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Is there a superiority of the stone volume measured in 3-D non-contrast tomography to the stone area in predicting the stone-freeness of the retrograde intrarenal surgery success?

Retrograd intrarenal cerrahinin taşsızlığını öngörmede üç boyutlu kontrastsız bilgisayarlı tomografi ile ölçülen taş volümünün taş alanına bir üstünlüğü var mıdır?

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Abstract
Purpose: To examine the predictive effect of preoperative stone volume (SV) against stone area (SA) on stone-free status (SF) following retrograde intrarenal surgery (RIRS).
Materials and methods: We retrospectively examined the medical records of 68 RIRS patients with renal calculi who were eligible. Patients having Non-Contrast Tomography (NCCT) before and subsequent to RIRS were included, however staghorn stones and inability to access were omitted. SF status was determined by the absence of visible stones on the NCCT three months after RIRS. Using a software reconstruction tool using 3-D NCCT, a radiologist determined stone load characteristics, such as SA and SV. Using a logistic regression model, the assessment of potential SF status determinants was conducted.
Results: Age, stone density, quantity and position of stones, usage of access sheath, failed prior SWL, and procedures were not substantially linked with non-SF status, however gender (p=0.014), SA (p=0.001), and SV (p=0.002) were strongly associated with non-SF status. The association between SV and SA was strong (r=0.866, p<0.001). A pairwise assessment of the ROC curves for SV and SA revealed no statistically significant difference in their specificities (p=0.274). Nevertheless, the multivariate analysis showed that SA was the sole independent predictor of SF status (p=0.001).
Conclusions: Both SA and SV were strongly suggestive of SF status after the RIRS. However, SA was only identified as an independent predictor of SF status after RIRS and as a sufficient predictor of SF status after RIRS.

Key words: Stone burden, 3-D measurement, lazer litotripsi, success treatment.

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Öz
Amaç: Retrograd intrarenal cerrahi (RIRC) sonrasında preoperatif taş volümü (TV) ve taş alanı (TA) ölçümlerinin taşsızlık durumu (TD) üzerine prediktif etkisini değerlendirmek.
Gereç ve yöntem: Böbrek taşları için RIRC yapılan, çalışma kriterlerine uygun 68 hastanın medikal kayıtlarını retrospektif olarak değerlendirdik. Operasyon öncesi ve sonrası kontrastsız bilgisayarlı tomografileri (KBT) olan hastalar çalışmaya dahil edilirken, sataghorn taşı olan ve taşa ulaşılamayan hastalar çalışma dışı bırakıldı. TD durumu RIRC operasyonu sonrasındaki 3. aydaki KBT'de görülebilir taş olmaması olarak tanımlandı. Bir radyolog 3 boyutlu KBT üzerindeki bir yazılım programı kullanarak TA ve TV gibi taş yükü karakteristiklerini tespit etti. Lojistik regresyon analizleri kullanılarak potansiyel TD tanımlayıcılarının değerlendirilmesi yapıldı.
Bulgular: TD ile taşın dansisitesi, lokalizasyonu ve sayısı, erişim kılıfı kullanımı, önceden geçirilmiş başarısız SWL ve operasyonlar ilişkili bulunmazken, cinsiyet, TA ve TV güçlü şekilde ilişkili bulundu (p=0,014), (p<0,001), ve (p=0,002), sırasıyla. TA ve TV'nin pairwise ROC eğri analizleri kıyaslandığında özgünlükleri açısından TD belirlemede aralarında istatistiki anlamlı bir fark olmadığı görüldü (p=0,274). Bununla birlikte, multivariate analizler SA'nın TD'yi belirlemede tek bağımsız prediktör olduğunu ortaya koydu (p=0,001).
Sonuç: Hem SA hem de SV RIRC operasyonu sonrasında TD'yi tahmin etmede fikir vericidir. Bununla birlikte SA, RIRC operasyonu sonrasında TD'yi bilmede tek bağımsız prediktördür ve tek başına yeterlidir.

Anahtar kelimeler: Taş yükü, 3 boyutlu ölçüm, lazer litotripsi, tedavi başarısı.

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Introduction

Pretreatment stone load is an independent determinant in patients receiving retrograde intrarenal surgery (RIRS) stone-free rates (SFRs) [1-4]. On plain X-ray, IVU, or non-contrast-enhanced CT (NCCT), the maximum stone length or stone surface area has historically been measured [5, 6].

European Association of Urology (EAU) suggests using maximum stone diameters to forecast stone load [7]. Due to the fact that kidney stones are irregular three-dimensional objects, two-dimensional measures may not be sufficient to accurately forecast stone load [8, 9]. EAU advises using a scalene ellipsoid formula to assess stone volume (SV). Recent research shown, however, that the scalene ellipsoid formula cannot offer an exact volume for all stones, since the typical shape of renal stones varies with diameter [10]. Using contemporary CT scanning tools, it is possible to precisely quantify the volume of a stone using 3D reconstruction [11]. Few studies have focused on this topic to yet, therefore it has not yet been conclusively determined [12, 13].

In the current research, we wanted to assess the prediction value of SV and stone area (SA) on SF status following RIRS using a specialized CT software reconstruction tool.

Materials and methods

Patients

We analyzed the medical records of 387 patients who had RIRS for renal calculi between October 2009 and January 2014 and recruited 68 individuals who met the inclusion criteria. Before and after RIRS, each patient was obliged to have a documented radiographic evaluation of the urinary tract by NCCT. Exclusion criteria included staghorn stones, inability to reach the site of the stones, and pediatric patients (less than 18 years of age). The demographic information, positioning of the access sheath, past SWLs and operations on the same side, as well as the quantity and location of the stones, were documented. A post-operative month 3 (POM 3) NCCT was used to classify patients as SF or non-SF. SF status was defined as the absence of any visible stone on the NCCT at POM 3.

Technique

Each patient had surgery under either general or spinal anesthesia. The standard lithotomy posture for patients was a modified combination Trendelenburg (head inclined about 20 degrees). During the procedures, a Storz Flex-XTM 2 (Karl Storz, Tuebingen, Germany, 7.5 F) flexible ureterorenoscope was used. Under endoscopic observation, the rigid ureterorenoscope was first introduced into the bladder. Through a working channel, a polytetrafluoroethylene-coated, 0.0035-inch guide wire was introduced into the ureter. Under the help of a guide wire, the rigid ureterorenoscope was inserted into the ureter. The second guide wire (sensitive, 0.0035 inch) was put into the other working channel of the ureterorenoscope after the ureterorenoscope was in the ureter. After removing the rigid ureterorenoscope, the access sheath was placed over the PTFE-coated guide wire. If it was difficult to insert the access sheath, the flexible ureterorenoscope was inserted without the access sheath. The visual picture was linked with the fluorescence image in order to enter the correct calyces. For lithotripsy, a 270-micron laser fiber was used. The holmium laser was calibrated at a rate of 10-25 Hz and an energy level of 0.5-0.8 joules. Stones were fractured until they were tiny enough (2 mm) to pass through the urinary system without difficulty. We implanted a 4.7 F ureteral double-j stent at the end of the procedures and withdrew it two weeks following RIRS.

Clinical and imaging evaluations

An expert radiologist reexamined the NCCTs to determine the number and location of kidney stones in the collecting system, as well as the SV, SA, and mean HU.

Statistical examination

The data were analyzed using SPSS (SPSS, Chicago, IL) and MedCalc (version 12.7.7) software. The Shapiro-Wilk test was performed to determine if variables were normally distributed.

The normally distributed variables are reported as mean standard deviation and compared using the Student's ttest. The non-normally distributed variables were given as median (minimum-maximum) and compared using Mann-Whitney U. ROC regression analysis was performed to evaluate the predictive abilities of age, mean HU, SV, and SA. The value of the threshold was established using the Youden Index. J. ROC curves for SV and SA were compared. Additionally, continuous data were presented as mean standard deviation (SD). To compare categorical variables provided as "n" or percentage (%), the Chi-Square Test and Fisher's Exact Test were used. Using the Spearman's rho test, the correlation between SA and SV was determined. We utilized a logistic regression model to undertake univariate and multivariate evaluation. All relevant factors were accounted for in the multivariate model (backward stepwise logistic regression method). All statistical tests were deemed significant if $p<0.05$. Chi-square tests and multivariate analysis using the Backward Stepwise Logistic Regression Method were used to identify determinants of stone-free status.

The quantity of stones was separated into two categories: solitary stones and stones with 2 sides. Lower pole, mid-pole+upper pole+renal pelvis, and multifocal stones are the three classifications of stone placement.

Results

Characteristics of patients and operative results

The average age was 51.73±13.70 (range: 18.0-80) years. There were 36 male patients (52.9%) and 32 female patients (47.1%). Lower pole, middle pole, upper pole, renal pelvis, and multifocal stone patients numbered 23, 10, 3, 17, and 15, respectively. The average total stone area and volume was 1.15 (min-max=0.28-5.89) cm^2 and 1.27 (min-max=0.32-9.35) cm^3, respectively. The average Hounsfield Unit value was 276.10±111.16 HU. The number of patients free of kidney stones was 54 (79%). The following metrics indicated significant differences between the SF and non-SF groups in favour of woman (p=0.014). Both SA and SV were associated with SF (p<0.001) and SV (p=0.002), respectively. Stone density, location and quantity of stones, age, past unsuccessful SWL, previous failed surgeries, and the use of an access sheath did not vary between the SF and non-SF groups. The background and treatment results are compared in Table 1 according to the stone status at POM3.

Correlation between two stone burden parameters

The Spearman's correlation test revealed that SA and SV are highly correlated (0.866 Spearman's rho) (p<0.001). This association was statistically significant (Figure 1).

Establishment of cutoff points

Area under the ROC curve (AUC) values for the SA and SV were 0.810 and 0.765, respectively (Figure 2).

Both stone load indicators were strongly predictive of SF at POM 3 (for SA p<0.001 and for SV p=0.001).

The ROC curves suggested that the SA and SV cutoff thresholds were 1.84 cm^2 and 1.650 cm^3, respectively. For SA, sensitivity was 85.19 (95% confidence interval: 72.9-93.4) and specificity was 71.43 (95% confidence interval: 41.9-91.6). For SV, the sensitivity was 75.93 (95% confidence interval: 62.4-86.5) and the specificity was 71.43 (95% confidence interval: 41.4-91.6). A pairwise assessment of the ROC curves for SA and SV revealed no statistically significant difference in their specificities (p=0.274). The AUC value for age was 0.689% (p=0.027), while the age cutoff value was 38 years. It had a sensitivity of 90.74 (95% confidence interval [CI]:79.7-96.9) and a specificity of 42.86 (95% CI:17.7-71.1). Also suggestive of SF status at POM 3 was not age.

Multivariate analysis of SF status predictors

Our univariate analysis revealed that the SA (p<0.001), SV (p=0.002), and gender (p=0.014) were significantly linked with non-SF at POM3.

In our backward stepwise logistic regression model, we kept the age and SA parameters. However, the SA was only an independent predictor of SF status (p=0.001) OR=12.68 (95% CI=2.933-54.825). The findings of univariate and multivariate analyses are summarized in Table 2.

Table 1. Comparison of patient and stone data between cases with stone-free and non-stone-free at postoperative month 3 after RIRS

	SF at POM3 (n=54)	Non – SF at POM 3 (n=14)	*p*
Age (years)	51.66±14.04	52.00±12.79	0.936[a]
≤38	9 (81.8%)	2 (18.2%)	1.000[b]
>38	45 (78.9%)	12 (21.1%)	
Gender			
Male	24 (66.7%)	12 (33.3%)	0.014[b]
Female	30 (93.8%)	2 (6.3%)	
Number of stones			
1	38 (86.4%)	6 (13.6%)	0.054[b]
≥2	14 (63.6%)	8 (36.4%)	
Renal stone location			
Lower pole	17 (73.9%)	6 (26.1%)	0.121[b]
Mid-pole, Upper pole, Renal pelvis	27 (90.0%)	3 (10.0%)	
Multiple location	10 (66.7%)	5 (33.3%)	
Stone Burden (Cumulative)			
Area (cm^2)	0.97 (0.28-4.76)	2.12 (0.78-5.89)	<0.001[c]
≤1.84 cm^2	46 (92%)	4 (8%)	<0.001[b]
>1.84 cm^2	8 (44.4%)	10 (55.6)	
Volume (cm^3)	1.150 (0.032-8.090)	2.895 (0.720-9.350)	0.002[c]
≤1.650 cm^3	41 (91.1%)	4 (8.9%)	0.001[b]
>1.650 cm^3	13 (56.5%)	10 (43.5%)	
Stone Density (Mean Hounsfield Unit)	272.83±113.32	288.71±105.43	0.637[a]
Use of access sheath			0.523[b]
Need	35 (76.1%)	11 (23.9%)	
No need	19 (86.4%)	3 (13.6%)	
Failed previous SWL			0.584[b]
Yes	24 (75%)	8 (25%)	
No	30 (83.3%)	6 (16.7%)	
Failed previous operations			0.758[b]
Yes	17 (77.3%)	5 (22.7%)	
No	37 (80.4%)	9 (19.6%)	

[a] Independent Samples test, [b] Chi-square test [c] Mann-Whitney U test
SF=Stone-free; POM=Postoperative month; SWL=Shock-wave lithotripsy

Table 2. Univariate and multivariate analysis of stone status after RIRS

Parameter	Category	Non-SF rate	Univariate *p*	Multivariate *p*	OR	95% CI
Age (years)	>38 ≤38	21.1% 18.2%	1.000	-	-	-
Gender	Female* Male	6.3% 33.3%	0.014	0.063	_	_
Number of stones	1 ≥2	13.6% 36.4%	0.054	-	_	_
Area (cm^2) (cumulative)	≤1.84 * >1.84	8% 55.6%	<0.001	0.001	12.68	2.93-54.83
Volume (cm^3) (cumulative)	≤1.650 * >1.650	8.9% 43.5%	0.003	_	_	_

Model significancy; $p<0.001$ (Omnibus Tests of Model Coefficients) for Hosmer and Lemeshow Test $p=0.326$ *reference value

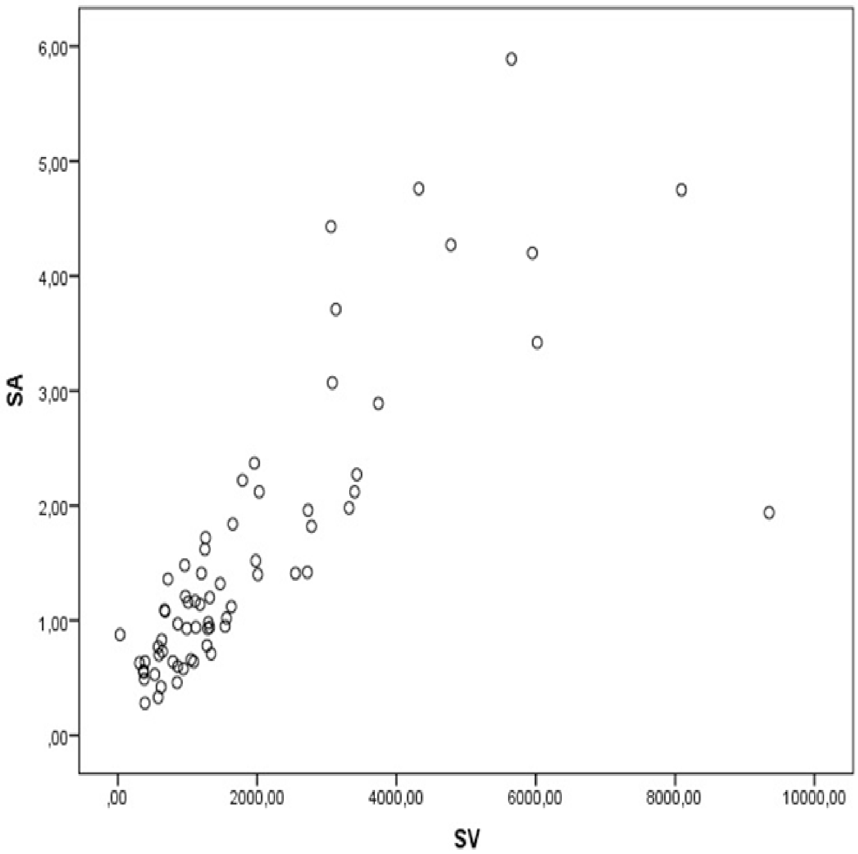

Figure 1. Scatter diagram for stone volume and stone area

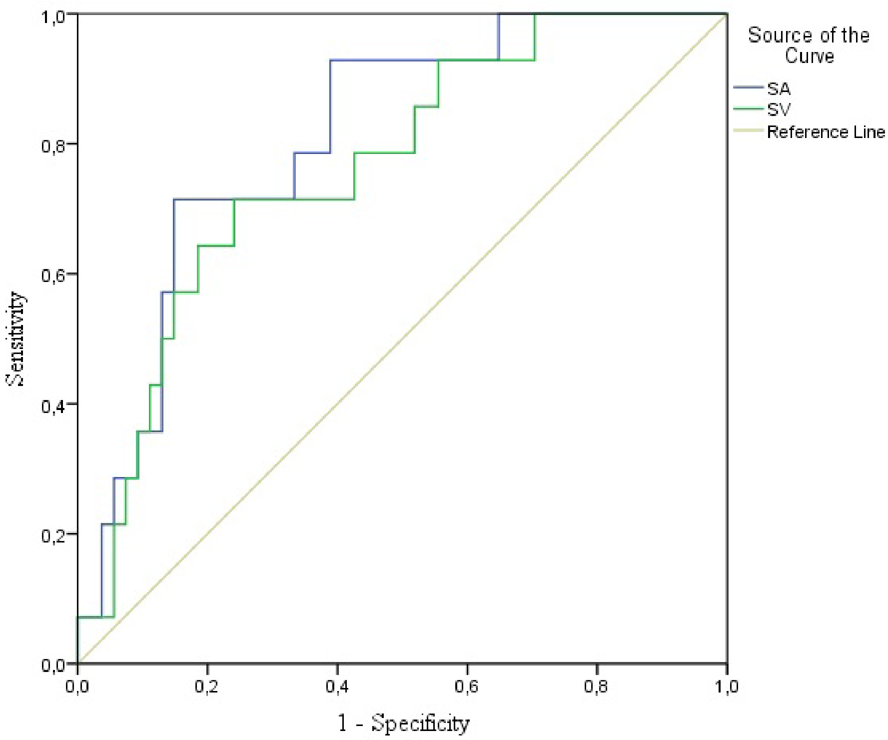

Figure 2. ROC curves of Stone area and stone volume for predicting stone-free stat

Discussion

In this work, we examined the importance and value of SV in predicting SF status after RIRS. The SA was computed by multiplying the longest dimension of the stone in axial plan by its perpendicular dimension in 3D NCCT. On 3D-NCCT, the SV was assessed using software intended to quantify tissue density within a certain range inside a defined area of interest. As a result, we hypothesized that the SV may be superior than the SA in predicting SF status for the reasons stated above, and that there may be high correlations between these stone load metrics. Our Spearmen test demonstrated high connections between SA and SV, as anticipated. In univariate analysis, SV was identified as a clinical predictor of SF status, although suggesting a lower value of predictability for SF status than SA. In addition, a pairwise assessment of the ROC curves of SA and SV revealed that their specificities for predicting stone status following RIRS were not significantly different. However, the SA outperformed the SV in predicting non-SF status after RIRS. Our multivariate backward logistic regression analysis demonstrated, however, that only SA is an independent predictor of SF status after RIRS. SV as determined by NCCT, is the most accurate predictor of SF status after extracorporeal shock wave lithotripsy (ESWL) [8, 9]. In addition, the SV was revealed to be an independent predictor of SF status following RIRS [1, 4, 13]. Thus, our findings seemed to vary from those of previously published research. However, SA has also been demonstrated to be prognostic of SF status following RIRS and linked well with SV [1, 4]. In these experiments, SA was estimated using KUB films and SV using NCCT. They discovered a significant relationship between SA and SV. Based on what we discovered and what others have indicated, SA as assessed by KUB films may be sufficient to determine SF status after RIRS.

Our ROC analysis determined that the SA cutoff value is 1.84 cm^2. This cutoff value predicted SF status with great sensitivity and specificity. According to a recent research, this figure for the predicted stone area is 1.25 cm^2 [1]. According to a previous research by the same authors, the traced stone area is 1.50 cm^2 [4]. We determined the SV threshold to be 1.650 cm^3. Previous research has indicated values between 0.84 cm^3 and 1.120 cm^3 [1, 4]. These thresholds were not comparable to ours. In addition, we can report that the imaging modalities, assessment methodology, and characterization of SF status vary amongst investigations.

In our investigation, we discovered that the SF rate after RIRS was somewhat greater in solitary stones than in non-solitary stones (p=0.054), but was not a predictor of SF status on its own. This data revealed that stone load had a far greater effect on SF status after RIRS than stone count. Our result was consistent with earlier findings [1, 4].

After RIRS, we determined that the location of the stone was not statistically significant for SF status. EAU standards identify lower pole stone as an adverse criterion for SF status [14]. We eliminated patients whose stones could not be accessible in order to prevent our findings from being corrupted by theirs, since we were interested in the effect of SV on the SF status of RIRS. According to us, this may have been the reason why we were unable to determine its effect on SF status after RIRS.

This research has significant limitations. Due to the retrospective nature of the study, confounding variables and measurement bias cannot be addressed to the same extent as in prospective randomized research. Another limitation was that this research only included findings from a single institution. Reviewing the relevant literature, we can state that published data regarding the imaging modalities, measuring methodology, and characterization of SF status are heterogeneous. Thus, further homogenous research from many sites are required.

In conclusions, SA was a predictor independent of SF status after RIRS. SV was strongly suggestive of SF status after RIRS, but it was not a predictor of SF status on its own. These predictors of SF status have cutoff values of 1.84 cm^2 for SA and 1.650 cm^3 for SV. These cutoff points may aid doctors in predicting the state of SF after RIRS. With the exception of stone load measures, the quantity of stones was not predictive of SF status. Based on prior publications and our results, it is possible that the SA evaluated by KUB films is sufficient to predict SF status in clinical practice.

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

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Ethics committee approval: The study was conducted without ethics commission approval because it was conducted before the years of 2020.

Authors' contributions to the article

H.K. have constructed/constructed the main idea and hypothesis of the study. Y.K., E.O. and B.C. developed the theory and arranged/edited the material and method section. B.C. and Y.K. have done the evaluation of the data in the Results section. Discussion section of the article written by Y.K. and H.K who also reviewed, corrected and approved. In addition, all authors discussed the entire study and approved the final version.