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Threshold Point of the Total Stone Volume Matter on Decision of Flexible Ureteroscopy

Total Taş Hacminin Değerlendirilmesinde Eşik Değerinin Fleksibl Üreterorenoskopi Kararı Üzerine Etkisi

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ABSTRACT Objective: To determine optimal patients who appropriate for flexible ureteroscopy (FURS) treatment of kidney stones, and the precise cut-off volume value to regard success of FURS. **Material and Methods:** We retrospectively analysed; 164 FURS procedures for kidney stone treatment between December 2012- October 2016 at our centre. Stone Free Rates (SFR) of the procedure was controlled with Non-Contrast CT (NCCT) at the end of the first month. The success rate was determined as the absence of stone fragments or clinical insignificant residual fragments <4 mm. Demographic features, clinical findings and outcomes were recorded. Multivariate analyses were performed to find independent factors and ROC curve was plotted to mark threshold points. Patients are classified according to volume as group 1 (under the cut-off value) and group 2 (beyond the cut-off volume). Area Under Curve (AUC) was used to define a relation between Total Stone Volume (TSV) and operative outcomes. **Results:** The mean TSV was 364.6±295.9 mm^3, and the overall SFR was 124 (75.6%). We identified that TSV beyond the 330 mm^3 volume SFR significantly decrease, operative time and fluoroscopy time remarkably increase as well. The AUC for the TSV and outcomes were 0.743, 0.754, 0.731 respectively. Patients whose TSV smaller than 330 mm^3 were 93 (56.7%) and the rest of patients 51(43.3%) have larger stone volume. SFR is significantly lower and fluoroscopy, the operative time longer in group two patients. **Conclusion:** TSV is the strongest influential factor for the SFR. FURS should be kept in mind firstly for the renal stones TSV <330mm^3, for larger stones other treatment modalities could be thought.

Keywords: Threshold limit values; kidney calculi; ureteroscopy

ÖZET Amaç: Böbrek taşı tedavisinde fleksibl üreterorenoskopi (FURS) tedavisine uygun hastaların belirlenmesi ve FURS tedavisinin başarısını değerlendirmesinde net bir eşik değerinin hesaplanması. **Gereç ve Yöntemler:** Kliniğimizde Aralık 2012 Ekim 2016 tarihleri arasında böbrek taşı tedavisi için FURS tedavisi uygulanmış 164 vaka geriye dönük tarandı. Yapılan işlemin taşsızlık oranı birinci ayın sonunda çekilen kontrastsız bilgisayarlı tomografi (BT) ile değerlendirildi. Başarı oranını belirlerken; BT'de kalkül görülmemesi ya da klinik olarak anlamsız kabul edilen (<4 mm) kalküllerin görülmesi başarı olarak kabul edildi. Demografik özellikler, klinik bulgular ve sonuçlar kayıt altına alındı. Bağımsız faktörleri ve ROC eğrisini belirlemek için çok değişkenli analizler yapıldı. Hastalar taş hacimlerinin eşik değerlerinin üstünde ve altında olmalarına göre iki gruba ayrıldılar. Eğri altında kalan alan, toplam taş hacmi (TTH) ile operasyon sonuçları arasındaki ilişkiyi tanımlamak için kullanıldı. **Bulgular:** Ortalama TTH 364,6±295,9 mm^3 ve toplam taşsızlık oranı 124 (%75,6) idi. Total taş hacmi 330 mm^3 üstünde olan değerler için taşsızlık oranında ciddi bir azalma izlenirken, fluroskopi ve operasyon sürelerinde de uzama olduğu görüldü. TTH ve sonuçlar için eğri altında kalan alan sırası ile; 0,743, 0,754, 0,731 olarak bulundu. 93 (%56,7) hastanın TTV 330 mm^3'den küçük, geri kalan 51 (%43,3) hastanın ise fazla idi. İkinci grupta operasyon başarısında ciddi anlamda düşüş olduğu görülürken, fluroskopi ve operasyon sürelerinde de uzama olduğu belirlendi. **Sonuç:** TTH, taşsızlık oranını etki eden en önemli faktördür. TTV 330 mm^3'den düşük olan hastalarda FURS ilk tedavi seçeneği olarak düşünülmeli iken, daha büyük volümlü taşlarda diğer tedavi yöntemleri göz önünde bulundurulmalıdır.

Anahtar Kelimeler: Eşik limit değerler; böbrek taşları; üreteroskopi

Urolithiasis is a common public health problem and prevalence vary from 1% to 20 depends on the geography, ethnic, dietary and genetic variables.[1] Unfortunately, the incidence of this disease has increased recently due to the sedentary lifestyle of our era and changes in our dietary habits.[2,3] Urinary stones can cause pain, metabolic problems and infections.[4] Those problems lower the quality of life and become an economic issue for the nations. Based on this truth; governments and medical societies try to define a guideline to approach the urinary stones with the considering optimal patient's therapy and the guidance of wide-based high volume studies.[5,6]

Kidney stones are essential and more challenging part of urinary stones. European Urology Association guidelines recommend flexible ureteroscopy (FURS) for smaller than 2 cm and percutaneous nephrolithotomy (PNL) for bigger than 2 cm kidney calculi.[7] Stone is usually regarded as the mean diameter of the surface which is often at the CT. However; calculi are asymmetric spherical bodies correlates with volume; one dimension measurement is not properly accurate with the correct size.[8]

Management of disease using with only conventional CT-based determination decreases the stone free rate (SFR) and increases the complications. It is not fair to tar large, long stone with large, short stone because of the similar wideness. PNL can cause higher morbidity and longer hospital stays so that it can be an over treatment for small volume stones.[9] The success rates of FURS procedures are weak and also additional inter ventions may be needed in the bigger stones treatment. So; it lowers the quality of life (QoL) and increases the health care costs.[10,11] Against this background; stone length in the evaluation of renal calculi is accustomed mistake and stone volume is a more powerful predictor for the approach stone treatment and follow-up.[12-15] We aimed to define the real cut-off value for the determination of appropriate treatment modality which gives us higher success rate, lower morbidity and cost.

MATERIAL AND METHODS

PATIENTS AND CHARACTERISTICS

We have analysed retrospectively 164 FURS procedures for kidney stone treatment between December 2012 with October 2016 in our centre. Patients' demographic features, previous medical and surgical history were reviewed. Previous stone surgeries were classified to the number and endoscopic or open. Preoperative findings such as hydronephrosis grade, stone side, count, volume, location, Hounsfield unit and absence pigtail stent were recorded. Operative time, fluoroscopy time, hospitalisation time and complications were regarded with the other parameters. An estimated volume was calculated using general formula (TSV: stone width × stone length × stone depth × π × 0.167) by using non-contrast CT.[16-18] Five patients were excluded because of the unsuccessful access or uncompleted procedures with the technical problems such as broken FURS. The success rate of the procedure controlled with plain radiograph for kidney, ureters and bladder (KUB) or CT at the end of the first month. The stone-free rate was determined as the absence of stone fragments or clinical insignificant residual fragments <4 mm.

All patients were informed about the alternative treatment modalities, the requirement of the additional session and interventions and longer antibiotic treatment duration. The research was conducted according to the principles of the Declaration of Helsinki. Assigned written informed consent form was taken from all patients; one copy was delivered to patients.

OPERATION TECHNIQUES

All procedures were performed under general anaesthesia with the five different FURS devices (Karl Storz, Flex X2, Tuttlingen, Germany) by surgeons who have operation experience higher than 30 cases. After the placement of double 0.035-inch polytetrafluoroethylene-coated guidewire (Boston Scientific, Marlborough, Massachusetts, USA), Ureteral Access sheath (9.5/11.5 Fr, Cook Medical, Bloomington, Indiana, USA) was inserted over one of the guidewires with the C-arm fluoroscopy device. Unless the Access sheath insertion were done, co-axial insertion with flexible was tried. All patients were inserted 4.8/6, Fr Double J stent (Coloplast, Humlebæk, Denmark) for two and three weeks. The stone fragmentation had been done with Ho: Yag laser (273 µm fibres, Quanto system 30W Litho, Samarate (VA), Italy).

STATISTICAL METHODS

SPSS 21 (SPSS, Inc., Chicago, IL) Software was utilised for data analysis. Variables distributions were regarded as the Kolmogorov-Smirnov test ($p < 0,05$) and if it was found as a nonparametric; Quantitive variables were conducted using the Mann- Whitney U test. Independent T-test was used for a normal distribution. Qualitative data were analysed with the Chi-square test or Fisher Exact test. Logistic regression analysis was used to measure an odds ratio. Roc Curve was plotted to determine an absolute cut-off value and the predictive value of this point provided by Under Curve (AUC). Correlation analyses performed to define a relation between Total Stone Volume (TSV), SFR and confirmed by ROC curve.

RESULTS

Totally 164 procedural cases were regarded in this present study and 101 (61.6%) of them are male. The mean age was 43.6 ± 13.8 years and mean TSV was 364.6±295.9 mm^3. More than 50% of the patients have previous stone surgery history and stone sides were similar between the right and left kidney. Table 1 demonstrates the demographics, medical features of the patients and stone characteristics. Double J stent was inserted to all patients and ureteric access sheath was used in all cases except two cases because of the unsuccessful insertion attempt, the coaxial technique had been undergone.

TSV, operative outcomes were regarded to define a cut-off value. This analysis showed that thres-

TABLE 1: Demographic features of the patients and stone characteristics.

Groups	Number	Percentage	Mean±SD	Minumum	Maximum
Patient	64				
Age(years)m			43.6± 13.8	14	78
Gender					
Female	63	38.4			
Male	101	61.6			
BMI			27.8±5.9	18.7	48.9
Hypertension	37	22.6			
Diabetes	23	14			
Hyperlipidemia	19	11.6			
Previous Open Stone Su	23	14.5		1	4
Previous Endo Stone Sur	93	57.1		1	14
Stone Side (R/L)	83/81	50.6/49.4			
Preop Double J	57	34.8			
Stone count(number)			1.72	1	7
Stone volume (mm^3)			364.6±295.9	14.9	2269.3
Stone Density(HU)			1099.3±361.3	310	1890
Stone Location					
Upper pole	19	11.5			
Middle calycx	43	26.2			
Lower Pole	94	57.3			
Pelvis	55	33.5			
Proximal Ureter	6	3.6			

hold values for stone size: 330 mm^3, fluoroscopy time: 7 sec and operative time: 65 min. Roc Curve was plotted and AUC demonstrated the level of significance as a 0.743, 0.754, 0.731 respectively. Log regression analyses determined the odds ratio (3.1) to compare the success rates of groups (Figure 1).

Patients whose TSV beyond the threshold value (Group 1) operative time ($p<0.001$) and fluoroscopy time ($p<0.001$) significantly longer than the patients smaller than cut-off value (Group 2). The success rate of the operation was also remarkably higher ($p<0.001$) and complications were common in the Group 2 (TSV >330 mm^3). There were not any significant correlation with the hospitalisation time, stone density and TSV (Table 2).

High fever occurred in six patients and they were treated long-term anti-biotherapy conservatively (Clavien Grade 2). Serious complications such as Clavien grade 3a happened in the three patients. Ureteral perforation occurred, it was confirmed by retrograde pyelography and Double-J stent could not be inserted so; percutaneous nephrostomy tube was performed in these patients. The ureteral tissue came back to normal appearance after three weeks later controlled by ureterorenoscopy.

Ethical approval: All procedures performed in studies involving human participants were in accordance with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

DISCUSSION

Kidney stones prevalence was 8.8% and men were more affected compared with women. The prevalence has increased remarkably and demonstrated by the contemporary studies.[19] By the way, kidney stones, directly and indirectly, cost effective also may cause labour loss. Medical expenses, pharmacy utilizations and work-loss time related with the urinary stones have a tremendous impact on the healthcare costs.[20] Different studies were done to seek the economic burden of kidney stones. Pearle et al. mentioned that annual spending were more than 2 billion American dollars.[21] Therefore; healthcare providers and governments have tried to

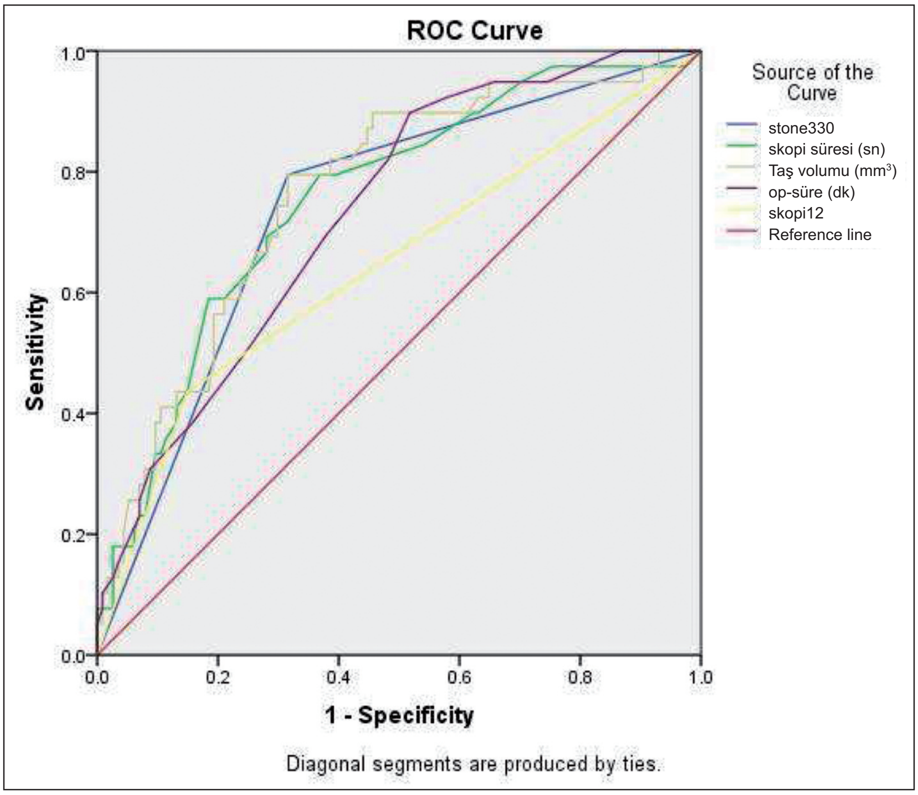

FIGURE 1: Roc Curves demonstrate the thresholds points and AUC.

TABLE 2: Procedures outcomes based on groups which classified on stone volume value.

	Group I (TSV <330 mm³)	Group II (TSV>330 mm³)	Overall	p
Stone-Free Rate	85 (91.4%)	39 (54.9%)		.000chi-fe
Hospitalization Time (Hour)	30.2±21.6	31.6±21.6	30.9±21.6	.411 mn
Operative Time (Min)	66.2±22.1	87.3±22.8	75.4±24.7	.000 it
Flouroscopy Time (Sec)	7.8±8.7	19.1±24.3	12.6±18	.000 mn
Stone Density (HU)	1059.2±357.3	1149.5±362.6	1099.3±361.3	.063 mn
Perioperative Complication				.073 chi
Clavien 2	4	2		
Clavien 3a	0	3		
	Coa (2-2.2%)	**Coa (1-1.4%)**	**Coa (3-1.8%)**	
Access Sheath	9.5 Fr (79-59%)	9.5 Fr (55-78%)	9.5 Fr (134-81.7%)	
Diameter (Fr)	11.5 Fr (11-13.6%)	11.5 Fr (13-18.3%)	11.5 Fr (24-14.6%)	
	14 Fr (1-1.7%)	14 Fr (2-2.8%)	14 Fr (3-1.8%)	

TSV: Total Stone Volume, Chi-fe: Chi-Square- Fisher exact test, MN: Mann-Whitney U test, it : Independent T-test, Coa: Co- axial Access.

define strategies to increase the cost-effectivity such as first prevention track.[22]

Endourological developments have widespread gained for last two decades; in parallel to the developments in medicine, technology and lifestyle changes, the prevalence of urinary stone and treatment expenses has risen.[23] Because of the enormous economic burden; urological societies established methods as efficient, safe, and low cost for kidney stone treatments. For instance; treatment recommendations related to the size of the stone. PNL >20 mm, shock wave lithotripsy (SWL)/FURS for stones <20 mm.[7] Treatment spendings vary from the surgeon's choice; Schoenthaler et al. Reported that endoscopes and disposable materials costs are significantly lower compared with the FURS for a medium size kidney stone.[24]

Determination of the treatment modality which is safest, cheapest, most efficient and what criteria should be considered as a priority is unknown. Stone size could be first parameters to define the way. All guideline recommendations based on the size of the stone as one dimension, however; stones are asymmetric and spherical bodies their volume predictions could be more accurate.[25] Volumetric measurement prevents the discordance of the stone size and interobserver variability. Therefore, it gives more certain aspects to approaching the renal stones. Although the guidelines maintain this accustomed inaccuracy; a few previous studies used a volumetric measurement to evaluate the kidney stone.[26] Ito et al. studied that larger stone volume prolonged the operative time.[27] Another research of the same group mentioned that stone volume is independent predictors of SFR.[28] Patel et al. recommend that stone volume measurement by NCCT could be used for surveillance of kidney stone.[29]

The target of the present study is to correct this discordance of our approach the kidney stone treatments. A few research had been done in this field such as; Ito et al. developed a nomogram to predict the SFR and they used a threshold value to classified the TSV 500 and 1000 mm^3.[14] Bandi et al. found that the TSV of < 500 μL was treated effectively by SWL of the solitary stones of the kidney.[12] Another study indicated that SWL is an effective treatment for 360 mm^3 volume kidney stones.[30] The risk of future symptomatic events increase the size of the asymptomatic kidney stone (79 mm^3-280 mm^3) was reported by Selby et al.[13]

Our study is naturally retrospective and enrolled relatively small patient number but has a several strengths points. Cut off volume measurement has not been reported yet to decide either FURS or PNL and it demonstrates strong relation with the outcomes. Definitive values were found on fluoroscopy and operative time to predict the SFR. Our work represents the priority in the literature with this aspects. High volume and validation studies should be done to increase the reliability of this value. It will be applicable and can change the guidelines.

In conclusion; TSV is the strongest factor to manage the kidney stone treatment. Beyond this threshold value prolongs operative, fluoroscopy time and increases the complications rates in FURS. So; to improve the SFRs and reduce the complications, other treatment modalities should be preferred.

Conflict of Interest

None of the authors declared any financial support.

Author Contrubutions

Idea/Concept: *Sinan Levent Kireççi;* ***Design:*** *Sinan Levent Kireççi;* ***Control/Supervision:*** *Cumhur Yeşildal;* ***Data Collection:*** *Musab İlgi;* ***Analysis and/or Interpretation:*** *Musab İlgi;* ***Literature Review:*** *Ayhan Dalkılıç;* ***Writing the Article:*** *Cumhur Yeşildal;* ***Critical Review:*** *Ayhan Dalkılıç;* ***References and Fundings:*** *Cemil Kutsal.*

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