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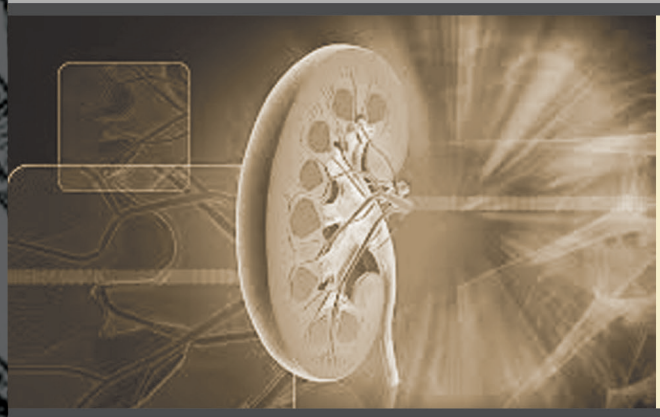

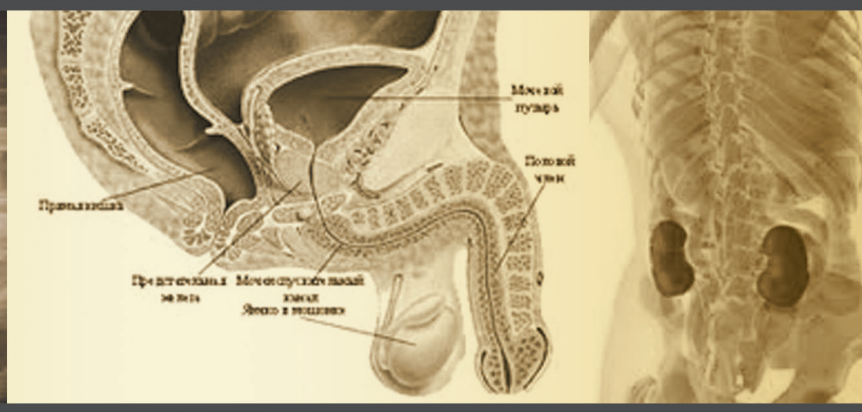

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2. Organization as Author

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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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ORIGINAL RESEARCH
Endourology

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Journal of Urological Surgery, 2017;4:106-108

Our Retrograde Intrarenal Surgery Experience with Horseshoe Kidney

At Nalı Böbrekte Retrograd İntrarenal Cerrahi Deneyimlerimiz

Tufan Süelözgen, Cemal Selçuk İşoğlu, Mustafa Karabıçak, Mehmet Yiğit Yalçın, Sezgin Yeni, Yusuf Özlem İlbey

University of Health Sciences, Tepecik Training and Research Hospital, Clinic of Urology, İzmir, Turkiye

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

Retrograde intrarenal surgery is currently popular, and at present it is seen as an alternative approach to percutaneous nephrolithotomy for stones over 2 cm. A threshold number for the learning curve is not available in the literature. Therefore, it should be performed in experienced centers in kidneys that do not have a normal anatomy like a horseshoe kidney.

Abstract

Objective: To share our experience with retrograde intrarenal surgery (RIRS) done in patients with horseshoe kidney anomaly.
Materials and Methods: Data from 107 patients who underwent RIRS for kidney stones between 2013 and 2016 in our clinic was retrospectively analyzed and 6 patients with horseshoe kidney anomaly detected on computed tomography (CT) were included in the study. Achieving stone-free status or having residual stones of ≤4 mm were considered operational success.
Results: The mean age of the patients was 44.5±6.7 years. Four patients were male (66.6%) and two were female (33.3%). The mean stone size was 14.5±4.1 (10-22) mm. Three patients had pelvis stones (50%) and the rest 3 (50%) had lower calyx stones. Two patients (33.3%) were found to be stone-free on post-operative non-contrast CT results.
Conclusion: RIRS should be performed by experienced surgeons in patients with horseshoe kidney.
Keywords: Kidney stone, horseshoe kidney, retrograde intrarenal surgery

Öz

Amaç: Amacımız at nalı böbrek anomalisine sahip hastalardaki retrograd intrarenal cerrahi (RIRC) deneyimlerimizi paylaşmaktır.
Gereç ve Yöntem: 2013-2016 yılları arasında kliniğimizde RIRC yapılan 107 hastanın verileri geriye dönük olarak incelendi ve bilgisayarlı tomografide (BT) at nalı böbrek anomalisine sahip olduğu belirlenen 6 hasta çalışmaya dahil edildi. Tamamen taşsızlık veya 4 mm'den daha az rezidü operasyon başarısı olarak kabul edildi.
Bulgular: Çalışmaya alınan hastaların yaş ortalaması 44,5±6,7 yıldı. Hastaların dört tanesi erkek (%66,6) iki tanesi kadındı (%33,3). Ortalama taş boyutu 14,5±4,1 (10-22) mm idi. Üç hastada pelvis taşı (%50) ve kalan üç hastada ise alt kaliks taşı mevcuttu. Postoperatif istenen kontrastsız BT'de iki hastada (%33,3) taşsızlık izlendi.
Sonuç: At nalı böbrek anomalisine sahip hastalarda RIRC deneyimli cerrahlar tarafından uygulanmalıdır.
Anahtar Kelimeler: Böbrek taşı, at nalı böbrek, retrograd intrarenal cerrahi

Introduction

The main goal in kidney stone treatment is to achieve the longest stone-free period with the smallest morbidity rate as possible. The search for less invasive techniques and the technological developments are still ongoing. Today, the primary approach for renal stones larger than 2 cm in diameter is percutaneous nephrolithotomy (PNL). However, another possible first-choice option is retrograde intrarenal surgery (RIRS), especially in extracorporeal shock wave lithotripsy (ESWL)-resistant stones

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measuring 1-2 cm in diameter (1). Although RIRS is a relatively common treatment method for kidney stones recently, there are not many publications about RIRS in horseshoe kidneys. Therefore, we would like to share our experience with RIRS surgery done in patients with horseshoe kidney anomaly.

Materials and Methods

Data from 107 patients who underwent RIRS for kidney stones between 2013 and 2016 in our clinic was retrospectively reviewed. Patients over 18 years of age with full set of demographic and post-operative data were included in the study. Patients with horseshoe kidney anomaly detected on computed tomography (CT) were included in the study. Patients' data were reviewed in terms of age, sex, stone location, stone diameter, stone-free status and post-operative complications. The longest axis of the stone measured was recorded as the stone diameter. Success status was defined as either no residue or a residue smaller than 4 mm on control CT taken on the 1st month of operation. Due to the retrospective nature of our study, there was no available data on patients who had residual stones after surgery.

Procedure

The procedure was performed under general anesthesia after urine cultures were detected as sterile. Patient was positioned from trendelenburg position to lithotomy position. Orifices were checked using a 22 F cystoscope. Routine rigid ureterorenoscopy and routine stenting were not performed before operation. Following insertion of a hydrophilic guide catheter, a 9.5-12F urethral access sheet was introduced. A flexible ureterorenoscopy was placed (Storz Flex X2©) and stones were fragmented using the Holmium-YAG laser (Litho 20 W Quantasystem®). Laser energy was adjusted to 0.8-1 Joule and the frequency was set as 5-8 Hz. A 200 µm laser probe was used. Dusting method is preferred for lithotripsy. All patients received a routine post-operative double-J stent (DJS) following surgery.

Results

A total of six patients with horseshoe kidney anomaly were included in the study. The mean age of the patients was 44.5±6.7 years. Four patients were male (66.6%) and two were female (33.3%). The mean stone size was 14.5±4.1 (10-22) mm and all stones were opaque. Three patients had pelvis stone (50%) and the rest 3 (50%) had lower calyx stones. Except for one patient, none of the patients required a preoperative DJS. Three (50%) patients had a previous ESWL history. Two patients (33.3%) were stone-free according to the post-operative non-contrast CT results (Table 1). None of the patients showed any intraoperative or early post-operative complication.

Discussion

Fuchs and Fuchs (2) have reported the first RIRS experience using a flexible ureterorenoscopy in 1990. With the recent advances in technology in addition to widespread use of the technique, today RIRS is used along with ESWL and PNL for kidney stone management. RIRS gained more popularity with similar stone-free rates and low complication profile seen in PNL technique (3). Lately, some authors argue that RIRS is a viable treatment option in treating 1-4 cm stones (4,5).

The European Association of Urology guidelines use stone size and location for determining treatment algorithm in kidney stones (1). However, kidney stone management in kidney anomalies is still a controversial subject. A study reported RIRS as a first-line treatment option in difficult cases such as bleeding diathesis, urinary diversion, morbid obesity, horseshoe kidney or calyx diverticulitis (6). In our study, we discussed the results of RIRS in our patients with horseshoe kidney anomaly.

Horseshoe kidney is the most commonly diagnosed fusion anomaly in kidneys. It is seen in 1 out of 400 live births. This anomaly is characterized by the anterior position of the renal pelvis and higher placement of ureteral exit. It causes insufficient drainage, urinary stasis and tendency for stone formation (7).

Table 1. Pre- and post-operative data of the patients included

	Age	Sex	Pre-operative ESWL	Stone localization	Preoperative DJS	Stone size (mm)	Stone-free	Intraoperative complications	Post-operative complications
Patient 1	58	Female	No	Pelvis	Yes	22	No	No	No
Patient 2	50	Male	Yes	Lower calyx	No	10	No	No	No
Patient 3	58	Female	No	Lower calyx	No	13	No	No	No
Patient 4	49	Male	Yes	Pelvis	No	15	No	No	No
Patient 5	33	Male	No	Lower calyx	No	12	Yes	No	No
Patient 6	19	Male	No	Pelvis	No	15	Yes	No	No

ESWL: Extracorporeal shock wave lithotripsy, DJS: Double-J stent

RIRS in horseshoe kidney was first reported in 2005 in a study including four patients with horseshoe kidneys and stone-free status was achieved in 3 of them (8). Another study including 17 patients done by Molimard et al. (9) reported a stone-free rate of 88.2%. No major complications were reported and the success rate was found to be comparable to PNL results. The study reported a mean stone size as 16 mm and all surgeries were performed by very experienced surgeons (9). Another study reported a stone-free rate of 70% in 25 renal units and low complication rates (10). Gokce et al. (11) in their study done on 23 patients, reported a stone-free rate of 73.9% with a mean stone size of 16.9±4.1 mm.

In our study, stone-free status was achieved in two (33%) patients based on non-contrast CT 1 month after surgery. This is a relatively low success rate in comparison with the results of the previous studies in the literature. This is thought to be caused by the insufficient experience with RIRS surgery in our clinic. In addition, the surgeries were not all performed by the same surgeon.

Study Limitations

There are not enough learning curve studies, thus, the sufficiency of RIRS technique (12). For that reason, we could not find a clear answer to the question "when RIRS should be performed in kidney anomalies?" However, one should be certain that the surgeon is experienced enough before attempting to use this technique in surgery of kidneys with anomalies. The main limitations of the study include its retrospective design, relatively low number of patients and the fact that the surgeries were not performed by the same surgeon.

Conclusion

For high stone-free rates, RIRS for horseshoe kidneys should be performed in experienced centers.

Ethics

Ethics Committee Approval: Retrospective study.

Informed Consent: Retrospective study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

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

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What are the Predictive Factors of the Cure and Complication Rates for Midurethral Slings in the Treatment of Stress Urinary Incontinence in Women: A Multicenter and Multivariate Analysis Study

Kadınlarda Stres Tip İdrar Kaçırma Tedavisinde Midüretral Slinglerin Başarı ve Komplikasyon Oranlarını Etkileyen Faktörler Nelerdir: Çok Merkezli ve Multivaryan Analiz Çalışması

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

To our knowledge, this was the biggest multicenter study about midurethral slings in our country. We hope the results will be a guide for the surgeons.

Abstract

Objective: Predictive factors that could affect the cure and complication rates of midurethral slings (MUS) in the treatment of stress urinary incontinence (SUI) were investigated.

Materials and Methods: A total of 594 women (outside-in transobturator in 285, inside-out transobturator in 91, and retropubic in 218) with SUI and who had undergone MUS were evaluated. The median age was 53.9 (27-82) years. Univariate analyses were done using chi-square test, Student's t-test and the Mann-Whitney U test. Multivariate analyses were done using logistic regression analysis to determine predictive factors affecting cure and complication rates.

Results: The mean follow-up time was 48 months. The subjective cure rate was 84% and complication rate was 11.2%. On univariate and multivariate analyses, the cure rate was found to be increased in younger patients [odds ratio (OR): 0.97, 95% confidence interval (CI): 0.95-0.99, p=0.038] and in patients with pure SUI (OR: 2.17, 95% CI: 1.31-3.60, p=0.002). The type of surgery was the only statistically significant parameter affecting the complication rate, which was significantly higher in retropubic MUS procedure (OR: 6.28, 95% CI: 3.51-11.22, p<0.001).

Conclusion: MUS is an effective and safe surgical procedure in the treatment of SUI. In this study, age and type of incontinence were the only significant predictive factors affecting the cure rate. Our study suggests that retropubic approach could be considered a risk factor for complication after MUS.

Keywords: Stress urinary incontinence, midurethral sling, transobturator, retropubic, complication

Öz

Amaç: Kadınlarda stres tip idrar kaçırma (STİK) tedavisinde midüretral sling (MUS) uygulanmasının sonuç ve komplikasyon oranlarını etkileyen prediktif faktörleri araştırdık.

Gereç ve Yöntem: Ürodinamik STİK tespit edilip MUS uygulanan 594 kadın hasta (285 transobturator dıştan içe, 91 transobturator içten dışa, 218 retropubik) araştırıldı. Ortalama yaş 53,9 (27-82) idi. Univaryan analizde ki-kare, Student-t ve Mann-Whitney U testleri kullanıldı. Multivaryan

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Öz

analizde lojistik regresyon testi kullanılarak kür ve komplikasyon oranlarını predikte eden faktörler araştırıldı.
Bulgular: Ortalama 48 ay takip süresinde subjektif kür oranı %84 olurken komplikasyon oranı %11,2 oldu. Univaryan ve multivaryan analizde kür oranının genç hastalarda [p=0,038, göreceli olasılıklar oranı (OR): 0,97, %95 güven aralığı (GA): 0,95-0,99] ve saf STİK olan hastalarda (p=0,002, OR: 2,17, %95 GA: 1,31-3,60) arttığı tespit edildi. Uygulanan cerrahi tipinin komplikasyon oranlarına etki eden tek prediktif faktör olduğu tespit edildi ki bu retropubik MUS'de anlamlı olarak daha yüksekti (OR: 6,28, %95 GA: 3,51-11,22, p<0,001).
Sonuç: Kadınlarda STİK cerrahi tedavisinde MUS başarıyla uygulanabilmektedir. Yapılan çalışmada yaş ve idrar kaçırma tipinin kür oranlarına etki eden prediktif faktörler olduğu bulunurken, uygulanan cerrahi tipinin komplikasyon oranlarını etkileyen tek prediktif faktör olduğu tespit edildi.
Anahtar Kelimeler: Stres tip idrar kaçırma, orta üretra gevşek sling, transobturator, retropubik, komplikasyon

Introduction

Stress urinary incontinence (SUI) is a common condition in women, with a prevalence of 35.5% in urology and obstetrics and gynecology outpatient clinics in Turkey (1), similar with that in the other European countries with the rate of 35% (2).

The main goal of the surgical treatment of SUI is to restore continence with minimal morbidity. Midurethral slings (MUS) are defined and performed continuously for the treatment of female SUI. Tension-free vaginal tape (TVT), which is a minimally invasive technique, was described in 1995 by Ulmsten and Petros (3) and has been used for the treatment of SUI in women. Despite the high success rates ranging from 84% to 95% that were notified for TVT, (4,5,6,7), there are concerns regarding its operative safety. Most perioperative complications of the TVT procedure have been related to penetration into the retropubic space (8,9). Transobturator tape (TOT), which was described by Delorme et al. (10) in 2001, was adopted because of perioperative and postoperative complications of TVT.

The aim of this study was to evaluate the predictive factors that could affect the effectiveness and complication rates of MUS, which has been performed for the surgical treatment of SUI in 5 medical centers in Turkey since 1999.

Materials and Methods

In this study, we included a total of 594 women (outside to in transobturator in 285, inside to out transobturator in 91, retropubic in 218) from 5 medical centers in Turkey, who were diagnosed with urodynamic SUI and underwent a MUS operation between October 1999 and August 2011 (Table 1). The study was approved by the İstanbul University Cerrahpaşa Faculty of Medicine Local Ethics Committee (approval number: 32821). Consent form was filled out by all participants.

The median age was 53.9 (27-82) years. A postoperative follow-up period of less than 6 months was the exclusion criterion in this study.

Patients presenting with stress or mixed (stress + urgency) type urinary incontinence were evaluated with medical history, physical examination, urinalysis, urine culture, 3-day bladder diary and multichannel urodynamic studies. Provocative stress test was performed in all patients and urethral mobility and pelvic organ prolapse (POP) were evaluated. The urodynamic study consisted of uroflowmetry, measurement of post-void residual urine, 1-h pad test, cystometry and measurement of valsalva leak point pressure. Most of the urodynamic investigations in this study were performed according to the standards of International Continence Society (ICS) "Good Urodynamic Practice" after it was published (11) and the ICS terminology was used for all definitions (12). The International Consultation on Incontinence Questionnaire-Short Form (ICIQ-SF) was used as a patient reported outcome measure after the validation of the Turkish version in 2004 (13). In total, 246 of 594 women had completed ICIQ-SF.

All patients underwent retropubic or transobturator placement of midurethral slings as previously defined (1,6) either using ready to use slings or homemade meshes by experienced surgeons or residents. All patients received intravenous antibiotic at the beginning of the operation. The operations were performed under local or general anesthesia. Cystoscopy was performed in all TVT patients, however, it was done in TOT patients if there was a hematuria or any difficulties during the passage of the trocars. The catheter was removed in the evening of the operation day in TVT group and immediately after the operation in TOT group.

Two outcome measures were evaluated; subjective cure rate and complication rate. Subjective cure was defined as the statement of the women of not experiencing any loss of urine upon

Table 1. The number of patients recruited by each of the five centers

Institution	n	%
İstanbul University Cerrahpaşa Faculty of Medicine	307	51.7
İzmir Ege University	91	15.3
İstanbul Marmara University	81	13.6
Kocaeli University	67	11.3
Ankara Gazi University	48	8.1
Total	594	100

physical activity, coughing or sneezing. Any amount of leakage was considered as surgical failure. Reported complications were bleeding, bladder perforation, other organ injury, retention, voiding dysfunction, de novo urgency, urinary infection, pain, and skin complications.

Statistical Analysis

Statistical analysis was done to assign the factors that had a significant impact on the effectiveness and complication rates of MUS. Statistical analyses were done with SPSS version 15.0. Univariate analyses were done using chi-square test, Student's t-test and the Mann-Whitney U test. Multivariate analyses were done using logistic regression analysis.

Results

The median follow-up period was 48 months. Patient characteristics are shown in Table 2. Preoperative evaluation findings and operative characteristics are shown in Table 3 and Table 4, respectively. Subjective cure rate was 84% and overall complication rate was 11.2%.

In univariate analysis, age, having stress incontinence (rather than mixed or urge incontinence), presence of detrussor overactivity in preoperative urodynamic investigation, use of a ready to use mesh, and concurrent POP repair were the factors that had a significant influence on the improvement of subjective cure rate (Table 5). However, number of delivery and pregnancies, comorbidity [diabetes mellitus (DM), neurologic disease], preoperative ICIQ-SF score, abdominal leak point pressure (ALPP) and experience of surgeon did not affect the subjective outcome. In multivariate analysis, increased age was a factor that negatively affected subjective cure rate and only to have a "stress type of incontinence" proved to improve cure rate (Table 6).

Univariate analysis of factors that could affect complication rate is shown in Table 7. Complication rate in the retropubic MUS patients were significantly higher compared to that in transobturator (either "inside-out" or "outside-in") MUS patients (50/168 vs. 17/359, respectively) (p<0.001). The type of mesh used also seemed to affect complication rate in univariate analysis. The complication rate was higher in patients who were operated with homemade meshes compared to those operated with ready to use meshes (17/71 vs. 50/456, respectively) (p=0.01). In multivariate analysis, only the type of surgery proved to affect complication rate (Table 8). Table 9 shows the complications with respect to types of MUS.

Table 2. Patient characteristics

Mean age (years)	**53.9 (±10.7)**
Body mass index	28.6 (20-70)
Type of incontinence	
Mixed type	298 (50.2%)
Stress type	282 (47.5%)
Urge type	13 (2.2%)
Number of pregnancies	4.2 (±2.4)
NSD	2.9 (±1.6)
Sectio	0.07 (±0.3)
Previous pelvic surgery	
No	441 (74.2%)
Hysterectomy	43 (7.2%)
MUS	21 (3.5%)
POP	21 (3.5%)
Other	33 (5.7%)
No data	35 (5.9%)

NSD: Normal spontaneous delivery, MUS: Midurethral sling, POP: Pelvic organ prolapse

Table 3. Preoperative findings

Qmax in uroflowmetry	27.1 (±8.3)
PVR	10.5 (±23)
VLPP	65.4 (±33.2)
DOA in cystometry	11.5% (68/594)
ICIQ-SF score	16.3 (±3.6)

PVR: Post-void residual, VLPP: Vesical leak point pressure, DOA: Detrussor overactivity, ICIQ-SF: International Consultation on Incontinence Questionnaire-Short Form

Table 4. Operative characteristics

Mean operative time (min)	36.4	±24.1
Mean hospital stay (hours)	39.5	±22.3
Type of anesthesia		
General	359	60.4%
Spinal	199	33.5%
Local	5	0.8%
Experience of surgeon		
Experienced	476	80.1%
Asistant	118	19.9%
Route of MUS insertion		
TOT outside in	285	48.0%
Retropubic	218	36.7%
TOT inside out	91	15.3%
Source of mesh		
Ready to use	506	85.2%
Home made	88	14.8%
Co existance POP surgery		
Yes	65	10.9%
No	529	89.1%

MUS: Midurethral sling, TOT: Transobturator tape, POP: Pelvic organ prolapse

Table 5. Univariate analysis of factors that could effect surgical outcome

Variable	Cured	Not cured	p
Age, mean (±SD)	53.7 (±10.5)	56.2 (±11.3)	0.04**
Number of NSD, mean (±SD)	2.8 (±1.5)	3.3 (±1.7)	0.11**
Number of pregnancies, mean (±SD)	4.1 (±2.3)	4.3 (±2.4)	0.06**
Comorbidity (DM, neurologic disease)			
Yes	32	8	0.47*
No	436	81	
Type of incontinence			
Mixed	218	59	0.003*
Stress	239	29	
Urge	15	2	
Preoperative ICIQ-SF score, mean (±SD)	16.3 (±3.6)	16.2 (±4.0)	0.72**
DOA in urodynamics			
Yes	44	19	0.01*
No	429	71	
ALPP, mean (±SD)	64.6 (±35.3)	63.1 (±29.1)	0.44**
Type of surgery			
TOT outside in	228	55	0.57*
TOT inside out	82	9	
Retropubic	163	26	
Type mesh used			
Ready to use	433	72	0.001*
Home made	40	18	
Concurrent POP repair			
Yes	45	15	0.04*
No	428	75	
Experience of surgeon			
Experienced	377	68	0.37*
Not experienced	96	22	

*Chi-square

**Student's t-test

SD: Standard deviation, NSD: Normal spontaneous delivery, DM: Diabetes mellitus, ICIQ-SF: International Consultation on Incontinence Questionnaire-Short Form, DOA: Detrussor overactivity, ALPP: Abdominal leak point pressure, TOT: Transobturator tape, POP: Pelvic organ prolapse

Table 6. Multivariate analysis of factors that could effect surgical outcome

	B	SE	Wald	df	p	Exp (B)
Age	-0.02	0.01	4.29	1	0.038	0.97
Type of incontinence, stress	0.77	0.25	9.1	1	0.002	2.1
Type of mesh (home made vs. ready to use)	0.62	0.34	4.34	1	0.067	1.87
Concurrent POP repair	-0.52	0.44	1.35	1	0.244	0.59
DOA in urodynamics	-0.57	0.33	2.90	1	0.088	0.56

POP: Pelvic organ prolapse, DOA: Detrussor overactivity, B: Coefficient, SE: Standard error, df: Degree of freedom, Exp (B): Confidence interval of odds ratio

Table 7. Univariate analysis of factors that could effect complication rate

Variable	Complication	No complication	p	Total
Age, mean (±SD)	52.6 (±9.0)	54.0 (±10.9)	0.28**	
Number of NSD, mean (±SD)	2.97 (±1.6)	2.95 (±1.5)	0.91**	
Number of pregnancies, mean (±SD)	4.6 (±2.6)	4.1 (±2.4)	0.16**	
Comorbidity (DM, neurologic disease)				
Yes	5	41	0.9*	46
No	62	478		540
Preoperative ICIQ-SF score, mean (±SD)	15.3 (±4.7)	16.3 (±3.5)	0.65***	
DOA in urodynamics				
Yes	10	58	0.34*	68
No	57	468		526
ALPP, mean (±SD)	59.3 (±30.7)	65.9 (±34.9)	0.15**	
Type of surgery				
TOT outside in	11	274	0.000*	285
TOT inside out	6	85		91
Retropubic	50	168		218
Type mesh used				
Ready to use	50	456	0.01*	506
Home made	17	71		88
Postoperative ICIQ-SF score, mean (±SD)	5.0 (±6.2)	3.1 (±5.6)	0.25***	
Concurrent POP repair				
Yes	5	60	0.33	65
No	62	467		529
Experience of surgeon				
Experienced	60	416	0.40*	476
Not experienced	7	111		118

*Chi-square

**Student's t-test

***Mann-Whitney U

SD: Standard deviation, NSD: Normal spontaneous delivery, DM: Diabetes mellitus, ICIQ-SF: International Consultation on Incontinence Questionnaire-Short Form, DOA: Detrussor overactivity, ALPP: Abdominal leak point pressure, TOT: Transobturator tape, POP: Pelvic organ prolapse

Table 8. Multivariate analysis of factors that could effect complication rates

	B	SE	Wald	df	p	Exp (B)
Type of surgery (Transobturator vs. retropubic)	-0.888	0.182	23.7	1	0.000	0.411
Type of mesh (home made vs. ready to use)	-0.611	0.414	2.174	1	0.140	0.543

B: Coefficient, SE: Standard error, df: Degree of freedom, Exp (B): Confidence interval of odds ratio

Discussion

In the present study, the age of the patients and the type of incontinence were found to be independent factors affecting the cure rates of MUS in the treatment of SUI in women. There are studies assessing the risk factors affecting cure and complication rates after MUS (14,15,16). The factors that have been demonstrated to affect success following MUS procedure were the type of incontinence, previous continence surgery, age, body mass index, usage of anticholinergic medications preoperatively, concurrent prolapse surgery and the type of surgery (14,15,16).

There are several studies that demonstrated the relationship between the age of the patient and success of MUS. Chen et al. (17) reported that the success rate of transobturator MUS was greater in women aged 60 years old or younger, compared with those older than 60 years [odds ratio (OR): 11.7; 95% confidence interval (CI): 1.8-76]. Patient age was found the only statistically significant parameter affecting the cure rate in another study

Table 9. The complications with respect to types of midurethral sling

	Transobturator		Retropubic		
	n	%	n	%	
Overall complications	17/359	4.7	50/168	29.7	0.001*
Immediate complications	1	0.3	3	1.8	
• Hemorrhage	-	-	1	0.6	
• Bladder perforation	1	0.3	2	1.2	
Short term complications	16	4.4	47	27.9	
• Voiding dysfunction	8	2.2	31	18.4	
• Infections	1	0.3	3	1.8	
• Pain	2	0.5	8	4.7	
• Skin infection and erosion	5	1.4	5	3.0	

*Chi-square test

and the cure rate was significantly lower in TVT patients over 55 years of age (18). However, there are also several studies that have demonstrated satisfactory outcomes after TVT in elderly patients (19,20). Nonetheless, elderly is known to be a greater risk for morbidity in any surgery. In this study, the subjective cure rate was lower in elderly patients (OR: 0.97, 95% CI: 0.95-0.99, p=0.038).

Mixed urinary incontinence was found to be a significant independent predictor for failure in our study. Holmgren et al. (21) reported that the long-term (8 years) cure rate after TVT in women with mixed urinary incontinence was lower than in women with pure SUI (21). However, others have found that the presence of urge symptoms did not reduce the success rates (22,23). Existing literature showed the difference between the mixed and pure SUI, however, those studies mostly included patients who were treated with retropubic MUS (21,23). Our study included both retropubic and transobturator groups and demonstrated that to have a pure SUI improved the success rate 2.17 times (OR: 2.17, 95% CI: 1.31-3.60, p=0.002) greater than mixed incontinence. Postoperative urge incontinence remains one of the most significant reasons for patient dissatisfaction and patients with mixed urinary incontinence should be informed preoperatively about the lower cure rates.

Although the type of mesh, concurrent prolapse repair and detrussor overactivity were significant in univariant analysis, they were not affecting the outcome of the surgery significantly in multivariate analysis. Some other studies indicated these variables as independent risk factors for surgical outcome (14,15,16). In a recent study, it was reported that concomitant prolapse surgery decreased the likelihood of surgical failure after MUS (14), and that concurrent prolapse surgery, taking anticholinergic medications preoperatively and increased age were independent risk factors affecting successful outcome after MUS (16).

In the present study, number of delivery and pregnancies, comorbidity (DM, neurologic disease), ALPP, and preoperative ICIQ-SF score did not affect the surgical outcome. However, it was observed that women with an ALPP of 60 cm H_2O or less had 12 times greater risk for continued SUI than women with a ALPP of more than 60 cm H_2O (24). In this study, we found no relationship between ALPP and treatment outcome. Pregnancy, delivery and other conditions, such as comorbidities, have been evaluated in the literature and identified as risk factors for SUI (25), however, they were not found as independent risk factors for outcome in our study. In addition, preoperative ICIQ-SF score that revealed the degree of incontinence and quality of life of the women did not affect the surgical outcome, although 246 of 594 women had completed ICIQ-SF score sheet in this study.

The complication rate in the retropubic MUS patients was significantly higher compared to that in transobturator (either "inside out" or "outside in") MUS patients. The type of the surgery predicts the complication rate of MUS. In addition, our study demonstrated that among the predictive factors that could affect the complication rates associated with MUS. Only the type of surgery proved to affect complication rate.

The complication rates are higher with retropubic routes than with transobturator tapes (26), although there are some studies against this conclusion (27,28,29). For instance, a randomized comparative trial suggested that patients in transobturator group had more complications than the retropubic group (27). However, in another study, it was demonstrated that TOT was equally effective as TVT with fewer complication, and the authors suggested that TOT would be the procedure of choice (30). In our opinion, the study design is important when comparing the complications rate between two groups. Minor complications included in the study (e.g._groin pain) and follow-up time could affect the complication rates of MUS. Similarly, Latthe et al. (31) reported that the rate of major complications, such as bladder injuries and haematomas, was higher in TVT than in TOT. However, groin/thigh pain and vaginal injuries were lower in TVT than

in TOT (31). Additionally, operator experience may be another important factor for the complication rates. However, experience of surgeon did not affect the outcome and complication rate of the surgery in our study. Hence, most of the surgeries were performed by experienced surgeons with residents observing by experienced surgeons during the procedure in our study. In the existing literature, there are several major complications after retropubic MUS, such as nerve, bowel or major vascular injuries, pelvic hematoma, necrotizing fasciitis, ischiorectal abscess, and even death (26). Notwithstanding, the majority of complications were not reported in small randomized controlled trials. In the present study, reported complications were bleeding, bladder perforation, other organ injury, retention, voiding dysfunction, de novo urgency, urinary infection, pain, and skin complications (Table 9). The risk of complication in retropubic MUS was 6.28 (95% CI: 3.51-11.22, p<0.001) times higher than in transobturator MUS in a 48-month follow-up period.

Study Limitations

Some limitations should be pointed out with regard to our study design. The retrospective nature was the first bias of our study. Besides, this study was not a randomized trial. However, it was a multicenter study including sites throughout the country. The operations were performed by different surgeons and this point could be thought as another bias. However, the cure rate was not affected by the experience of the surgeon.

Conclusion

We conclude that age of the patient and type of incontinence were significant predictive factors affecting the cure rate for MUS in women with SUI. Risk factors for treatment failure are similar for TVT and TOT. However, retropubic approach should be considered a high risk factor for complication after MUS.

Ethics

Ethics Committee Approval: The study was approved by the İstanbul University Cerrahpaşa Faculty of Medicine Local Ethics Committee (approval number: 32821).

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

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: O.D., B.Ç., C.Özyurt, T.T., C.Ö., İ.Ş., Concept: S.Ç., O.D., C.Özyurt, C.Ö., B.Ç., Design: S.Ç., O.D., T.T., B.Ç., Data Collection or Processing: S.Ç., N.M., C.Ö., S.Çiftçi, L.İ., İ.Ş., Analysis or Interpretation: S.Ç., O.D., N.M., A.Ş., Literature Search: C.Özyurt, İ.Ş., N.M., T.T., Writing: S.Ç., N.M., T.T., O.D.

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The Effect of Ureteral Stent Placement Before Radical Prostatectomy on the Safety of Ureteral Dissection and the Surgeon's Comfort

Radikal Prostatektomi Öncesi Üreteral Stent Yerleştirilmesinin Güvenli Üreteral Diseksiyona ve Ameliyat Konforuna Etkisi

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

It has been reported that placing ureteral stents during robot-assisted laparoscopic radical prostatectomy particularly in patients with a large median lobe after the incision of the anterior bladder neck makes the ureteral dissection procedure safer. We recommend this procedure particularly for patients with a large median lobe, a ureteral orifice that atypically opens closer to the bladder neck, a large ureterocele, a severe ureteral kink, and a history of pelvic radiotherapy or transurethral resection of the prostate.

Abstract

Objective: This study investigated the role of preoperative ureteral stent placement in reducing the risk of ureteral injury, an intraoperative complication of radical retropubic prostatectomy (RRP), and its contribution to the surgeon's comfort.

Materials and Methods: Open RRP was performed in 66 patients diagnosed with localized prostate cancer in our clinic between 2010 and 2015. The patients were divided into two groups; group 1 (n=34) underwent surgery without ureteral stent placement and group 2 (n=32) had surgery following the placement of a ureteral stent. The cases were preoperatively evaluated by suprapubic and transrectal ultrasonography. Perioperative and postoperative complications of all cases were determined. Both groups were assessed in terms of ureteral injury, operative time, and surgeon's comfort.

Results: The mean age of the patients in group 1 and group 2 was 61.12±5.92 (50-72) years and 63.58±6.2 (51-75) years, respectively. The mean prostate volume was 76.8±2.41 and 72.4±3.53 cc in groups 1 and 2, respectively. The mean operative time was 143.9±3.06 minutes in group 1 and 136.8±2.83 minutes in group 2. Partial ureteral injury occurred in three patients in group 1 and was repaired intraoperatively. Of these patients, two had previously undergone radiotherapy for prostate cancer and it was difficult to perform prostate dissection intraoperatively. The remaining patient had a history of transurethral resection of the prostate. No ureteral injury was observed in any of the patients in group 2.

Conclusion: Preoperative ureteral stent placement in selected patients can facilitate ureteral dissection and reduce ureteral injury risk.

Keywords: Prostatic neoplasms, prostatectomy, ureter, stents

Öz

Amaç: Bu çalışmada ameliyat öncesi üreteral stent yerleştirilmesinin radikal retropubik prostatektomi (RRP) ameliyatının intraoperatif bir komplikasyonu olan üreter yaralanması riskinin azaltılmasındaki rolü ve cerrahi konfora katkısı değerlendirilmiştir.

Gereç ve Yöntem: 2010-2015 yılları arasında kliniğimizde lokalize prostat kanseri saptanan 66 hastaya açık RRP ameliyatı yapılmıştır. Hastalar iki gruba ayrılmıştır; grup 1 (n=34) üreteral stent yerleştirilmeden ve grup 2 (n=32) sistoskopi eşliğinde bilateral üreteral stent yerleştirildikten sonra

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Öz

opere edilmiştir. Olgular preoperatif olarak suprapubik ve transrektal ultrasonografi ile değerlendirilmiştir. Bütün olguların peroperatif ve postoperatif komplikasyonları tespit edilmiştir. Her iki grup üreteral yaralanma, ameliyat süreleri ve cerrahın ameliyat konforu açısından değerlendirilmiştir.

Bulgular: Bu çalışmadaki grup 1 ve grup 2 hastaların sırasıyla, yaş ortalaması 61,12±5,92 (50-72) ve 63,58±6,2 (51-75) yıl, prostat volümleri 76,8±2,41 ve 72,4±3,53 cc olarak tespit edilmiştir. Ortalama ameliyat süreleri grup 1 için 143,9±3,06 dakika iken, grup 2 için 136,8±2,83 dakika olarak gerçekleşmiştir. Grup 1'deki hastaların üç tanesinde ameliyat sırasında kısmi üreteral yaralanma oluşmuş ve intraoperatif olarak onarılmıştır. Bu hastalardan iki tanesi daha önce prostat kanseri sebebiyle radyoterapi alan hastalar olup intraoperatif olarak prostat diseksiyonu güçlükle yapılabilmiştir. Bir hastada ise geçirilmiş transüretral prostat rezeksiyonu öyküsü tespit edilmiştir. Grup 2'deki hastaların hiçbirinde üreteral yaralanma oluşmamıştır.

Sonuç: Seçilmiş hastalara ameliyat öncesinde üreteral stent yerleştirilmesi üreteral diseksiyonu kolaylaştırabilir ve üreteral yaralanma riskini azaltabilir.

Anahtar Kelimeler: Prostat tümörleri, prostatektomi, üreter, stentler

Introduction

Prostate cancer is one of the most common malignancies seen in Turkey as well as across the world and has varying treatment modalities. Radical retropubic prostatectomy (RRP) is a common treatment method for localized prostate cancer. Developed 60 years ago, this operation involves the removal of the entire prostate gland between the bladder and the urethra (1). Approximately 30 years ago, Walsh and Donker (2) developed a neuroprotective technique. Despite all the improvements in the RRP technique, intraoperative and postoperative complications are more frequently seen compared to other operations. Studies have suggested the placement of ureteral stents or use of intravenous indigo carmine to prevent ureteral injury in RRP (3,4). We consider that ureteral stents deployed in selected patients before RRP are an effective method of reducing the risk of intraoperative ureteral injury and contributing to surgeon's comfort.

Materials and Methods

Open RRP was performed in 66 patients with localized prostate cancer in our clinic between 2010 and 2015. The patients were divided into two groups: group 1 consisted of 34 patients who had open RRP without ureteral stent placement. Group 2 comprised 32 patients who had undergone the same operation following bilateral ureteral stent placement with cystoscopy. Patients who were diagnosed with prostate cancer were preoperatively evaluated by hemogram, biochemistry, chest X-ray, abdominal tomography or magnetic resonance imaging. In cases where necessary, whole-body scintigraphy was performed and the disease was confirmed to be localized. Furthermore, suprapubic and transrectal ultrasonography was undertaken for all patients preoperatively to assess intravesical pathology, prostate volume and median lobe of the prostate. Patients presenting with large median lobe, ureteral orifice that atypically opens closer to the bladder neck, large ureterocele, severe ureteral kink, nodule or hardness on rectal examination and history of pelvic radiotherapy or transurethral resection of the prostate were included in the study. Patients presenting with bladder cancer on ultrasound were excluded from the study. Table 1 shows the demographic characteristics of patients included in the study. All patients were treated with the same technique by the same surgeon. Both groups were evaluated for ureteral dissection and surgeon's comfort during the operation. This study was designed retrospectively and all patients signed an informed consent agreement.

Operation Technique

Under general anesthesia, cystoscopy was performed on patients of group 2 in the lithotomy position to insert a bilateral ureteral d-J stent. The operation was started with a subclavian median incision in the supine position and bilateral pelvic lymphadenectomy was undertaken to perform complete staging. The endopelvic fascia was opened and completely separated from the prostate levator muscle and made spherical. In patients with large prostates and narrow and deep anatomy of the pelvis, the puboprostatic ligaments were cut. In the remaining patients, the puboprostatic ligaments were left intact. Then, the dorsal venous complex was ligated and cut, and the urethra was removed.

Following the removal of the urethra, the rectourethral fibers, vas deferens, and seminal vesicles were dissected. In young patients presenting with normal findings on rectal examination and low risk, the neurovascular bundle was preserved. The rectal catheter that was inserted preoperatively allowed a safer dissection intraoperatively. Following the separation of the lateral pedicles, the border between the bladder and the prostate was detected and the bladder neck was incised from the anterior to the posterior to separate the prostate from the mesentery; thus, the prostatectomy procedure was completed. After this procedure, the bilateral stents were clearly visible and the intestines around the ureter orifices were confirmed to be intact (Figure 1). In cases where necessary, the bladder neck was narrowed and reconstructed with eversion using the "tennis

racket" technique. Following the removal of the ureteral stents, vesicoureteral anastomosis was completed with an average of 6 sutures. After a leakage test to confirm that there was no extravasation, the procedure was terminated by closing each layer. A head light and magnification were used during the operation.

Statistical Analysis

The data was analyzed with the Statistical Package for the Social Sciences v. 16 (SPSS Inc, Illinois, USA). Continuous data was expressed as mean ± standard deviation. The statistical comparisons of age, prostate volume and operation time were performed by a paired sample t-test. The Kruskal-Wallis H test was used in the analysis of the demographic characteristics of the patients. A p value of less than 0.05 was considered statistically significant.

Results

The mean age of the patients in group 1 was 61.12±5.92 (50-72) and those in group 2 was 63.58±6.2 (51-75) years. The mean prostate volume in group 1 and group 2 was 76.8±2.41 cc and 72.4±3.53 cc, respectively. The mean operative time was 143.9±3.06 in group 1 and 136.8±2.83 minutes in group 2 (Table 2). There was no statistically significant difference between the two groups in terms of age, prostate volume and duration of operation (p>0.05). Partial ureteral injury occurred in three patients in group 1 during the dissection of the posterior bladder neck. One of these patients had a history of transurethral resection of the prostate. Damage to the left ureteral orifice due to dissection was detected intraoperatively and repaired by implanting it into the bladder mucosa after placing the ureteral d-J stent. The remaining two patients had a history of pelvic radiotherapy, which made it difficult to dissect the tissues resulting in a partial injury to the distal ureter during the dissection of the bladder neck from the posterior. This injury was noticed during the operation and primarily repaired following the insertion of the d-J stent. None of the patients in group 2 presented with any complication. The stents placed in the group 2 patients were removed intraoperatively prior to vesicoureteral anastomosis.

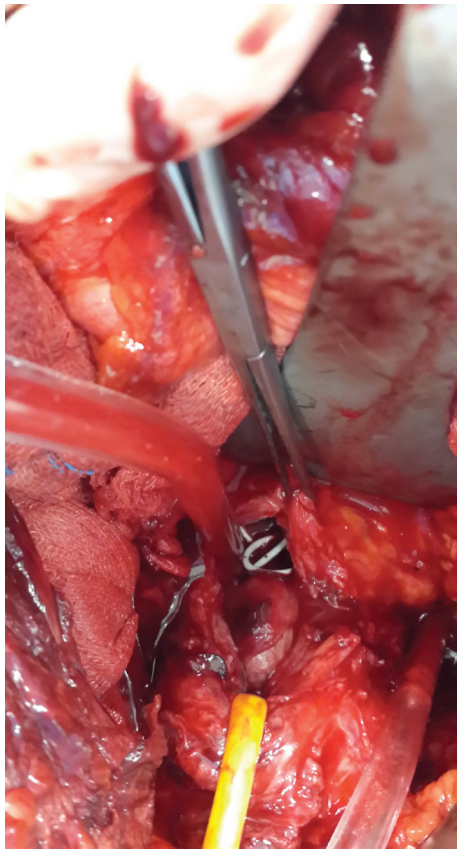

Figure 1. The appearance of a large median lobe (arrow) and ureteral d-J stents during the resection of the bladder neck

Discussion

Radical prostatectomy is the only method that has been reported to have an advantage over conservative treatments concerning survival rate, particularly for patients with a life expectancy of

Table 1. The demographic characteristics of the patients

	Group 1 (n=34)	Group 2 (n=32)	*p
Large median lobe	15	17	0.74
Atypically located orifices	1	3	0.81
Bladder tumour	-	-	-
Ureterocele	-	1	0.76
Radiotherapy or TUR* history	5	4	0.82
Solitary kidney	-	1	0.77
Nodule or hardness on rectal examination	7	5	0.64

*Kruskal-Wallis H test was used in all comparisons

TUR: Transurethral resection

Table 2. A comparison of the two groups in terms of age, prostate volume and operation time

	Group 1 (n=34)	Group 2 (n=32)	p*
Age (year)	61.12±5.92	63.58±6.2	0.897**
Prostate volume (cc)	76.8±2.41	72.4±3.53	0.75**
Operation time (minute)	143.9±3.06	136.8±2.83	0.674**

*Paired sample t-test

**There was no statistically significant difference between the two groups in terms of age, prostate volume and operation time

more than 10 years and for those included in the low risk group (5). This procedure has one of the longest learning curves in terms of the anatomical localization of the prostate and the surrounding structures. Radical prostatectomy involves many intraoperative and postoperative complications and its success depends on the use of a good technique. The most important intraoperative complication is hemorrhage, which arises from venous structures and may require transfusion. In different case series, average blood loss has been reported to be 1500 mL (6). In addition to hemorrhage, rectal injury and obturator nerve injury during pelvic lymphadenectomy may be seen (7).

Another complication that can be seen intraoperatively is ureteral injury, which mostly occurs during dissection of the posterior bladder neck (3,8). Although the incidence changes depending on the experience of the surgeon and the particular case, it has been reported to vary between 0 and 4.7% (4). It is beyond doubt that preoperative stent placement reduces the risk of ureteral injury particularly in patients with a large median lobe, atypical cases in which the ureteral orifice is too close to the bladder neck, and patients with a history of transurethral resection or pelvic radiotherapy. These stents may be used temporarily and removed at the end of the operation before performing vesicoureteral anastomosis. Another method of preserving ureteral orifices is to use intravenous indigo carmine (4). However, this method has received little attention from researchers.

It cannot be reliably predicted in advance which cases have more risk for ureteral injury. Studies reporting a higher risk in patients with a large median lobe have suggested the use of a temporary ureteral stent or intravenous indigo carmine depending on the surgeon's preference after dissecting the anterior bladder neck in order to prevent ureteral injury during the dissection of the posterior bladder neck in these patients (3,4). In clinical practice, in certain cases, we place a ureteral stent by cystourethroscopy with the patient in the lithotomy position before proceeding to open RRP. Cystourethroscopy offers a more detailed assessment of the urethra and the bladder mucosa and helps identify small bladder pathologies and the localization of ureteral orifices that cannot be detected in preoperative imaging. In the current study, ureteral injury was not observed in any of the patients who underwent surgery after the placement of a d-J stent. We consider that patients with high risk for ureteral injury are those with a large median lobe, a ureter orifice that is atypically close to the bladder neck, a large ureterocele, a severe ureteral kink, and a history of pelvic radiotherapy or transurethral resection of the prostate. In addition, preoperative ureteral stent placement may be an advantage in patients with poor renal function or a solitary kidney. Undertaking this procedure by cystourethroscopy for all cases may be disadvantageous in terms of cost. However, placement of a ureteral stent in the described cases would not only facilitate surgery and allow a safer dissection but may also prevent morbidity due to ureteral injury and reduce additional tests and treatment cost for patients.

In open RRP, after dissecting the bladder neck, surgeons try to monitor ureteral orifices and urine jet, however, observing these structures with the naked eye is both troublesome and extends the duration of the procedure. Ureteral stents placed preoperatively not only reduce the risk of ureteral injury during dissection and allow safer dissection, but also demonstrate ureteral orifices immediately after the dissection of the bladder neck and prevent the prolongation of the operation time. These stents should be removed after placing vesicoureteral anastomotic sutures. It has been reported that placing ureteral stents during robot-assisted laparoscopic radical prostatectomy particularly in patients with a large median lobe after the incision of the anterior bladder neck makes the ureteral dissection procedure safer (3). However, to the best of our knowledge, there is no study in the literature reporting endoscopic placement of a ureteral stent before open RRP.

Study Limitations

The limitation of this study is that it is performed in a small number of patients. Prospectively randomized trials with greater numbers of patients may contribute to this issue.

Conclusion

Ureteral stent placement in open radical prostatectomy is not routinely required. However, it may be useful in selected cases that are at risk for dissection. In RRP, ureteral stent placement by cystourethroscopy makes bladder neck dissection safer and reduces the risk of intraoperative ureteral injury without significantly affecting the operation time. We recommend this procedure particularly for patients with a large median lobe, a ureteral orifice that atypically opens closer to the bladder neck, a large ureterocele, a severe ureteral kink, and a history of pelvic radiotherapy or transurethral resection of the prostate.

Ethics

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

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

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Diagnostic Role of F-18 Fluorodeoxyglucose Positron-Emission Tomography/Computed Tomography in Restaging of Upper Urinary Tract Urothelial Carcinoma

Üst Üriner Sistem Transizyonel Hücreli Karsinomlarının Yeniden Evrelendirilmesinde F-18 Florodeoksiglukoz Pozitron-Emisyon Tomografisi/Bilgisayarlı Tomografinin Tanısal Rolü

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

There are quite few data in the literature about re-staging of upper urinary tract urothelial carcinoma with positron-emission tomography/computed tomography (PET/CT). We may see in the study that PET/CT detects local recurrence and distant metastasis with high specificity.

Abstract

Objective: To retrospectively evaluate contribution of F-18 fluorodeoxyglucose positron-emission tomography/computed tomography (^{18}FDG-PET/CT) to re-staging of upper urinary tract urothelial carcinoma (UTUC).

Materials and Methods: This study included a total of 17 patients (12 males and 5 females), who underwent nephroureterectomy due to UTUC and ^{18}FDG-PET/CT between July 2007 and April 2015. The mean age of the patients was 64.3±9.96 years (range: 45-79). ^{18}FDG-PET/CT was performed for re-staging 6-24 months after nephroureterectomy (mean: 18 months). Nearly 1 hour after intravenous injection of 555 MBq of F-18 FDG, the patients underwent whole-body PET scanning from the skull base to the upper thighs after 6 hours of fasting, and nearly 1 hour after all body CT scanning performed in the craniocaudal direction. By using CT data for attenuation correction, FDG-PET images were reconstructed.

Results: ^{18}FDG-PET/CT scans proved negative findings in three patients (17.7%) and positive findings in 14 patients (82.3%). Suspicious recurrent or metastatic lesions were confirmed by histopathology or clinical follow-up. Sensitivity of ^{18}FDG-PET/CT was 93% and the specificity was 75%.

Conclusion: ^{18}FDG-PET/CT defines local recurrence and far metastases with high specificity in re-staging of operated UTUC. It is thought that the procedure could play an important role in decisions regarding radiotherapy or chemotherapy and post-operative follow-up after the operation and could affect the whole decision-making process.

Keywords: Upper urinary tract urothelial carcinoma, positron-emission tomography, positron-emission tomography/computed tomography, re-staging

Öz

Amaç: Üst üriner sistem ürotelyal karsinomlarının (UTUC) yeniden evrelendirilmesinde F-18 florodeoksiglukoz pozitron-emisyon tomografisi/bilgisayarlı tomografinin (^{18}FDG-PET/BT) katkısını retrospektif olarak incelemektir.

Gereç ve Yöntem: Temmuz 2007 ile Nisan 2015 tarihleri arasında UTUC nedeniyle nefroüreterektomi yapılan ve yeniden evreleme amacıyla ^{18}FDG-PET/BT çekilen 17 hasta (12 erkek, 5 kadın) çalışmaya dahil edildi. Hastaların ortalama yaşı 64,3±9,96 yıl idi (yaş aralığı: 45-79). Yeniden evreleme için ^{18}FDG-PET/BT çalışması nefroüreterektomi sonrası 6-24 ay sonra (ortalama 18 ay) yapıldı. Hastalar taramadan önce 6 saat boyunca aç bırakıldı ve kafa tabanından üst uyluk bölgesine kadar olan alanda F-18 FDG 555 MBq intravenöz enjeksiyonundan yaklaşık 1 saat sonra tüm vücut PET taraması yapıldı. Tüm vücut BT taraması kraniokaudal yönünde yapıldı. FDG-PET imajları doğrulama için BT dataları kullanılarak rekonstrükte edildi.

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Öz

Bulgular: ^{18}FDG-PET/BT görüntüleme üç hastada (%17,7) negatif, 14 hastada (%82,3) pozitifti. Şüpheli tekrarlayan veya metastatik lezyonlar histopatolojik olarak ya da klinik izlem ile teyit edildi. ^{18}FDG-PET/BT'nin duyarlılık ve özgüllüğü sırasıyla %93 ve %75 idi.
Sonuç: Opere UTUC'nin yeniden evrelemesinde ^{18}FDG-PET/BT lokal nüks ve/veya uzak metastazları yüksek doğrulukta saptayabilmektedir. Operasyon sonrası takip ile radyoterapi ve kemoterapi kararının verilmesi ve tedavi sonrası takibin yapılmasında önemli bir rol oynayabileceği ve karar vermeyi etkileyebileceği düşünülmektedir.
Anahtar Kelimeler: Üst üriner sistem ürotelyal karsinoma, pozitron-emisyon tomografisi, pozitron-emisyon tomografisi/bilgisayarlı tomografi, yeniden evreleme

Introduction

Urothelial cancers are the fourth most common cancers after prostate or breast cancers, lung, and colorectal cancers (1). However, upper urinary tract urothelial carcinoma (UTUC) is an extremely rare cancer and accounts for 5-10% of all urothelial cancers (2). The estimated annual incidence of UTUC in Western countries is about one or two new cases per 100.000 inhabitants. The rate of concomitant bladder carcinoma ranges between 8% and 13% in patients diagnosed with UTUC. Of these patients, 30-51% develop recurrence in the bladder, and ipsilateral recurrence occurs in 2-6% (3). An invasive cancer is present in 60% of patients at the diagnosis of UTUC. The disease makes a peak in patients aged 70-80 years, and the ratio of male to female is 3:1. There have been familial/hereditary cases of UTUC linked to hereditary nonpolyposis colorectal carcinoma (1). Environmental carcinogens and smoking are the most important etiological factors. Furthermore, the polymorphism reducing the activity of sulfotransferase which triggers the development of UTUC is the only genetic etiological factor described in the literature (4). Histopathologically, these tumors are classified similar to bladder cancers as carcinoma *in situ* (CIS), low-grade and high-grade. Multidetector computed tomography urography (MDCTU) is the gold standard method in the diagnosis of UTUC (5). UTUCs invading the muscle wall usually have a very poor prognosis. The 5-year cancer-specific survival is <50% for pT2/pT3 and <10% for pT4 (6). Gender and localization of the tumor are considered to be of no prognostic significance. Advanced age, presence of lymphovascular invasion, presence of necrosis, sessile growth pattern of the tumor, and presence of CIS may predict poor prognosis (1). Radical nephroureterectomy with excision of the bladder cuff is the gold standard treatment for UTUCs, regardless of the location of theatumor in the upper urinary tract (7). All patients should be followed up after radical nephroureterectomy for possible development of metachronous bladder tumor. Cisplatin-based chemotherapy regimens can be used in UTUCs. However, adjuvant chemotherapy achieves a recurrence-free rate of up to 50% but has minimum impact on survival (8). Adjuvant radiotherapy can achieve local disease control (9).

UTUC requires follow-up with cytology, cystoscopy, ureterorenoscopy, and MDCTU after surgery. However, diagnosis of distance metastases and local recurrence remain challenging in operated UTUC. Moreover, there is a need for a diagnostic test providing high sensitivity and specificity in determining residual disease and monitoring response to treatment after radiotherapy and chemotherapy. F-18 fluorodeoxyglucose positron-emission tomography/computed tomography (^{18}FDG-PET/CT) is the most important diagnostic instrument providing functional and anatomical images. The most important aim of this study was to define the role of ^{18}FDG-PET/CT in re-staging UTUC after surgery. The histological conclusions (where available) or the total clinical and radiological workup (MDCTU, magnetic resonance imaging) were used as a standard reference.

Materials and Methods

A total of 7938 patients were evaluated and 10553 ^{18}FDG-PET/CT scans were performed in the nuclear medicine department between July 2007 and April 2015. In this patients group, 17 [12 males (70.5%) and 5 females (29.5%)] were diagnosed with operated upper urinary tract carcinoma and underwent ^{18}FDG-PET/CT for re-staging of the tumor. ^{18}FDG-PET/CT study was performed after nephroureterectomy in all patients. PET/CT was made once 6-24 months post-operatively. All patients were diagnosed with transitional cell carcinoma (TCC) based on histopathological and immunohistochemical evaluation. The mean age of the patients was 64.3±9.96 years (range: 45-79). According to the grading system of the European Association of Urology (EAU) for upper urinary tract TCC, two patients (11.7%) had low-grade and 15 patients (88.3%) had-high grade tumor. The patients were re-evaluated with ^{18}FDG-PET/CT for re-staging due to suspicion of disease recurrence besides other radiologic or clinical analyses done to perform routine follow-up. These patients were evaluated retrospectively, and pathological findings and ^{18}FDG-PET/CT data were recorded.

All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation and with the Helsinki Declaration of 1975, as revised in 2000. The study does not have approval of the ethical committee as it is retrospective but, informed consent

was obtained from all patients for being included in the study. Additional information consent was obtained from all patients for which identifying information is included in this article.

Imaging and Interpretation of Data

F-18 fluorodeoxyglucose was synthesized using an in-house cyclotron (Siemens) and an automated synthesis system according to the authorized procedure. After five hours of fasting, blood glucose level of each patient was measured, and the patient was then intravenously injected with 370 MBq of F-18 FDG. One hour after F-18 FDG injection, a CT scan without contrast agent was performed, covering the area from the vertex to the proximal thigh, and the images were used for attenuation correction and image fusion. This was followed by whole-body 3D PET acquisition with 8 bed positions of 3 minutes of emission scan time each using a dedicated PET/CT scanner (HI-REZ Biograph 6, Siemens) which provides an in-plane spatial resolution of 4.8 mm, an axial field view of 16.2 cm. The PET data were reconstructed using a Gaussian filter with an ordered-subset expectation maximization algorithm (3 iterations, 8 subsets), re-oriented in transverse, coronal and sagittal planes, and assessed by comparing them with corresponding CT images.

PET scans were analyzed visually and semi-quantitatively using maximum standardized uptake value (SUV_{max}) measurement. SUV was expressed in terms of body weight (SUVbw - g/mL). The parameters such as patient's weight (kg), height (cm), radioactivity during injection (MBq), residual radioactivity (MBq) after the injection, starting time of injection, and half-life of the radioisotope (taken as standard 109.8 minutes for 18-FDG) were calculated automatically by the software.

Two experienced nuclear medicine physicians reviewed blindly and independently the hybrid FDG PET/CT scans as positive or negative for a primary tumor site. Every focal tracer uptake that deviated from physiological distribution was considered in favour of disease spread. The background deviation and activity difference between the suspected lesion and the surrounding tissues were used to differentiate benign from malignant lesions. Therefore, SUV_{max}>2.5 threshold was employed.

Statistical Analysis

All statistical data analyses were calculated using SPSS statistics software (version 16.0; SPSS, Inc., Chicago, Illinois, USA). All statistical data analyses were calculated using Fisher's exact test. P<0.05 was considered to indicate a statistically significant difference.

Results

^{18}FDG-PET/CT scans presented negative findings in three patients (17.7%) and positive findings in 14 patients (82.3%). Four patients (23%) had widespread metastases with high SUV involving at least two organs (lungs, bone, lymph nodes, etc.). Eleven patients (64.7%) had lymph node metastasis (mean SUV_{max}: 5.8, min: 3.6, max: 11.3), four patients (23%) had bone metastasis (mean SUV_{max}: 8.8, min: 5.4, max: 14.8), and three patients (17.6%) had liver metastasis. None of the patients had metachronous bladder carcinoma or disease recurrence in the contralateral upper urinary tract. PET scans were negative in all patients classified as low grade according to the EAU grading system, and patients with high-grade tumor showed positive findings on PET (Table 1). The results of ^{18}FDG-PET/CT scans according to histological grade are presented in Table 1. The rate of PET-positive studies is higher if the grade of the tumor is high. The mean SUV_{max} was 7.1 (min: 3.6, max: 17) in patients with positive PET/CT findings. ^{18}FDG-PET/CT results correlated with histological subtype in possibility charts (p<0.05). Suspicious recurrent or metastatic lesions were confirmed by histopathology or clinical follow-up. Sensitivity and specificity of ^{18}FDG-PET/CT were 93%, 75% respectively (Figures 1, 2, 3, and 4).

Discussion

UTUC is associated with extremely poor prognosis. Radical nephroureterectomy and bladder cuff excision is the gold standard treatment method for UTUCs regardless of the localization of the tumor in the upper urinary tract (7). Since local recurrence and metastatic disease substantially decline survival in patients with UTUC, establishing exact diagnosis and providing prompt treatment are of crucial importance. Re-staging of the disease, minimizing false-positivities and false-negativities, and more importantly, recognition of metastatic disease constitute the most important and realistic part of determining the treatment strategy. In the light of current literature data, current follow-up programs routinely used in clinical follow-up of operated UTUC in general focus on the search for the presence of metachronous bladder carcinoma and/or upper urinary tract tumor. ^{18}FDG-PET/CT is the most significant diagnostic instrument that provides functional and anatomical images.

Establishing the diagnosis of primary UTUC using ^{18}FDG-PET

Table 1. Positron-emission tomography/computed tomography results according to histological findings and grade of the primary tumor

TCCa histological grade	PET/CT positive n, (%)	PET/CT negative n, (%)
Low grade	0	2 (100%)
High grade	15 (100%)	0

TCC: Transitional cell carcinoma, PET/CT: Positron-emission tomography/computed tomography

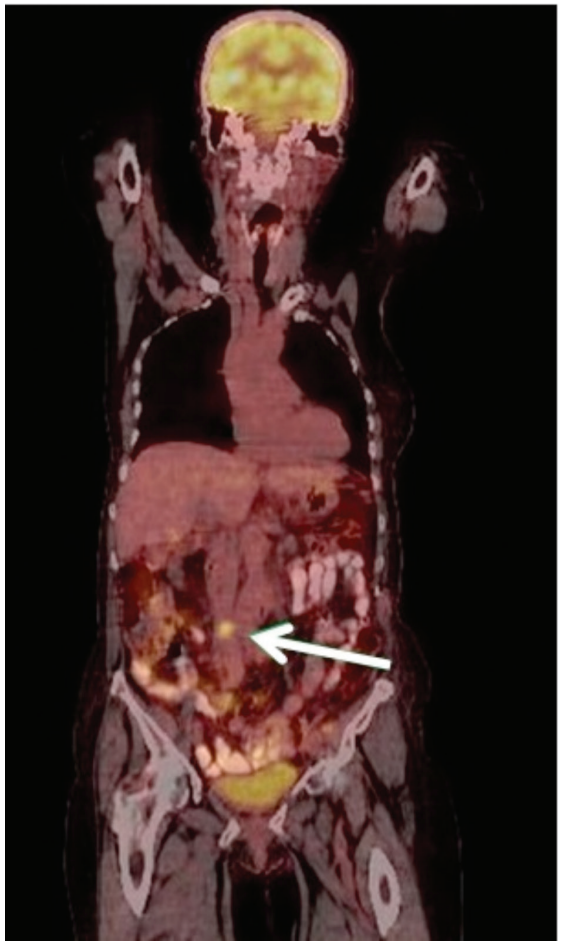

Figure 1. The coronal reconstruction of F-18 fluorodeoxyglucose positron-emission tomography/computed tomography scans shows interaortocaval lymphadenopathy (arrow), maximum standardized uptake value: 7.2

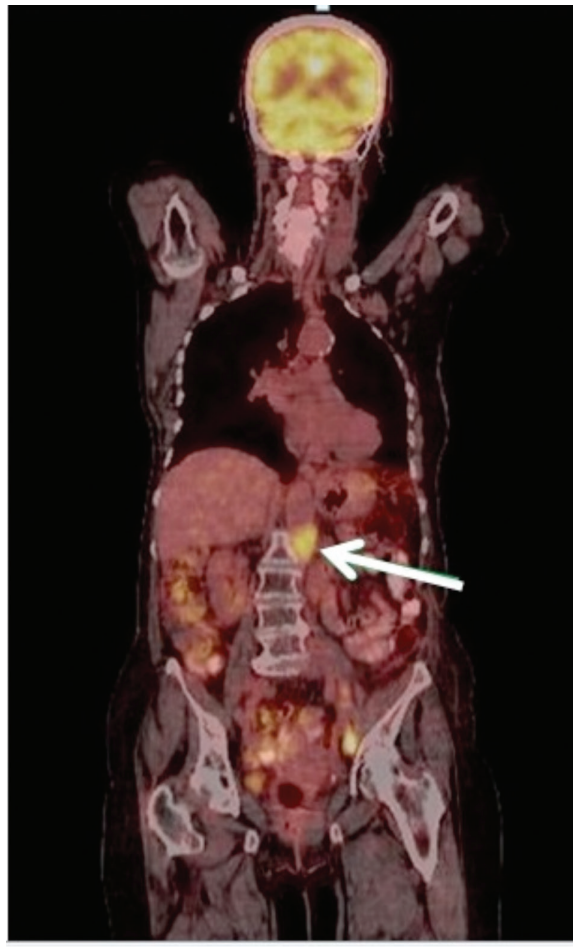

Figure 2. The coronal reconstruction of F-18 fluorodeoxyglucose positron-emission tomography/computed tomography scans shows paraaortic lymphadenopathy (arrow), maximum standardized uptake value: 10.0

scans is challenging due to of the physiological urinary activity of FDG. The physiological ^{18}FDG excretion of the renal collecting system should be differentiated from malignant pathological activity. The excretion of ^{18}FDG from pelvicalyceal system limits the sensitivity and specificity of the procedure in diagnosing urothelial cancers. The low expression of glucose transporters responsible for intracellular deposition of ^{18}FDG is one the most important reasons for reduced sensitivity in diagnosing primary urothelial carcinomas (10). However, re-staging of UTUC using ^{18}FDG-PET/CT scans after radical nephroureterectomy overcomes the challenges pertaining to the urinary tract in monitoring response to treatment after chemotherapy and radiotherapy. Therefore, it allows the diagnosis of the lesions with higher accuracy and specificity. This method has some limitations only in diagnosing upper urinary tract tumors and metachronous bladder tumor. However, this did not appear as a limitation in the current study due to the fact that none of the patients had local recurrence in the bladder and other parts of upper urinary tract.

The most distinctive feature of the cancer tissue is that it shows higher glucose metabolism than normal tissues (Warburg effect) (11). High uptake of FDG in cancerous lesions of the transitional carcinoma was first demonstrated by Harney et al. (12) in rats. Drieskens et al. (13) found that metabolism-based anatomical information gathered by the addition of FDG-PET to CT provided high diagnostic accuracy in pre-operative staging of invasive transitional cancers particularly invasive bladder carcinoma. A study by Watanabe et al. (14) demonstrated hypermetabolism in TCC of the upper urinary tract and suggested that FDG-PET imaging might be also useful in detecting primary and metastatic lesions of TCC of the renal pelvis. Diuresis has been known to effectively decrease the background radioactivity in the urinary tract and hence facilitate the identification of hypermetabolic lesions on FDG-PET (15). 11C-methionine PET has been reported to be superior to F-18 FDG PET (16). 11C-choline was also tried due to its low level of urinary excretion. In the literature, studies conducted by Picchio et al. (17) and Gofrit et al. (18) found that PET or PET/CT scans using 11C-choline were superior to CT alone in diagnosing lymph node metastases in patients

Figure 3. The coronal F-18 fluorodeoxyglucose positron-emission tomography/computed tomography scans show soft tissue metastasis in the left psoas muscle (arrow), maximum standardized uptake value: 11.3

Figure 4. Maximum intensity projection images of a patient, interaortocaval lymphadenopathy (arrow)

with UTUC. UTUCs commonly spread to hilar, abdominal, para-aortic, paracaval regional lymph nodes (19). In particular, nephrectomy eliminates the problem of superimposition in visualizing metastasis to ipsilateral lymph nodes and provides high diagnostic accuracy.

In this regard, the sensitivity of ^{18}FDG-PET/CT scans in diagnosing regional lymph nodes can be further increased. Furthermore, FDG activity in the residual tissue after radiotherapy and chemotherapy may be useful in re-staging of the disease. MDCTU is used to detect lymph node or distant metastases however, it is known that metastasis can also come about in normal-sized lymph nodes. Therefore, false-negative results in MDCTU are a handicap for the use of this method in re-staging of UTUCs. Sun et al. (20) found positive correlation between the sensitivity of FDG and grade and stage of UTUCs. In their series of 27 patients with urothelial malignancies, Sun et al. (20) stated that PET could have a role in the prognosis of UTUC. In this study, the sensitivity and positive predictive value of FDG PET and CT were 67% vs. 59% and 90% vs. 84%, respectively (20). In a series of 13 cases with metastatic UTUC reported by Dou et al. (21), PET/CT was used in re-staging of the disease. In the study, a SUV of 3.8 was detected for the metastatic lymph nodes measuring 10 mm (±2.2) in average. In these patients, the presence of metastatic disease was confirmed by pathological examination. After re-staging, the sensitivity and specificity were 87.5% and 92.3, respectively. Dou et al. (21) concluded that ^{18}FDG-PET/CT might play an important role in deciding on initial therapy and re-staging due to high sensitivity and specificity of this method in diagnosing local and/or distant metastases in patients with UTUC. Although average size of the lymph nodes was not available in the present study, 11 patients (64.7) were found to have lymph node metastasis. The mean SUV in these patients was 5.8 (min: 3.6, max: 11.3). The high sensitivity and specificity reported for ^{18}FDG-PET/CT in diagnosing patients with lymph node metastasis in the present study supports current literature data. The diagnostic performance reported for PET/CT scans in the literature is summarized in Table 2. We suggest that FDG-PET/CT is valuable in diagnosing lymph node metastasis considering the fact that this method detected lymph node metastasis with high accuracy in 64.7% of the patients in the present study. We assume that the fact that problems caused by physiologic renal excretion of FDG disappeared in all patients who underwent nephroureterectomy is particularly important in detecting lymph node metastasis. Therefore, PET/CT is particularly recommended when lymph node metastasis

Table 2. Diagnostic performance of positron-emission tomography and positron-emission tomography/computed tomography studies in the literature

Author	Modality	n	Sensitivity, %	Specifity, %	Accuracy, %	PPV, %	NPV, %
Sun et al. (20)	PET/CT	27	59 (67)	-	-	84 (90)	-
Dou et al. (21)	PET/CT	13	87.5	92.3	-	-	-
Present study	PET/CT	17	93	75	93.3	75	89

PPV: Positive predictive value, NPV: Negative predictive value, PET/CT: Positron-emission tomography/computed tomography

is suspected due to its high sensitivity in detecting metastasis in normal-sized lymph nodes. Considering the fact that the mean SUV was 5.8 for lymph node metastasis and all patients had high-grade UTUC in the present study, ^{18}FDG-PET/CT can provide useful information in patients with high-grade tumor and patients suspected to have lymph node metastasis. In the present study, four patients (23%) had bone metastasis with a mean SUV of 8.8 (min: 5.4, max: 14.8). There have been studies reporting that PET/CT offered high predictive value in detecting bone metastasis. Wu et al. (22) compared F-18 FDG PET and technetium-99m methylene diphosphonate bone scans and documented higher sensitivity and accuracy of PET in detecting bone metastases in patients with renal cell carcinoma. PET/CT is also superior to bone scintigraphy in demonstrating lytic bone metastasis. It has been suggested that ^{18}FDG-PET/CT would be especially useful in patients with prostate cancer with lytic skeletal metastasis (23). ^{18}FDG-PET/CT can diagnose UTUC with bone metastasis with high sensitivity and specificity when considering the disadvantages of bone scintigraphy having high rates of false-positive results caused by degenerative bone lesions.

The metabolic rate of low grade TCCs is close to that of normal tissues. The increased glucose metabolism in patients with high grade UTUC allows visualization of the lesions on the detector due to increased FDG uptake. In the present study, 17 patients underwent ^{18}FDG-PET/CT for re-staging of the disease. Despite small sample size, ^{18}FDG-PET/CT showed negative findings in all patients with low-grade tumor. On the other hand, ^{18}FDG-PET/CT showed positive findings in all patients with high-grade UTUC. Consistent with the literature data, there was a correlation between the tumor grade and positive PET/CT findings.

False-positive or false-negative results in FDG uptake cannot be related only to glucose metabolism of tumor tissue. The researches have showed that ^{18}FDG-PET/CT scans can render data solely in the existence of a number of and increased tumor cells with abnormal glucose metabolism (10^4-10^7). Such diagnostic insufficiencies are particularly important in metastasis to solid organs such as the lungs and liver. In general, ^{18}FDG-PET/CT cannot precisely evaluate metastasis measuring less than 5 mm in size. After all studies, we still do not know why lung lesions below this threshold do not produce high SUVs. This can be caused by movement artifacts and low metabolic activity of the metastatic lesion. Decrease in movement artifacts using steady techniques, achieving a better spatial resolution and finding a higher cut-off SUV amounts for such lesions can extend diagnostic exactness (24).

The findings of PET/CT scans must be verified by histopathological work-up in order to confirm disease recurrence. Theoretically, PET/CT remains the standard imaging technique. However, in daily practice, this can be rarely possible because of clinical reasons, feasibility of the procedure and effective advantages of this approach in the absence of a radical surgical intention. In our study, histological verification was available in four patients and all the other ones were compared with clinical and radiological findings. In one patient with mediastinal lymphadenopathy with a SUV of 5.5, the existence of metastasis was confirmed by endobronchial ultrasound-guided biopsy. In another patient, solitary lung metastasis (SUV: 5.1) was confirmed by metastasectomy, and the patient was administered with cisplatin-based chemotherapy.

Study Limitations

The limitation of the study is its retrospective nature. A number of selection bias may have been demonstrated as it is probably that only those patients with UTUC suspected to have recurrence were referred for PET/CT.

Conclusion

^{18}FDG-PET/CT images supply complete structural-metabolic data and have the potential to significantly decrease the false-positives of PET and CT performed individually. In spite of the limitations of our study due to its retrospective design and absence of systematic histological confirmation of pathological uptake, our outcomes are in compliance with the literature and suggest that ^{18}FDG PET/CT is characterised by high sensitivity and negative predictive value and could be useful in restaging UTUC. It is considered that the procedure could play a critical role in decisions regarding radiotherapy or chemotherapy and post-operative follow-up after the operation.

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Ethics

Ethics Committee Approval: All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation and with the Helsinki Declaration of 1975, as revised in 2000. The study does not have approval of the ethical committee as it is retrospective.

Informed Consent: Informed consent was obtained from all patients for being included in the study. Additional information consent was obtained from all patients for which identifying information is included in this article.

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Utility of Flexible Ureterorenoscopy and Laser Lithotripsy in the Treatment of Multiple Intrarenal Stones

Multipl Böbrek Taşlarında Fleksibl Üreterorenoskopi ve Lazer Litotripsinin Etkinliği

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

Only a few reports have described ureteroscopic treatment of multiple intrarenal stones. Extracorporeal shock wave lithotripsy and percutaneous nephrolithotomy have some disadvantages with multiple intrarenal stones. The present study showed that flexible ureterorenoscopy with laser lithotripsy was an effective and safe treatment option in patients with multiple intrarenal stones.

Abstract

Objective: We aimed to determine the safety and efficacy of flexible ureterorenoscopy and Holmium laser lithotripsy in treating multiple intrarenal stones.
Materials and Methods: We identified 32 consecutive patients with multiple intrarenal stones who underwent flexible ureterorenoscopy and/or laser lithotripsy performed by a single surgeon. Informed consent was obtained from all participants before treatment. Each patient was evaluated in terms of stone location, stone number, stone size, stone burden (cumulative stone length), body mass index, operative time, stone-free rate, and perioperative complications.
Results: The median age of the patients was 38 years [interquartile range (IQR), 34.25-52.00]. The patients had a total of 75 intrarenal calculi. The average number of stones per patient was 2.50 (IQR, 2.0-3.0). The median total stone burden per patient was 23.0 mm (IQR, 19.0-28.0 mm). Twenty-one patients (65.5%) had stone burdens >20 mm, and 11 (34.5%) had burdens ≤20 mm. The overall final stone-free rate was 78.1%. The stone-free rates for patients with stone burdens ≤20 mm and >20 mm were 81.8% (9/11) and 76.2% (16/21), respectively (p=0.544). A perioperative complication (urinary leakage) occurred in one patient. Postoperative complications were recorded in four (12.5%) patients; a urinary tract infection in one, pain requiring parenteral medication in two, and hematuria in one.
Conclusion: Flexible ureterorenoscopy combined with laser lithotripsy may be an effective treatment option for patients with multiple intrarenal stones; we noted only a few minor complications. The success rate was higher in patients with stone burdens ≤20 mm.
Keywords: Flexible ureterorenoscopy, laser lithotripsy, multiple renal stones

Öz

Amaç: Multipl böbrek taşlarının tedavisinde fleksibl üreterorenoskopi ile birlikte Holmium lazer kullanımını etkinlik ve güvenlik açısından değerlendirmeyi amaçladık.
Gereç ve Yöntem: Kliniğimizde multipl böbrek taşı nedeni ile tek cerrah tarafından fleksibl üreterorenoskopi ve lazer litotripsi yapılan 32 hasta retrospektif olarak değerlendirildi. Hastaların yaşı, cinsiyeti, vücut kitle indeksi, operasyon süresi, taşlarının yeri, boyutu, sayısı, yükü, taşsızlık oranı ve komplikasyonlar kaydedildi. Taş yükü böbrek içindeki taşların uzunlukları toplamı olarak hesaplandı. Taşsızlık, operasyon sonrası 3. ayda taş olmaması veya böbrek içinde <3 mm taş olması olarak değerlendirildi.
Bulgular: Ortanca hasta yaşı 38 [çeyrekler arası aralık (IQR), 34,25-52,00] yıl idi. Hastalarda toplam 75 intrarenal taş vardı. Hasta başı ortanca taş sayısı ve taş yükü sırasıyla 2,50 (IQR, 2,0-3,0) 50 ve 23,0 mm (IQR, 19,0-28,0 mm) idi. Hastaların 21'inde (%65,5) taş yükü >20 mm iken 11 (%34,5) hastanın ≤20 mm idi. Toplam taşsızlık oranı %78,1 idi. Bu oran taş yükü ≤20 mm ve >20 mm olan hastalarda sırasıyla %81,8 (9/11) ve %76,2 (16/21) idi (p=0,544). Bir hastada operasyon sırasında idrar kaçağına neden olan üreter perforasyonu gelişti, double-J kateter ile tedavi edildi. Dört hastada (%12,5) postoperatif komplikasyon izlendi (iki hasta paranteral tedavi gerektirecek ağrı, bir hastada hematüri, bir hastada ise idrar yolu enfeksiyonu).

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Öz

Sonuç: Böbrek içi multipl taş tedavisinde fleksibl üreterorenoskopi ile birlikte lazer litotripsi düşük komplikasyon oranı ve yüksek başarıya sahiptir. Bu taşların tedavisinde ilk tercih kullanılabilmesi için ileri dönük kör karşılaştırmalı çalışmalara ihtiyaç vardır.
Anahtar Kelimeler: Fleksibl üreterorenoskopi, lazer litotripsi, multipl böbrek taşları

Introduction

Huffman et al. (1) were the first to perform retrograde intrarenal surgery (RIRS) in 1983. They used a rigid ureteroscope to deliver ultrasonic lithotripsy to a pelvic stone. Since that time, flexible ureteroscopes have been developed and the Holmium laser has been used for fragmentation. The advances in endoscopic imaging technology include enhanced deflection ability, increased durability, and reductions in diameter. Thus, the role played by RIRS in stone surgery has expanded.

The European Association of Urology guidelines on urolithiasis recommend different treatment modalities according to renal stone size and location (2). Thus, the recommended first-line treatment for renal stones >20 mm in diameter is percutaneous nephrolithotomy (PCNL), and both extracorporeal shock wave lithotripsy (ESWL) and endourology (RIRS and PCNL) for renal stones 10-20 mm in diameter. While ESWL is not recommended as the first-line treatment for lower pole renal stones in the presence of unfavourable factors, RIRS is strongly recommended (2). Nevertheless, there is no clear recommendation for multiple renal stones. In the treatment of these stones, because flexible ureterorenoscopy can readily reach different calices, it may have a higher success rate, especially for multiple stones in different locations. With PCNL and ESWL, there is also a need for multiple interventions for multiple renal stones in different locations. Although only a few studies have evaluated RIRS for the treatment of multiple renal stones, they have reported low interventions with high success rates (3,4,5,6,7).

In the present study, we sought to determine the safety and efficacy of flexible ureterorenoscopy and Holmium laser lithotripsy in treating multiple renal stones.

Materials and Methods

We retrospectively reviewed data on nephrolithiasis patients treated in our institution (İzmit Konak Hospital) from July 2013 to April 2015. We identified 32 consecutive patients with multiple intrarenal stones who underwent flexible ureterorenoscopy and laser lithotripsy performed by a single surgeon. All patients were informed about other treatment modalities such as PCNL and ESWL. Flexible ureterorenoscopy was performed based on patient preferences. Informed consent was obtained from all participants before treatment. All patients were evaluated prior to treatment by computed tomography (CT) running a dedicated stone protocol. Each patient was evaluated in terms of stone location, stone number, stone size, stone burden (cumulative stone length), body mass index (BMI), operative time, stone-free rate (SFR), and perioperative complications. The total stone burden was the sum of all stone diameters (3,6,8). Preoperative urinalyses and cultures were performed and appropriate antibiotics were prescribed if necessary. Operations were delayed in such cases. The operation time was defined as the time between commencement of endoscopy and placement of the double-J stent. Stone-free status was defined as the absence of stone fragments other than asymptomatic, insignificant residual fragments <3 mm in diameter.

Technique

Each patient was placed in the dorsal lithotomy position under general anaesthesia, and intravenous antibiotics were commenced. First, ureteroscopy was performed using an 8-9.5-F semi-rigid ureteroscope (Karl Storz, Germany) guided by a 0.038 mm diameter guidewire. The ureter was evaluated in terms of pathologies (stones, obstructions, and so forth) and subjected to dilation before placement of an access sheath [9.5/11.5, 11.0/13.0, 12.0/14.0-F (Cook, Boston Scientific)] to allow optimal visualisation, maintaining a low intrarenal pressure, and facilitating extraction of stone fragments. If an access sheath could not be placed, a double-J stent was placed and the operation was re-scheduled for 2 weeks later (passive dilation). A 7.2-F flexible ureteroscope (Storz FLEX-X2, Germany) through which a 270 µm laser fibre was used for treatment. The Holmium laser energy was set to 0.4-1.2 J delivered at 5-12 Hz (Dornier 20W Laser, Germany). In cases of large stones (>1 cm), we prefer low frequency and high power to fragment and collect the parts. In the case of small stones, we prefer high frequency and low power to dust it. We used 2.2-F tipless nitinol baskets (NCircle, Ngage, Cook Medical, Limerick, Ireland) for retrieval of stone fragments >2 mm in diameter. Postoperatively, a 6-F 26 cm long double-J stent was placed based on the surgeon's preference. This stent was removed under local anaesthesia, using a flexible or rigid cystoscope, within 3 weeks postoperatively. Residual fragment status was assessed via non-contrast CT, or renal ultrasonography (US) plus a plain frontal supine radiograph of the kidneys, ureters, and bladder (KUB) (only patients with radiopaque stones), 3 months after removal of the double-J stent.

Statistical Analysis

Statistical analyses were performed with the SPSS for Windows software (version 21.0; SPSS, Inc., Chicago, Illinois). Mean and

standard deviations were calculated for normally distributed numerical data, while median and interquartile ranges (IQRs) were obtained for numerical data with skewed distributions. The Pearson χ^2 test and Fisher's exact test were used to compare SFRs. The Mann-Whitney U test was used to compare operation times. A p value of <0.05 was taken to indicate statistical significance.

Results

On retrospective analysis, there were 32 patients: Twenty-four males and eight females. The median age was 38.00 years (IQR, 34.25-52.00) (Table 1). As regarding the weight of the patients, eight had normal weight (BMI: 18.50-24.99 kg/m^2), 13 patients were overweight (BMI: 25.00-29.99 kg/m^2) while 13 patients were obese (BMI ≥30.00 kg/m^2). The patient stone demographics are shown in Table 2. There were a total of 75 intrarenal calculi. The median stone number per patients was 2.50 (IQR, 2.0-3.0). The median total stone burden per patient was 23.0 (IQR, 19.0-28.0). Twenty-one patients (65.5%) had a stone burden >20 mm, and 11 patients (34.5%) had a stone burden ≤20 mm.

Evaluation of intraoperative and postoperative data is shown in Table 3. Passive dilatation with double-J stent was applied in three patients (access sheath application error). The overall median operation time was 67.50 minutes (IQR 60.00-80.00). Operation time was significantly longer in patients with stone burden >20 mm [76.52 (IQR 60.00-85.00) minute] compared to those with ≤20 mm [60.00 (IQR 40.00-60.00) minute] (p=0.026). The overall SFR was 78.1%. SFRs for patients with a stone burden ≤20 mm and >20 mm were 81.8% (9/11) and 76.2% (16/21), respectively (p=0.544). Significant residual fragments (≥3 mm) were found in seven patients. The total stone burden was >20 mm in these five patients, while ≤20 mm in two patients (one with a history of open renal surgery).

Perioperative complication (urinary leakage) was occurred in one patient with a 20-mm stone burden. He was treated with only a double-J stent. A follow-up CT scan at 1 month after double-J removal showed ureteral healing without any complication. Postoperative complications were recorded in four (12.5%) patients (two had ≤20 mm and two had >20 mm stone burden), including urinary tract infection in one, pain with requiring parenteral medication in two, and hematuria in one patients, respectively. The patient with urinary tract infection was admitted to the hospital for intravenous antibiotics. He was discharged home after 48 h and fully recovered in 15 days.

Table 1. Patient characteristics

Number of patients (n)	32
Gender	
Male, n (%)	24 (75%)
Female, n (%)	12 (25%)
Age, [median (IQR)]	38 (34.25-52.00)
Body mass index (kg/m^2) [median (IQR)]	28 (26.00-31.75)

IQR: Interquartile range

Table 2. The stone demographics

Stone laterality	
Right, n (%)	13 (40.6%)
Left, n (%)	18 (56.3%)
Bilaterally, n (%)	1 (3.1%)
Stone location	
Renal pelvis, n (%)	23 (71.9%)
Lower pole, n (%)	28 (87.5%)
Mid-pole, n (%)	15 (46.9%)
Upper pole, n (%)	8 (25.0%)
Number of stones per patients (n), median (IQR)	2.50 (2.0-3.0)
Total stone burden per patients (mm), median (IQR)	23.0 (19.0-28.0)

IQR: Interquartile range

Discussion

Intrarenal stones are treated with ESWL, PCNL, or RIRS depending on stone size and location (2,9). However, no consensus on the management of multiple intrarenal stones has yet emerged. The optimum approach must be associated with minor morbidity and a minimal need for recurring intervention.

Both ESWL and endourology are recommended first-line treatment options for renal stones <20 mm in diameter (2). However, EWSL SFRs are significantly decreased under the following circumstances: shock-wave-resistant stones (formed

Table 3. Evaluation of intraoperative and postoperative data

Operation time (minutes), median (IQR)	67.50 (60.00-80.00)
Passive dilatation, n (%)	3 (9.4%)
Use rate of access sheath, n (%)	31 (96.9%)
Hospitalisation time (hours), median (IQR)	24.00 (22.00-24.00)
Peroperative complication, n (%)	1 (3.1%)
Postoperative double-J catheterization, n (%)	29 (90.6%)
Postoperative complication, n (%)	4 (12.5%)
Stone free rate (overall), n (%)	25 (78.1%)
Stone free rate (≤20 mm), n (%)	9 (81.8%)
Stone free rate (>20 mm), n (%)	16 (76.2%)

IQR: Interquartile range

of calcium oxalate monohydrate, brushite, or cystine); the presence of a steep infundibular-pelvic angle; the presence of a long lower pole calyx (>10 mm); and the presence of a narrow infundibulum (<5 mm) (2). The ESWL SFRs fell as the BMI increased (2). In the current study, 13 (40%) patients were overweight and 13 (40%) were obese; the SFR was >78%. ESWL is contraindicated in pregnant patients and in those with bleeding disorders. In addition, no more than 3-5 sessions of EWSL should be conducted (2). Furthermore, ESWL often requires multiple sessions (e.g., in patients with steinstreise formations) and is associated with longer treatment periods than are other surgical methods in patients with multiple stones (10,11). ESWL is associated with higher rates of residual fragment regrowth (21-59%) (12,13) and dysrhythmia (11-59%) (12,14). Consequently, there is a need for alternative treatments for patients with multiple renal stones.

PCNL, the first-line treatment for stones >20 mm in diameter, affords very high SFRs (2). However, the presence of multiple, but separated, kidney stones usually require repeat access or re-operation, and possibly also adjunctive (i.e., endourological) procedures. The most common postoperative complications are fever, bleeding, urinary leakage, and difficulties attributable to residual stones (2). Seitz et al. (15) showed that after PCNL, Clavien 1 complications (deviations from the normal postoperative course without the need for pharmacological treatment or an intervention) occurred in up to 88.1% of patients. Clavien 2 complications (including a need for blood transfusion and/or parenteral nutrition) occurred in 7% of patients. Clavien 3 complications (requiring re-intervention) developed in 4.1% of patients. Clavien 4 complications (life-threatening) developed in 0.6% of patients, and Clavien 5 complications (death) developed in 0.04% (15). The risks of these complications increased when procedures were repeated. De et al. (16) conducted a systematic review and meta-analysis comparing PCNL with RIRS. PCNL afforded significantly higher SFRs but was associated with more complications and a greater postoperative decrease in hemoglobin level. RIRS yielded a significantly higher SFR than micro-PCNL but a lower SFR than standard PCNL (16).

Currently, RIRS is increasingly used in patients with advanced indications. Only a few reports have described ureteroscopic treatment of multiple intrarenal stones (3,4,5,6,7). Breda et al. (3) evaluated 51 patients with multiple intrarenal stones [a total of 161 intrarenal calculi, mean number of stones/patient 3.1±1 (2-6), stone burden 21±6 mm]. The overall SFRs after one and two procedures were 64.7% and 92.2%, respectively. The SFRs for patients with stone burdens >20 mm and <20 mm were 85.1% and 100%, respectively. Two operative complications developed, one major (sepsis) and four minor (3). Herrera-Gonzalez et al. (4) evaluated 125 patients, and the SFR after a single RIRS procedure was 74.4%. Takazawa et al. (5) studied 51 patients (with a total of 146 stones, 37 unilateral and 14 bilateral) who underwent 65 ureteroscopic procedures. The SFR after a single session was 80% (41/51). In patients with stone burdens <20 mm and ≥20 mm, the single-session SFRs were 92% (23/25) and 69% (18/26), respectively. No major intraoperative problems were noted (5). Alkan et al. (6) evaluated 41 patients [173 intrarenal stones; mean number of stones/patient 3.6±3.0; mean stone burden 22.2±8.4 mm (12-45 mm)]. The overall SFR was 91.7%. The SFRs for patients with stone burdens <20 mm and >20 mm were 100% (23/23) and 84% (21/25), respectively. Minor complications developed in six patients, but no major complications were noted (6). In the present study, we evaluated the RIRS success rates in patients with multiple intrarenal stones who underwent a single procedure. Similar to the cited studies, the overall SFR was 78.1%. When the patients were divided into those with stone burdens ≤20 mm and >20 mm, the SFRs were 81.8% and 76.2%, respectively. The overall SFR for a single procedure was higher than in studies by Breda et al. (3) and Herrera-Gonzalez et al. (4), similar to that by Takazawa et al. (5), and lower than in that by Alkan et al. (6), as described above. However, the SFR of the patients with stone burden ≤20 mm seemed to be lower versus the cited studies. Most of these studies did not state the number of sessions when they divided patients according to stone burden. Thus, it is expected that the very high SFRs in patients with stone burden <20 mm were probably caused by multiple procedures. Urinary system anatomies and stone localizations are also possible factors contributing to the lower SFRs.

In the present study, we encountered five minor complications (one operative and four postoperative). These were not correlated with increasing stone size. The numbers of postoperative complications were the same both in patients with stone burden ≤20 mm (n=2) and those with stone burden >20 mm (n=2). Additionally, a perioperative complication was seen in one patient with a stone burden ≤20 mm. The mean operation time was significantly higher with total stone burden >20 mm, as expected.

Study Limitations

The present study had some limitations. First, the retrospective nature of the study is important. In addition, there was no control group. Thus, further comparative, prospective studies are needed to draw final conclusions. Later, we evaluated residual fragment status via non-contrast CT or US plus KUB. We preferred US plus KUB in patients with radiopaque stones, because this avoided redundant exposure to X-rays from the CT scan. This may have caused insignificant measurement variability with respect to residual stones, due to the difference in accuracy between these imaging methods. Third, it is known that the SFRs of stone retrieval techniques show variability

according to the localization of the stone in the kidney. Thus, it would be better to compare SFRs with fixed locations and fixed stone burdens.

The total stone burden is calculated by several methods (cumulative diameter, surface area, and volume). In clinical practice, the most widely used parameter is cumulative diameter (3,6,8), as in the present study. However, since this parameter does not show stone width or depth, stone volume has been proposed to be a more reliable method for confirming stone-free status. Ito et al. (17) retrospectively analyzed 243 patients with radiopaque renal stones. They measured the preoperative stone burden according to both cumulative diameter (mm, KUB) and stone volume (mm^3, non-contrast CT). They obtained a plain KUB film on postoperative day 1 in all cases to assess the presence of stones. They defined stone-free status as no detectable stone on KUB images. SFRs at postoperative day 1 after URS were 79.43% (<20 mm stones) and 29.4% (≥20 mm stones). They found that cumulative stone burden calculated according to stone volume was more predictive of the presence of stones on postoperative day 1 on plain KUB versus the cumulative stone diameter, especially for stones ≥20 mm. However, this was a retrospective observational study. The SFR was much lower in stones of ≥20 mm compared with <20 mm stones. Postoperative day 1 is a very important time point for assessing the real stone-free status.

Conclusion

In conclusion, we found that flexible ureterorenoscopy with laser lithotripsy was an effective treatment option in patients with multiple intrarenal stones; only a few minor complications were encountered. The success rates were higher in patients with stone burdens <20 mm. Randomised comparative studies are needed before flexible ureterorenoscopy can be recommended as a first-line treatment for multiple intrarenal stones.

Ethics

Ethics Committee Approval: This article is based on a retrospective study. All data were collected from the hospital record system, and the study was performed in accordance with the ethical standard laid down in the 1964 Declaration of Helsinki and its later amendments.

Informed Consent: Informed consent was obtained from all participants before treatment.

Peer-review: Externally peer-reviewed.

Authorship Contributions

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

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CASE REPORT
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Extrarenal Retroperitoneal Angiomyolipoma: A Rare Case

Ekstrarenal Retroperitoneal Anjiyomiyolipom: Nadir Bir Olgu

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Abstract

Angiomyolipomas are benign tumors consisting of smooth muscles, vessels, and fat tissue. They are generally located on the kidneys; extrarenal angiomyolipoma is rare. Apart from the kidneys, angiomyolipomas are seldom located in the retroperitoneal area. Moreover, it is quite difficult to diagnose angiomyolipomas located in the retroperitoneal area. Due to the low amount of fat, negative density may not be identified by computed tomography (CT). The purpose of this report was to discuss the case of a retroperitoneal angiomyolipoma that clinically resembles a surrenal tumor and cannot be clearly discriminated from surrenal tissue on CT.

Keywords: Angiomyolipoma, density, kidney, retroperitoneum, tomography

Öz

Anjiyomiyolipomlar düz kas, damar ve yağ dokusundan oluşan benign tümörlerdir. Genellikle böbreğe yerleşirler, ekstrarenal anjiyomiyolipom nadir görülür. Anjiyomiyolipomun böbrek dışında retroperitoneal bölgeye yerleşimine oldukça az rastlanır. Retroperitoneal bölgeye yerleşen anjiyomiyolipomlara tanı koymak oldukça zordur. Yağ miktarının az olması nedeniyle bilgisayarlı tomografide (BT) negatif dansite saptanmayabilir. Bu olgu sunumumuzda klinik belirtileri sürrenal tümörü andıran ve BT'de sürrenal dokusuyla net ayrımı yapılamayan retroperitoneal anjiyomiyolipom olgusunu tartışmayı amaçladık.

Anahtar Kelimeler: Anjiyomiyolipom, dansite, böbrek, retroperiton, tomografi

Introduction

An angiomyolipoma (AML) consists of mature fat tissue, thick blood vessels, and soft muscle cells (1). AMLs are frequently located on the kidneys. Although most cases are sporadic, 20% are accompanied by tuberous sclerosis (2). Retroperitoneal AML may cause abdominal pain and increased abdominal discomfort. The diagnosis of renal AML is established using computed tomography (CT), showing negative fat density [between -10 and -100 Hounsfield unit (HU)] with an accuracy rate of 86% (3,4). In extrarenal AMLs, negative density may not be revealed due to the low amount of fat tissue, which complicates diagnosis (5). In our study, we discussed the rarely encountered case of a retroperitoneal AML.

Case Presentation

A 45-year-old male patient presented to our clinic with the complaint of pain on the right side of his body. A mass lesion (5x6 cm), which could not be clearly discriminated from the surrenal tissue in the right retroperitoneal area, was identified using ultrasonography. Abdominal CT showed a mass lesion measuring 5x6.5 cm with a density of 40 HU on the right side that could not be clearly discriminated from the surrenal tissue (Figure 1). The patient, who occasionally suffered from blood pressure attacks, was pre-diagnosed with pheochromocytoma or adrenocortical carcinoma. He was prepared for surgery by the endocrine clinic. Informed consent was obtained from the patient.

The mass was reached employing the open retroperitoneal approach. The mass was found to be located between the

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kidney and the surrenal tissue, independent of both organs. The whole mass was resected. Pathological examination of the lesion revealed vascular structures with thick walls containing no elastic lamina, mature adipose tissue focuses, and fascicles made of intense spindle cells around these structures. In the immunohistochemical examination, spindle cells were reactively identified through S100 SMA and Desmine HBM45. In the immunohistochemical study, S-100 reactivity was determined in the adipocyte areas, whereas CD34 and CD31 were positively identified in the vascular areas. The Ki-67 proliferative index was found to be low (5-10%) in all three components of the tumoral formation. Based on all the data, the case was interpreted in favor of "retroperitoneal AML" (Figure 2).

Discussion

AML was defined in 1951 by Morgan et al. (6). It is characterized by various amounts of vessels, muscles, and fat tissues. Although it is substantially observed to be sporadic, it is accompanied by tuberous sclerosis in 20% of cases. AML accompanied by tuberous sclerosis is frequent in the third or fourth decade of life and especially among women. These tumors are mostly observed to be asymptomatic, small, multifocal, and bilateral. Sporadic cases are observed as bigger, single, and unilateral masses (7) in patients aged between 40 and 70 years.

Tumors located in the retroperitoneal area are not common. The diagnosis before surgery is established via radiological screening. In the retroperitoneal area, lymph node metastasis may be observed after lymphoma, liposarcoma, leiomyosarcoma, schwannoma, paraganglioma, and testicular tumors (8). Retroperitoneal AML is a rare tumor. In the English literature, only 11 cases of retroperitoneal AML have been reported. Typically, these tumors grow towards the vascular pedicle and may cause abdominal pain and hemorrhagic shock (9). Although the radiological diagnosis of renal AML is straightforward, the diagnosis of extrarenal AML is difficult. Since fat density is low in these tumors, a negative density may not be identified, which complicates the diagnosis (10).

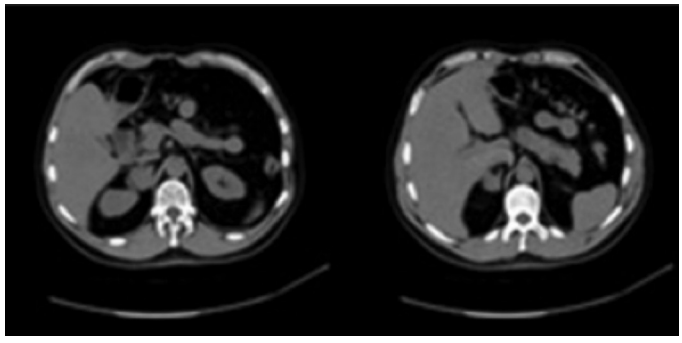

Figure 1. Mass with 5x6 cm size is seen in right surrenal area in tomography

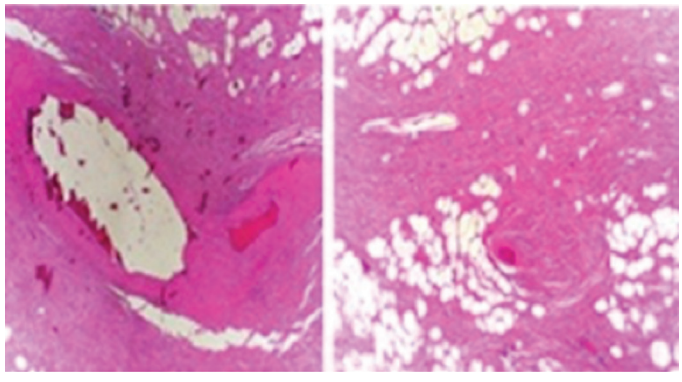

Figure 2. Microscopic image of lesion through hematoxylin and eosin

In our case, the density was measured as 40 HU due to the low amount of fat. As it could not be clearly discriminated from the surrenal tissue on CT, the mass lesion was thought to be primary surrenal tumor. However, in surgical exploration, the lesion was seen to be independent of the surrenal tissue. If AML could been diagnosed through radiology before surgery and the size of the tumor had been small, the patient could be managed via active surveillance. However, the patient has been operated on.

Consequently, the radiological diagnosis of renal AML is easy while the diagnosis of extrarenal retroperitoneal AML is more difficult. Since there is a lower fat density in these tumors, they may not be detected due to negative density.

Ethics

Informed Consent: Informed consent was obtained from the patient.

Peer-review: Externally peer-reviewed.

Authorship Contributions

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

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

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CASE REPORT
Urooncology

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Transitional Cell Bladder Cancer in a 12-Year-Old Male Patient: A Case Report

On İki Yaşındaki Erkek Hastada Transizyonel Hücreli Mesane Kanseri: Olgu Sunumu

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Abstract

Bladder tumors are rarely seen in childhood. However, transitional cell carcinoma of the bladder may be observed in this age group. Although they are generally low grade and the relapse rates are low, close follow-up is recommended. A 12-year-old child was brought to our clinic with the complaint of painless haematuria. Ultrasound initially detected a polypoid lesion on the right wall of the bladder. Pathological analysis revealed low-grade urothelial cancer without evidence of invasion (pTa). Bladder tumors, despite rarely seen in pediatric age group, should be considered in the differential diagnosis for patients with the complaint of macroscopic haematuria.

Keywords: Bladder cancer, pediatrics, transitional cell carcinoma

Öz

Mesane tümörleri çocukluk çağında nadir görülmektedir. Bu yaş grubunda görülen değişici epitelyal hücreli mesane tümörü çoğunlukla düşük evre ve düşük nüks oranına sahip olmakla birlikte yakın takibi önerilmektedir. Bu olgu sunumunda ağrısız makroskopik hematüri şikayeti ile polikliniğe başvuran 12 yaşındaki erkek hastayı sunmayı amaçladık. Hastanın üriner sistem ultrasonografisinde mesane sağ yan duvarda polipoid bir lezyon saptandı. Patolojik incelemede düşük dereceli non-invaziv ürotelyal kanser tanısı aldı (pTa). Mesane tümörü, pediatrik yaş grubunda nadir gözlenmesine rağmen makroskopik hematüri şikayeti ile başvuran hastalarda ayırıcı tanıda düşünülmesi gerekmektedir.

Anahtar Kelimeler: Mesane kanseri, pediatrik, transizyonel hücreli karsinom

Introduction

Bladder tumours (BTs) are rarely seen in childhood. Many reasons and risk factors for BT in adults have been described but etiology and prognosis of BTs in children could not be totally clarified as they are rarely seen in childhood. Transitional cell carcinoma of the bladder is caused by tumors peaking in 6th and 7th decades of life and observed 3-4 times more frequently in males than in females. Additionally, it has been reported that white ethnicity was associated with a greater risk (39:1) (1). While BTs of epithelial origin are common in adults, mesoderm-originated BTs are more commonly observed in children. In this paper, we aimed to present a case of transitional cell carcinoma of the bladder which is rarely seen in children.

Case Presentation

A 12-year-old child was brought to our clinic with the complaint of painless macroscopic haematuria for the last 2 months. Physical examination was normal. His body mass index was 27 kg/m^2. No erythrocyte and leukocyte were seen in urinalysis. His family history, environmental tobacco smoke and environmental factors were unremarkable. On urinary tract ultrasonography (USG), a polypoid nodular lesion 8.3x6 mm in dimension was detected on the right inferolateral wall of the bladder and the upper urinary system was natural. In the cystoscopy performed with general anaesthesia, bilateral ureter orifices were observed to be natural as well as a polypoid lesion stuck nearly 2 cm lateral to the right orifice on the right wall of the bladder.

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Monopolar transurethral resection (TUR) was performed using pediatric resectoscope to the lesion simultaneously (Figure 1) and no other lesion was seen in the bladder.

Postoperative bladder irrigation was applied until the 1st postoperative day. The urethral catheter was removed on the 3rd postoperative day and the patient was discharged. His pathologic assessment revealed low-level non-invasive papillary urothelial carcinoma (TaG1) (Figure 2, 3).

The patient was subjected to follow-up and cystoscopy 3 months later. Written informed consent was obtained from the parents of the patient.

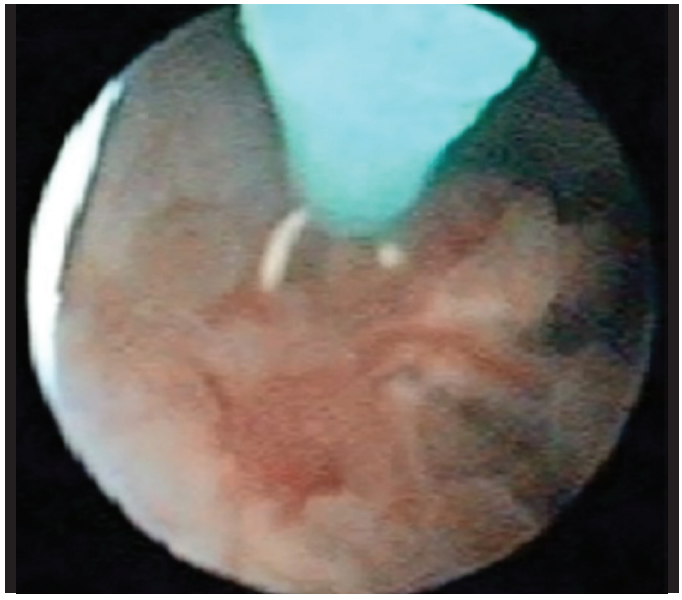

Figure 1. Transurethral resection of the papillary tumor on the right side wall of the urinary bladder

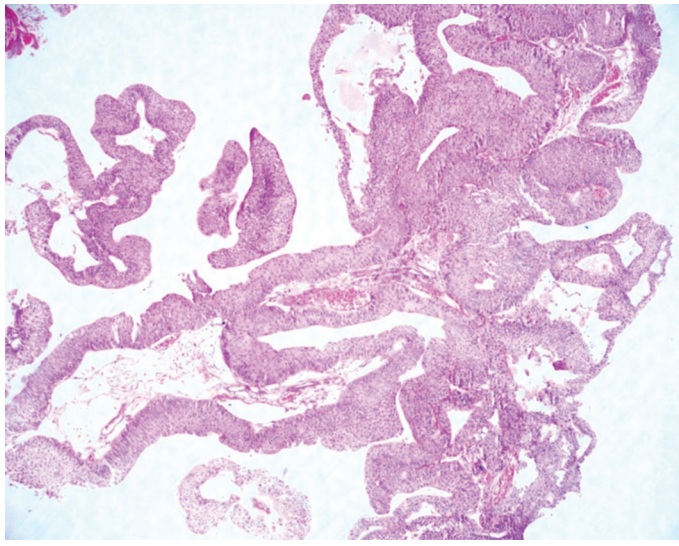

Figure 2. Low power microscopic magnification (hematoxylin and eosin, x40) of the lesion: Frondlike papillary projections that include thickened multilayered urothelium and fragments of apparently normal bladder mucosa was observed. There was not any lamina propria invasion in papillary neoplasm areas

Discussion

BT is the 11th most common cancer worldwide. Most of the diagnosed BTs were reported to be non-muscle invasive bladder cancer.

BTs are rarely seen in childhood. In childhood, bladder cancer was first reported in 1924 (2). Recently, Lerena et al. (2) reported 125 cases of urothelial tumors diagnosed in patients younger than 20 years of age.

Although childhood BTs are generally mesoderm-originated, tumors of epithelial origin are seen far less. Many factors, such as social and genetic factors, occupational exposures, dietary habits, radiation exposure, aromatic amines, exposure to cyclophosphamide, and smoking habit play significant roles in adults. Bladder stones, Schistosoma haematobium, chronic irritation and infection are also among the factors increasing the risk of cancer. However, chronic irritation and infections were blamed in the aetiology, although the effect of these risk factors in childhood could not be totally clarified (3). Moreover, it was detected that some genetic factors are influential in terms of aetiology. In a study conducted by Keetch et al. (4), high Ki67 expression and low cycline D1 expression were found to be correlated with higher relapse rates. Although reduced p27 Kip1 expression increases the risk of recurrence in elderly individuals, it was not correlated with the increase of relapse risk in youngers. These data make us think that development and progression of BTs are shaped as a result of different molecular pathways and genetic factors (4).

The patients generally seek medical advice with the complaint of painless macroscopic haematuria. Our patient also sought

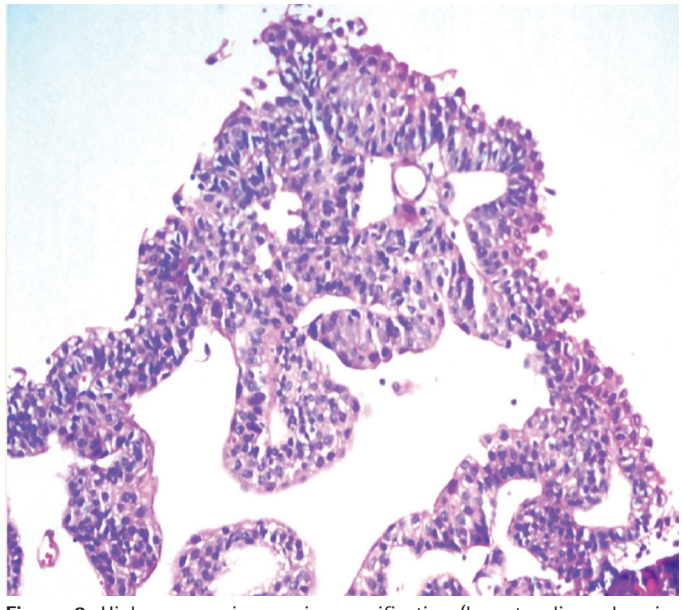

Figure 3. High power microscopic magnification (hematoxylin and eosin, x200) of the lesion: Loss of polarity, several suprabasal mitotic figure and cytologic atypia findings such as nuclear enlargement, hyperchromasia, mild differences in shape and prominent nucleoli were determined

medical advice with this complaint. Williamson et al. (5) reported that the diagnosis of BTs might be delayed in children because of reluctance to undergo evaluation.

USG is a significant method in diagnosis. The patients are generally seen in the low stage. In 21-patient research of Fine et al. (6), low- and high-grade tumors were seen in 18 and 3 patients respectively. Urothelial papilloma was observed in 2 patients and a total of 12 patients were younger than 15 years, of whom 7 were younger than 10 (6). In childhood, transitional cell carcinoma of the bladder usually has a lower grade and stage than in older patients. Our patient also was a low-grade patient.

Transurethral resection of bladder tumour conducted under general anaesthesia is the standard procedure for treatment. There is consensus on postoperative intravesical treatment for pediatric patients (2,6). Many authors use management guidelines that have been published for adults. Both mitomycin C and Bacillus Calmette-Guerin have been used in children, however, efficacy of intravesical treatments has not been defined due to the rarity of transitional cell carcinoma of the bladder in children (7). Postoperative intravesical treatment was not applied to our patient also.

Patient follow-up is important. There is no standardized follow-up procedure for children. USG and urinary cytology are the methods to be used, but the non-invasive nature is their advantage. Diagnostic cystourethroscopy is an efficient method. However, it requires general anaesthesia and has a risk of urethral damage in pediatric patients. Bujons et al. (3) recommended a follow-up of 2 years by cystourethroscopy twice a year, annual USG and urinary cytology. Although transitional cell carcinoma of the bladder seen in this age group has low-grade and relapse rates, close follow-up and cystoscopy at 3 months are recommended. If the result is negative, subsequent cystoscopy is advised 9 months later, and then, yearly for 5 years according to the European Association of Urology (EAU) guidelines. We have planned cystoscopy and ultrasound according to EAU Guidelines on Bladder Cancer every 3 months for the first year and then yearly for 5 years.

As a conclusion, BT, despite rarely seen in pediatric age group, should be considered in the differential diagnosis for patients with the complaint of macroscopic haematuria.

Ethics

Informed Consent: Written informed consent was obtained from the parents of the patient.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: M.Ç.Ç., L.S., Concept: M.Ç.Ç., S.S., H.E., Design: M.Ç.Ç., S.S., H.E., Data Collection or Processing: M.Ç.Ç., S.S., N.Ö.K., Analysis or Interpretation: L.S., H.E., Literature Search: M.Ç.Ç., S.S., N.Ö.K., Writing: M.Ç.Ç., L.S., N.Ö.K.

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

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CASE REPORT
Functional Urology

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Continent Idiopathic Vesicovaginal Fistula Coexisting with Moyamoya Disease

Moyamoya Hastalığıyla Birlikte Kontinan İdiyopatik Vezikovajinal Fistül

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Abstract

The most common cause of vesicovaginal fistula in developed countries is iatrogenic injury whereas in developing countries the leading cause is obstetric complications. Spontaneous vesicovaginal fistula is extremely rare. In this case report, a 23-year-old female patient with moyamoya disease and a stable right ovarian cyst and a vesicovaginal fistula without any underlying factor is discussed. She was fully continent. If there is any possible relationship between vesicovaginal fistula and moyamoya disease, it needs further investigations.
Keywords: Continent, idiopathic, incidental, moyamoya disease, vesicovaginal fistula

Öz

Vezikovajinal fistül; gelişmiş ülkelerde en sık iatrojenik nedenlere bağlıyken, gelişmekte olan ülkelerde en sık obstetrik nedenlere bağlıdır. Spontan vezikovajinal fistül çok nadirdir. Yirmi üç yaşında stabil ovaryan kist nedeniyle takipli hastada insidental saptanan nedeni belli olmayan, tamamen kontinan olan olgu sunulmuştur. Moyamoya hastalığı ve vezikovajinal fistül arasında ilişki olduğunu belirlemek için ek çalışmalara ihtiyaç vardır.
Anahtar Kelimeler: Kontinan, idiyopatik, insidental, moyamoya hastalığı, vezikovajinal fistül

Introduction

Vesicovaginal fistula (VVF) is the abnormal anatomic communication between the female bladder and vagina. Usually presents itself as continuous urinary incontinence. There are many etiologic risk factors such as obstetric trauma, pelvic surgery, infections, congenital abnormalities, foreign materials, malignancy and pelvic radiation (1). Due to high education and sociocultural levels, the incidence seems to be low in the developed countries. On the other hand, in the developing countries, there is an obviously high incidence and prevalence. Considering the low level of medical informative feed-back mechanisms and poor obstetrics health care services, it seems very hard to keep VVF patient data that can be used for epidemiological research studies. In those areas, due to high maternal mortality and obstetric complications, the incidence of VVF is significantly increased (2). In this paper, we report a female patient with known moyamoya disease and a stable right ovarian cyst who was regularly followed up by the departments of neurology, gynecology and presented with radiological and cystoscopy findings of incidentally diagnosed asymptomatic continent VVF.

Case Presentation

A 23-year-old obese female patient was first seen 5 years ago in the obstetrics and gynecology outpatient clinic with the complaint of irregular periods. She had regular menstrual periods and no gynecological complaint since then. Transvaginal ultrasonography showed a 17 mm right ovarian cyst and follow up was recommended.

In 2009, she attended the neurology outpatient clinic with the complaint of recurrent headache. Transcranial Doppler

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ultrasonography and cranial magnetic resonance imaging (MRI) revealed a stenotic occlusion at the supraclinoid portion of the right internal carotid artery and decreased blood flow on the right middle cerebral artery suggesting moyamoya disease. She has been followed by the neurology department since then.

At her last visit to the gynecology outpatient clinic in November 2014, a pelvic ultrasonography revealed a 63x60x68 mm cystic appearance presenting with an internal echo pattern in the genital tract. Further radiological investigation done by an abdominopelvic MRI showing at the beginning of the screening that the vagina seemed to be normal but on the 30th minutes, radiopaque intensity of the bladder was same with the appearance of the vagina without an obvious VVF tract (Figure 1). She was referred to our female urology department. We planned computed tomography (CT) urography for identification of the possible fistula tract. On the CT scan, the urine including contrast material filled the vagina through a VVF tract in the mid vagina (Figure 2). After complete micturition, the vagina and the bladder completely emptied.

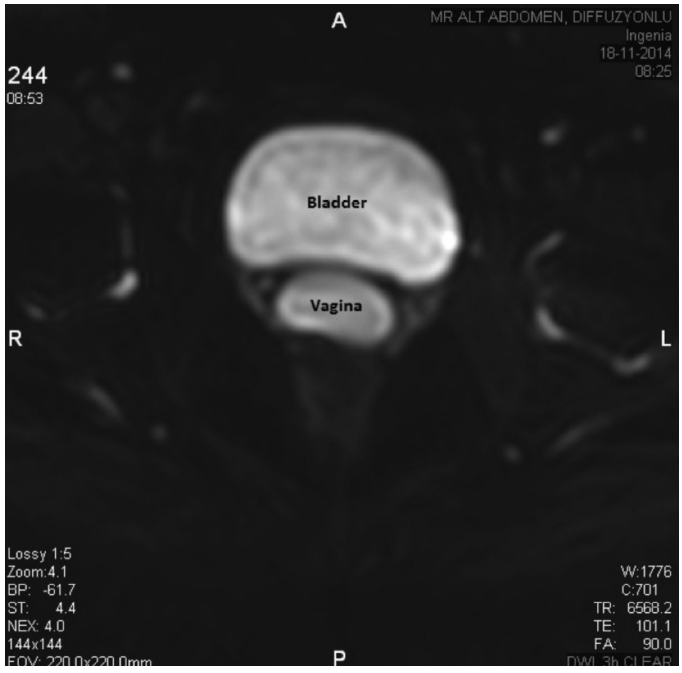

Figure 1. Magnetic resonance imaging scan showing the contrast material filled the vagina

Figure 2. Computed tomography scan showing the mid vaginal fistula tract and the filled vagina with the same intensity of the urine in the bladder

On her gynecological examination it was observed that she had an intact annular hymen with no history of any sexual intercourse, urogenital trauma, pelvic surgery, labor or pelvic radiotherapy predisposing to the occurrence of VVF. Her routine urine analysis and urine culture revealed no pyuria, bacteriuria nor microscopic hematuria.

The fistula tract was identified in the bladder by flexible cystoscopy and verified by administration of methylene blue. Although VVF repair was recommended, the neurology department did not clear her for any type of anesthesia. At this point, routine follow-up was recommended.

Discussion

This case is unique and extraordinary because of complete continence and having none of the underlying etiological factors related to VVF as we searched the literature. Normally being an asymptomatic patient relieved the presence of fistula tract under the radiological examination due to over-distended bladder.

VVF leads to continuous incontinence and urinary leakage that gradually affects the patient's psychosocial situation and physical health. VVF patients have a higher incidence of suffering from depression, anxiety and other psychological disorders (3).

Moyamoya disease is a radiologically diagnosed disease which presents generally intimal thickening of the distal segments of inferior cerebral artery also proximal segments of the anterior and middle cerebral arteries. The underlying mechanism of the disease are not well understood. Due to the stenotic segments, the arterial blood flow decreases and weak collaterals develop in order to ensure the blood supply to these areas. This appearance on the radiological images looks like "puff of smoke" which is called moyamoya in Japanese (4). The typical histological finding of the disease is intimal thickening of the arteries without vasculitis. Moyamoya disease is well described and having a high incidence in the Far East areas especially in the Japanese population, nevertheless, a few studies in the literature showed that the disease could also be seen in the Western populations

and other ethnic groups (5). Few case reports also described extracranial presentation of moyamoya disease (6). In our case, we could not clearly describe a relationship between the pelvic arterial blood supply alteration due to moyamoya disease and pelvic ischemia leading to formation of VVF.

Moyamoya disease has high morbidity and risks of perioperative complications and outcomes related to general anesthesia which restrict the use of anesthetic agents (7). We informed the patient about the untreated VVF risks and complications, such as recurrent urinary tract infections and altered kidney functions due to chronic irritation leading to malignant transformation. She did not accept any treatment modality. Follow-up was recommended since there was no residual urine in the bladder and the vagina.

Due to full continence and no underlying etiological factors leading to VVF, this is the first and unique case reported in the literature. Although moyamoya disease rarely shows extracranial presentation such as pelvic arterial alteration, VVF might be related with it. It could be taken into consideration that small diameter VVF and asymptomatic VVF with high anesthesia risks could be followed up without any surgical treatment. Although we could not obviously show a relationship between moyamoya disease and VVF leading the formation of VVF further investigations are warranted.

Ethics

Informed Consent: Consent form was filled out by the participant.

Peer-review: Externally peer-reviewed.

Authorship Contributions

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

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CASE REPORT
General Urology

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Journal of Urological Surgery, 2017;4:143-144

Ectopic Prostate Originating from the Anterior Bladder Wall

Mesane Ön Duvarı Kaynaklı Ektopik Prostat

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Abstract

Ectopic prostate in the urinary bladder is quite rare. The presenting complaint may vary according to the location of the prostate tissue in the bladder. Patients usually present with hematuria, dysuria, bladder neck obstruction, kidney failure, and urinary tract infections. In this paper, we present a case of ectopic prostate arising from the anterior bladder wall.
Keywords: Ectopic prostate, bladder front wall, embryology

Öz

Mesane içinde prostat ektopisi nadir rastlanan bir durumdur. Başvuru nedenleri ektopik prostat dokusunun mesane içindeki yerine göre değişebilir. Genellikle hematüri, dizüri, mesane çıkım obstrüksiyonu, böbrek yetmezliği ve üriner sistem enfeksiyonu ile prezente olurlar. Biz bu çalışmada mesane ön duvarı kaynaklı ektopik prostat olgusunu sunuyoruz.
Anahtar Kelimeler: Ektopik prostat, mesane ön duvar, embriyoloji

Introduction

"Ectopia" or "Ectopy" refers to congenital displacement or abnormal positioning of an organ or body part. Ectopic prostate is a rare condition. The most common place for ectopic prostate has been reported to be posterior urethra (1). In the literature, there are other reported sites such as sacrum, bladder, uterus, cervix, vagina, testicles, seminal vesicles and retrovesical area (2,3,4,5,6).

In this paper, we present a case of ectopic prostate arising from the anterior bladder wall.

Case Presentation

A 75-year-old male patient presented to our clinic with the complaint of macroscopic hematuria for the past 3 days. Physical examination was unremarkable. Digital rectal examination revealed grade 1 benign prostatic hyperplasia. Liver and kidney function tests were normal. Total prostate-specific antigen (PSA) level was 2 ng/dL.

Ultrasonography showed bladder wall thickening.

Abdominal computed tomography depicted advanced bladder wall thickening and soft tissue density which produced mass-like images (Figure 1).

The patient underwent cystoscopy under local anesthesia with an initial diagnosis of bladder tumor.

Two wide-based, polypoid, solid and hyperemic masses were resected from the anterior bladder wall. The bigger mass had a diameter of 3 cm.

Immunohistochemical examination showed prostatic-type polyp and ectopic prostate tissue (Figure 2).

The patient was given detailed approval for use in scientific publication.

Discussion

The generally accepted opinion on the mechanism of ectopia in the medicine community is that it is a congenital condition

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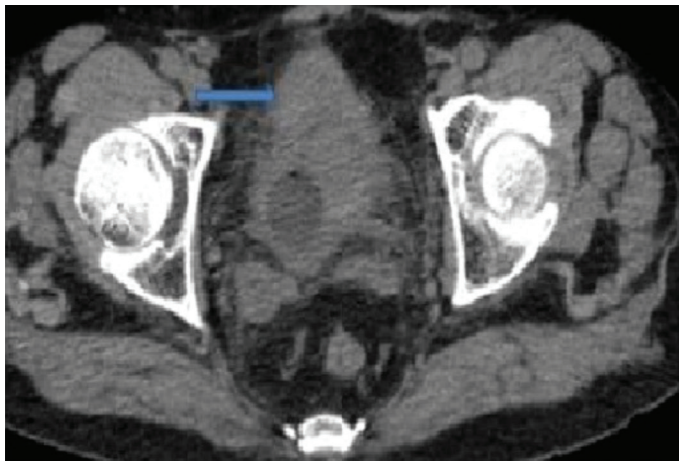

Figure 1. Ectopic prostate originating from front wall of the bladder-radiological view

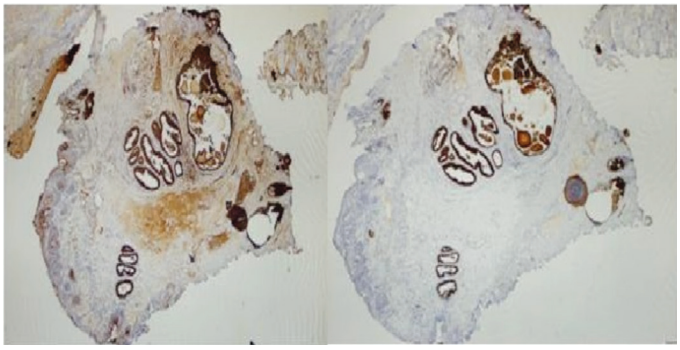

Figure 2. Ectopic prostate originating from front wall of the bladder-histopatological view

which develops during embryonic development stage. The bladder and urethra are derived from the primitive urogenital sinus. This formation continues with the prostate in the 3rd month. Abnormal migration of prostate cells with differentiation abilities can cause ectopia in rare cases (1).

The definite diagnosis is made following histopathological examination of the mass. Prostatic glands are stained easily using prostate acid-phosphatase and PSA (2).

Ectopic prostate within the bladder is quite rare (4).

The main complaint can be various due to different placement of the prostate tissue within the bladder. The patients usually present with hematuria, dysuria, bladder neck obstruction, kidney failure and urinary tract infections (2).

The masses within the bladder can be seen either as a flat or polypoid structure. Flat masses are usually observed around the bladder neck whereas polypoid masses are mainly located on the bladder wall (7).

Although there is a reported case of malignant transformation in the literature, recurrence following surgery has not been reported (1).

Ethics

Informed Consent: Consent form was filled out by the participant.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: S.Ü., A.S.D., Concept: S.Ü., A.S.D., Design: S.Ü., O.K., Data Collection or Processing: S.Ü., A.C.E., Analysis or Interpretation: S.Ü., F.Ç.Ü., Literature Search: S.Ü., Y.Y., Writing: S.Ü.

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CASE REPORT
Urooncology

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Perivascular Epithelioid Cell Tumor of the Kidney: A Rare Case Report

Böbreğin Perivasküler Epiteloid Hücre Tümörü: Nadir Bir Olgu Sunumu

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Abstract

Perivascular epithelioid cell tumors are rare mesenchymal tumors composed of histologically and immunohistochemically distinctive perivascular epithelioid cells. They are mostly benign, however, malignant tumors with aggressive behavior and distant metastasis can also occur. The standard treatment is surgical excision. Here, we report a case of a 25-year-old male with a 4 cm-mass located in the inferior pole of the left kidney, treated by surgical excision.
Keywords: Kidney tumor, perivascular epithelioid cell tumor, partial nephrectomy

Öz

Böbreğin perivasküler epiteloid hücre tümörleri nadir görülen histolojik ve immünohistokimyasal olarak farklı perivasküler epiteloid hücrelerden oluşan mezenkimal tümörlerdir. Çoğunluğu benign tümörlerdir; fakat malign olanları agresif seyredebilir ve metastaza yol açabilir. Standart tedavi yöntemi ise cerrahi eksizyondur. Olgumuzda 25 yaşında sol böbrek alt polünde 4 cm kitle saptanan ve cerrahi olarak eksize ettiğimiz hastayı sunmayı amaçladık.
Anahtar Kelimeler: Böbrek tümörü, perivasküler epiteloid hücre tümörü, parsiyel nefrektomi

Introduction

Perivascular epithelioid cell tumors (PEComas) of the kidney are a group of tumor family covering classical angiomyolipoma (AML), microscopic AML (microhamartoma), intraglomerular lesions, cystic AML, epithelioid AML, oncocytoma-like AML and lymphangiomyomatosis of the renal sinus. The World Health Organization (WHO) defines PEComa as a "mesenchymal tumor that contains perivascular epithelioid cells presenting histological and immunohistochemical differences". While classical AML is benign, epithelioid AMLs are defined as potentially malign mesenchymal lesions for their capacity to develop local recurrence and metastasis (1,2,3). Surgical treatment may be required in AML for symptoms such as hemorrhage and pain, or for the risk of malignancy in tumors that cannot be differentiated from AML in the case of PEComa and certain variants of AML (3,4,5).

This case report aimed to present a patient who undergone retroperitoneoscopic partial nephrectomy due to a renal mass and diagnosed with PEComa after pathological examination.

Case Presentation

We planned magnetic resonance imaging (MRI) in a 25-year-old male patient, who was admitted to our clinic due to left-sided flank pain, with no pathological finding during the examination and laboratory tests, however, with a suspicious mass lesion located at the inferior pole of the left kidney detected during ultrasonographic examination. It was decided to perform surgical excision after detection of a 4 cm tumoral lesion in the inferior pole of the left kidney on MRI (Figure 1). We performed left retroperitoneoscopic partial nephrectomy in our clinic. The total operative time was 90 minutes with the warm ischemia time

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of 14.5 minutes. There was no perioperative complication and the patient was discharged on day 3 after removal of the drain given the positive postoperative general status of the patient. The patient was diagnosed with PEComa following human melanoma black-45 (HMB-45) monoclonal antibody expression and 2 mitoses under 50x magnification during pathological examination. 400x magnified images are given in Figure 2, 3, 4 with the actin, HMB-45 and haematoxylin and eosin staining of the mass. The surgical margins were negative with no other foci according to the thoracic computed tomography (CT) and abdominal MRI, and the patient is still under follow-up with no local recurrence and metastasis by postoperative month 18.

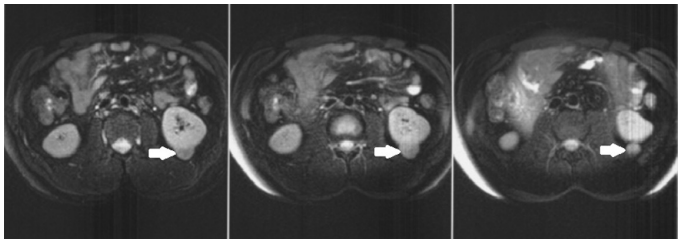

Figure 1. Magnetic resonance imaging image of the 4 cm tumoral lesion of the patient at the inferior pole of the left kidney

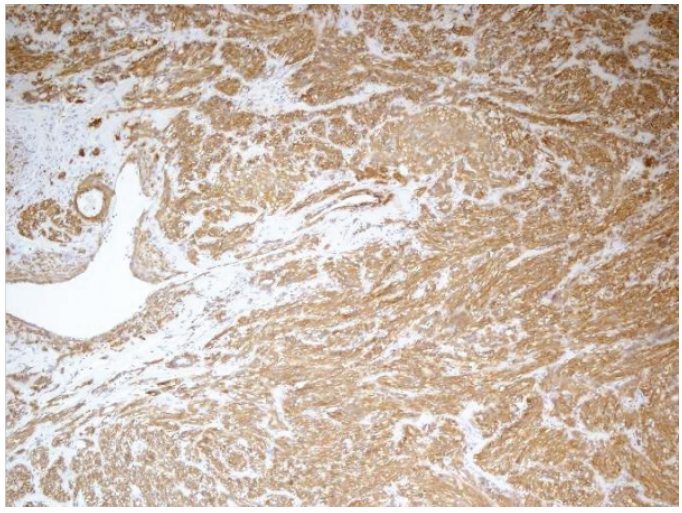

Figure 2. Diffuse actin expression of perivascular epithelioid cell tumor under microscopic immunohistochemical examination (200x magnification)

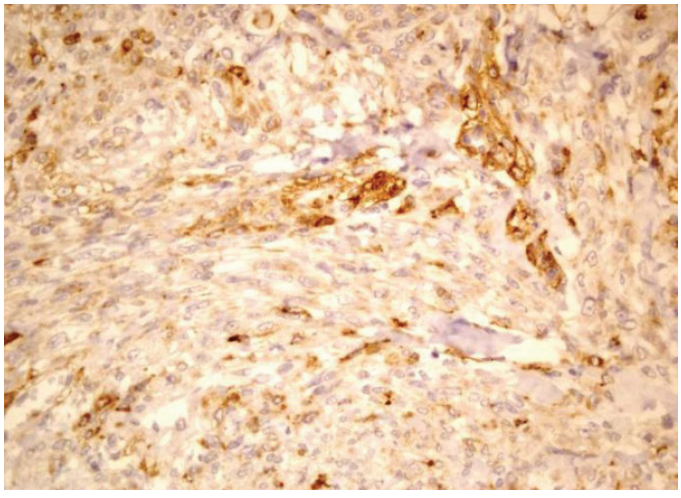

Figure 3. Focal human melanoma black-45 expression of perivascular epithelioid cell tumor under microscopic immunohistochemical examination (400x magnification)

Discussion

The concept of perivascular epithelioid cell first emerged in 1992, which was followed by introduction of the term PEComa 4 years afterwards (1,6). In 2002, the WHO defined PEComa as a mesenchimal tumor that contains perivascular epithelioid cells presenting histological and immunohistochemical differences (7). There is no particular disease-specific complaint of the patient. Patients may present with general symptoms such as nausea, dyspepsia, intermittent pain and loss of appetite. Yet, majority of the patients are asymptomatic. Our case presented with left-sided flank pain. Although there is no specific lab test that may contribute to diagnosis, radiological work-up has limited relevance (6). Studies report several radiological definitions of PEComa's. Some studies present an association between presence of arteriovenous hypervascularity on CT cross-sections and PEComa (8,9). Most of the CT and MRI exams indicate that majority of the lesions are heterogeneous in arterial and venous phases while they are mildly hypodense in the late phase. However, diagnostic accuracy of these methods has been reported to be 15.7-22.7% (10). Table 1 shows the radiological characteristics of patients diagnosed with PEComa in a study of 32 cases (4). The table also presents radiological characteristics of AML types (11,12,13). MRI was used as the imaging modality in our case but it failed to provide a definitive preoperative diagnosis. Differential diagnosis of the tumor significantly depends on its differentiation from AML due to malignancy risk of the tumor (1,2). Presence of fat, a diagnostic finding for AML, may be demonstrated on MRI. Although T1-weighted images provide high signal intensity on the fat tissue, this is not characteristic for AML. Renal cell carcinoma and hemorrhagic

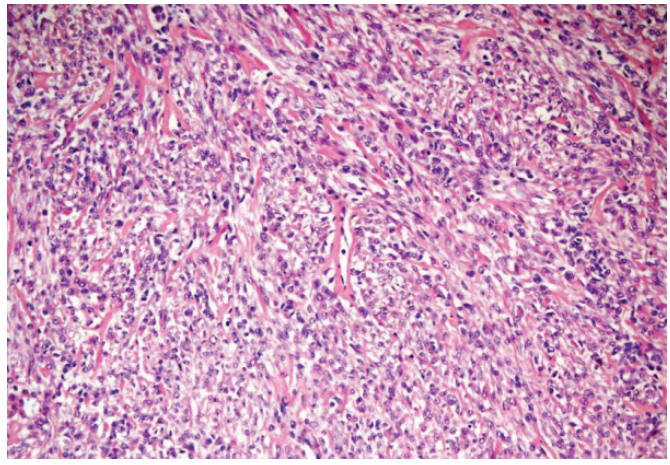

Figure 4. Hematoxylin and eosin staining of perivascular epithelioid cell tumor under microscopic examination (200x magnification)

Table 1. Radiologic and predictive characteristics for the evaluation of perivascular epithelioid cell tumor-angiomyolipoma (4,11,12,13)

	MRI; n (%)	CT; n (%)
Tan et al. (4) - PEComa		
Hypointense at T1-weighted images and hyperintense and hypodense and isodense at the T2-weighted images	6/15 (40)	10/32 (31.2)
Well defined margin and a regular shape	12/15 (80)	26/32 (81.2)
Heterogeneous and significant increase during the arterial and venous phases	10/15 (66.6)	21/32 (65.6)
Morosi et al. (11) - AML		
Heterogeneous, rich in fat, hyperdense in fat, but hypodense in muscle and intralesional vessel	-	10 (100)
Tsukada et al. (12) - epithelioid AML		
Heterogeneous	5/8 (62.5)	-
>45 HU	6/8 (75)	
Solid component and hypointense at T2		3/8 (37.5)
Jinzaki et al. (13) - fat poor AML	-	-
Absence of fat at CT		

MRI: Magnetic resonance imaging, CT: Computed tomography, PEComa: Perivascular epithelioid cell tumor, AML: Angiomyolipoma, HU: Hounsfield unit

cysts may also present a similar image. Furthermore, chemical shift and india ink artifacts are also used (3,5,14). Indications for surgical treatment in AML are based on recovery of symptoms including hemorrhage and pain, nevertheless surgical treatment may be necessary for pathological definitive diagnosis and treatment due to lack of differentiation of preoperative AML and the risk of malignancy in some variants (3,5,14).

Standard treatment for PEComas is surgical resection involving the healthy tissue. Although many are benign, local recurrences and distant metastasis are also possible; there are even cases where distant metastasis was reported following surgical resection of the primary tumor (15). That is exactly the reason why long-term follow-up of PEComa's is recommended. Some studies reported possible use of positron emission tomography in tumor follow-up (16).

Definitive tumor diagnosis relies on pathologic work-up. Pathologically, PEComas contain epithelial-like cells closely associated with dilated vascular channels. It is the basic feature of cells to have an epithelial cell-like morphology and clear eosinophilic cytoplasm characterized by pre-melanosomes, hemidesmosomes and intensive cytoplasmic glycogen gathered with weak intra-cellular connections. Another important feature is that the tumor presents a melan-A expression that triggers HMB-45, microphthalmia transcription factor and melanocytic differentiation of the tumor (2,17). HMB-45 is the most sensitive melanocytic determinant of PEComa (2,17). Our case showed positive staining of tumor cells, a diffuse staining with actin, desmin and caldesmon and focal with HMB-45 and melan-A. There was no staining with CD117, CD34 and S100.

In PEComas, presence of high mitotic activity [>1/50 high-power field (hpf)], atypical mitotic figures, coagulative tumor necrosis, pleomorphism and nuclear atypia, hypercellularity, infiltrative growth pattern, and big tumor size (>70 mm) have been shown to be associated with the malignancy potential (17). Our case had 2/50 hpf mitotic activity, a tumor size of 32 mm but no hemorrhage, necrosis and vascular invasion. Since the patient had only one of the risk factors, i.e., high mitotic activity, the tumor was initially assessed as a benign tumor. Yet, considering the presence of a risk factor and the malignancy potential of the tumor, the patient was put in close follow-up for the possibility of post-resection distant organ metastasis or local recurrence.

In conclusion, what should be kept in mind for the differential diagnosis of PEComa and renal angiolipoma is that these are tumors require close follow-up and good knowledge of pathological risk factors due to their malignancy potential following surgical excision since clinical behavior of these tumors is not precisely known.

Ethics

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

Peer-review: External and internal peer-reviewed.

Authorship Contributions

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

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Urooncology

Doi: 10.4274/jus.2017.04.019

Re: A Prospective Study of Health-Related Quality-of-Life Outcomes for Patients with Low-Risk Prostate Cancer Managed by Active Surveillance or Radiation Therapy

Banerji JS[1], Hurwitz LM[2], Cullen J[3], Wolff EM[4], Levie KE[5], Rosner IL[6], Brand TC[7], L'Esperance JO[8], Sterbis JR[9], Porter CR[10]

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EDITORIAL COMMENT

The treatment options for low-risk prostate cancer (PCa) include active surveillance (AS), external-beam radiation therapy (EBRT), and radical prostatectomy all with 5-year survival rates over 95%. However, each treatment option also carries the risk of negative effects on health-related quality of life (HRQoL). AS has been gaining popularity in recent years, however, data are lacking on its effects on HRQoL. This study aimed to determine whether patients with low-risk PCa, who undergo EBRT, report poorer HRQoL outcomes compared to those managed with AS over a 3-year period. The study population was identified from the Center for Prostate Disease Research Multicenter National Database. Inclusion criteria included a biopsy-confirmed diagnosis of PCa in patients aged 75 years or younger. "Low-risk" PCa was defined using the National Comprehensive Cancer Network criteria: clinical stage T1-T2a, biopsy Gleason score ≤6, and prostate-specific antigen <10 ng/mL. HRQoL data were collected using 2 validated questionnaires: the Expanded Prostate Cancer Index Composite which is designed to evaluate urinary, bowel, sexual, and hormonal function and bother experienced within the past 4 weeks and the 36-item Medical Outcomes Study Short Form (SF-36) survey which measures general, physical and mental health. Of the 499 eligible patients with low-risk PCa, 103 (21%) selected AS and 60 (12%) were treated with EBRT. At baseline, both treatment groups reported comparable HRQoL. EBRT patients experienced significantly worse bowel function and bother at 1 year and 2 years compared to patients managed with AS. Patients who received EBRT were significantly more likely to experience a decrease in more than one functional domain (urinary, sexual, bowel, or hormonal) at 1 year. The limitations of the study include a short follow-up period, small sample size and inability to measure individual physician treatment preferences or recommendations. In addition, 27% of EBRT patients received the therapy at a dose lower than currently recommended dose. Keeping these limitations in mind and that these findings require validation, this study supports the use of AS as a way to preserve HRQoL among low-risk PCa patients.

Özgür Yaycıoğlu, MD

Andrology

Doi: 10.4274/jus.2017.04.020

Re: Preclinical Evaluation of a TEX101 Protein ELISA Test for the Differential Diagnosis of Male İnfertility

Korbakis D[1,2], Schiza C[1,3], Brinc D[3], Soosaipillai A[3], Karakosta TD[1,4,] Légaré C[5], Sullivan R[5], Mullen B[3], Jarvi K[2,6], Diamandis EP[1,2,3,4], Drabovich AP[1,3,4]

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BMC Med 2017;15:60. doi: 10.1186/s12916-017-0817-5.

EDITORIAL COMMENT

Seminal plasma (SP) is enriched with testis-derived proteins, mRNA and metabolites. Due to blood-testis and blood-epididymis barriers, testis-specific biomarkers are not found in blood serum. Therefore, evaluation of semen and SP could be an option for non-invasive diagnosis of male infertility. In this study, the authors evaluated the performance of TEX101 ELISA in large cohort of fertile, subfertile and infertile men besides the validation of this test as a prognostic biomarker of sperm retrieval in patients with non-obstructive azoospermia (NOA). Impressively, TEX101 differentiated between pre- and post-vasectomy samples with 100% sensitivity and 100% specificity. As a marker of differentiation between NOA and obstructive azoospermia, combination of TEX101 with ECM1 increased sensitivity to detect NOA from 69% to 81% at 100% specificity. In addition, a cut-off value of TEX101 ≥0.6 ng/mL provided 73% sensitivity at 64% specificity for predicting sperm or spermatid retrieval in men with NOA. The prediction of sperm retrieval by TEX101 was comparable to blood serum protein (the area under the curve value=0.64; 71% sensitivity at 68% specificity) (1). Testicular sperm extraction is still the only option for men with NOA. Most of the patients and supposes accept sperm extraction procedure even if they had a very little chance of sperm recovery. Better biomarkers to predict sperm recovery from testicular sperm extraction operation in NOA patients are still required.

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Emre Bakırcıoğlu, MD

Andrology

Doi: 10.4274/jus.2017.04.021

Re: Post-Thaw Recovery of Rare or Very Low Concentrations of Cryopreserved Human Sperm

Kathrins M[1], Abhyankar N[2], Shoshany O[2], Liebermann J[3], Uhler M[3], Prins G[2], Niederberger C[2]

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Fertil Steril 2017;107:1300-1304. doi: 10.1016/j.fertnstert.2017.04.016.

EDITORIAL COMMENT

In men with azoospermia due to spermatogenic dysfunction (ASD) or men with very low sperm count "severe oligospermic men", sperm cryopreservation is very important back-up to save these sperms for future *in vitro* fertilization procedures. However, technical difficulties with cryopreservations are still a problem for men with very low sperm count. The most detrimental outcome of cryopreservation of very low concentrations of sperm is the absence of identifiable sperm after thawing. In this study, the authors investigated the cases of failure to retrieve any sperm after thawing of low concentrations of cryopreserved sperm. In this retrospective study, 55 men [83 intracytoplasmic sperm injection (ICSI) cycles] who met the inclusion criteria were included. Five different couples underwent 5 ICSI cycles (6.0%) however, no sperm were identified after thawing. Four of these cases (8.5%) were in the group of "rare sperm only" and one (2.8%) in the group of <100,000 total sperm. It was observed that the ability to locate sperm after thawing was not statistically significantly associated with the pre-cryopreservation parameters and sperm source. The findings documented in this study could be valuable information for couples suffering from ASD who are in the process of decision making whether to start ovulation induction before or after surgical sperm retrieval.

Emre Bakırcıoğlu, MD

Transplant Survey

Doi: 10.4274/jus.2017.04.022

Re: Body Mass Index as a Predictor of Outcomes Among Pediatric Kidney Transplant Recipient

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Pediatr Transplant 2017. doi: 10.1111/petr.12992.

EDITORIAL COMMENT

In the adult population obesity is a serious problem for patients requiring kidney transplantation by causing delayed graft function (DGF) and deep wound infections which in the long run having a negative impact on graft and patient survival. However, there are controversial reports regarding the pediatric population. In this retrospective largest cohort study authors have examined the association between body mass index (BMI) and patient outcomes among 13014 primary pediatric kidney transplant recipients (<18 years old) between 1987 and 2013 from United Network for Organ Sharing database. After stratifying the patients into five categories according to their BMI based on their Z scores, which was established by World Health Organization. The majority of the patients (12588) was in the Z score category of -2 to +2 and was used as the reference group. -3 (thin) and +3 (obese) categories were evaluated for differences in graft and patient survival. There was no difference in graft or patient survival and no differences in rates of DGF among obese children compared to normal and underweight children undergoing kidney transplantation. However, these results should be interpreted very carefully because of its retrospective nature and also reflection of just one nation. Childhood obesity is a serious problem with increasing prevalence and obese children with end stage kidney disease should not be eliminated from having a kidney.

Yarkın Kamil Yakupoğlu, MD

Transplant Survey

Doi: 10.4274/jus.2017.04.023

Re: Incidence and Risk Factors of Early Surgical Complications in Young Renal Transplant Recipients: A Persistent Challenge

Rodricks N[1], Chanchlani R[1,2,3,4], Banh T[1], Borges K[1], Vasilevska-Ristovska J[1], Hebert D[2], Patel V[1], Lorenzo AJ[5], Parekh RS[1,2,4,6,7]

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Pediatr Transplant 2017. doi: 10.1111/petr.13006.

EDITORIAL COMMENT

Renal transplantation in children younger than 5 years of age is technically challenging and associated with increased mortality and graft loss. In this retrospective cohort study, the authors have examined the incidence and risk factors for early post transplant surgical complications in 83 recipients who were younger than 5 years old over three decades (1985-2014) which was divided into two periods. The incidence of surgical complications was 26.5% within 30 days post-transplant with vascular thrombosis being the most common complication in both periods. The number of complications did not significantly differ between two periods, however, the incidence rate of graft failure was higher in the first period. The authors have also highlighted the negative impact of early surgical complications on the graft and patient survival when compared to patients without complications. In a subgroup analysis of those with only vascular complications, children with abnormal coagulation profile were 3 times more prone to development of vascular complications, however, it was not significant. In this very young population, early surgical problems play a major role in graft failure and mortality. Kidney transplantation is still the best option for this very unique population in experienced centers. However, prevention of vascular complications require further optimization. Randomized controlled trials are required to determine the type, duration and benefits of prophylactic anticoagulant therapy in young children.

Yarkın Kamil Yakupoğlu, MD

Basic Research

Doi: 10.4274/jus.2017.04.024

Re: MicroRNA-210-3p Depletion by CRISPR/Cas9 Promoted Tumorigenesis through Revival of TWIST1 in Renal Cell Carcinoma

Yoshino H[1], Yonemori M[1], Miyamoto K[1], Tatarano S[1], Kofuji S[2], Nohata N[3], Nakagawa M[1], Enokida H[1]

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Oncotarget 2017;8:20881-20894. doi: 10.18632/oncotarget.14930.

EDITORIAL COMMENT

Recently, a new tool based on a bacterial clustered regularly interspaced short palindromic repeats (CRISPR)-associated protein-9 (Cas9) nuclease from *Streptococcus pyogenes* has created a new hope for scientific researches. This new approach can modify targeted permanent mutations on the genome. The functions of CRISPR and CRISPR-associated genes are essential in adaptive immunity in some bacteria and archaea, enabling the organisms to respond to and eliminate invading genetic material. The CRISPR/Cas9 system requires only the redesign of the crRNA to change target specificity. This contrasts with other genome editing tools, including zinc finger and transcription activator-like effector nucleases, where redesign of the protein-DNA interface is required. In the urology literature, previous studies showed that five miRNAs (miR-885-5p, miR-1274, miR-210-3p, miR-224 and miR-1290) were upregulated the most in clear cell renal cell carcinoma (RCC). In this research, the authors identified twist-related protein 1 (TWIST1) as a key target of miR-210-3p. They utilized the CRISPR/Cas9 gene editing system to deplete miR-210-3p in RCC cell lines (786-o, A498 and Caki2). They suggested that high TWIST1 and low miR-210-3p expression was associated with poorer overall and disease-free survival as compared to low TWIST1 and high miR-210-3p expression. According to this research, CRISPR/Cas9 system to study specific miRNAs and other non-coding RNAs in areas of cancer can be useful as a targeted genome-editing tool. This tool will be crucial in urooncology researches in the near future.

Fehmi Narter, MD, PhD

Basic Research

Doi: 10.4274/jus.2017.04.025

Re: Physical Aspects of Cancer Invasion

Guiot C, Pugno N, Delsanto PP, Deisboeck TS

University of Torino, Department of Neuroscience, CNISM, Torino, Italy

Phys Biol 2007;4:P1-6. doi: 10.1088/1478-3975/4/4/P01.

EDITORIAL COMMENT

One of the current research topics is invasion mechanism of cancer cells. Invasiveness, one of the properties of tumor progression, contains the tumor's ability to expand into the host tissue due to biochemical and biomechanical processes. Invasion mechanisms are investigated on models ranging from microscopic to macroscopic scales. Microscopic models are suitable to describe malignant transformations in the cellular level (biochemical, genetic, etc.). Macroscopic models of solid tumor growth may be related to the universal laws of physics (pressure, heat, etc.). Another described model is mesoscopic version and this design is intermediate type between microscopic and macroscopic levels. Tumor invasion is controlled by three parameters: tumor surface tension, microenvironmental pressure and tumor radius. The authors noted the two main cancer invasive mechanisms, namely "smooth margin" invasive mass and "fingering", as a progressive damage growth in comminuted solids or a drop splashing in liquids.

They suggested that "composite" models are more logical to explain cancer invasion mechanism. Additionally, for diagnostic and therapeutic purposes of the neoplastic growth, a multilevel approach that includes both micro and macroscopic scales and its mesoscopic bridging level may be most promising. For completely understanding the invasion mechanisms of the cancer cells, there is a need for further research about this topic.

Fehmi Narter, MD, PhD

Doi: 10.4274/jus.1594
Journal of Urological Surgery, 2017;4:156-158

Intraoperative Frozen Section in Uropathology: When and How?

Üropatolojide İntraoperatif Frozen İnceleme: Ne Zaman ve Nasıl?

Yelda Dere

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Introduction

Frozen section, which is also known as intraoperative pathology consultation, is one of the most challenging expertise of surgical pathology practice due to many reasons, such as inadequate sampling, freezing artefacts on the tissue section and necessity of quick decision due to the limitation of time, and is being used in many surgical operations in order to choose the right procedure for the patients (1,2). The surgeons should share the patient's clinical data with the pathologist for the method to be successful and specify the expectations from the pathologist for choosing the most appropriate treatment option (1). In addition, both the surgeon and the pathologist must know the advantages and the limitations of the frozen section, specify the indications and act between these limits.

Frozen Section in Genitourinary Pathology

Various indications and problems associated with the frozen section can be counted in every organ-specific disease in genitourinary system pathology and, some of them are summarized as follows:

1. Evaluation of the Surgical Margins

a) Frozen section is generally studied during radical prostatectomy (RP) in high-risk patients (high biopsy Gleason score and high prostate-specific antigen level), especially when nerve sparing or robotic surgery is being used (2,3). The most conflicting artefacts are crushed tissues, cauterization and heat artefacts as well as freezing artefacts. In such conditions, deeper sections or additional tissue fragments may be needed due to difficulty in assessing small carcinomatous glands, nucleolar prominence and myoepithelial layer. If the suspicion for margin positivity continues, even if many sections were cut and additional tissue fragments were sectioned, the margin status can be given by observing the permanent paraffin blocks (2).

b) As the indications of partial nephrectomy widen, the evaluation of the surgical margins in partial nephrectomies became the most common indication of the frozen section in renal tumors (4). Two types of tissues can be sent for frozen section analysis. The surgeon may send a small fragment of tumor bed parenchyma which can be fully assessed for frozen section or the whole partial nephrectomy specimen. When the whole specimen is sent, the surgeon must ink the parenchyma side of the surgical margin in order to preserve its orientation (5). However, as most of the tumors treated with partial nephrectomy are well defined or capsulated, many authors stated that the macroscopic view of the surgeon is generally accepted enough for the evaluation of the margins without frozen section (6).

c) The evaluation of the surgical margins of the ureters and urethra during radical cystectomy is the most common frozen section study among all genitourinary pathologies (2,7). In frozen section, reporting mild and moderate dysplasia should be avoided as they have no clinical. However, reporting the presence of high grade dysplasia or carcinoma *in situ* is important depending on the necessity of additional marginal excision. The rate of high grade dysplasia or carcinoma *in situ* in ureteral margins has been reported to be 4.8-9% in the literature (8). Diagnosis based on frozen section can be difficult depending on the effects of applied treatments, cauterization or freezing artefacts (Figure 1, 2). In addition, pathologists should always keep in mind that the reactive urothelium can show atypical cellular morphology and search additional features such as loss of polarity, nuclear hyperchromasia and high nucleus/cytoplasmic ratio before diagnosing dysplasia.

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d) In testicular tumors, evaluation of surgical margins is a very rare indication which is only used in testis sparing surgical procedures (7).

e) Evaluation of surgical margins is the most common indication for frozen section in penile surgeries (7). The urethral margin sent for frozen section analysis should include corpus spongiosum, corpus cavernosa, penile fascia and the skin and the distal margin should be inked by the surgeon in order to orientate the pathologist (7). When the whole penectomy specimen is sent for frozen section, the pathologist must be sure that the proximal surgical margin is located upright in the frozen section.

2. The Diagnosis of the Tumor and Tumor Type

a) There are no indications for frozen section during RP, radical cystectomy or penectomy for the diagnosis of the tumor as they are generally diagnosed by transurethral needle biopsies, resections or incisional biopsies (2,7,9).

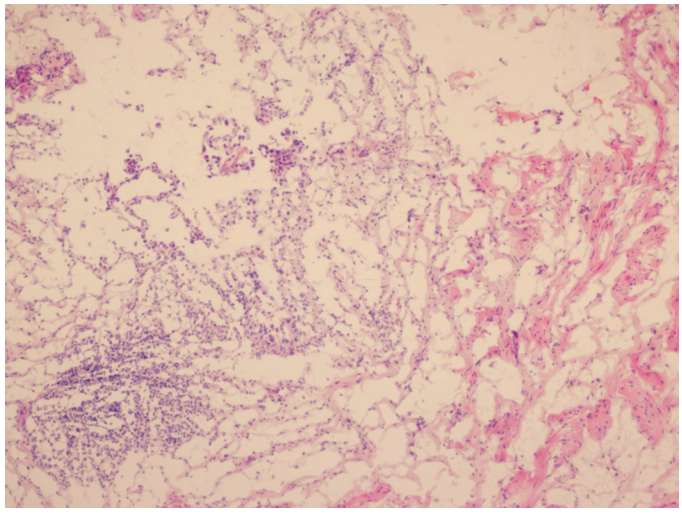

Figure 1. Frozen section of ureter with fragmentation and freezing artefacts which has given a frozen diagnosis of carcinoma *in situ*, hematoxylin and eosin, x100

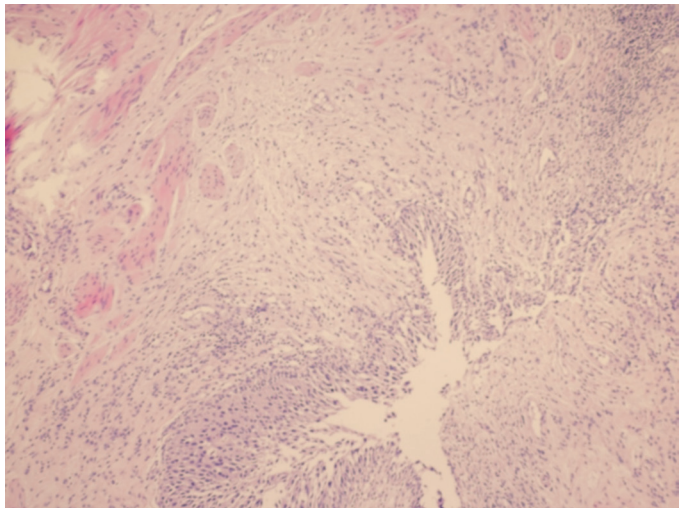

Figure 2. Permanent paraffin section of the same ureter, hematoxylin and eosin, x100

b) The histological type of renal tumors is the rarest indication of frozen section which rarely affects the surgical operation. Although for tumors with specific morphologic features can be diagnosed easily, oncocytic or cystic changes, papillary growth pattern, angiomyolipomas with low fat configuration, and high grade tumors may complicate the diagnostic approach (2). Additionally, it is important to make differential diagnosis between renal cell tumors and urothelial carcinoma because of the necessity of ureterectomy during surgical procedure.

c) The type of testicular malignant germ cell tumors has no effect on the type of surgical procedure, thus there is no indication for frozen section (1). However, in some testicular and most paratesticular lesions, frozen section is important in order to ensure the testis sparing surgery. Prepubertal age,

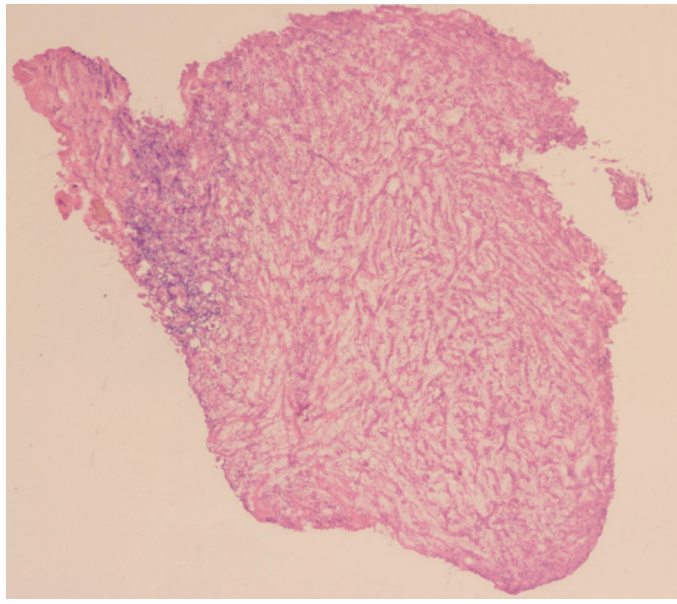

Figure 3. Frozen section of a paratesticular tumor: the patient was given a frozen diagnosis concordant with adenomatoid tumor and operated by partial orchiectomy, hematoxylin and eosin, x40

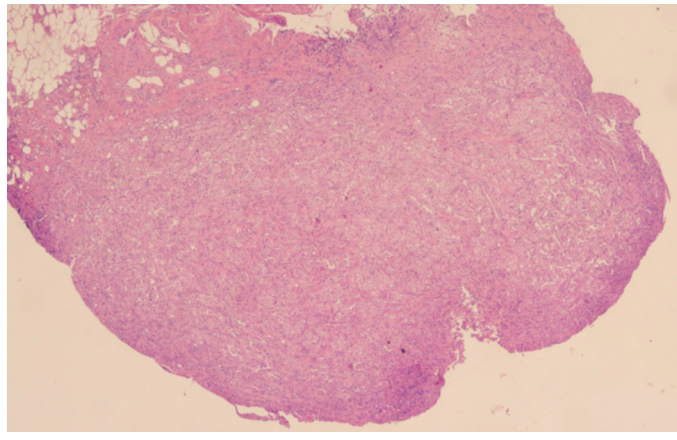

Figure 4. Permanent paraffin section of the same case with the final diagnosis of adenomatoid tumor, hematoxylin and eosin, x40

inflammatory or infectious nonneoplastic lesions (such as sperm granuloma) and benign neoplastic lesions (such as adenomatoid tumor, lipoma) need frozen section for preventing redundant orchiectomies (Figure 3, 4) (2,7).

3. The Evaluation of Lymph Nodes

Frozen sections of the lymph nodes are studied by the same procedure in all genitourinary malignancies. The lymph nodes are macroscopically examined first and the suspicious cut surface is being sectioned for microscopic evaluation regardless of the primary malignancy (2). The specificity of frozen section diagnosis of the lymph nodes has been reported to be very high in many studies (10). However, the adipose tissue replacing the lymph node in older patients and the difficulty in freezing and sectioning adipose tissue must be considered in false negativity which has been reported to be as high as 33% in RPs (10).

In conclusion, frozen section study has many advantages and limitations in uropathology as in other systems. Thus, pathologists and urologists must be aware of the exact indications and the limitations of the frozen section.

Keywords: Frozen section, intraoperative consultation, uropathology

Anahtar Kelimeler: Frozen inceleme, intraoperatif konsültasyon, üropatoloji

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Ethics

Peer-review: Internally peer-reviewed.

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