3D voluminometry of urolithiasis as a predictor of success in ureterorenoscopic (URS) treatment

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Abstract Stone burden is a predictor of stone free rate (SFR) after ureterorenoscopy (URS). 2D measurements (X-Ray/CT) may unreliable predict actual stone burden. This study was performed to evaluate 3D measurements as a predictor of SFR after URS compared to 2D measurements. A retrospective study (2008–2019) was performed on patients with a single stone and preoperative CT-scans. Stone size was assessed by three conventional 2D methods and an automated 3D measurement. Primary outcome was SFR after four weeks. Secondary outcomes involved the need for subsequent procedure and complications. 227 patients were included, SFR was 74.9%. 3D measurement correlated significantly with SFR (OR: 0.980). Unfortunately, no predictive value was observed. 3D measurement demonstrated a significant correlation to complications (OR: 0.966). Low interobserver variability (0.891 vs 0.782 respectively) was found in the 2D and 3D measurements. It was concluded that, although 3D voluminometry correlates significantly to SFR and complications, these approach harbors no predictive value.

Keywords 2D measurement · Stone burden · Stone free · Kidney stone · Ureter stone · Volume

3D-metingen voor nierstenen als voorspeller van succes bij ureterorenoscopische (URS) behandelingen

Samenvatting ‘Steenload’ is een voorspeller voor steenvrij-status na ureterorenoscopie (URS). Huidige 2D-metingen (X-BOZ/CT-scan) bepalen onnauwkeurig de daadwerkelijke steenload. Deze studie werd uitgevoerd om te bepalen of 3D-metingen een betere voorspeller zijn voor het steenvrij zijn na URS vergeleken met 2D-metingen. Er werd een retrospec-tieve studie (2008–2019) uitgevoerd met patiënten met een enkele uretersteen en een peroperatieve CT-scan. Grootte van de steen werd bepaald aan de hand van drie gebruikelijke meetmethoden (2D) en een geautomatiseerde 3D-meting. Primaire uitkomst was steenvrij na vier weken. Secundaire uitkomsten waren de noodzaak van een tweede procedure, en complicaties. 227 patiënten werden geïncludeerd, 74,9% was steenvrij na URS. 3D-metingen correleerden significatief met steenvrij (OR 0,980) en complicaties (OR 0,966). Helaas kon geen voorspellende waarde worden bepaald. Tussen de 2D- en 3D-metingen werd een lage interobserver variabiliteit (0,891 vs. 0,782) gevonden. Geconcludeerd werd dat, hoewel 3D-metingen correleren met een steenvrij-status en complicaties, deze metingen vooral nog geen voorspellende waarde hebben.

Trefwoorden 2D-metingen · Steenload · Steenvrij · Niersteen · Uretersteen · Volume

Introduction

Kidney stones are well known for their acute colic pain and is frequently paired with fever and/or renal function deterioration. The lifetime incidence of symptomatic urolithiasis is estimated to be between
2% and 15% in the Western population [1, 2]. Up to 80% of the patients with urolithiasis pass their stone spontaneously with or without the use of analgesics or medical expulsive therapy (MET) when stones are less than 4 mm [3]. All other patients are more likely to receive active treatment. The size, position, shape of the stone and patient characteristics at presentation are factors that influence treatment decisions [4, 5]. Unfortunately, not all stones can be removed during one surgical procedure. A well-known important factor that plays a role in the success (complete removal of all stones) after active treatment is the size of the stones or so-called stone burden. In daily practice, size is measured by several two-dimensional (2D) methods such as the longest stone axis, mean stone axis or stone surface area (length × width) on non-contrast enhanced CT-scan or abdominal X-ray [2, 6].

Since urolithiasis are irregular three-dimensional (3D) structures that often have different geometric shapes, 2D measurements may inaccurately predict stone volume and not reflect the actual total stone burden [5, 7]. Some studies have investigated 3D measurements of urolithiasis to predict spontaneous passage and outcomes of treatment after Shockwave Lithotripsy (SWL). They showed 3D measurements to be a clinically significant independent predictor of success [8–11]. Regarding ureterorenoscopy (URS), reports have been published that indicate the potential use of 3D measurements [10, 12]. So far, for percutaneous treatment no advantage has been found of 3D measurements on treatment outcome [13].

This study was designed to investigate if automated 3D volume measurements have a higher predictive value of stone-free rates (SFR) after URS compared to conventional 2D measurements. Secondary outcomes include complications and need for secondary procedure. Our goal is to introduce a potential pretreatment tool for counseling urolithiasis patients about their chance of stone-free status after URS and the potential need for a secondary procedure or the occurrence of complications.

Methods

For this retrospective study, we identified patients who were treated by ureterorenoscopy (URS) for urolithiasis from April 2008 to October 2019 at the Canisius Wilhelmina Hospital Nijmegen, the Netherlands. Criteria for inclusion were: age > 18 years and single (clinically relevant) stone diagnosed by CT-scan. Patients with multiple stones, obscure stones and no available preoperative CT-scans were excluded from the study. Our institutional review board approved this study and the need for signed informed consent was waived (ref. 035-2020).

Preoperative, peroperative and postoperative characteristics of all patients were recorded and saved in a database (CastorEDC). Preoperative characteristics included age, sex, stone position, stone side, stone density, renal function and mean size of the stone. Stone position was classified as ureteral (proximal or distal) or renal (upper-, mid-, lower pole, pelvis). Urinary position was based on stone position above (proximal) or below (distal) the iliac vessels.

Perioperative characteristics involved the use of a semi-rigid or flexible ureterorenoscope. For proximal and renal stones a reusable Olympus Flex URF-V3 or a disposable PUSEN ureterorenoscope was used and when needed, an ureteral access sheath was applied. An Olympus semi-rigid ureterorenoscope was used for distal/proximal ureteral stones [12]. Postoperative characteristics were stone-free status, complications, mean stone density and need for second surgery. Stone-free status was considered if no identifiable stone was present after the URS procedure determined by the operating urologist or confirmed by CT-scan 4 weeks postoperatively (mainly assessed by urologist).

Stone measurement

All measurements were performed on a non-contrast CT-abdomen. All CT-images were examined on the axial reconstruction with 1.5 mm slice thickness. The maximum height (longest axis, LA) and width of the stones in mm were measured manually and were recorded in the database. The mean stone diameter (AvgA) was calculated by summing up height and width, divided by two. Based on the manual measurements of the mean stone diameter in mm, we calculated an ‘expected volume’ using the formula for spheres: $V = \frac{4}{3}\pi r^3 \text{ (in mm}^3\text{)}$ [14].

For 3D measurements we applied an automated measurement tool from the Philips Intellispace Portal 8.0 (2015, Amsterdam, The Netherlands). These measurements were applied on the same CT-images and same slices (axial view) where urolithiasis have been recorded in the manually measured (2D) volume. This tool calculates volume based on voxel size of a selected segment.

Interobserver variability

To explore if the measurements in this study are performed accurately and reliably, we also tested the interobserver variability. A subset of 30 patients were randomly selected for this test. The measurements were performed by a team of three observers: an abdominal radiologist, an endo-urologist and a student-researcher. Slice numbers of the CT-scan in which the urolithiasis were detected, have been given separately to the observers in order to prevent applying measurements on inequivalent stones (in the case of existing irrelevant multiple stones). All measurements were collected and saved in the Castor database.
**Statistical analysis**

All analyses were performed with SPSS software version 25.0 (IBM Corp.). To compare the continuous and categorical variables between the stone free and residual stone patients we applied the Mann-Whitney-U Test and an Independent T-samples Test for continuous variables; Pearson’s chi-squared test and Fisher’s exact test for categorical variables. We decided to use Mann-Whitney-U Test instead of the regular t-test due to the absence of normally distributed data in the four size measurement methods. The different volume measurement methods, manual (2D) vs automated volume (3D), were compared by a paired sample t-test. A multivariate logistic regression analysis was performed to determine the correlation of stone-free status (primary outcome), complications and need for secondary procedure (secondary outcomes) for the four different measurement methods. Other variables that may independently contribute to stone-free status, such as the mean stone density (HU), the procedure (URS) type and the stone position were accounted for. Predictive accuracy for primary and secondary outcomes of each of the stone size measurement methods was assessed by using receiver operating characteristic (ROC) analysis. A $p$-value < 0.05 was considered to indicate statistically significant results in all analyses. Interobserver variability was evaluated by interrater correlations calculated via the Intraclass Correlation Coefficient (ICC), applying the Two Way Mixed model attaining an Absolute Agreement between the three observers.

**Results**

A total of 227 patients met the inclusion criteria (Tab. 1). The mean age was 50.6 years and 63.9% were men. Stones were overall located in the kidney (26%) or ureter (74%). 170 patients (74.9%) were classified as stone free. Type of URS, semi rigid or flexible, were equally used for the procedures. Stone size measurements (2D and 3D), stone position, and type of URS procedure appeared to be significantly different in the SF-group compared to the group that had residual stones. Complications such as pain, infection, discomfort by JJ catheter, hematuria and urine retention were only found in 12.3% of the cases. A secondary procedure was needed in 20.1% of all patients.

**Stone measurement**

The respective median values for longest axis, mean axis, 2D volume and 3D volume were 6.0 mm, 5.0 mm, 65.5 mm³ and 117.0 mm³. The difference between the SF- and RS-group in stone size measurements were respectively 6.0 mm vs 7.0 mm (LA, $p = 0.017$), 5.0 mm vs 6.0 mm (AvgA, $p = 0.018$), 65.5 mm³ vs 113.1 mm³ (2D, 3D volumetry of urolithiasis as a predictor of success in URS treatment)

| Variable                  | Total       | Stone-free status (SFS) | Residual stone (RS) | $p$-value |
|---------------------------|-------------|-------------------------|---------------------|-----------|
| n                         | 227         | 170 (74.9%)             | 57 (25.1%)          | 0.607     |
| Age                       | 50.6 ± 13.8 | 50.9 ± 14.5             | 49.8 ± 11.6         | 0.607     |
| Gender                    |             |                         |                     | 0.875     |
| – Male                    | 145 (63.9%) | 108 (74.5%)             | 37 (25.5%)          |           |
| – Female                  | 82 (36.1%)  | 62 (75.6%)              | 20 (24.4%)          |           |
| Stone position            |             |                         |                     | 0.018     |
| – Distal                  | 75 (33.0%)  | 64 (85.3%)              | 11 (14.7%)          |           |
| – Proximal                | 93 (41.0%)  | 72 (77.4%)              | 21 (22.6%)          |           |
| Ureteral                  |             |                         |                     |           |
| – Pelvis                  | 23 (10.1%)  | 12 (52.2%)              | 11 (47.8%)          |           |
| – Lower pole              | 25 (11.0%)  | 16 (64.0%)              | 9 (36.0%)           |           |
| – Middle pole             | 6 (2.6%)    | 3 (50.0%)               | 3 (50.0%)           |           |
| – Upper pole              | 5 (2.2%)    | 3 (60.0%)               | 2 (40.0%)           |           |
| Renal                     |             |                         |                     | 0.002     |
| – Semi rigid              | 99 (43.6%)  | 83 (83.8%)              | 16 (16.2%)          |           |
| – Flexible                | 101 (44.5%) | 64 (63.4%)              | 37 (36.6%)          |           |
| – Not defined             | 27 (11.9%)  | 23 (85.2%)              | 4 (14.8%)           |           |
| Manual 2D, mm³            | 65.5 (33.5–179.6) | 65.5 (33.5–143.8) | 113.1 (47.7–268.1) | 0.019     |
| Automated 3D by ISP, mm³  | 117.0 (55.0–235.0) | 111.0 (53.0–210.0) | 160.0 (75.0–352.0) | 0.013     |
| Long axis, mm             | 6.0 (4.0–8.0) | 6.0 (4.0–8.0)     | 7.0 (5.0–9.0)      | 0.017     |
| Mean size, mm             | 5.0 (4.0–7.0) | 5.0 (4.0–6.5)     | 6.0 (4.5–8.0)      | 0.018     |
| Mean stone density, HU    | 1145.2 ± 255.8 | 1178.3 ± 266.7   | 1156.7 ± 219.1    | 0.255     |

**Table 1** Pre-, peri- and postoperative patient characteristics between the SF and RS group

$bold = significant finding$
Patients had a mean stone density of 639.5 Hounsfield Unit (HU). The automated 3D volume measurement was found to be significantly higher than the manual 2D volume measurement (117.0 [55.0–235.0] mm\(^3\) vs 65.5 [33.5–179.6] mm\(^3\); \(p \leq 0.001\)). Multivariate logistic regression analysis of the four stone size assessment methods (LA, AvgA, 2D volume, 3D volume respectively), accounting for stone position, was performed (Tab. 2 and 3; in the electronic supplementary material (ESM) Tab. 1 and 2). Regarding all four methods, stones located in the distal ureter are statistically significantly more likely to be successfully treated.

For the primary outcome, stone free after four weeks, only automated 3D volume measurement (OR 0.980, 95% CI: 0.967–0.994, \(p = 0.006\)) was statistically significantly correlated. ROC curve analysis for stone-free status (SFS) at four weeks postoperatively (Fig. 1a), showed no difference in AUC values (AUC = 0.605, 0.605, 0.604, 0.610 respectively) for the four measurements.

For the secondary outcomes, the need for secondary procedure and complications, none of the measurements is considered as an independent factor (Tab. 2 and 3; ESM Tab. 1 and 2). All the different measurement methods seem to have close similar accuracy in predicting the need for secondary procedure (Fig. 1b), respectively AUC = 0.580 (LA), 0.587(AvgA), 0.589 (2D) and 0.602 (3D). The AUC did not reveal any statistically significant differences.

Regarding complications after URS, automated 3D voluminometry was found to be a statistically significant correlator (OR 0.996, CI: 0.934–0.999, \(p = 0.044\)). Position of the stone did not have an

**Table 2** Logistic regression analysis on the effect of the longest stone axis (LA) measurement on stone-free-status four weeks after URS, need for secondary procedure and the occurrence of complications, accounted for stone position

| Predictor                  | SFS 4 weeks post URS | Secondary procedure | Complications |
|----------------------------|----------------------|---------------------|--------------|
|                            | OR (95% CI)          | \(p\)               | OR (95% CI)  | \(p\)       | OR (95% CI)  | \(p\)       |
| Longest stone axis, mm     | 0.918 (0.824–1.023)  | 0.123               | 1.026 (0.913–1.153) | 0.666        | 0.890 (0.759–1.043) | 0.149        |
| Position                   |                      |                     |              |             |              |             |
| – Distal                   | 3.165 (1.444–6.939)  | \(0.004\)           | 0.306 (0.129–0.724) | \(0.007\)   | 0.415 (0.151–1.140) | 0.088        |
| – Proximal                 | 2.011 (0.907–4.460)  | 0.086               | 0.628 (0.274–1.439) | 0.272        | 0.532 (0.189–1.501) | 0.233        |
| – Renal                    | 1.0 (ref)            | 1.0 (ref)           | 1.0 (ref)    |             |              |             |

\(p\)-value < 0.05 is considered statistically significant

CI confidence interval, OR Odds Ratio, ref reference category, SFS stone-free status

**Table 3** Logistic regression analysis on the effect of the automated (3D) volumenmeasurement on stone-free-status four weeks after URS, need for secondary procedure and the occurrence of complications, accounted for stone position

| Predictor                  | SFS 4 weeks post URS | Secondary procedure | Complications |
|----------------------------|----------------------|---------------------|--------------|
|                            | OR (95% CI)          | \(p\)               | OR (95% CI)  | \(p\)       | OR (95% CI)  | \(p\)       |
| Automated volume 3D, per 10 mm\(^3\) | 0.980 (0.967–0.994)  | \(0.006\)           | 1.010 (0.997–1.023) | 0.137        | 0.986 (0.934–0.999) | \(0.044\)    |
| Position                   |                      |                     |              |             |              |             |
| – Distal                   | 2.965 (1.365–6.439)  | \(0.006\)           | 0.366 (0.144–0.780) | \(0.011\)   | 0.379 (0.140–1.022) | 0.055        |
| – Proximal                 | 1.924 (0.871–4.251)  | 0.106               | 0.679 (0.300–1.534) | 0.352        | 0.497 (0.177–1.398) | 0.185        |
| – Renal                    | 1.0 (ref)            | 1.0 (ref)           | 1.0 (ref)    |             |              |             |

\(p\)-value < 0.05 is considered statistically significant

CI confidence interval, OR Odds Ratio, ref reference category, SFS stone-free status

Fig. 1 Receiver Operating Characteristic (ROC) curve analysis of stone-free status (a), need for secondary procedure (b) and complications occurring (c) for all four measuring methods
influence on the occurrence of complications. The AUC reported no statistically significant differences (Fig. 1c).

In Tab. 4 the SFR, need for secondary procedure and the occurrence of complications were correlated to three stone size categories (<200, 200–400, >400 mm³) when using a 3D volume measurement and a 2D volume measurement. Patients with stones >400 mm³ had a significant lower chance of achieving stone-free status.

**Interobserver variability**

For assessment of the interobserver variability, we randomly selected 30 patients, performed the measurements by three independent observers and calculated the Intraclass Correlation Coefficient (ICC). An intrerrater correlation of 0.891 vs 0.782 respectively in the manual vs automated volume measurement method was attained in this analysis (Tab. 5).

**Discussion**

Urolithiasis are 3D structures that can adopt complex geometric shapes. Stone size is typically assessed by measuring the longest stone axis, mean stone axis or surface area (which are considered as 2D measurements) on a plain abdominal CT-scan. Measuring one axis or a surface area fails to provide exact volumetric information since it is limited by the inability to measure the second or third dimension [9, 15]. It is known that success of surgical treatment (stone free) for urolithiasis depends on the actual size of the stone. A 3D measurement could possibly provide a better representation about the actual stone size (stone burden). This study was designed to investigate and validate if automated software-based 3D voluminometry of urolithiasis has a better predictive value for stone-free status after URS compared to conventional 2D measurements.

We found that automated 3D voluminometry predicts complications and SFS better than 2D measurements. Stone position, procedure type and mean stone density did not influence the results regarding complications. Our data showed that small stones (<400 mm³) indicate a higher chance of success compared to large stone (>400 mm³). Although the correlation of 3D measurements with SFS and complications, the predictive accuracy between the four methods was not significantly different (Fig. 1). Based on the logistic regression models and ROC curves, an actual clinical benefit for automated 3D volume measurement, could not be determined. Only one study has explored the predictive value of automated 3D volume on SFS after percutaneous nephrolithotomy (PCNL) and found similar results [13].

To our knowledge, our cohort is the largest used to explore the value of 3D voluminometry as a predictor of success after URS treatment of urolithiasis. Nevertheless, it is a retrospective study that included a small heterogeneous group of patients from one institute with renal and ureteral single stones. Another bias in our study is that stone treatment during URS was performed by individual surgeons preferences and patient characteristics. In our institute we used a low power Holmium laser, but settings and technique (dusting or fragmenting) differed. All these settings could affect the effectiveness of the treatment [16]. Unfortunately, because of our study design, this data could not be retrieved. A larger prospective multi-institutional trial could reveal more reliable correlations of 3D measurements with the outcomes after URS [9]. Furthermore, in our clinic, we evaluate SFS on plain CT-abdomen four weeks postoperatively or by visual control during surgery. Unfortunately this latter clinical observation does not correlate with actual SFS when assessed by radiographic studies [17]. Other studies have shown that residual stone
fragments could also pass spontaneously in many patients even after four weeks. A postoperative CT after 12 weeks could provide a higher chance of SFS [10]. In this study, only patients with a single stone were included. Although a majority of patients that present themselves in our clinic have a single stone, a large group has multiple stones. For now it remains unclear if there is a clinical benefit of pre-operative 3D voluminometry in this group of patients.

For this study we applied 3D reconstruction software from the Philips Intellispace Portal. This software was used because it was already available in our hospital and has been applied in several clinical domains. So far, no studies have examined the use in analyzing urolithiasis [18]. Future software updates, more specifically adjusted to evaluation of urolithiasis, could improve the efficiency and accuracy of stone volume measurement [19]. Unfortunately, medical centers use different types of software for reviewing radiological images. Therefore, it is difficult to extrapolate our results to other hospitals. Ideally, a tool should be developed that can be applied on all different types of software.

We assume 3D stone voluminometry to be an easily obtainable measurement that could represent actual stone burden for all urolithiasis patients. A trained observer (radiologist or urologist) requires less than two minutes to assess the stone volume in the Intellispace Portal in case of a single stone [9]. Nevertheless, there are some significant shortcomings for 3D stone volume assessment. In case of multiple stones, which is related to lower SFR, radiologist will need more time to assess total stone volume. In daily practice, urologists can determine the clinical relevance of multiple stones better than a radiologist. Therefore, the clinical implication for urologists could possibly not be as high as described in previous studies [20, 21].

When the measurement of stone size is essential in treatment decision and success rates, the reproducibility of stone size measurements (interobserver variability) are also important [19]. The results in this study, demonstrated low variabilities and a high reproducibility values (ICC 0.891 vs 0.782) between observers. According to our findings, we can conclude that the automated volume measurement is reliable and reproducible [19].

Although 3D-stone voluminometry correlates significantly better to SFS and the occurrence of complications, it harbors no predictive value. Automated volume assessment of urolithiasis is easily performed and highly reproducible. More studies need to be performed to fully elucidate the potential of 3D-measurements regarding success rates after URS and other surgical treatments for urolithiasis.

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