JOURNAL OF ENDOUROLOGY
Volume 33, Number 9, September 2019

Pp. 742–749
DOI: 10.1089/end.2019.0130



# The Impact of Stone Multiplicity on Surgical Decisions for Patients with Large Stone Burden: Results from ReSKU

Samuel Zetumer, BA,[1] Scott Wiener, MD,[2] David B. Bayne, MD,[2] Manuel Armas-Phan, BS,[1]
Samuel L. Washington III, MD,[2] David T. Tzou, MD,[3] Marshall Stoller, MD,[2] and Thomas Chi, MD[2]

## Abstract

***Introduction:*** American Urological Association (AUA) guidelines recommend percutaneous nephrolithotomy (PCNL) for total stone burden greater than 20 mm, yet it is unclear if the number of stones affects adherence to this guideline. We aim to assess the impact of stone multiplicity on the choice of ureteroscopy (URS) *vs* PCNL as a first-line therapy for patients with high burden (>20 mm), and examine whether the AUA guideline-discordant care impacts patient outcomes.
***Materials and Methods:*** Data were collected from the Registry for Stones of the Kidney and Ureter (ReSKU) database, a prospectively collected registry of patients with stone disease. Multivariate logistic regression (MLR) was used to estimate the association between stone multiplicity and the decision to perform URS for high stone burden (>20 mm) patients. MLR was further used to estimate the association between performing URS and the following outcomes: stone-free rate, need for a second operation, and complications. Postoperative hospital stay was compared between patients receiving URS *vs* PCNL using Student's *t*-test.
***Results:*** One hundred twenty-five patients were included in this analysis. For patients with total stone burden exceeding 20 mm, those with more than three stones had roughly nine times the likelihood of undergoing URS over PCNL compared with patients with a single stone (adjusted odds ratio 9.21, confidence interval [95% CI] 2.55–40.58, $p = 0.001$). Stone-free rates, Clavien–Dindo scores, and frequency of second-look operations did not differ significantly between URS and PCNL patients. URS patients were discharged an average of 1.26 days earlier than patients who received PCNL (95% CI 0.72–1.81, $p < 0.001$).
***Discussion:*** Stone multiplicity strongly predicts which patients with stone burden >20 mm will undergo URS and who will undergo PCNL. These deviations from AUA guidelines do not appear to worsen patient outcomes. These results suggest that careful consideration of each patient may warrant deviation from guidelines.

**Keywords:** kidney stone, kidney calculi, renal stone, cumulative stone diameter, stone multiplicity, ureteroscopy, percutaneous nephrolithotomy

## Introduction

One in 11 Americans will be diagnosed with nephrolithiasis, and an estimated 25% of patients diagnosed with nephrolithiasis will receive surgical management at least once during their lifetime.[1] For large stone burdens greater than 20 mm, the American Urological Association (AUA) guidelines recommend percutaneous nephrolithotomy (PCNL) as first-line therapy.[2] However, many tertiary stone centers report safe outcomes treating some patients who have large stone burdens with ureteroscopy (URS) instead.[3–5] It's unclear how stone multiplicity, that is, the number of stones in the affected renal unit, influences deviations from AUA-concordant care.

While the factors that push urologists toward one operation or another are not well characterized, stone multiplicity arises as an important factor in other contexts. For example, stone multiplicity has previously been shown to independently predict lower postoperative stone-free rate after both URS and PCNL.[6,7] Stone multiplicity has also been effectively incorporated into scoring systems to predict case complexity, postoperative complications, and the need for second

[1]University of California, San Francisco School of Medicine, San Francisco, California.
[2]Department of Urology, University of California, San Francisco, San Francisco, California.
[3]Division of Urology, Department of Surgery, University of Arizona, Tuscon, Arizona.

operations.[8,9] However, no study to date has examined how stone multiplicity is association with surgical approach, URS *vs* PCNL, when treating patients with high stone burden.

We hypothesize that among patients with stone burden of >20 mm, the presence of multiple stones on preoperative imaging predicts the provider choosing URS rather than PCNL. Furthermore, we hypothesize that postoperative outcomes do not differ significantly between those treated with URS and PCNL. We aim to assess the impact of stone multiplicity on the choice of URS *vs* PCNL as first-line therapy for patients with stone burden >20 mm, and examine whether AUA guideline-discordant care impacts patient outcomes.

## Materials and Methods

### Study participants and inclusion criteria

From October 2015 through November 2018, all consenting patients treated for urinary stone disease at the University of California, San Francisco (UCSF) Urology Department, were prospectively enrolled into the Registry for Stones of the Kidney and Ureter (ReSKU), the methodology of which has been previously described.[10]

Adult ReSKU patients were included in this study if they had >20 mm aggregate stone burden visualized on CT and subsequently underwent either URS or PCNL as a first operation. Patients who underwent PCNL with a concurrent ipsilateral URS were grouped with patients who received PCNL alone for the purposes of these analyses.

### Exclusion criteria

Patients who were pregnant during a first visit or had a known bleeding diathesis were excluded, as these are absolute contraindications for PCNL.

### Data collected

The following demographic and comorbid characteristics were collected at the time of the first clinic visit: age, reported gender, ethnicity (Hispanic/non-Hispanic), body mass index, current medications, and prior surgeries at outside institutions.

From CT imaging, radiographic data were collected regarding the stone's location, total stone burden, multiplicity, and the presence of any complex genitourinary anatomy. The list of genitourinary anatomical anomalies considered ''complex'' is listed in Supplementary Appendix SA1. Guy's stone score, a nomogram for determining PCNL case complexity, was also determined for each renal unit.[9] Cumulative stone diameter (CSD), defined as the sum of the largest diameters of each stone visualized in a single renal unit, was used as the measure of total stone burden. CSD was measured by the attending urologist at the time of patient's first clinical visit using electronic calipers. High CSDs have consistently shown to be predictive of lower stone-free rates, increased need for second operations, and increased likelihood of complications.[3,11] This measure, rather than surface area or volume, was chosen because it is the most common measure of stone burden and is the measure used by both the AUA and the European Association of Urology (EAU) in their guidelines.[12]

The following data were collected from each operation: operating surgeon, operation type (URS or PCNL), and whether or not visual clearance of stone fragments was achieved at the conclusion of the operation. From postoperative encounters, data were collected regarding the timing of hospital discharge, Clavien–Dindo scores for postoperative complications, and whether residual stones were visualized on postoperative imaging. Clavien–Dindo scores were measured on a scale from 1 to 5 as previously described.[13]

Dates of subsequent surgeries and follow-up appointments were also collected for each patient. For each patient, right and left renal units were analyzed separately.

### Surgical techniques

Flexible ureteroscopy (LithoVue; Boston Scientific, Marlborough, MA) was used for a majority of URS cases, with semirigid URS reserved for mid-distal ureteral stones. Ureteral access sheaths were used in a majority of cases. Lithotripsy was accomplished with holmium:YAG laser (200 or 365 micron tip), with laser strength ranging from 20 to 120 W. Fragmentation and basketing were preferred, and performed in approximately three-fourths of cases, with dusting also occurring in about half of those. Stone-free status was assessed intraoperatively with ultrasound and URS. Stone-free status was assessed postoperatively with ultrasound, kidney, ureter, and bladder radiograph (KUB), and/or rarely CT, all within the first 3 weeks after the operation. Approximately 50% of patients received multiple imaging modalities.

Unless the patient's anatomy or disease burden necessitated an alternative approach, PCNLs were accomplished with suction lithotripsy following by flexible nephroscopy, all through a single tract dilated to 24F. Less than 10% of patients required multiple tracts. Concurrent URS, either antegrade or retrograde, was performed when patients had either high stone burden in the mid-distal ureter in addition to their renal stone burden, or when nephroscopy alone was unable to achieve stone-free status. At the conclusion of the operation, a nephrostomy tube was placed. Nephrostomy tubes were typically removed on postoperative day (POD) 1. Stone-free status was assessed intraoperatively and immediately postoperatively with antegrade nephrostogram, KUB, and/or CT. Approximately two-thirds of patients had stones-free status assessed with multiple modalities.

Patients who began the operation with PCNL and required concurrent URS were grouped with patients who received PCNL alone for this study. However, to ensure that results did not depend on cases in which both of these modalities were utilized, all analyses were completed once with these patients included and once with these patients removed (see the Sensitivity Analyses section below).

### Statistical and graphical analyses

Summary statistics were used to describe demographic and clinical characteristics. Mean and standard deviation (SD) were used to describe continuous variables. Frequencies were reported for categorical variables.

The primary analysis estimated the degree to which stone multiplicity predicted surgical approach (URS *vs* PCNL). Chi-squared statistics and univariate logistic regressions were used for categorical and continuous variables, respectively. Next, multivariate logistic regression (MLR) was used to estimate the degree to which stone multiplicity predicted the surgical approach while controlling for the identity of the operating surgeon, demographic features of the patient, and other radiologic characteristics of the stones.

After visual examination of the results of the primary analysis, the three primary authors (S.Z., S.W., and D.B.) designed three patient profiles to distinguish between patients who received AUA-concordant care and patients who received AUA-discordant care (i.e., PCNL or URS). Each profile was created to maximize the discrimination between patients who underwent URS and those who underwent PCNL, while maintaining simple and understandable definitions for each profile.

The secondary analysis investigated whether post-procedural outcomes differed between those who underwent URS and PCNL. The outcomes of interest included the presence of residual stones at the conclusion of the operation, the presence of residual stones on radiographic imaging taken within 3 weeks after the operation, significant postoperative complications (defined as Clavien–Dindo score >1), the need for a second operation within 90 days of the first operation, and the length of postoperative hospital stay. Chi-squared and MLR were used to determine the degree to which the surgical approach, URS or PCNL, predicted the dichotomous outcomes (presence of residual stones, significant postoperative complications, and the need for a second operation). Student's *t*-test was used to measure the difference in the length of hospital stay between URS and PCNL patients.

### *Sensitivity analyses*

Three sensitivity analyses were conducted for both primary and secondary analyses. First, all analyses were repeated after excluding patients with complex anatomy. Second, all analyses were repeated after excluding patients who underwent both PCNL and URS. Third, all analyses were repeated after excluding all patients with any ureteral stones. These sensitivity analyses were conducted to increase the generalizability of any results to patient populations with varying levels of disease complexity.

Statistical analyses and figures were completed using R software (version 3.4.0; The R Foundation for Statistical Computing). Adjusted odds ratios (aOR) were reported for each MLR. A *p*-value less than 0.05 was considered statistically significant.

## Results

### *Patient demographics and data quality*

One thousand one hundred ninety-four patients were enrolled in the ReSKU between October 2015 and November 2018, of which 125 met inclusion criteria, providing 129 renal units for the primary analysis. Patient and renal unit characteristics are shown in Table 1. Mean CSD was 39.7 mm (SD 17.1). Seventy-nine renal units (61%) contained more than 1 stone, 45 renal units (35%) contained more than 3 stones.

### *Primary analysis: association between stone multiplicity and choice of URS*

Of the 129 renal units available for the primary analysis, 96 (74.4%) underwent PCNL and 33 (25.6%) underwent URS. Among the 96 PCNL cases, URS was also performed in 24 (18% of all cases). In a univariate analysis, patients with two or three stones had four times the odds of undergoing URS (OR 4.00, $\chi^2 = 8.21$, $p = 0.04$). Patients with more than three stones had a similar increase in odds of undergoing URS (OR 3.67, $\chi^2 = 8.21$, $p = 0.04$).

In a multivariate analysis controlling for demographic features, CSD, and operating urologist, patients with a renal unit containing more than three stones had over nine times the odds of undergoing URS when compared with patients with a renal unit containing a single stone (aOR 9.21, confidence interval [95% CI] 2.55–40.58, $p = 0.002$, Table 2). Patients with two to three stones had approximately two times the odds of undergoing URS, although this result was not statistically significant (aOR 1.93, 95% CI 0.55–7.18, $p = 0.31$). For every 10 mm increase in CSD, the odds of undergoing URS decreased by 65% (OR 0.35, 95% CI 0.19–0.58, $p < 0.001$). Figure 1 demonstrates the findings of the multivariate analysis: the likelihood of choosing URS decreases for every 10 mm increase in CSD over 20 mm, but the likelihood of performing URS increases when more stones are present. Excluding patients with complex anatomy (9 cases), patients with any ureteral stones (21 cases), or patients who received both PCNL and URS (24 cases) did not change the significance or magnitude of these results (Supplementary Data: Sensitivity Analysis).

After this analysis, three patient profiles were created to describe the influence of stone multiplicity on clinical decision-making (Fig. 2). Eighty-nine percent of the 94 patients in Profile 3, with either one stone or CSD greater than 35 mm, were managed with PCNL. Eleven out of 12 (92%) of the patients in Profile 1, with more than three stones and CSD less than 35 mm were managed with URS. Roughly half of the 23 patients who were in neither Profile 1 nor Profile 3 were managed with URS (47%) or PCNL (53%; see Profile 2 of Fig. 2).

### *Secondary analysis: association between operation type and outcomes*

Of the 125 patients available for the primary analysis, 101 (81%) received postoperative imaging within 3 weeks of the operation, and 96 (76%) had at least 90 days of follow-up data available to query for second operations. For each outcome, patients with missing data were excluded from that outcome's analysis.

After controlling for patient characteristics and radiologic features, URS was not significantly associated with residual stone burden visualized at the conclusion of surgery (aOR 1.24 95% CI 0.29–4.77, $p = 0.76$) or on postoperative imaging (aOR 0.70 95% CI 0.034–5.11, $p = 0.76$). URS patients did not have higher rates of complication (aOR of Clavien–Dindo >1: 0.78, 95% CI 0.08–8.25, $p = 0.83$) when compared with PCNL. Out of all patients in this study, only two PCNL patients experienced a postoperative complication requiring surgical intervention (Clavien–Dindo ≥3). URS patients did not have an increased likelihood of a second operation within 90 days of the first (aOR 0.71, 95% CI 0.49–8.43, $p = 0.32$) compared with PCNL patients. The median date of discharge was POD 2 and POD 0 for PCNL and URS patients, respectively. URS patients were discharged an average of 1.26 days earlier than PCNL patients (95% CI: 0.72–1.81 days, $p < 0.001$). CSD was significantly associated with the likelihood of residual

TABLE 1. PATIENT DEMOGRAPHICS, RADIOLOGIC FEATURES, AND INTRAOPERATIVE CHARACTERISTICS

| *Patient demographics* | *ReSKU cohort* (n=*125*) | *URS cohort* (n=*30*) | *PCNL cohort* (n=*95*) |
|---|---|---|---|
| Age (mean ± SD) | 57.5 ± 16.0 | 61.5 ± 15.5 | 56.1 ± 15.9 |
| Gender, *n* (% total) | | | |
| Female | 42 (34) | 12 (40) | 30 (32) |
| Male | 83 (66) | 18 (60) | 65 (68) |
| Ethnicity, *n* (% total) | | | |
| Non-Hispanic | 104 (83) | 28 (93) | 76 (80) |
| Hispanic | 19 (15) | 2 (7) | 17 (20) |
| BMI (kg/m$^2$, mean ± SD) | 31.1 ± 8.5 | 30.9 ± 9.3 | 31.3 ± 8.5 |
| *Radiologic features* | *Renal units* (n=*129*) | *Renal units* (n=*33*) | *Renal units* (n=*96*) |
| CSD, mm (mean ± SD) | 39.7 ± 17.1 | 43.2 ± 17.6 | 29.7 ± 10.4 |
| Stone number, *n* (% total) | | | |
| 1 | 50 (39) | 6 (18) | 44 (46) |
| 2–3 | 34 (26) | 12 (36) | 22 (23) |
| >3 | 45 (35) | 15 (45) | 30 (31) |
| Guy's stone score, *n* (%) | | | |
| Grade I | 15 (12) | 2 (6) | 13 (14) |
| Grade II | 49 (38) | 20 (61) | 29 (30) |
| Grade III | 47 (37) | 11 (33) | 36 (38) |
| Grade IV | 16 (13) | 0 (0) | 16 (17) |
| Location (*n*)[a] | | | |
| Upper pole | 51 | 13 | 38 |
| Interpolar | 62 | 19 | 43 |
| Lower pole | 97 | 27 | 71 |
| Caliceal diverticulum | 0 | 0 | 0 |
| Renal pelvis | 72 | 8 | 65 |
| Ureteropelvic junction | 13 | 2 | 11 |
| Proximal ureter[b] | 13 | 5 | 8 |
| Other ureters[b] | 9 | 4 | 5 |
| Complex anatomy[b], *n* (% total) | 9 (7) | 1 (3) | 8 (8) |
| *Operative characteristics* | *Renal units* (n=*129*) | *Renal units* (n=*33*) | *Renal units* (n=*96*) |
| Preoperative stent, *n* (%) | 23 (18) | 6 (18) | 17 (18) |
| Operative time, minutes (mean ± SD) | 119 ± 52 | 95 ± 48 | 126 ± 50 |
| Operating urologist ID, *n* (% total) | | | |
| 1 | 52 (40) | 12 (36) | 40 (42) |
| 2 | 77 (60) | 21 (64) | 56 (58) |

[a]Renal units with stones in more than one location were counted once for each occupied location.
[b]These patients were excluded in subsequent sensitivity analyses.
BMI = body mass index; CSD = cumulative stone diameter; PCNL = percutaneous nephrolithotomy; SD, standard deviation; URS = ureteroscopy.



stones (aOR 1.64, 95% CI 1.12–2.27, $p = 0.013$) and need for a second operation (aOR 1.45, 95% CI 1.04–2.077, $p = 0.03$, Table 3).

Repeating all secondary analyses after excluding patients with complex anatomy (9 cases), patients with any ureteral stones (21 cases), or patients who underwent URS during their PCNL (24 cases) did not change the significance of these results (Supplementary Data: Sensitivity Analysis).

## Discussion

Our study demonstrates that for stone burden >20 mm, stone multiplicity was significantly associated with undergoing URS rather than the intervention recommended by the AUA guidelines, PCNL. In the primary analysis, patients with more than three stones demonstrated a ninefold increase in the odds of undergoing URS when compared with those with a single stone. We then found that undergoing URS was not associated with significant differences in postoperative complications, rates of residual stone burden, or the need for a second operation. Undergoing URS was associated with significantly shorter hospital stays, as prior research has consistently demonstrated.[14–16] Notably, the significance of findings from both analyses did not change after controlling for demographic features, radiologic characteristics, or the operating urologist, nor did these results change after excluding patients with complex anatomy, ureteral stones, or patients who required both PCNL and URS.

In this cohort, we demonstrate that URS remains a viable surgical option for patients with a CSD greater than 20 mm while not exposing patients to an increased risk of a second operation or lower stone-free rates compared with PCNL. Prior research has shown that this is typically not the case:

Table 2. Features Associated with Choosing Ureteroscopy as First-Line Therapy for Patients with Over 20 mm of Stone Burden

| *Patient demographics* | *Odds ratio* | *Adjusted odds ratio* | *95% confidence interval* |
|---|---|---|---|
| Age (per decade) | 1.25 NS | 1.20 | 0.87–1.71 NS |
| Gender (male) | 0.79 NS | 0.78 | 0.27–2.28 NS |
| Ethnicity (Hispanic) | 0.29 NS | 0.60 | 0.08–3.07 NS |
| BMI (per 10 kg/m$^2$) | 0.99 NS | 1.11 | 0.62–1.98 NS |
| Radiologic features | | | |
| CSD (per 10 mm) | 0.46*** | 0.35*** | 0.19–0.58*** |
| Stone number | | | |
| 1 | 1 | 1 | (Reference) |
| 2–3 | 4.00* | 1.93 | 0.55–7.18 NS |
| >3 | 3.67* | 9.21** | 2.55–40.58** |
| Complex anatomy | 0.34 NS | 0.31 | 0.01–3.89 NS |
| Operating urologist (2 *vs* 1) | 1.25 NS | 2.50 | 0.62–4.69 NS |

*$p<0.05$; **$p<0.01$; ***$p<0.001$.
NS, nonsignificant.



URS operations, on average, achieved stone-free status at lower rates than PCNL.[17,18] This seems particularly true for patients with large burden.[5]

We believe that the nature of stone multiplicity contributed to our increased stone-free rate for URS compared with the published literature. During URS, a given volume of smaller stones offers fewer large flat surfaces for dusting when compared with a single large stone, which may encourage a fragmentation and basketing technique over dusting.[19,20] This technique is associated with improved stone-free rates when compared with dusting.[21] Furthermore, because stone volume is proportional to the cube of the diameter of the stone, multiple stones of a given CSD have less volume when compared with a single stone of the same CSD. For any given CSD, therefore, operations on multiple stones create less debris than operations on single stones. Since lower levels of debris are also associated with higher stone-free rates,[20] it is reasonable that URS on multiple smaller stones may have higher stone-free rates than URS on single large stones. These two factors may contribute to a higher stone-free rate for URS for select patients, comparable with the stone-free rate of PCNL in certain circumstances.

Our findings suggest that focusing only on CSD, as per AUA guidelines, may provide an incomplete assessment of the true stone burden present in any renal unit. While CSD is strongly associated with surgical outcomes and is the most common measure of aggregate burden,[3,11] there are major drawbacks to using this metric in isolation for surgical decision-

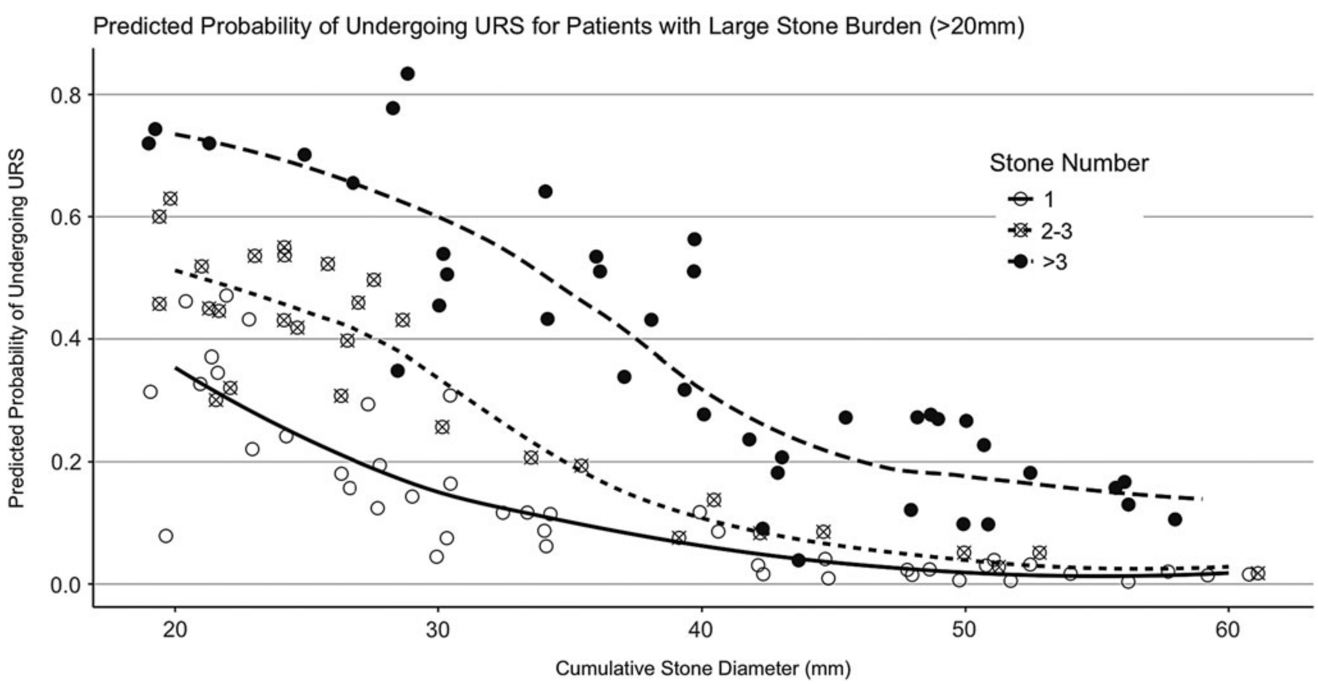


**FIG. 1.** Relationship between CSD, stone multiplicity, and the likelihood of undergoing URS. Predicted probabilities were determined by a multivariate logistic regression model fit to patient demographics, CSD, stone multiplicity, the presence of complex anatomy, and operating urologist. As CSD increases, the likelihood of undergoing URS decreases. As stone number increases, the likelihood of URS increases. CSD = cumulative stone diameter; URS = ureteroscopy.

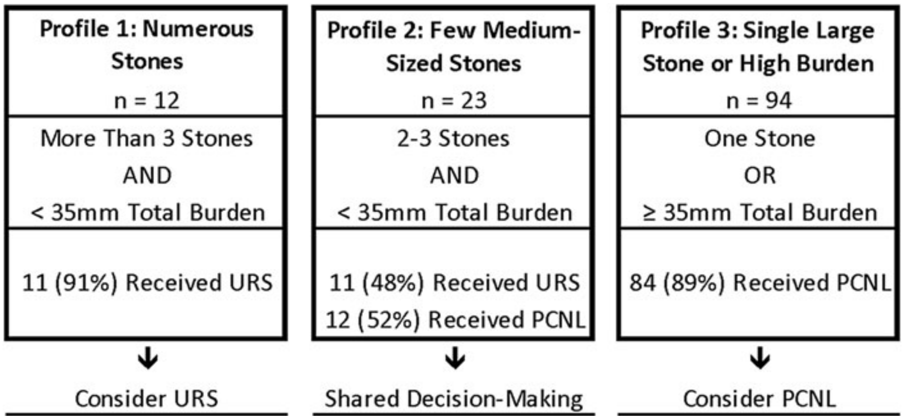


**FIG. 2.** Suggested profiles to aid the surgical management of patients with CSD >20 mm. A majority of patients in Profile 1, who had more than three stones and relatively low burden (<35 mm), were managed with URS. Patients in Profile 2, who had two to three stones and low burden, were split between URS and PCNL. A majority of patients in Profile 3, who had one stone or relatively high burden (>35 mm), were managed with PCNL. PCNL = percutaneous nephrolithotomy.



making. For example, a stone measuring 10×3×3 mm would have the same CSD as a stone measuring 10×9×9 mm, but a ninefold difference in volume.[22] The CSD-volume discrepancy also exists when multiple stones are present: a similar ninefold difference exists between the volume of a 30 mm spherical stone and the volume of three 10 mm spherical stones. This discrepancy is reduced but not eliminated when surface area is substituted for CSD: it would take nine of these small stones to have the same surface area as the large stone, but the volume of the larger stone would still be three times the volume of all nine smaller stones. While CSD and surface area have demonstrated clinical utility, they may not be sufficient to guide management in the case of irregularly shaped stones or, as this analysis demonstrates, multiple stones. Given these challenges, it is possible that guidelines referencing only CSD do not capture the full complexity of stone management.

As written, AUA guidelines recommend that patients with single large stones should be managed similarly to patients with many medium-sized stones.[23] However, the research used to develop and support this guideline has considerable variation in its reporting of stone. For example, some studies exclude patients with multiple stones, while others include all patients with CSD over 20 mm, even those with many small stones.[14,15,24] This methodologic heterogeneity precludes the possibility of thoroughly analyzing the impact of stone multiplicity on surgical decisions and outcomes. Our findings suggest that a more comprehensive assessment of stone

Table 3. Features Associated with Adverse Postoperative Outcomes for Patients with Over 20 mm of Stone Burden

| | *Odds of adverse outcome* | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | *Residual stones visualized at conclusion of surgery* | | *Residual stones present on postoperative imaging* | | *Second operation required* | | *Clavien score >1* | |
| | *Odds ratio* | *Adjusted odds ratio* | *Odds ratio* | *Adjusted odds ratio* | *Odds ratio* | *Adjusted odds ratio* | *Odds ratio* | *Adjusted odds ratio* |
| *Patient demographics* | | | | | | | | |
| Age (per decade) | 1.05 NS | 0.91 NS | 0.96 NS | 0.93 NS | 0.84 NS | 0.78 NS | 0.70* | 0.62 NS |
| Gender (male) | 0.82 NS | 0.91 NS | 0.79 NS | 0.88 NS | 0.68 NS | 0.67 NS | 9.02* | 10.6 NS |
| Ethnicity (Hispanic) | 0.24 NS | 0.16 NS | 1.45 NS | 0.99 NS | 1.53 NS | 0.91 NS | 1.56 NS | 0.16 NS |
| BMI (per 10 $kg/m^2$) | 1.02 NS | 1.13 NS | 1.04 NS | 1.48 NS | 1.02 NS | 1.39 NS | 1.10* | 4.15** |
| *Radiologic features* | | | | | | | | |
| CSD (per 10 mm) | 1.44** | 1.64** | 1.46* | 1.44* | 1.45** | 1.45* | 0.90 NS | 0.79 NS |
| Stone number | | | | | | | | |
| 1 (Reference) | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| 2–3 | 0.66 NS | 0.81 NS | 0.98 NS | 1.13 NS | 0.44 NS | 0.51 NS | 0.13 NS | 0.03 NS |
| >3 | 1.02 NS | 0.65 NS | 1.46 NS | 0.99 NS | 0.98 NS | 0.71 NS | 0.26 NS | 0.25 NS |
| Complex anatomy | 0.59 NS | 0.37 NS | 0.97 NS | 0.87 NS | 0.66 NS | 0.46 NS | 1.74 NS | 1.83 NS |
| *Intraoperative features* | | | | | | | | |
| Intervention type | | | | | | | | |
| PCNL (Reference) | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| URS | 0.65 NS | 1.24 NS | 0.33 NS | 0.70 NS | 0.96 NS | 0.71 NS | 0.36 NS | 0.78 NS |
| Operating urologist (2 *vs* 1) | 1.90 NS | 1.14 NS | 1.31 | 1.00 NS | 1.31 NS | 1.15 NS | 0.22* | 0.77* |

$^*p < 0.05$; $^{**}p < 0.01$.

burden may augment AUA guideline statements and provide better guidance for practicing urologists. A re-examination of the guidelines with a focus on both stone burden and multiplicity may be necessary.

This study has some limitations. Patient preference is a factor in surgical decision-making that was not available for analysis in this study. It has been reported that $\sim$30% of patients with high burden received URS because of patient preference.[5] However, it is extremely unlikely for patient preference to confound the results of this analysis because preferences do not influence stone multiplicity, and so cannot bias the association between multiplicity and surgical decisions. More likely, the reverse is true: stone multiplicity influences both the urologist and patient preferences during shared decision-making, which in turn influences which operation is chosen. Guidelines that reflect this thinking—that multiple stones should influence surgical decisions in certain circumstances—may better serve urologist and patient alike.

In addition, all patients in this cohort were treated at a high-volume tertiary care center by two surgeons with expertise in URS and PCNL. This presents two challenges to interpreting these results. First, patient complexity is high in this cohort, so it is initially unclear the degree to which these results generalize to other patient populations. However, the significance of these results did not change when excluding patients with complex anatomy, patients with ureteral stones, or patients whose disease burden necessitated the use of both PCNL and URS. The results of these sensitivity analyses demonstrate that our findings generalize to patients with less complicated disease burden. Second, expertise or surgeon preference of the two surgeons at this center may contribute to the success of URS for patients with burden above 20 mm. This reduces the generalizability of these results to centers and urologists less familiar with these procedures. As more institutions adopt the ReSKU, however, it will be possible to confirm these results prospectively across multiple centers.

As a final limitation, it is possible that another metric, such as a stone location, Guy's stone score, or surface area, may serve as a better measure by which to differentiate between patients who should receive URS and those who should receive PCNL. However, both the Guy's stone score and stone location are intimately related to stone multiplicity: patients with multiple stones have higher Guy's scores, and it is uncommon for many stones to exist in one isolated region of the kidney.[9] Multiplicity is integral to these other descriptors of disease burden.[25] Our results demonstrate that any association between these metrics and surgical decisions is, at least in part, due to stone multiplicity.

Surface area has the potential to replace CSD as a better measure of stone burden, but it is unlikely that surface area alone can discriminate URS patients from PCNL patients. Point in case, after review of a small subgroup of patients from this cohort who received URS, 7 of 10 had more than 400 $mm^2$ of stones, distributed among many small stones throughout the renal unit. Although they had ''high burden'' as measured by surface area, treating these patients with PCNL would have likely required multiple tracts or concurrent URS. Furthermore, our results did not show that CSD was useless. This measure was significantly associated with surgical choice and some surgical outcomes (Tables 1 and 2). However, it was not enough—it was a necessary but not sufficient piece of information, as demonstrated by the multivariate analysis. To decide an operation on the basis of burden alone, whether measured with CSD or surface area, is to ignore important features of this disease.

## Conclusion

Stone multiplicity drives the decision to use URS for patients with total burden >20 mm. This choice, which deviates from AUA guidelines, does not appear to negatively impact patient care. Future work should continue to explore the optimal intervention for patients with high burden and multiple stones.


## Acknowledgments

The authors acknowledge David Glidden, PhD and Michael Kohn, MD, MPP for their assistance with data presentation and statistical analyses.


## Declarations

The authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or nonfinancial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this article.

## Author Disclosure Statement

S.Z., S.W., D.B.B., M.A.P., S.L.W., D.T.T. have no competing financial interests. M.S. is a cofounder of Applaud Medical and the Ravine Group, and consultant for Boston Scientific and BARD. T.C. is a consultant for Boston Scientific and BARD.

## Supplementary Material

Supplementary Appendix SA1
Supplementary Data

## References


1. Scales CD, Smith AC, Hanley JM, Saigal CS. Prevalence of kidney stones in the United States. Eur Urol 2012;62: 160–165.
2. Assimos D, Krambeck A, Miller NL, et al. Surgical Management of Stones: American Urological Association/Endourological Society Guideline, PART II. J Urol 2016;196:1161–1169.
3. Ito H, Kawahara T, Terao H, Ogawa T, Yao M, Kubota Y, Matsuzaki J. The most reliable preoperative assessment of renal stone burden as a predictor of stone-free status after flexible ureteroscopy with holmium laser lithotripsy: A single-center experience. Urology 2012;80:524–528.
4. Baş O, Tuygun C, Dede O, et al. Factors affecting complication rates of retrograde flexible ureterorenoscopy: Analysis of 1571 procedures—A single-center experience. World J Urol 2017;35:819–826.
5. Scotland KB, Rudnick B, Healy KA, et al. Retrograde ureteroscopic management of large renal calculi: A single institutional experience and concise literature review. J Endourol 2018;32:603–607.

6. Smith A, Averch TD, Shahrour K, et al. A nephrolithometric nomogram to predict treatment success of percutaneous nephrolithotomy. J Urol 2013;190:149–156.
7. Jeong H, Oh S, Oh JJ, et al. The acceptable criterion of stone burden and the significant factors to choose retrograde intrarenal stone surgery or miniaturized percutaneous nephrolithotomy for the treatment of renal stones >10 mm. J Endourol 2017;31:1012–1018.
8. Yarimoglu S, Polat S, Bozkurt IH, et al. Comparison of S.T.O.N.E and CROES nephrolithometry scoring systems for predicting stone-free status and complication rates after percutaneous nephrolithotomy: A single center study with 262 cases. Urolithiasis 2017;45:489–494.
9. Thomas K, Smith NC, Hegarty N, Glass JM. The Guy's Stone Score—Grading the complexity of percutaneous nephrolithotomy procedures. Urology 2011;78:277–281.
10. Chang HC, Tzou DT, Usawachintachit M, et al. Rationale and Design of the Registry for Stones of the Kidney and Ureter (ReSKU): A prospective observational registry to study the natural history of urolithiasis patients. J Endourol 2016;30:1332–1338.
11. Merigot de Treigny O, Bou Nasr E, Almont T, Tack I, Rischmann P, Soulié M, Huyghe E. The cumulated stone diameter: A limited tool for stone burden estimation. Urology 2015;86:477–481.
12. Ito H, Kawahara T, Terao H, et al. Utility and limitation of cumulative stone diameter in predicting urinary stone burden at flexible ureteroscopy with holmium laser lithotripsy: A single-center experience. PLoS One 2013;8:e65060.
13. Dindo D, Demartines N, Clavien P-AA. Classification of surgical complications: A new proposal with evaluation in a cohort of 6336 patients and results of a survey. Ann Surg 2004;240:205–213.
14. Akman T, Binbay M, Ozgor F, et al. Comparison of percutaneous nephrolithotomy and retrograde flexible nephrolithotripsy for the management of 2–4 cm stones: A matched-pair analysis. BJU Int 2012;109:1384–1389.
15. Bryniarski P, Paradysz A, Zyczkowski M, et al. A randomized controlled study to analyze the safety and efficacy of percutaneous nephrolithotripsy and retrograde intrarenal surgery in the management of renal stones more than 2 cm in diameter. J Endourol 2012;26:52–57.
16. Hyams ES, Shah O. Percutaneous nephrostolithotomy versus flexible ureteroscopy/holmium laser lithotripsy: Cost and outcome analysis. J Urol 2009;182:1012–1017.
17. Kang SK, Cho KS, Kang DH, Jung HD, Kwon JK, Lee JY. Systematic review and meta-analysis to compare success rates of retrograde intrarenal surgery versus percutaneous nephrolithotomy for renal stones >2 cm. Medicine (Baltimore) 2017;96:e9119.
18. Zhang W, Zhou T, Wu T, et al. Retrograde intrarenal surgery versus percutaneous nephrolithotomy versus extracorporeal shockwave lithotripsy for treatment of lower pole renal stones: A meta-analysis and systematic review. J Endourol 2015;29:745–759.
19. Weiss B, Shah O. Evaluation of dusting versus basketing-can new technologies improve stone-free rates? Nat Rev Urol 2016;13:726–733.
20. Santiago JE, Hollander AB, Soni SD, Link RE, Mayer WA. To dust or not to dust: A systematic review of ureteroscopic laser lithotripsy Techniques. Curr Urol Rep 2017;18:1–9.
21. Humphreys MR, Shah OD, Monga M, et al. Dusting versus basketing during ureteroscopy—Which technique is more efficacious? A prospective multicenter trial from the EDGE research consortium. J Urol 2018;199:1272–1276.
22. Pozniak MA, Borman EJ, Zelinski N, et al. Automated renal stone volume measurement by noncontrast computerized tomography is more reproducible than manual linear size measurement. J Urol 2011;186:2275–2279.
23. Pradère B, Doizi S, Proietti S, Brachlow J, Traxer O. Evaluation of guidelines for surgical management of urolithiasis. J Urol 2018;199:1267–1271.
24. Pan J, Chen Q, Xue W, et al. RIRS versus mPCNL for single renal stone of 2–3 cm: Clinical outcome and cost-effective analysis in Chinese medical setting. Urol Res 2013;41:73–78.
25. Verma A, Tomar V, Yadav S. Complex multiple renal calculi: Stone distribution, pelvicalyceal anatomy and site of puncture as predictors of PCNL outcome. Springerplus 2016;5:1–6.

Address correspondence to:
*Thomas Chi, MD*
*Department of Urology*
*University of California, San Francisco*
*400 Parnassus Avenue*
*6th Floor Urology Clinic A610*
*Box 0330*
*San Francisco, CA 94143-0330*

*E-mail:* tom.chi@ucsf.edu

**Abbreviations Used**

AUA = American Urological Association
BMI = body mass index
CSD = cumulative stone diameter
CT = computed tomography
KUB = kidney, ureter, and bladder radiograph
MLR = multivariate logistic regression
PCNL = percutaneous nephrolithotomy
ReSKU = Registry for Stones of the Kidney and Ureter
UCSF = University of California, San Francisco
URS = ureteroscopy