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Manuscripts should be prepared according to ICMJE guidelines (http://www. icmje.org/). Original manuscripts require a structured abstract. Label each section of the structured abstract with the appropriate subheading (Objective, Materials and Methods, Results, and Conclusion). Case reports require short unstructured abstracts. Letters to the editor do not require an abstract. Research or project support should be acknowledged as a footnote on the title page.

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

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Turkish abstract texts should be written in accordance with the Turkish Dictionary and Writing Guide of the Turkish Language Association.

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Materials and Methods: Important methods should be written respectively.



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Results: Important findings and results should be provided here.

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

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

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

Article length: Not to exceed 3000 words.

Original researches should have the following sections:

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

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Statistics: Describe the statistical methods used in enough detail to enable a knowledgeable reader with access to the original data to verify the reported results. Statistically important data should be given in the text, tables and figures. Provide details about randomization, describe treatment complications, provide the number of observations, and specify all computer programs used.

Results: Present your results in logical sequence in the text, tables, and figures. Do not present all the data provided in the tables and/or figures in the text; emphasize and/or summarize only important findings, results, and observations in the text. For clinical studies provide the number of samples, cases, and controls included in the study. Discrepancies between the planned number and obtained number of participants should be explained.

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

Discussion: This section should include a discussion of the data. New and important findings/results, and the conclusions they lead to should be emphasized. Link the conclusions with the goals of the study, but avoid unqualified statements and conclusions not completely supported by the data. Do not repeat the findings/results in detail; important findings/results should be compared with those of similar studies in the literature, along with a summarization. In other words, similarities or differences in the obtained findings/results with those previously reported should be discussed.

Study Limitations: Limitations of the study should be detailed. In addition, an evaluation of the implications of the obtained findings/results for future research should be outlined.

Conclusion: The conclusion of the study should be highlighted.

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

Examples of References:

1. List All Authors

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

2. Organization as Author

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

3. Complete Book

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

4. Chapter in Book

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



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5. Abstract

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

6. Letter to the Editor

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

7. Supplement

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

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How I do?

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Comparison of Stone Scoring Systems in Predicting Outcomes of Percutaneous Nephrolithotomy in Patients with Solitary Kidney

Tek Böbrekli Hastalarda Uygulanan Perkütan Nefrolitotominin Sonuçlarını Tahmin Etmede Taş Skorlama Sistemlerinin Karşılaştırılması

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

There are various studies in the literature evaluating the efficacy of stone scoring systems in predicting the outcomes and postoperative complications of percutaneous nephrolithotomy. The treatment of kidney stones in patients with solitary kidney is a challenge for the surgeon. When we searched the literature, we observed that there is no study evaluating the efficacy of scoring systems in patients with solitary kidney. In our study, it was shown that Clinical Research Office of the Endourology Society nomogram was the most effective factor in predicting the outcome of the surgery, but both scoring systems were not effective in predicting postoperative complications.

Abstract

Objective: To assess efficacy of the Guy's Stone score (GSS) and Clinical Research Office of the Endourological Society (CROES) nomogram in predicting outcomes of percutaneous nephrolithotomy (PCNL) in patients with solitary kidney.

Materials and Methods: Ninety patients with solitary kidney, who underwent PCNL between 2010 and 2018 in our center, were evaluated. Demographic characteristics and preoperative laboratory results of the patients were recorded. Operative time, duration of anesthesia, access number, stone location, supracostal access, stone-free (SF) rate, complication rate, nephrostomy tube removal time and length of hospital stay were recorded.

Results: Data of patients with residual stones and SF patients were compared. In the analysis of groups; GSS, CROES score, stone burden, preoperative creatinine value, multiple accesses and presence of staghorn stone were found to be significant factors related with SF status. When data was evaluated according to complication status, stone burden, GSS, CROES score, multiple accesses and stone location were significant factors. In multivariate analysis, the most significant factors in predicting SF and complication status were CROES score (p=0.019) and stone burden (p=0.012), respectively.

Conclusion: PCNL is an effective method in the treatment of stones in solitary kidney. CROES score is a better predictor of SF status in patients with solitary kidney. Patients with high stone burden are more prone to complications.

Keywords: Percutaneous nephrolithotomy, Solitary kidney, Guy's Stone score, CROES nomogram

Öz

Amaç: Guy Taş skorunun (GSS) ve Endouroloji Derneği Klinik Araştırma Ofisi (CROES) nomogramının tek böbrekli hastalarda perkütan nefrolitotomi (PCNL) sonuçlarını öngörmedeki etkinliğini değerlendirmek.

Gereç ve Yöntem: Kliniğimizde 2010 ve 2018 yılları arasında PCNL uygulanan tek böbrekli 90 hasta değerlendirildi. Hastaların demografik özellikleri ve preoperatif laboratuvar sonuçları kaydedildi. Operasyon süresi, anestezi süresi, akses sayısı, taş yerleşimi, suprakostal erişim, taşsızlık oranı (TO), komplikasyon oranı, nefrostomi çekim süresi ve hastanede kalış süresi kaydedildi.

Bulgular: Rezidüel taşlı ve taşsız hastaların verileri karşılaştırıldı. Grupların analizinde; GSS, CROES skoru, taş yükü, preoperatif kreatinin değeri,

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çoklu akses ve staghorn taş varlığı TO durumu ile ilişkili önemli faktörlerdi. Veriler komplikasyon durumuna göre değerlendirildiğinde; taş yükü, GSS, CROES skoru, çoklu akses ve taş yerleşimi önemli faktörlerdi. Çok değişkenli analizlerde TO ve komplikasyon durumunu öngörmede en önemli faktörler sırasıyla CROES skoru (p=0,019) ve taş yükü (p=0,012) idi.

Sonuç: PCNL, tek böbrekli hastalarda taşların tedavisinde etkili bir yöntemdir. CROES skoru tek böbreği olan hastalarda TO durumu için daha iyi bir belirleyicidir. Yüksek taş yükü olan hastalar komplikasyonlara daha yatkındır.

Anahtar Kelimeler: Perkütan nefrolitotomi, Tek böbrek, Guy Taş skoru, CROES nomogramı

Introduction

Renal stone treatment in solitary kidney is a challenge for urologists. Although it is hard to make decision for surgeons in the treatment of the patients with solitary kidney, there is no different recommendation in the current guidelines for such special cases. In the current European Association of Urology guidelines, while retrograde intrarenal surgery (RIRS), percutaneous nephrolithotomy (PCNL) and extracorporeal shock wave lithotripsy (ESWL) are equally suggested for the treatment of stones in the range 1 to 2 cm, PCNL is the treatment of choice for kidney stones larger than 2 cm (1). In the literature, there are various studies evaluating the effectiveness of PCNL in solitary kidneys, which revealed stone free rates (SFRs) between 59% and 100% (2,3,4,5,6). Despite the satisfactory success rate of the procedure, many surgeons may prefer less invasive methods considering the possible complications especially in patients with solitary kidney. As known, PCNL is described as a safe method for stone removal, however, it is associated with some complications such as fever, urinary tract infection, bleeding requiring transfusion, neighboring organ injury, loss of the kidney and death (7). Additionally, it should be taken into consideration that patients with solitary kidney have a thicker parenchyma as a result of compensatory hypertrophy and are more prone to bleeding. Possibility of total nephrectomy due to uncontrollable bleeding, which leads to a life-long hemodialysis or transplantation requirement, is a primary concern for the patient and the surgeon.

Recently, different stone scoring systems have been developed to assist surgeons in predicting surgical outcomes of PCNL (8,9,10,11). Guy's Stone score (GSS) and the Clinical Research Office of the Endourological Society (CROES) nomogram are two of the most widely used scoring systems. GSS consists of four grades based on stone burden, stone location, and anatomical features of the kidney. Higher GSS is associated with decreased SFR. The CROES nomogram is consisted of variables such as size, number and location of the stone, previous treatment, presence of staghorn stone and number of cases treated per year in the institution. Each factor has a score between 0 and 100 and SFR correlates positively with the increase of the total score. In the previously published articles, it was demonstrated that both scoring systems were correlated well with SFR (12,13,14) and they had similar ability in predicting surgical outcomes (15,16,17,18).

In the current study, we aimed to analyze the data of patients with solitary kidney who underwent PCNL in our institute and assess the efficiency of GSS and CROES nomogram in predicting stone-free status and complication status.

Materials and Methods

After institutional review board approval (protocol no: 2011-KAEK-25 2018/10-02), the data of 90 patients with solitary kidney, who underwent PCNL between November 2010 and June 2018 was, evaluated.

The procedure was performed in patients with stones greater than 2 cm, patients with ESWL-resistant stones, and patients who selected PCNL after receiving information about treatment alternatives.

Patients, who had congenital solitary kidney, patients who had a contralateral kidney which is non-functional or which contributes less than 15% to total function (19) and those who had undergone nephrectomy, were included in the study.

Preoperative Evaluation

Detailed physical examinations, history taking, blood count, blood biochemistry assays, estimated glomerular filtration rate (eGFR), urine analysis and urine culture were performed. The Chronic Kidney disease epidemiology collaboration formula was used to calculate eGFR (20). Kidney-ureter-bladder radiography, ultrasonography and computed tomography (CT) were performed for each patient. Stone size was calculated using CT images. The two largest diameters were multiplied to calculate the stone burden. All the calculations (stone size, GSS, CROES score) were performed by the same surgeon.

Prophylactic antibiotic administration was performed one hour prior to the procedure. Appropriate antibiotic therapy was administered in patients with positive urine culture and the procedure was delayed until the sterile urine culture was seen.

Surgical Procedure

The procedures were performed under general anesthesia by different experienced surgeons. Following the insertion of a 6 F ureteral catheter, the patients were turned to the prone position. Contrast agent was injected through the catheter to visualize the renal collecting system. Access was performed under fluoroscopic guidance. After access was obtained, a guide wire was inserted into the collecting system. Serial dilators were used to dilate the access tract and a 30 F Amplatz sheath was positioned. Stone fragmentation was performed with a pneumatic lithotripter. The fragments were extracted using a stone basket or a grasper. Smaller fragments were extracted by irrigation. At the end of the procedure, antegrade pyelography was performed to check stone clearance and a nephrostomy tube was inserted under fluoroscopy guidance.

The demographic characteristics of the patients, such as age, gender, and laterality, operative time, anesthesia time, access number, stone location (located in a single calyx or in multiple calyces), presence of supracostal access, SFR, complication rate, nephrostomy removal time and length of hospital stay were recorded and evaluated.

The nephrostomy catheter was removed after recovery of hematuria. Stone clearance was assessed with CT 3 weeks after the procedure. If there were no stone fragments on the images, the procedure was defined as SF. Clinically insignificant residual fragments (CIRFs) were defined as the presence of fragments <4 mm which are non-obstructive, non-infectious and asymptomatic. PCNL-associated complications were recorded and classified according to the Clavien classification (21,22).

Statistical Analysis

Distribution of continuous variables was evaluated using the one-sample Kolmogorov-Smirnov test. Comparisons between groups were evaluated using the Pearson's chi-squared test and Fisher exact test for categorical variables and using the Mann-Whitney U test or independent samples t-test for continuous variables. Logistic regression analysis was performed to evaluate the independent factors associated with complication and SF status. Statistical analysis was performed using SPSS 16.0 for windows software (SPSS, Inc., Chicago, IL) and a p value of less than 0.05 was considered statistically significant.

Results

Of the 90 patients who underwent PCNL, 60 were male and 30 were female. The median age of the patients was 52 years (21-83). The procedures were performed for stones in the right kidney in 47 patients and in the left kidney in 43. Descriptive values of the total cohort are showed in Table 1. The causes of having solitary kidney were contralateral nephrectomy (50 patients), non-functional kidney (11 patients), congenital agenesis (8 patients) and contralateral kidney which contributed less than 15% to total renal function in dimercaptosuccinic acid scintigraphy (21 patients).

The data of the patients with residual stones and SF patients were compared. Patients with CIRFs were included in the group

with residual stones. The SF rate was 81.1% (73 patients) after a single session. The procedure was unsuccessful in 5 patients and there were CIRFs found on the images in 12 patients. ESWL was performed after 5 unsuccessful operations and stone clearance was achieved in 3. In the patients with CIRFs, the stones were stable, so they were followed up. In the analysis of the groups; GSS (p=0.005), CROES score (p=0.001), stone burden (p=0.002), preoperative creatinine value (p=0.009), multiple accesses (p=0.003), presence of staghorn stone (p=0.001), and to have stones located in multiple calyces (p=0.043) were the significant factors associated with SF status. Although the median creatinine value was significantly higher in patients with residual stones, eGFR was not found to be a significant factor. The evaluation of factors associated with SF status is demonstrated in Table 1.

In our series, complications occurred in 17 patients. There were 5 grade 1, 15 grade 2 and 2 grade 3 complications (Table 2). When the patients were evaluated according to the complication status, stone burden (p<0.001), GSS (p=0.05), CROES score (p=0.005), multiple accesses (p=0.003) and presence of staghorn stone (p=0.009) were the statistically significant factors (Table 3).

Univariate and multivariate analyses of the factors affecting SF status and complication status are demonstrated in Table 4. In the multivariate analysis by using the forced-entry method, no independent factor associated with SF or complication status was found. In backward elimination, the most significant factor to predict SF status was CROES score (p=0.019) and the most significant factor to predict complication status was stone burden (p=0.012).

Discussion

PCNL in patients with solitary kidney poses a significant challenge for the urologist. Taking the sole functioning kidney into account, the aims of the procedure should be to achieve maximum stone clearance in a single session and avoid complications affecting renal function. When we searched the literature, we found various studies assessing the efficacy of nephrolithometric systems in predicting surgical outcomes. However, we could not find a topic comparing the efficacy of those for PCNL in solitary kidney.

In a study performed by Bucuras et al. (2), data of 189 patients with solitary kidney who underwent PCNL was compared with patients with two normal functioning kidneys. SFR was significantly lower (65.4% to 76.1%) and blood transfusion rate was higher (10.1% to 5.6%) in patients with solitary kidney. Also a higher cardiovascular risk and American Society of Anesthesiologists (ASA) score were seen in this group. The higher rate of blood transfusion was related with factors such as higher ASA score, more prevalent anticoagulant use and thicker parenchyma. No statistically significant difference was observed

Table 1. Total cohort and association of factors with stone-free status								
	Total Cohort (n=90)	Patients with no residual stone (n=73)	Patients with residual stone (n=17)	р				
Age (years) [median (min-max)]	52 (21-83)	51 (21-83)	53 (24-81)	0.613				
Gender, n/%	-	-	-	0.341				
Male Female	60/66.7 30/33.3	47/64.4 26/35.6	13/76.5 4/23.5					
Side, n/%	-	-	-	0.850				
Right Left	47/52.2 43/47.8	38/52 35/48	9/53 8/47	-				
Mean hemoglobin, (g/dL) (mean \pm SD)	13.744 <u>+</u> 1.85	13.76±1.66	13.69 <u>+</u> 2.58	0.890				
Preoperative creatinin (g/dL) [median (min-max)]	1.2 (0.5-3.2)	1.2 (0.5-3.2)	1.6 (0.9-2.6)	0.009				
Preoperative GFR (mg/dL) (mean \pm SD)	63.72 <u>+</u> 25.65	66.18±25.10	53.16 <u>+</u> 26.08	0.06				
Stone burden (mm ²) [median (min-max)]	588 (150-4900)	500 (150-4459)	1600 (225-4900)	0.002				
CROES score [median (min-max)]	208.5 (100-320)	218 (100-320)	158 (118-277)	0.001				
GSS [median (min-max)]	2 (1-4)	2 (1-4)	3 (1-4)	0.005				
Access number, n/%	-	-	-	0.003				
Single Multiple	55/61.1 35/38.9	50/68.5 23/31.5	5/29.4 12/70.6	-				
Stone location, n/%	-	-	-	0.043				
Single Multiple	41/45.6 49/54.4	37/50.7 36/49.3	4/23.5 13/76.5	-				
Staghorn stone, n/%	-	-	-	0.001				
Yes No	17/18.9 73/81.1	9/12.3 64/87.7	8/47.1 9/52.9	-				
Supracostal access, n/%	-	-	-	0.101				
Yes No	23/25.6 67/74.4	16/21.9 57/78.1	7/41.2 10/58.8	-				
Hydronephrosis, n/%	-	-	-	0.380				
Yes No	61/67.8 29/32.2	51/69.9 22/30.1	10/58.8 7/41.2	-				
Anesthesia time (minute) [median (min-max)]	90 (55-360)	90 (55-360)	90 (65-100)	0.229				
Operation time (minute) [median (min-max)]	55 (15-300)	50 (15-300)	55 (45-60)	0.869				
Hospitalization day [median (min-max)]	3 (1-7)	3 (1-7)	3 (1-5)	0.165				
SD: Standard deviation, GFR: Glomerular filtration rate, CROES: Clinical Maximum	Research Office of the Endourologi	ical Society nomogram, GS	S: Guy's Stone score, min: Mini	mum, max:				

between the groups when the rates of other complications (fever, hydrothorax, perforation, etc.) were evaluated. The significantly lower SFR was associated with surgeon's not taking risks in stone removal in solitary kidneys to avoid complications (2). In another study, data of 412 patients with single functioning kidney was investigated. SFR and complication rate were 91.3% and 19.2%, respectively. Blood transfusion was required in 19 patients (4.6%) and it was associated with uremia and lower preoperative hemoglobin levels due to the uremia (23). In our study, the mean GFR value was lower in patients with residual stones and in patients with complications, however, no statistically significant difference was revealed.

Table 2. Complications according to Clavien classification					
Clavien grade 1					
Fever, n/%	5/5.55				
Clavien grade 2					
Blood transfusion, n/%	15/16.7				
Clavien grade 3					
Nephrostomy tract urine leakage requiring Double J-stent, n/%	2/1.8				

Wong and associates evaluated data of 22 PCNLs which were performed in 17 solitary kidney patients. SFR was 59%. There

were 3 Clavien 2 complications (sepsis in 2 patients, blood transfusion in 1) and 2 Clavien 3 complications (double J -stenting requirement). The relatively low SFR was associated with higher GSS than in similar studies evaluating the outcomes of PCNL in solitary kidney (4).

In a study performed by Torricelli and co-workers, data of 27 patients with solitary kidney who underwent PCNL were evaluated. SFR was 67%. Postoperative complications occurred in 8 patients (29.6 %) (5 Clavien 2 and 3 Clavien 3). GSS was calculated for each patient and 45% of the patients were classified as having GSS 3 or 4. Conversely with our study, GSS was not associated with complication status. On univariate

analysis, prolonged operative time was the only factor associated with complication status (24).

As mentioned above, there are several studies comparing the efficacy of GSS and CROES nomogram in the literature. In a study performed by Bozkurt et al. (15), the efficacy of GSS and CROES nomogram in predicting SFR and complication rate was compared. Both scoring systems had similar accuracy in predicting SFR. Also the analysis showed that both scoring systems revealed significant efficacy in predicting postoperative complications (15). In a multicenter study performed by Labadie et al. (16), a total of 246 patients, who underwent PCNL between 2009 and 2012, were evaluated. Multivariate logistic

Table 3. Association of factors with complication status							
	Patients without complication (n=73)	Patients with complication (n=17)	р				
Age (years) [median (min-max)]	54 (21-83)	52 (34-70)	0.556				
Gender, n/%	-	-	0.446				
Male Female	50/68.5 23/31.5	10/58.8 7/41.2	-				
Side, n/%	-	-	0.790				
Right Left	39/53.4 34/46.6	8/47 9/53	-				
Mean hemoglobin (g/dL) [mean \pm SD]	13.97±1.77	13.15±1.90	0.113				
Preoperative creatinin (mg/dL) [median (min-max)]	1.2 (0.5-3.1)	1.3 (0.7-3.2)	0.615				
Preoperative GFR (mg/dl) [mean \pm SD]	64.66±25.24	59.69±27.82	0.475				
Stone burden (mm ²) [median (min-max)]	452 (150-4900)	1600 (500-4459)	<0.001				
CROES score [median (min-max)]	216 (100-320)	158 (137-289)	0.005				
GSS [median (min-max)]	2 (1-4)	2 (1-4)	0.05				
Access number, n/%	-	-	0.003				
Single Multiple	50/68.5 23/31.5	5/29.4 12/70.6	-				
Stone location, n/%	-	-	0.138				
Single Multiple	36/49.3 37/50.7	5/29.4 12/70.6	-				
Staghorn stone, n/%	-	-	0.009				
Yes No	10/13.7 63/86.3	7/41.2 10/58.8	-				
Supracostal access, n/%	-	-	0.24				
Yes No	18/22.8 61/77.2	5/29.4 12/70.6	-				
Hydronephrosis, n/%	-	-	0.065				
Yes No	46/63 27/37	15/88.2 2/11.8	-				
Anesthesia time (minute) [median (min-max)]	90 (55-190)	85 (55-360)	0.749				
Operation time (minute) [median (min-max)]	55 (15-145)	60 (20-300)	0.531				
Hospitalization day [median (min-max)]	3 (1-7)	3 (1-7)	0.448				
SD: Standard deviation, GFR: Glomerular filtration rate, CROES: Clinical Research Office of the Endou Maximum	rological Society nomogram,	GSS: Guy's Stone score, min:	Minimum, max:				

Table 4. Univariate and multivariate analyses of factorsaffecting stone-free status and complication status								
	p values							
		Multivariate analysis						
	Univariate analysis	Logistic regression (enter method)	Logistic regression (backward– stepwise method)					
Stone-free status	Stone-free status							
Stone burden CROES score GSS Access number Stone location Staghorn stone	0.003 0.002 0.002 0.005 0.048 0.002	0.502 0.124 0.361 0.118 0.191 0.464	0.019 (Step 5) 0.095 (Step 5)					
Complication status								
Stone burden CROES score GSS Access number Staghorn stone	0.001 0.008 0.027 0.005 0.013	0.111 0.375 0.328 0.080 0.514	0.012 (Step 4) 0.093 (Step 4)					

CROES: Clinical Research Office of the Endourological Society nomogram, GSS: Guy's Stone score,

Continuous variables: CROES, GSS, stone burden

Categorical variables: Access number (single-multiple), stone location (single calyxmultiple calyces), staghorn stone (yes-no)

regression analysis showed that all the scoring systems were significantly correlated with SF status. Also, GSS and S.T.O.N.E nephrolithometry score were significantly associated with length of hospital stay and estimated blood loss while CROES score was not (16).

In the current study, SFR and complication rate were consistent with other studies. However, we found a higher rate of blood transfusion in our series. This condition was related with a more protective clinical approach to patients with solitary kidney and larger stone size compared to other studies. In the analysis, stone burden was associated with SFR and complication rate. The main purpose of this study was to evaluate the efficacy of GSS and CROES score in predicting SFR and complication status in patients with solitary kidney. Both scoring systems were correlated with SFR and complication status. In multivariate analysis of factors affecting SFR, CROES score was the only independent factor associated with SF status.

Concerns of patients and surgeons about the complications of PCNL are more disturbing before procedures on single functioning kidney. Recently, RIRS has been reported to provide a high SFR with low complication rate and relatively less life-threatening complications (25,26). RIRS was defined as a successful treatment modality for stones in solitary kidneys but a decrease in SFR was reported especially for stones larger than 2 cm (27). Requirement of follow-up procedures after RIRS may add new risks and prolong the duration of treatment. We think that especially in solitary kidney, the modality of stone treatment should be selected according to surgeon's experience and patient's status.

The predictability of complications is an advantage for surgeon in the pretreatment patient preparation and peroperative decision taking. We think that the development of a PCNLspecific tool for predicting complication status is important. Our analysis revealed that neither GSS nor CROES score was effective enough in predicting complication prior to PCNL in solitary kidneys.

There are some limitations of the current study. First, the data was collected from a retrospective cohort. Second, we could not evaluate the efficacy of S.T.O.N.E nephrolithometry score due to lack of stone density in our cohort. Third, it was a single-center study which may limit generalizability.

Conclusion

PCNL is an effective method in the treatment of renal stones in solitary kidney. CROES nomogram score is a better tool in predicting SF status in patients with solitary kidney who are candidates for PCNL. Patients with high stone burden are more prone to complications. Further studies should be performed to evaluate the efficacy of nephrolithometric scoring systems in predicting surgical outcomes after PCNL in patients with solitary kidney.

Ethics

Ethics Committee Approval: Institutional review board approval (protocol no: 2011-KAEK-25 2018/10-02).

Informed Consent: Retrospective study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

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The Efficacy of N-acetylcysteine Against Renal Oxidative Stress After Extracorporeal Shock Wave Treatment: An Experimental Rat Model

N-asetilsisteinin Ekstrakorporeal Şok Dalga Tedavisi Sonrasında Oluşan Renal Oksidatif Stres Hasarına Karşı Etkinliği: Deneysel Rat Modeli

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

Current study confirmed that shock wave lithotripsy (SWL) causes oxidative stress as expressed by a remarkably increased plasma oxidative stress index in blood samples of SWL-treated rats as the first time in literature. SWL also produced acute renal damage as tubular damage and interstitial inflammation. N-acetylcysteine (NAC) was found to be effective in decreasing SWL-induced oxidative stress and also may protect to some extend certain histological alterations. This experimental model provides an important background for subsequent clinical trials on protective role of NAC in patients receiving SWL.

Abstract

Objective: To evaluate effects of renal extracorporeal shock wave lithotripsy (SWL) on plasma Oxidative Stress index (OSI) and to observe histopathological alterations in an experimental model. Secondly, protective role of N-acetylcysteine (NAC) was investigated.

Materials and Methods: A total of 24 rats were randomly divided into 3 groups as control (group 1), SWL + saline (group 2), and SWL + NAC (group 3). Study groups were further divided into two subgroups as short-term and long-term. In groups 2 and 3, 2000 shock waves were applied. Intraperitoneal saline was administered in group 2, and intraperitoneal NAC was given to group 3. No treatment was administered to group 1. Blood samples and nephrectomy specimens were obtained for biochemical and histopathological examinations, respectively. OSI was calculated by measuring plasma total antioxidant status (TAS) and total oxidant status (TOS). Acute and chronic histopathological damage were evaluated by light microscopy.

Results: SWL caused a remarkable increase in oxidative stress. Strikingly, TOS levels were significantly lower (p=0.027) and TAS levels were significantly higher (p=0.006) in rats with SWL + NAC (group 3). As a result, OSI was lower (p=0.013). This effect was particularly significant in the short-term subgroup. It was also concluded that tubular damage and interstitial inflammation were higher in the SWL group (p=0.022). These acute histological alterations were slighter in rats with NAC.

Conclusion: The current study demonstrated that SWL can cause severe oxidative stress and acute renal damage by increasing free oxygen radical production. NAC was effective in decreasing SWL-induced oxidative stress and preventing certain histological alterations to some extent. **Keywords:** Extracorporeal shock wave lithotripsy, Kidney, Oxidative stress, Rat

Öz I

Amaç: Bu çalışmanın amacı deneysel bir modelde renal ekstrakorporeal şok dalga litotripsisinin (ESWL) plazma Oksidatif Stres indeksi (OSİ) üzerindeki etkilerini değerlendirmek, histopatolojik değişiklikleri gözlemlemek ve N-asetilsisteinin (NAC) koruyucu rolünü araştırmaktır.

Gereç ve Yöntem: Toplam 24 rat rastgele 3 gruba; kontrol (grup 1), SWL + salin (grup 2) ve SWL + NAC (grup 3) olarak ayrıldı. Çalışma grupları ayrıca kısa ve uzun süreli olarak iki alt gruba ayrıldı. Grup 2 ve 3'te 2000 şok dalga ESWL uygulandı. Grup 2'de intraperitoneal salin ve grup 3'e



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intraperitoneal NAC verildi. Grup 1'e tedavi uygulanmadı. Biyokimyasal ve histopatolojik incelemeler için sırasıyla kan örnekleri ve nefrektomi örnekleri alındı. OSİ, plazma toplam antioksidan seviyesi (TAS) ve toplam oksidan seviyesi (TOS) ölçülerek hesaplandı. Akut ve kronik histopatolojik hasar ışık mikroskobu ile değerlendirildi.

Bulgular: ESWL, oksidatif streste belirgin bir artışa neden oldu. Grup 3'teki ratlarda TOS düzeyleri anlamlı olarak düşük (p=0,027), TAS seviyeleri anlamlı derecede yüksek saptandı (p=0,006). Sonuç olarak, OSİ daha düşük saptandı (p=0,013). Bu etki kısa süreli alt grupta daha anlamlıydı. Ayrıca SWL grubunda tübüler hasar ve interstisyel enflamasyonun daha yüksek olduğu sonucuna varıldı (p=0,022). Bu akut histolojik değişiklikler NAC verilen ratlarda daha az saptandı.

Sonuç: Mevcut çalışma, ESWL'nin serbest oksijen radikal üretimini artırarak şiddetli oksidatif stres ve akut böbrek hasarına neden olabileceğini göstermiştir. NAC, ESWL'nin neden olduğu oksidatif stresi azaltmada ve bazı histolojik değişikliklerin oluşumunu engellemede etkili olduğu görülmüştür.

Anahtar Kelimeler: Ekstrakorporeal şok dalga litotripsisi, Böbrek, Oksidatif stres, Sıçan

Introduction

Urinary Stone disease represents a major common health problem all over the world. There have been remarkable changes in the indications for surgical treatment as a result of the technological development in endourologic instruments (1). Nevertheless, extracorporeal shock wave lithotripsy (SWL) remains the initial treatment modality for the majority of patients with renal stones. Moreover, current guidelines suggest that SWL remains the least-invasive procedure for stone management in children (2). Therefore, long-term tissue effects of SWL are needed to be investigated despite its long-term proven efficacy. There have been several reports proposing that SWL causes oxidative stress due to renal ischemia-reperfusion injury (3,4,5). Furthermore, some agents have been tested to prevent SWL-induced renal oxidative stress (6,7).

N-acetylcysteine (NAC) is a well known antioxidant (8). NAC inhibits activation of c-Jun N-terminal kinase, p38 MAP kinase and redox-sensitive activating protein-1 and nuclear factor kappa B transcription factor activities regulating expression of numerous genes. Furthermore, NAC can prevent apoptosis and promote cell survival by activating extracellular signal-regulated kinase pathway (8). It is also proposed that NAC can modify DNA. Thereby, NAC has a preventive role in several processes as reducing endothelial dysfunction, inflammation, fibrosis, and invasion.

The objective of this experimental study was to investigate the effects of SWL on plasma oxidative stress, and to observe possible histopathological alterations in rat kidneys. Moreover, we aimed to detect the protective role of NAC administration during SWL treatment.

Materials and Methods

Animals

All experiments in this study were performed in accordance with the Universal Declaration of Animal Rights (Paris, 1978) and were approved by the Local Animal Ethics Committee (1001/03). Twenty-four female Wistar-Albino rats all aged 12 weeks with a range of weight of 175-250 g were used in the present study. The animals were housed in cages with 9 rats at maximum. The animals lived at a temperature range from 18°C to 20°C and a 12 h light and dark cycle. Sample size estimates were based on data from previous studies (9).

Experimental Groups and Procedures

The animals were randomly assigned to three groups according to weight by using simple randomization method (Figure 1). Study groups (2 and 3) were further randomly divided into two subgroups as short-term (14 days) and long-term (28 days). Group 1 (6 rats) constituted control animals without any SWL and NAC. Group 2 (9 rats) underwent SWL and received intraperitoneal saline at a dose of 1 mL/kg/day for 14 (shortterm) or 28 days (long-term) as placebo treatment. Group 3 (9 rats) also underwent SWL, and these rats received intraperitoneal NAC (Asist[®], Husnu Arsan, Turkiye) at a dose of 300 mg/kg/day for 14 (short-term) or 28 days (long-term).

Control group had no intervention at all. In groups 2 and 3, contrast material was administered through an intravenous catheter that was placed in the rat tail vein, and a collecting system was visualized under fluoroscopy with general anesthesia by administrating 1mg/kg intramuscular injection of ketamine HCl (Rompun[®], Bayer, Germany) and xylazine HCl (Ketalar[®], Eczacibasi, Turkiye) (10 mg/kg). The anesthetized rats were then fixed at the thorax and hip in the supine position on the platform of the lithotripter. This maneuver allowed direct entry of the shock waves through the abdominal wall into the left



Figure 1. Study flowchart

kidney tissue. Then, the lower pole of the left kidney was treated after it was localizated using fluoroscopy. A total of 200 shock waves were applied to the left kidney with an amplitude of 18 kV and a rate of 60 SW/minute (PCK Stonelith-V5 Lithotripter, Ankara, Turkiye) at a single setting.

The final procedure was performed on the 14th day following SWL in the short-term subgroups and on the 28th day following SWL in the long-term subgroups, respectively. The rats in the group 1 were also operated on the 14th day. A midline laparotomy was performed, and blood samples were collected from the vena cava by syringe for biochemical analyses. After the kidneys had been excised, they were longitudinally bisected; one hemisection was fixed in formalin solution, embedded in paraffin and stained with hematoxylin-eosin (H&E) for microscopic examination.

The blood samples were centrifuged at 12000 rpm at 4°C for 10 min., and then stored at 80°C for biochemical tests. The Oxidative Stress index (OSI) was calculated by measuring plasma total antioxidant status (TAS) and total oxidant status (TOS) by using a novel, colorimetric and fully automated method for measuring total antioxidant response against potent free radical reactions as described by Erel (10,11). The tests were performed by an auto-analyzer (Beckman Coulter AU480, Japan) by using appropriate kits (Rel Assay, Turkiye). TAS results were expressed as mmol Trolox Eqiv./L, while TOS values were expressed as μ mol H2O2 Eqiv./L. OSI was calculated by using the formula OSI (arbitrary unit) = TOS (μ mol H2O2 Eqiv./L)/TAS (μ mol Trolox Eqiv./L).

Histological investigation that was evaluated by the same pathologist involved acute and chronic damage. Acute renal damage was evaluated by 4 parameters: 1. tubular damage, 2. interstitial inflammation and hemorrhage, 3. dilatationcongestion in the glomerular and vascular structures, and 4. increase in inflammatory cells. A scoring system was separately used for these histological parameters as "0 (normal morphology)", "1 (mild)", "2 (moderate)" and "3 (severe)". The evaluation was made semiquantitatively. In each preparation, 30 sites were evaluated and rated on average (12). Renal glomeruli, tubule, interstitium and arteries were evaluated histopathologically regarding the parameters mentioned above. The evaluation was done as follows; score 1=mild (6-25%); score 2=moderate (26-75%); score 3=heavy (76-100%) (13). The mean score was calculated for each subgroup. On the other hand, chronic renal damage was examined by using 2 parameters: tubular atrophy and interstitial fibrosis (12). Tubular atrophy was graded as "0 (normal morphology)", "1 (<10%)", "2 (10-25%)", "3 (25-50%)", "4 (50-75%)", and "5 (>75%)". Interstitial fibrosis was scored similarly with acute damage parameters as from 0 to 3.

Statistical Analysis

Statistical analysis was done using the Statistical Package for Social Sciences, ver. 15.0 for Windows, (SPSS, Chicago, IL). The Kruskal-Wallis test was used for comparison of the groups and significant differences were determined using the Dunn's posthoc test. A p value of less than 0.05 was considered statistically significant.

Results

Biochemical Analysis

Remarkably elevated TOS values were observed in rats undergoing SWL i.e. group 2 (Table 1). However, group 3 (SWL + NAC) had significantly low TOS values compared to group 2 (p=0.027). The median TOS value was 15.38 µmol H2O2 Eqiv./L and 16.27 H2O2 Eqiv./L in rats with SWL + saline (group 2) at short term (14 day) and long term (28 day), respectively. NAC administration (group 3) decreased these values to 8.58 H2O2 Eqiv./L at short term and 10.92 H2O2 Eqiv./L at long term (Table 1). Consequently, NAC administration improved the TOS almost two times in the third group. Similarly, the median TAS value was 0.96 µmol TroloxEgiv./L in the short term of group 2 (SWLsaline). This value was increased to 1.19 µmol TroloxEqiv./L by 14 day NAC injection (group 3). This difference was significant (p=0.006). As a result of these, OSI (TOS/TAS) was lower in the NAC group (p=0.013). This effect was particularly significant in the short-term subgroup. As much as two times higher OSI values were measured in rats that underwent SWL without NAC. While the median OSI was 7.21 arbitrary units at the 14 day with NAC (group 3), it was 16.72 arbitrary units in the SWL group without NAC (group 2) (Table 1). Even the control group had an OSI value of 10.555 arbitrary units that was higher but not significant compared to NAC group.

Histological Investigation

Tubular damage as an acute damage parameter was found to be prominent in rats receiving SWL. Control group had a median score of 0.5 for tubular damage. This value was increased up to 2 in the SWL + saline group (group 2) both in short- and long-term subgroups. This difference was significant (p=0.022). Although not significant, NAC application decreased this tubular damage score down to 1 and, 1.5 at short and long term, respectively. In figure 2, histological views of the tubular damage are shown with respect to groups. Similarly, interstitial inflammation was not observed at all in the control group. SWL caused a prominent increase in this score up to 2 both at 14 and 28 days in group 2. These changes in interstitial inflammation were statistically significant (p=0.002). Although not-significant, this score was decreased to 1 by NAC application in group 3 (Table 2). The rest of the acute damage parameters namely, dilatation-congestion

Table 1.The comparison of biochemical oxidative stress parameters between groups									
	Group	n	Mean	Median	Standard deviation	min	max	р	
	1	6	11.126	11.12 ^{ab}	1.5804	8.46	12.89		
	2-short	5	15.254	15.38 ^b	3.8641	11.52	20.70		
TOS	3-short	5	8.976	8.58ª	1.4356	7.64	11.00	0.027	
(μποι π ₂ 0 ₂ εφιν./ε)	2-long	4	21.595	16.27 ^b	15.885	9.01	44.83		
	3-long	4	10.43	10.92 ^{ab}	3.1326	6.25	13.63	1	
	1	6	1.0866	1.09 ^{ab}	0.0826	1.00	1.23	0.006	
	2-short	5	0.976	0.96 ^b	0.0622	0.92	1.06		
IAS (umol TroloxEaiy/L)	3-short	5	1.204	1.19ª	0.0823	1.09	1.31		
	2-long	4	1.2675	1.165 ^{ab}	0.2518	1.10	1.64		
	3-long	4	1.855	1.685 ^{ab}	0.8456	1.09	2.96		
	1	6	10.253	10.555ª	1.3485	7.69	11.50	1	
	2-short	5	15.634	16.72ª	3.7261	11.42	19.53		
OSI (Arbitrony unit)	3-short	5	7.508	7.2 ^b	1.5439	6.11	10.09	0.013	
	2-long	4	18.105	11.85 ^{ab}	15.350	7.97	40.75		
	3-long	4	7.1175	6.93 ^{ab}	4.5532	2.11	12.5		

TOS: Total oxidant status; TAS: Total antioxidant status; OSI: Oxidative Stress index, Group 1: Control group, Group 2: SWL + saline, Group 3: SWL + NAC, Short:14 days, Long: 28 days SWL: Extracorporeal shock wave lithotripsy, NAC: N-acetylcysteine, ^{a, b, ab}: The letters (a, b, ab) in the upper right side of median values of the groups were used to show whether the differences between the groups were significant. If there is a statistically significant difference between the groups, they carry different letters (like a and b). If there is the letter (ab), it does not differ from the group with a, and the group with b letter, Min: Minimum, Max: Maximum

in the glomerular and vascular structures, and increase in inflammatory cells, were not different between the groups (Table 2). Similarly, no difference in chronic renal damage parameters, such as tubular atrophy and interstitial fibrosis, was noticed between the groups.

Discussion

SWL constitutes a milestone in the management of Urinary Stone disease (2). Particularly, the higher clinical success in children with renal stones signifies the clinical utilization of SWL. However, possible histological and functional alterations in renal tissue after SWL treatment has gained a tremendous concern, and several well-designed experimental trials have focused on this issue.

One of the possible mechanisms for SWL-related renal damage is increased oxidative stress due to renal ischemia-reperfusion injury (3,4,5). An experimental model on rabbits demonstrated a statistically significant decrease in tissue scavenger enzyme levels (i.e. formation of free oxygen radicals) after SWL in dose dependent manner (5). A similar trail on 69 rats clearly demonstrated a significant increase in malondialdehyde (MDA) levels and decrease in superoxide dismutase (SOD) activity as markers for oxidative stress after SWL (14). They further reported that total saponins of astragalus which is the main component of. A mongholicus can decrease shock waveinduced kidney injury not only by scavenging oxygen free radicals but also inhibiting the expression of p-selectin (14).



Figure 2. Tubular damage between the groups. A) Control group: tubular damage (normal, score 0) (htte x400). B) Group 2 (swl + saline) at 14 day: tubular damage (severe, score 2) (htte x400). C) Group 3 (swl + nac) at 14 day: tubular damage (moderate, score 1) (htte x400)

The same authors performed a subsequent trial on rats; they confirmed that shock wave significantly increased the level of MDA and decreased SOD activity in both blood and renal homogenates (7). The study group receiving astragalosides, a novel antioxidant agent, could be protected from shock waveinduced renal oxidative injury. Furthermore, a clinical trial on 120 patients with renal SWL treatment proposed that oral antioxidant administration was associated with reduced mean serum concentration of MDA, higher levels of serum ascorbic acid and serum albumin, lower alpha-tocopherol/cholesterol ratio, lower urinary albumin and beta-2 microglobulin levels

Table 2. The comparison of histological alterations between groups									
	Group	n	Mean	Median	Standard deviation	min	max	р	
	1	6	0.5	0.50°	0.548	0	1		
	1-short	5	1.6	2.00 ^b	0.548	1	2		
Tubular damage	3-short	5	1.2	1.00 ^{ab}	0.837	0	2	0.022	
	2-long	4	2.0	2.00 ^b	0.0	2	2		
	3-long	4	1.5	1.50 ^{ab}	0.577	1	2		
	1	6	0.0	0.00ª	0.00	0	0		
	2-short	5	2.0	2.0 ^b	0.707	1	3		
Interstitial inflammation	3-short	5	1.0	1.0 ^{ab}	1.00	0	2	0.002	
	2-long	4	2.0	2.00 ^b	0.00	2	2		
	3-long	4	1.0	1.00 ^b	0.00	1	1		
	1	6	0.5	0.50	0.548	0	1	0.291	
	2-short	5	1.2	1.00	0.447	1	2		
Congestion	3-short	5	0.6	1.00	0.548	0	1		
	2-long	4	0.75	1.00	0.50	0	1		
	3-long	4	0.75	1.00	0.50	0	1		
	1	6	0.00	0.00	0.00	0	0		
	2-short	5	1.20	1.50	0.20	0	2		
Increase in inflammatory cells	3-short	5	1.00	1.50	0.50	0	2	0.287	
	2-long	4	0.75	1.00	0.541	0	1		
	3-long	4	0.75	1.00	0.541	0	1		
	1	6	0.00	0.0	0.0	0	0		
	2-short	5	2.00	2.00	0.50	1	3		
Fibrosis	3-short	5	1.00	1.50	0.50	1	2	0.299	
	2-long	4	2.00	2.00	0.0	2	2		
	3-long	4	1.00	1.00	1.00	1	1		
	1	6	0.00	0.00	0.00	0	0		
	2-short	5	0.00	0.00	0.00	0	0		
Tubular atrophy	3-short	5	0.00	0.00	0.00	0	0	1.00	
	2-long	4	0.00	0.00	0.0	0	0		
	3-long	4	0.00	0.00	0.00	0	0		

Group 1: Control group, Group 2: SWL + saline, Group 3: SWL + NAC, Short: 14 days, Long: 28 days SWL: Extracorporeal shock wave lithotripsy, NAC: N-acetylcysteine ^{a, b, ab}: The letters (a, b, ab) in the upper right side of median values of the groups were used to Show whether the differences between the groups were significant. If there is a statistically significant difference between the groups, they carry different letters (like a and b). If there is the letter (ab), it does not differ from the group with a, and the group with b letter

(15). They concluded that SWL generates free radicals through ischemic/reperfusion injury mechanism, and oral administration of antioxidant may protect these patients from short-term renal injury caused by SWL. A similar study by Ozguner et al. (6) showed that shock wave exposure caused a significant rise in MDA, urine N-acetyl-beta-glucosaminidase (NAG) activity, uric acid and white cell counts as markers of oxidative stress. On the other hand, a novel free radical scavenger, caffeic acid phenethyl ester, reduced the rise in MDA, NAG, uric acid and white cell counts growiding a protection against SWL-induced free radical damage. In another study on 12 rats, it was demonstrated that

SWL caused oxidative stress and impaired the antioxidant and trace element levels in the kidneys of rats (16). They reported higher MDA levels, and reduced glutathione levels, lower SOD, and glutathione peroxidase activities in SWL group. A clinical trial reported elevated plasma and urinary nitric oxide levels after SWL (3). Plasma and urinary MDA levels also showed statistically significant elevation after SWL. Another clinical trial proposed that SWL caused a severe alteration in activities of glucose-6-phosphate dehydrogenase, SOD and catalase in the erythrocyte haemolysate (17). They concluded that erythrocyte lipid peroxidation might be induced and antioxidative defense

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mechanism may be transiently impaired by SWL. A prospective, randomized, double-blind, placebo-controlled clinical trial on 100 patients with SWL treatment showed a clinical efficacy of coenzyme Q10 (CoQ10) as an oral powerful antioxidant with vasoactive properties in preventing renal injury (18). CoQ10 showed improvement in vasoactive hormone parameters, Vascular Resistance index on Doppler ultrasound and interleukin levels suggesting a protection in renal function, and also vasoactive and inflammation parameter values. In an experimental pig model of SWL, acute oxidative stress and inflammatory responses were localized to the renal medulla within the focal zone of the lithotripter (19). Melatonin as a potent endogenous free radical scavenger was tested on rabbits after SWL (20). The mean levels of MDA, uric acid and white cell counts as markers of oxidative stress were significantly lower in the melatonin-treated group suggesting a protective effect of melatonin. Another experimental rabbit model showed that antioxidant defense potential of the SWL-treated tissues was reduced, and MDA levels were increased (21). Administration of vitamin E plus C combination ameliorated antioxidant defense potential in part, prevented increases in MDA levels in the SWLtreated tissues. All these experimental SWL models and some clinical studies propose that SWL produces significant oxidative stress. Current trial also confirms that SWL application caused a remarkable decline in TAS levels and a significant rise in TOS levels. Consequently, a notable raise in OSI was observed in rats undergoing SWL. In this study, OSI values were reported by measuring TAS and TOS in blood samples of SWL-treated rats as the first time in the literature for detecting SWL-related oxidative stress. We also used a novel colorimetric and fully automated method for measuring total antioxidant response against potent free radical reactions (10,11).

Histological alterations due to SWL treatment were also reported by several well-designed experimental trials. Chronic morphological changes, such as tubular injury and interstitial fibrosis, were observed in rats after SWL (12). The authors also suggested that nuclear factor κB (NF κB) was important in the progression of SWL-induced long-term renal damage and also shock wave exposure up-regulated the expression of transforming growth factor- β 1. According to an electron microscopic investigation on rabbit model, some significant subcellular changes, such as endothelial injury, damage to glomerular basal membrane, etc., were observed in the SWLtreated renal tissue (22). Acute morphological changes, such as glomerular bleeding, tubular dilatation, atrophy and partial necrosis, have been reported in rat kidneys after SWL (22). Investigation by scanning electron microscopy revealed a tubular loss of microvilli and cilia. It was postulated that longterm lesions were due to the venous rupture occurred during SWL, especially in thin arcuatae veins. This resulted in interstitial hematoma. Later on, hematomas progressed to interstitial

fibrosis. Finally, blood supply in these areas was reduced and secondary changes, such as glomerular-tubular atrophy and sclerosis, followed. Similarly in a rat SWL model, gross interstitial hemorrhage, subcapsular hematomas, and hemorrhages into the renal pelvis were detected by using vascular casting procedures (23). All these histological investigations showed that SWL causes some significant morphological alterations in experimental models. In this study, tubular damage and interstitial inflammation, acute damage parameters, were also found to be prominent in rats receiving SWL. However, no finding of chronic renal damage, such as tubular atrophy and interstitial fibrosis, was noticed after SWL. This observation may be due to the fact that chronic changes require a longer period to develop. We can conclude that SWL produces significant oxidative stress which in turn results in acute renal damage such as tubular damage and interstitial inflammation.

NAC, a potent antioxidant, was tested to prevent oxidative damage in renal tissues. In a rat model, carbon dioxide pneumoperitoneum was used to induce oxidative stress (24). It was reported that administration of NAC provided a complete protection against decline in glomerular filtration rate following pneumoperitoneum. In a randomized, double-blind, controlled clinical trial on chronic hemodialysis patients, administration of NAC suggested to reduce oxidative stress without major side-effects (25). In another experimental study, it was shown that NAC could protect rat kidney against aspartame-induced oxidative stress (26). Similarly, it has been concluded that NAC showed effective restoration of oxidative stress biomarkers including MDA, SOD, and glutathione peroxidase (27). In this experimental model, rats that received intraperitoneal NAC at a dose of 300 mg/kg/day for 14 or 28 days showed a significant improvement of TOS as much as two times than the rats without NAC. Similarly, median TAS value was remarkably increased by NAC injection. Consequently, OSI was lower in the NAC group. Almost two times higher OSI values were measured in rats that underwent SWL without NAC. Therefore, this study showed that NAC has a protective role against oxidative stress associated with SWL. Moreover, tubular damage and interstitial inflammation as acute damage parameters were found to be less prominent in rats receiving NAC. The current trial suggests that NAC administration during SWL can prevent renal oxidative stress, and then, some subsequent morphological alterations may also be improved by NAC.

The limitations of the study include that pre-SWL oxidative stress measurements would be appropriate, however, obtaining blood samples from rats requires anesthesia. Second point, contrast material used to visualize the kidney may affect renal functions. Thirdly, larger study groups would be more powerful, however, the number of rats were restricted in accordance with the "3R (reduction, refinement, replacement) rule", also taking

into account similar studies in the literature and practices of the animal ethical committee.

Conclusion

Current study confirmed that SWL causes oxidative stress as expressed by remarkably increased plasma OSI in blood samples of SWL-treated rats as the first time in the literature. SWL also produced acute renal damage as tubular damage and interstitial inflammation. NAC was found to be effective in decreasing SWL-induced oxidative stress and also it was assumed that it may protect against certain histological alterations to some extent. This experimental model provides an important background for subsequent clinical trials on protective role of NAC in patients receiving SWL.

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Ethics

Ethics Committee Approval: All experiments in this study were performed in accordance with the Universal Declaration of Animal Rights (Paris, 1978) and were approved by the Local Animal Ethics Committee (10-01/03).

Informed Consent: Local Animal Ethics Committee approval was obtained and compliance with the international animal rights declaration.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: D.B., K.Ç., Design: D.B., K.Ç., Y.Ş., Data Collection or Processing: D.B., Y.Ş., Analysis or Interpretation: D.B., K.Ç., H.E., Literature Search: D.B., K.Ç., Y.Ş., A.Y., Writing: D.B., A.Y., E.B.

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Laparoscopic Transperitoneal Simple, Radical and Partial Nephrectomy: A Single Center Experience

Laparoskopik Transperitoneal Basit, Radikal ve Parsiyel Nefrektomi: Tek Merkez Klinik Tecrübemiz

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

Laparoscopic surgery has become a standard technique for better results for both oncologic and non-oncologic diseases, especially in urology, as in other disciplines. The higher the surgeon's experience in laparoscopic surgery, the shorter the operative time, the lesser the blood loss and the shorter the hospital stay. Currently, as the urologists gain experience in laparoscopy, they perform more complex operations such as partial nephrectomy in a shorter time, with less blood loss and complications. It should be kept in mind that there may be more perirenal adhesions in laparoscopic simple nefrectomy patients and care should be taken for possible complications.

Abstract

Objective: To present our initial experience on laparoscopic transperitoneal nephrectomies and to report the perioperative and postoperative outcomes in patients with kidney tumor.

Materials and Methods: We retrospectively evaluated clinical data, laboratory results and radiological findings of 40 patients who underwent laparoscopic renal surgery performed by a single surgeon in a single center between November 2017 and May 2019. Thoracoabdominopelvic computed tomography was performed in all patients.

Results: A total of 40 patients (26 males (65%), 14 females (35%) with a median age of 58.7 years underwent laparoscopic transperitoneal nephrectomy. Sixteen patients underwent laparoscopic simple nephrectomy (LSN) for nonfunctional kidney, 20 patients with solid renal tumors underwent laparoscopic radical nephrectomy (LRN), and four patients underwent laparoscopic partial nephrectomy (LPN) for solid renal mass. The mean operative time was 207.9±79.1, 218.9±57.5 and 175.0±75.0 minutes for LSN, LRN and LPN, respectively. The mean length of hospital stays was 3.0±1.3, 2.7±0.6 and 2.7±1.5 days, respectively. Conversion to open surgery was done in 2 patients who underwent LRN and in two patients who underwent LSN due to intraoperative bleeding and intraperitoneal adhesions, respectively. We experienced postoperative complication only in one patient (2.5%) who underwent LSN.

Conclusion: Advances in technology and surgical experience have led to an increase in laparoscopic kidney surgery even for advanced renal tumors. Serious complications may occur mainly in the early stages of the learning curve, but complication rates and operative time significantly decrease by the surgeons' experience. Complicated and more extensive tumors make surgeons more experienced in advanced laparoscopic treatment techniques. **Keywords:** Complication, Experience, Laparoscopy, Renal tumor

Öz

Amaç: Laparoskopik transperitoneal nefrektomi konusunda ilk deneyimimizi sunmak ve böbrek tümörü olan hastalarda perioperatif ve postoperatif sonuçları bildirmek.



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Gereç ve Yöntem: Kasım 2017-Mayıs 2019 tarihleri arasında tek bir merkezde aynı cerrah tarafından laparoskopik böbrek cerrahisi ile ameliyat edilen 40 hastanın klinik verilerini, laboratuvar sonuçlarını ve radyolojik bulgularını retrospektif olarak değerlendirdik. Torakoabdominopelvik bilgisayarlı tomografi tüm hastalar için rutin olarak yapıldı.

Bulgular: Toplam kırk hastaya (26 erkek (%65), 14 kadın (%35) ortanca yaş 58,7 yıl) laparoskopik transperitoneal nefrektomi uygulandı. Hastaların 16'sına fonksiyonel olmayan böbrek için laparoskopik basit nefrektomi (LBN) uygulandı; solid böbrek tümörü olan 20 hastaya laparoskopik radikal nefrektomi (LRN), dört hastaya da solid böbrek kitlesi için laparoskopik parsiyel nefrektomi (LPN) uygulandı. Ortalama operasyon süreleri LBN, LRN ve LPN için sırasıyla 207,9±79,1, 218,9±57,5 ve 175±75,0 dakikaydı. Ortalama hastanede kalış süresi sırasıyla 3,0±1,3, 2,7±0,6 ve 2,7±1,5 gündü. LRN uygulanan iki hastada ve LBN yapılan iki hastada, sırasıyla intraoperatif kanama ve intraperitoneal adezyonlar nedeniyle açık nefrektomiye geçildi. Postoperatif komplikasyon sadece LBN uygulanan bir hastada (%2,5) saptandı.

Sonuç: Teknoloji ve cerrahi tecrübedeki gelişmeler ile laparoskopik böbrek cerrahisi ileri böbrek tümörleri için bile tercih edilen yöntem haline gelmiştir. Özellikle öğrenme eğrisinin erken aşamalarında ciddi komplikasyonlar ortaya çıkabilir, ancak komplikasyon oranları ve çalışma süreleri cerrahın tecrübesiyle önemli ölçüde azalır. Komplike ve daha büyük tümörler, ileri laparoskopik tedavi teknikleri için cerrahları daha deneyimli hale getirmektedir.

Anahtar Kelimeler: Laparoskopi, Böbrek tümörü, Tecrübe, Komplikasyon

Introduction

The European Association of Urology and the American Urological Association recommend the surgical approach as a primary treatment modality for kidney tumors (1,2). Evolution in minimally invasive treatment techniques has led to laparoscopic surgery, the standard treatment procedure for stage T1 kidney tumors (3,4). Laparoscopic nephrectomy (LN) offers oncological results similar to those of open nephrectomy with the advantages of shorter hospital stay, faster recovery, less pain and blood loss (5,6).

In this study, we aimed to report our experience and postoperative outcomes in patients who underwent laparoscopic transperitoneal nephrectomy due to nonfunctioning kidney or kidney tumor.

Materials and Methods

After receiving Institutional Board approval from the Clinical Research and Ethics Committee of Zonguldak Bülent Ecevit University (Zonguldak, Turkiye) (33479383/37), we retrospectively reviewed the medical record of 40 patients with different pathologies who underwent a laparoscopic transperitoneal simple, radical or partial nephrectomy between November 2017 and May 2019. We recorded the demographic characteristics, such as gender and age, as well as body mass index, type of surgery, American Society of Anesthesiologists risk, preoperative and postoperative hemoglobin and creatinine levels, operative time, postoperative drainage, hospital stay and histopathological diagnoses, in addition to R.E.N.A.L nephrometry scores in those with kidney tumor.

In the R.E.N.A.L nephrometry scoring system; (R) represents maximum tumor radius, (E) endophytic/exophytic properties of the mass, (N) tumor distance to the collecting system, (A) anterior/posterior descriptor and, (L) represents the location relative to the polar line. Each parameter was scored from 1 to 3 according to the anatomy of the tumor, and the total score was calculated. A total score of 4-6 means low, 7-9 intermediate and 10-12 high tumor complexity.

Statistical Analysis

The Statistical Package for the Social Sciences v. 18.0 (SPSS Inc, Chicago, IL, USA) was used for statistical analysis. Data were given as mean \pm standard deviation, percentages, or numbers. A p value <0.05 was accepted as significant.

Surgical Procedure

We performed transperitoneal laparoscopic surgery with the patient placed in 70-degree lateral decubitus position. A 12 mm optical camera port was inserted 5 cm lateral to the level of the umbilicus after 20 mmHg pneumoperitoneum was created using a Veress needle. The second 10 mm trocar was placed subxiphoidally and, finally, a 5 mm trocar was placed about two cm medial and superior to the anterior superior iliac crest to create a triangular shape under direct vision for the left side. For right-sided tumors, we used an additional 5 mm port for liver retraction. In the intraabdominal pressure of 12 mmHq, the colon was medialized with the help of a grasper and scissors over the Toldt line. The renal artery and vein were dissected and separately clipped using Hem-o-lok (Weck Closure Systems; Research Triangle Park, NC) clips. The kidney was released from the surrounding tissues by dissecting with a LigaSure device. For partial nephrectomy, after renal pedicle dissection, we clamped the main renal artery using a bulldog clamp (Figure 1a) and resected the tumor with safe margins. Using a 2-0 absorbable polyglactin suture, we closed the renal parenchyma in a running fashion (Figure 1b). The bulldog clip was removed, the renal artery was opened, and the intraabdominal pressure was decreased to 5 mmHg to control bleeding. We removed the specimens via the trocar incision using an endo bag (Endo Catch Gold, Medtronic, MN) and placed a drain at the surgery site. In the early postoperative period, we used a patient-controlled analgesia pump and paracetamol for pain relief.



Figure 1. Renal artery was clamped using a bulldog clamp (1a) and renal parenchyma was closed in a running fashion using a 2-0 absorbable polyglactin suture (1b)

Table 1. Demographic data of patients who were treated withlaparoscopic transperitoneal renal surgery				
Gender Male (n, %) Female (n, %)	26 (65.0%) 14 (35.0%)			
Age (years)	58.7±12.3			
BMI (kg/m²)	27.3 <u>±</u> 4.8			
Left side (n, %) Right side (n, %)	24 (60.0%) 16 (40.0%)			
Mean tumor diameter (cm)	4.9 <u>±</u> 2.4			
Laparoscopic transperitoneal nephrectomy Simple (n) Radical (n) Partial (n)	16 20 4			
BMI: Body Mass index				

Results

A total of 40 patients were included in the study. Twenty-six were male (65%) and 14 were female (35%). The mean age was 58.7 ± 12.3 years, the mean body mass index was 27.3 ± 4.8 kg/m2 and the mean tumor diameter was 4.9 ± 2.4 cm. Sixteen patients had right-sided (40%), and 24 had left-sided disease (Table 1).

Low, moderate and high total R.E.N.A.L nephrometry scores were recorded in eight, seven and nine patients, respectively. The mean operative time was 207.9 ± 79.1 , 218.9 ± 57.5 and 175.0 ± 75.0 minutes for simple nephrectomy, radical nephrectomy and partial nephrectomy, respectively. After mobilization of the patients on postoperative day 1, we removed the urethral Foley catheter. The mean length of hospital stay was 5.0 ± 2.8 , 3.7 ± 0.9 and 3.7 ± 2.0 days and the mean duration of drain use stays was 3.0 ± 1.3 , 2.7 ± 0.6 and 2.7 ± 1.5 days for laparoscopic simple nephrectomy (LSN), laparoscopic radical nephrectomy (LRN) and laparoskopik parsiyel nefrektomi (LPN), respectively (Table 2).

Sixteen patients underwent LSN for nonfunctioning kidney, 20 underwent LRN, and 4 patients underwent LPN for kidney tumor. Conversion to open surgery was needed in four patients (10%) due to intraabdominal adhesions or bleeding (due to significant vascular injury (n=1), splenic laceration (n=1), and in remaining two patients, due to significant intraperitoneal adhesions. Intraoperatively, 1 patient with renal artery injury

Table 2. Perioperative and postoperative findings of patients who were treated with laparoscopic transperitoneal renal surgery					
	LSN (n=16)	LRN (n=20)	LPN (n=4)		
Operation time (min), (mean ± standard deviation)	207.9±79.1	218.9±57.5	175.0±75.0		
Hospital stay (days) (mean \pm standard deviation)	5.0±2.8	3.7±0.9	3.7±2.0		
Mean drainage (days), (mean \pm standard deviation)	3.0±1.3	2.7 <u>±</u> 0.6	2.7±1.5		
Mean hemoglobine level (g/dL), (mean \pm standard deviation) Preoperative Postoperative	14.4±1.7 13.2±1.8	13.7±1.3 12.3±1.2	14.1±0.7 12.5±0.5		
Mean creatine level (mg/dL), (mean ± standard deviation) Preoperative Postoperative	1.0±0.2 1.0±0.3	0.8±0.2 1.0±0.2	0.7±0.2 0.8±0.1		
Mean ASA1 score (mean \pm standard deviation)	2.0±0.2	2.4±0.6	2.5±1.0		
Mean R.E.N.A.L nephrometry score (mean ± standard deviation)	-	8.8±1.9	4.5 <u>+</u> 0.5		
Total intraoperative complications (n) Renal arterial injury (n) Splenic injury (n)		2 1 1			
Conversion to open surgery (n) Due to adhesions (n) Due to visceral injury (n) Due to vessel injury (n)	2 2 - -	2 - 1 1	- - - -		
Postoperative complications (n) Duodenal perforation (n)	1				
LSN: Laparoscopic simple nephrectomy, LRN: Laparoscopic radical nephrectomy, LPN: Laparoscopic p	partial nephrectomy, ASA1;	American Society of And	esthesiologists ¹ , min: Minimum		

Table3.Pathologicalresultsofthelaparoscopictransperitonealrenalsurgeries							
	LSN (n=16)	LRN (n=20)	LPN (n=4)				
Benign (n)	16	-	1				
Oncocytoma (n)	-	3	1				
RCC ¹							
Clear cell (n)	-	9	2				
Papillary (n)	-	2	-				
Chromophobe (n)	-	5	-				
Carcinosarcoma (n)	-	1	-				
RCC1: Renal cell carcinoma, LSN: Laparoscopic simple nephrectomy, LRN: Laparoscopic radical nephrectomy, LRN: Laparoscopic nartial nephrectomy							

received 5 units and 1 patient with splenic injury received 2 units of blood.

In a patient who underwent right LSN due to nonfunctioning kidney with stone formation, duodenal perforation occurred in the postoperative second day which was successfully repaired (2.5%). Histopathological evaluation revealed benign lesions in 4 patients (16.6%) and malignant lesions in 20 (83.3%) (Table 3).

Discussion

The laparoscopic approach for the treatment of T1 renal tumors has been accepted as the standard surgical method by the development of laparoscopic devices in addition to the laparoscopic experience. LN has been shown to have advantages such as faster recovery, fewer painkillers, early mobilization, shorter hospital stay and early oral feeding compared to open surgery (5,6). Shorter mean time to normal activity (3.6 versus 8.1 weeks) and shorter mean time to full recovery (8.2 versus 29.3 weeks) have been reported for LN compared to open nephrectomy with similar oncological outcomes (7,8,9,10).

All patients underwent a standard transperitoneal laparoscopic approach in our clinic with the advantages of larger working space, presence of prominent anatomical landmarks, and better maneuverability due to the distance between ports. Retroperitoneal laparoscopy provides shorter hospital stay and lower complication rates. It can easily be applied in patients who had previous abdominal surgery with similar oncological outcomes, and it has also the advantage of early renal hilar control (11). However, working in a small space is the main limiting factor (12). The surgeon's experience and preference is the most critical factor in choosing a transperitoneal or retroperitoneal approach. Because of our increasing experience in transperitoneal laparoscopy, we routinely use the transperitoneal approach in our clinic.

In 2010, Demir et al. (13) reported their first experiences of laparoscopic approach on 32 patients with the mean operative

time of 181 and 179 min for LRN and LSN, respectively. In their study including 482 LN procedures (344 via transperitoneal approach and 138 via retroperitoneal approach) performed in 14 centers, Rassweiler et al. (14) found that the mean operative time for transperitoneal approach was 178 min. The longest operative time for laparoscopic radical nephrectomy was given as 300 minutes in the literature (15,16,17). The mean operative time in our study was consistent with the literature (200.6 min).

Four patients required conversion to open surgery due to severe intraperitoneal adhesions, vascular injury and splenic laceration (10%). However, all the open conversions occurred in the initial stage of laparoscopic surgery. The rate of conversion to open surgery has been reported to be between 14% and 4% in the literature (18,19,20). In our study, perirenal adhesions and duodenal perforation were mostly observed in LSN patients. Akkoc et al. (21) reported two vascular injuries (7.1%) in twenty eight LSN patients. In addition to the surgeon's experience, the higher the total R.E.N.A.L nephrometry score, the higher the likelihood of vascular complications. Considering that the number of patients with moderate and high R.E.N.A.L nephrometry score was 16, it could be assumed that these patients were quite complicated cases. The rate of vascular injury complication associated with laparoscopic surgery has been reported to be 0.03%-2.7% (22,23,24). Nevertheless, in the present study, the rate of significant vascular damage was 2.5%, which was consistent with the literature.

Study Limitations

Initial experience and postoperative outcomes of patients who underwent laparoscopic transperitoneal simple, radical or partial nephrectomy were reported in this study. However, this study has some limitations including

- 1) Small sample size,
- 2) Lack of long-term follow-up,
- 3) The study was not designed as randomized controlled study.

Conclusion

With the advances in technology and surgical experience, LN has become the preferred method even for advanced renal tumors. Serious complications may occur mainly in the early stages of the learning curve, but complication rates and operative time significantly decrease by the surgeons' experience. Complicated and more extensive tumors make surgeons more experienced in advanced laparoscopic treatment techniques

Ethics

Ethics Committee Approval: Institutional Board Approval was obtained from Clinical Research and Ethics Committee of Zonguldak Bülent Ecevit University (33479383/37).

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

Peer-review: Internally peer-reviewed.

Authorship Contributions

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

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Can Neutrophil Count, Lymhocyte Count and Neutrophil-tolymphocyte Ratio Predict Fever Following Percutaneous Nephrolithotomy in Patients Without Risk Factors?

Risk Faktörü Olmayan Hastalarda, Perkütan Nefrolitotomi Sonrası Ateşi Öngermede, Nötrofil, Lenfosit Sayısı ve Nötrofil-Ienfosit Oranı Etkin Midir?

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

Preoperative blood parameters could be good indicator to define patients without risk factors for post-percutaneous nephrolithotomy fever.

Abstract

Objective: To examine the relationship of neutrophil counts, lymphocyte count and neutrophil-to-lymphocyte ratio (NLR) with postoperative fever in patients undergoing percutaneous nephrolithotomy (PCNL).

Materials and Methods: A total of 519 patients aged over 18 years, who underwent PCNL between January 2005 and January 2013 and had a preoperative white blood cell count between 4000-12,000/µL, were included in this study. Conditions that could lead to postoperative fever or impact blood parameters constituted the exclusion criteria. At the postoperative period, the patients were divided into two groups based on the presence of fever. Age, gender, Body Mass index, stone size, number of percutaneous access, duration of operation, preoperative white blood cell count, neutrophils, lymphocytes, and NLR were compared. The relationship of these parameters with fever was evaluated with univariate and multivariate analyses.

Results: The group with fever included 50 patients and the group without fever, 469 patients. The difference between the two groups was statistically significant in terms of neutrophil and lymphocyte counts, and NLR. Univariate analysis revealed that preoperative thrombocyte count, lymphocyte count, neutrophil count, and NLR were the parameterss significantly related with fever, yet, in multivariate analysis, the only statistically significant parameters related with post-PCNL fever were age, thrombocyte count, and white blood cell count.

Conclusion: When risk factors for fever are excluded, lymphocyte count and NLR appear to be easy-to-use and affordable diagnostic markers to predict postoperative fever in patients undergoing PCNL.

Keywords: Bacteremia, Fever, PCNL, Neutrophil-lymphocyte ratio

Öz

Amaç: Perkütan nefrolitotomi (PNL) yapılan hastalarda lenfosit sayısı ve nötrofil lenfosit oranı (NLO) ile post operatif ateş arasındaki ilişkiyi değerlendirmek.

Gereç ve Yöntem: Ocak 2005 - Ocak 2013 tarihleri arasında PNL yapılan 519 hasta çalışmaya alındı. Çalışmaya; 18 yaş ve üzeri, preoperatiferatif beyaz küre sayısı 4000-12,000 10³/µL arasında olan hastalar alındı. Postoperatif dönemde ateş yapabilecek ya da kan parametrelerini etkileyecek durumlar çalışma dışı bırakıldı. Postoperatif dönemde hastalar ateşi 38,5 °C üzeri olan ve ateşi olmayan olarak iki gruba ayrıldı.

Bulgular: Ateş olan grupta 50 hasta, ateş olmayan grupta 469 hasta vardı. Gruplar arasında yaş, cinsiyet, Beden Kitle indeksi, giriş sayısı, taş boyutu, beyaz küre ve trombosit sayısı bakımından istatistiksel olarak anlamlı farklılık yoktu. Ancak nötrofil sayısı, lenfosit sayısı ve NLO değerleri arasında

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her iki grup arasındaki fark istatistiksel olarak anlamlı bulundu. Univaryant analizde preopeatif trombosit, lenfosit, nötrofil sayısı ve NLO anlamlıyken multivaryant analizde yaş, trombosit ve beyaz küre sayısı anlamlı çıkmıştır.

Sonuç: PNL yapılan hastalarda ateş oluşturabilecek risk faktörleri dışladığında lenfosit sayısı ve NLO postoperatif ateşi öngörmede kullanılabilecek kolay ve ucuz bir tanı aracı olarak gözükmektedir.

Anahtar Kelimeler: Bakteriyemi, Ateş, PNL, Nötrofil-lenfosit oranı

Introduction

Percutaneous nephrolithotomy (PCNL) is a minimally-invasive method commonly used to remove kidney stones. The frequency of postoperative fever has been reported at a rate of 16.7% to 35% even in patients undergoing appropriate prophylactic antibiotic therapy and having a sterile urine culture (1,2,3). Urinary extravasation and bacteremia are the most likely causes of fever after PCNL (1). Although it is very important to isolate the causative microorganism for the diagnosis of bacterial infection in the postoperative period, it is not always possible and urinary and blood cultures may return negative. On the other hand, the techniques performed to elucidate the etiology of fever are time-consuming and may also generate pseudo-negative results due to many factors, antibiotics used for prophylactic purposes being in the first place (4,5). This leads to a prolonged hospital stay and an increased cost of patient care. Despite their limited use in early diagnosis of bacterial infections, C-reactive protein, white blood cell count and neutrophil count are the most commonly used parameters (6,7,8). More superior parameters include procalcitonin, proadrenomedullin, IL-6, and IL-8 (9). However, the fact that they are not available in all centers and impose higher costs limits their use. Recently, neutrophil-to-lymphocyte ratio (NLR) seems to be an effective biomarker as a simple and useful parameter for early diagnosis of bacterial infections (10,11). These tests, however, are used for early diagnosis of bacterial infection after emergence of fever. No single parameter has been proposed yet to predict postoperative fever even after the exclusion of preoperative factors that may cause fever.

In the present study, we aimed to investigate whether neutrophil count, lymphocyte count, and NLR obtained from routine preoperative blood tests can be used in predicting fever following PCNL in patients with no risk factors for infection.

Materials and Methods

The local ethical committee approved the study. Written and verbal consent was obtained from all patients before the operation. Data of 1.039 patients, who underwent PCNL between January 2005 and January 2013 and had complete patient records, were retrospectively evaluated. The study included patients of both genders aged over 18 with a preoperative white blood

cell count between 4000 and 12,000/ μ L. The exclusion criteria included preoperative urinary system obstruction, proliferation in preoperative and/or postoperative urine culture, preoperative and/or postoperative blood transfusions, preoperative urinary diversion and/or intervention, presence of postoperative residual stone, presence of malignancy, and presence of hematologic diseases. Patients who had postoperative complication Clavien grade II and above were excluded from the study. The cohort was composed of patients who had only Clavien grade I complication. A total of 519 patients were included.

Ceftriaxone and ciprofloxacin were used for prophylaxis in the preoperative period while the patients were on the operating table. Conventional PCNL technique was employed. In the lithotomy position, a 6 Fr ureteral catheter was placed first, and then prone position was given. Under X-ray fluoroscopy percutaneous access was made with an 18 G needle after retrograde pyelography via ureteral catheter. Once the guide wire was sent to the pelvicalyceal system, the tract was dilated up to 30 Fr and an access sheath was placed. The stone was visualized with a 26 Fr nephroscope, broken into pieces by pneumatic and ultrasonic lithotripters, and collected with forceps. At the end of operation, a 20 Fr nephrostomy tube was placed in all cases. The postoperative nephrostomy tube was removed in 2-4 days after hematuria resolved. All operations were performed by three experienced surgeons who had completed their individual learning curve. Routine analgesic regimen-deksketoprofen trometamol IV/p.o.- twice a day was ordered for all patients until the nephrostomy tube was removed. Postoperative observation of a body temperature of 38.5 °C in three consecutive measurements in the ear at hourly intervals was accepted as fever. Body temperature measurement was used because it was the only available method during the study period. The patients were divided into two groups as those with and without fever. Age, gender, body mass index, stone size, number of percutaneous access, duration of operation, postoperative counts of white blood cells, neutrophils, lymphocytes, and thrombocytes were all recorded and NLR was calculated.

Statistical Analysis

The Kolmogorov-Smirnov test was used to test the normality of the study data. Categorical variables in both groups were compared using the chi-square test. The Mann-Whitney U test was used to compare non-parametric variables. A p value of less than 0.05 was considered statistically significant. To predict postoperative fever, a receiver operating characteristic (ROC) analysis was performed for the variables that were significantly different between the two groups. Sensitivity, specificity, area under curve, confidence interval, positive predictive value (PPV) and negative predictive value (NPV), as well as Youden index (J index) values were calculated. To define potential preoperative factors associated with post-PCNL fever, univariate and multivariate analyses with logistic regression were performed.

Results

The group with fever included 50 patients (33 males and 17 females), while the one without fever included 469 patients (296 males and 173 females). The median age in the group with fever was 44 years (24-80), while it was 46 (18-83) years in the group without fever. The age, gender, Body Mass index, number of percutaneous access, stone size, duration of operation, preoperative counts of white blood cells, neutrophils, lymphocytes, and thrombocytes, and NLR values are summarized in Table 1.

	Fever (+) n=50	Fever (-) n=469	р
Age (years)	44 (24-80)	46 (18-83)	0.994 [∞]
Sex (n)	-	-	-
Male/female	33/17	296/173	0.679*
Body Mass index (kg/m ²)	24.7	27.5	0.134 [∞]
(min-max)	(21-37)	(17.4-49.6)	-
#of Access (n)	1	1	0.866*
(min-max)	(1-3)	(1-6)	-
Stone size (mm ²)	220	250	0.376 [∞]
(min-max)	(100-1600)	(100-1200)	-
Operative time (min)	70	90	0.387 [∞]
(min-max)	(15-220)	(10-572)	-
White blood cell count	7720	6810	0.062 [∞]
(min-max)	(1770-11980)	(4200-11710)	-
Neutrophil count	5280	3930	<0.001 [∞]
(min-max)	(1610-9110)	(1100-10100)	-
Lymphocyte count	1657	2500	<0.001 [∞]
(min-max)	(520-2450)	(100-6820)	-
Thrombocyte count	252	262	0.074 [∞]
(10³/µL) (min-max)	(53-416)	(111-522)	-
NLR	3.295	2.050	<0.001 [∞]
(min-max)	(1.46-12.85)	(0.35-32.4)	-

There was no significant difference between the two groups in terms of age, gender, Body Mass index, number of percutaneous access, stone size, and preoperative white blood cell and thrombocyte counts. However, the difference between the two groups was significant in terms of neutrophil count, lymphocyte count, and NLR values. Sensitivity, specificity, area under curve, cut-off value, 95% confidence interval, PPV, NPV, and J index value were calculated for neutrophil count, lymphocyte count, and NLR values with the help of ROC analysis. NLR had a sensitivity of 86%, specificity of 55.2%, area under curve of 0.733, PPV of 16%, NPV of 97%, J index of 0.4122; neutrophil count had a sensitivity of 60%, specificity of 71%, area under curve of 0.670, PPV of 18%, NPV of 94%, and J index of 0.3186; and lymphocyte count had a sensitivity of 88%, specificity of 58%, area under curve of 0.725, PPV of 18%, NPV of 97%, and J index of 0.4621 (Table 2, Table 3). ROC curves calculated for neutrophil count, lymphocyte count, and NLR values are provided in Figure 1. Univariate analysis revealed that age (p=0.006), preoperative neutrophil count (p<0.001), lymphocyte count (p<0.001), NLR (p=0.038) and thrombocyte count (p=0.05) were significant factors affecting post-PCNL fever. The significant parameters in multivariate analysis, on the other hand, were age (p=0.025), thrombocyte count (p=0.011) and white blood cell count (p=0.045), which were not significant in univariate analysis (Table 4).

Ceftriaxone was used in 498 patients and ciprofloxacin was used in 21 patients. Fever was observed in 48 (9.6%) patients given ceftriaxone for prophylaxis and 2 (9.5%) (patients given ciprofloxacin. There was no difference between fever rates of two types of prophylactic antibiotics (p=0.671).

Discussion

Various regimens of antibiotic prophylaxis are implemented to prevent upper urinary system infections and urosepsis (12,13,14). There is a general tendency to apply a short-term antibiotic course, which typically lasts 48 hours after PCNL (15). However, as we showed in our previous study, application of a single-dose preoperative antibiotic is sufficient in patients with a clean preoperative urine culture and no risk factor for upper urinary system infection (16).

Today, there is no diagnostic test to predict post-PCNL fever preoperatively. Different prophylactic and therapeutic protocols may be employed if this possibly-bacteriologic complication is foreseeable, thus the cost of unnecessary antibiotics and overtreatment of patients can be prevented. Previous studies have shown that inflammatory processes increase neutrophil count and reduce lymphocyte count, while NLR is a simple and useful parameter to detect systemic inflammation (17). Goodman et al. (18) demonstrated NLR, rather than lymphocyte

index of receiver operating characteristic analysis								
	Cut-off value	Sensitivity (%)	Specificity (%)	Area under curve (%95 Cl)	± SE	PPV (%)	NPV (%)	J index
NLR	>2.21	86	55.2	0.733 (0.693 -0.770)	0.0290	16	97	0.4122
Neutrophil (10 ³ /µL)	>5	60	71.8	0.670 (0.628-0.710)	0.0421	18	94	0.3186
Lymphocyte (10 ³ /µL)	≤2.17	88	58.2	0.725 (0.685-0.763)	0.0262	18	97	0.4621
SE: Standard error, CI: Confidence interval, PPV: Positive predictive value, NPV: Negative predictive value, NLR: Neutrophil-to-lymphocyte ratio, J Index: Youden index								

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Table 3. Cross table of neutrophil counts, lymphocyte counts, and neutrophil-lymphocyte ratio

		Fever (+) n (%)	Fever (-) n (%)	Total n
Neutrophil count (103/µL)	>5	30 (60%)	133 (28%)	163
	<5	20 (40%)	336 (72%)	356
Lymphocyte count (10³/µL)	<2.17	44 (88%)	196 (41%)	240
	>2.17	6 (12%)	273 (59%)	279
Neutrophile-	>2.21	43 (86%)	210 (44%)	253
lymphocyte ratio	<2.21	7 (14%)	259 (56%)	266
Total (n)	-	50	469	-



Figure 1. Receiver operating characteristic curves of neutrophil, lymphocyte, neutrophil-to-lymphocyte ratio

NLR: Neutrophil-to-lymphocyte ratio

count, to be a more specific parameter for appendicitis. It has also been shown that lymphocytopenia and NLR predict bacteremia to a better extent than common infectious disease parameters in emergency care units (10). Another study found eosinophil count and NLR to be prognostic factors in bacteremia (11). NLR has been found to predict community-acquired pneumoniaassociated mortality better than neutrophil, white blood cell, and lymphocyte count as well as CRP (19). De Jager et al. (10) reported a sensitivity, specificity, PPV, and NPV of 72%, 63%, 67.6%, and 73.4%, respectively, for NLR. They found an area under curve of 0.73 for lymphocyte and NLR.

According to our results, we detected that lymphocyte count and NLR were more sensitive in predicting post-PCNL fever for patients without fever. In addition, we found that lymphocyte count was the most sensitive parameter with respect to J index. We found cut-off levels of $\leq 2170/\mu$ L and > 2.21 for lymphocyte count and NLR, respectively. These cut-off levels may show variability depending on the patient population, and type and severity of inflammation. The reason for lower PPV in this study may be the high number of patients who were included in the fever (-) group. Presence of more patients in the fever (-) group makes NPV more important. According to the results of our study, 97% of patients without postoperative fever can be estimated by considering NLR and lymphocyte count. We think that postoperative fever and bacteremia can be prevented by various antibiotic prophylaxis strategies and therapeutic

		Univariate 95% Cl*	Post-PCNL Fever		Multivariate 95% Cl	
				Odds ratio		p
	Odds ratio					
Sex	0.881	0.477-1.629	0.687	-	-	-
Neutrophil count	1.432	1.207-1.699	<0.001	-	-	-
Lypmhocyte count	0.408	0.201-0.608	<0001	-	-	-
NLR	1.061	0.996-1.131	0.038	-	-	-
Stone size	1	0.998-1.001	0.749	-	-	-
BMI	0.948	0.868-1.036	0.239		-	-
Thrombocyte count	0.996	0.992-1.000	0.050	0.992	0.987-0.998	0.011
White blood cell count	1.142	0.963-1.355	0.126	1.262	1.005-1.584	0.045
Age in years	1.031	1.009-1.054	0.006	1.035	1.004-1.067	0.025

Table A. Haller State and multiplication second with former often noventenceus nonhvalithete

regimens in patient groups considered at risk (NLR \geq 2.21, lymphocyte count \leq 2170) based on NLR and lymphocyte count.

Lymphocyte count, neutrophil count, NLR and platelet count are statistically significant preoperative factors affecting post PNCL fever in univariate analysis. In multivariate analysis, this is only valid for age, platelet count and white blood cell count. Upon a look into the literature, Tang et al. (20) emphasized that NLR ratio was an independent factor in predicting post-PCNL Systemic Inflammatory Response syndrome. Similar to our study, Cetinkaya et al. (21) indicated that NLR was important in predicting post-PCNL fever in univariate analysis, but not in multivariate analysis. Sen et al. (22) demonstrated that the NLR after post-PCNL septicemia was an independent factor in multivariate analysis with a threshold value which is close to the one in our study (>2.5). We think that the reason as to why the NLR value in our study was not significant in the multivariate analysis was the varying number of patients in the two groups (469 vs 50).

In addition to its retrospective nature, other weaknesses of this study may be listed as follows: having a small number of patients with fever, absence of stone analysis and culture data, lack of risk analysis for patients' comorbidities, and the fact that NLR was a significant factor in univariate analysis but not in multivariate analysis. Also, the fact that two different antibiotics were used for prophylaxis is another limiting factor in this study. Many studies showed that sepsis rates are not different for ceftriaxone and ciprofloxacin (16). Moreover, fluoroquinolones are not recommended anymore due to potential side effects in the current Urological Infection Guideline by the European Urology Association (23). In this study, ceftriaxone was used for prophylaxis mostly. Ciprofloxacin was used in a small group of patients and fever rates were not different between two antibiotics. Due to the retrospective nature of this study patients given ciprofloxacin as prophylaxis were included in this study. We have not used fluoroquinolones for prophylaxis before PCNL since 2012.

Conclusion

Post-PCNL fever is encountered at a considerable rate despite all prophylactic measures. A simple and affordable diagnostic modality to predict it would prevent unnecessary antibiotic use and decrease treatment costs. In addition, appropriate prophylaxis would prevent postoperative fever. Hence, we think that preoperative neutrophil and lymphocyte counts, as well as NLR are diagnostic tools to predict postoperative fever when risk factors for fever are excluded. Further prospective, randomized studies are needed on this subject.

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Prested In: This study was presented as e-poster at the 3rd International Meeting Challenges in Endourology and Functional Urology 2013 in Paris.

Ethics

Ethics Committee Approval: The local ethical committee approved the study. Abdullah Demirtaş, Numan Baydilli (protocol no.: 2013/198).

Informed Consent: Written and verbal consent was obtained from all patients before the operation.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: A.D., Design: A.D., Data Collection or Processing: N.B., G.S., Ş.T.T., T.D., Analysis or Interpretation: A.D., N.B., T.D., Literature Search: A.D., N.B., Ş.T.T., Writing: A.D., N.B., Ş.T.T.

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

Financial Disclosure: The authors declare that they have no

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Comparison of Hounsfield Unit and Intraoperative "GATA Scale" Score to Determine Requirement of DJ Stent Insertion in Ureteral Stone Treatment

Üreter Taşı Tedavisinde DJ Stent Yerleştirme Gerekliliğini Belirlemek İçin Hounsfield Ünitesi ve İntraoperatif "GATA Skala" Puanının Karşılaştırılması

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

This work contrary to what is known show that there is a relationship between hounsfield unit and stone size, New scale sets the criteria for DJ stent placement.

Abstract

Objective: In this study, we aimed to determine the contribution of hounsfield unit (HU) measurement with non-contrast-enhanced computed tomography to the treatment of a single ureteral stone, and compare the value of HU and intraoperative "GATA scale" score in deciding for DJ stent placement in patients with a single ureteral stone.

Materials and Methods: Ninety patients diagnosed with a single ureteral stone in our clinic between January 2018 and September 2018 were evaluated prospectively. We planned a new scale called "GATA scale" with three benchmarks. The validity and reliability of HU were compared with those of GATA scale score. Statistical significance was defined as p<0.05.

Results: The mean stone volume at diagnosis was $245.29\pm23.9 \text{ mm}^3$. The mean HU of ureteral stones was 1065.21 ± 33.5 . The mean total score according to GATA scale was 6.44 ± 0.2 . To determine the threshold value for factors affecting stent placement after lithotripsy, receiver operating characteristic analysis was performed for stone volume, laser duration, total energy to complete laser lithotripsy and GATA scale score and showed that the optimal thresholds were 164.01 mm^3 , 4.25 mins, 1004 W and 7.5, respectively.

Conclusion: In clinical practice, GATA scale can be used in decision making for DJ stents placement. Stent placement following lithotripsy is recommended especially in patients with a stone volume of greater than 160 mm³ or total energy to complete laser lithotripsy over 1000 W or laser duration longer than 4 minutes or GATA scale score higher than 7.

Keywords: Ureteral stone, Hounsfield unit, Laser lithotripsy

Öz

Amaç: Bu çalışmada, kontrastsız bilgisayarlı tomografi ile hounsfield ünitesi (HÜ) ölçümünün üreter taşı tedavisine katkısını belirlemeyi ve DJ yerleştirilmesi gereksinimini belirlemek için HÜ ve intraoperatif "GATA skala" puanlarının karşılaştırılmasını amaçladık.

Gereç ve Yöntem: Ocak 2018 ve Eylül 2018 tarihleri arasında kliniğimizde tek bir üreter taşı tanısı konan 90 hasta prospektif olarak değerlendirildi. Üç kriter ile "GATA ölçeği" adı verilen yeni bir ölçek planladık. HÜ'nün geçerliliği ve güvenilirliği için GATA skala skoru ile karşılaştırıldı. İstatistiksel anlamlılık p<0,05 olarak tanımlandı.

Bulgular: Üreteral taşı olan hastalarda tanıda ortalama taş hacmi 245,29±23,9 mm³ idi. Üreter taşlarının ortalama HÜ değeri 1065,21±33,5 idi. GATA ölçeğine göre ortalama toplam puan 6,44±0,2 idi. Litotripsi sonrası stent yerleşimini etkileyen faktörlerin eşik değerlerini belirlemek için taş hacmi,

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lazer süresi, tamamlanan lazer litotripsinin toplam enerjisi ve GATA skala skoru için alıcı işletim karakteristiği analizi yapıldı ve optimal eşik sırasıyla 164,01 mm³, 4,25 dakika, 1004 W ve 7,5 saptandı.

Sonuç: Klinik pratikte, GATA skalası, DJ stentlerin yerleştirme kararında kullanılabilir. Özellikle taşın hacmi 160 mm³'ün üzerinde veya toplam enerji 1000 W'nun üzerinde veya lazer süresi 4 dakikadan fazla veya GATA skalası 7'den fazla ise, litotripsiden sonra stent yerleştirilmesi önerilir. Anahtar Kelimeler: Üreteral taş, Hounsfield ünitesi, Lazer litotripsi

Introduction

Urinary system stones have an important place in urology practice. The prevalence of urolithiasis in economically developed countries has been reported to range between 4% and 20% (1). Large stones may cause obstruction and small ones may produce severe flank or lower abdominal pain. Location of pain varies with the location of the stone. Standard evaluation includes a detailed medical history and physical examination. In the evaluation of acute flank pain, non-contrast-enhanced computed tomography (NCCT), which can determine stone density and plays a role in deciding the modality of treatment is the gold standard (2,3). However, risks associated with radiation due to computed tomography (CT) scanning causes anxiety in everyone. Thus, low-dose and ultra-low-dose protocols are preferred. However, it should be noted that the diagnostic accuracy decreases as the dose decreases (4). Accuracy of hounsfield units (HU) may be queried considering all the above concerns.

In this study, we aimed to determine the contribution of HU measurement to choosing the correct treatment option for a single ureteral stone, and to demonstrate the accuracy or fallibility. Also, we planned to investigate the right alternatives that can be used instead of HU and contribute to clinical practice.

Materials and Methods

Patient Population

A total of 90 patients, 77 males and 13 females, who underwent holmium laser lithotripsy (LL) using semirigid ureteroscope for the treatment of single ureteral stone in our clinic between January 2018 and September 2018 were prospectively reviewed.

Inclusion and Exclusion Criteria

Patients aged 18 years and older having a single ureteral stone were enrolled in the study. Patients, who were found to have missing data during data recording, evaluation or analysis, were excluded from the study. Patients under the age of 18, patients with surgical failure and patients who received combined therapy (LL and pneumatic lithotripsy) were not included in the study.

Study Design

The study was designed as a prospective study and was conducted according to the principles of the Declaration of Helsinki. No additional test or assessment other than the evaluations performed for the diagnosis of ureteral stone in routine urology practice was done (physical examination, radiography and NCCT).

Age, gender, presence and location of pain, presence of additional disease, history of previous shock-wave lithotripsy or surgery for urolithiasis, smoking habit, stone location, stone volume, opacity of stone, degree of hydronephrosis, presence of ureteral stenosis or ureteral orifice stenosis and presence or absence of ureteral stent placement were recorded.

All patients were evaluated with NCCT preoperatively. Stone protocol NCCT was performed using a 64 detector row helical CT scanner at 120 kV, 240 mA, with 1.25 mm collimation. Stone location was recorded for each patient. Stone location was classified as proximal ureteral, mid ureteral and intramural ureteral. Stone volume was calculated by measuring the three dimensions of the stone in millimeters and then using the formula: length x width x height x π x 1/6 (5,6). HU calculations were performed for each stone in 3 different areas on CT images and the mean value was taken.

Surgical Procedure

Ureteroscopy (URS) with holmium LL (URS-LL) was performed by four urologists (minimum 5 years of experience in the field). We used semirigid ureteroscope 27000 L/K or 27001 L/K (diameter proximal and distal, 7/6.5 and 8/7 Fr, respectively) models of Storz (Germany) and Holmium-YAG laser by the Sphinx 80 Litho (Power Suite 80 W, Katlenburg-Lindau, Germany) for lithotripsy. Excitation/emission wavelengths of the laser fiber were 230/365 µm with an output energy of 0.5/4.5 J and a pulse repetition rate of 4/30 Hz. In URS, the calculi were targeted; dusting was preferred as the main option or the stones were fragmented into pieces as small as possible and stones >4 mm were removed with a basket catheter. Smaller fragments were expected to pass spontaneously. The efficacy of lithotripsy was evaluated by ultrasound and abdominal X-ray one day later.

A New "GATA" Scale

To compare HU to intraoperative findings; stone hardness, intraoperative laser duration and the total energy to complete

LL were intraoperatively recorded. We designed a guestionnaire for the surgeons to fill immediately after each URS. Then, all the patients were divided into three groups according to results for the balanced distribution of the patients in all groups. There were 29, 30 and 31 patients in group 1, 2 and 3, respectively (according to stone hardness, intraoperative laser duration and the total energy to complete LL). Three main subjects were scored from 1 to 3 in the questionnaire. Stone hardness was scored from 1 to 3 (soft, medium-hard and hard). Laser duration that is defined as the time between beginning and end of lithotripsy was calculated and scored from 1 to 3 (0-3.99 min, 4-7.99 min and >8 min). The total energy to complete LL for each stone was calculated by multiplying pulse energy (J) by frequency (Hz) and scored from 1 to 3 (0-999 W, 1000-2499 W and >2500 W). Total score of the scale was between 3 and 9 point. HU and GATA scale score were compared statistically to find the accuracy of HU.

Statistical Analysis

Statistical analyses were performed using SPSS Statistics 22.0 software (SPSS Inc., Chicago, IL, USA) and Microsoft Excel computer programs. The normality hypothesis was tested using the Kolmogorov-Smirnov test during data analysis. Descriptive statistics for continuous variables were presented as mean and standard deviation. Pearson's correlation coefficient and Spearman's correlation coefficient were used for correlation analyses of the parameters. Also, multinomial logistic regression was evaluated to determine the significance of the risk/effect parameters. Receiver operating characteristic (ROC) curve was applied to determine the cut-off value for significant parameters. Statistical significance was defined as p<0.05.

Results

The mean age of the patients was 45.8 ± 1.52 years (range, 21-75 years). Regarding primary presenting complaints, flank pain was present in 95.55% (86/90). Left flank pain was observed in 51.11% of cases. 24.44% (22/90) of patients had a history of surgical procedure for urinary calculi, and 72.72% (16/22) underwent lithotripsy. 30% (27/90) of patients had a history of shock-wave lithotripsy. Additional disease was found in 28.88% (26/90) of patients. Diabetes Mellitus, hypertension and coronary artery disease were detected in 4, 12 and 4 patients, respectively. 6 of 26 patients had a combination of these diseases. 22.22% (20/90) of patients was smoker or tobacco user.

The location of the stone was proximal ureter, mid ureter and intramural ureter in 37.77% (34/90), 41.11% (37/90) and 21.11 (19/90) of patients, respectively. The mean stone volume at diagnosis in patients with ureteral calculi was 245.29 ± 23.9 mm³. Hydronephrosis was found in 91.11% (82/90) of patients

with ureteral calculi and the degree of hydronephrosis was grade 1 in 26.82%, 2 in 39.02%, 3 in 32.92% and grade 4 in 1.21% of patients. The mean HU was 1065.21 ± 33.5 (Table 1). 74.44% (67/90) of patients had opaque, 21.11% (19/90) had semi-opaque and 4.44% (4/90) had non-opaque stones.

The mean GATA scale score was 6.44 ± 0.2 . 17.77% (16/90) of patients had soft, 27.77% (25/90) had medium-hard and 54.44% (49/90) had hard stones. The mean laser duration was 8.18 ± 0.89 min. The mean total energy to complete LL was $3258.18\pm630W$ (Table 1).

Stent placement after URS-LL was performed in 66.66% (60/90). In 30 patients, stent placement was not required. The GATA scale score was statistically significantly higher in patients who required DJ stent placement (p<0.0001). All patients were successfully treated.

There was a statistically significant positive correlation between HU and total GATA scale score. The Spearman's correlation coefficient was 0.49 for this result. There was a statistically significant positive correlation between stone size and HU (p<0.05). Also, there was a statistically significant positive correlation between opacity of stones and HU or GATA scale score (p<0.05). There was no statistically significant correlation between the size of ureteral stenosis or ureteral orifice stenosis and HU or GATA scale score.

To determine the threshold value for factors affecting stent placement after lithotripsy, ROC analysis performed for stone volume, laser duration, total energy to complete LL and GATA scale score showed that the optimal threshold values were 164.01 mm³ (sensitivity: 60%; specificity: 70%), 4.25 mins (sensitivity: 68%; specificity: 73%) 1004 W (sensitivity: 80%; specificity: 60%) and 7.5 (sensitivity: 45%; specificity: 90%), respectively. (AUC_{stone volume}=0.70, AUC_{laser duration}= 0.73, AUC_{laser} =0.75 and AUC_{GATA scale score}=0.71) (Table 2 and 3) (Figure 1).

Discussion

Especially in Western countries, urinary stones are one of the most common urological diseases (7). Diagnosis of ureteral stones is rapid using low-dose CT (8). The EAU 2018 urolithiasis

Table 1. Evaluation of descriptive characteristics in patients with ureteral stone were managed by URS-LL					
Variable	Mean <u>+</u> standart deviation (n=90)				
Age (years)	45.8 <u>+</u> 1.52				
Volume of stone (mm ³)	245.29 <u>+</u> 23.9				
Hounsfiel unit (HU)	1065.21 <u>+</u> 33.5				
Laser duration (min)	8.18±0.89				
Laser energy (W)	3258.18±630				
GATA scale score	6.44±0.2				

	A	Standard	A	Asymptotic 95% confidence interval	
	Area	error ^a	Asymptotic sig. ^o	Lower bound	Upper bound
Stone volume	0.707	0.057	0.001	0.595	0.819
Laser duration	0.733	0.054	0.000	0.626	0.839
Laser energy	0.754	0.055	0.000	0.646	0.861
GATA scale score	0.718	0.057	0.001	0.607	0.830
^{a:} Under the non-parametric assumption ^{b:} Null hypothesis, true area=0.5					

Table 2. Area under the curve of stone volume, laser duration, laser energy and GATA scale score. Evulation of success in these parameters to predict of stent placement

Table 3. Receiver operating characteristic curve of stone volume, laser duration, laser energy and GATA scale score and sensitivity and specificity ratios of threshold values

Variable	Cut-off value	Sensivity	Specificity	LR+	LR-
Stone volume	164.01 mm3	60	70	2	0.57
Laser duration	4.25 mins	68.3	73.3	2.55	0.44
Laser energy	1004 W	80	60	2	0.33
GATA scale score	7.5	45	90	4.5	0.61
LR: Likelihood ratio					



Figure 1. Diagonal segments are produced by ties

ROC: Receiver operating characteristic

guideline strongly recommends evaluation of HU on NCCT for ureteral stones (9). HU can be used for diagnosis and selection of the treatment options. However, these methods do not predict the composition of stones with high accuracy.

HU, HU density or HU_{diff} can be used for assessment of ureteral stones (10). These parameters have been evaluated in the literature and their success has been proven in many studies with different results. Baran et al. (11) and Deshmukh and et al. (12) reported that kidneys in patients with calculi have a comparatively high renal cortex and papillae densities than in normal population. However, when the articles were examined in detail, there was no statistically significant difference between

some poles of the kidney. These findings support some concerns such as heterogeneity of the measuring area or variability of HU values. In the literature, there are a lot of studies for estimating stone composition with HU values. In some studies, it was reported that HU on NCCT could differentiate just calcium from non-calcium stones (13,14,15). Patel et al. (16) found that HU measurement of urinary stones on NCCT may be used for differentiation of various calcium stone subtypes. However, Stewart et al. (17) reported that for calcium stones, the ability of HU on NCCT to predict stone composition was limited. For brushite stones, HU and HU density can help predict stone composition (18). In another study, Motley et al. (19) reported that neither HU density nor mean HU value was able to identify urinary stones in vivo and to evaluate radiodensities of ureteral stones; HU density was better than HU value. These results show that the HU value changes due to differences in stone composition. However, HU measurements are affected by the heterogeneity of the stone as well as the metabolic structure of the stone. In our study, 49% correlation which was found in our cohort contributes to the debate on the reliability of this method. Deciding by HU value when evaluating treatment options leads to a wrong decision in approximately 50% of cases.

HU can be used in choosing among treatment options (SWL, URS-LL or percutaneous antegrade removal) for ureteral stones. Ouzaid et al. (20) reported that HU was a prognostic factor for success of extracorporeal shockwave lithotripsy (SWL) and 970 HU represented the most sensitive (100%) and specific (81%) point on the ROC curve. Thus, urinary stones with a mean stone density of >1000 HU is deemed to be resistant to SWL (21). El-Assmy et al. (22) found that a stone attenuation of \leq 600 HU was

a significant independent predictor of SWL success in children. However, HU does not seem to be a predictive parameter for stone expulsion (23). In our cohort, the mean HU value was 1065.21. In our study, there was no correlation between HU value and GATA scale score in patients with a high HU value. Therefore, HU evaluation led us to perform URS-LL in some patients instead of SWL and SWL instead of URS-LL in some patients, which resulted in treatment failure. Also SWL is not a cost-effective treatment option (24). For this reason, a wrong treatment choice leads to a high cost.

In the treatment, rigid or flexible ureterorenoscopes can be used (25). URS-LL has high stone-free rates in all locations of the urinary tract and with all stone types and sizes (26). In URS-LL, fragmentation may be more advantageous than dusting for complete initial stone clearance (27). In our cases, URS-LL was usually performed for fragmentation and the success rate was 100% for ureteral stones. However, dusting method may be preferred especially for stones in the upper urinary tract. However, we did not need it because we routinely used stone cone in our cases.

Routine stenting is not necessary before URS or after uncomplicated URS (complete stone removal). In addition to stone removal, minimal damage to the ureter, such as edema, by using laser energy or URS during operation can lead to severe pain in the postoperative period. Therefore, stone removal is not the only criterion for stenting. However, intraoperative criteria for stent placement are not objective. A scoring based on laser energy, duration of the procedure or intraoperative evaluation has not been done before. Therefore, we think that cutoff values used in our study are extremely important. In addition, ureteral catheters may be routinely used for the first 24 hours after the operation in patients. Especially in cases with high energy and long operative time, removal of the ureteral catheter can be waited for up to 48 hours after the operation.

Study Limitations

The present study has several limitations. This is a single-center study with a small sample size. In our cases, we do not routinely use metabolic evaluation for ureteral stone patients after surgery and accept the fact that not all patients were operated on by a single surgeon experienced in the field of endourology. For these reasons, we believe that larger case series will be more effective in the interpretation of these findings, especially in the evaluation of GATA scale score.

Conclusion

HU is used for decision of treatment modality in patients with ureteral stones. But we found that HU had a weak correlation

with intraoperative GATA scale score. Thus, HU led to false choice in approximately half of the patients. Also GATA scale score can be use in decision making for DJ stent placement. Especially if the volume of the stone is over 160 mm³ or the total energy is over 1000 W or the laser duration is more than 4 minutes or GATA scale score more than 7, stent placement after lithotripsy is recommended.

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Ethics

Ethics Committee Approval: Institutional review board (IRB) approval was acquired from our clinic committee.

Informed Consent: Informed consent was obtained from all individual participants included in the study.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Concept: C.E., Ö.Y., Design: C.E., Data Collection or Processing: C.E., Y.E.K., S.A., S.E.Ş., Analysis or Interpretation: C.E., Ö.Y., M.C.T., Literature Search: C.E., H.H.T., Writing: C.E., Ö.Y.

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Contents of Urinary System Stones in North Marmara Region and Their Distribution by Gender

Kuzey Marmara Bölgesi'nde Üriner Sistem Taşlarının İçeriği ve Cinsiyete Göre Dağılımı

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

This article examines the stone contents in the northern Marmara Region and provides up-to-date information.

Abstract

Objective: We aimed to determine the contents of kidney stones in our country by evaluating the results of the stone analysis of patients who underwent surgery due to ureteral or kidney stones or experienced spontaneous stone expulsion.

Materials and Methods: Data of patients with urolithiasis who underwent surgery due to ureteral or kidney stones or experienced spontaneous stone expulsion in our clinic between 1999 and 2019 were retrospectively analyzed.

Results: Results of 1304 urinary system stone analyses were obtained. 869 (66.6%) patients were male and 435 (33.4%) were female. The maleto-female ratio was 1.99:1. The mean age of the patients was 43.2±15.3 years. Among 1304 urinary system stones, 734 (56.3%) had a single component, while 570 (43.7%) contained more than one substance. The most common stone type was calcium oxalate monohydrate (43%) and the second most common stone type was the composition of calcium oxalate monohydrate and calcium oxalate dihydrate (21.3%). The rate of uric acid stone was 6.8% and the rate of cystine stone was 2.1%. Any amount of calcium oxalate, uric acid and cystine were observed in 85.3%, 12.2% and 5.4% of urinary tract stones, respectively.

Conclusion: Urinary system stone disease is approximately two times more frequent in men than in women in Turkiye and the most common stone component is calcium oxalate.

Keywords: Urolithiasis, Calcium oxalate, Uric acid, Cystine

Öz

Amaç: Üreter veya böbrek taşı sebebiyle opere edilen veya spontan taş düşüren hastaların taş analiz sonuçlarını değerlendirerek ülkemizdeki böbrek taşlarının içeriğini belirlemeyi amaçladık.

Gereç ve Yöntem: Kliniğimizde 1999-2019 yılları arasında üreter veya böbrek taşları sebebiyle opere edilen veya spontan taş düşüren ürolitiazis hastalarının verileri retrospektif olarak incelendi.

Bulgular: Toplam 1304 üriner sistem taş analizi sonucu elde edildi. Hastaların 869'u (%66,6) erkek, 435'i (%33,4) kadındı. Erkek/kadın oranı 1,99:1 idi. Hastaların yaş ortalaması 43,2±15,3 idi. 1304 üriner sistem taşından 734'ü (%56,3) tek bir bileşene sahipken, 570'i (%43,7) birden fazla bileşen içermekteydi. En yaygın taş tipi kalsiyum okzalat monohidrat (%43) taşı ve ikinci en sık taş tipi ise kalsiyum okzalat monohidrat ve kalsiyum okzalat dihidrat (%21,3) bileşimiydi. Ürik asit taşı oranı %6,8 ve sistin taşı oranı %2,1 idi. Üriner sistem taşlarında herhangi bir miktarda kalsiyum okzalat, ürik asit ve sistin sırasıyla %85,3, %12,2 ve %5,4 oranında gözlendi.

Sonuç: Üriner sistem taş hastalığı Türkiye'de erkeklerde kadınlara göre yaklaşık iki kat daha sık görülmektedir ve en yaygın taş bileşeni kalsiyum oksalattır.

Anahtar Kelimeler: Ürolitiyazis, Kalsiyum okzalat, Ürik asit, Sistin



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Introduction

The incidence of urinary system stone disease has gradually increased in the United States of America, Europe, and the Far East after World War 2 (1). It has been reported that the prevalence of urinary system stone disease varied between 1% and 20% (2). In a study made in Turkiye in 1991, the prevalence of urinary system stone disease was found to be 14.8% and the prevalence of stones in males was 1.5 times higher than in females (3).

The incidence of urinary system stone disease depends on many factors such as geographical, climatic, hereditary, ethnic and nutritional characteristics. Infectious causes, anatomic anomalies, and drug use also may play a role in stone formation. Urinary system stones may be formed by many different substances. While some stones are formed by a single substance, some others may contain more than one substance. In addition to treatment, determining stone content is important for preventing recurrence (2). Spontaneously passed or surgically removed urinary system stones can be used for analysis. Different methods are used for stone analysis.

Our aim in this study was to present the content of urinary system stones commonly observed in our country by evaluating the stone analysis results of patients who were operated through open, endoscopic or laparoscopic methods or experienced stone expulsion after extracorporeal shock wave lithotripsy (ESWL) or spontaneously. Thus, the contribution can be made to form different health policies to prevent kidney stones, a severe public health problem.

Materials and Methods

After obtaining local ethics committee approval (20/05/2019-2019/243), data of urinary system stone patients who underwent open nephrolithotomy, nephropyelolithotomy, percutaneous nephrolithotomy, open or laparoscopic pyelolithotomy and ureterolithotomy, semi-rigid or flexible ureterorenoscopy and ESWL due to kidney or ureteral stone in our clinic or passed stones spontaneously between 1999 and 2019 were examined retrospectively. All female and male patients with data on stone analysis results were included in the study without age restriction. Examined parameters included demographic information and stone analysis results. First stone analyses based on the chronological order were considered for patients who had multiple operations. Patients without data on stone analysis results were excluded from the study.

Stone analyses were made using infrared spectroscopy, X-ray diffraction or polarization microscopy in different laboratories by expert chemists.

Statistical Analysis

IBM SPSS statistics for Mac version 21 (Chicago, IL, USA) was used for data analysis. While constant variables were given in mean \pm standard deviation, categorical variables were given in numbers and percentages. In the comparison of the two groups, the Mann-Whitney U test was used for numeric data and chisquare tests were used for categorical variables. A p value of less than 0.05 was considered statistically significant.

Results

Urinary system stone analysis results of a total of 1304 patients were obtained. Eight hundred and sixty-nine patients (66.6%) were male and 435 (33.4%) were female. The male-to-female ratio was 1.99:1. The age of the patients varied from 2 to 72 with an average of 43.2±15.3 years. While 734 urinary system stones out of 1304 (56.3%) had a single component, 570 (43.7%) contained more than one substance. The stones were divided into 16 subgroups based on analysis results (Figure 1). The most common stone type was calcium oxalate monohydrate (43%) followed by stones composed of calcium oxalate monohydrate and calcium oxalate dihydrate with a rate of 21.3%. The incidence of uric acid stones and cystine stones was 6.8% and 2.1%, respectively. Different amounts of calcium oxalate were observed in 85.3%, uric acid in 12.2% and cystine 5.4% of in urinary system stones. The average age of patients with cystine stone was significantly lower than others (30.9±20.8 years vs 43.9±14.6 years; p<0.01) (Figure 2). No relationship could be shown between calcium oxalate, cystine and uric acid stone content and gender (p=0.741, p=0.515 and p=0.419, respectively).



Figure 1. The distribution of stone according to ingredients



Figure 2. Stone distribution according to age

Discussion

Urinary system stone disease is a prevalent public health problem around the world although it is more commonly observed in some regions. Its prevalence has been reported to be over 10% especially in countries with high standards of living, reaching 37% in some regions with an increasing stone prevalence in the last 20 years (2). 50% of individuals with urinary system stone disease have the possibility of recurrent stone formation within five years. Thus, in addition to treating the current stone, preventing recurrent stone formation is of vital importance. Thus, the European Association of Urology guidelines recommends stone analysis in all patients who have their first stone (2).

In a study made by Muslumanoglu et al. (4), the prevalence of urinary system stone disease was found to be between 11.1% and 13.2%. Stone prevalence was reported to increase with age both in males and females and while it is 8% in individuals younger than 25 years of age, it was 26.6% in those 45-55 years of age. Based on the distribution of stone patients in different regions, the prevalence was found to be lowest in the Black Sea region with 9.5%, while it was highest in the Aegean Region with 12.6%. Stone patients in Marmara Region constituted 11.4% of all stone patients in Turkiye. In another study made with 6453 stone patients by Karabacak et al. (5) in our country, calcium oxalate stones were the most commonly detected kidney stones with a rate of 80.4%. These were followed by uric acid stones with a rate of 4.8%, cystine stones with 3.1% and phosphatecontaining (dahlite, brushite, struvite, whitlockite) stones with 3.3%. The male-to-female ratio was reported to be 2:1. Similar to the study by Karabacak et al. (5) calcium oxalate stones were

the most common stone content and the male/female ratio was 1.99:1 in our study.

When stone analysis results of individuals having symptomatic kidney stone for the first time were examined in a study made by Singh et al. (6) in the United States, it was found that the content of stones was calcium oxalate in 76%, hydroxyapatite in 18% and uric acid in 4.8% of patients. Symptomatic recurrence rate in 10 years was detected to be nearly 50% in brushite, struvite and uric acid stones and 30% in calcium oxalate and hydroxyapatite stones. These results could not be provided as we do not have data on recurrence in our current study.

In a study made by Ye et al. (7) it was shown that among 49.317 stone samples, 16.361 were formed (33.2%) by a single component, 20.370 (41.3%) by two components and 11.314 (22.9%) by three components. While the most common stone content was calcium oxalate with a rate of 65.9%, carbapatite followed this with 15.6%, urate with 12.4%, struvite with 2.7% and brushite with 1.7%. In our study, 56.3% of the stones contained a single substance.

In another study made by Safarinejad (8), it was shown that urinary system stone disease prevalence increased with age and while it was 0.9% between the ages of 15 and 29, it increased to 8.2% between the ages 60 and 69 (p=0.001). The average age of the patients was 43.2 ± 15.3 years in our study.

In a study made by Tyson et al. (9) in Ireland, it was found that 94.5% of urinary system stones contained different amounts of calcium. The rate of stones containing calcium oxalate and phosphate mixture was reported to be 73.1% and pure calcium oxalate stone rate was reported to be 2.5%. In total, any amount of uric acid was found in 9.6% of stones and struvite in 13.7%. Pure cystine was detected in 1.1% of stones, as expected. Any amount of uric acid was found in 12.2% of stones in our current study, this rate was 5.4% for cystine. High cystine stone rate can be explained by genetic background.

In a study made by Luo et al. (10) in China, it was reported that 69.4% of 732 patients who had stone analysis were male and 30.6% were female. The male-to-female ratio was 2.27:1. In this study, it was observed that 63.8% of the stones contained a single component. The most common stone type was ammonium urate with a prevalence rate of 35.6% in males and 33.4% in females. Calcium oxalate monohydrate stones were detected in 30.9% of males and 31.2% of females. When evaluated in age groups, stone formation peaked between 1 and 3 years of age for individuals under 18 years of age and between 19 and 40 for those over 18 years of age. We did not find any relationship between stone type and gender in our study. The average age of patients who had only cystine as a component was significantly lower than those without cystine.

Study Limitations

Our study has some limitations. First of all, this is a retrospective study. Lack of knowledge of the ethnical backgrounds, body mass index and urinary system stone recurrence conditions of the patients precluded more detailed analysis. Also, the fact that the study covered patients in a period of 20 years, which is a long period, may have affected the stone analysis methods and results. Stone analyses not made in a single center may have caused the differences.

Conclusion

Urinary system stones are observed nearly two times more frequently in males than in females in Turkiye. The most common stone component is calcium oxalate.

Ethics

Ethics Committee Approval: Obtaining local ethics committee approval (20/05/2019-2019/243).

Informed Consent: This study does not include any patient.

Peer-review: Internally peer-reviewed.

Authorship Contributions

Concept: E.G., K.G.Ş., Design: E.G., K.G.Ş., Supervision: E.G., Data Collection or Processing: E.G., K.G.Ş., Analysis or Interpretation: E.G., K.G.Ş., Literature Search: E.G., K.G.Ş., Writing: E.G., K.G.Ş.,

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

Financial Disclosure: The authors declare that they have no relevant financial.

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Urooncology

Predictive Value of Neutrophil-to-Lymphocyte and Platelet-to-Lymphocyte Ratio Measured Prior to Prostate Biopsy

Prostat Biyopsisi Öncesi Ölçülen Nötrofil Lenfosit ve Trombosit Lenfosit Oranının Prediktif Değeri

Hüseyin Eren

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

The effect of inflammation parameters on prostate cancer has been shown previously. This study will examine the role of blood parameters on detecting clinically significant prostate cancer. Maybe, this may prevent to do unnecessary biopsy.

Abstract

Objective: We planned to investigate the value of neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) in predicting prostate cancer (PCa).

Materials and Methods: We enrolled 302 male patients who underwent prostate biopsy between January 2013 and June 2018. We recorded anthropometric indices, demographic parameters, physical examination, laboratory values, in addition to results of radiologic imaging and pathological examination. The patients were divided into two groups as patients with benign prostatic hyperplasia (BPH) and those with PCa. We investigated the association of NLR and PLR with histopathology.

Results: The mean age of the patients was 66.2±8.2 years. Patients with prostate adenocarcinoma were older, had higher prostate-specific antigen (PSA) concentrations, neutrophil count, and had lower hemoglobin, platelet count and prostate volume (PV) compared to patients with BPH. Receiver operating characteristic analysis identified that NLR values above 2.43 indicated 1.68 fold (95% Cl: 1.06-2.66; p=0.028) higher risk for prostate adenocarcinoma. NLR correlated positively with age, and PSA, negatively with hemoglobin and platelet count. NLR and PV were the independent predictors of biopsy histopathology.

Conclusion: We demonstrated that NLR is independently associated with PCa in patients undergoing prostatic biopsy due to high PSA levels. **Keywords:** Neutrophil to lymphocyte ratio, Platelet to lymphocyte ratio, Prostate cancer, Benign prostatic hyperplasia

Öz

Amaç: Prostat biyopsisi öncesinde nötrofil lenfosit oranı (NLR) ve trombosit lenfosit oranının (PLR) prostat kanserini öngörmede değerini araştırmayı planladık.

Gereç ve Yöntem: Ocak 2013 - Haziran 2018 tarihleri arasında prostat biyopsisi yapılan 302 hasta çalışmaya alındı. Antropometrik veriler, demografik özellikler, fizik muayene bulguları, laboratuvar değerleri, radyolojik görüntüleme sonuçları ve patolojik sonuçlar kaydedildi. Hastalar patoloji sonuçlarına göre benign prostat hiperplazisi (BPH) ve prostat kanseri olarak 2 gruba ayrıldı. NLR ve PLR histopatoloji sonucuna etkisi istatistiksel olarak karşılaştırıldı.

Bulgular: Hastaların yaş ortalaması 66,2±8,2 yıl idi. Gruplar arasında yaş, nötrofil, hemoglobin, platelet, NLR, prostat-spesifik antijen (PSA) ve prostat volümü açısından anlamlı fark bulundu. Alıcı işletim karakteristiği analizinde NLR 2,43 üzerinde olan hastalarda prostat kanseri görülme olasılığının BPH'ye göre 1,68 (%95 Cl: 1,06-2,66; p=0,028) kat daha fazla olduğu izlendi. NLR ile yaş, nötrofil ve PSA arasında pozitif korelasyon, lenfosit, hemoglobin ve trombosit arasında negatif korelasyon saptandı. Çoklu analizde NLR ve PV'nin prostat kanseri için bağımsız belirteçler olduğu görüldü.

Sonuç: PSA değerinin yüksek olması nedeniyle prostat biyopsisi yapılan hastalarda NLR'nin prostat kanseri ile bağımsız bir şekilde ilişkili olduğu gösterildi.

Anahtar Kelimeler: Nötrofil lenfosit oranı, Trombosit lenfosit oranı, Prostat kanseri, Benign prostat hiperplazisi

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Introduction

Prostate cancer (PCa), 15% of all cancers, is the second most common cancer in men, with approximately 1.1 million new diagnoses worldwide in 2012 (1). Therefore, several methods, such as digital rectal examination (DRE), prostate-specific antigen (PSA) screening, PSA density, PSA velocity and doubling time, PCa antigen 3 (PCA3) and multi-parametric magnetic resonance imaging (mpMRI) are used in clinical practice for early diagnosis (2,3). PSA testing is the most commonly used screening method and a serum level above 4 ng/mL is generally accepted as an indication for prostate biopsy (4). The latest updated European Association of Urology guideline recommends the combination of 12-core biopsy and MR-guided fusion biopsy. However, today, transrectal ultrasonography (TRUS)-guided 12-core biopsy is still the standard technique used for the diagnosis of PCa (5).

Inflammation is one of the important factors in the etiology of carcinogenesis (6). In recent years, many studies demonstrated the relationship of blood biomarkers, such as neutrophil-tolymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR), with inflammation and immune response in cancer patients (7,8). Circulating neutrophils and mediators, such as vascular endothelial growth factor, tumor necrosis factor α , interleukin 1 (IL-1) and IL-6 may affect the progression of the cancer (9). Previous studies showed the relationship of NLR with overall survival, and progression-free survival (PFS) in patients with PCa (10,11,12,13,14). Some studies identified elevated PLR as a poor prognostic factor in some cancers, such as gastric, ovarian, and renal cell cancer. In their study evaluating NLR and PLR in patients with BPH and PCa, Kaynar et al. (15) reported that a statistically significant difference was found in mean PLR between the groups only when the PSA level was ≥ 10 ng/mL.

In the present study, we planned to investigate the value of NLR and PLR prior to prostate biopsy in predicting PCa.

Materials and Methods

We enrolled 447 male patients who were admitted to the urology clinic of our hospital between January 2013 and June 2018 with a PSA above 4 ng/mL and/or suspicious DRE findings that would necessitate prostate biopsy. We recorded patient information including anthropometric indices, demographic parameters, physical examination, laboratory values, in addition to results of radiologic imaging and pathological examination. Urine test was performed all patients to exclude urinary tract infection before biopsy procedure. Urine culture and antiobiogram were performed in patients with a sign of active infection. Patients who had negative culture after treatment and a PSA level above 4 ng/mL were also included. Enrolled patients underwent TRUS-guided 12-core prostate biopsy. All prostate biopsies were performed by the same urologist (Dr. H.E). Blood samples were collected via antecubital vein in the morning following an 8-hour fasting period. NLR and PLR were calculated using laboratory records.

We excluded patients with previous prostate biopsy (n=12), prostatic surgery (n=28), hematologic disorder (n=6), oncologic disease (n=13), history of radiotherapy (n=5) and chemotherapy (n=9), those using medications causing bone marrow suppression (n=2) and patients who had high-degree intraepithelial neoplasia (n=7), inflammation (n=30), prostatitis (28), and atypical small acinar proliferation in pathological examination. The remaining 302 patients, forming the study group, were further stratified as patients with BPH or PCa. Anthropometric indices, demographic characteristics, hematological values, and pathological results were compared between the groups.

The study was approved by the Recep Tayyip Erdoğan University Institutional Ethics Committee (2019/111) (Rize, Turkiye).

Statistics Analysis

Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS) 20.0 (IBM, Chicago, USA). Categorical values were displayed as percentages; continuous variables were expressed as mean ± standard deviation The Kolmogorov-Smirnov test was used to evaluate the normality of the distributions of population. Since the distribution was not normal, Mann-Whitney U test with a Bonferroni correction test was used to compare the independent variables between the groups. Spearman analysis was used for correlation. We performed receiver operating characteristic (ROC) analysis to calculate threshold value for NLR. Multivariate analysis including independent variables [Body Mass index (BMI), age, smoking, prostate volume (PV)] of the univariate test was performed in order to demonstrate the effect of NLR on pathologic results. A p value of <0.05 was considered statistically significant.

Results

The mean age of the patients was 66.2 ± 8.2 years. Anthropometric characteristics and laboratory values are presented in Table 1. Forty-three (14.2%) patients were smokers. 153 patients (50.7%) had BPH, and the remaining 149 had prostatic adenocarcinoma. The PCa grade according to the International Society of Urologic Pathologists (ISUP) classification and Gleason score of patients with prostatic adenocarcinoma were as follows: ISUP 1 (n=90) 29.8%, ISUP 2 (n=31) 10.3%, ISUP 3 (n=15) 5%, ISUP 4 (n=2) 0.7%, ISUP 5 (n=10) 3.3%; Gleason 6 (n=90) 29.8%, Gleason 7 (n=46) 15.2%, Gleason 8 (n=2) 0.7%, and Gleason 9 (n=10) 3.3%, respectively.

ROC analysis identified a threshold of 2.43 (area under the curve: 0.584; 95% Cl: 0.520-0.649, p<0.001), with the sensitivity of

61.7%, specificity of 51.6%, positive predictive value of 55%, and the negative predictive value of 58%. NLR values above 2.43 indicated 1.68 times (95% Cl=1.06-2.66; p=0.028) higher risk of prostatic adenocarcinoma (Figure 1).

Patients with prostatic adenocarcinoma were older, had higher PSA concentrations, neutrophil count, and had lower hemoglobin, platelet count and PV compared to patients with BPH (Table 2). The remaining parameters were similar between the groups.

Table 1. Anthropometric indices and laboratepatients	ory results of all
Characteristics	Mean ± SD
Waist circumference, cm, mean (SD)	28.11±4.31
WBC, mean (SD)	8.37±3.48
Neutrophil, mean (SD)	5.74±3.07
Lymphocyte, mean (SD)	1.87 <u>+</u> 0.92
Hemoglobin, mean (SD)	13.25±2.45
Platelet, mean (SD)	230.01±74.70
NLR, mean (SD)	3.99±3.65
PLR, mean (SD)	150.98±116.29
PSA ng/mL, mean (SD)	18.48±73.21
PV, mean (SD)	70.01±39.16
WPC: White blood call NIP: Neutraphil to lymphosyster ra	tio DLD: Platalat to

WBC: White blood cell, NLR: Neutrophil-to-lymphocyte ratio, PLR: Platelet-tolymphocyte ratio, PSA: Prostate-specific antigen, PV: Prostate volume, SD: Standard deviation



Figure 1. Neutrophil-to-lymphocyte ratio ROC curve of neutrophilto-lymphocyte ratio above 2.427 revealed 61.7% sensitivity and 51.6% specificity for prostatic carcinoma.

Table 2. Comparison of anthropometric indices, demographic features and blood parameters between the groups						
	BPH n=153 (50.7%)	Prostate Ca n=149 (49.3%)	р			
Age mean, (SD)	64.98±7.77	67.37 <u>±</u> 8.44	0.017			
BMI mean, (SD)	28.28±3.99	27.93 <u>+</u> 4.62	0.292			
WBC mean, (SD)	8.02±3.02	8.72 <u>+</u> 3.87	0.179			
Neutrophil mean, (SD)	5.34 <u>+</u> 2.78	6.16±3.29	0.049			
Lymphocyte mean, (SD)	1.92 <u>+</u> 0.78	1.81±1.05	0.085			
Hemoglobin mean, (SD)	13.77 <u>+</u> 2.30	12.72 <u>+</u> 2.50	0.001			
Platelet mean, (SD)	241.37±78.88	218.36±68.47	0.006			
NLR mean, (SD)	3.62±3.71	4.37±3.56	0.011			
PLR mean, (SD)	152.32±136.61	149.61±91.27	0.932			
PSA mean, (SD)	7.35±7.27	29.91±102.89	0.001			
PV mean, (SD)	73.88 <u>+</u> 39.48	66.05 <u>+</u> 38.56	0.026			
RPH: Benign prostatic hyperplasia Ca: Cancer BMI: Body Mass index WBC: White						

BPH: Benign prostatic hyperplasia, Ca: Cancer, BMI: Body Mass index, WBC: White blood cell, NLR: Neutrophil-to-lymphocyte ratio, PLR: Platelet-to-lymphocyte ratio, PSA: Prostate.specific antigen, PV: Prostate volume, SD: Standard deviation

Spearman correlation analysis demonstrated a strong correlation between NLR and PLR (r=0.602). Additionally, NLR significantly positively correlated with age and PSA and negatively with hemoglobin and platelet count (Table 3).

We performed multivariate analyses including age, smoking, BMI, NLR and PV. We identified NLR and PV as the independent predictors of PCa (Table 4).

Discussion

In the present study, we investigated the relationship between the blood parameters and prostate biopsy histopathology. We demonstrated that increased age, neutrophil count, and NLR were associated with PCa and that PCa was more likely than BPH above a certain NLR threshold. Moreover, we demonstrated that NLR and PLR were strongly related. NLR correlated positively with age and PSA, negatively with hemoglobin and platelet count. However, only NLR and PV were the independent predictors of PCa.

Elevated PSA levels and suspicious DRE are the main indications for prostate biopsy. TRUS-guided and MRI fusion biopsies are currently the most commonly used methods to detect PCa (5). Despite being specific for prostate, PSA may rise due to BPH, prostatitis and trauma thus, may lead to unnecessary biopsy (16). Serial PSA testing, including PSA density, PSA velocity, PSA doubling time, free:total PSA ratio and PCA3 is used to avoid unnecessary biopsy procedures, however, none of them alone may reliably suggest definitive diagnosis of PCa. Recent guidelines recommend additional imaging methods, such as mpMRI, which increase the cost of PCa diagnosis (5). We know that chronic inflammation and ensuing cell proliferation

Table 3. Correlations between study parameters										
	Age	Neutrophil	Lymphocyte	Hemoglobin	Platelet	PSA	PV	NLR	BMI	PLR
Age	1									
Neutrophil	-0.010	1								
Lymphocyte	-0.227**	-0.075	1							
Hemoglobin	-0.227**	-0.225**	0.300**	1						
Platelet	-0.140*	0.051	0.260**	0.236**	1					
PSA	0.183**	0.011	-0.124*	-0.149**	0.031	1				
PV	0.207**	0.037	-0.040	0.011	-0.040	0.237**	1			
NLR	0.143*	0.732**	-0.664**	-0.343**	-0.124*	0.118*	0.056	1		
BMI	-0.205**	-0.083	0.141*	0.187**	0.057	-0.151**	0.025	-0.139*	1	
PLR	0.085	0.062	-0.492**	-0.111	0.279**	0.039	0,043	0.602**	-0.074	1
PSA: Prostate specific antigen	PSA: Prostate specific antigen; PV: Prostate volume; NLR: Neutrophil-to-lymphocyte ratio; BMI: Body Mass index; PLR: Platelet-to-lymphocyte ratio, *: p<0.05 is considered statistically									

PSA: Prostate specific antigen; PV: Prostate volume; NLR: Neutrophil-to-lymphocyte ratio; BMI: Body Mass index; PLR: Platelet-to-lymphocyte ratio, *: p<0.05 is considered statistically significant, **: p<0.01

 Table 4. Logistic regression analysis to identify independent

 predictors of prostate cancer

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Independent variables	OR	95% Cl	р		
Age	1.02	0.991-1.053	0.17		
Smoking	1.01	0.506-2.017	0.97		
BMI	1.00	0.996-1.012	0.36		
NLR	1.12	1.025-1.227	0.012		
PV	0.99	0.984-0.997	0.005		
BMI: Body Mass index, NLR: Neutrophil-to-lymphocyte ratio, PV: Prostate volume					

contribute to carcinogenesis, and many cancers arise from sites of chronic inflammation (17). Since inflammation is implicated in carcinogenesis, blood biomarkers may be used in order to improve diagnosis of PCa. Recently, inexpensive biomarkers, such as NLR, and PLR, are being used in predicting malignancies (18). In a Swedish cohort, it was documented that elevated prediagnostic inflammatory markers were significantly associated with PCa, and high leukocyte count was related with increased risk of PCa in young men (19). Similarly, in a Finnish cohort, an increased PCa risk with high leukocyte count has been reported (20).

NLR is a sign of immune activity. Low lymphocyte count is associated with immunosuppression in several cancers (19). NLR is raised in patients with aggressive or high-grade tumors, which also reflects poor survival (18,21). Although Kamali et al. (22) and Khosropanah et al. (23) could not document an association between NLR and PCa, several other studies identified a positive relationship and proposed to use NLR as a biomarker for the diagnosis of PCa (2,16,24). Our study also supports this hypothesis.

Thrombocytosis is often encountered in malignant tumors with poor survival (25). The reason for that association may be evasive action of tumor cells from immune system by platelets. Platelets may also interact with tumor cells via ligands and help vascular adhesion of malignant cells (26). The relationship of PLR with PCa is not clear. A meta-analysis showed an association between PLR and overall and PFS (27). Yuksel at al. (9) and coworkers reported that a high PLR was a predictor of PC. We could not document an association between PCa and PLR in our study.

Study Limitations

The major limitation of the study was its retrospective design. Another important aspect is including only patients with BPH as the control group. Biopsy-proven prostatitis might be compared as well. However, our study includes two large groups with similar size, which is a strong aspect.

Conclusion

We demonstrated that NLR was independently associated with PCa in patients who underwent prostatic biopsy due to high PSA levels.

Ethics

Ethics Committee Approval: The study was approved by the Recep Tayyip Erdoğan University Institutional Ethics Committee (2019/111) (Rize, Turkiye).

Informed Consent: Informed consent was obtained from all patients

Peer-review: Externally peer-reviewed.

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

Financial Disclosure: The author declare that they have no relevant financial.

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Comparison of Standard Open Wound Care and Vacuum-assisted Closure Therapy in Fournier's Gangrene

Fornier Gangreni Tedavisinde Standart Açık Yara Pansumanı ve Vakum Yardımlı Kapamanın Karşılaştırılması

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

The effect of VAC in therapy of Fournier's gangrene.

Abstract |

Objective: Management of Fournier's gangrene (FG) includes large wound debridement, broad-spectrum antibiotic, wound care and re-debridement if necessary. The aim of our study was to compare standard open wound care and vacuum-assisted closure (VAC) therapy in patients with FG.

Materials and Methods: Thirty-three patients (29 males and 4 females) who underwent surgery for FG were enrolled in the present study. The data was evaluated retrospectively. The patients were divided into two groups according to wound care after large wound debridement. Standard open wound care with antibiotic pomade was performed twice a day in 14 patients and VAC therapy was performed every 48-72 hours in 17 patients. The data of the two groups were compared.

Results: Twenty-three (69.7%) patients had Diabetes Mellitus and 20 patients (60%) had poor hygiene. The re-debridement rate in patients who received standard open wound care was statistically higher than in those who underwent VAC therapy (p=0.016). There were no statistically significant differences in mortality rate, length of hospital stay and need for reconstruction between the groups. When the data were analyzed, no statistically significant difference was found in FG Severity index score, length of hospital stay and mortality rate. However, the relationship between mortality rate and location of lesion was statistically significant (p=0.03). Four patients died, 3 (75%) due to wide necrotizing fasciitis extending to the abdominal wall.

Conclusion: The present study showed that the technique used for wound care did not influence mortality, need for reconstruction and length of hospital stay. The only advantage of VAC therapy was decreased re-debridement rate in patients with FG.

Keywords: Fournier's gangrene, Wound care, Vacuum-assisted closure therapy, VAC

Öz

Amaç: Fornier gangreninin tedavisi, agresif yara debridmanı, geniş spektrumlu antibiyotik kullanımı, yara bakımı ve gerekirse tekrar debridman gerektirir. Çalışmamızın amacı Fornier gangrenli hastaların tedavisinde klasik yara bakımının ve vakum yardımlı kapama malzemelerinin karşılaştırılmasıdır.

Gereç ve Yöntem: Çalışmaya Fornier gangreni nedeniyle cerrahi yapılan otuz üç hasta (29 erkek ve 4 kadın) dahil edildi. Veriler retrospektif olarak değerlendirildi. Hataların 23 tanesi (%69,7) Diyabet hastalığı vardı ve 20 hastada (%60) kötü hijyen mevcuttu. Hastalar debridman sonrası yara bakımına göre 2 gruba ayırıldı. On dört hastaya antibiyotikli pomad ile günde 2 kez standart yara pansumanı yapıldı. On yedi hasta, 48-72 saatte bir değişen VAC tedavisi ile takip edildi. İki grubun verileri karşılaştırıldı.

Bulgular: Hastaların 23 tanesi (%69,7) Diyabet hastalığı vardı ve 20 hastada (%60) kötü hijyen mevcuttu. Klasik pansuman ile takip edilen hastalarda tekrar debridman oranları VAC ile takip edilen hastalara göre istatistiksel olarak fazlaydı (p=0,016). Mortalite oranları, hastanede yatış süreleri ve

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rekonstrüksiyon ihtiyaçlarında anlamlı farklılık saptanmadı. Veriler analiz edildiğinde FG Şiddeti indeksi skorlarında, hastanede yatış süresinde ve mortalite oranlarında istatistiksel bir fark bulunmadı. Ancak mortalite oranı ile lezyon lokalizasyonu arasındaki ilişki istatistiksel olarak anlamlıydı (p=0,03). Mortalitenin görüldüğü 4 hastanın 3'ü (%75) abdominal duvara yayılan geniş nekrotizan fasiit nedeniyle öldü.

Sonuç: Bu çalışma, yara bakımı tekniğinin mortalite, rekonstrüksiyon ihtiyacı ve hastanede yatış süresini etkilemediğini göstermiştir. VAC tedavisinin tek avantajı yeniden debridman oranındaki azalmadır.

Anahtar Kelimeler: Fornier gangreni, Yara bakımı, Vakum yardımlı kapama, VAC

Introduction

Fournier's gangrene (FG), a rare necrotizing fasciitis of the genital, perineal and perianal regions, was first described in 1764 and then named by Jean-Alfred Fournier in 1883 (1,2). It is more common in developing countries and males are affected 10-fold more commonly than females (3). FG is a urological emergency and requires immediate hospitalization. Early diagnosis is very important to decrease the rate of mortality related to the disease. Treatment of FG includes urgent large surgical debridement, broad-spectrum antibiotic therapy, wound care therapy and re-debridement if necessary. In spite of this aggressive management, mortality rate of the disease has been reported to be 7.5-45% (4).

Wound care therapy after radical surgical debridement is an important part of treatment. Different approaches, including standard open wound therapy, vacuum-assisted closure (VAC) therapy and negative pressure wound therapy (NPWT), have been used for wound care. VAC therapy and NPWT have recently become popular in the postoperative management of FG. Different approaches to open wound care, such as sterile dressing, Dakin's solution and topical honey, have been investigated. Recently, effectiveness of VAC and NPWT in postoperative treatment of FG has been evaluated (5). The aim of our study was to compare the effects of VAC and open standard wound care on wound healing after radical debridement.

Materials and Methods

A total thirty-three patients (29 males and 4 females) with FG, who underwent radical surgical debridement in the departments of general surgery, urology and plastic and reconstructive surgery in Manisa Celal Bayar University between January 2002 and May 2018, were enrolled in the present study. Data on medical history, symptoms, physical examination findings, such as size and location of the lesion, were analyzed retrospectively. The data on laboratory tests, surgical debridement and postoperative wound care were evaluated. The diagnosis of FG was based on the medical history and clinical symptoms including tenderness and/or erythema of the perianal, perineal or genital region, skin edema, fluctuation and/or crepitation of the subcutaneous tissue, gangrene or necrosis, purulent discharge and fever. Patients who had no necrotizing fasciitis

and had only limited perineal or scrotal abscess were excluded from the study. Fournier's Gangrene Severity index (FGSI) was calculated to measure the severity of FG (6). In the FGSI, 9 parameters, including temperature, heart and respiratory rates, white blood cell count, hematocrit, serum sodium, potassium, creatinine and bicarbonate levels, are scored (the degree of deviation from normal is graded from 0 to 4). The patients in the study were divided into two groups according to the management of wound care (VAC therapy and open standard wound care) after surgical debridement. Standard open wound care was performed with antibiotic pomade twice a day. VAC therapy was performed once every 48-72 hours. The data of the groups were analyzed statistically. The local ethics committee approved the study protocol.

Statistical Analysis

Statistical analysis was carried out using the Statistical Package for the Social Sciences for Windows, version 18.0 (SPSS, IL, USA). Differences in variables between the groups were analyzed using the chi-square and Mann-Whitney U tests. A p value of less than 0.05 was considered statistically significant.

Results

In the present study, the mean age of the participants was 56.21±14.02 years. Twenty three patients (69.7%) had Diabetes Mellitus (DM) and 8 (24.2%) had hypertension (HT). The mean length of hospital stay (day), FGSI score and debridement area (cm²) were 23.87±14.25, 5.09±3.20 and 119.18±103.22, respectively. Twelve patients (36.4%) underwent reconstruction surgery after debridement and wound care therapy. Four patients (12.1%) died during hospitalization. When mortality rates according to extension of lesions were evaluated, the mortality rate in patients who had necrotizing fasciitis extending to the abdominal wall was statistically significant higher (p<0.05). The mortality rates in patients with abdominal wall, perineal and scrotal and/or penile extension were 30% (3/10), 14.3% (1/7) and 0% (0/16), respectively. There was no statistically significant difference in mean age, FGSI score, debrided area and rate of DM and HT between VAC and open standard therapy groups (Table 1). Although the mortality rate, length of hospital stay and need for reconstruction were similar between the two groups, the

rate of re-debridement in VAC group was statistically lower than in open standard wound care group (p<0.5) (Table 2).

Table 1. Comparison of the mean age, Fournier's GangreneSeverity index scores, debrided areas and rates of DiabetesMellitus and hypertension in vacuum-assisted closure therapyand open standard wound care

	VAC therapy (n=17)	Open standard wound care (n=16)	р
Age (years)	59.52±12.30	52.68±14.88	0.15
FGSI score	4.70±3.05	5.50±3.40	0.42
Debrided area (cm ²)	135.11±112.49	102.25 <u>+</u> 9	0.48
DM	13/17 (76.4%)	10/16 (62.5%)	0.46
HT	3/17 (17.6%)	5/16 (31.2)	0.43
V/AC: Voouum assisted alos	ura ECSI: Equippior's Ca	narona Sovarity inday DM	·Diabatas

VAC: Vacuum-assisted closure, FGSI: Fournier's Gangrene Severity index, DM: Diabetes Mellitus, HT: Hypertension

 Table 2. Comparison of mortality rates, hospitalization times, needs for re-debridement and reconstruction in vacuum-assisted closure therapy and open standard wound care

	VAC therapy (n=17)	Open standard wound care (n=16)	р			
Mortality rate during hospitalization	1/17 (5.9%)	3/16 (18.8%)	0.35			
Hospitalization times (days)	23.11±13.13	24.68 <u>+</u> 15.74	0.78			
Re-debridement rate	4/17 (23.5%)	11/16 (68.7)	0.001*			
Reconstruction rate	8/17 (47.1%)	4/16 (33.3%)	0.17			
VAC: Vacuum-assisted closure, *Statistically significant difference (chi-square test)						

Discussion

The treatment of FG includes radical surgical debridement of necrotized tissue, broad-spectrum antibiotics and hemodynamic support with fluids (7). The other important principle in the management of FG is wound care after initial radical debridement (5,8). Open debrided wounds are generally managed with sterile dressing and povidone iodine or antibiotic. Some studies have compared various open wound approaches such as with povidone iodine, Dakin's solution and topical honey and noticed both advantages and disadvantages (9,10). Recently, NPWT and VAC therapy have become popular treatment options for wound care in FG. However, there have been a few studies about these approaches for postoperative therapy of FG in the literature. VAC therapy for the postoperative treatment of FG was first reported by Weinfeld et al. (11) in 2005. They used VAC therapy for the management of debrided wounds in three patients who had FG and reported that all patients achieved successful genital wound coverage. The results of the other two studies that investigated the outcomes of VAC therapy for postoperative management of

FG were similar to the results of the first study (12.13). Assenza et al. (12) investigated six male cases of FG who had DM and suggested that VAC was a time-saving method. The results of their study showed that VAC decreased length of hospital stay, patient discomfort and number of medications and improved significantly quality of life. Similar to this study, Cuccia et al. (13) evaluated the outcomes of VAC for postoperative wound therapy in six patients who had very extensive FG (the mean FGSI was 10.5). They reported that VAC therapy was effective in cleaning and preparing the wounds, and decreased the length of hospital stay and patient discomfort. However, the two important limitations of these two studies were small sample size and absence of control group. Our study compared VAC and open standard wound therapy, and had larger study populations than in their studies. Our results showed that the length hospital stay in patients who underwent VAC and open standard wound therapy were statistically similar.

According to the best of our knowledge, there have been two studies (14,15) that compared VAC and open standard wound therapy for postoperative management of FG. Ozturk et al. (14) compared VAC (n=5) and conventional therapy (n=5) for the management of FG following initial debridement in a small number of patients. The results of their study showed that VAC and conventional therapies were equally effective in healing the wounds and the total costs of them were statistically similar. The results also indicated that with the use of VAC, patients had less pain and dressing changes, and greater mobility. They found that hands-on treatment time was reduced for physicians using VAC. In conclusion, they suggested that VAC therapy was an economical and effective option for wound therapy after debridement. They also noticed that the patients and physicians were more satisfied with VAC therapy than with conventional wound therapy. We did not investigate physicians' satisfaction but the hands-on treatment time in VAC group was shorter than in open standard group, because VAC and open standard wound therapy were performed once every 2-3 days and twice a day, respectively. Although the length of hospital stay and need for reconstruction were statistically similar between the groups, re-debridement rate in VAC group was significantly lower than in open standard group. Czymek et al. (15) evaluated 35 patients with FG. Nineteen patients underwent VAC therapy and other 16 patients were managed with antiseptic dressing after debridement. They noticed that VAC therapy was associated with longer hospital stay and lower mortality. They stated that a partial explanation was that some patients with severe sepsis died in the first 3 days and could not undergo VAC therapy. In our study, there was no statistically significant difference in mean age, FGSI score, debrided area, and DM and HT rates between the two groups (VAC and open standard). Two groups with similar features in comorbidity and FG were compared in our study. Therefore, the outcomes of our study are more valuable than that of above mentioned studies. We found that length hospital stay, mortality rate and reconstruction rate were statistically similar between the groups. The results of our study showed that VAC and conservative open therapy in the postoperative treatment of FG had similar effectiveness but the advantage of VAC therapy was less needs for re-debridement. The limitations of the present study were small and retrospective design. So we suggest that further prospective studies comparing VAC and standard open wound therapy in larger study groups are warranted.

Conclusion

The results of our study indicated that length of hospital stay and reconstruction rate were similar between VAC and open standard wound therapy for postoperative treatment of FG. Moreover, the most important advantage of VAC therapy was decreasing re-debridement rates. Lower re-debridement rate and dressing frequency in VAC therapy might decrease hands-on treatment time and increase physician satisfaction. Therefore, we think that VAC therapy is more comfortable than open standard wound therapy for patients and physicians.

Ethics

Ethics Committee Approval: The local ethics committee approved the study (protocol no: 03.02.2020–68).

Informed Consent: Retrospective study.

Peer-review: Internally peer-reviewed.

Authorship Contributions

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Andrology

Micro-Doppler Ultrasonography-assisted Microsurgical Varicocelectomy: First Time in Turkiye

Türkiye'de İlk Kez Mikro-doppler Ultrasonografi Yardımlı Mikrocerrahi Varikoselektomi

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

According to our knowledge there is no report about intra-operative micro-Doppler ultrasound utilization during microsurgical varcicocelectomy procedure in Turkiye. This study demonstrates its first utilization, effectiveness and safety in our country.

Abstract

Objective: The magnification of the operative microscope or loop used in microsurgical varicocelectomy facilitates defining the anatomical structures. Even if the microsurgical approach is chosen, still, there is a 1% chance of iatrogenic testicular artery ligation and this may lead to the testicular atrophy. In this study, our aim was to present the efficacy and safety of the micro-Doppler ultrasound (USG) used during microsurgical varicocelectomy for the first time in Turkiye.

Materials and Methods: A total of 46 patients with clinical varicocele underwent microsurgical varicocelectomy from May 2018 to July 2019. The da Vinci surgical system (CordaMed, İstanbul) was used in 5 patients and a standard operating microscope was used in 41 patients. Once the spermatic cord was brought up during the surgery, the velocity time integral microvascular Doppler system (Deltamed, Ankara) was used to identify the testicular vessels. The micro-Doppler USG probe allowed differentiation of the vessel by hearing the arterial pulsation audio.

Results: Microsurgical varicocelectomy was performed in 46 patients and 48 spermatic cord units. The mean number of spermatic veins that were ligated in each spermatic cord unit was 3.05 (2-5) and each spermatic cord unit had mean 1.4 (1-3) spermatic arteries that were preserved. The mean follow-up duration was 9 months and none of the patients developed testicular atrophy after the procedure.

Conclusion: The use of micro-Doppler USG in micro-surgical varicocelectomy seems to be an effective and safe method that facilitates the identification of testicular vessels. With the aid of micro-Doppler USG, even very small size arteries could be easily identified and iatrogenic damage could be avoided.

Keywords: Varicocelectomy, Microsurgery, Testicular arter injury, Micro-Doppler ultrasonography

Öz∣

Amaç: Mikrocerrahi varikoselektomide kullanılan ameliyat mikroskobunun veya loop gözlüğün büyütme özelliği anatomik yapıların tanımlanmasına yardımcı olsa bile %1 oranında iyatrojenik testiküler arter bağlanması ihtimali mevcuttur ve bu durum testis kaybına kadar gidebilir. Bu çalışmada mikrocerrahi varikoselektomi ameliyatı esnasında ülkemizde ilk kez kullanılan mikro-Doppler ultrasonografi (USG) cihazının etkinliği ve güvenilirliği sunmak amaçlanmıştır.

Gereç ve Yöntem: Mayıs 2018 ile Temmuz 2019 tarihleri arasında klinik varikoseli olan toplam 46 hastaya mikrocerrahi varikoselektomi ameliyatı yapılmıştır. Beş hastada da Vinci Robotik Platform (CordaMed, İstanbul) kullanılmış, 41 hastada ise standart ameliyat mikroskobu kullanılmıştır. Ameliyat esnasında spermatik kord subinguinal insizyondan çıkarıldıktan sonra damarların tanımlanması aşamasında testiküler arter-internal spermatik ven ayrımında hız zaman integrali mikro-Doppler ultrason probu (Deltamed, Ankara) kullanılmıştır. Mikro-Doppler USG probu artere temas ettiği esnada işitsel yolla arteriyel pulsasyonun duyulması ile damar ayrımının yapılmasını mümkün kılmıştır.

Bulgular: Kırk altı hastanın 2'sinde bilateral olmak üzere toplam 48 spermatik kord ünitesine mikro-cerrahi varikoselektomi işlemi uygulanmıştır. Ameliyat esnasında kullanılan mikro-Doppler ultrason probu sayesinde testiküler arterler ve internal spermatik venler çok rahat bir şekilde tanımlanabilmiştir. Ameliyat esnasında ortalama 3,05 (2-5) spermatik ven bağlanmış ve ortalama 1,4 spermatik arter (1-3) korunmuştur. Ortalama



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takip süresi 9 ay olan hastaların %67'sinde sperm parametrelerinde düzelme izlenmiş olup hiçbir hastada ameliyattan sonra testiküler atrofi izlenmemiştir.

Sonuç: Mikro-cerrahi varikoselektomi ameliyatında mikro-Doppler ultrason probu kullanılması testiküler arter ve internal spermatik ven ayırımını kolaylaştıran etkin ve güvenli bir yöntemdir. Mikro-Doppler ultrason probu sayesinde çok küçük boyuttaki arterler bile çok kolay tanımlanabilir ve ameliyat esnasında iyatrojenik hasardan kaçınılabilir.

Anahtar Kelimeler: Varikoselektomi, Mikrocerrahi, Testiküler arter hasarı, Mikro-Doppler ultrasonografi

Introduction

Today, various techniques from open to laparoscopic surgery, from microsurgery to percutaneous embolization have been defined for the repair of a varicocele which is accepted as the most common reversible reason of male infertility. Microsurgical approach has the lowest recurrence rate and the lowest postoperative complication rate and therefore it is preferred as the most efficient technique (1). The magnification of the operative microscope or loop used in microsurgical varicocelectomy facilitates defining the anatomical structures. Even if microsurgical approach is chosen, still, there is a 1% chance of iatrogenic testicular artery ligation and this may lead to the testicular atrophy (2). Therefore, identification of the veins and arteries that are dissected and ligated during a varicocelectomy is very important.

The use of micro-Doppler ultrasonography (USG) in varicocelectomy surgery has been firstly identified in 2010 (3). It has been shown that more internal spermatic arteries were preserved and more spermatic veins were ligated when the micro-Doppler USG was used (3). According to the 2017 Public Hospitals Statistics Report, in only public hospitals, 37,000 varicocelectomy surgeries were performed in 2017 in our country (4). Despite this high number, to our knowledge, there have been no reports of the use of micro-Doppler USG in varicocelectomy surgery in our country. In this study, our aim was to present the efficacy and safety of the micro-Doppler USG used during microsurgical varicocelectomy for the first time in Turkiye.

Materials and Methods

The hospital ethical committe approval was obtained and the informed consent was signed by each patient before the surgery. A total of 46 patients with clinical varicocele underwent microsurgical varicocelectomy using a velocity time integral micro-Doppler USG probe (Deltamed, Ankara) from May 2018 to July 2019. The da Vinci surgical system (CordaMed, İstanbul) was used in 5 patients and a standard operating microscope was used in 41 patients.

The standard microsurgical varicocelectomy surgery principles were obeyed during the surgeries. An approximately 1-2 cm

subinguinal incision was made and the spermatic cord was exposed and extracted to the surface through the incision. Then, depending on the joint decision of both the surgeon and the patient, the robotic platform or the surgical microscope was brought in and the microsurgical stage of the operation began. In this phase, initially the cremaster muscle was cut by cautery parallel to longitudinal axis of the spermatic cord. Then, with blunt and sharp dissections the vascular structures of the spermatic cord were identified. At this point, each vascular structure was examined several times by using the micro-Doppler USG probe and the artery-vein distinction was confirmed (Figure 1). The micro-Doppler USG probe allowed differentiating the vessel by hearing the arterial pulsation. All dilated veins were cut and ligated and the surgery was completed following the standard techniques.

Results

Microsurgical varicocelectomy was performed in 46 patients and 48 spermatic cord units. Indications for the surgery were: oligospermia in 29 patients, pain in 9 patients, pain and oligospermia in 6 patients, and azoospermia in 2 patients. The mean age of the patients was 27 years (18-47) and the mean duration of surgery was 38 (30-50) minutes. The testicular arteries and the internal spermatic veins were very easily identified with the assistance of the micro-Doppler USG probe



Figure 1. Use of intra-operative micro-Doppler ultrasonography

used during the surgery. The mean number of spermatic veins that were ligated in each spermatic cord unit was 3.05 (2-5) and each spermatic cord unit had mean 1.4 (1-3) spermatic arteries that were preserved. The mean follow-up duration was 9 months and none of the patients developed testicular atrophy after the procedure.

Discussion

The European Association of Urology Infertility Guidelines recommends varicocelectomy in men with a clinical varicocele, oligozoospermia and otherwise unexplained infertility in the couple (5). It was shown in a meta-analysis that assessed randomized controlled trials comparing the current varicocelectomy techniques, patients operated via the microsurgical approach have higher pregnancy rates, lower recurrence rates and less postoperative hydrocele complications (1). The magnification of the operating microscope or loop used in microsurgical varicocelectomy clearly facilitates identifying the anatomical structures, however, it does not eliminate the iatrogenic testicular artery injury risk completely. In a retrospective study evaluating 2102 patients operated via microsurgical approach by using a surgical microscope providing magnification of 25x, it was shown that accidental ligation of the testicular artery occurred in 0.9% of the patients and testicular atrophy developed in 5% of these patients with ligation of the testicular artery (2).

There may be many causes of the accidental artery ligation during microsurgery varicocelectomy (2). For example, smaller testicular arteries may not allow perceiving the arterial pulsation. In another theory, aggressive manipulations may cause arterial spasm and makes it difficult to identify the artery during dissection of the vessels. Another potential explanation is that the arteries may be present behind the complex branches of the veins or very close to them. Due to all of these potential risks, arteries may be accidentally ligated and testicular loss may occur.

In addition to the magnification of the operating microscope for the identification of the vessels in the spermatic cord during varicocelectomy procedure, urologists have been directed to other methods as well. In this context, Cocuzza et al. (3) first evaluated the value of systematic use of intraoperative Doppler USG during microsurgical subinguinal varicocele repair in 2010. In this study, 225 spermatic cord units that underwent microsurgical varicocelectomy by using micro-Doppler USG and 152 spermatic cord units that underwent microsurgical varicocelectomy without micro-Doppler USG were compared and it was shown that more veins were ligated (8.0 vs 7.3), more arteries were preserved (1.6 vs 1.3) and fewer arterial injuries were seen (0 vs 2) in the micro-Doppler USG group. In a randomized controlled trial evaluating the use of intraoperative Doppler USG, surgical outcomes of 85 patients who underwent Doppler USG-assisted microscopic subinguinal varicocelectomy and and 87 patients without Doppler USG were compared. It was observed that the intraoperative Doppler USG group had shorter operative time (42 min vs 53 min), greater number of protected arteries (1.9 vs 1.3) and greater number of spermatic veins ligated (7.8 vs 7.0) (6). Varicocelectomy is a very common surgery in our country. According to the statistical report made by the General Directorate of Public Hospitals in 2017, only in public hospitals, 2499 bilateral and 11957 unilateral varicocelectomy procedures were performed in Turkiye. (4). Considering the fact that private and university hospitals were not included in this report, the actual number of procedures would be way beyond these numbers. Considering the number of microsurgical varicocelectomies reaching tens of thousands a year and the probability of spermatic artery damage in 1% and resulting testicular atrophy in 5% of them, it may be estimated that tens of patients would suffer from complications leading to testicular loss due to a such simple operation as varicocelectomy. Therefore, as surgeons, it is our responsibility to take precautions in order to minimize the odds of these complications.

The use of intraoperative Doppler USG for the subinguinal microsurgical varicocelectomy procedure increases our knowledge about the anatomy of the spermatic cord. In a mapping study including 24 patients who underwent subinguinal varicocelectomy by using intraoperative Doppler USG, it was found that the mean number of ligated spermatic veins was 4.7 for each spermatic unit and 44.1% of these veins were found in the upper-medial quadrant of the spermatic cord (7). Similar to our study, the mean number of spermatic arteries was 1.33 for each spermatic cord in this study.

Conclusion

The use of operative microscope or surgical loops does not seem enough to protect accidental testicular arterial injury. The use of micro-Doppler USG in micro-surgical varicocelectomy seems to be an effective and safe method that facilitates identification of testicular vessels. With the assistance of micro-Doppler USG, even very small size arteries can be easily identified and iatrogenic damage can be avoided.

Ethics

Ethics Committee Approval: The hospital ethical committe approval was obtained.

Informed Consent: the informed consent was signed by each patient before the surgery.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: A.G., A.E., Design: A.G., A.E., Data Collection or Processing: A.G., G.K., Analysis or Interpretation: A.G., M.A., Literature Search: A.G., A.E., Writing: A.G., M.A., A.E.

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Effects of Chronic Renal Failure on Surgical Outcomes of Laparoscopic Nephrectomy for Benign Diseases? A Comparative Study

Kronik Böbrek Yetmezliğinin Benign Hastalıklar Sebebiyle Yapılan Laparoskopik Nefrektomide Cerrahi Sonuçlar Üzerine Etkisi Var mı? Karşılaştırmalı Bir Çalışma

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

It is known that chronic renal failure (CRF) patients come up with metabolic disturbances such as metabolic acidosis, increased risk of bleeding and a higher infection rate. However, data regarding outcome of laparoscopic nephrectomy in patients with CRF is scarce. Results of our study indicated that patients with chronic kidney disease can be counselled that surgical outcomes are comparable to patients with normal kidney function in laparoscopic nephrectomy.

Abstract

Objective: The aim of this study was to compare surgical outcomes of laparoscopic nephrectomy (LN) for benign diseases in patients with chronic renal failure (CRF) undergoing hemodialysis with their non-CRF counterparts.

Materials and Methods: A retrospective chart review of patients who underwent LN between 2008 and 2019 was conducted. Patients with CRF requiring hemodialysis were defined as group 1 whereas those with normal renal function prior to surgery were defined as group 2. Operative and postoperative parameters, such as complications, American Anesthesiologists Association scores, perioperative bleeding, length of stay and Hb drop, as well as demographic data, were reviewed.

Results: There were 22 patients in group 1 (13 females and 9 males) and 43 patients in group 2 (27 females and 16 males). There was no statistically significant difference between the groups with regards to mean intra operative bleeding (62.7 ± 62.3 mL vs 55.9 ± 54.7 mL, p=0.652) and Hb drop (0.9 ± 0.8 g/dL vs 1.1 ± 1.0 g/dL, p=0.475). The mean length of hospital stay was 3.8 ± 1.0 days in group 1 whereas it was 3.4 ± 1.3 days in group 2 (p=0.263). No conversion to open surgery was needed in the cohort. Complications were observed in 2 patients in group 1, both of which were blood transfusions and 3 patients in group 2 which were surgical site infection treated with iv antibiotics, delayed return of bowel movements and atelectasis that fully recovered after respiratory physiotherapy.

Conclusion: Surgical outcomes in LN for benign urological problems in patients with CRF are comparable to those in patients with normal kidney function.

Keywords: Laparoscopic, Nephrectomy, Complications, Chronic renal failure, Outcome

Öz

Amaç: Bu çalışmanın amacı kronik böbrek yetmezliği (KBY) nedeniyle hemodiyalize (HD) giren hastalarda benign sebeplerle yapılan laparoskopik nefrektomi (LN) sonuçlarını normal böbrek fonksiyonuna sahip hastalarla karşılaştırmaktır.

Gereç ve Yöntem: Kliniğimizde 2008 ile 2019 yılları arasında benign sebeplerle LN yapılmış olgular retrospektif olarak değerlendirilmiştir. KBY nedeniyle HD'ye giren hastalar grup 1, normal böbrek fonksiyonuna sahip hastalar grup 2 olarak adlandırılmıştır. Gruplar arası cerrahi ve cerrahi dışı parametreler (Amerikan Anestezistler Derneği skoru, perioperatif kanama, hastane yatış süresi, hemoglobin düşüşü ve demografik bilgiler) karşılaştırılmıştır.

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Bulgular: Grup 1'de 22 hasta mevcut (13 kadın, 9 erkek) iken grup 2'de 43 hasta (27 kadın, 16 erkek) vardı. İki grup arasında perioperatif kanama (62,7±62,3 mL vs. 55,9±54,7 mL, p=0,652) ve hemoglobin düşüşü (0,9±0,8 g/dL vs. 1,1±1,0 g/dL, p=0,475) açısından fark saptanmadı. Grup 1 için ortalama hastanede yatış süresi 3,8±1,0 gün iken grup 2'de 3,4±1,3 gün olarak bulundu (p=0,263). Çalışmaya dahil edilen hiç bir hastada açık cerrahiye geçiş olmadı. Grup 1'de 2 hastada komplikasyon (kan transfüzyonu) gözlenirken grup 2'de 3 hastada komplikasyon izlendi (iv antibiyotik ile tedavi edilen yara yeri enfeksiyonu, uzamış barsak hareketi geri dönüşü, fizyoterapi ile gerileyen atelektazi).

Sonuç: Benign sebeplerle yapılan LN açısından HD bağımlı KBY'li hastalar ile normal böbrek fonksiyonuna sahip hastalar arasında cerrahi sonuçlar açısından fark yoktur.

Anahtar Kelimeler: Laparoskopik, Nefrektomi, Komplikasyon, Kronik böbrek yetmezliği, Sonuç

Introduction

Laparoscopic nephrectomy (LN) is a globally accepted method for patients requiring nephrectomy for benign diseases. Advantages of laparoscopic surgery for benign diseases have been well defined in the literature (1). A subgroup of patients who undergo LN is chronic renal failure (CRF) patients. These patients undergo nephrectomy due to several causes (vesicoureteric reflux, urolithiasis, urinary tract infections, etc.), generally prior to renal transplantation in order to optimize graft survival. It is known that CRF patients come up with metabolic disturbances such as metabolic acidosis, increased risk of bleeding and a higher surgical site infection rate (2). However, data regarding outcomes of LN in patients with CRF is scarce (3).

The aim of this study was to compare surgical outcomes of LN in patients with CRF (undergoing hemodialysis) with those who have normal renal function, thus, evaluate if CRF would alter surgical outcomes.

Materials and Methods

After obtaining local ethics board approval (date: 29.04.2019, no.: 72300690-799), a retrospective chart review of patients, who underwent LN between 2008 and 2019, was conducted. Patients with incomplete data were excluded. Patients with CRF were defined as group 1, whereas their counterparts who have normal renal function (normal serum creatinine level) prior to surgery were defined as group 2. Group 2 consisted of consecutive patients who underwent LN for benign diseases. All patients in group 1 were under hemodialysis. Indications for nephrectomy and pre-operative serum creatinine levels were noted. Of note, the main reason for nephrectomy in group 1 was preparation for renal transplantation. Demographic data of the patients were retracted. Operative and postoperative notes such as American Anesthesiologists Association (ASA) scores, perioperative bleeding, length of hospital stay and hemoglobin (Hb) drop were also reviewed. Complications were assessed as per the Clavien-Dindo classification system (4).

A single surgeon (EÖ) performed the surgeries. All patients in group 1 received hemodialysis one day before the surgery. Operative technique of transperitoneal nephrectomy, in brief, was as follows; the patients were placed in a lateral decubitus position at 90 degrees to the operating table under general anesthesia. After mobilization of the colon, the ureter was found and control of the hilum was obtained. Specimens were extracted by extending the incision at the level of the more caudal port. In cases where bilateral nephrectomy was required, one additional port was used for the contralateral side.

Statistical Analysis

For statistical analysis, all numeric values were tested for normal distribution. Data are shown as mean \pm standard deviation for those with normal distribution while median (range minimum and maximum) were used for those that does not. Non-parametric values were tested using the Wilcoxon signed-rank test, and parametric values were tested using the Student's t-test. Chi-square and Fischer's exact tests were executed for nominal variables. GraphPad software was used and a p value of <0.05 was considered statistically significant.

Results

Our cohort comprised a total of 65 patients out of 71. There were 22 patients in group 1 (13 females and 9 males) and 43 patients in group 2 (27 females and 16 males). There were no statistically significant differences in terms of gender ratio and age between the two groups. The mean pre-operative creatinine level in group 1 was 3.4 ± 0.9 mg/dL and 0.7 ± 0.07 md/dL in group 2 (p<0.0001). The mean Body Mass index (BMI) value in patients with CRF and those with normally functioning kidneys was 21.4 ± 3.8 and 25.6 ± 5.8 , respectively (p=0.003). Median ASA score was 2 in group 1 (range 2-3) and 1 in group 2 (range 1-3). A total of 28 nephrectomies were performed in group 1 (left side in 10, right side in 6, and bilateral in 6 patients), while 24 patients underwent left nephrectomy and 19 patients underwent right nephrectomy in group 2 (Table 1).

In patients with CRF, indication for LN was non-functioning kidney due to urolithiasis (source of recurrent infection) in 13 patients and vesicoureteral reflux in 9. On the other hand, 26 patients underwent nephrectomy because of non-functioning kidney due to urinary stone disease, 9 patients due to unilateral reflux nephropathy, 6 patients due to ureteropelvic junction obstruction, 1 patient due to vascular thrombosis as well as another one for obstructing megaureter in group 2.

surgery between the groups (107.2+35.8 min vs 111.0+41.3 min, p=0.715). Also, there was no statistically significant difference between the groups with regards to mean intra operative bleeding (62.7±62.3 mL vs 55.9±54.7 mL, p=0.652) and Hb drop $(0.9\pm0.8 \text{ g/dL vs } 1.1\pm1.0 \text{ g/dL}, p=0.475)$. The mean length of hospital stay was 3.8±1.0 days in group 1 and 3.4±1.3 days in group 2 (p=0.263). No conversion to open surgery was required in the cohort (Table 2).

Complications were observed in 2 patients in group 1 both of which were blood transfusions (grade 2). Of note, one of those patients underwent bilateral nephrectomy and the other has previously undergone percutaneous nephrolithotomy on the ipsilateral side. Further, complications were observed in 3 patients in group 2. One patient faced with surgical site infection treated with iv antibiotics (grade 2), one patient had delayed return of bowel movements (grade 1) and another one had atelectasis that fully recovered after respiratory physiotherapy (grade 1). Of these patients in group 2, the first patient had a previous open surgery for a ipsilateral kidney stone, the second one had total abdominal hysterectomy and bilateral salpingo-oopherectomy

Table 1. Overview of the patients							
	Group 1	Group 2	р				
Number of patients (n)	22	43	-				
Gender (Female/male)	9/13	27/16	-				
Laterality (Left/right/bilateral)	10/6/6	24/19/0	-				
Age (years)	34.2 <u>+</u> 17.1	38.6 <u>+</u> 16.6	0.329				
Mean Body Mass index (kg/m²)	21.4 <u>+</u> 3.8	25.6±5.8	0.003				
Median ASA score (range)	2 (2-3)	1 (1-3)	-				
Mean pre-operative serum creatinine (mg/dL)	3.48±0.94	0.77±0.07	>0.0001				
Nephrectomy indications Urolithiasis Vesioureteric reflux Ureteropelvic junction obstruction Vascular thrombosis Obstructive megaureter	13 9	26 9 6 1 1					
ASA: American Society of Anesthesiolog	ASA: American Society of Anesthesiologists						

Table 2. Operative outcome of the patients						
	Group 1	Group 2	р			
Duration of surgery (mins)	107.27±35.85	111.07±41.37	0.715			
Perioperative blood loss (mL)	62.7 <u>+</u> 62.3	55.9 <u>+</u> 55.7	0.652			
Hb drop (mg/dL)	0.98±0.89	1.17±1.06	0.475			
Length of hospital stay (days)	3.8±1.0	3.4 <u>+</u> 1.3	0.263			
Hb: Hemoglobin						

Ölçücüoğlu et al. Effects of Chronic Renal Failure on L/S Nephrectomy

Table	2	Detiente			line Alex
lable	J.	Patients	with	comp	licatio

Table 3. Patients with complications			
	Complication	Clavien grade	
Group 1 #1 #2	Blood transfusion Blood transfusion	Grade 2 Grade 2	
Group 2 #1 #2 #3	Surgical site infection treated with Ab Delayed return of bowel movements Atelectasis recovered after physiotherapy	Grade 2 Grade 1 Grade 1	
Ab: Antibiotics			

Discussion

LN has been an alternative to open nephrectomy since it was first introduced back in 1991 (5). Throughout the years, there have been major advancements in the technique, technology and indications. Currently, laparoscopy is the standard of care in patients with renal cell carcinoma when oncological outcomes would not be jeopardized (6). Also, many studies to date confirmed that LN is a viable alternative for benign diseases (1,7).

LN in patients with CRF, on the other hand, poses another challenge for urologists. Reduced platelet function, serum electrolyte abnormalities, anemia, hypertension, and vascular and cardiac problems are only a few problems that surgeons encounter when dealing with CRF patients especially when they are on dialysis (8,9).

A study by Sanli et al. (3) indicated that comparable surgical outcomes could be achieved in patients undergoing hemodialysis. Similarly, our results indicate no significant difference in complication rates between the groups. In addition, duration of surgery, Hb drop and length of stay was not statistically different from their counterparts with normal kidney function.

It should be remembered that nephrectomy for benign diseases are not always easy and several complications might be observed even if the patients have normally functioning kidneys (10). In a large group of CRF patients, Shoma et al. (11) evaluated results of native nephrectomy prior to renal transplantation that is very similar to group 1 in our series, and showed that only 4% of the cases required conversion to open surgery. Also, they have experienced 4 major complications i.e. pneumothorax, hematoma, colonic injury and bleeding. Additionally, it has been shown that learning curve had an impact on conversion to open surgery in LN in CRF patients (3). However, in our cohort, none of the patients required conversion.

Our comparative analysis also indicated that a lower BMI value may be observed in patients with CRF, which might be a consequence of their metabolic status. Interestingly, 5 of 6 patients with complications in the whole cohort have had prior abdominal or ipsilateral urinary tract surgery. Although it is hard to establish firm conclusions, previous abdominal/urinary tract surgery seems to complicate LN, based on our results.

Limitations of our study include retrospective nature and relatively low patient number while comparative analysis of CRF patients and patients who have normal renal function is an important aspect of this study.

Conclusion

CRF does not increase operative or post-operative complication rates. Patients with CRF can be counselled that surgical outcomes are comparable to those in patients with normal kidney function in LN even though there is no standardized recommendation or guidelines to use laparoscopy for nephrectomy in benign urological problems.

Ethics

Ethics Committee Approval: The study were approved by the Ankara City Hospital of Local Ethics Committee (date: 29.04.2019, no.: 72300690-799).

Informed Consent: Retrospective study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: M.İ.D., E.Ö., A.M.B., Design: M.İ.D., A.M.B., Data Collection or Processing: M.İ.D., E.Ö., A.M.B., Analysis or Interpretation: M.İ.D., Literature Search: M.İ.D., Writing: M.İ.D.

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

Financial Disclosure: The authors declare that they have no relevant financial.

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Evaluation of Surgical Outcomes in Different Hypospadias Types by HOSE Score

Farklı Hipospadias Tiplerinde Cerrahi Sonuçların HOSE Skoru ile Değerlendirilmesi

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

Hypospadias objective scoring evaluation score is an objective and reliable scoring system that can be used to evaluate the results of hypospadias surgery.

Abstract I

Objective: We aimed to present outcomes of hypospadias surgery with the help of the Hypospadias objective scoring evaluation (HOSE) system and to demonstrate the reliability of the HOSE.

Materials and Methods: Data of patients, who were operated for hypospadias in our clinic between January 2017 and March 2019, were retrospectively analyzed. The parameters included demographic data, location of the meatus preoperative, postoperative complications, follow-up period, recurrence and postoperative HOSE score.

Results: A total of 46 patients were included in the study. The mean age of the patients was 8.5 ± 5.4 years. Fifteen patients had distal hypospadias, 13- subcoronal, 9- penile, 6- proximal and 3 had glanular hypospadias. Tubularized incised plate urethroplasty was performed in 35 patients, Bracka 2- stage repair in 6 patients and meatal advancement and glanduloplasty in 3 and, the onlay flap technique was used in 2 patients. The mean postoperative HOSE score was 14.6±1.7. The lowest HOSE score was found in patients with proximal hypospadias and the highest HOSE score was in those with glanular hypospadias (12.6 versus 15.6) (p=0.26). When HOSE scores of the patients were evaluated by a different physician, the mean HOSE score was found to be 14.5±1.7. There was no significant intraobserver variation (Kappa score: 0.698), (p<0.0001).

Conclusion: HOSE is an objective and reliable scoring system that can be used to evaluate the outcomes of hypospadias surgery. **Keywords:** Hypospadias, HOSE, Penile reconstruction

Öz 🛛

Amaç: Hipospadias cerrahisi sonuçlarını Hypospadias objective scoring system (HOSE) skorlama sistemi yardımıyla sunmayı ve HOSE skorlamasının güvenilirliğini ortaya koymayı amaçladık.

Gereç ve Yöntem: Kliniğimizde Ocak 2017 - Mart 2019 yılları arasında hipospadias nedeni ile opere edilen hastaların verileri retrospektif olarak incelendi. İncelenen parametreler hastaların demografik verileri, hipospadias lokalizasyonu, peroperatif ve postoperatif komplikasyonlar, takip süresi, nüks olup olmadığı, postoperatif HOSE skorundan oluşmakta idi.

Bulgular: Çalışmaya toplam 46 hasta dahil edildi. Hastaların ortalama yaşı 8,5±5,4 yıl idi. Hastaların hipospadias mea yerleşimleri, 15'i distal, 13'ü subkoronal, 9'u mid penil, 6'sı proksimal, 3'ü glanüler şeklinde idi. Hastaların 35'ine TİPU, 6 tanesine iki basamaklı Braca, 3 tanesine MAGPI ve 2 tanesine onlay flep yapılmıştı. Hastaların postoperatif ortalama HOSE skoru değeri 14,6±1,7 idi. HOSE skoru proksimal hipospadiası olanlarda en düşük iken glanüler hipospadiası olanlarda en yüksek idi, 12,6'ya karşın 15,6 (p=0,26). Farklı bir hekim tarafından aynı hastaların HOSE skoru değerlendirildiğinde ortalama HOSE skoru 14,5±1,7 bulundu. Gözlemciler arasında değerlendirme açısından farklılık bulunmadı (Kappa skoru: 0,698), p<0,0001).

Sonuç: HOSE skoru hipospadias cerrahisinin sonuçlarının değerlendirilmesinde kullanılabilecek objektif ve güvenilir bir skorlama sistemidir. **Anahtar Kelimeler:** Hipospadias, HOSE, Penil rekonstrüksiyon

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Introduction

Hypospadias is a common congenital anomaly affecting one out of every 200 to 300 newborn males (1). Hypospadias surgery also aims functional recovery in addition to improving cosmetic appearance (2). More than 200 techniques have been defined for the surgical treatment of hypospadias. Some of these surgical techniques may have more complications (3). While a straight penis in erection, a meatus near the tip of the glans, ability to urinate in a standing position and being able to have sexual intercourse were found to be satisfactory in the evaluation of surgical success in the past, a functionally and cosmetically normal penis is aimed today. Evaluation of hypospadias surgery outcomes sheds light on future clinical practice (4).

Different scoring systems for assessment of hypospadias surgery outcomes have been suggested (5,6,7,8). Surgical success and functional results of hypospadias surgery can be predicted with these scoring systems. Our aim in this study was to present the outcomes of hypospadias surgery performed in our study using the hypospadias objective scoring evaluation (HOSE) system and also to investigate the reliability of the HOSE.

Materials and Methods

After obtaining local ethics committee approval (protocol no. 2019-241; 20.05.2019), records of patients, who underwent surgery due to hypospadias in our clinic between January 2016 and March 2018, were retrospectively analyzed. The examined parameters were demographic characteristics, location of the maetus, peroperative and postoperative complications, follow-up duration, recurrence data and HOSE score in the postoperative 12th month. The HOSE is a 5- point scoring system evaluating meatal location, meatal shape, urinary stream, erection and presence of fistula. The minimum total score is 5 and the maximum is 16 points (9).

Seven out of a total of 55 patients who had hypospadias operation were excluded from the study due to previous hypospadias surgery and two others were excluded as they were over the age of 18 and the study covered 46 patients in total.

Statistical Analysis

IBM SPSS statistics for Mac version 21 (Chicago, IL, USA) was used for data analysis. While constant variables were given in mean ± standard deviation, categorical variables were given in numbers and percentages. The Kolmogorov-Smirnov test was used to test normal data distribution. For the comparison of two groups, the Mann-Whitney U test was used for numerical data and chi-square tests were used for categorical variables. The One-Way ANOVA was used for comparing numerical data of more than two groups. Intraobserver reliability was measured using the kappa coefficient.

Results

A total of 46 patients were included in the study. The mean age of the patients was 8.5+5.4 years. Fifteen patients had distal (meatus located on the glans or distal shaft), 13- subcoronal (just below the glans penis), 9- penile (in the midshaft), 6- proximal (at the penosocratal junction) and 3 patients had glanular hypospadias (meatus on the glans penis but not at the tip). Thirty five of the patients underwent tubularised incised plate urethroplasty (TIPU), 6 had Bracka 2- stage repair and 3 had meatal advancement and glanuloplasty incorporated (MAGPI), and the onlay flap technique was used in 2 patients. The average duration of catheterization was 12.1±4.6 days. The average length of hospital stay was 3.2±0.9 days and the average followup period was 22.7±15.6 months. Recurrence was observed in 13 patients after 4.9±4.8 months in average. Among the patients with recurrence, 10 (76.9%) had urethrocutaneous fistula, 2 (15.4%) had meatal stenosis and 1 (7.6%) had wound infection. The mean postoperative HOSE score was 14.6±1.7. While HOSE score was lowest in patients with proximal hypospadias, it was highest in patients with glanular hypospadias (12.6 vs 15.6) (p=0.26). 11 patients had a total HOSE score below 14 (23.9%) and 35 patients (76.1%) had 14 and above (Table 1).

When the groups with and without complication were examined, the mean HOSE score in the group with and without complication was 13 ± 1.75 and 15 ± 1.05 , respectively (p=0.106).

Tablo 1. Hypospadias objective scoring evaluation			
1) Meatal location			
Distal 4			
Proximal glanular 3			
Coronal 2			
Penile shaft 1			
2) Meatal shape			
Vertica I 2			
Circular 1			
3) Urinary Stream			
Single stream - 2			
Spray 1			
4) Erectile function			
Straight 4			
Mild angulation (<10°) 3			
Moderate angulation (>10°, <45°) 2			
Severe angulation (>45°) 1			
5) Fistula			
None 4			
Single-subcoronal or more distal 3			
Single-proximal 2			
Multiple or complex 1			

Although no statistically significant difference was detected in HOSE score between the groups, the lowest HOSE score was found in the complication group.

When the relationship between surgical method and HOSE score was examined, the mean HOSE score in 35 patients who had TIPU was 14.9 ± 1.4 while it was 13.5 ± 2.3 (p=0.167) in those who underwent surgery performed using other methods (MAGPI, onlay flap, Bracka). No significant difference was detected in HOSE score when surgical methods were compared but HOSE score was higher in TIPU group. The mean HOSE score was found to be 14.5 ± 1.7 when the HOSE scores of the patients were evaluated by a different doctor. There was no significant intraobserver variance (Kappa score: 0.698), (p<0.0001).

Discussion

Hypospadias is one of the most difficult fields of urogenital reconstructive surgery. Many different techniques have been suggested for hypospadias repair. Complication rates, cosmetic appearance of the penis, urination and sexual functions, quality of life and psychosexual life should be considered when evaluating outcomes of hypospadias surgery. Today, different scoring systems are used for evaluating the surgical outcomes. Some of these are HOSE, hypospadias objective penile evaluation (5), Pediatric Penile Perception Score (6), Mureau (7) and Hadidi (8) scores (4). All these different scoring systems have their unique positive and negative aspects. In this study, we used HOSE to evaluate our hypospadias surgery outcomes.

HOSE score was defined by Holland et al. (9) in 2001. In an original study, randomly selected 20 patients were evaluated nearly 12 months after hypospadias surgery and HOSE score was given by four different observers (two doctor, one nurse and one relative of patient) to the patients and no significant intraobserver variation was observed (mean weighted kappa: 0.66). As a result, it was stated that HOSE score was a reproducible, objective outcome measure and independent of the preoperative severity of the defect (9).

In our study, no significant intraobserver variation of HOSE score was observed (Kappa: 0.69).

In a study made by Aulagne et al. (1) on 48 patients aged 20-35 years who had been operated due to severe posterior hypospadias in childhood, 27 follow-up patients were administered HOSE and a quality of life questionnaire prepared by the authors. Satisfaction rate in 21 patients with a HOSE score of 14 or above was 71%, it was 51% in patients with a HOSE score below 14.

In another study including 55 patients, 34.5% of the patients had acceptable outcomes with a total HOSE score of 14-16. HOSE score and uroflowmetry were suggested as simple, non-

invasive and non-expensive techniques for evaluating long-term outcomes of hypospadias surgery (10).

In another study including 99 patients who underwent hypospadias repair using the meatal mobilization technique, 94% of patients reached the maximum of 16 points and 6% had 12-15 points on the HOSE symptom score (11). In our current study, the HOSE score of 14 and above in 76.1% of the patients may be explained by the fact that some of these patients had severe proximal hypospadias.

Conclusion

HOSE is an objective and reliable scoring system which can be used to evaluate outcomes of hypospadias surgery.

Ethics

Ethics Committee Approval: Ethics committee approval was received on 20.05.2019

Informed Consent: All patients had given written informed consent before the surgery for giving permission for the use of the collected data at any time.

Peer-review: Internally peer-reviewed.

Authorship Contributions

Concept: Y.A., E.G., Design: Y.A., E.G., Data Collection and/or Processing: Y.A., E.G., Analysis and/or Interpretation Y.A., E.G., Literature Research: Y.A., E.G., Writing: Y.A., E.G.

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

Financial Disclosure: No financial support.

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Assessment of Positioned Instillation of Contrast Cystography in Children with Recurrent Urinary Tract Infections

Tekrarlayan İdrar yolu Enfeksiyonu olan Çocuklarda Pozisyonel Yerleştirilen Kontrast Sistografinin Değerlendirilmesi

© Hülya Nalçacıoğlu¹, © Deniz Demirci², © İsmail Dursun³, © Numan Baydilli², © Varol Nalçacıoğlu², © Sibel Yel³, © Funda Baştuğ¹, © Zübeyde Gündüz³, © Hakan Poyrazoglu³ , © Ruhan Düşünsel ³

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

Positioned instillation of contrast (PIC) cystogram is used as a diagnostic tool for the examination of vesicoureteral reflux in patients with recurrent febrile urinary tract infections (UTIs) without any signs of reflux on conventional voiding cystourethrography (VCUG). In this current study, we described our pediatric single center experience with PIC cystogram in recurrent UTIs whose reflux is not identified on conventional VCUG. We hope that this study leads to further development and widespread use of PIC cystography in pediatric diagnostic practice as well as to optimize the algorithm for the treatment of children with febrile UTIs to reveal occult VUR.

Abstract

Objective: Vesicoureteral reflux (VUR) is considered the most important predisposing factor for urinary tract infection (UTI). Renal damage due to VUR, subsequently renal scarring and the possibility of reflux nephropathy warrant early detection of VUR. Our aim was to evaluate the value of positioned instillation of contrast (PIC) cystography in the detection of VUR in children with recurrent UTI and a normal voiding cystourethrography (VCUG).

Materials and Methods: PIC cystography was performed in each child with the indication of recurrent UTI with a normal VCUG between June 2015 and November 2017.

Results: Thirty-four children (32 girls, 2 boys) aged 7 to 17 years (median, 10 years), were examined. Twenty (58.8%) patients had normal ultrasound and 12 patients (35.3%) had bilateral scars detected using 99mTc-dimercaptosuccinic acid (DMSA). Thirty-one (91.2%) patients were shown to have VUR on PIC cystography. Nine (29%) patients had no renal scar with positive PIC and 3 (12%) patients had scars with negative PIC. Scars were detected in 13 (72.2%) patients with grade I-II VUR, and 4 (30.8%) with grade III-IV VUR had no scars on DMSA. There was no significant difference between the results of PIC and DMSA renal scan. Twenty-six patients (76.5%) with PIC-VUR underwent simultaneous endoscopic injections. During the postoperative follow-up with an average of 12 months, 27 patients showed no evidence of febrile UTIs.

Conclusion: Based on our results, PIC cystogram seems to be a good alternative to invasive voiding cystourethrogram in screening children for VUR. **Keywords:** Recurrent urinary tract infections, Positioned instillation of contrast cystogram, Children, Occult reflux

Öz∣

Amaç: Vezikoüreteral reflü (VUR) idrar yolu enfeksiyonu (İYE) için en önemli predispozan faktördür. VUR'ye bağlı böbrek hasarı, böbrekte skar oluşumu ve reflü nefropatisi olasılığı, VUR'nun tespiti için en önemli gerekçelerdir. Amacımız, voiding sistoüretrografi (VCUG) reflü tespit edilmemiş tekrarlayan idrar yolu enfeksiyonlu (İYE) çocuklarda VUR saptanmasında konumlu kontrast yerleştirme (PIC) sistografinin değerlendirilmesidir. Gereç ve Yöntem: Haziran 2015 - Kasım 2017 tarihleri arasında VCUG'de reflü tespit edilmemiş tekrarlayan İYE'li çocuklara PIC sistografi yapıldı. Bulgular: Otuz dört çocuk, yaşları 7-17 arasında değişen (yaşları ortanca, 10 yaş) 32'si kız olan çocuklar incelendi. Yirmi (%58,8) hastada normal US,



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12 hastada (%35,3) 99m-Tc-dimerkaptosüksinik asit (DMSA) kullanılarak iki taraflı skar tespit edildi. Otuz bir (%91,2) hastanın PIC sistografisinde VUR olduğu görüldü. Dokuz (%29) hastada PIC pozitif, renal skar yoktu ve 3 (%12) hastada negatif PIC ile skar vardı. DMSA'da grade I-II VUR'li 13 (%72,2) hastada ve grade III-IV VUR'lu 4 hastada (%30,8) skar saptanmadı. PIC sistografide reflü ile DMSA'da skar arasında anlamlı ilişki bulunmadı. PIC-VUR'u olan 25 hastaya (%76,5) eş zamanlı endoskopik enjeksiyon yapıldı. Postoperatif dönemde ortalama 12 ay takipte olan 27 hastada ateşli İYE tekrarlamadı.

Sonuç: Elde ettiğimiz sonuçlara göre, PIC sistogram VCUG'de reflü tespit edilmemiş tekrarlayan İYE'li çocuklarda VUR saptanmasında alternatif bir tanı aracı olarak kullanılması yararlı görülmektedir.

Anahtar Kelimeler: Rekürren üriner sistem enfeksiyonları, Konumlu kontrast yerleştirme sistogramı, Çocuklar, Gizli reflü

Introduction

Vesicoureteral reflux (VUR) is considered a common predisposing factor for urinary tract infections (UTIs) with an incidence of 25-40% in children (1,2,3). Recurrent UTIs associated with VUR can lead to reflux nephropathy, a principal cause of end-stage renal disease in children (4,5). Therefore, early detection and timely treatment of VUR is important in reducing the risk of permanent renal damage.

Voiding cystourethrography (VCUG) is the most widely used fluoroscopic technique in most clinics to confirm VUR as an initial evaluation of children with febrile or recurrent UTIs. However, technique-related and patient preparation-related variables may affect the reliability and accuracy of voiding cystourethrogram (VCUG). Many variables such as different types and sizes of catheters, rate of bladder filling, concentration of contrast agents or intermittent nature of VUR contribute to this problem (2,6,7,8,9,10).

Rubenstein et al. (11) were the first to introduce positioned instillation of contrast (PIC) cystogram which is a new diagnostic tool for detecting VUR in patients with recurrent febrile UTIs despite a normal VCUG. The main advantage of PIC cystography is subureteric injection at the same session when occult VUR is detected. Although there are limited reports on PIC cystogram, the incidence rate of febrile UTI is lowered significantly by treatment of VUR identified by PIC cystography (12,13,14)

The aim of our study was to evaluate the value of PIC cystography in the detection of VUR in children with recurrent UTIs all of whom had negative VCUG findings.

Materials and Methods

We retrospectively reviewed data of 34 pediatric patients who underwent PIC cystography between June 2015 and November 2017. PIC cystography is performed on each child with an indication of recurrent UTI with negative VCUG. This study was approved by the Erciyes University Faculty of Medicine, Institutional Review Board and Ethics Committee (project no.: 2017/543). The patients' parents or legal guardians gave consent for the use of their data for research purposes. The term "recurrent UTI was defined as more than one episode of pyelonephritis, or one episode of pyelonephritis plus at least one episode of cystitis, or at least three episode of cystitis. All patients were admitted or referred for the evaluation of recurrent UTI and imaging data including renal ultrasonography (US), VCUG, and Tc-99m-dimercaptosuccinic (DMSA) acid renal scintigraphy scans were analyzed in detail upon admission. Exclusion criteria were as follows: presence of anatomic abnormalities such as duplex systems/posterior urethral valves or bladder problems including neurogenic bladder. Lower urinary tract dysfunction (LUTD) was defined by clinical findings, including urgency, urge incontinence, enuresis, hesitancy, intermittent voiding, and weak stream. Children with abnormal voiding patterns were assessed and managed without urodynamic test prior to PIC cystography. Renal scars were evaluated using DMSA based on the criteria of Goldraich et al. (15). A DMSA scan was performed 3-6 months after infection was diagnosed.

Once the bladder was emptied, PIC cystography was performed by using a 9.5 F or 11 F pediatric cystoscope with the patient in the dorsal lithotomy position during endoscopy. The cystoscope beak was placed close to the ureteral orifice and the ureteral orifices were identified and evaluated for their trigonal appearance (patulous or not).

Contrast agent was placed at a height of 1 meter above the level of the bladder and flowed toward the orifice via the irrigation port of the cystoscope while the fluoroscopy was performed to evaluate VUR. The bladder was emptied after the procedure was completed. All patients were on antibacterial prophylaxis and had negative culture at the time of the procedure. The grade of PIC-VUR was described by adapting the system of the international reflux classification (16).

If VUR was detected, endoscopic treatment was performed in the same session, surgical reimplantation was performed later. Postoperative follow-up evaluation was done at 1 month with renal and bladder US and urinalysis and culture when indicated. Antimicrobial prophylaxis was continued at this time. Success was defined as having no further febrile UTIs. VCUG and DMSA scans were not performed after antireflux treatment.

For each patient, data were recorded as outlined below.

(a) Demographic and clinical information; (b) imaging data including renal US, VCUG, and DMSA scan; (c) follow-up data including antimicrobial prophylaxis and the presence of recurrent UTIs. The clinical outcome focused on postoperative febrile UTIs.

Statistical Analysis

All statistical calculations were made using the Statistical Package for the Social Sciences 22.0 (SPSS IBM Corp, Armonk, New York, USA). The characteristics of the patients were determined using descriptive statistics. Results are given as median (minimum–maximum) or proportion. Categorical variables were evaluated using the chi-square test. Statistical significance was accepted as p<0.05.

Results

Thirty-four children (32 girls and 2 boys) aged 7-17 years (median: 10 years) were identified retrospectively. Twenty-one (61.8%) patients had a history of febrile, 13 patients had afebrile recurrent UTIs. Demographic and clinical data of patients are summarized in Table 1.

Renal US was normal in 20 children and abnormal (hydronephrosis) in 14. The DMSA renal scan was normal in nine patients and abnormal in 25. Unilateral and bilateral renal scarring was confirmed in 13 (38.2%) and 12 (35.3%) patients, respectively. Thirty-one of the 34 (91.2%) patients demonstrated reflux on PIC cystogram; PIC-VUR was unilateral in 10 patients and bilateral in 21 patients. Among these patients, 18 had grade I-II VUR and 13 had grade III-IV VUR. Nine patients (29%) with positive PIC had no renal scar, and 3 (12%) patients with negative PIC had scars. Scars were detected in 13 (72.2%) patients with grade I-II VUR, and 4 (30.8%) patients with grade III-IV VUR had no scar on DMSA. There was no significant difference between the results of PIC and DMSA renal scan. 10 of the 34 patients who presented with febrile UTIs had dysfunctional voiding.

Twenty-six (76.5%) of the 31 patients with PIC-VUR underwent simultaneous endoscopic injection of a bulking agent, dextranomer/hyaluronic acid copolymer. Ureteroneocystostomy was performed in 4 (11.8%) patients. One patient, who had grade I PIC-VUR with no scars on DMSA, did not undergo antireflux surgery. Six patients who had abnormal voiding patterns and managed for LUTD, had subsequent febrile UTIs in the followup period and PIC-VUR was detected. 2 patients who had grade I-II and 4 with grade III-IV VUR underwent endoscopic therapy.

The postoperative follow-up interval was from 5 to 22 months with an average of 12 months. During this time, 27 of the 34 patients were on follow-up. After PIC-VUR treatment, 27 patients showed no evidence of febrile UTIs. Seven of 27 patients experienced afebrile UTIs. All the 7 patients were girls (mean age:

11.14 \pm 3.28 years) and 6 of the 7 patients demonstrated PIC-VUR; 2 patients had grade I-II VUR and 4 had grade III-IV VUR. There were no repeat VCUG and DMSA scans after endoscopic therapy because the infections were not febrile. The 7 female patients demonstrated LUTD despite pelvic floor therapy and behavioural interventions, their afebrile UTIs persisted.

No significant association was found between PIC cystography results and the frequency of UTI, kidney US findings, and DMSA scans (p=0.289, p=0.773 and p=0.276, respectively). In contrast, a significant association was found between the PIC results and gender (p=0.034). PIC cystogram did not identify VUR in 3 patients (8.8%). Due to few number of patients with negative

Table 1. Clinical characteristics of children underwent PICcystography with recurrent urinary tract infections			
Variables	Study population (n=34)		
Age (years) (mean <u>+</u> SD)	10.19 <u>+</u> 2.64		
Gender (n, %)			
• Female	32 (94.1)		
• Male	2 (5.9)		
UTIs (n, %)			
• Febrile	21 (61.8)		
• Afebrile	13 (38.2)		
Dysfunctional voiding (on medical history) (n, %)	10 (29.4)		
US findings n (%)			
Normal	20 (58.8)		
Abnormal (hydronephrosis)	14 (41.2)		
DMSA Scan Findings (n, %)			
Unilateral scar	13 (38.2)		
Bilateral scars	12 (35.3)		
PIC-VUR (n, %)			
• No VUR	3 (8.8)		
• grade I-II VUR	18 (52.9)		
• grade III-IV VUR	13 (38.2)		
Intervention (n, %)			
• Endoscopic	26 (76.5)		
Open reimplantation	4 (11.8)		
Medical therapy	4 (11.8)		
Clinical follow-up (months)	12.62 <u>+</u> 5.43 (5-22) (median)		
UTIs after surgery (n, %)			
• None	27 (79.4)		
• Febrile	0		
• Afebrile (all of them performed by endoscopic therapy)	7 (20.5)		
VCUG: Voiding cystourethrography, UTIs: Urinary tract infections, US: Ultrasound, VUR: Vesicoureteral reflux, DMSA: 99mTc-dimercaptosuccinic acid			

PIC cystogram results, we cannot make a firm conclusion that PIC cystogram is alternative to VCUG.

Discussion

VCUG is the most widespread used method as the first modality for the detection of VUR in children (1,2,3,4). However, the biggest challenges physicians face in clinical practice is managing children who had recurrent febrile UTIs with normal VCUG findings. In our study, we focused on the predictive value of showing occult reflux with PIC cystogram and the clinical its effect on recurrent UTIs in patients considered without VUR using standard imaging techniques. We found that 31 of the 34 (91.2%) patients had significant degrees of reflux detected using PIC cystography and the episodes of febrile UTIs were not repeated during follow-up; in some patients there was a decrease in non-febrile UTIs. Although no consensus is available regarding the role of PIC cystogram in children with recurrent UTIs, the findings reported in our study are strikingly similar to those reported previously (11,12,13,14,17,18,19,20,21,22,23).

In the first report by Rubenstein et al. (11), the authors state that PIC cystogram was performed in 30 children with recurrent febrile UTI and normal VCUG, and VUR was detected in all of these children with PIC cystogram. They also no VUR in the control group. During the postoperative 8-months follow-up, none of the patients had recurrent febrile UTIs, similar to that reported by our study. In a study of 39 patients with recurrent febrile UTIs from four centers, PIC-VUR was found in 82% of the patients (12). Tareen et al. (17) reported that patients with recurrent febrile UTIs without VUR on VCUG should underwent PIC cystogram. Based on these studies, PIC cystogram appeared to be a promising method but, despite high sensitivity, it proved to be less practicable than VCUG.

An important point is to further evaluate whether PIC-positive reflux is truly clinically significant or not. Following a review of these initial studies, a multi-institutional study was performed to evaluate the clinical outcome of postoperative followup of PIC-VUR in 118 patients, focusing on the incidence of postoperative febrile UTIs. The authors showed that the episodes of febrile UTIs was significantly reduced after treatment (13). Another study found a relationship between PIC-VUR grades and severity of renal scarring on DMSA (21). Tareen et al. (17) stated that PIC cystography should be the next step in patients who had a second UTI and had signs of scarring in DMSA and who had no VUR on VCUG. Recently, Haberal et al. (14) from Turkiye examined 198 patients who underwent PIC cystography and reported a reflux rate of 58.3% in patients with UTIs. The authors concluded that PIC was an effective diagnostic method for revealing occult VUR. In addition, they found that 37.5% of the unscarred renal units had VUR. They found no significant

difference between the results of PIC-VUR and renal scarring on DMSA, in contrast to the findings of Tareen et al. (17). This result is compatible with our findings. Given that, in our cohort, 9 (29%) patients with positive PIC had no renal scars and 3 (12%) patients with negative PIC had scars. Among these patients, 18 had grade I-II VUR and 13 had grade III-IV VUR. Scars were detected in 13 (72.2%) patients with grade I-II VUR, and 4 (30.8%) patients with grade III-IV VUR had no scars on DMSA. We found no statistically significant relationship between the presence of scar in DMSA and PIC-VUR. The most important question is whether we should perform PIC cystograms in patients with recurrent infections in whom reflux cannot be shown and who have no scars on DMSA. In view of the literature, VUR can be seen independent of renal scarring (14,17). Patients with PIC-VUR without renal scarring may not be at risk for renal damage, but they may benefit clinically when a causative factor can be treated by reducing or eliminating future febrile infections.

Haberal et al. (14) found that the infection-free rate in the follow-up was slightly higher in the patients with PIC-VUR, but it was not significantly different from patients who were PIC-negative. They emphasized that the clinical benefit of PIC cystography is not yet clear despite its diagnostic advantage of detecting occult VUR in patients with febrile UTI. In a study of 42 patients with recurrent febrile UTIs from Turkiye, the infection-free rate was found as 80.5% after PIC cystography and concurrent subureteric injection (22). In our cohort, 31 patients demonstrated PIC-VUR and 30 of the 31 patients were treated via endoscopic injection or ureteral reimplantation; none of them had recurrent febrile UTIs during the follow-up. Despite tha curve of febrile UTIs cured, seven female patients with lower urinary tract dysfunction experienced afebrile UTIs during the follow-up. It also appeared that UTIs in girls were more often associated with dysfunctional voiding. The initial DMSA scan was normal in all THE seven patients; therefore, neither DMSA nor VCUG were repeated. Our patients who had LUTD still have higher rates of recurrent UTIs compared with those without LUTD at baseline. The results highlight that there appeared to be a stronger association between VUR and recurrent UTIs in children with LUTD. Although VUR is associated with the risk of recurrent UTI and renal scarring, there has been increased appreciation of other factors, such as bladder and bowel dysfunction, which is an important contributor to the recurrence of UTI, VUR persistence and renal scarring (23). Despite pelvic floor therapy and behavioural interventions, recurrent afebrile UTIs were still present. It may be assumed that LUTD in these patients was the result of an incompetent vesicoureteral junction.

Study Limitations

This study has a number of limitations. As a retrospective study with a relatively small sample size, it lacks the statistical power required to reach firm conclusions on the superiority of
any VUR assessment technique. Patients with reflux on VCUG examination were not included in this study, which makes it difficult to interpret subgroup findings of PIC cystography. In this study, we found that PIC-VUR was demonstrable in most cases of recurrent febrile UTIs with normal standard VCUG findings. Despite its advance in determination VUR, we could not state that PIC cystogram is an alternative method to VCUG without insufficient PIC-negative results. Another important limitation is that the PIC process requires general anesthesia. However, it should be stated here that this method is valuable in that it permits examination of the urethra, urinary bladder, and ureteral orifices, and simultaneously allows for subureteric injection for the treatment in patients with PIC-VUR.

Conclusion

In conclusion, our study shows that PIC cystography may be used as a diagnostic method for predicting VUR in children with recurrent febrile UTIs when VCUG is normal. In addition, after the diagnosis of occult reflux, simultaneous subureteric injection provided the cessation of febrile UTI and decreased the rate of afebrile UTIs in some of our patients. For this reason, the main advantage of PIC cystography is both showing occult reflux and allowing for subureteric injection in patients with PIC-VUR at the same session.

We recommend PIC cystography in children who had recurrent febrile UTI with no VUR on VCUG and scars in DMSA. We hope that this study leads to further development and widespread use of PIC cystography in pediatric diagnostic practice as well as to optimize the algorithm for the treatment of children with febrile UTIs to reveal occult VUR.

Ethics

Ethics Committee Approval: This study was approved by the Erciyes University Faculty of Medicine Institutional Review Board and Ethics Committee (project no.: 2017/543).

Informed Consent: The patient's parents or legal guardians gave consent to use their data for research purposes.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: H.N., D.D, I.D Design: H.N., N.B., Data Collection and/or Processing: D.D., N.B., V.N., S.Y., F.B., Analysis and/or Interpretation: H.N., Z.G., H.P., R.D., Literature Research: H.N., N.B., Writing: H.N.

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Resistant Hypokalemia Improving After Radical Nephrectomy: A Case Report

Olgu Sunumu: Radikal Nefrektomi Sonrası Düzelen Dirençli Hipokalemi

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Abstract

Paraneoplastic syndromes are systemic disorders developing in response to any neoplasm and may have various clinical symptoms depending on the affected organ system. Hypercalcemia, one of the renal cell carcinoma (RCC) – Related Paraneoplastic syndromes, occurs in approximately 20% of patients with RCC. Although clinical conditions such as paraneoplastic hypercalcemia and polycythemia are more common complications of RCC, there are rarer paraneoplastic syndromes such as hepatic dysfunction, galactorrhea and Cushing's syndrome. It has been reported that RCC accounted for 2% of all cancers responsible for for Cushing's syndrome and the symptoms associated with Cushing's syndrome remited after surgical treatment. In our patient, although serum isolated adrenocorticotropic hormone, aldosterone and cortisol levels were normal, there was treatment resistant hypokalemic metabolic alkalosis and this was not related to Cushing's syndrome. Complete normalization of the clinical picture and laboratory values after radical nephrectomy suggests that hypokalemic metabolic alkalosis may be a Paraneoplastic syndrome associated with RCC. **Keywords:** Carcinoma, Adenocarcinoma, Hypopotasemia, Hypokalemia, Cushing's syndrome, Nephrectomy, Radical Nephrectomy, Oncology, Urooncology

Öz∣

Paraneoplastik sendromlar, herhangi bir neoplazmaya yanıt olarak gelişen sistemik bozukluklardır ve etkilenen organ sistemine bağlı olarak çeşitli klinik semptomlara neden olabilir. Böbrek hücreli kanser (RCC) ile ilişkili Paraneoplastik sendromlardan biri olan hiperkalsemi, RCC hastalarının yaklaşık %20'sinde görülür. Paraneoplastik hiperkalsemi ve polisitemi gibi klinik durumlar RCC'nin daha sık görülen komplikasyonları olmasına rağmen, hepatik disfonksiyon, galaktore ve Cushing sendromu gibi daha nadir Paraneoplastik sendromlar da vardır. Paraneoplastik Cushing sendromu, RCC'nin Cushing sendromundan sorumlu tüm kanserlerin %2'sini oluşturduğunu ve Cushing sendromuyla ilişkili semptomların cerrahi eksizyondan sonra giderildiğini bildirmiştir (6). Hastamızda serum izole adrenokortikotropik hormon, aldosteron ve kortizol düzeyleri normal olmasına rağmen tedaviye dirençli hipokalemik metabolik alkaloz vardı ve bu Cushing sendromu ile ilişkili değildi. Radikal nefrektomi sonrası klinik tablonun ve laboratuvar değerlerinin tamamen normale dönmesi, hipokalemik metabolik alkolozun RCC ile ilişkili bir Paraneoplastik sendrom olabileceğini düşündürmektedir.

Anahtar Kelimeler: Karsinom, Adenokarsinom, Hipopotasemi, Hipokalemi, Cushing sendromu, Nefrektomi, Radikal Nefrektomi, Onkoloji, Üroonkoloji

Introduction

Paraneoplastic syndromes are systemic pathologies that may occur due to any malignancy and affect various organ systems (1). The classical triad of palpable mass, flank pain and hematuria is seen in 15% of patients with renal cell carcinoma (RCC), whereas the probability of developing RCCrelated Paraneoplastic syndrome is 40% (1). The most common paraneoplastic complication of RCC is hypercalcemia (2). Other RCC-related Paraneoplastic syndromes include Cushing's syndrome (1). Symptoms of Cushing's syndrome may include nausea, vomiting, hypokalemia and metabolic alkalosis (3). In our case, nausea, vomiting, hypokalemia and metabolic alkalosis suggested Cushing's syndrome which may develop due to RCC. However, the patient's findings were not consistent with Cushing's syndrome. No similar case has been reported in the literature previously.

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Case Report

A 53-year-old male patient presented with the complaints of weakness, abdominal pain, nausea and vomiting. These complaints were present for about 1 month and increased gradually in recent days. Physical examination revealed no pathological findings other than central obesity. He had a history of hypertension. Abdominal ultrasonography revealed a 10 cm mass in the left kidney. Whole body computed tomography revealed an exophytic solid mass of 14 cm in length and approximately 10x9.5 cm in transverse dimensions in the lower pole of the left kidney. There was no evidence of renal vein invasion. No pathological finding and a typical distant metastasis were detected in both adrenal glands (Figure 1, 2).

Written informed consent was obtained from the patient and left radical nephrectomy was planned and preoperative preparations were started. The results of blood analysis were as follows: potassium – 2.5 mEq/L (reference range: 3.5–5 mEq/L), creatinine – 1.7 mg/dL (0.7–1.3 mg/dL), sodium – 133 mEq/L (136– 145 mEq/L), hemoglobin – 9.8 g/dL (13.1–17.2 g/dL), hematocrit – 27.9% (39–50%), and urine pH – 6. Nephrology consultation was obtained and potassium chloride (KCL) replacement (infusion in



Figure 1. The appearance of the mass on computed tomography



Figure 2. The appearance of calcification in the mass on computed tomography

1000 cc saline at 60 meq and 10 hours) was initiated according to the recommendations. Nausea and vomiting were controlled by antiemetic treatment during the hospitalization period. However, despite repeated KCL replacement several times, the patient's potassium level did not increase significantly. The values were as follows: PH - 7.55, HCO3 - 37.4 mmol/L (22-26), and PCO2 - 43.2 mmHq (35-45) potassium - 2.5 mEq/L (3.5-5).

Endocrinology consultation was requested according to the recommendations of the nephrology clinic. The tests requested by endocrinologists revealed the followings: total cholesterol - 139 mg/dL (<200), triglyceride - 186 mg/dL (<150), high density lipoprotein cholesterol: 22 mg/dL (>55), LDL cholesterol (calculated using the Friedewald equation) - 80 mg/dL (<130), isolated adrenocorticotropic hormone (ACTH) (morning) - 42.6 pg/mL (<46), TSH - 1.9 μ IU/mL (0.27-4.2), FT4 - 1.47 ng/dL (0.93-1.7), cortisol (morning) - 13.11 μ g/dL (4.82-19.5), 17-OH progesterone - 79 ng/dL (20-250), and aldosterone - 5.0 ng/dL (2-18). Acetazolamide tablets were started by the nephrology clinic due to alkalosis, and he was operated under KCL replacement therapy (infusion in 1000 cc saline for 60 meq and 10 hours) and left radical nephrectomy was performed.

The level of potassium was 4.2 mEq/L (3.5-5) and pH was 7.39 on the first postoperative day, and potassium was 4.4mEq/L (3.5-5) and pH was 7.40 at the first postoperative month. Histopathological investigation of the surgical specimen revealed chromophobe RCC and negative surgical margins.

Discussion

RCC is the 6th most common cancer in males and 10th in females (4). The incidence of RCC is increasing due to the widespread use of abdominal imaging especially for musculoskeletal complaints or gastrointestinal complaints (5).

Although clinical conditions such as paraneoplastic hypercalcemia and polycythemia common in RCC, there are less common Paraneoplastic syndromes such as hepatic dysfunction, galactorrhea and Cushing's syndrome (1). Riggs and Sprague (6) reported that RCC accounted for 2% of all cancers responsible for Cushing's syndrome and the symptoms associated with Cushing's syndrome remitted after surgical treatment. RCCinduced Cushing's syndrome is thought to be due to ectopic ACTH secretion by tumor cells (6). In patients undergoing radical or partial nephrectomy, Cushing's syndrome can be treated by eliminating ectopic ACTH-producing tumor cells. Elevated levels of ACTH in the postoperative period may be associated with disease recurrence or progression (7).

Naert et al. (8) reported a case of necrotizing myopathy in a patient with a right renal mass in whom a remission of myopathy was observed after radical nephrectomy.

Hypokalemic metabolic alkalosis may occur in patients with Cushing's syndrome (9). In our patient, although serum ACTH, aldosterone and cortisol levels were normal, there was resistant hypokalemic metabolic alkalosis and this was not related with Cushing's syndrome. The complete normalization of the clinical picture and laboratory values after radical nephrectomy suggests that hypokalemic metabolic alkalosis may be a Paraneoplastic syndrome associated with RCC.

Ethics

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

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: F.K., M.S.K., M.D., Design: F.K., M.S.K., M.D., Data Collection and/or Processing: M.D., Analysis and/or Interpretation: A.Ş., F.K., M.S.K., M.D., Literature Research: M.D., Writing: M.D.

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Bladder Sparing Surgical Treatment in a Patient with Pelvic Lipomatosis

Pelvik Lipomatozisli Bir Olguda Mesane Koruyucu Cerrahi Tedavi

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Abstract |

Pelvic lipomatosis is an uncommon benign disease characterized by the excessive growth of mature fat tissue in the perivesical and perirectal areas. A 61-year-old male patient, who was admitted with voiding difficulty, underwent bladder-sparing surgery with excision of adipose tissue for pelvic lipomatosis. The case is presented and discussed with the relevant literature. **Keywords:** Pelvic lipomatosis, Treatment, Surgery

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Öz

Pelvik lipomatozis, perivezikal ve perirektal bölgelerde aşırı matür yağ dokusu büyümesi ile karakterize nadir ve benign bir hastalıktır. İdrar yapma zorluğu ile başvuran 6 yaşındaki erkek hastaya pelvik lipomatosis için mesane koruyucu yağ doku eksizyonu cerrahisi uygulandı. Olgu ilgili literatür eşliğinde sunuldu ve tartışıldı.

Anahtar Kelimeler: Pelvik lipomatozis, Tedavi, Cerrahi

Introduction

Pelvic lipomatosis is a benign proliferative disease characterized by excessive growth of large amounts of mature fat tissue often accompanied by cell infiltration and fibrosis in the pelvic retroperitoneal space (1,2). It was first defined by Engels (3) in 1959 and was termed "pelvic lipomatosis" by Fogg and Smyth (4) in 1968. Until 2005, 198 cases had been reported (5). The PubMed screening showed that additional 116 cases in a total of 18 studies have been published since 2005 (6). The incidence pelvic lipomatosis has been reported to be 0.6–1.7 per 100.000 hospital admissions in the USA (7). The male-female ratio of pelvic lipomatosis ranges between 10:1 and 27:1 (2,5,8,9). Heyns et al. reported that the mean age at diagnosis was 48 years with a range from 9 to 80 years (2). Tong et al. reported that pelvic lipomatosis was seen in the same family members (10) and was more common in blacks, but this is uncertain (11). The etiology of pelvic lipomatosis is not clear (2,9). Obesity, endocrine disorders, posterior urethral obstruction, recurrent urinary system infections, and steroid treatment have been proposed to be possible mechanisms (2,9). Finally, it may be related to an anomaly in the HMG-IC gene (10) or significant changes in the whole genome methylation level (12).

Symptoms are caused by extrinsic compression of the urinary system, the lower intestinal tract and the vascular system (2,9). There are no disease-specific findings in the physical examination (2,9).

The methods used in the diagnosis of pelvic lipomatosis are computed tomography (CT) and magnetic resonance imaging (1,8). There are bilaterally compressed, fixed, superiorly and anteriorly dislocated bladder (inverted tear-drop, pear, gourd or banana-shaped), superomedially displaced lower third part of the ureter, prolongation and anterior displacement

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of the prostatic urethra by increased adipose tissue, besides hydroureteronephrosis (1,8). When pelvic lipomatosis coexists with cystitis glandularis, filling defects may be seen in the related bladder wall (1,2). We present herein a case of a 61-year-old man with pelvic lipomatosis treated by bladder-sparing surgery and discuss the relevant literature.

Case Report

A 61-year-old male patient presented with the complaints of slow urine stream and frequency. He had a history of urolithiasis surgery and hypertension. The patient's body mass index was 43 kg/m2. On digital rectal examination, the prostate was unremarkable. The patient's blood creatinine, urea nitrogen, and total prostate-specific antigen values were 2.5 mg/dL, 50 mg/dL and 2.2ng/mL, respectively. Urinalysis revealed hematuria and pyuria. Urine culture and tuberculosis test were negative.

Non-contrast abdominal CT revealed bilateral grade 4 hydronephrosis, cranially displaced bladder and increased pelvic adipose tissue (Figure 1a, 1b). On nephrostogram, no contrast passage from the right ureter to the urinary bladder and from the left kidney to the left ureter was observed (Figure 1c, 1d). There was no reflux on voiding cystourethrography (Figure 2). Detrusor overactivity and outflow obstruction were detected in pressure-flow study. Histopathological examination of the bladder biopsy specimens revealed follicular cystitis.

Subsequently, the fatty tissue surrounding the bladder was excised preserving the bladder and by employing a previously described technique (13). Histopathological examination



Figure 1. Non-contrast abdominal computed tomography. A) Bilateral grade 4 hydronephrosis. B) High-density perivesical adipose tissue and cranially replacement of the urine bladder. The nephrostography. C) A very tortuous right ureter, and no contrast passage from the right distal ureter to the urine bladder. D) There is no ureteral contrast passage from the left kidney



Figure 2. The urine bladder form is impaired, craniocaudal length is increased, and vesicoureteral reflux is absent on the cystogram

revealed mature adipose tissue development. Four months after surgery, post-void residual urine volume and serum creatinine value were 45 cc and 1.66 mg/dL, respectively. There were grade 1 hydronephrosis of the right kidney and grade 2 hydronephrosis of the left kidney in the three-year follow-up of the patient. Voiding difficulty and the quality of life of the patient improved after the operation. Control cystoscopy could not be performed because of patient refusal.

A written informed consent from patient was obtained.

Discussion

Pelvic lipomatosis has serious complications such as obstructive renal failure (2,5,9), hypertension (2,9), thrombosis, urinary calculi, and bladder adenocarcinoma (2,9,14). Approximately three-quarters of cases of pelvic lipomatosis have been reported to be associated with proliferative cystitis, a premalignant lesion, such as cystitis glandularis, cystitis cystica, or cystitis follicularis (2,9,10,11,14).

Differential diagnostic considerations include pelvic hematoma, urinoma, extensively enlarged lymph nodes, lymphoma, liposarcoma, a large lymphocele, pelvic venous collaterals formed by inferior vena cava obstruction, and abscess or iliopsoas hypertrophy (1,2,9).

In their study including 84 patients with pelvic lipomatosis, Chen et al. (11) reported that nearly 80% of patients had various degrees of bladder outlet obstructions according to urodynamics. None of the non-obstructed patients had disease progression at follow-up (11). There is no standardized algorithm for the treatment of pelvic lipomatosis. The efficacy of different treatment modalities such as weight loss, antibiotics, steroids, and radiotherapy has not been proven (2,9). In the management of this disease, a conservative approach is preferred for patients with minor symptoms and without renal impairment (2,9,13,15).

If patients have severe hydronephrosis and uremia, urinary diversion (double J stent placement, ureteral reimplantation, nephrostomy, ureterostomy or conduit) is recommended to prevent renal impairment (2,5,8,9,11,15). The alternative to this approach is removal of the fat tissue in the treatment of pelvic lipomatosis. The first successful treatment of pelvic lipomatosis by extirpation of the lipomas was reported by Carpenter in 1973 (16). Ballesteros reported the second case of perivesical lipomatosis in which the fat deposits were successfully removed surgically in 1977 (17). Halachmi et al. described an ultrasonic-assisted lipectomy technique for the treatment of pelvic lipomatosis (15). Ali et al (13). reported a case of pelvic lipomatosis in a 45-year-old male patient in whom a bladder-sparing excision of the adipose tissue was performed. Recently, Ge et al. reported satisfactory outcomes in their study investigating long-term efficacy of a novel treatment modality for pelvic lipomatosis, a combination of pelvic mass extirpation and ureteral reimplantation (18).

We consider that excision of pelvic adipose tissue using the bladder-sparing technique in suitable patients may give satisfactory results. The procedure can be attempted before major surgery, such as cystectomy and ileal loop diversion, to avoid major surgical interventions.

Ethics

Informed Consent: A written informed consent from patient was obtained.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: F.T., A.Ö., Concept: F.T., Design: F.T., Data Collection or Processing: Ö.K., U.C., Analysis or Interpretation: F.T., Literature Search: F.T., Writing: F.T., Ö.K., U.C., A.Ö.

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A Rare Variant of Urethral Duplication: Type-3 Bladder and Complete Urethral Duplication

Üretra Duplikasyonun Nadir Bir Formu: Tip-3 Mesane ve Üretranın Komplet Duplikasyonu

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Abstract

Urethral duplication is a rare congenital anomaly with several anatomical variations. Persistence of duplicated urethra and related sphincter mechanism are mainly the reasons for the symptoms. We here present a 9-month-old boy with a rare form of duplication with each portion of the duplicated bladder having its own urethral opening.

Keywords: Urethra duplication, Bladder duplication, Effmann classification

Öz 🛽

Üretral duplikasyon, farklı anatomik varyasyonları olan nadir bir konjenital anomalidir. Semptomlar genellikle duplike üretranın devamlılığı ve sfinkter mekanizması ile olan ilişkisine bağlıdır. Bu olgu sunumunda, 9 aylık bir erkek çocuğunda üretra duplikasyonun nadir bir formu olan her biri kendi üretral açıklığına sahip, duplike mesane anlatılmaktadır.

Anahtar Kelimeler: Urethra duplikasyonu, Mesane duplikasyonu, Effmann klasifikasyonu

Introduction

Congenital urethral duplications present with two urethral meas; one orthotopic and one ectopic (1). Wide range of anatomical variants of urethral duplications may be asymptomatic or may show a double urinary stream during micturition. However the range of described urinary symptoms is wide and includes incontinence, urinary tract infection (UTI), urinary retention and outflow obstruction. This rare case presents a normal orthotopic bladder and urethra, with an additional abortive vesical duplication connected to a second passive urethra.

Case Report

A 9-month-old boy with double urethra was referred to our clinic. Physical examination revealed a retractable foreskin and double urethra with functional ventral urethra and hypoplastic

dorsal urethra. There was no medical history of UTI or antenatal hydronephrosis that may be associated with urinary tract anomalies.

Initially, endoscopic surgery was performed using a 0° optic 9.5 Fr pediatric urethro-cystoscope with the patient under general anesthesia. Placing a guide wire and a 4 Fr urethral catheter through the dorsal and ventral urethra helped easy identification (Figure 1). Cystoscopy was performed. A zebra guide wire was placed into the dorsal urethra and the guide wire was not seen in the ventral urethra due to complete urethral duplication. Fluoroscopic images of the dorsal and ventral urethra revealed vesical duplication, dorsal urethra connected to an atrophic bladder and a ventral urethra connected to a normal orthotopic bladder (Figure 2). Finally, a circumcision was performed. The patient was asymptomatic during the 1-year follow-up period.



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Figure 1. A passive dorsal mea and an active ventral mea of double urethra



Figure 2. Fluoroscopic images of bladders connected to ventral (active) and dorsal (passive) urethras

Discussion

Urethral duplication is a rare congenital anomaly, usually with more functional ventral urethra. Effmann et al. (2) classified the anomaly into three types depending on the completion of the duplication (partial/accessory blind tract-type 1, complete-type 2), and association with bladder duplication (type 3) (2). The Y-subtype duplication constitutes 6-30% of all urethral duplications (3). The Effmann classification is the most known functional classification and covers most of the anomalies; however, it does not differentiate sagittal from coronal duplication (4). Various duplications that differ in terms of clinical picture, anatomy and management of the disease could be described by the definition of "urethral duplication" (5). This type of case has been reported previously in the Effmann classification. Similar to our case, most patients have no symptoms or may have the main symptom such as double urinary stream during micturition, incontinence, UTI and urinary retention or obstruction. Urethral duplications may include a wide spectrum of anomalies and recent reports presented various urethral duplications that were not listed in previous classifications (6,7).

The management of urethral duplications is decided based on urological symptoms and cosmetic deformities. If surgery is necessary, functional urethra should be preserved after identification of the active or passive urethra.

Ethics

Informed Consent: Informed consent was obtained from the patient.

Peer-review: Externally peer-reviewed.

Authorship Contributions

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

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From the Scalpel to the Water

Neşterden Suya

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To the Editor,

In the twentieth century, the surgical treatment of benign prostatic hyperplasia (BPH) is changing, hand to hand, with currently available technologies that are reshaping surgical procedures, evolving from open to minimally invasive approaches.

Men with clinically significant lower urinary tract symptoms (LUTS) due to BPH can be treated with drugs or surgically. Surgical intervention is an appropriate treatment for patients with moderate-to-severe LUTS, with acute urinary retention or other BPH-related complications.

For many years, transurethral resection of the prostate (TURP) has been considered the gold standard for surgical treatment of BPH; nowadays Holmium laser enucleation of the prostate is challenging the role of traditional TURP. In 1999, TURP represented the 81% of surgical treatment for BPH versus 39% of 2005 (1).

The laser treatments have been developed in the last 15 years; laser resections can be performed using different kinds of energy: coagulative, cutting and vaporizing laser (2). It is safe with good haemostatic properties, able to treat bladder calculi at the same time and suitable for prostates of different volumes, of choice in the increasing number of patients on antiplatelet therapy.

The first laparoscopic simple prostatectomy was described in 2002 (3). In 2008, the first single-port simple laparoscopic prostatectomy was performed (4). In the recent years, laparoscopy has shown significant technological improvements, including introduction of 4K Ultra HD video equipment, 3D HD video systems, miniaturized instruments with 7 degrees of freedom, and ergonomic platforms. Not the least, also robot-assisted simple prostatectomy has been described with a 3-arm da Vinci Surgical System. Robotic surgery allows robotic arms to replicate the hand movements of the surgeon with greater precision with filtering out any tremor in the surgeon's hands while providing enhanced visualization in high definition 3 dimensional images and improvement in human performance (5,6).

We are waiting for smaller robotic platforms with better maneuverability, providing force feedback and eye tracking capabilities to move the scope inside the patient according to the surgeons' eye movements.

Recently, a new robotic system, used in endourology, is under investigation: the AquaBeam®-system for robot-assisted aquablation of the prostate. By using the power of water, pulsating near the speed of sound, the robot removes the prostatic tissue automatically. It is for the first time a surgical approach allows to eliminate the need for one surgical assistant!

We are witnesses of a revolution not only in the surgical approach to the patient but also of the environment where surgical interventions take place; hybrid operating rooms offer new visualization technologies to provide high-definition, 3-dimensional, real-time images guidance and to perform combined open, minimally invasive and image-guided procedures in the same theatre.

We are moving towards minimally invasive surgery with a switch from direct, hands-on surgical approaches to indirect, "hands-off" approaches as well as towards hybrid operating rooms which allow robotic surgery and telesurgery.

At the beginning, the growing interest in commercial spaceflight and the need of defense departments to have a trauma Pod that



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would allow surgeons to perform operations on soldiers from a distance have increased the demand for telerobotic surgeries. Nowadays it is reality, with more than one surgical procedures described; the current robotic platforms enable remote access, without the need for the surgeon to be present physically in the operating theatre.

Furthermore, the use of tablets and smartphones to talk with patients, colleagues and hospitals will be the new way of communication.

The introduction of virtual reality simulation in the 1990s paved the way for surgical simulation. At the beginning of the century, simulators have been introduced for laparoscopic surgery and they are currently at our disposal for robotic training too. Simulators allow trainees to acquire surgical skills in a safe and controlled environment.

On the whole, surgical procedures, instruments, operating rooms, way of communication, training courses, all has changed in the recent years.

We have reached the 'technological and smart surgery era' and 'mobile healthcare'.

Keywords: BPH, LUTS, Surgery, Technological era

Anahtar Kelimeleri: BPH, LUTS, Cerrahi, Teknolojik dönem

Informed Consent: Unnecessary.

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UROLOGIC SURVEY

Transplant Survey

DOI: 10.4274/jus.galenos.2020.07.001



Re: Low-intensity Shockwave Therapy for Erectile Dysfunction in Kidney Transplants Recipients. A Prospective, Randomized, Double Blinded, Sham-Controlled Study with Evaluation By Penile Doppler Ultrasonography

Yamaçake KGR¹, Carneiro F², Cury J¹, Lourenço R¹, Françolin PC², Piovesan AC¹, Srougi M¹, Nahas WC¹, Antonopoulos IM¹

¹São Paulo University Faculty of Medicine, Department of Urology, São Paulo, Brazil ²São Paulo University Faculty of Medicine, Department of Radiology, São Paulo, Brazil Int J Impot Res. 2019;31(3):195-203. doi: 10.1038/s41443-018-0062-2

EDITORIAL COMMENT

Erectile dysfunction (ED) remains a very common problem in patients with end-stage renal disease even among kidney transplant recipients. Nonsurgical treatment alternatives for ED consist of oral phosphodiesterase type 5 inhibitors and intracavernosal injections of vasodilating agents. In this double-blind, single-center, prospective, randomized, and sham-controlled trial, the authors evaluated the efficacy of low-intensity extracorporeal shockwave therapy (Li-ESWT) for the first time for the treatment of ED in 20 kidney transplanted men. The patients were followed for 12 months with International Index of Erectile Function Questionnaire (IIEF) score, Erection Hardness score (EHS) and penile Doppler. The mean IIEF and EHS scores were better on every follow-up in the Li-ESWT group, however, no difference was observed in penile Doppler findings. In this setting, Li-ESWT appears to be a treatment alternative for the treatment of ED in kidney transplant recipients. Nevertheless, the mechanism of action is suggesting neoangiogenesis; this effect has not been confirmed by penile Doppler in this study.

Yarkın Kamil Yakupoğlu, MD

Transplant Survey

DOI: 10.4274/jus.galenos.2020.07.002



Re: Post-renal Transplant Urolithiasis in Children: An Increasingly Diagnosed Complication: A Retrospective Cohort Study

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Arch Dis Child. 2020;105(1):69-73. Doi: 10.1136/archdischild-2019-317203

EDITORIAL COMMENT

The prevalence of kidney stones in the general population is increasing not only in adults but also in the pediatric population with a greater frequency in girls compared with boys. Urolithiasis is an uncommon complication, usually presenting with unusual findings in kidney transplant recipients. However, if left untreated, it can be a potential cause for graft loss. In this retrospective cohort study, the investigators evaluated the frequency, risk factors and characteristics of post kidney transplantation (KTx) urolithiasis in 142 pediatric kidney transplant recipients over two decades (1995-2016) in an Australian hospital. Only 8 of 142 (5.6%) male recipients were diagnosed with stones; the rate is higher than the previously reported (2.7%-5%) in the early 2000s. Interestingly, stone formers were significantly younger at the time of transplantation and weighed substantially less than non-stone formers. Time to presentation was bimodal; three stones were diagnosed in the first 3 months after KTx, whereas the initial postoperative ultrasound studies were negative for urolithiasis; retained sutures and recurrent urinary tract infections were the most likely causes for early occurrences. The remainder stones were identified 2-4 years after KTx. All stones contained calcium oxalate, 3 were mixed with calcium phosphate and there were only one uric acid stone. Although hypercalciuria was present in 5 (83.3%), none had hyperuricosuria and hypercalcemia. Graft loss due to urolithiasis was not experienced in this cohort. Besides being a single-center study, its relatively small sample size and retrospective characteristics make it hard to make some strong comments regarding the prevalence of childhood urolithiasis and biochemical risk factors in pediatric KTx population, however, there is an increase in the frequency of urolithiasis in parallel with the increase in the general pediatric population.

Yarkın Kamil Yakupoğlu, MD