



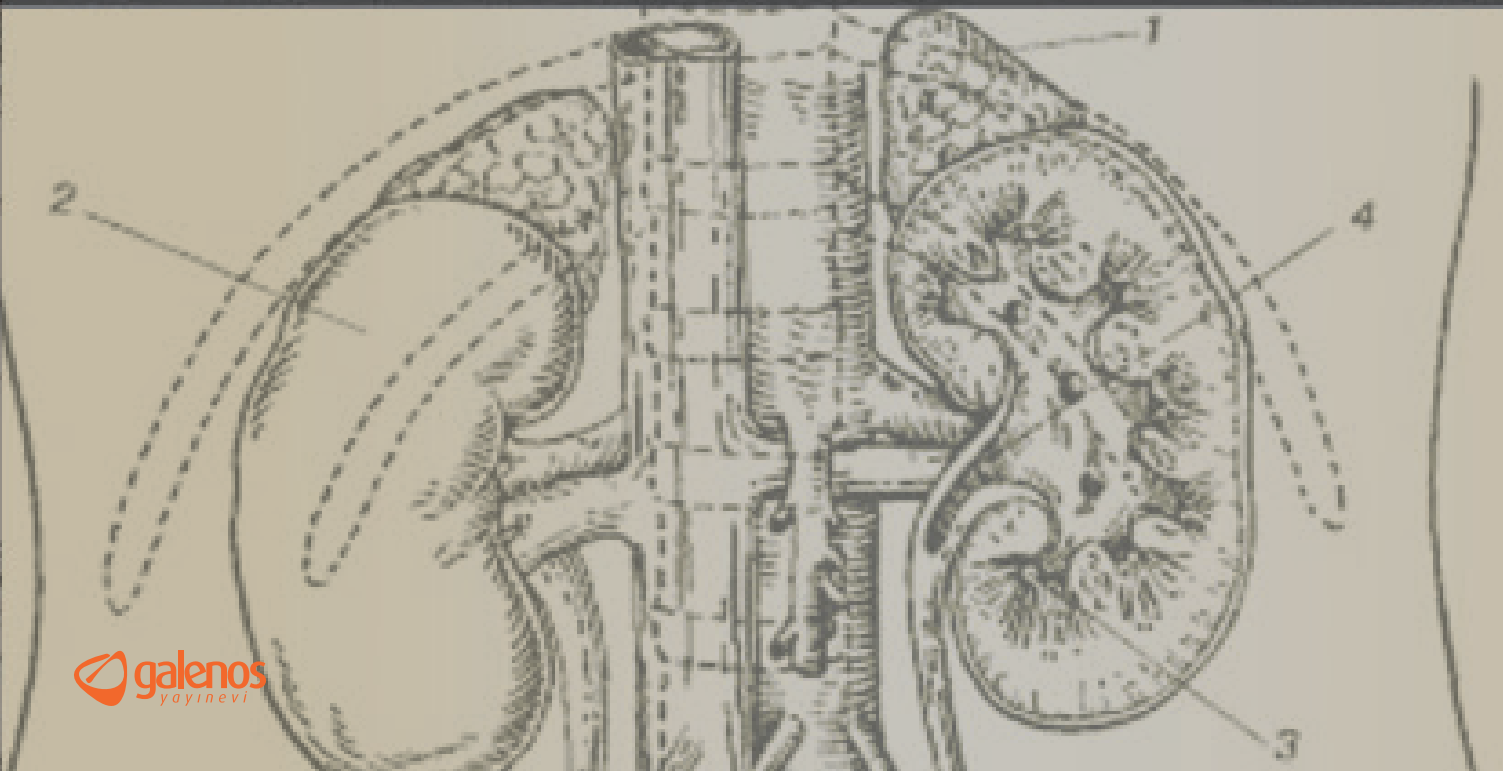
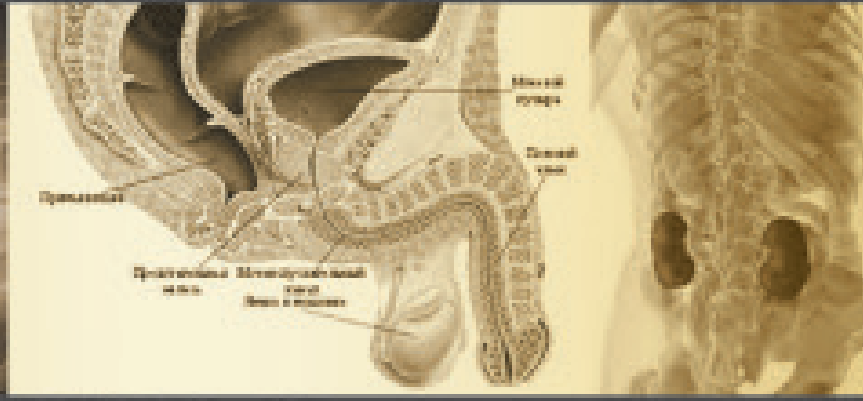
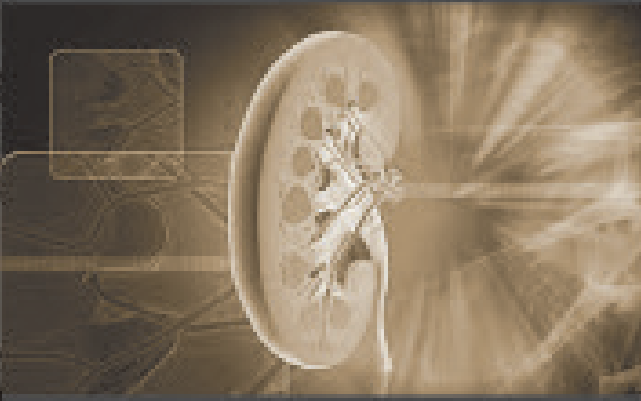
Society of
Urological
Surgery
in Türkiye

E-ISSN 2148- 9580

JOURNAL OF UROLOGICAL SURGERY

Volume 5 / Issue 3 / September 2018

www.jurolsurgery.org



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Technical and other assistance should be provided on the title page.

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Title: The title should provide important information regarding the manuscript's content.

The title page should include the authors' names, degrees, and institutional/professional affiliations, a short title, abbreviations, keywords, financial disclosure statement, and conflict of interest statement. If a manuscript includes authors from more than one institution, each author's name should be followed by a superscript number that corresponds to their institution, which is listed separately. Please provide contact information for the corresponding author, including name, e-mail address, and telephone and fax numbers.

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Abstract

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Materials and Methods: Important methods should be written respectively.

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Results: Important findings and results should be provided here.

Conclusion: The study's new and important findings should be highlighted and interpreted.

Other types of manuscripts, such as case reports, reviews and others will be published according to uniform requirements. Provide at least 3 keywords below the abstract to assist indexers. Use terms from the Index Medicus Medical Subject Headings List (for randomized studies a CONSORT abstract should be provided (<http://www.consort-statement.org>).

After keywords in original research articles there must be a paragraph defining "What is known on the subject and what does the study add".

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Abstract length: Not to exceed 250 words. "What is known on the subject and what does the study add" not exceed 100 words.

Article length: Not to exceed 3000 words.

Original researches should have the following sections:

Introduction: The introduction should include an overview of the relevant literature presented in summary form (one page), and whatever remains interesting, unique, problematic, relevant, or unknown about the topic must be specified. The introduction should conclude with the rationale for the study, its design, and its objective(s).

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Comparisons, and statistically important values (i.e. p value and confidence interval) should be provided.

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References

Cite references in the text, tables, and figures with numbers in parentheses. Number references consecutively according to the order in which they first appear in the text. Journal titles should be abbreviated according to the style used in Index Medicus (consult List of Journals Indexed in Index Medicus). Include among the references any paper accepted, but not yet published, designating the journal and followed by, in press. Authors are solely responsible for the accuracy of all references.

Examples of References:

1. List All Authors

Ghoneim IA, Miocinovic R, Stephenson AJ, Garcia JA, Gong MC, Campbell SC, Hansel DE, Fergany AF. Neoadjuvant systemic therapy or early cystectomy? Singlecenter analysis of outcomes after therapy for patients with clinically localized micropapillary urothelial carcinoma of the bladder. *Urology* 2011;77:867-870.

2. Organization as Author

Yaycioglu O, Eskicorapci S, Karabulut E, Soyupak B, Gogus C, Divrik T, Turkeri L, Yazici S, Ozen H; Society of Urooncology Study Group for Kidney Cancer Prognosis. A preoperative prognostic model predicting recurrence-free survival for patients with kidney cancer. *Jpn J Clin Oncol* 2013;43:63-68.

3. Complete Book

Wein AJ, Kavoussi LR, Novick AC, Partin AW, Peters CA. *Campbell-Walsh Urology*, 10th ed. Philadelphia, Elsevier&Saunders, 2012.

4. Chapter in Book

Pearle MS, Lotan Y. Urinary lithiasis: etiology, epidemiology, and pathogenesis. In: Wein AJ, Kavoussi LR, Novick AC, Partin AW, Peters CA. *Campbell-Walsh Urology*, 10th ed. Philadelphia, Elsevier&Saunders, 2012, pp 1257-1323.

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5. Abstract

Nguyen CT, Fu AZ, Gilligan TD, Kattan MW, Wells BJ, Klein EA. Decision analysis model for clinical stage I nonseminomatous germ cell testicular cancer. *J Urol* 2008;179:495a (abstract).

6. Letter to the Editor

Lingeman JE. Holmium laser enucleation of the prostate-If not now, when? *J Urol* 2011;186:1762-1763.

7. Supplement

Fine MS, Smith KM, Shrivastava D, Cook ME, Shukla AR. Posterior Urethral Valve Treatments and Outcomes in Children Receiving Kidney Transplants. *J Urol* 2011;185(Suppl):2491-2496.

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Article length: Not to exceed 1000 words.

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How I do?

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Tables, Graphics, Figures, and Images

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A Comparison of Epidural Anesthesia without Motor Block Versus General Anesthesia for Percutaneous Nephrolithotomy

Perkütan Nefrolitotomide Motor Bloksuz Epidural Anestezi ile Genel Anestezinin Karşılaştırılması

© Sedat Öner¹, © Burak Acar², © Efe Önen¹, © Metin Kılıç¹, © Mustafa Murat Aydos¹, © Murat Demirbaş¹, © Ali Ekber Yüreklî³

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What's known on the subject? and What does the study add?

Today, epidural anesthesia in percutaneous nephrolithotomy operations is as effective as general anesthesia, safe and comfortable for the surgeon. This is why it is preferred in some clinics. We are on the lookout for its use even further, as it offers additional advantages such as less postoperative analgesic requirements and shorter operating times for the surgery room.

Abstract

Objective: The study carried out to compare the operative parameters and stone clearance in patients who underwent percutaneous nephrolithotomy (PNL) under epidural anesthesia (EA) without motor block versus those who underwent PNL under general anesthesia (GA).

Materials and Methods: We retrospectively reviewed 2 groups of patients who underwent PNL at our institute between January 2014 and September 2014. Group 1 consisted of 69 consecutive patients who underwent PNL under EA without motor block and group 2 consisted of 69 consecutive patients who underwent PNL under GA. Patients general characteristics, stone features, surgical parameters, duration of surgery, time spent in the operating room, postoperative analgesic requirements, complications, stone clearance rate and mean length of hospital stay were compared between the 2 groups.

Results: The two groups were similar in terms of mean age, gender, stone size and previous surgery. Operative time, access site, mean access number, postoperative fever, drainage, mean hemoglobin drop, stone-free rate, duration of nephrostomy tube and length of hospitalization were also similar between the groups. The time spent in the operating room, blood transfusion rate and postoperative analgesic requirements in EA group were significantly lower than those in GA group.

Conclusion: PNL under EA without motor block is as effective and safe as PNL under GA and it offers some advantages as with lower parenteral analgesic requirements, lower transfusion rates and lesser usage of operation room.

Keywords: Epidural, Anesthesia, Percutaneous nephrolithotomy

Öz

Amaç: Çalışma, motor bloksuz epidural anestezi (EA) altında perkütan nefrolitotomi (PNL) uygulanan hastalara karşı genel anestezi (GA) uygulanan hastaların operasyon parametrelerini ve taş temizlenmesini karşılaştırmak için yürütülmüştür.

Gereç ve Yöntem: Ocak 2014 ile Eylül 2014 tarihleri arasında kliniğimizde PNL uygulanan iki grup geriye dönük olarak incelendi. Grup 1, motor bloksuz EA uygulanan ardışık 69 hasta ve grup 2 de GA altında PNL uygulanan ardışık 69 hastadan oluştu. İki grup arasında hastaların genel özellikleri, taş özellikleri, cerrahi parametreler, ameliyat süresi, ameliyat odasındaki süre, postoperatif analjezik gereksinimleri, komplikasyonlar, taş temizleme oranı ve ortalama hastanede kalış süreleri karşılaştırıldı.

Bulgular: İki grup arasında yaş, cinsiyet, taş boyutu ve daha önce yapılan cerrahi açısından benzerlik vardı. Her iki grupta da operasyon süresi, erişim yeri, ortalama erişim sayısı, ameliyat sonrası ateş, drenaj, ortalama hemoglobin düşmesi, taşsızlık oranı, nefrostomi süresi ve hastanede yatış süresi benzerdi. Ameliyat odasında geçen süre, kan transfüzyon oranı ve EA grubundaki postoperatif analjezik gereksinimleri GA grubundakilere göre anlamlı derecede düşüktü.

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Received: 02.01.2018 **Accepted:** 08.05.2018

Cite this article as: Öner S, Acar B, Önen E, Kılıç M, Aydos MM, Demirbaş M, Yüreklî AE. A Comparison of Epidural Anesthesia without Motor Block Versus General Anesthesia for Percutaneous Nephrolithotomy. J Urol Surg 2018;5(3):143-148.

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Sonuç: Motor bloksuz EA ile yapılan PNL, GA altındaki PNL kadar etkili ve güvenlidir olup daha az parenteral analjezik gerekliliği, daha düşük transfüzyon oranları ve ameliyat odasının daha kısa süreli kullanımı gibi bazı avantajlar sunmaktadır.

Anahtar Kelimeler: Epidural, Anestezi, Perkütan nefrolitotomi

Introduction

Percutaneous nephrolithotomy (PNL) is the primary treatment modality for the management of most renal stones, especially for patients with large and multiple kidney stones (>2 cm), staghorn stones and cases of failed shock-wave lithotripsy (1,2,3,4). PNL is generally carried out under general anesthesia (GA) in the prone position (1,5). However, GA is associated with higher rates of complication than regional anesthesia (RA) (6). Endotracheal tube migration and neurologic problems at the time of position transition may arise during PNL under GA (7). Furthermore GA has the risk of pulmonary complications; randomized controlled studies indicated that RA reduces postoperative mortality and other serious problems (7,8,9). There have been a few studies conducted to compare PNL under RA and GA with respect to operative parameters (10,11).

The present study was carried out as a prospective randomized study to compare surgical parameters, stone clearance, complication rates and postoperative pain between patients undergoing PNL under RA [epidural anesthesia (EA) without motor block] and those undergoing PNL under GA, and whether EA was a good alternative to GA in PNL.

Materials and Methods

Two groups of patients who underwent PNL between January 2014 and September 2014 at our institute were retrospectively reviewed. Group 1 consisted of 69 consecutive patients who underwent PNL under EA without motor block and group 2 consisted of 69 consecutive patients who underwent PNL under GA. The type of anesthesia was decided by the anesthesiologist regardless of the comorbid conditions or the characteristics of the kidney stones. Patients under the age of 17 years and above the age of 80 years, with an American Society of Anesthesiologists (ASA) score above 3, with bilateral kidney stones, with solitary kidney, with radio-lucent stones and those requiring additional urological surgeries such as endopyelotomy and ureteroscopy were excluded. History taking, physical examination, preoperative laboratory tests (urinalysis, urine culture, complete blood count, renal function tests and liver function tests) and radiologic evaluation including kidney-ureter-bladder (KUB) plain images, urinary ultrasound and/or intravenous urography and/or computed tomography (CT) were performed in all patients.

Patients with urine culture positive for microorganism were treated according to urine culture before the operation.

Calculated stone surface area was evaluated by multiplying the maximum diameter, width, $\frac{1}{4} \pi$ of the stone seen on the plain radiography.

Chest X-ray and electrocardiogram were performed as a part of a fitness test for anesthesia and adequate blood was arranged. Written informed consent for the procedure both EA and GA was taken prior to the operation.

This retrospectively designed study was approved by Local Ethics Committee of University of Health Sciences Bursa Yüksek İhtisas Training and Research Hospital (approval number: 2011-KAEK-25 2016/09-07).

Epidural Anesthesia without Motor Block

Epidural catheter was introduced through an 18G needle in the intervertebral space at the T12-L1 level to produce sensorial anesthesia between T6 and S4 segments (from the kidney to the penile urethra) outside the operation room by an experienced anesthesiologist (A.Y.). A test dose (lidocaine 3 mL with adrenaline 1:200.000) was administered. After that a 20 mL solution containing 5 mg 0.5% bupivacaine and 0.05 mg fentanyl per mL was injected through the epidural catheter and 15-20 minutes later, the patients were put into the operating room under sensorial anesthesia. Maintenance of anesthesia was supplied by the injection of the same solution in the amount of 10 mL per 90 minutes. By the administration of the drug in this concentration, only sensorial anesthesia was established (without motor block). Sedation of patients was done by intravenous administration of 50 µg fentanyl or 0.01 mg/kg diazepam, if necessary. Postoperative pain control was provided by injection of 15-20 mL solution containing 3 mg 0.05% bupivacaine and 0.05 mg fentanyl in each milliliter, through the epidural catheter when needed (minimum 120 minutes interval) in group 1. Postoperative pain control in group 2 was provided by the intramuscular injection of diclofenac sodium (150 mg/day) or meperidine (200 mg/day) until the patients could take the diclofenac sodium per orally.

Percutaneous Nephrolithotomy Technique

Standard PNL operation was done in both groups by an experienced urologist (S.O.). Cystoscopy and 6F ureteral catheterization were performed in the lithotomy position, after which the patients were shifted to the prone position. Puncture of the appropriate calyx was performed by an 18G needle under biplanar fluoroscopy guidance after imaging of the renal collecting system by the contrast material injection through the ureteral catheter. Sequential amplatz dilation of

the tract over a 0.038 guidewire was performed and finally a 30F working sheath was kept in the collecting system and a 26F nephroscope was inserted. Normal saline was used for irrigation. The stones were fragmented with pneumatic lithotripter and the fragments were extracted with forceps. Stone clearance was assessed by the fluoroscopic control and a 16F reentry nephrostomy catheter was placed at the end of the operation. The nephrostomy catheter was removed after 24-72 hours depending on the clearance of hematuria.

Duration of EA, mean time elapsed between entrance to operating room to cystoscopy start time, mean time from entrance to operating room to the beginning of the PNL operation, in-room time and duration of operation were recorded. Operation time was calculated as the time elapsed (in minutes) from the puncture of pelvicalyceal system until the insertion of the nephrostomy tube.

PNL-associated complications, such as hemorrhage requiring transfusion, fever, prolonged urinary drainage, severe urosepsis, pleural injury, colon injury, and hemorrhage requiring arterial embolization, perirenal hematoma, and death were classified according to the modified Clavien classification. Also complications, such as pain, hypotension, nausea and vomiting depending on the anesthesia, during the operation and postoperative period were recorded.

Our criteria for blood transfusion included a postoperative hemoglobin level of <10 mg/dL with ongoing hematuria and/or hemodynamic instability. In case of supracostal or upper calyceal puncture, chest X-ray was ordered to assess pleural injury. Stone clearance was evaluated by the KUB X-ray and/

or CT scan 3 weeks after surgery. Patients with no opacities on the X-ray and/or CT scan were considered stone free; those with opacities under 4 mm were considered to have clinically insignificant residual fragments.

Statistical Analysis

Statistical Package for the Social Sciences for Windows was used in the evaluation of the data of the study. Student's t-test, the Mann-Whitney U test and Pearson's coefficient were used for the evaluation of quantitative variables and χ^2 test was used for the evaluation of the qualitative variables. A p value of less than 0.05 was considered statistically significant.

Results

The patient and stone characteristics are shown in Table 1. The two groups were similar in age, sex, body mass index, ASA scores, location of stones, involvement of renal units, existence of hydronephrosis, and history of previous kidney operation.

There was no complication associated with epidural catheter placement procedure in group 1. All patients in group 1 passed to prone position themselves because of EA without motor block, the others passed that position with the help of operating room staff.

Two female patients (7.4%) and 8 male patients (19.0%), who received EA, complained of slight pain during cystoscopy when the cystoscope passing the bladder neck. Operation continued after additional injection of analgesics through the epidural catheter in these patients. Nausea-vomiting and hypotension

Table 1. Patient and stone characteristics

Characteristic	Group 1 (EA) (n=69)	Group 2 (GA) (n=69)	Significance
Mean age (years)	46.0 (19-79)	43.9 (17-77)	0.36
Male/female	42/27	37/32	0.51
Mean BMI (kg/m ²)	28.6±6.3 (19-47.2)	28.3±5.9 (18-46.8)	0.44
Mean ASA score	1.3	1.2	0.18
Site of stone			0.45
Single calyx	13	12	
Pelvic	19	17	
Pelvic + single calyx	11	12	
Multiple calyx	20	25	
Staghorn	6	3	
Hydronephrosis			0.59
Yes	46	42	
No	23	27	
Stone area (mm ²)	760 (64-2952)	678 (120-2162)	0.38
Right/left kidney	35/34	28/41	0.35
Previous stone surgery	18 (26.0%)	15 (21.7%)	0.42

EA: Epidural anesthesia, GA: General anesthesia, BMI: Body mass index, ASA: American Society of Anesthesiologists

associated with EA (Clavien 1) were seen in 3 patients (4.3%) and 7 patients (10.1%) in group 1, respectively.

Operative findings are shown in Table 2. There was no difference in operative time, number of access (single or multiple access), access site, mean access number, fluoroscopy time, postoperative creatinine change, postoperative fever (Clavien 1), prolonged drainage (exceeding 72 hours) requiring double-j catheter insertion (Clavien 3A), stone-free rate, duration of nephrostomy tube and length of hospitalization (Table 2). Although the mean hemoglobin drop was similar between the groups, hemorrhage requiring blood transfusion (Clavien 2) rate was significantly lower in group 1. Overall in-room time in group 1 patients was significantly lower than in group 2 patients (Table 2). Parenteral analgesic requirement was significantly higher in group 2 (Table 2). There were no parenteral analgesic requirements in group 1 patients.

No patient required second-look PNL in both groups.

Discussion

PNL is the first-line treatment choice for managing renal stone disease, although several new techniques, such as retrograde intrarenal surgery and modification of PNL, have been introduced (11). PNL is mostly performed under GA, although it can be done also under RA (6,10,12,13,14,15,16). However, patients undergoing GA are more likely to have severe morbidities, such as drug-induced anaphylaxis, complications associated with endotracheal tube during the change of the position from lithotomy to prone, and cardiovascular, pulmonary and neurologic complications, than those receiving RA (14). During supracostal or upper pole puncture, patients can follow verbal commands and control respiration more easily under RA. In addition, advantages of RA over GA have been demonstrated in many other operations (17,18).

Mostly combined spino-EA (CSEA) is used as RA in PNL operations. Kuzgunbay et al. (6) compared the efficacy and safety in 37

Table 2. Operative parameters

Characteristic	Group 1 (EA) (n=69)	Group 2 (GA) (n=69)	Significance
Mean operation time (min)	58.7 (6-135)	60.8 (10-132)	0.69
Mean time for the administration of epidural anesthesia (min)	5.3 (3-12)	-	-
Mean time from entrance to operation room to start of cystoscopy (min)	13.5 (5-44)	21.6 (10-40)	0.00
Mean time from entrance to operation room to the beginning of the PNL operation (min)	36.5 (14-187)	42.4 (18-84)	0.05
Mean duration in operation room (min)	103.0 (49-230)	117.8 (55-190)	0.01
Number of access			0.75
Single	56	57	
Multiple	13	12	
Access site			0.45
Upper calyx	11 (13%)	11 (13%)	
Middle calyx	33 (39%)	38 (45%)	
Lower calyx	40 (48%)	35 (42%)	
Mean access number	1.2 (1-3)	1.2 (1-5)	0.95
Fluoroscopy time (min)	2.5	2.4	0.91
Mean hemoglobin drop (g/dL)	1.9±0.08	2.1±0.26	0.13
Serum creatinine (mg/dL)			0.69
Preoperative	1.15±0.57	1.04±0.25	
Postoperative	1.13±0.51	1.05±0.28	
Blood transfusion	6 patients (8.6%)	15 patients (21.7%)	0.03
Postoperative fever	3 patients (4.3%)	2 patients (2.8%)	0.68
Prolonged drainage	1 patient (1.4%)	1 patient (1.4%)	0.33
Stone free	63 patients (91.3%)	64 patients (92.7%)	0.83
Mean duration of nephrostomy tube (days)	2.2	2	0.23
Mean hospitalization time (days)	3	3	0.81
Parenteral analgesic requirements	None	1.9 times (0-4)	0.01

EA: Epidural anesthesia, GA: General anesthesia, PNL: Percutaneous nephrolithotomy

patients who underwent PNL under CSEA and 45 patients under GA. They concluded that PNL under CSEA was effective and safe as PNL under GA. Karacalar et al. (19) reported the superior results of spinal combined epidural anesthesia (SCEA) compared to GA in some aspects such as patient satisfaction, less postoperative pain and shorter duration of postoperative analgesic medication use. They observed no difference in the incidence of vomiting, itching, hypotension and bradycardia between the groups but higher rate of nausea was found in GA group. In their prospective randomized study comparing PNL under GA and PNL under SCEA, Sing et al. (10) found that the mean analgesic requirement within 24 hours was lower and hospital stay was shorter in SCEA group. RA is equally effective and safe compared to GA.

Studies comparing PNL under RA with PNL under GA have compared mostly spinal anesthesia (SA) or SCEA with GA. There is limited number of studies comparing PNL under EA with PNL under any other type of anesthesia. In a study of 50 patients comparing PNL under EA with PNL under GA, Tangpaitoon et al. (14) reported that EA had some advantages over GA including less nausea/vomiting, less postoperative pain, less analgesic drug usage and more patient satisfaction. There was no difference in postoperative hemoglobin values, operation time, postoperative complication, success rate and hospital stay between patients receiving EA and GA. However, the authors did not state if motor block was provided or not.

There are also a small number of studies comparing PNL under EA with PNL under the other RA techniques. Nandanwar et al. (20) compared PNL under EA and PNL under SA and they reported that segmental epidural block was better than SA in terms of hemodynamic stability, postoperative analgesia, patient satisfaction and reduced incidence of nausea and vomiting. They also stated that EA was difficult to execute and took longer time to act as compared to spinal block which limits its use (20).

In our study, epidural catheter was placed outside the operating room and the patients got into the operating room under sensorial anesthesia for using time efficiently. The duration of surgery was similar between the 2 groups. There was no recovery time in EA unlike GA. With these advantages, the time spent in the operating room in EA group was significantly lower than that in GA group (Table 2). Since effective use of time in operating room is important, especially in clinics with excess surgical workload, EA can be superior to GA in this regard.

GA is prone to complicate in terms of vascular, pulmonary and neurological issues, especially during changing patient's position from lithotomy to prone (21). In our EA technique, we used a low concentration of local anesthetics with opioids and obtained sensorial and sympathetic block without any motor block. Thus, all the patients in EA group got the prone position

themselves and were protected from the risk of complications during the position change under GA.

Some patients (2 women and 8 men) complained of slight pain during the passage of cystoscope through the bladder neck which is innervated more caudally. As known, epidural space widens caudally and the nerves are thicker and obtaining sensorial block is harder at that level. The efficiency of EA in that level also depends on the diffusion time of the anesthetic agent. The pain in these patients was probably due to the fact that the anesthetic agent did not reach to sacral segments or delayed. In these circumstances, operation can be continued by additional drug administration through epidural catheter or intravenous sedation with the mixture of fentanyl and diazepam.

To create percutaneous renal access and to continue PNL operation under EA are not different from that under GA, at least in our clinic. We did not experience any problem during the access formation under EA even in the upper pole, except in one patient. Thus, the number of upper pole access in EA group was similar to that in GA group (Table 2). PNL operation was continued after additional drug administration in that patient.

Another advantage of EA over GA is that you can cooperate with the patient during the surgery. Respiratory maneuvers necessary for avoiding pleural injury could be done more rapidly and easily.

Hypotension can be observed in PNL under EA because of sympathetic blockage. Nausea and vomiting are usually caused by hypotension. We observed hypotension and nausea-vomiting in 10.1% and 4.3% of patients, respectively. In these situations, sympathomimetics, antiemetics and volume expanders were used for treatment. Preoperative adequate hydration is more important in this aspect.

Although the mean hemoglobin drop was similar between the groups, the patients in EA group required significantly fewer blood transfusions (Table 2). Our criteria for blood transfusion were not only hemoglobin drop but also ongoing hematuria and/or hemodynamic instability. Although we could not show the main reason in the content of the literature, the significant difference in blood transfusion rates between the groups may be due to blood transfusion in patients with ongoing hematuria and/or hemodynamic instability.

Patient controlled analgesia through the epidural catheter provides postoperative pain control very well and minimize pulmonary and thromboembolic complications associated with postoperative pain-related mobilization restriction. It also protects patients from unnecessary analgesic injections and its possible complications, such as abscess, cellulitis and phlebitis. Thus, patients in EA group were not exposed to any parenteral analgesic injection, while patients in GA group were exposed to significantly more parenteral injection in our study (Table 2).

EA did not prolong operative time and did not reduce success rate in PNL. It did not shorten length of hospitalization, but kept the patients more comfortably in that period.

Study Limitations

The limitations of this study are lack of perioperative and postoperative blood pressure variegation measurements and visual analog scale scores and its retrospective nature.

Our study is perhaps the first study in the literature which compares the surgical parameters, stone clearance and postoperative analgesic requirements following PNL under EA without motor block and under GA. However, further prospective randomised controlled studies are needed.

Conclusion

PNL under EA without motor block is equally effective and safe compared to PNL under GA. The advantages of EA over GA are less usage of operating room, self-positioning of patients from the lithotomy to the prone position, less early postoperative pain and less parenteral analgesic use without changing operative parameters and success rate.

Ethics

Ethics Committee Approval: This retrospectively designed study was approved by Local Ethics Committee of University of Health Sciences Bursa Yüksek İhtisas Training and Research Hospital (approval number: 2011-KAEK-25 2016/09-07).

Informed Consent: Because of its retrospective nature, no written informed consent was obtained from the patients.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: S.Ö., B.A., M.K., Concept: S.Ö., B.A., Design: S.Ö., B.A., Data Collection or Processing: S.Ö., E.Ö., A.E.Y., Analysis or Interpretation: B.A., Literature Search: M.M.A., M.D., Writing: S.Ö., E.Ö., B.A.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

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Hospital Readmissions Due to Subcapsular Renal Hematoma After Flexible and Rigid Ureterorenoscopy

Fleksibl ve Rijid Üreterorenoskopi Sonrası Görülen Subkapsüler Hematom Nedeniyle Hastaneye Yatışların Karşılaştırılması

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What's known on the subject? and What does the study add?

The literature regarding subcapsular hematoma after ureterorenoscopy is scarce. To our knowledge, this is the first study that compares flexible vs rigid ureterorenoscopy techniques. Our results indicate hospitalization rates due to subcapsular hematoma after ureterorenoscopy is statistically not different between two groups.

Abstract

Objective: The aim of this study is to compare the rates of hospitalization due to subcapsular renal hematoma (SRH) following flexible ureterorenoscopy (FURS) and semirigid ureterorenoscopy (RURS) for the treatment of ureteral and renal stones.

Materials and Methods: Patients who have been treated with FURS and RURS at two different institutions between March 2009 and February 2014 were enrolled in the study. Patient files and hospital records were reviewed. Pneumatic lithotripter was used in RURS while holmium:yttrium aluminium garnet laser was used for FURS. Subcapsular hematoma diagnosis was based on clinical and radiological findings. Comparative analysis of patients with SRH in terms of age, sex, stone size/position, degree of preoperative hydronephrosis, duration of surgery and size of hematoma was done.

Results: A total of 1187 patients were found to have undergone ureteroscopic intervention due to ureteral or renal stones. RURS was performed in 992 (83.6%) patients and FURS was performed in 195 patients (16.4%). Of the 992 patients who underwent RURS, postoperative SRH occurred in 6 patients (0.6%). Postoperative SRH occurred in 3 patients (1.5%) who underwent FURS. Of the 9 patients who developed SRH, blood transfusions were needed in three patients and one patient was treated with percutaneous drainage catheter insertion. No patient underwent open surgery. There was no statistically significant difference between the two types of surgeries with regard to age, stone size/localization, degree of preoperative hydronephrosis, duration of surgery and size of SRH ($p>0.05$).

Conclusion: SRH is a rare complication following RURS and FURS. There is no statistically significant difference in the risk for this specific complication between FURS and RURS.

Keywords: Subcapsular hematoma, Ureterorenoscopy, Complication, Rigid, Flexible

Öz

Amaç: Bu çalışmanın amacı üreter ve böbrek taşlarının endoskopik tedavisinde fleksibl ve rijid üreterorenoskopi sonrası ortaya çıkan subkapsüler hematom olgularının hastaneye yatışlarını karşılaştırmaktır.

Gereç ve Yöntem: İki farklı hastanede Mart 2009 ve Şubat 2014 yılları arasında yapılmış olan fleksibl ve rijid üreterorenoskopi olguları retrospektif olarak tarandı. Hasta dosyaları ve hastane kayıtları incelendi. Rijid üreterorenoskopi için pnömotik, fleksibl üreterorenoskopi için holmium lazer kullanıldı. Subkapsüler hematom tanısı klinik ve radyolojik olarak konuldu. Hastalar iki grup için de yaş, cinsiyet, taş boyutu ve yeri, işlem öncesi hidronefroz derecesi, operasyon süresi ve hematom boyutu açısından karşılaştırıldı.

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Received: 21.03.2018 **Accepted:** 01.06.2018

Cite this article as: Taken K, Güneş M, Ergün M, Dönmez Mİ. Hospital Readmissions Due to Subcapsular Renal Hematoma After Flexible and Rigid Ureterorenoscopy. J Urol Surg 2018;5(3):149-153.

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Bulgular: Toplamda 1187 hastanın üreterorenoskopik girişim geçirmiş olduğu bulundu. Rijid üreterorenoskopi 992 hastaya (%83,6), fleksibl üreterorenoskopi ise 195 hastaya (%16,6) uygulandı. Rijid üreterorenoskopi grubunda 6 (%0,6), fleksibl üreterorenoskopi grubunda ise 3 hastada (%1,5) işlem sonrası subkapsüler renal hematoma geliştiği saptandı. Bu 9 hastanın üçünde kan transfüzyonu gerekirken, birinde de perkütan drenaj kateteri yerleştirilmesi gerekliliği oldu. Hiçbir hastada açık cerrahi gerekmedi. İki hasta grubunda belirtilen parametreler açısından hiçbir fark bulunamadı ($p>0,05$).

Sonuç: Rijid ve fleksibl üreterorenoskopi sonrası görülebilen subkapsüler hematoma nadir bir komplikasyondur. Bu komplikasyonun gelişme riski fleksibl ve rijid üreterorenoskopi gruplarında benzerdir.

Anahtar Kelimeler: Subkapsüler hematoma, Üreterorenoskopi, Komplikasyon, Rijid, Fleksibl

Introduction

Ureteroscopic lithotripsy is a highly effective and minimally invasive procedure in the treatment of ureteric and renal stones (1). The increased benefit, efficacy, and success due to ureteroscopy and intra-corporal lithotripsy over time have been credited to the development of efficient and flexible ureteroscopes, laser lithotripters, and various other accessories. Flexible ureterorenoscopy (FURS) and laser lithotripsy has become increasingly popular in the treatment of large renal stones because of decreased morbidity rates and hospital stay, coupled with high stone-free rates that are similar to percutaneous nephrolithotomy (PCNL) (2,3).

Subcapsular renal hematoma (SRH) is a rare complication that may follow urologic procedures such as shock wave lithotripsy, ureterorenoscopy, and PCNL (4,5,6). The objective of this study was to compare hospitalization due to SRH following FURS and semirigid ureterorenoscopy (RURS) in the treatment of ureteral and renal stones.

Materials and Methods

Patients who were treated with FURS and RURS at two institutions between March 2009 and February 2014 were enrolled in the study. Patient files and hospital records were retrospectively reviewed after approval of the Yüzüncü Yıl University Ethics Committee (approval number: 2015-00/122), and provided written informed consent.

The endoscopic procedures were performed by one of 4 urologists using general anesthesia with the patients in the lithotomy position. A pneumatic lithotripter was used in RURS and a holmium:yttrium aluminium garnet (Ho:YAG) laser was used for FURS. The diagnosis of ureteric and renal stones was made using intravenous pyelography or computed tomography (CT). For ureteroscopy, an 8.5/9.5 Fr semirigid ureteroscope (Richard Wolf GmbH, Knittlinger, Germany) and a 6/8.8 Fr flexible ureteroscope (Richard Wolf GmbH, Knittlinger, Germany) were used. For lithotripsy, a pneumatic lithotripsy device (Elmed-Vibrolith, Ankara, Türkiye), and a Ho:YAG laser (Richard Wolf GmbH, Knittlinger, Germany) with 270 and 365 μ laser fibers were used. A safety guide wire was inserted for guidance of the

rigid ureteroscope without dilating the ureteric orifice under fluoroscopy. For FURS, a 12 Fr ureteral access sheath was used in all patients. Continuous irrigation was supplied from 1 meter above the level of the patient to obtain and sustain a clear operative visual field during all procedures. Moreover, manual hand pumps were used when continuous irrigation became insufficient. For laser lithotripsy, the laser energy was applied at 0.8–1.5 J with a pulse rate of 5–10 Hz. The pneumatic lithotripter was used at 4–10 bar pressure with a pulse rate of 4–10 Hz. Stone fragmentation was completed when a particle size of 2–3 mm was achieved. No effort was made to extract or remove stone fragments. After the procedure, an indwelling 4.7 Fr 26 cm JJ stent was placed and left *in situ* for 3 weeks when necessary. Kidney, ureter, and bladder imaging and ultrasonography were used during follow-up.

SRH was suspected in patients with side pain, fever, or hematuria following procedures and those patients were immediately evaluated by CT. Upon diagnosis of SRH, all patients were admitted to hospital. Appropriate analgesic and antibiotic therapies were initiated. A comparative analysis was conducted in patients with SRH in terms of age, sex, stone size/position, degree of preoperative hydronephrosis, duration of surgery, and size of hematoma.

Statistical Analysis

All data were analyzed using Statistical Package for the Social Sciences version 13.0 (SPSS Inc., Chicago, United States of America). Descriptive statistics for the continuous variables were presented as mean \pm standard deviation, and minimum and maximum values. The categorical variables were represented as absolute numbers and percentages. The Mann-Whitney U test was used to compare RURS and FURS groups. In addition, Z-test and Fisher's exact test were performed to determine the differences between the two proportions. A p value of >0.05 was considered significant.

Results

A total of 1187 patients were found to have undergone ureteroscopic intervention due to ureteral or renal stones. The patients comprised 804 (67.7%) men and 383 (32.3%) women with a mean age of 39 ± 20.8 years (range, 20–79 years). RURS

was performed in 992 (83.6%) patients and FURS was performed in 195 (16.4%). All patients with SRH presented with severe ipsilateral flank pain accompanied by other symptoms such as gross hematuria, fever, and abdominal pain. The patients were hospitalized for a week, antibiotherapy and analgesics were administered, and a complete blood count and follow-up was performed. Table 1 presents the clinical features and outcomes of the 9 patients who presented with SRH after ureteroscopy.

Of the 992 patients, who underwent RURS, 6 patients (5 males and 1 female) with a mean age of 36.3 years (range, 20-67 years) were hospitalized because of postoperative SRH (0.6%). The mean stone size was 1.58 cm (range, 0.7-3.1 cm). The stones were in the proximal (n=2), mid (n=2), and distal ureter (n=1), and 1 was in the renal pelvis of the kidney. Preoperative ultrasonography revealed mild hydronephrosis in one patient, and three and two patients presented with moderate and severe hydronephrosis, respectively. In the SRH group, two patients required manual pump irrigation and another two had a postoperative JJ stent inserted.

Among the 195 patients who underwent FURS, 3 patients (1.5%) (3 men, 1 woman) with a mean age of 46.6 years (range, 24-79 years) were hospitalized after developing SRH. The mean stone size was 1.46 cm (range, 0.8-2.5 cm). The stone was located in the proximal ureter in one patient, whereas the remaining two patients had lower caliceal stones. One of the patients presented with mild hydronephrosis; the other two had moderate hydronephrosis. Also, one patient had a JJ stent postoperatively and another was on anti-platelet therapy. Table 2 presents the comparative results of SRH for surgery types according to stone localizations. There was no statistically significant difference in length of hospital stay between patients undergoing FURS

or RURS who developed SRH and those without SRH ($p>0.05$). Table 3 presents the descriptive statistics and comparative results for surgery types. There was no statistically significant difference between the two types of surgery with regards to age, stone size/localization, degree of preoperative hydronephrosis, duration of surgery, and size of SRH ($p>0.05$).

Blood transfusion was needed in 3 patients, two of whom were in the RURS group. Only a woman aged 24 years, who presented with fever (38.5 °C) and a 9.5 cm SRH after RURS, needed percutaneous drainage. She was discharged after 1 week of close follow-up. No patient underwent open surgery or angioembolization because of SRH.

Discussion

The causes of SRH include renal trauma, tumors, vascular diseases, infections, renal cystic diseases, and bleeding disorders (7,8,9). An incidence of lower than 0.4% has been reported

Table 2. Comparative results of subcapsular renal hematoma for surgery types according to stone locations

Stone localization	RURS	SRH	FURS	SRH	p value*
Kidney	25	1	91	2	0.521
Proximal ureter	183	2	99	1	0.948
Middle ureter	245	2	4	0	0.156
Distal ureter	539	1	1	0	---
Total	992	6	195	3	0.172

RURS: Semirigid ureterorenoscopy, FURS: Flexible ureterorenoscopy, SRH: Subcapsular renal hematoma
* $p<0.05$

Table 1. Clinical features and outcomes of the 9 patients with subcapsular renal hematoma

	Age/sex	Procedure	Stone location	Stone size (mm)	Degree of preoperative hydronephrosis	Duration of operation (mins)	Size of hematoma (cm)	Treatment
1	45/m	RURS	Right, kidney	18	Moderate	80	5	Conservative
2	67/m	RURS	Left, proximal	7	Moderate	40	3	Conservative
3	23/m	RURS	Left, proximal	17	Severe	80	7	Blood transfusion
4	39/m	RURS	Right, middle	31	Severe	70	5	Conservative
5	20/f	RURS	Left, middle	12	Mild	30	4	Conservative
6	24/m	RURS	Left, distal	10	Moderate	40	9.5	Blood transfusion and drainage
7	24/f	FURS	Right, kidney	11	Mild	48	3.5	Conservative
8	79/m	FURS	Left, kidney	25	Moderate	60	4	Blood transfusion
9	37/m	FURS	Right, proximal	8	Moderate	35	3.5	Conservative

RURS: Semirigid ureterorenoscopy, FURS: Flexible ureterorenoscopy, m: male, f: female

Table 3. Descriptive statistics and comparative results for surgery types

		n	Mean	p value*
Age	RURS	6	36.33	0.521
	FURS	3	46.67 (24-79)	
	Total	9	39.78 (20-79)	
Stone size	RURS	6	15.83 (7-31)	0.855
	FURS	3	14.67 (8-25)	
	Total	9	15.44 (7-31)	
Duration of surgery	RURS	6	56.67 (30-80)	0.548
	FURS	3	47.67 (35-60)	
	Total	9	53.67 (30-80)	
Size of hematoma	RURS	6	5.58 (3-10)	0.213
	FURS	3	3.67 (3.5-5)	
	Total	9	4.94 (3-10)	

RURS: Semirigid ureterorenoscopy, FURS: Flexible ureterorenoscopy
*p<0.05

following ureterorenoscopy (5,8,10). Different mechanisms have been suggested for the development of SRH following ureteroscopy, including guide wire manipulation; fornix rupture secondary to high irrigation pressure; postoperative double-j stent placement; increased intrapelvic pressure in hydronephrotic kidneys, which results in tension, kinking and/or obstruction in the main vascular structures; recanalization of ureters following ureteroscopy; and sudden expansion and rupture of the compressed parenchyma.

Previous authors have defined the risk factors as stone size, hydronephrosis degree, surgery duration, and irrigation fluid pressure (4,5,10). Precautions such as using low pressure irrigation during procedures are advised. These precautions may include ceasing fluid flow or ureteroscope removal, and placing a 8-10 Fr urethral catheter into the bladder during surgery in cases that are predicted to take a long time (7,10). In a study by

Rehman et al. (11), it was demonstrated that use of a 12/14 Fr access sheath could keep intrarenal pressure below 20 mmHg during maximum irrigation flow. In our series, preoperative hydronephrosis, JJ stent placement, exposure to high intrapelvic pressure, and aspirin intake were factors that facilitated SRH. However, it is impossible to make a conclusion about the exact etiologic factors because there were too few patients in the study group.

The most common symptoms in patients with SRH include side pain, fever, hematuria, palpable mass, and bloodloss-related symptoms (5,9). All of our patients had side pain and fever. The time interval between the initial surgery and the corrective operation varied between 3 and 7 days, which has been reported to be between the 10th hour and 20th day in the literature (10). Interestingly, with the exception of one patient, who presented with side pain and fever on the 20th day, the mean time between surgery and the time of re-admittance in our study was 5.4 days.

Historically, Kendall et al. (12) proposed radical nephrectomy as a treatment when there is no apparent etiology and the contralateral kidney appears normal after careful pathologic examination, because of the high incidence of small renal tumors. Currently, it has been reported that operative exploration was not necessary in most unexplained cases because of the diagnostic accuracy of CT (13,14,15). Chiu et al. (10) reported post-ureteroscopy SRH in 4 (0.36%) out of 1114 patients. In their report, they documented that one patient underwent urgent angiography after a significant drop in the hemoglobin level, but no embolization was needed. Another patient underwent ultrasonography-guided drainage of the hematoma, and one had an emergency open clot evacuation because of significant compression on the kidney by the hematoma (10). Meng et al. (9) diagnosed 8 (0.4%) of 1918 patients as having SRH after ureteroscopy. They managed five patients with small and uninfected hemorrhage conservatively, but reported that three patients with infective and large hemorrhage were managed using percutaneous nephrostomy (n=1) and percutaneous subcapsular drainage (n=2). Super-selective renal arterial embolization has also been reported in the literature for the treatment of SRH after flexible ureteroscopic laser lithotripsy (16).

All patients who present with symptomatic SRH should be hospitalized. The first-line treatment in patients with SRH should be conservative. This approach includes antibiotic treatment, pain control, and close follow-up of hemoglobin levels. Initial creatinine levels should also be monitored. In cases of hemodynamic deterioration, open surgery or percutaneous drainage of the hematoma are recommended rather than conservative treatment (6,10,11). None of our patients required open surgical interventions or arterial embolization, but percutaneous drainage was performed in one patient because

of a huge hematoma that was infected. Blood transfusion was needed in three patients. No residual hematoma was detected on CT scans at the 6th month follow-up checks.

Study Limitations

There have been few studies to date that directly reported comparative analyses and outcomes of patients hospitalized with SRH after ureteroscopy. Our study was limited because of its retrospective nature and relatively small number of patients with SRH. Therefore, the statistical comparisons may be insufficient. However, our study showed that the risk of hospitalization because of SRH following RURS and FURS was comparable and low.

Conclusion

SRH is a rare complication that may follow ureterorenoscopy. It should be suspected in patients who present with symptoms of side pain, fever, or hematuria following ureterorenoscopic stone treatment. The risk of hospitalization for this specific complication was statistically same in the FURS and RURS groups.

Ethics

Ethics Committee Approval: This study was approved by the Yüzüncü Yıl University Ethics Committee (approval number: 2015-00/122).

Informed Consent: Consent form was filled out by all participants.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: K.T., M.G., M.E., Concept: K.T., M.G., Design: K.T., M.İ.D., Data Collection or Processing: K.T., M.G., M.E., Analysis or Interpretation: K.T., M.İ.D., Literature Search: K.T., M.İ.D., Writing: K.T.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

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Previous Open Stone Surgery: Is It a Risk Factor for Bleeding in Percutaneous Nephrolithotomy

Perkütan Nefrolitotomide Kanama: Daha Önce Açık Taş Cerrahisi Geçirmiş Olmak Bir Risk mi?

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What's known on the subject? and What does the study add?

Although there are many reports examining the effects of previous open stone surgery on percutaneous nephrolithotomy, its possible effects on bleeding in percutaneous nephrolithotomy is still controversial in the literature.

Abstract

Objective: The aim of this study is to determine whether previous open stone surgery is a risk factor for bleeding in patients undergoing percutaneous nephrolithotomy (PNL).

Materials and Methods: Data of patients who underwent PNL in our clinic between 2007 and 2015 were reviewed retrospectively. Eighty-two patients underwent PNL and had a history of previous ipsilateral open surgery. A control group was created with 82 patients randomly selected among PNL patients with no history of open surgery. The groups were evaluated in terms of preoperative demographic data, operative success and complications, especially hemorrhage requiring transfusion.

Results: The groups were similar in terms of demographic data and stone burden. One patient of each group was administered intraoperative blood transfusion. There was no statistically significant difference between the two groups in terms of postoperative blood transfusion ($p=0.245$).

Conclusion: In our study, it can be said that previous open stone surgery does not increase potential complication of bleeding in PNL.

Keywords: Percutaneous nephrolithotomy, Open stone surgery, Bleeding

Öz

Amaç: Bu çalışmanın amacı perkütan nefrolitotomi (PNL) yapılan hastalarda daha önce açık taş cerrahisi geçirmenin kanama için bir risk faktörü olup olmadığını belirlemektir.

Gereç ve Yöntem: 2007-2015 yılları arasında kliniğimizde PNL yapılan hastaların verileri geriye dönük olarak incelendi. PNL yapılan ve aynı taraftan daha önce açık operasyon öyküsü olan 82 hasta mevcuttu. PNL yapıp, açık operasyon öyküsü olmayan hastalardan randomize olarak 82 hasta seçildi ve kontrol grubu oluşturuldu. Preoperatif demografik veriler, operasyon başarısı ve özellikle transfüzyon gerektiren kanama ve diğer komplikasyonlar açısından gruplar değerlendirildi.

Bulgular: Gruplar demografik veriler ve taş yükü açısından birbirine benzerdi. Her iki grupta birer hastaya intraoperatif kan transfüzyonu yapıldı. Postoperatif kan transfüzyonu açısından gruplar arasında istatistiksel olarak fark saptanmadı ($p=0,245$).

Sonuç: Çalışmamızda daha önce açık taş cerrahisi geçirmiş olmanın PNL'de kanama komplikasyonu ihtimalini artırmadığından bahsedilebilir.

Anahtar Kelimeler: Perkütan nefrolitotomi, Açık taş operasyonu, Kanama

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Received: 02.06.2018 **Accepted:** 26.06.2018

Cite this article as: Süelözgen T, İlbey YÖ. Previous Open Stone Surgery: Is It a Risk Factor for Bleeding in Percutaneous Nephrolithotomy? J Urol Surg 2018;5(3):154-157.

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Introduction

Percutaneous nephrolithotomy (PNL) is a minimally invasive surgical procedure considered the first choice in the treatment of kidney stones larger than 2 cm (1). Despite appropriate surgical and medical treatment, stone disease can recur in about half of the cases within 5-7 years (2). In this situation, PNL may be required in patients who underwent open stone removal in the past. Perinephric scar tissue, calyceal scarring, and distortion due to the previous surgery have been reported to affect subsequent interventions (3). Although there are many reports examining the effects of previous open stone surgery on PNL, its possible effects on bleeding in PNL is still controversial in the literature. In our study, we examined if previous open stone surgery would increase the risk of bleeding in PNL or not.

Materials and Methods

The patients included in the study were retrospectively evaluated and divided into two groups and written informed consent was obtained from all patients. Eighty-two patients, who underwent PNL and had previous ipsilateral open stone surgery between 2007 and 2015, were included in group 1. Data on age, gender, duration of operation, duration of fluoroscopy, and bleeding requiring intraoperative transfusion were noted. Postoperative complications were also noted. For the control group, group 2, 82 patients were randomly selected from PNL patients who did not have open stone surgery before. All patients were evaluated with non-contrast computed tomography (CT) preoperatively. PNL was decided with respect to stone size or after unsuccessful extracorporeal shockwave lithotripsy. The number of open stone surgeries the patients underwent could not be obtained accurately from the records due to the retrospective design of our study.

Isolated renal pelvis or isolated calyx stones were classified as simple stones; pelvis and calyx stones or staghorn stones as complex stones. Patients with positive bacterial culture were treated with appropriate antibiotics. All patients underwent operation when their urine cultures were sterile.

Procedurally, the patients were placed in the lithotomy position under general anesthesia. Using a 26 F cystoscope, a 6 F ureteral catheter was inserted. The patient was then turned to the prone position and contrast medium was administered through the urethral catheter. An 18 G access needle was introduced into the collecting system through the selected calyx under fluoroscopy. A guide wire was introduced after clear urine flow was observed. Following 6 F dilation with Amplatz dilator, tract was created in accordance with the single step technique using 25-30 F dilator. We had no patients in whom access failed. The stones were fragmented using a 27 F nephroscope and an ultrasonic

lithotripter. A 14 F Malecot catheter was placed postoperatively in all patients. In patients without complications, the Malecot catheter was removed on postoperative day 1-3. All patients were re-evaluated with non-contrast tomography after postoperative month 1. Detecting no stones or some small stone fragments ≤ 4 mm was recognized as success.

Statistical Analysis

Summary statistics were used for continuous variables (mean, standard deviation, standard error). Associations between categorical variables were analysed using χ^2 test. When the expected number of observations in one or more categories was ≤ 5 , we used the Fisher's exact test. The independent-samples t-test and the Mann-Whitney U test were used to compare differences between two independent groups. Data were analyzed using SPSS version 15.0 software (SPSS Inc., Chicago, United States of America). A p value of less than 0.05 was considered statistically significant.

Results

Of the 82 patients in group 1, 47 (57.3%) were male and 35 (42.7%) were female, with a mean age of 48.2 ± 14.0 years. The mean operative time was 102 ± 266 minutes and the mean duration of fluoroscopy was 230 ± 294 seconds. Forty-two patients had simple stones (51.2%) while 40 (48.8%) had complex stones.

In group 2, 46 (56.1%) of 82 patients were male and 36 (43.9%) were female, with a mean age of 44.05 ± 17 years. The mean duration of operation was 134 ± 44 minutes and the mean duration of fluoroscopy was 194 ± 44 seconds. In group 2, 43 (52.4%) patients had simple and 39 (47.6%) patients had complex stones. There was no statistically significant difference between the groups in terms of the above mentioned variables (Table 1).

Table 1. Significant demographic data

	Group 1 (n=82)	Group 2 (n=82)	p value
Mean age (\pm SD)	48.24 \pm 14	44 \pm 17	0.96
Gender (%)			0.87
Male	47 (57.3%)	46 (56.1%)	
Female	35 (42.7%)	36 (43.9%)	
Operation site (%)			0.92
Right	54 (65.9%)	42 (51.2%)	
Left	28 (34.1%)	40 (48.8%)	
Stone burden (%)			0.92
Simple	42 (51.2%)	43 (52.4%)	
Complex	40 (48.8%)	39 (47.6%)	

SD: Standard deviation

Table 2. Intraoperative data and postoperative complications

	Group 1 (n=82)	Group 2 (n=82)	p value
Operation time (min)	102	134	0.17
Fluoroscopy time (sec)	230	194	0.36
Multiple access (%)	5 (6.1)	12 (14.6)	0.12
Intraoperative blood transfusion (%)	1 (1.2)	1 (1.2)	1
Postoperative blood transfusion (%)	3 (3.6)	0	0.24
Postoperative fever (%)	5 (6.1)	12 (14.6)	0.12
Operation success (%)	66 (79.2)	70 (85.3)	0.4
Additional intervention (DJS) (%)	2 (2.4)	0	0.24

DJS: Double J stent

Double access was required in 5 (6.1%) patients of group 1 and in 12 (14.6%) patients of group 2 (p=0.122).

Intraoperative blood transfusion was performed for one patient of each group.

Blood transfusion was performed due to postoperative hemodynamic instability in 3 patients (3.7%) of group 1. None of the patients required transfusion in the control group and there was no statistically significant difference between the groups (p=0.245). Postoperative fever was observed in 5 (6.1%) patients of group 1 and in 12 (12.6%) patients of the control group. There was no difference between the groups in terms of postoperative fever (p=0.122).

Double J stent was implanted in 2 patients (2.4%) in group 1 due to prolonged wound drainage. The stents were removed one month after the operation. There was no need for additional surgical intervention in any patients.

Residual stones were observed in 17 (20.7%) patients of group 1 and in 12 (14.6%) patients of group 2 on CT performed on postoperative 1st month. There was no significant difference between the groups in terms of operative success (Table 2).

Discussion

PNL is the first choice surgical method to be used in the treatment of kidney stones ≥ 2 cm in size, but complications are observed in almost one fourth of patients (23.3%) despite developing technology and increasing experience. Post-PNL bleeding is a very common complication. Although bleeding is treated with conservative methods in most of the cases, bleeding requiring transfusion is considered a complication and has been reported at different rates (1%-55%) in the literature (4). Many factors predicting bleeding in PNL were examined

in studies. Stone size, presence of staghorn stones, prolonged operative time and a need for multiple accesses are known to increase bleeding complication requiring post-PNL transfusion (4,5). It is controversial whether previous ipsilateral open stone surgery is a risk factor for bleeding complication requiring transfusion or not. It has been reported that retroperitoneal scar tissue and pelvicalyceal structures with scars may complicate all operational stages from access to fragmentation, especially maneuvering with the nephroscope (6).

In their study comparing 65 patients with previous nephrolithotomy and 117 patients without any history of renal surgery, Basiri et al. (7) observed no difference in terms of complications including bleeding. Said et al. (8), however, stated that previous open surgery can be an important determinant for hemorrhage and transfusion requirement in PNL. Yesil et al. (9) reported that severe hemorrhages requiring angioembolization were frequent in their 42 patients who underwent open renal surgery. Sofikerim et al. (10) determined that the incidence of bleeding requiring transfusion was nearly twice as high in the group with open surgery, suggesting that this was a predisposing factor for bleeding complication.

In our study, blood transfusion was performed in one patient in group 1 and one patient in group 2 (p=1). Postoperatively, three patients (3.6%) of group 1 had bleeding requiring transfusion while no transfusion was required in the control group. However, the results were not found to be statistically significant (p=0.12). There was no problem, such as pseudoaneurysm or arteriovenous fistula, in our patients who required angioembolization. Interestingly, there are also some reports indicating that previous open renal stone surgery reduced blood loss during PNL (11).

PNL success was stated to decrease in patients with previous open stone surgery in some studies (12). In our study, stone-free rates were 79.2% in the group with previous operation and 85.3% in the control group, and there was no statistically significant difference in success rate between the groups. Our success rates are consistent with the literature.

Study Limitations

The retrospective design, the fact that different surgeons performed the operations and relatively limited number of patients can be mentioned as the major limitations of our study.

Conclusion

Despite limited number of patients in the study, it is possible to state that previous open renal stone surgery is not a risk factor for bleeding complication requiring transfusion in PNL. However, further studies with larger patient groups are needed in order to reach definite conclusion on this issue.

Ethics

Ethics Committee Approval: Retrospective study.

Informed Consent: It was taken.

Peer-review: Externally peer-reviewed.

Authorship Contributions

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

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

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Comparison of Efficacy and Complications of Holmium Laser and Pneumatic Lithotripters Used in the Ureterorenoscopic Treatment of Proximal Ureter Stones, a Multi-Center Study of Society of Urological Surgery Aegean Study Group

Proksimal Üreter Taşlarının Üreterorenoskopi ile Tedavisinde Kullanılan Holmiyum Lazer ve Pnömatik Litotriptörlerin Etkinlik ve Komplikasyonlarının Karşılaştırılması, Ürolojik Cerrahi Derneği Ege Çalışma Grubu'nun Çok Merkezli Bir Çalışması

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What's known on the subject? and What does the study add?

Türkiye is an endemic region for urinary system stone disease and the incidence rate is 14.8%. Currently, ureterorenoscopy, where laser and pneumatic energy sources are used as lithotripter, is the first choice in the treatment of ureteral stones. The aim of this multi-centered study was to compare the efficacy of holmium laser and pneumatic lithotripters used in the ureterorenoscopic treatment of proximal ureteral stones and investigate their complications.

Abstract

Objective: The aim of this study is to compare the efficacy and complications of holmium laser and pneumatic lithotripsy used in the ureterorenoscopic treatment of proximal ureteral stones.

Materials and Methods: Data of 638 patients, who underwent ureterorenoscopy (URS) due to proximal ureteral stones in different centers, were obtained from patient files. The patients were divided into two groups according to the type of lithotripter used: group 1; laser lithotripter (n=324; 50.8%) and group 2; pneumatic lithotripter (n=314; 49.2%). URS was considered successful upon determination stone-free status with the imaging methods after treatment. The effectiveness and the complications of holmium:yttrium-aluminum-garnet laser and pneumatic lithotripsy were compared.

Results: The total success rate of URS was 82.6% and the complication rate was 8.1%. The mean age of patients was similar between the groups; however, the body mass index values, stone surface area and stone Hounsfield unit were significantly higher in group 1. Although the mean operative time, complication rate and the mean length of hospital stay were similar between the groups; the URS success and postoperative ureteral

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Received: 19.06.2018 **Accepted:** 27.06.2018

Cite this article as: İrer B, Şen V, Erbatu O, Yıldız A, Ongün Ş, Çınar Ö, Cihan A, Şahin M, Şahin MO, Üçer O, Kızılay F, Bozkurt O. Comparison of Efficacy and Complications of Holmium Laser and Pneumatic Lithotripters Used in the Ureterorenoscopic Treatment of Proximal Ureter Stones, a Multi-Center Study of Society of Urological Surgery Aegean Study Group. J Urol Surg 2018;5(3):158-163.

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J stent use rates were significantly higher in group 1 and the push-back rate was significantly higher in group 2.

Conclusion: If laser lithotripsy is available in a clinic, we believe that it is better to use it as the first option in the treatment of proximal ureter stones. However, considering that it is not easy to access laser lithotripters due to their high cost in Turkey, pneumatic lithotripters may be an effective and inexpensive alternative that can also be safely used in these cases.

Keywords: Complication, Laser lithotripter, Pneumatic lithotripter, Proximal ureter stone, Ureter stone

Öz

Amaç: Bu çalışmanın amacı proksimal üreter taşlarının üreterorenoskopi (URS) ile tedavisinde kullanılan holmiyum lazer ve pnömatik litotriptörlerin etkinlik ve komplikasyonlarını karşılaştırmaktır.

Gereç ve Yöntem: Proksimal üreter taşı nedeni ile farklı referans merkezlerde URS yapılan toplamda 638 hastanın verileri retrospektif olarak tarandı. Hastalar kullanılan litotriptör türüne göre 2 gruba ayrıldı: Grup 1; lazer litotriptör (n=324; %50,8) ve grup 2; pnömatik litotriptör (n=314; %49,2). URS başarısı, tedavi sonrası yapılan görüntüleme tetkiklerinde taşsızlık saptanması olarak alındı. Holmium:yttrium-aluminum-garnet lazer ve pnömatik litotriptörlerin başarı ve komplikasyon oranları karşılaştırıldı.

Bulgular: Toplamda URS başarısı %82,6 ve genel komplikasyon oranı ise %8,1 idi. Lazer litotriptör kullanılan hastalarla pnömatik litotriptör kullanılan hastalar demografik veriler ve taş özelliklerine göre karşılaştırıldıklarında; her iki grubun yaş ortalamaları benzerdi ancak hastaların vücut kitle indeks değerleri, taş alanı ve Hounsfield ünitesi değerleri grup 1'de anlamlı olarak yüksek saptandı. Grup 1 hastalarında şok dalgasıyla böbrek taşı kırılma öyküsü olanlar anlamlı olarak daha fazla saptandı. Her iki grup operasyon sonuçlarına göre ve komplikasyon oranlarına göre karşılaştırıldığında; operasyon süresi, komplikasyon oranları ve hastanede yatış süreleri açısından benzer olarak saptansa da URS başarısı ve postop üreteral J stent kullanımı grup 1'de anlamlı olarak yüksek; push back oranları ise grup 2'de anlamlı olarak yüksek saptandı. Her iki gruptaki komplikasyonlar Clavien-Dindo sınıflamasına göre karşılaştırıldığında anlamlı bir fark saptanmadı.

Sonuç: Eğer kliniklerde lazer litotripsisi mevcutsa, proksimal üreter taşları tedavisinde ilk seçenek litotriptör olarak kullanılmasının daha uygun olacağı kanısındayız. Ancak ülkemizde yüksek maliyetleri nedeni ile lazer litotriptörlere ulaşımın çok da kolay olmadığını düşünürsek; etkin ve ucuz bir yöntem olan pnömatik litotriptörler de güvenle bu olgularda kullanılabilir.

Anahtar Kelimeler: Komplikasyon, Lazer litotripsisi, Pnömatik litotripsisi, Proksimal üreter taşı, Üreter taşı

Introduction

The prevalence of urinary system stone disease has been reported to be 4-20% in economically developed countries (1,2). The incidence of stone disease varies according to geographical, climatic, ethnic, racial, dietary and genetic factors (3,4). In Turkey, it is an endemic disease with a rate of 14.8% (5).

Methods that can be used in the treatment of ureteral stones include conservative treatment-monitoring, medical expulsive therapy, extra-corporal shock wave lithotripsy (ESWL), and ureterorenoscopy (URS). If there is no indication for active stone removal, the first treatment option is either conservative monitoring or medical expulsive treatment. According to the European Association of Urology guidelines, if there is an indication for active stone removal (for stones that are not likely to pass spontaneously and in the presence of symptoms, such as persistent pain despite adequate analgesic treatment, persistent obstruction, and renal insufficiency), the first treatment choice for proximal ureteral stones is URS if the stone is larger than 10 mm and ESWL or URS if the stone size is less than 10 mm (6). Studies have shown that the success of URS is affected by the size, location, number and composition of the stone, whether it is impacted, and the lithotripter that is used (7,8). With the development of technology, various energy sources, including ultrasonic, pneumatic, electrohydraulic and laser lithotripters have begun to be used for stone fragmentation (9,10). Currently, the most common ones are pneumatic and laser lithotripters, both have certain advantages and disadvantages (11). In this

study, we aimed to compare the efficacy of holmium laser and pneumatic lithotripsy used in URS for proximal ureteral stones and to investigate their complications according to the Clavien-Dindo classification.

Materials and Methods

Patients and Data Collection

A total of eight centers were included in the study. Data of patients, who underwent URS due to proximal ureteral stones in different reference centers, were obtained from patient files. A total of 638 patients underwent ureteroscopic lithotripsy. The patients were divided into two groups according to the type of lithotripter: group 1; laser lithotripter (n=324; 50.8%) and group 2; pneumatic lithotripter (n=314; 49.2%). Stones located in the region between the ureteropelvic junction and the pelvic brim in the ureter were accepted as proximal stones and included in the study. The stones that were immobilized, embedded in the ureteric mucosa, and had mucosa-folded on them during the endoscopic visualization, were evaluated as impacted stones. URS was considered successful upon determination stone-free status with the imaging methods after treatment. All patients were evaluated postoperatively by non-contrast computed tomography or abdominal radiography. Stone surface area is calculated by multiplying the stone length by stone width in mm. Data on patients' perioperative double J stent requirement, gender, stone push-back status, general complication rate and Clavien-Dindo grade and URS success rate (stone-free)

were collected. The effectiveness and the complications of holmium:yttrium-aluminum-garnet (YAG) laser and pneumatic lithotripsy were compared.

This study was conducted retrospectively and approved by the Ethics Committee of Dokuz Eylül University with number 2018/03-03. Written informed consent was not obtained from patients.

Surgical Technique

Sterile urine culture was provided prior to the procedure. Cefazolin (1 g IV) was administered following spinal or general anesthesia. The choice of anesthesia type was mostly determined by the preference of anesthetists in the centers participating in the study. In the lithotomy position, 5% lidocaine gel was applied to the urethra. All the procedures were performed by semirigid ureteroscopes with an 8 or 9 Fr distal tip. A guidewire with 3 cm flexible tip was used routinely to guide ureteroscope. If stone access was achieved, a holmium laser or a pneumatic lithotripter was used for stone fragmentation. Lithotripter selection was made according to the facilities in the centers participating in the study. A 16 or 18 Fr Foley catheter was introduced into the bladder with the completion of the operation and was withdrawn on the same day or one day later.

Statistical Analysis

Pearson's chi-square test was used to compare the difference in types of anesthesia method between the two groups. If the smallest theoretical frequency was <5, the Fisher's exact test was used to analyze the variables. An independent-samples t-test was conducted to compare outcomes for URS with holmium:YAG laser and pneumatic lithotripsy. Data were analyzed using the SPSS (version 23.0) statistical program. A p value of less than 0.05 was considered statistically significant.

Results

Of the 638 patients included in the study, 424 (66.5%) were male and 214 (33.5%) were female. The mean age was 44.9±14.4 years, and 208 patients (32.6%) had co-morbidities, of whom 188 (29.5%) were undergoing medical treatment. Approximately half the patients had a history of stone passing (n=304, 47.6%). Among these patients, 183 (28.7%) had previously undergone ESWL and 98 (15.4%) had a history of stone surgery. The operation was performed under general anesthesia in 329 patients (51.6%) and spinal anesthesia in 309 (48.4%). The mean duration of the operation was calculated as 45.1±19.1 min. There was no residual stone in 527 patients (82.6%), and the complication rate was 8.1% (n=52). Table 1 presents the demographic data of the patients, general characteristics of the stones and detailed information about the operations.

When the laser lithotripter group (group 1; n=324, 50.8%) and the pneumatic lithotripter group (group 2; n=314, 49.2%) were compared in terms of demographics and stone characteristics, it was found that the mean ages were similar (44.5±13.2 vs 45.2±15.5, respectively, p=0.542), but the mean body mass

Table 1. Demographic data and stone characteristics of the patients

Age (mean ± SD)	44.88±14.41
BMI (kg/m ²) (mean ± SD)	26.2±3.5
Stone area (mm ²) (mean ± SD)	83.7±57.2
Hounsfield unit (mean ± SD)	883.7±380.4
Operation time (minutes) (mean ± SD)	45.13±19.13
Hospitalization time (days) (mean ± SD)	1.78±2.00
	n, %
Gender	
Male	424 (66.5%)
Female	214 (33.5%)
Comorbidity	
Yes	208 (32.6%)
No	430 (67.4%)
Medication	
Yes	188 (29.5%)
No	450 (70.5%)
Previous stone disease history	
Yes	304 (47.6%)
No	334 (52.4%)
Previous ESWL history	
Yes	183 (28.7%)
No	455 (71.3%)
Stone side	
Left	324 (50.8%)
Right	314 (49.2%)
Lithotripter	
Laser	324 (50.8%)
Pneumatic	314 (49.2%)
Anesthesia	
Spinal	309 (48.4%)
General	329 (51.6%)
Ureteral J stent	
Yes	396 (62.1%)
No	242 (37.9%)
Complication	
Yes	52 (8.1%)
No	568 (89.0%)
Ureteroscopy	
Successful	527 (82.6%)
Unsuccessful	111 (17.4%)

SD: Standard deviation, BMI: Body mass index, ESWL: Extra-corporal shock wave lithotripsy

index values, stone surface area and Hounsfield unit (HU) values were significantly higher in group 1 than in group 2 (26.9±3.4 vs 25.7±3.6, p<0.001; 90.7±64.4 vs 76.4±47.6, p=0.002; and 973.7±410.2 vs 814.3±340.6, p<0.001, respectively). The number of patients with a history of ESWL and number of operations performed under general anesthesia in group 1 was higher than in group 2 (33% vs 24.2%, p=0.014 and 68.2% vs 34.4%, p<0.001, respectively). In group 2, co-morbidities were more common (25.9% for group 1 and 39.5% for group 2, p<0.001), and a higher number of operations were performed under spinal anesthesia (31.8% for group 1 and 65.6% for group 2, p<0.001) (Table 2).

When the two groups were compared for surgical outcomes and complication rates; the results were similar in terms

Table 2. Relationship of demographic data and stone characteristics with the lithotripter type

	Group 1 (laser) n=324	Group 2 (pneumatic) n=314	p
Age (years)	44.5±13.3	45.2±15.5	0.542
BMI (kg/m ²)	26.9±3.4	25.7±3.6	<0.001
Stone area (mm ²)	90.7±64.4	76.4±47.6	0.002
Hounsfield unit	973.7±410.2	814.3±340.6	<0.001
Gender			
Male	226 (69.8%)	198 (63.1%)	0.079
Female	98 (30.2%)	116 (36.9%)	
Co-morbidity			
Yes	84 (25.9%)	124 (39.5%)	<0.001
No	240 (74.1%)	190 (60.5%)	
Type of anesthesia			
Spinal	103 (31.8%)	206 (65.6%)	<0.001
General	221 (68.2%)	108 (34.4%)	
Stone side			
Right	160 (49.4%)	164 (52.2%)	0.261
Left	164 (50.6%)	150 (47.8%)	
Previous stone disease history			
Yes	152 (46.9%)	162 (51.6%)	0.383
No	172 (53.1%)	152 (48.4%)	
Previous ESWL history			
Yes	107 (33%)	76 (24.2%)	0.014
No	217 (67%)	238 (75.8%)	
Previous stone operation history			
Yes	53 (16.4%)	45 (14.3%)	0.478
No	271 (84.6%)	269 (85.7%)	

BMI: Body mass index, ESWL: Extra-corporal shock wave lithotripsy

of duration of operation, complication rates and length of hospital stay (44.7±20.7 min vs 45.6±17.3 min, p=0.533; 7.7% vs 8.6%, p=0.396; and 1.8±1.0 days vs 1.8±2.7 days, p=0.864, respectively), the URS success and postoperative ureteral J stent use were significantly higher in group 1 than in group 2 (89.8% vs 75.2%, p<0.001 and 75.9% vs 47.8%, p<0.001, respectively), whereas the push back rate was significantly higher in group 2 (3.5%) compared to group 1 (1.2%) (p<0.001) (Table 3).

There was no significant difference between the two groups in the rate of complication according to the Clavien-Dindo classification (p=0.525). The most common complication was postoperative fever (n=24, 3.8%), followed by lumbar pain (n=11, 1.7%), urosepsis (n=5, 0.8%), ureteral perforation (n=5, 0.8%), urinary tract infection (n=5, 0.8%), postoperative hematuria (n=1, 0.2%), and arrhythmia (n=1, 0.2%).

Discussion

Although ESWL has been used as the first option for the treatment of proximal ureteral stones, with the recent developments in ureterorenoscopes leading to the reduction in their diameter and the emergence of flexible devices, URS has become the first treatment choice, in particular for stones

Table 3. The effect of lithotripter type on operation outcomes

	Group 1 (laser) n=324	Group 2 (pneumatic) n=314	p
Operation time (minute)	44.7±20.7	45.6±17.3	0.533
Double j stent			
Positive	246 (75.9%)	150 (47.8%)	<0.001
Negative	78 (24.1%)	184 (52.2%)	
Push-back to the collecting system			
Positive	4 (1.2%)	11 (3.5%)	0.050
Negative	320 (98.8%)	303 (97.6%)	
Complication			
Positive	25 (7.7%)	27 (8.6%)	0.396
Negative	299 (92.3%)	287 (91.4%)	
Clavien classification			
Clavien 1	20 (6.2%)	16 (5.1%)	0.525
Clavien 2	2 (0.6%)	4 (1.3%)	
Clavien 3	2 (0.6%)	3 (1.0%)	
Clavien 4	1 (0.3%)	4 (1.3%)	
Negative	299 (92.3%)	304 (91.4%)	0.525
Length of stay (day)	1.8±1.0	1.8±2.7	0.864
Ureterscopy success rate			
Successful	291 (89.8%)	236 (75.2%)	<0.001
Unsuccessful	33 (10.2%)	78 (24.8%)	

>10 mm (6). The technical improvement of lithotripters used predominantly for stone fragmentation has led to an increase in the URS success rates and decrease in the complication rates (7,12). Today, the most commonly used devices are laser and pneumatic lithotripters.

Laser lithotripters first came into use in the late 1980s with dye-laser technology (13,14). Recently, a very commonly preferred technique is holmium laser, which is capable of performing fragmentation by providing energy through small-diameter quartz fibers that can pass through the working channels of the smallest ureterorenoscopes (15). Holmium:YAG laser is able to fragment all types of stones, including hard calcium oxalate monohydrate and cystine stones, and can perform stone breaking with an ablative effect and dusting. The success rates of laser lithotripsy, which has been widely used in the treatment of proximal ureteral stones, have been reported to be 81.8-90.9% (7,15,16). In the current study, the success of URS in patients with proximal ureter stones who underwent laser lithotripsy was found to be 89.8%, consistent with the literature.

Pneumatic lithotripters, which began to be manufactured in the early 1990s, are the most preferred devices in current medical practice in Turkey due to having the lowest cost and successful treatment outcomes (17). The working principle of a pneumatic lithotripter is that the metal probe passing through the straight endoscopic channel within the ureteroscope and directly contacting the stone is driven forward with a projectile created by means of the air pressure generated by the pneumatic lithotripter, and as a result of the applied force, the stone is fragmented. The success rates of pneumatic lithotripters in the treatment of proximal ureteral stones have been reported to vary between 75% and 90.5% (12,18,19,20). Similarly, in the current study, this rate was found to be 75.2%. In this study, we found that laser lithotripsy had a higher success rate for the treatment of proximal ureteral stones than pneumatic lithotripsy (89.8% and 75.2%, respectively). The most important reason for this is the significantly higher rate of push-back observed in pneumatic lithotripsy (3.5%) compared to laser lithotripsy (1.2%). In a study conducted with 100 patients, Tipu et al. (21) reported push-back rates of 16% and 4% in pneumatic and laser lithotripsy, respectively. In a retrospective study of 1,296 patients who underwent pneumatic lithotripsy, the push-back rate for proximal ureteral stones was found to be 1.6% (12). In a randomized controlled trial, Razzaghi et al. (22) reported a push-back rate of 17.9% in the pneumatic group and no push-back in the laser group after evaluating 56 patients in each group. These varying push-back rates in the literature may be due to the different number of patients and the operations being performed by different surgeons.

In URS, the complication rates range from 9% to 25%, and the majority are minor complications that do not require any

intervention (23). Some studies in the literature have also compared complications according to the type of lithotripter used for the treatment of proximal ureteral stones. Bapat et al. (8) and Tipu et al. (21) reported a significantly lower complication rate in patients undergoing laser lithotripsy, whereas Kassem et al. (18) and Aydemir et al. (20) did not find any significant difference between the two groups in terms of complications. In the current study, we did not observe any significant difference in the rate of complication according to the Clavien-Dindo classification between patients who underwent laser lithotripsy and those who underwent pneumatic lithotripsy.

Despite the higher URS success rate in the laser lithotripsy group in our study, the use of ureteral J stent was also significantly higher in this group. This may be due to the significantly higher parameters of preoperative history of ESWL, stone area and stone HU in the laser lithotripsy group compared to the pneumatic lithotripsy group. Strohmaier et al. (24) pointed that lower URS success rates in patients with a preoperative history of ESWL might be a result of mucosal edema that primarily occurred following ESWL. Similarly, in a study investigating the significance of stone size in the treatment of distal ureteral stones, Tuğcu et al. (25) reported that in patients with a preoperative history of ESWL, the URS operation was more difficult due to mucosal edema and the stones having become impacted. In the same study, it was found that as the size of ureteral stones increased, the complications increased but there was no statistically significant difference. In their study including 154 patients, Taş et al. (26) investigated the incidence of ureteral stenosis in patients undergoing pneumatic lithotripsy for the treatment of distal ureteral stones and found high rates of ureteral J stent implantation associated with increased mucosal edema, ureteral perforation, and high stone burden. In a recently published study, it was also reported that in patients who underwent flexible URS, the high values of stone HU prolonged the operative time and were associated with residual stone fragments (27). As the HU value indicating stone fragility increases, fragmentation of the stone may become more difficult, increasing the possibility of residual stones and requirement of ureteral J stent placement.

Study Limitations

Our study has some limitations, such as having a retrospective and multi-center design. For this reason, a complete standardization of surgical (different surgeons and ureterorenoscopes) and anesthetic (different anesthetist) applications have not been achieved.

Conclusion

In the treatment of proximal ureter stones, the success rates of laser lithotripsy were found to be higher than those of pneumatic lithotripsy, while the complication rates were similar. If laser lithotripsy is available in a clinic, we believe that it is

better to use it as the first option in the treatment of proximal ureter stones. However, considering that it is not easy to access laser lithotripters due to their high cost in Turkey, pneumatic lithotripters may be an effective and inexpensive alternative that can also be safely used in these cases.

Ethics

Ethics Committee Approval: This study was approved by the Ethics Committee of Dokuz Eylül University with number 2018/03-03.

Informed Consent: Written informed consent was not obtained from patients because this was a retrospective study.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: B.İ., V.Ş., O.E., A.Y., Ş.O., Ö.Ç., A.C., M.Ş., M.O.Ş., O.Ü., F.K., O.B., Concept: B.İ., V.Ş., M.O.Ş., O.Ü., F.K., O.B., Design: B.İ., V.Ş., M.O.Ş., O.Ü., F.K., O.B., Data Collection or Processing: B.İ., V.Ş., O.E., A.Y., Ş.O., Ö.Ç., A.C., M.Ş., M.O.Ş., O.Ü., F.K., O.B., Analysis or Interpretation: B.İ., Literature Search: V.Ş., Writing: B.İ., V.Ş.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

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Does Platelet Mass Index Play a Role in Predicting Biochemical Recurrence in Localized Prostate Cancer?

Lokalize Prostat Kanserinde Trombosit Kitle İndeksinin Biyokimyasal Nüksü Öngörmede Yeri Var mıdır?

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What's known on the subject? and What does the study add?

The literature data used to predict early recurrence of localized prostate cancer need to be expanded, but studies should be continued.

Abstract

Objective: The aim of this study is to investigate the association of preoperative platelet mass index (PMI) with tumor pathologic features and postoperative biochemical recurrence in patients undergoing radical prostatectomy due to localized prostate cancer.

Materials and Methods: Data of 141 patients, who underwent radical prostatectomy for localized prostate cancer between April 2004 and April 2017, were retrospectively screened. Patient age, preoperative prostate-specific antigen (PSA) level, platelet count, mean platelet volume and PMI value, neutrophil-lymphocyte ratio (NLR), tumor grade, Gleason score, tumor volume, lymph node involvement, surgical margin positivity and biochemical recurrence at 3 months were all noted. The relationship of preoperative PMI value with age, PSA, pathologic parameters, surgical margin positivity and biochemical recurrence was evaluated.

Results: The mean age of the patients was 61.79±5.98 years, the mean PSA value was 9.50±6.69 ng/mL, mean PMI was 2003.91±486.69, and the mean NLR was 2.79±2.06. There was no correlation of PMI value with PSA, pathological stage, Gleason score, lymph node involvement, tumor volume, surgical margin positivity, and biochemical recurrence. There was statistically significant negative correlation between PMI and Gleason score.

Conclusion: In our study, we could not demonstrate preoperative PMI as a prognostic factor for early biochemical recurrence in patients undergoing radical prostatectomy for prostate cancer. To achieve a better conclusion that we can generalize, there is a need for prospective studies with larger patient series.

Keywords: Platelet mass index, Inflammation, Prostate cancer

Öz

Amaç: Bu çalışmanın amacı, lokalize prostat kanseri nedeniyle radikal prostatektomi yapılan hastalarda preoperatif trombosit kitle indeksi (PMI) ile tümörün patolojik özellikleri ve postoperatif biyokimyasal nüks arasındaki ilişkiyi araştırmaktır.

Gereç ve Yöntem: Nisan 2004 ile Nisan 2017 arasında lokalize prostat kanseri nedeniyle radikal prostatektomi yapılan 141 hastanın verileri retrospektif olarak tarandı. Hastaların yaş, preoperatif prostat spesifik antijen (PSA), trombosit sayısı, ortalama trombosit hacmi ve PMI değerleri, N/L oranı, tümör evresi, Gleason skoru, tümör hacmi, lenf nodu tutulumu, cerrahi sınır pozitifliği ve 3. ayda biyokimyasal nüks olup olmadığı kaydedildi. Ameliyat öncesi PMI değerinin yaş, PSA, patolojik parametreler, cerrahi sınır pozitifliği ve biyokimyasal nüks ile olan ilişkisi incelendi.

Bulgular: Hastaların yaş ortalaması 61,79±5,98 yıl, ortalama PSA değeri 9,50±6,69 ng/mL, ortalama PMI değeri 2003,91±486,69 ve ortalama N/L oranı 2,79±2,06 idi. PMI değeri ile PSA, patolojik evre, Gleason skoru, lenf nodu tutulumu, tümör hacmi, cerrahi sınır pozitifliği, biyokimyasal nüks arasında bir korelasyon izlenmedi. PMI ile Gleason skoru arasında istatistiksel olarak anlamlı negatif korelasyon izlendi.

Sonuç: Çalışmamızda prostat kanseri nedeniyle radikal prostatektomi uygulanmış hastalarda ameliyat öncesi PMI değerini, erken biyokimyasal nüks için prognostik bir faktör olarak gösteremedik. Genellemen yapabileceğimiz daha iyi bir sonuç elde etmek için, daha geniş hasta serileri ile prospektif olarak tasarlanmış çalışmalara ihtiyaç vardır.

Anahtar Kelimeler: Trombosit kitle indeksi, Enflamasyon, Prostat kanseri

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Received: 01.03.2018 **Accepted:** 04.06.2018

Cite this article as: Girgin R, Çınar Ö, Bulut E, Önal CF. Does Platelet Mass Index Play a Role in Predicting Biochemical Recurrence in Localized Prostate Cancer? J Urol Surg 2018;5(3):164-169.

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Introduction

Although prostate cancer is now accepted as an important cause of male deaths, the mystery over the behavior of cancer cells is still ongoing. Prostate-specific antigen (PSA) screening can be used in the diagnosis of early-stage prostate cancer, but the pathological features of cases undergoing radical surgery continue to be questioned. For this reason, there is still a need to update the information on prostate cancer. The relationship between cancer formation and inflammation has become a very interesting subject nowadays and the evidence about the link between these two conditions is increasing day by day. It has been shown that increased angiogenesis as a result of inflammation caused by infection, autoimmunity, chronic irritation, and tumor and resulting from treatments, contributes to carcinogenesis (1). The relationship between tumor survival and inflammation has been tried to be shown using neutrophil-lymphocyte ratio (NLR) in many cancer types. It is known that platelets play an important role not only in achieving hemostasis but also in inflammatory reactions and in immunological responses (2,3,4,5). Mean platelet volume (MPV) has been previously reported to be a marker of platelet activation, but, recently, platelet mass index (PMI) calculated by multiplying platelet count by MPV was claimed to be a better parameter of inflammation than MPV in a study (6,7).

In this retrospective study, we aimed to investigate the association of preoperative PMI with tumor pathologic features and postoperative biochemical recurrence in patients undergoing radical prostatectomy due to localized prostate cancer.

Materials and Methods

Data of patients, who underwent radical prostatectomy for localized prostate cancer at Zonguldak Bülent Ecevit University, Health Practice and Research Center, Clinic of Urology between April 2004 and April 2017 by four expert surgeons in urooncology, were retrospectively screened following the approval of Bülent Ecevit University Local Ethics Committee (protocol number: 2018-23-17/01). Using hospital records, patients' age, preoperative PSA, platelet count, MPV and PMI value, NLR, tumor grade, Gleason score, tumor volume, lymph node involvement, surgical margin positivity, and biochemical recurrence at 3 months were analyzed. A total of 141 patients with written consent and at least 6 months of follow-up were included in the study. PMI value was examined in relation to age, PSA, pathologic parameters, surgical margin positivity and biochemical recurrence. Biochemical recurrence was accepted when an additional treatment started at the third month control with an increase of PSA value or if there was a persistent increase in PSA value at the 6th month control.

Statistical Analysis

Mean, standard deviation, median lowest, highest, frequency and ratio values were used in the descriptive statistics of the data. The distribution of the variables was measured by the Kolmogorov-Smirnov test. The Kruskal-Wallis test and the Mann-Whitney U test were used in the analysis of quantitative independent data. In correlation analysis, the Spearman correlation coefficient was used. SPSS 18.0 program was used for statistical analysis.

Results

The mean age of the patients was 61.79 ± 5.98 years, the mean PSA value was 9.50 ± 6.69 ng/mL, the mean PMI was 2003.91 ± 486.69 , and mean NLR was 2.79 ± 2.06 . The preoperative data of the patients are summarized in Table 1. The mean tumor volume was 9.20 ± 8.42 cm³. Four (2.8%) patients had lymph node involvement, while 66 (47.6%) patients had positive surgical margin; 25 (17.5%) patients had biochemical recurrence at the third month control. The distribution of patients according to preoperative PSA levels and pathologic variables is shown in Table 2. The relationship between surgical margin involvement and histopathological findings is shown in Table 3. There was no correlation of PMI value with PSA, pathological stage, Gleason score, lymph node involvement, tumor volume, surgical margin positivity, and biochemical recurrence (Table 4). The correlation of NLR with PSA, pathological stage, Gleason score, lymph node involvement, tumor volume, surgical margin positivity, and biochemical recurrence is shown in Table 5. NLR was statistically significantly lower in lymph node-positive patients. Analysis of correlation between NLR and age, PSA, Gleason score and tumor volume and between PMI and age, PSA, Gleason score and tumor volume are shown in Table 6. There was a statistically significant negative correlation between PMI and Gleason score.

Table 1. Preoperative data of the patients

	Min	Max	Mean \pm SD
Age (year)	42	74	61.79 \pm 5.98
Total PSA (ng/mL)	2.41	36.72	9.50 \pm 6.69
Platelet count (K/ μ L)	130	461	243.02 \pm 66.13
MPV (fL)	6.7	11.5	8.3 \pm 0.93
PMI	962	3558.3	2003.91 \pm 486.69
Neutrophil count (K/ μ L)	0.6	17.2	4.96 \pm 2.25
Lymphocyte count (K/ μ L)	0.5	4.6	2.07 \pm 0.72
NLR	0.31	17.20	2.79 \pm 2.06
Tumor volume (cm ³)	0.12	38.5	9.20 \pm 8.42

PSA: Prostate-specific antigen, MPV: Mean platelet volume, PMI: Platelet mass index, NLR: Neutrophil-lymphocyte ratio, Min: Minimum, Max: Maximum, SD: Standard deviation

Table 2. The distribution of patients according to preoperative prostate-specific antigen levels and pathologic variables

		n	%
PSA (ng/mL)	0-4	4	2.8
	4-10	95	66.4
	10-20	30	21.0
	20<	12	8.5
Clinical stage	T2a	21	14.7
	T2b	11	7.7
	T2c	42	29.4
	T3a	55	38.5
	T3b	12	8.4
Surgical margin	Negative	75	52.4
	Apex	29	20.3
	Basal	12	8.4
	Multifocal	25	17.5
Lymphovascular invasion	Negative	123	86.0
	Positive	17	11.9
Perineural invasion	Negative	51	35.7
	Positive	90	62.9
Seminal vesicle invasion	Negative	128	89.5
	Positive	13	9.1
Lymph node invasion	Negative	137	95.8
	Positive	4	2.8
Third month biochemical recurrence	No	116	81.1
	Yes	25	17.5

PSA: Prostate-specific antigen

Discussion

It is known that the development of tumor cells in our body activates an inflammatory response. Systemic inflammation also suppresses the anti-tumor immune system, thus facilitating cancer progression and metastasis (8,9,10,11,12,13). Previously, biomarkers of inflammation, such as NLR, platelet-lymphocyte ratio and C-reactive protein, have been shown to be valuable prognostic factors in many cancers (8,10,11,12,14,15,16,17). During the inflammatory process, many mediators that activate thrombocytes are released. Platelets secrete various growth factors that support angiogenesis, cell proliferation and metastasis (15,16,17,18,19). Tumor-associated thrombocyte aggregation forms a barrier against T-cells by forming a protective shield around the tumor cells (20,21).

While localized prostate cancer treatment and follow-up schemes are created, many biochemical and pathological data are benefited from. Prostate cancer may show differences between treatment strategies when cases become resistant to castration. Thus, the idea of using simple blood tests to guide the experts is available for a long time. NLR is the most studied parameter for this purpose. However, in the literature, we have not seen any study evaluating such a relationship with PMI in prostate cancer.

In our study comparing the NLR with preoperative PSA value, pathologic data and the presence of biochemical recurrence in patients with localized prostate cancer undergoing radical prostatectomy, NLR was lower in lymph node-positive patients and it was statistically significant. Unlike our work, a significant correlation was found between high NLR and lymph node positivity in a study with 1688 patients performed by Zhang et al. (22). However, in their study with 217 cases, Kwon et al. (23) found a positive relationship only between NLR and Gleason score. On the other hand, we did not observe a relationship with other parameters.

PMI is a biomarker that has recently attracted the attention of researchers. In the first study about PMI, it has been reported that unnecessary platelet transfusions in neonatal intensive care units could be prevented (24,25,26,27). There is an inverse

Table 3. Distribution of histopathological findings with surgical margin involvement

		Surgical margin involvement n (%)*				p
		Non	Apex	Basal	Multifocal	
Gleason score	5-6	51 (68.0)	13 (17.3)	5 (6.7)	6 (8.0)	0.003
	7	22 (40.0)	13 (23.6)	6 (10.9)	14 (25.6)	
	8 and above	2 (18.2)	3 (27.3)	1 (9.1)	5 (45.5)	

* Percentages are given in parentheses, p<0.05

Table 4. Correlation between platelet mass index value and biochemical and pathological variables

PMI		Min-max	Median	Mean ± SD	p*
PSA (ng/mL)	0-4	1579-2456	1789	1903±384	0.588
	4-10	962-3558	1923	1989±502	
	10-20	1340-2978	1899	1985±412	
	20<	1235-3091	2097	2202±571	
Clinical stage	T2	1047-3273	1938	2017±442	0.548
	T3	962-3558	1913	1990±534	
Gleason	5-6	962-3558	2049	2077±497	0.157
	7	1066-3091	1847	1922±476	
	8<	1322-2468	2009	1915±423	
Tumor volume (cm ³)	≤5	962-3273	1962	2013±459	0.533
	5<	1066-3558	1908	2007±509	
Surgical margin	(-)	1047-3273	1938	2003±432	0.968
	(+)	962-3558	1877	2005±546	
Lymph node invasion	(-)	962-3558	1932	2009±491	0.164
	(+)	1448-1883	1742	1704±186	
Biochemical recurrence	(-)	962-3558	1918	2005±492	0.929
	(+)	1235-3091	1998	2032±468	

PSA: Prostate-specific antigen, PMI: Platelet mass index, Min: Minimum, Max: Maximum, SD: Standard deviation
*p<0.05

Table 5. Correlation between neutrophil-lymphocyte ratio and biochemical and pathological variables

NLR		Min-max	Median	Mean ± SD	p*
PSA (ng/mL)	0-4	1.6-3.5	2.04	2.31±0.82	0.920
	4-10	0.32-17.2	2.25	2.87±2.33	
	10-20	0.87-7.22	2.09	2.61±1.49	
	20<	1.09-5.07	2.54	2.88±1.37	
Clinical stage	T2	0.32-9.6	2.43	2.89±1.98	0.444
	T3	0.91-17.2	2.07	2.7±2.17	
Gleason	5-6	0.88-9.6	2.41	2.81±1.66	0.433
	7	0.32-17.2	2	2.88±2.66	
	8<	1-4.18	2.09	2.31±0.95	
Tumor volume (cm ³)	≤5	0.91-9.6	2.17	2.76±1.71	0.835
	5<	0.32-17.2	2.22	3.03±2.3	
Surgical margin	(-)	0.78-9.6	2.33	2.73±1.73	0.882
	(+)	0.32-17.2	2.1	2.87±2.41	
Lymph node invasion	(-)	0.32-17.2	2.23	2.83±2.08	0.02
	(+)	1-1.96	1.24	1.36±0.44	
Biochemical recurrence	(-)	0.32-17.2	2.2	2.9±2.18	0.688
	(+)	1.09-6.56	2.11	2.84±1.48	

PSA: Prostate-specific antigen, NLR: Neutrophil-lymphocyte ratio, Min: Minimum, Max: Maximum, SD: Standard deviation
*p<0.05

Table 6. Analysis of correlation between neutrophil-lymphocyte ratio and platelet mass index value

		Age	PSA	Gleason	Tumor volume
NLR	r	-0.003	0.036	-0.99	-0.002
	p	0.972	0.674	0.242	0.985
		Age	PSA	Gleason	Tumor volume
PMI	r	-0.119	0.005	-0.16	-0.037
	p	0.158	0.95	0.049	0.667

PSA: Prostate-specific antigen, NLR: Neutrophil-lymphocyte ratio, PMI: Platelet mass index
Spearman correlation coefficient

relationship between platelet count and platelet volume in order to keep PMI stable, and therefore platelet activity at a constant value. Apart from PMI value, high MPV value and larger platelet diameter were found to be associated with increased platelet activity (28).

It is seen in the literature that MPV has different prognostic significance in different cancers. However, how MPV values affect prognosis remains to be discussed. High MPV value is significant in breast and hepatocellular carcinomas, but it gains significance when decreasing in lung cancer (29,30,31,32,33). It is not possible to reach a definite result with MPV today. Elevation in platelet count was found to be associated with metastasis development and poor prognosis in some solid cancers (34,35). This is being explained by the overproduction of megakaryocyte colony-stimulating cytokines (36). On the other hand, it has been also claimed that platelets act as a protective shield against circulating tumor cells (37). Takeuchi et al. (38,39) showed that the higher the platelet counts and platelet-lymphocyte ratio the poorer the prognosis of breast cancer. The prognostic value of increase in the number of platelets in renal cell carcinoma cases has also been investigated, but the results were different from each other (36).

In this pioneer study, a negative correlation between PMI and Gleason score was found which was to be statistically significant. We assume that the low number of patients may be misleading. We did not observe a statistically significant difference between PMI values and biochemical recurrence among patients.

Study Limitations

There were some limitations in this study. First, the retrospective nature of the study makes it difficult to obtain generalizable results. The lack of long-term follow-up results of patients was the other limitation of this study. The low number of patients treated at a single institution also weakens the power of influence of the study.

Conclusion

Our study demonstrates that preoperative PMI is not a prognostic factor for early biochemical recurrence in patients undergoing radical prostatectomy for prostate cancer. When the literature is examined, it is emphasized that platelet count and platelet volume may be prognostic factors in some advanced cancers. To achieve the same result for PMI values in prostate cancer, there is a need for prospective studies with larger patient series.

Ethics

Ethics Committee Approval: This study was approved by Bülent Ecevit University Local Ethics Committee (protocol number: 2018-23-17/01).

Informed Consent: Written consent was taken from all patients.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: R.G., E.B., Ö.Ç., Concept: R.G., Design: R.G., Data Collection or Processing: C.F.Ö., E.B., Analysis or Interpretation: R.G., E.B., Ö.Ç., Literature Search: C.F.Ö., Writing: R.G.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

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Gender-related Differences in Surgically Treated Patients with Renal Cell Carcinoma

Cerrahi Olarak Tedavi Edilen Böbrek Tümörü Hastalarının Cinsiyete Özgü Farklılıkları

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What's known on the subject? and What does the study add?

The gender-related differences of the patients who have surgically treated renal cell carcinoma are already known for the Europe and America. However, in the literature, there is no information about these differences for Turkish population. Our study may guide future studies with similar concept with more patients in our population.

Abstract

Objective: The aim of the study was to investigate gender-specific differences in the Turkish patients with renal cell carcinoma (RCC) undergoing radical or nephron-sparing nephrectomy and compare the results with those in other regions.

Materials and Methods: Data of 76 patients, who were clinically diagnosed with RCC and underwent radical or nephron-sparing nephrectomy from January 2011 to August 2017, were retrospectively evaluated. Age and gender of the patients and the size, histological type, grade and pathological stage of the tumors were recorded. A chi-square test was used for comparing categorical variables, whereas the Student's t-test was used for the same purpose in the continuous variables.

Results: Of the 67 patients, 39 (58.2%) were male and 28 (41.8%) were female; male-to-female ratio was 3:2. The mean age of the male and female patients was 63.4±11.7 years and 59.3±14.3 years, respectively and the mean tumor size was 5.7 and 5.3 cm, respectively. There were differences in mean age, tumor size and Fuhrman grade, however, none of them reached the level of statistical significance. Twenty four of the male and 25 of the female patients had low-stage, 15 of the male and 3 of the female patients had high-stage disease. Thus, the male patients had higher stage disease than the female patients and the difference was statistically significant (p=0.011).

Conclusion: Turkish women with RCC had significantly lower stage disease than Turkish men, although grade and size of the tumor did not present a statistically significant difference. The results were similar with other European studies.

Keywords: Renal cell carcinoma, Gender, Difference, Radical, Nephron sparing, Nephrectomy

Öz

Amaç: Çalışmamızın amacı, radikal ya da nefron koruyucu cerrahi ile tedavi edilmiş renal hücreli karsinomlu (RHK) hastalarımızın cinsiyete özgü farklılıklarını değerlendirmek ve bunu diğer bölgeler ile karşılaştırmaktır.

Gereç ve Yöntem: Ocak 2011 ile Ağustos 2017 arasında klinik olarak RHK tanısı almış ve radikal veya nefron koruyucu nefrektomi operasyonu geçirmiş olan 76 hastanın verileri retrospektif olarak gözden geçirildi. Hastaların yaşları ve cinsiyetleri ile tümörlerinin boyutu, histolojik tipi, derecesi ve patolojik evreleri bulundu. Kategorik değişkenlerin değerlendirilmesinde ki-kare testi, sürekli değişkenlerin değerlendirilmesinde ise Student's t-testi kullanıldı.

Bulgular: Altmış yedi hastanın 39'u (%58,2) erkek, 28'i (%41,8) ise kadındı ve erkek/kadın oranı 3:2 idi. Erkeklerin ortalama yaşı 63,4±11,7; kadınların ise 59,3±14,3 yılı idi. Ortalama tümör boyutu erkeklerde 5,7; kadınlarda ise 5,3 cm idi. Ortalama yaş, tümör boyutu ve Fuhrman derecesinde fark saptanmasına rağmen anlamlı seviyeye ulaşmadı. Erkeklerin 24'ü düşük, 15'i yüksek; kadınların ise 25'i düşük, 3'ü yüksek evreli hastalığa sahipti. Yani erkekler istatistiksel olarak anlamlı şekilde kadınlardan daha yüksek evreli hastalığa sahipti (p=0,011).

Sonuç: Sonuç olarak, kadın popülasyonumuz erkekler göre anlamlı şekilde daha düşük evreli tümöre sahip olmasına rağmen, tümörlerin derecesi ve boyutları anlamlı bir farklılık göstermedi. Sonuçlarımız Avrupa çalışmalarıyla uyumlu bulundu.

Anahtar Kelimeler: Böbrek hücreli karsinom, Cinsiyet, Farklılık, Radikal, Nefron koruyucu, Nefrektomi

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Received: 08.04.2018 **Accepted:** 20.06.2018

Cite this article as: Akarken İ, Dere Y, Tarhan H, Deliktaş H, Şahin H. Gender-related Differences in Surgically Treated Patients with Renal Cell Carcinoma. J Urol Surg 2018;5(3):170-173.

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Introduction

Currently, kidney cancer is the ninth most common malignancy in men and 14th most common in women, it is also the 16th most common cause of death from cancer worldwide. There were an estimated 338.000 new cases and 143.000 deaths from kidney malignancies in 2012 (1). Cancers originating from renal parenchyma cells account for nearly 85 percent of the newly diagnosed kidney cancers in the United States of America. Other types of kidney cancers include renal pelvis cancer (12%) and rare malignancies (2%). Clear cell carcinoma comprises more than 70% of renal cell carcinoma (RCC) and papillary carcinoma (15%) and chromophobe carcinoma (5%) are the other main histologic types (2). The incidence of RCC has been gradually increasing in the United States of America and Europe in the past thirty years (3). Also, there is a two-fold increase in mortality and a five-fold increase in new cases of RCC when compared with 70's (4).

Despite the increasing rates, the incidence of RCC amongst genders is distinctly different. The rates were about twice as high for males than for females. However, the ratio has remained approximately same (5). Hormonal and reproductive factors which include the use of hormone therapy, oral contraceptives and parity may be the reason behind this gender-specific difference in incidence (6). Some studies indicate that men present with RCC with higher stage, larger tumors and at younger age than women (7). Most of the previous studies on gender-specific features of RCC included patients from Europe or the United States of America and there is little information about the gender-specific features of Turkish patients with RCC in the literature.

The aim of the study was to investigate gender-specific differences in the Turkish patients with RCC undergoing radical or nephron-sparing nephrectomy and compare the results with those in other regions.

Materials and Methods

After Muğla Sıtkı Koçman University Local Ethics Committee's approval with 180085 decision number, data of 76 patients, who were clinically diagnosed with RCC and underwent radical or nephron-sparing nephrectomy in our department from January 2011 to August 2017, were retrospectively evaluated. A total of nine patients were excluded from the study because they had non-RCC pathological type tumors (5 oncocytoma, 2 fat-poor angiomyolipoma and 2 upper urothelial cell carcinoma). Therefore, 67 patients were included in the study.

In addition to the age and gender of the patients, data on the size, histological type, grade and pathological stage of the tumors were obtained. All the pathologic materials were

processed according to the standard procedures and assessed by an experienced genitourinary pathologist at our institution. The 2009 American Joint Committee on Cancer tumor-node-metastasis (TNM) staging system was used to assign pathological stages (8). The Fuhrman grading system was used for nuclear grading (9).

Statistical Analysis

Pearson's chi-square test was used for comparing categorical variables, whereas the Student's t-test was used for the same purpose in continuous variables. Very few patients died during the study, consequently, no survival analysis could be conducted. The software Statistical Package for the Social Sciences 22.0 (SPSS Inc., Chicago, United States of America) was used to assess data. A p value of less than 0.05 was considered statistically significant.

Results

The clinicopathological features of the patients and comparison results are shown in Table 1. Of the 67 patients; 39 (58.2%) were male and 28 (41.8%) were female; male-to-female ratio was 3:2. The mean age of the male and female patients was 63.4±11.7 years and 59.3±14.3 years, respectively and the mean tumor size was 5.7 cm and 5.3 cm, respectively. There were differences in mean age, tumor size and Fuhrman grade, however, none of them reached the level of statistical significance. Twenty four of the male and 25 of the female patients had low-stage, while 15 of the male and 3 of the female patients had high stage disease. Thus, the incidence of high stage disease in male patients was higher than in female patients and the difference was statistically significant (p=0.011). Papillary RCC was found in 3 of the male and 2 of the female patients and chromophobe RCC was detected in 1 of the males and 2 of the females. Because of the low number of cases, the histological subtypes were not included in the analysis.

Discussion

To the extent of our knowledge, there is no study in the literature which investigates the gender-related differences in patients with RCC in the Turkish population. Although the present cohort represent only a small part of the Turkish population with RCC, it may guide the further studies with larger cohorts and be used to compare the results with the other regions of the world.

Largest studies in the literature, which were conducted with more than thirty thousand patients, have shown that the male-to-female ratio for patients with RCC was nearly 2:1. Aron et al. (10) assessed the results of 35.336 patients and found a male-to-female ratio of 7:4, while Stafford et al. (11) reached the same result with 39.434 patients. Moreover, Woldrich et al. (12) found

Table 1. The clinicopathological features and comparison results of the patients

Variable	Total	Male	Female	p value
Patients, n (%)	67	39 (58.2)	28 (41.8)	0.222
Mean (SD)				
Age (years)	61.73 (12.9)	63.4 (11.7)	59.3 (14.3)	0.200
Tumor size (cm)	5.5 (2.5)	5.7 (2.4)	5.3 (2.6)	0.465
Pathological tumor stage				
				0.011
T1	34	17	17	-
T2	15	7	8	-
T1+T2 (low stage)	49	24 (61.53)	25 (89.28)	-
T3	14	12	2	-
T4	4	3	1	-
T3+T4 (high stage)	18	15 (38.46)	3 (10.72)	-
Fuhrman grade				
				0.982
G1	6	2	4	-
G2	30	19	11	-
G1+G2 (low grade)	36	21 (53.8)	15 (53.57)	-
G3	17	9	8	-
G4	14	9	5	-
G3+G4 (high grade)	31	18 (46.15)	13 (46.42)	-

SD: Standard deviation, G: Grade

a ratio of 8:5 with more than 236.000 cases. Contrary to these studies, we found a male-to-female ratio of 3:2. In line with our study, Schrader et al. (13) from Germany and Hew et al. (14) from Netherlands demonstrated the same ratio. Although the ratio varies, the incidence of RCC is higher in males than in females. Despite the lack of evidence, some studies have suggested that hormonal and reproductive factors may explain the low incidence of RCC in women (6,15).

Most of the large population-based studies indicated that female patients were older than males at the time of diagnosis (13,14). A study by Woldrich et al. (12) including 236.930 patients showed that the mean age of females and males were 64.3 and 62.9 years, respectively. In addition, Stafford et al. (11) and Aron et al. (10) reached similar results regarding the age difference between genders. However, in a study by Lee et al. (16) performed in South Korea, there was no statistically significant difference in mean age between genders. Unlike most of the articles in the literature, in our study, the mean age of males was higher than females, but the difference did not reach the level of statistical significance. Consistent with our study, Chen et al. (17) found that compared with male patients, female patients were younger, but the difference was not significant.

There are conflicting results about difference in tumor size between genders in the publications. Some of the previous studies found no difference in the tumor size between genders (16,17,18). However, Hew et al. (14) and Aron et al. (10) found that the mean tumor size in females were smaller than in males. In accordance, we found that the mean tumor size in females was smaller, but the difference was not statistically significant. Contrary to these results, the mean tumor size in females was higher in a non-significant level, in a study by Lee et al. (16).

Because of the low number of our cases, we converted the Fuhrman grading system into low grade and high grade by merging grade 1 with 2 and grade 3 with 4, respectively. The same process was repeated for the TNM staging of the tumors. Females tend to have more low-grade tumors (10,14,17). However, we found no significant difference in tumor grade between genders in our study. Schrader et al. (13) assessed 780 patients treated with nephrectomy and found no difference in grades, in line with our study. Women present with lower stage tumors than man despite the different staging systems (10,11,12,19,20). In agreement with previous studies, we also found that female patients had lower stage tumors. Hew et al. (14) reported less common pT3 stage tumors in women,

interestingly, except in those younger than 40 years. However, May et al. (21) assessed the results of 6136 patients with RCC and reported no significant difference in tumor stage between genders. Currently there is no clear explanation for the pathological difference in RCC between genders. However, gender-specific molecular markers and hormone receptors in RCC may play a major role in clarifying this difference.

Further nationwide, multicenter studies with more detailed data collection are warranted for better understanding of the gender-related differences in Turkish patients with RCC.

Study Limitations

The limitations of our study must be noted. In addition to its retrospective design, we could only assess patients who underwent surgery. Moreover, as a result of small sample size; neither we could conduct histologic subtype analysis nor survival analysis. We did not have sufficient data about female clinical characteristics, such as age of menopause, pregnancy or parity. Also, information about the potential risk factors, symptoms, and incidental detection rates were lacking. Such information may be useful in explaining gender-related differences.

Conclusion

Turkish women with RCC had significantly lower stage tumors than Turkish men, although stage and size of tumor did not present a statistical significant difference. Also, the difference between mean age did not reach the significant level. Gender-related differences in patients with RCC in the Turkish population are similar with that in other regions of the world, but larger scale studies are needed.

Ethics

Ethics Committee Approval: The study was approved by the Muğla Sıtkı Koçman University Local Ethics Committee with 180085 decision number.

Informed Consent: The study is retrospective.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: İ.A., Y.D., H.T., H.D., H.Ş., Concept: İ.A., H.Ş., Design: İ.A., H.Ş., Data Collection or Processing: İ.A., Y.D., H.T., H.D., Analysis or Interpretation: İ.A., Y.D., Literature Search: İ.A., H.T., H.D., Writing: İ.A.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

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Outcomes of Laparoscopic Transperitoneal Pyeloplasty for the Treatment of Ureteropelvic Junction Obstruction in Adult Patients

Üreteropelvik Bileşke Darlığı Nedeniyle Erişkin Hastalarda Uygulanan Laparoskopik Transperitoneal Pyeloplasti Sonuçları

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What's known on the subject? and What does the study add?

There are limited studies related to laparoscopic pyeloplasty in adult patients. The technique may be a gold standart treatment method in this patient group. Our study shows that the technique has low complication rate.

Abstract

Objective: Laparoscopic transperitoneal pyeloplasty (LTP) is being widely preferred in the treatment of ureteropelvic junction obstruction (UPJO). This study aims to assess the outcomes of treatment efficacy of LTP performed in our clinic for the treatment of UPJO in adult patients.

Materials and Methods: Data of patients, who underwent LTP procedure in our clinic between 2004 and 2017, were reviewed retrospectively. Data of 116 patients in total were included in the study. The cases were reviewed in terms of demographic characteristics, complaints at admission, and clinical, laboratory and radiological findings. The patients were divided into two groups and correlation of demographic data (age, age group, and gender), side and presence of kidney stone with the presence of crossing vessel was investigated. Chi-square test, Student's t-test and Fisher's exact test were applied for statistical analysis.

Results: The mean age of the patients was 29.9 (19-51) years. Eight patients were the secondary patients who underwent open surgery upon diagnosis of UPJO. Forty-one (35.3%) patients had the anomaly of crossing vessel compression, 17 (14.6%)-kidney stone, 5 (4.3%)-solitary kidney and 3 (2.5%) had horseshoe kidney. The mean operating time was 124 (80-245) minutes. No statistically significant correlation of the presence of crossing vessel with age, gender, side and presence of stone was found. The mean length of hospital stay was 3.05 (2-11) days and the mean postoperative follow-up time was 44 (12-120) months. Success rate was found to be 93.1%. One (0.8%) patient had perioperative and 10 (8.6%) patients had postoperative complications.

Conclusion: LTP is a feasible, effective and reliable option in the treatment of UPJO with low complication rate and high success rate.

Keywords: Laparoscopy, Pyeloplasty, Ureteropelvic junction, Obstruction

Öz

Amaç: Laparoskopik transperitoneal pyeloplasti (LTP), üreteropelvik bileşke darlığı (ÜPBD) tedavisinde artan bir sıklıkta tercih edilmektedir. Bu çalışmada, kliniğimizde ÜPBD tedavisinde uyguladığımız LTP yönteminin tedavi etkinliği üzerine sonuçlarını değerlendirmeyi amaçladık.

Gereç ve Yöntem: Kliniğimizde 2004 ve 2017 yılları arasında LTP uygulanan hastaların verileri retrospektif olarak incelendi. Toplam 116 hastanın verileri çalışmaya dahil edildi. Olguların demografik özellikleri, başvuru yakınmaları, klinik, laboratuvar ve radyolojik görüntü bulguları incelendi. Hastalar iki gruba ayrılarak demografik veriler (yaş, yaş grubu, cinsiyet), taraf ve böbrek taşı varlığı ile çaprazlayan damar varlığı arasındaki ilişki araştırıldı. İstatistiksel analizde ki-kare, Student's t-testi, Fisher exact testi kullanıldı.

Bulgular: Hastaların ortalama yaşı 29,9 (19-51) idi. Hastaların 8 tanesi ÜPBD tanısıyla açık cerrahi uygulanmış olan sekonder hastalardı. Hastaların 41'inde (%35,3) çaprazlayan damar basısı, 17'sinde (%14,6) böbrek taşı, 5'inde (%4,3) soliter böbrek ve 3'ünde (%2,5) de at nalı böbrek anomalisi saptandı. Operasyon süresi ortalama 124 (80-245) dakikaydı. Çaprazlayan damar varlığı ile yaş, cinsiyet, taraf ve taş varlığı arasında istatistiksel

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Received: 26.02.2018 **Accepted:** 27.04.2018

Cite this article as: Demirdağ Ç, Ozman O, Çitgez S, Önal B, Talat Z. Outcomes of Laparoscopic Transperitoneal Pyeloplasty for the Treatment of Ureteropelvic Junction Obstruction in Adult Patients. J Urol Surg 2018;5(3):174-179.

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anlamli ilişki saptanmadı. Hastanede yatış süresi ortalama 3,05 (2-11) gün, operasyon sonrası izlem süresi ortalama 44 (12-120) aydı. Başarı oranı %93,1 olarak saptandı. Hastaların 1'inde (%0,8) peroperatif, 10'unda (%8,6) ameliyat sonrası komplikasyon gözlemlendi.

Sonuç: LTP, düşük komplikasyon oranları, yüksek başarı oranları ile ÜPBD tanılı hastaların tedavisinde uygulanabilir, etkin ve güvenilir bir seçenektir.

Anahtar Kelimeler: Laparoskopji, Pyeloplasti, Üreteropelvik bileşke, Darlık

Introduction

Ureteropelvic junction obstruction (UPJO) is the most common congenital cause of upper urinary tract obstruction resulting in progressive dilatation of the renal collecting system (1). Clinical signs of UPJO include flank pain, renal colic and infection; and may result in progressive loss of renal function (1). The gold standard for the treatment of UPJO is open pyeloplasty, described by Anderson-Hynes, with a success rate of over 90% (2,3). Minimally invasive approaches in UPJO are endoscopic treatment, laparoscopic pyeloplasty and robotic pyeloplasty.

Laparoscopic pyeloplasty was first introduced in 1993 by Schuessler et al. (4) and was started to be used as a minimally invasive option at a level which can compete with open pyeloplasty in terms of success rates. Beside the improvement offered by this treatment option, the most important superiority for the patients is that the treatment is less invasive and thus results in low morbidity.

The aim of this study was to present the outcomes and associated complications in an adult patient group, who underwent laparoscopic transperitoneal pyeloplasty (LTP).

Materials and Methods

Data of 116 patients who underwent LTP in our clinic between 2004 and 2017 was retrospectively reviewed. Demographic characteristics, complaints at admission and the clinical, laboratory and radiologic findings of the patients were investigated. Indications for surgery were symptomatic UPJO such as pain, urinary tract infection, impaired renal function, and/or decline in renal function over time monitored on a diuretic renal scan. Laparoscopic approach was performed in all cases.

Perioperative complications were classified according to the Satava (5) classification and the postoperative complications according to the Clavien classification (6). The patients were followed up postoperatively on the basis of radiologic and laboratory findings. For assessment purposes, ultrasonography (US) was taken at month 1-3 postoperatively and mercaptoacetyltriglycine (MAG-3) scintigraphy at month 6 postoperatively and, the follow-up intervals were planned accordingly.

The patients were divided into two groups according to the presence of crossing vessels. Demographic data (age, age group,

and gender), side, previous renal surgery and presence of kidney stone were investigated in both groups.

This was a retrospective study and all patients provided written informed consent. Ethics committee approval was not obtained because of the retrospective design of the study.

Statistical Analysis

The data was analyzed with the Statistical Package for the Social Sciences version 16 (SPSS Inc., Illinois, United States of America). Chi-square test, Student's t-test and Fisher's exact test were used in statistical analysis. A p-value of less than 0.05 was considered statistically significant.

Results

Data of 116 patients in total was included in the study (Table 1). The mean age was 29.9 (19-51) years. Seventy-six patients were male and 40 were female. Sixty-eight patients had UPJO on the left side whereas 48 patients on the right side. There were 17 (14.6%) patients who had kidney stone and 41 (35.3%) patients had crossing vessel. There were 3 (2.5%) patients with horseshoe kidney anomaly, whereas 5 (4.3%) patients had solitary kidney. In 8 (6.9%) patients, there was a history of previous pyeloplasty surgery. The mean operating time was 124 (80-245) minutes. While the colon was medialized in 108 patients, the transmesocolic approach was used in 8 patients. Y-V plasty was performed in 11 patients and dismembered pyeloplasty in 105 patients. Intraoperative double-J stent was laparoscopically implanted in all patients.

The mean length of hospital stay was 3.05 (2-11) days and the mean postoperative follow-up time was 44 (12-120) months. During the perioperative period, grade 3 complication was observed in 1 (0.8%) patient on the basis of the Satava classification; whereas during the postoperative period, 2 (1.7%) patients had grade 1, 7 (6%) patients had grade 2 and 1 (0.8%) patient had grade 3 complications on the basis of the Clavien classification (Table 2). In 1 patient, perioperative colon injury was observed during port insertion. Primary repair was performed laparoscopically in this patient. During the postoperative period, 3 patients had prolonged extravasation of urine, 5 patients had paralytic ileus and 2 had high fever. Percutaneous nephrostomy catheter was inserted in one of the patients who developed extravasation of urine. Eight (6.9%) patients had recurrent obstruction during the follow-up. Endopyelotomy was performed in 7 (6.1%) of these patients

Table 1. Characteristics of patients and demographic datas

Patient characteristics	n
Number of patients	116
Age (year)	
Mean (range)	29.9 (19-51)
Sex	
Female	40 (34.5%)
Male	76 (65.5%)
Side	
Left kidney	68 (58.6%)
Right kidney	48 (41.4%)
Primer/secondar	
Primer	108 (93.1%)
Secondar	8 (6.9%)
ASA score (mean)	1.4
Concomitant renal abnormality	
Crossing vessel	41 (35.3%)
Kidney stone	17 (14.6%)
Solitary kidney	5 (4.3%)
Horseshoe kidney	3 (2.5%)
HCT level (preoperative)	
Mean (range)	39 (26-45)
Creatinine level (preoperative)	
Mean (range)	0.90 (0.5-1.3)
Clinical features	
Pain	58 (50.0%)
No symptom	31 (26.7%)
Urinary system infection	21 (18.1%)
Hematuria	6 (5.2%)

ASA: American Society of Anaesthesiologists, HCT: Hematocrit

for recurrence. Two of these patients were tertiary cases, who underwent LTP following open pyeloplasty. Nephrectomy was performed in one patient.

No statistically significant correlation of the presence of crossing vessel with age, gender, side, previous renal surgery, and presence of stone was found (Table 3).

Discussion

Since it was first defined by Schuessler et al. (4) in 1993 as a surgical treatment of UPJO, laparoscopic management of this condition has become an ideal alternative to open and endoscopic techniques. The decision for open, laparoscopic, endoscopic or robotic managements depends on the preference and experience of the surgeon with each method having its own pros and cons. The endoscopic and laparoscopic developments in the last 2 decades and recent robotic developments in the last

Table 2. Per- and postoperative findings

Per- and postoperative findings	n
Operation time (min)	
Mean (range)	124 (80-245)
Approach	
Colon reflecting	108 (93.1%)
Transmesocolic	8 (6.9%)
Technique	
Dismembered	105 (90.5%)
Y-V plasty	11 (9.5%)
Bleeding (mL)	
Mean (range)	38 (22-53)
HCT level (postoperative)	
Mean (range)	37.8 (26-43)
Creatinine level (postoperative)	
Mean (range)	0.93 (0.5-1.3)
Peroperative complications according to Satava classification	
Grade 3	1 (0.8%)
Postoperative complications according to Clavien classification	
Grade 1	10 (8.6%)
Grade 2	2 (1.7%)
Grade 3	7 (6.0%)
Hospitalization time (days)	
Mean (range)	3.05 (2-11)
Results	
Succeed	108/116 (93.1%)
Recurrence	8/116 (6.9%)
Follow-up (months)	
Mean (range)	44 (12-120)

HCT: Hematocrit

Table 3. The correlation between crossing vessel and demographic datas

Variables	Crossing vessel (+)	Crossing vessel (-)	p
Age (year, mean)	29.16±14.9	30.11±14.87	0.99*
Male gender	28/41	48/75	0.52**
Left side	24/41	44/75	0.82**
Kidney stone	3/41	14/75	0.23***

*Student's t-test, **chi-square test, ***Fisher exact test

5-10 years have shifted the surgeon's preference to minimally invasive techniques. All factors including cost, available surgical equipments and experience are determinant in the surgical technique to prefer. It has been reported by many series that operative time in open pyeloplasty was significantly shorter than in laparoscopic pyeloplasty. Yet, laparoscopic pyeloplasty has

become the method of choice as gold standard therapy in some centers due to advantages of shorter time of hospitalization and less analgesic requirement (7,8). In our series, all cases were treated laparoscopically. The success rate of 93.1% reported in our study is comparable to the results reported by experienced laparoscopic surgeons in the literature (9,10,11).

The most significant symptom in adult patient group with UPJO is pain. UPJO may be found in work-ups done upon complaints of pain with micturition and blood in urine. UPJO may also be coincidentally found during tests run for other complaints without any symptom at all (12). In our series, 50% of patients presented with pain, 18.1% with urinary tract infection and 5.2% with hematuria. 26.7% of patients were diagnosed as asymptomatic.

Almost 30% of the patients have crossing vessel at the UPJ (13). In our series, 41 (35.3%) patients presented with crossing vessel, 17 (14.6%) with kidney stone, 5 (4.3%) with solitary kidney and 3 (2.5%) presented with horseshoe kidney anomaly. Correlation of the presence of crossing vessel with UPJO or the effect of vascular transposition or ligation on results of pyeloplasty is debatable. Zeltser et al. (14) detected crossing vessel in almost 20% of patients with a normal UPJ. On the other hand, patients presenting with UPJO were found to have crossing vessel more commonly than the normal population (15). Almost 35.3% of the patients in our study had crossing vessel. There was no statistically significant relationship between presence of crossing vessel and any demographic feature.

Dismembered pyeloplasty is the most frequently preferred surgical technique (16). The advantage of dismembered pyeloplasty is removal of the narrow segment, and yet it is technically more challenging than non-dismembered pyeloplasty since the ureter is divided (4). Since the ureter is not divided in non-dismembered pyeloplasty, the first suture, in particular, is put without tension with a shorter anastomosis time. There is an obvious need for more scientific data to conclude whichever method is better for patients. In our series, 82% of the patients underwent dismembered pyeloplasty.

Although the Anderson-Hynes dismembered pyeloplasty is the most common technique, there are many different techniques applicable according to the pelvic anatomy. Foley Y-V plasty is the most commonly used non-dismembered technique. This technique designed for high ureteral access cannot be applied when the lower pole vessel needs to be transposed. However, crossing vessel has not always been shown to be responsible for UPJO (17). Furthermore, the success rate of Y-V plasty applied in the presence of crossing vessel is comparable to Anderson-Hynes plasty (10). In our series, 1 out of 10 patients undergoing Foley Y-V plasty presented with crossing vessel. It was decided in these cases that the crossing vessels could not be responsible for the external compression since they were localized to the proximal

of the UPJ. Besides, the UPJ extends more to the proximal in Y-V plasty moving away from the crossing vessel.

The study presenting our 14-year laparoscopic pyeloplasty experience confirms that Y-V plasty was rather preferred in the first years, later on replaced totally by dismembered pyeloplasty. Other authors sharing their first 100-case experiences have shown to prefer the Y-V technique in the same ratios (9,10,11). Nevertheless, these studies did not report until when and how much this technique was applied down the learning curve.

Presence of stone does not hinder the laparoscopic technique in the presence of UPJO. Ramakumar et al. (18) published a 20-case series having undergone simultaneous pyelotomy in 2002. Similarly, preoperative assessment of 17 (14.6%) cases revealed stone in our study, following which laparoscopy-guided simultaneous pyelolithotomy was applied.

Although horseshoe kidney may look as a challenge for laparoscopic approach, it has been reported in a few studies (19,20). In our series, 3 (2.5%) patients with horseshoe kidney anomalies underwent LTP. Consequently, laparoscopic pyeloplasty has been successfully applied in patients with renal anomalies.

Laparoscopic pyeloplasty can successfully be applied in recurrent patients who had previous surgery for UPJO. However, it is not at all times easy to create a favorable space and make ureter dissection due to the adhesences resulting from a previous surgery. The operator is expected to have advanced laparoscopic experience to make a tension-free anastomosis (21). In our series, 8 (6.9%) patients had a history of open pyeloplasty. Six (5.2%) of these patients did not develop recurrence during follow-up, whereas 2 (1.7%) patients had recurrent obstruction. One (0.8%) patient had endopyelotomy. The other (0.8%) patient had failed and thus later required nephrectomy.

The transmesocolic approach was used in 8 (6.9%) patients of our series. In particular, in left-sided UPJOs, incision and dissection through the Toldt line for colon mobilization in transperitoneal approach restrict laparoscopic vision due to bleeding and fog and extend the operating time. For this reason, transmesocolic approach is preferred by certain centers for left-sided UPJO. There are reports of shorter operating times in the literature when compared to the transperitoneal method in other series (22,23). Although the transmesocolic technique lasts shorter as the colon is not taken down, this technique is not widely preferred since it is eligible for younger and lean patients with low mesenteric adipose tissue (24). This technique was preferred in only 8 (6.9%) patients in our series. No comparison was made since we had a low number of patients with the transmesocolic approach.

There are series of pyeloplasty performed without use of double-J stent in the literature (25,26). There are studies suggesting that

stentless pyeloplasty is a safe and feasible technique. In 2007, Shalhav et al. (27) published the outcomes of 5 of their patients in whom they performed laparoscopic stentless pyeloplasty. Dismembered technique was preferred for all patients. Double-J stent was used in all patients who underwent LTP in our study. Double-J stent was removed on postoperative month 1 in average.

During the perioperative period 1 (0.8%) patient had grade 3 complication on the basis of the Satava classification; and during the postoperative period, 2 (1.7%) patients had grade 1, 7 (6%) patients had grade 2 and 1 (0.8%) patient had grade 3 complication on the basis of the Clavien classification (Table 2). One patient (0.8%) had perioperative left colon injury during port insertion. Primary repair was performed laparoscopically in this patient. This patient did not have any associated problem postoperatively. The postoperative complication rate was found to be 8.6%. Two (1.7%) patients had high fever (grade 1), 3 (2.6%) patients had prolonged extravasation of urine (grade 2) and 5 (4.3%) patients had paralytic ileus (grade 2). These patients improved during postoperative follow-up with medical treatment. Percutaneous nephrostomy catheter was inserted in one (0.8%) of the patients with extravasation of urine (grade 3 complication).

The mean follow-up time was 44 (12-120) months. There is no common consensus about the follow-up duration. In our clinic, US was taken at month 1-3 postoperatively and MAG-3 scintigraphy at month 6 postoperatively for assessment purposes and the follow-up intervals were planned accordingly. During the follow-up, 8 (6.9%) patients had recurrent obstruction. Endopyelotomy was applied in 7 (6.1%) patients for recurrence. Two (1.7%) of these patients were tertiary cases, who underwent LTP following open pyeloplasty. One (0.8%) patient had nephrectomy. Complications are similar when compared to the literature (9,10,11).

Study Limitations

Outcomes and complication rates in adult patients who underwent LTP in our center are presented in this study. This study suggests that LTP is technically feasible in adult patients with UPJO. However, our study has several limitations. The data were collected longitudinally and verified retrospectively, which could have introduced error. Another limitation of our study is that we did not compare the technique with open surgery. However, we performed the general principles of open surgery during the procedure. Despite these limitations, our results suggest that LTP is a safe and feasible treatment in the management of UPJO. Future studies should be prospectively designed to overcome the existing limitations.

Conclusion

LTP is an effective and safe approach in surgical treatment of adult patients diagnosed with UPJO. It may be a first-line

therapy with its low complication rates, eligibility in patients with anatomic variations and short hospital stay.

Ethics

Ethics Committee Approval: Ethics committee approval was not applied because of retrospective design of the study.

Informed Consent: All patients provided a signed informed consent form.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: Ç.D., B.Ö., Concept: Ç.D., O.Ö., Design: Ç.D., S.Ç., Data Collection or Processing: Ç.D., B.Ö., S.Ç., Analysis or Interpretation: S.Ç., O.Ö., Z.T., Literature Search: O.Ö., Writing: Ç.D., B.Ö., O.Ö.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

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Prevalence and Possible Risk Factors of Overactive Bladder Symptoms in Women Living in the City of İzmir

İzmir İlinde Yaşayan Kadınlarda Aşırı Aktif Mesane Semptomlarının Prevalansı ve Olası Risk Faktörleri

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What's known on the subject? and What does the study add?

Overactive bladder is a condition that affects quality of life and daily social, emotional and physical activities of patients. This study aims to evaluate the prevalence and possible risk factors of overactive bladder symptoms among women living in a western city of Türkiye, İzmir.

Abstract

Objective: We aimed to evaluate the prevalence and possible risk factors of overactive bladder symptoms (OABS) among women living in a western city of Türkiye, İzmir.

Materials and Methods: A questionnaire and the validated Overactive Bladder Symptom Score were filled by urologists with face-to-face interview. The prevalence of OABS and independent possible risk factors of OABS such as age, obesity, systemic diseases, educational level, marital status and number of births were analyzed. The participants with OABS and without OABS were compared in terms of possible risk factors.

Results: A total of 719 women were included and the prevalence of OABS was 42.8% in our study. The prevalence of OABS with urinary incontinence (UI) (OAB_{wet}) was 69.2% and the prevalence of OABS without UI (OAB_{dry}) was 30.8% and nocturia was the most common OABS besides urgency. There was a statistically significant association between OABS and presence of nocturia and UI types ($r=0.363$, $p<0.001$, $r=0.568$, $p<0.001$). The key risk factors for OABS according to multivariate analysis were obesity, hypertension, diabetes mellitus, marital status and lower education level.

Conclusion: The prevalence of OABS was 42.8% among adult Turkish women in the city of İzmir. Obesity, hypertension, diabetes mellitus, lower education and being married were significantly related to OABS in women.

Keywords: Overactive bladder symptoms, Prevalence, Risk factors, Urinary incontinence

Öz

Amaç: Türkiye'nin batı kenti İzmir'de yaşayan kadınlarda aşırı aktif mesane semptomlarının (AAMS) prevalansını ve olası risk faktörlerini değerlendirmeyi amaçladık.

Gereç ve Yöntem: Validasyonu yapılmış Aşırı Aktif Mesane Semptom Skoru (OABSS) formunu içeren anket, katılımcılarla yüz yüze görüşme ile ürologlar tarafından dolduruldu. AAMS prevalansı ve yaş, obezite, komorbidite, eğitim düzeyi, evlilik durumu ve doğum sayısı gibi AAMS'nin bağımsız olası risk faktörleri değerlendirildi. AAMS olan ve olmayan katılımcılar olası risk faktörleri açısından karşılaştırıldı.

Bulgular: Çalışmamıza toplam 719 kadın dahil edildi ve AAMS prevalansı %42,8 idi. İdrar kaçırma ile birlikte olan AAMS prevalansı %69,2, idrar kaçırma birlikteliği olmaksızın AAMS prevalansı %30,8 olarak bulundu ve acil sıkışma hissi ile birlikte en sık görülen semptom noktüriydi. AAMS ile noktüri ve idrar kaçırma tipleri arasında istatistiksel olarak anlamlı ilişki vardı ($r=0,363$, $p<0,001$, $r=0,568$, $p<0,001$). Çok değişkenli analize göre AAMS için temel risk faktörleri obezite, hipertansiyon, diabetes mellitus, evlilik durumu ve düşük eğitim seviyesi idi.

Sonuç: İzmir ilindeki yetişkin Türk kadınlarında AAMS prevalansı %42,8 idi. Obezite, hipertansiyon, diabetes mellitus, düşük eğitim ve evli kadınlar arasında AAMS ile anlamlı ilişki vardı.

Anahtar Kelimeler: Aşırı aktif mesane semptomları, Prevalans, Risk faktörleri, İdrar kaçırma

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Received: 17.05.2018 **Accepted:** 22.05.2018

Cite this article as: İrer B, Şen V, Bozkurt O, Demir Ö, Esen A. Prevalence and Possible Risk Factors of Overactive Bladder Symptoms in Women Living in the City of İzmir. J Urol Surg 2018;5(3):180-187.

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Introduction

Overactive bladder (OAB) is a condition that affects health-related quality of life and daily social, emotional and physical activities of patients (1). The International Continence Society (ICS) defines OAB as urgency, with or without urgency urinary incontinence (UUI), usually with frequency and nocturia (2). In several population-based studies, the prevalence of OAB symptoms (OABS) has been reported to be between 11% and 32.6% (3,4,5). Although patients with OABS (with or without UUI) have high level depression, sexual problems, and distress in daily life, most patients do not consult a doctor for any treatment and continue to suffer from OABS (3).

The underlying causes of the pathophysiology of OABS have not been fully established. For this reason, many studies have been conducted in many countries to establish the causes and risk factors for OABS in their populations. Aging, chronic diseases, such as diabetes mellitus (DM) and hypertension, obesity, socioeconomic status, being married and childbirth have been shown to be associated with OABS (5,6,7,8,9,10).

There are several studies in the literature comparing the risk factors for OABS, lower urinary tract symptoms and urinary incontinence (UI) in the Turkish population and showing the effect of these conditions on the quality of life of patients (11,12,13). In this study, we aimed to evaluate the prevalence and possible risk factors for OABS and severity of OABS among adult women living in a western city of Turkiye, İzmir, with face-to-face interviews by experienced urologists.

Materials and Methods

This study was approved by the Ethics Committee of Dokuz Eylül University with number 2016/05-35. The cohort included all women over 18 years of age who accepted to participate in the study and completed the informed consent form on a weekend for International Women's Day Campaign at İzmir International Fair. The questionnaire used in the study was completed by participants during face-to-face interviews with urologists. Participants who were unable to respond to questionnaire due to cognitive disability and who had dementia or any neurological disease were excluded from the study. Also women having symptoms of cystitis, such as dysuria and fever, and those receiving antibiotic therapy for urinary tract infections were excluded from the study.

The questionnaire consisted of 2 parts. Socioeconomic and demographic features such as age, occupation, level of education, parity, marital status, and physician referral status, as well as systemic diseases such as hypertension, DM, coronary artery disease, chronic obstructive pulmonary disease, etc. and previous operation history were evaluated in the first part;

the validated International Consultation on Incontinence Questionnaire-Short Form (ICIQ-SF) (14) and Overactive Bladder Symptom Score (OABSS) (15) were administered in all participants in the second part. Definitions for OABS and UI types were used according to the standard definitions of the ICS (2). The 8-item Overactive Bladder Questionnaire (OAB-V8) consists of 8 questions each of which can be graded by the patient within a scale of never (0); few (1); sometimes (2); quite a few (3); usually (4); and always (5). Thus, the total score ranges from a minimum of 0 to a maximum of 40. A total score of 8 or greater on the OABSS indicates high risk for OAB (15). Therefore, for subsequent analysis, we classified women with an OABSS greater than 8 as having OABS (group 1) and women with an OABSS less than 8 as having no OABS (group 2). The participants with or without OABS were evaluated in terms of risk factors such as age, comorbidities, parity, presence or absence of incontinence, status of doctor consultation, education level, marital status and total ICIQ-SF score and OABSS. The participants were also divided into 3 groups according to age distributions and each group was evaluated in terms of OABS status.

Statistical Analysis

Categorical variables were compared with chi-square test and continuous variables were compared with independent samples t-test. Multivariate regression analysis was used to define the potential risk factors for OAB. The results were expressed as adjusted odds ratio with 95% confidence interval. Statistical analyses were performed with Statistical Package of Social Sciences version 22.0 (SPSS, Chicago, Illinois, United States of America) and a p value of less than 0.05 was considered statistically significant.

Results

The mean age of 719 women participating in the study was 51.2 ± 11.1 years. Socioeconomic and demographic characteristics, comorbidities, UI status and OABS of the participants are presented in Table 1. The prevalence of OABS was 42.8% and the prevalence of UI was 50.3% in the study. In the participants with OABS, the prevalence of OABS with UI (OAB_{wet}) was 69.2% and the prevalence of OABS without UI (OAB_{dry}) was 30.8%. In this study, the incidence of frequency, nocturia, UUI was found to be 72.3%, 61.8%, 42.7% and 37.7%, respectively. In our study, 86.7% of participants with OABS consulted a doctor previously, whereas 13.3% of participants did not consult a doctor ($p < 0.001$).

In this study, we showed using univariate analysis that the most significant potential risk factors associated with OABS were age ($p < 0.001$), DM ($p < 0.001$), hypertension ($p < 0.001$), parity ($p < 0.001$), education level ($p = 0.002$), marital status ($p < 0.001$) and

obesity ($p < 0.001$) (Table 2). However, there were no statistically significant relationship between OABS and the other possible risk factors (Table 2). Patients with OABS had more frequent UI and nocturia than patients without OABS (Table 3). In addition,

Table 1. Socioeconomics and demographic characteristics, comorbidities, continence and overactive bladder symptoms status of participants

Age (mean \pm SD)	51.2 \pm 11.1
Number of births (parity) (range)	1.8 (0-10)
Overactive Bladder Symptom Score (mean \pm SD)	9.0 \pm 8.6
ICIQ-SF Score (mean \pm SD)	4.1 \pm 5.1
BMI (mean \pm SD)	28.7 \pm 3.3
Age group	
≤ 40 years (n, %)	119 (16.6%)
40-60 years (n, %)	472 (65.6%)
≥ 60 years (n, %)	128 (17.8%)
Marital status	
Never married (n, %)	88 (12.2%)
Divorced (n, %)	125 (17.4%)
Married (n, %)	506 (70.4%)
Education level	
Primary and secondary school (n, %)	310 (43.1%)
High school (n, %)	225 (31.3%)
College and higher education (n, %)	184 (25.6%)
Comorbidities	
Diabetes mellitus (n, %)	100 (13.9%)
Hypertension (n, %)	238 (33.1%)
Thyroid diseases (n, %)	28 (3.9%)
Coronary artery disease (n, %)	34 (4.7%)
Chronic obstructive pulmonary disease (n, %)	8 (1.1%)
Number of births (parity)	
Nulliparous (n, %)	128 (17.8%)
< 3 births (n, %)	442 (61.5%)
≥ 3 births (n, %)	149 (20.7%)
Urinary incontinence	
Yes	362 (50.3%)
No	357 (49.7%)
Urinary incontinence types	
Stress UI (n, %)	250 (69.1%)
Urge UI (n, %)	62 (17.1%)
Mixed UI (n, %)	50 (13.8%)
Overactive Bladder Symptom Score ≥ 8	
Yes (group 1)	308 (42.8%)
No (group 2)	411 (57.2%)
Status of doctor consultation	
Yes	393 (54.7%)
No	326 (45.3%)

UI: Urinary incontinence; SD: Standard deviation, BMI: Body mass index, ICIQ-SF: International Consultation on Incontinence Questionnaire-Short Form

there were statistically significant association and correlation between OABS severity and presence of nocturia and UI types ($r = 0.363$, $p < 0.001$, $r = 0.568$, $p < 0.001$). When we examined the relationship of age with OABS severity and storage symptoms, we found a statistically significant difference between age groups in terms of OABS severity and storage symptoms especially nocturia and UI (Table 4). Body mass index (BMI), total OABSS and frequency of nocturia increased with age (Table 4).

According to our results, major risk factors for OABS were DM, hypertension, obesity, marital status and low level of education in multivariate logistic regression analysis (Table 5). When we evaluated univariate and multivariate analyses, we found that some variables showed different relationships with OABS. There was a statistically significant difference in age and parity between participants with and without OABS ($p < 0.001$) (Table 2), whereas the statistical significance was not observed in multivariate analysis (Table 5).

Discussion

OAB is a chronic disease and it is defined by the ICS as urgency, with or without UUI, usually with frequency and nocturia (2). The present study was designed as a community-based survey to evaluate the risk factors and the prevalence of OABS in women, living in İzmir, a western city of Türkiye. In our study population, the prevalence of OABS was 42.8%. According to age groups, the prevalence of OAB was 27.7% in those below 40 years of age, 44.9% in those aged 40-60 years, and 49.2% in women above 60 years of age. The European Prospective Investigation into Cancer and Nutrition study showed that the global prevalence of OABS was 11.8% and 51% of men and 56% of women aged 40-59 years suffered from storage symptoms (3). In two different studies conducted in Japanese women, the prevalence of OABS was ranged between 8.1% and 11% (6,7). Kim et al. (8) reported that the prevalence of OABS was approximately 5.2% among adult Korean women. The prevalence of OABS was found to be 6.0% in the Chinese population (9). The differences between the prevalence rates in our study and other studies may be related to inclusion criteria, such as age, race, systemic diseases, definition variety of OABS, design of questionnaires and survey methods. Most of these studies were planned at outpatient clinics and the participants were interviewed via telephone or internet and the OABSS questionnaire was not used for determination of OABS. Although reaching a wider range of participants in surveys conducted via telephone and internet, the disadvantage of such studies is the time allocated for participation is limited and attendees' participation in the questionnaires is low. For these reasons, it may be more difficult to evaluate the actual situation of participants during telephone and internet interviews than in face-to-face interviews. This may lead to differences in OABS

Table 2. Distribution of potential risk factors between overactive bladder symptoms groups

	Group 1 n=308	Group 2 n=411	p value
Age (mean ± SD)	53.0±10.3	49.8±11.6	0.035
Parity (number of births) (mean ± SD)	2.0±1.2	1.6±1.2	<0.001
BMI (mean ± SD)	29.4±3.2	28.2±3.3	0.W
Total OAB Symptom Score	16.9±7.7	3.2±2.2	<0.001
Frequency of nocturia	1.8±1.5	0.6±0.7	<0.001
Diabetes mellitus (n, %)			
Yes	61 (19.8%)	39 (9.5%)	<0.001
No	247 (80.2%)	372 (90.5%)	
Hypertension (n, %)			
Yes	132 (42.9%)	106 (25.8%)	<0.001
No	176 (57.1%)	305 (74.2%)	
Hyperthyroidism (n, %)			
Yes	9 (2.9%)	10 (2.4%)	0.686
No	299 (97.1%)	401 (97.0%)	
Hypothyroidism (n, %)			
Yes	6 (1.9%)	3 (0.7%)	0.146
No	302 (98.1%)	408 (99.3%)	
Coronary artery disease (n, %)			
Yes	19 (6.2%)	15 (3.6%)	0.055
No	289 (93.8%)	396 (96.4%)	
Chronic obstructive pulmonary disease (n, %)			
Yes	5 (1.6%)	3 (0.7%)	0.115
No	303 (98.4%)	408 (99.3%)	
Education level (n, %)			
Primary and secondary school	155 (50.3%)	155 (37.7%)	0.002
High school	90 (29.2%)	135 (32.8%)	
College and higher education	63 (20.5%)	121 (29.4%)	
Marital status			
Never married	21 (6.8%)	67 (16.3%)	<0.001
Divorced	50 (16.2%)	75 (18.2%)	
Married	237 (76.9%)	269 (65.5%)	
Number of births (parity)			
Nulliparous	33 (10.7%)	95 (23.1%)	<0.001
<3	199 (64.6%)	243 (59.1%)	
≥3	76 (24.7%)	73 (17.8%)	
Obesity			
Yes	125 (40.6%)	100 (24.3%)	<0.001
No	183 (59.4%)	311 (75.7%)	
Age groups			
<40 year	33 (10.7%)	86 (20.9%)	0.001
40-60 year	212 (68.8%)	260 (63.3%)	
>60 year	63 (20.5%)	65 (15.8%)	

OAB: Overactive bladder, SD: Standard deviation, BMI: Body mass index
One-way ANOVA test for continuous variable and chi-square test for categorical variable

Table 3. Relationship of presence of overactive bladder symptoms with urinary incontinence types and nocturia

	Group 1 (n=308)	Group 2 (n=411)	p value	r value
UI types (n, %)				
None UI	47 (15.3%)	310 (75.4%)	<0.001	0.568
UUI	51 (16.6%)	11 (2.7%)		
SUI	162 (52.6%)	88 (21.4%)		
MIU	48 (15.6%)	2 (0.5%)		
Nocturia (n, %)				
Yes	253 (82.1%)	220 (53.5%)	<0.001	0.363
No	55 (17.9%)	191 (46.5%)		

UI: Urinary incontinence, SUI: Stress incontinence, UUI: Urgency urinary incontinence, MIU: Mixed urinary incontinence
Pearson's correlations and chi-square test for categorical variable

Table 4. Distribution of overactive bladder symptoms severity, storage symptoms, body mass index and frequency of nocturia according to age groups

	≤40 year n=119	40-60 year n=472	60 year< n=128	p value
Frequency (n, %)				
No	34 (28.4%)	126 (26.7%)	39 (30.5%)	0.679
Yes	85 (71.6%)	346 (73.3%)	89 (69.5%)	
Urgency (n, %)				
No	74 (62.2%)	271 (57.4%)	67 (52.3%)	0.294
Yes	45 (37.8%)	201 (42.6%)	61 (47.7%)	
Nocturia (n, %)				
Yes	51 (42.9%)	191 (40.5%)	33 (25.8%)	0.005
No	68 (57.1%)	281 (59.5%)	95 (74.2%)	
UUI (n, %)				
Yes	90 (75.6%)	286 (60.6%)	72 (56.3%)	0.003
No	29 (24.4%)	186 (39.4%)	52 (43.8%)	
OABSS ≥8				
No	86 (72.3%)	260 (55.1%)	65 (50.8%)	0.001
Yes	33 (27.7%)	212 (44.9%)	63 (49.2%)	
BMI (mean ± SD)	28.2±3.1	28.7±3.4	29.5±3.0	0.003
Total OABSS (mean ± SD)	6.6±7.6	9.2±8.6	10.7±9.0	0.001
Frequency of nocturia (mean ± SD)	0.8±1.0	1.1±1.3	1.4±1.3	0.002

UUI: Urgency urinary incontinence, BMI: Body mass index, SD: Standard deviation, OABSS: Overactive Bladder Symptom Score
Pearson's correlations and chi-square test for categorical variable

prevalence. Unlike previous studies, according to the best of our knowledge, our study was the first community-based study designed as face-to-face interviews and the OABSS was filled by experienced urologists.

There are few studies evaluating the prevalence of OABS in Türkiye. Zumrutbas et al. (11) reported that the prevalence of storage symptoms was 64.1% in women in a western city of Türkiye, Denizli. In our study, the prevalence of frequency, nocturia, urgency and UUI was found to be 72.3%, 61.8%, 42.7% and 37.7%, respectively.

OABS is defined by the ICS as wet and dry for more precise diagnosis of OAB and for more effective treatment. Most of studies in the literature have found different results on the prevalence of OAB_{dry} and OAB_{wet}. Wang et al. (9) showed that the prevalence of OAB_{wet} was 70.0% and the prevalence of OAB_{dry} was 30.0% among individuals with OAB. Wen et al. (10) showed that the OAB_{dry}-to-OAB_{wet} ratio was about 1:1. In present study, the prevalence of OAB_{wet} was 69.2% and the prevalence of OAB_{dry} was 30.8% in individuals with OAB and the OAB_{dry}-to-OAB_{wet} ratio was about 2.3:1. Similar to the differences in the

Table 5. Potential risk factors associated with overactive bladder symptoms

Variable	Overactive bladder symptoms			
	B coefficient	Odds ratio	95% CI	p
Age	0.011	1.012	0.995-1.028	0.176
Diabetes mellitus	-0.485	0.616	0.384-0.989	0.045
Hypertension	-0.532	0.588	0.412-0.839	0.003
Parity (>2 delivery)	0.318	1.374	0.819-2.307	0.229
Obesity	-0.734	0.480	0.344-0.670	<0.001
Marital status (married)	-0.509	0.601	0.404-0.893	0.012
Education level (primary school)	0.501	1.650	1.093-2.490	0.017

B: Beta regression coefficient, CI: Confidence interval
Multivariate regression analyses

studies of the OABS prevalence, the cause of the difference may be related to study design and age, gender and comorbid conditions of the participants involved in the study.

Many studies in the literature aimed to determine the risk factors for OABS. Possible risk factors for OABS include advanced age, obesity, hypertension, drug use, lower educational level, marital status, parity, and alcohol consumption (8,9,10). In present study, according to multiple logistic models, DM, hypertension, being married, low education level and obesity were associated risk factors for OABS.

Previous researchers have pointed to an increase in the prevalence of OABS associated with aging (3,8,9). This increase may be explained by aging processes that cause deterioration of the bladder functions due to decreased muscle and neurological activities, changes in physical status by aging and age-related factors such as menopause and systemic diseases. In this study, patients with OABS were older than those without OABS. As the age increased, frequency of OABS, especially nocturia and UI, also increased. Moreover, we found that aging-related systemic diseases such as DM, obesity and hypertension were key risk factors for OABS.

Previous studies reported that there was an association between DM and OABS (8,9,16). In addition, Kaplan et al. (17) examined the urodynamic findings in DM patients and found detrusor overactivity in 55% of patients. One of the late complications of DM is peripheral neuropathy (17). The cause of diabetic neuropathy includes impaired glucose metabolism, ischemia, superoxide-induced free radical formation, damaged axonal transport, and metabolic derangement of the Schwann cell resulting in segmental demyelination and impairment of nerve conduction (18). Therefore, peripheral neuropathy can cause detrusor overactivity and may be an important risk factor for

OABS (19). Consistent with the literature, in our study, DM was a significant risk factor for OABS.

Obesity was demonstrated to be a risk factor that was significantly associated with OABS in several studies (8,9,10,20). A patient with a BMI greater than 30 kg/m² is at increased risk for the onset of OABS (20,21). Our results showed a significant association between OABS and obesity. This association can be explained by mechanical, neuroendocrine and inflammatory factors. Obesity may increase bladder pressure which, in turn, causes or increases detrusor instability and results in OABS (22). On the other hand, adipose tissue may increase autonomic nerve activity by secreted leptin hormone, especially noradrenergic sympathetic nerves, and increased sympathetic activity results in urinary frequency (23). Furthermore, obesity is associated with a chronic inflammatory response resulting in oxidative stress, increased acute phase reactants, and activation of inflammatory signaling pathways (24). Due to the increase in concentrations of interleukin (IL)-1, IL-6, and tumor necrosis factor alpha in detrusor may result in overactivity (25).

In the literature, there are few studies linking hypertension to OABS (8,26). However, there are many studies showing the relationship of OAB with hypertension and metabolic syndrome (27,28,29). Kim et al. (8) showed significant associations between OABS and hypertension. Hypertension and vascular risk factors result in increased ischemia, which leads to structural changes in the bladder (30). Moreover, when the bladder blood flow decreases because of hypertension, adenosin triphosphate and prostaglandin E2 release from the urothelium and contractions occur in the bladder (31). Therefore, hypertension and vascular risk factors can lead to OABS. Similarly to the previous study, hypertension was found to be a risk factor for OABS in this study.

Low education level and being married are the possible risk factors of OABS in women. Previous studies and our study demonstrated a clear relationship between low education level and risk of OABS (9,32). Smoking, poor hygiene and urinary tract infections may be more frequent in people with lower education levels, while those with higher education levels tend to search better health behaviors and consequently have a healthier lifestyle. However, there are conflicting results in the literature suggesting that being married was a risk factor for OABS. Similar to our results, Wang et al. (9) demonstrated that being married was a risk factor for OABS. On the contrary, Kim et al. (8) found that unmarried status was significantly related to OABS. The reason for this disparity may depend on the age, socioeconomic level, type of delivery and number of births of the participants.

Despite the considerable physical, social and psychological morbidity related with OABS, many patients do not consult

healthcare professionals. OABS, especially storage problems, may embarrass patients, thus, patients may not volunteer to talk to their doctor about these complaints. Additionally, patients with OABS may believe that no effective treatment was available for OABS. Milsom et al. (33) reported that 40% of individuals with OABS did not seek medical help. Üçer et al. (34) showed that 57% of patients with OAB symptoms had not been previously admitted to hospital. In our study, this rate was found to be 13.7%.

Study Limitations

The current study has some limitations. First, we evaluated the participants on a weekend for International Women's Day Campaign at İzmir International Fair and in a limited time, the number of participants can be considered relatively small compared to previous studies. Second, urinalysis was not performed to identify urinary tract infections. However, the OAB-V8 was filled by urologists during face-to-face interviews; patients, who complained of fever and dysuria and have recently been treated for cystitis, were identified with anamnesis and excluded from the study.

Conclusion

The prevalence of OABS in Turkish women was high and OABS affected almost half of the adult women and risk factors associated with OABS were similar to those in other countries. In accordance with the previous studies, obesity, medical comorbidities such as DM and hypertension, marital and low education were key risk factors for OABS and aging was associated with the presence of OABS and storage symptoms. According to the best of our knowledge, our study was the first community-based study designed as face-to-face interviews by experienced urologists. We assume that our study may contribute to the literature since it determines OABS prevalence and risk factors in women living in a western city of Türkiye, İzmir.

Ethics

Ethics Committee Approval: This study was approved by the Ethics Committee of Dokuz Eylül University with number 2016/05-35.

Informed Consent: All participant completed the informed consent form.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: B.İ., V.Ş., O.B., Ö.D., A.E., Concept: B.İ., V.Ş., O.B., Ö.D., A.E., Design: B.İ., V.Ş., O.B., Ö.D., A.E., Data Collection or Processing: B.İ., V.Ş., Analysis or Interpretation: B.İ., V.Ş., O.B., Literature Search: B.İ., Writing: B.İ., O.B.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

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A Case Report of Prostatic and Peritoneal Hemangioendothelioma

Prostatik ve Peritoneal Hemanjiyoendoteliyoma: Bir Olgu Sunumu

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Abstract

Epithelioid hemangioendothelioma is a rare endothelial neoplasm that is uncommonly described in the urinary system. To date, only one case has been described as originating from the prostate. We report a second case of prostatic epithelioid hemangioendothelioma, this one in a 71-year-old man. Epithelioid hemangioendothelioma was found on transurethral resection of the prostate with discovery of extensive peritoneal dissemination.

Keywords: Hemangioendothelioma, Vascular neoplasms, Prostatic neoplasms

Öz

Epiteloid hemanjiyoendoteliyoma; ürolojik sistemde olağandışı olarak tanımlanan nadir bir endotelial neoplazmdir. Bugüne kadar, prostattan kaynaklanan tek bir olgu tarif edilmiştir. Bu yazıda; 71 yaşındaki bir erkek hastada, literatürde ikinci olarak görülen bir prostatik epiteloid hemanjiyoendoteliyoma olgusu sunulmuştur. Epiteloid hemanjiyoendoteliyoma, prostatın transüretal rezeksiyonu sırasında geniş peritoneal yayılımın görülmesi ile saptanmıştır.

Anahtar Kelimeler: Hemanjiyoendoteliyoma, Vasküler neoplazmlar, Prostatik neoplazmlar

Introduction

Epithelioid hemangioendothelioma (EHE) is a rare endothelial neoplasm first described by Weiss and Enzinger (1) in 1982. EHE is part of a family of hemangioendotheliomas and is characterized by proliferation of epithelioid endothelial cells. It is thought to have biologic behavior intermediate between that of hemangiomas and angiosarcomas (2). Initially believed to be characterized by low malignant potential, however, it is now documented to have high local recurrence potential, and even metastatic risk in nearly one-third of cases (3).

EHE occurs at a spectrum of ages most commonly involving the soft tissues, lungs, liver, and bones. Rarely is it found in the urinary system (4) and to date only one case has been described as originating from the prostate (3). Here, we present a case of EHE initially found on transurethral resection of the prostate (TURP) with subsequent discovery of extensive peritoneal involvement.

Case Presentation

A 71-year-old man with a significant cardiovascular medical history as well as benign prostatic hyperplasia (BPH) and renal cell carcinoma presented with 1 week of painless gross hematuria and lightheadedness. One month previously, he had open infra-renal aortic aneurysm repair and removal of infected stent graft with subsequent aortobifemoral bypass. Computed tomography (CT) scan of the abdomen and pelvis showed a possible endovascular leak and what was thought to be a 3.0x3.0 cm prostatic abscess in the right lobe of the prostate.

Due to the signs of sepsis and his recent history of aneurysm repair and grafting, the patient was placed on broad spectrum antibiotics and taken urgently to the operating room for drainage of the prostatic abscess via TURP. The left lobe of the prostate had the typical appearance of BPH. The tissue in the right lobe was clearly abnormal; a thick white material was encountered, but no frank abscess was identified.

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Received: 09.05.2017 **Accepted:** 17.07.2017

Cite this article as: Lao M, Beshai B, Ricci A, Wagner J. A Case Report of Prostatic and Peritoneal Hemangioendothelioma. J Urol Surg 2018;5(3):188-190.

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Histologic analysis revealed adenomatous and fibromuscular stromal hyperplasia with chronic active inflammatory changes, squamous metaplasia of prostatic ducts, bland infarction and reactive glandular and stromal atypia. Dissecting in-between benign prostatic ducts and acini were solid clusters of atypical epithelioid cells with ample eosinophilic cytoplasm and limited lumen formation. Occasional characteristic "blister cells" were noted. Mitoses were rare. No overt malignant cytologic features were seen with no evidence of hemorrhagic necrosis. Immunohistochemical assays from cluster of differentiation 31, cluster of differentiation 34, factor 13a, friend leukemia integration-1 transcription factor and erythroblast transformation-specific-related gene were positive consistent with vascular phenotype and denying prostatic carcinoma. Histology was interpreted as vascular tumor of intermediate malignant potential (i.e. EHE, Figure 1).

After TURP, the patient had an unstable clinical course and continued to deteriorate. CT angiogram showed large fluid collections measuring 8.6 cm and 5.7 cm. Given the patient's clinical course, he was brought to surgery where exploratory laparotomy revealed 5 liters of blood clot and peritoneal cancerous dissemination involving the small bowel, peritoneal walls, and omentum. It was unclear whether the fluid collections were iatrogenic seromas or malignant ascites. Initial frozen section indicated malignancy and final pathology revealed

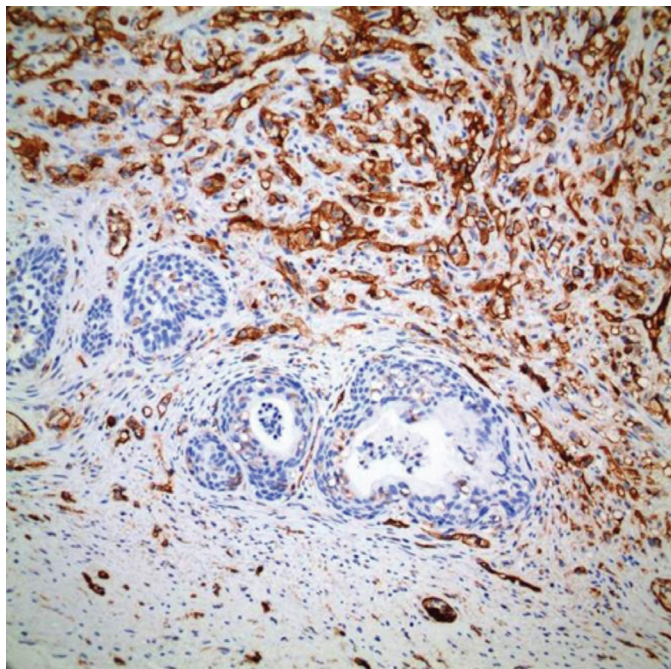


Figure 1. Prostate (transurethral resection of the prostate), cluster of differentiation 31, original magnification, 200x: cluster of differentiation 31 highlights the cytoplasm and membranes of infiltrative tumor cells, sparing normal prostatic glands and stroma, with a strong internal control expression in normal blood vessels. Such strong cluster of differentiation 31 positivity confirms the neoplasm's vascular origin

malignant EHE. Peritoneal histology was of higher grade than the prostate tumor, resembling epithelioid angiosarcoma (Figure 2). The patient expired shortly thereafter.

All of the procedures described in this report were standard of care. The patient provided informed consent for the standard of care procedures described per hospital requirements, however no informed consent for research was needed as this was not a research study.

Discussion

EHE is a rare endothelial vascular neoplasm. The incidence is less than 0.1 per 100,000 people, and the mean age at diagnosis is 42 years with a slight female prevalence (5). EHE usually originates in soft tissues, liver, lungs, or bone; rarely has it been reported to originate in the urinary system. When discovered in the bladder, the common presenting complaint is hematuria (4). When involving the kidney, it can be discovered on imaging as a heterogeneous mass (6). In our patient, imaging suggested the possibility of a prostatic abscess. EHE typically has a better prognosis than classic angiosarcoma, but with higher potential for metastatic disease than other hemangioendotheliomas (2).

The diagnosis of EHE cannot be made on imaging studies but rather requires a biopsy for histologic and immunohistochemical examination. The differential diagnosis should always include primary or metastatic epithelioid angiosarcoma, and even poorly

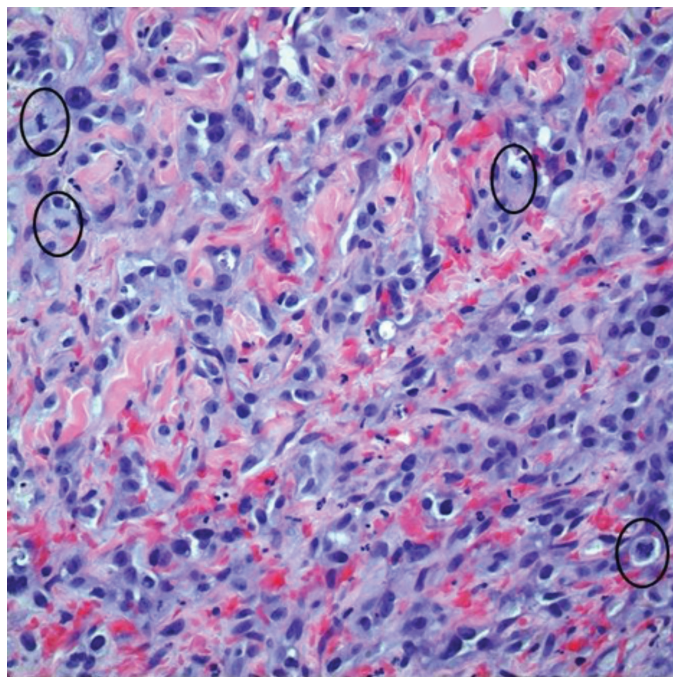


Figure 2. Peritoneal nodule, hematoxylin and eosin, original magnification, 400x: in contrast to tumor cells seen in prostatic primary, the epithelioid cells here show higher grade of atypia, pleomorphism, and hyperchromasia. In addition, increased mitotic activity is present (circles)

differentiated prostatic carcinoma (3). In the case presented here, the differential diagnosis also included prostate abscess, prostate adenocarcinoma, and a non-adenocarcinomatous cancer of the prostate. In contrast to EHE, angiosarcoma shows a greater degree of cellular pleomorphism, nuclear hyperchromatism, necrosis, and higher mitotic rate. There are no clear cut radiographic features to strongly suggest EHE, but there are some features that might be commonly seen. Imaging might reveal evidence of a mass that is often solid in appearance. Contrast-enhanced CT might reveal heterogeneous hypodense nodules with a ring-like low density border and a lower density center. Magnetic resonance imaging might show heterogeneous hypointense lesions on T1-weighted images and hypertense lesions on T2-weighted images (7).

Due to its rarity, no consensus exists on the management of urologic EHE. Clinical behavior can vary depending on the site of the disease. Surgical resection with clear margins should be performed if possible. In those with inoperable disease, a period of observation to assess tumor behavior is reasonable. Durable spontaneous regression has been reported (8). The role of medical therapy remains unclear. It is uncertain if pharmacological options have any real efficacy given the variable natural history of urologic EHE. Management has included chemotherapy and drugs that exploit angiogenic pathways and receptors for vascular endothelial growth factor. Studies have also reported using paclitaxel, bevacizumab, sunitinib, interferon-alpha, doxorubicin, 5-fluorouracil, cyclophosphamide, vinblastine, carboplatin, thalidomide, and etoposide (9). A novel gene fusion product, WWTR1-CAMTA-1 may inform future therapies (10). Radiotherapy has no place in the management of these tumors. The current report illustrates the differential diagnosis and management of this rare condition in a case that is particularly unique as it originated in the prostate. To our knowledge, ours' is only the second such case to be presented in the literature.

Acknowledgements

We thank Tara McLaughlin, PhD for her administrative and editorial assistance in revising and preparing this manuscript for publication.

Ethics

Informed Consent: All of the procedures described here were

standard of care. The patient provided informed consent for the standard of care procedures described, however no informed consent for research was needed as this was not a research study.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: J.W., M.L., B.B., Concept: J.W., M.L., B.B., A.R., Design: J.W., M.L., B.B., A.R., Data Collection or Processing: J.W., M.L., B.B., A.R., Analysis or Interpretation: J.W., M.L., B.B., A.R., Literature Search: M.L., B.B., Writing: J.W., M.L., B.B., A.R.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support

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Nephron-sparing Surgery without Angioembolization in Giant Angiomyolipoma: Is it Feasible?

Dev Anjiyomiyolipomda Anjiyoembolizasyon Olmadan Nefron Koruyucu Cerrahi: Uygulanabilir mi?

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Abstract

Varying sizes of renal angiomyolipoma (AML) have been reported in the literature, with the general consensus that a size greater than 10 cm can be termed a giant AML. Our patient presented with increasing abdomen girth since last 3 years. Contrast-enhanced computed tomography scan of the abdomen confirmed the presence of "AML" arising from the upper and mid pole of the right kidney with similar small foci in the contralateral kidney. The patient underwent nephron-sparing surgery with preserving the right lower pole with enucleation of multiple small foci in the right kidney. The surgical specimen, which was confirmed to be AML histopathologically, was 40 cm × 20 cm × 15 cm in size and 7000 g in weight. This represents the case of the largest AML with a dimension of up to 40 cm and managed by nephron-sparing surgery without prior angioembolization. AML larger than 10 cm is usually considered to be giant AML in the literature.

Keywords: Angioembolization, Giant angiomyolipoma, Nephron-sparing surgery, Renal angiomyolipoma, Nephrectomy

Öz

Literatürde çeşitli boyutlarda renal anjiyomiyolipom olguları bildirilmiştir ve 10 cm'den daha büyük olanlar için dev AML terimi genel ortak görüştür. Olgumuz, son üç yıldır artan karın şişliği ile başvurdu. Kontrastlı batin tomografisi hem sol böbrekte küçük ve çok odaklı hem de sağ böbreğin üst ve orta bölümünden köken alan büyük boyutlarda anjiyomiyolipomlar saptadı. Sağ böbreğin orta ve üst bölümüne uygulanan parsiyel nefrektomiye ek olarak alt kutuptaki küçük odaklara da enükleasyon uygulanarak, nefron koruyucu cerrahi yapıldı. Cerrahi örnek 40 cm × 20 cm × 15 cm boyutlarında ve 7000 g ağırlığında olup, histopatolojik açıdan AML olduğu doğrulandı. Bu, 40 cm'ye kadar bir boyuta sahip en büyük AML olgusudur ve öncesinde anjiyoembolizasyon olmaksızın nefron koruyucu cerrahi yapılmıştır. Boyutu genellikle 10 cm'den büyük olan AML, literatürde dev AML olarak kabul edilir.

Anahtar Kelimeler: Anjiyoembolizasyon, Dev anjiyomiyolipom, Nefron koruyucu cerrahi, Renal anjiyomiyolipom, Nefrektomi

Introduction

Renal angiomyolipoma (AML) is a benign tumor composed of adipose tissue, abnormal blood vessels and smooth muscle. AML is usually diagnosed incidentally on ultrasound but symptoms may vary from flank pain, palpable flank mass and hematuria to life-threatening hemorrhage (52%-91%) especially in those larger than 4 cm. Giant AML is usually managed by transarterial embolization (TAE), partial nephrectomy or total nephrectomy

as described in the literature. Our case represents the largest AML with a dimension of up to 40 cm which was managed by nephron-sparing surgery in the form of partial nephrectomy without prior embolization.

Case Presentation

A 35-year-old female patient presented with bloating sensation and increasing abdomen girth since last 3 years. Ultrasound

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Received: 16.05.2017 **Accepted:** 28.07.2017

Cite this article as: Arya A, Bhatyal H, Narang V, Agarwal S. Nephron-sparing Surgery without Angioembolization in Giant Angiomyolipoma: Is it Feasible? J Urol Surg 2018;5(3):191-193.

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revealed a large hyperechoic and heterogeneous mass arising from the right kidney and extending toward other side of the abdomen. Her serum creatinine level was 0.8 mg/dL. Contrast-enhanced computed tomography (CT) scan of the abdomen confirmed the presence of AML of size 35 cm × 18 cm arising from the upper and mid pole of the right kidney with multiple feeding vessels and similar small foci in the contralateral kidney (Figure 1). Magnetic resonance imaging of the brain revealed no signs of tuberous sclerosis and that were suggestive of sporadic AML. The possible treatment options including nephron-sparing surgery and total nephrectomy were explained to the patient. Midline abdomen

incision was taken from the xiphisternum to the pubic symphysis. A large mass arising from the upper and mid pole of the right kidney with multiple small foci in the lower pole was seen. The mass was mobilized and delivered partly outside the abdomen with intact vascularity for easy access to the renal pedicle from the inferior aspect. The renal pedicle was isolated and encircled by a vessel loop (Figure 2). Right partial nephrectomy involving the upper and mid poles was done with excision of 3 superficial lesions in the lower pole and preserving the remaining lower pole of the right kidney. Renal defect was closed with interrupted 2/0 vicryl sutures over an absorbable hemostat (Surgicel) after closure

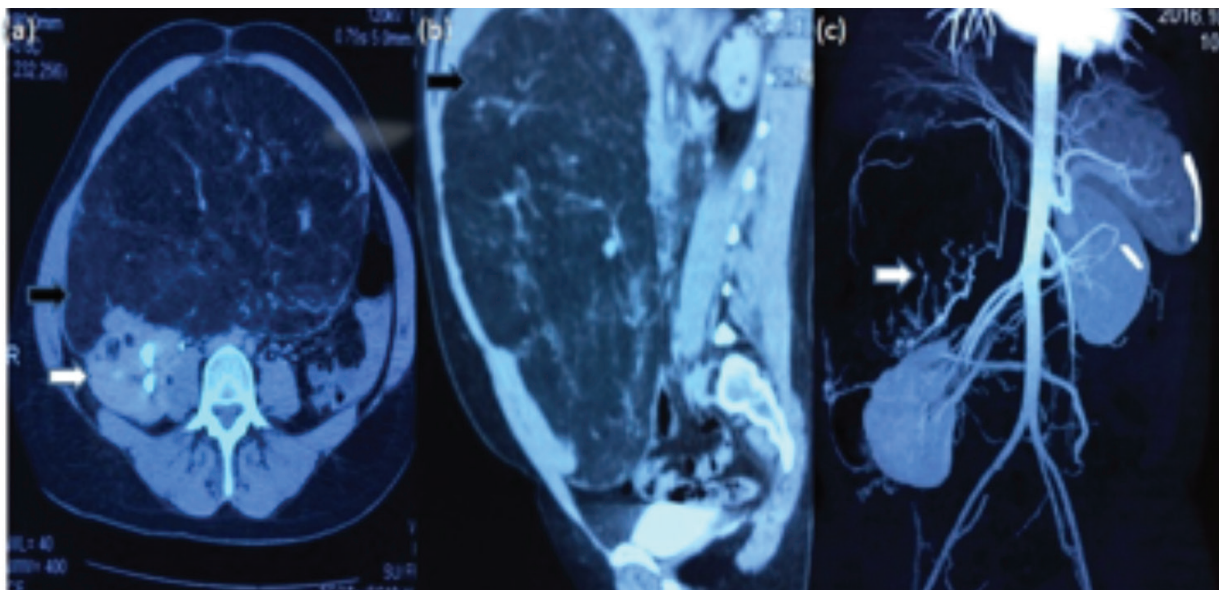


Figure 1. Computed tomography scan, a) Transverse, b) Sagittal image showing giant angiomyolipoma (black arrow) arising from upper and mid pole of right kidney and normal right lower pole (white arrow) with multiple small foci of angiomyolipoma, c) Computed tomography angiography demonstrates giant angiomyolipoma with multiple feeding vessels (white arrow)

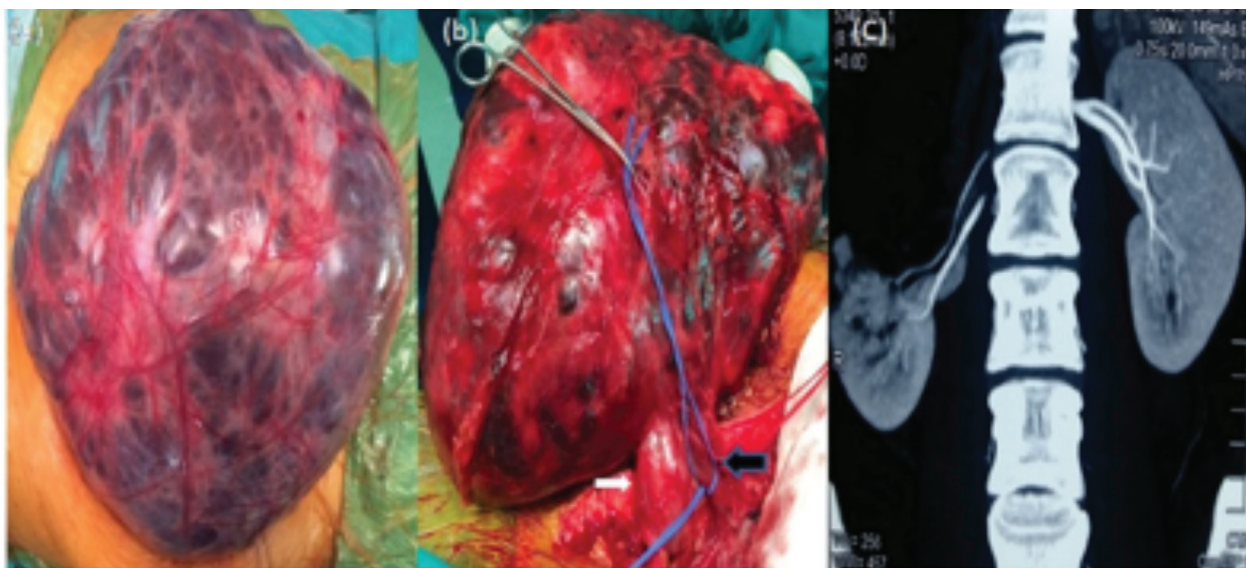


Figure 2. Intraoperative finding of a) giant angiomyolipoma delivered out of the abdomen, b) Giant angiomyolipoma with normal remaining right lower pole (white arrow) and renal pedicle (black arrow), c) Postoperative computed tomography angiography demonstrates normal functioning remaining right lower pole with intact vascularity and no recurrence

of the collecting system separately. The total warm ischemia time was 10 minutes with no major blood loss intraoperatively. The patient was discharged on day 7 with a serum creatinine level of 0.9 mg/dL. The mass was grossly measured 40x20x15 cm and weighed 7000 g. Histopathology of the specimen confirmed the presence of AML. CT renal angiography revealed normal functioning of the remaining right lower pole (6.4x4.1 cm) with no recurrence (Figure 2) after 6 months.

Written informed consent was obtained by participant.

Discussion

AML measuring over 10 cm is considered giant AML. AML larger than 4 cm usually requires treatment due to great risk of bleeding. Treatment could vary from TAE to surgical intervention in the form of either nephron-sparing surgery or total nephrectomy. TAE may obviate the need of emergency surgical intervention in the form of total nephrectomy especially in stable patients with retroperitoneal hemorrhage associated with giant AML. However, this comes with the risk of Post-embolization syndrome. These patients can be managed later on by elective nephron-sparing surgery due to the decrease in size of AML (30%-50%) (1). We managed our patient with giant AML by nephron-sparing surgery without prior embolization to avoid the risk of Post-embolization syndrome which is observed especially in large tumors. Giant AML usually managed by total nephrectomy (2). We should always attempt to preserve the renal function by nephron-sparing surgery in giant AML because they mostly arise from a small portion of normal kidney (3,4). Very few studies are there with regards to nephron-sparing surgery in giant AML with low complication rates of up to 12% and low local recurrence rates (5). There have been case reports of giant AML managed by preoperative embolization followed by partial nephrectomy (6,7). Very few case reports of giant AML managed by partial nephrectomy without angioembolization have been described in the literature, but the size of AML in that case was 24 cm (8,9). Our case represent the largest AML (40x20x15 cm) ever reported which was managed by nephrectomy with excision of multiple lesions in the remaining kidney without the need for prior embolization. AML could be sporadic or familial in association with tuberous sclerosis complex (TSC). It is very difficult to carry out partial nephrectomy in familial AML due to multiple and larger lesions. AML with TSC is usually associated with upregulation of mammalian target of rapamycin (mTOR) pathway. mTOR inhibitors, such as sirolimus and everolimus, should be considered in the management of familial AML prior

to nephron-sparing surgery as these agent decrease the size of the lesion and make the patient amenable to nephron-sparing surgery which is otherwise difficult to carry out.

Ethics

Informed Consent: Written informed consent was obtained by participant.

Peer-review: Internally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: A.A., H.B., V.N., S.A., Concept: A.A., H.B., V.N., S.A., Design: A.A., H.B., V.N., S.A., Data Collection or Processing: A.A., H.B., V.N., S.A., Analysis or Interpretation: A.A., H.B., V.N., S.A., Literature Search: A.A., H.B., V.N., S.A., Writing: A.A., H.B., V.N., S.A.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

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Case Report: A Truck Driver with Pelvic Pain

Olgu Sunumu: Pelvik Ağrısı Olan Bir Kamyon Şoförü

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Abstract

Extraskelatal myxoid kondrosarkoma (EMC) is a relatively rare soft tissue malignancy, originally described in the 1950s and characterized as a distinct entity from chondrosarcoma of the bone in the 1970s. These tumors most commonly originate in the proximal extremities, and their occurrence in the genitourinary tract is exceedingly rare, with few case reports citing origination in its component organs. We present a clinical case report of an EMC originating from the base of the penis with significant local involvement of the bony pelvis.

Keywords: Extraskelatal, Myxoid, Chondrosarkoma, Genitourinary

Öz

Ekstraskeletal miksoid kondrosarkom (EMK), başlangıçta 1950'li yıllarda tarif edilen ve 1970'li yıllarda kemik kondrosarkomundan ayrı bir varlık olarak karakterize edilen, nispeten nadir yumuşak doku malignitesidir. Bu tümörler en sık proksimal ekstremitelerden köken alırlar, genitoüriner sistemde görülme sıklığı son derece nadirdir ve komponent organlardan köken alan az sayıda olgu sunumu mevcuttur. Kemik pelvisinin anlamlı lokal tutulumu ile birlikte penis tabanından kaynaklanan EMK'li klinik bir olgu sunuyoruz.

Anahtar Kelimeler: Ekstraskeletal, Miksoid, Kondrosarkom, Genitoüriner

Introduction

Extraskelatal myxoid chondrosarcoma (EMC) is a rare type of sarcoma of the soft tissues that usually presents as a slow-growing mass in men in their 50-60s (1,2). They are distinct from chondrosarcoma, and are characterized by a multinodular growth of primitive chondroblast-like cells in an abundant myxoid matrix. Most patients present with tumor development in the proximal extremities and show slow progression of disease; however, late local recurrence and metastases do occur (2). The presence of this type of tumor in the soft tissues of the genitourinary tract was first described in 1973 with its presence noted in the scrotum (3). Subsequent case reports have re-demonstrated its presence in the scrotum as well as its occurrence in the spermatic cord, perineum and vulva; however these cases appear to be extremely rare. We present a case report of an EMC originating at the base of the penis, as well as a review of the literature on this rare entity.

Case Presentation

A 63-year-old male presented to our institution for evaluation due to a painful mass overlying his suprapubic area that had begun to interfere with his occupation. He noted the mass was first noticed around one year prior to his presentation, but that it seemed to grow rapidly over the few months prior to him seeking medical attention. Other than discomfort, he had relatively few symptoms with no constitutional or voiding symptoms. On physical examination, he had a large, non-mobile, firm mass that encompassed the suprapubic area and tracked into both inguinal creases. This area was overlying the regional lymph nodes, so adenopathy was not able to be assessed. A computed tomography scan showed a large suprapubic mass surrounding the base of the penis. He underwent an open, excisional biopsy in the operating room with pathology showing EMC. Following pathologic diagnosis, a contrast-enhanced magnetic resonance

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Received: 26.05.2017 **Accepted:** 14.09.2017

Cite this article as: Rademaker NJ, Dooley WC, El Amm C, White J, Cross BW. Case Report: A Truck Driver with Pelvic Pain. J Urol Surg 2018;5(3):194-196.

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imaging of the abdomen and pelvis was obtained that showed a heterogeneous lobulated mass infiltrating the soft tissues around the base of the penis, extending into the perineum with left-sided extension above the urogenital diaphragm and extending out the left sciatic notch (Figure 1). His metastatic survey was negative.

A multidisciplinary case was undertaken with the urology, orthopedic surgery, surgical oncology, and plastic and reconstructive surgery services. Radical excision of a 28.5 cm tumor was performed that included total penectomy with perineal urethrostomy, right orchiectomy due to tumor invasion of the right spermatic cord, left orchiopexy, complex scrotoplasty, radical resection of the bilateral pubis, superior rami and inferior rami and complicated recreation and closure of the pelvic floor musculature (Figure 2). A double layer of biological graft material was folded and sutured for a 2 cm four-layer central band to become the replacement neopubis. This was bone anchored in place and anterior and posterior flaps were utilized to rebuild missing anterior abdominal wall musculature by suturing the back layer inside and anterior to external muscle fascia. Pelvic floor reconstruction was then performed by attaching both

layers to ischium via bone anchors and the bladder neck was re-suspended from the neopubis, opening in layers for urethral passage. Lastly, soft tissue external coverage was created by rotational regional flaps. He was admitted to the intensive care unit postoperatively for flap checks. On postoperative day two, his flap began to appear ischemic and he was taken back to the operating room for debridement of the anterolateral thigh flap with subsequent replacement with a vertical rectus abdominis myocutaneous flap. Following this, he had an uneventful remaining postoperative course and he was discharged home on oral antibiotics with a Foley catheter, multiple Jackson-Pratt (JP) drains and home health for dressing changes. He has been seen in follow-up with subsequent removal of his Foley catheter and JP drains. His surgical sites and flap remain healthy and viable. The pathological margins were negative and microscopic histology demonstrated rearrangement of the *NR4A3* (9q31.1) and *EWSR1* (22q12) genes in 90% of cells, consistent with the pathological diagnosis of EMC. He will be followed with serial imaging at three months intervals.

Written informed consent was completed by participant.

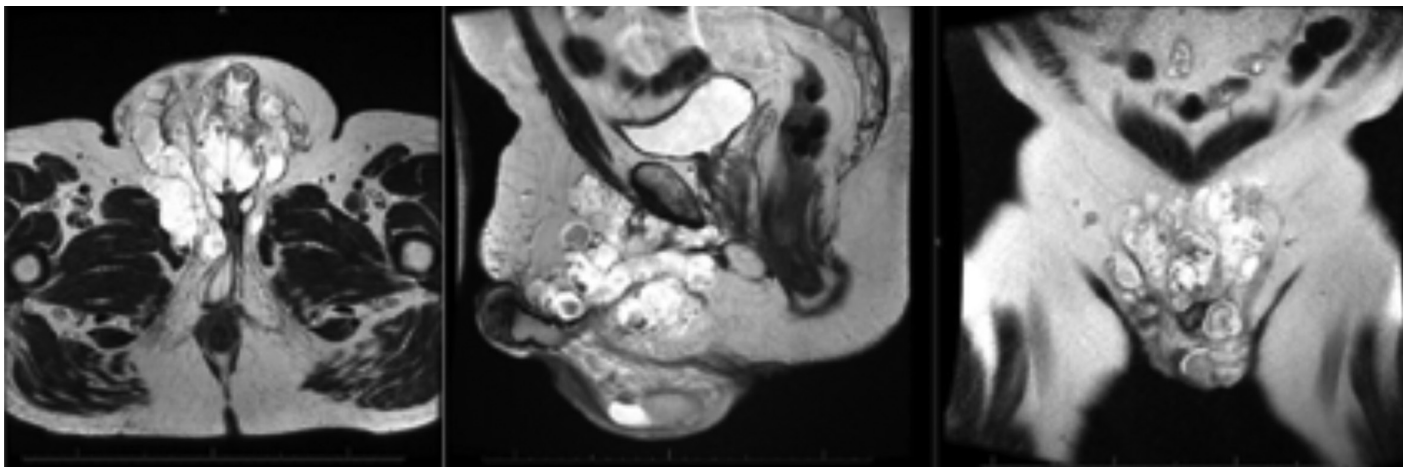


Figure 1. 3 Tesla magnetic resonance imaging of the pelvis showing diffuse tumor involvement of the bony pelvis and its component organs



Figure 2. a) Radical pelvic mass excision undertaken by multidisciplinary team with dissection showing the following: 1- bladder, 2- prostate, 3- bulbar urethra, b) Pelvic floor reconstruction showing biological mesh and neo-pubis, c) Soft tissue coverage with regional rotational flaps

Discussion

EMC is a rare soft tissue tumor that comprises <3% of all sarcomas (4). They commonly develop in the deep compartments of the proximal extremities in the 5th to 6th decade with a 2:1 predilection for male patients (2).

EMC is a unique tumor with fusion (or chimeric) genes (4,5,6). There have been four specific translocations identified, but the most common translocation is t (9;22) (q22;q12), found in approximately 75-80% of cases, which results in a fusion of *EWSR1* gene at 22q12 to the nuclear receptor subfamily 4, group A, member 3 gene (*NR4A3*) at 9q22. Given their sensitivity and specificity, a combination of real-time polymerase chain reaction and fluorescent *in situ* hybridization is felt to be a sensitive and specific method for diagnosis (4).

As noted above, EMC is usually discovered as a localized process with only 10-15% of patients having metastasis at presentation. They do; however, have a propensity for local recurrence and metastasis despite an indolent course. Large tumors (>10 cm) and metastatic disease at diagnosis are indicative of a poor prognosis. Patients presenting without metastatic disease have been shown to have a 35-40% chance of developing local recurrence by 3.5 years. The risk of subsequent development of distant recurrence or metastasis is thought to be around 25-30% by 3.5 years. Recent retrospective reviews show 5, 10, and 15-year overall survival rates of 82%, 65%, and 58%, respectively (7).

Surgical resection is the mainstay of treatment, but there are limited data regarding options for the treatment of unresectable or metastatic disease (2,7,8). Chemotherapy appears to have minimal benefit in the treatment of this disease process, with poor response rates noted across several studies (7,8). More recently, sunitinib has shown some promise in small studies with genotypic/phenotypic analyses that support a correlation between chemotherapeutic response and the presence of the *EWSR1-NR4A3* fusion gene (9).

Ethics

Informed Consent: It was taken.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: B.W.C., W.C.D., C.E.A., J.W., Concept: N.J.R., B.W.C., Design: N.J.R., B.W.C., Data Collection or Processing: N.J.R., Analysis or Interpretation: N.J.R., Literature Search: N.J.R., Writing: N.J.R., B.W.C., W.C.D., C.E.A., J.W.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

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Bladder Carcinoma in a 24-Year-Old Patient: A Case Report and Review of the Literature

Yirmi Dört Yaşındaki Hastada Mesane Kanseri: Olgu Sunumu ve Literatür Derlemesi

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Abstract

Urothelial bladder carcinoma is a rare condition in young patients. Clinicians have less inclination to perform cystoscopy in this age group because benign causes of hematuria are more common. Thus, diagnostic delays of up to one year may occur. We report a 24-year-old male patient with urothelial bladder cancer. Clinical behavior and prognosis in young individuals are controversial. The definitions of "young patient" are highly variable and different World Health Organization pathological classification systems are used for reporting. Generally, it presents as a low-stage and low-grade disease, nevertheless, it may present with high-grade tumors, even with muscle-invasive cancer.

Keywords: Bladder cancer, Urothelial, Young patient, Review, Case

Öz

Ürotelyal mesane kanseri genç hastalarda nadir görülür. Bu yaş grubunda hematürinin benign sebepleri daha sık olduğundan, hekimler sistoskopi yapma konusunda çok istekli değildirler. Bu nedenle tanıda bir yıla varan gecikmeler yaşanabilmektedir. Yirmi dört yaşında erkek hastada, genç hastalarda klinik davranışı ve prognozu belirsiz olan ürotelyal mesane kanserini rapor ettik. "Genç hasta" terimi çok değişken olarak kullanılmış ve farklı WHO patolojik klasifikasyon sistemleriyle raporlanmıştır. Genel olarak hastalık düşük-derece ve evre ile seyrederek ancak, yüksek dereceli hatta kasa invaziv hastalık bile görülebilmektedir.

Anahtar Kelimeler: Mesane kanseri, Ürotelyal, Genç hasta, Derleme, Olgu

Introduction

Bladder carcinoma has been reported to be a common malignancy with an estimated 15580 deaths and 74690 new cases globally in 2013 (1). It is typically a disease of older individuals; the majority of patients are above 60 years of age at the time of diagnosis. Urothelial bladder carcinoma (UBC) is a rare condition in patients aged below 40 years, furthermore, much rarer in the first two decades of life with reported incidence rates of only 0.1% to 0.4% (2). There is controversy regarding the clinical behavior and prognosis of UBC in young patients.

Case Presentation

The patient was a healthy 24-year-old male who had no history of smoking or exposure to chemicals. He presented to our

clinic after having painless macroscopic hematuria. Physical examination was unremarkable. The urinalysis was positive for blood cells and there were no signs of infection and, other laboratory tests were normal. Initially, the patient was sent for a urinary ultrasound scan which revealed a 2x2 centimeters hyper-echoic lesion on the right side of the bladder; both of the kidneys were normal. His urine was confirmed to be sterile by urine culture and cytology of the urine was negative for aberrant cells. Diagnostic cystoscopy confirmed the papillomatous lesion on the right side of the bladder at the 8 o'clock position (Figure 1). Soon after, deep transurethral resection of the lesion was carried out down to the muscle. The postoperative period was uneventful. Pathology of the lesion was reported as papillary urothelial neoplasm of low malign potential (PUNLMP) (Figure 2). Control cystoscopy at the 3rd month has shown no recurrence in the follow-up; the next cystoscopy was planned for the 12th

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Received: 16.08.2017 **Accepted:** 19.09.2017

Cite this article as: Akarken İ, Şahin H, Tarhan H, Deliktaş H, Çetinkaya M. Bladder Carcinoma in a 24-Year-Old Patient: A Case Report and Review of the Literature. J Urol Surg 2018;5(3):197-199.

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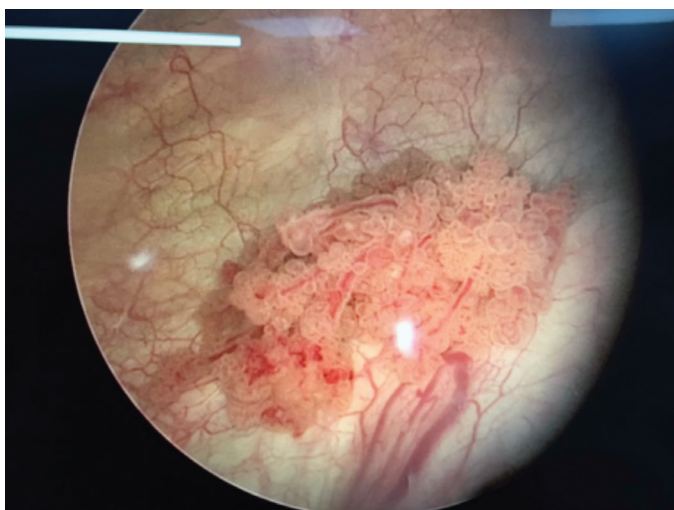


Figure 1. Cystoscopic view of the tumor

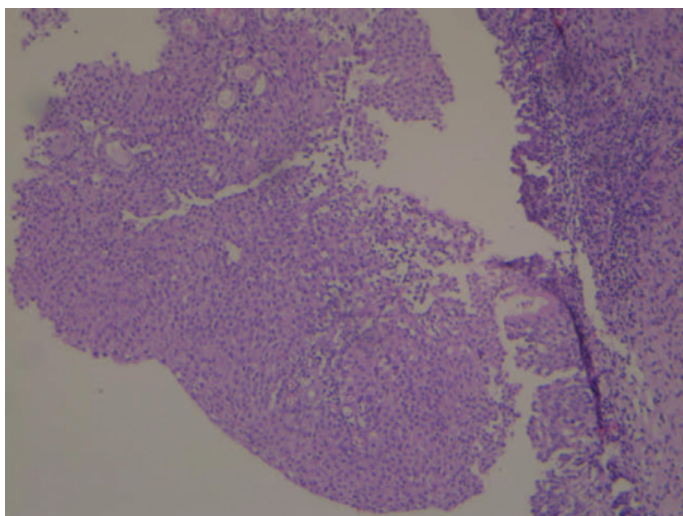


Figure 2. Microscopic view of the tumor

month. The informed consent was obtained from the patient for publication.

Discussion

UBC in young individuals is very rare and only 1% of cases are detected in the first 40 years of life. Its incidence dramatically increases with age. In people aged over the 70 years, the incidence rate of UBC is 15-20 times higher than in those aged 30-50 years (3).

Nearly all patients with UBC typically present with macroscopic and painless hematuria (4). In this age group, the clinicians have less inclination to perform cystoscopy. In a study, cystoscopy was performed in 40% of children who presented with macroscopic hematuria and UBC was detected in only 1% (5). Therefore, diagnostic delays of up to one year may occur. Ultrasound imaging is very sensitive for detecting UBC and proven to be a

reliable diagnostic tool. Computed tomography is particularly useful for assessing the upper urinary system and distant metastasis. Urine cytology has limited use in the diagnosis of UBC because it has very low sensitivity.

There is controversy on the clinical behavior and prognosis of UBC in young patients which can be explained with several reasons. Firstly, the definitions of "young patient" are highly variable. The vast majority of the studies have included patients below 40 years of age as "young patient", while others have used 20 or 30 years of age as a cut-off point. Recently, in the age group below 20 years, the disease was found to have clinical and pathological features different from that in older (6). Secondly, different World Health Organization (WHO) pathological classification systems have been used for reporting. The histopathological reporting classification system was last overhauled by the WHO in 2016.

The younger patients with UBC have low-stage and -grade disease while the incidence of high-grade tumors gradually increases with age. Na et al. (7) analyzed 42 patients and found pTa in 33, pT1 in 4, pT2 or higher in 5 and low-grade in 31, high-grade in 11 patients. Moreover Wang et al. (8) found that 5-year survival was better in young patients (93.8%) than in older ones (85.1%). The largest study, with more than 150 patients, showed that the vast majority of patients had PUNLMP (40.3%), furthermore, UBC could be highly aggressive in 18% of high-grade and muscle-invasive type tumors (9).

It is widely accepted that conversion of the 1973 WHO classification to the 2004 WHO classification would result in down-grading of a significant proportion of grade 1 tumors to PUNLMP (10). Especially in patients under 30 years of age, in whom grade 1 tumors predominate, it is likely that majority of urothelial carcinomas from studies published before the 2004 WHO system would have been classified as PUNLMP, as reported by Fine et al. (11). In that study, 23 UBC patients were reclassified according to the 2004 WHO classification system and more than half of tumors were found to be PUNLMP. It is reasonable to conclude that PUNLMP dominates in patients under 30 years of age. Even if PUNLMP may recur in up to 36% of patients, it has a low risk of progression (3.7%) and this progression generally occurs as a low-grade pTa lesion (12). Another importance of the term is that the diagnosis of "cancer" can be avoided in young patients.

There have been some studies investigating the relationship between recurrence of UBC and age. Na et al. (7) showed that only 7.1% of patients under 40 years of age had recurrences, while 38% of patients over 60 years of age had recurrence. Moreover, Ozbey et al. (13) reported that the mean time to first relapse was 37.7 months in young patients and 9.9 months in older patients, therefore the older age group may have more rapid recurrence.

Several studies were conducted to understand the molecular level why young patients had more low-grade and -stage tumors. Wild et al. (14) reported that genetic alterations which are frequently found in older patients are extremely rare under 20 years of age. Similarly, Owen et al. (15) showed lower epigenetic alteration rates in individuals under the age of 20 years.

Hematuria in young patients should be investigated in detail. By using the term PUNLMP, the diagnosis of "cancer" can be avoided and it is particularly important in young patients who usually have favorable outcomes. In the management of UBC in young patients, the grade and stage of the tumor are more critical than the age factor, as in older patients.

Ethics

Informed Consent: The informed consent was obtained from the patient.

Peer-review: Internally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: H.D., H.Ş., Concept: İ.A., H.Ş., Design: İ.A., M.Ç., Data Collection or Processing: İ.A., H.T., Analysis or Interpretation: İ.A., Literature Search: İ.A., H.T., H.D., Writing: İ.A.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

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Multifocal Synchronous Chromophobe, Papillary, and Clear Cell Renal Cell Carcinoma in a Single Kidney

Tek Bir Böbrekte Çok Odaklı Eş Zamanlı Kromofob, Papiller ve Berrak Hücreli Tipte Renal Hücreli Karsinom

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Abstract

We present a unique case of concurrent chromophobe, clear cell, and papillary renal cell carcinomas (RCC) in three separate sites in the same kidney after partial nephrectomy. We review the literature of synchronous RCC of up to two histologic subtypes, which is rare in occurrence.

Keywords: Chromophobe, Clear cell carcinoma, Papillary, Partial nephrectomy, Renal cell carcinoma

Öz

Bu çalışmada, parsiyel nefrektomi sonrası aynı böbreğin üç ayrı bölgesinde eş zamanlı kromofob, berrak hücreli ve papiller renal hücreli karsinomu (RHK) olan eşsiz bir olgu sunulmuştur. Eş zamanlı iki histolojik alt tip bile oldukça nadir görülmektedir. Literatür eşliğinde eş zamanlı çoklu alt tip RHK gözden geçirilmiştir.

Anahtar Kelimeler: Kromofob, Berrak hücreli karsinom, Papiller, Parsiyel nefrektomi, Renal hücreli karsinom

Introduction

Multifocal, synchronous renal cell carcinoma (RCC) in a same kidney is rare. Most case reports describe up to two histologic subtypes of RCC, which were found synchronously with either benign tumors or a primary malignancy of another organ. Given the rarity of this scenario, the long-term prognosis is unknown.

Case Report

We present a case of a healthy 70-year-old man who was found to have a right renal mass and benign cysts on workup of vague abdominal pain. He denied flank pain, gross hematuria, voiding symptoms, or constitutional symptoms including fever,

weight loss, and night sweats. He had no significant medical comorbidities or history of malignancy. He was a non-smoker and had no occupational exposures. He had no family history of urologic malignancies. On examination, he was obese with a body mass index of 36. His skin was unremarkable without cutaneous lesions. There was neither tenderness nor palpable masses on abdominal examination. His renal function was normal with a creatinine of 1.0 mg/dL and glomerular filtration rate of 75.

A computed tomography scan of the abdomen and pelvis with and without intravenous contrast revealed several lesions of the right kidney (Figure 1). In the anterior interpolar region, there was a partially exophytic, heterogenous, solid, enhancing mass (44 to 94 HU) measuring 3.4 cm, concerning for RCC. There was

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Received: 18.09.2017

Accepted: 15.10.2017

Cite this article as: Delto JC, Abello A, El Hussein S, Fukuma B, Alexis J, Mastrogiovanni L, Bhandari A. Multifocal Synchronous Chromophobe, Papillary, and Clear Cell Renal Cell Carcinoma in a Single Kidney. J Urol Surg 2018;5(3):200-202.

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a 2.2 cm mildly dense lesion (29 HU) in the anterior superior pole suggestive of a hemorrhagic/proteinaceous cyst. In the mid to lower pole, there were two adjacent, mildly dense, largely homogenous lesions with no discernable contrast enhancement. The posterior lesion was 4 cm and exhibited near-fluid attenuation with no enhancement, compatible with a cyst. The anterior lesion was 3.1 cm with mildly increased density (26 HU) and no significant contrast enhancement (32 HU) suggestive of a hemorrhagic/proteinaceous cyst. A bone scan was negative for metastasis.

After extensive discussion, the patient elected to undergo robotic partial nephrectomy of the solid anterior interpolar mass. The other lesions were thought to be benign cysts that did not warrant excision. However, at the time of surgery, while exposing the solid tumor, the lower pole lesion was identified and it appeared to be a complex cystic mass, concerning for malignancy. Thus, both tumors were excised separately. There was a simple cyst in the upper pole that was decorticated and the cyst wall was sent for pathologic examination. All three lesions were removed with a total warm ischemia time of 27 minutes. The remainder of the surgery was unremarkable. He was discharged home on postoperative day two.

Pathologic examination revealed multiple histologic subtypes of RCC. The solid tumor in the interpolar region was composed of eosinophilic cells that were positive for CD117, showed

membranous staining for cytokeratin 7 and focal positivity for vimentin, supportive of the diagnosis of eosinophilic variant of chromophobe RCC (Figure 2A). The lower pole tumor was morphologically a papillary RCC, supported by diffuse positive staining for racemase (Figure 2B). The upper pole cyst was a cystic clear cell RCC (Figure 2C). The neoplastic cells were positive for keratin AE1/3, paired box gene 8 and vimentin, with a Fuhrman nuclear grade of 1. All margins were negative.

The patient was seen in follow-up six weeks postoperatively, doing well with excellent renal function. Given such rare pathology and multifocality, the patient may be at higher risk for recurrence. He will be followed with a magnetic resonance imaging three months postoperatively.

Written informed consent was not required at our institution for case report. Patient is not identified.

Discussion

Synchronous renal tumors of varying pathology in the same kidney is a rare phenomenon. There have been reports of concurrent RCC and benign tumors such as oncocytoma and angiomyolipoma (AML) as well as other primary malignancies such as adrenal (1,2). To our knowledge, this is the first report of multifocal RCC with synchronous tumors of three different histologic subtypes in one kidney: chromophobe, clear cell, and papillary.

There have been only a few case reports of two synchronous RCCs appearing in the same kidney. Na et al. (3) reported a case of an adult patient with autosomal dominant polycystic kidney disease on hemodialysis who was found to have multiple



Figure 1. Computed tomography abdomen/pelvis with intravenous contrast. Sagittal view of right kidney with renal lesions: A) Anterior interpolar solid partially exophytic, heterogenous enhancing mass. B) Two adjacent hemorrhagic/proteinaceous cysts. C) Superior pole simple cyst

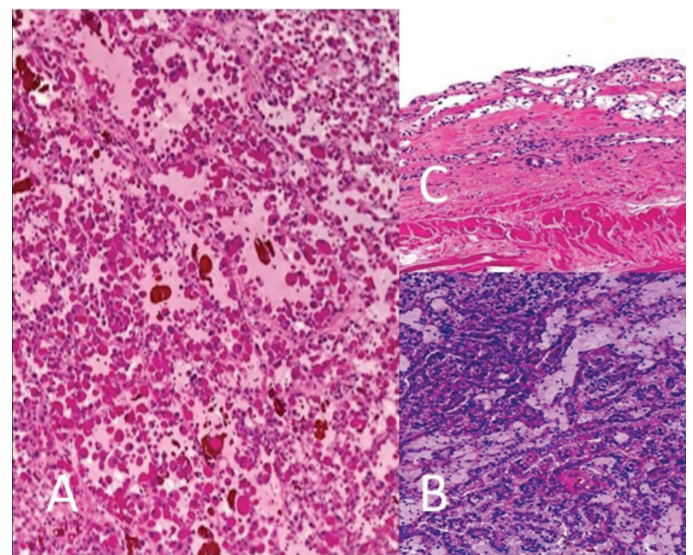


Figure 2. A) Anterior solid lesion with eosinophilic variant of chromophobe renal cell carcinoma. B) Posterior, lower pole lesion with papillary renal cell carcinoma. C) Upper pole cyst with cystic clear cell renal cell carcinoma

lesions of both papillary and clear cell RCC in the same radical nephrectomy specimen. The patient had no evidence of disease at three-month follow-up. Synchronous chromophobe and papillary RCC has been reported in a solitary kidney with two distinct masses (4). Interestingly, Roehrl et al (5) described a patient with a single 5 cm renal mass that was found to have components of chromophobe and papillary RCC. Three months after radical nephrectomy, the patient was without evidence of disease.

There have been few reports of synchronous RCCs with AML. Jun et al. (6) reported a radical nephrectomy specimen containing separate lesions including chromophobe RCC, clear cell RCC, and AML. Similarly, Kang et al. (7) reported synchronous chromophobe RCC, clear cell RCC, and an AML in a 62-year-old woman with tuberous sclerosis, who was healthy and without evidence of recurrence six months postoperatively.

The natural history and prognosis for a patient with multiple synchronous RCC lesions of varying subtypes are unknown, given its inherently rare nature. Moreover, the follow-up period of 3-6 months for the patients with two subtypes of RCC in these previously mentioned case reports is short and information about long-term outcome is lacking. All reported patients were treated with radical nephrectomy for multiple tumors. Our patient was treated with partial nephrectomy and found to have negative margins. Our patient may have a potential for worsened prognosis or even a higher likelihood of recurrence given three synchronous types of RCC. Moreover, in the event that adjuvant treatments may be required, regimens may be difficult to determine given the varying nature of each neoplasm. However, since the patient underwent a partial nephrectomy and has excellent renal preservation, the choice of adjuvant therapy is not limited by renal function.

In conclusion, the occurrence of multiple, synchronous, ipsilateral renal neoplasms including chromophobe, clear cell, and papillary RCC is rare and prognostic information is not widely available. Thus, careful monitoring and close follow-up of such patients is critical.

Ethics

Informed Consent: This was not required at our institution for case report. Patient is not identified.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: J.C.D., A.B., S.E.H., J.A., B.F., L.M., Concept: J.C.D., A.B., Design: J.C.D., A.B., Data Collection or Processing: J.C.D., S.E.H., B.F., Analysis or Interpretation: J.C.D., A.B., S.E.H., B.F., L.M., J.A., Literature Search: A.A., J.C.D., Writing: J.C.D., A.B., A.A.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

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A Rare Case of the Urinary Bladder: Small Cell Carcinoma

Mesane Nادر Görülen Olgu: Küçük Hücreli Karsinom

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Abstract

Small cell carcinoma generally originates from the lungs. However, rarely, it could be observed in organs other than the lungs. Primary small cell carcinoma of the bladder is a rare and aggressive disease and it generally presents itself with metastasis. Although there has not been a consensus on the method of treatment for this rare disease, multimodal treatment is recommended. In this study, we present long-term results of transurethral resection in a patient with non-muscle-invasive primary small cell carcinoma who refused additional treatments.

Keywords: Small cell carcinoma, Bladder tumor, Multimodal treatment

Öz

Küçük hücreli kanser çoğunlukla akciğer orijinlidir. Fakat nadiren akciğer dışı organlarda da görülebilir. Mesanenin primer küçük hücreli karsinomu nadir görülen ve çoğunlukla metastazlarla seyreden agresif bir hastalıktır. Nadir görülmeleri nedeni ile tedavisinde fikir birliği sağlanmamış olsa da multimodal tedavi önerilmektedir. Bu çalışmada ek tedavileri kabul etmeyen, kas invaziv olmayan primer küçük hücreli mesane kanserli bir olgunun sadece transüretal rezeksiyon sonrası uzun dönem sonuçları sunulmuştur.

Anahtar Kelimeler: Küçük hücreli kanser, Mesane tümörü, Multimodal tedavi

Introduction

Small cell carcinoma of the bladder is a very rare tumor accounting for less than 1% of all bladder cancers (1). It is much aggressive than the commonly seen types of cancers of the bladder and urothelial carcinoma and is associated with poor prognosis. Clinically, it has similarities with urothelial carcinoma. Patients with small cell carcinoma of the bladder typically present with macroscopic hematuria and rarely with signs of bladder irritation. Additionally, rarely, there may be signs of abdominal pain and urinary system obstruction. Although there has not been a consensus on the treatment because of its rarity, multidisciplinary approach, including radical cystectomy (RC), chemotherapy and radiation therapy, is recommended to increase the chance of cure and life expectancy.

Case Presentation

This study was retrospective and patient approval was obtained. An 86-year-old female patient presented to our clinic with a

bladder mass which was detected incidentally. Ultrasonography showed a 14x9 mm hyperechoic, vascularized solid lesion in the right lateral wall protruding into the lumen. Complete transurethral resection of bladder tumor (TURBT) was performed. Pathologic examination revealed lamina propria-invasive small cell carcinoma which was not invading the muscularis propria (Figures 1, 2). Thoracoabdominal computed tomography showed primary bladder small cell carcinoma with no lung pathology. Although there was muscle tissue in the specimen in pathologic examination, restaging-TUR was performed in order to do better staging after four weeks and no tumor formation was recognized in the pathologic examination. Additional treatment options, such as RC and radiotherapy were recommended to the patient by giving information on the aggressiveness of the disease, however, the patient did not accept any treatment. In the four-year follow-up of the patient who came to controls irregularly, no pathologic findings were detected in the control cystoscopies and systemic evaluations.

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Received: 17.04.2017 **Accepted:** 21.10.2017

Cite this article as: Kervancıoğlu E, Dirim A, Yılmaz Akçay E. A Rare Case of the Urinary Bladder: Small Cell Carcinoma. J Urol Surg 2018;5(3):203-205

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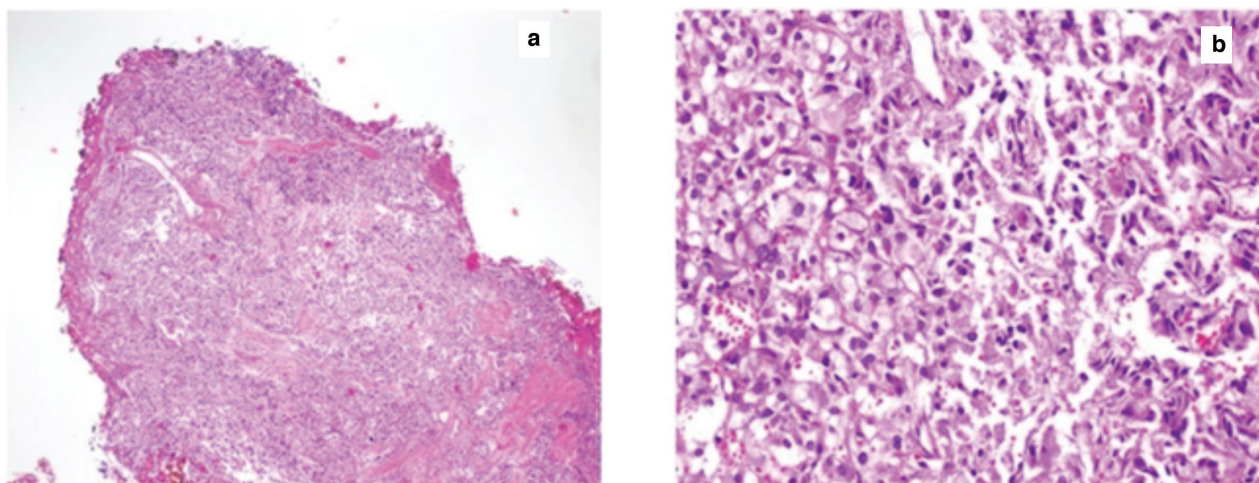


Figure 1. a) Small cell carcinoma of urinary bladder; tumor is composed of sheets and nests of atypical small cells (hematoxylin and eosin, 40x), b) Higher magnification of tumor cells with scant cytoplasm and hyperchromatic nucleus (hematoxylin and eosin, 200x)

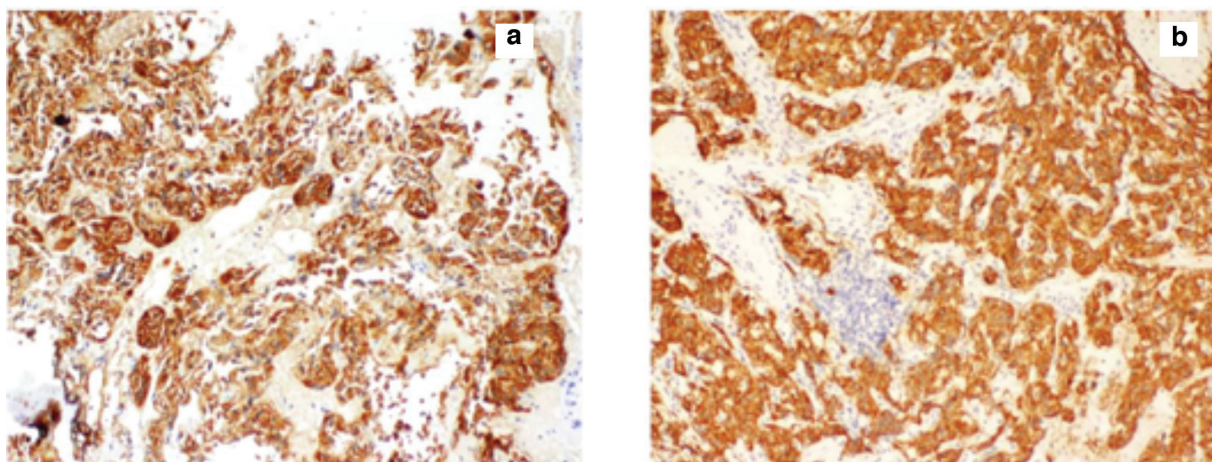


Figure 2. a) Immunostaining for synaptophysin is diffusely positive (100x), b) Immunostaining for chromogranin A is diffusely positive (100x)

Discussion

Small cell carcinoma of the bladder was first defined by Cramer et al. (2) in 1981. The ratio between male and female patients is 5/1 and it is seen commonly in the 6th decade of life (3). Pathologic diagnosis can generally be established via TURBT or immunohistochemical analysis of RC samples (4). Preoperative urine cytology may be useful for diagnosis, however this method has a low specificity (5).

It is much aggressive than the commonly seen urothelial carcinomas of the bladder and has poor prognosis. Nearly 40% of patients with small cell carcinoma present at an advanced stage (6). In one study, it has been reported that 66% of patients had lymph node metastasis detected during RC (3). Our case belongs to the rare group of patients with non-muscle invasive disease followed up with re-TUR evaluation. The explanation for the absence of the expected aggressive features can be made based on this situation.

There is no standard treatment for small cell carcinoma of the bladder. Local treatment options are TURBT, RC and radiation therapy as for urothelial carcinoma. High recurrence and poor survival rates have been reported for the disease which cannot be controlled with only TURBT (7). According to the experiences of Mayo Clinic, if there is not any metastasis, RC should be performed for patients with bladder small cell carcinoma. Systemic chemotherapy should be planned for patients with metastasis. Chemotherapy following RC is not indicated for patients with stage 2 disease but is considered for those with stage 3 and 4 disease (8). Neoadjuvant chemotherapy and RC combination as multimodal therapy has been reported to provide longer survival when compared with RC alone (9). On the other hand, Cheng et al. (3) have reported that there was no difference in 5-year survival between patients treated with RC and those who received no treatment.

In some selected patients with localized low-stage bladder small cell carcinoma, TURBT, radiotherapy and partial cystectomy can

be performed. RC is thought to be the best method to totally remove the mass, however, it only improves survival in patients with localized tumor (10).

As a result, since it is an aggressive disease and is rarely seen, there is no standard treatment approach to the management of small cell carcinoma of the bladder. It is seen that in muscle invasive disease, there must be RC and in metastatic disease, multimodal treatment is required in the light of recent studies. However, in rare situations like our case, non-muscle-invasive disease may occur. There have not been many studies in the literature regarding non-muscle-invasive bladder small cell carcinoma. We believe that our study will be useful in the topic. However, it is obvious that large-scale studies are needed.

Ethics

Informed Consent: Consent form was filled out by participant.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: E.K., A.D., Concept: E.K., Design: E.K., Data Collection or Processing: E.K., E.Y.A., Analysis or Interpretation: A.D., Literature Search: E.K., Writing: E.K.

Conflict of Interest: No conflict of interest was declared by the authors

Financial Disclosure: The authors declared that this study received no financial support

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“Accidental” Diagnosis of a Silent Giant Hydronephrosis

Sessiz Bir Dev Hidronefrozun “Rastlantısal” Tanısı

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Abstract

Giant hydronephrosis is defined as the presence of more than 1000 mL of fluid in the collecting system. While usually affecting children, uncommonly, adults may be affected, and it can be mistakenly diagnosed as a tumor. We present a case of silent giant hydronephrosis in an adult, misdiagnosed initially as a tumor, and subsequently confirmed as giant hydronephrosis postoperatively.

Keywords: Giant hydronephrosis, Computed tomography, Calculus, Renal tumor

Öz

Dev hidronefroz, toplayıcı sistemde 1000 mL'den daha fazla sıvının varlığı olarak tanımlanmaktadır. Genellikle çocukları etkilerken, nadiren yetişkinler de etkilenebilir ve yanlışlıkla bir tümör olarak teşhis edilebilir. Başlangıçta tümör olarak yanlış tanı konulan ve akabinde ameliyat sonrası sessiz dev hidronefroz olarak onaylanan bir yetişkinde, sessiz dev hidronefroz olgusunu sunuyoruz.

Anahtar Kelimeler: Dev hidronefroz, Bilgisayarlı tomografi, Taş, Renal tümör

Introduction

Giant hydronephrosis in the paediatric population is most commonly due to ureteropelvic junction obstruction; in more than half of these cases, this obstruction is functional rather than anatomical. When occurring in adults, this clinical entity presents a diagnostic challenge, as more often than not, a diagnosis of a tumor will be made. Cross sectional imaging via computed tomography (CT) or magnetic resonance imaging allows a detailed assessment to be made prior to surgical planning. We describe, in our experience, a patient with silent giant hydronephrosis due to a ureteric calculus, who was eventually diagnosed with silent giant hydronephrosis post trauma. The preoperative CT findings in our case are described.

Case Presentation

A previously well 54-year-old man presented with acute onset hematuria and lower abdominal pain, after falling down while riding his bicycle. This was the first episode. He had no other complaints.

On physical examination, the abdomen appeared mildly distended. Minimal tenderness was noted on palpation of the lower abdomen, with no obvious bruising. Laboratory test results were all normal, except for red blood cells present in urinalysis.

A suspicion of injury to the urogenital organs prompted an urgent contrast enhanced CT of the abdomen which showed a huge mass, mainly located on the right side of the abdomen, occupying almost the entirety of the abdomen, measuring approximately 15 cm x 25 cm x 35 cm (antero-posterior x width x cranio-caudal). It was seen that the mass was displacing the liver superiorly, the bowels and most of the abdominal organs confined to the left side, and the pelvic organs inferiorly. Minimal enhancement with septation was noted; with an area of avid enhancement posteriorly, and heterogenous enhancement centrally (Figures 1a, b). An 8 mm calculus was seen in the proximal right ureter, which was displaced from its normal anatomical position (Figure 2). No invasion of the surrounding structures was seen. A renal tumor with incidental finding of calculus was initially suspected.

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Received: 25.07.2017 **Accepted:** 19.09.2017

Cite this article as: Md Noh MSF, Abdul Rashid AM. “Accidental” Diagnosis of a Silent Giant Hydronephrosis. J Urol Surg 2018;5(3):206-208.

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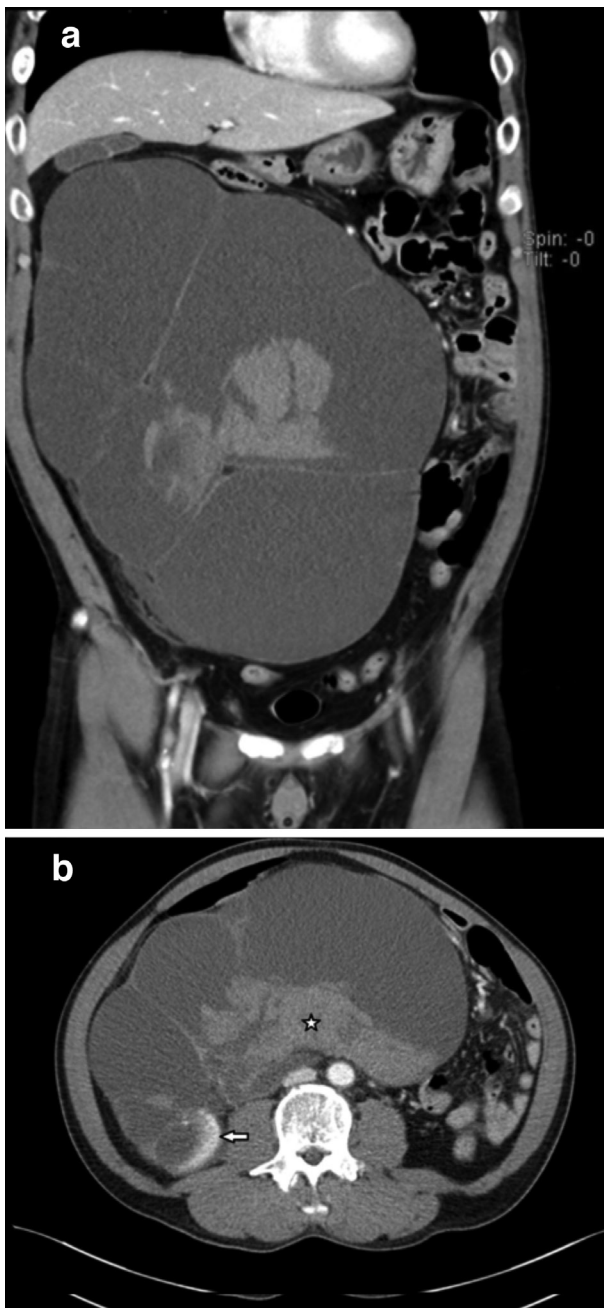


Figure 1. Computed tomography images in coronal (a) and axial (b) sections showing; a) The huge renal mass is seen here displacing the abdominal organs, b) Note an area of avid enhancement posteriorly (arrow), and minimal enhancement of the renal parenchyma with a central solid heterogenous focus (star); which was initially thought to represent a tumor/hematoma

The patient then underwent an open right nephrectomy. A total of 1500 mL of blood stained fluid was collected intraoperatively. Histopathological examination revealed features of chronic hydronephrosis with an incarcerated calculus in the proximal right ureter. No atypical cells suggestive of malignancy. Patient otherwise recovered well postoperatively. Informed consent was obtained, and patient's anonymity has been maintained.



Figure 2. Computed tomography image in coronal section showing the incarcerated calculus in the displaced proximal right ureter (arrow)

Discussion

Giant hydronephrosis was defined by Stirling (1) in 1939, as the presence of more than 1000 mL of fluid in the collecting system (2,3). Most cases occur in children; uncommonly in adults and result from obstruction by calculus (4). When present, they may often be misdiagnosed and mistaken for a tumor (4,5). This was demonstrated in our case. Among the differentials for giant cystic masses in the abdomen include intraperitoneal cysts (mesenteric or choledochal), retroperitoneal cysts (renal, adrenal, or pancreatic in origin), ovarian cysts and tumors, and to a certain extent, gross ascites. Once the diagnosis has been established, evaluation of renal function may be undertaken via nuclear studies, prior to deciding whether to proceed with nephrectomy. In the event that renal function is satisfactory, nephrectomy may be avoided. Other conditions where nephrectomy may not be chosen as the definitive treatment include bilateral disease, and disease affecting a younger age group. In our case, as the contralateral kidney was functioning normally, and that there were signs of active hemorrhage in the diseased kidney, total nephrectomy was deemed the most appropriate treatment plan.

Ethics

Informed Consent: It was obtained.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: M.S.F.M.N., A.M.A.R., Concept: M.S.F.M.N., Design: A.M.A.R., Data Collection or Processing: M.S.F.M.N., Analysis or Interpretation: M.S.F.M.N., Literature Search: M.S.F.M.N., A.M.A.R., Writing: M.S.F.M.N.

Conflict of Interest: The authors declared no conflict of interest.

Financial Disclosure: The authors declared that this study received no financial support.

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A Rare Cause of Acute Urinary Retention: Urethral Caruncle

Nadir Bir Akut Üriner Retansiyon Sebebi: Üretral Karünkül

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Abstract

A urethral caruncle is a benign tumor formation in the vascular structure originating from the posterior wall of the external urethral meatus primarily occurring in postmenopausal women. A vesical globe was identified in a 71-year-old patient admitted to our outpatient clinic with the complaints of vaginal bleeding and inability to urinate. Vaginal examination revealed a 2.5x2.5 cm urethral caruncle. The patient's bladder was emptied via the insertion of a 16 F urethral catheter. Caruncle excision was performed, and the patient was started on local estrogen therapy and followed up.

Keywords: Urethra, Caruncle, Vesical globe

Öz

Üretral karünkül genellikle postmenapozal dönemdeki kadınlarda eksternal üretral meanın arka duvarından kaynaklanan vasküler yapıda benign bir tümöral oluşumdur. Polikliniğimize idrar yapamama ve vajinal kanama şikayeti ile başvuran 71 yaşındaki hastada glob vezikale tespit edildi. Vajinal muayenesi esnasında 2,5x2,5 cm boyutlarında üretral karünkül tespit edilen hastaya 16 F üretral kateter yerleştirilerek mesane boşaltıldı. Karünkül eksizyonu yapılan hasta, lokal östrojen tedavisi başlanarak takibe alındı.

Anahtar Kelimeler: Üretra, Karünkül, Glob vezikale

Introduction

Urethral caruncle is a lesion that is generally seen in postmenopausal women. It originates from the posterior wall of the urethra and protrudes from the external urethral meatus. These lesions have high visibility and are usually smaller than 1 cm (1). They contain loose vascular connective tissues covered by hyperplastic urothelial and squamous and flat epithelial cells. Histologically, depending on the state of inflammation, vascularity, and fibrosis, there are three subtypes of urethral caruncle; papillomatous, angiomatous, and granulomatous. Despite being asymptomatic when small, large caruncles may cause bleeding and difficulty in urination. Although the etiology is not completely known, hypoestrogenemia is presumed to be effective and positive results can be obtained with estrogen replacement therapy or local estrogens (2).

Case Presentation

A 71-year-old female patient was admitted to our outpatient clinic with the complaints of vaginal bleeding and inability to urinate for the last 10 hours. Physical examination revealed a vesicle globe. During the insertion of a transurethral catheter, a dark red 2.5x2.5 cm polypoid lesion of a vascular structure protruding out of the urethral meatus was observed. It contained sites of bleeding foci and had an overlying hematoma (Figure 1). The bladder was emptied of approximately 700 cc urine using a 16 F catheter. The patient's history revealed a gradual reduction in urine flow for the last three years and the presence of blood stains on her underwear over the past week. In the constructed ultrasonography, no pathology was observed in the bladder but a grade 4 hydronephrosis was identified in the left kidney. Computed tomography showed grade 4 hydronephrosis in the left kidney (Figure 2). The level of estrogen was determined to

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Received: 26.07.2017 **Accepted:** 22.10.2017

Cite this article as: Akdemir F. A Rare Cause of Acute Urinary Retention: Urethral Caruncle. J Urol Surg 2018;5(3):209-211.

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Figure 1. A dark red polypoid lesion with hematoma foci of the vascular structure outside the urethral meatus

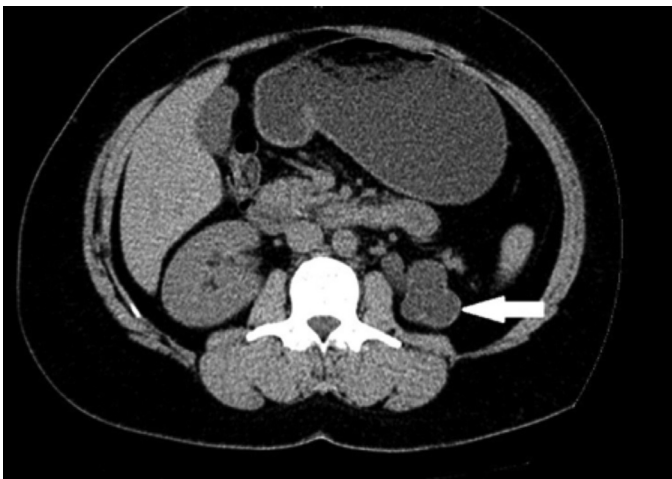


Figure 2. Grade 4 hydronephrosis image in the left kidney (arrow)

be 5 pg/mL. The patient was scheduled for surgical excision of the urethral caruncle. Following preparations and obtaining the patient's informed consent, diagnostic cystoscopy was performed under general anesthesia. There were no other lesions in the bladder; however, common trabeculations, cellulite, and small diverticula were observed. Following the insertion of a 16 F transurethral catheter, the urethral caruncle was excised and the urethral mucosa was sutured to the meatus. During this procedure, it was observed that the patient's vagina and urethra were atrophic and fragile. After the operation, the patient was started on local estrogen therapy. No postoperative complication occurred. The catheter was removed five days after the operation and the patient was able to urinate without

difficulty. The patient was followed up for the detection of recurrence. Histopathological examination of the mass revealed urethral caruncle.

Discussion

The most common benign tumor in female urethra is a urethral caruncle. Although it is usually seen in the postmenopausal period, it can also develop at younger ages. Urethral caruncles are reddish, raspberry-like, hemorrhagic lesions usually smaller than 1 cm. Small-sized caruncles are usually asymptomatic; however, when they grow, they may cause urinary retention. The malignancy rate has been reported as 1.6% (2,3,4).

Although caruncles are usually benign, they should be surgically excised and histopathologically examined since they may be the indicators of lymphoma, clitoral venous thrombosis, urethral thrombosis, pseudoneoplastic lesions, urethral polyps, malign melanoma, intestinal heterotypic, angiomatous lesions, and diastolic urethral stenosis (5,6,7,8,9,10,11). Microscopically, a caruncle is surrounded by an epithelial layer and consists of connective tissues formed by dense inflammatory cells, in particular the polymorphonuclear cells. In addition, reactive patterns, such as fibrocapillary proliferation (granulomatous), hypervascularity (angiomatous), epithelial hyperplasia (papillomatous), or intestinal metaplasia (mucinous), may also be observed (12).

Although urethral caruncles do not usually result in complaints other than cosmetic distress, they sometimes lead to bleeding observed as blood stains on underwear, painful urination with an intermittent split stream, and acute urinary retention (13). In addition to these conditions, the differential diagnosis of a urethral caruncle should include the elimination of other diseases that cause paraurethral masses, such as senile urethritis, skeletal abscess, infected urethral diverticulum, ectopic ureterocele, Gartner's duct cyst, residual Mullerian cyst, vaginal wall cyst, and urethral-vaginal neoplasms. It has been reported that small urethral caruncles can be treated with topical estrogen, anti-inflammatory treatment, and cryoablation. Large caruncles blocking the urinary flow should be surgically excised (14). Biopsy and histopathological examination are the only way of excluding the possibility of malignancy irrespective of the size of the mass. Furthermore, in patients with estrogen deficiency, recurrence may be observed albeit rare and after a long period.

In conclusion, despite usually being considered as benign formations, urethral caruncles do require a histopathological examination for a definitive diagnosis. The elimination of estrogen deficiency, particularly in postmenopausal patients, would also prevent future complications.

Ethics

Informed Consent: It was obtained.

Peer-review: Externally peer-reviewed.

Financial Disclosure: The author declared that this study received no financial support.

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Re: Antibiotics for Asymptomatic Bacteriuria in Kidney Transplant Recipients

Coussement J, Scemla A, Abramowicz D, Nagler EV, Webster AC

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Cochrane Database Syst Rev 2018;2:CD011357. doi: 10.1002/14651858.CD011357.pub2.

EDITORIAL COMMENT

Asymptomatic bacteriuria (AB), defined as bacteriuria without signs or symptoms of urinary tract infection (UTI), is observed up to more than 50% of kidney transplant recipients. In this Cochrane systematic review, besides the efficacy of treating AB with antibiotics in kidney transplant recipients to prevent symptomatic UTIs, also all-cause mortality and the indirect effects of UTI (acute rejection, graft loss, worsening of graft function) were investigated. For this purpose, The Cochrane Kidney and Transplant Register of Studies (which includes searches of Central, MEDLINE, Embase, conference proceedings, the International Clinical Trials Register, and clinicaltrials.gov) was searched until 1 September 2017 and the authors included two studies (212 participants) comparing antibiotics versus no treatment and had identified three on-going studies. Data were pooled across two studies (total of 212 patients) and overall, the incidence of symptomatic UTI varied between 19% and 31% in the groups not treated for AB. Persistence of AB was high regardless of treatment and although the available data were limited, so far, there is still no evidence to suggest antibiotic treatment of AB would improve patient and graft outcomes such as all-cause mortality, graft loss, acute rejection, hospitalization for UTI or graft function. Although the data on adverse reactions were also very limited, however, there seemed to have been no severe adverse event attributable to the antibiotic treatment and non-severe adverse events appeared to be infrequent. Including the results of these ongoing randomised controlled trials in further meta-analyses will help provide more reliable evidence whether to treat AB in kidney transplant recipients.

Yarkın Kamil Yakupoğlu, MD



Re: Retro-peritoneal Cooling for Kidney Preservation from Multi-organ Cadaver Donors

Salazar-Bañuelos A, Monroy-Cuadros M, Henriquez-Cooper H

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Am J Surg 2018;215:802-803. doi: 10.1016/j.amjsurg.2017.12.015.

EDITORIAL COMMENT

Good organ preservation is the key to successful organ transplantation and adequate cooling of organs plays a major role in the preservation. However, in the era of multi-organ retrieval, the kidneys are usually the last organs to be procured as they are considered the most resistant to warm ischemia. In spite of cold perfusion and the application of intra-abdominal ice, retroperitoneal warming of kidneys from the psoas muscles somehow cannot be prevented from the posterior aspect of the kidneys. The right and left kidneys of the 21 deceased donors undergoing multi-organ procurement were randomized to either the experimental group where a bag constructed of surgical sponge, tied in its four corners was filled with ice and placed between the kidney and the psoas muscle, versus the control group where the kidney was left in place in contact with the muscles. There was a significant difference between in extraction temperature of the kidneys between the experimental group and control group (8 °C vs 11.6 °C). The clinical significance of this reduction in extraction temperature remains uncertain, and no clinical outcomes are reported. The technique is simple, reproducible, low-risk, and does not bring any additional cost, thus, larger randomized controlled studies focusing on the clinical outcomes would be planned using this technique.

Yarkin Kamil Yakupoğlu, MD



Re: More Extensive Lymph Node Dissection at Radical Prostatectomy is Associated with Improved Outcomes with Salvage Radiotherapy for Rising Prostate-specific Antigen After Surgery: A Long-term, Multi-institutional Analysis

Fossati N¹, Parker WP², Karnes RJ³, Colicchia M³, Bossi A⁴, Seisen T⁴, Di Muzio N⁵, Cozzarini C⁵, Noris Chiorda B⁵, Fiorino C⁵, Gandaglia G¹, Bartkowiak D⁶, Wiegel T⁶, Shariat S⁷, Goldner G⁸, Battaglia A⁹, Joniau S⁹, Haustermans K¹⁰, De Meerleer G¹⁰, Fonteyne V¹¹, Ost P¹¹, Van Poppel H⁹, Montorsi F¹, Briganti A¹, Boorjian SA¹²

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Eur Urol 2018;74:134-137. doi: 10.1016/j.eururo.2018.02.024.

EDITORIAL COMMENT

Residual, unresected lymph node disease has the potential to be a source for recurrence after salvage radiotherapy (sRT). The importance of pelvic lymph node dissection at the time of radical prostatectomy (RP) with regard to recurrence risk following sRT has not been previously determined. Therefore, the authors investigated whether the extent of nodal dissection at RP is associated with oncologic outcomes following sRT in men with increasing prostate-specific antigen (PSA) levels after surgery. They performed a multi-institutional review of men treated with sRT with a rising PSA after RP. The associations between lymph node yield and biochemical recurrence (BCR) as well as clinical recurrence (CR) after sRT were assessed. Seven hundred twenty eight patients were identified; of these, 221 were diagnosed with BCR and 116 with CR during a median follow-up of 8.4 years. The risk of BCR after sRT was inversely associated with the number of nodes resected, and increased extent of dissection was associated with a decreased risk of CR after sRT. The authors concluded that their data support the importance of an extensive lymph node dissection at surgery that may be used in prognosis assessment when sRT is being considered.

The authors should be congratulated for investigating an inventive notion which will pave the way for further work on the effects of surgical technique on treatments downstream in multi-modal approach to high-risk prostate cancer. However, the multi-institutional, retrospective design of the study cautions us to be watchful for inherent flaws such as non-standardized surgical as well as sRT technique, timing and indications for sRT, pathological processing and reporting, etc.

Özgür Yaycıoğlu, MD, FEBU



Re: Calcium Role in Human Carcinogenesis: A Comprehensive Analysis and Critical Review of Literature

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Cancer Metastasis Rev 2016;35:391-411. doi: 10.1007/s10555-016-9634-0.

EDITORIAL COMMENT

Calcium is the most abundant mineral in the human body especially in the bones and teeth. A few amount of total calcium is physiologically active (1%), as signaling molecules; it plays major roles in biological systems importance of calcium has been appreciated over the years especially in cancer. Free calcium is associated to the many cellular processes such as cancer initiation, promotion, and progression. Its role is very crucial in cancer-related molecular mechanisms such as signaling pathway. In the literature, the relationship between calcium metabolism and many different cancers, such as breast, colon and prostate cancers, has been investigated. Two distinct mechanisms relating calcium homeostasis to cancer pathways have been described. The first pathway is calcium store-dependent, and the second is rather calcium influx-dependent. These mechanisms are responsible for cellular life and control mechanisms over cell death, growth, and division. As a result, calcium could also function as a first messenger in cancer. These responsible mechanisms are alterations in cell surface calcium-sensing receptor, alterations in transmembrane calcium trafficking protein expression, the role of non-membrane-bound calcium-binding proteins, resistance to apoptosis, increased compartmental calcium concentration initiating cancerous transformation, the cytoplasmic effects of high intracellular calcium, habituation of cells to lower levels of calcium. These theories may contribute to cancer research for the development of new diagnosis, prognosis, and treatment tools and options based on calcium signaling.

Fehmi Narter, MD, PhD



Re: INSL3 in the Benign Hyperplastic and Neoplastic Human Prostate Gland

Klonisch T, Müller-Huesmann H, Riedel M, Kehlen A, Bialek J, Radestock Y, Holzhausen HJ, Steger K, Ludwig M, Weidner W, Hoang-Vu C, Hombach-Klonisch S

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Int J Oncol 2005;27:307-15.

EDITORIAL COMMENT

Insulin-like peptide 3 (INSL3), relaxin-like factor is a member of the relaxin/insulin gene family. It is expressed in testicular Leydig cells. It is critical for testis descent in boys. INSL3 is essential in the first phase of testis descent for the growth of the gubernaculum testis.

The INSL3 hormone is a marker of testicular Leydig cells in the post-pubertal testis. In this study, the authors investigated the expression of human INSL3 in patients with benign prostate hyperplasia, prostate intraepithelial neoplasia and prostate carcinoma tissues. An autocrine/paracrine INSL3-LGR8 ligand receptor system within the human prostate has been proven. LGR8 has been identified as the INSL3/relaxin receptor and was shown *in vitro* to promote a strong proliferative response in fetal rat gubernaculum cells upon exposure to rat INSL3. As a result of this study, they have demonstrated for the first time the presence of a potentially functional INSL3-LGR8 ligand receptor system in human benign hyperplastic and neoplastic prostate and identified INSL3, motility enhancing factor for the human prostate carcinoma cell line PC-3. INSL3 may be a biomarker that represents the Leydig cell function. Moreover, with further comprehensive studies, it may be considered as a marker like testosterone for detection of castration level like testosterone in prostatic carcinoma.

Fehmi Narter, MD, PhD



Re: Whole Exome Sequencing of a Consanguineous Turkish Family Identifies a Mutation in GTF2H3 in Brothers with Spermatogenic Failure

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Urology 2018. pii: S0090-4295(18)30622-8. doi: 10.1016/j.urology.2018.06.031.

EDITORIAL COMMENT

In this study, the authors investigated the genetic cause of spermatogenetic failure in a consanguineous Turkish family with four infertile and three fertile brothers by using whole exome sequencing (WES). Two brothers were azoospermic with follicle stimulating hormone, luteinizing hormone and total testosterone levels within the normal range. One of them had a pathology report showing maturation arrest. Both have had microdissection testicular sperm extraction operation without sperm recovery. Spermogram in other two brothers showed oligoasthenoeratozoospermia (OAT) with a sperm count of 2.2 and 7 million/mL. DNA extraction was obtained for WES in all infertile brothers and parents, who were first-degree cousins, to investigate possible candidate gene(s) which passed to the siblings via Mendelian inheritance. A non-synonymous variant in general transcription factor 2H subunit 3 (GTF2H3) in chromosome 12 was identified in the family. This variant was confirmed to be homozygous in the two azoospermic brothers and heterozygous in the two brothers with OAT. GTF2H3 codes for the protein subunit p34 which comprises part of the GTF2H and this transcription factor has been shown to play a critical role in activating retinoic acid receptor alpha (RAR alpha). RAR alpha has also been shown to be essential in spermatogenesis in human. In this study, the authors proposed that GTF2H3 variant may lead a dysfunction of transcription factor 2H activation of RAR alpha leading to spermatogenetic failure.

Emre Bakircioglu, MD



Re: Life Quality Change After Inflatable Penile Prosthesis Implantation

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Aging Male 2018;1-7. doi: 10.1080/13685538.2018.1487393.

EDITORIAL COMMENT

In this study, the authors investigated whether inflatable penile prosthesis implantation alters the quality of life in patients who suffered erectile dysfunction (ED). Forty-one patients who underwent penile prosthesis implantation were evaluated. The mean age of the patients was 59.9 years. A 2-piece prosthesis was implanted in 30 patients and a 3-piece prosthesis in 11. The Turkish version of the 36-Item Short Form Health Survey was used to evaluate the quality of life of the patients before and 1 year after the surgery. ED patients were classified according to the ED etiology (diabetic, cardiovascular and pelvic surgery) and the type of prosthesis implanted. In all the groups, a significant improvement was observed in quality of life after surgery and the most prominent improvement was observed in diabetic patients.

It is the first study in the literature to evaluate the changes in quality of life of patients with ED after penile prosthesis implantation.

Emre Bakırcıoğlu, MD