ER status					
Positive	232 (65.4)	78.0 (77.5-78.0)	82.7	4.7	**<0.001**
Negative	123 (34.6)	72.1 (70.5-73.0)	63.6	-8.5	0.190
HER2 status					
Positive	67 (18.9)	69.2 (67.7-69.2)	67.5	-1.7	0.603
Negative	218 (61.4)	78.6 (77.7-79.5)	78.4	-0.2	0.188
Grade					
Low	57 (16.1)	87.5 (87.5-87.5)	91.6	4.1	0.160
Moderate	176 (49.6)	76.9 (76.3-76.9)	78.0	1.1	0.147
High	122 (34.4)	69.2 (67.5-70.0)	66.0	-3.2	0.703
Neoadjuvant chemotherapy					
Yes	42 (11.8)	54.8 (52.4-59.5)	70.1	15.2	**0.001**
No	313 (88.2)	78.5 (78.2-78.8)	76.9	-1.6	0.688

*: using mean predicted 5-year overall survival by PREDICT, +: difference between the predicted and observed 5-year overall survival (predicted - observed), #: Chi-square goodness-of-fit test comparing predicted and observed mortality estimates, CI: confidence interval, ER: estrogen receptor, HER2: human epidermal growth factor receptor 2

Prognostic Factors for Survival in Patients with Breast Cancer

The factors that affect 5-year overall survival in this cohort of 585 patients were shown in Table 2. The number of deaths from breast cancer in 5 years was 47.2% (n=276). The means survival time in stage III and IV disease were 44.6 (95% CI: 41.6-47.6) and 25.3 (95% CI: 22.4-28.3) months, respectively. The prognostic factors contributing to death were identified with the Cox proportional hazards regression model. A significant factor can be defined as a factor associated with death caused by breast cancer.

The stage at diagnosis, surgical treatment, and radiotherapy were found as significant prognostic factors contributing to breast cancer death. For the stage of disease, patients with stage III (p=0.005) and IV (p<0.001) disease had an increase in the hazard of death of 5.80 times and 10.61 times compared with stage I disease. For patients who did not receive surgical treatment, the hazard of death increased by 2.29 times compared to those who underwent surgical intervention (p<0.001). Patients who did not undergo radiotherapy also showed an increased hazard of death by 1.92 times compared to those who underwent radiotherapy (p<0.001). Age, ethnicity, and patient delay of more than 3 months to hospital visits were not significantly associated with an increased risk of death in patients with breast cancer. Patients who did not receive neoadjuvant chemotherapy showed a lower risk of death, with a hazard ratio of 0.63 in comparison to the patients who received neoadjuvant chemotherapy (p=0.003).

DISCUSSION

From the study, PREDICT seems to accurately predict the 5-years overall survival of the study population in Kuala Terengganu. The result was consistent with previous studies conducted in Asia countries (8,9,11,12). Studies concluded that the PREDICT tool accurately estimated the 5- and 10-year overall survival in Asian populations, with some exceptions within their subgroup. From our result, PREDICT overestimates the 5-year overall survival in patients with tumor sizes from 2 to 5 cm, ER-positive breast cancer, and those who underwent neoadjuvant chemotherapy.

In patients with ER-positive breast cancer, PREDICT overestimated the 5-year overall survival by 4.7%. Among the 355 patients (stage I to III), 65.4% (n=232) expressed ER receptors and were offered endocrine therapy as adjuvant therapy in the form of tamoxifen or aromatase inhibitors after surgery. Five years of endocrine therapy in hormone receptor-positive patients are proven to reduce the recurrence rate from 26.1% to 15.4%, increasing the overall survival in ER-positive breast cancer patients (13). Among all the patients with ER-positive breast cancer, 87.5% (n=203) were given hormonal therapy. However, only 53.7% (n=109) of them completed hormonal therapy for at least five years. This might contribute to the lower observed 5-year overall survival compared to PREDICT. A study was done in East Coast Malaysia, with a similar demographic background to our populations, mainly Malay populations. The percentage of diagnosis delays for

Table 2. Prognostic factors for survival in patients with breast cancer (n=585)

	n (%)	Crude HR (95% CI)	Wald statistics (df)	p#
Age				
<40 years	103 (17.6)	1.00		
40-64.9 years	412 (70.4)	0.87 (0.64-1.18)	0.76 (1)	0.383
≥65 years	70 (12)	0.72 (0.47-1.11)	2.21 (1)	0.137
Ethnicity				
Non-Malay	29 (5.0)	1.00		
Malay	556 (95)	1.98 (0.81-4.89)	2.22 (1)	0.137
Stage at diagnosis				
Stage I	33 (5.6)	1.00		
Stage II	196 (33.5)	2.14 (0.61-7.52)	1.42 (1)	0.234
Stage III	168 (28.7)	5.80 (1.69-19.94)	7.80 (1)	**0.005**
Stage IV	188 (32.1)	10.61 (3.09-36.49)	14.06 (1)	**<0.001**
Surgical treatment				
Yes	462 (79)	1.00		
No	123 (21)	2.29 (1.73-3.00)	33.73 (1)	**<0.001**
Radiotherapy				
Yes	339 (40.9)	1.00		
No	346 (59.1)	1.92 (1.41-2.62)	16.96 (1)	**<0.001**
Neoadjuvant chemotherapy				
Yes	381 (65.1)	1.00		
No	204 (34.9)	0.63 (0.47-0.86)	8.76 (1)	**0.003**
Symptoms to first visit				
<3 months	207 (35.4)	1.00		
≥3 months	223 (38.1)	1.21 (0.92-1.58)	1.89 (1)	0.169

#: Cox proportional hazards regression test, HR: hazard ratio, CI: confidence interval

more than three months was 72.6% as patients tend to seek alternative treatment, such as traditional medicine, due to cultural beliefs. Interpretation of the symptoms as not dangerous is associated with delay in presentation. This is because most of the time it was not painful, not other associated symptoms and they felt well. Other factors, which include negative perception towards side effects of chemotherapy, non-cancer interpretation, and negative attitude towards therapy, contribute to delays in diagnosis and non-compliance to treatment planned (14).

The other factor that showed a significant difference between the observed and predicted values is among the patients who received neoadjuvant chemotherapy. PREDICT overestimated the survival by 15.2%. As PREDICT was developed in the UK, the selection of patients for neoadjuvant chemotherapy might be different compared to our center. Patients with high-risk features such as triple-negative breast cancer or HER2-enriched breast cancer will be offered neoadjuvant chemotherapy even in early breast cancer, as the pathological complete response rate is higher than luminal breast cancer (15). However, this practice is not a routine in our center. Neoadjuvant is often offered to patients with locally advanced breast cancer in which the tumor was deemed unresectable at initial diagnosis. The chemotherapy aims to downsize the tumor to allow resection of the tumor and closure of the wound later. Among the 42 patients (stage I to III) who received neoadjuvant chemotherapy, the mean tumor size was 6±2.9 cm, and 76.2% (n=32) of them presented with stage III disease at their initial presentation. Only 23.8% (n=10) of patients were stage II breast cancer who underwent neoadjuvant chemotherapy. This might contribute to the difference in the observed and predicted survival values.

As for the factors associated with death from breast cancer, 585 patients have been identified and analyzed using the Cox proportional hazards regression model. The late-stage presentation of breast cancer, no surgical treatment, and no radiotherapy showed significant results, which were associated with a higher risk of death in patients with breast cancer. Cancer staging is an important prognostic factor in breast cancer (4). Of the patients, 60.8% (n=356) patients presented with stage III and IV disease at initial presentation with a mean survival time of 44.6 (95% CI: 41.4-47.6) months and 25.3 (95% CI: 22.4-28.3) months respectively, and a 5-year survival rate of 34.0% (n=121) in stage III and stage IV disease. This result was consistent with the study by Pathy et al. (4), conducted at the UMMC and the National University Hospital, Singapore, that showed a 5-year survival rate of 30.2%. Stage III diseases are associated with higher mortality compared with stage I disease, with a hazard ratio of 5.8; meanwhile, stage IV diseases are 10.6 times at risk of death compared to stage I disease. A bigger mean tumor size also has been observed in the present study, with a mean tumor size of 5.3 cm, compared with 2.6 cm in the same study (4). Larger tumor size is related to delay in presentation. The study showed a delay in presentation for more than 3 months associated with a bigger tumor size, 2.3 cm, compared with 1.8 cm without delay. However, there was no significant difference in outcome compared between patients with and without diagnosis delay of more than three months (16).

Many factors are causing a patient delay in seeking medical treatment. From a study, patients who go for alternative therapy (odds ratio (OR): 1.77), who had breast ulcer (OR: 5.71), palpable axillary lymph nodes (OR: 2.19), false diagnostic test (OR: 5.32), non-cancer interpretation (OR: 1.68), and negative attitude toward therapy (OR: 2.09) are more likely to result in a delay in seeking treatment (14). Other factors, such as negative perception towards side effects of chemotherapy, fear of surgery and treatment, fear of being unable to take care of

the family after treatment, and fear of husband may divorce them and remarry. All these factors contribute to patient delay in seeking treatment (14). Delays in treatment carry significant morbidity. Patient delay seeking treatment for more than three months was found to be associated with higher mortality with a 12.0% lower 5-year survival rate (17). Other factors, such as Malay ethnicity, stage III or IV at diagnosis, and patients without surgical treatment had lower survival rates (10). However, from our study, delay in seeking treatment for more than three months did not significantly increase the risk of death in patients with breast cancer, with a hazard ratio of 1.21. This was consistent with the study by Tartter et al. (16).

Multiple treatment options are available in patients with breast cancer, such as surgery, endocrine therapy, radiotherapy, chemotherapy, bisphosphonate, and targeted therapy. However, not all options are available in all centers. Surgery remains the mainstay of treatment in patients with breast cancer. From our study, patients who did not undergo surgery had a risk of 2.3 times death compared with those who underwent surgery. The findings in the present study are consistent with the findings of Pathy et al. (4) and Bello et al. (18). Other than that, the risk of death in patients who did not undergo radiotherapy is 1.9 times higher. Studies have shown that radiotherapy reduces local recurrence risk and improves overall survival (19). Patients who did not receive neoadjuvant chemotherapy show a lower risk of death, with a hazard ratio of 0.63. As in our center, 92% of patients who received neoadjuvant chemotherapy are diagnosed with locally advanced disease at initial presentation. This might result in a higher risk of death than those who did not receive neoadjuvant chemotherapy.

The strength of this study is that this study is the first study that validated the use of the PREDICT tool among patients in the East Coast. However, the limitation of this study is that this is a single-center study. The number of patients involved might not be representative of the management and outcome of breast cancer in Malaysia, particularly in the East Coast. This is because the different center has their own practice in managing breast cancer patients and not all centers have a breast and endocrine surgeon, so the outcome might be different. Data from other centers are needed to represent the whole population in Malaysia. In addition, PREDICT overestimated the 5-year overall survival in a few of the subgroups. Therefore, we need to improve our current practice to meet the international standard.

CONCLUSION

PREDICT tool proved to be accurate in predicting 5-year overall survival in our center. It may be a valuable tool during consultation and aid in treating our patients. The clinician will be able to provide an estimated 5-years overall survival rate to the patient according to different treatment options. However, it overestimates survival in some subgroups, such as patients with tumor sizes from 2 to 5 cm, ER-positive breast cancer, and those who underwent neoadjuvant chemotherapy. In addition, patients who presented at later stages of the disease and those who did not undergo surgery and radiotherapy are among the factors related to a higher risk of death in breast cancer patients. The patient's delay in seeking treatment for more than three months seems unrelated to a higher risk of death.

Ethics Committee Approval: The study was approved by the Human Research Ethics Committee, Universiti Sains Malaysia (13.02.2022, USM/JEPeM/21090640) and the Medical Research & Ethics Committee, Ministry of Health Malaysia (19.08.2021, NMRR-21-1560-59266 (IIR)).

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Evaluation of the Association of Serum Uric Acid Levels and Stroke in Emergency Department Patients

Acil Servis Hastalarında Serum Ürik Asit Düzeyi ve İnme İlişkisinin Değerlendirilmesi

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ABSTRACT

Aim: Stroke is a leading cause of disability and fatality. While clinical and imaging methods are commonly used in stroke management, biochemical parameters such as serum uric acid (SUA) level are largely overlooked. This study aimed to examine the relationship between high or low SUA levels and both ischemic and hemorrhagic stroke.
Material and Methods: This is a retrospective, single-center observational study. The study included all consecutive patients who were consulted from the emergency department (ED) to neurology and/or neurosurgery between January 1, 2023, and December 31, 2023. Data of the patients were obtained from the hospital computer system and ED records. While SUA levels of ≤2.8 mg/dL indicated hypouricemia, levels of ≥7 mg/dL were considered hyperuricemia.
Results: A total of 1186 adult patients were included in the study. It was observed that 484 of them were diagnosed with stroke, 394 were ischemic stroke, and 90 were hemorrhagic stroke. Stroke patients had higher median SUA levels ($p<0.001$). The median SUA level of ischemic stroke patients was higher than hemorrhagic stroke patients ($p<0.001$). Hyperuricemia increased the risk of ischemic stroke 2.4-fold (OR: 2.402, 95% CI: 1.792-3.221, $p<0.001$). Hypouricemia decreased the risk of ischemic stroke (OR: 0.272, 95% CI: 0.129-0.577, $p<0.001$).
Conclusion: SUA levels are associated with stroke and ischemic stroke. Hyperuricemia may be useful as an additional parameter to strengthen the diagnosis of possible stroke in ED. SUA levels of patients at risk for stroke can be useful in terms of follow-up of these patients and the precautions to be planned.
Keywords: Emergency department; stroke; uric acid.

ÖZ

Amaç: İnme, sakatlık ve ölümlerin önde gelen nedenlerinden biridir. İnme yönetiminde klinik ve görüntüleme yöntemleri yaygın olarak kullanılırken, serum ürik asit (SUA) düzeyi gibi biyokimyasal parametreler büyük ölçüde göz ardı edilmektedir. Bu çalışmada, yüksek veya düşük SUA düzeyleri ile hem iskemik hem de hemorajik inme arasındaki ilişkinin incelenmesi amaçlanmıştır.
Gereç ve Yöntemler: Bu çalışma retrospektif, tek merkezli gözlemsel bir çalışmadır. Çalışmaya 1 Ocak 2023 ile 31 Aralık 2023 tarihleri arasında acil servisten nöroloji ve/veya beyin cerrahisine konsülte edilen tüm ardışık hastalar dahil edilmiştir. Hastaların verileri hastane bilgisayar sisteminden ve acil servis kayıtlarından elde edilmiştir. ≤2,8 mg/dL olan SUA düzeyleri hipoürisemiyi gösterirken, ≥7 mg/dL olması hiperürisemi olarak kabul edildi.
Bulgular: Çalışmaya toplam 1186 yetişkin hasta dahil edildi. Bunların 484'ünün inme tanısı aldığı, 394'ünün iskemik inme, 90'ının ise hemorajik inme olduğu görüldü. İnme hastalarının medyan SUA düzeyleri daha yüksekti ($p<0,001$). İskemik inme hastalarının medyan SUA düzeyi hemorajik inme hastalarından daha yüksekti ($p<0,001$). Hiperürisemi iskemik inme riskini 2,4 kat artırmıştır (OR: 2,402; %95 GA: 1,792-3,221; $p<0,001$). Hipoürisemi iskemik inme riskini azaltmıştır (OR: 0,272; %95 GA: 0,129-0,577; $p<0,001$).
Sonuç: SUA düzeyleri inme ve iskemik inme ile ilişkilidir. Hiperürisemi, acil serviste olası inme tanısını güçlendiren ek bir parametre olarak yararlı olabilir. İnme açısından riskli hastaların SUA düzeyleri bu hastaların takibi ve planlanacak önlemler açısından faydalı olabilir.
Anahtar kelimeler: Acil servis; inme; ürik asit.

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INTRODUCTION

Stroke is one of the leading causes of mortality and disability worldwide and stroke is thought to be responsible for 11% of deaths (1). According to estimates, there were 9.5 million new stroke cases and 2.7 million deaths in 2016. 50% of people who become disabled due to stroke complications are under the age of 70, which increases the burden of stroke on the healthcare system and expenditures. The vast majority of strokes are ischemic strokes. Although less common, hemorrhagic strokes are also a cause of serious mortality and morbidity (2,3). Hypertension, diabetes mellitus, obesity, and cardiovascular diseases are known risk factors for stroke (4-7). In addition, studies have shown that high serum uric acid (SUA) level, i.e. hyperuricemia, increases the risk of stroke (2,5,8-10).

Uric acid is produced in the human body as a result of the metabolism of purine nucleotides. The majority of uric acid is excreted through the kidneys and the rest through the intestines. Uric acid is an important antioxidant and is involved in the scavenging of free radicals. Hypouricemia causes a decrease in antioxidant capacity and all tissues and organs are exposed to oxidative stress (11,12). SUA levels show differences between societies and genders. Normal SUA levels are generally shown between 3 mg/dl and 6.8 mg/dl in the literature (11,13).

It is known that SUA level has a u-shaped effect on renal diseases, cardiovascular diseases, and all-cause mortality, both low and high levels increase the risk (13-15). Studies suggesting that hypouricemia is associated with neurological diseases such as Parkinson's, Alzheimer's, and multiple sclerosis are also available in the literature (16-18).

Studies in the literature examining the association between stroke and SUA levels generally focus on the association between hyperuricemia and ischemic stroke. Although the strong association between hyperuricemia and ischemic stroke has been demonstrated in many studies in the literature, studies showing the effect of hypouricemia on the development of ischemic stroke have remained limited. On the other hand, studies examining the effect of SUA levels on the development of hemorrhagic stroke are also very limited. This study aimed to investigate the effects of low and high SUA levels on the development of ischemic and hemorrhagic stroke.

MATERIAL AND METHODS

Study Setting and Design

This is a retrospective, single-center observational study. It was performed in the emergency department (ED) of a tertiary university hospital in Turkey with approximately 120,000 admissions per year. The study was initiated after local ethics committee approval (Non-Invasive Health Research Ethics Committee of Düzce University, approval ID: 2024/13, dated: February 5, 2024) was obtained. The study was conducted on patients aged 18 years and older who were admitted to the ED between January 1, 2023, and, December 31, 2023.

Adult patients admitted to the ED during the indicated period who were consulted with neurology or neurosurgery departments were identified through the hospital computer system and included in the study. Data on admission diagnosis, comorbid disease, computed tomography (CT) and diffusion magnetic resonance imaging (MRI) reports, consultation reports, SUA, and serum electrolyte levels were obtained from the hospital computer system and ED archive records.

Selection of Participants and Study Protocol

All patients admitted to the ED department aged 18 years and old, being consulted to neurology and/or neurosurgery departments from the ED were included in the study. Patients with incomplete data, patients without CT or MRI examination, pregnant women, and patients referred to our hospital from another hospital were excluded from the study. Among the total of 116,916 ED admissions during the study period, the number of admissions aged 18 years and over was 110,469.

Normal values of SUA level have been shown to range between 3 mg/dl and 6.8 mg/dl in various studies (11,13). There are also studies in which the normal range of uric acid was determined differently according to gender (2,5). In this study, patients with SUA level ≤2.8 mg/dl for both gender groups were grouped as hypouricemic patients. Patients with SUA level ≥7 mg/dl were grouped as hyperuricemic patients, again valid for both gender groups. The other values were named normouricemia.

The diagnoses of stroke, hemorrhagic stroke, and ischemic stroke were obtained from the consultation notes written by neurologists and/or neurosurgeons after evaluation of the patient's clinical condition and CT and/or MRI imaging findings. Descriptive statistical data of the patients included in the study in terms of the scanned parameters were generated. Stroke and non-stroke patient groups were compared with each other in terms of the characteristics screened in the study. Ischemic stroke and hemorrhagic stroke groups were compared in terms of demographic data, SUA levels, and serum electrolyte levels. Odds ratio values were calculated for the development of ischemic and hemorrhagic stroke in hyperuricemia, hypouricemia, and comorbid diseases screened in the study. Finally, patients were divided into 3 groups, hypouricemic, normouricemic, and hyperuricemic according to SUA values, and comparisons were made between the groups in terms of the parameters screened in the study.

Statistical Analysis

Compliance with normal distribution was evaluated by the Kolmogorov-Smirnov test, Shapiro-Wilk test, and histogram. Continuous data were compared between two groups by the Mann-Whitney U test and between three groups by the Kruskal-Wallis test. The relationship between categorical variables was analyzed by Pearson's chi-square test or Fisher's exact test. Bonferroni correction was applied since three group comparisons were made. Continuous data were summarized by median, $25^{th,}$ and 75^{th} percentile, minimum-maximum, and categorical data were summarized by frequency and percentage. Statistical software IBM SPSS v.23 was used for these analyses. The significance level was set as $p<0.05$.

RESULTS

During the study period, 1186 patients were consulted from the ED to the neurology and/or neurosurgery department. 64 patients had an SUA level of ≤2.8 while 231 patients had an SUA level of 7 mg/dl or higher. Out of all the patients included in the study, 484 were diagnosed with stroke in the ED. Among these patients, 394 were diagnosed with ischemic stroke and 90 were diagnosed

with hemorrhagic stroke. The median age of the patients included in the study was 68 (range, 18-97) years and 48.2% (n=572) of the patients were female. The median age of the patients with a diagnosis other than stroke was 65 (range, 18-97), and the median age of patients with a diagnosis of stroke was 72 (range, 21-97) years. The median age of stroke patients was statistically significantly higher (p<0.001). There was no significant difference in gender between stroke and non-stroke patients (p=0.866). The median SUA level of all the patients included in the study was 5.3 mg/dL, while this level was 5.1 mg/dL in non-stroke patients and 5.7 mg/dL in stroke patients. The median SUA level was statistically significantly higher in stroke patients (p<0.001). The most common comorbid diseases included in the study were hypertension at 56.9% (n=675), diabetes mellitus at 32.5% (n=386), and cardiac diseases at 33.1% (n=393). The hypertension rate was 47.6% (n=334) in non-stroke patients and 70.5% (n=341) in stroke patients and there was a significant difference between the groups (p<0.001). Comorbid diseases and median electrolyte levels, and comparisons between stroke and non-stroke patient groups were shown in Table 1.

The median age of ischemic stroke patients in the study was 71.5 (range, 21-97) years and 48.7% (n=192) were female. In hemorrhagic stroke patients, the median age was 73 (range, 38-96) years and the female sex ratio was 44.4% (n=40). There was no significant difference between hemorrhagic and ischemic stroke groups in terms of age (p=0.803) and gender (p=0.463). The median SUA level of ischemic stroke patients was significantly higher than hemorrhagic stroke patients (5.8 vs 5.1 mg/dL, p<0.001). Comparison of ischemic stroke and hemorrhagic stroke patients in terms of age, gender, SUA, and serum electrolyte levels were shown in Table 2.

Table 1. Comparison of characteristic features and serum electrolyte levels among patients with and without stroke

	Non-Stroke (n=702)	Stroke (n=484)	p
Age (years)*	65 (48-77) [18-97]	72 (63-80) [21-97]	**<0.001**
Gender (female), n (%)	340 (48.4)	232 (47.9)	0.866
Uric Acid (mg/dL)	5.1 (4.0-6.2) [1.0-16.1]	5.7 (4.6-7.0) [2.1-20.6]	**<0.001**
Sodium (Meq/L)	138 (136-140) [112-172]	138 (136-140) [123-168]	0.230
Potassium (Meq/L)	4.20 (3.91-4.58) [2.37-6.95]	4.36 (4.00-4.72) [2.92-5.97]	**<0.001**
Chloride (Meq/L)	103 (99-105) [76-130]	103 (101-105) [81-121]	**0.038**
Calcium (mg/dL)	9.2 (8.9-9.6) [5.5-13.7]	9.3 (8.9-9.6) [6.7-16.9]	0.140
Phosphate (mg/dL)	3.21 (2.69-3.72) [0.76-9.14]	3.27 (2.84-3.75) [0.87-8.78]	0.126
Magnesium (mg/dL)	1.98 (1.82-2.11) [0.99-3.37]	1.97 (1.82-2.11) [1.10-3.19]	0.959
Hypertension, n (%)	334 (47.6)	341 (70.5)	**<0.001**
Diabetes Mellitus, n (%)	204 (29.1)	182 (37.6)	**0.002**
Hearth Diseases, n (%)	206 (29.3)	187 (38.6)	**<0.001**
Asthma and COPD, n (%)	61 (8.7)	46 (9.5)	0.630
Renal Failure, n (%)	26 (3.7)	15 (3.1)	0.570
Malignancies, n (%)	78 (11.1)	36 (7.4)	**0.035**
History of Stroke, n (%)	104 (14.8)	93 (19.2)	**0.045**

COPD: chronic obstructive pulmonary disease, *: values presented as median (interquartile range, 25th-75th percentile) [minimum-maximum]

Table 2. Comparison of characteristic features and serum electrolyte levels among patients with ischemic and hemorrhagic stroke

	Ischemic Stroke (n=394)	Hemorrhagic Stroke (n=90)	p
Age (years)*	71.5 (64-80) [21-97]	73 (59-80) [38-96]	0.803
Gender (female), n (%)	192 (48.7)	40 (44.4)	0.463
Uric Acid (mg/dL)	5.8 (4.8-7.2) [2.3-20.6]	5.1 (4.1-6.3) [2.1-12.5]	**<0.001**
Sodium (Meq/L)	138 (136-140) [123-168]	139 (137-141) [126-150]	**0.013**
Potassium (Meq/L)	4.40 (4.00-4.79) [2.92-5.91]	4.11 (3.73-4.56) [3.10-5.97]	**<0.001**
Chloride (Meq/L)	103 (100-105) [82-121]	104 (102-106) [81-113]	0.098
Calcium (mg/dL)	9.3 (8.9-9.6) [6.7-11.9]	9.3 (9.0-9.5) [8.1-10.9]	0.488
Phosphate (mg/dL)	3.28 (2.86-3.75) [0.90-8.28]	3.25 (2.77-3.80) [0.87-6.29]	0.707
Magnesium (mg/dL)	1.97 (1.82-2.11) [1.10-3.19]	1.97 (1.85-2.10) [1.37-3.03]	0.611
Hypertension, n (%)	281 (71.3)	60 (66.7)	0.383
Diabetes Mellitus, n (%)	157 (39.8)	25 (27.8)	**0.033**
Hearth Diseases, n (%)	162 (41.1)	25 (27.8)	**0.019**
Asthma and COPD, n (%)	39 (9.9)	7 (7.8)	0.536
Renal Failure, n (%)	12 (3.0)	3 (3.3)	0.887
Malignancies, n (%)	32 (8.1)	4 (4.4)	0.230
History of Stroke, n (%)	75 (19.0)	18 (20.0)	0.834

COPD: chronic obstructive pulmonary disease, *: values presented as median (interquartile range, 25th-75th percentile) [minimum-maximum]

The presence of hyperuricemia increased the risk of ischemic stroke 2.4-fold (OR: 2.402, 95% CI: 1.792-3.221, p<0.001). In the presence of hypouricemia, the risk of ischemic stroke was significantly reduced (OR: 0.272, 95% CI: 0.129-0.577, p<0.001). In the presence of hypertension, the risk of ischemic stroke increased 2.5-fold (OR: 2.512, 95% CI: 1.939-3.255, p<0.001). Diabetes mellitus increased the risk of ischemic stroke 1.6-fold (OR: 1.629, 95% CI: 1.264-2.099, p<0.001) and heart disease increased the risk of ischemic stroke approximately 1.7-fold (OR: 1.696, 95% CI: 1.317-2.183, p<0.001). When similar comparisons were made between the hemorrhagic stroke group and the non-hemorrhagic stroke group, no significant results were obtained showing that hyperuricemia, hypouricemia, hypertension, diabetes mellitus, heart diseases, or history of stroke caused an increase or decrease in the risk of hemorrhagic stroke. The effects of hyperuricemia, hypouricemia, and comorbid diseases on the risk of ischemic and hemorrhagic stroke were shown in Table 3.

The rate of hypertension was 46.9% (n=30) in the hypouricemic group, 54.0% (n=481) in the normouricemic group, and 71.0% (n=164) in the hyperuricemic group. There was a significant difference in the rate of hypertension between SUA groups and the rate of hypertension was higher in the hyperuricemic group (p<0.001). The stroke rate was 21.9% (n=14) in the hypouricemia group, and 38.4% (n=342), and 55.4% (n=128) in the normouricemia and hyperuricemia groups, respectively. Stroke rates were significantly different in all three SUA groups and stroke rate was higher in the hyperuricemia group (p<0.001). When SUA groups were compared in terms of ischemic stroke, the rates of all three groups were significantly different and the rate of ischemic stroke was higher in the hyperuricemia group (12.5%, n=8 vs 30.4%, n=271, vs 49.8%, n=115, p<0.001). No significant difference was found between SUA groups in terms of hemorrhagic stroke rates (9.4%, n=6, vs 8.0%, n=71, vs 5.6%, n=13, p=0.419). Comparisons between SUA-level groups in terms of age, gender, comorbid diseases, and stroke types were shown in Table 4.

DISCUSSION

Stroke is one of the most important causes of mortality and disability in today's world. Stroke at an early age can lead to early death as well as long life expectancy with disability. The ages at which stroke occurs differ between societies and geographies. In studies performed in Eastern societies where the population is relatively poorer, stroke is usually seen frequently in the 60s, whereas in Western societies, which are more socioeconomically developed, stroke cases become more frequent after the 70s. In some studies performed in different societies, stroke rates were found to be higher in male patients and some female patients (6,8,19-21). In our study, the median age of stroke patients was 72 years and this result is similar to Western societies with better economic conditions. In Turkey, the country where the study was conducted, this situation should be attributed to easy access to health services and effective treatments for diseases that increase the risk of stroke due to the social state policies implemented rather than to better economic conditions. In our study, no significant difference was found between genders in terms of stroke rates.

Table 3. Comparison of the patients with ischemic stroke to those without, and patients with hemorrhagic stroke to those without, based on the serum uric acid levels and comorbidities

	Ischemic Stroke (n=394)			Hemorrhagic Stroke (n=90)		
	OR	**95% CI**	**p**	**OR**	**95% CI**	**p**
Hypouricemia (SUA ≤2.8 mg/dL)	0.272	0.129-0.577	**<0.001**	1.278	0.536-3.050	0.579
Hyperuricemia (SUA ≥7 mg/dL)	2.402	1.792-3.221	**<0.001**	0.680	0.371-1.247	0.210
Hypertension	2.512	1.939-3.255	**<0.001**	1.564	0.993-2.464	0.054
Diabetes Mellitus	1.629	1.264-2.099	**<0.001**	0.783	0.485-1.263	0.315
Hearth Diseases	1.696	1.317-2.183	**<0.001**	0.761	0.472-1.227	0.261
History of Stroke	1.291	0.940-1.773	0.113	1.281	0.746-2.199	0.369

SUA: serum uric acid, OR: odds ratio, CI: confidence interval

Table 4. Comparison of SUA-level groups in terms of demographic data, comorbid diseases, and stroke diagnoses

	Hypouricemia SUA ≤2.8 mg/dL (n=64)	**Normouricemia SUA 2.9-6.9 mg/dL (n=891)**	**Hyperuricemia SUA ≥7 mg/dL (n=231)**	**p#**
Age (years)*	62 (45-74) [20-90] [a]	68 (53-78) [18-97] [a]	74 (64-82) [21-97] [b]	**<0.001**
Gender (female), n (%)	51 (79.7) [a]	409 (45.9) [b]	112 (48.5) [b]	**<0.001**
Hypertension, n (%)	30 (46.9) [a]	481 (54.0) [a]	164 (71.0) [b]	**<0.001**
Diabetes Mellitus, n (%)	21 (32.8) [a,b]	274 (30.8) [b]	91 (39.4) [a]	0.044
Hearth Diseases, n (%)	13 (20.3) [a]	275 (30.9) [a]	105 (45.5) [b]	**<0.001**
History of Stroke, n (%)	10 (15.6) [a,b]	137 (15.4) [b]	50 (21.6) [a]	0.072
Malignancies, n (%)	9 (14.1) [a]	79 (8.9) [a]	26 (11.3) [a]	0.253
Stroke, n (%)	14 (21.9) [a]	342 (38.4) [b]	128 (55.4) [c]	**<0.001**
Ischemic Stroke, n (%)	8 (12.5) [a]	271(30.4) [b]	115 (49.8) [c]	**<0.001**
Hemorrhagic Stroke, n (%)	6 (9.4) [a]	71 (8.0) [a]	13 (5.6) [a]	0.419

SUA: serum uric acid, #: Bonferroni correction was applied since three group comparisons were made (p<0.016 indicates a statistically significant difference, [a,b,c]: different letters written as exponents indicate statistically significant differences, *: values presented as median (interquartile range, 25th-75th percentile) [minimum-maximum]

In the literature, the rate of ischemic strokes in all strokes is shown to be between 70% and 87% (2,4,19,20,22). In our present study, ischemic strokes constitute more than 80% of all stroke patients and our findings are similar to the literature.

Hypertension, diabetes mellitus, cardiovascular diseases, and dyslipidemias are comorbid diseases which are risk factors for stroke (5,6,8,19,21). Studies have shown that more than 60% of stroke patients have high arterial blood pressure values measured at presentation and more than 70% of stroke patients, whether hemorrhagic or ischemic, have a diagnosis of hypertension (23). In our study, the most common comorbid diseases in stroke patients were hypertension, cardiovascular diseases, and diabetes mellitus. All three of these comorbid diseases are observed at a higher rate in stroke patients than in non-stroke patients. The diagnosis of hypertension reaches 70% in the stroke patient group. This is similar to the literature and clearly demonstrates the relationship between hypertension and stroke. In our study, hypertension increased the risk of ischemic stroke approximately 2.5 times. In terms of hemorrhagic stroke, no statistically significant increase in risk due to hypertension was found, contrary to the findings in the literature. It is thought that further studies with a larger sample size and a more general population will provide results on the relationship between hemorrhagic stroke and hypertension that will match the data in the literature. In our study, the risk of ischemic stroke increased approximately 1.6-fold in the presence of cardiovascular disease and 1.6-fold in the presence of diabetes mellitus. No significant increase in the risk of hemorrhagic stroke due to comorbid diseases was detected.

There are many studies showing that hyperuricemia is a risk factor for ischemic stroke (2,5,8-10). It is also known that comorbid diseases including hypertension, diabetes mellitus, and cardiovascular diseases which increase the risk of stroke are observed more frequently in hyperuricemic patients (2,11,12,24). In our study, median uric acid level was significantly higher in stroke patients compared with non-stroke patients. In our study, the rate of ischemic stroke was also significantly higher in the hyperuricemic patient group and hyperuricemia increased the risk of ischemic stroke approximately 2.4-fold. Our findings in terms of the relationship between hyperuricemia and ischemic stroke are similar to the literature. The first diagnosis of many diseases is made in EDs. The diagnostic power of EDs depends on the clinical experience of the physicians working there as well as the available tests and imaging methods. In many health centers other than tertiary care, MRI or CT examination to confirm the diagnosis of stroke cannot be performed. In the light of the findings of our study, it can be said that hyperuricemia is an additional parameter to strengthen the preliminary diagnosis of stroke in patients presenting to EDs with symptoms suspicious for stroke. Hyperuricemic patients presenting with stroke-like symptoms to an ED where CT or MRI imaging cannot be performed may be given priority over normouricemic patients when referring to centers where imaging can be performed.

There are no adequate studies in the literature on the relationship between hypouricemia and stroke. The findings of our study show that both stroke and ischemic stroke rates were significantly lower in the hypouricemic patient group. In addition, the risk of ischemic stroke was significantly lower in hypouricemic patients compared to non-hypouricemic patients. Hypouricemia detected in patients admitted to the ED with findings suspicious for stroke may give ED physicians an idea that the patient may not have an ischemic stroke. However, the final diagnosis should be made by imaging modalities such as CT and MRI.

Adding SUA levels to the blood parameters checked during hospital admissions or health screenings of patients at risk for stroke will be beneficial for the follow-up of these patients. In patients with hyperuricemia, performing the necessary tests for hypertension, diabetes mellitus, and cardiovascular diseases, which are known to increase the risk of stroke, and starting treatment immediately if these diseases are detected may be beneficial in minimizing the risk of stroke.

There are few studies showing that SUA-lowering treatments are associated with a lower stroke risk (25). In the light of our findings, we think that SUA-lowering treatments may reduce the risk of ischemic stroke in normouricemic and hyperuricemic patients who are at risk for ischemic stroke. Further studies on this subject will contribute to the literature.

In our study, no difference was found between the groups formed according to SUA levels in terms of hemorrhagic stroke rates, and no significant conclusion was reached regarding whether hyperuricemia or hypouricemia increases or decreases the risk of hemorrhagic stroke. In our search, we found that one study concluded that high SUA levels increased the risk of hemorrhagic stroke (4). However, we could not find any data on the relationship between hemorrhagic stroke and SUA levels except for the mentioned study. Our study shows that SUA levels are not related to the development of hemorrhagic stroke and in this respect, it is not similar to the other study, further studies will provide a better understanding of the subject.

Firstly, our study is single-center and retrospective. Secondly, SUA level was measured once in each patient in the study; SUA levels before or after admission are not known. Thirdly, urinary uric acid was not measured in the study; the causes of hypouricemia or hyperuricemia cannot be known. Fourthly, the medications used by the patients were not evaluated in our study; it is not known whether the patients were taking medications that may affect SUA levels.

CONCLUSION

Hypertension is the comorbid disease that increases the risk of ischemic stroke the most (approximately 2.5-fold) and 70% of stroke patients have hypertension. Stroke and ischemic stroke patients have higher median uric acid levels and hyperuricemia rates. Hyperuricemia increases the risk of ischemic stroke approximately 2.4 times. Hypouricemia decreases the risk of ischemic stroke. There is no such relationship in terms of hemorrhagic stroke. In patients who present to the ED with findings suspicious for stroke but in whom MRI or CT cannot be performed, SUA level may give the physician an idea about the preliminary diagnosis. SUA level to be examined during the follow-up of patients at risk for ischemic stroke may be useful in terms of stroke risk assessment.

Ethics Committee Approval: The study was approved by the Non-Invasive Health Research Ethics Committee of Düzce University (05.02.2024, 2024/13).

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The Effect of Prolotherapy and Dry Needling on Pain and Foot Functions in Hallux Valgus

Halluks Valgusta Proloterapi ve Kuru İğnelemenin Ağrı ve Ayak Fonksiyonları Üzerine Etkisi

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ABSTRACT

Aim: Hallux valgus is a common foot deformity that causes significant pain and functional impairment. This study aimed to compare the effectiveness of prolotherapy and dry needling in treating mild to moderate hallux valgus pain.
Material and Methods: Patients with hallux valgus deformity experiencing refractory pain after orthotic and analgesic treatment, and treated with prolotherapy (52 patients, 68 feet) or dry needling (49 patients, 57 feet) methods were included in the study. Each group received three treatment sessions at 3-week intervals. Clinical assessments were performed using the visual analog scale (VAS) and American Orthopedic Foot and Ankle Society (AOFAS) scores at baseline, in the third month, and twelfth month.
Results: Both groups showed significant improvement in VAS and AOFAS scores after treatment ($p<0.001$). In the prolotherapy group, the VAS score decreased from 6 (range, 4-8) in the pre-treatment period to 2 (range, 1-5) both in the third and twelfth months ($p<0.001$). In the dry needling group, the VAS score decreased from 6 (range, 4-7) in the pre-treatment period to 4 (range, 2-7) both in the third and twelfth months ($p<0.001$). While the AOFAS scores improved to 75 (range, 63-85) in the third month and 76 (range, 60-80) in the twelfth month in the prolotherapy group ($p<0.001$), improved to 56 (range, 44-75) in the third month and 50 (range, 36-75) in the twelfth month in the dry needling group ($p<0.001$).
Conclusion: Both prolotherapy and dry needling effectively treat hallux valgus pain and improve foot function, with prolotherapy showing superior effectiveness.
Keywords: Conservative; dry needling; symptomatic hallux valgus; pain; prolotherapy.

ÖZ

Amaç: Halluks valgus, ayağın yaygın bir deformitesi olup önemli ağrı ve fonksiyonel bozukluğa neden olabilir. Bu çalışmanın amacı hafif ve orta dereceli halluks valgus ağrısının tedavisinde proloterapi ve kuru iğnelemenin etkinliğini karşılaştırmaktır.
Gereç ve Yöntemler: Ortez ve analjezik tedavi sonrası dirençli ağrı yaşayan halluks valgus deformitesi olan ve proloterapi (52 hasta, 68 ayak) veya kuru iğneleme (49 hasta, 57 ayak) ile tedavi edilen hastalar çalışmaya dahil edildi. Her grup 3 haftalık aralıklarla üç tedavi seansı aldı. Görsel analog skala (visual analog scale, VAS) ve Amerikan Ortopedik Ayak ve Ayak Bileği Derneği (American Orthopedic Foot and Ankle Society, AOFAS) skorları kullanılarak klinik değerlendirmeler başlangıçta, üçüncü ayda ve on ikinci ayda yapıldı.
Bulgular: Her iki grup da tedavi sonrası VAS ve AOFAS skorlarında anlamlı iyileşme gösterdi ($p<0,001$). Proloterapi grubunda, VAS skoru tedavi öncesi 6'dan (aralık, 4-8) hem üç ve hem de on ikinci aylarda 2'ye (aralık, 1-5) düştü ($p<0,001$). Kuru iğneleme grubunda, VAS skoru tedavi öncesi 6'dan (aralık, 4-7) hem üç ve hem de on ikinci aylarda 4'e (aralık, 2-7) düştü ($p<0,001$). AOFAS skorları, proloterapi grubunda, üçüncü ayda 75'e (aralık, 63-85) ve on ikinci ayda 76'ya (aralık, 60-80) yükselirken ($p<0,001$), kuru iğneleme grubunda üçüncü ayda 56'ya (aralık, 44-75) ve on ikinci ayda 50'ye (aralık, 36-75) yükseldi ($p<0,001$).
Sonuç: Hem proloterapi hem de kuru iğneleme halluks valgus ağrısını etkili bir şekilde tedavi eder ve ayak fonksiyonunu iyileştirir, ancak proloterapi daha üstün sonuçlar gösterir.
Anahtar kelimeler: Konservatif; kuru iğneleme; semptomatik halluks valgus; ağrı; proloterapi.

INTRODUCTION

Hallux valgus is a common foot deformity characterized by the lateral deviation of the great toe over 15° and associated pain (1). Multiple predisposing factors contribute to hallux valgus, but no specific etiological mechanism has been definitively identified (2). The lateral deviation causes metatarsal rotation and valgus at the metatarsophalangeal joint, resulting in joint instability, decreased range of motion, and pain. Muscle imbalances around the joint further exacerbate the deformity (3).

Treatment options for hallux valgus include both surgical and nonsurgical methods. Nonsurgical treatments such as orthotic devices, physical therapy, and footwear modifications are commonly used for mild to moderate deformities (4). Surgical intervention is often reserved for severe cases but carries risks of postoperative complications (5). Recently, local injections like prolotherapy and dry needling have been used effectively for various musculoskeletal disorders, including hallux valgus (5,6). Prolotherapy involves injecting hypertonic dextrose to promote natural healing, while dry needling uses thin needles at trigger points to alleviate pain (7,8).

Prolotherapy aims to strengthen ligaments, tendons, and joint capsules by inducing local inflammation, leading to tissue regeneration and pain relief. Dry needling induces biochemical changes in muscle function, affecting pain, inflammation, and blood flow (9-11). This study aimed to evaluate the effectiveness of these treatments in patients with hallux valgus pain unresponsive to conventional therapies.

MATERIAL AND METHODS

This study was approved by the ethics committee of the University of Health Sciences (03.06.2021, 258). Informed consent was obtained from all participants, and the study adhered to the principles of the Declaration of Helsinki.

Patient Selection

Patients diagnosed with painful hallux valgus deformity between March 2020 and April 2021, and who had persistent pain after at least six months of orthotic and analgesic treatment were included in this retrospective study. Exclusion criteria were: age below 18 years, absence of pain, rheumatic or systemic inflammatory diseases, neuromuscular disorders, diabetes mellitus, history of foot infections or surgeries, recent corticosteroid injections, bleeding tendencies, and pregnancy. Patients with hallux valgus angles greater than 40° or less than 15° were also excluded. A total of 120 patients, 60 in prolotherapy and 60 in dry needling groups were included in the study (Figure 1).

Treatment Protocol

Prolotherapy injections (3.6 mL dextrose, 15% solution, and 0.4 mL lidocaine) were administered using a 27-gauge needle at three points around the medial capsule of the metatarsophalangeal joint under aseptic conditions. Dry needling was performed similarly at three trigger points around the medial capsule. Both treatments were given three times at 3-week intervals. Patients were blinded to the treatment method. Post-treatment, patients were advised to rest, avoid long walks, and use standard analgesics (500 mg acetaminophen three times daily for three days). No home exercises or splints were recommended (Figure 2).

Clinical Evaluation

The visual analog scale (VAS) and the American Orthopedic Foot and Ankle Society (AOFAS) scores were recorded at baseline, third month, and twelfth month. The VAS is a tool used to measure a patient's pain intensity, where patients rate their pain on a scale from 0 (no pain) to 10 (worst possible pain). The AOFAS score is a comprehensive assessment used to evaluate foot and ankle function, which includes parameters such as pain, function, and alignment of the forefoot. These evaluations were conducted to monitor the effectiveness of the treatments over time.

Statistical Analysis

Descriptive statistics were presented as mean±standard deviation for normally distributed data, median, 25^{th}-75^{th} percentile, minimum-maximum for non-normally distributed data, and number and percentage for categorical data. The Shapiro-Wilk test was used to assess normality. Comparisons between groups utilized t-tests for normally distributed data and Mann-Whitney U tests for non-normally distributed data. Changes in VAS and AOFAS scores over time were analyzed using the Friedman test, with post-hoc Wilcoxon tests for pairwise comparisons. Statistical analyses were conducted using IBM SPSS Statistics v.20, and $p<0.05$ was considered statistically significant.

RESULTS

Eleven patients in the dry needling group and six patients in the prolotherapy group did not complete the follow-up. Additionally, two prolotherapy patients withdrew due to severe pain and hypotension during injection. Thus, 49 patients in the dry needling group and 52 in the prolotherapy

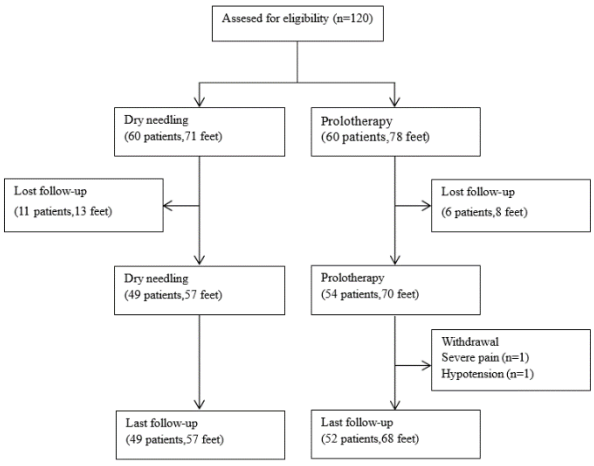

Figure 1. Flowchart of subjects in the study

Figure 2. A) dry needling method, **B)** prolotherapy procedure

group completed the treatment protocol. Demographic characteristics, including body mass index (BMI), were similar between the groups (Table 1).

Both groups showed significant improvement in VAS scores post-treatment ($p<0.001$). In the prolotherapy group, VAS scores decreased from 6 (range, 4-8) in the pre-treatment period to 2 (range, 1-5) both in the third and twelfth months. In the dry needling group, VAS scores decreased from 6 (range, 4-7) in the pre-treatment period to 4 (range, 2-7) both in the third and twelfth months. The improvement of the VAS scores in the prolotherapy group was higher than in the dry needling group both in the third and twelfth months ($p<0.001$). Both groups showed significant improvement in post-treatment AOFAS scores ($p<0.001$). In the prolotherapy group, AOFAS scores improved from 75 (range, 63-85) in the third month to 76 (range, 60-80) in the twelfth month. In the dry needling group, AOFAS scores improved from 56 (range, 44-75) in the third month to 50 (range, 36-75) in the twelfth month. It was observed that the improvement in the prolotherapy group was better than in the dry needling group (Table 2).

DISCUSSION

This study compared the effectiveness of prolotherapy and dry needling in treating hallux valgus pain. Both treatments significantly reduced pain and improved foot function, but prolotherapy showed superior results in both VAS and AOFAS scores at the third and twelfth months.

The pathogenesis of hallux valgus involves the failure of the first metatarsosamoid ligament, medial collateral ligament, and medial capsule, leading to joint instability and muscle imbalance (12). Non-surgical treatments aim to alleviate pain and improve function (13,14). Prolotherapy, a regenerative injection therapy, induces local inflammation and tissue regeneration, thus reducing pain without significant side effects (15). The findings of the present study align with previous studies showing the efficacy of prolotherapy in various musculoskeletal conditions (16,17).

Dry needling relieves pain by targeting hypersensitive trigger points in muscles, tendons, and ligaments (18,19). Although its exact mechanism is unclear, dry needling is effective in treating various musculoskeletal pain conditions. Our study showed that dry needling also alleviates pain in hallux valgus patients, although less effectively than prolotherapy.

Prolotherapy injections stimulate healing by inducing local inflammation, resulting in the production of new fibrous tissue, thus strengthening the ligaments, tendons, and joint capsules. This mechanism leads to decreased pain and improved function (20,21). Dry needling, on the other hand, works by causing microtrauma to the tissues, which triggers the body's natural healing response and results in pain relief and improved muscle function (22,23).

The significant improvement in both VAS and AOFAS scores in the prolotherapy group suggests that this treatment is more effective in reducing pain and improving foot function compared to dry needling. The findings support the use of prolotherapy as a viable non-surgical treatment option for patients with mild to moderate hallux valgus who do not respond to conventional therapies.

The study lacked a control group, and larger sample sizes with diverse clinical evaluations are needed. Additionally, the lack of long-term follow-up beyond twelve months limits the ability to assess the sustained effectiveness of the treatments. Nevertheless, this study provides valuable insights into the comparative effectiveness of prolotherapy and dry needling in treating hallux valgus.

CONCLUSION

Both prolotherapy and dry needling are effective in treating hallux valgus pain and improving foot function. Prolotherapy demonstrated superior results than dry needling both in pain management and functional improvement in hallux valgus. Both methods can be considered viable options for the non-surgical treatment of mild to moderate hallux valgus.

Table 1. Baseline demographic characteristics of the groups

	Prolotherapy (n=52)	**Dry Needling (n=49)**	**p**
Age (years)	48.25±11.41	49.29±8.12	0.602
BMI (kg/m^2)	26.65±3.28	27.08±3.68	0.713
Gender, n (%)			
Female	39 (75.0)	40 (81.6)	0.420
Male	13 (25.0)	9 (18.4)	
Side, n (%)			
Left	16 (30.8)	26 (53.1)	
Right	20 (38.4)	15 (30.6)	0.058
Bilateral	16 (30.8)	8 (16.3)	

BMI: body mass index, descriptive statistics reported as mean±standard deviation

Table 2. VAS and AOFAS scores of the groups in pre-treatment visit and post-treatment visits

	Prolotherapy (n=52)		**Dry Needling (n=49)**		**p****
	Mean±SD	**Median (IQR) [min-max]**	**Mean±SD**	**Median (IQR) [min-max]**	
VAS					
Pre-treatment	6.19±1.20	6 (5-7) [4-8]	5.55±0.91	6 (5-6) [4-7]	**0.006**
3rd month	2.40±1.01	2 (1-3) [1-5]	4.33±1.04	4 (3-5) [2-7]	**<0.001**
12th month	2.54±1.07	2 (1-3) [1-5]	4.16±1.01	4 (3-5) [2-7]	**<0.001**
p*		**<0.001**		**<0.001**	
AOFAS					
Pre-treatment	35.92±7.67	36 (30-45) [23-52]	35.12±6.60	36 (28-42) [23-48]	0.600
3rd month	74.67±5.58	75 (68-80) [63-85]	56.35±7.88	56 (50-65) [44-75]	**<0.001**
12th month	73.44±5.47	76 (67-79) [60-80]	49.96±7.80	50 (45-63) [36-75]	**<0.001**
p*		**<0.001**		**<0.001**	

SD: standard deviation, IQR: interquartile range (25th-75th percentile), VAS: visual analog scale, AOFAS: American Orthopedic Foot and Ankle Society, *: Friedman test, **: Mann-Whitney U test

Ethics Committee Approval: The study was approved by the Gülhane Scientific Research Ethics Committee of the University of Health Sciences (03.06.2021, 258).

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The Relationship between Idiopathic Intracranial Hypertension and Obstructive Sleep Apnea: Is Obesity the Only Mediating Factor between the Two?

İdiyopatik İntrakraniyal Hipertansiyon ve Obstrüktif Uyku Apnesi Arasındaki İlişki: İkisi Arasındaki Tek Aracı Faktör Obezite mi?

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ABSTRACT

Aim: This study aimed to investigate the possible reciprocal relationship between idiopathic intracranial hypertension (IIH) and obstructive sleep apnea (OSA).
Material and Methods: This cross-sectional study was conducted from October 2023 to February 2024. Patients with IIH and age and gender-matched controls without IIH were included. Information on age, gender, comorbidities, smoking, and alcohol consumption was recorded. Body mass index (BMI) was calculated, and a BMI ≥30 was considered obese. Berlin questionnaire and STOP-BANG questionnaire were administered to all participants. High risk for OSA was determined if participants responded affirmatively to at least three out of the eight questions on the STOP-BANG questionnaire, or if two out of the three categories showed positive results on the Berlin questionnaire.
Results: Sixty patients with IIH and 120 controls participated. There were no significant differences between groups regarding age (p=0.437) and gender distribution (p=0.716). The percentage of obese subjects was significantly higher in the IIH group (p<0.001). The Berlin and STOP-BANG results showed that the IIH group had higher risks for OSA than the control group. Multivariate logistic regression analysis revealed obesity as the only factor independently associated with high-risk classification with the Berlin questionnaire. In the STOP-BANG survey, higher age, male gender, obesity, and hyperlipidemia were independently related to high-risk classification.
Conclusion: Obesity is a common risk factor for both OSA and IIH. The coexistence of OSA and IIH may cause increased morbidity and mortality rates in both diseases. Therefore, we recommend that patients with IIH be screened for OSA risk.
Keywords: Pseudotumor cerebri; obstructive sleep apnea; body mass index; obesity.

ÖZ

Amaç: Bu çalışmanın amacı idiyopatik intrakraniyal hipertansiyon (İİH) ve obstrüktif uyku apnesi (OSA) arasındaki olası karşılıklı ilişkiyi araştırmaktır.
Gereç ve Yöntemler: Bu kesitsel çalışma Ekim 2023 ile Şubat 2024 tarihleri arasında gerçekleştirilmiştir. İİH'li hastalar ve İİH'si olmayan yaş ve cinsiyet uyumlu kontroller çalışmaya dahil edilmiştir. Yaş, cinsiyet, komorbiditeler, sigara içme ve alkol tüketimine ilişkin bilgiler kaydedilmiştir. Vücut kitle indeksi (VKİ) hesaplanmış ve VKİ ≥30 olanlar obez olarak kabul edilmiştir. Tüm katılımcılara Berlin anketi ve STOP-BANG anketi uygulanmıştır. Katılımcılar STOP-BANG anketindeki sekiz sorudan en az üçüne olumlu yanıt verdiğinde veya Berlin anketinde üç kategoriden ikisi olumlu sonuç verdiğinde OUA için yüksek risk belirlenmiştir.
Bulgular: Altmış İİH hastası ve 120 kontrol grubu katılmıştır. Gruplar arasında yaş (p=0.437) ve cinsiyet dağılımı (p=0.716) açısından anlamlı fark yoktu. Obez bireylerin yüzdesi İİH grubunda anlamlı derecede yüksekti (p<0.001). Berlin ve STOP-BANG sonuçları, İİH grubunun kontrol grubuna göre OUA için daha yüksek risk taşıdığını göstermiştir. Çok değişkenli lojistik regresyon analizi, Berlin anketinde yüksek risk sınıflandırması ile bağımsız olarak ilişkili tek faktörün obezite olduğunu ortaya koymuştur. STOP-BANG anketinde ise yüksek yaş, erkek cinsiyet, obezite ve hiperlipidemi bağımsız olarak yüksek risk sınıflandırması ile ilişkili bulunmuştur.
Sonuç: Obezite hem OSA hem de İİH için ortak risk faktörüdür. OSA ve İİH birlikteliği her iki hastalıkta da artmış morbidite ve mortalite oranlarına neden olabilir. Bu nedenle, İİH'li hastaların OSA riski açısından taranmasını öneriyoruz.
Anahtar kelimeler: Psödotümör serebri; obstrüktif uyku apnesi; vücut kitle indeksi; obezite.

INTRODUCTION

Idiopathic intracranial hypertension (IIH), commonly recognized as pseudotumor cerebri, is a pathological state characterized by the symptomatic elevation of intracranial pressure devoid of discernible causative factors (1,2). IIH is rare but has a markedly higher frequency among obese individuals and middle-aged females (1,3,4), and thus, there is a rising incidence in parallel with increasing global obesity (5). IIH manifests with characteristic clinical indicators of elevated intracranial pressure (6) and is linked to diminished quality of life and heightened cardiovascular risk.

Obstructive sleep apnea (OSA) is a prevalent disorder characterized by total or partial upper airway obstruction during sleep, leading to various associated symptoms (7). It is related to obesity and older age and is more common in men (4). OSA similarly correlates with diminished quality of life and elevated susceptibilities to type 2 diabetes, cardiovascular diseases, hypertension, and heightened mortality rates (8). Recent studies have reported a relationship between OSA and papilledema (9-11). Perhaps more interestingly, the pathophysiology of OSA has been associated with cerebral venous dilatation and increased intracranial pressure due to hypoxia and hypercapnia episodes during sleep (12).

Despite affecting different demographics, obesity appears to be a shared characteristic of patients with OSA and IIH, potentially suggesting shared pathophysiology and other common risk factors (4,13,14). Although some cross-sectional studies have made notable findings suggesting a relationship between IIH and OSA (15), there is no definitive evidence about the effect of OSA on IIH or vice versa. However, considering that both diseases are independent risk factors for increased risk of morbidity, especially cardiovascular morbidity, the coexistence of these diseases may cause a synergistic effect. Therefore, it will be essential to determine the risks and relationships between OSA and IIH to understand pathophysiology or diagnostic approaches which can be complicated. It is widely acknowledged within the academic sphere that polysomnography is the definitive diagnostic tool for identifying OSA; however, its customary application in screening procedures presents certain inherent complexities (16). In the context of OSA, the Berlin and STOP-BANG questionnaires serve as validated screening instruments to evaluate the likelihood of disease onset (17).

This study aimed to explore the potential bidirectional association between IIH and OSA, a correlation that remains inadequately elucidated. This investigation is conducted by employing the Berlin and STOP-BANG questionnaires among patients clinically diagnosed with IIH. It was also a secondary aim to investigate other factors associated with IIH and increased OSA risk.

MATERIAL AND METHODS

Study Design and Participants

A cross-sectional investigation was conducted within the Neurology Department of our institution, spanning from October 2023 to February 2024. Patients who were followed up with a diagnosis of IIH in our hospital's neurology inpatient or outpatient clinic and a control group matched with these patients in terms of age and gender were included in the study. IIH diagnoses were made according to the revised diagnostic criteria (modified Dandy criteria) for IIH (18). The IIH criteria were briefly as follows: (i) presence of signs and symptoms of increased intracranial pressure, (ii) absence of localizing findings other than abducens nerve palsy, (iii) cerebrospinal fluid opening pressure ≥25 cmH_2O, (iv) normal cerebrospinal fluid composition, and (v) normal neuroimaging, exclusion of venous sinus thrombosis (18). Volunteers for the control group were recruited from individuals attending the neurology outpatient clinic whose clinical evaluations did not indicate elevated intracranial pressure. The healthy control group was matched to the patient group in terms of sex and age.

The shared exclusion criteria for both cohorts encompassed individuals under 18, those lacking the cognitive capacity to respond to the questionnaire, pregnant or breastfeeding individuals, those diagnosed with sleep disorders, and individuals unwilling to volunteer for the study. Patients with secondary causes of increased pressure such as intracranial mass, cerebral venous thrombosis, etc., and those with complaints suggestive of these pathologies were excluded from both patient and control groups. The research protocol was comprehensively delineated to the participants, and their written consent, signifying their informed acknowledgment and agreement, was obtained. The study protocol was structured to adhere to anticipated ethical considerations, aligning with the principles outlined in the Declaration of Helsinki and subsequent revisions, and received approval from the pertinent local ethics committee (Başakşehir Çam and Sakura City Hospital, dated 13.09.2023, and numbered 422).

Data Collection, Definitions, and Tools

The IIH diagnosis-related information of the patients was obtained by retrospective scanning of our hospital's digital records. All data of the participants (including healthy controls) who volunteered to participate in the study were obtained by examining their information at first admission during the study period. After written consent was obtained, we recorded age, sex, comorbidity information, smoking and alcohol consumption status. Only those who actively smoked tobacco products and consumed alcohol were defined as users of tobacco or alcohol. Presenting symptoms for patients with IIH were recorded. The height and weight measurements of the participants were taken and body mass index (BMI) was calculated as weight/height^2 (kg/m^2). Participants were grouped according to their BMI <18.5 as underweight, 18.5-24.9 as normal weight, 25.0-29.9 as overweight, and ≤30 as obese (19). The Berlin and STOP-BANG questionnaires were administered to all participants.

Berlin Questionnaire

The Berlin questionnaire contains ten questions in 3 categories and one measurement (BMI). The first six questions concern snoring (first dimension), and questions 7 to 9 concern daytime sleepiness (second dimension). High blood pressure was questioned in the third dimension, and BMI was measured. The patient's family members verified answers to questions about snoring. In the first and second dimensions, two or more positive responses indicating recurrent symptoms (>3-4

times/week) were considered to show positivity. A history of high blood pressure or a BMI of more than 30 kg/m^2 was considered positive for the third dimension. Patients who were positive for two or more categories were considered to have a high risk for OSA (16,20). The validity of the Berlin questionnaire in Turkish was confirmed by Karakoc et al. (21).

STOP-BANG Questionnaire

The STOP-BANG questionnaire encompasses a set of inquiries consisting of eight binary (affirmative/negative) interrogatives and four supplementary demographic inquiries about sleep apnea symptoms. Moreover, it incorporates four queries constituting the STOP segment, which assesses variables such as snoring, fatigue, witnessed apnea events, hypertension, BMI, age, neck circumference, and male gender. Each affirmative response to the questionnaire prompts an allocation of 1 point, while each negative response warrants 0 points, resulting in a cumulative score ranging from 0 to 8. If 3 out of the 8 questions in the STOP-BANG survey received affirmative answers, the individual was considered to be at high risk for OSA (22).

Outcome Measures

The principal aim of the investigation was to examine the autonomous correlations between the occurrence of IIH and a heightened probability of OSA. The secondary outcomes of the study were to investigate other variables associated with IIH and increased OSA risk.

Statistical Analysis

Statistical analysis was conducted using IBM SPSS Statistics for Windows, Version 25.0 (IBM Corp., Armonk, NY, USA). Statistical significance was defined as $p<0.05$. Histograms and Q-Q plots were employed to assess the normal distribution of variables. Descriptive statistics were reported as mean ± standard deviation for normally distributed continuous variables, median (25th percentile - 75th percentile) for non-normally distributed continuous variables, and frequency (percentage) for categorical variables. Normally distributed continuous variables underwent analysis via Student's t-test, while non-normally distributed continuous variables were analyzed using the Mann-Whitney U test. Categorical variables were subjected to chi-square, Fisher's exact, or Fisher-Freeman-Halton tests. Logistic regression analyses were conducted to identify significant factors independently associated with high risk on the Berlin and STOP-BANG questionnaires. Variables were initially assessed via univariate regression analysis, with statistically significant variables subsequently included in multivariate analysis.

RESULTS

The study comprised 60 individuals diagnosed with IIH and 120 healthy participants. The IIH group exhibited a median age of 33 (interquartile range (IQR), 27-43.5) years whereas the control group had a median age of 31 (IQR, 27-40) years. Females represented 86.67% (n=52) of the IIH group and 83.33% (n=100) of the control group. No statistically significant differences were observed among the groups concerning age (p=0.437) and gender distribution (p=0.716). The proportion of individuals with normal weight was notably greater within the control group, while the prevalence of obesity was markedly elevated among participants in the IIH group ($p<0.001$). The prevalence of diabetes mellitus (p=0.007) and respiratory diseases (p=0.043) exhibited statistically significant elevation within the IIH group compared to the control group. According to the Berlin questionnaire results, the percentage of patients with positivity for dimension 1 (p=0.008), dimension 2 ($p<0.001$), and dimension 3 ($p<0.001$) was higher among IIH patients. Furthermore, patients categorized as having high risk for OSA were statistically significantly more common among those with IIH, based on the Berlin ($p<0.001$) and the STOP-BANG (p=0.004) questionnaires (Table 1).

Subsequently, multivariate logistic regression analysis was conducted, indicating that obesity emerged as the sole factor exhibiting an independent association with the

Table 1. Comparison of demographics, symptoms, and questionnaire results with regard to groups

	IIH (n=60)	Control (n=120)	p
Age (years)	33 (27 - 43.5)	31 (27 - 40)	0.437†
Gender, n (%)			
Female	52 (86.67)	100 (83.33)	0.716§
Male	8 (13.33)	20 (16.67)	
BMI (kg/m^2)	32.64±6.32	26.63±5.10	**<0.001**‡
BMI Groups, n (%)			
Underweight	0 (0.00)	3 (2.50)	**<0.001**¶
Normal weight	8 (13.33)	50 (41.67)	
Overweight	11 (18.33)	28 (23.33)	
Obese	41 (68.33)	39 (32.50)	
Comorbidities, n (%)			
Diabetes mellitus	8 (13.33)	3 (2.50)	**0.007**$^{\#}$
Hypertension	6 (10.00)	7 (5.83)	0.363$^{\#}$
Hyperlipidemia	3 (5.00)	7 (5.83)	1.000$^{\#}$
Heart diseases	3 (5.00)	2 (1.67)	0.335$^{\#}$
Respiratory diseases	4 (6.67)	1 (0.83)	**0.043**$^{\#}$
Thyroid diseases	1 (1.67)	4 (3.33)	0.666$^{\#}$
Epilepsy	1 (1.67)	0 (0.00)	0.333$^{\#}$
Smoking, n (%)	16 (26.67)	34 (28.33)	0.953§
Alcohol use, n (%)	4 (6.67)	8 (6.67)	1.000$^{\#}$
Symptoms, n (%)			
Headache	55 (91.67)	-	-
Dizziness	15 (25.00)	-	-
Tinnitus	39 (65.00)	-	-
Visual problems	46 (76.67)	-	-
Berlin Q., n (%)			
Dimension 1 positive	29 (48.33)	34 (28.33)	**0.008**§
Dimension 2 positive	35 (58.33)	28 (23.33)	**<0.001**§
Dimension 3 positive	39 (65.00)	38 (31.67)	**<0.001**§
High risk	35 (58.33)	33 (27.50)	**<0.001**§
STOP-BANG Q., n (%)			
High risk	27 (45.00)	29 (24.17)	**0.004**§

IIH: idiopathic intracranial hypertension, BMI: body mass index, Q: questionnaire, †: Mann-Whitney U test, ‡: Student's t-test, §: chi-square test, $^{\#}$: Fisher's exact test, ¶: Fisher-Freeman-Halton test, descriptive statistics were presented as mean ± standard deviation for normally distributed continuous variables, median (25th - 75th percentile) for non-normally distributed continuous variables, and frequency (percentage) for categorical variables

attainment of a "high risk" outcome based on the Berlin questionnaire (odds ratio (OR): 9.366, 95% confidence interval (CI): 4.222-20.776, p<0.001). IIH (OR: 2.148, 95% CI: 0.985-4.684, p=0.055) was not found to be significant (Table 2).

High age (OR: 1.047, 95% CI: 1.002-1.094, p=0.042), male sex (OR: 5.692, 95% CI: 1.992-16.263, p=0.001), obesity (OR: 9.934, 95% CI: 3.948-24.996, p<0.001) and hyperlipidemia (OR: 17.905, 95% CI: 1.576-203.424, p=0.020) were found independently associated with being designated as "high risk" by the STOP-BANG questionnaire. Again, IIH (OR: 1.734, 95% CI: 0.743-4.048, p=0.203) was not independently associated with high-risk results from the STOP-BANG questionnaire (Table 3).

DISCUSSION

Idiopathic intracranial hypertension is a rare condition that occurs mainly in obese patients, and its etiology is unknown. Diagnostic criteria and treatment guidelines for IIH are still being modified (23). While the precise pathophysiological mechanisms underlying IIH remain elusive, obesity, hormonal irregularities, and OSA have been posited as potential risk factors contributing to the onset of IIH (9-11). On the contrary, studies on IIH as a risk factor for increased OSA risk are quite limited. This study aimed to examine the interconnection between IIH and OSA. Consequently, our findings revealed an increased likelihood of OSA among patients diagnosed with IIH compared to those without the condition.

Additionally, the IIH group had a higher BMI, percentage of obese patients, and percentage of patients with diabetes mellitus and respiratory diseases. Nonetheless, IIH did not emerge as an autonomous factor predisposing individuals to a heightened risk of OSA as per the evaluations derived from the Berlin and STOP-BANG questionnaires. As per the Berlin questionnaire, obesity was identified as the sole autonomous predictor associated with a heightened risk of OSA. As indicated by the STOP-BANG questionnaire, advanced age, male gender, obesity, and hyperlipidemia emerged as independent predictors correlating with an elevated risk of OSA. Although IIH is more prevalent among young individuals and women, OSA is more common in older individuals and men. However, several investigations have indicated an increased likelihood of IHH

Table 2. Logistic regression analysis results for high risk of Berlin questionnaire

	Univariate		Multivariate	
	OR (95% CI)	**p**	**OR (95% CI)**	**p**
Age	1.057 (1.024 - 1.091)	**0.001**	1.040 (0.997 - 1.085)	0.071
Gender (male)	2.155 (0.955 - 4.865)	0.065		
Obesity	12.758 (6.127 - 26.566)	**<0.001**	9.366 (4.222 - 20.776)	**<0.001**
Hypertension	10.614 (2.275 - 49.521)	**0.003**	1.268 (0.171 - 9.426)	0.817
Hyperlipidemia	4.169 (1.040 - 16.712)	**0.044**	1.463 (0.203 - 10.566)	0.706
Heart diseases	1.101 (0.179 - 6.762)	0.917		
Respiratory diseases	2.538 (0.413 - 15.593)	0.315		
Thyroid diseases	6.937 (0.759 - 63.417)	0.086		
Smoking	1.013 (0.517 - 1.984)	0.970		
Alcohol use	0.813 (0.235 - 2.808)	0.743		
IIH	3.691 (1.925 - 7.078)	**<0.001**	2.148 (0.985 - 4.684)	0.055

OR: odds ratio, CI: confidence interval, IIH: idiopathic intracranial hypertension, Nagelkerke R^2: 0.422

Table 3. Logistic regression analysis results for high risk of STOP-BANG questionnaire

	Univariate		Multivariate	
	OR (95% CI)	**p**	**OR (95% CI)**	**p**
Age	1.065 (1.031 - 1.101)	**<0.001**	1.047 (1.002 - 1.094)	**0.042**
Gender (male)	4.478 (1.931 - 10.385)	**<0.001**	5.692 (1.992 - 16.263)	**0.001**
Obesity	10.403 (4.833 - 22.388)	**<0.001**	9.934 (3.948 - 24.996)	**<0.001**
Diabetes mellitus	6.722 (1.711 - 26.411)	**0.006**	0.901 (0.131 - 6.213)	0.916
Hypertension	8.768 (2.309 - 33.290)	**0.001**	0.477 (0.062 - 3.692)	0.478
Hyperlipidemia	23.553 (2.904 - 191.025)	**0.003**	17.905 (1.576 - 203.424)	**0.020**
Heart diseases	1.494 (0.243 - 9.199)	0.665		
Respiratory diseases	3.453 (0.561 - 21.268)	0.182		
Thyroid diseases	1.494 (0.243 - 9.199)	0.665		
Smoking	0.617 (0.293 - 1.299)	0.204		
Alcohol use	1.639 (0.497 - 5.407)	0.417		
IIH	2.567 (1.329 - 4.959)	**0.005**	1.734 (0.743 - 4.048)	0.203

OR: odds ratio, CI: confidence interval, IIH: idiopathic intracranial hypertension, Nagelkerke R^2: 0.470

in individuals with OSA, and conversely. It is noteworthy that IIH alone leads to a twofold increase in the risk of cardiovascular morbidity (8). It is widely recognized that OSA represents a notable predisposing factor for the onset of type 2 diabetes, cardiovascular diseases, hypertension, and mortality (5). The concurrent occurrence of OSA in individuals diagnosed with IIH, or conversely, may be associated with an increased susceptibility to adverse health outcomes and mortality, potentially demonstrating a synergistic effect. Thus, assessing the potential coexistence of OSA in individuals with IIH, or vice versa, examining the likelihood of IIH in patients at elevated risk for OSA may mitigate individual or synergistic risks associated with morbidity and mortality linked to these respective conditions. Moreover, identifying additional risk factors contributing to these associations and implementing preventive measures against these factors could help prevent potential increases in adverse outcomes.

Although polysomnography stands as the primary diagnostic modality for OSA, its utilization is often deemed impractical (16). Alternative diagnostic tools have been developed to address these challenges. The Berlin and STOP-BANG questionnaires represent readily deployable screening instruments that have exhibited sensitivity in discerning the propensity for OSA (13). We therefore evaluated the increased risk of OSA with these two questionnaires. The IIH group had significantly higher positivity for the dimensions and overall results with these tests. In addition, the percentage of patients with diabetes mellitus and respiratory diseases was significantly higher in the IIH group compared to those without IIH. In a prospective study, BMI exhibited a statistically significant elevation in the cohort diagnosed with IIH compared to the control group. The percentage of patients with positive results for Berlin questionnaire dimensions 1 and 2 was significantly higher in the IIH group compared with the control group (13). In another study, the Berlin questionnaire was applied simultaneously with polysomnography in patients with IIH. While 75% of those with a high-risk Berlin questionnaire score had polysomnography-confirmed OSA, 70% of those with a low-risk Berlin questionnaire score did not have OSA (16). Another investigation demonstrated that following adjustments for BMI, males diagnosed with IIH exhibited a notably higher likelihood of presenting with a positive Berlin questionnaire or a documented history of OSA (19). A comprehensive retrospective cohort study showed that individuals with untreated sleep apnea had a twofold more significant risk of developing IIH. Moreover, following adjustments for age, gender, BMI, and concurrent medical conditions, continuous positive airway pressure therapy for OSA seemed to lower the likelihood of developing IIH (24). Yiangou et al. (4) demonstrated that individuals diagnosed with IIH who also presented with OSA exhibited poorer papilledema severity and visual field recovery after 12 months compared to those without OSA, notwithstanding similar alterations in intracranial pressure. This observation implies that OSA might worsen papilledema and visual dysfunction through shared or potentially synergistic pathways with IIH. Moreover, numerous prior investigations have indicated a heightened incidence of OSA among individuals diagnosed with IIH (10,11,15,25). However, some studies claim the opposite and report no connection between OSA and IIH. In a recent prospective study, no association was observed between OSA and IIH in terms of opening pressure and the severity of papilledema (26). Another investigation determined that the frequency and intensity of OSA among individuals diagnosed with IIH did not exceed anticipated levels relative to factors such as age, gender, ethnicity, BMI, and menopausal status (15). Youssef et al. (27) indicated that IIH did not constitute a predisposing factor for the occurrence or severity of OSA. While the majority of research aims have posited that individuals diagnosed with IIH encounter a heightened susceptibility to OSA, findings from the present study corroborate these assertions. However, the available evidence is insufficient to assert that IIH alone is an autonomous risk factor contributing to an elevated likelihood of developing OSA. Given that obesity, a significant confounding variable, represents a prevalent risk factor shared by both OSA and IIH.

The most important known common risk factor for both OSA and IIH is obesity. The frequency of IIH and OSA is escalating in tandem with the growing prevalence of obesity on a global scale (4,25,28). In the current study, mean BMI and percentage of obese patients were significantly higher in the IIH group compared to those without IIH. Although IIH did not emerge as an autonomous variable associated with a heightened risk of OSA based on the outcomes of multivariate analysis, obesity independently stood out as a risk factor contributing to elevated susceptibility to OSA across both survey methodologies. Several studies have illustrated bariatric surgery's clinical and economic efficacy in managing IIH (4,14,29,30). Yiangou et al. (4) investigated the effects of bariatric surgery on intracranial pressure, papilledema, OSA prevalence, and severity in women with IIH. They showed that bariatric surgery improved all of these characteristics in patients with IIH. In a 5-year randomized clinical trial, changes in the intracranial pressure of women diagnosed with IIH were investigated 12 months after bariatric surgery, showing significant decreases in post-operative data collection (14). It is essential at this point to note that high BMI is recognized as the strongest predictor of OSA, regardless of IIH (25). Our study showed that high BMI is a significant risk factor for both OSA and IIH, supporting previous studies. However, no definitive evidence links IIH as a risk factor to OSA. The link between IIH and OSA may be based on BMI value, possibly as a causative risk factor or a mediating parameter. However, it remains uncertain whether the existence or management of OSA influences the clinical trajectory of IIH. This issue needs to be investigated in more detail with more comprehensive, multicenter studies involving a large number of subjects.

Just as the frequency relationship between IIH and OSA is unclear, the pathophysiological connection mechanisms are also unclear (4). While the causal relationship between OSA and IIH remains ambiguous, pathophysiological and clinical associations probably exist between IIH, OSA, and obesity. Measurements of cerebrospinal fluid pressures reaching as high as 750 mm H_2O have been documented in individuals experiencing OSA during episodes of nocturnal apnea, indicating a potential correlation between OSA and elevated intracranial pressure (9,31). It is speculated that OSA and obesity may cause an increase in

the number of retinol-binding proteins that transport vitamin A or retinol in the blood, resulting in increased cerebrospinal fluid production and possibly decreased absorption. Another possible mechanism is that increased intra-abdominal pressure due to obesity and OSA leads to increased central venous pressure, preventing the absorption of cerebrospinal fluid. Hypoxia and hypercapnia induced by OSA can lead to cerebral vasodilation and augmented cerebral blood flow, thereby contributing to heightened intracranial pressure. Cerebral edema arising from hypoxia due to OSA could instigate a rise in intracranial pressure via the apneic stress response, liberation of excitatory neurotransmitters, or compromise of the blood-brain barrier, particularly in susceptible individuals (4,13,16,30,32-34). Additionally, it is already well known that OSA can negatively affect visual functions by causing microangiopathic complications (35,36). Intermittent nocturnal hypoxia as a result of OSA is thought to worsen the visual consequences of IIH by causing exacerbation of optic nerve ischemia. Based on these data, we recommend that all patients diagnosed with IIH be screened for the risk of OSA. However, for this screening purpose, using polysomnography, the gold standard in diagnosing OSA, has some difficulties, as mentioned above. The high-risk classification derived from the Berlin questionnaire demonstrates a sensitivity of 86% and specificity of 77% in identifying OSA compared to results obtained from sleep studies (20). Specific references have cited the STOP-BANG questionnaire as possessing the greatest sensitivity (84%) among screening assessments for identifying OSA in contrast to the Epworth Sleepiness Scale (69%) and the Berlin questionnaire (68%). However, it exhibits lower specificity (38%) compared to the Epworth Sleepiness Scale (74%) (4). According to the results of these two surveys in our study, findings indicating a high risk of OSA in patients with IIH were obtained. Nevertheless, the present investigation did not permit the examination of the accuracy of the Berlin and STOP-BANG questionnaires in diagnosing OSA, as polysomnography was not conducted on the study participants. Therefore, more data is needed regarding the usability of these questionnaires in detecting OSA risk in patients with IIH.

The current study was conducted in a single center, limiting its external validity. The number of participants in the IIH group was relatively small because IIH is not a common disease. OSA evaluation was made through surveys. Polysomnography was not applied because it was not compatible with study practice. Significant differences in comorbidity and BMI between IIH and control groups have made it difficult to evaluate the pure OSA risk in patients with IIH. A possible longitudinal relationship between IIH and OSA has been ignored because the time to diagnosis of patients with IIH is not available. Longitudinal studies tracking improvement in IIH after treatment of OSA or obesity are required to definitively comment on the cause-and-effect relationship between IIH, OSA, and obesity. This study was not designed to investigate which morbidities OSA causes to increase the risk in patients with IIH. Examining these factors will substantially enhance comprehension of the synergistic impacts of these two conditions on concurrent medical conditions.

CONCLUSION

Patients with IIH showed higher rates of obesity and a higher risk of OSA compared to the control group. However, IIH was not an independent predictor of high OSA risk. Male sex, older age, obesity, and hyperlipidemia are independent factors associated with a high risk of OSA. Obesity represents a prevalent risk factor shared by both OSA and IIH. The coexistence of OSA and IIH may cause a synergistic effect on increased morbidity and mortality rates in both diseases. Henceforth, individuals diagnosed with IIH should undergo screening for OSA risk utilizing the Berlin and STOP-BANG questionnaires or other validated screening methodologies.

Ethics Committee Approval: The study was approved by the Clinical Research Ethics Committee of Başakşehir Çam and Sakura City Hospital (13.09.2023, 422).

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The Importance of Aneurysm Morphology and Perianeurysmal Environment in Aneurysmal Subdural Hematomas

Anevrizmal Subdural Hematomlarda Anevrizma Morfolojisi ve Perianevrizmal Ortamın Önemi

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ABSTRACT

Aim: Aneurysmal subdural hematoma (anSDH) is an uncommon condition associated with significant mortality risk. This study focused on the relationship between morphology and the perianeurysmal environment by comparing aneurysm location and clinical outcomes.
Material and Methods: A total of 486 patients with aneurysmal subarachnoid hemorrhage were retrospectively analyzed for accompanying subdural hematoma (SDH) cases. Demographic information, rebleeding, discharge, and 6 months of the modified Rankin scale scores (favorable and unfavorable) were recorded. The aneurysms were divided into 3 groups: internal carotid artery (ICA), anterior cerebral artery (ACA), and middle cerebral artery (MCA). Other parameters included aneurysm morphology, SDH width, intracerebral hematoma (ICH) volume, the presence of intraventricular hematoma, and distance to the subdural space.
Results: Concomitant SDH was detected in 19 (3.9%) patients. Aneurysms were located in the ICA, 10 (52.6%); MCA, 8 (42.1%); and ACA, one (5.3%). The mean size was 9.5±4.3 mm, and there was a significant difference in aneurysm size between the ICA and MCA (p=0.025). In six supraclinoid aneurysms (posterior communicating and anterior choroidal arteries), the aneurysm dome was in the inferior lateral projection. No significant differences were observed between patients with favorable and unfavorable modified Rankin scale in terms of clinical and aneurysm morphological characteristics, except for increased ICH volume (p=0.020) and shift effects (p=0.030).
Conclusion: The size and dome projection of ICA supraclinoid segment aneurysms may be important risk factors for SDH. We also believe that aneurysm localization may have a limited impact on clinical outcomes in the context of SDH.
Keywords: Subdural hematoma; aneurysm morphology; perianeurysmal environment.

ÖZ

Amaç: Nadir rastlanan anevrizmal subdural hematom (anSDH) oldukça yüksek mortaliteye sahiptir. Bu çalışma anevrizma yerleşimi ve klinik sonuçları karşılaştırılarak morfoloji ve perianevrizmal ortam arasındaki ilişkiye odaklanmıştır.
Gereç ve Yöntemler: Anevrizmal subaraknoid kanaması olan toplam 486 hasta, eşlik eden subdural hematom (SDH) olguları açısından retrospektif olarak analiz edildi. Demografik bilgiler, tekrar kanama, taburculuk ve 6 aylık modifiye Rankin skalası (olumlu ve olumsuz) kaydedildi. Anevrizmalar 3 gruba ayrıldı: internal karotid arter (internal carotid artery, ICA), anterior serebral arter (anterior cerebral artery, ACA), ve orta serebral arter (middle cerebral artery, MCA). Diğer parametreler arasında anevrizma morfolojisi, SDH genişliği, intraserebral hematom (intracerebral hematoma, ICH) hacmi, intraventriküler hematom varlığı ve subdural boşluğa olan mesafe yer aldı.
Bulgular: Eşlik eden SDH 19 (%3,9) hastada tespit edildi. Anevrizmaların 10'u (%52,6) ICA, 8'i (%42,1) MCA ve biri (%5,3) ACA'da yerleşmişti. Ortalama boyut 9,5±4,3 mm idi ve ICA ile MCA arasında anevrizma boyutu açısından anlamlı bir fark vardı (p=0,025). Altı supraklinoid anevrizmada (posterior komünikan ve anterior koroidal arterler) anevrizma kubbesi inferior lateral projeksiyonda idi. Modifiye Rankin skalasına göre olumlu ve olumsuz değerlendirilen hastalar arasında artmış ICH hacmi (p=0,020) ve orta hat kayma etkisi (p=0,030) dışında klinik ve anevrizma morfolojik özellikleri açısından anlamlı bir fark gözlenmedi.
Sonuç: ICA supraklinoid segment anevrizmalarının boyutu ve kubbe projeksiyonu SDH için önemli risk faktörleri olabilir. Ayrıca, anevrizma lokalizasyonunun SDH bağlamında klinik sonuçlar üzerinde sınırlı bir etkiye sahip olabileceğine inanıyoruz.
Anahtar kelimeler: Subdural hematom; anevrizma morfolojisi; perianevrizmal ortam.

INTRODUCTION

While intracranial aneurysm rupture is associated with subarachnoid hemorrhage (SAH), subdural hematoma (SDH) usually occurs because of trauma and anticoagulant use. Aneurysmal subdural hematoma (anSDH) is a rare condition that usually occurs due to the rupture of a posterior communicating artery (PComA) aneurysm (35-41%) (1-3). These cases are associated with poor clinical outcomes, with a mortality rate of 70% (4).

Aneurysms develop in the subarachnoid spaces bounded by the arachnoid space, bones, brain parenchyma, and dura. The subarachnoid space forms the center of the perianeurysmal environment (PAE) and is associated with aneurysm growth and rupture (5-7). It is logical to associate PAE with additional bleeding such as intracerebral hematoma (ICH), intraventricular hematoma (IVH), and SDH after rupture.

Neurovascular imaging is necessary to determine the source of bleeding and treatment plans for SDH (8). Computed tomography (CT) angiography is a minimally invasive method that provides clinicians with rapid and precise morphological information for easy access. This is the first study to determine the diagnosis and treatment of aneurysms in most patients (9).

Studies of anSDH have mostly focused on the mechanisms of its formation, management, and prognosis. Studies on aneurysm morphology and PAE are rare. In this article, we present a series of patients with SDH components in addition to SAH after aneurysm rupture. We focused on aneurysm morphology and its relationship with PAE by comparing aneurysm locations and clinical outcomes. In doing so, we aimed to highlight the critical features that may pose a risk of anSDH and affect the clinical outcomes of patients with unruptured aneurysms.

MATERIAL AND METHODS

Medical records, surgical videos, and reports of 486 patients with aneurysmal SAH treated at our institution were retrospectively analyzed to detect and assess the development of any accompanying SDH. The inclusion criterion was an age of >18 years. The exclusion criteria were isolated falcine or tentorial SDH, poor image quality, the presence of bleeding diathesis, and a history of anticoagulant use. Medical records were reviewed, and the following data were collected: demographic information, World Federation of Neurosurgical Societies (WFNS) grade, rebleeding, treatment methods, discharge, and modified Rankin Scale (mRS) score at the sixth month.

We evaluated SDH size, midline shift (MLS), the presence of ICH and IVH, and aneurysm features (morphological and PAE) on CT and CT angiography, which are frequently used to determine the diagnosis and treatment. ICH was diagnosed based on CT scans at admission, and the ICH volume was calculated using the formula, A×B×C/2 (10). All intraparenchymal hemorrhages ≥10 ml were defined as ICH (11). Aneurysms were categorized into three groups based on their location: internal carotid artery (ICA) including ophthalmic artery, anterior choroidal artery (AChoA), and PComA, middle cerebral artery (MCA), and anterior cerebral artery (ACA). The cross-sectional width of the aneurysmal sac at its widest point was measured as aneurysm size. Aneurysms were classified into three morphological types: irregular, bleb, and lobulated. The other morphological parameters assessed were multiplicity and thrombosis. Measurements were obtained using DCOM format with 2D and 3D software (version V4.4EU; Synapse 3D Fujifilm Medical Systems, USA), which can be used on a personal computer.

The PAE was visualized using 3D CT angiography. Based on the aneurysm shape and projection, the relationships (distance to the subdural space and overlap) with the brain parenchyma, dura, and bone structures were examined.

The choice of treatment (surgery or endovascular) was determined after a multidisciplinary evaluation, considering the general medical and neurological status, the presence of a mass effect due to SDH or ICH, and aneurysm morphology. Clinical status at discharge and at 6 months was categorized as favorable (mRS 0-3) or unfavorable (mRS 4-6) outcomes. Patients were divided into two groups based on aneurysm location (MCA and ICA) and clinical outcomes (favorable and unfavorable). ACA aneurysms were excluded from the comparative statistical evaluation because there was only one. MCA and ICA groups were compared for clinical and morphological parameters to assess the risk of AnSDH. The study was conducted following the guidelines and was approved by the ethics committee of Bursa Yüksek İhtisas Training and Research Hospital (11.08.2021, 2021/08-17).

Statistical Analysis

For statistical analysis, JASP (0.16.1) and Jamovi (2.2.5.0, The JAMOVI Project, Sydney, Australia, 2022) were used. Continuous data with normal distribution were presented with mean and standard deviation, while continuous variables without normal distribution were reported with median, minimum, and maximum values for descriptive statistics Categorical variables were displayed as numbers and percentages. For normality, Shapiro-Wilk, Kolmogorov-Smirnov, and Anderson-Darling tests were used. Pearson's chi-square and Fisher's exact tests were used to compare the two category components, while RxC tables were analyzed with the Fisher-Freeman-Halton test. To compare two groups with normally distributed numerical variables, an independent sample t-test was employed. The Mann-Whitney U test was used to compare the two groups with non-normally distributed variables. The statistical significance level was set at $p<0.05$.

RESULTS

AnSDH was detected in 19 (3.9%) patients. The mean age of the patients was 64.2±11.4 years, and 14 (73.7%) were >60 years old. Ten (52.6%) of the patients were female. The mean WFNS score at presentation was 3.7±0.9, the same at the time of intervention. Ten (52.6%) aneurysms were located in the ICA (seven PComA, two ophthalmic, and one AChoA), eight (42.1%) in the MCA, and one (5.3%) in the ACA. The initial mean maximal SDH thickness was 9.7±5.9 mm, and the mean MLS was 8.4±5.9 mm. The mean MLS due to an MCA aneurysm was 12.8±2.9 mm, significantly different from an ICA aneurysm ($p=0.012$). SDH occurred on the right side in ten (52.6%) patients, on the left side in eight (42.1%), and bilaterally in one (5.3%). All patients presented with Fisher grade 4 SAH, of them 17 (89.5%) had ICH. All patients with MCA aneurysm rupture-induced SDH had ICH, with a median volume of

46.1 (range, 36-84) ml, the median volume of the ICA aneurysms was 18 (range, 8-44) ml. ICH volumes due to MCA aneurysm rupture were significantly higher (p=0.020). IVH was observed in four (21.1%) patients (Table 1).

While the shortest distance between the MCA aneurysm and subdural space was <10 mm, the mean distance between the ICA aneurysm and subdural space was 2.6±2.9 mm. Six (75%) aneurysms, except for two MCA aneurysms, were found to be directed towards the brain parenchyma. Four (50%) projections of MCA aneurysms were temporal, two (25%) were frontal, and two (25%) were sylvians. While eight (80%) ICA aneurysms overlapped with the brain parenchyma, both ophthalmic artery aneurysms were associated with both the parenchyma and the subdural space. It was observed that the projections of six (60%) ICA aneurysms were lateral, two (20%) were anterosuperior, and two (20%) were posterolateral. It was observed that the projection of 75% of supraclinoid aneurysms (PComA and AChoA) was in an inf-lateral direction. Rebleeding was observed in two patients (10.5%).

The mean aneurysm size was 9.5±4.3 mm, and there was a statistically significant difference in the sizes of the ICA and MCA aneurysms (p=0.025). Eight (42.1%) aneurysms were ≥10 mm in size and mostly ICA aneurysms. While seven (36.8%) aneurysms had an irregular shape, six (31.6%) had blebs, and six (31.6%) were lobulated. Multiplicity and thrombosed aneurysms were present in three (15.8%). Sixteen (84.2%) patients underwent aneurysm clipping, and three (15.8%) underwent endovascular coiling.

The mRS values at discharge and 6 months were the same, and nine (47.4%) patients had favorable outcomes. The mortality rate was 42.1% (n=8). The factors affecting the clinical outcomes were ICH volume (p=0.020) and shift effects (p=0.030). No other clinical or aneurysm morphological features showed a statistically significant difference between the patients with favorable and unfavorable outcomes. The most important factor affecting clinical outcomes was the WFNS score (p=0.010).

DISCUSSION

Risk factors for anSDH include old age, sentinel headache before SAH, PComA aneurysm, and ICH on the initial CT (4,12). SDH occurs in approximately 0.5-7.9% of anSAHs (13). This was similar to the rate observed in the present study (approximately 3.8%). In our study, 73.7% of the patients were aged 60 years and older. 36.8% of the study participants had a PComA aneurysm and the rate of ICH on the initial CT scan was 89.5%. Our findings support those of previous studies on the possible risk factors. However, most previous investigations did not include additional data regarding the relationship between specific aneurysm morphology and PAE.

Bleeding into the subdural space, either directly or via the subarachnoid space, is the most frequently discussed theory on the mechanism of SDH development (14). Therefore, PAE

Table 1. Patient characteristics

No	Age	Gender	WFNS	Location	Subdural Size (mm)	Shift (mm)	IVH	ICH	mRS	mRS (6 months)	Aneurysm Size (mm)	Death	Morphology	Multiplicity	Thrombosed	Re-bleed	Treatment	Subdural Dis. (mm)	Projection
1	55	M	5	MCA	6	14	N	Y	UF	UF	9	Y	Irregular	N	N	N	Clips	≥10	Frontal
2	89	F	5	ICA-OphtA	19	10	N	Y	UF	UF	16	Y	Lobulated	N	Y	Y	Clips	0	Inf-lateral
3	61	F	4	MCA	9	16	Y	Y	UF	UF	15	N	Irregular	N	N	N	Clips	≥10	Temporal
4	75	F	2	ICA-PComA	4	0	N	N	F	F	5	N	Blep	N	N	N	Coil	2.7	Inf-lateral
5	62	M	2	ACA-PComA	5	3	N	Y	F	F	6	N	Irregular	Y	N	N	Clips	3.7	Anterior
6	41	F	3	MCA	8	10	Y	Y	F	F	7	N	Lobulated	N	N	N	Clips	≥10	Temporal
7	67	M	4	MCA-ETB	4	14	N	Y	F	F	6	N	Irregular	N	N	N	Clips	≥10	Frontal
8	59	M	4	MCA	3	16	Y	Y	UF	UF	4	Y	Blep	N	N	N	Clips	≥10	Temporal
9	70	M	3	ICA-OphtA	11	6	N	Y	F	F	13	N	Lobulated	N	N	N	Clips	0	Anterior
10	60	M	5	ICA-PComA	13	0	N	Y	UF	UF	12	Y	Irregular	N	Y	N	Clips	1.8	Inf-lateral
11	48	M	3	ICA-PComA	7	0	N	Y	F	UF	10	N	Irregular	Y	N	N	Clips	3.8	Inf-lateral
12	55	F	4	ICA-PComA	16	11	Y	Y	UF	UF	7	N	Blep	N	N	N	Clips	4	Inf-posteric
13	60	M	4	MCA	20	14	N	Y	UF	UF	5	Y	Lobulated	N	N	N	Clips	≥10	Sylviyan
14	65	F	3	ICA-PComA	3	0	N	Y	F	F	4	N	Lobulated	N	N	N	Coil	3	Inf-lateral
15	68	F	5	MCA	12	11	N	N	UF	UF	5	Y	Blep	N	N	Y	Clips	≥10	Temporal
16	63	F	4	ICA-AChoA	11	6	N	N	F	F	14	N	Blep	N	N	N	Clips	2	Inf-lateral
17	74	M	3	ICA-PComA	10	4	N	N	F	F	13	N	Blep	N	N	N	Coil	4.8	Inf-posteric
18	63	F	4	MCA	5	8	N	Y	UF	UF	9	Y	Lobulated	Y	N	N	Clips	≥10	Frontal
19	85	F	4	ICA-PComA	22	17	N	N	UF	UF	17	Y	Irregular	N	Y	N	Clips	1.5	Inf-lateral

WFNS: World Federation of Neurosurgical Societies, IVH: intraventricular hematoma, ICH: intracerebral hematoma, mRS: modified Rankin Scale, Dis: distance, M: male, F: female, MCA: middle cerebral artery, ICA: internal carotid artery, ACA: anterior cerebral artery, OphtA: ophthalmic artery, PComA: posterior communicating artery, AChoA: anterior choroidal artery, ETB: early temporal branch, Y: yes, N: no, F: favorable, UF: unfavorable

can be considered the primary factor in the development of anSDH. As the aneurysm dome grows, dense adhesions develop with the arachnoid membrane, causing the basal cistern to fuse almost completely with the wall of the aneurysm. Especially in ICA aneurysms, when this adherent dome protrudes towards the skull base dura (bleb or lobule), the PAE-subdural space distance decreases (Figure 1). To date, aneurysm size has not been reported as a risk factor for anSDH (4,12,14,15). Our findings showed that ICA aneurysms were significantly larger than MCA aneurysms. Additionally, 70% of ICA aneurysms were 10 mm or larger in size. Another striking finding was that the projection of six (75%) of the eight ICA-supraclinoid aneurysms was inferolateral (Figure 2). The distance of these aneurysms to the nearest dural anatomical structures (anterior clinoid process) was 2.6 (range, 0-4.8) mm. In our study, the distance between all MCA aneurysms and the subdural space was greater than 10 mm. The mean length of the ICA-supraclinoid segment was 14.8±3.0 mm (16). In fact, it was reported that this length was shorter in the presence of a PComA aneurysm (17). If these segment aneurysms tend towards the petroclinoid area in the subdural space, where the ICA passes, and reach large sizes, this naturally increases the risk of acute SDH. Considering these close anatomical connections at the skull base, our findings suggest that medium-large (10 mm and above) and inferior lateral projection ICA-supraclinoid segment aneurysms are potential risk factors for the development of anSDH.

Another hypothesis on the etiology of anSDH is the leakage of a large amount of blood from the parenchyma into the subdural space through tears in the parenchyma and arachnoid membrane (14). Aneurysms surrounded by brain tissue, such as MCA aneurysms (Figure 3), are associated with a high risk of ICH (12). Spontaneous ICH is defined as bleeding with a volume of 25-30 mL (18). No specific volume has been defined for SAH with ICH as it is associated with widespread subarachnoid clots and edema that can affect cerebral circulation. The presence of an accompanying SDH complicates the situation. In our study, ICH was observed in 89.5% of the patients with SDH. In previous studies, the association between anSDH and ICH has ranged from 27% to 63% (4,19). The high rate observed in our study may be attributable to the inclusion of all hematomas measuring ≥10 ml as ICH. However, we believe that ICH is frequently observed after aggressive aneurysmal rupture, extending into the subdural space.

Another remarkable finding was that, although ICH volumes and MLS were significantly higher in the MCA group than in the ICA group, there was no significant difference in the clinical results. We believe that the fact that the accompanying hematoma in SDH cases did not have a significant effect on clinical outcomes despite increasing volumes may be due to altered vascular circulation and impaired cerebral perfusion after SAH. Consistent with previous studies (4,12,19), the most important factor affecting clinical outcomes in our study

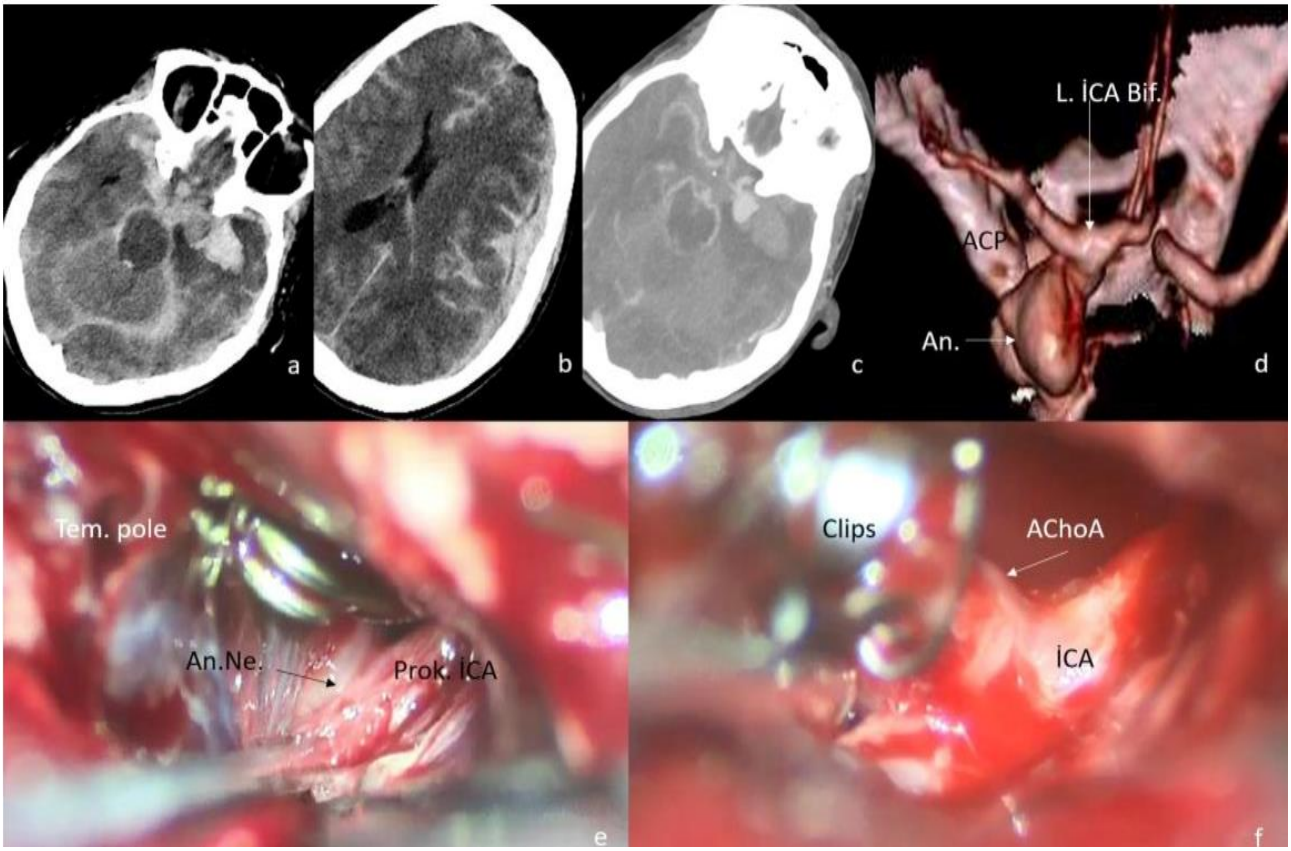

Figure 1. a,b) Initial computed tomography (CT) scan showing diffuse subarachnoid hemorrhage, left temporal intracerebral hematoma, and subdural hematoma in the convexity, **c,d)** On CT angiography, a 14-mm saccular aneurysm was observed in the anterior choroidal artery(AChoA) extending to the anterior fossa dura, **e,f)** After emergency surgery, drainage of the hematoma and subdural hematoma, and temporary clipping, the AChoA aneurysm is clipped (patient number, 16)

L. ICA Bif: left internal carotid artery bifurcation, ACP: anterior clinoid process, An: aneurysm, An.Ne: Aneurysm neck, Tem: temporal, Pro: proximal

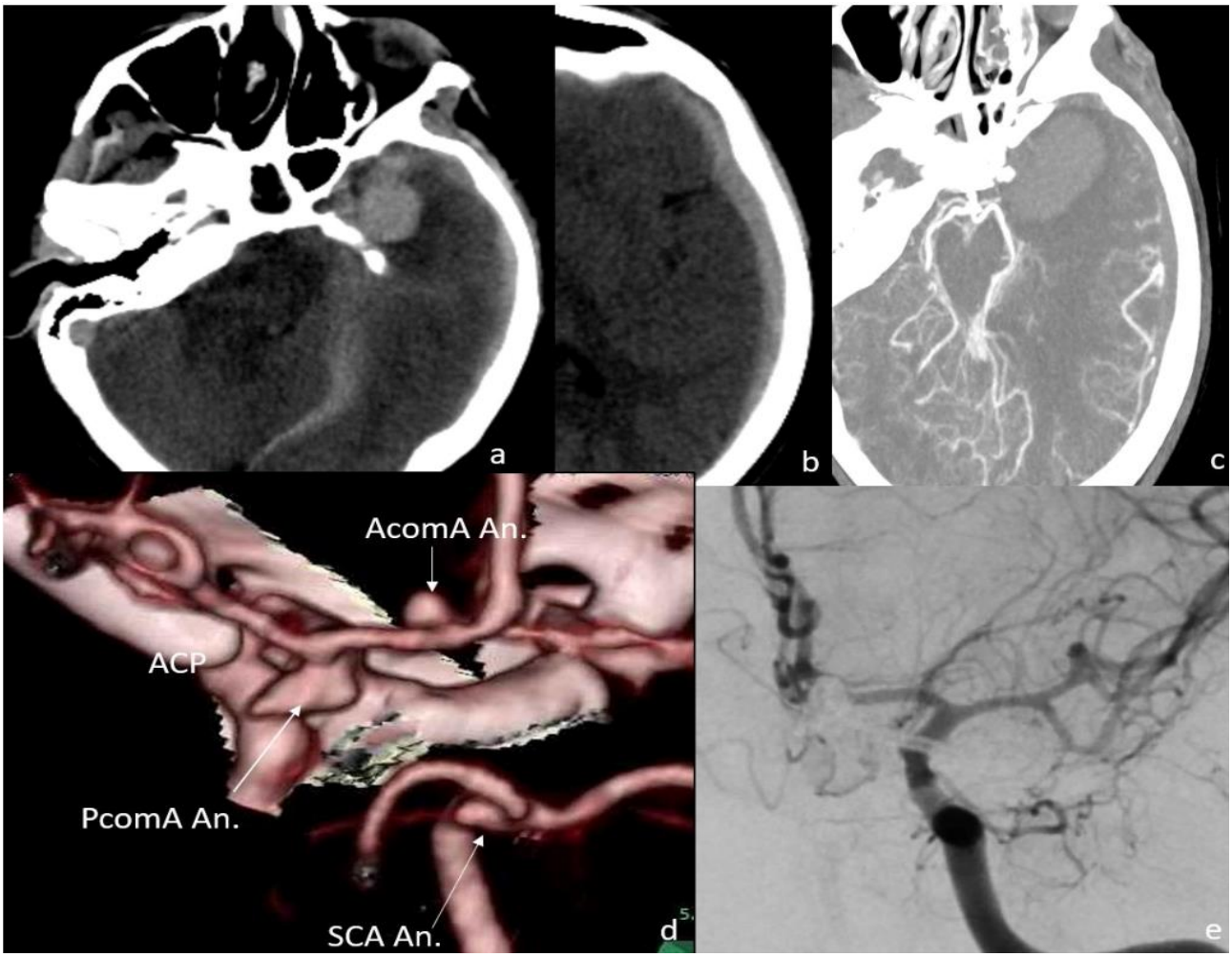

Figure 2. a,b) Computed tomography (CT) showing diffuse subarachnoid hemorrhage, intracerebral hematoma starting from the left temporal pole and extending to the convexity, and subdural hematoma, **c,d)** CT angiography revealed saccular aneurysms in the inferior laterally oriented posterior communicating artery (PComA), superior cerebellar artery (SCA), and anterior communicating artery (AComA), considering that the PComA aneurysm was bleeding, consistent with a hematoma, emergency surgery was performed, clip ligation of PComA and AComA aneurysms was performed in the same session, **e)** postoperative digital subtraction angiography image (patient number, 11)
ACP: anterior clinoid process, An: aneurysm

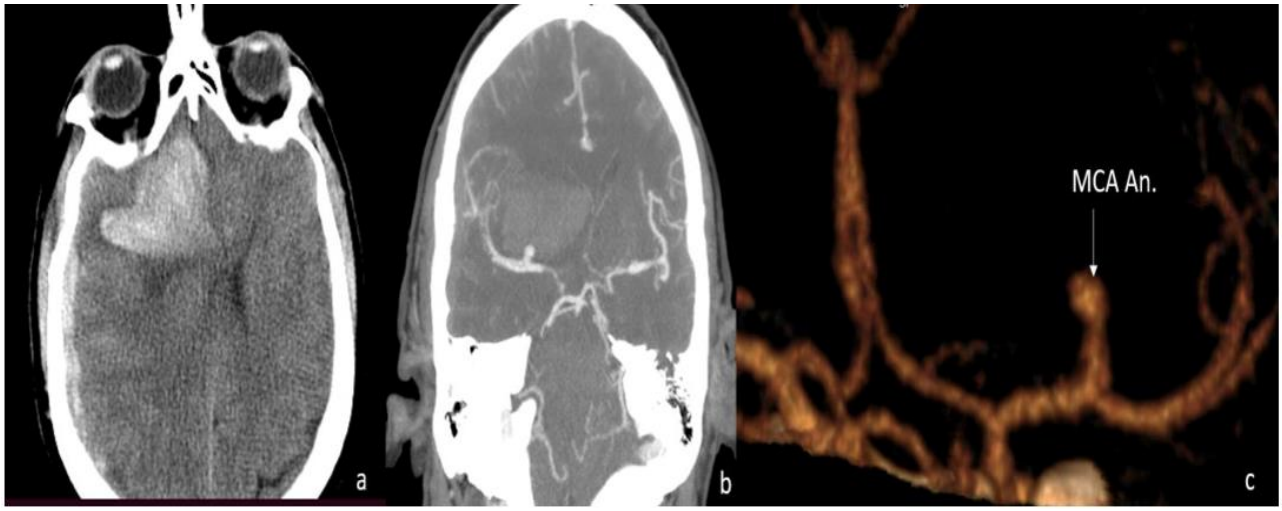

Figure 3. a) right temporal intracerebral hematoma (ICH) and subdural hematoma (SDH) were observed on computed tomography (CT), **b,c)** a right middle cerebral artery early branch aneurysm is detected on CT angiography, emergency surgery was performed by clip ligation and SDH-ICH drainage, (patient number, 7)
MCA: middle cerebral artery, An: aneurysm

was the WFNS score. In addition, aneurysm morphology and localization did not significantly affect clinical results. Although the results of our study are important, additional research with a larger sample size is required.

This study has several limitations. The small sample size limited subgroup analysis, hence, some therapeutically relevant findings may not have been statistically significant. 3D neuroimaging provided extensive information on aneurysm morphology, but a high-resolution MRI is needed to determine the link between aneurysms and their surroundings. Future studies should evaluate the relationship between aneurysm morphology and arachnoid membrane and dura, especially in patients with and without supraclinoid anSDHs.

CONCLUSION

The relationship between aneurysm morphology and PAE in the etiology of anSDH is clear, and the size and dome projection of ICA aneurysms, particularly supraclinoid ICA aneurysms, may be an additional risk factor. The findings of our study may also help determine the prognosis of unruptured supraclinoid aneurysms. Furthermore, our study showed that the specific localization of aneurysms and concomitant bleeding (IVH and ICH) did not significantly affect the clinical outcomes of anSDH.

Ethics Committee Approval: The study was approved by the Ethics Committee of Bursa Yüksek İhtisas Training and Research Hospital (11.08.2021, 2021/08-17).

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Comparison of ICSI and Spontaneous Pregnancy Outcomes in Women with Unexplained Infertility

Açıklanamayan İnfertilite Tanısı Almış Kadınların ICSI ve Spontan Gebelik Sonuçlarının Karşılaştırılması

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ABSTRACT

Aim: This study aimed to investigate whether there is a difference between the results of intracytoplasmic sperm injection (ICSI) pregnancies and subsequent spontaneous pregnancies with a diagnosis of unexplained infertility.
Material and Methods: In this retrospective study, a total of 48 women who first conceived with ICSI and then achieved spontaneous pregnancy were included. Duration and causes of infertility, time to spontaneous conception, pregnancy outcomes, and maternal and neonatal complications were evaluated.
Results: Maternal age was older in the spontaneous pregnancy group compared to the ICSI group (p=0.029). The gestational age at delivery was found similar in both groups. Although birth weight was higher in the spontaneous pregnancy group, the difference between the groups was not statistically significant (p=0.382). The time to achieve pregnancy was shorter in the spontaneous pregnancy group (p=0.001). Gestational diabetes was significantly higher in the spontaneous pregnancy group (p=0.001), while amniotic fluid abnormality, gestational hypertension (p=0.001), and preterm delivery (p=0.001) were significantly higher in the ICSI group. While the number of babies with the 1st-minute low Apgar score was higher in the ICSI group (%4.16 vs 2.08%, p=0.001), the 5th-minute Apgar score was similar.
Conclusion: Even if couples are evaluated as infertile, it should be taken into consideration that they can achieve spontaneous pregnancy. It may be rational to wait for spontaneous pregnancy in eligible couples with unexplained infertility and not to refer the patient for early assisted reproductive techniques.
Keywords: ICSI; spontaneous pregnancy; pregnancy outcomes; unexplained infertility.

ÖZ

Amaç: Bu çalışmada, açıklanmayan infertilite tanısı alarak intrasitoplazmik sperm enjeksiyonu (intracytoplasmic sperm injection, ICSI) ile elde edilen gebelikler ile daha sonradan elde edilen spontan gebeliklerin sonuçları arasında bir farklılık olup olmadığının incelenmesi amaçlanmıştır.
Gereç ve Yöntemler: Retrospektif nitelikteki bu çalışmaya önce ICSI ile gebe kalmış ve sonrasında ise spontan gebelik elde etmiş olan toplam 48 kadın dahil edildi. İnfertilite süreleri ve nedenleri, spontan gebelik elde etmek geçen süre, gebelik sonuçları ile maternal ve neonatal komplikasyonları değerlendirildi.
Bulgular: ICSI grubu ile karşılaştırıldığında, maternal yaş spontan gebelik grubunda daha büyüktü (p=0,029). Doğum anındaki gebelik haftası her iki grupta benzer bulundu. Spontan gebelik grubunda doğum ağırlığı daha yüksek olmasına rağmen gruplar arasındaki fark istatistiksel olarak anlamdı değildi (p=0,382). Gebelik elde etmek için geçen süre spontan gebelik grubunda daha kısaydı (p=0,001). Gestasyonel diyabet spontan gebelik grubunda daha yüksek iken (p=0,001), amnion mai anormalliği, gestasyonel hipertansiyon (p=0,001) ve preterm doğum (p=0,001) ICSI grubunda anlamlı olarak daha yüksekti. 1. dakika düşük Apgar skoru olan bebek sayısı ICSI grubunda daha yüksekken (%4,16'ya karşı %2,08 p=0,001), 5. dakika Apgar skoru benzerdi.
Sonuç: Çiftler infertil olarak değerlendirilse bile sonrasında spontan gebelik elde edebilecekleri göz önünde bulundurulmalıdır. Açıklanamayan infertilite tanısı almış uygun çiftlerde spontan gebelik için beklemek ve hastayı erkenden üremeye yardımcı teknikler için yönlendirmemek akılcı bir tutum olabilir.
Anahtar kelimeler: ICSI; spontan gebelik; gebelik sonuçları; açıklanamayan infertilite.

INTRODUCTION

The commonly used definition of infertility is the inability to achieve pregnancy for 12 months despite unprotected intercourse (1). Many couples suffer from this situation. In the studies conducted, 12.6%-17.5% of couples were diagnosed with infertility, although the population and region screened varied (2). This means that around 50 million couples worldwide are seeking treatment for infertility (3,4). In women, tubal and uterine disorders, ovulation dysfunction and endocrinologic disorders often cause infertility, while in men, abnormal sperm count and function, obstruction of the reproductive tract, and hormonal disorders cause infertility. But in some couples, conventional methods cannot reveal the cause of infertility. This condition is called unexplained infertility (5). Infertility treatment has been available for more than 40 years. However, infertility treatment requires extensive biomedical and surgical interventions (6). All of these treatments are mentally, physically, and economically exhausting for the couple in addition to the high cost, especially in case of repeated treatment failure. For this reason, it is important that the resources allocated for treatment are used rationally. Another noteworthy issue is that 18-20% of all couples who had previously achieved pregnancy by receiving infertility treatment were able to conceive spontaneously afterward (7,8). This brings to mind the question of whether couples are referred early for assisted reproductive technology (ART) treatment. In terms of pregnancy outcomes, ART pregnancies carry a greater risk of adverse perinatal outcomes such as preeclampsia, gestational hypertension, and gestational diabetes than spontaneous pregnancies (9).

This study aimed to compare the live births of women who had undergone in vitro fertilization (IVF) treatment for unexplained infertility and the live births achieved by spontaneous pregnancies of these women.

MATERIAL AND METHODS

This retrospective cohort study was conducted between April 2018 and April 2022 in the Department of Obstetrics of Duzce University, a tertiary medical center, after obtaining institutional review board (Non-interventional Health Research Ethics Committee of Düzce University, 02.05.2017, 77) approval. Informed consent was obtained from all participants included in the study. The study population consisted of 48 women who were treated for unexplained infertility and had a singleton live birth and then became pregnant spontaneously and had a singleton live birth. Demographic data, pregnancy data, and delivery information of the patients who were included in the study and delivered in our hospital were obtained from the electronic data recording system of our hospital. Gestational age at birth was determined by adding 14 days after an embryo transfer in ART pregnancies and by the last menstrual period or first-trimester sonography in spontaneous pregnancies. Gestational diabetes mellitus was defined as an abnormal fasting blood glucose level or an abnormal glucose tolerance test result between 24 and 28 weeks of gestation (10). Gestational hypertension was diagnosed when blood pressure was 140/90 mmHg and above, not accompanied by proteinuria and similar systemic findings after the 20th week of pregnancy (11). Preeclampsia is a pregnancy disorder characterized by new-onset hypertension, typically occurring after 20 weeks of gestation and often near term. While it is frequently accompanied by new-onset proteinuria, some women may exhibit hypertension and other signs or symptoms of preeclampsia without the presence of proteinuria (12). Based on previous studies examining perinatal outcomes of pregnancies after IVF and spontaneous conception (13), to investigate whether major adverse obstetric outcomes were relevant and whether there was a 30% increase in the rate of major adverse obstetric outcomes, we included all women who met the inclusion criteria.

Statistical Analysis

The data in the study were analyzed using IBM SPSS Statistics for Windows v.21.0 (IBM Corp, Armonk, NY). The normality was evaluated using the Shapiro-Wilk test. The quantitative data are presented as the median, minimum, and maximum values, or mean, and standard deviation, and the categorical data as numbers and percentages. Statistical analyses were performed using the Mc-Nemar test and Wilcoxon signed rank test when appropriate. Data were determined at the 95% confidence level and a p-value of <0.05 was accepted as statistically significant.

RESULTS

Subsequent spontaneous pregnancies of 48 women who had previously undergone ICSI for unexplained infertility and had a live birth were evaluated in this study.

In terms of demographic data, maternal age was statistically significantly higher in the spontaneous pregnancy group (30.2±5.02 vs 27.1±5.36 years, p=0.029). While gestational week (39.3±2.12 vs 37.4±3.52, p=0.051) and birth weight (3390±588 vs 3270±741 gram, p=0.382) were similar between the groups, the time required to achieve pregnancy was significantly shorter (3.17±2.56 vs 4.12±2.87 years, p=0.001) in the spontaneous pregnancy group (Table 1.)

While gestational diabetes was found significantly higher in the spontaneous pregnancy group (6.25% vs 4.16%, p=0.001), amniotic fluid abnormality, gestational hypertension (8.33% vs 6.25%, p=0.001), and preterm delivery (10.4% vs 6.25%, p=0.001) were significantly higher in the ICSI group (Table 2).

Although the number of babies with 1st-minute low APGAR scores was higher in the ICSI group (4.16% vs 2.08%, p=0.001), the 5th-minute Apgar scores were similar for both groups (2.08% vs 2.08%, p=1.000). No perinatal mortality was observed in both groups. Although

Table 1. Clinical characteristics of the ICSI and spontaneous pregnancy groups

	ICSI (n=48)	Spontaneous (n=48)	p
Maternal age (year)	27.1±5.36	30.2±5.02	**0.029**
Gestational week	37.4±3.52	39.3±2.12	0.051
Birth weight (gram)	3270±741	3390±588	0.382
Time to achieve pregnancy (year)	4.12±2.87	3.17±2.56	**0.001**

ICSI: intracytoplasmic sperm injection, data were shown as mean±standard deviation

Table 2. Pregnancy and labor complications

	ICSI (n=48)	Spontaneous (n=48)	p
Gestational diabetes	2 (4.16)	3 (6.25)	**0.001**
Polihidramios	3 (6.25)	2 (4.16)	**0.001**
Oligohidramnios	3 (6.25)	2 (4.16)	**0.001**
Gestational hypertension	4 (8.33)	3 (6.25)	**0.001**
Preeclampsia	3 (6.25)	3 (6.25)	1.000
Preterm labor	5 (10.4)	3 (6.25)	**0.001**
Placental abruption	1 (2.08)	0 (0.00)	-

ICSI: intracytoplasmic sperm injection, data were shown as number (percentage)

Table 3. Maternal and neonatal outcomes

	ICSI (n=48)	Spontaneous (n=48)	p
1st-minute Apgar <7	2 (4.16)	1 (2.08)	**0.001**
5th-minute Apgar <7	1 (2.08)	1 (2.08)	1.000
Perinatal mortality	0 (0.00)	0 (0.00)	-
Cesarean delivery	40 (83.3)	43 (89.6)	0.383

ICSI: intracytoplasmic sperm injection, data were shown as number (percentage)

the cesarean section rate was higher in the spontaneous pregnancy group (89.6% vs 83.3%, p=0.383), but the difference was not statistically significant (Table 3).

DISCUSSION

The main finding from this study is that adverse perinatal outcomes are more common in ICSI pregnancies, although the women who become pregnant are the same. Although the gestational age at delivery is similar, clinicians may choose to end ICSI pregnancies earlier in the presence of pregnancy complications. We believe that the main motivation for this is the desire of the couple to take home a live baby.

Similar to our study, Hayashi et al. (13) evaluated ART pregnancies and found that the frequency of preterm delivery and placental invasion anomalies increased in ART pregnancies, while vaginal delivery rates decreased. While the underlying mechanisms for adverse obstetric outcomes in pregnancies of subfertile women remain unclear, potential explanations include the medical conditions that led to subfertility, sperm factors, and, in ART pregnancies, ovarian stimulation, embryo culture, and freezing (14). Raatikainen et al. (15) compared women who conceived after ART and women who achieved spontaneous pregnancy in a subfertile population and found similar rates of preterm delivery, need for neonatal intensive care unit (NICU), and low Apgar score. They concluded that infertility treatment alone cannot be associated with adverse pregnancy outcomes. In our study, preterm delivery and low Apgar score rates were higher in the ICSI group. Similar to us, Ludwig et al. (7) in their study on spontaneous pregnancies after ART found that 20% of couples became spontaneously pregnant within 2 years. In the couples included in our study, the time to achieve pregnancy after ICSI was approximately 3 years. In our study, the average age of women undergoing ICSI is relatively higher. These women have a longer fertility period ahead of them. The likelihood of spontaneous pregnancy after ICSI increases inversely with the woman's age (7). Couples who have a live birth after ART should definitely receive family planning counseling. The unexpected, spontaneous conception of additional children can lead to unanticipated social, economic, and psychological effects, especially for families experiencing multiple births after undergoing ICSI treatment. It should be emphasized that spontaneous pregnancy rates after ART are not low at all, couples who want to conceive again can conceive naturally, and couples who do not want to have children should use a contraceptive method.

The major limitation of our study is its retrospective design and relatively small sample size. Our study cohort was composed of women from a single hospital, making it challenging to generalize our findings to the broader female population. However, spontaneous pregnancies after ART is a critical issue, although it is not covered much in the literature and the information on this subject is very limited. With this study, we aimed to fill this gap in the literature.

CONCLUSION

When infertile couples are evaluated, especially those who are young age may be given a chance for spontaneous pregnancy for a while longer instead of being referred for ART quickly. In ART pregnancies, both the cost to achieve pregnancy is high and pregnancy complications are more common. Further studies are needed to validate these findings in clinical practice.

Ethics Committee Approval: The study was approved by the Non-interventional Health Research Ethics Committee of Düzce University (02.05.2017, 77).

Conflict of Interest: None declared by the authors.

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Comparison of Nasal Anthropometric Measurements of Turks Living in Different Geographical Regions

Farklı Coğrafi Bölgelerde Yaşayan Türklerin Nazal Antropometrik Ölçümlerinin Karşılaştırılması

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ABSTRACT

Aim: Determining the anthropometric characteristics of the nose, which is located in the center of the face, plays an important role not only in surgical procedures but also in identifying ethnic differences. This study aimed to examine the nasal similarities and differences between Kazakhs and Turks who have lived in different regions for more than a thousand years.
Material and Methods: The study included 200 Turkish students and 200 Kazakh students. For each student, sixteen distance measurements and five angle measurements of the nose were taken. The photographs were taken using a digital camera mounted on a tripod, with a distance of 1.50 meters between the photographer and the student participating in the study. Digital photographs of the front, left side, and base of the nose were taken in the Frankfurt Horizontal Plan, which is the standard head position. The photographs were transferred to the DIGIMIZER software, where measurements were made using anthropometric points previously determined.
Results: The findings reveal that among both societies, nasal measurements tend to be greater for males compared to females. Conversely, females exhibit higher nasofrontal (p=0.001) and nasolabial (p=0.001) angles compared to males. Moreover, Turks generally exhibit greater nasal length (p=0.001), width (p=0.001), and height (p=0.037) than Kazakhs, whereas tend to have lower nasofrontal (p=0.001) and nasolabial (p=0.001) angles than Kazakhs.
Conclusion: Nasal anthropometric measurements for males were generally higher than for females. In addition, all measurements differed between Turks and Kazakhs. The results of this study will be useful for future anthropometric studies.
Keywords: Anthropometry; nose; Kazakh; Turk.

ÖZ

Amaç: Yüzün merkezinde yer alan burnun antropometrik özelliklerinin belirlenmesi, sadece cerrahi işlemlerde değil, aynı zamanda etnik farklılıkların belirlenmesinde de önemli bir rol oynamaktadır. Bu çalışmanın amacı, bin yıldan fazla bir süredir farklı bölgelerde yaşayan Kazaklar ve Türkler arasındaki burun benzerliklerinin ve farklılıklarının incelenmesidir.
Gereç ve Yöntemler: Çalışmaya 200 Türk öğrenci ve 200 Kazak öğrenci dahil edildi. Her bir öğrenci için burnun on altı adet mesafe ve beş adet açı ölçümü alındı. Fotoğraflar, fotoğrafçı ile çalışmaya katılan öğrenci arasında 1,50 m mesafe olacak şekilde, tripod üzerine yerleştirilmiş dijital fotoğraf makinesi kullanılarak çekildi. Burnun ön, sol taraf ve tabanının dijital fotoğrafları, başın standart pozisyonu olan Frankfurt Yatay Planında çekildi. Fotoğraflar DIGIMIZER yazılımına aktarıldı ve daha önce belirlenen antropometrik noktalar kullanılarak ölçümler yapıldı.
Bulgular: Elde edilen bulgular, her iki toplumda da burun ölçümlerinin erkeklerde kadınlara göre daha büyük olma eğiliminde olduğunu ortaya koydu. Tersine, kadınlar erkeklere kıyasla daha yüksek nazofrontal (p=0,001) ve nazolabial (p=0,001) açılar göstermekteydi. Ayrıca, Türkler genel olarak Kazaklardan daha büyük burun uzunluğu (p=0,001), genişliği (p=0,001) ve yüksekliği (p=0,037) sergilerken, Kazaklara göre daha düşük nazofrontal açı (p=0,001) ve nazolabial (p=0,001) açılara sahip olma eğilimindeydi.
Sonuç: Erkekler için nazal antropometrik ölçümler genellikle kadınlara göre daha yüksekti. Ayrıca, tüm ölçümler Türkler ve Kazaklar arasında farklılık gösteriyordu. Bu çalışmanın sonuçları gelecekteki antropometrik çalışmalar için yararlı olacaktır.
Anahtar kelimeler: Antropometri; burun; Kazak; Türk.

INTRODUCTION

Anthropometry is a universally applicable method that can reveal the proportions and dimensions of the human body (1). Anthropometric measurements, utilized to define human morphology, gender, ethnic origin, or age, also serve as benchmarks in clinical diagnosis and for pre-, and post-operative patients (2). This approach has been employed to determine anthropometric measurements of populations, and numerous studies have been conducted to examine various parts of the human body anthropometrically. The results of such studies in different populations and at different periods considerably determine the standards for those populations (1,3). The aesthetic appeal of facial features has significantly improved in recent years. Numerous researchers have dedicated their efforts to this subject, conducting studies aimed at objectively measuring facial beauty (4-7). In this context, it is crucial to reveal the anthropometric characteristics of the nose, as it plays a pivotal role in the natural and harmonious appearance of the human face, contributing significantly to facial aesthetics (8). In addition to ethnicity, gender, and genetic factors, the structure of the nose varies as the skeletal system evolves throughout life for various reasons. Future studies will use these factors to establish standards that will play an important role in surgical procedures and in determining societal norms (3,9). According to studies conducted among people living in different geographies, nasal anthropometric measurements vary (10,11).

This study aimed to investigate how the anthropometric measurements of noses differ between individuals of Kazakh Turks and Turkey Turks, despite originating from the same lineage. As far as we know, there is no study in the literature comparing the nasal anthropometric measurements of Turks and Kazakhs. We hypothesized that these differences have emerged due to varied cultural interactions in distinct geographical regions throughout history.

MATERIAL AND METHODS

The required sample size was calculated as 350 with the G*Power v.3.1.9.6 (effect size, d=0.6; power, 1-ß=0.85). The study included 400 healthy individuals selected by random sampling method, comprising 200 Turkish students (100 females and 100 males) aged between 18 and 30 years from Ahi Evran University, and 200 Kazakh students (100 females and 100 males) aged between 18 and 30 years from Ahmet Yesevi University.

All participants had no history of nasal trauma or surgical procedures, and their body mass index (BMI) fell within specified limits (18.5-24.5 kg/m^2). Photographs of Turkish students were taken at Ahi Evran University, and Kazakh students at Ahmet Yesevi University. The photographs were taken using a digital camera mounted on a tripod, with a distance of 1.50 m between the photographer and the student participating in the study. Digital photographs of the anterior, lateral, and basal views of the nose were taken in the "Frankfurt Horizontal Plane" with each participant seated in a chair, head upright, eyes forward, and pupils fixed at the midway point (12). Prior to the study, informed consent was obtained from the individuals participating in this study. The study was approved by the Erciyes University Clinical Research Ethics Committee before commencement (Decision no: 2017/311).

The photographs were transferred to the DIGIMIZER software. The transferred photographs were utilized to identify anthropometric points including nasion (n), subnasale (sn), pronasale (prn), alare (al), soft nasal tip point (al'), and columella top point (c') for measuring the width of the columella. Additionally, wing margin point (ac), wing thickness point (alI), subalare (sbal), gnathion (gn), and labiale superior (ls) were determined. For each individual's nose, 13 distances and five angles between these anthropometric points were measured. Anthropometric points and abbreviations used in nasal measurements are shown in Table 1. Soft tissue landmarks in the anterior, lateral, and basal views are described in Table 2. To ensure

Table 1. Anthropometric points and abbreviations used in nasal measurements

Measurements	Anthropometric Point	Abbreviation	Figure
Nose length	Nasion-Pronasale	n-prn	1A,B
Nose tip protrusion length	Subnasale-Pronasale	sn-prn	1B,C
Columella length	Subnasale-Columella	sn-c	1C
Nasal root width	Maxillofrontale-Maxillofrontale	mf-mf	1A
Nose fold width	Alare'-Alare'	al'-al'	1A,C
Nose width	Alare-Alare	al-al	1A,C
Anatomical nose width	Alarcurvatur-Alarcurvatur	ac-ac	1A,C
Columella width	Columella'-Columella'	c'-c'	1C
Nostril floor width	Subalare-Subalare	sbal-sbal	1C
Nose height	Nasion-Subnasale	n-sn	1B
Distance between alar curvature and pronasal	Alar curvatur-Pronasale	ac-prn	1C
Distance between subalar and pronasal	Subalare-Pronasale	sbal-prn	1C
Right nose wing thickness	AlareI-AlareI	alI-alI	1C
Nasofrontal angle	Glabella-Nasion-Pronasale	g-n-prn	1D
Nasofacial angle	Pronasal-Nasion-Gnathion	prn-n-gn	1D
Nasal tip angle	Nasion-Pronasale-Subnasale	n-prn-sn	1D
Nasolabial angle	Pronasale-Subnasale-Labiale Superior	prn-sn-ls	1D
Wing inclination angle	Alare-Pronasale-Alare	al-prn-al	1C

Table 2. Soft tissue landmarks on the anterior, lateral, and basal views

Measurement points	Description	Figure
Glabella (g)	The midpoint between the eyebrows	1A,B
Nasion (n)	The point where the sutura internasalis and sutura frontonasalis meet	1A,B
Pronasale (prn)	The midpoint of the apex nasi	1A-C
Subnasale (sn)	The midpoint where the base of the columella (the lower edge of the septum nasi between the two nostrils) joins the upper lip	1A-C
Labiale superior (ls)	The midpoint of the upper vermillion line	1B
Gnathion (gn)	The midline point of the lower edge of the mandible	1A,B
Top of Columella (c)	It is the point at the junction of the nasal wings, soft nasal tip, and columella (the lower edge of the septum nasi between the two nostrils)	1C
Maxillofrontale (mf)	The point where the nasofrontal and maxillofrontal canal intersect	1A
Alare (al)	It is the point where the nose protrudes the most laterally on both sides when viewed from the opposite side of the face	1A-C
Soft Nasal Tip (al')	It is the point showing the two domes formed by Cartilago alaris major at the tip of the nose	1A-C
Wing Thickness Point (alI)	These are the points where the middle part of the nose wings are taken as a level and used to measure their thickness	1C
Wing Edge Point (ac)	It is the most lateral point of the wing groove where each wing meets the base	1A-C
Subalare (sbal)	Landmark on the skin of the upper lip where the bases of the nasal wings disappear from view	1C
Columella Width Point (c')	It is the point where the columella tapers and curves at a level higher than the base of the columella	1C
Nasofrontal Angle (g-n-prn)	It is the angle formed between the nose and forehead as it continues from the dorsum nasi to the forehead	1D
Nasofacial angle (prn-n-gn)	It is the angle formed between the plane passing through the glabella-gnathion points perpendicular to the ground and the nasal dorsum	1D
Nasal Tip Angle (n-prn-sn)	It is the angle formed by combining the nasion, pronasal, and subnasal points	1D
Wing inclination angle (al-prn-al)	It is the angle formed between the right and left alar points and the pronasal point	1D
Nasolabial Angle (prn-sn-ls)	It is the angle formed between the upper lip and the base of the columella	1D

measurement reliability, the measurements were repeated twice by one investigator and then averaged. The anthropometric points utilized for the measurements, as determined on the photographs, are illustrated in Figure 1.

Statistical Analysis

The data normality was evaluated using the Kolmogorov-Smirnov and Shapiro-Wilk tests. The Q-Q graphs and histograms were analyzed. An independent t-test was used for group comparisons. Statistical analysis was performed using the SPSS v.16.0 software package. A significance level of $p<0.05$ was utilized for all statistical analyses.

RESULTS

The mean age of the individuals was 24.07±1.05 years. Linear and angular measurements in Turks and Kazakhs were shown in Table 3. Most of the linear and angular measurements at the nose measured in this study were higher in Turks than in Kazakhs, except for sn-c (p=0.003), nasal tip angle (p=0.001), nasofrontal (p=0.001) angle, and nasolabial angle (p=0.001). These measurements were found higher in Kazakhs.

It was observed that there were sex-related differences in the measured parameters. The measured values of males were generally higher than those of females. However, females demonstrated higher values than males in the nasofrontal and nasolabial angles (Table 4).

While there were no statistically significant differences between the genders among the Turkish students, in terms of the values of the measurements alI-alI left (p=0.134), and alI-alI right (p=0.119), sn-c (p=0.457), wing inclination angle (p=0.083), and nasal tip angle (p=0.452), significant differences were found in the rest of the parameters.

On the other hand, statistically significant differences were found between Kazakh males and Kazakh females in terms

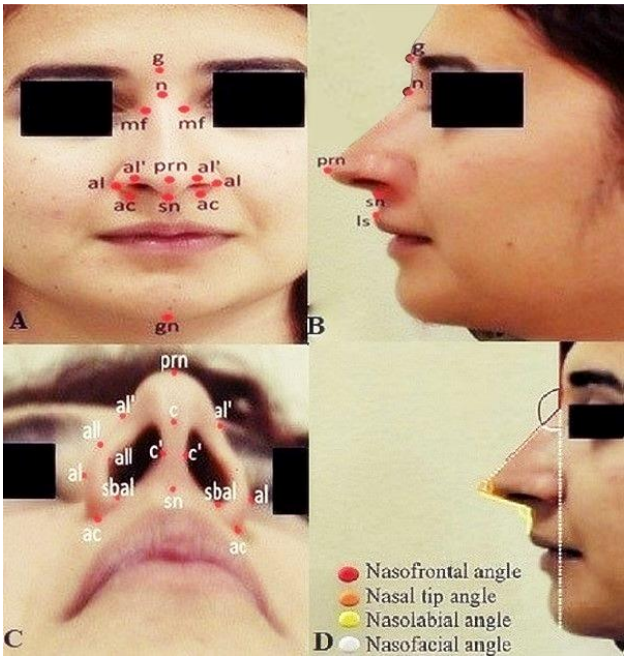

Figure 1. A) Anterior, **B)** lateral, and **C)** basal views of the anthropometric points used, and **D)** the nasal angles from the lateral view of the nose

Table 3. Linear and angular measurements at the nose in Turk and Kazakh students

Measurement	Turk (n=200)	Kazakh (n=200)	p
ac-ac	33.17±3.62	25.87±2.93	**<0.001**
ac-prn (L)	31.53±3.08	26.83±3.33	**<0.001**
ac-prn (R)	31.52±3.04	27.10±3.43	**<0.001**
al'-al'	26.43±2.93	20.61±2.66	**<0.001**
al-al	36.39±3.53	28.85±3.39	**<0.001**
alI-alI (L)	4.62±0.85	3.80±0.85	**<0.001**
alI-alI (R)	4.70±0.80	3.96±0.76	**<0.001**
c'-c'	6.81±0.91	5.40±0.81	**<0.001**
mf-mf	17.60±1.75	17.06±2.28	**0.009**
n-prn	50.66±4.52	47.28±6.12	**<0.001**
n-sn	55.81±5.15	54.67±5.66	**0.037**
sbal-prn (L)	25.62±2.77	22.28±2.98	**<0.001**
sbal-prn (R)	25.45±2.72	22.61±3.01	**<0.001**
sbal-sbal	24.64±3.65	17.56±2.36	**<0.001**
sn-c	11.13±1.59	11.66±1.91	**0.003**
sn-prn	21.20±2.55	19.29±2.54	**<0.001**
Wing inclination angle	81.73±8.39	68.15±6.78	**<0.001**
Nasal tip angle	77.51±5.85	91.95±4.84	**<0.001**
Nasofacial angle	35.38±6.00	28.62±5.12	**<0.001**
Nasofrontal angle	141.14±12.27	148.87±7.81	**<0.001**
Nasolabial angle	104.25±14.58	110.11±10.72	**<0.001**

L: left, r: right, linear measurements are reported in mm, and angles are in degrees

of the measurements of ac-ac (p=0.021), c'-c' (p=0.008), mf-mf (p<0.001), n-prn (p<0.000), n-sn (p<0.001), wing inclination angle (p<0.001) nasofacial angle (p=0.046), and nasofrontal angle (p<0.001), while there was no significant difference between genders in other measured parameters.

When the linear and angular distances measured by the marked reference points in Turk and Kazakh males were compared, sn-c (p=0.044), nasal tip angle (p<0.001), nasofrontal angle (p<0.001), and nasolabial angle (p<0.001) were found to be higher in Kazakh males, while the other parameters were statistically significantly higher in Turk males (p<0.001 for all parameters).

While sn-c (p=0.027) and mf-mf (p<0.001) values were higher in Kazakh females, other linear measurements were found to be higher in Turk females. Kazakh females exhibited higher values in nasal tip angle (p<0.001) and nasofrontal angle (p<0.001), whereas Turk females showed higher values in nasofacial angle (p<0.001) and wing inclination angle (p<0.001). Despite the nasolabial angle being measured higher in Kazakh females than in Turk females, statistical analysis did not reveal any significant difference (p=0.460).

DISCUSSION

Identifying the anthropometric features of the nose, pivotal for the natural and harmonious appearance of the human face, and their contribution to aesthetic appeal, underscores the importance of conducting comparative studies across diverse societies. Such endeavors are crucial

Table 4. Linear and angular measurements of the nose in Turk and Kazakh students by gender

Measurement	Gender		Turk (n=200)	Kazakh (n=200)	p
	Male (n=100)		34.90±3.22	25.39±2.88	**<0.001**
ac-ac	**Female (n=100)**		31.43±3.14	26.35±2.91	**<0.001**
		p	**<0.001**	**0.021**	
	Male (n=100)		32.55±3.04	26.92±3.61	**<0.001**
ac-prn (L)	**Female (n=100)**		30.51±2.78	26.75±3.04	**<0.001**
		p	**<0.001**	0.103	
	Male (n=100)		32.51±3.01	27.32±3.74	**<0.001**
ac-prn (R)	**Female (n=100)**		30.53±2.75	26.89±3.08	**<0.001**
		p	**<0.001**	0.377	
	Male (n=100)		27.63±2.74	20.25±2.78	**<0.001**
al'-al'	**Female (n=100)**		25.24±2.62	20.97±2.49	**<0.001**
		p	**<0.001**	0.053	
	Male (n=100)		38.23±3.14	28.69±3.49	**<0.001**
al-al	**Female (n=100)**		34.56±2.89	29.01±3.29	**<0.001**
		p	**<0.001**	0.478	
	Male (n=100)		4.71±0.88	3.86±0.88	**<0.001**
alI-alI (L)	**Female (n=100)**		4.53±0.81	3.74±0.81	**<0.001**
		p	0.134	0.319	
	Male (n=100)		4.79±0.80	3.92±0.82	**<0.001**
alI-alI (R)	**Female (n=100)**		4.61±0.80	3.99±0.69	**<0.001**
		p	0.119	0.574	

L: left, r: right, linear measurements are reported in mm, and angles are in degrees

Table 4. Linear and angular measurements at the nose in Turk and Kazakh students by gender (continued)

Measurement	Gender		Turk (n=200)	Kazakh (n=200)	p
	Male (n=100)		7.16±0.89	5.25±0.78	**<0.001**
c'-c'	**Female (n=100)**		6.46±0.79	5.55±0.81	**0.009**
		p	**<0.001**	**0.008**	
	Male (n=100)		18.21±1.72	15.91±1.76	**<0.001**
mf-mf	**Female (n=100)**		16.98±1.56	18.22±2.16	**<0.001**
		p	**<0.001**	**<0.001**	
	Male (n=100)		52.87±3.73	50.25±5.91	**<0.001**
n-prn	**Female (n=100)**		48.46±4.17	44.30±4.75	**<0.001**
		p	**<0.001**	**<0.001**	
	Male (n=100)		58.40±4.53	56.32±5.91	**<0.001**
n-sn	**Female (n=100)**		53.22±4.39	53.03±4.90	**<0.001**
		p	**<0.001**	**<0.001**	
	Male (n=100)		26.37±2.93	22.63±3.18	**<0.001**
sbal-prn (L)	**Female (n=100)**		24.86±2.40	21.94±2.74	**<0.001**
		p	**<0.001**	0.103	
	Male (n=100)		25.97±2.93	22.97±3.26	**<0.001**
sbal-prn (R)	**Female (n=100)**		24.93±2.40	22.25±2.71	**<0.001**
		p	**<0.001**	0.091	
	Male (n=100)		26.12±3.65	17.63±2.33	**<0.001**
sbal-sbal	**Female (n=100)**		23.15±3.00	17.48±2.39	**<0.001**
		p	**<0.001**	0.650	
	Male (n=100)		11.21±1.62	11.72±1.90	**0.044**
sn-c	**Female (n=100)**		11.04±1.57	11.60±1.94	**0.027**
		p	0.457	0.666	
	Male (n=100)		21.89±2.61	19.17±2.78	**<0.001**
sn-prn	**Female (n=100)**		20.50±2.95	19.42±2.29	**0.001**
		p	**<0.001**	0.487	
	Male (n=100)		82.76±9.20	64.92±5.74	**<0.001**
Wing inclination angle	**Female (n=100)**		80.70±7.39	71.37±6.21	**<0.001**
		p	0.083	**<0.001**	
	Male (n=100)		77.20±5.86	91.36±4.70	**<0.001**
Nasal tip angle	**Female (n=100)**		77.83±5.86	92.55±4.92	**<0.001**
		p	0.452	0.082	
	Male (n=100)		36.33±6.46	29.35±5.11	**<0.001**
Nasofacial angle	**Female (n=100)**		34.42±5.37	27.90±5.06	**<0.001**
		p	**0.024**	**0.046**	
	Male (n=100)		133.58±11.37	145.04±8.15	**<0.001**
Nasofrontal angle	**Female (n=100)**		148.71±7.60	152.70±5.17	**<0.001**
		p	**<0.001**	**<0.001**	
	Male (n=100)		99.35±12.60	109.71±10.85	**<0.001**
Nasolabial angle	**Female (n=100)**		109.16±14.83	110.51±10.63	0.460
		p	**<0.001**	0.598	

L: left, r: right, linear measurements are reported in mm, and angles are in degrees

for establishing standards tailored to the specific characteristics of examined communities. In the current study, anthropometric measurements of the noses of Kazakh Turks and Turkish Turks were conducted to reveal the similarities and differences.

In the present study, the nasal height (n-sn) measured in Turkish males (58.40 mm) was observed to be lower than values reported by Farkas et al. (13) in their study of various ethnic groups, including Iranian (62.6 mm), Bulgarian (61.6 mm), and Portuguese (59.5 mm) males. Additionally, it was found to be higher than ethnic groups, Japanese (56.9 mm), Italian (56.9 mm), Greek (55.5 mm), and Slovenian (56.2 mm) males. In the present study, the nasal height (n-sn) measurement in (56.32 mm) Kazakh males was found to be lower than males from other ethnic groups except Greek and Slovenian males (13).

In the study, the nasal height (n-sn) of a Turkish female was measured as 53.22 mm, while that of a Kazakh female was 53.03 mm. These measurements are similar to both Japanese (53.3 mm) and Han Chinese (53.87 mm) females reported in Farkas et al. (13).

In the present study, the nose length (n-prn) in Turkish males (52.87 mm) which was found to be higher than that of Kazakhs (50.25 mm), was also found higher than Italians with 51.00 mm (3), Chinese with 48.84 mm (8), Han Chinese with 48.43 mm (14), Saudi Arabians with 50.6 mm (15), Nigerians with 47.8 mm (10), and North Americans with 50 mm (16). The nose length (n-prn) in Turkish females (48.46 mm) which was higher than Kazakhs (44.30 mm), was also higher than Italians with 46.46 mm (3), Chinese with 46.68 mm (8), Saudi Arabians with 43.3 mm (15), and North Americans with 44.7 mm (16). However, it exhibited similarity with the Han Chinese at 48.34 mm (14) and Egyptian females at 48.46 mm (17).

Farkas et al. (13) compared nose width (al-al) among different ethnic groups. According to their findings, the highest measurement in males was observed in individuals of Indian descent (42.6 mm), while the lowest measurement was found in Italians (32.1 mm). As for Turkish males in the present study, their nose width (al-al) measurement (38.23 mm) surpassed the measurements of individuals from Azerbaijan (35.7 mm), Greece (35.7 mm), Italy (32.1 mm), Iran (35.3 mm), and Egypt (32.4 mm). However, it was lower than the measurements of individuals from Bulgaria (42.6 mm) and India (43.4 mm). Kazakh males in the present study had the lowest nose width (al-al) measurement (28.69 mm) compared to all these ethnic groups. Among females, the highest measurement belonged to individuals from Singapore (37.2 mm), whereas the lowest was in Egyptian females (29.3 mm). The nose width (al-al) of Turkish females (34.56 mm) in the present study, was higher than the measurements of North Americans (31.4 mm), Italians (29.5 mm), and Egyptians (29.3 mm). However, it was lower than the Singaporean (37.2 mm) and Japanese (37.1 mm) females. Additionally, the nose width (al-al) value of Kazakh females (29.01 mm) was found to be similar to the measurements of Italian (29.5 mm), Slovakian (30.6 mm), and Egyptian (29.3 mm) females (13).

The angle values related to the nose are examined in Table 5, it is generally observed that nasofrontal, nasal tip, and nasolabial angles are higher in females in most ethnic groups, while the nasofacial angle is higher in males. Among males, the nasofacial angle is highest in Saudi Arabians (15) and lowest in Kazakhs. In females, this value is highest in Egyptians (17) and lowest in Kazakhs. The wing inclination angle is higher in Kazakh females compared to Kazakh males in the present study, while it is similar between males and females in Turks and other ethnic groups. In both genders, the wing inclination angle is lower in Kazakhs compared to other ethnic groups.

In males, the lowest value of nasofrontal angle was found in Iranian males (18) and the highest value was found in Chinese (8) males. In females, the highest value was found in Kazakhs, and the lowest value was found in Kenyan females (19). However, this angle was similar between North American (16) and Iranian (18) males. The highest nasolabial angle among males belonged to Kazakh males, while the lowest belonged to Kenyan males (19).

The nasofacial angle values were similar among Turkish in this study, Indian (20), and Iranian (18) males. In females, this value was found to be highest in Kazakhs in the present study, and lowest among Kenyans (19). In males, the nasal tip angle had the lowest value in Turks in the present study, and the highest value in Chinese (8). In females, the lowest value of the nasal tip angle was detected in Turkish females in the present study, and the highest value was detected in Saudi Arabian females (15).

The determination of the anthropometric characteristics of the nose located at the center of the face plays an important

Table 5. Comparison of nasal angle measurements in different ethnic groups

Study	Ethnicity	Nasofrontal angle		Nasofacial angle		Nasal tip angle		Nasolabial angle		Wing inclination angle	
		Male	Female	Male	Female	Male	Female	Male	Female	Male	Female
Present Study	Turkey	133.58	148.71	36.33	34.42	77.20	77.83	99.35	109.16	82.76	80.70
	Kazakhstan	145.04	152.70	29.35	27.90	91.36	92.55	109.71	110.51	64.92	71.37
Sforza et al., 2011 (3)	Italy					93.84	94.99				
Dong et al., 2010 (8)	China	138.19	144.04			94.16	96.19	104.3	103.42		
Li et al., 2014 (14)	China (Han)	132.6	138.7			87.94	90.85	100.9	98.97		
Al-Qattan et al., 2012 (15)	Saudi Arabia	135.9	145.9	41.4	33.3	90.5	97.3	100.4	102.3	92.3	89.3
Choe et al., 2006 (16)	North America		134.3		29.9				104.2		
Mohammed Ali, 2014 (17)	Eygpt	134.97	139.5	39.94	38.79			100.61	102.06	75.43	74.45
Fariaby et al., 2006 (18)	Iran	126	134	36	36			97	98		
Virdi et al., 2019, (19)	Kenya	127.3	127.9					85.5	85.2		
Mehta et al., 2017 (20)	India	135.91	141.18	36.85	35.08			102.53	106.18		

role not only in defining surgical operations and the aesthetic standards of societies but also in the classification of human populations and the identification of ethnic differences. Anthropometric measurements of the nose in different ethnic groups are crucial for nasal surgery because the goal of the surgery is to achieve good long-term functional and aesthetic outcomes. Therefore, clinical data should be supported by quantitative data obtained from anthropometric results (21,22).

CONCLUSION

When nose measurements among ethnic groups are compared, similarities and differences are observed among specific groups. In the parameters measured in the present study, values for males were generally higher than for females based on gender. However, females had higher values in the nasofrontal and nasolabial angles. While the nasolabial angle and n-sn value exhibited similarities in Turkish and Kazakh females, other measurements showed differences between Turkish and Kazakh populations.

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Developing A Mobile Application to Determine the Psychological Wellness of University Students

Üniversite Öğrencilerinin Psikolojik İyilik Halini Belirlemek İçin Bir Mobil Uygulama Geliştirilmesi

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ABSTRACT

Aim: This study aimed to develop a mobile application to assess the psychological well-being of university students.
Material and Methods: Using an innovative and interdisciplinary approach, this study follows a rigorous methodology from September 2022 to June 2023. The development of the mobile application followed a systematic and structured process to ensure functionality, usability, and reliability. Throughout all stages of development, professional support was sought from information technology to ensure the technical robustness, reliability, and effectiveness of the application. The study embraces four developmental stages including needs identification, technical development, intervention design, and promotion. These stages ensure a student-centered approach, while the application itself offers insights into depression, anxiety, stress, relationship violence attitudes, addiction, Internet addiction, sleep quality, and eating disorders.
Results: A unique and all-inclusive mobile application was created to assess and enhance the psychological well-being of university students. With the real-time emotion monitoring feature of the application, students may keep an eye on their present emotional states and develop self-awareness. If long-term negative emotions are detected, the early warning system is activated and implemented. It provides uninterrupted referrals to qualified professionals for immediate response and support in emergency situations and an enhanced feedback mechanism for user complaints and suggestions. It also provides sensitive evaluation and triage processes by creating an anonymous system record to provide instant support, when necessary. The application also includes stress management guidance for students.
Conclusion: This application provides real-time data that offers mental health professionals a comprehensive overview of students' psychological states.
Keywords: Mobile applications; student; health services; undergraduate.

ÖZ

Amaç: Bu çalışmada, üniversite öğrencilerinin psikolojik iyilik halini belirlemek için bir mobil uygulama geliştirilmesi amaçlanmıştır.
Gereç ve Yöntemler: Yenilikçi ve disiplinler arası bir yaklaşıma sahip olan bu çalışma, Eylül 2022'den Haziran 2023'e kadar uzanan titiz bir metodoloji izlemektedir. Mobil uygulamanın geliştirilmesi, işlevselliğini, kullanılabilirliğini ve güvenilirliğini sağlamak için sistematik ve yapılandırılmış bir süreç izlemiştir. Geliştirmenin tüm aşamalarında, uygulamanın teknik sağlamlığını, güvenilirliğini ve etkinliğini sağlamak için bilgi teknolojilerinden profesyonel destek alınmıştır. Çalışma, ihtiyaç belirleme, teknik geliştirme, müdahale tasarımı ve tanıtım aşamalarından oluşan dört gelişim aşamasını kapsamaktadır. Bu aşamalar öğrenci merkezli bir yaklaşım sağlarken, uygulama, depresyon, anksiyete, stres, ilişki şiddeti tutumları, bağımlılık, internet bağımlılığı, uyku kalitesi ve yeme bozukluklarına ilişkin içgörüler sunmaktadır.
Bulgular: Psikolojik iyilik hallerini değerlendirmek ve geliştirmek amacıyla üniversite öğrencilerine özel, kapsamlı bir mobil uygulama geliştirildi. Uygulamanın gerçek zamanlı duygu takibi özelliği ile öğrenciler anlık duygusal durumlarını izleyebilir ve öz farkındalık kazanabilirler. Uzun süreli olumsuz duyguların tespit edilmesi durumunda, erken uyarı sistemi etkinleştirilerek eyleme geçmektedir. Acil durumlarda anında müdahale ve destek için nitelikli profesyonellere kesintisiz yönlendirme ve kullanıcı şikayetleri ve önerileri için geliştirilmiş bir geri bildirim mekanizması sağlamaktadır. Ayrıca gerektiğinde, anında destek sağlamak için anonim sistem kaydı oluşturarak duyarlı bir değerlendirme ve triyaj süreçleri sağlamaktadır. Uygulama öğrencilerin stres yönetimi yönlendirmelerini de içermektedir.
Sonuç: Bu uygulama, ruh sağlığı profesyonelleri için öğrencilerin ruhsal durumuna ilişkin genel bakış sağlayan gerçek zamanlı veri sunmaktadır.
Anahtar kelimeler: Mobil uygulamalar; öğrenci; sağlık hizmetleri; üniversite.

INTRODUCTION

University students face a range of academic, emotional, and economic stressors throughout their lives. Simultaneously, students are tasked with several developmental challenges such as self-discovery, forming close relationships with the opposite sex, making career choices, and gaining independence (1,2). When university students are unable to successfully manage developmental tasks and stress sources, their psychological well-being can be negatively impacted, potentially leading to depression, anxiety, eating disorders, substance abuse disorders, and other mental health issues (3-5).

In this period, the concept of 'psychological well-being,' which has gained importance in preventing mental issues, is defined as a state of wellness in which an individual can cope with the normal stresses of life, use their own abilities, contribute to their community, and work productively and fruitfully. Research shows that individuals with a high level of psychological well-being (flourishing) have better physical health, higher life satisfaction, and psychological resilience; are likely to have positive future expectations; experience more positive emotions; are happier and more optimistic; and suffer less from symptoms of psychological distress such as depression, anxiety, and stress (6-8).

Mental health is paramount in preventing and resolving stress, challenges, and other mental health issues, particularly those experienced by university students. In recent years, there has been increasing interest in employing technology to support the mental well-being of university students, particularly through the development and implementation of mobile applications. Mobile mental health applications enhance accessibility to mental health resources for students, enabling individual progress monitoring and timely interventions (9-11).

Recent years have witnessed a rapid increase in the use of mobile applications and smartphones among the 18-25 age group, as reported by Gökbulut B (12). While specific data on the rate of mobile device usage based on Internet technologies among the young population in Turkey are not available, it is estimated to be high. The interest of youth in mobile technologies has led the mobile application industry to focus on applications that have attracted their attention (13). Moreover, the use of mobile applications in the health sector has rapidly increased in recent years. Applications developed specifically to address mental health issues of individuals have been instrumental in managing stress and anxiety and enhancing psychological well-being (14). Mobile health applications reduce the cost of obtaining professional help and increase accessibility to mental health (15).

The COVID-19 pandemic has exacerbated the need for mental health support among university students by adversely affecting their academic and social lives. This scenario underscores the pivotal role that mobile mental health applications can play in extending support to students during challenging times (15-18).

Contemporary research has aimed to assess the efficacy and usability of mobile mental health applications among university students. These findings illustrate that well-designed applications can assist students in managing stress and bolstering mental health. Students exhibit positive attitudes towards using these applications and have emphasized their potential as a valuable resource (9,11,19).

Despite recognizing the potential of mobile mental health applications, further research is imperative to comprehend their impact on student's mental well-being and effectively integrate them into university support systems. Moreover, the exploration of students' attitudes and behaviors regarding seeking psychological help is crucial, as individual attributes, sociocultural factors, and prior experiences influence this process and the likelihood of accepting help (20-22). Universities must ensure the provision of viable and effective mental health resources to their students and cultivate a positive attitude toward utilizing these resources. This could potentially increase the likelihood of students seeking and accepting help from stressful situations. The mental well-being of university students is a priority, and universities must establish effective support systems to address this (21).

As psychiatric nurses, we endeavored to develop a mobile application that takes responsibility for identifying mental health issues in young individuals and evaluating appropriate treatment and support options. Mobile mental health applications are suitable for monitoring, supporting, and providing timely intervention for students' mental health. However, it is also crucial to assess the effectiveness of these applications and the attitudes of students towards receiving help and to conduct further research on this subject (22).

The aim of this study was to develop a mobile application to determine the psychological well-being of university students. This study explored the use of mobile applications to support university students' mental well-being, their attitudes toward seeking professional help, and the obstacles they encounter. The insights gained about students will aid in the refinement of university support systems and provide more effective solutions to support their mental health. This study aimed to develop a mobile application to assess the psychological well-being of university students and is anticipated to contribute significantly to understanding and supporting the mental health needs of university students on a broader scale.

MATERIAL AND METHODS

This descriptive study involved the development of mobile device applications. The mobile application program was developed at Düzce University, between September 2022 and June 2023. The development of the mobile device application followed a systematic and structured process involving various stages to ensure functionality, usability, and reliability. Throughout all stages of development, professional support was sought from information technology and computer engineering firms to ensure the technical robustness, reliability, and effectiveness of the application. Each stage of the development process was meticulously planned and executed with an emphasis on creating a user-friendly, reliable, and effective mobile application. The involvement of professional information technology and computer engineering support plays a crucial role in refining the technical aspects of the application, contributing to its overall success and efficacy.

The key steps followed during the development of the application are as follows:

Preparation of Mobile Application: At the foundational stage, the core elements, objectives, and scope of the

mobile application were established. In the development of mobile application modules, an extensive literature review was initially conducted focusing on the factors affecting the psychological well-being of university students and related mobile health applications. Subsequently, a roadmap was established to determine the needs of the university students. The project team integrated the data obtained from the literature review with students' needs to create modules through a dynamic process. The details of these stages are given below.

Identification of Student Needs: To identify student needs, a group of 14 community leaders from universities was gathered. Meetings with this team were intended to introduce the mobile application and determine the needs of students. Throughout the process, students' ideas were continuously solicited (via the WhatsApp group). Another method used to identify needs was the evaluation of applications made to the "Psychological Counseling and Guidance Unit" within the university. The reasons for applications by approximately 1000 students who sought assistance from this unit in the last five years were examined, and content analyses were conducted. Decisions regarding the assessment scale to be used in the application were made by considering the analysis results and information obtained from literature reviews related to the subject. At this stage, the application was also accepted for support by "Düzce University Scientific Research Projects" (project number: 2021.16.01.1163), and a special logo was designed for mobile applications. Following the decision of the university senate, the name of the application was determined to be "MODUM".

System Architecture and Software Preparation for Mobile Applications: The overall system architecture is designed to outline the structural framework and interactions within an application. The necessary software preparations were performed to establish a solid base for the functionality and features of the application.

The development of the MODUM Mobile Application Program consists of nine steps.

Step 1: Creation of systematic entry using student numbers
Step 2: Design of the login screen and informative areas, development of login functionalities and other connections
Step 3: Execution of front-end developments, creation of services for database and insert operations
Step 4: Testing of login and content screens
Step 5: Implementation of the notification infrastructure to be included in the application, design of reporting screens
Step 6: Creation of APIs for database connections
Step 7: Design of live monitoring screens, establishment of front-end and back-end API connections
Step 8: Conducting screen tests
Step 9: All tests were completed for mobile applications

Preparation of Mobile Application Infrastructure Components: The essential infrastructure components were prepared to ensure that the underlying elements supporting the application were robust and reliable.

Infrastructure Components: To examine the implemented application from an infrastructure-component perspective, Microsoft SQL was used as the database. NET Core is used for backend development, flutter for mobile devices, and angular for the web interface. The server infrastructure of the university was employed to handle multiple client requests and minimize security vulnerabilities. For media content such as images and videos, Amazon S3 services are preferred for their expertise in security and speed.

System Architecture: The system comprises four main components: API, mobile applications (Android and iOS), web panel, and database. Each domain operates in physically and software-isolated environments. The administrative panel of the software is web-based and written in an angular format. The database relationship (backend) was programmed using Net Core and the software database was written using Microsoft SQL. The software data tab was designed to comply with the relational database architecture. The software's mobile interface was written using Flutter, and the mobile application was operated on iOS version 10+ and Android version 7+ devices.

Development of the Mobile Application Flow Diagram: A comprehensive flow diagram was prepared to visually represent the workflow of the application and identify the interaction points within the application.

Login Screen: Users can enter the system on the login screen by typing the first six digits of their student number, age, and gender, followed by pressing the login button. In addition, the text for the Personal Data Protection Law (in Turkish KVKK) is in the middle of the page (Figure 1). The login screen does not collect any data in the category of 'personal data.' The data collected by the application only include whether the student is under or over 25 years old, their gender, and the faculty information they are registered with. These data are defined as tertiary data and are protected by the university's information technology network. Students not registered with the university or external participants can access the application using the codes of faculty departments associated with Düzce University. Random access is not permitted. After three random attempts, the system was locked.

Mood Diary Screen: This screen displays a total of nine emotions. In addition to the basic emotions found in the literature (23,24), the screen also includes emotions suggested by students based on the test results of the application. The user can select one of the nine emotional states displayed on the screen based on their mood. Upon making this choice, students can see the mood of other students in their department as a percentage below the emoji. The student then receives a motto as feedback related to the chosen emoji. Mottos were categorized according to their emotional expressions. Students can make emotional choices up to six times in 24 hours, once every four hours (Figure 1).

MOD Assessment Screen: Underneath the question "Do you want to feel better physically or mentally?", there is a section on mental and physical health, including the topic of reducing stress management.

Psychological Well-Being Screen: When an area is clicked, scale items related to that field are displayed. Points are accumulated as questions are answered and reverse items are processed. Assessment results can be viewed from the "my results" screen and are also reflected directly on the student's screen (Figure 2). Notifications appear on the screen regarding the scale scores and mean scores, guiding the student.

Stress Management Screen: Sleep aid and stress management sections contain "breathing exercise" and "body scan exercise," which are known to be effective tools for stress management, from Mindfulness applications (Figure 3).

Figure 1. Login screens

Figure 2. Assessment surveys

Figure 3. Stress management screens

MODUM Safety Screen: There is the "Women's Support Application" (in Turkish "KADES") application to share security issues related to the students themselves or others in emergencies. Emergency situations involving students or others were classified and organized into a flowchart.

Support for Friends in Need: Especially the section "if something is happening to a friend" is created to support students who are unreachable due to the inability to ask for help, stigmatization, and lack of awareness. A short survey will identify the emergencies of students, categorize them, and invite them for consultation.

MODUM Suggestions and Complaints Screen: This screen is categorized as on- or off-campus. Student issues are identified using data-mining techniques and conveyed to relevant departments. All the features of the application are shown on the map in Figure 4.

Preparation for Intervention within the Application: A triage system has been established within the application to cater to the support needs that may arise from university students. The system, arranged with yellow, orange, and red codes, plans to meet the student requests accordingly. A mental health professional (psychiatric nurse) plan was created to establish initial contact with the students and direct them toward triage. The details of the student triage are shown in Figure 5.

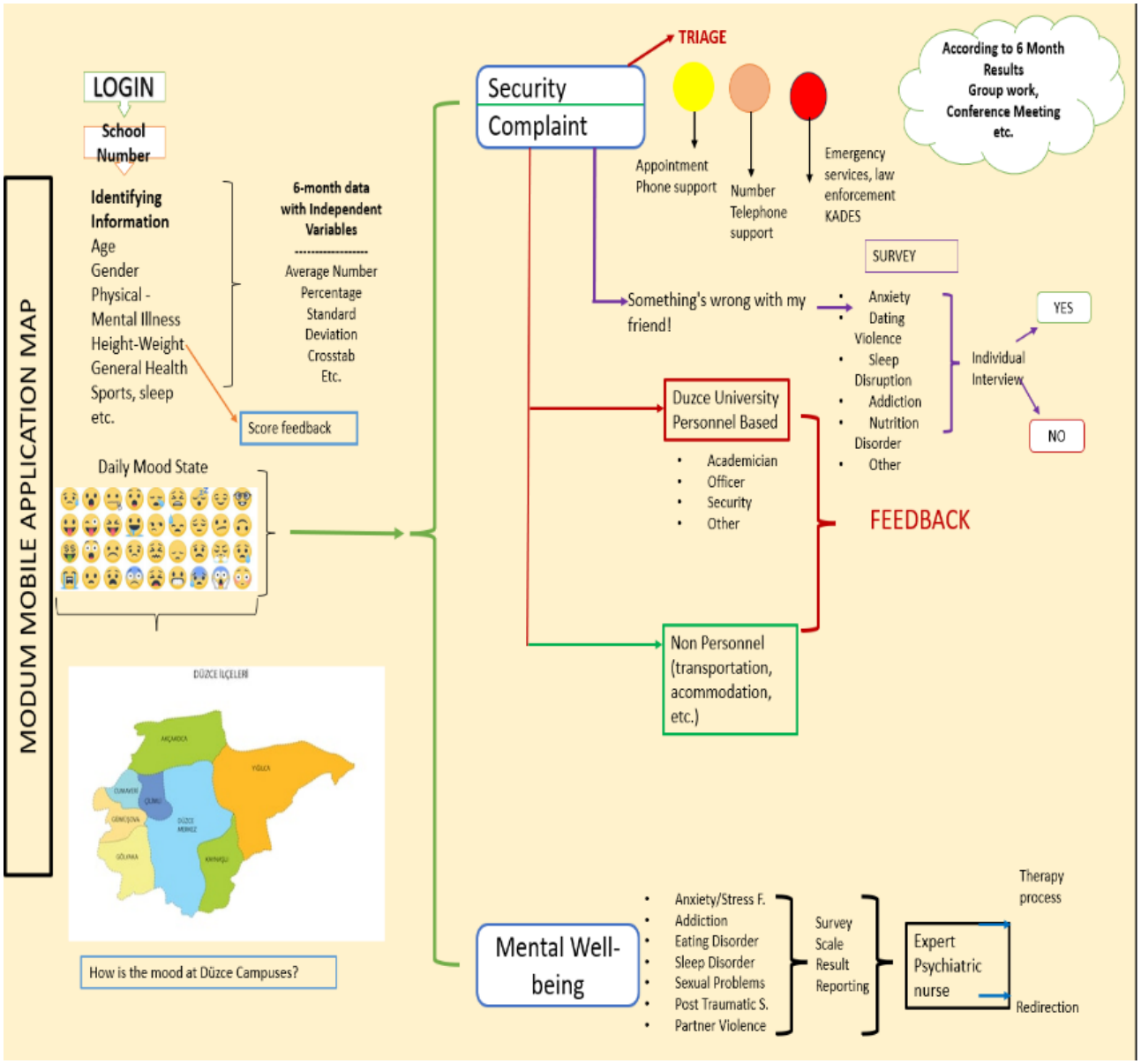

Figure 4. Application map

Testing the Mobile Application: The MODUM application was tested in two stages. In the first stage, the technical/structural features were tested, and in the second stage, the content, flow, and functionality of the algorithms were tested.

Technical/Structural Testing: To test the technical features and design of the application, feedback was sought from the students on various types of phones and usage habits. For this purpose, students from the university's associate degree in computer science programs were invited to participate in this research. A total of 200 students in the computer science department were informed about the MODUM application and research. Of these, 80 volunteers downloaded the MODUM application to their phones and tested it in terms of technical features. Simultaneously, the MODUM researchers used the application for three months, and student feedback was considered through an interactive process. At the end of three months, technical and structural errors and deficiencies were revised to finalize the application.

Testing of Content, Flow, and Algorithms: During this stage, the 'MODUM Application Assessment Form' created by researchers using literature resources was used. For this assessment, students from the university's Faculty of Health Sciences, Nursing Department were sampled. The reason for choosing this faculty was their experience in biopsychosocial health assessment and that they were receiving face-to-face education during the application process (due to online education triggered again by the earthquake in Turkey on February 6, 2023). A total of 120 nursing students in face-to-face education were informed of the study. Of these, 32 students who met the inclusion criteria (actively attending the university face-to-face, with at least six months of study duration, and without any physical/psychological disorders that could impair the use of the application or understanding of the questions) volunteered to participate in the sample.

Preparation of the Mobile Application Introduction: Three videos introducing the application were prepared and filmed in collaboration with the university's communication

and promotion coordination unit. These videos were published on university websites for all students.

Data Collection Instruments

Depression, Anxiety, and Stress Scale (DASS-42): The scale developed by Lovibond was adapted to Turkish by Akın and Çetin (25) with validity-reliability analyses conducted. It comprises 42 items graded on a 4-point Likert scale, covering depression, anxiety, and stress dimensions (26).

Dating Violence Attitude Scale: This scale was validated and tested for reliability by Terzioğlu et al. (27). It comprises 28 items on a 5-point Likert scale, measuring attitudes towards violence in dating relationships.

Addiction Profile Index (API): This scale was developed by Ögel et al. (28) to measure factors related to addiction, and consists of 37 questions on a 4-point Likert Scale.

Young Internet Addiction Test - Short Form: Adapted to Turkish by Kutlu et al. (29) and consisting of 12 items scored on a 5-point Likert scale measuring the level of Internet addiction.

Pittsburgh Sleep Quality Index (PSQI): The scale was developed by Buysse et al. (30), and adapted for Turkish by Agargun et al. (31). It is a self-report scale consisting of 24 questions to evaluate sleep quality and disturbances over a one-month time interval.

Eating Attitude Test: It is a 40-item, 6-point Likert-type scale developed by Garfinkel et al. (32,33) and adapted to Turkish by Savaşır and Erol (34), designed to measure symptoms of anorexia nervosa.

The MODUM Application Assessment Form: This form was prepared by the researchers with 10 questions based on a literature review. It is designed to evaluate users' physiological and psychological states using both open- and close-ended questions and application visuals.

Ethical and Legal Aspects of the Research

For the research, necessary permissions were obtained from the Scientific Research and Publication Ethics Committee of Düzce University (dated 30.09.2021, and numbered 219). All students involved in the research were informed in writing and verbally about the details of the research, and an "Informed Consent Form" was used. Institutional permission was obtained for retrospective evaluations of admissions made to the "Psychological Counseling and Guidance Unit." It was explicitly stated in writing and verbally that the information obtained from the research would not be used anywhere outside the research report, and that individuals could withdraw from the research whenever they wished. Legal advice regarding the protection of personal data for mobile applications was obtained from Düzce University.

The overall system architecture is designed to outline the structural framework and interactions within an application. The necessary software preparations were performed to establish a solid base for the functionality and features of the application.

Study Limitations

Conducting the study at a single center poses a limitation in terms of the generalizability of the research findings. The criterion for the study was that participants had to own and use a smartphone. Another limitation was the anonymity of the application. In this regard, text regarding the Personal Data Protection Law (in Turkish "KVKK") was placed on the application's login screen.

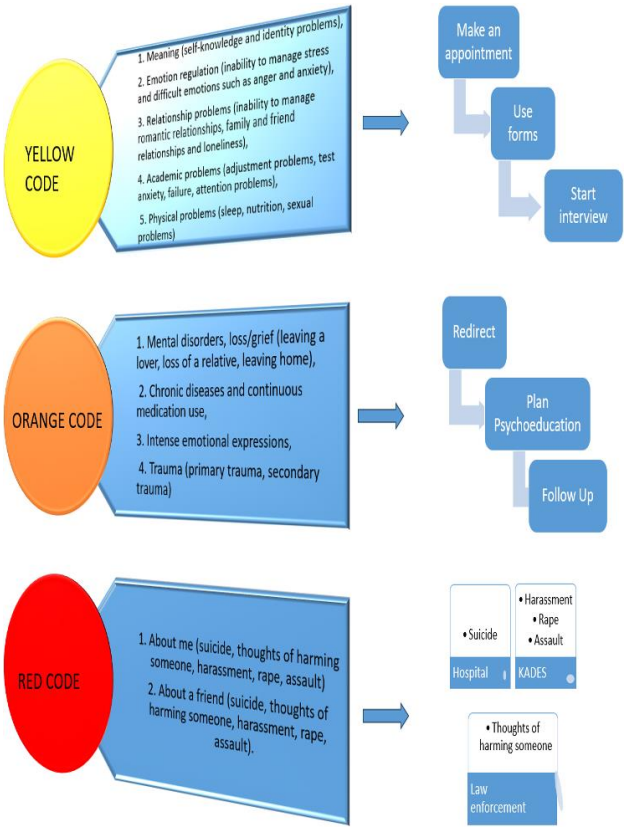

Figure 5. Students' triage

RESULTS

A preliminary assessment of the MODUM application was conducted to elicit users' real-world experiences, development suggestions, and overall evaluations. Development suggestions were presented to students for their opinions, anticipating that they would provide a comprehensive understanding of how the application could be optimized in terms of aesthetics, functionality, user information, and content.

A preliminary assessment of the MODUM application was conducted using the MODUM Application Assessment Form, which was designed to measure user perspectives on various critical aspects of the application. A total of 32 student responses from the university were received for this assessment. Of the students, 96.9% (n=31) liked the MODUM design, 96.9% (n=31) found the application user-friendly and easy to use, 93.8% (n=30) trusted the application's privacy measures, 90.6% (n=29) believed that the application would be beneficial to university students, 96.9% (n=31) were satisfied with the application's speed, 93.8% (n=30) recommended the application to other friends, and 87.5% (n=28) reported the content of the application to be adequate.

Suggestions for application development were presented under the following headings:

Content Enhancement: Suggestions were made to improve the clarity of the content, explicitly stating the purpose of the application and increasing the use of symbols that express emotions.

User Experience: Some students provided feedback on aesthetic and interactive features, such as color harmony, increasing the number of emoji, and interactive notifications.

Information and Transparency: Recommendations were made to provide user information at the initial login, elaborate on privacy details more thoroughly, and offer insights about the application content in the Play Store.
Emotional and Cognitive Feedback: The feelings and thoughts of the participants offer insights into the general acceptance of the application.
Overall Evaluation: Most participants expressed positive sentiments about the application's engaging design, its potential to create emotional awareness, and their perception of professionalism.
Considering these findings, the following steps are recommended for the further development of MODUM applications.

- Conducting detailed user research to understand user needs and expectations better,
- Focusing on the suggestions brought up by participants regarding privacy, content, and user experience,
- Maintaining and enhancing the positive aspects identified by users while making necessary adjustments in areas perceived negatively,
- Supporting the application's continuous improvement by establishing regular feedback collection and evaluation processes.

Our mobile application, designed to assess and support the psychological well-being of university students, was integrated with a series of functionalities to ensure a comprehensive user experience. The results obtained for these functionalities are described in detail below:

DISCUSSION

In recent years, the increased use of mobile health applications among university students has emerged as one of the most exciting developments in the health sector. Analyses in this realm reveal the substantial role of these applications in assessing and improving the mental health of students. These students often face psychological health problems exacerbated by various factors, including academic stress, social pressure, and lack of sleep (35-37). In this context, instant access and intervention provided by mobile health applications are recognized as significant steps in addressing these problems (18,38,39).
Particularly during the COVID-19 pandemic, the isolation and uncertainty experienced have heightened the importance of such applications (40). The economic accessibility of mobile health applications, proven to have similar effectiveness as traditional therapies, is also advantageous for students (11,19,21). Customized applications for students are reportedly more effective than general health applications as they accurately assess and address the specific needs of students. This emphasizes the necessity of designing applications tailored to the target audience rather than generalized ones (22,37). A study by Lee and Jung (14) suggested that mindfulness-based applications such as DeStressify can offer effective alternative support for the mental health of university students. Universities and other institutions could benefit from promoting the use of DeStressify or other Mindfulness-based mobile health applications for students interested in anxiety management or self-guided health support based on mindfulness. In addition to these programs, this study introduced a new application to evaluate the mental and physical health of students, particularly focusing on the context of Turkey.
However, despite these positive prospects, potential problems exist, such as concerns about the protection of personal data and security (39). Developers and healthcare providers must implement necessary security measures to ensure the safe widespread use of such applications. Significant issues and inconsistencies related to privacy in mobile health applications have been observed, and clinicians must be aware of the benefits and risks of mobile health applications and communicate them clearly to patients (41). The integration of artificial intelligence and new technologies can enhance the effectiveness and user-friendliness of mobile health applications (42).
The current study, aimed at developing a mobile application (MODUM) for monitoring and improving the psychological well-being of university students, presents significant findings that align with the global trends observed in mobile health application usage among university students, as well as some unique insights pertinent to the Turkish context.
Studies indicate a general acceptance of mobile application-based interventions among college students for managing stress, anxiety, and depression, emphasizing the effectiveness and proactive role these tools can play in mental health management (1).
The MODUM application's high user satisfaction rates echo findings from studies that found that pharmacy students using mobile health applications reported higher e-health literacy (2). This indicates not only readiness but also a positive perception of mobile health solutions among Turkish students. In a broader study examining Turkish college students' attitudes towards mental health applications, it was observed that while many students were aware of such applications, their usage remained relatively low. Students expressed an interest in applications that provide stress management tools and mood tracking, which aligns with the features offered by the MODUM application (3).
MODUM's feature of real-time emotional tracking is relevant to Lee and Jung's (14) analysis of the DeStressify application, where mindfulness-based applications were effective in reducing anxiety. The capability of MODUM to enable users to monitor their emotional states provides a direct tool for self-awareness and stress management, a critical aspect during challenging times such as the COVID-19 pandemic, as seen in Spain’s increased reliance on mental health applications (4).
The MODUM application focuses on providing content that is not only adequate but also educational, aligning with the need for increased education in the usage of mobile health applications, as highlighted in the study on Istanbul pharmacy students. The feedback on content adequacy (87.5% positive) suggests a well-received approach, yet also points towards an area for continuous improvement.
Concerns regarding the security and privacy of mobile health applications are a common barrier to wider adoption, as noted in studies from Morocco, and broader privacy concerns have been discussed in Turkish studies (5). The MODUM's development process includes stringent measures to protect user data, mirroring the global need for secure mobile health solutions.
The acceptance and integration of mobile health applications such as MODUM into university health

systems is crucial. This study's emphasis on a structured and rigorous development process ensures the reliability and functionality of the applications, which could facilitate their integration into university support systems, thereby enhancing their utility and acceptance among students.

The findings from the MODUM application development and evaluation study not only reinforce the global recognition of mobile applications as viable tools for enhancing mental health among university students but also highlight specific aspects such as real-time monitoring and educational content that are critical for their success. Future research should focus on overcoming barriers related to privacy and security and enhancing the educational components of these applications to ensure they meet the diverse needs of the student population. In addition, continual feedback mechanisms and iterative improvements are crucial for maintaining the relevance and efficacy of these applications in a rapidly evolving digital landscape.

In Turkey, we observed the absence of a mobile application designed to assess and monitor the physical and mental health of university students. Our examinations have revealed that existing mobile applications mainly introduce universities and focus on logistics subjects, but they lack a section to identify the individual needs of students. This study was the first of its kind in Turkey and was designed to address the gap in health development among university students.

CONCLUSION

The results of this study can be grouped as follows:

Innovative Application Development: This research successfully developed a comprehensive and innovative mobile application specifically designed to assess and enhance the psychological well-being of university students, addressing an essential unmet need in higher education institutions.

Real-Time Emotional Tracking: The application uniquely incorporates real-time emotional tracking, allowing students to monitor and gain awareness of their immediate emotional states, activating an early warning system for prolonged negative emotions to prompt acknowledgment and action.

Comprehensive Health Monitoring and Professional Referral: The application facilitated holistic health monitoring, provided students with a detailed review of their mental and physical health statuses, and enabled seamless referrals to qualified professionals for immediate intervention and support in urgent situations.

Data-Driven Approach: A standout feature of the application is its ability to utilize real-time data reporting, offering insights into the mental state of students across multiple campuses and enabling the development of programs specifically tailored to address the diverse needs of the student population proactively.

Enhanced Security and Privacy: While illustrating the transformative potential of mobile health applications in mental healthcare for university students, the study also highlighted the crucial need for advancements in security and privacy to foster the wider adoption and efficacy of such technologies in the context of higher education.

University years are pivotal for both the personal and academic development of young individuals, as preserving their mental and physical health directly affects their academic achievements. However, current technological tools and mobile applications usually focus on logistics needs and overlook students' psychological well-being. A serious deficiency in this domain has been observed in Turkey, and the application developed is expected to fill this gap and contribute to students.

The findings of this study demonstrate that mobile health applications developed to evaluate and support the mental conditions of university students offer unique benefits, but also encounter certain challenges. For future advancements in this field, more extensive research on the efficiency, safety, and user-friendliness of these applications is crucial. One of the most important steps in this field is directing attention to understanding students' specific needs and designing applications to meet these needs. Efforts to overcome security and privacy concerns can facilitate the adoption of this technology by a broader audience. Continuous research and development efforts are crucial to ensure the efficacy and safety of such applications, with real-world data and user experience playing a significant role in making these applications more effective and user-friendly.

Ethics Committee Approval: The study was approved by the Scientific Research and Publication Ethics Committee of Düzce University (30.09.2021, 219).

Conflict of Interest: This manuscript was produced based on the doctoral thesis of Dilek Demirezen, the first author, and all authors declare that there is no conflict of interest.

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Overview of Early Complications in Decompressive Craniectomy

Dekompresif Kraniyektomide Erken Komplikasyonlara Genel Bakış

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ABSTRACT

Aim: The aim of this study was to investigate the prevalence and time of occurrence of complications in patients with seamless duraplasty after reverse question mark incision, and the morbidity and mortality rates after surgery.

Material and Methods: Twenty-four patients admitted with different supratentorial indications and underwent decompressive craniectomy and seamless duraplasty between 2019 and 2023, were retrospectively included in this study. The patient's age, gender, etiological reason at admission, and Glasgow coma score before surgery were recorded. The types of complications, their time of occurrence, their relationships with each other, and the procedures performed were recorded.

Results: The median time for complications during one-month follow-up was 7 (range, 1-28) days. A total of 18 complications were observed in 15 (62.5%) patients. While 7 (46.7%) of 15 patients with complications died within one month of follow-up, 7 (77.8%) of 9 patients without complications died. Although the mortality rate was higher in patients without complications, there was no statistically significant difference between patients with and without complications (p=0.210). The survival rate in the first month was 53.3% in patients with complications and 22.2% in patients without, and the median survival time was 5 days in patients with complications and 8 days in patients without complications (p=0.214).

Conclusion: The onset time and management of the complications is crucial during the first month after decompressive craniectomy which has high mortality and morbidity rates, since the complications can lead to each other, and also these complications can cause serious economic and labor loss.

Keywords: Decompressive craniectomy; complication; early period.

ÖZ

Amaç: Bu çalışmanın amacı dikişsiz duraplasti hastalarında ters soru işareti kesisi sonrası komplikasyon görülme sıklığı ve ortaya çıkma zamanı ile ameliyat sonrası morbidite ve mortalite oranlarının araştırılmasıdır.

Gereç ve Yöntemler: 2019 ve 2023 yılları arasında farklı supratentoryal endikasyonlarla başvuran ve dekompresif kranyektomi ve dikişsiz duraplasti uygulanan 24 hasta geriye dönük olarak bu çalışmaya dahil edildi. Hastaların yaşı, cinsiyeti, başvuru sırasındaki etiyolojik nedeni ve ameliyat öncesi Glasgow koma skoru kaydedildi. Komplikasyonların türleri, oluşma zamanları, birbirleriyle ilişkileri ve yapılan işlemler kaydedildi.

Bulgular: Bir aylık takipte komplikasyona kadar geçen medyan süre 7 (aralık, 1-28) gündü. Hastaların 15'inde (%62,5) toplam 18 komplikasyon görüldü. Komplikasyon gelişen 15 hastanın 7'si (%46,7) bir aylık takip süresi içinde hayatını kaybederken, komplikasyon gelişmeyen 9 hastanın 7'si (%77,8) hayatını kaybetti. Komplikasyon gelişmeyen hastalarda mortalite oranı daha yüksek olmasına rağmen komplikasyon gelişen ve gelişmeyen hastalar arasında istatistiksel olarak anlamlı fark yoktu (p=0,210). İlk ay sağkalım oranı, komplikasyon gelişen hastalarda %53,3 ve gelişmeyen hastalarda %22,2, ortanca sağkalım süresi komplikasyon gelişen hastalarda 5 gün, komplikasyon gelişmeyen hastalarda ise 8 gün idi (p=0,214).

Sonuç: Mortalite ve morbidite oranları yüksek olan dekompresif kranyektomi sonrası ilk bir ay içerisinde komplikasyonların birbirine neden olabilmesi ve aynı zamanda ciddi ekonomik ve iş gücü kaybına yol açması nedeniyle komplikasyonların başlangıç zamanı ve yönetimi oldukça önemlidir.

Anahtar kelimeler: Dekompresif kranyektomi; komplikasyon; erken dönem.

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INTRODUCTION

Decompressive craniectomy (DC) is a surgical method that aims to reduce morbidity and mortality rates in cases with high intracranial pressure that do not respond to medical treatment (1-3). DC was first described by Kocher (4) and Cushing (5,6) and is used in different intracerebral pathologies, especially; it is also used as a last remedy in cases such as traumatic brain injury (TBI), middle cerebral artery (MCA) infarction, acute subdural hematoma (ASDH), acute encephalitis, cerebral toxoplasmosis, subdural empyema and subarachnoid hemorrhage (7-14).

There is no consensus on the application of this surgical method, which is used as a last remedy to control intracranial high pressure in neurosurgery practice. Although different incision types have been described to ensure a large frontotemporoparietal DC (at least 12x15x15 cm) and avoid incision complications, the standard large frontotemporoparietal reverse question mark (RQM) incision continues to be the most used method today (15).

Again, to prevent complications, different procedures are applied, such as sealing the dura in a watertight manner or laying it on the area without performing duraplasty. Watertight closure of the dura has been found in many studies to show no significant difference in preventing cerebrospinal fluid (CSF) leakage and infection compared to rapid closure decompressive craniectomy without duraplasty (16). On the contrary, many studies have reported that watertight duraplasty should not be used in DC because non-watertight duraplasty may shorten the operation time while the possibility of complications remains the same (2,16,17).

Regardless of which method is applied, it is clear that they do not have a significant advantage over each other in terms of complications that may occur. DC is still a rescue surgery with serious and frequent complications. Understanding the type and burden of potential complications, the timeline and the reasons for their occurrence will be key to designing high-quality randomized controlled trials in the future. The aim of this study was to investigate the prevalence and time of occurrence of complications in patients with seamless duraplasty after RQM incision and to examine the possible morbidity and mortality after surgery.

MATERIAL AND METHODS

Twenty-four patients aged 18 and over, who applied to our clinic with different supratentorial indications and underwent DC and seamless duraplasty between 2019 and 2023, were retrospectively included in this study. The patient's age, gender, etiological reason at admission, and Glasgow coma score (GCS) before the surgery were recorded. Ethical approval for the study was obtained from the Non-interventional Health Research Ethics Committee of Düzce University (01.04.2024, 2024/076). All surgical procedures were performed under general anesthesia and within the first 24 hours. All patients underwent imaging with computed tomography (CT) before and after the operation, neurological and physical examinations of the patients were evaluated during daily visits, and cranial CT and magnetic resonance imaging (MRI) were performed when necessary. The types of complications, their time of occurrence, their relationships with each other, and the procedures performed were recorded. DC was performed as described by Gudeman et al (18). In this procedure, after a skin incision starting from the zygoma, approximately 1 cm in front of the tragus, passing approximately 5 cm behind the auricle and extending to the hairline on the same side, the temporalis muscle was rolled antero-inferiorly and a craniectomy extending up to 12 cm in diameter was performed. The craniectomy was extended below the temporal bone and the dura was opened in a curvilinear manner. After the main procedure for the primary cause (such as intracerebral hematoma, empyema, subdural hematoma evacuation), if any, the dura was laid on the area and a drain was placed in the epidural area. The bone flap was placed in the abdomen. The drains used were removed after 3 days.

Statistical Analysis

Statistical analyses were performed with IBM SPSS v.22. The distribution of numerical data was examined with the Shapiro-Wilk test and the homogeneity of variance with the Levene test. One-way analysis of variance or the Kruskal-Wallis test was used for group comparisons, depending on the distribution of the data. Categorical data were analyzed by Pearson chi-square, Fisher's exact, or Fisher-Freeman-Halton test. Kaplan-Meier curves were compared with the log-rank test. Descriptive statistics for numerical variables were reported as mean and standard deviation or median, interquartile range, minimum, and maximum values, depending on the distribution of the data. Categorical data were reported as frequency and percentage. The statistical significance level was considered as 0.05.

RESULTS

The mean age of the patients included in the study was 62.4±20.9 (range, 19-90) years, and 13 (54.2%) of the patients were male and 11 (45.8%) were female. Surgical indications were acute ischemic stroke (AIS) in 8 (33.3%) patients, intracerebral hemorrhage (ICH) in 7 (29.2%) patients, ASDH in 5 (20.8%) patients, and acute epidural hematoma (AEDH) in 4 (16.7%) patients. The median GCS of the patients before the surgery was 6 and ranged from 4 to 12.

The median time for complications during a one-month follow-up was 7 (range, 1-28) days. Complications were observed in 15 (62.5%) of the 24 patients who underwent DC. A total of 18 complications were observed since there were two different complications in one patient and three different complications in another. The two different complications seen in the same patient were hydrocephalus and meningitis, respectively, while the patient who suffered three different complications had external cerebral herniation, wound infection, and hydrocephalus. The frequency of complications and their onset times were shown in Table 1.

During the first month, 14 (58.3%) patients died. GCS was 8 or lower in all patients who died. When examined in terms of GCS, 14 of 18 patients (77.8%) with GCS scores of 8 or lower died, while all 6 patients with GCS scores above 8 were still alive one month later. The mortality rate was statistically significantly higher in those with a GCS of 8 or lower (p=0.002).

While all patients presenting with AIS had a GCS of 8 or less, 4 (80%) patients with ASDH, 5 (71.4%) patients with ICH, and 1 (25%) patient with AEDH had a GCS of 8 or less. The highest rate of patients with a GCS of 8 or less was seen in patients with AIS, and this rate did not differ statistically significantly in ASDH and ICH, while it was significantly lower in the patients with AEDH compared to all other etiologies (p=0.035). No significant difference was detected in terms of age, gender, complications, and one-month mortality rates according to the etiology of the patients (Table 2).

The survival rate in the first month was 12.5% in patients with AIS, 42.9% in ICH, 60% in ASDH, and 75% in acute epidural hematoma (p=0.030, Figure 1).

While 7 (46.7%) of 15 patients with complications died within a one-month follow-up period, 7 (77.8%) of 9 patients without complications died within a month. Although the mortality rate was higher in the patients without complications, there was no statistically significant difference between patients with and without complications (p=0.210).

The survival rate in the first month was 53.3% in patients with complications and 22.2% in patients without complications, and the median survival time was 5 days in patients with complications and 8 days in patients without complications (p=0.214, Figure 2).

DISCUSSION

DC is a surgical method used as a last remedy in cases where medical treatment of high intracranial pressure is inadequate due to different etiological reasons. Although it is claimed that this procedure reduces mortality, it is an indisputable fact that patients face the risk of many different complications after the operation, which will negatively affect their quality of life. Being able to predict the timing of these complications that occur after surgery will provide a significant advantage in managing the process correctly. Complications are divided into two groups, early and late, according to the time of occurrence. Complications seen within one month are classified as early complications and are generally seen during hospitalization (19).

It has been reported in the literature that the general complication rate after DC surgery is around 53.9% (20), and in the present study, complications were observed in 15 (62.5%) of the patients who underwent DC.

The overall prevalence of DC-related CSF leak/fistulas has been shown to be up to 6.3% (21). In our study, the CSF

Table 1. The frequency and onset time of complications

Complication Type (n=18)	n (%)	Time (day)
Cerebrospinal fluid leakage	5 (27,8)	1, 1, 4, 14, 25
Contralateral intracranial hematoma	1 (5,6)	3
Hydrocephalus	2 (11,1)	5, 25
External Cerebral Herniation	2 (11,1)	7, 7
Subdural Hygroma	1 (5,6)	10
Incision Site Infection	2 (11,1)	10, 10
Incision Site Ulseration	3 (16,7)	4, 15, 15
Sinking Skin Flap Syndrome	1 (5,6)	28
Meningitis	1 (5,6)	30
Total	**18**	

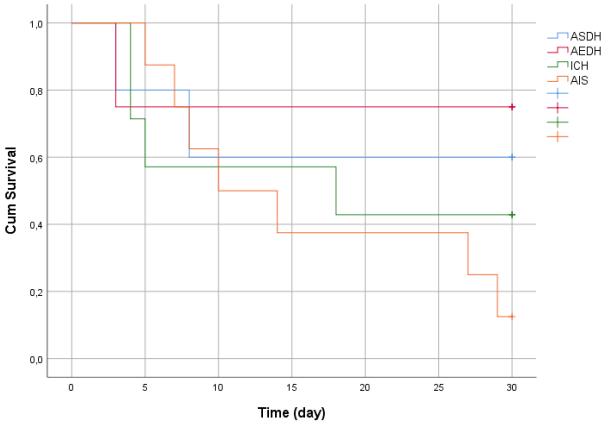

Figure 1. The survival rate in the first month according to the indications

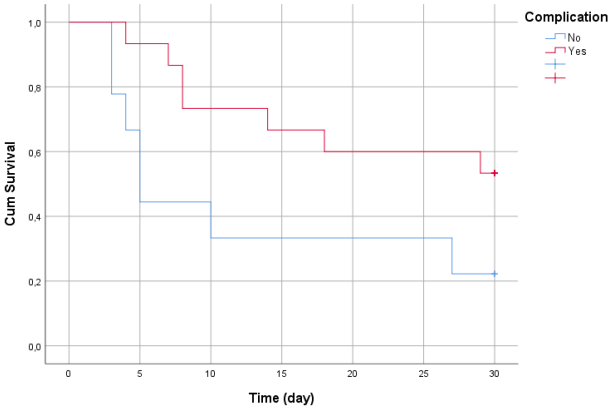

Figure 2. The survival rate in the first month in patients with and without complications

Table 2. Comparison of the demographic and clinical characteristics according to the etiology

	ASDH (n=5)	AEDH (n=4)	ICH (n=7)	AIS (n=8)	p
Age (year)	63.6±29.1	61.0±28.9	64.1±8.8	60.9±22.7	0.990
Gender, n (%)					
Male	3 (60.0)	2 (50.0)	4 (57.1)	4 (50.0)	0.981
Female	2 (40.0)	2 (50.0)	3 (42.9)	4 (50.0)	
GCS	7 (4) [5-10]	10 (5) [6-12]	5 (5) [4-10]	6 (2) [4-8]	0.089
GCS, n (%)					
≤8	4 (80.0)	1 (25.0)	5 (71.4)	8 (100)	**0.035**
>8	1 (20.0)	3 (75.0)	2 (28.6)	0 (0.0)	
Complication, n (%)	3 (60.0)	3 (75.0)	4 (57.1)	5 (62.5)	0.947
One-month mortality, n (%)	2 (40.0)	1 (25.0)	4 (57.1)	7 (87.5)	0.180

ASH: acute subdural hematoma, AEDH: acute epidural hematoma, ICH: intracerebral hemorrhage, AIS: acute ischemic stroke, GCS: Glasgow coma score

leak rate was 27.8%. Although Vieira et al. (2). stated that the risk of CSF leakage does not increase if the arachnoid is intact during the DC procedure, and therefore whether the dura is sutured or not does not cause a significant difference in the frequency of this complication, we think that in our study, the free laying of the dura and high intracranial pressure increased the rate of this complication.

CSF leakage, which is the most common complication we see in patients in whom we performed DC, was observed on days 1, 4, 14, and 25. Ban et al. (20) in their study including 89 patients, reported the average time for CSF leak was 7.0±4.2 days. In all patients with CSF leakage, a solution was achieved with tight dressing and head elevation.

In general, the frequency of contralateral or distant hematoma following DC was found to be 8.6% (21). In this study, this rate was 5.6%. New and expanding hematomas are characteristically reported in the first few days after DC, and the disappearance of the buffering effect after falling ICP is held responsible (20,22). These bleedings may vary as contusion, epidural hematoma, subdural hematoma, and intracerebral hematoma. It has been shown that after DC, contralateral hematoma occurs on average after 2.1 days (22), and ipsilateral hematoma occurs after 1.5 days (20). In our study, in one patient who underwent DC surgery 3 days prior, a brain CT scan was performed after mental status decline. The imaging showed contralateral hematoma. It regressed spontaneously without the need for surgical intervention.

Hydrocephalus

The incidence of hydrocephalus varies between 0.7% and 86%, depending on etiological causes (23). In our study, the prevalence was observed as 11.1%. Although it is generally classified in the late-term complications group, hydrocephalus was detected in two patients on the 5th day and 25th day, respectively in our study. In the patient with hydrocephalus seen on the 25th day, external cerebral herniation and wound ulcerations were observed to have developed sequentially. In the patient who suffered hydrocephalus on the 5th day, after a series of lab tests it was concluded that meningitis had developed. CSF circulation disorders are held responsible for hydrocephalus. We performed ventriculoperitoneal shunt surgery on our patient who developed hydrocephalus on the 25th day. In the latter patient who developed meningitis after hydrocephalus, we first performed medical intervention with antibiotics, after the condition had resolved external ventricular drainage surgery was performed followed by VP shunt surgery.

External Cerebral Herniation

External cerebral herniation was defined by Yang et al. (22) as the protrusion of cerebral tissue more than 1.5 cm from the middle of the DC. Its incidence was found to be 25% in studies. In our study, it was 11.1%. Inadequate craniectomy is held responsible for its etiology. In patients with insufficient craniectomy, the condition becomes worse due to the compression of the venous structures at the bone edges after brain edema (7). While in studies external cerebral herniation was observed within the first 14 days (19), in our case it was observed on the 7th day, consistent with the literature. We determined that the external cerebral herniation in our case was due to inadequate craniectomy, and we enlarged the craniectomy defect in one patient, and a spontaneous regression of hernia was observed one month later in the other patient.

Subdural Hygroma

The pathophysiology of subdural hygroma, the most common CSF circulation disorder, is unclear. Extra-axial collections have been reported to occur after DC in 53% of patients, even if hydrocephalus was controlled (21). In our study, the prevalence was 5.6%. Subdural hygroma was observed an average of 8 days after DC, and it was observed that it prolonged the hospital stay and caused deterioration in the neurological picture (21). In our case, it was seen after 10 days. The condition regressed with a tight dressing.

Incision Site Complications

Incision site complications include ulceration, necrosis, and insufficient wound healing. In one study, the rate was found to be 10%. In our study, wound infection was 11.1% and wound ulceration was 16.7%. The causes of these complications, apart from patient-specific factors, have been blamed on large skin flaps and damage to the temporal artery (21). We observed local wound infections on the 10th day and ulceration on the 4th and 15th days. We treated it with oral antibiotics and wound care.

Meningitis

In our study, meningitis was diagnosed in 1 (5.6%) patient on the 30th day after hydrocephalus, with CSF samples taken after on the basis of clinical observations and laboratory values. Antibiotic treatment was applied.

Sinking Skin Flap Syndrome

This complication is also called trephine syndrome (24). This condition, which includes many cognitive and emotional symptoms, was later defined as sinking skin flap syndrome to also describe focal neurological disorders. The difference between the external environment and intracerebral pressure causes the skin to collapse in the surgical area (25). Although a study has shown that it can occur at any time between 3 days and 7 years, it is stated that it is most common on the 30th day and its incidence is 10% (19). In our study, it was seen on the 28th day and its rate was 5.6%.

In our study, the most common surgical indication was AIS, and since all of them had a GCS below 8, we think that AISs cover an important area in patients who underwent DC. Although complications are seen to be higher in those with a GCS score of 8 and lower in those with a GCS score above 8, no statistically significant difference is observed, and the reason why the mortality rate is 77.8% in those without complications and 46.7% in those with complications can be explained by the shorter lifespan in those with lower GCS.

The main limitations of the study are its single-centered nature, its retrospective character, and its low number of patients, which makes statistical analysis difficult.

CONCLUSION

The fact that complications can be seen at any time from the first day to the 30th day, even after the first month after DC, has high mortality and morbidity rates, and those complications can cause each other, that it causes serious economic and labor loss, is why it is called a last resort salvage surgery and that complications It reveals the time of emergence and the need for management.

Ethics Committee Approval: The study was approved by the Non-interventional Health Research Ethics Committee of Düzce University (01.04.2024, 76).

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Evaluation of YouTube Videos as a Source of Information about Dementia Care

Demans Hastalarının Bakımı Konusunda Bilgi Kaynağı Olarak Youtube Videolarının Değerlendirilmesi

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ABSTRACT

Aim: Digital platforms such as YouTube are popular sources of health-related information. Although there are studies evaluating the quality of different online medical content, studies focusing on the quality of dementia-related content are limited. This study aimed to investigate the quality of YouTube videos related to dementia patient care.
Material and Methods: Using the term "Dementia care" on the YouTube platform, 100 English videos that met the inclusion criteria were identified and analyzed. In addition to video popularity measurements, to evaluate content quality, the global quality scale (GQS), modified DISCERN scale, Journal of the American Medical Association (JAMA) quality scale, and the patient education materials assessment tool for audio/visual materials (PEMAT-A/V) are used.
Results: It was observed that most of the videos were uploaded by non-academic health institutions (36%) and health professionals (23%). When the content of the videos was evaluated, it was determined that general care strategies were the most common content with 52%. Scores indicating high levels of reliability and accuracy were determined on all applied content quality scales. Videos sourced from academic healthcare institutions were found to have the highest scores on content quality scales. In correlation analyses, video metrics such as duration, view ratio, number of comments, and video power index values were positively correlated with content quality scores.
Conclusion: Videos about dementia patient care on YouTube generally exhibit high popularity and content quality. Individuals seeking information about dementia care on online platforms should be directed to videos uploaded by healthcare institutions.
Keywords: Dementia; dementia care; YouTube.

ÖZ

Amaç: YouTube gibi dijital platformlar sağlıkla ilgili bilgiler için popüler kaynaklardır. Farklı çevrimiçi tıbbi içeriklerin kalitesinin değerlendirildiği çalışmalar yapılmış olsa da, demansla ilgili içeriklerin kalitesine odaklanan çalışmalar sınırlıdır. Bu çalışmanın amacı, demanslı hasta bakımıyla ilişkili YouTube videolarının kalitesini değerlendirmektir.
Gereç ve Yöntemler: YouTube platformunda "Dementia care" terimi kullanılarak, dahil etme kriterlerini karşılayan 100 İngilizce video belirlendi ve analiz edildi. Video popülerlik ölçümlerinin yanı sıra, içerik kalitesini değerlendirmek için, küresel kalite ölçeği (global quality scale, GQS), modifiye DISCERN skalası, Journal of the American Medical Association (JAMA) kalite ölçeği ve işitsel/görsel materyaller için hasta eğitim materyalleri değerlendirme aracı (patient education materials evaluation tool for audio/visual, PEMAT-A/V) kullanılmıştır.
Bulgular: Videoların büyük çoğunluğunun akademik olmayan sağlık kuruluşları (%36) ve sağlık profesyonelleri (%23) tarafından yüklendiği görülmüştür. Videoların içeriği değerlendirildiğinde, genel bakım stratejilerinin %52 ile en yaygın içerik olduğu tespit edilmiştir. Uygulanan içerik kalitesi ölçeklerinin tümünde yüksek güvenilirlik ve doğruluk düzeylerine işaret eden skorlar saptanmıştır. Akademik sağlık kurumları kaynaklı videoların, içerik kalitesi ölçeklerinde en yüksek puanlara sahip olduğu görülmüştür. Korelasyon analizlerinde, süre, görüntüleme oranı, yorum sayısı ve video güç indeksi değerleri gibi video metrikleri, içerik kalitesi skorlarıyla pozitif yönde korelasyon göstermiştir.
Sonuç: YouTube platformunda yer alan demanslı hasta bakımıyla ilgili videolar, genel olarak yüksek popülerlik ve içerik kalitesi sergilemektedir. Çevrimiçi platformlarda demans bakımı hakkında bilgi arayan bireylerin, sağlık kuruluşları tarafından yüklenen videolara yönlendirilmeleri uygun olacaktır.
Anahtar kelimeler: Demans; demans bakımı; YouTube.

INTRODUCTION

The prevalence of dementia is increasing as the global population ages. Presently, over 55 million people worldwide are living with dementia, and around 10 million new cases are diagnosed each year. Dementia is recognized as one of the leading causes of disability and dependency among older adults worldwide (1,2). Dementia syndromes, particularly Alzheimer's disease, which accounts for 60-70% of dementia cases, pose numerous practical challenges for patients, families, healthcare providers, and healthcare systems. Following a dementia diagnosis, patients and their families require practical information and guidance to manage the condition effectively. They seek information on various topics, including maintaining daily living activities, ensuring home safety, financial planning, engaging with formal support services and care teams, guardianship, and legal matters (2,3). Patients' relatives and caregivers increasingly utilize digital platforms to gather information on these topics (4).

Addressing these issues effectively can improve disease management and enhance patient, family, and caregiver experience (5,6).

In recent years, the internet and social media platforms have become prevalent resources offering numerous opportunities to access health information, among other topics. Video-sharing platforms are often preferred by users over traditional websites for obtaining health information (7). YouTube, the leading video-sharing platform, ranks as the second most visited website globally, following Google, according to data from November 2023 (https://www.statista.com/statistics/1201889/most-visited-websites-worldwide-unique-visits). In this regard, YouTube is among the most frequently utilized sources for health-related information (7,8-11). Similar to other health topics, YouTube offers a wide range of medical content related to dementia care and support for patients and their families. This content includes information on different aspects of the disease, evaluation of treatment options, and offering psychosocial support (11-16). Additionally, YouTube offers substantial convenience for healthcare professionals and institutions in achieving their objectives, such as reaching their target audience and providing education. However, there are concerns regarding the potential negative impacts of health-related content. The primary issue is the risk of the uncontrolled spread of misleading or false information, which can lead to significant challenges within the healthcare system for both patients and healthcare professionals (7,8). Therefore, it is essential to verify the reliability, accuracy, and quality of the information obtained and ensure access to reliable content. Numerous studies in the literature have been conducted for this purpose, presenting scales and methods to evaluate the quality of medical content on online platforms (8,9,11,17-22). While some of these studies concentrate on dementia-related content, none specifically examine videos related to dementia care (12-16,20).

This study aimed to assess and evaluate the reliability, accuracy, understandability, applicability, and popularity of dementia care-related videos on YouTube, focusing specifically on their suitability as a source of information for patients seeking such content.

MATERIAL AND METHODS

Since the study did not involve human subjects, approval from a clinical research ethics committee was not required. This decision is consistent with practices observed in similar previous studies. In determining our methods, we adhered to recommendations from previous studies and literature reviews that evaluated the quality of medical content on online platforms (11,19,22).

Video Search

The video search was conducted on January 10, 2024, using the keyword 'dementia care' on the YouTube platform. To ensure unbiased results, all cookies and search history were cleared. To replicate the experience of an ordinary user, the default selection was set to "relevance-based ranking." Given that research indicates individuals typically explore only the initial search results, approximately 60-200 videos, our study focused on analyzing the top 100 most relevant videos. We included only English-language videos and excluded duplicates, videos shorter than 60 seconds or longer than 60 minutes, scientific meeting recordings, medical lectures, videos with audio issues, and irrelevant content as stated in previous literature (9,11). URLs for the 100 videos meeting the inclusion criteria were saved for further analysis. Two neurologists independently reviewed all videos, and any differing evaluations were re-examined and finalized.

Video Analytics

Information such as the title, country of origin, video source, days since publication, image quality, video duration (in seconds), and total number of views, comments, likes, and dislikes up to the search date were recorded. The video power index (VPI), which measures the popularity and impact of video content, was computed using the formula VPI= (like ratio × view ratio) / 100. The view ratio was calculated by dividing the number of views by the number of days since publication (view ratio= total views / days since publication). The like ratio was calculated as like ratio= (number of likes × 100) / (number of likes + number of dislikes). To evaluate the quality of video content, the global quality scale (GQS), modified DISCERN score, the Journal of the American Medical Association (JAMA) benchmark score, and patient education materials assessment tool audio/visual (PEMAT-A/V) were utilized (11,19,23,24).

The global quality scale (GQS) is a widely used scale designed to assess the overall quality of content on a spectrum from poor to excellent. This five-point Likert scale considers key elements such as content flow, information quality, and ease of use. A higher score on the scale indicates better quality and utility. Scores of 1 or 2 suggest low educational quality, 3 indicate intermediate quality, while scores of 4 or 5 indicate high educational quality (11,19,24).

The modified DISCERN tool consists of five questions that assess content for its reliability, clarity, and impartiality. Each question receives a score of either 1 or 0, indicating whether the content meets the established criteria. The total score from these questions determines the overall quality, with higher scores suggesting increased reliability and less bias in the information provided (11,19,24).

JAMA benchmark criteria assess the quality of online health information based on authorship, accurate citation

of sources, currency of information, and disclosure of conflicts of interest. Each criterion earns one point, with a maximum score of four points indicating the highest level of reliability and accuracy (11,19,24,25).

The PEMAT-A/V assesses the quality and clarity of patient education materials, including videos and multimedia presentations. Its goal is to ensure that health information is communicated effectively to patients in a clear and actionable manner, using straightforward language. The assessment consists of 12 items for the understandability domain and five items for the actionability domain. The overall score is reported as a percentage (26).

Statistical Analyses

IBM SPSS v.20 (Armonk, NY: IBM Corp. Released 2011) package program was used for statistical analyses. The distribution of normality was assessed by using the Shapiro-Wilk test. Descriptive statistics regarding the numeric data were presented as mean±standard deviation and median, minimum-maximum. Comparisons of video quality scores among different publishers and video types were performed by the Kruskal-Wallis test. Correlations between quality scores and video analytics were evaluated via Spearman's correlation test. A two-tailed p-value of <0.05 was considered statistically significant.

RESULTS

We watched the first 162 videos from the search results and selected 100 videos that met the inclusion criteria. The total duration of the 100 videos was approximately 703 minutes (around 42.232 seconds), with a median duration of 272 (range, 65-2024) seconds. The total number of views was 2 982 054, with a median of 13879 views. Upon analyzing the country of origin, most (80%, n=80) of the videos were from the United States of America. Videos from the United Kingdom accounted for 11% (n=11), and 9% (n=9) were from other countries. Regarding video sources, non-academic healthcare systems contributed the most content with 36 (36%) videos, followed by healthcare professionals with 23 (23%) videos, academic health organizations (where authors were affiliated with a university or research group) with 22 (22%) videos, and TV/educational websites with 19 (19%) videos. Of the videos, 90 (90%) featured high-definition (≥720p) image quality. The others were in standard definition (480p) with 6 (6%) and low definition (≤360p) with 4 (4%) videos. Regarding the content of the videos, the most prevalent topic was general care strategies featured in 52% (n=52) of the videos. Behavioral problems were addressed in 21% (n=21) of the videos, while 18% (n=18) focused on care centers, and 9% (n=9) discussed social and financial support systems. The median GQS score, which assesses the educational quality of the videos, was 4 (range, 1-5), indicating high quality. The median score on the modified DISCERN scale was 4 (range, 2-4), suggesting high reliability, and the median JAMA benchmark score of the videos was 4 (range, 1-5), indicating high quality. The median PEMAT-A/V scores were 80% (range, 38-100) for understandability and 66% (range, 0-100) for actionability. Video descriptive features and analytics were summarized in Table 1.

We found that VPI, which measures the popularity and impact of video content, varied by video source. Videos from academic sources had statistically significantly higher VPI scores compared to those from non-academic and TV/educational websites ($p<0.001$, and $p=0.023$, respectively). Furthermore, videos sourced from healthcare professionals had significantly higher VPI scores than those from non-academic sources ($p=0.008$).

In evaluating content quality by the source of videos, we observed differences in content quality scales (Table 2). Videos from academic health organizations had higher GQS scores compared to those from non-academic health organizations and TV/educational websites ($p=0.001$, and $p=0.005$, respectively). Modified DISCERN scores were significantly higher in videos sourced from academic health organizations than in those from non-academic health organizations ($p=0.008$). When comparing video sources in terms of JAMA scores, videos from academic health organizations had significantly higher scores than those from TV/educational websites ($p=0.045$). For PEMAT A/V understandability scores, videos from healthcare professionals scored significantly higher than those from TV/educational websites and non-academic health organizations ($p=0.025$, and $p=0.010$, respectively). Differences were also observed in PEMAT A/V actionability scores across video sources. Videos from academic health organizations had significantly higher scores than those from non-academic health organizations and TV/educational websites (both $p<0.001$). Additionally, videos from healthcare professionals had significantly higher PEMAT A/V actionability scores than those from non-academic health organizations ($p=0.013$).

Correlation analyses revealed positive correlations between video analytics, such as video duration, view ratio, number of comments, VPI, and content quality scales, including GQS, modified DISCERN, JAMA, and PEMAT A/V scores (Table 3).

DISCUSSION

In this study, we assessed the quality and usefulness of YouTube videos as sources of information on dementia care, focusing on the 100 most relevant videos. Our findings indicate that these videos generally exhibit high content quality and reliability scores when evaluated using the GQS, DISCERN, JAMA, and PEMAT A/V scales. Furthermore, we observed significant variations in content quality based on the source of the videos. Videos from academic health institutions consistently received the highest scores across the VPI, GQS, modified DISCERN, JAMA, and PEMAT A/V assessment tools. Correlation analyses revealed that video analytics metrics, such as video duration, view ratio, number of comments, and VPI values, were positively correlated with accuracy and reliability in the content quality scales.

To the best of our knowledge, this study is the first to specifically examine the utility of online platforms as resources for dementia care information. However, there are some studies in the literature that evaluate online content discussing dementia.

For instance, Lam and Woo (16) found that YouTube effectively adapted educational videos on dementia for the elderly over three years, demonstrating its value in reaching diverse age groups. Similarly, YouTube has been identified as an increasingly popular platform for delivering culturally sensitive dementia education to Chinese

Americans (15). Another study comparing YouTube to talk-based educational workshops on dementia highlighted YouTube's utility in providing dementia-related information to Chinese Americans (14). In these three studies, analyses were conducted only on video metrics, and the lack of use of content quality assessment scales limits the reliability of the results. Despite these insights, these studies lacked content quality assessments.

Table 1. Video descriptive and analytics

	Mean±SD	Median	IQR	Min-Max
Duration (second)	422.32±41.95	272	167-513.25	65-2024
Number of views	108715.29±31096.43	13879	3577-74797	22-2313299
Time since publication (day)	2473.72±468.07	2064.5	966.5-3044	1-45301
Number of likes	1516.75±424.05	229.5	20.75-977.5	1-24444
Academic health organization	1897.36±3250.10	1150	78-1917	13-15084
Non-academic healthcare systems	984.33±4059.05	88	11-457	1-24444
Healthcare professional	1931.43±4291.74	568	291-988	8-15843
TV/educational website	1582.84±5573.39	87	8-301	1-24443
Number of dislikes	54.67±19.38	3	0-17	0-1254
Number of comments	90.64±26.77	10.5	0-68.25	0-1496
View ratio	46.96±10.68	14.32	2.38-45.13	0.1-816.84
Like ratio	97.34±0.76	98.68	96.79-100	25-100
VPI	45.53±10.22	13.98	2.37-43.91	0.09-776.98
GQS	3.94±0.09	4	3-5	1-5
Modified DISCERN	3.44±0.06	4	3-4	2-4
JAMA	3.68±0.06	4	3-4	1-5
PEMAT A/V 1	72.04±1.66	80	60-80	38-100
PEMAT A/V 2	56.04±2.96	66	33-66	0-100

VPI: video power index, GQS: global quality scale, JAMA: Journal of the American Medical Association, PEMAT-A/V: patient education materials assessment tool audio/visual, 1: understandability, 2: actionability, SD: standard deviation, IQR: interquartile range (25^{th}-75^{th} percentile)

Table 2. Analyses of content quality by video sources

	Academic Health Organization (AC)	Non-Academic Healthcare Systems (Non-AC)	Healthcare Professional (HP)	TV/Educational Website (TV)	p
	Mean±SD Median (IQR) [min-max]	Mean±SD Median (IQR) [min-max]	Mean±SD Median (IQR) [min-max]	Mean±SD Median (IQR) [min-max]	
GQS	4.55±0.15 5 (4-5) [3-5]	3.64±0.13 4 (3-4) [2-5]	4.13±0.17 4 (4-5) [2-5]	3.58±0.23 4 (3-4) [1-5]	**<0.001**
DISCERN	3.77±0.11 4 (4-4) [2-4]	3.22±0.11 3 (3-4) [2-4]	3.61±0.13 4 (3-4) [2-4]	3.26±0.16 3 (3-4) [2-4]	**0.004**
JAMA	3.91±0.06 4 (4-4) [3-4]	3.64±0.11 4 (3-4) [1-4]	3.83±0.14 4 (3-4) [2-5]	3.32±0.20 4 (3-4) [1-4]	**0.042**
PEMAT A/V 1	78.41±2.40 80 (80-80) [50-100]	67.92±2.68 73 (55-80) [40-100]	78.78±3.33 80 (75-90) [40-100]	64.32±4.34 70 (40-80) [38-90]	**0.001**
PEMAT A/V 2	82.38±5.36 100 (66-100) [33-100]	40.48±4.26 33 (33-66) [0-100]	63.26±4.15 66 (66-66) [33-100]	41.25±5.63 33 (33-66) [0-66]	**<0.001**
VPI	81.47±25.12 54.3 (7.9-90.6) [1.9-521.2]	14.31±3.41 4.8 (1.3-15.8) [0-79.1]	50.09±14.35 27.5 (13.2-58.6) [1-263.7]	57.52±40.40 6.6 (0.7-28.6) [0.1-776.9]	**<0.001**

GQS: global quality scale, JAMA: Journal of the American Medical Association, PEMAT-A/V: patient education materials assessment tool audio/visual, 1: understandability, 2: actionability, VPI: video power index, SD: standard deviation, IQR: interquartile range (25^{th}-75^{th} percentile), post hoc test results of groups; GQS: AC vs Non-AC: p=0.001, AC vs TV: p=0.005; Modified DISCERN: AC vs Non-AC: p=0.008; JAMA: AC vs TV: p=0.045; PEMAT A/V 1: Non-AC vs HP: p=0.010, HP vs TV: p=0.025; PEMAT A/V 2: AC vs Non-AC: p<0.001, AC vs TV: p<0.001, Non-AC vs HP: p=0.013; VPI: AC vs Non-AC: p<0.001, AC vs TV: p=0.023, Non-AC vs HP: p=0.008

Table 3. Correlation coefficients between content quality scores and video analytics

	GQS		DISCERN		JAMA		PEMAT-A/V 1		PEMAT-A/V 2	
	r_s	p	r_s	p	r_s	p	r_s	p	r_s	p
VPI	0.430	**<0.001**	0.309	**0.002**	0.269	**0.007**	0.413	**<0.001**	0.535	**<0.001**
Video duration	0.399	**<0.001**	0.392	**<0.001**	0.448	**<0.001**	0.428	**<0.001**	0.292	**0.005**
View ratio	0.434	**<0.001**	0.315	**0.001**	0.272	**0.006**	0.419	**<0.001**	0.536	**<0.001**
Number of comments	0.480	**<0.001**	0.475	**<0.001**	0.421	**<0.001**	0.520	**<0.001**	0.624	**<0.001**
Image quality	-0.154	0.126	-0.139	0.167	0.041	0.686	-0.177	0.078	-0.153	0.148

GQS: global quality scale, JAMA: Journal of the American Medical Association, PEMAT-A/V: patient education materials assessment tool audio/visual, 1: understandability, 2: actionability, VPI: video power index, r_s: Spearman's rho

Tang et al. (27) analyzed YouTube video content related to Alzheimer's disease, considering video metrics, content, audience participation, and speaker features. However, they did not assess content quality.

Recent research by Bizpınar et al. (12) evaluated YouTube videos as a source of information on mild cognitive impairment (MCI), revealing that 96% of the videos fell into the useful/very useful category based on content quality scales. Similarly, a study on informational videos about Alzheimer's disease found that English-language videos generally scored high on content quality scales (20). These findings align with our study's results, which also utilized similar quality scales to evaluate the content quality of dementia care videos. Notably, our study observed a higher ratio of videos with useful content quality compared to studies examining videos on various medical topics (18,28-31). The high content quality of dementia care videos in our study can be attributed to their predominantly healthcare professional and academic center origins. Existing literature supports the notion that videos involving healthcare professionals tend to meet higher standards of quality and reliability (7,12,24,32).

Our results regarding the high content quality of dementia care-related videos highlight the potential of YouTube as a useful and adequate information acquisition tool for patients and their relatives.

In our study, we found a positive correlation between video analytics —including video duration, view ratio, number of comments, and VPI— and content quality scale scores. This aligns with findings from other studies (2,27,32,33). While our findings suggest that viewers tend to select videos with higher educational and content quality regarding dementia care, it's important to note that video popularity doesn't always equate to video reliability or quality. Metrics like the GQS, modified DISCERN, JAMA, and PEMAT A/V scores assess specific content quality elements such as accuracy, reliability, understandability, and actionability. In contrast, VPI reflects the perceived value of the video content. Supporting our view, some studies on medical content have indicated that videos popular among viewers may lack content quality (7,28,30,34). We recommend creating a video format that takes into account the standards set by content quality scales to increase the view ratio of informative content about dementia by the target audience.

Online platforms, particularly video-sharing sites like YouTube, have created extensive avenues for patients and their families to access information about various aspects of diseases, evaluate treatment options, and receive psychosocial support (22,24). However, the uncontrolled nature of the sources and content on these platforms can lead to inaccuracies and unreliability, potentially negating the positive effects and misguiding patients and their families (7,8,24). Therefore, monitoring the quality and reliability of health-related content is crucial. Standardizing these evaluations can be achieved using appropriate content quality assessment scales. The most commonly utilized scales for this purpose in the literature include GQS, Modified DISCERN, and JAMA (7,8,24). We also used the PEMAT A/V scale in addition to other scales. Despite the increasing availability and use of audiovisual educational materials such as videos, scales specifically developed to evaluate these materials are limited. PEMAT A/V is superior to other quality assessment tools in its ability to reliably evaluate audiovisual materials. PEMAT is also the first tool to measure actionability, an increasingly emphasized goal of patient education materials. The use of PEMAT A/V is an important advantage, therefore increasing the reliability of the results of our study (26). It is worth noting that the actionability scores of the videos analyzed in our study were relatively lower compared to the understandability scores. Developing video content with enhanced actionability will further elevate the educational quality of videos related to dementia care.

Our study has several limitations that warrant consideration. Firstly, we focused only on the videos in English-language, which may limit the applicability of our findings to non-English-speaking audiences. Secondly, relying on a single keyword for video selection, although aimed at identifying the most relevant videos, could be viewed as a limiting factor. Lastly, our focus solely on videos from YouTube, excluding content from other websites or social media platforms, may not capture the full spectrum of available information on dementia care across online platforms.

CONCLUSION

This study is the first to specifically analyze YouTube videos focusing on dementia care, highlighting the platform's potential as a valuable and accurate resource for the public seeking information on dementia patient care. Given the ease of accessing healthcare information online and the challenges physicians face in controlling misinformation, educational videos on platforms like YouTube must be uploaded by academics and healthcare professionals to ensure the dissemination of reliable content. Also, to enhance viewership and educational quality, we recommend creating video formats that adhere to established content quality standards. Future research should focus on identifying gaps in the realm of online healthcare education materials and on customizing content to effectively address the specific needs of the target audience.

Ethics Committee Approval: Since our study was not an experimental study including human or animal subject, ethics committee approval was not required.

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Delusional Pregnancy in a Patient with Epilepsy: A Case Report

Epilepsi Tanılı Hastada Gebelik Sanrısı: Bir Olgu Sunumu

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ABSTRACT

Interictal psychosis is a psychotic symptom that is not temporally related to epileptic seizures. Pregnancy delusion is defined as a person's fixed belief that she is pregnant despite objective evidence that she is not pregnant. In this case report, pregnancy delusion was described in a patient with epilepsy. A 31-year-old woman with epilepsy was admitted to a psychiatric ward. The patient, whose pregnancy test results were never positive, believed that she was pregnant. It was learned that her identical twin had experienced reproductive-sexuality-themed psychotic symptoms 10 years ago. The patient was hospitalized for three weeks and discharged in remission with paliperidone 6 mg/day and biperiden 2 mg/day. Caution should be exercised when using antipsychotics because of their epileptogenic effects. Pregnancy delusion in epilepsy is rare. In addition to this rare condition, it is noteworthy that reproductive-sexual delusions were reported in the patient's twin brother who was diagnosed with epilepsy.
Keywords: Pseudocyesis; epilepsy; psychosis.

ÖZ

İnteriktal psikoz, epileptik nöbetlerle zamansal olarak ilişkili olmayan psikotik bir semptomdur. Gebelik sanrısı, bir kişinin hamile olmadığına dair nesnel kanıtlara rağmen hamile olduğuna dair sabit inancı olarak tanımlanır. Bu vaka raporunda, epilepsili bir hastada gebelik sanrısı tanımlanmıştır. Otuz bir yaşında epilepsi hastası bir kadın psikiyatri servisine yatırılmıştır. Gebelik test sonuçları hiçbir zaman pozitif çıkmayan hasta gebe olduğuna inanıyordu. Hastanın tek yumurta ikizinin 10 yıl önce üreme-cinsellik temalı psikotik belirtiler yaşadığı öğrenildi. Üç hafta hastanede yatan hasta paliperidon 6 mg/gün ve biperiden 2 mg/gün tedavisiyle remisyonla taburcu edilmiştir. Epileptojenik etkileri nedeniyle antipsikotik kullanırken dikkatli olunmalıdır. Epilepside gebelik sanrısı nadirdir. Bu nadir duruma ek olarak, hastanın epilepsi tanısı almış ikiz kardeşinde de üreme-cinsel sanrıların bildirilmiş olması dikkat çekicidir.
Anahtar kelimeler: Yalancı gebelik; epilepsi; psikoz.

INTRODUCTION

Epilepsy stands as one of the most common chronic neurological diseases worldwide, with a reported prevalence of 0.4-1% (1). Psychiatric disorders frequently accompany epilepsy, with studies indicating that 39-54.1% of diagnosed patients exhibit such comorbidities (2). A systematic review revealed that around 6% of individuals diagnosed with epilepsy -eight times more than the general population- experience psychotic disorders (3).

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Factors such as the onset of epilepsy before the age of ten and temporal lobe origin increase the risk of developing psychosis. Additionally, there is a suggestion that controlling seizures and the use of antiepileptic drugs may heighten the risk of psychosis. In this context, the concept of 'forced normalization,' a significant phenomenon in the relationship between psychiatric disorders and epilepsy, deserves attention (4). Two main hypotheses attempt to explain the relationship between epilepsy and psychosis. The first suggests that recurrent epileptic seizures predispose individuals to psychosis due to their neurotoxic effect, while the second posits that epilepsy and psychosis result from common neurodevelopmental disorders or nonspecific diffuse brain damage (5). Supporting the second hypothesis, neuropathological, neuroimaging, and genetic findings indicate similarities in structural brain abnormalities and genetic irregularities between patients with schizophrenia and epilepsy (3).

Psychotic symptoms in epilepsy patients are categorized as ictal, post-ictal, and interictal. Interictal psychosis, not associated with seizures, generally exhibits a clinical appearance similar to schizophrenia (2). Unlike schizophrenia, interictal psychosis presents more prominent positive symptoms, with less impairment in cognitive functions and overall functionality (6).

Pregnancy delusion, classified as a somatic delusional disorder within the schizophrenia spectrum and other psychotic disorders in the Diagnostic and Statistical Manual of Mental Disorders-5 (DSM-5), involves a fixed belief in pregnancy despite clear objective evidence to the contrary. Unlike pseudocyesis, pregnancy delusion lacks physical symptoms of pregnancy (7,8). The etiology of pregnancy delusion and pseudocyesis involves various biological, social, and psychological factors. Both conditions are rare, with limited literature available on their occurrence in patients diagnosed with epilepsy (8). This case report aimed to contribute to the existing literature by discussing the interictal psychosis observed in a patient diagnosed with epilepsy, emphasizing the central theme of pregnancy delusion.

CASE REPORT

A 31-year-old female patient, a high school graduate, and housewife, second among five siblings, and an identical twin, has been evaluated for compulsory hospitalization at the psychiatry outpatient clinic, accompanied by her father. Her husband, from whom she has been separated for two months, applied to the court, citing the patient's psychiatric symptoms. The court issued a 'decision to hospitalize the patient in the psychiatric ward.' During the interview, accusatory statements by both the patient and her father against her husband were prominent. The patient claimed her husband sought hospitalization to facilitate divorce, denying any psychiatric illness. She also disclosed a terminated pregnancy due to violence from her husband five months ago. Medical records revealed a previous diagnosis of bipolar disorder, but the patient hadn't adhered to the recommended treatment.

Further examination of medical records revealed consistently negative human chorionic gonadotropin (hCG) values despite frequent pregnancy test visits. The family physician noted the patient's insistence on blood tests, doubting negative results. The patient claimed to have seen the gestational sac in an ultrasound but believed doctors were concealing it.

In her medical history, the patient had been treated for focal epileptic seizures since childhood, with the last seizure occurring two years ago. Currently on lacosamide 150 mg 2*1, the patient's last psychiatric treatment, olanzapine 2.5 mg, was discontinued due to sleepiness. Compulsory hospitalization led to her admission for organized treatment. Routine blood tests, brain magnetic resonance imaging, and electroencephalography were normal.

The patient's parents, both teachers, had no known psychiatric diagnosis but shared their daughter's pregnancy delusions, asserting her lack of psychiatric illness. The patient's identical twin, also diagnosed with epilepsy, had been hospitalized in a psychiatric ward a decade ago. Born prematurely, the twin experienced the first epileptic seizure at 55 days and exhibited psychiatric symptoms ten years ago. Despite admission to psychiatry, she left the clinic prematurely at her family's request without completing treatment.

Mental State Examination

The individual appeared to be her stated age, appropriately dressed for her sociocultural level, displayed good self-care, was slightly overweight, maintained eye contact, responded to questions purposefully, and exhibited a normal speech rate and amount. She presented a defensive attitude, affective irritability, and a dysphoric mood. Consciousness was clear, and she demonstrated orientation, and cooperation, with no psychopathological findings in perception. Her intelligence level was clinically normal, abstract thinking ability was intact, but there was an impairment in her ability to evaluate reality. The content of her thoughts included delusions of seeing evil in her husband and a delusion of pregnancy. Psychomotor agitation was observed.

Clinical Course

Hospitalized with a DSM-5 diagnosis of delusional disorder, the patient actively participated in clinic and garden activities. Psychometric evaluations indicated scores of 17 points on the young mania rating scale (YMRS), 22 points on the brief psychiatric rating scale (BPRS), 21 points on the scale for the assessment of positive symptoms (SAPS), and 2 points on the scale for the assessment of negative symptoms (SANS).

In interviews, accusatory and suspicious thoughts towards her husband were prominent. She reported frequent visits to the gynecology outpatient clinic, claiming to have seen a gestational sac on ultrasonography, contrary to physicians' findings. Risperidone 1 mg/day treatment was initiated and gradually increased. Considering the patient's epilepsy diagnosis, a consultation with the neurology unit recommended continuing the current epilepsy treatment (lacosamide 150 mg 2*1).

On the third day, the patient reported body rashes and refused medication, though no dermatologic lesion was found on examination. Non-compliant attitudes towards risperidone were noted in the patient and her parents, leading to a decision to reorganize treatment. Considering prolonged-release formulations for better compliance, paliperidone 3 mg/day was initiated. The patient remained compliant, exhibited no issues with peers, and expressed a desire to study medicine. Accusatory speeches against her

husband continued during occasional doctor visits, where she alleged violence resulting in a miscarriage, unsupported by physical examination findings. The patient adhered to paliperidone treatment, with the dose increased to 6 mg/day. Serum prolactin levels were monitored, and repeated psychometric tests showed symptom improvement (YMRS: 4, BPRS: 14, SAPS: 6, SANS: 0 points). Outpatient treatment was decided, and the patient was discharged on the 22nd day with follow-up plans. Informed consent was obtained from the patient and her family, who continue regular outpatient follow-up.

DISCUSSION

Psychotic symptoms associated with epilepsy are not clearly categorized in DSM-5, leading to difficulties in diagnosis (3). The bidirectional relationship between epilepsy and psychiatric disorders may pose challenges in clinical practice (9). These patients may present with various clinical manifestations, leading to potential misdiagnosis. In fact, our patient's past diagnosis of bipolar disorder supports this observation. The less impaired functionality in interictal psychosis, the prominence of positive symptoms, and the onset of epilepsy preceding psychosis may aid in distinguishing it from primary psychotic disorders (6).

Studies indicate a poor prognosis for interictal psychoses, with a small proportion recovering spontaneously, while approximately two-thirds persist beyond six months (10,11). While no specific guidelines exist for managing interictal psychoses, applying treatment schemes for initial psychotic episodes is recommended. Besides using antiepileptic drugs to control seizures, using antipsychotic drugs for a period has been emphasized for managing psychotic symptoms (10).

In our case, the addition of antipsychotic drugs to antiepileptic treatment resulted in regression of psychotic symptoms. Choosing an antipsychotic drug for interictal psychosis lacks a clear answer, necessitating caution due to the epileptogenic effects of these drugs. Particularly, chlorpromazine and clozapine are well-known to lower seizure thresholds (12).

Some authors argue against distinguishing between the delusion of pregnancy and pseudocyesis, suggesting their continuous nature (13). Consequently, disorders in the pseudocyesis differential diagnosis should also be considered in delusions of pregnancy. Although many neurological, endocrine, and metabolic diseases are implicated in this delusion, the association with epilepsy is not commonly emphasized (13). Interestingly, a case similar to ours, involving delusions of pregnancy in a young female diagnosed with epilepsy, has been reported, necessitating further studies to unveil the relationship between epilepsy and delusions of pregnancy (14).

In the literature, it is noted that patients with pregnancy delusions provide responses aligned with their sociocultural level, contrary to medical evidence (10). In our case, the patient claimed to recognize the gestational sac on USG, attributing it to her high school child development studies, challenging the doctors' findings.

Reproductive and sexuality-themed delusions accompanying pregnancy delusion have been suggested (13). Similarly, it is intriguing that the identical twin of our patient developed such delusions. Both siblings, treated for epilepsy since infancy, suggest common neurobiological processes in the pathogenesis.

Our case revealed that the patient's parents also shared the delusion of pregnancy, resembling a rare instance of shared psychosis syndrome known as "Folie-à-deux," where delusions transfer to another person in a close relationship. A reported case in the literature involves a married couple sharing the delusion of pregnancy (15). The involvement of the patient's relatives in psychosis complicates treatment as family support becomes challenging to obtain.

In summary, key points from our case report include the absence of appropriate classification and diagnostic criteria for epilepsy-related psychotic symptoms, the potential for misdiagnosis due to varied clinical presentations in interictal psychosis, and the occurrence of delusions of pregnancy as part of interictal psychosis. The development of reproductive-sexuality-themed delusions in the patient's identical twin, both treated for epilepsy since infancy, hints at common neurobiological processes in the pathogenesis. Pregnancy delusions might extend beyond the individual, impacting social life.

In conclusion, the need for guidelines in diagnosing and treating interictal psychosis is evident. Further neurobiological studies exploring the relationship between epilepsy and pregnancy delusion are crucial. We believe our study can raise awareness among clinicians regarding this subject.

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Unilateral Double Superior Cerebellar Artery Variation: A Cadaveric Case Report

Unilateral Çift Arteria Superior Cerebelli Varyasyonu: Bir Kadavra Vaka Raporu

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ABSTRACT

The superior cerebellar artery (SCA) is a vessel anterior to the brainstem, usually originating from the basilar artery (BA). In this case, a different course of left SCA in a 74-year-old male cadaver was reported. The origin of the SCA was found to be a unilateral double root at the left side on the anterior surface of the pons. The distances of the starting points of roots to the bifurcation of BA were 31.09 mm on the right side, on the left side the rostral root was 33.84 mm and the caudal root was 30.95 mm. The diameter of the right SCA was 2.37 mm, the left rostral root was 2.05 mm and the caudal root was 1.24 mm. Knowing the course of SCA, and especially morphological variations, will be helpful for the clinical branches in preventing complications during surgical operations, evaluating angiographic examinations, and diagnosing and treating neurovascular diseases.
Keywords: Anatomy; duplication; superior cerebellar artery; variation; cadaver.

ÖZ

Arteria superior cerebelli (ASC), beyin sapının önünde bulunan bir damar olup genellikle arteria basilaris (AB)'ten köken alır. Bu olguda 74 yaşındaki erkek bir kadavrada sol ASC'nin farklı seyri bildirilmektedir. ASC'nin kökeninin sol tarafta pons'un ön yüzünde unilateral çift kök halinde olduğu tespit edildi. Köklerin başlangıç noktalarının bifurcatio basilaris'e olan uzaklıkları sağ tarafta 31,09 mm, sol tarafta üst kök 33,84 mm ve alt kök 30,95 mm idi. Sağ ASC çapı 2,37 mm, sol üst kökün çapı 2,05 mm ve alt kökün çapı ise 1,24 mm idi. ASC'nin seyrinin ve özellikle morfolojik varyasyonların bilinmesi, cerrahi operasyonlar sırasında komplikasyonların önlenmesinde, anjiografik tetkiklerin değerlendirilmesinde ve nörovasküler hastalıkların teşhis ve tedavisinde klinik branşlara faydalı olacaktır.
Anahtar kelimeler: Anatomi; duplikasyon; arteria superior cerebelli; varyasyon; kadavra.

INTRODUCTION

The superior cerebellar artery (SCA) is the most rostral artery of the infratentorial vessels. It originates a few millimeters proximal to the origin of the posterior cerebral artery (PCA), the terminal branches of the basilar artery (BA) at the anterior of the brainstem. It then passes just below the oculomotor nerve (1-3). Each SCA has a short trunk. The rostral (medial-vermian) and caudal (lateral-marginal) branches are separated from this trunk. These branches run along the pontomesencephalic sulcus and bifurcate on the upper surface of the cerebellum, passing around the superior cerebellar peduncle. In the beginning, its rostral and caudal branches run parallel to each other. The rostral branch turns medially towards the lateral faces of the mesencephalon and inferior colliculus, where it arcs upward at the border of the

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superior colliculus and runs over the upper part of the vermis. It feeds the superolateral cerebellar hemisphere. Its deeper branches provide the nuclei of the cerebellum. It also gives branches along its course that feed the laterotegmental part of the upper part of the pons. Its posterior branches feed the superior cerebellar peduncle. Its caudal branch extends forward and provides the hemisphere of the cerebellum (4-7).

The SCA, which is located in the posterior cranial fossa in terms of origin and location, is the vessel with the least variation in the vertebrobasilar system (1,8). Although the SCA is considered the most consistent artery of the infratentorial branches, variations in its anatomy are noteworthy. Different variation possibilities of the SCA have been described in the literature: duplication, triplication, early bifurcation, fenestration, flattening, hypoplasia, and origin from the PCA (6,9-11). Duplication is among the most common anatomical variations of SCA. In addition to its variations, SCA is clinically important because of its close relationship with the oculomotor, trochlear, and trigeminal nerves. SCA plays an important role in the development of trigeminal neuralgia. However, due to its anatomical variability, SCA can trigger other neurovascular compressions (NVC), such as hemifacial spasm, oculomotor nerve palsy, and ocular neuromyotonia. In addition, it may be associated with ischemic syndromes and aneurysm development, emphasizing its clinical importance. Specific anatomical variants, such as the caudal course of the SCA trunk, may increase the risk of NVC (12).

Knowing the anatomical variations in the origin of SCA is important for anatomists, neurosurgeons, neurologists, and radiologists. The presence of variations can influence the plan of surgical and radiologic procedures. Therefore, a descriptive knowledge of the anatomy of this region with variable vascular structures would be useful to clinical anatomy at any stage of surgical planning. This study aimed to contribute to the literature by presenting the variation detected during routine cadaveric head dissection.

CASE REPORT

SCA variation was observed in a 74-year-old male cadaver during routine dissection for educational purposes at Tokat Gaziosmanpaşa University Faculty of Medicine, Department of Anatomy. First, a coronal incision was made on the scalp between the zygomatic processes of the os frontale passing over the frontal eminence. Then, another sagittal incision was made on the medial line starting from the midpoint of this incision and ending at the level of the external occipital protuberance. Finally, an incision was made horizontally from the end of the second incision to the level of the asterion on each side, and the scalp was opened anteriorly and laterally. The calvaria was cut open with an oscillating bone saw. After the dura mater was visualized, the cranial nerves were carefully dissected individually. Then, the spinal cord was cut at the level of the foramen magnum, and the brain was separated from the skull base. When the VA and BA were examined, it was found that the SCA was separated from the BA as two separate roots for the left side (Figure 1).

The branching and path of the roots were checked. In the course of the rostral root, it was observed that it was divided into two terminal branches distributed in the superior-medial part of the vermis and cerebellum close to the vermis. The second root followed a course close to the normal SCA course. It is divided into two branches, rostrally and caudally, on the anterior surface of the pons, with the caudal root distributed to the lateral part and the rostral root distributed between the vermis and the lateral edge (Figure 2). Both sides were in contact with the oculomotor nerve. The distance to the bifurcation basilaris was measured to determine whether there was a difference in the point of separation of the roots from the BA. The separation point of the right root was 31.09 mm, the separation point of the left rostral root was 33.84 mm and the separation point of the lower left root was 30.95 mm. To check whether there was a difference in vessel diameters, the diameters of the right and left roots were measured. The right root was 2.37 mm in diameter, while the left rostral root was 2.05 mm and the lower root was 1.24 mm. In addition, considering its close neighborhood with the trigeminal nerve, the distance between them was measured to see if there was an effect. The right trigeminal nerve exited 5.57 mm caudal to the right SCA. The left trigeminal nerve exited 8.26 mm caudal to the rostral root of the left SCA, 2.14 mm caudal to the rostral root, and 2.04 mm rostral to the caudal root of the lower root of the left SCA. No variation was found in the branching and course of the right SCA.

DISCUSSION

Since aneurysms and ischemic cerebrovascular diseases occurring in the posterior cranial fossa are evaluated by angiography, it is essential to know the vascular variations in this region (13). SCA occlusions may be asymptomatic depending on the regions involved in the brainstem and cerebellum. SCA occlusions are usually asymptomatic because of the anastomoses of the vessels in the region (14,15).

Some studies have reported that duplications are caused by problems in the connection of arteries during the embryonic period (16,17). Mani et al. (18) reported unilateral duplication of SCA in 28%, bilateral duplication in 8%, and unilateral triplication in two patients. Hardy et al. (14) reported that 43 of the 50 SCAs they examined in their study showed a single SCA, and 7 of them showed duplication. In a study by Avcı et al. (19), 67% of SCAs were single, 26% showed duplication, and 7% showed triplication. The case presented in this study was similar to the study of Arifoğlu et al. (1), the SCA originates from the BA as a single root on the right side and as two separate roots on the left side, and the caudal part branches again.

Mani et al. (18) reported that the oculomotor nerve runs between the PCA and SCA. They argue that these two arteries will be a reference for surgical operations on the nerve. In our case, we found that the rostral and caudal two roots traveled under the oculomotor nerve. Therefore, the thesis of Mani et al. (18) is not always valid in cases with duplication, and taking the arteries as a reference may mislead the diagnosis and treatment. Uchino et al. (16) suggested that SCA anomalies may cause compression syndromes in the adjacent nerves. In our case, the SCA was in contact with the oculomotor nerve, which supports the hypothesis of Uchino et al. (16).

Vascular variations are frequently encountered in cadaveric and autopsy studies. Knowledge of the course of SCA and morphologic variations is essential for preventing complications during surgical operations and for effective diagnosis and treatment of neurovascular diseases.

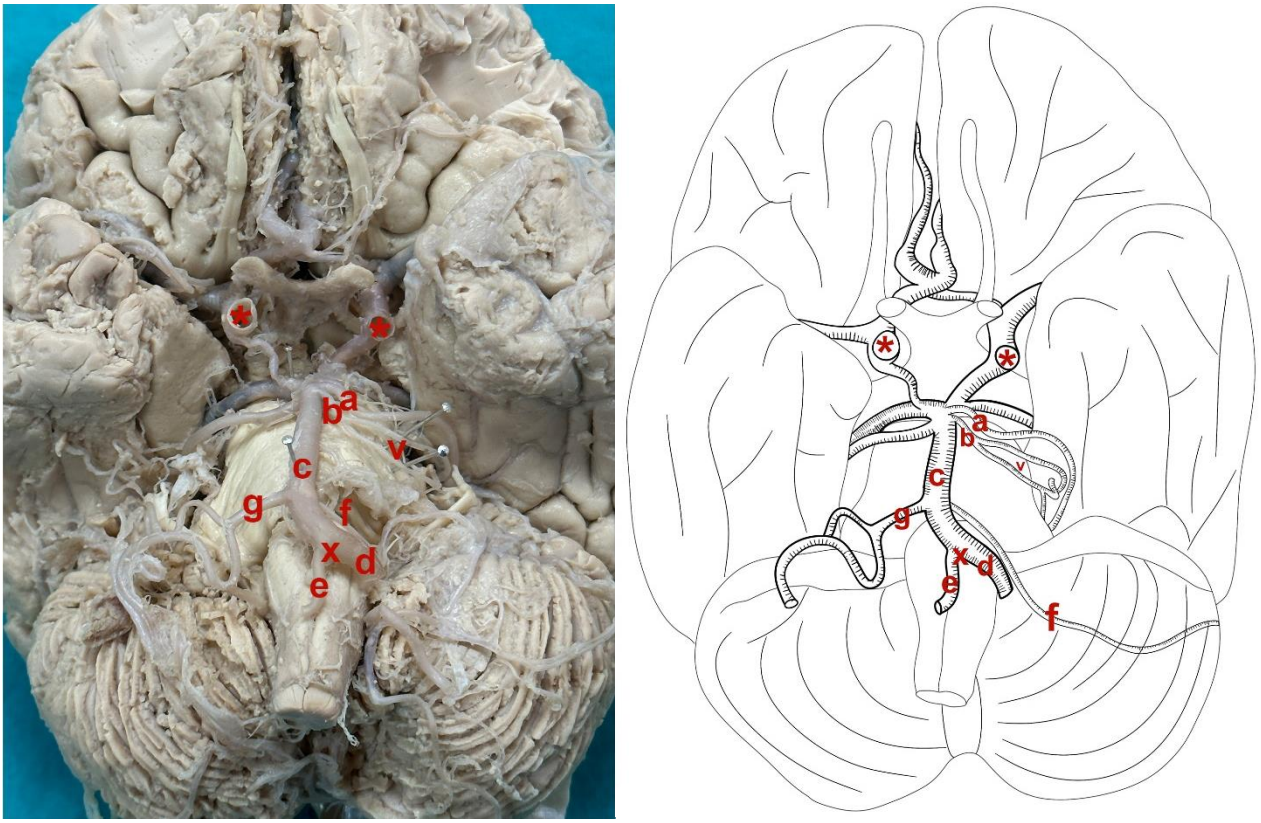

Figure 1. Left side, duplication of superior cerebellar artery, *: internal carotid artery, a: rostral root of superior cerebellar artery, b: caudal root of superior cerebellar artery, c: basilar artery, d: left vertebral artery, e: right vertebral artery, f: left anterior inferior cerebellar artery, g: right anterior inferior cerebellar artery, x: bifurcation; v: trigeminal nerve

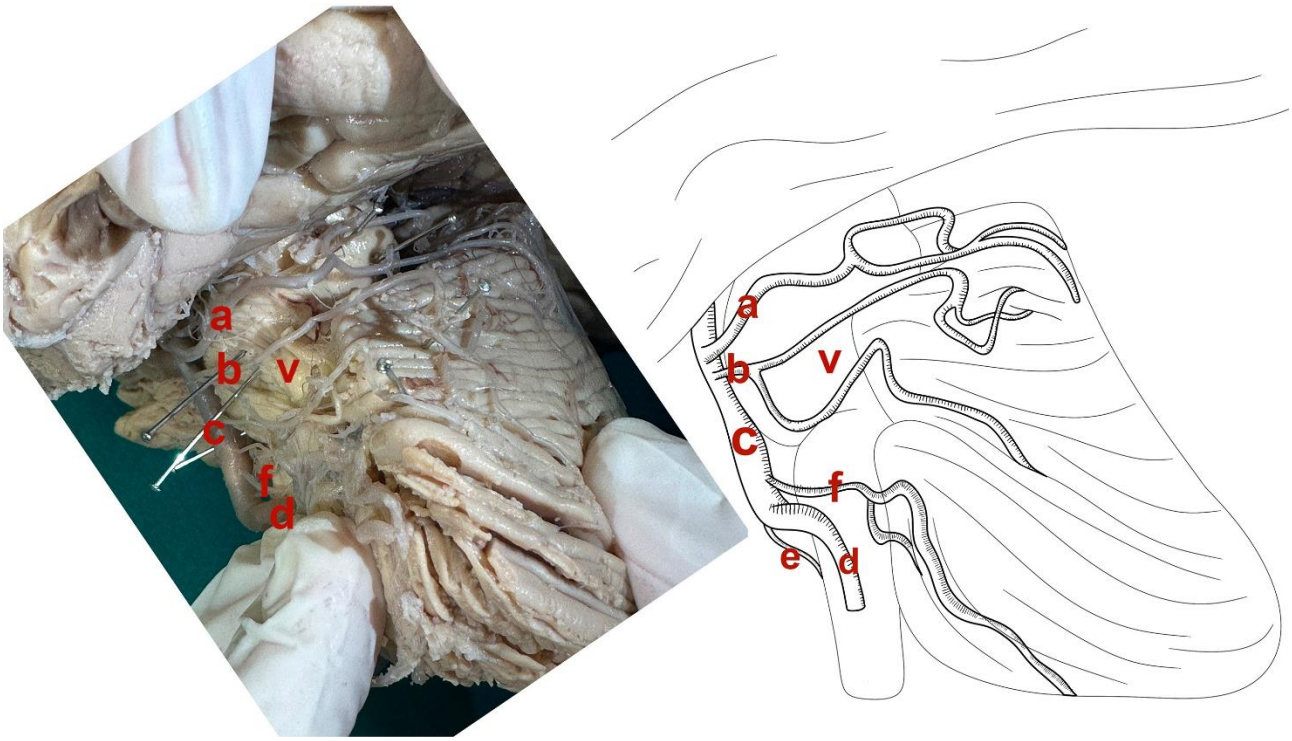

Figure 2. Left lateral aspect of the superior cerebellar artery, a: rostral root of superior cerebellar artery, b: caudal root of superior cerebellar artery, c: basilar artery, d: left vertebral artery, e: right vertebral artery, f: left anterior inferior cerebellar artery

Informed Consent: Since our study was a case report including a cadaveric study, there was no consent form.

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A Rare Cause of Macroscopic Hematuria: Ureteral Fibroepithelial Polyp: A Case Report

Makroskopik Hematürinin Nadir Bir Nedeni: Üreteral Fibroepitelyal Polip: Bir Olgu Sunumu

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ABSTRACT

Fibroepithelial polyps are rare, benign, non-epithelial tumors of the urinary system. They can occur throughout the entire urinary system, including the renal pelvis, ureter, bladder, and urethra, which are lined with urothelium. These polyps originate from the stromal structure, formed by the combination of mesodermal and urothelial cells. The most common clinical complaint of patients with fibroepithelial polyps is unilateral flank pain. In some cases, this pain may be accompanied by hematuria, dysuria, and pollakiuria, which are irritative lower urinary tract symptoms. In this case report, a case of a giant ureteral fibroepithelial polyp in a patient who was admitted to our clinic with macroscopic hematuria and left flank pain was presented. Following the diagnosis of a giant polyp in the left ureter, we treated the patient with endoscopic ablation using a Holmium-YAG laser device under ureteroscopy guidance.
Keywords: Hematuria; fibroepithelial; ureteroscopy.

ÖZ

Fibroepitelyal polipler üriner sistemin oldukça nadir görülen, iyi huylu, epitelyal olmayan tümörleridir. Böbrek pelvisi, üreter, mesane ve üretra da dahil olmak üzere üroepitelyum ile döşeli, üriner sistemin tamamında ortaya çıkabilirler. Mezodermal ve üroepitelyal hücrelerin birleşiminden oluşan stromal yapıdan köken alırlar. Fibroepitelyal polipli hastaların kliniğe en sık başvuru şikayeti tek taraflı yan ağrısıdır. Bazı durumlarda yan ağrısına hematüri, dizüri, pollaküri gibi irritatif alt üriner sistem semptomları da eşlik edebilir. Bu olgu sunumunda, makroskopik hematüri ve sol yan ağrısı şikayetleri ile kliniğimize başvuran bir hastada dev üreter fibroepitelyal polip sunulmuştur. Sol üreterde dev polip tanısı konulan hastaya üreteroskopi eşliğinde Holmium-YAG lazer cihazı kullanılarak endoskopik ablasyon uygulandı.
Anahtar kelimeler: Hematüri; fibroepitelyal; üreteroskopi.

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INTRODUCTION

Fibroepithelial polyps (FEPs) are rare, benign, nonepithelial tumors of the urinary system. They originate from the stroma composed of mesodermal and transitional epithelial cells. While the majority of FEPs are located in the ureter (most commonly in the proximal ureter), approximately 15% are found in the renal pelvis, and they are less commonly observed in the urethra and bladder (1). They tend to be unilaterally located, with left-ureteral involvement being twice as common as right-sided involvement (2). In cases where a radiolucent filling defect originating from the proximal ureter is observed on intravenous urography (IVU) or retrograde ureterography

and the cytology is negative, FEP should be suspected (3). Currently, IVU and retrograde ureterography, which are imaging methods for the diagnosis of FEP, have been replaced by computed tomography (CT) urography with technological developments. Since FEPs typically occur in the ureteropelvic junction (UPJ), most cases can be followed up with a diagnosis of congenital UPJ obstruction, which is a cause of hydronephrosis in childhood (4). With this case, we aimed to examine a 44-year-old female patient with left ureteral FEP, which is considered an extremely rare cause of macroscopic hematuria and left flank pain, both clinically, radiologically, and histopathologically. Additionally, we aimed to contribute to the literature by successfully treating patients through endoscopic ablation using a Holmium-YAG laser.

CASE REPORT

A 44-year-old female patient presented to our clinic with complaints of macroscopic hematuria and left flank pain. Physical examination revealed tenderness at the left costovertebral angle, but no other pathological findings were detected. Laboratory investigations revealed >400 erythrocytes per field in the microscopic examination of complete urinalysis, while leukocytes and nitrites were negative. Kidney function parameters were within the normal reference range. Ultrasound examination revealed mild dilation of the collecting systems in the left kidney. To elucidate the etiology of the patient's hematuria and left flank pain, a CT urography examination was performed. On CT urography, the right urinary tract and right kidney were observed to be normal. The left kidney was also normal; no stones were detected in the left ureter. Images of the pyelographic phase revealed a tubulonodular hypodense lesion, approximately 80 mm in length, in the proximal section of the left ureter, causing no significant ureteral expansion or partial filling of the lumen. Contrast material passing into the ureter was observed at the periphery of the lesion. The ureter was normal in width both proximal and distal to the segment containing the lesion; no dilation was observed in the collecting system of the left kidney. Due to the lack of geometric configuration and size of the lesion, density measurements could not be performed, and it was not clear whether the lesion was solid. Given the patient's macroscopic hematuria, it was considered that the lesion in the ureter could be associated with a solid lesion that partially fills the lumen (Figure 1). Cystoscopy was performed on the patient under general anesthesia and no pathological findings were found except for hematuric jet flow coming from the left ureteral orifice. Therefore, a diagnostic ureterorenoscopy was performed on the patient. At the level of the left proximal ureter, a pedunculated polypoid mass approximately 7 cm in length, almost completely obstructing the lumen, was observed (Figure 2). The base of the polypoid mass was ablated with a Holmium-YAG laser and separated from the ureteral wall. Subsequently, using foreign body forceps, all tissue was removed in a single piece and sent to the pathology laboratory for definitive diagnosis. The excision material macroscopically appeared tubular with all surfaces covered with mucosa and a pedunculated structure resembling a stalk at the surgical margin (Figure 3). Then, a 4.8Fr 26 cm pigtail catheter was placed in the patient's left ureter. No complications were encountered. Histopathological examination of the excised sections revealed chronic inflammatory cells, fibroblasts, and congested vascular structures in the loose, edematous stroma at the center of the lesion. The surface of the lesion was lined with urothelial epithelium (Figure 4). No mitotic figures were observed in the epithelium. The lesion did not show continuity at the surgical margin. Immunohistochemical studies revealed no significant increase in proliferative activity with Ki-67 in the urothelial epithelium or lesion stroma. Urothelial cells with umbrella cells were observed with cytokeratin 20. In conclusion, the lesion was reported as a FEP.

In the patient's follow-up ultrasound the third postoperative week after the removal of the pigtail catheter, no hydronephrosis was observed. No pathological findings were found in the blood and urine tests and control urinary system ultrasound of the patient,

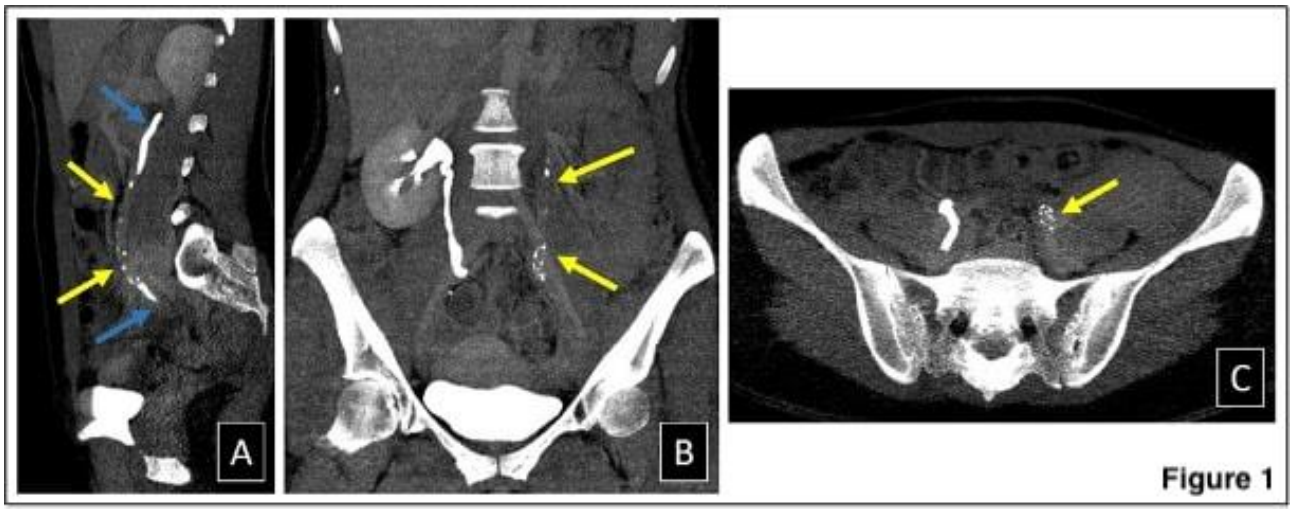

Figure 1. A) Sagittal, **B)** coronal, and **C)** transverse plane maximum intensity projection images of the pyelographic phase of the computed tomography urography examination, a hypodense lesion partially filling the lumen along the segment in the left ureter (yellow arrows) is observed, the ureter segments proximal and distal to this segment are of normal width (blue arrows)

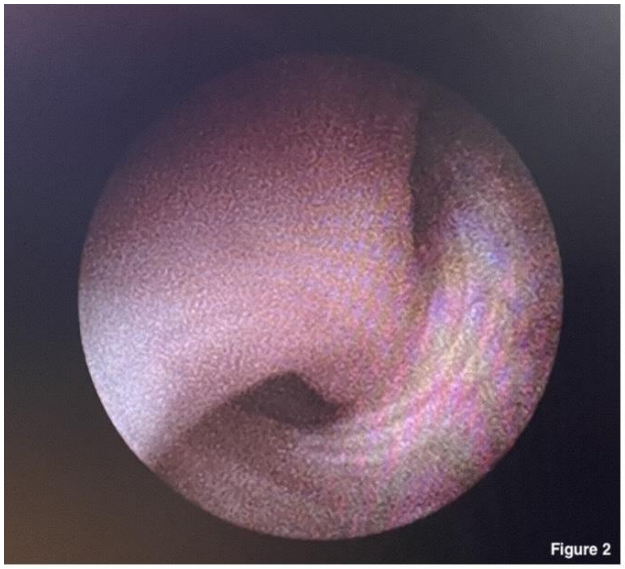

Figure 2. Image of the FEP in the lumen of the left ureter

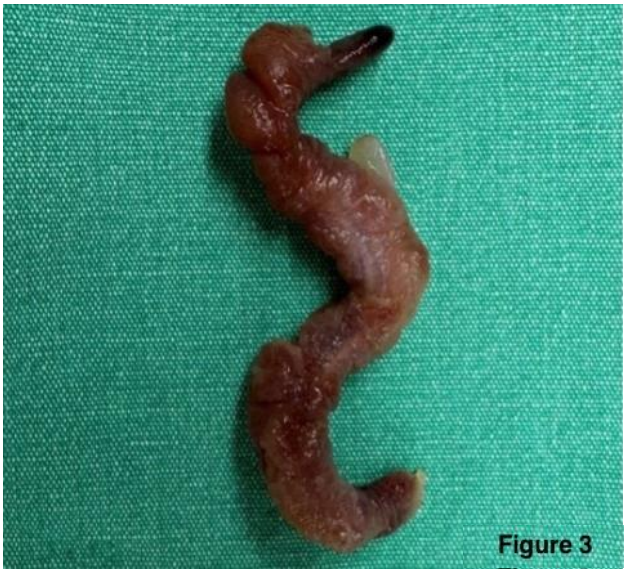

Figure 3. Macroscopic view of the excision material

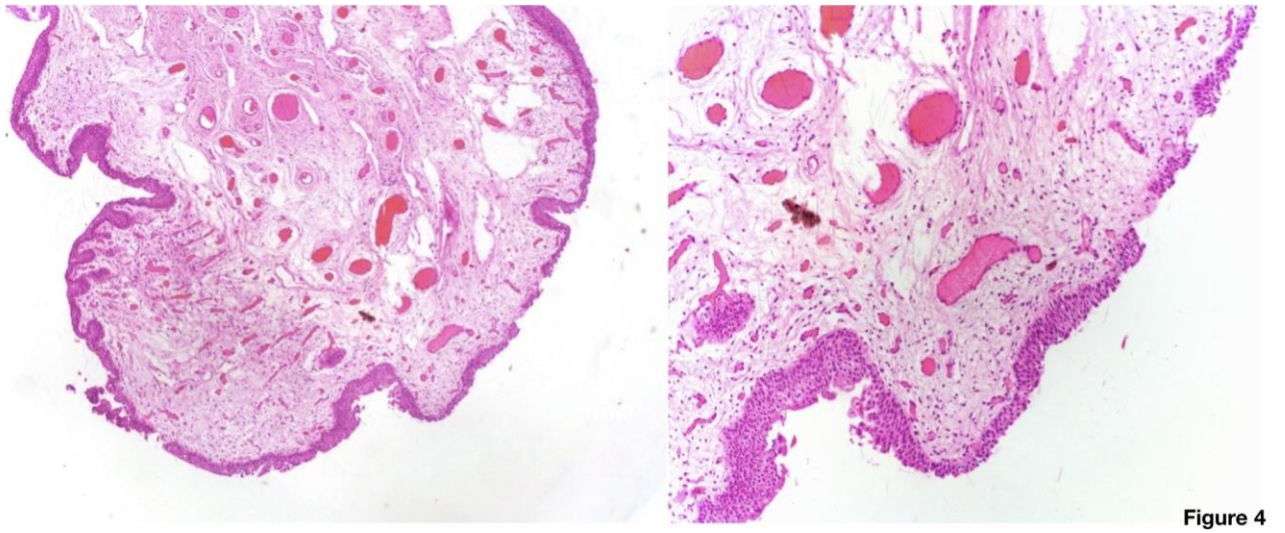

Figure 4. The urothelial epithelial lining on the surface and a central fibrovascular core structure were observed (H&E, x40)

who achieved control in the third month. Verbal and written consent was obtained from the patients for the study.

DISCUSSION

Among FEPs, the majority are benign mesodermal tumors originating from the ureter. Histologically, FEPs are composed of structures with a surface covered by normal uroepithelium and a loose fibrovascular stroma (5). Although classified as benign hamartomas due to their histological structure, cases with accompanying malignant and cystic degeneration have been reported in the literature (6,7). The most common presentations for patients with FEP are colicky flank pain (79%) and hematuria (50%), while symptoms such as dysuria, pollakiuria, and pyuria may also be present (8). In the past, open surgical methods were used for the treatment of FEPs. However, currently, minimally invasive methods such as percutaneous, ureterorenoscopic, and laparoscopic techniques are employed. Currently, the most commonly used treatment modality for FEPs is ureterorenoscopic ablation with a Holmium-YAG laser, and most studies highlight this method (9,10). Another minimally invasive approach is the percutaneous antegrade approach, which is preferred especially for polyp ablations in the proximal ureter and renal pelvis (5). The laparoscopic method is crucial for the treatment of polyps that are too large to be completely excised with endoscopic treatment and has replaced open surgical excision (6). Childs et al. (5) applied open surgical procedures to the first 10 out of 22 patients in their study, while they performed ureterorenoscopic ablation in 11 other patients and percutaneous ablation in 1 patient. They reported that they achieved complete treatment success with endoscopic methods as well. Sun et al. (10) showed that large FEPs with an average size of 11 cm can be treated with ureterorenoscopic ablation by applying this procedure to all 5 patients. Kijvikai et al. (6) treated a 17 cm fibroepithelial polyp via laparoscopic excision. There are differences of opinion regarding preoperative biopsy in the literature. While Childs et al. (5) argued in their study that biopsy is mandatory because differentiation from

urothelial carcinoma cannot be made with radiological imaging or ureterorenoscopic view, Sun et al. (10) reported that biopsy is not necessary in patients with a typical appearance of FEPs, and after frozen examination in case of suspicion, ablation can be performed. In our case, due to the typical appearance of FEPs in the radiological and endoscopic images, the tumor was completely excised by applying the Holmium-YAG laser ablation procedure. Laser ablation was applied to the base of the polypoid mass. Studies have shown that the depth of long FEPs may be short, and long FEPs can be treated with ablation at this point (5,10).

At the 3-month postoperative follow-up, urinalysis, hemogram, biochemical parameters, and urinary system ultrasound were performed, and no pathological findings were detected.

In conclusion, FEPs can be successfully treated by applying Holmium-YAG laser ablation through ureterorenoscopy, which is a minimally invasive method.

Informed Consent: Written informed consent was obtained from the patient for publication and accompanying images.

Conflict of Interest: None declared by the authors.

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Migraine Causality in Alpha-1 Antitrypsin Deficiency

Alfa-1 Antitripsin Eksikliğinde Migren Nedenselliği

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ABSTRACT

Alpha1-antitrypsin (A1AT) is an anti-inflammatory mediator with antiprotease activity associated with anti-inflammatory and immunomodulatory effects in various inflammatory conditions. A1AT deficiency (A1ATD) has been associated with various hyperinflammatory diseases, such as lung disease (emphysema and bronchiectasis), liver disease (chronic hepatitis, cirrhosis, and hepatoma), and skin diseases (panniculitis). Migraine with aura is one of the common migraine subtypes associated with neuroimmunologic activation and neuroinflammation which is associated with cortical spreading depression and glial hyperinflammation in etioradiopathogenesis, and the main mechanisms explained so far are hyperinflammation of pro-inflammatory mediators, sensitivity of trigeminal nerve fibers and pain-conjugated glial cells activation. In this case report, a causative perspective of migraine with aura and A1ATD was presented through etioradiopathogenetics mechanisms that show the central reflections of systemic hyperinflammatory processes, and the importance of peripheral hyperinflammatory conditions in migraine etiology was examined.
Keywords: Alpha-1 antitrypsin deficiency; cortical spreading depression; hepatocerebral pathways; migraine; neuroimmune activation; neuroinflammation.

ÖZ

Alfa1-antitripsin (A1AT), çeşitli inflamatuar durumlarda anti-inflamatuar ve immünomodülatör etkilerle ilişkili antiproteaz aktivitesine sahip bir anti-inflamatuar aracıdır. A1AT eksikliği (A1ATE), akciğer hastalığı (amfizem ve bronşektazi), karaciğer hastalığı (kronik hepatit, siroz ve hepatoma) ve cilt hastalıkları (pannikülit) gibi çeşitli hiperinflamatuar hastalıklarla ilişkilendirilmiştir. Auralı migren, etyopatogenezinde kortikal yayılan depresyon ve glial hiperinflamasyonla ilişkili nöroimmünolojik aktivasyon ve nöroinflamasyonla ilişkili olan yaygın migren alt tiplerinden biri olup şimdiye kadar açıklanan ana mekanizmalar, proinflamatuar mediatörlerin hiperinflamasyonu, trigeminal sinir liflerinin duyarlılığı ve ağrıyla konjuge glial hücrelerin aktivasyonudur. Bu vaka raporunda, sistemik hiperinflamatuar süreçlerin santral yansımalarını gösteren etioradiopatogenetik mekanizmalar üzerinden auralı migren ve A1ATE'nin nedensel bir perspektifi sunulmuş ve periferik hiperinflamatuar durumların migren etiyolojisindeki önemi incelenmiştir.
Anahtar kelimeler: Alfa-1 antitripsin eksikliği; kortikal yayılan depresyon; hepatoserebral yollar; migren; nöroimmün aktivasyon; nöroinflamasyon.

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INTRODUCTION

Alpha-1 antitrypsin deficiency (A1ATD) is an autosomal recessive disease caused by a mutation in the SERPINA1 gene. A1AT is an anti-inflammatory mediator with antiprotease activity (1) associated with anti-inflammatory and immunomodulatory effects in various inflammatory conditions, such as rheumatoid arthritis, diabetes

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mellitus, cystic fibrosis, and asthma (2). A1ATD has been associated with various hyperinflammatory diseases, such as lung disease (emphysema and bronchiectasis), liver disease (chronic hepatitis, cirrhosis, and hepatoma), and skin diseases (panniculitis). Migraine with aura (MWA) is among the most common migraine type that the pathogenesis is associated with neuroimmunologic activation and neuroinflammation, which is thought to be associated with cortical spreading depression (CSD) and glial hyperinflammation (3). Current data obtained from animal models have shown that CSD occurs as a result of the release of proinflammatory mediators, activation of trigeminal nerve fibers and inflammation, as well as specific neuroinflammatory markers showing an increase in pain-conjugated glial activation on positron emission tomography (PET) (3). In this case report, a causative perspective of MWA in a patient diagnosed with A1ATD was presented through etioradiopathogenetics mechanisms that show the central reflections of systemic hyperinflammatory processes, and the importance of peripheral hyperinflammatory conditions in migraine etiology was examined.

CASE REPORT

A 35-year-old female patient was admitted with a headache and imbalance in gait that had been going on for six months. Her headache was a migratory character that could continue for over 24 hours and was localized in the right frontoparietal area with a throbbing quality. Her headache was accompanied by a feeling of conjugate photophobia and nausea induced by a movement that causes difficulties in daily life activity. There was a complaint of vision loss in both eyes, which started about 5-10 minutes before the headache, which she referred to as a serrated area in all directions. She did not describe a constrained view or diplopia in her neurological examination. In her medical history, she was diagnosed with A1ATD syndrome three months ago. Serum liver tests and abdominal ultrasonography (USG) were performed at the internal medicine clinic where the patient applied with the complaint of right upper quadrant pain. In serum examinations, elevation in liver function tests showed mild to severe steatosis in liver parenchyma and mild severe mesenteric panniculitis in the mesenteric root periphery, which was detected in USG (Figure 1. A). With the current findings, the patient was referred for biopsy for diagnostic evaluation of hepatocellular pathologies. The patient's liver biopsy showed mild-stage fibrosis (Figure 1. B). Dynamic liver magnetic resonance imaging (MRI) and triphasic upper/lower abdomen computed tomography (CT) showed no additional hepatobiliary pathology. There was no significant emphysematous appearance on the patient's thorax CT. In serum tests performed for hepatobiliary pathologies, a low A1AT level of 45 mg/dL (normal range, 93-224 mg/dL) was detected (turbidimetric method). Pulmonary function tests were normal. Liver function studies revealed elevated serum alanine aminotransferase (ALT) level of 245 U/L (average, 71-236 U/L), aspartate aminotransferase (AST) level of 155 U/L (average 68-148 U/L), and triglyceride level of 324 mg/dL (normally <150 mg/dL). Alkaline phosphatase and γ-glutamyl transferase were normal. With these results, the patient was diagnosed with A1ATD, and ursodiol was started during the follow-up period. Cranial MRI and MR angiography were performed regarding the patient's current complaints, and nonspecific ischemic gliotic areas in the bilateral frontal hemispheres were detected. There were no abnormalities regarding vasculitis in the serum parameters (i.e., erythrocyte sedimentation rate, serum protein immunofixation electrophoresis, complement C3, C4, etc.). The patient, who met almost all criteria for MWA and whose metabolic disorder continued at the time of admission, was followed up with non-steroidal anti-inflammatory drug (NSAID) therapy. During follow-up, there was no response to NSAID treatment as attack treatment, and the patient was switched to flunarizine (5 mg/per day) treatment. A significant improvement was observed when switching to flunarizine in prophylaxis.

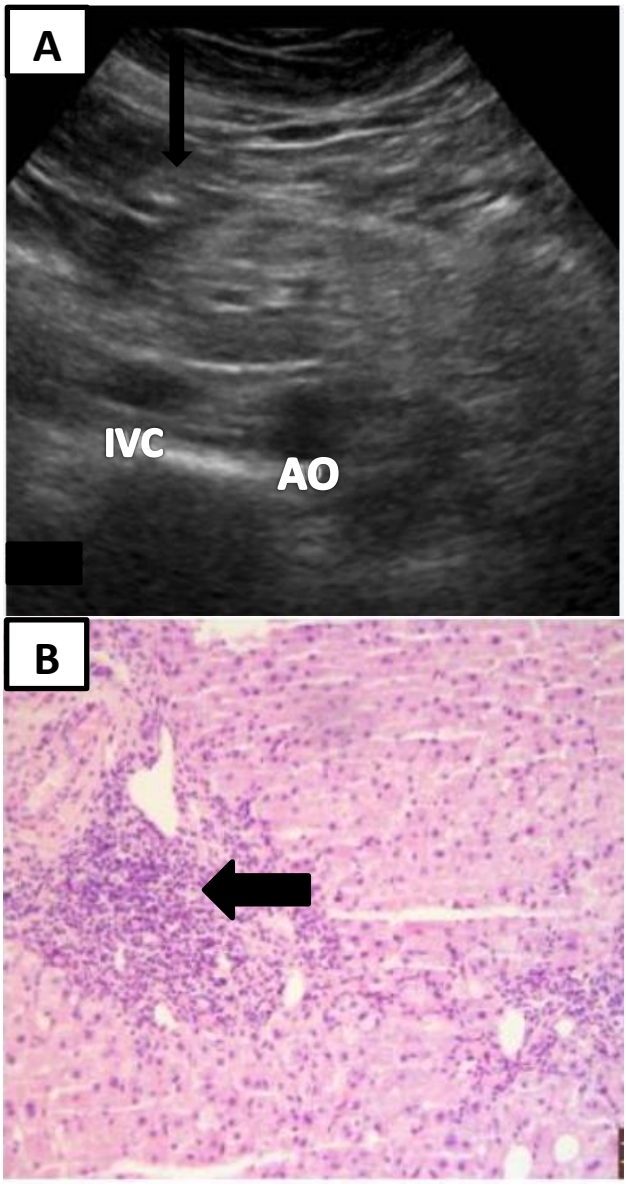

Figure 1. A) Abdomen ultrasonography showed mild to severe steatosis in liver parenchyma and mild severe mesenteric panniculitis in the mesenteric root periphery (black arrow), IVC: inferior vena cava, AO: aorta abdominalis, **B)** mild stage fibrosis was observed in the liver biopsy (black arrow)

DISCUSSION

A1AT is a glycoprotein produced mainly in the liver and acts primarily as a serine protease inhibitor to prevent the destruction of pulmonary structures by neutrophil elastase. It also has an immunomodulatory and anti-inflammatory effect as a positive acute phase reactant and its serum level increases in response to inflammatory stress in order to maintain the balance of proinflammatory processes (4). In studies on the relationship between A1ATD and inflammatory processes, A1ATD has been shown to be associated with proinflammatory mediators, including interleukin-1β (IL-1β) and complement activation. Also, increased levels of complement receptor-associated C3d and IL-1β have been shown in individuals with A1ATD with ZZ genotype (5,6). In a different study, NLRP3 expression by innate immune cells (mainly macrophages), which is conducted by the TLR-NF-κB pathway, results in an increase of the cellular contents of the pro-IL-1β and NLRP3 inflammasome in response to Alu RNA through TLR7 activation was reported in A1ATD (7).

MWA is a subtype of migraine that accounts for approximately 25% of all cases and is accompanied by visual (more than 90%), sensory, and motor auras before pain, of which association with various neuroinflammatory processes has been reported (3). The CSD model is among the mechanisms explained in the process of pain progression. This mechanism is a slow (2-5 mm/min) and spontaneous progressive depolarization of neurons and glia with low excitation thresholds in the cortical gray matter. This spreading process has been associated with hyperinflammation and has been reported to cause sensitization and activation of trigeminal afferents in the cranium (3). One of the most important studies examining the relationship between MWA and hyperinflammation so far was carried out by Hadjikhani et al. (8) that evaluated PET/MRI data of 18kDa translocator protein (an inflammatory marker) in the simultaneously acquired 11C-PBR28 PET on 11 MWA patients and mean tracer uptake (SUVR) in four regions of interest comprising the meninges plus the adjacent parameningeal tissues (PMT) were measured. Higher SUVR in PMT overlying occipital cortex was observed compared to control patients. The study detected increased signal (i.e., augmented 11C-PBR28 binding reflecting increased 18-kD translocator protein (TSPO) expression) in the meningeal and parameningeal areas in MWA patients, as evidence of persistent extra-axial inflammation evident in the occipital area. As a result of this study, it was concluded that the meningeal inflammatory process, which may develop due to various etiopathogenic inductors and progress with CSD, may contribute to hyperinflammation in the MWA pathophysiology (3).

In this case report, a patient diagnosed with de novo MWA after being diagnosed with A1ATD is discussed. The patient first applied with gastrointestinal complaints, and a significant increase in serum liver tests, as well as hepatic fibrosis on biopsy and panniculitis on abdominal USG, were detected. Following A1ATD diagnosis with existing hepatic pathology, MWA began without a previous migraine resume. In a study investigating potential connections between common genotypes of the SERPINA1 gene and cluster headache (CH), significant findings were revealed (9). The study found a significant difference in CH attack frequency in patients who are heterozygous or homozygous M allele carriers. This suggests a potential relationship between the presence of an S or Z allele and a higher attack frequency in CH, with potential implications for future research and clinical practice.

In a different study, 20 patients diagnosed with medication-overuse headaches, including migraine, and 18 healthy controls were included in the study. Proteomic analysis was performed using mono- (SDS-PAGE) and two-dimensional gel electrophoresis (2-DE) followed by liquid chromatography-tandem mass spectrometry (LC-MS/MS). This thorough analysis revealed disturbances in specific proteins in the serum of the patients, including A1AT, immunoglobulin heavy constant alpha 1, retinol-binding protein, and transthyretin, as a result of 2-DE combined with LC-MS/MS analysis (10). The causality of A1ATD and migraine is still doubtful and although no objective explanation has been made for the etiopathogenesis of this coexistence, there is a series of immunological and inflammatory evidence that both are triggered and aggravated by hyperinflammatory processes as pathophysiological inductors.

CONCLUSION

Various headache types have been described in several studies, especially in patients with hepatopulmonary diseases, and it is unclear in which mechanisms this causality occurs. The current studies suggest that various autoimmune inflammatory processes that cause differentiation in proteomic patterns may be critical players in the etiology of different headache types, particularly those associated with hyperinflammatory processes like migraine. There are also different opinions that the possible co-existence with proinflammatory mediators propagation from the peripheral hepatic system to the central nervous system and cause denovo migraine attacks by triggering the hyperinflammatory condition that can be detected in MWA patients' meningeal and parameningeal tissues. These findings open new avenues for future research, inspiring us to delve deeper into the etioradiopathogenetic changes during disease courses. New studies are needed in this field.

Informed Consent: Written informed consent was obtained from the patient for publication and accompanying images.

Conflict of Interest: The patient's data used in the figure was applied for a fee by units specialized in the relevant field in a private clinic, and it is stated that it was used with the patient's consent. There is no conflict of interest.

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- Etik kurul onay bilgisi GEREÇ ve YÖNTEMLER bölümünde kurul adı, onay tarihi ve sayısı ile birlikte belirtilmelidir.
- Eğer çalışmada direkt-indirekt ticari bağlantı veya maddi destek veren kurum mevcut ise yazarlar; kullanılan ticari ürün, ilaç, firma vb. ile ticari hiçbir ilişkisinin olmadığını veya varsa nasıl bir ilişkisinin olduğunu (konsültan, diğer anlaşmalar), editöre sunum sayfasında belirtmelidirler.
- Yazarlar çalışma ile ilgili kişisel ve finansal tüm ilişkilerin bildirilmesinden sorumludur. Makalenin başvurusu ve/veya değerlendirmesi ile ilişkili herhangi bir çıkar çatışması olup olmadığının açıkça beyan edilmesi gerekmektedir.
- Makalelerin bilimsel ve etik kurallara uygunluğu yazarların sorumluluğundadır.

BAŞVURU DOSYALARI

Makaleler aşağıda belirtilen şekilde ayrı dosyalar halinde sisteme yüklenmelidir.

Telif Hakkı Devir Formu: Başvuru sırasında sistemden alınacak Telif Hakkı Devir Formu tüm yazarlar tarafından makaledeki yazar sıralamasına uygun şekilde imzalanmış olmalıdır.

Başvuru Mektubu: Makalenin türü, daha önce hiç bir yerde yayınlanmamış ve/veya yayınlanmak üzere değerlendirme sürecinde olmadığı, varsa çalışmayı maddi olarak destekleyen kişi ve kuruluşlar ve bu kuruluşların yazarlarla olan ilişkileri (yoksa olmadığı) belirtilmelidir. Makalenin konusuyla ilgili olarak önerilen, yazarlarla ve kurumlarıyla ilgisi olmayan en az iki hakemin adları, akademik unvanları, kurumları, iletişim bilgileri ve e-posta adresleri yazılmalıdır. Editörlerin hakemleri seçme hakkı saklıdır.

Başlık Sayfası: Makalenin başlığını (İngilizce ve Türkçe), 40 karakteri geçmeyen kısa başlık, tüm yazarların adlarını, akademik unvanlarını, ORCID® numaralarını, kurumlarını, e-posta adreslerini ve ayrıca sorumlu yazarın adını, yazışma adresini, telefon numarasını, e-posta adresini içermelidir. Makale daha önce bilimsel bir toplantıda sunulmuş ise toplantı adı, tarihi ve yeri (yoksa sunulmadığı) belirtilmelidir.

Ana Metin: Makalenin başlığı (İngilizce ve Türkçe), 40 karakteri geçmeyen kısa başlık, Öz (İngilizce ve Türkçe), Anahtar kelimeler (İngilizce ve Türkçe), Ana Metin (gönderilen makalenin türüne uygun olarak bölümlere ayrılmış), Kaynaklar, Tablolar ve Şekil açıklamaları yer almalıdır.

Etik Kurul Onay Belgesi: Tüm araştırma makaleleri için Etik Kurul Onay Belgesi ayrı bir dosya olarak yüklenmelidir.

Not: Makalede şekil, resim veya fotoğraf varsa bunların da her biri ayrı birer dosya olarak yüklenmelidir.

MAKALE TÜRÜNE GÖRE KULLANILMASI GEREKEN BÖLÜMLER

Araştırma Makalesi

BAŞLIK (İngilizce ve Türkçe), KISA BAŞLIK, ÖZ (İngilizce ve Türkçe), Anahtar kelimeler (İngilizce ve Türkçe), GİRİŞ, GEREÇ VE YÖNTEMLER, BULGULAR, TARTIŞMA, SONUÇ, KAYNAKLAR

ÖZ ve ABSTRACT çeviri açısından uyumlu olmalı ve her biri kendi içinde 200-250 kelime arasında olmalıdır.

ABSTRACT, "Aim, Material and Methods, Results, Conclusion" şeklinde yapılandırılmalıdır.

ÖZ, "Amaç, Gereç ve Yöntemler, Bulgular, Sonuç" şeklinde yapılandırılmalıdır.

Derleme (Sadece Davetli)

BAŞLIK (İngilizce ve Türkçe), KISA BAŞLIK, ÖZ (İngilizce ve Türkçe), Anahtar kelimeler (İngilizce ve Türkçe), GİRİŞ, Konu ile İlgili Alt Başlıklar, SONUÇ, KAYNAKLAR

ÖZ ve ABSTRACT çeviri açısından uyumlu olmalı ve her biri kendi içinde 150-200 kelime arasında olmalıdır.

Olgu Sunumu

BAŞLIK (İngilizce ve Türkçe), KISA BAŞLIK, ÖZ (İngilizce ve Türkçe), Anahtar kelimeler (İngilizce ve Türkçe), GİRİŞ, OLGU SUNUMU, TARTIŞMA, KAYNAKLAR

ÖZ ve ABSTRACT çeviri açısından uyumlu olmalı ve her biri kendi içinde 100-150 kelime arasında olmalıdır.

Diğer

Bu üç temel makale türü dışındaki (editöre mektup, editöryel yorum/tartışma vb.) yazıların hazırlanmasında da genel yazım kuralları geçerlidir. Bu tür yazılarda başlık ve öz bölümleri yoktur. Kaynak sayısı 5 ile sınırlıdır. İthaf olunan makale sayı ve tarih verilerek belirtilmelidir. Yazının sonunda yazarın ismi, kurumu ve adresi yer almalıdır. Mektuba cevap, editör veya makalenin yazarları tarafından, yine dergide yayınlanarak verilir.

YAZARLARA BİLGİLENDİRME

YAZIM KURALLARI
- Makaleler Microsoft Word® belgesi olarak hazırlanmalıdır.
- Sayfa kenarlarında 2,5 cm boşluk bırakılmalıdır.
- Sayfa numaraları sayfanın sağ alt köşesine yerleştirilmelidir.
- Tüm metinler 12 punto Times New Roman karakteri kullanılarak çift satır aralığı ile sola hizalanmış olarak yazılmalıdır.

ANAHTAR KELİMELER
- Anahtar kelime sayısı en az 2 olmalı, kelimeler birbirlerinden noktalı virgül (;) ile ayrılmalıdır.
- Türkçe anahtar kelimeler Türkiye Bilim Terimleri (TBT)'ne (http://www.bilimterimleri.com), İngilizce anahtar kelimeler Medical Subject Headings (MESH)'e (http://www.nlm.nih.gov/mesh/MBrowser.html) uygun olarak verilmelidir.

İSTATİSTİKSEL YÖNTEMLER
- Tüm araştırma makaleleri biyoistatistik açıdan değerlendirilmeli ve uygun plan, analiz ve raporlama ile belirtilmelidir. Bu makalelerde, GEREÇ VE YÖNTEMLER bölümünün son alt başlığı "İstatistiksel Analiz" olmalıdır.
- Bu bölümde çalışmada kullanılan istatistiksel yöntemler ne amaçla kullanıldığı belirtilerek yazılmalı, istatistiksel analiz için kullanılan paket programlar ve sürümleri belirtilmelidir.
- p değerleri ondalık üç basamaklı (p=0,038; p=0,810 vb.) olarak verilmelidir.
- Makalelerin biyoistatistik açıdan uygunluğunun kontrolü için ek bilgi www.icmje.org adresinden temin edilebilir.

KISALTMALAR
- Terim ilk kullanıldığında parantez içinde kısaltmayla birlikte açık olarak yazılmalı ve tüm metin boyunca aynı kısaltma kullanılmalıdır.
- Uluslararası kullanılan kısaltmalar Bilimsel Yazım Kurallarına uygun şekilde kullanılmalıdır.

TABLOLAR VE ŞEKİLLER
- Metinde ilgili cümlenin sonunda (Tablo 1) ve/veya (Şekil 1) şeklinde belirtilmelidir.
- Tablolar (başlıklarıyla birlikte) ve şekiller (açıklamalarıyla birlikte) kaynaklardan sonra ve her biri ayrı bir sayfada olacak şekilde metnin sonuna eklenmelidir.
- Tablo başlıkları tablo üstünde (Tablo 1. Tablo başlığı), şekil açıklamaları ise şeklin altında (Şekil 1. Şekil açıklaması), ilk harfleri büyük olacak şekilde yazılmalıdır.
- Tablolarda ve şekillerde kısaltma veya sembol kullanılmış ise altında dipnot olarak açıklanmalıdır.
- Şekiller ve fotoğraflar, .png, .jpg vb. formatta ve en az 300 dpi çözünürlükte ayrı dosyalar halinde yüklenmelidir.
- Şekil ve fotoğraf alt yazıları, son tablonun olduğu sayfadan sonra, ayrı bir sayfada sırasıyla verilmelidir.
- Daha önce basılmış şekil, resim, tablo, grafik vb. kullanılmış ise yazılı izin alınmalı ve açıklama olarak belirtilmelidir. Bu konudaki hukuki sorumluluk yazarlara aittir.

TEŞEKKÜR
- Eğer çıkar çatışması/çakışması, finansal destek, bağış ve diğer bütün editöryel (İngilizce/Türkçe değerlendirme) ve/veya teknik yardım varsa, bu bölümde, KAYNAKLAR bölümünden önce belirtilmelidir.

KAYNAKLAR
- Kaynaklar, kullanım sırasına göre numaralandırılmalı ve metin içinde ilgili cümlenin sonunda parantez içinde numaralarla (1) veya (1,2) veya (3-5) şeklinde verilmelidir.
- Kaynaklar dizini, metin içinde kaynakların kullanıldığı sıraya göre oluşturulmalıdır.
- Yazar sayısı 6 veya daha az ise tüm yazarlar belirtilmeli, 7 veya daha fazla ise ilk 6 yazar belirtildikten sonra "et al." eklenmelidir.
- Kongre bildirileri, kişisel deneyimler, basılmamış yayınlar, tezler ve internet adresleri kaynak olarak gösterilmemelidir.
- DOI tek kabul edilebilir online referanstır.

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Al-Habian A, Harikumar PE, Stocker CJ, Langlands K, Selway JL. Histochemical and immunohistochemical evaluation of mouse skin histology: comparison of fixation with neutral buffered formalin and alcoholic formalin. J Histotechnol. 2014;37(4):115-24.

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