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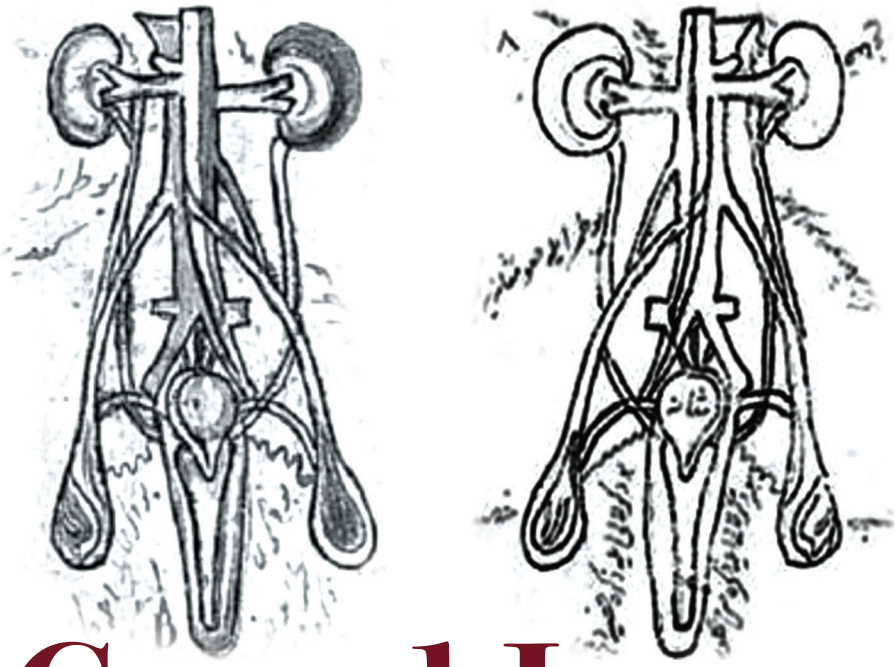

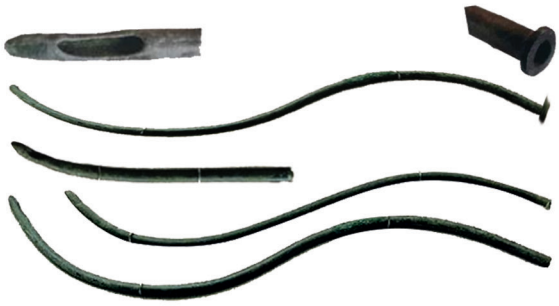

Grand Journal of UROLOGY

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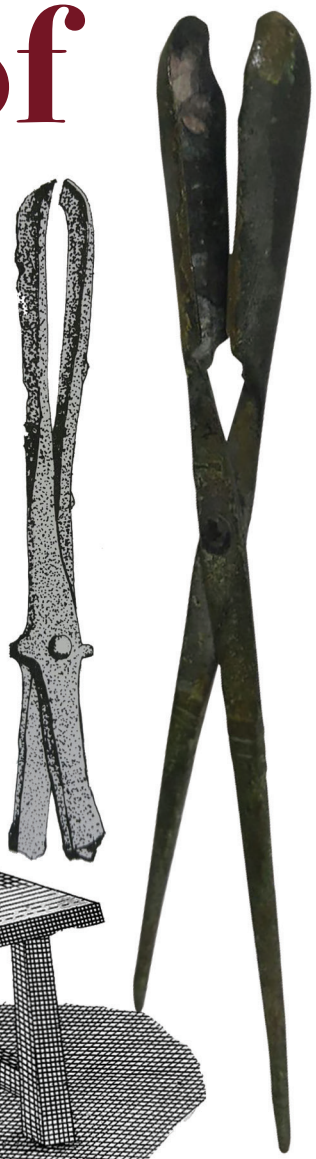

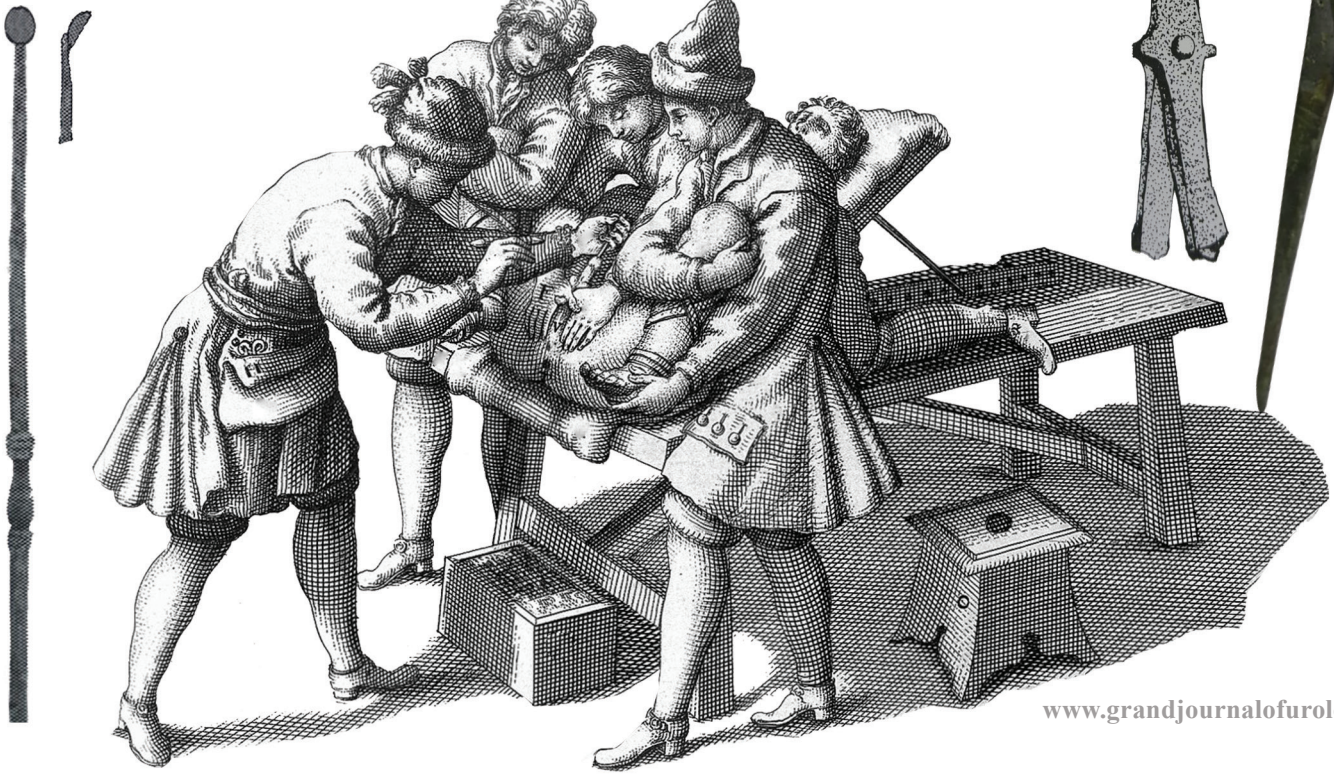

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Grand Journal of UROLOGY

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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 www.grandjournalofurology.com. The journal guidelines, technical information, and the required forms are available on the journal's web page.

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- Turkish (if the article is sent from Turkey) and English short title of the article, not exceeding 50 characters.
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- Name, institution, e-mail, mobile phone and address of the corresponding author.

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- At least 2.5 cm margins must be left on all sides of each page.
- If there is, figure should be sent separately, it should not be in the main text.
- 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.
- Abbreviations should be defined when first mentioned and then used consistently.
- Abbreviations should not be used in the title. Abbreviations can be used if they occur three or more times in the abstract, but must be re-introduced in the main text.
- Footnotes can be used to provide additional information, which may include a quotation of a reference in the reference list. It should not consist of just one reference and never include bibliographic details of a reference. It should also not contain any figures or tables.
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- Tables and figures should be numbered with parentheses in the text.

The main text should contain the following sections in order:

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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, Gereçler ve Yöntemler, Bulgular, Sonuç).

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)? http://www.nlm.nih.gov/mesh/MBrowser.html 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.

Author Instructions

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.

Editorial Comment: It aims to present a brief critical comment on the research article published in the journal by experts or highly reputable reviewers. The authors are selected and invited by the journal to provide such comments. It does not include abstract, keyword, table, figure, image, and other media elements.

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Article Type	Number of Authors	Font Word	Summary of Word	Source	Table
Research	12	4000	450	30	5
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Case Report	8	1500	250	15	1
Clinical Image	5	500	N/A	10	0
Letters to the Editor	5	500	N/A	5	1

Acknowledgments (If Available)

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-Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Authors must indicate the existence of a conflict of interest. If there is no conflict of interest, it should be declared (For more information: https://grandjournalofurology.com/static.php?id=32).

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Manuscripts should be edited according to the Elsevier-Vancouver reference style.

-References should be numbered in square brackets in the text.

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

- Articles with six and fewer authors

[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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Descriptions of the figures related to the article should be written in order under this title.

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- The cover letter should include the article's title, the article type, and the corresponding author's full name.

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- The corresponding author should make a declaration that the article is not currently published elsewhere, accepted, or reviewed simultaneously.

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- Figures should always be defined in consecutive numerical order in the text.

- Figures, graphics, and photographs must be submitted as separate files (in TIFF or JPEG format) via the application system.

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

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The articles can be withdrawn after acceptance until corrected proof are sent by the author(s) to the editorial office. After this stage, the article's withdrawal will only be approved for the most compelling and inevitable reasons. Author (s) who prefer to request a withdrawal of their manuscript is obliged to fill in the Withdrawal Form, declaring the reasons and submit the scanned version signed with each author's original signature to the editorial board e-mail at info@grandjournalofurology.com. If the reason is acceptable, the author may retract the article without any penalty for withdrawal. Unless the withdrawal request of manuscripts whose copyrights have been transferred to the Grand Journal of Urology is approved, the author(s) cannot send their work to another journal for evaluation.

Contents

Contents

Editorial

Dear colleagues,

I am honored to share with you the third issue of 2022 of the Grand Journal of Urology (Grand J Urol) with the contributions of many respected researchers and authors.

Our journal has been abstracted/indexed in EBSCOhost, J-Gate, Index Copernicus International (World of Journals List), EuroPub, SciLit, ResearchGate, ScienceGate and Google Scholar international databases. As of these achievements, the Grand Journal of Urology (GJU) has taken its place among the journals indexed by international databases.

Grand Journal of Urology (GJU) aims to carry written and visual scientific urology studies to academic platforms and to make significant contributions to the science of urology.

In this issue of our journal, there are many valuable articles under the subheadings of Andrology, General Urology, Laparoscopic and Robotic Surgery, Female 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
September 2022
Assoc. Prof. Ekrem GUNER, MD
Editor-in-Chief

Original Article – General Urology

Grand J Urol 2022;2(3):87-92
DOI: 10.5505/GJU.2022.32032

The Retrospective Analysis of 54 COVID-19 Patients With Retroperitoneal Bleeding in One Center

Tek Merkezde Retroperitoneal Kanamalı 54 COVID-19 Hastasının Retrospektif Analizi

Yusuf Kasap[1], Muhammed Emin Polat[1], Kazim Ceviz[1], Lutfi Ihsan Boyaci[1], Emre Uzun[1], Samet Senel[1], Esin Olcucuoglu[2]

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Cite as: Kasap Y, Polat ME, Ceviz K, Boyaci LI, Uzun E, Senel S, Olcucuoglu E. The retrospective analysis of 54 COVID-19 patients with retroperitoneal bleeding in one center. Grand J Urol 2022;2(3):87-92.

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Abstract

Objective: We aimed to analyze and report the outcomes of patients with retroperitoneal bleeding (RPB) among our COVID-19 inpatients under anticoagulation therapy.
Materials and Methods: We retrospectively analyzed 54 patients who were anticoagulated with low- molecular-weight heparin (LMWH) and developed RPB during COVID-19 treatment in the hospital, either in intensive care unit or non-intensive care unit services, between March 2020 and March 2021. The patients' demographic and clinical data were analyzed, and we compared the laboratory results at the time of admission and during episodes of RPB. The patients were divided into conservative and interventional treatment groups. We compared the size of retroperitoneal hematoma, anticoagulant doses, erythrocyte suspension transfusion rates, presence of hyperinflammation syndrome between these groups. Also, treatment modalities and mortality status were shown. The hematoma size and erythrocyte suspension transfusion rates were compared between groups, and their correlation with anticoagulant dose and age were analyzed as well.
Results: In the management of RPB that developed, 48 (88.9%) patients were approached conservatively, 4 (7.4%) patients underwent angioembolization, and 2 (3.7%) patients laparotomy. Mortality was observed in 14 (25.9%) patients. Relevant laboratory parameters as lactate dehydrogenase, procalcitonin, interleukin-6 levels and lymphocyte counts were elevated exceedingly, while the hemoglobin values were significantly lower during episodes of RPB ($p=0.007$, $p=0.044$, $p=0.031$, $p=0.018$ and $p<0.001$, respectively). Also, there was a significant correlation between increased LMWH doses and size of the hematomas ($p=0.044$).
Conclusion: Patients experiencing RPB while receiving anticoagulants due to COVID-19 need active treatment depending on the dose of anticoagulants they are using. Considering the patient's clinical need, it may be a logical approach to start treatment with the lowest possible dose of an anticoagulant.

Keywords: heparin, anticoagulant treatment, COVID-19, retroperitoneal hematoma, mortality

Öz

Amaç: Yatarak tedavi gören COVID-19 hastalarımız arasında antikoagülan tedavi gören retroperitoneal kanamalı (RPK) hastaların sonuçlarını analiz ve rapor etmeyi amaçladık.
Gereçler ve Yöntemler: Mart 2020 ile Mart 2021 tarihleri arasında hastanemizde yoğun bakım veya yoğun bakım dışı servislerde COVID-19 tedavisi sırasında düşük molekül ağırlıklı heparin (DMAH) tedavisi ile antikoagülasyon sağlanan ve RPK gelişen 54 hasta retrospektif olarak incelendi. Hastaların demografik ve klinik verileri analiz edildi, başvuru ve RPK anındaki laboratuvar sonuçları karşılaştırıldı. Hastalar konservatif ve girişimsel tedavi gruplarına ayrıldı. Bu gruplar arasında retroperitoneal hematom boyutu, antikoagülan dozları, eritrosit süspansiyon transfüzyon oranları, hiperinflamasyon sendromu varlığı karşılaştırıldı. Ayrıca tedavi modaliteleri ve mortalite durumu da gösterildi. Hematom boyutu ve eritrosit süspansiyonu transfüzyon oranları karşılaştırıldı, antikoagülan dozu ve yaş ile korelasyonları analiz edildi.
Bulgular: Hastalarda gelişen RPK yönetiminde 48 (%88,9) hastaya konservatif olarak yaklaşıldı, 4 (%7,4) hastaya anjiyoembolizasyon, 2 (%3,7) hastaya laparotomi uygulandı. Mortalite 14 (%25,9) hastada gözlendi. Laboratuvar sonuçlarında RPK sırasında laktat dehidrojenaz, prokalsitonin, interlökin-6 düzeyleri ve lenfosit düzeyleri daha yüksek, hemoglobin düzeyi anlamlı olarak daha düşüktü (sırasıyla $p=0,007$, $p=0,044$, $p=0,031$, $p=0,018$ ve $p<0,001$). Ayrıca artmış DMAH dozu ile hematom boyutu arasında anlamlı bir ilişki vardı ($p=0,044$).
Sonuç: COVID-19 nedeniyle antikoagülan alan hastalarda aktif tedavi gerektiren RPK, antikoagülan dozu ile ilişkilidir. Hastanın klinik ihtiyacı göz önüne alındığında mümkün olan en düşük doz antikoagülan ile tedaviye başlamak akılcı bir yaklaşım olabilir.

Anahtar kelimeler: heparin, antikoagülan tedavi, COVID-19, retroperitoneal hematom, mortalite

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Introduction

COVID-19 is a widespread and life-threatening viral infection that frequently appears with respiratory symptoms and fever [1]. It can also affect other systems, such as cardiovascular, hepatobiliary, or hematologic systems [2,3]. Retroperitoneal bleeding (RPB) is another life-threatening condition that can manifest due to trauma, vascular lesions, tumors, surgical procedures, anticoagulant treatment, or idiopathic risk factors [2,4]. The hypercoagulable state occurs secondary to the effect of the virus or increased cytokine secretion [5]. Therefore, anticoagulant treatments are recommended widely in COVID-19 patients, and the risk of bleeding concomitantly increases [1,5]. Due to the thromboembolic complications and the bleeding risk of the viral infection, the predictability of bleeding is becoming an important issue requiring safe use of anticoagulants [1]. To predict and prevent this complication, we analyzed the clinical and laboratory results of 54 RPB cases among anticoagulated COVID-19 inpatients. We aimed both to describe incidence, morbidity, and mortality rates related to RPB, also search for factors that affect bleeding to improve clinicians' knowledge.

Materials and Methods

This study was approved by the local institutional review board (University of Health Sciences Ankara City Hospital, approval number- 2021/E2-21-229) and The Turkish Ministry of Health. It was carried out in accordance with the Basic Principles of WMA Declaration of Helsinki–Ethical Principles for Medical Research Involving Human Subjects.

A total of 16.211 inpatients diagnosed as COVID-19 based on the results of polymerase chain reaction (PCR) tests of nasopharyngeal swabs or computed thorax tomographies (CT Thorax) and started to receive anticoagulant treatment (low-molecular-weight heparin-LMWH) in our hospital between 12.03.2020- 12.03.2021 were analyzed. Among them, 3583 patients were treated in the intensive care units (ICUs). Fifty-four patients who developed RPB during follow-up were included in this study. Before hospitalization and treatment, the patients diagnosed with RPB and those already using LMWH due to other indications before the diagnosis of COVID-19 disease was made were excluded.

Data were retrospectively retrieved from the hospital's electronic database. We collected data related to demographic characteristics (age, gender), comorbidities, clinical symptoms (fever, cough, dyspnea, fatigue, myalgia), and results of relevant laboratory parameters [serum creatinine (SCr) (0.67-1.17), lactate dehydrogenase (LDH) (1-247 IU/L), international normalized ratio (INR) (0.8-1.2), activated partial thromboplastin time (aPTT) (9.8-14 second), fibrinogen (1.7-4.2 mg/dL), D-dimer (<550 ng/mL), procalcitonin (0-0.1 ng/mL), ferritin (22-322 µg/L), hemoglobin (13.5-17.2 g/dL), lymphocyte (1.1-4.5 x10^9/L), platelet counts (150-400 x10^9/L), C-reactive protein (CRP) (0-5 mg/L), interleukin-6 (IL-6) (0-50 pg/ml)] at admission and during RPB, radiological imaging (retroperitoneal hematoma size), and treatment protocols of the patients (conservative, angioembolization, laparotomy). Creatinine, LDH, INR, aPTT, fibrinogen, D-dimer, procalcitonin, ferritin, hemoglobin, lymphocyte, platelet, CRP, IL-6 values collected at both admission and during bleeding episodes, were compared.

The anticoagulation dose was determined in consideration of patients' body mass index (BMI) and risk factors for thromboembolism: increased D-dimer, fibrinogen levels, and thrombotic disease history.

Criteria of hyperinflammation syndrome were used to predict severity of COVID-19 infection. We described the hyperinflammation syndrome during the first hospitalization and bleeding episode with two or more of these criteria: LDH >300 IU/L, ferritin >500 mcg/L, D-dimer >1000 ng/mL, lymphocyte count <1000 cell/mm^3 [5].

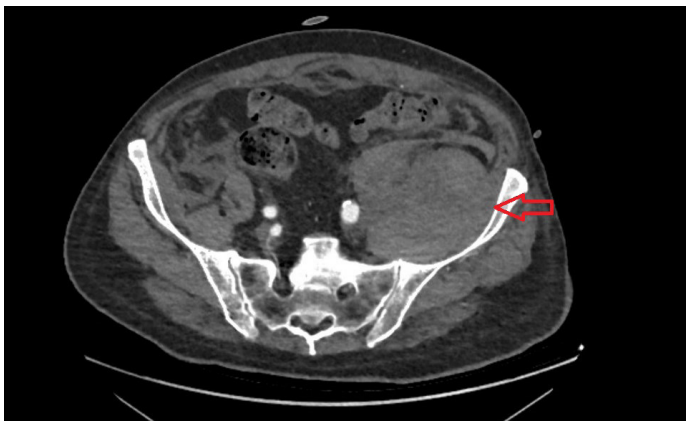

Figure 1. The arterial phase CT imaging of the retroperitoneal bleeding

Retroperitoneal hematoma was detected with CT scanner (Model: General Electrics-Revolution ES CT Scanner) of the abdomen (**Figure 1**). Length, width, and height of the retroperitoneal hematomas were measured. The greatest dimension measured was accepted as hematoma size. We defined the symptomatic period as the time elapsed between hospitalization and detection of the bleeding.

The patients were grouped according to the treatment they received (conservative treatment, angioembolization or surgical intervention: laparotomy) to analyze the factors affecting the requirement for treatment. Conservative treatment options indicated the cessation of anticoagulant treatment or decreasing its dose, follow-up of the immobilized patient and transfusions of blood products like erythrocyte suspension (ES), platelets or coagulation factors. Also, angioembolization of the active bleeding vessels and laparotomy to control bleeding were applied when transfusion rates of the patients increased enormously. Decreased hemoglobin values and the hemodynamic instability which was hardly managed with vasopressor medications were the main indications for intervention. Laparotomy was applied when interventional radiology was not available, and when surgical intervention for hemorrhagic complications is needed. When the interventional radiology was available, angioembolization was applied to these patients. However, the clinical picture did not allow us to use active treatment methods sometimes, for example in some patients we couldn't use any interventional method despite the need for increased rates, and amounts of ES transfusions and hemodynamic instability which didn't respond to the vasopressor treatment.

Table 1. Demographic, clinical, laboratory and treatment characteristics of patients

	Total (n=54)
Demographic data	
Age (year) (Mean ± SD)	70.7±12.8
Gender, female, n (%)	19 (35.2)
Comorbidities	
Hypertension, n (%)	36 (66.7)
Diabetes mellitus, n (%)	13 (24.1)
Asthma/COPD, n (%)	10 (18.5)
CAD, n (%)	20 (37)
CVA, n (%)	10 (18.5)
CKD, n (%)	13 (24.1)
Clinical data	
Fever, n (%)	13 (24.1)
Cough, n (%)	16 (29.6)
Dyspnea, n (%)	18 (33.3)
Fatigue, n (%)	12 (22.2)
Myalgia, n (%)	11 (20.4)
Symptoms duration (day) (mean)(min-max)	13 (1-29)
Hospitalization time (day) (mean)(min-max)	26 (0-95)
Mortality, n (%)	14 (25.9)
Laboratory results during admission and RPB time	
During admission LDH (IU/L) (median)(min-max)	344 (156-1038)
During RPB LDH (IU/L) (median)(min-max)	396.5 (207-16843)
p	**0.007**
During admission INR (median)(min-max)	1.1 (1-2.1)
During RPB INR (median)(min-max)	1.1 (0.8-3)
p	0.574
During admission D-dimer (ng/mL) (median)(min-max)	1515 (300-35200)
During RPB D-dimer (ng/mL) (median)(min-max)	2350 (510-709000)
p	0.253
During admission procalcitonin (ng/mL) (median)(min-max)	0.1 (0-511)
During RPB procalcitonin (ng/mL) (median)(min-max)	0.3 (0-11.7)
p	**0.044**
During admission ferritin (µg/L) (median)(min-max)	517 (31-4600)
During RPB ferritin (µg/L) (median)(min-max)	620.5 (68-111016)
p	0.056
During admission hemoglobin (g/dL) (median)(min-max)	12.2 (6.1-18.3)
During RPB hemoglobin (g/dL) (median)(min-max)	9.2 (4.1-13.6)
p	**<0.001**
During admission lymphocyte (cell/mm3) (median)(min-max)	735 (310-4280)
During RPB lymphocyte (cell/mm3) (median)(min-max)	850 (310-8780)
p	**0.018**

During admission IL-6 (pg/mL) (median)(min-max)	32.5 (2.8-992)
During RPB IL-6 (pg/mL) (median)(min-max)	36.8 (3-16241)
p	**0.031**
Medical treatment	
Anticoagulant dose (mL), n (%)	0.8 (0.4-1.2)
RPB treatment	
Conservative, n (%)	48 (88.9)
Angioembolization, n (%)	4 (7.4)
Laparotomy, n (%)	2 (3.7)

COVID-19: coronavirus disease-19; COPD: chronic obstructive pulmonary disease; CVA: cerebrovascular accident; CKD: chronic kidney disease; ES: erythrocyte suspension; LDH: lactate dehydrogenase; INR: international normalized ratio; IL-6: interleukin-6; RPB: retroperitoneal bleeding

Table 2. Comparison of clinical data of patients

Retroperitoneal bleeding administration	**Conservative (n=48, 88.9%)**	**Angioembolization/Laparotomy (n=6, 11.1%)**	**p**
Retroperitoneal hematoma size (cm) (median)(min-max)	10.5 (2-32)	20 (6-25)	0.116
Anticoagulant dose (mL) (median)(min-max)	0.8 (0.4-1.2)	1.2 (0.8-1.2)	**0.016**
ES transfusion rates (Unit) (median)(min-max)	5 (0-24)	9 (6-15)	**0.01**
Hyperinflammation syndrome during admission, n (%)	38 (79.2)	5 (83.3)	0.646
Hyperinflammation syndrome during RPB, n (%)	40 (83.3)	5 (83.3)	0.685

COVID-19: coronavirus disease-19; ES: erythrocyte suspension

Table 3. Correlation of retroperitoneal hematoma size, anticoagulant dose, erythrocyte suspension transfusion rate and age

	Retroperitoneal hematoma size		**ES transfusion rate**	
	r	**p**	**r**	**p**
Retroperitoneal hematoma size			0.186	0.178
Anticoagulant dose	0.263	**0.044**	0.09	0.52
ES transfusion rate	0.186	0.178		
Age	0.162	0.242	0.005	0.971

aPTT: activated partial thromboplastin time; COVID-19: coronavirus disease-19**;** ES: erythrocyte suspension; RPB: retroperitoneal bleeding

Also, two treatment groups were compared according to the size of retroperitoneal hematomas, anticoagulant dose, ES transfusion rate**,** hyperinflammation syndrome present at both admission and during bleeding episodes.

The hematoma size and ES transfusion rates were compared between groups. Their correlation with anticoagulant dose and age was analyzed as well.

Statistical Analysis

SPSS 22 software (IBM SPSS Statistics, IBM Corporation, Chicago, IL, USA) package program was used for the statistical analysis. This SPSS program is a frequently used up-to-date program that yields accurate results. The conformity of the variables to the normal distribution was examined using the Shapiro-Wilk tests. Variables were expressed as mean ± standard deviation or median (minimum-maximum) values. Mann-Whitney U test was used to compare groups in terms of non-categorical parameters. Categorical variables were expressed as percentages. Fisher's exact tests were used to compare categorical variables. Wilcoxon test was used to evaluate the significance of the differences between both groups. Correlation between parameters was evaluated with the Spearman test. Cases with a p-value below 0.05 were considered statistically significant.

Results

The RPB was seen in a total of 54 patients including 38 patients hospitalized in ICU, and 16 in non-ICU services.

The mean age of the patients was 70.7±12.8 years, and the study population consisted of 19 (35.2%) female cases. All patients received anticoagulant therapy (LMWH) as part of their COVID-19 treatment. In addition to LMWH treatment, 21 patients who had coronary artery disease (CAD) and/or cerebrovascular accident (CVA) were using their routine acetylsalicylic acid containing drugs before bleeding. In the management of RPB, 48 (88.9%) patients were approached conservatively, 4 (7.4%) patients underwent angioembolization, and 2 (3.7%) patients laparotomy. Fourteen (25.9%) patients exited. Only one patient (16.6%) died after laparotomy among the interventionally treated patients. Furthermore, 13 patients (39.5%) died in the conservatively treated group.

We compared the laboratory data at the time of admission and during RPB. Accordingly, at the time of RPB, LDH, procalcitonin, IL-6 levels and lymphocyte levels were higher, while the hemoglobin values were statistically significantly lower ($p=0.007$, $p=0.044$, $p=0.031$, $p=0.018$ and $p<0.001$, respectively).

Demographic, clinical, laboratory data and treatment modalities of the patients are shown in **Table 1**. The anticoagulant dose and ES transfusion rates of the patients who required active treatment (angioembolization or laparotomy) due to RPB were higher than the patients who were approached conservatively ($p=0.016$ and $p=0.01$, respectively). There was no significant difference between these two groups regarding retroperitoneal hematoma size and the presence of hyperinflammation syndrome at the time of admission and RPB (**Table 2**). In the subsequent analysis, a positive correlation was found between the anticoagulant dose given to the patients and the size of the developing retroperitoneal hematoma ($r=0.263$, $p=0.044$) (**Table 3**).

Discussion

This study aimed to analyze the RPB complication in the COVID-19 patients who had undergone anticoagulant treatment due to a high risk of thrombosis [6]. The increasing rate of this condition causes unpredictable clinical deterioration and needs to be identified at an early stage [5]. Before this study, only case series were trying to identify and describe this condition [5,7]. To our knowledge, this is the first study that evaluates a large series of patients with RPB.

The most important cause of death in COVID-19 patients is thromboembolism due to the cytokine storm and altered coagulation profiles of the patients [1,8,9]. To avoid this complication, the authors have recommended anticoagulation treatment [10,11]. However, there is no standard dose that can provide a totally safe environment for patients because the clinic of each patient is unique, and the predisposition to this complication may vary [5,10]. In our study, the hematoma size increased with the increasing dose of the anticoagulant. The anticoagulant doses and the ES transfusion rates of the interventional treatment group were higher than the conservative group. So that, if we decrease the use of unnecessarily administered high-dose anticoagulants, we may treat RPB with only conservative treatment.

In a case series, incidence rate of RPB was declared as 7.6 per 1000 hospitalizations among patients infected with COVID-19 [5]. The rate of retroperitoneal bleeding was 0.10% among patients admitted to our hospital, especially to ICUs. Also, in all patients who underwent anticoagulant treatment, the rate of bleeding was 0.003%. It seems that the need for ICU may increase the rates of retroperitoneal bleeding. In ICUs, the increased cytokine storm of the patients and increased susceptibility to the DIC may make bleeding easier with anticoagulation.

For the treatment of RPB, there are different recommendations. Still, the first step must include conservative approaches like stopping the anticoagulant drugs, initiation of intravenous fluid resuscitation, balanced transfusion of ES and coagulation products in case of need, and monitorization of the immobilized patient to avoid additional trauma [1,5]. These first-step treatments are vital because if we control the bleeding, we can decrease the number of healthcare workers who will make therapeutic interventions [1]. However, if the patient needs an intervention for his/her survival, we need to choose the proper treatment modality according to the patient's clinical condition [5]. In our hospital, we applied laparotomy in 3.7% and angioembolization in 7.4% of the patients.

The other risk factors for RPB have been indicated as age, presence of comorbidities including hypertension (HT), chronic kidney disease (CKD) and diabetes mellitus (DM) [5]. Also, increased aPTT levels, and disseminated intravascular coagulation (DIC) increase the risk and worsen the prognosis of this condition [2,5,12]. In our results, the mean age of the patients was 70.7 years, and all of them were using LMWH. The patients had HT (6.7%), CAD (37%), and DM (24%). We did not find a significant difference between aPTT values of the patients during the bleeding episodes, but LDH, procalcitonin, lymphocyte and IL-6 values were significantly higher in these patients during the bleeding period compared to their baseline values. We think that proinflammatory cytokines like IL-6, indicators of hyperinflammation syndrome like LDH-lymphocyte count and procalcitonin levels which indicate increased level of infection may provide information about propensity for the retroperitoneal hemorrhage parallel to the severity of infection.

Our study also has limitations. First of all, our study was designed retrospectively. In addition, the small number of patients is one of the limitations. Due to the restriction of the data, we could not analyze the non-RPB control group. However, we think that our study will be an essential source for the RPB clinic, as this study was performed during COVID-19 epidemic with the highest number of patients reported in the literature.

Conclusion

Patients experiencing RPB while receiving anticoagulants due to COVID-19 need active treatment depending on the dose of anticoagulants they are using Considering the patient's clinical need, it may be a logical approach to start treatment with the lowest possible dose of an anticoagulant. Nevertheless, we need more studies to identify a safe dose of LMWH treatment. Also, the clinicians must be aware of this complication and its risk factors. They must not hesitate to make interventions to decrease the mortality rates due to RPB in case of need.

Ethics Committee Approval: This study was approved by University of Health Sciences Ankara City Hospital Review Board (approval date and number 07.04.2021/E2-21-229) and Turkish Ministry of Health.
Informed Consent: An informed consent was obtained from all the patients or relatives.
Publication: The results of the study were not published in full or in part in form of abstracts.
Peer-review: Externally and internally peer-reviewed.
Authorship Contributions: There is not any contributions who may not be listed as authors. Concept – Y.K., M.E.P.; Design – Y.K., M.E.P., K.C.; Supervision –Y.K., S.S., E.O., Resources – M.E.P., K.C., L.I.B.; Materials – Y.K., M.E.P., K.C.; Data Collection and/or Processing – M.E.P., K.C., S.S.; Analysis and/or Interpretation – M.E.P., E.U.; Literature Search – M.E.P., E.U.; Writing Manuscript – Y.K., M.E.P., S.S.; Critical Review – E.O.
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Original Article – Laparoscopic and Robotic Surgery

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Comparison of Open and Laparoscopic Simple Prostatectomy Outcomes: Experiences of a Single Surgeon

Açık ve Laparoskopik Basit Prostatektomi Sonuçlarının Karşılaştırılması: Tek Cerrah Deneyimi

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Abstract

Objective: To compare the open simple prostatectomy (OSP) and laparoscopic simple prostatectomy (LSP) performed due to benign prostatic enlargement greater than 80 cc.
Materials and Methods: Between January 2015 and July 2021, patients who underwent OSP and LSP were retrospectively screened. The patients' demographic, preoperative, perioperative, and postoperative data were noted and compared.
Results: The data of a total of 90 patients, including 55 (61.1%) cases in the OSP and 35 cases (38.9%) in the LSP group were analyzed. Age, comorbidity rates, and body mass index scores of the patients were comparable. There was also no significant difference in the preoperatively calculated mean prostate volume, and Qmax of the cases. The mean operative time was significantly longer for LSP ($p<0.0001$). The median blood loss was 368 cc (250) and 80 cc (35) in the OSP and LSP groups, respectively, indicating significantly higher values in the OSP group ($p<0.0001$). The mean hospital stay was statistically significantly higher in the OSP group (8.1±4.3 days) compared to the LSP group (3.6±1 days) ($p<0.0001$). Minor complications were observed in 21 (38.2%) patients in the OSP and five (14.2%) patients in the LSP group with a significant intergroup difference ($p=0.007$).
Conclusion: Laparoscopic technique is a safe and effective procedure for large prostatic adenomas. Compared to open surgery, LSP has a longer operative time but is associated with greater patient comfort and lower complication rates.

Keywords: open simple prostatectomy, laparoscopic simple prostatectomy, benign prostatic enlargement, bladder outlet obstruction

Öz

Amaç: Bu çalışmada >80 cc üzeri benign prostat büyümesi sebebiyle açık basit prostatektomi (ABP) ve laparoskopik basit prostatektomi (LBP) yapılan hastaların verilerini karşılaştırmayı hedefledik.
Gereçler ve Yöntemler: Ocak 2015-Temmuz 2021 tarihleri arasında ABP ve LBP uygulanan hastalar geriye dönük olarak tarandı. Hastalara ait demografik veriler, preoperatif, peroperatif ve postoperatif döneme ait veriler not edildi ve karşılaştırıldı.
Bulgular: ABP grubunda 55 (%61,1) hasta, LBP grubunda 35 (%38,9) hasta olmak üzere toplam 90 hastanın verileri incelendi. İki grup arasında yaş, komorbidite oranları ve vücut kitle indeksi arasında anlamlı fark izlenmedi. Gruplar arasında preoperatif prostat hacmi, IPSS ve Qmax değerleri arasında anlamlı fark izlenmedi. LBP grubunda anlamlı yüksek operasyon süresi izlendi ($p<0,0001$). ABP grubunda median kan kaybı 368 cc (250) ve LBP'de median 80 cc (35) olarak hesaplandı ve ABP'de anlamlı yüksek değerler saptandı ($p<0,0001$). Hastanede kalış süreleri ABP grubunda ortalama 8,1 ± 4,3 gün ve LBP grubunda 3,6 ± 1 gün olarak saptandı ve ABP için anlamlı yüksek olarak saptandı ($p <0,0001$). ABP grubunda 21 (%38,2) hastada, LBP grubunda 5 (%14,2) hastada minör komplikasyon izlendi ve iki grup arasında anlamlı fark izlendi ($p=0,007$).
Sonuç: Büyük prostat adenomlarına yönelik olarak uygulanan simple prostatektomi operasyonu laparoskopik olarak güvenli ve efektif olarak uygulanabilir. Açık cerrahiye oranla LBP, daha uzun operasyon süresine sahip olmakla birlikte, daha belirgin hasta konforu ve daha düşük komplikasyon oranları ile ilişkilidir.

Anahtar kelimeler: açık basit prostatektomi, laparoskopik basit prostatektomi, iyi huylu prostat büyümesi, mesane çıkım tıkanıklığı

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Introduction

Bladder outlet obstruction (BOO) due to benign prostatic hyperplasia (BPH) is one of the most common causes of lower urinary tract symptoms (LUTS) in men. Transurethral resection of the prostate (TUR-P) is the standard surgical technique to be applied in patients with a prostate volume of 30-80 cc [1]. According to the current guidelines, open simple prostatectomy (OSP), holmium laser enucleation of the prostate (HoLEP), and bipolar enucleation are recommended techniques in the presence of enlarged adenoma tissue (>80 cc), and short-term and long-term functional outcomes of these methods are reported to be comparable [2].

The main limitations of OSP are its relatively higher morbidity and blood transfusion rates (7-14%) [3,4], while those of the HoLEP technique is its longer learning curve, unavailability in some centers [5]. The bipolar enucleation technique shows a similar safety profile to HoLEP [6,7]. In addition to these techniques, Mariano et al. described the laparoscopic simple prostatectomy (LSP) in 2002 and Sotelo et al. described robot-assisted simple prostatectomy (RASP) in 2008 [8,9]. LSP and RASP, which are classified as minimally invasive simple prostatectomy (MISP) techniques, have been found to provide similar functional outcomes, as well as having common advantages compared to the open surgery in terms of blood loss and hospital stay. LSP is one of the main alternatives to OSP, but it has some disadvantages such as its higher cost, requirement of special equipment, and their inapplicability in every clinic [10].

This study aims to compare the perioperative and postoperative results and long-term functional outcomes of the OSP and LSP operations performed by a single surgeon in our clinic.

Materials and Methods

On receiving the ethics committee approval (Umraniye Training and Research Hospital Ethics Committee, approval date and number 2022/37); patients who underwent OSP or LSP performed by a single surgeon between January 2015 and July 2021 were retrospectively screened. Patients operated at the beginning of the learning curve for LSP were not included in the study. Patients with a prostate volume of <80 cc, missing data, history of previous prostatic or urethral surgery or urethral stenosis, neurovesical dysfunction and/or prostate cancer, and those with a postoperative follow-up period of fewer than six months were excluded from the study. Among the patients with significant LUTS and a prostate volume greater than 80 cc, surgical treatment was recommended for those with a preoperative International Prostate Symptom Score (IPSS) of ≥12 and/or Quality of Life (QoL) score of ≥4 and/or post-void residual (PVR) urine of >50 ml if they were unresponsive to medical treatment and/or upon patient request [11].

Surgical Technique

For OSP, preoperative cystourethroscopy was performed. Through Pfannenstiel incision the Retzius space was reached. Two sutures were placed on the bladder. The bladder was opened, and the prostate gland was released with cautery. Subsequently, digital enucleation of the prostate from its capsule was performed. Hemostatic sutures were placed on the bladder neck at the 5, 7, 1, and 11 o'clock positions. The bladder wall was closed in two layers. A drain was placed in the Retzius space. The abdominal wall was closed in layers.

LSP was performed under general anesthesia with the patient in the supine position. Prophylactic antithrombotic agents and antibiotics were administered. A two-way 18-Fr Foley catheter was introduced transurethrally into the bladder. A 2-cm midline skin incision was made immediately below the umbilicus. Following the incision of the rectus fascia, the rectus muscles were dissected bluntly to enter into the extraperitoneal space. A minimal area was created with finger dissection and using a balloon trocar (Spacemaker™ Pro Access & Dissector System Covidien, Dublin, Ireland), Retzius space sufficient for surgical manipulations was exposed under direct vision. One 10-mm trocar was inserted as the camera port, and three 5-mm trocars as the working ports. Working trocars were placed 2 cm lateral to the anterior iliac crest on the right and left sides, and the other 5-mm trocar was placed lateral to the rectus sheath on the right. After the excision of periprostatic fatty tissue, an incision was made into the prostate capsule until adenoma tissue was reached without descending to the lateral of the capsule. After adenoma tissue was identified, the entire adenoma tissue was dissected sharply or bluntly using harmonic (HARMONIC® Ethicon, Raritan, New Jersey, USA) or monopolar scissors. Hemostasis was achieved in case of need, with bipolar or harmonic scissors. In patients with an enlarged prostate, the incision was extended laterally if necessary. Adenoma tissue was removed and taken into an endobag. The bladder neck mucosa and posterior prostatic capsule were trigonized with 3/0 polyglactin sutures. A three-way Foley catheter was inserted transurethrally into the bladder. The prostatic capsule was sutured continuously with 2/0 polyglactin sutures. After confirming that there was no leakage, a drain was placed in the Retzius space, and the bladder was continuously irrigated with saline solution. The specimen was morcellated with scissors until it could be drawn out through the skin incision and taken into the bag. In cases with bladder stones, the stones were extracted through the capsular incision. Any bladder diverticulum was also simultaneously resected.

Descriptive and Perioperative Analyses

Preoperatively, age, body mass index (BMI), medical history, serum PSA, routine biochemistry and coagulation parameters, presence of indwelling bladder catheter, maximum urinary flow (Qmax) and uroflowmetry parameters, IPSS, IPSS-QoL Index, International Index of Erectile Function-5 (IIEF-5) scores were recorded. Prostate dimensions were measured using transrectal ultrasonography (TRUS). In the presence of suspected prostate cancer, a TRUS-guided biopsy was performed preoperatively. Operative time and intraoperative blood loss were evaluated as perioperative parameters and duration of catheterization, length of hospital stay, drain dwell times, and decrease in hemogram as postoperative parameters. Complications were classified according to the Clavien-Dindo classification system and

divided into early and late stages according to their occurrence before or after the first postoperative 30 days [12].

To evaluate functional outcomes, uroflowmetry parameters, IPSS, IPSS-QoL index, and IIEF-5 scores were evaluated at postoperative six months. The pad test was used to evaluate the status of urinary continence. Continence was defined as the absence of any pad use due to urinary leakage. In addition, the development of urethral stricture, bladder outlet obstruction, residual adenoma tissue, and postoperative acute urinary retention was noted.

Statistical Analysis

Categorical data were presented as numbers and percentages. Mean and standard deviation values were calculated for numerical data. The Kolmogorov-Smirnov test was used to test the normality of the distribution of numerical data. The Student's t-test was used to compare normally distributed numerical data. The Mann-Whitney U test was performed to compare the mean values of data without normal distribution. The frequencies of categorical variables were compared with the Pearson chi-square and Fisher's exact tests. A p-value below 0.05 was considered statistically significant. Statistical analyses were undertaken using the Statistical Package of Social Sciences version 21 (IBM SPSS Statistics; IBM Corp., Armonk, NY).

Results

The data of a total of 90 patients, including 55 (61.1%) cases in the OSP and 35 (38.9%) cases in the LSP group, were analyzed. The mean age of the whole patient group was 68 ± 6.5 years. The age, comorbidity rates, BMI, and the American Society of Anesthesiologists (ASA) scores the proportion of patients with preoperative catheters and concurrent bladder stones, preoperatively measured PSA values and the number of TRUS-guided biopsies performed were comparable. The mean prostate volume was 153.5 ± 55.2 cc in the OSP group and 148.2 ± 39.4 cc in the LSP group, indicating lack of any significant intergroup difference. Both groups also did not significantly differ in terms of the preoperatively measured bladder capacity and PVR values. The number of median lobes and bladder diverticula were also comparable between groups. Lastly, no significant intergroup differences were detected in terms of the preoperative Qmax, IPSS-QoL, and IIEF-5 values.

Considering perioperative parameters, the mean operative time was 107.8 ± 19 minutes in the OSP group and 152.1 ± 42.6 minutes in the LSP group, revealing a significant intergroup difference ($p<0.0001$). The median blood loss was 368 cc (250) and 80 cc (35) for the OSP and LSP groups, respectively, indicating a significantly higher blood loss in the OSP group ($p<0.0001$). When the transfusion rates in the perioperative and postoperative periods were compared between both groups,

1. Preoperative, peroperative and postoperative datas

Parameters (mean ± SD)	**Total n=90**	**Group 1 55 (61,1)**	**Group 2 35 (38,9)**	**p**
Age (years)	68 ± 6,5	68,4 ± 6,4	67,3 ± 6,7	0,429
BMI (kg/m^2)	25,6 ± 2	25,7 ± 1,8	26,1 ± 1,3	0,367
PSA (ng/ml)	8 ± 4,8	8 ± 5	8,1 ± 4,6	0,963
Preop Hct (%)	41 ± 3,9	41,3 ± 4	40,5 ± 3,8	0,322
Prostate volume (cc)	151,4 ± 49,5	153,5 ± 55,2	148,2 ± 39,4	0,623
Preop. bladder capacity (cc)	136 ± 55,5	135 ± 54,3	137,6 ± 58,1	0,833
Preop. PVR$^+$ (cc)	167,5 (148,7)	180 (156)	155 (100)	0,788$^{\&}$
Preop. Qmax (mL/sc)	6,6 ± 2,8	6,7 ± 2,9	6,5 ± 2,5	0,806
Preop. IPSS	32,4 ± 2,1	32,2 ± 2,2	32,6 ± 2	0,429
Preop. IPSS- QoL Index	5,5 ± 0,5	5,4 ± 0,5	5,6 ± 0,4	0,090
Preop. IIEF-5	18 ± 2,5	17,8 ± 2,5	18,4 ± 2,7	0,265
Operation time (min)	125,1 ± 37,2	107,8 ± 19	152,1 ± 42,6	**<0,0001**
Peroperative blood loss$^+$ (cc)	290 (365)	368 (250)	80 (35)	**<0,0001$^{\&}$**
Htc decrease	8,5 ± 4,7	10,8 ± 4,5	5 ± 2	**<0,0001**
Drain time (day)	3,8 ± 2,4	5 ± 2,3	1,8 ± 0,4	**<0,0001**
Foley cathater (day)	6,2 ± 3,1	7,6 ± 3,3	4 ± 0,5	**<0,0001**
Hospital stay (day)	6,3 ± 4,1	8,1 ± 4,3	3,6 ± 1	**<0,0001**
Follow up (month)	11,5 ± 3,8	11,3 ± 2,7	11,8 ± 4,3	0,239

BMI: body mass index; Hct: hematocrit; PVR: post voiding residual urine; IPSS: international prostate symptom score; QoL: quality of life; IIEF-5: international index of erectile function & Mann-Whitney U Test + Presented as median (IQR)

significantly higher values were found in the OSP group ($p<0.0001$). The mean duration of follow-up with a drain was 5 ± 2.3 days in the OSP group and 1.8 ± 0.4 days in the LSP group, with a significantly longer follow-up period for the OSP group ($p<0.0001$). The duration of follow-up with a Foley catheter in the postoperative period was also found to be significantly longer in the OSP group ($p<0.0001$). The mean length of hospital stay was significantly higher in the OSP group (8.1 ± 4.3 days) compared to the LSP group (3.6 ± 1 days) ($p<0.0001$). Preoperative, perioperative, and postoperative data are shown in **Table 1**.

As a result of the pathological evaluation, BPH was detected in 72 (80%), chronic prostatitis in 15 (16.6%), and Gleason 3+3 prostate adenocarcinoma in three (3.3%) patients. Patients with prostate cancer were included in the active surveillance protocol, and any increase in PSA levels was not observed during their follow-up. The distribution of pathological data was similar.

Complications were observed in 31 (34.4%) patients in the perioperative and early postoperative periods including 26 (28.8) minor (Clavien Grade 1-2) and five (5.5%) major (Clavien Grade 3-4) complications. Minor complications were observed in 21 (38.2%) patients in the OSP and five (14.2%) patients in the LSP group, with a statistically significant intergroup difference ($p=0.007$). Major complications were observed in four patients (7.2%) in the OSP and one (2.8%) patient in the LSP group, indicating lack of any intergroup significant difference. The patients with a fever, wound infection, and subileus were followed up conservatively, while those who developed urinary retention after catheter removal were followed up with an intraurethral Foley catheter for three days. In case of the obstruction of the catheter due to a clot, irrigation was applied. Endoscopic operations were performed on the patients who could not be treated with irrigation. Reoperation was required in one (1.1%) patient in the OSP group due to bleeding. Sepsis was observed in two (2.2%) patients in the OSP group, who were then referred to the intensive care unit. Complications are presented in **Table 2**.

In the late postoperative period, incontinence was observed in three (5.4%) patients and stricture development in one (1.8%) patient in the OSP group without any intergroup difference. The patients who developed incontinence were given medical treatment, and those who developed stenosis were treated with the appropriate surgical method.

The parameters of functional outcomes evaluated at the preoperative and postoperative six months revealed that the increase in the bladder capacity was significantly higher in the LSP group than in the OSP group ($p<0.0001$). While no significant difference was observed between the two groups regarding the changes in the PVR and IIEF-5 parameters, the changes in the Qmax, IPSS, and IPSS-QoL Index parameters were significantly higher in the LSP group ($p<0.0001$ for all) (**Table 3**).

Discussion

Among the operations performed for enlarged prostate tissue, the OSP technique is applied as the first choice in many centers, despite all other recent developments [13]. In a study conducted in the United States of America between 2002 and 2012, Pariser et al., reported an annual decrease of 145 cases undergoing OSP, while there was a gradual increase in the use of minimally invasive techniques [14]. In a meta-analysis undertaken in 2021 comparing different operations performed on prostates with a volume of over 60 cc, HoLEP, enucleation of the prostate with a diode laser, bipolar energy, and LSP were found to be superior to OSP and monopolar TURP [15].

In 2012, Asimakopoulos et al., conducted a systemic review of existing literature concerning LSP and reported that LSP provided lesser blood loss, shorter postoperative catheterization time, and hospital stay compared to open surgery. In that review, longer operative time was noted as the only disadvantage of LSP [16]. In another study on this subject, Autorino et al. stated that extirpative and reconstructive parts were the challenging steps that complicated MISP [17].

Porpiglia et al. reported that the operative times of the OSP and LSP techniques were similar [18]. However, Garcia-Segui and Gascon-Mir determined the operative time as 101.2 minutes for OSP and 135.2 minutes for LSP and noted a significant intergroup difference [19]. In a meta-analysis conducted in 2019, it was stated that MISP techniques had longer operative times compared to OSP [20]. In this study, the operative time was 107.8 ± 19 minutes for OSP and 152.1 ± 42.6 minutes for LSP, with a significantly longer operative time for LSP ($p<0.0001$). We consider that these differences in operative times reported in the literature may be related to differences in prostate volumes, surgical experience, and anatomical variations. Although our study was not aimed at this, we think that operative times may be shortened with the increase in surgical experience.

In our study, the median blood loss was 368 cc (250) in the OSP and 80 cc (35) in the LSP group, indicating a significantly higher blood loss in the OSP group ($p<0.0001$). Similarly, in previous studies, significantly lower amounts of bleeding were detected in patients who underwent LSP [18,19]. A meta-analysis determined that MISP techniques provided lower bleeding rates compared to OSP [20]. It is considered that the ability of MISP techniques to enlarge images through advanced imaging methods facilitated more effective hemostasis of the vessels of proliferative prostate tissue and associated bleeding thus resulting in lower bleeding rates [21].

In this study, significantly lower hematocrit levels, higher transfusion and catheter irrigation rates, longer catheter dwell times, delayed drain and Foley catheter withdrawal times, and prolonged hospital stay were observed in the OSP group in the early postoperative period. In previous studies, the catheter dwell times were similarly found to be significantly higher in the OSP group [8,19,22]. In contrast, Porpiglia et al., did not detect a significant difference between the catheter dwell times of the surgical groups [18]. In the current study, the length of hospital stay was determined as 8.1 ± 4.3 days for the OSP group and 3.6 ± 1 days for the LSP group ($p<0.0001$), which is in agreement with many studies in the literature [19,22]. However, there are also studies suggesting that there is no significant difference in the length of hospital stay between the two techniques [18,19]. In a meta-analysis, a significant difference was found in favor of LSP in terms of catheter dwell times and length of hospital stay [20]. We consider that the reason for these contradictory findings

Table 2. Early and late complications

Early Complication	**Total n=90**	**Group 1 55 (61,1)**	**Group 2 35 (38,9)**	**p**
Minor Complications				**0,007**
Grade 1				
Fever	5 (5,5)	4 (7,2)	1 (2,8)	
Wound site infection	3 (3,3)	3 (5,4)	0 (0)	
Ileus	1 (1,1)	0 (0)	1 (2,8)	
Grade 2				
Transfusion	12 (13,3)	11 (20)	1 (2,8)	
Urinary retention after catheter removal	3 (3,3)	2 (3,6)	1 (2,8)	
Clot retention (need irrigation)	2 (2,2)	1 (1,8)	1 (2,8)	
Major Complications				0,385
Grade 3b				
Endoscopic clot removal	1 (1,1)	1 (1,8)	0	
Reintervention	1 (1,1)	1 (1,8)	0	
Open conversion	1 (1,1)	-	1 (2,8)	
Grade 4				
Sepsis	2 (2,2)	2 (3,6)	0 (0)	
Late Complications				
Incontinence (n; %)	3 (3,3)	3 (5,4)	0 (0)	0,079[!]
Stricture (n; %)	1 (1,1)	1 (1,8)	0 (0)	0,611[!]

!: Fisher Exact Test

Table 3. Functional outcomes

Parameters (mean ± SD)	**Total n=90**	**Group 1 55 (61,1)**	**Group 2 35 (38,9)**	**p**
Increase of bladder capacity (cc)	209,1 ± 116,8	168 ± 103,3	273,7 ± 108,3	**<0,0001**
Decrease of PVR (cc)	130,7 ± 79,7	128,1 ± 77,4	134,8 ± 84,2	0,702
Increase of Qmax (mL/sc)	18,1 ± 9,4	13,9 ± 6,3	24,8 ± 9,7	**<0,0001**
Change of IPSS	29 ± 2,6	28,1 ± 2,5	30,3 ± 2,2	**<0,0001**
Change of IPSS- QoL index	4,7 ± 0,9	4,3 ± 0,8	5,2 ± 0,6	**<0,0001**
Decrease of IIEF-5	0,9 ± 0,4	0,9 ± 0,3	0,9 ± 05	0,387

PVR: post voiding residual urine; IPSS: international prostate symptom score; QoL: quality of life; IIEF-5: international index of erectile function

in the literature is that parameters such as drain, and catheter withdrawal times, and hospital stay may vary depending on surgical and clinical preferences.

In a study undertaken by Manfredi et al., the rates of intraoperative, and early postoperative complications during the one-year follow-up period were reported as 2%, and 14%, respectively, while the complication rate was 5% in the late postoperative period [23]. In another study comparing the RASP and LSP techniques, Pavan et al., detected 3.1% minor and 2.1% major complication rates in the LSP group in the postoperative period, which were significantly lower compared to the RASP group [24]. Pariser et al. reviewed the national inpatient sample data of 35,000 patients who underwent simple prostatectomy over 10 years, and determined that minimally invasive techniques were associated with fewer complications [14]. When the total complication rates were evaluated in a meta-analysis, significantly lower complication rates were noted for the MISP group compared to the OSP group [20]. In our study, complications were observed in 34.4% of the patients in the perioperative and early postoperative periods.

After any surgery performed with the indications of BOO/BPH, questionnaires such as IPSS and IPSS-QoL, and parameters such as Qmax, bladder capacity, and PVR are important measures for monitoring the efficacy of treatment. Manfredi et al. investigated the long-term results of patients who underwent LSP, and showed that the Qmax values significantly increased in the early postoperative period, and maintained in the long term. In the same study, significant improvements were found in the IPSS and IPSS-QoL index scores in the early postoperative period, while no significant change was found concerning the IIEF-5 scores [23]. In a study comparing the RASP and LSP techniques, Pavan et al., reported significant improvements in all functional parameters in the postoperative period for both techniques. The authors also stated that the techniques applied did not have any effect on sexual function [24]. A meta-analysis could not demonstrate any difference between OSP and MISP in terms of functional outcomes [20].

In our study, as a result of the comparison of functional outcomes measured at the postoperative sixth month, LSP provided significant improvements in bladder capacity, Qmax value, and IPSS and IPSS-QoL index scores. Compared to open surgery, laparoscopic surgery has the advantage of obtaining a clearer image by providing a larger bleeding-free environment thanks to improved optical magnification and intra-abdominal pressure created. We believe that subcapsular dissection of the enlarged prostate in the bleeding-free environment is achieved more easily and bleeding control is realized with fewer sutures thanks to these advantages. We believe that the significant difference obtained in parameters such as IPSS and Qmax, which we think is related to QoL, is achieved thanks to such advantages offered by LSP.

Thanks to relatively lower amount of blood loss achieved in laparoscopic operations compared to open surgery, the need for transfusion is lowered with decreased complication rates. In addition, LSP has other advantages. Indeed, it is less painful and analgesic requirement is lesser in the early postoperative period with shorter hospital stay, and catheter dwell time. The advantages of the minimally invasive nature of laparoscopic surgery were also demonstrated in our study, as has been generally shown in the literature in studies comparing the laparoscopic and open techniques.

Although the data were collected prospectively, the retrospective nature of the analysis and the small number of patients were the limitations. In addition, presenting the data of a single surgeon who had completed the learning curve and the experiences of a single center has created an obstacle to the generalizability of the findings. It should also be kept in mind that similar results may not be obtained in less experienced centers. There is also a need for further studies with longer follow-up periods.

Conclusion

Laparoscopic technique is a safe and effective procedure for large prostatic adenomas. Compared to open surgery, LSP has a longer operative time but is associated with greater patient comfort and lower complication rates.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of University of Health Science, Umraniye Training and Research Hospital (Approval date and number: 10/02/2022-37).
Informed Consent: Written informed consent was obtained from patients who participated in this study.
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 – F.Y.S.; Design – F.Y.S.; Supervision – F.Y.S.; Resources – F.Y.S.; Materials – F.Y.S.; Data Collection and/or Processing – F.Y.S.; Analysis and/or Interpretation – F.Y.S.; Literature Search – F.Y.S.; Writing Manuscript – F.Y.S.; Critical Review – F.Y.S.
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Frequency of ISUP 2014 Grade Group Upgrading in Radical Prostatectomy Patients and Associated Risk Factors: A Retrospective Study and Multivariate Analysis

Radikal Prostatektomi Hastalarında ISUP 2014 Grade Grup Yükselmesi Sıklığı ve İlişkili Risk Faktörleri: Retrospektif Bir Çalışma ve Çok Değişkenli Analiz

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Abstract

Objective: The primary aim of this study is the determination of International Society of Urological Pathology (ISUP) grade group (GG) upgrading prevalence and its risk factors in prostate cancer patients.
Materials and Methods: This study was conducted on 117 patients who all underwent open radical prostatectomy in our institution between 2011 and 2020. Patients who received neoadjuvant therapy prior to surgery and had metastasis in lymph nodes or bones were excluded from the study.
Results: In 28 (23.9%) cases ISUP GG had upgraded in final pathology. While grade group of 81 (69.2%) patients did not change, it was downgraded in the remaining 8 (6.8%) cases. In the univariate analysis for the predictors of ISUP GG upgrade, ISUP GG distribution in biopsy pathology (OR: 0.46, 95% CI: 0.26-0.82, p=0.009), positive core fraction (PCF) (OR: 0.07, 95% CI 0.01-0.85, p=0.037), greatest positive core percentage (GPC) (OR: 0.12, 95% CI: 0.02-0.68, p=0.016) and extraprostatic invasion extended (EPI-extended) (OR: 2.95, 95% CI: 1.16-7.49, p=0.023) were all identified as significant factors. When these significant factors were analyzed in multivariate logistic regression analysis, biopsy ISUP grade (OR: 0.38, 95% CI: 0.18-0.79, p=0.01), greatest percentage of cancer (GPC) (OR: 0.10, 95% CI 0.01-0.78, p=0.027) and EPI-extended (OR 14.9, 95% CI:3.1-71.9, p=0.01) were shown as independent predictors.
Conclusion: ISUP GGs of a significant number of patients upgrade in the final pathology. Initial biopsy ISUP score and greatest positive core percentage in the biopsy are independent predictors of ISUP GG upgrade risk. EPI-extended was also significantly higher in ISUP upgrade group. Tumor upgrade risk should be considered prior to prostate cancer treatment.

Keywords: prostate neoplasms, urologic surgical procedures, male, pathology

Öz

Amaç: Çalışmamızın ana amacı prostat kanseri hastalarında, ISUP Grade Grup (GG) yükselmesi oranının tespiti ve ilgili risk faktörlerinin tanımlanmasıdır.
Gereçler ve Yöntemler: Bu çalışma, 2011-2020 yılları arasında, hastanemizde açık radikal prostatektomi ve bilateral lenfadenektomi operasyonu geçiren 117 hastada gerçekleştirilmiştir. Cerrahi öncesi neoadjuvan tedavi alan, lenf nodu pozitifliği ya da uzak metastazı olan hastalar çalışma dışı bırakılmıştır.
Bulgular: Hastaların 28'inde (%23,9), ISUP grade grubu final patolojisinde yükselmiştir. Grade grubu değişmeyen veya azalan hastaların sayısı ise 81 (%69,2) ve 8'dir (%6,8). ISUP GG yükselmesinin tek değişkenli analizinde, biyopsideki ISUP GG`u (OR 0.46, 95% CI 0.26-0.82, p=0.009), pozitif kor oranı (OR 0.07, 95% CI 0.01-0.85, p=0.037), en yüksek pozitif kor yüzdesi (OR 0.12, 95% CI 0.02-0.68, p=0.016) ve geniş ekstra prostatik invazyonu (OR 2.95, 95% CI 1.16-7.49, p=0.023) prediktif faktörler olarak belirlenmiştir. Bu faktörlere çok değişkenli analiz uygulandığında, biyopsi ISUP grubu (OR 0.38, 95% CI 0.18-0.79, p=0.01), GPC (OR 0.10, 95% CI 0.01-0.78, p=0.027) ve geniş ekstra prostatik invazyonu (OR 14.9, 95% CI 3.1-71.9, p=0.01) bağımsız prediktif faktörler olarak bulunmuştur.
Sonuç: Final patolojide önemli bir sayıda hastanın ISUP grade grubu artmaktadır. İlk biyopsi ISUP grade grubu ve en yüksek pozitif kor yüzdesi, ISUP GG yükselmesinin bağımsız prediktörleridir. Ekstra prostatik invazyon da ISUP yükselme grubunda anlamlı oranda daha fazla görülür. Prostat kanseri tedavisi öncesinde tümör grubu yükselme ihtimali değerlendirilmelidir.

Anahtar kelimeler: prostat kanseri, ürolojik cerrahi işlemler, erkek, patoloji

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Introduction

Prostate cancer is the most common malignancy of men except skin cancers and causes significant mortality and morbidity [1]. There is a wide variety of therapy options for prostate cancer ranging from conservative managements like watchful waiting and active surveillance to definitive treatments such as radical prostatectomy, radiotherapy and brachytherapy [2]. Gleason score (GS) classification of prostate biopsy specimens is a vital part of management algorithm [2,3]. GS is especially important for choosing between active surveillance and definitive treatment options like surgery or radiotherapy [2]. However, upgrade of Gleason scores has been reported in subjects who underwent radical prostatectomy following an active surveillance protocol period. The discrepancies between pathologic upgrade rates ranged between 14-55% in different series [4-8]. Furthermore, this pathologic upgrade rate has been increasing in recent years [9]. This phenomenon may lead to either overtreatment (surgery or radiotherapy) of subjects as a result of overgrading of needle biopsy specimens or under treatment (active surveillance) of them following an understaged biopsy [4]. Gleason grading system was modified by the grading group classification in order to improve identification of low-grade cancers [10,11]. The 2014 International Society of Urological Pathology (ISUP) grading system classifies Gleason grades into 5 tiers with corresponding Gleason scores as follows: Grade group 1 (ISUP GG 1): GS< 6; GG 2: GS 3+4=7 ; GG 3: GS 4+3=7; GG 4: GS 4 and GG 5: GS 9 and 10. The stratification of GS 7 into two separate parts with different survival outcomes and treatment requirements as well as comforting patients by naming GS≤ 6 cancers as GG 1 are important aspects of this classification system [12].

The primary aim of this study is the determination of ISUP GG upgrading prevalence and its risk factors in a group of cases who underwent prostate needle biopsy or radical prostatectomy. Investigation of prostate cancer grade group upgrading using a relatively recent system (ISUP 14 GG) encompassing all risk groups is the essence of this article.

Material and Methods

This study was conducted on 117 patients who all underwent open radical prostatectomy with bilateral lymphadenectomy in University of Health Sciences, Sisli Hamidiye Etfal Training and Research Hospital between 2011 and 2020 after approval of Clinical Research Ethics Board was obtained (date and number: 2021/3156). Patients who received any kind of neoadjuvant therapy prior to surgery and had metastases in lymph nodes or bones were excluded (n=25). Patients from all risk groups were included in the research since our objective was the investigation of ISUP GG upgrade in non-metastatic surgery candidates in prostate cancer group. However, majority of the cases (75%) were still in low-risk group with PSA levels <10 ng/dl, ISUP grade 1 or 2 and clinical stage of T1c or T2a. The data were analyzed retrospectively. Demographic, and clinical data of the patients including age, preoperative PSA levels, prostate volumes (cc) measured by ultrasound (formula=length x width x height x 0.52) and clinical stage of the cancer were investigated and recorded. PSA density was calculated by dividing PSA values with prostate volumes in cc.

Postoperative pathology reports were used for this retrospective analysis without re-examining pathology slides. Histopathologic examinations of all the surgical, and the majority of the needle biopsy specimens were performed in our institution by the same pathologists. Our analysis included external needle biopsy specimens having at least 12 biopsy cores in which number of positive cores and tumor length/percentage, Gleason grades and patterns were recorded. Assessment of pathologies was performed according to Gleason score classification, including primary and secondary Gleason patterns. Pathologies were also stratified according to the new ISUP 2014 grading group system [11]. Any transition from lower ISUP group to a higher one was accepted as ISUP GG upgrading. Needle biopsy pathology parameters may be listed as: ISUP grade grouping (determined from Gleason grades recorded in the original pathology reports), number of positive cores (PCN), positive core fraction (PCF: number of positive cores/total number of cores), extended PCF (PCF >50%), greatest percentage of cancer cells in a single core (GPC), total sum of positive core percentages (TPC), biopsy core ratio of percentages (BCR%: TPC/ (Core number x100)), total core length with cancer (TCL), biopsy core ratio of length (BCR mm: TCL/total biopsy length in mm) and absence/presence of prostatic intraepithelial neoplasia (PIN) and high grade PIN (HGPIN). Postoperative pathology parameters included ISUP grade grouping, weight of the specimen, calculated volume (volumetric calculation from the 3 dimensions of prostate specimen in cc, presence/absence of PIN and HGPIN, extraprostatic capsule invasion (EPI) and extended EPI (EPIe), seminal vesicle invasion (SVI), lymphovascular invasion (LVI), apex invasion, bladder neck invasion (BNI), lymph node metastasis [13,14]. Unilateral/bilateral nature of the cancer was assessed in histopathological examinations of both biopsy and surgical specimens. Patients with ≤pT2 and ≥pT3 tumors detected in surgical specimens were classified as cases with local and locally advanced prostate cancers, respectively.

Statistical Method

Statistical analysis was performed with IBM SPSS Statistics 15.0.0 (Chicago, IL). Descriptive analysis of categorical parameters was reported as numbers and percentages while continuous data were given either as mean and standard deviations (SD) or median and interquartile range (IQR) for variables with normal and abnormal distribution, respectively. In cases of abnormal distribution, numerical differences between two dependent groups were estimated with Mann-Whitney U test. In case of normal distribution, numerical differences were compared by independent samples t-test. Ratio differences between two dependent groups were compared by McNemar and McNemar-Bowker tests. Correlation of nonparametric numerical variables was determined using Spearman correlation analysis. Binary univariate and multivariate logistic regression analysis was utilized in order to estimate predictive factors. Fraction and ratios were sometimes expressed as a number fraction between 0, and 1 and sometimes as a percentage. Statistical significance was assumed in cases of $p<0.05$.

Results

A total of 117 patients were included in this study. **Table 1** shows the baseline demographics, clinical, and pathology features of the cohort. Median age at surgery was 63 (interquartile range (IQR) 57-67 years), PSA and PSA density were 8.7 ng/ml (IQR: 5.8-22) and 0.21 (IQR: 0.13-0.60), respectively. Median positive core fraction (PCF) and greatest percentage of a single core (GPC) were 33% (IQR: 17%-50%) and 60% (IQR: 40%-90%), respectively. In addition, biopsy core ratio of length (BCR mm) and percentages (BCR%) were found as 8% (4-19%) and 10% (5-20%), respectively. Median total length of positive cores (TCL mm) was 10.1 mm (IQR: 2.9-20.3). The rate PIN positivity was 23.9% (n=28) and 87.2% (n=102) for biopsy and surgical pathology specimens, respectively whereas the corresponding rates were 15.3% (n=18) and 78.6% (n=92) for high grade prostatic intraepithelial neoplasia (HGPIN). In 76 of 89 patients without perineural invasion (PNI) detected in their biopsy specimens, PNI was revealed in the surgical pathology material with a statistically significant (23.9% vs 87.2%, p<0.001) intergroup difference. Furthermore, HGPIN was detected in the final pathology of 77 patients who had not HGPIN in biopsy specimens, and the HGPIN was disclosed in the final pathology of 78.6% the patients. The differencein the rates of HGPIN detected in biopsy and surgical pathology specimens was statistically significant (15.3% vs 78.6%, p<0.001). In addition, 40 (34.2%) of these 117 patients had extraprostatic invasion (EPI), including 27 (23.1%) cases with extended EPI. Seminal vesicle invasion was detected in 10 (8.6%) patients, whereas surgical margin positivity and apex positivity were present in 41 (35%) and 54 (46.6%) cases, respectively.

The distribution of ISUP grade groups detected in biopsy specimens in the indicated number of patients was as follows: GG 1, n=38 (32%); GG 2, n=49 (31.9%); GG 3, n=21 (17.9%); GG 4, n=8 (6.8%, and GG 5, n=1 (0.9%), while their distribution in surgical pathology specimens of these patients changed as shown: GG 1, n=23 (19.7%); GG 2, n=57 (48.7%); GG 3, n=25 (21.4%); GG 4, n=7 (6.0%), and GG 5, n=5 (4.3%). The difference in ISUP GG distribution estimated for biopsy, and surgical pathology specimens was statistically significant (p=0.03). In other words, in 28 (23.9%) cases, ISUP upgrading was observed in the final surgical pathology compared to biopsy pathology. Furthermore, there was no change in ISUP scores in 81 (69.23%) patients, and downgrading was observed in the final pathology scores in 8 (6.84%) cases (**Table 2**).

When the patients were classified into ISUP upgrading (Group 2) and non-upgrading (Group 1) groups, which also included downgraded cases; groups 1 and 2 had 89 (76.1%) and 28 (23.9%) patients, respectively. These two groups were compared using chi-square, and Mann-Whitney U tests, and statistically significant intergroup differences were found as for the distribution of ISUP GGs (p=0.01), positive core fractions, greatest percentage of cancer and EPI extended. PCF (33% vs 25%, p=0.05) and GPC (70% vs 45%, p=0.01) were both statistically lower in the upgrading group, while EPI extended was detected in significantly higher rates in the upgrading group (18.0% vs 39.3%, p=0.02). In the univariate analysis of the same parameters in biopsy pathology specimens, ISUP GG

Table 1. The overall patient and pathology characteristics

Descriptive (n=117)	Median (IQR)
Age at surgery (years)	63 (57-67)
PSA (ng/ml)	8.7 (5.8-22)
PSA density (ng/ml^2)	0.21 (0.13-0.60)
US volume (cc)	40 (30.5-58.5)
Calculated volume (cc)	41.6 (31.1-62.2)
Specimen weight (g)	45 (34.75-56.25)
Positive core number (PCN)	4 (2-6)
Positive core fraction (PCF)	0.33 (0.17-0.50)
Greatest percentage of single core (GPC)	0.60 (0.40-0.90)
Total sum of positive core percentages (TPC)	1.15 (0.60-2.60)
Biopsy core ratio of length (BCR, mm)	0.08 (0.04-0.19)
Biopsy core ratio of % (BCR %)	0.10 (0.05-0.20)
Total core length with cancer (TCL, mm)	10.1 (2.9-20.3)
ISUP GG upgrade +	28 (23.9%)
ISUP GG upgrade -	89 (76.1%)
Biopsy PIN +	28 (23.9%)
Surgery PIN +	102 (87.2%)
Biopsy HGPIN +	18 (15.3%)
Surgery HGPIN +	92 (78.6%)
EPI +	40 (34.2)
EPI extended +	27 (23.1%)
SVI +	10 (8.6%)
LVI +	5 (4.3%)
Margin +	41 (35.0%)
Apex invasion +	54 (46.2%)
BNI+	15 (12.8%)
Biopsy bilateral	42 (35.9%)
Surgery bilateral	82 (70.1%)
Local advanced	47 (40.2%)
Lymph node +	6 (5.1%)

All the continuous data with abnormal distribution according to Kolmogorov-Smirnov and Shapiro-Wilk test were expressed as median value and interquartile range. Interquartile range in parenthesis were the 25th and 75th percentile values of the data. US: ultrasound; BCR mm: biopsy core ratio of length (total positive core length in mm/total core length); BCR%: biopsy core ratio of percentages (BCR%: TPC/ (core number x100)); ISUP GG: international society of urological pathology 2014 grade group; PIN: prostatic intraepithelial neoplasia; HGPIN: high grade PIN; EPI: extra prostatic capsule invasion; SVI: seminal vesicle invasion; LVI: lenfo-vascular invasion; BNI: bladder neck invasionw

Table 2. The distribution of ISUP Gleason groups in biopsy and surgery pathologies

		ISUP GG Surgery					
		1	**2**	**3**	**4**	**5**	**Total**
ISUP GG Bx	**1**	21	14	1	1	1	**38 (32%)**
	2	2	40	5	2	0	**49 (41.9%)**
	3	0	3	16	1	1	**21 (17.9%)**
	4	0	0	3	3	2	**8 (6.8%)**
	5	0	0	0	0	1	**1 (0.9%)**
	Total	**23 (19.7%)**	**57 (48.7%)**	**25 (21.4%)**	**7 (6.0%)**	**5 (4.3%)**	**117**

distribution (OR 0.46, 95% CI 0.26-0.82, p=0.009), positive core fraction (PCF) (OR 0.07, 95% CI 0.01-0.85, p=0.037) greatest positive core percentage (OR 0.12, 95% CI 0.02-0.68, p=0.016) and extraprostatic invasion extension (EPI-extended) (OR 2.95, 95% CI 1.16-7.49, p=0.023) were all identified as significant factors (**Table 3**). When these significant factors were analyzed in multivariate logistic regression analysis (backward method), biopsy ISUP grade (OR 0.38, 95% CI 0.18-0.79, p=0.01), GPC (OR 0.10, 95% CI 0.01-0.78, p=0.027) and EPI extended (OR 14.9, 95% CI 3.1-71.9, p=0.01) were shown as the independent predictors of ISUP GG upgrade from biopsy to surgery (**Table 4**).

Discussion

Since the development of prostate cancer grading system by Donald Gleason 50 years ago, Gleason grading system has been a controversial issue among urologic pathologists. Grading system, classification of atypical lesions and the discrepancy between the histopathologic reports of biopsy and surgical specimens may be counted among these contradictory topics [5,15,16]. Epstein et al. explained the reasons of these differences as pathology errors, borderline grades and sampling error [4]. Furthermore, Gleason score of 7 encompassed both 3+4 and 4+3 pathologies, which may require different managements with their differentiating risk factors. Therefore, in the year 2014 a new grading grouping system was proposed by a pathology consultation in which all GS≤ 6 was classified as ISUP G1 and GS 7 was divided into two compartments as ISUP GG 2: 3+4, and ISUP GG 3: 4+3. This new system (ISUP GG 2014), which was a modification of 2005 updates, allowed an accurate stratification of tumors, described the lowest grade as 1 instead of 6 and thereby reduced patient anxiety [17]. This system also classified some of the atypical lesions such as cribriform glands, glomeruloid glands and mucinous carcinoma as Gleason pattern of 4 and thus increased their risk factor [11].

In the light of all these developments, we deemed the usage of ISUP GG system to assess the Gleason grade upgrade from biopsy to surgery. Furthermore, accurate GG identification is necessary not only for the decision of active surveillance and definitive treatment but also for the correct risk stratification of the cancer, informing patient and planning the definitive post-treatment options in advance. As a result, we preferred to report GG upgrading in a heterogeneous cohort who underwent open radical prostatectomy in our hospital. ISUP GG upgrade was observed in 23.9% of our 117 patients. While in our univariate analysis, biopsy ISUP grade, PCF and GPC were significant parameters, only biopsy ISUP GG and GPC kept their significance in the multivariate analysis. In addition, extended EPIe was the only significant surgical pathology parameters which was significantly associated with upgrading in both univariate and multivariate analysis.

Independent predictors of pathology grade upgrading identified in different studies may be listed as non-white race, older age, higher PSA levels, cancer positive biopsy fraction, prostate volume, prostate density and tumor percentage of >50% per core [18-23]. In a recent study, cancer upgrade has been shown to have a positive correlation with increased levels of TNF-alpha and a negative correlation with high levels of IL-6 (24). In an article by Epstein al., GS upgrading from ≤6 to a higher grade happened in 36.3% of 7643 cases [4]. Even after multidisciplinary consultations, tumor upgrades remained high ranging from 43% to 63.8% (20, 21). In their study of 7643 patients, they identified increasing age, PSA levels, maximum percentage of cancer, per core number and decreasing radical prostatectomy specimen weight as predictors of biopsy upgrade from GS of 5-6 (ISUP 1). Greatest percentage of prostate cancer, showing the extension of the tumor in prostate was identified as a significant predictor of upgrading in our investigation, similar to other studies [4,21,23,25]. In a multicenter study of 1159 patients, PSA levels, percent of positive biopsy cores and small prostate volumes were suggested as predictive factors for upgrading [23]. Schiffmann et al. indicated tumor involvement per core (≥50%) as the most strong predictor for upgrading besides the number of positive cores, PSA values and age in their study of 1331 cases [21]. Although positive core fraction could not keep its significance in our multivariate analysis, several studies reported it as a significant predictor [4,18,21]. In another study by Brasetti et al., GG upgrade was reported in 41.4% of the patients with a number of positive biopsy cores and PSA density as the predictors [26]. The relation between positive cores and upgrade of GG 1 cancers was confirmed again in a study of 1966 patients with an upgrade rate of 40% and 59% for very low and low-risk cancers, respectively [27]. Finally Capitanio et al., reported that Gleason upgrade rate was reduced by half (23.5% vs 47.9%, p<0.001) when greater number of biopsy cores were obtained (18 cores vs 10-12 cores) [28].

Extended extraprostatic extension (EPIe) was the only

Table 3. The comparison of ISUP GG upgrading and non-upgrading groups in terms of clinical, biopsy and surgical pathologic parameters

	ISUP Upgrade (-)	ISUP Upgrade (+)	p
n (%)	89 (76.1%)	28 (23.9%)	
Age (years)	61.4 ± 6.9	65.0 ± 6.3	0.8
Clinical stage (Pt1c vs T2)	48 (68.6%) 22 (31.4%)	15 (75%) 5 (25%)	0.58
PSA ng/ml [1]	6.9 (5.7-15)	8.3 (5.2-13.4)	0.54
PSAd [1] (ng/ml^2)	0.19 (0.14-049)	0.19 (0.11-0.38)	0.68
US vol [1] (cc)	39.0 (30.0-50.3)	40.0 (33.0-60.0)	0.85
Calculated vol [1] (cc)	40.5 (29.2-56.4)	39.3 (33.5-62.5)	0.51
Specimen weight [1] (gr)	41.5 (33.5-55.2)	46.5 (36.3-69.7)	0.99
Biopsy ISUP 1 2 3 4 5	 21 (23.6%) 42 (47.2%) 19 (21.3%) 6 (6.7%) 1 (1.1%)	 17 (60.1%) 7 (25.0%) 2 (7.1%) 2 (7.1%) 0 (0%)	**0.01**
PCN [1]	4 (2-6)	3.0 (1.25-5.0)	0.13
PCF [1]	0.33 (0.19-0.44)	0.25 (0.11-0.42)	**0.05**
PCF >50 %	23 (25.8%)	5 (17.9%)	0.38
GPC (%) [1]	0.70 (0.40-0.90)	0.45 (0.3-0.67)	**0.01**
TPC (mm) [1]	1.15 (0.69-2.60)	0.85 (0.36-1.30)	0.06
BCR % [1]	0.09 (0.06-0.20)	0.08 (0.03-0.11)	0.06
TCL (mm) [1]	12.2 (5.7-27.1)	8.6 (2.2-13.1)	0.06
BCR mm [1]	0.09 (0.05-0.23)	0.08 (0.03-0.09)	0.06
Biopsy PIN +	23 (25.8%)	5 (17.9%)	0.38
Surgery PIN +	76 (85.4%)	26 (92.9%)	0.52
Biopsy HGPIN +	11 (12.4%)	7 (25.0%)	0.13
Surgery HGPIN +	68 (76.4%)	24 (85.7%)	0.29
EPI total +	27 (30.3%)	13 (46.4%)	0.11
EPI extended +	16 (18%)	11 (39.3%)	**0.02**
SVI +	6 (6.8%)	4 (14.3%)	0.24
LVI +	3 (3.3%)	2 (7.2%)	0.59
Margin +	30 (33.7%)	11 (39.3%)	0.59
Apex invasion +	41 (46.1%)	13 (46.4%)	0.97
BNI +	10 (11.3%)	5 (17.9%)	0.34
Biopsy bilateral	32 (35.9 %)	10 (35.7 %)	0.98
Surgery bilateral	60 (67.4%)	22 (78.6%)	0.26
Local advanced +	33 (37.1%)	14 (50%)	0.22
Lymph node +	3 (3.4%)	3 (10.7%)	0.15

All the continuous data with abnormal distribution according to Kolmogorov-Smirnov and Shapiro-Wilk test were expressed as median value and interquartile range. Interquartile range in parenthesis were the 25th and 75th percentile values of the data. Continuous data with normal distribution was expressed as mean value and standard deviation (only age in this group US: ultrasound; PCN: positive cores number; PCF: positive core fraction; GPC: greatest percentage of cancer cells in a single core; TPC: total sum of positive core percentages; BCR mm: biopsy core ratio of length (total positive core length in mm/total core length); BCR%: biopsy core ratio of percentages (BCR%: TPC/ (core number x100)); TCL: total core length with cancer; ISUP GG: international society of urological pathology 2014 grade group; PIN: prostatic intraepithelial neoplasia; HGPIN: high grade PIN; EPI: extra prostatic capsule invasion; SVI: seminal vesicle invasion; LVI: lenfo-vascular invasion; BNI: bladder neck invasion

1: The continuous data showed non-normal distribution and therefore expressed as medians (IQR)

Table 4. Binary logistic regression analysis for ISUP upgrade (univariate and multivariate)

	Univariate Analysis		Multivariate Analysis	
	OR (95% CL)	**p**	**OR (95% CL)**	**p**
Biopsy ISUP	0.461 (0.26-0.82)	0.009	0.38 (0.18-0.78)	0.01
Positive core Ffraction (PCF)	0.066 (0.01-0.85)	0.037		
Greatest positive core (GPC)	0.120 (0.02-0.68)	0.016	0.10 (0.02-0.78)	0.03
EPI extended +	2.952 (1.16-7.49)	0.023	14.9 (3.01-71.9)	0.001

Only statistically significant data in the univariate analysis was shown in this table. Binary univariate and multivariate logistic regression analysis was utilized in order to estimate predictive factors. PCF: positive core fraction; GPC: greatest percentage of cancer in a single core; ISUP GG: international society of urological pathology 2014 gradeg; EPI: extra prostatic capsule invasion

significantly associated surgical pathology factor with upgrading in our study. When compared with the non-upgrading group other factors such as SVI (6.8% vs 14.3%), LVI (4.1% vs 9.1%), lymph node positivity (3.9% vs 12%), and surgical pT3 vs pT2 (37.1% vs 50%) showed much higher prevalence in the upgrading group, without any statistical significance. Tilki et al. demonstrated a significantly higher prevalence of these factors (EPE, SVI, LVI, margin positivity) in the upgrading group [5]. In another study by Abedi et al., 32.8% of patients had a Gleason score upgrade, and also they histopathologically detected significantly higher rates of EPI, SVI and positive lymph node invasion in surgical specimens [16]. These results support the idea that Gleason score upgrading in PCa indicates a tendency to become invasive/locally advanced cancers. Some of our results might not attain a level of statistical significance probably due to limited number of patients, but may achieve statistical significance if the study could be performed with larger number of patients.

Limitations of this study are its retrospective nature, inclusion of pathology reports of multiple surgeons and pathologists in the study. The relatively subjective sampling procedure of needle biopsy, especially when performed by different surgeons, may increase heterogeneity of the biopsy group. While all of our identified predictive parameters (PCF, GPC, EPIe) are in accordance with literature, the rates of PCF and GPC were paradoxically lower in the upgrade group. While this finding is in contrast with previous literature which indicates high volume/ extension of tumor leads to tumor upgrading, our data is consistent in its own accord. Total tumor length, BCR% and BCR mm were also lower in the upgrade group in addition to PCF and GPC. As a hypothesis, this discrepancy might be due to the inclusion of all risk groups instead of only lower tier ones. Otherwise, this might also be due to accurate identification of Gleason grade in the biopsy as a result of higher cancer tissue available.

Conclusion

ISUP Grade Groups may allow better understanding of prostate cancer pathologies for both surgeons and pathologists. However, discrepancy between histopathological classifications of biopsy and surgical specimens in terms of PIN, HGPIN, ISUP grade groups still continues. A significant number of patients with low-grade ISUP scores are upgraded in the final pathology. Initial ISUP score and greatest percentage of cancer-positive cores in the biopsy specimens were independent predictors of ISUP upgrade risk. Extended extraprostatic invasion was also significantly higher in the IUSP upgrade group. Tumor upgrade risk should be considered prior to prostate cancer treatment.

Ethics Committee Approval: The ethical principles were designed under Helsinki Declaration and the study was approved by University of Health Sciences, Sisli Hamidiye Etfal Training and Research Hospital, Clinical Research Ethical Board at 2021 (16.02.2021/3156).
Informed Consent: An informed consent was obtained from all the patients for research.
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Frequency of Hydroureteronephrosis in Patients With Pelvic Organ Prolapse and the Effect of Hydronephrosis on Urodynamic Parameters

Pelvik Organ Prolapsuslu Hastalarda Hidroüreteronefroz Sıklığı ve Hidronefrozun Ürodinamik Parametrelere Etkisi

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Abstract

Objective: This study aims to evaluate the frequency of hydronephrosis and the effect of hydronephrosis on urodynamic parameters in patients with advanced-stage pelvic organ prolapse (POP).
Materials and Methods: This retrospective cross-sectional study was conducted between July 2019 - February 2020 with 66 patients who were admitted to the urogynecology outpatient clinic with symptomatic advanced-stage POP. Urinary system ultrasonography and urodynamic examination were performed on all patients before the operation. The severity of prolapse in the study population was evaluated using the POP-Q system. Urinary system ultrasonography was performed by radiologists. Demographic data, POP time, and urodynamic parameters were compared in hydronephrosis and non-hydronephrosis cases.
Results: The general frequency of hydronephrosis among the patients was 19.7% (13/66 patients). It was found that the weight (p=0.0001) and body mass index (p=0.004) levels were higher in patients with hydronephrosis. There was no significant difference in the duration of POP, the presence of detrusor overactivity, and other urodynamic parameters in patients with or without hydronephrosis.
Conclusion: There was no relationship found between hydronephrosis and urodynamic parameters. In line with these data, urinary system ultrasonography is recommended for all patients with POP due to the high frequency of hydronephrosis and the consequences of hydronephrosis leading to renal failure.

Keywords: pelvic organ prolapse, hydronephrosis, urodynamics

Öz

Amaç: Bu çalışma, ileri evre pelvik organ prolapsusu (POP) olan hastalarda hidronefroz sıklığını ve hidronefrozun ürodinamik parametrelere etkisini değerlendirmeyi amaçlamaktadır.
Gereçler ve Yöntemler: Bu retrospektif kesitsel çalışma Temmuz 2019 - Şubat 2020 tarihleri arasında ürojinekoloji polikliniğine semptomatik ileri evre POP ile başvuran 66 hasta ile yapıldı. Ameliyat öncesi tüm hastalara üriner sistem ultrasonografisi ve ürodinamik muayene yapıldı. Çalışma popülasyonundaki prolapsus şiddeti POP-Q sistemi kullanılarak değerlendirildi. Üriner sistem ultrasonografisi radyologlar tarafından yapıldı. Hidronefroz ve hidronefroz olmayan olgularda demografik veriler, POP süresi ve ürodinamik parametreler karşılaştırıldı.
Bulgular: Hastalar arasında genel hidronefroz sıklığı çalışmamızda %19,7 (13/66 hasta) idi. Hidronefrozlu hastalarda kilo (p=0,0001) ve vücut kitle indeksi (p=0,004) düzeylerinin daha yüksek olduğu bulundu. Hidronefrozu olan ve olmayan hastalarda POP süresi, detrüsör aşırı aktivitesinin varlığı ve diğer ürodinamik parametrelerde anlamlı bir fark saptanmadı.
Sonuç: Hidronefroz ile ürodinamik parametreler arasında bir ilişki saptanamadı. Bu veriler doğrulutusunda; hidronefroz sıklığının yüksek olması ve hidronefrozun böbrek yetmezliğine kadar giden sonuçlarının olması sebebiyle POP hastalarının tümüne üriner ultrasonografi yapılması önerilir.

Anahtar kelimeler: pelvik organ prolapsusu, hidronefroz, ürodinami

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Introduction

Pelvic organ prolapse (POP) is defined as the descent of the pelvic organs into or out of the vagina. It can be seen in about half of women giving birth. It causes urogenital symptoms and sexual dysfunction. The main reason is the loss of pelvic support [1]. In gynecology, hydronephrosis is present in many diseases, including severe genital mechanical defects, endometriosis, and postoperative iatrogenic lesions. The prevalence of hydronephrosis is shown to be significantly related to the severity of prolapse [2,3]. In this study, we aimed to investigate the frequency of pelvic hydronephrosis and the effect of hydronephrosis diagnosed by ultrasonography on urodynamic parameters in patients with symptomatic POP.

Material and Methods

After approval local ethics committee (approval number 2020/382), symptomatic female patients with stage 3-4 POP based on pelvic organ prolapse quantification (POP-Q) whose ages were ranging between 30 to 80 years and who were admitted to the urogynecology outpatient clinic in Bakirkoy Dr. Sadi Konuk Training and Research Hospital, Gynecology and Obstetrics Clinic between July 1, 2019, and February 1, 2020, were evaluated. Preoperative urinary system ultrasonography and urodynamic examination were performed for all patients. Patients with urinary obstruction secondary to abdominal or pelvic tumor, obstructive kidney stones, vesicoureteral reflux, ureteral strictures, chronic renal failure, patients with adhesions, endometriosis, previous prolapse surgery, and patients who had a hysterectomy were defined as the exclusion criterion. A total of 81 patients with stage 3 and 4 POP, who underwent corrected urodynamics and urinary ultrasonography were included in the study. Among these patients, 7 patients were excluded because of insufficient anamnesis, 5 patients due to kidney disease, and 3 patients as the preoperative urodynamic study results could not be obtained. Regardless of the stage in the urinary system ultrasonography, all patients with hydroureteronephrosis constituted the study group, and the patients without hydroureteronephrosis constituted the control group. A total of 66 patients, (13 in the study group and 53 in the control group) were included in the study.

Preoperative urodynamics report of patients in both groups was obtained from computer-based hospital records. Detailed anamnesis of these patients, including age, height, weight, body mass index (BMI), parity, and duration of POP (years) were obtained from the files of the patients.

Urinary system ultrasonography with Voluson E8 (General Electrics, USA) device was performed by a radiologist on all of the patients. Urodynamics with prolapse reduction was also performed in these patients. The urodynamic procedure was performed using a multi-channel urodynamic system under International Continence Society (ICS) standards [4]. Uroflowmetry was performed at the beginning and post-void residual (PVR) volume was measured. After bladder evacuation, catheters were placed in the rectum and bladder for filling cystometry. While the patient was in the sitting position, the bladder was filled with sterile saline at room temperature. At the time of filling cystometry, first desire to void, strong desire to void, maximum cystometric capacity, P vesical (Pves), P detrusor (Pdet), P abdominal (Pabd), bladder compliance, detrusor overactivity (DO), valsalva leak point pressure (VLPP), and lowest detrusor pressure at which urinary leakage occurs in the absence of a detrusor contraction or an increase in abdominal pressure (detrusor leak point pressure, DLPP) values were recorded. Detrusor overactivity was considered as involuntary detrusor contraction at any pressure that could occur spontaneously or with stimulation during the filling phase in cytometry. Then, bladder emptying was evaluated by a pressure-flow study. In uroflowmetry, maximum flow rate (Qmax), time to reach maximum flow rate, voided volume, and PVR values were recorded. The Liverpool nomogram was used to evaluate uroflowmetry [5]. Study group and control group urodynamic study results (maximal flow rate, time to reach maximum flow rate, void volume, PVR, detrusor overactivity, compliance, maximal vesical pressure, maximal detrusor pressure, maximum bladder capacity, bladder volume at first desire to void, bladder volume at severe desire to void, VLPP, DLPP) were compared with age, parity, and BMI.

Statistical Analysis

In this study, which was carried out to investigate the effect of hydroureteronephrosis on urodynamic parameters in patients with POP, 30 patients were reached as a result of the pilot application designed to compare the PVR levels of the control group (no hydronephrosis) and the study group (with hydronephrosis), the potency was found to be 0.82. Based on this power of influence, a power analysis was made with GPower 3.1.9.2. As a result of the analysis, in the design of the comparison of PVR levels between the two groups, the group ratio was 0.24, 80% power, 95% confidence level, and 0.82 effect power, 52 cases for the control group and 12 cases for the study group. It was determined that a minimum of 64 cases in total should be included in the study.

Statistical analysis was performed using the SPSS 23 (statistical package for the social sciences) package program. The demographic variables of patients, the number of units (n), percentage (%), mean, and median (min-max) values were given for continuous variables. The normal distribution test of continuous variables was done with the Kolmogorov Smirnov test. Frequency and percentage values were given for categorical variables. Chi-square analysis was used for the relationships between categorical variables. Where appropriate, categorical variables were evaluated with Fisher's exact test. Independent sample t-test was used for the comparison of two groups in continuous independent variables with normal distribution, and Mann-Whitney U-test was used for two-group comparisons in variables that did not fulfill the normal distribution assumption. $P<0.05$ value was considered significant.

Results

The data of 66 patients were evaluated. The mean age of the patients was 62.3±10.53 years (32-79 years). The mean BMI of the patients was found to be 28.28±3.47. The overall incidence

of hydronephrosis among the patients was 19.7% (**Table 1**).

Detrusor overactivity was detected in 38.46% of patients with hydronephrosis and in 32.08% of patients with hydronephrosis, respectively, and there was no significant difference between the two groups (p=0.746) (**Table 2**).

It was determined that the patient group with hydronephrosis had higher weight (p=0.0001) and BMI (p=0.004). There was no significant difference between the two groups in terms of age, parity, and duration of POP (**Table 3**).

There was also no significant difference found between the two groups in terms of other urodynamic parameters (**Table 4**).

Discussion

The relationship between POP and hydronephrosis has been known for a long time, but the literature on the prevalence of hydronephrosis in these patients is largely variable. The reason for this variability may be related to the differences in POP stages and the duration of POP [3,6-12]. If left untreated, severe cases of POP may develop hydronephrosis or renal failure [13] and if the POP is corrected, regression of hydronephrosis may be possible [2]. The prevalence of hydronephrosis is shown to be significantly related to the severity of POP [2,14]. Based on this knowledge, we included patients with at least grade 3-4 POP to better investigate the relationship between urodynamics and hydronephrosis. Also, patients who had a previous hysterectomy, incontinence, or POP surgery were not included in the study because ureter or bladder damage could not be excluded. In previous studies, the prevalence of hydronephrosis in patients treated for POP was reported to range from 7.7% to 30.6% [3,6-12,14]. In this study, the frequency of hydronephrosis in patients with advanced stages of POP was found to be 19.7%, similar to the current international literature. No previous cross-sectional studies investigating the frequency of hydronephrosis in patients with POP have been found in our country. The high rate of hydronephrosis reported in this study indicates that renal ultrasonography should be performed before deciding on follow-up or surgical treatment in patients with POP.

POP and stress urinary incontinence coexist in up to 80 percent of women with pelvic floor dysfunction [15]. Advanced-stage POP can mask urinary incontinence by kinking the urethra. Selection of the optimal reconstructive surgical procedure and adding an anti-incontinence procedure may be challenging to surgeons as the POP repair can unmask urinary incontinence in previously continent women or even worsen the existing urinary symptoms.

There are three possible accepted strategies for potential stress urinary incontinence at the time of symptomatic treatment in women without stress urinary incontinence. One of the strategies is performing concurrent surgeries for POP and stress urinary incontinence, regardless of preoperative POP reduction and urinary stress testing. This will lead to attendant surgical risk, that is unnecessary for the patient. The other one is performing only POP surgery and making another incontinence surgery if needed related to postoperative urinary symptoms. This strategy can lead to a second anesthesiologic preparation. In our clinical practice, we choose the last strategy by performing POP reduction urodynamic testing in combination with medical

Table 1. Distribution of hydronephrosis

	n	%
None	53	80.3
Present	13	19.7
Total	66	100

Table 2. Detrusor overactivity according to the presence of hydronephrosis

Detrusor overactivity	Without hydronephrosis n:53		With hydronephrosis n:13		p
	n	%	n	%	
None	36	67.92	8	61.54	0.746
Present	17	32.08	5	38.46	

*Fisher Exact Test; P<0.05 was considered statistically significant

Table 3. Age, height, weight, BMI, POP duration, and parity analysis according to the presence of hydronephrosis

	Without hydronephrosis n:53	With hydronephrosis n:13	
	Avg+SD Med. (Min.-Max.)	Avg+SD Med. (Min.-Max.)	P
Age	62.04±10.44 64- (32-79)	63.38±11.27 64- (42-79)	0.710
Height	159.23±5.94 160- (150-170)	157.85±5.52 160- (150-165)	0.421
Weight	69.57±6.73 70- (55-85)	76.92±5.22 75- (70-85)	**0.0001***
BMI	27.68±3.22 27.11- (20.2-37.77)	30.74±3.49 29.38- (26.34-37.77)	**0.005***
Parity	3.62±2.4 3- (1-12)	3.62±3.07 3- (1-13)	0.691
POP Duration (year)	4.87±5.24 3-(1-25)	5.77±3.49 5-(1-12)	0.128

*Student t-test, Mann Whitney U test; P<0.05 was considered statistically significant

Table 4. Evaluation of urodynamic parameters according to the presence of hydronephrosis

	Without hydronephrosis **n:53**	**With hydronephrosis** **n:13**	
Urodynamic parameters	Avg+SD Med. (Min.-Max.)	Avg+SD Med. (Min.-Max.)	**P**
Residual amount of urine	67.23±90.33 32- (0-375)	81.92±87.25 57- (0-211)	0.548*
Bladder volume at first desire to void	142.47±99.57 125- (26-565)	125.92±48.54 128- (47-187)	0.564
Bladder volume at strong desire to void	308.79±121.24 282- (103-610)	302±113.48 270- (153-497)	0.855
Max. bladder capacity	406.53±127.65 387- (200-714)	396±90.33 419- (223-514)	0.780
Detrusor leak point pressure	35.13±27.86 30.5- (5-102)	40.17±53.51 27.5- (5-140)	0.773
Valsalva leak point pressure	68.38±52.56 61.5- (3-220)	89.83±46.08 118- (15-120)	0.184*
Maximum urine flow rate	10.17±10.58 6- (0-48)	7.38±7.92 4- (0-20)	0.396*
Voiding volume	132.47±167.66 53- (0-614)	108±144.71 28- (0-446)	0.565*
Bladder compliance	33.35±23.1 27.3- (2.8-82.1)	34.63±21.48 32.9- (0-82.8)	0.856
Time to reach max. flow rate	6.38±10.22 3- (0-56)	4.77±8.36 3- (0-31)	0.601
Pves (max. vesical pressure)	119.6±29.7 118- (48-181)	127.31±44.11 116- (60-221)	0.452
Pdet (maximal detrusor pressure)	69.62±38.97 63- (15-216)	62.08±40.28 52- (16-163)	0.536

*Mann Whitney U test-Student's t-test; $P<0.05$ was considered statistically significant

history for the assessment occult stress urinary incontinence in patients planning POP surgery. We add incontinence surgery if urinary incontinence is demonstrated by prolapse reduction [16].

In our study, a relationship between urodynamic results and the presence of hydronephrosis in POP patients was also investigated, and no significant difference was observed in urodynamic parameters. In other words, it is not possible to predict hydronephrosis based on urodynamic results. Therefore, renal ultrasonography should be performed to investigate the presence of hydronephrosis, even if urodynamics has been performed in patients with POP who are scheduled for follow-up or surgery.

As a result of the study, there was no significant difference between the duration of POP and the frequency of hydronephrosis. In a study conducted on 140 patients with stage 1-4 prolapse between 2009 and 2012, it was stated that the probability of hydronephrosis increased as the duration of prolapse increased [8]. The reason for this difference may be due to the high number of patients and the inclusion of all stages of POP even the asymptomatic stages in the study.

A significant difference was found between the group with and without hydronephrosis in terms of weight and associated BMI is a valuable secondary result of our study. No similar results were found in previous literature. These results can be

attributed to high abdominal pressure which can be a factor in the progression of POP. It can be postulated that high abdominal pressure due to weight may increase hydroureteronephrosis. To understand this relationship more clearly, it should be investigated in more detail with different studies in the future.

In our study, a retrospective analysis was performed on a sample group of 66 people in a local education and training hospital. Although this may be a weakness the study has enough statistical power to press on our valuable finding "the urodynamics does not have the efficient role for the prediction of hydronephrosis in patients with POP". Using a multi-channel urodynamic system following ICS standards is also a strength of our study. To make a more detailed evaluation of this issue, a larger patient group can be followed and examined for a longer period.

Conclusion

According to the results of our study, no correlation was found between hydronephrosis and urodynamic parameters. Weight and BMI have a significant effect on the progression of hydronephrosis. In line with these data, urinary system ultrasonography is recommended for all patients with POP due to the high frequency of hydronephrosis and the consequences of hydronephrosis leading to renal failure. There is a need for prospective studies with larger numbers of patients to obtain definitive results on this issue.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of University of Health Science, Dr. Sadi Konuk Training and Research Hospital (Approval date and number: 07/09/2020-382).
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Case Report – Andrology

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A Rare Cause of Infertility: 48XXYY Syndrome

İnfertilitenin Nadir Görülen Bir Nedeni: 48XXYY Sendromu

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Abstract

In the evaluation of a 32-year-old male patient who was referred to our clinic with the complaint of gynecomastia and primary infertility, ennuchoid structure, hypergonadotropic hypogonadism, and azoospermia were detected. Based on these findings, the genetic evaluation revealed the presence of 48XXYY syndrome. In this case report, we aimed to report the diagnostic algorithm and management of 48 XXYY syndrome. It should be noted that fertility should not be expected in patients with 48XXYY syndrome.

Keywords: male infertility, azoospermia, Y-chromosome deletions, Klinefelter syndrome

Öz

Otuziki yaşında jinekomasti ve primer infertilite şikâyeti nedeni ile kliniğimize yönlendirilen erkek hastanın yapılan değerlendirilmesinde ennuchoid yapı, hipergonadotropik hipogonadizm, azospermi saptanmıştır. Bu bulgulara dayanarak yapılan genetik incelemede 48XXYY sendromu tespit edilmiştir. Bu olgu sunumunda 48XXYY sendromunun tanı algoritmasını ve hastalık yönetimini sunmayı amaçladık. 48XXYY sendromlu hastalarda doğurganlığın beklenmemesi gerektiği unutulmamalıdır.

Anahtar kelimeler: erkek infertilitesi, azospermi, Y-kromozom delesyonları, Klinefelter sendromu

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Introduction

The incidence of infertility, which is the inability to achieve conception at the end of one year despite regular attempts at unprotected sexual intercourse, ranges from 7% to 15% [1]. Infertility is an important problem that causes loss of self-confidence, mental disorders, sexual dysfunction and social withdrawal in couples. Male factor infertility is present in approximately half of all infertile couples [2]. In the etiology of male infertility, several congenital or acquired factors such as urogenital abnormalities, varicocele, undescended testis, infections of the genital tract, metabolic and endocrine disorders, testicular failure, immunologic problems, cancer, drugs, radiotherapy, altered lifestyle, and genetic factors have been reported [3].

Apparently, genetic factors, especially in oligozoospermic and azoospermic patients, have been increasingly investigated in recent years. Genetic examination in infertility is important in terms of revealing the etiological factor and predicting the pregnancy potential, and the need for future counseling. Klinefelter syndrome (KS), known as 47XXY, can be seen in up to 10% of the cases with nonobstructive azoospermia and in one in 500-1000 live births [4]. Various variants of Klinefelter syndrome have been reported. Here, a case with a genetic diagnosis of 48XXYY, which is a very rare variant of Klinefelter syndrome, will be presented.

Case

A 32-year-old male patient, who was followed up in the endocrinology clinic due to gynecomastia, was referred to our clinic for fertility evaluation. Informed consent form was obtained from the patient. It was understood from his past medical history that he had been born with a normal spontaneous vaginal delivery at term and a normal birth weight. The patient's penile erection was normal, but he was never married and had no sexual partner. We noted that the patient had learning difficulties. In addition, tremor was observed in the hands of the patient during the physical examination. The patient was 192 cm tall, and weighed 90 kg with a body mass index (BMI) of 24.45 kg/m^2, and blood pressure of 125/80 mmHg. In addition, physical examination revealed eunuchoid appearance, reduced muscle mass, long arms and legs. Routine hematologic and biochemical parameteres such as complete blood count, results of hepatic and renal function tests were within normal ranges.

In the hormonal evaluation of the patient, levels of testosterone (1.74 ng/mL: 1.93-8.36 ng/mL), FSH (60.61 mIU/mL: 0.7-11.1 mIU/mL), and LH (35.82 mIU/mL: 0.8-7.6 mIU/mL) were as indicated. Other serum hormone levels were within normal limits. No pathological finding was detected in the pituitary parenchyma or sellar cavity in the MRI examination of the case. In scrotal ultrasonography, the dimensions of the left, and right testes were measured as 13x10x19 mm, and 11x18x10 mm, respectively. Millimetric calcification was observed in the upper pole of the right testis. Upon detection of azoospermia in the requested semen analysis, genetic analysis was performed. Genetic evaluation revealed the presence of a 48XXYY syndrome (**Figure 1**). Based on these findings, the patient was told that he had no fertility potential.

Discussion

Knowing the genetic causes in the etiology of infertility is important for obtaining correct information and applying the optimal treatment approach to the patients. While the risk of chromosomal anomaly is up to 4% in those with sperm counts less than 5 million compared to the general population, the risk increases even more in cases with nonobstructive azoospermia [5]. Genetic disorders manifest themselves as sex chromosomal anomalies or autosomal chromosomal anomalies. Sex chromosome aneuploidies are the most frequently occurring chromosomal abnormalities with an incidence of 1 in 400 births [6]. The most common sex chromosomal anomalies are KS and its variants. Patients with KS have 47XXY in 80-90%, and 48,XXXY, 48,XXYY, 49,XXXXY or 46,XY/47,XXY mosaicism or other structurally abnormal sex chromosomes in 10-20% of the cases [7].

The 48XXYY variant, which is seen in 2.3% of KS cases, was first reported by Muldal and Ockey in 1960 [8]. The 48,XXYY syndrome affects 1 in 18,000 to 50,000 male births. This syndrome is hypothesized to result from double nondisjunction during meiosis in spermatogenesis. In this syndrome, patients usually present to clinics with abdominal obesity, small testicles, learning difficulties, behavioral disorders, skeletal deformities, or delayed puberty [6,7]. The patient in this case report was sent to our clinic for infertility evaluation. In a study of 95 patients, the diagnosis of 48,XXYY syndrome had been made between the ages of 1-5 in 37%, between the ages of 6-10 in 25%, and at the age of ≥ 11 years in 27% of the cases [8]. Although the diagnosis is usually made in adolescence according to the findings mentioned above, prenatally diagnosed cases have been also reported [9,10]. It has been reported that only 30% of the cases are diagnosed based on the symptoms secondary to an endocrinological disorder [10,11].

The additional X and Y chromosomes lead to disorders of testicular dysgenesis and hypergonadotropic hypogonadism. Accordingly, this syndrome is characterized as azoospermia and small testicles as in our case. In the literature, testicular volumes between 1-4 mL have been detected in cases with this

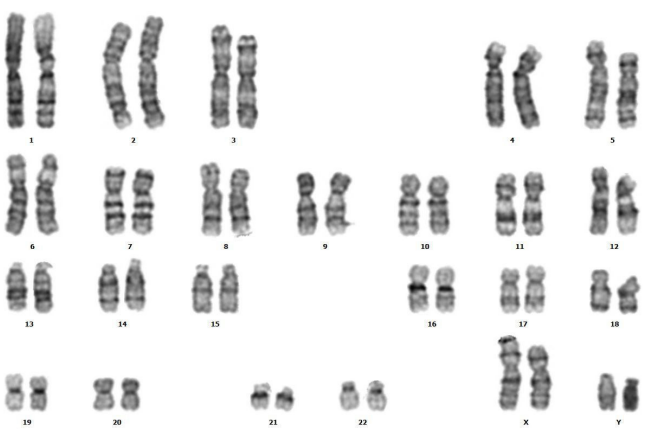

Figure 1. Analysis showing the 48,XXYY karyotype of the patient. GTG, G-banded karyotypes

syndrome [11]. In these cases, testosterone insufficiency may cause gynecomastia and decrease in muscle mass. Our patient had gynecomastia. In one study, the incidence of gynecomastia was reported to be 25% in adolescents and 41% in adults [12]. Another remarkable finding in these cases is related to their body structures. In a clinical study, Borgaonkar et al., reviewed the reported data of 53 patients and concluded that 48,XXYY cases are taller starting from an earlier age, compared to the growth parameters of the general population as in our case [13]. In addition, cardiac, cerebral and pulmonary defects, recurrent respiratory tract infections, strabismus, neurological symptoms, or diabetes mellitus may occur [11,14]. According to these findings, 48,XXYY syndrome has been defined as a different clinical and genetic disorder by some researchers. In the literature, achievement of in vitro fertility has been reported in only one case with 48XXYY syndrome [15].

The 48XXYY syndrome is an extremely rare genetic disorder and should always be considered in the etiology of male infertility when evaluating azoospermic cases. When 48XXYY syndrome is detected, guidelines strictly recommend informing the patient and in case of need his relatives in detail regarding impossibility of spontaneous fertility.

Ethics Committee Approval: N / A.
Informed Consent: An informed consent was obtained from the patient.
Publication: The results of the study were not published in full or in part in form of abstracts.
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Authorship Contributions: Any contribution was not made by any individual not listed as an author. Concept – H.Z., N.A.; Design – H.Z., N.A.; Supervision – F.E.; Resources – H.Z., N.A.; Materials – H.Z., N.A.; Data Collection and/or Processing – H.Z., N.A.; Analysis and/or Interpretation – H.Z., F.E., N.A.; Literature Search – H.Z., N.A.; Writing Manuscript – H.Z., N.A.; Critical Review – F.E.
Conflict of Interest: The authors declare that they have no conflict of interest.
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Case Report – Urological Oncology

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Well-differentiated and Dedifferentiated Giant Paratesticular Liposarcoma: A Report of Two Cases and a Review of the Literature

İyi Diferansiye ve Dediferansiye Paratestiküler Dev Liposarkomu: İki Olgu Sunumu ve Literatürün Gözden Geçirilmesi

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Abstract

Paratesticular liposarcomas (PLSs) are mostly painless, slow-growing and extremely rare inguinal or scrotal masses. Reports of approximately 270 cases have been published in the literature so far, but only a few of them contain information about giant PLSs exceeding 10 cm in size. Correct diagnosis and treatment is important as PLSs tend to cause local relapses and distant metastases. Here, we aimed to present, and evaluate a dedifferentiated (24 cm), and a well-differentiated (12 cm) giant PLS in the light of the literature data.

Keywords: paratesticular, mass, liposarcoma, giant, sarcoma

Öz

Paratestiküler liposarkomlar (PLS) çoğunlukla ağrısız, yavaş büyüyen ve oldukça nadir görülen inguinal veya skrotal kitlelerdir. Literatürde şu ana kadar yaklaşık 270 vaka bildirilmiştir; ancak bunlardan sadece birkaçı 10 cm'yi aşan dev PLS hakkında bilgi içermektedir. PLS lokal relapslara ve uzak metastazlara neden olma eğiliminde olduğundan doğru tanı ve tedavi önemlidir. Burada 24 cm dediferansiye ve 12 cm iyi diferansiye dev PLS'si olan 2 olguyu sunmayı ve literatürü değerlendirmeyi amaçladık.

Anahtar kelimeler: paratestiküler, kitle, liposarkom, dev, sarkom

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Introduction

Liposarcomas, soft tissue malignancies originating from mesodermal tissues, account for around 20% of all sarcomas. They are generally seen in the retroperitoneal area and extremities [1]. Approximately 12% of liposarcomas originate from the spermatic cord, testicular tunica and epididymis and are called paratesticular liposarcomas (PLSs) [2]. When the tumor diameter exceeds 10 cm, the PLS is classified as "giant" [3]. According to a recent meta-analysis, there are 265 PLS cases in the literature, and only a few cases of giant PLS [4]. Due to its rarity, there is no standard guideline regarding the incidence, diagnosis, recurrence and treatment of PLS [5]. In this case report, we aimed to present our treatment approach for two cases of giant LPS.

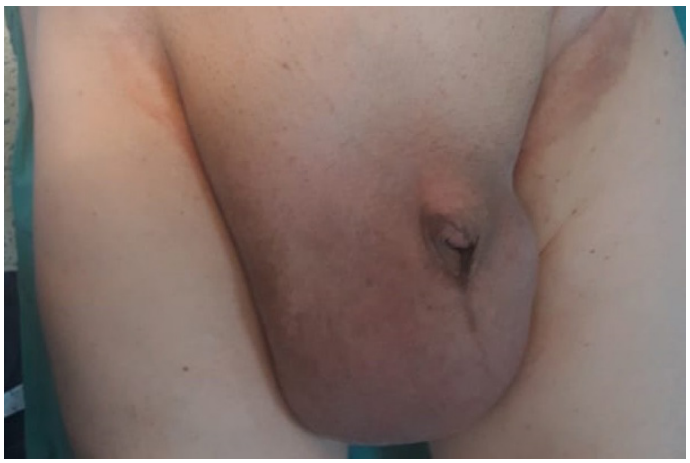

Figure 1. Preoperative view of the giant mass

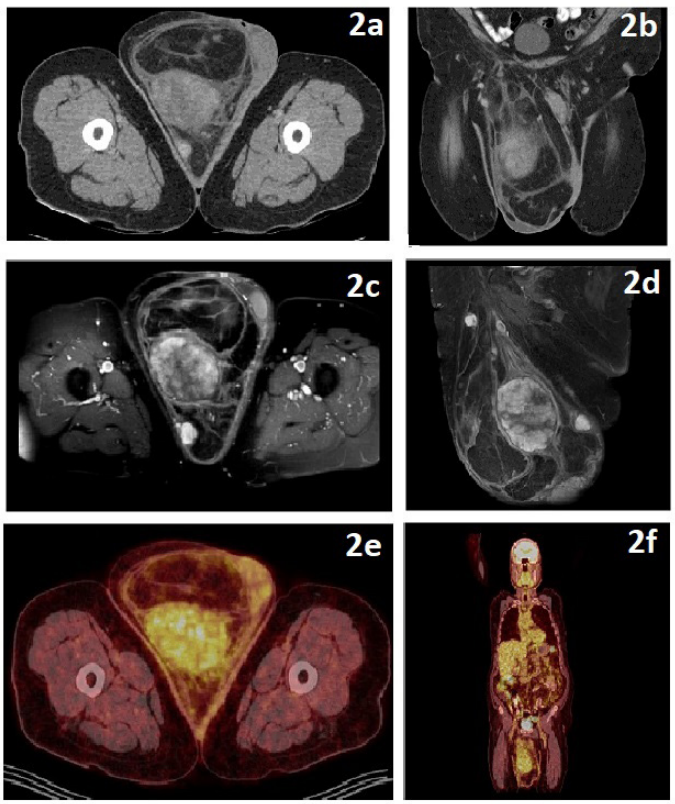

Figure 2. 2ab: Axial and coronal CT images; 2cd: Axial and sagittal MRI images; 2ef: Axial and coronal PET scan images

Case 1

A 63-year-old male patient presented to our outpatient clinic with a painless slowly growing scrotal mass that has been present for about 7 months (**Figure 1**). Physical examination revealed a giant solid mass in the right hemiscrotum. The mass lacked normal testicular tissue as detected during palpitation. The patient's preoperative levels of alpha-fetoprotein (AFP) (1.87 ng/mL), beta-human chorionic gonadotropin (β-hCG) (<1.20 ng/mL), and lactate dehydrogenase (LDH) (173 ng/mL) were as indicated. The contrast-enhanced computed tomography showed a solid mass of approximately 13.5x18.5x23.5 cm in size with heterogeneous fatty tissue containing septa and heterogeneous opacification extending from the right inguinal canal towards the right hemiscrotum (**Figures 2a, and b**). There were no signs of metastases in other organs. On examination, other soft tissues were normal. Magnetic resonance imaging (MRI) showed a solid mass of approximately 13.5x18.5x23.5 cm in size containing septa and heterogeneous fatty tissues herniated from the right inguinal canal towards the right hemiscrotum (**Figures 2c, and d**). Nodular heterogeneous opacifications in different sizes were observed in the superior (1.5x1.5 cm), in the middle (6.5x8.5 cm) and in the immediate inferior (2.5x2 cm) part of the mass. The positron emission tomography (PET) scan (F-18 FDG) imaging of the patient indicated increased 18fluorine-fluorodeoxyglucose (18F-FDG) uptake in the 9.0x6.5 and 3.0x2.2 cm solid components of the 18.0x12.5x24.0 cm fat- density septated mass lesion extending from the right inguinal canal into the scrotum (SUVmax: 8.0) (**Figures 2e, and f**). Thereupon, radical orchiectomy and hemiscrotectomy were performed through a right inguinal incision (**Figures 3a, and b**). A tumor weighing 2590 g with dimensions of 22x18x10 cm, and a negative surgical margin was sent to pathology and reported as dedifferentiated liposarcoma. The dedifferentiated component had the characteristics of myxofibrosarcoma which positively stained with immunohistochemically applied CDK4 (cyclin-dependent kinase-4) for the oncoprotein MDM2 (mouse double minute 2) and negatively with musicarmine stain (**Figures 4a, and b**).

The patient was administered 4 cycles of doxorubicin (50 mg) and ifosfamide (4 g) chemotherapy in the second postoperative month. In order to increase local control following chemotherapy, radiotherapy with a total of 28 fractions (50.4 Gy) and fractional doses of 1.8 Gy was applied using a Siemens Artiste Linear Accelerator Device (Siemens Medical Solutions,

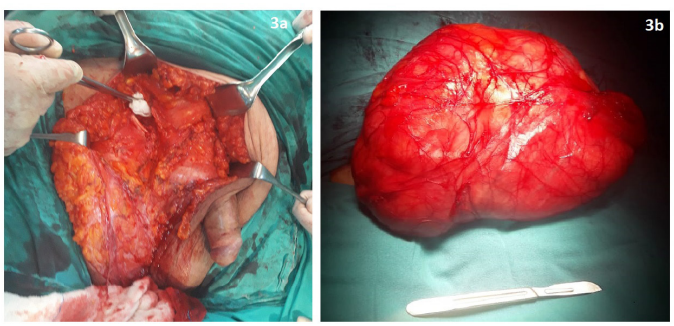

Figure 3. 3a: Surgical area after removal of the mass; 3b: Postoperative view of the giant mass

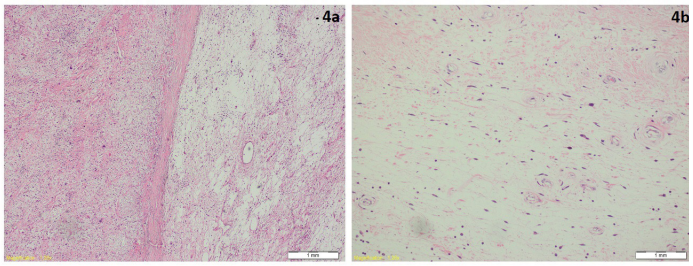

Figure 4. 4a: Sharp transition between dedifferentiated and well-differentiated components in hematoxylin-eosin staining at 4x magnification; 4b: Atypical spindle cells between mature lipocytes in connective tissu

Figure 5. 5abc: Sagittal, coronal and axial section view of the giant scrotal mass in MRI

Figure 6. Postoperative view of the giant mass

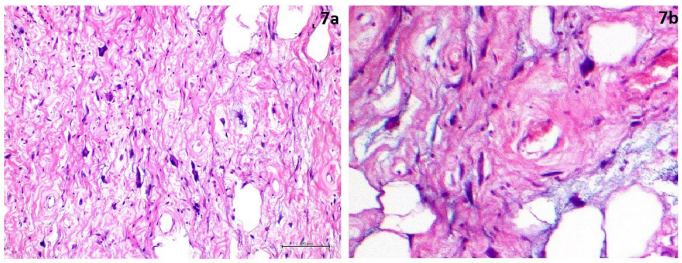

Figure 7. 7ab: In hematoxylin eosin staining at 40x magnification, prominent pleomorphic atypical cells with lipoblasts in eosinophilic background and myxoid changes in the background

Concord, CA, USA) with 6 MV photon energy. No recurrence was detected in the follow-up PET scan (F-18 FDG) obtained at the postoperative 18th month.

Case-2

A 58-year-old male patient was admitted to our outpatient clinic with a painless left hemiscrotal mass that has been growing for about a year. On physical examination, a 12 cm-mass filling the left hemiscrotum was palpated and normal testicular tissue could be partially palpated next to the mass. The patient's preoperative levels of AFP (2.82 ng/mL), β-hCG (<1.20 ng/mL), and LDH (250 ng/mL) were as indicated. MRI revealed a mass in the left hemiscrotum that completely filled the scrotum (**Figures 5a,b, and c**). It has widest dimensions of 12x7.7x7.6 cm and demonstrated heterogeneous necrotic areas in T1 hypo T2-weighted series. Heterogeneous opacifications in post-contrast series, increased diffusion and diffusion restriction in some places were observed. No signs of metastasis were observed. Radical orchiectomy was performed through a right inguinal incision (**Figure 6**). Pathological examination revealed a solid lesion weighing 1440 g and having dimensions of a 14x13x6.5 cm adjacent to but not involving the testicle. The capsule of the lesion was enveloped with typical testicular tissue. Negative surgical margins were obtained. Pathology report suggested a well differentiated liposarcoma. Focal positive nuclear staining was observed with immunohistochemically applied CDK4, but not with MDM2. It also stained positively for S100 protein (**Figures 7a, and b**). The patient was also evaluated by medical oncology due to the possibility of need for additional postoperative treatment. No additional treatment was recommended. No residual tumor or metastases were detected in the patient's postoperative 3rd month follow-up with PET scan (F-18 FDG).

Discussion

PLSs are mostly painless, slow-growing and extremely rare inguinal or scrotal masses [5]. Their origins are difficult to determine due to the complex anatomical structure of the scrotum and inguinal region, but presumably they originate most frequently (76%) from the spermatic cord [6]. In 2002, World Health Organization (WHO) classified liposarcomas based on their histology as well- differentiated, dedifferentiated, myxoid, round cell, and pleomorphic liposarcomas [7]. PLSs are mostly seen in adult patient groups aged between 50 and 60 years

[8]. Compared to well-differentiated low-grade liposarcomas, dedifferentiated liposarcomas have a more aggressive course and tend to have higher local recurrence rates, potential for distant metastasis, and a higher risk of death [9]. In metastatic cases, lung, bone, abdomen, and paraspinal soft tissue metastases are more common [10]. Therefore, application of imaging modalities that examine the thoracic, abdominal, and scrotal surgical regions would be appropriate for metastasis screening. For metastasis screening, we preferred to use PET scan, which is currently used primarily in many metastatic cancer types.

When the tumor diameter exceeds 10 cm, it is called a giant PLS [3]. They manifest as large scrotal mass lesions appearing just below the superficial inguinal ring [7]. Generally, these masses are misdiagnosed as hydrocele, epididymal cyst, inguinal hernia, hematocele or lipoma [9]. On ultrasonography (US), PLSs appear as heterogeneous, solid, hypoechoic lesions with relatively low vascularity, and sometimes liquefaction may accompany if necrosis is present [5,7]. However, US cannot always distinguish PLS from lipomas if the tumor is small or if it is a well-differentiated PLS with a homogeneous fat pattern [11]. Paratesticular liposarcomas are usually seen as heterogeneous mass lesions compatible with fat density in contrast-enhanced CT images. Contrast-enhanced CT can also provide important information regarding staging and follow-up [6]. Another useful imaging technique is MRI, which is the gold standard in the staging of soft tissue tumors. It does not only provide precise information about tumor foci, but also characterizes and defines the extent of local tumor spread [12].

Our Case 1 came with more than one screening examination (CT, MRI and PET) applied in another center before consulting to us. However, our Case 2 applied directly to us. We preferred MRI as preoperative imaging, primarily because of its superiority over the other imaging techniques in demonstrating the surgical site and surrounding soft tissues. On the same day, we made the surgical decision without wasting time in line with the accelerated reports submitted to us by the radiology physicians. In our opinion, it may be more appropriate to use other imaging methods (CT or PET scan) in the postoperative follow-up of metastases. Diagnosis of PLS is mainly made based on the histopathological, immunohistochemical and cytomorphological features of the mass lesion.

When a diagnosis of PLS is suspected, an urgent radical procedure must be performed to avoid the high risk of local recurrence and worsening of the prognosis. The gold standard in PLS treatment is radical orchiectomy with high ligation of the spermatic cord. Wide excision and hemiscrotectomy can also be performed in cases where the mass is larger and local invasion is suspected [13]. The issue of lymph node dissection is controversial. There is not enough data to show that superficial inguinal or retroperitoneal lymph node dissection has any therapeutic efficacy [6]. However, some studies have suggested the application of lymphadenectomy limited to the radiologically detected suspicious lymph nodes [14]. Surgical margin positivity is a risk factor for early recurrence and distant metastases [15]. A clinical study showed that 3-year local recurrence-free survival rates were 100%, and 29% in cases with negative, and positive surgical margins, respectively.

Generally, since liposarcomas are the most radiosensitive types of the sarcomas, radiotherapy is used for local control. In some cases of liposarcomas, remission has been achieved with radiotherapy alone, but the results in PLS are not yet clear. If surgical margin positivity is observed after surgical resection or if there is evidence of a tumor showing a high grade and aggressive behavior, adjuvant radiotherapy may be applied to the inguinal region and scrotum in addition to surgery to prevent local recurrence [16]. Recurrence may occur after radiotherapy in dedifferentiated aggressive tumors. Data on the effectiveness of chemotherapy in metastatic PLS are limited. However, some recent studies have recommended the use of doxorubicin, vincristine and cyclophosphamide [15]. Although the place and effectiveness of adjuvant therapies in the treatment of scrotal liposarcoma are controversial, our first case is one of the largest scrotal liposarcoma cases in the literature, which led us to apply adjuvant therapy more aggressively. However, further studies are needed to define a standard treatment in this regard. With the information we have, application of this type of specific treatment was decided for the patient.

It is important to inform young patients about sperm preservation before orchidectomy. The patient should be informed of the possibility of the presence of dysfunctional testicular tissue remaining after orchiectomy. Apart from this, the information that potential use of adjuvant chemotherapy, and radiotherapy in case of need may adversely affect fertilization, should be shared with the patient. Although long-term infertility after radiotherapy is rarely observed in studies on testicular tumors, it has been found that chemotherapy may cause long-term infertility in a dose-dependent manner. Therefore, the patients who cannot preoperatively preserve their sperms, should be informed about this adverse outcome of chemotherapy before application of adjuvant treatments [17].

In our study, two PLSs were successfully treated and the patients were cured. However, the short postoperative follow-up period of our patients stands out as a limitation of our study. In order to contribute more precise information to the literature, meta-analyses of the cases with longer follow-up periods cited in the literature should be conducted.

Conclusion

PLSs are extremely rare malignant soft tissue tumors. Contrast-enhanced CT and MRI are prominent methods in diagnosis, but the final diagnosis of PLS is made based on histopathological and immunohistochemical evaluation. The gold standard treatment method is radical orchiectomy, and when necessary, a multimodal approach including radiotherapy and chemotherapy is recommended. Long-term follow-up is required due to the risk of local recurrence and distant metastases.

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Case Report – General Urology

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A Rare Cause of Acute Urinary Retention in a Young Man: Zinner Syndrome

Genç Bir Erkekte Akut Üriner Retansiyonun Nadir Bir Nedeni: Zinner Sendromu

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Abstract

Zinner syndrome is a rarely seen congenital anomaly characterized with developmental defects of mesonephric (Wolffian) duct including obstruction of the ejaculatory duct, an ipsilateral seminal vesicle cyst, and an ipsilateral renal agenesis. Patients may present with genitourinary system complaints, or they may be completely asymptomatic and detected incidentally. Minimally invasive cyst aspiration and surgical treatment are mainly aimed for symptomatic relief. In this article, a rare case of Zinner Syndrome presenting with signs of urinary retention is presented.

Keywords: Zinner, seminal vesicle cyst, urinary retention, renal agenesis

Öz

Zinner sendromu, ejakülatör kanal obstrüksiyonu, ipsilateral seminal vezikül kisti ve ipsilateral renal agenezi gibi mezonefrik (Wolffian) kanal gelişim bozukluğu ile karakterize nadir görülen bir konjenital anomalidir. Hastalar genitoüriner sistem şikayetleri ile başvurabileceği gibi tamamen asemptomatik olup tesadüfen saptanabilir. Minimal invaziv kist aspirasyonu ve cerrahi tedavi esas olarak semptomatik rahatlamayı amaçlar. Bu makalede nadir görülen ve üriner retansiyon bulgusu ile başvuran bir Zinner Sendromu vakası sunulmuştur.

Anahtar kelimeler: Zinner, seminal vezikül kist, üriner retansiyon, renal agenezi

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Introduction

Zinner syndrome is a rarely seen congenital anomaly characterized by developmental defects of mesonephric (Wolffian) duct. The classic triad includes ejaculatory duct obstruction, an ipsilateral seminal vesicle cyst, and an ipsilateral renal agenesis. It was first described by A. Zinner in 1914 [1]. Bladder neck, half of the trigone, urethra, vas deferens, seminal vesicles, and epididymis in men develop from the distal mesonephric duct under the influence of testosterone and anti-Müllerian hormone. During embryogenesis, developmental disorders of the distal mesonephric duct affect the formation of the ipsilateral kidney, ureter, vas deferens, and seminal vesicles. The ejaculatory duct obstruction results in cystic dilatation of seminal vesicles because of the accumulation, and retention of seminal fluid. Patients may present with genitourinary system complaints, or they may be completely asymptomatic and detected incidentally. In this paper, we report a case of a 32-year-old male patient who presented with acute urinary retention, and diagnosed as Zinner syndrome based on radiological examinations.

Case

A 32-year-old male patient was admitted to the emergency department complaining of an inability to urinate for hours. He had been complaining of frequent episodes of difficult micturition for three weeks. He had no known urological or systemic diseases. His vital signs were within normal limits at the time of admission. Suprapubic tenderness and distension due to a distended urinary bladder were revealed upon physical examination. No abnormality was detected during the physical examination of the external genitalia. The results of urinalysis, hematological and biochemical blood tests were within normal limits. Following the insertion of a 16-F urethral catheter, he was referred to the urology department for further examination.

Abdominopelvic ultrasound (US) was performed and a hypertrophic left kidney (Grade 1) with increased echogenicity was seen and the right kidney could not be visualized. A lobulated multiloculated cystic lesion of approximately 7.5x6.0 cm in size in the posterior region of the bladder compressing the prostate and the bladder was observed. Then, a magnetic resonance imaging (MRI) of the lower abdomen was performed. On MRI, cystic enlargement reaching 3.5 cm in diameter at the widest point of the left seminal vesicle and compressed bladder was detected. The left seminal vesicle was not separate from this cystic lesion (**Figure 1**). Fluid-fluid levels were noted in the dilated left vas deferens possibly secondary to dense, proteinous content. The left ureter showed indentation with cystic enlargement to the base of the bladder, consistent with ureterocele which apparently terminated proximally at the level of the left sacroiliac joint. The right ureter, right seminal vesicle, and prostate were morphologically normal.

The radiological findings of the left seminal vesicle cyst with ipsilateral renal agenesis, tubular enlargement of ipsilateral vas deferens, and left ureterocele with blind-ending proximal ureter led to the establishment of the diagnosis of Zinner syndrome, which is a mesonephric duct anomaly. Since acute urinary retention developed, transrectal needle aspiration was performed under the guidance of transrectal US (**Figure 2a**). Cystic dilatation regressed completely after aspiration (**Figure 2b**) of a dark-colored liquid (**Figure 3**). The urethral catheter was removed at the 24th hour after percutaneous aspiration. The patient was discharged after he urinated without difficulty. A control visit was scheduled for approximately one month after the procedure.

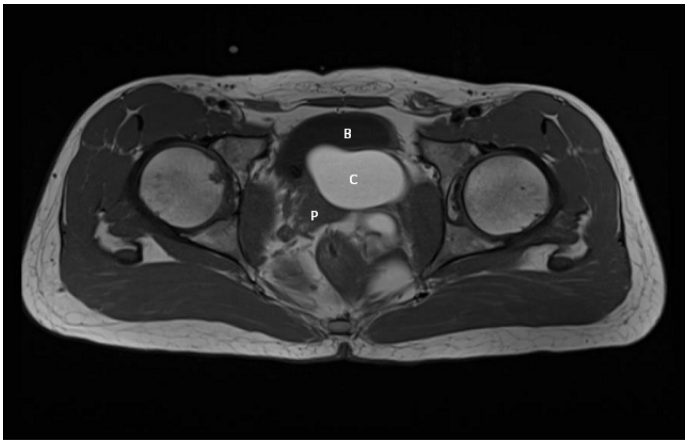

Figure 1. Axial T1-weighted images of MRI. The cystic lesion (C) at the level of the left seminal vesicle compresses on the bladder (B) from the posterior and on the prostate (P) from the lateral

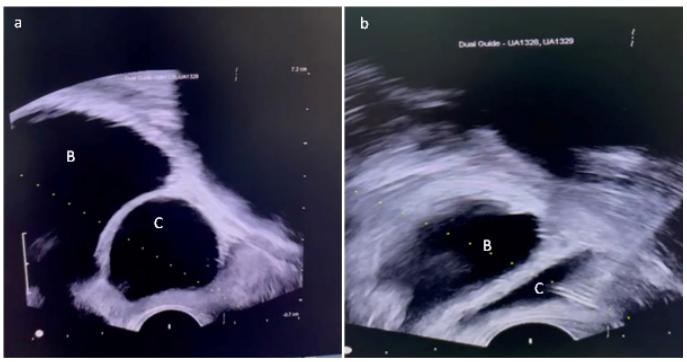

Figure 2. Sagittal view of transrectal ultrasound before (a) and after (b) transrectal needle aspiration of cystic lesion (C) on the posterior of the bladder (B). It was observed that the cystic lesion shrunk and disappeared after aspiration

Figure 3. Dark-colored aspirated liquid of cystic lesion

Discussion

Current hypotheses regarding the pathogenesis of Zinner syndrome are related to disruptions in the development of the mesonephric duct or Wolffian duct. In normal embryological development, the mesonephric duct performs some basic renal functions. Also, the presence of testosterone in males stimulates the distal end of the mesonephric duct to differentiate into the epididymis, vas deferens, seminal vesicles, and bladder trigone. Dysfunction of signaling pathways during development of the distal mesonephric duct may result in agenesis or dysplasia of the ureteral bud (and subsequently the ipsilateral kidney) or genital adnexal structures (such as the ipsilateral seminal vesicle) [2].

In this case report, we are presenting a case of Zinner syndrome that referred to us with acute urinary retention and the diagnosis was established based on MRI findings. Then, we performed transrectal aspiration of the cyst under US guidance. We performed radiological tests during control visits to see if there was any recurrence of cysts. Recurrence of cysts was not observed during control visits. The patient did not have urinary retention or difficulty urinating again. Zinner syndrome is mostly asymptomatic. Symptoms classically occur at the age of peak sexual and reproductive activity due to the accumulation of seminal fluid in the seminal vesicles. Most of the symptomatic cases present with lower urinary tract symptoms such as enlarged seminal vesicle cyst, dysuria, pollakiuria, painful ejaculation, perineal pain, and epididymitis. Although rare, patients may also present with infertility [3], hematospermia [4], scrotal pain [5], and difficult micturition [6]. Because this syndrome has broad-spectrum symptoms, the diagnosis of infertility may be delayed. In pediatric age, congenital seminal vesicle cysts may be asymptomatic and may be diagnosed incidentally during routine radiological imaging during postnatal US scanning for urinary tract anomalies or during neonatal US in patients with suspected prenatal renal malformation. Seminal vesicle cysts are present from birth but grow and become symptomatic in adolescence or adulthood [7].

Zinner syndrome is diagnosed radiologically using various imaging methods. The gold standard diagnostic imaging techniques include US or CT in the first stage and MRI imaging as a further examination [8]. Ureteral anomalies may present in different forms in Zinner syndrome. The ipsilateral ureter may be completely agenetic [2] or may present as a blind-ending ureterocele [9] or ureter opening into the seminal vesicle [10].

As a treatment modality incidentally asymptomatic or minimally symptomatic cases may be followed up. Treatment is mainly aimed at symptomatic relief. In a recently published systematic review of 214 cases, surgery was the most common treatment approach performed. Surgery can be performed as an open, robotic, or laparoscopic vesiculectomy. Seminal vesiculoscopy, transurethral unroofing of the cyst, and transurethral resection of the ejaculatory duct are other rarely applied surgical treatment options. Percutaneous drainage and transrectal aspiration are less invasive methods that can be applied as an alternative to surgery. In a study recurrence was reported in 8 out of 19 (47.4%) patients who had undergone transrectal cyst aspiration requiring surgical treatment [11].

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Letter to the Editor – Andrology

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DOI: 10.5505/GJU.2022.58076

Re: Ozlu et al.: False Penile Fracture: Case Series and Literature Review [Grand J Urol 2021;1(1):9-13]

Re: Özlü ve ark.: Yalancı Penil Fraktür: Olgu Serisi ve Literatürün Gözden Geçirilmesi [Grand J Urol 2021;1(1):9-13]

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Dear editor,

We have read with great interest, the case series and literature review of false penile fracture by Ozlu et al. in which the authors share clinical experience with more than 100 patients over a 13-year period [1]. By examination of operative reports, they retrospectively evaluated the patients with a pre-diagnosis of penile fracture and frankly reported a misdiagnosis rate of approximately 8%. This ratio is comparable and consistent with the literature [2-5]. Examining the patient clinical and operative characteristics, shown as a table on a separate page, we see that only two of total eight false penile fracture cases underwent radiological examination. Magnetic resonance imaging (MRI) was preferred in these patients, and it was stated that one of them was MRI positive (patient 4) and the other was MRI false positive (patient 2). Patients with a tunical tear in preoperative MRI, but no tear in surgical exploration were considered to have false penile fracture. Since only ligation procedures were performed on both MRI positive and MRI false positive patients, we think that such a distinction is confusing and not necessary. Perhaps ultrasonography could be preferred for the remaining six patients for whom radiological examination was not performed, due to its easy accessibility and provide medical recording. However, an ideal radiographic imaging modality is still lacking so far [6]. Although there are some clinical differences between false and true penile fractures, the two conditions cannot be clearly distinguished from each other either clinically or radiologically [3].

Consequently, we would like to encourage Ozlu et al., on a very diligently written and quite informative article that briefly summarizes the studies that have already been published and the approach to the patient with penile fracture. Urologists somehow have to base the definitive diagnosis of penile fracture on surgical exploration in order to eliminate serious long-term potential problems of an overlooked tunical tear.

Sincerely yours.

Ethics Committee Approval: This article does not contain any studies with human participants performed by the author.
Authorship Contributions: Any contribution was not made by any individual not listed as an author. Concept – B.K.A., O.L.O.; Design – B.K.A., O.L.O.; Supervision – B.K.A., O.L.O.; Resources – B.K.A., O.L.O.; Materials – B.K.A., O.L.O.; Data Collection and/or Processing – B.K.A., O.L.O.; Analysis and/or Interpretation – B.K.A., O.L.O.; Literature Search – B.K.A., O.L.O.; Writing – B.K.A., O.L.O.; Critical Review – B.K.A., O.L.O.
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SUBJECT INDEX / Volume 2, 2022