

## Grand Journal of UROLOGY

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# Grand Journal of UROLOGY

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### Aims and Scope

Grand Journal of Urology (Grand J Urol) is an open access, peer-reviewed journal publishing original scientific articles in the field of urology. It aims to issue scientific publications on Andrology (Male Sexual Disfunction, Infertility), Endourology, Female Urology, Functional Urology, General Urology, Genitourinary Radiology, History of Urology, Laparoscopic and Robotic Surgery, Minimally Invasive Urology, Neurourology, New Technology and Techniques, Pediatric Urology, Reconstructive Urology, Renal Transplantation, Urolithiasis, and Urological Oncology. It is published electronically three times a year (January, May, September), and the language of publication is English.

The target audience of the journal includes, urology specialists, residents in urology and other specialists who are interested in the field of urology. The journal aims to publish original scientific articles, clinical research, reviews, case reports, clinical images, editorial comments, and letters to the editor that are prepared in accordance with the ethical guidelines. Mini reviews, clinical updates, surgical techniques, and a guideline of guidelines that are in the scope of the journal are considered for publication and/or invited by the editor. All manuscripts must be submitted via the online submission system at <u>www.grandjournalofurology.com</u>. The journal guidelines, technical information, and the required forms are available on the journal's web page.

Only articles that have not been published elsewhere or are not reviewed for publication may be submitted. Grand J Urol does not accept multiple submission and duplicate submission even though the previous one was published in a different language. The journal's publication policy is based on independent and unbiased double-blinded peerreviewed principles. Following the online article submission, the journal's fast publishing process is an important policy, with our members of the Advisory Board and referees, peerreviewes are conducted to the highest standards and feedbacks are provided in the shortest time possible. The journal reserves the right to request any research material related to the article.

### Mission

The mission of the Grand J Urol (GJU) is to distribute urological medical data to the World as well as create a supportive and vibrant scientific platform to connect and explore ideas by publishing articles related to all fields of urology. The GJU aims to address current urological issues at both national and international levels, start debates, and exert an influence on decision-makers all over the world by integrating science in everyday life.

The Grand Journal of Urology encourages and enables academicians, researchers, and specialists to publish their valuable research in urology branch.

### **Basic Publication Rules**

The primary aim of the journal is to publish original articles with high scientific and ethical quality and serve as a good example of medical publications in the World. The Grand Journal of Urology's editorial policy (evaluation and publication processes) is shaped according to the guidelines of international organizations such as the International Council of Medical Journal Editors (ICMJE), the World Association of Medical Editors (WAME), the Council of Science Editors (CSE), the Committee on Publication Ethics (COPE), the US National Library of Medicine (NLM), the World Medical Association (WMA), the US Office of Research Integrity (ORI), the European Association of Science Editors (EASE), and the International Society of Managing and Technical Editors (ISMTE), and National Information Standards Organization (NISO). The journal also is in conformity with the Principles of Transparency and Best Practice in Scholarly Publishing (https://doaj.org/apply/transparency/).

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- Turkish (if the article is sent from Turkey) and English title of the article.

- Turkish (if the article is sent from Turkey) and English short title of the article, not exceeding 50 characters.

- Authors' names, institutions and ORCID IDs.

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- Line breaks must be double spaced type.

- At least 2.5 cm margins must be left on all sides of each page.

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- If there is, table should be in the main text.

- All references, tables and figures should be cited in the main text and numbered according to the order they appear in the main text.

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- The limitations of the original articles should be declared in the Discussion section before the conclusion paragraph.

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The main text should contain the following sections in order:

### Abstract

Original articles and review articles should be a maximum of 300 words and structured (Objective, Methods, Results, Conclusion). Case reports should have a maximum of 200 words and be unstructured. If the article is sent from Turkey, Turkish abstract should be sent (Amaç, Gerecler ve Yöntemler, Bulgular, Sonuc).

### **Keywords**

4 to 6 keywords, can be used for indexing purposes should be provided. Keywords should be selected from Medical Subject Headings (MeSH) databases prepared by the National Library of Medicine (NLM).

What is Medical Subject Headings (MeSH)? <u>http://</u><u>www.nlm.nih.gov/mesh/MBrowser.html</u> is a wide range of medical-biological terms list used for the classification of articles in main international article search directories and databases, aimed to standardize medical-biological terminology and updated continuously, from which keywords of English articles can be chosen.



### Manuscript

Original Article: It is the most crucial article type since it provides new data based on original research. The main text should be structured with the subtitles of Introduction, Materials and Methods, Results, Discussion, and Conclusion.

Statistical analysis is often required to support the results. It should be done according to international statistical reporting standards. Information on statistical analysis should be given under a separate subtitle under the Material and Methods section, and the statistical methods applied during the process should be specified.

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Case Report: Rare cases, situations that pose difficulties in diagnosis and treatment, cases that offer new treatments or reveal information not included in the literature are considered. The main text should contain the subtitles Introduction, Case Presentation, and Discussion.

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Ethics committee approval is required in accordance with the National Ulakbim TR Index criteria for research/ original article studies using patients' data, even if they are retrospective, and this approval document should be attached when submitting the article (For more information: https://grandjournalofurology.com/static.php?id=32).

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[1], [3-5], [6,9], [8-12,16].

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[1] Guner E, Seker KG, Arikan Y, Huseynov C, Sam E, Ozdal OL. Aktuelle Urol. 2020; 51: 285-289. https:// doi.org/10.1055/a-1117-2776.

- Article with more than six authors

[2] Karabulut D, Karabulut U, Caglar FN, Ekşi M, Yenice MG, Guner E, et al. The association between CHA2DS2-VASc score and erectile dysfunction: a cross-sectional study. Int Braz J Urol. 2019; 45: 1204-1208. https://doi.org/10.1590 / S1677-5538. IBJU.2019.0058.

- Book

[3] Sweetman SC. Martindale the Complete Drug Reference. 34th ed. London: Pharmaceutical Press; 2005.

- Book chapter

[4] McKenna K. Ejaculation. In: Knobil E, Neil J, editors. Encyclopedia of Reproduction, New York: Academic Press; 1999, p. 1002-8.

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Peer review is an integral part of scientific publishing that confirms the validity of the manuscript. Independent researchers in the relevant research area assess submitted manuscripts for originality, validity, and significance to help editors determine whether a manuscript should be



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After receipt of the article through the electronic submission system, it will be considered by Assistant Editor. The texts will be checked in terms of accordance with Journal's Instructions for Authors format and plagiarism by using iThenticate similarity Check system for identifying. After the first check, the Assistant Editor will forward the relevant articles to the Editorin-Chief. The Editor-in-Chief will check the article in terms of Journal's scope, style and format, originality, and scientific quality. Each manuscript will be sent to at least two external, independent reviewers who are experts in their fields by the Editor-in-Chief/Associate Editors to guarantee a double-blind evaluation process. Evaluating the articles in a short period of 4-6 weeks by the referees and sending feedback to the authors is a policy considered by the journal for the fast publication process.

We are applying the same steps to the doubleblind peer-review process when we got the in-house submission.

### Revision

When sending a revised version of an article, a response to reviewers letter should be sent to in which all the criticisms put forward by the referees are evaluated and commented individually. Simultaneously, the changes made should be specified in the text by marking them in red. An article must be re-submitted within 30 days of being sent to the author(s) for revision. If the author (s) think that additional time is required, they must demand this extension before the first 30 days expires.

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# SURNAL OF

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### Editorial

### Editorial

Dear colleagues,

I am honored to share with you the first issue of 2025 (volume 5, issue 1) of the Grand Journal of Urology (Grand J Urol) with the contributions of many respected researchers and authors.

Grand Journal of Urology (GJU) aims to carry written and visualscientific urology studies to academic platforms and to make significant contributions to the science of urology. Our journal has been abstracted/indexed in Tubitak Ulakbim TR Index, EBSCOhost, J-Gate, SciLit, ResearchGate and Google Scholar international databases. As of these achievements, the Grand Journal of Urology (GJU) has taken its place among the journals indexed by national and international databases. In this issue of our journal, there are many valuable articles under the subheadings of Andrology, Endourology, Female Urology, Pediatric Urology and Urological Oncology. I hope that these carefully prepared articles will make important contributions to valuable readers, researchers and the urology literature.

On this occasion, I would like to express my heartfelt gratitude to our authors who have contributed to our journal with their articles, to our reviewers who have meticulously evaluate the articles.

Respectfully yours January 2025 Assoc. Prof. Ekrem GUNER, MD Editor-in-Chief



### Exploring the Link Between Diagonal Earlobe Crease (Frank's Sign) and the Severity of Erectile Dysfunction

Diagonal Kulak Memesi Kıvrımı (Frank Belirtisi) ile Sertleşme Bozukluğu Şiddeti Arasındaki İlişkinin Araştırılması

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### Abstract

**Objective:** To investigate the relationship between Frank's sign (FS), a diagonal fold of the earlobe, and the severity of erectile dysfunction (ED), focusing on FS as a potential prognostic marker for ED, particularly its vascular components.

**Materials and Methods:** A prospective study was conducted on 114 male patients aged 18-80 years at the Andrology Clinic of Haydarpaşa Numune SUAM. Participants were stratified according to International Index of Erectile Function-5 (IIEF-5) scores. FS presence, body mass index (BMI), lipid profiles and inflammatory markers (NLR, PLR) were recorded. Statistical analyses assessed the association between FS, ED severity and cardiovascular risk factors.

**Results:** A significant correlation was found between FS and ED severity, especially for bilateral FS (p=0.000). Patients with FS had higher BMI and LDL levels, indicating a strong association with cardiovascular risk factors. Atherogenic index and PLR were also significantly associated with ED (p=0.018, p=0.003).

**Conclusion:** FS, especially bilateral FS, is closely associated with ED severity and its vascular pathology, suggesting its potential use as a prognostic marker in the evaluation of ED. Further research is needed to confirm these findings and to explore the integration of FS into clinical practice.

Keywords: Frank's sign, erectile dysfunction, cardiovascular risk factors

### Özet

Amaç: Kulak memesindeki diagonal kıvrım olan Frank belirtisi (FB) ile erektil disfonksiyon (ED) şiddeti arasındaki ilişkiyi araştırmak, özellikle de FB'nin ED'nin vasküler bileşenleri için olası bir prognostik belirteç olarak kullanımını değerlendirmek.

Gereçler ve Yöntemler: Haydarpaşa Numune SUAM Androloji Kliniği'nde 18-80 yaş aralığındaki 114 erkek hasta üzerinde prospektif bir çalışma yapıldı. Katılımcılar, Uluslararası Erektil Fonksiyon İndeksi-5 (IIEF-5) skorlarına göre sınıflandırıldı. FB varlığı, beden kitle indeksi (BKİ), lipid profilleri ve inflamatuar belirteçler (NLR, PLR) kaydedildi. İstatistiksel analizler, FB, ED şiddeti ve kardiyovasküler risk faktörleri arasındaki ilişkiyi değerlendirdi.

**Bulgular:** FB ile ED şiddeti arasında, özellikle bilateral FB'de anlamlı bir ilişki bulundu (p=0.000). FB olan hastaların daha yüksek BKİ ve LDL seviyelerine sahip olduğu gözlendi, bu da kardiyovasküler risk faktörleriyle güçlü bir ilişki olduğunu gösterdi. Aterojenik indeks ve PLR de ED ile anlamlı şekilde ilişkiliydi (p=0.018, p=0.003).

**Sonuç:** FB, özellikle bilateral FB, ED şiddeti ve vasküler patolojisi ile yakından ilişkilidir ve ED'nin değerlendirilmesinde prognostik bir belirteç olarak kullanılma potansiyeline sahiptir. Bu bulguların doğrulanması ve FB'nin klinik uygulamaya entegrasyonu için daha fazla araştırmaya ihtiyaç vardır.

Anahtar kelimeler: Frank belirtisi, erektil disfonksiyon, kardiyovasküler risk faktörleri

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### Introduction

Erectile dysfunction (ED) is a multifactorial disorder that is common in men and has a significant impact on quality of life. Its pathophysiology is complex and includes neurogenic, psychogenic, endocrine and, most importantly, vascular components [1,2]. Vascular aetiologies have led to ED being frequently recognised as an early sign of cardiovascular disease (CVD). In this context, it has been suggested that ED may act as a subclinical indicator of CVD [2]. There is increasing evidence in the literature of the effects of inflammation and oxidative stress on erectile function. The study by Roumeguere et al. shows that elevated levels of IL-18 and myeloperoxidase-dependent oxidised LDL in the corpus cavernosum impair endothelial function by inhibiting e-NOS mRNA expression. These findings support the critical role of inflammation and oxidative stress in the pathophysiology of ED [3].

Frank's sign (FS), defined by Sanders T. Frank in 1973, is known as a diagonal fold in the earlobe and has been reported in the literature as a physical marker of cardiovascular disease [4]. This marker has attracted attention because of its association with coronary artery disease and other atherosclerotic conditions. Several studies have shown that FS is associated with endothelial dysfunction, inflammation and oxidative stress [5]; endothelial dysfunction and inflammation are factors that play a critical role in the pathogenesis of atherosclerosis and are among the basic pathophysiological mechanisms of ED. Metabolic syndrome is a cardiometabolic disorder consisting of components such as abdominal obesity, hypertension, dyslipidaemia and insulin resistance, and is strongly associated with ED [6].

The fact that FS is associated with these components of the metabolic syndrome raises the question of the usefulness of this physical marker in predicting ED. It has been reported in the literature that FS impairs endothelial function as an indicator of inflammation and oxidative stress in the vessel wall. Therefore, it is thought that FS may be a predisposing factor that may predispose to the development of ED. Indeed, the fact that ED and CVD share common risk factors makes it necessary to investigate the prognostic value of FS [6,7].

The aim of this article is to review the potential role of FS in the prediction of ED and its use in clinical practice. A comprehensive review of the existing literature will assess the relationship between FS and ED and CVD, its prognostic value and its place in clinical practice. This evaluation should contribute to the development of new approaches to the use of FS in the diagnosis and management of ED.

### **Matherials and Methods**

Our study, which was approved by the Haydarpaşa Numune Training and Research Hospital Clinical Research Ethics Committee on 19 June 2023 with decision number HNEAH-KAEK 2023/128, is a prospective study. Written informed consent was obtained from all participants. Men aged 18-80 years with ED as defined by the International Index of Erectile Function-5 (IIEF-5), scoring less than 22 points and with normal hormonal parameters were enrolled in the study between 1 May 2023 and 23 July 2023 at the SBU Haydarpaşa Numune SUAM Andrology Clinic. As a control group, 33 patients were enrolled who had no complaints of ED or scored 22 points and above on the IIEF-5 and who met other inclusion criteria. Exclusion criteria included men with ED secondary to hormonal deficiency, those under 18 or over 80 years of age, and those who were unwilling to consent or unable to communicate effectively.

Each participant underwent a comprehensive physical examination and a detailed medical history was taken. Height, weight, body mass index (BMI), presence of diabetes mellitus (DM), and whether FS was unilateral or bilateral were recorded. Laboratory tests were performed on the morning after the clinic visit on an empty stomach, including glucose, lipid profile and complete blood count. Based on IIEF-5 scoring, patients were classified as having severe ED (scores 5-7), moderate ED (scores 8-11), mild-moderate ED (scores 12-16), mild ED (scores 12-1), and normal (scores 22-25). The neutrophil/lymphocyte and platelet/lymphocyte ratios, atherogenic index (LDL/HDL) and coronary risk index (total cholesterol/HDL) were calculated and recorded from the hemogram and lipid profile.

### Statistical Analysis

SPSS 25.0 (IBM, NY, USA) was used for statistical analysis. Normality tests were assessed using the Kolmogorov-Smirnov test. Descriptive statistical methods (mean, standard deviation, frequency, ratio, percentage) were used to evaluate the study data. Mann-Whitney U test and chi-squared test were used for paired groups. Statistically significant p-value was defined as <0.05.

### Results

Our study included 114 male patients, of whom 81 (71%) had ED complaints and 33 (29%) did not. FS was present in 57 of our patients and there was no FS in 57 of our patients. The age range of our patients was  $52.36\pm10.87$  years. The IIEF-5 score of our patients with ED was minimum 6 and maximum 21 (15.74±3.10).

The mean age was  $52.22 \pm 10.66$  years in patients with ED and  $52.72 \pm 11.53$  years in patients without ED; there was no statistically significant difference in age between the two groups (p=0.743). The mean BMI of patients with ED was  $29.03 \pm 4.90$ , whereas the mean BMI of patients without ED was  $26.19 \pm 3.66$ . This difference was statistically significant (p=0.002). It shows that patients with ED had a higher BMI (**Table 1**).

When the lipid profile of our patients was evaluated, the VLDL values were  $34.25 \pm 22.45 \text{ mg/dL}$  in patients with ED and  $39.34 \pm 18.96 \text{ mg/dL}$  in patients without ED. This difference was not statistically significant (p=0.072). LDL levels were  $128.48 \pm 68.49 \text{ mg/dL}$  in patients with ED and  $96 \pm 32.81 \text{ mg/dL}$  in patients without ED, and this difference in LDL levels was statistically significant (p=0.007). HDL levels were  $45.30 \pm 17.46 \text{ mg/dL}$  in patients with ED and  $49.30 \pm 20.86 \text{ mg/dL}$  in patients without ED and this difference was not statistically significant (p=0.373). The mean triglyceride level was  $175.86 \pm 123.86 \text{ mg/dL}$  in patients with ED and  $196.72 \pm 94.80 \text{ mg/dL}$  in patients without ED and this difference was not statistically significant (p=0.053). Patients with ED had a total cholesterol level of  $190.58 \pm 36.69 \text{ mg/dL}$  and patients without ED had a total cholesterol level of  $183 \pm 38.42 \text{ mg/dL}$ . The difference in

	ED (n:81)	Non-ED (n:33)	Р
Age	52.22±10.66	52.72±11.53	0.743*
BMI	29.03±4.90	26.19±3.66	0.002*
VLDL	34.25±22.45	39.34±18.96	0.072*
LDL	128.48±68.49	96±32.81	0.007*
HDL	45.30±17.46	49.30±20.86	0.373*
Trigliserid	175.86±123.86	196.72±94.80	0.053*
Total Kolesterol	190.58±36.69	183±38.42	0.219*
Coronary Risk Index	4.56±1.53	4.23±1.65	0.193*
Aterojenik Risk Index	3.19±2.54	2.29±1.07	0.018*
NLR	1.95±0.74	1.93±0.66	0.536*
PLR	107.20±35.84	125.27±32.72	0.003*

**Table 1.** Demographic characteristics of patients non-ED and ED

 Table 3. The relationship between frank's sign

\*\*: Chi-Square test

frank's sign and ED

ED

Non-ED

subgroup presence and ED						
	Frank's					
	Frank's Sign (-)	Unilateral	Bilateral	P**		
ED	31 (%54.3)	13 (%65)	37 (%100)	0.000		
Non-ED	26 (%45.7)	7 (%35)	0			
	57 (%100)	20 (%100)	37 (%100)			

Table 2. The relationship between the presence of

Frank's Sign (+)

50 (%87.7)

7 (%12.3)

57 (%100)

1 00

P\*\*

0.000

Frank's Sign (-)

31 (%54.3)

26 (%45.7)

57 (%100)

\*\*: Chi-Square test

**Table 4.** The relationship between the presence of frank's sign and ED subgroup

	Frank's Sign (+)	Frank's Sign (-)	P**
Severe	1 (%1.7)	1 (%1.7)	0.000
Moderate	5 (%8.7)	0 (%0)	
Mild to moderate	27 (%47.4)	8 (%14)	
Mild	17 (%29.8)	22 (%38.6)	
No ED	7 (%12.4)	26 (%45.7)	
	57 (%100)	57 (%100)	

\*\*: Chi-Square test

	Frank's	up		
	Frank's Sign (-)	P**		
Severe	1 (%1.7)	0 (%0)	1 (%2.7)	0.000
Moderate	0 (%0)	0 (%0)	5 (%13.5)	
Mild to Moderate	8(%14)	4 (%20)	23 (%62.2)	
Mild	22 (%38.1)	9 (%45)	8(%21.6)	
No ED	26(%45.7)	7 (%35)	0 (%0)	
	57 (%100)	20 (%100)	37 (%100)	

**Table 5.** The relationship between the presenceof frank's sign subgroup and ED subgroup

\*\*: Chi-Square test

\*: Mann-Whitney U Test

cholesterol levels was not significant (p=0.219) (Table 1).

When the relationship between Coronary Risk Index (CRI) and Atherogenic Risk Index and ED was evaluated, the mean values were  $4.56 \pm 1.53$  and  $3.19 \pm 2.54$  in patients with ED and  $4.23 \pm 1.65$  and  $2.29 \pm 1.07$  in patients without ED, respectively. Although no statistically significant correlation was found between CRI and ED, a statistically significant correlation was found between Atherogenic Index and ED (p=0.193, p=0.018) (Table 1).

When the relationship between neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR), which are inflammatory biomarkers, and ED was evaluated, NLR was found to be  $1.95 \pm 0.74$  and PLR was  $107.20 \pm 35.84$  in patients with ED. In patients without ED, NLR was  $1.93 \pm 0.66$  and PLR was  $125.27 \pm 32.72$ . Although the relationship between NLR and ED was not statistically significant, the relationship between PLR and ED was statistically significant (p=0.536, p=0.003) (Table 1).

When the relationship between FS and ED was evaluated, 87.7% of patients with FS had ED complaints, but 45.7% of patients without FS did not have ED complaints. There is a statistically significant relationship between the presence of FS and ED (p=0.000) (Table 2).

When the relationship between FS subgroups and ED was evaluated, 22.8% of patients had ED in the unilateral presence of FS, whereas all patients had ED complaints in the bilateral presence. There is statistical significance between FS subgroup analysis and ED (p=0.000) (Table 3).

When FS and ED subgroup analysis was evaluated, 45.7% of patients without FS had no ED complaint and 29.8% of patients with FS had mild ED, 47.4% had mild-moderate ED, 8.7% had moderate ED and 1.7% had severe ED. The relationship between the severity of ED in patients with FS was statistically significant (p=0.000) (**Table 4**).

When analysing the FS subgroup and the ED subgroup, it was observed that ED was more severe in patients with bilateral FS than unilateral (p=0.000) (**Table 5**) (**Figure 1**).

### Discussion

Our study is one of the first to investigate the relationship between FS and ED, and to examine in detail the link between this physical marker and the vascular component of ED. FS was first described by Sanders T. Frank in 1973 and has been associated with coronary artery disease (CAD) and other atherosclerotic conditions. FS has been accepted in the literature as a physical marker of cardiovascular disease, making the association of FS with vascular pathologies such as ED even more significant [4,8]. When the association of FS findings with the presence of chronic diseases in healthy young Turkish population and first degree relatives was evaluated, it was observed that chronic diseases including CAD, cerebrovascular disease and peripheral vascular disease were observed in first degree relatives of patients with Frank's sign findings [9].

Stoyanov et al., in their autopsy study, arterial fibrosis in the myocardium and fibrosis in deep tissues and nerves were observed in patients with Frank's sign, and it has been accepted as an indicator of vascular and neuronal dysfunction [10]. However, the association of FS with endothelial dysfunction and vascular inflammation plays an important role in understanding the mechanisms underlying the strong association of this physical marker with ED. When the relationship between FS and CAD was evaluated by Wang et al, more severe vessel obstruction was observed on coronary angiography in patients with bilateral FS findings (OR, 5.690; 95% CI (3.4-9.3),  $p \le 0.001$ ) [11]. In line with our hypothesis, our study found a significant correlation between the presence of ED in patients with FS and its severity in bilateral cases.

There is a significant association between ED and metabolic syndrome. In recent years, an increased likelihood of ED has been reported in patients with metabolic syndrome [6]. Çulha et al., in the study evaluating the relationship between atherogenic index and ED, a significant correlation was found between ED and high atherogenic index, but no significant correlation was found between BMI and LDL levels [12]. Similarly, in our study, a significant correlation was found between the level of atherogenic index and ED, but a significant correlation was also found between BMI and LDL levels and ED.

The effect of haematological parameters on acute and chronic inflammation has recently been the subject of much debate. It has been observed that the value of haematological parameters in predicting CVD and ED may be similarly influenced by inflammation. Liao et al., in the study in which they evaluated the relationship between haematological parameters and cholesterol metabolism and ED, a statistically significant correlation was found between LDL, NLR, PLR values and ED, and a negative correlation was found with BMI [13]. In our study, a statistically significant correlation was observed between high LDL and PLR levels and ED.

This relationship between FS and ED severity may have important applications in clinical practice. In particular, the bilateral presence of FS may indicate conditions in which the vascular component of ED is more severe, and in these cases patients may need to be monitored more closely. In addition, the presence of FS may be used as an additional tool to determine the risk of CVD in individuals diagnosed with ED. This may help in the development of early diagnosis and treatment strategies to prevent vascular complications of ED.



**Figure 1.** The relationship between the presence of frank's sign subgroup and ED subgroup

### Conclusion

The presence of FS, especially in bilateral cases, shows a significant correlation with the severity of ED and the underlying vascular pathophysiology. The results of our study suggest that FS may be considered as a potential prognostic marker in the diagnosis and management of ED. Although the limitations of the study include the small sample size and singlecentre design, it should be noted that these factors do not fully affect the clinical validity of our findings and provide important contributions to the existing literature. In addition, the lack of control for lifestyle factors such as smoking and physical activity are limitations that should be taken into account when considering the generalisability of the results. However, even with these limitations, it is believed that this study provides a valuable perspective on the clinical potential of FS in the diagnosis and treatment of ED.

**Ethics Committee Approval**: Ethical approval for this study was obtained from Haydarpaşa Numune Training and Research Hospital Clinical Research Ethics Committee (Approval number: HNEAH-KAEK 2023/128, Date: 19 June 2023).

**Informed Consent:** An informed consent was obtained from all the patients.

**Publication:** The results of the study were not published in full or in part in form of abstracts.

Peer-review: Externally peer-reviewed.

Authorship Contributions: Any contribution was not made by any individual not listed as an author. Concept – R.K., E.T.; Design – R.K., E.T.; Supervision – R.K., M.İ.Ö.; Resources – Ö.Y., İ.A.; Materials – Ö.Y., İ.A.; Data Collection and/or Processing – R.K., E.T.; Analysis and/or Interpretation – R.K., E.T.; Literature Search – Ö.Y., İ.A.; Writing Manuscript – R.K., E.T.; Critical Review – R.K., M.İ.Ö.

**Conflict of Interest:** The authors declare that they have no conflicts of interest.

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### Mean Monocyte Count Predicts Testicular Salvage in Children with Testicular Torsion

Ortalama Monosit Sayısı Çocuklarda Testis Torsiyonunda Testisin Kurtarılmasını Öngörüyor

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### Abstract

**Objective:** This study aimed to investigate hematological parameters and related factors predicting testicular salvage in patients diagnosed with testicular torsion in children.

**Materials and Methods:** The data of 86 patients under the age of 18 years, who underwent emergency scrotal exploration for testicular torsion between January 2013 and December 2019, were retrospectively analyzed. The patients were divided into two groups as Group 1 (Successful Salvage - Detorsion: 63 patients), and Group 2 (Failed Salvage - Orchiectomy: 23 patients). Demographic data, clinical features, laboratory tests and radiological examinations were evaluated.

**Results:** The mean age was  $13.7 \pm 3.3$  years (Group 1:  $13.50 \pm 3.84$ , Group 2:  $14.47 \pm 1.64$  years). The duration of symptoms was significantly higher in Group 2 ( $5.12 \pm 2.54$  vs.  $15.08 \pm 6.30$  hours, p<0.001). Among the hematological parameters, the mean monocyte count was statistically significantly higher in Group 2 than in Group 1 (Group 1:  $0.62 \pm 0.27$ , Group 2:  $0.99 \pm 0.51$  103 µ/L, p: 0.001). Multivariate analysis showed that the duration of symptoms and monocyte count were independent risk factors in predicting testicular salvage. (p < 0.001, p = 0.042, respectively) **Conclusion:** This study shows that the mean monocyte count, in addition to the duration of symptoms, is a simple hematological parameter that can contribute to the prediction of testicular salvage in children with testicular torsion.

Keywords: testicular torsion, testicular fixation, orchiectomy, monocytes, salvage, viability.

### Özet

Amaç: Bu çalışmada, çocuklarda testis torsiyonu tanısı almış hastalarda testisin kurtarılmasını öngören hematolojik parametreler ve ilgili faktörler araştırıldı.

Gereçler ve Yöntemler: Ocak 2013 ile Aralık 2019 arasında testis torsiyonu nedeniyle acil skrotal eksplorasyon uygulanan 18 yaş altı 86 hastanın verileri retrospektif olarak analiz edildi. Hastalar Grup 1 (Başarılı Kurtarma - Detorsiyon: 63 hasta) ve Grup 2 (Başarısız Kurtarma - Orşiektomi: 23 hasta) olmak üzere iki gruba ayrıldı. Demografik veriler, klinik özellikler, laboratuvar testleri ve radyolojik incelemeler değerlendirildi.

**Bulgular:** Ortalama yaş 13,7 ± 3,3 yıldı (Grup 1: 13,50 ± 3,84, Grup 2: 14,47 ± 1,64 yıl). Semptomların süresi Grup 2'de anlamlı olarak daha yüksekti ( $5.12 \pm 2.54$  vs. 15.08 ± 6.30 saat, p<0.001). Hematolojik parametreler arasında, ortalama monosit sayısı Grup 2'de Grup 1'den istatistiksel olarak anlamlı şekilde daha yüksekti (Grup 1: 0.62 ± 0.27, Grup 2: 0.99 ± 0.51 103 µ/L, p: 0.001). Çok değişkenli analiz, semptomların süresi ve monosit sayısının testis kurtarmayı tahmin etmede bağımsız risk faktörleri olduğunu gösterdi. (sırasıyla p < 0.001, p = 0.042)

**Sonuç:** Bu çalışma, semptomların süresine ek olarak ortalama monosit sayısının testis torsiyonu olan çocuklarda testis kurtarmayı tahmin etmeye katkıda bulunabilecek basit bir hematolojik parametre olduğunu göstermektedir.

Anahtar kelimeler: testis torsiyonu, testis fiksasyonu, orşiektomi, monosit, kurtarma, yaşayabilirlik.

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### Introduction

Testicular torsion is a urological emergency requiring urgent diagnosis and treatment which may lead to organ loss as a result of gonadal necrosis and may cause infertility problems in the future. Although it is observed in all age groups, it is more common in children [1].

The main treatment of testicular torsion is emergency surgery and the decision of detorsion and testicular fixation or orchiectomy is made during surgery. In the absence of objective criteria for assessing testicular viability, the fate of the testis is entirely at the discretion and experience of the surgeon. There are a limited number of parameters that can be used to predict preoperative testicular salvage. The most important factor known to predict testicular salvage is the duration of symptoms. As reported in the literature, irreversible testicular loss begins after the first 6 hours [2].

In recent years, there have been many studies evaluating hematological parameters in the differential diagnosis of testicular torsion [3]. However, only a limited number of studies have investigated the role of hematological parameters in predicting the possibility of preoperative testicular viability/ orchiectomy. The results are conflicting and there is still no consensus. In addition, most of these studies include the adult age group [4-9].

In this study, we investigated the role of preoperative hematological parameters in predicting testicular salvage in children undergoing emergency scrotal exploration for testicular torsion.

### **Materials and Methods**

After obtaining local ethics committee approval (Decision no: 2020/482), the medical records of 131 patients operated on for testicular torsion between January 2013 and December 2019 were retrospectively reviewed. 86 patients under 18 years of age with complete medical records were included in the study. Exclusion criteria: Patients who underwent manual detorsion, patients over 18 years of age, missing study data, liver dysfunction, renal dysfunction, hematological diseases, inflammatory diseases and known malignancy. Demographic data (age), clinical characteristics (duration of symptoms, place of presentation, time of presentation, season of presentation), complete blood count (CBC), radiological parameters (scrotal color Doppler ultrasonography [CDUS]), and operative results (viability, degree of torsion) were analyzed.

Complete blood counts were obtained using a hematology analyzer (Coulter Gen-S Haematology Analyser; Beckman Coulter Corp, Hialeah, FL, USA). Hematological parameters included white blood cell (WBC), neutrophil, lymphocyte, monocyte, eosinophil, basophil, platelet count (PLT), mean platelet volume (MPV) and mean corpuscular volume (MCV). Neutrophil-tolymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) were calculated by dividing neutrophil count by lymphocyte count and platelet count by lymphocyte count, respectively. All patients underwent scrotal CDUS before surgery.

All patients were taken to emergency surgery. After determining the type and degree of testicular torsion during scrotal exploration, the testes were detorsioned and rewarmed with warm saline for more than 10 minutes. For testicular viability, a three-step bleeding test was performed as recommended by Arda and Özyaylalı [10]. According to the results of the bleeding test, orchiectomy or detorsion-testicular fixation was decided. All testes removed after orchiectomy were subjected to histopathological examination for final confirmation. Tissue necrosis was confirmed in all patients. Patients who underwent successful salvage - detorsion were defined as Group 1 and patients who underwent failed salvageorchiectomy were defined as Group 2.

The parameters determined between the two groups were compared. The primary aim of this study was to determine the role of preoperative hematological parameters in predicting testicular salvage in patients undergoing emergency surgery for testicular torsion. The secondary aim was to investigate the factors influencing the prediction of testicular salvage.

### Statistical Analysis

Categorical data were presented as percentages and numbers. For continuous variables, data were presented as mean and standard deviation. The normality of the distribution of continuous variables was assessed using the Shapiro-Wilk test. Means of two normally distributed groups were compared using the Student t-test. The Mann-Whitney U test was used when they were not normally distributed. Frequencies of categorical variables were compared using the Pearson chi-square test or Fisher's exact test. Statistical significance was accepted at P<0.05. Univariable and multivariable logistic regression tests were used to determine factors predicting testicular salvage. Receiver operating characteristic (ROC) curve analysis was performed to determine cut-off values and areas under the curve (AUC) for the variables. Statistical analysis was performed using the Statistical Package of Social Sciences version 21 (IBM SPSS Statistics; IBM Corp., Armonk, NY).

### Results

The mean age of the patients was  $13.7 \pm 3.3$  years and the age range was 2-18 years. Age, degree of torsion, place of presentation, time of presentation, season of presentation and scrotal CDUS results were not significantly different between the groups (p > 0.05). There was a statistically significant difference in the duration of symptoms between the two groups (group 1:  $5.12 \pm 2.54$ , group 2:  $15.08 \pm 6.30$  hours, p < 0.001). Although mean WBC, neutrophil, lymphocyte, platelet, and hemoglobin levels were higher in Group 2, no statistically significant difference was found (p>0.05). The mean monocyte count was statistically significantly higher in Group 2 than in Group 1 (group 1: 0.62  $\pm$  0.27, group 2: 0.99  $\pm$  0.51  $\mu/L$ , p: 0.001). Although the mean MCV, MPV, NLR, and PLR were higher in Group 1 than in Group 2, no statistically significant difference was found (p > 0.05). The results of the comparisons between groups are shown in Table 1.

Univariate analysis showed that testicular salvage was associated with the duration of symptoms and monocyte count. Multivariate analysis showed that monocyte count (OR = 4.308, P = 0.042) and symptom duration (odds ratio [OR] = 1.052, P < 0.001) were independent risk factors for testicular salvage (**Table 2**). The monocyte count was significantly lower in the successful salvage group than in the failed salvage group (P < 0.01).

Table 1. Comparison	of patient characteristics an	nd haematological	parameters between groups
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Variables	Group 1 (Successful Salvage-detorsion)	Group 2 (Failed salvage- orchiectomy)	P value
Number of patients	63	23	
Mean age $\pm$ SD, year	13.50 ± 3.84	14.47 ± 1.64	0.685¥
Duration of symptoms, hour	$5.12 \pm 2.54$	$15.08 \pm 6.30$	<0.001¥
Torsion degree	513 ± 182	592 ± 149	0.070*
Mean WBC count $\pm$ SD, $10^3 \mu/L$	11.91 ± 4.16	13.06 ± 4.88	0.283*
Mean Neutrophil count $\pm$ SD, $\mu/L$	8.99 ± 3.88	$9.83 \pm 4.77$	0.417*
Mean Lymphocye count $\pm$ SD, $\mu/L$	$1.92 \pm 0.74$	$2.00 \pm 1.61$	0.818*
Mean Monocyte count $\pm$ SD, $\mu/L$	$0.62 \pm 0.27$	$0.99 \pm 0.51$	0.001¥
Mean PLT count $\pm$ SD,10 <sup>3</sup> $\mu$ /L	285 ± 70	301 ± 57	0.320*
Mean Hemoglobin count $\pm$ SD, g/dL	$14.0 \pm 1.56$	$14.3 \pm 1.34$	0.376*
Mean MCV count ± SD,fL	83.1 ± 6.6	82.9 ± 5.2	0.904*
Mean MPV count ± SD,fL	8.25 ± 1.34	8.21 ± 1.27	0.923*
Mean NLR count ± SD	$7.09 \pm 5.31$	5.0 ± 3.94	0.099*
Mean PLR count ± SD	$210 \pm 145$	$179 \pm 74$	0.904¥
Admission place Emergency department Urology clinic	59 (96.7) 2 (3.3)	21 (91.3) 2 (8.7)	0.301&
Admission date Weekdays Weekend	46 (75.4) 15 (24.6)	20 (87) 3 (13)	0.250#
Admission season Spring Summer Autumn Winter	18 (29.5) 9 (14.8) 13 (21.3) 21 (34.4)	6 (26.1) 1 (4.3) 8 (34.8) 8 (34.8)	0.423#
Scrotal CDUS No blood flow Equal Decreased	51 (83.6) 4 (6.6) 6 (9.8)	21 (91.3) 0 (0.0) 2 (8.7)	0.657&

SD: standart deviation; WBC: white blood cell; PLT: platelet; MCV: mean corpuscular volume; MPV: mean platelet volume; NLR: neutrophil-to-lymphocyte ratio; PLR: platelet-to-lymphocyte ratio; CDUS: colour Doppler ultrasonography; \*Indipendent T test; #Yates' Chi-Square; ¥ Mann-Whitney U test; & Fisher's Exact Test

The prediction of preoperative testicular salvage by duration of symptoms and monocyte count was further evaluated using the ROC curve. According to the ROC analysis, the best cut-off point for the duration of symptoms was 7.5 hours (sensitivity 100%, specificity 80.6%, area under the curve (AUC) 0.968, p: < 0.001, 95% confidence interval 0.938-0.999), the best cut-off point for monocyte count was 0.82  $\mu$ /L (sensitivity 59.1%, specificity 74.1%, AUC: 0.672, p = 0.018, 95% confidence interval 0.533-0.812) (**Table 3**.) The ROC analysis of these parameters is shown in **Figure 1**.

### Discussion

Testicular torsion is a urological emergency with adverse outcomes such as orchiectomy. Studies show that initial misdiagnosis, degree of torsion, ischemia time and sonographic findings are predictors of testicular salvage [11-14]. In addition to anamnesis, physical examination, clinical features and radiological findings, simple hematological parameters have been investigated in limited studies to determine testicular salvage. Most of these studies have included adult populations.

Table 2.	To predict	preoperative	testicular salvag	ge univariable a	nd multivariable bin	ary logistic	regression analysis
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		Univariable	ble Multivariable			
	OR	95% CI	P value	OR	95% CI	P value
Age (year)	1.102	0.934-1.301	0.250			
Duration of symptom (hour)	1.051	1.028-1.075	<0.001	1.052	1.028-1.077	<0.001
Torsion degree	1.003	1.000-1.006	0.074			
WBC count	1.000	1.000-1.000	0.282			
Neutrophil count	1.051	0.934-1.182	0.413			
Lymphocyte count	0.957	0.663-1.381	0.815			
Monocyte count	4.574	1.293-16.176	0.018	4.308	0.804-23.091	0.042
PLT count	1.004	0.996-1.011	0.318			
Hemoglobin	1.175	0.824-1.675	0.372			
MCV	0.995	0.920-1.076	0.903			
MPV	0.981	0.674-1.429	0.922			
NLR	0.910	0.812-1.020	0.104			
PLR	0.998	0.994-1.002	0.346			
Admission (Urology clinic)	2.810	0.372-21.227	0.317			
Admission (weekdays)	2.174	0.566-8.354	0.258			
Admission seasonal	1.127	0.757-1.679	0.556			
Scrotal CDUS (No blood flow)	2.059	0.415-10.207	0.377			

OR: oddsratio; CI: confidence; WBC: white blood cell; PLT: platelet; MCV: mean corpuscular volume; MPV: mean platelet volume; NLR: neutrophil-to-lymphocyte ratio, PLR: platelet-to-lymphocyte ratio; USG: ultrasonography

Table 3. ROC curve analysis of duration and monocyte count for testicular salvage

	AUC	95% CI	P-value	Cut of value	Sensitivity - specificity
Variables					
Duration	0.968	0.938-0.999	<0.001	7.5	% 100 - % 80.6
Monocyte count ( $\mu$ /L)	0.672	0.533-0.812	0.018	0.82	% 59.1- % 74.1

ROC: receiver operating characteristic; AUC: area under the curve; CI: confidence interval

Our study was conducted only in children under 18 years of age. In our study, multivariate analysis for determinants of testicular salvage showed that the duration of symptoms was a significant determinant, similar to previous studies [12,15]. However, among hematological parameters, multivariate analysis showed that only mean monocyte count was a significant determinant. According to the results of our study, in ROC analysis, mean monocyte count was found to be an independent predictive factor in addition to symptom duration in predicting testicular salvage.

Our study is consistent with the results of the study conducted by Merder et al. on pediatric and adult patients [4]. In

this study, data of 88 patients, 61 of whom had orchidopexy and 27 of whom had orchidectomy, were retrospectively analyzed. According to the results of this study, the duration of symptoms and monocyte count were found to be statistically significantly higher in the orchiectomy group [4]. Similarly, in another study, Yılmaz et al. reported that monocyte count, monocyte-to-eosinophil ratio (MER), and C-reactive protein (CRP) levels were found to be statistically higher in the orchiectomy group in patients with testicular torsion, while the only significant variable in multivariate logistic regression analysis for testicular viability was monocyte count [8]. In another study conducted

by Chen et al. only in the pediatric age group, it was reported that monocyte count was an independent predictive factor for testicular salvage [16]. Monocytes are the largest white blood cell type and one of the most basic components of the innate immune system. Approximately 3 -10 % of white blood cells are monocytes. Circulating monocytes and their differentiated forms play an important role in inflammation and have both pro- and anti-inflammatory effects [17]. In addition to the inflammatory response, monocytes play a role in the ischaemic process [18]. In our study, the fact that the mean monocyte count was found to be higher in the orchiectomy group may be interpreted as a result of a longer inflammatory and ischaemic process.

Hematological parameters have been investigated in some studies in the literature due to their cheap, easy and quick results. NLR is a laboratory marker of systemic inflammation and is routinely measured in peripheral blood [19]. In the study by Barkasi et al. in which complete blood count parameters and CRP were evaluated, although NLR, PLR, and CRP levels were found to be high in the orchiectomy group, they did not find a statistically significant relationship with laboratory parameters in predicting testicular viability [9]. Although the duration of symptoms was the most reliable parameter predicting testicular viability in the study by Jang et al., the authors showed that NLR may be useful in predicting testicular viability in patients between 3-12 hours [6]. In our study, except for monocytes among hematological parameters, other parameters and NLR and PLR derived from these parameters did not show a statistically significant difference between both groups.

Another study in the literature reported that the duration of symptoms, the degree of torsion of the spermatic cord and especially the MPV may be predictive of testicular viability in cases of testicular torsion [7]. The authors found that, in patients with testicular torsion, MPV was significantly higher. In another study evaluating the predictive role of MPV, Peretti et al. reported that MPV was a parameter predictive of testicular viability in patients with testicular torsion presenting with symptom duration of less than 6 hours [5]. According to the results of multivariate analyses of another study performed in the pediatric age group, WBC and MPV were shown to be associated with the risk of surgical outcome in addition to the cause of testicular torsion and intervention time [20]. In our series, the duration of symptoms and the degree of testicular torsion were higher in the orchiectomy group and the MPV was lower in contrast to the literature data. Although there was a statistically significant difference in symptom duration, there was no statistically significant difference between the degree of torsion and MPV values.

A recent study of retrospective histopathological examination of viability in cases of testicular torsion concluded that at least 10% of testicular torsion cases undergoing orchiectomy could be salvaged. The authors stated that the duration of symptoms is not a clear predictor of testicular damage and that it is not always correct to decide whether or not to perform orchiectomy based on the subjective macroscopic appearance of the affected testis [21]. Therefore, hematological parameters may help determine viability.

In a 7-year retrospective cohort study of factors predicting testicular viability by analyzing the American Child Health Information System database, orchiectomy was reported in 918 (31.9%) of 2,876 patients operated on with the diagnosis

### ROC Curve



Diagonal segments are produced by ties.

**Figure 1.** Receiver operating characteristic (ROC) curve for testicular salvage

of testicular torsion. The analysis did not show any difference according to season or geographical region. Factors that increased the risk of orchiectomy included age between 1 and 9 years, race, and lack of private insurance [22]. Another study investigating factors predictive of testicular salvage in children reported that the duration of symptoms and degree of torsion predicted testicular salvage on multivariate analysis. In addition, the authors stated that testicular torsion is more common in the winter season and caution should be taken [23]. In our study, there was no statistically significant difference between groups according to age and season.

One of the most important limitations of our study is its retrospective methodology. Secondly, some acute phase reactants such as CRP level, erythrocyte sedimentation rate and procalcitonin level were not included because they are not routinely checked and are expensive. Thirdly, detorsion and orchiectomy were performed by different surgeons with different surgical volumes and experience with testicular torsion. Finally, although our study was a single-center study, this was compensated for by the large sample size.

### Conclusions

This study demonstrated that the mean monocyte count, in addition to the duration of symptoms, is a simple hematological laboratory finding that may contribute to the differentiation of testicular salvage in cases diagnosed with testicular torsion. There is a need for prospective, controlled studies with larger patient series on this subject. Ethics Committee Approval: Ethical approval for this study was obtained from Bakırköy Dr. Sadi Konuk Training and Research Hospital Clinical Research Ethics Committee (Decision no: 2020/482).

**Informed Consent:** An informed consent was obtained from all the patients.

**Publication:** The results of the study were not published in full or in part in form of abstracts.

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### Analysis of 79 Patients with Forgotten Ureteral Stents: 10-Year Experience in a Single Tertiary Care Center Unutulmus Üreteral Stentli 79 Hastanın Analizi:

## Tek Bir Üçüncü Basamak Merkezinin 10 Yıllık Deneyimi

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### Abstract

**Objective:** Double J (DJ) stents are frequently used, especially in urological surgeries, to relieve obstruction and provide urine flow from the kidney to the bladder, to heal the ureter, and to prevent complications. In the literature, it was determined that up to 12% of patients with ureteral stents have forgotten ureteral stents (FUS). In this study, we aimed to present our 10-year experience of FUS treatment.

**Materials and Methods:** The medical records of patients treated with the diagnosis of FUS (those with stents for >6 months) between January 2014 and June 2024 were retrospectively reviewed. The reasons for the DJ stent placement, the center where the stent was placed (those placed in our own clinic and forgotten or those placed in an external center and forgotten and referred to us), duration of the stent, symptoms at presentation, and treatments performed were noted. **Results:** The study included 79 patients. The mean age of the patients was  $49.4\pm21.3$  years, with a range of 25-90 years. Of patients, 60.8% were unaware of the presence of a stent. The mean stent duration was  $24\pm39.4$  months (range 6-300 months) and 52 (65.8%) patients had encrustation. There were 4 (5.1%) patients with solitary kidneys. The mean postoperative hospitalization time was  $5.6\pm4.5$  days. The majority of patients underwent DJ stent placement after ureteroscopic lithotripsy (34.2%) and due to obstructed ureteral stones (31.5%). The most common symptoms at presentation were storage lower urinary tract symptoms (22.8%), dysuria (21.5%), recurrent urinary tract infection (16.5%) and flank pain (15.2%). Three (3.8%) patients underwent open nephrectomy due to non-functioning kidney. All remaining patients were treated endoscopically.

**Conclusion:** FUS often causes more morbidity than treatment of the primary disease. Although it can be successfully treated with endourological surgeries, the main goal should be to prevent the development of this complication.

Keywords: endoscopic surgical procedure, ureteral calculi, urolithiasis, urinary catheters

### Özet

Amaç: Özelikle ürolojik cerrahilerde obstrüksiyonun giderilip böbrekten mesaneye idrar akışının sağlanması, üreterin iyileşmesi ve komplikasyonların önlenmesi amacıyla double-J (DJ) stentler sıklıkla kullanılmaktadır. Literatürde üreteral stent takılan hastaların %12'ye kadarında unutulmuş üreteral stent (FUS) olduğu saptanmıştır. Bu çalışmada biz FUS tedavisinde 10 yıllık kendi deneyimlerimizi sunmayı amaçladık.

Gereçler ve Yöntemler: Ocak 2014 ile Haziran 2024 tarihleri arasında FUS (>6 ay stenti olanlar) tanısıyla tedavi edilen hastaların tıbbi kayıtları retrospektif olarak incelendi. Hastaların DJ stent takılma nedenleri, stentin takıldığı merkez (kendi kliniğimizde takılan ve unutulan veya dış merkezde takılıp unutulup bize başvuranlar), stentli kalma süreleri, başvuru semptomları ve yapılan tedaviler not edildi.

**Bulgular:** Çalışmaya 79 hasta dahil edildi. Hastaların ortalama yaşı 49.4±21.3 yıl olup yaş aralığı 25-90 yıl idi. Hastaların %60,8'i stent varlığından habersizdi. Ortalama stent süresi 24±39.4 ay (6-300 ay) idi ve 52 (%65,8) hastada enkrustasyon vardı. Soliter böbrekli 4 (%5,1) hasta vardı. Ameliyat sonrası ortalama hastanede kalış süresi 5.6±4.5 gündü. Hastaların büyük çoğunluğuna üreteroskopik litotripsi sonrası (%34.2) ve obstrukte üreter taşları nedeniyle (%31.5) DJ stent takıldı. Başvuru anındaki en sık görülen semptomlar depolama alt üriner sistem semptomları (%22.8), dizüri (%21.5), tekrarlayan üriner sistem enfeksiyonu (%16.5) ve yan ağrısı (%15.2) idi. Non-fonskiyone böbrek nedeniyle 3 (%3.8) hastaya açık nefrektomi operasyonu uygulandı. Geri kalan hastaların tamamı endoskopik olarak tedavi edildi.

**Sonuç:** FUS sıklıkla primer hastalık tedavisinden daha çok morbiditeye neden olmaktadır. Her ne kadar endoürolojik ameliyatlarla başarılı tedavi edilebilse de bu komplikasyonun gelişiminin önlenmesi ana hedef olarak belirlenmelidir.

Anahtar kelimeler: endoskopik cerrahi işlemler, ureter taşı, ürolitiazis, üriner kateterler

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### Introduction

Ureteral double-J (DJ) stents have an important place in urology practice. DJ stents are frequently used, especially in urological surgeries, to relieve obstruction and provide urine flow from the kidney to the bladder, to heal the ureter, and to prevent complications. Historically, Zimskind et al. first relieved ureteral obstruction by endoscopically inserting a DJ stent in 1967 [1]. However, ureteral stents have a certain period of use. In general, they must be removed or replaced within 6 weeks to 6 months. This is because, in addition to their serious benefits, there is serious literature information indicating that they increase morbidity and mortality when they remain longer than the specified periods [2-4]. It is very important to comply with this period and to raise awareness of patients. However, despite it being explained many times in writing and verbally, some patients forget that they have a stent. In the literature, it was determined that up to 12% of patients with ureteral stents have forgotten ureteral stents (FUS) [5]. Studies about the complications of FUS found that DJ stent occlusion, encrustation, migration, stone formation, hydronephrosis, renal failure, sepsis and even death may occur [6].

Another important issue with FUS is how the stent duration affects treatment. When we look at the studies, it is more difficult to treat stents that remain in place for more than one year [7]. In addition, treatment approaches may vary depending on the location and size of encrustation and whether the stent is fragmented or not. Extracorporeal shockwave therapy (ESWL), endoscopic cystolithotripsy (EnCLT), ureteroscopic lithotripsy (URLS), percutaneous nephrolithotomy (PCNL) and open surgery can be performed for the management of FUS complications [7,8]. In this study, we aimed to present our 10year experience of FUS treatment.

### **Materials and Methods**

After obtaining approval from the local ethics committee of Adana City Training and Research Hospital (Date: 11.09.2024, Approval No:5/145), the medical records of patients treated with the diagnosis of FUS (those with stents for >6 months) between January 2014 and June 2024 were retrospectively reviewed.

The reasons for the DJ stent placement, the center where the stent was placed (those placed in our own clinic and forgotten or those placed in an external center and forgotten and referred to us), duration of the stent, symptoms at presentation, and treatments performed were noted. All patients underwent serum creatinine level, complete blood count, urinalysis, urine culture, direct urinary system radiography, and ultrasound before treatment. Non-contrast computed tomography was performed in patients with complicated (fragmented/migrated stent) and radiolucent stones. Those with urinary tract infections before surgery were treated. Single dose cephalosporin prophylaxis was administered before all procedures.

EnCLT, URSL and PCNL surgeries were performed to manage complications related to FUS and to remove the stent. In patients with minimal encrustation observed on preoperative imaging, cystoscopy-guided stent removal was attempted. In patients with encrustation at the lower end of the stent, enCLT was performed with a pneumatic lithotriptor in the dorsal lithotomy position. The stent was then gently removed with a ureteroscopic grasper. If the stents could not be removed, a ureteral catheter was placed next to the stents to visualize the collecting system with radiocontrast injection. The patient was placed in the prone position and PCNL was performed and the stent was removed. In patients with encrustation of the ureter, retrograde URSL was performed under fluoroscopic guidance using semirigid ureteroscope. Nephrectomy was performed in patients with non-functioning kidneys.

### Statistical Analysis

Qualitative variables are expressed as frequency and percentage. Age, indwelling time of stent, and hospitalization time are shown as mean and standard deviation.

### Results

The study included 79 patients. The mean age of the patients was  $49.4\pm21.3$  years, with a range of 25-90 years. Of patients, 60.8% were unaware of the presence of a stent. The mean stent duration was  $24\pm39.4$  months (range 6-300 months) and 52 (65.8%) patients had encrustation. There were 4 (5.1%) patients with solitary kidneys. The mean postoperative hospitalization time was  $5.6\pm4.5$  days. Demographic and clinical data of the patients are summarized in **Table 1**.

Table 1. Demographic and clinical data of patients

Parameters	
Age, years (mean±SD)	49.4±21.3
Nationality, n (%)	
Turkish	65 (82.3)
Syrian	14 (17.7)
Gender, n (%)	
Male	54 (68.4)
Female	25 (31.6)
Stent inserted center, n (%)	
Our clinic	43 (54.4)
Other clinic	36 (45.6)
Reasons, n (%)	
Forgot	31 (39.2)
Did not know	48 (60.8)
Indwelling time (months)	24±39.4
Site, n (%)	
Right	41 (51.9)
Left	38 (48.1)
Stent related complications, n (%)	
Encrustation	52 (65.8)
Migration	7 (8.9)
Fragmentation	3 (3.8)
Solitary kidney, n (%)	4 (5.1)
Hydronephrosis presence, n (%)	18 (22.8)
Hospitalization time (days)	5.6±4.5

The majority of patients underwent DJ stent placement after URSL (34.2%) and due to obstructed ureteral stones (31.5%) (**Table 2**). The reasons for DJ stent placement are shown in Table 2.

The most common symptoms at presentation were storage lower urinary tract symptoms (LUTS) (22.8%), dysuria (21.5%), recurrent urinary tract infection (UTI) (16.5%) and flank pain (15.2%) (**Table 3**). The complaints of the patients at presentation are summarized in Table 3.

Three (3.8%) patients underwent open nephrectomy due to non-functioning kidney. All remaining patients were treated endoscopically. EnCLT and URSL treatments were applied in a single session, while a second session was performed in cases requiring PCNL. The stents of 22 (27.8%) patients with FUS were extracted by grasping them with forceps during simple cystoscopy in a single session. After treatment, stents were re-implanted in 23 patients and removed after 6 weeks. Treatments performed for FUS are summarized in **Table 4**.

### Discussion

One in every ten patients who receive ureteral stents is diagnosed with FUS. The definition of FUS varies among studies (>3, >6, >12 months) [8]. While stents cause symptoms such as dysuria, hematuria, urgency, frequency, and flank pain in the early period, serious conditions such as stent obstruction, migration, encrustation, spontaneous fragmentation, ureteroarterial and ureterointestinal fistula can develop in the late period [9]. It is a known fact that the longer the FUS period, the higher the frequency of complications and the severity of the complications [8].

The presenting symptoms were addressed in many studies in the literature. Patil et al. stated that the most common presenting symptoms were dysuria (80%) and storage LUTS (53.3%) in their study with 30 patients [7]. Damiano et al. found that flank pain (25.3%) and storage LUTS (18.8%) were common [10]. It was also observed that as the indwelling time of the DJ stent increased, the possibility of bacterial colonization and infection increased [11]. This risk is higher in women especially and dysuria, storage LUTS, recurrent UTI and flank pain complaints are the main symptoms of patients [12].

As the stent duration increases, the probability of encrustation increases [13]. Encrustation is usually observed at the proximal and distal ends of stents. The mid-ureteral parts are less, or mildly, encrusted [8]. In a study investigating the causes of encrustation, a history of past stones increased encrustation at the proximal end of the stent, while patient age and urinary tract infection increased encrustation at the distal end [14]. In one study, the encrustation rate was reported as 76.3% in stents that remained in place for more than 12 weeks [15]. In another study including 69 patients with stent duration of more than six months, the encrustation rate was found to be 73.9% and the encrustation size increased as the duration increased [16]. Jain et al. found that the encrustation size was large in those with a history of urinary system stone disease [17]. This study included FUS patients with a duration of more than 6 months and the overall encrusting rate was 65.8%. In 38 patients, the stent indwelling time was more than 12 months and the encrustation rate was 81.6%. If we look at the reasons for DJ stent placement in the literature, Patil et al. [7] reported that DJ stents were most frequently placed after URSL and PCNL, and Al-Hajjaj et al. [18] reported that DJ stents

#### Table 2. Reasons for Double-J stent placement

Parameters	n, (%)
Infection	3 (3.8)
URSL	27 (34.2)
ESWL	1 (1.3)
PCNL	6 (7.6)
Pregnancy	2 (2.5)
Cystectomy	1 (1.3)
Trauma	1 (1.3)
Retroperitoneal fibrosis	1 (1.3)
Urolithiasis	25 (31.5)
Ureteral compression (malign)	3 (3.8)
Unknown	9 (11.4)

URSL: ureteroscopic lithotripsy; ESWL: extracorporeal shockwave lithotripsy; PCNL: percutaneous nephrolithotomy

Table 3. Presenting symptoms of patients

Parameters	n, (%)
Fever	2 (2.5)
Dysuria	17 (21.5)
Hematuria	6 (7.6)
Flank pain	12 (15.2)
Storage LUTS	18 (22.8)
Recurrent UTI	13 (16.5)
Asymptomatic	11 (13.9)

LUTS: lower urinary tract symptoms; UTI: urinary tract infection

Table 4. Forgotten Double-J stents treatment methods

Parameters	n, (%)
SCSR	22 (27.8)
SCSR with EnCLT	9 (11.4)
SCSR with URSL	15 (19)
EnCLT and URSL and SCSR	11 (13.9)
EnCLT and PCNL and antegrade SR	2 (2.5)
URSL and PCNL and antegrade SR	6 (7.6)
PCNL and antegrad SR	4 (5.1)
EnCLT and URSL and PCNL and antegrade SR	7 (8.9)
Open nephrectomy	3 (3.8)

SCSR: simple cystoscopic stent removal; EnCLT: endoscopic cystolithotripsy; URSL: ureteroscopic lithotripsy; PCNL: percutaneous nephrolithotomy; SR: stent removal

were frequently placed after URSL. In our study, similar to the literature, DJ stents were placed in most patients either due to obstructed ureteral stones or after URSL.

Although there is no definitive treatment algorithm for FUS, treatment decisions should be made after evaluating imaging findings (encrustation, stone size, migration, fragmentation) and renal function. While stents can be removed in some patients with simple cystoscopy, combined endourological treatments can be applied in complicated cases. The presence of stones in the proximal part of the stent is associated with an increase in the number of sessions, a prolongation of the treatment period, and an increase in complications [16,19]. In one study, 15 ureteral stents that remained in place for 20 months could not be removed by simple cystoscopy [20]. Mahmood et al., in their study with 52 FUS (stent duration >3 months), mostly applied cystoscopic stent removal, URSL and combined endourological treatments [21]. Gupta et al. frequently used cystoscopy and ureteroscopy methods to remove stents in 23 FUS (stent duration >6 months) patients [9]. In the study by Patil et al. (stent duration >6 months), ureteroscopy and PCNL methods were applied more [7]. In this study, endourological surgeries were applied more, in line with the literature.

The use of ESWL in the management of FUS patients has been shown in studies [21,22]. However, this method does not provide sufficient benefit in patients with severe encrustation and high stone burden [8]. However, it may increase the success of endourological treatments [23]. There were patients in our center who used ESWL for FUS treatment, but we did not include them in the study because ESWL was mostly unsuccessful in these patients and patient data were insufficient.

In order to prevent FUS and related complications, detailed information should be provided to patients who have DJ stents after urological surgeries, the complications that may develop when the stent remains in place for longer than the specified period should be explained, adequate fluid intake should be encouraged, stone prophylaxis should be initiated in appropriate patients and antimicrobial treatments should be applied for prophylaxis [8]. In order to prevent FUS development, McCahy et al. kept records of those who had DJ stents on the computer and developed a model that reminded the urologist about the expired stents [24]. Patients can also be reminded verbally by e-mail, SMS (short message service, or text message) or by calling their registered numbers when their stent expiration date has passed [22].

If we look at the limitations of our study, the small number of patients, being a single-center study, the absence of postoperative complication data, the absence of stone analysis, and the absence of cost analysis are the main limitations of the study.

### Conclusion

FUS often causes more morbidity than treatment of the primary disease. Although it can be successfully treated with endourological surgeries, the main goal should be to prevent the development of this complication.

**Ethics Committee Approval**: This study was performed according to the Helsinki Declaration and with permission from the local ethics committee of Adana City Training and Research Hospital (Date: 11.09.2024, Approval No:5/145).

**Informed Consent:** An informed consent was obtained from all the patients.

**Publication:** The results of the study were not published in full or in part in form of abstracts.

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### Comparative Analysis of Polyacrylamide Hydrogel Injections and Trans-obturatuar tape in the Treatment of Stress Urinary Incontinence in Women: Evaluation of Efficacy and Safety Outcomes

Kadınlarda Stres İdrar Kaçırma Tedavisinde Poliakrilamid Hidrojel Enjeksiyonları ve Trans-obturatuar Bantların Karşılaştırmalı Analizi: Etkinlik ve Güvenlik Sonuçlarının Değerlendirilmesi)

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### Abstract

**Objective:** To compare the efficacy and safety of polyacrylamide hydrogel (PAHG) injections with trans-obturatuar tape (TOT) surgery for managing stress urinary incontinence (SUI) in women and to assess treatment outcomes.

**Materials and Methods:** This retrospective cohort study involved 61 women diagnosed with SUI from 2022 to 2024. The study divided the patients into two groups: one comprising 32 patients who underwent TOT surgery and another comprising 29 patients who received PAHG injections. The key variables analyzed included demographic data, operation time, hospital stay, and patient satisfaction measured using the visual analog scale (VAS). Complications were recorded using the Clavien-Dindo classification. Statistical analyses were performed to identify the factors influencing the outcomes, including independent sample t-tests and regression models.

**Results:** The TOT group showed a higher treatment success rate, with 93.75% of patients having a resolution of SUI symptoms than the PAHG group (82.76%). PAHG demonstrated advantages in shorter operation times (mean difference, 8.31 minutes, p<0.001), absence of catheterization, and shorter hospital stays (mean difference of 20.24 hours, p<0.001). TOT was associated with higher rates of complications such as vaginal discharge (43.75%) and groin pain (28.12%), whereas the PAHG group reported no such complications.

**Conclusion:** TOT surgery provides higher success rates for SUI treatment; however, PAHG injections offer a viable, minimally invasive alternative with a lower risk of complications. Future research needs to involve larger sample sizes and include long-term follow-up to validate and refine these findings.

Keywords: stress incontinence, polyacrylamide hydrogels, trans-obturatuar tape, mid-urethral slings, treatment outcome, patient satisfaction

### Özet

Amaç: Kadınlarda stres üriner inkontinansın (SUI) tedavisinde poliakrilamid hidrojel (PAHG) enjeksiyonları ile trans-obturatuar band cerrahisinin etkinliğini ve güvenilirliğini karşılaştırmak ve tedavi sonuçlarını değerlendirmek.

Gereçler ve Yöntemler: Bu retrospektif kohort çalışmasına 2022-2024 yılları arasında SUI tanısı alan 61 kadın dahil edildi. Çalışma hastaları iki gruba ayırdı: biri trans-obturatuar band ameliyatı geçiren 32 hasta, diğeri PAHG enjeksiyonu yapılan 29 hastadan oluşuyordu. Analiz edilen temel değişkenler arasında görsel analog ölçeği (VAS) kullanılarak ölçülen demografik veriler, operasyon süresi, hastanede kalış süresi ve hasta memnuniyeti yer aldı. Komplikasyonlar Clavien-Dindo sınıflaması kullanılarak kaydedildi. Sonuçları etkileyen faktörleri belirlemek için bağımsız örneklem t-testleri ve regresyon modelleri dahil olmak üzere istatistiksel analizler yapıldı.

**Bulgular:** Trans-obturatuar band grubu, PAHG grubuna göre (%82.76) hastaların %93.75'inde SUI semptomlarında düzelme ile daha yüksek bir tedavi başarı oranı gösterdi. PAHG, daha kısa ameliyat süreleri (ortalama fark, 8.31 dakika, p<0.001), kateterizasyon olmaması ve daha kısa hastanede kalış süresi (ortalama fark 20.24 saat, p<0.001) avantajlar göstermiştir. Trans-obturatuar band vajinal akıntı (%43.75) ve kasık ağrısı (%28.12) gibi komplikasyon oranları ile ilişkili iken, PAHG grubunda böyle bir komplikasyon bildirilmedi.

Sonuç: Trans-obturatuar band SUI tedavisi için daha yüksek başarı oranları sağlar; bununla birlikte, PAHG enjeksiyonları, daha düşük komplikasyon riski ile uygun, minimal invaziv bir alternatif sunar. Gelecekteki araştırmaların daha büyük örneklem boyutlarını içermesi ve bu bulguları doğrulamak ve iyileştirmek için uzun vadeli takibi içermesi gerekir.

Anahtar kelimeler: stres inkontinans, poliakrilamid hidrojel, trans-obturatuar band, orta üretral askı, tedavi sonucu, hasta memnuniyeti

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### Introduction

Stress urinary incontinence (SUI) is a common health problem affecting millions of women worldwide and seriously impairing their quality of life. Defined by the International Continence Society (ICS) as "involuntary leakage of urine during exertion, exercise, sneezing, or coughing", SUI is a condition that about half of women experience at some point in their lives [1]. SUI notably contributes to physical and psychological discomfort that negatively affects individuals' social life and overall quality of life.

Recent complications in the surgical treatment of SUI have notably undermined confidence in traditional treatment methods. Mesh-based surgical approaches, such as transobturator tape (TOT), have been associated with serious complications including bladder injury and mesh erosion [2]. In this context, there is growing interest in alternative treatment modalities that are less invasive and reduce the risk of mesh-related complications.

Given the complications associated with traditional meshbased surgeries, our study turns to emerging alternatives such as PAHG (polyacrylamide Hydrogel) injections, aiming to evaluate their efficacy and safety. Degradation-resistant PAHG was approved by the Food and Drug Administration (FDA). This polymer gel contains 2.5% cross-linked polyacrylamide and 97.5% water for injection and is considered a promising option for treating urinary incontinence [3]. However, available data on the long-term efficacy and safety of PAHG injections are limited, making it imperative to compare this treatment option with other surgical methods.

This study aimed to compare the efficacy and safety of PAHG injections with those of TOT surgery for the treatment of SUI, to reveal the differences between these two methods, and to determine which of these treatment options is more appropriate in clinical practice. By filling the knowledge gaps in the existing literature, we aimed to provide evidence-based recommendations to improve patient satisfaction and outcomes in SUI treatment.

### **Materials and Methods**

### **Data Collection**

This study included 61 patients who underwent surgery for SUI between October 2022 and March 2024. Data, including demographic details, medical history, preoperative examinations, and postoperative outcomes, were obtained from the patient records. Preoperative cough stress and Q-tip test results were also recorded. The classification of urethral mobility, critical for surgical decision-making, ranges from 0° (indicating no movement) to > 30°, which represents excessive mobility [4,5]. The post-treatment outcomes were evaluated using the Global Response Assessment Scale, while any complications were categorized based on the Clavien-Dindo system.

### **Eligibility Criteria**

Patients included in the study did not differentiate between mixed and pure urinary incontinence. Stress incontinence was sufficient. Therefore, the presence of intrinsic sphincteric deficiency (ISD) is not considered a valid criterion for exclusion of any procedure. Patients with recurrent urinary tract infections, neurogenic bladder, neurological disorders with severe functional impairment, or mental health problems were excluded. Previous surgical interventions for stress urinary incontinence were considered exclusion criteria for participation in the study because they may confound the study results and, therefore, were not included in the analysis. Minimally invasive urodynamic studies were not conducted on uncomplicated patients and were, thus, beyond the scope of this study. A visual analog scale was used to evaluate patient satisfaction after the procedure.

### **Treatment Decision Criteria**

The decision to perform TOT or administer PAHG injections was based on a combination of clinical evaluations and patientspecific factors. Key considerations included:

Urethral Mobility: Patients with significant urethral hypermobility (as indicated by a Q-tip test angle  $>30^\circ$ ) were more likely to undergo TOT due to its higher efficacy in such cases.

Patient Preferences: Patients who desire a less invasive option with shorter recovery times were guided toward PAHG injections.

Body mass index (BMI) and comorbidities: TOT was preferred for patients with higher BMI (>35) or those who required greater structural support, while PAHG injections were recommended for patients with lower BMI or those unsuitable for surgical procedures due to comorbidities.

Previous Treatment History: Since no patients had prior treatments for SUI in this study, all interventions were considered first-line. Patients with contraindications for anesthesia or surgery were prioritized for PAHG injections.

Physician Assessment: The attending physician's clinical judgment, based on the patient's medical history, physical examination, and risk-benefit analysis, played a crucial role in the final decision.

### **Ethical Considerations**

Patients were apprised of the objective of the surgical operation and the potential risks and advantages associated with the procedures involved. Prior to and following the surgical intervention, the patients were informed that the obtained data could be used in a scientific study by safeguarding their personal information, and they provided written informed consent before the procedures commenced. This study adhered to the ethical guidelines of the Declaration of Helsinki and was approved by the Ethics Committee of Burhan Nalbantoğlu State Hospital (Number: YTK1.01, project code 29/24).

### Treatment and Follow-up Protocol

The trans-obturator type (out-in technique) procedure was applied to all patients. Polyacrylamide hydrogel injection was performed using a product-specific endoscope, endoscopy kit, and injection needle (23-gauge), and 2-3 cc was injected at 3-4 distinct locations at the junction of the bladder neck and urethra.

The primary objective was to eradicate stress urinary incontinence as a measure of success. The patients' postoperative 6th-week stress incontinence was assessed via telephone. Bladder overactivity following the procedure is regarded as a complication in patients diagnosed with pure stress incontinence. Postoperative satisfaction was assessed using a visual analog scale. The global evaluation scale indicated that the treatment success had a response rate exceeding 50%. During the evaluation, patients were questioned about their inclination to submit themselves to the procedure again and recommend it to their friends.

#### **Data Analysis**

A power analysis was performed using G-power software to evaluate the validity of the study and dependability of the outcomes obtained. In the power analysis, the effect size (d) was determined to be 0.8, which indicates that there was a mediumhigh-level effect in our study. According to the power analysis results, the probability of a type I error ( $\alpha$ ) was 8.61%, the probability of a type II error ( $\beta$ ) was 8.61%, and the statistical power  $(1-\beta)$  was 91.38. The categorical data encompassed the nature of the treatment, including TOT/PAHG, as well as the classification of urinary incontinence, such as mixed or pure. Moreover, it contains information on potential complications, including vaginal discharge and groin pain. The quantitative data examined in this study comprised several variables, such as patient age, body mass index (BMI), frequency of urinary incontinence episodes per day, operation time, hospital stay, and visual analoge scale (VAS) satisfaction score. These variables were analyzed using descriptive statistics, and an independent sample t-test was used to compare the results between the TOT and PAHG groups. The tables provide a summary of the descriptive statistics. Categorical data were expressed as numbers (n) and percentages, whereas quantitative data were presented as mean ± standard deviation (SD). Regression and correlation tests were conducted to determine the factors influencing the treatment outcomes. Data analysis was performed using SPSS version 28.0 software.

### Results

This study included patients with a mean age of  $58\pm12.1$  years. A total of 29 patients underwent PAHG, while 32 underwent TOT. The mean BMI was calculated to be  $25.7 \pm 4.8$  kg/m<sup>2</sup>. The mean number of incontinences per day was  $3\pm1.1$  (range 2-7). None of the patients had undergone any prior surgical intervention or pharmacological treatment for SUI. A total of 48 patients were diagnosed with mixed-type stress incontinence, while 13 patients had pure SUI. Upon examination, all patients exhibited a hypermobile urethra, as determined by the Q-tip test, which had a result greater than 30°. Among the 17/58 patients with mixed-type stress incontinence, 17 received anticholinergic agents, local estrogen replacement, and medical treatment for constipation. Five patients in the TOT group and three patients in the PAHG group had a BMI > 35. The characteristics of the groups according to the surgical technique are shown in **Table 1**.

The treatment success rate was 30 (93.75%) in patients who underwent TOT. In 2 (6.25%) patients, no incontinence was observed with provocation in the lithotomy position; however, incontinence was detected while standing. Urinary incontinence in five (17.24%) patients in the PAHG group resolved completely a few days after the procedure but returned afterward. Three of the five patients with urinary incontinence after PAHG injection had a BMI > 35.

Table 1. Characteristic features of the surgical technique groups

Group (n)	TOT (32)	PAHG (29)	P-Value
Age (years)	$55.6 \pm 11.7$	$62.5 \pm 11.8$	0.58
BMI (kg/m <sup>2</sup> )	$27.4 \pm 5.7$	$23.9 \pm 2.7$	0.47
SUI type			0.91
- Mixed	25 (78.1%)	23 (79.3%)	
- Pure	7 (21.9%)	6 (20.7%)	
Urinary incontinence episodes	2.9 ± 1.1	3.1 ± 1.2	0.28
SUI duration (months)	$33.3 \pm 11.8$	$29.5 \pm 11.7$	0.31
Operation time (minutes)	20.3±4.05	12±2.7	0.01
Catheter duration (days)	$22.5 \pm 3.4$	Nil	0.01
Hospitalization duration (hours)	25.3±4.2	5.1±1.4	0.01
Follow-up time (months)	14.75±6.5	10.8±4.3	0.17
Global response assess- ment	32 (100%)	24 (82.75%)	0.19
Return of urinary incon- tinence	2 (6.25%)	5 (17.24%)	<0.05
VAS satisfaction score	$7.81 \pm 1.06$	8.06 ± 1.36	0.12

TOT: tension-free obturator tape; PAHG: polyacrylamide hydrogel injection; BMI: body mass index, SUI: stress urinary incontinence; VAS: visual analog scale for satisfaction evaluation

Both methods were assessed in terms of operative time, postoperative urethral catheter duration, and length of hospital stay by using an independent t-test. The mean difference in operative times was 8.31 minutes. According to Levene's test, the p-value was 0.054, suggesting that the variances were equal. Therefore, the mean operative time was notably shorter in the PAHG group (p < 0.001). The PAHG group did not experience catheterization, whereas the TOT group was catheterized for 22.53 hours. There was a statistically significant difference between the two groups regarding catheterization (p<0.001). In addition, there was a mean difference of 20.24 hours between postoperative hospitalization times, and the TOT group had a longer hospital stay (p<0.001). Statistical evidence revealed that the hospitalization requirements of the TOT group were more significant.

In a cross-tabulation analysis conducted using SPSS and employing the global response scale, 20 out of 32 patients in the TOT group were classified as "4," 10 as "5," and two as "2". For the PAHG group, 2 of 29 patients received a score of "0", 3 received a score of "2", 7 received a score of "4", and 17 received a score of "5". The results indicated a statistically significant difference between the two groups (p = 0.021). The postoperative VAS satisfaction score for the TOT group was 7.81±1.06, while that for the PAHG group was 8.06±1.36. Since the postoperative VAS satisfaction scores did not follow a normal distribution, the Mann-Whitney U test was used to compare the two groups, and no significant difference was observed between them (p=0.12).

The results of the linear regression analysis were used to

determine the factors that influenced the VAS satisfaction score. The p-value for treatment method was 0.835, while the p-value for age was 0.019. As age increased, the VAS satisfaction scores also increased. The p-values for the number of urinary incontinence episodes and the duration of urinary incontinence were 0.213 and 0.630, respectively, indicating that these variables did not notably affect the VAS satisfaction score. The p-value for BMI was 0.675, suggesting that this variable had no significant impact on the VAS satisfaction score. The factors that influenced treatment success were analyzed using a logistic regression model. The results showed that the variables were collectively significant (Overall Statistics: p=0.003). Specifically, the Treatment Method (p=0.014), age (p=0.548), number of Urinary Incontinence episodes (p=0.094), duration of Urinary Incontinence (p=0.293), and BMI (p=0.014) were all found to be statistically significant.

None of the patients had urinary retention or required clean intermittent catheterization. Of the 32 patients who received TOT after 7 days, 14 (43.75%) were found to have vaginal discharge (Clavien-Dindo grade II). The patients were administered vaginal antibacterial suppositories. Of the 32 individuals who underwent TOT, 9 (28.12%) experienced pain in the groin area (Clavien-Dindo grade I). The patients were treated with nonsteroidal anti-inflammatory drugs (NSAIDs) without requiring physical therapy or additional medical or surgical intervention. Twenty-three patients with TOT experienced postoperative vaginal bleeding in the form of spotting that soiled the pads or underwear. No bladder injury or mesh erosion was detected in any of the patients in the TOT group during the follow-up period (**Table 2**).

### Discussion

This study was conducted to evaluate the efficacy and safety of PAHG injections and TOT surgery for the management of SUI in women. Our results indicate that both options are effective in treating SUI; however, there are notable variations between the two. In our study, we found that the TOT method demonstrated greater treatment success than PAHG injections. While 6.25% of TOT-treated patients experienced persistent urinary incontinence, 17.24% of those in the PAHG group experienced recurrence of urinary incontinence in a relatively short time. Our findings align with existing literature on this subject [6]. However, the minimally invasive nature of PAHG offers advantages, particularly, a short operative time and no catheter

Table 2. Postoperative complication
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Complication Type	TOT Group (32)	PAHG Group (29)	P-value
Vaginal discharge	14 (43.75%)	0 (0%)	0.001
Groin pain	9 (28.12%)	0 (0%)	0.001
Urinary retention	0 (0%)	0 (0%)	-
Bladder injury	0 (0%)	0 (0%)	-
Mesh erosion	0 (0%)	0 (0%)	-
Urethral erosion	0 (0%)	0 (0%)	-
Vaginal bleeding*	23(71.8%)	0 (0%)	0.001

\*Staining on pads or underwear

requirement. These findings suggest that PAHG injections may be a potential treatment option for patients with a lower risk of complications, who wish to avoid invasive procedures.

The use of specific equipment for PAHG applications makes this method easy and standardized [7]. The use of PAHG may be considered for patients with hip issues who are placed in a restricted lithotomy position during mid-urethral sling procedures as it has demonstrated comparable treatment outcomes. In our case series, three patients were referred to the PAHG by their surgeons for this specific purpose.

When evaluated in terms of patient satisfaction, there was no statistically significant difference between the two methods; however, the satisfaction rates in the PAHG group tended to increase with age. In the literature, satisfaction rates with PAHG injections have been reported to range between 64% and 90% [4], which is consistent with our findings [4,8,9]. Despite the high success rates of the TOT method, the low complication rates and minimally invasive nature of PAHG injections may support the preference for this method in certain patient groups. However, in contrast to more invasive methods such as TOT and tension-free vaginal tape (TVT), no disparity in satisfaction rates has been detected in most studies [4].

Remarkably, patients with high BMI benefited less from PAHG injections, suggesting that the efficacy of this method may be related to BMI. However, the fact that patients with similar BMI benefited notably from TOT suggests that TOT may be more effective in this patient group. Although the sample size of our study was small, this finding suggests that BMI may be an important factor in treatment selection, and this issue should be examined in greater depth in studies with larger sample sizes.

The effect of surgical experience on treatment outcomes was an important finding of our study. The surgeons' long years of experience with the TOT method may explain the high success rates of this method, whereas less experience with PAHG injections may have led to lower success rates. This suggests that surgical experience and skill can notably influence treatment outcomes, especially with new or less commonly used methods [10,11].

With regard to complications, higher rates of vaginal discharge and groin pain were observed in the TOT group. These complications may be related to the invasive nature of TOT, and surgical techniques should be revised to reduce such complications [10,11]. The absence of such complications in the PAHG group suggests that the PAHG injections have an advantageous safety profile. Nevertheless, it is reasonable to anticipate low complication rates by carefully selecting the patients in the PAHG group [6,12]. Unfortunately, this study did not include long-term follow-up data. Long follow-up periods of up to 7 years have been documented in previous studies for PAHG patients with PAHG and are consistent with our observations [13].

This study has some limitations. First, the relatively small sample size limited the generalizability of our findings. Furthermore, the inhomogeneity of the patients and lack of separation between mixed-type and pure SUI cases may have affected the accuracy of the results. Furthermore, the absence of long-term follow-up data in this study introduces uncertainty, particularly concerning the long-term efficacy and safety of PAHG injections. Moreover, the fact that a single surgeon performed all the surgical procedures could have influenced the outcomes. Notably, while the surgeon had 17 years of experience in the TOT group, they had only two years of experience in the PAHG group. This disparity in experience may have affected the results and should be considered when interpreting the findings. Considering these limitations, randomized controlled trials with larger sample sizes and long-term outcomes should be conducted in the future [6].

### Conclusion

In conclusion, although the TOT method offers higher success rates, the minimally invasive nature and low complication rates of PAHG injections make this method an effective alternative in certain patient groups. Future studies should examine the costeffectiveness of these treatment methods and their impact on patient satisfaction by evaluating the long-term outcomes of both methods, using larger sample groups. Furthermore, multicenter studies conducted by different surgeons are recommended to better understand the impact of surgical experience and skills on treatment outcomes.

**Ethics Committee Approval**: This study was performed according to the Helsinki Declaration and with permission from the local ethics committee of Burhan Nalbantoğlu State Hospital (Number: YTK1.01, project code 29/24).

**Informed Consent:** An informed consent was obtained from all the patients.

**Publication:** The results of the study were not published in full or in part in form of abstracts.

Peer-review: Externally peer-reviewed.

Authorship Contributions: Any contribution was not made by any individual not listed as an author. All authors read and approved the final version of the manuscript. Concept – N.B., F.E.; Design – N.B., F.E.; Supervision – N.B., F.E.; Resources – N.B., F.E.; Materials – N.B., F.E.; Data Collection and/or Processing – N.B., F.E.; Analysis and/or Interpretation – N.B., F.E.; Literature Search – N.B., F.E.; Writing Manuscript – N.B., F.E.; Critical Review – N.B., F.E.

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### Penile Strangulation by Foreign Bodies - Varied Presentations, Unique Management Strategies and Outcomes - A Case Series with Review of Literature

Yabancı Cisimlerlerle Penil Strangülasyon- Çeşitli Sunumlar, Benzersiz Yönetim Stratejileri ve Sonuçlar- Literatürün Gözden Geçirildiği Bir Vaka Serisi

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### Abstract

Penile strangulation by foreign bodies is a true urological emergency causing varied outcomes based on the degree and duration of the strangulation. Irrespective of the presenting age and cause, disruption of blood flow to the penile tissues is the consequence leading to outcomes ranging from simple penile oedema to total penile gangrene. We hereby report five cases of adult penile strangulation, all of them presenting in the emergency department with variable intervals of strangulation after foreign body application. Three patients were managed by cutting the metallic rings by a motorized metal cutting device borrowed from the hospital electrical maintenance department as a desperate measure while one was managed with the thread unwinding method. The last case being plastic bottle neck strangulation was managed with disruption by heavy scissors.

Keywords: penile, strangulation, metallic ring, bottle neck, silk winding, foreign body

### Özet

Yabancı cisimlerle penil strangülasyon, strangülasyonun derecesine ve süresine bağlı olarak çeşitli sonuçlara neden olan gerçek bir ürolojik acil durumdur. Yaş ve nedenden bağımsız olarak, penis dokularına giden kan akışının bozulması, basit penis ödeminden total penis kangrenine kadar değişen sonuçlara yol açar. Burada, hepsi yabancı cisim uygulamasından sonra değişen boğulma aralıklarıyla acil servise başvuran beş yetişkin penis boğulması vakasını bildiriyoruz. Üç hasta, acil bir önlem olarak hastane elektrik bakım bölümünden ödünç alınan motorlu bir metal kesme cihazıyla metal halkaları keserek tedavi edilirken, biri iplik çözme yöntemi ile tedavi edildi. Son vaka olan plastik şişe boynu boğulması, ağır makaslarla kesilerek tedavi edildi.

Anahtar kelimeler: penis, stangülasyon, metalik halka, şişe boynu, ipek sarma, yabancı cisim

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### Introduction

Penile strangulation by foreign bodies is one such rare occasion that requires the urologist to rush to emergency for immediate intervention. Both motives and materials of strangulation have a long list ranging from application for sexual gratification by metallic rings to pranks gone wrong using threads [1]. Penile strangulation is seen over a varied age group of the population with cases even noted in the paediatric age group termed the penile tourniquet syndrome [2]. Irrespective of the cause, strangulation causes disruption of blood flow to the penile tissues leading to outcomes ranging from simple penile oedema to complete gangrene based on the duration and degree of strangulation. We here depict 5 cases of penile foreign body strangulation, their management and final outcomes with a brief review of scarce available literature on the subject.

### **Case Presentations**

### Case 1

A 60-year-old man came to emergency with complaints of penile pain and swelling secondary to a metal ring applied to the root of the penis 1 day back for sexual gratification. Physical examination revealed an oedematous, swollen penis with blistering of the shaft skin with a metal ring of approximately 8-10 mm thickness. As per institutional protocol and Medico legal concern, Penile Doppler was done which revealed preserved flow in both corpora cavernosa distal to the ring. Removal of the ring was initially attempted using more conservative measures like lubricants, corporal aspiration and threading but was unsuccessful due to the oedematous and engorged state of the penis. The patient was then immediately taken up under short sedation and removal of the ring was done using an electrical motorised cutting device [Figure 1]. Following removal of the ring, the penile oedema began to subside and at 30-day follow up, the patient had normal distal penile sensations and voiding function with an optimal Erection Hardness Score (EHS) of 4.

### Case 2

A 45-year-old man came to emergency with complaints of penile pain and swelling secondary to a metal ring applied to the root of the penis 10 days back under alcohol influence. Physical examination revealed an oedematous penis with blackening of skin at the shaft region and pressure ulceration noted at the site of metal ring application. Penile Doppler revealed high resistance flow seen in both cavernosal arteries with normal flow on the dorsal arteries and deep dorsal vein. After failure of initial conservative manoeuvres, the patient was taken up under short sedation and removal of the ring was done using an electrical motorised cutting device [Figure 2]. Following removal of the ring, the penile oedema began to resolve and at 30-day follow up, the patient had normal distal penile sensations and voiding function with an EHS of 4. The region of pressure ulceration granulated and healed well with regular wound care.

### Case 3

A 36-year-old man presented with complaint of diffuse penile swelling due to a metal ring applied at the base of the penis 4



**Figure 1.** Clinical photograph of the 1st case. a: Preoperative presentation; b: Representative intraoperative photograph; c: Retrieved metallic ring



**Figure 2.** Clinical photograph of the 2nd case. a: Preoperative presentation; b: Retrieved metallic ring; c: Post-operative photograph



**Figure 3.** Clinical photographs of the 3rd case. a: Preoperative presentation; b: Retrieved metallic ring; c: Post-operative photograph



**Figure 4.** Steps of the silk winding technique. a-b: Suture string is passed proximally through the metallic ring; c: The suture material was circumferentially wound around the penis just distal to the metallic ring followed by unwinding of the suture material from the proximal end causing distal sliding of the ring; d: Distal sliding of the ring facilitated by multiple subcutaneous punctures over the penile skin causing exudation of serosanguineous fluid and decompression of edema; e-f: The ring gently slided over the glans and removed intact

days back applied for sexual gratification. Physical examination revealed the oedematous shaft of penis distal to the constriction ring. Urgent Penile Doppler revealed high resistance monophasic flow in both cavernosal arteries proximal to the ring with no flow in cavernosal arteries distal to the ring. The patient was taken up for removal of the ring under sedation with an electrical motorised cutting device after failure of initial local manoeuvres [Figure 3]. Following removal, the penile oedema resolved and at the 30 day visit voiding function and distal penile sensation was normal with an optimal EHS of 4.

### Case 4

A 45-year-old man presented with complaints of inability to micturate and penile swelling due to a metal ring applied at the base of the penis 8 hours back applied for sexual gratification. Physical examination revealed the oedematous shaft of penis distal to the constriction ring with skin erosion at the site of ring application. Penile Doppler was suggestive of preserved flow in both corpora cavernosa distal to the ring. Initial conservative measures such as lubricant application, multiple skin punctures or corporal aspirations failed and then patient was taken up for removal of the ring under local anaesthesia with the silk unwinding technique [Figure 4]. Following removal of the ring, resumption of normal voids was observed and at 30 day follow up complete penile oedema resolution with normal voiding function and distal penile sensation was observed with an EHS of 4.

#### Case 5

A 60-year-old man presented with complaint of diffuse penile swelling and pain due to application of plastic bottle neck at the base of the penis 6 hours back for sexual gratification [Figure 5]. Physical examination revealed the oedematous penile shaft with bluish discolouration with corporal gas analysis revealing signs of ischemia. The patient was managed by disruption of the bottle neck by heavy scissors under sedation. removal, the Following penile oedema resolved and at 30 day follow up, normal voiding function and an optimal EHS of 4 was documented.



**Figure 5.** Clinical photograph of plastic bottle neck penile strangulation

### Discussion

Penile strangulation is an urological intervention necessitating immediate intervention by the urologist. Sexual gratification is the most common desired outcome for which penile strangulation is attempted in most cases. Penile strangulation is done by a large list of objects including heavy metal rings, plastic pipes, plastic bottle necks, sprockets or plumbing cuffs with metallic rings being the most troublesome of all these objects to device a removal strategy [1]. Patients usually present immediately or relatively early after their futile attempts at removing these objects fail, but chronic strangulation as late as 1 month post application has also been reported in literature [3]. Attempts to grade the severity of such injuries have been made by a number of authors in an attempt to judge prognosis. The most popular of them all was described by Bhat et al. who classified penile strangulation injuries as described below [4].

Grade I: Distal edema only.

Grade II: Distal edema, skin & urethral trauma, corpus spongiosum compression, decreased penile sensation.

Grade III: Skin & urethral trauma, no distal sensation.

Grade IV: Separation of corpus spongiosum, urethral fistula, corpus cavernosum compression, no distal sensation.

Grade V: Gangrene, necrosis or distal penile amputation. Harouchi et al. had devised a four-grade classification ranging from superficial skin loss (Grade I) to loss of glans (Grade IV) [5]. Silberstein et al. developed a two-tier grading system which categorised injuries into either low or high grade with the latter defined to be those ones that are likely to require a secondary surgical procedure post removal of the strangulating agent [6].

Irrespective of the aetiology, treatment involves prompt decompression by removal of the constricting ring. Various techniques have been described for removal of the constricting ring with cutting methods being the most commonly described. An account of published similar reports on foreign body penile strangulation has been summarised in **Table 1** [7–18] along with the various different techniques used in their management. Management strategies for metallic constricting foreign bodies

Table	1. Summary of	published literature	on foreign	body penile	strangulation and	l management
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No	Author	Age*	Foreign Body	Duration	Local Examination	Management
1	Kim Y G, Shin Y S & You J H. Urogenit Tract Infect [7]	51	Metal ring	4 days	Penile edema	Corporal blood aspiration with I & D of penile skin to reduce subcutaneous Penile edema
2	Dong et al. Case Rep Urol. [8]	64 57	Metal ring	12 hours 8 hours	Penile edema Penile edema	Silk winding method
3	Vyas K N & Solanki M I. Int Surg J. [9]	45	Metal ring	2 days	Pressure ulceration under the ring with distal penile edema	Silk winding method
4	Destinval C et al. J Pediatr Urol. [10]	13	Metal ring	2 hours	Penile edema	Gigli saw
5	Paonam S, Kshetrimayum N & Rana I. Urol Ann [11]	47	Metal ring	2 days	Penile edema	Dental micro motor cutting device
6	Chen, Michael Y.& Rukin, Nicholas J. JCU [12]	42	Metal ring	4 weeks	Penile edema	Motorised electric ring cutting device
7	Singh I et al. BMJ Case Rep [13]	33	Metal ring	2 weeks	Penile edema & Pressure necrosis/ulceration of penile skin under the ring	Motorised electric ring cutting device
8	Ichaoui et al . Case Rep Urol [14]	42	Metal ring	10 days	Penile edema & Pressure necrosis/ulceration of penile skin under the ring	Motorised electric ring cutting device
9	Saroj J K et al. Int Surg J. [15]	48	Metal ring	6 days	Penile Gangrene	Total penectomy + PU
10	Magdum et al. J Sci Soc. [16]	60	Plastic pipe	NM	Penile edema	Dental drill
11	Agarwal AA et al. BMJ Case Rep. [17]	45	Plastic bottle neck	18 hours	Penile edema	Heavy scissors
12	Dar NR et al. Pediatr Dermatol. [18]	5	Hair coil	4 weeks	Oedema of glans penis	Removal by dissecting forceps
13	Present case 1	60	Metal ring	1 day	Penile edema and blistering of penile skin	Motorised electric ring cutting device
14	Present case 2	45	Metal ring	5 days	Penile edema & Pressure necrosis/ulceration of penile skin under the ring	Motorised electric ring cutting device
15	Present case 3	36	Metal ring	4 days	Penile edema	Motorised electric ring cutting device
16	Present case 4	45	Metal ring	8 hours	Penile edema	Thread unwinding technique
17	Present case 5	60	Plastic bottle neck	6 hours	Penile edema	Heavy scissors

Age\*: In years; I & D: Incision and drainage; PU: Perineal urethrostomy; NM: Not mentioned

ranged from simpler measures like multiple subcutaneous needle punctures and corporal aspirations [7] to the more complex manoeuvres like the silk winding technique [8, 9] or disruption of the rings by cutting devices such as the gigli saw [10], dental drill [11] or the motorised cutting devices in extremely desperate situations [12-14]. Unlike the usual benign course in most of the above published literature, Saroj JK et al. described an unfortunate case of metallic ring penile constriction in a 48 year old patient which culminated in total penile gangrene and total penectomy [15]. Other foreign bodies that have been reported to cause strangulation include plastic pipes [16], plastic bottle necks [17] and human hair [18]. The human hair coil strangulation or the penile tourniquet syndrome is an unique but dangerous situation observed most often in circumcised children where strangulation occurs by the falling maternal hair that winds around the coronal sulcus and produces constriction leading to a wide variety of outcomes ranging from simple constriction to more severe consequences such as urethrocutaneous fistulas, partial penile transection or even an amputated glans penis [19]. Despite being a subject of constantly improving published literature, there exists no fixed protocol on management with most authors managing such cases with their own creative management techniques aimed at removing the constricting object with minimal morbidity. I Singh et al. [20] uniquely attempts to frame an algorithm based on different levels of injury encompassing all described methods on removal of strangulating penile foreign bodies that can be considered a prototype towards formation of more similar standardised management protocols in the future with collective review of available literature on the subject.

Campbell K et al. [21] reviewed long term sequalae of patients that underwent extrication of constricting penile foreign bodies. The authors reported long term sequalae in 24% of studied patients after removal of the constricting agent with the need for skin grafting and urethroplasties being the most commonly observed long term sequalae.

### Conclusion

Penile strangulation by constricting foreign bodies is one of those rare situations demanding emergent intervention from an urologist. Despite being a topic of constant improvisation and newer techniques of management, major lacunae does exist in areas like fixed protocols of management and follow up for long term sequalae. Larger studies on the subject concentrated on formation of such standard protocols seem to be the need of the hour to gain further insights into the topic.

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### Port Site Metastases After Incidental Upper Urinary Tract Urothelial Carcinoma: A Case Report

İnsidental Üst Üriner Sistem Ürotelyal Karsinomu Sonrası Port Yeri Metastazı: Bir Olgu Sunumu

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### Abstract

Upper urinary tract urothelial tumors are rarely seen. Only 5% of all transitional cell carcinomas (TCCs) originate from the upper urinary tract. Although skin metastases in urinary tumors are quite rare, the incidence of skin metastases in upper urinary tract TCCs is not exactly known due to the lack of published research on this subject. In this article, we aimed to present a lesion consistent with TCC metastasis in the left inguinal region of a patient who was operated on for a renal pelvic mass. A 61-year-old male patient underwent left laparoscopic nephrectomy because of a mass reported as renal cell carcinoma (RCC) in the upper pole of the left kidney. After the pathology result reported the presence of left renal TCC, the patient underwent left ureterectomy plus cuff resection in an another medical center. After this second operation, the skin lesion developing at the trocar entry site on the left inguinal region of the patient was reported as an abscess on imaging. The histopathology of the excised abscess was reported as TCC metastasis. There is no consensus on the treatment regimen for skin metastases of urothelial carcinomas, and these metastases have a relatively poor prognosis. One -year survival rate is generally 35%. The patient in our case received generitabine and cisplatin treatment and has been under oncology follow-up for twelve months.

Keywords: kidney cancer, metastasis, transitional cell carcinoma, skin

### Özet

Üst üriner sistem ürotelyal tümörleri nadiren görülür. Tüm transizyonel (değişici) hücreli karsinomların (TCC) sadece %5'i üst üriner sistemden kaynaklanmaktadır. Üriner sistem tümörlerinde cilt metastazları oldukça nadir görülmesine rağmen, üst üriner sistem TCC'lerinde cilt metastazı insidansı, bu konuda yayınlanmış araştırma eksikliği nedeniyle tam olarak bilinmemektedir. Bu makalede, renal pelvik kitle nedeniyle ameliyat edilen bir hastanın sol inguinal bölgesinde TCC metastazı ile uyumlu bir lezyonu sunmayı amaçladık. Altmış bir yaşında erkek hastaya sol böbrek üst polde renal hücreli karsinom (RHK) olarak rapor edilen kitle nedeniyle sol laparoskopik nefrektomi uygulandı. Patoloji sonucu sol renal TCC olarak bildirildikten sonra, hastaya başka bir tıp merkezinde sol üreterektomi artı kaf rezeksiyonu yapıldı. Bu ikinci ameliyattan sonra hastanın sol inguinal bölgesinde trokar giriş yerinde gelişen cilt lezyonu görüntülemede apse olarak rapor edildi. Eksize edilen apsenin histopatolojisi TCC metastazı olarak raporlandı. Ürotelyal karsinomların cilt metastazları için tedavi rejimi konusunda bir fikir birliği yoktur ve bu metastazlar nispeten kötü prognoza sahiptir. Bir yıllık sağkalım oranı genellikle %35'tir. Olgumuz gemsitabin ve sisplatin tedavisi almıştır ve on iki aydır onkoloji takibindedir.

Anahtar kelimeler: böbrek kanseri, metastaz, transizyonel hücreli karsinom, deri

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### Introduction

While TCC is most commonly seen in the bladder, it is also rarely seen in the upper urinary tract. Upper urinary tract TCC accounts for 5% of all TCCs [1]. Treatment approach for these TCCs generally involves open-laparoscopic or robotic nephroureterectomy and cuff resection. Laparoscopic surgery, which was first defined as a minimally invasive procedure by Clayman et al. in 1991 [2], has become quite frequently applied due to milder postoperative pain, shorter hospital stay, and faster recovery compared to open surgery. On the other hand, non-surgical treatment approaches may be given priority in metastatic disease.

Skin metastases originating from renal cell carcinoma (3.4-4.0%) bladder carcinoma (0.84-3.6%), prostate carcinoma (0.36-0.7%), and testicular germ cell tumors (0.4%) have been reported at indicated incidence rates [3]. The incidence rates of skin metastasis in TCCs originating from the upper urinary tract are not completely known. Port site metastasis (PSM), which is rare after laparoscopic surgery, is defined as a recurrent tumoral lesion in one or more trocar entry sites on the abdominal wall [4]. In urology practice, PSM was first reported in 1994 by Stolla et al. in a patient with bladder tumor [5]. After this first report, more than 50 urological PSM cases have been reported to date [6].

In this article, we present a case of TCC metastasis at the left inguinal port site three months after the patient's first operation for renal tumor.

### Case

A 61-year-old male patient with a renal stone who had undergone endourological surgery five years ago was admitted to our outpatient clinic with complaints of intermittent hematuria, and left flank pain. The hematuria was thought to have resulted from the stone. However, since the most recent ultrasonography (USG) of the patient revealed the presence of a solid lesion in the upper pole of the left kidney, contrast-enhanced abdominal magnetic resonance imaging (MRI) was performed which disclosed a 6 cm solid lesion in the upper pole of the left kidney, consistent with a renal cell carcinoma (RCC) (Figure 1).

When the computed tomography (CT) scans of the patient performed within the previous 5 years were examined, it was observed that a lesion, which had been mostly reported as a kidney cyst, remained in situ for a long time Left laparoscopic

nephrectomy was performed because the patient's most recent MRI revealed a lesion consistent with an RCC in his left kidney. Histopathology results revealed the presence of stage pT3a TCC with surgical margin negativity which invaded beyond muscular layer into peripelvic fat or renal parenchyma and also demonstrated lymphovascular invasion. Two months after nephrectomy, the patient underwent left laparoscopic ureterectomy and cuff excision in another center. The pathology results of the second operation revealed the presence of a benign lesion.

When the patient reapplied to our clinic three months after laparoscopic left ureterectomy and cuff excision, he complained of a painful swelling at the port site on the left inguinal region for three months. A contrast-enhanced CT scan reportedly demonstrated a mass lesion with a diameter of 3 cm localized lateral to the left psoas muscle, and another lesion with a diameter of 3 cm in the subcutaneous tissue of the left inguinal region consistent with an abscess (Figure 2). However, at this time, the patient had no fever, and inflammation markers were negative. Surgical excision was performed because fluid collection was not observed in the superficial USG performed for the lesion due to the presence of a suspect abscess. The pathology result of the surgical specimen was reported as metastatic lesion of TCC with surgical margin positivity. However, the lesion located lateral to the psoas muscle was not operated. The patient, who received 8 cycles of gemcitabine and cisplatin treatment, has been under oncology follow-up for 12 months. His current CT showed regression of the lesion localized lateral to the psoas muscle (Figure 3).

### Discussion

Urinary system TCCs generally metastasize to the lungs, liver, bones, heart and brain, and especially to regional lymph nodes. However, skin metastases are most common in the head, face, neck, abdomen, suprapubic regions, and extremities [7]. In our case, the skin metastasis appeared as a hyperemic mass lesion approximately 3 cm in diameter at the trocar entry site on the left inguinal region.

It has been reported that TCCs originating from the bladder cause skin metastasis more frequently than the TCCs of the renal pelvis [8,9]. However, the incidence of skin metastasis from TCCs originating from renal pelvis is not exactly known due to the lack of literature information.

Current clinical and laboratory procedures can hardly



Figure 1. Preoperative MRI image: Approximately 6 cm solid lesion in the left kidney



Figure 2. Control CT image after three months: 3 cm lesion on the left psoas muscle (yellow) and a 3 cm lesion on the skin in the left lower quadrant (red)

Figure 3. Control CT image after twelve months: Regression of the lesion in the lateral psoas

reveal metastases of TCCs. The diagnosis of skin metastasis of TCC is made based on pathological examination of the mass lesions after surgical excision. In addition, there are reports of cases diagnosed based on pathological examination of needle biopsy specimens [10]. In our case, the lesion considered to be an abscess based on radiological interpretation, so abscess was excised which prevented us to plan a wider excision with resultant development of positive surgical margins.

Although there are not enough data on the treatment of skin metastases of urinary TCCs, platinum-based treatments are generally used in most cases [11]. However, the prognosis of skin metastases of urinary TCCs are quite poor. Overall, one-year survival rate for metastatic urothelial carcinomas is 35%, even with the use of current chemotherapeutic agents [12].

Our patient has been on cisplatin and gemcitabine treatment for about twelve months, and he is currently being closely followed up by our urology and oncology clinics.

### Conclusion

In conclusion, PSM of urinary system TCCs is a rare condition with a very poor prognosis. Newly developed skin lesions should be considered as possible metastases, and should be closely followed up in patients treated for urinary TCC.

### **Ethics Committee Approval:** N / A.

**Informed Consent:** An informed consent was obtained from the patients.

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### A Rare Case: Primary Signet Ring Cell Carcinoma of Urinary Bladder Nadir Bir Vaka: Mesanenin Primer Taslı Yüzük Hücreli Karsinomu

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### Abstract

Primary signet ring cell carcinoma of the urinary bladder is a very rare tumor. At the time of diagnosis, patients are usually in an advanced stage and have a poor prognosis. It is a very rare tumor, case report presentations are important in the management of these patients. We report to a 41-year-old patient who presented with painless gross hematuria and abdominal pain for three months and was diagnosed with a bladder tumor. The patient was considered to have advanced stage disease due to the presence of liver metastasis at the time of diagnosis and was followed up with chemotherapy. After medical treatment, the patient died after a survival of more than 30 months.

Keywords: bladder, adenocarcinoma, signet ring cell

### Özet

Mesanenin primer taşlı yüzük hücreli karsinomu çok nadir görülen bir tümördür. Tanı anında hastalar genellikle ileri evrededir ve kötü prognoza sahiptir. Çok nadir görülen bir tümördür, olgu sunumları bu hastaların yönetiminde önemlidir. Üç aydır ağrısız makroskopik hematüri ve karın ağrısı ile başvuran ve mesane tümörü tanısı alan 41 yaşında bir hastayı sunuyoruz. Hasta tanı anında karaciğer metastazı varlığı nedeniyle ileri evre hastalık olarak kabul edildi ve kemoterapi ile takip edildi. Medikal tedavi başlangıcının ardından hasta 30 aydan uzun bir süre hayatta kaldıktan sonra hayatını kaybetmiştir.

Anahtar kelimeler: mesane, adenokarsinom, taşlı yüzük hücre

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### Introduction

Primary signet-ring cell carcinoma (PSRCC) is a rare tumor of the urinary bladder [1,2]. The most common type of bladder cancer is urothelial carcinoma, which occurs in 90% of all cases [3,4]. Cases of adenocarcinoma of the bladder are extremely low (2%) [3]. PSRCC of the bladder accounts for 0.12–0.6% among the different histological subtypes of bladder carcinomas [3,5].

PSRCC of the bladder was first described in 1955 by Otto Saphire [6]. To the present day, data on just over 300 cases with such a finding have been published [3]. In a research that has been performed between Sept 1991 and Aug 2016, and included a total of 2778 bladder cancer patients, only five (0.18%) patients were diagnosed with PSRCC [2].

Signet ring cell carcinoma (SRCC), classified as a subtype of adenocarcinoma, most commonly occurs in the colon and stomach. Evaluation of clinical, radiological and immunohistochemical findings of involvement of other systems is important in the differential diagnosis to determine the primary origin of cancer. Here, we aimed to share a rare case of PSRCC of the bladder who had a longer survival time than the median overall survival reported in the literature.

### Case

A 41-year-old male referred to internal medicine outpatient clinic with intermittent painless gross hematuria and abdominal pain ongoing for three months. The medical history of the patient included diabetes mellitus and thyroidectomy. The patient was using oral anti-diabetic and thyroid replacement therapies. Systemic examination was grossly normal.

The abdominal ultrasound revealed 63x45 mm protruding cystic lesion in the bladder lumen and two solid lesions in the liver, the largest of which is 28 mm in size. Computed tomography

scan revealed a 73x49x51 mm lesion with exophytic extension in the bladder (Figure 1), three metastatic lesions in the liver, the largest of which was 31 mm in segment 2 (Figure 2), and a 16 mm lymphadenopathy in the right external iliac chain. Trucut biopsy was performed from the lesion in the segment 2 of the liver. The pathology report showed carcinoma infiltration in extracellular mucin with diffuse appearance of signet-ring cells and glandular structures (Figure 3). The immunohistochemical findings included positivity for CK7, CK20, CDX2, and SATB2 with negative results for PAX8 and GATA3. Liver function tests were unremarkable. Upper gastrointestinal endoscopy and colonoscopy were not performed because no findings indicated a primary gastrointestinal cancer. Serum prostate-specific antigen (PSA) was 1,6 ng/ml (reference range(RR): 0,4 ng/ml), CA 19-9 2 U/ml (RR:0-37 U/ml), and carcinoembryonic antigen (CEA) 19.9 ng/ml (RR: <5 ng/ml). No other primary focus was detected in other system scans, so the bladder was considered as the primary site of the tumor.

As a result of the current findings, first-line gemcitabine plus cisplatin regimen was initiated. CEA level was 64 ng/ml at the initiation date of chemotherapy (CTh). After the third cycle of CTh, cisplatin was discontinued due to acute kidney injury (creatinine level increased to 2.5 mg/dl from its basal level of 0,8 mg/dl). After creatinine level decreased to 1.4 mg/ dl and remained stable, it was decided to continue the treatment with carboplatin and gemcitabine combination. After three cycles of this CTh regimen, partial response was detected on positron emission tomography-computerized tomography (PET-CT) scan and CEA level decreased to 5,3 ng/ml. Therefore, additional three CTh cycles was planned. After the sixth cycle, CTh was discontinued due to grade 3 thrombocytopenia. After the complete blood count results normalized, it was decided to continue the treatment with single agent capecitabine. Due to chronic kidney disease, capecitabine was initiated after renal



Figure 1. Primary tumour at the time of diagnosis

Figure 2. Liver metastases at the time of diagnosis

**Figure 3.** Carcinoma infiltration (H&E, Ax40, Bx100) forming glandular structures in the focal area with signet ring cell appearance in a large area within the liver tissue (stellate)

dose adjustment. After two months of treatment, CEA level increased to 50 ng/ml and macroscopic hematuria occurred. PET-CT scan was ordered after these findings. Although the primary lesion in the bladder was stable, a new metastatic lesion in the liver was detected. Because of the good response with first-line gemcitabine-platin combination, re-challenge with carboplatin and gemcitabine regimen was preferred. After three cycles of treatment, PET-CT imaging showed progression in metastatic liver lesions and new conglomerated lymphadenopathies in the external iliac region, although the primary lesion in the bladder was stable. After palliative radiotherapy (RT) was applied to the lesions in the bladder, liver, and external iliac region, it was decided to continue the treatment with second-line paclitaxel and carboplatin combination. CEA level was found as 22 ng/ml at the initiation of CTh. After two cycles of CTh, new metastatic lesions in the liver and lung were detected on PET-CT scan and third-line single agent docetaxel regimen was planned. After the third cycle of docetaxel, treatment was discontinued due to grade 3 anemia. PET-CT imaging was performed and new metastases were detected in the lung, liver and sacrum. Single agent vinorelbine was initiated after palliative RT to the sacral metastasis. One month after the 3rd cycle vinorelbine was administered, the patient was referred for cardiology consultation upon complaints of dyspnea and peripheral edema which had been present for one week. The patient was diagnosed as heart failure with low ejection fraction and was interned to the coronary intensive care unit. Acute decompensated heart failure treatment was started. Unfortunately, the patient died of acute decompensated heart failure in June 2023. Despite all interventions, the patient died 30 months after diagnosis.

### Discussion

Less than 2% of all primary bladder neoplasms are of the adenocarcinomas [4]. PRSCC of the urinary bladder is an extremely rare tumor as a subtype of adenocarcinoma, accounting for 0.24% of all bladder malignancies [3,5]. After the first two cases published in 1955, approximately 300 patients have been described in the English literature [2,6]. The disease is usually diagnosed at an incurable disease. Due to asymptomatic progression, advanced disease is present at the time of diagnosis, so the prognosis is poor. Also, the tumor is considered resistant to CTh and RT. [3,7].

The clinical presentations of PSRCC of the bladder are similar to those of bladder malignant tumors. Common presenting symptoms were hematuria and irritative voiding symptoms. Hong et al. investigated 32 patients with SRCC of the bladder, reported macroscopic hematuria in 59% of patients, bladder irritation symptoms in 25% [8]. The current information on diagnosis and treatment is based on case reports and small nonrandomized studies [3]. Identification of the primary localization requires the collaboration of radiology, pathology, urology and internal medicine. Hong et al. reported that SRCC of the bladder shows diffuse and infiltrative growth and therefore neoplastic lesions are often not recognized in the early stage of SRCC on cystoscopy [8]. On cystoscopy, the lesion is characterized as pedunculated, polypoid, sessile, or ulceroinfiltrative. Two thirds of the tumors secreted mucin and most accumulated in the interstitial area. Less frequently, mucin is secreted within

the lumen of the acinus and rarely, excess intracellular mucin shifts the nucleus into a peripheral crescent, giving the cells the appearance of a signet ring [9].

When diagnosing SRCC of the bladder, it is recommended to rule out a primary tumor that arises from outside the bladder [3]. Metastatic SRCC of bladder, the primary lesion is likely to originate from gastrointestinal tract. Patients should be examined for abdominal pain, nausea, vomiting, bloddy diarrehea and constipasion. Contrast CT of the abdomen/pelvis and gastrointestinal endoscopy can be used for clinical diagnosis. Immunohistochemistry is very useful in determining the origin of unknown primary site. Until now, there is no commonly accepted agreement on the immunohistochemical findings of primary SRCC of the bladder. CK20 is a cytokeratin typically expressed in the lower gastrointestinal tract, urothelium and Merkel cells. CK7 is expressed in lung, ovarian, endometrial and breast cancers [10]. CK20-positive/CK7-positive combination is seen in urothelial carcinomas and pancreatic/biliary cancers. Thomas et al. found positive expression of CK20 (78%), CK7 (67%), CDX2(33%) and β-catenin (78%) [11]. Hong et al. found positive expression GATA3 (72%), Ki-67 (63%), CEA (44%) and CK20 (28%) [8]. SRCCs of the gastrointestinal tract and bladder have similar immunohistochemical staining patterns. So immunohistochemistry is insufficient to distinguish between primary bladder tumor and metastasis of gastrointestinal origin [11]. In addition, the absence of nuclear positivity for β-catenin in the absence of an endoscopically visible lesion in the gastrointestinal tract supports a urinary bladder origin [1].  $\beta$ -catenin positivity is detected to the cell membrane, confirming a primary bladder origin [1]. Despite the lack of an identified serum marker for PSRCC of the urinary bladder, elevated CEA has been frequently reported. There is evidence that an increase in CEA level after surgery in SRCC patients is closely associated with disease progression and CEA is recommended to determine the degree of malignancy and to monitor the follow-up of SRCC [9]. In our case, we observed CEA elevation and we used in evaluation of treatment response.

Patients with SRCC present at a younger age, higher histologic grade and more advanced tumor stage than other bladder tumor subtypes [3]. Patients with SRCC have worse responses to RT and CTh than patients with urothelial carcinoma [4]. In the absence of consensus guidelines for the management of PSRCC, diagnosis in a multidisciplinary setting and input from relevant clinical subspecialties is required. Treatment options for SRCCs include surgery, RT and CTh. Surgical methods range from transurethral resection to radical cystectomy with urinary diversion. Currently, there is no standard CTh for PSRCCs of the bladder due to their rarity. In a case report of 12 cases of bladder SRCC treated with adjuvant CTh or CTh for metastatic disease, regimens containing carboplatin, cisplatin, gemcitabine, capecitabine and 5-fluoro-uracil were used [12]. We preferred cisplatin and gemcitabine, a standard combination for transitional carcinoma of the urinary bladder. Due to progression during follow-up, capecitabine, paclitaxel and docetaxel CTh agents were administered. When progression was detected on the last imaging, vinorelbine was initiated. Acute kidney injury and thrombocytopenia, which were thought to be related to chemotherapy, developed during treatment. In a retrospective study of 32 SRCC patients, 1-year and 2-year

survival rates were %53.1 and %9.4 respectively [8]. The same study also showed that GATA3 was an independent protective factor for prognosis (p <0.05) and T stage was an independent risk factor (p <0.05) [8]. In a series of 54 patients, 46% had stage 4 disease, with an overall survival rate of 43% at 2 years, in addition, no patient with stage 4 disease at diagnosis was alive 2 years later [7]. Liu et al found that the 3-year median survival for PSRCC of the bladder was 25.3% [13]. Thirty months after the diagnosis, the patient died of acute decompensated heart failure. The patient's 30-month survival month survival exceeds the typical survival reported for PSRCC patients. This is attributed to the favorable response to initial chemotherapt and the absence of serious systemic complications in the early period.

### Conclusion

PSRCCs of the bladder is very rare. When a diagnosis of SRCC is made, other sites, especially the gastrointestinal tract, should be investigated. Due to the rarity of the tumor and the lack of randomized trials, optimal treatment has not yet been determined. Treatment is usually similar to the traditional radical treatment of the bladder cancer. Consequently, further work is needed to investigate and consider potential barriers to the provision of appropriate care for these patients.

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