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REVIEW

Flexible ureteroscopy versus percutaneous nephrolithotomy as primary treatment for renal stones 2 cm or greater

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Abstract: The purpose of this review, based on the current evidence in the literature, is whether ureteroscopy (URS) is a comparable primary treatment option to the current gold standard of percutaneous nephrolithotomy (PCNL) for the treatment of large kidney stones 2 cm or greater. The lack of prospective randomized trials directly comparing URS and PCNL makes comparison challenging. The numerous studies are not standardized in terms of their definition of stone-free or how stone size is reported. In order to standardize comparison of results, we used a stone-free definition of <4 mm after one procedure per imaging of the author's choice, since how each patient was imaged postoperatively was not reported. The results from the literature show that moderately large stones from 2 to 3 cm treated ureteroscopically have similar outcomes to PCNL. Stone-free rates with URS decrease when stone size is above 3 cm. Our interpretation of the literature suggests that a current limitation of URS is that multiple procedures for URS would be required to achieve comparable stone-free rates to PCNL, particularly for stones greater than 4 cm.

Keywords: ureteroscopy, percutaneous nephrolithotomy, lithotripsy, urinary calculi

Introduction

The purpose of this review, based on the current evidence in the literature, is whether ureteroscopy (URS) is a comparable primary treatment option to the current gold standard of percutaneous nephrolithotomy (PCNL) for the treatment of large kidney stones 2 cm or greater. Such large stones remain a challenging problem for urologists to treat, and left untreated can lead to significant problems, such as obstruction, pain, and loss of renal function. Further, certain stones may be infected with urease-producing bacteria that can lead to recurrent urinary tract infections (UTIs), rapidly increasing stone burdens, and occasionally even sepsis and death. Unless significant comorbidities or other contraindications exist, complete removal of the stone is recommended in order to relieve obstruction, remove infectious bacteria, and preserve renal function.[1,2]

The symptoms and signs of nephrolithiasis were documented by Hippocrates in the fourth century BC. It was not until centuries later, in AD 1550, that Cardan performed the first recorded open nephrolithotomy at the same time of treatment of a lumbar abscess.[3] Subsequent developments focused on initiating surgical intervention prior to abscess formation or fistulization.[3] Hyrtl and Brödel in 1902 reported the finding of an avascular plane, Brödel white line, that permitted access to the renal collecting system via the parenchyma. This led to the development of the anatrophic nephrolithotomy, thus reducing bleeding that had been problematic with prior techniques.[3] In 1965, Gil-Vernet developed the extended pyelolithotomy, which became the access of choice for

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most open stone removals.[3] Much of the 1960s and 1970s was dominated by the open approach until the advancement of endoscopic technology occurred. This was a critical point in the development of the modern-day PCNL.

History of percutaneous nephrolithotomy

The first record of percutaneous access of the kidney dates back to 1865 at London's Great Ormond Street Hospital for Sick Children. Thomas Hillier described his repeated percutaneous tapping of a severely dilated right-sided hydronephrotic kidney, only in the end to lose his patient to urosepsis from a distal left ureteral stone.[4] This technique would not be investigated further until almost a century later, in 1955, when Goodwin et al documented 16 cases in which needle trocars were placed using X-ray fluoroscopy to drain hydronephrotic kidneys.[5] Twenty years later, in 1976, Fernström and Johansson showed that renal stones could be treated via percutaneous pyelolithotomy.[6] At that time, PCNL was primarily used only for stones less than 1.5 cm due to the limitations of the available stone-retrieval and fragmentation instruments. With the development of pneumatic and ultrasonic lithotripsy, large stones were then able to be removed through a small percutaneous tract.[7] High stone-free rates (SFRs) have been reported for large stone burdens treated by PCNL since the 1980s.[3] By 1987, Matlaga and Lingeman had shown that SFRs were similar between open anatrophic nephrolithotomy and PCNL, but PCNL had lower blood-transfusion rates and shorter hospital stays.[3] In his 1994 review of 101 patients, Lingeman et al showed that PCNL could achieve SFRs of 90% for lower-pole stones, which contrasted with an SFR of 59% in a review of 3000 extracorporeal shockwave lithotripsy (ESWL) procedures. In addition, SFRs achieved by PCNL were independent of stone burden, whereas SFRs with ESWL declined as stone size increased.[8] Lingeman's retrospective study was later followed by a prospective trial from Albala et al that demonstrated SFRs of 95% vs 37% for PCNL and ESWL respectively, validating the earlier reports.[9] However, in a recent analysis of the Clinical Research Office of the Endourological Society (CROES) PCNL global study, 1450 single large (>2 cm) non-staghorn calculi were reviewed. The analysis showed SFRs by PCNL of 90% for stone sizes of 2–3 cm. This dropped to 84% for stones greater than 4 cm, contrasting Lingeman's observation of PCNL SFRs being independent of size. This is likely because the CROES study analyzed data from significantly larger stones, as their range was from 2–6 cm and included surgeons of varying skill.[10] The percentage of patients requiring blood transfusion increased from 4.4% in the 2–3 cm group to 13.3% for stone sizes above 4 cm. While mean operative time increased by 20 minutes when stone size increased by 2 cm, the length of hospital stay did not significantly change from 4 days.[10] There are some inherent limitations with the CROES database that can make direct comparisons to studies with standardized treatment protocols difficult.

The combined European Association of Urology (EAU)/American Urological Association (AUA) Nephrolithiasis Guidelines Panel concluded that PCNL should be first-line treatment for stones greater than 1.5 cm in diameter based on SFRs from 85%–100%, which were achieved with low complication rates.[11] While there is no standardized definition of staghorn calculus, it generally refers to a stone that takes up a significant portion of the renal pelvis and branches into at least one calyx.[1] In 2005, the AUA proposed PCNL as the standard of care for the treatment of staghorn stones, and at present this remains the gold standard for removal of large renal stones (>2 cm).[1,12] Currently, open surgery is rarely used to treat nephrolithiasis, and there has been a trend towards percutaneous monotherapy without the aid of ESWL due to the advances in flexible nephroscopes, lithotriptors, and grasping devices.[1] The guideline authors emphasized at the time the need to investigate further the outcomes of ureteroscopy as first-line treatment for large stones.

History of ureteroscopy

Ureteroscopy inadvertently began in 1912, when Hugh Hampton Young passed a rigid cystoscope into the dilated ureters of a child with posterior urethral valves.[3,13] In the early 1970s, rigid ureteroscopes were used to treat distal ureteral stones. The first clinical use of an actively deflectable ureteroscope was reported by Takayasu et al in 1971. It had no irrigation, no working channel, and only minimal deflection.[14] In 1980, Karl Storz Endoscopy (Tuttlingen, Germany) created a longer ureteroscope that could reach the renal pelvis, and in combination with the development of pneumatic lithotripsy allowed for the treatment of larger upper-tract stones.[13] Early ureteroscopes were built with a stiff rod lens design with a resultant large diameter and rigidity. However, the development of fiber-optic cables allowed for the creation of thinner and more flexible ureteroscopes, which came into mainstream use in the early 1990s.[13] Rigid and semirigid (usually employing fiber optics) ureterscopes are still widely used today due to their larger working channels, excellent visibility, and ease of handling in the mid- and distal ureter.

Early flexible ureteroscopes lacked active deflection at the tip, as well as a channel for irrigation, thereby limiting visualization and access to stones at an acute angle to the probe. A major breakthrough for flexible ureteroscopy occurred with the development of both small-caliber fiber-optic Ho:yttrium aluminum garnet (YAG) laser fibers and highly flexible nitinol stone baskets. These devices can be easily passed through the smaller working channel of flexible ureteroscopes.[15] However, even small-caliber instruments can limit scope deflection and limit access to the desired calyx, especially the lower pole.[15] Scope manufacturers have worked on increasing the amount of deflection attainable by flexible ureteroscopes. By increasing active deflection from the conventional 170° to 270° in the Storz Flex-X2, immediate SFRs almost doubled from 38% to 70% due to improved successful treatment of lower-pole stones.[15] Since the 1990s, flexible ureteroscopes have continued to be improved, with a reduction in outer diameter, the introduction of digital "chip on the tip" technology, an enlarged field of view, and enhanced active primary and secondary deflection.[16] Today, the majority of stones in the collecting system can be accessed with flexible ureteroscopes.[16]

Ureteral access sheaths

Ureteral access sheaths (UASs) have provided another advance for ureteroscopy.[17] The fine dust created by Ho:YAG lithotripsy generated a need for improved irrigation flow to maintain adequate visualization. The development of the UAS allowed for continuous low-pressure irrigation during the procedure, resulting in improved visualization. The maintenance of a low-pressure system reduces the risk of pyelovenous backflow and subsequent risk of sepsis. The UAS also allows the surgeon to easily perform multiple passes with a ureteroscope during a procedure, thereby allowing for basket retrieval of stone fragments while simultaneously protecting the delicate ureter. L'esperance et al demonstrated that the use of a UAS increased SFR, defined as no stones on noncontrast computed tomography (CT) or intravenous urography 2 months postoperatively, by 12% when compared to no UAS use (79% vs 67% SFR, respectively).[18] Hyams et al performed a retrospective multicenter review of large stones (2–3 cm in size) treated ureteroscopically and found an SFR of 83% after one procedure. SFR was defined as residual fragments less than 4 mm in size on X-ray. A UAS was used in only 67% of the cases.[19] However in Riley et al's study of large stones treated ureteroscopically where a UAS was used in all cases, an SFR (defined as 2 mm or less on X-ray) of 91% after an average of 1.82 procedures was achieved.[20] Both the increase in number of procedures done per patient, as well as UAS use, likely contributed to the higher SFR (with stricter definition) in the Riley et al study and supports the results reported by L'esperance et al.

PCNL complications

While PCNL has reported high SFRs in the range of 78%–95%,[1,21] it is not without drawbacks. Complications such as intra- and postoperative bleeding, sepsis, pulmonary complications, and adjacent organ injury can all occur. Patients also typically require at least an overnight stay in hospital. The EAU, in their review of 12,000 PCNL procedures, found average transfusion rates to be approximately 7% (range 0%–20%) with an embolization rate of 0.4% (range 0%–1.5%).[12] Other complications can include thoracic injury, abdominal organ injury, sepsis, and death, with rates being 1.5% (0%–11.6%), 0.4% (0%–1.7%), 0.5% (0.3%–1.1%), and 0%–0.3%, respectively.[12] Even higher complication rates have been reported.[21,22] Bleeding is a risk factor in PCNL due to the arrangement of the parenchymal vasculature around the collecting system.[23] Percutaneous access can tear these vessels, leading to intraoperative and/or postoperative blood loss.[23] Stoller et al reported an average total blood loss (intraoperative + postoperative) of 2.8 g/dL in one stage, one-puncture PCNLs, and a transfusion rate of 14% in uncomplicated single-tract cases (n = 127).[24] They found that increasing the number of new tracts or having a collecting system tear doubled blood loss; however, the presence of a mature healed tract reduced the risk by 50%.[24] Similar conclusions were found in Kukreja et al's prospective study of 236 PCNL cases, where predictors of blood loss included tearing of the collecting system, operative time longer than 1 hour, dilation of new tracts, increased tract size, and increasing number of tracts. Predictors of perioperative transfusion included preoperative anemia, stone size, multiple tracts, and total blood loss. By deferring dilations on multiple tracts for stones ranging around 2 cm, the hemoglobin drop decreased from 3.3 to 1.7 g/dL. An overall transfusion rate of 7.9% was reported.[23] This contrasts an average 0.3 g/dL drop in hemoglobin for ureteroscopy.[25] Contemporary PCNL series have reported lower transfusion rates of 0.8%–2%, with no significant difference in bleeding between single-tract and multiple-tract treatments.[26,27] However, a recent international CROES study of 5800 PCNL cases performed worldwide reported high transfusion rates of 11.1% in fluoroscopic guided PCNLs in contrast to 3.8% in ultrasound (US)-guided cases. Multivariate analysis revealed this significant difference may be due to larger access sheaths used in the fluoroscopic group, while the imaging modality was no longer a significant determinant of bleeding or transfusions. While the CROES prospective study concluded no significant difference in SFR between US- or fluoroscopic-guided PCNLs, there was a heavier stone burden in the fluoroscopic group that was statistically significant. Also, more than double the number of US-guided PCNLs had preoperative CT diagnostic imaging done in contrast to the fluoroscopic group.[28]

Factors such as improved flexible nephroscopes, better video systems, improved instrumentation, balloon dilation, and increased surgeon experience are likely factors in the improved outcomes.[26] However, choice of surgical technique is not simply surgeon preference but may be significantly influenced by the patient's anatomy, comorbidities, and body habitus. In normal-weight patients, PCNL has achieved SFRs of 91% after one procedure and an overall success rate of 95% with multiple procedures.[9,21] As a result, the AUA and EAU recommend PCNL as first-line treatment for stones greater than 2 cm.[1,12] However SFRs in both the PCNL and URS literature are influenced by the author's definition of stone-free, the patient's renal anatomy and body habitus, the postoperative imaging used and the surgeon's skill level. CROES reported an overall SFR of 76% after one procedure, with 15% requiring a secondary intervention.[26] The relationship between stone size, composition, and SFR was not addressed in this specific report. A quarter of their sample had a large stone burden; however, what defined a large stone burden was not clear, nor was the percentage of these patients who required a secondary intervention.[26] In Soucy et al's retrospective study of 509 PCNLs for staghorn stones, an SFR of 78% was achieved after 9% underwent a secondary nephroscopy. By 3 months, an overall SFR of 91% was achieved, but significantly fewer patients who underwent multiple tracts were stone-free in contrast to those needing a single tract (78% vs 92%, respectively).[27] Twice as many complete staghorn stones required multiple tracts in comparison to partial staghorns.[27]

Effects of obesity on outcomes

In a CROES database study of 3700 patients, 62% of them were reported as at least overweight (body mass index [BMI] 25 to over 40), illustrating that this demographic makes up the majority of stone cases worldwide.[29] Female stone-formers were more likely to be obese, with twice as many women having a BMI over 40 (superobese) compared to men.[29,30] Patients with a BMI over 25 were also more likely to have diabetes and cardiovascular disease. Further, 23% of patients with a BMI over 40 were taking anticoagulants and had a significantly higher rate of staghorn stones.[29] In contrast, El-Assmy et al reported an even distribution of staghorn calculi in all BMI cohorts, and there was no associated increase in blood loss in diabetics despite correlations shown in other studies.[23,31] The contrasting results between the El-Assmy et al and CROES studies could be due to the different populations evaluated. El-Assmy et al's project gathered data from an Egyptian population, whereas the CROES study included a worldwide population from Asia, the Americas, and Europe.[29,31] Desai et al showed that North America (US, Canada, Mexico) had the highest percentage of patients presenting with staghorn stones (38.8%), and the CROES study showed that North America had the highest proportion of stone-formers that were obese (BMI 30–40) and superobese (BMI $>$ 40).[29,32] Not unexpectedly, as BMI increased with the CROES population, so did the percentage of patients with diabetes and coronary artery disease. This was not the case in El-Assmy et al's work, in which there was no statistically significant difference in diabetes or cardiovascular disease with increasing BMI.[29,31] Obesity in the setting of a Westernized/North American diet with high glycemic carbohydrates and animal protein has been associated with increased excretion of stone-forming metabolites and increased urine osmolality.[30] Diabetes, with increased excretion of sugar in the urine, promotes hypercalciuria.[30] Neither study evaluated the urinary electrolytes for each BMI cohort in the different countries, but diet, lifestyle, and comorbidities could be promoting staghorn formation in the obese American population. Alternatively, the incidence of diabetes and cardiovascular disease is underdiagnosed in this Egyptian population.

Obese patients have an increased skin-to-kidney distance, which can pose a technical challenge with percutaneous access and may require additional tracts if standard instruments are too short to reach the targeted stones.[33,34] Despite these potential risk factors for bleeding, current findings from several contemporary studies have shown no association between increasing BMI or history of anticoagulant use with blood loss and the need for transfusion.[29,31]

Even though current studies of PCNLs in obese patients (BMI 30–40) have shown no significant increase in bleeding, operating room (OR) time, hospital stay, or major complications, this is still a demographic of patients that is at increased risk for developing larger stones and staghorn calculi. Staghorn calculi often require multiple tracts due to their size and complex shape. Their complexity in turn has been associated with lower SFRs, and multiple tract placements are associated with increased bleeding risk.[24,27]

Reported mean OR times for PCNL are approximately 70 minutes, ranging from 40 minutes to 150 minutes in normal BMI patients.[31] With patients having a BMI of ≥40, there was a threefold greater retreatment rate, a 10% lower SFR, and a 30-minute increase in OR time.[29] The increase in OR time in the CROES study may have been compounded by a higher incidence of staghorn stones in the superobese patients.[29] After one procedure, SFRs of 43%–50% have been reported in obese patients after PCNL. This is significantly less than the SFRs reported for nonselective groups.[27,35,36]

Ureteroscopy: impact of stone size on stone-free rate

The development of new-generation flexible ureteroscopes with improved active deflection and smaller diameter have resulted in easier access to the entire collecting system and are associated with fewer complications and improved overall SFRs.[25,37] Recent studies have reported the successful treatment of stones greater than 2 cm with flexible URS.[19,20,37–49] One limitation of the current literature related to stone treatment is the lack of a standardized definition of stone-free. The definition of less than 4 mm on imaging not requiring a second procedure was used here as a standardized comparison between studies. SFR with this standardization is variable, as shown in Tables 1 and 2. Results show an inverse relationship between SFR and stone size, particularly above 4 cm. In studies that specified treating stones ranging from 2 to 4 cm, SFR ranged from 63% to 89% after one URS.[19,37,39,42,44,45] This decreased to 25%–75% when stones greater than 4 cm were treated.[20,38,39,41,47,48] Ricchiuti et al's study of 23 patients' SFR dropped from 88% to 60% to 40% for stone sizes 2–3 cm, 3–4 cm, and above 4 cm, respectively.[47] Mariani did report an overall SFR of 95% for stones ranging from 2 to 10 cm, but required an average of 1.7 procedures per patient.[41] Table 1 demonstrates that when multiple URSs were performed, the SFR range increased to 88%–97%. Hyams et al, in a retrospective study of 19 patients with stones ranging from 2 to 3 cm in size, reported an overall SFR of 95%, in which only one patient had to undergo two procedures,[19] whereas in Mariani's report of 16 patients with a stone size of 4–10 cm, up to six procedures were needed to achieve an overall SFR of 88%[43] (Table 1). This is in contrast to a CROES study reporting 85% of PCNLs needing only one procedure, but stone size was not specifically addressed in this report.[26] In Xue et al's study of PCNL for non-staghorn stones 4–6 cm in size, an SFR of 84% 1 month after surgery after one procedure was achieved.[10] In Soucy et al's study of staghorn calculi, the SFR was only 79% at 30 days postoperatively in stones that required multiple tracts and included patients that underwent two procedures.[27] In another CROES report, the SFR of staghorn compared to non-staghorn stones (57% vs 83%) differed significantly.[32] In a matched-pair analysis by Akman, elderly patients with stones up to 3 cm were treated with either PCNL or URS. While URS had a lower initial SFR of 82% after the first procedure, and 18% underwent a second procedure, an overall SFR at 3 months was comparable to PCNL (93% vs 96%, respectively).[50] URS also has the benefit of being primarily an outpatient procedure, thus reducing cost and the morbidity associated with inpatient admission.

Mean OR times

In general, the surgical time for PCNLs has been reported as shorter in comparison to URS.[19,25,47,48,50] Akman et al reported a mean OR time of 38.7 ± 11.6 minutes for PCNL in contrast to 58.2 ± 13.4 minutes for URS for stones 2–4 cm.[25] A similar comparison resulted in their matched-pair analysis of URS vs PCNL in the elderly. The mean total OR time was 64.5 ± 20.9 minutes and 40.7 ± 10.7 minutes, for URS and PCNL respectively.[50] In contrast, Bryniarski et al's study demonstrated a mean OR time of 100 minutes for PCNL versus 85 minutes for URS, with no significant difference in stone size between the groups.[46] Nguyen and Belis also had longer mean OR times for PCNL of 3 hours 35 minutes, compared to 2 hours and 11 minutes for URS.[51] Based on these findings, in some centers, URS has shown that it can achieve comparable OR times to PCNL. However, as illustrated in Table 2, there is significant variability in the OR times for URS. This may be due to surgeon experience, type of lithotripter used, whether the stone was simply fragmented or whether it was also basket-extracted, whether a UAS was used, and where the stones were located in the kidney.[32]

Complications in PCNL vs URS

Several reports suggest patients undergoing URS may have less Clavien level II or higher complications as compared to PCNL. In a CROES report of 5800 patients undergoing PCNL, 11% had Clavien level I complications including postoperative fever and pain, while 9.4% had Clavien level II or higher surgical complications, with an overall transfusion rate of 5.7%. Additional level II or greater complication rates reported included a 4.7% rate of urosepsis, a 3.1% rate of pleural injury, a 1.4% rate of renal hemorrhage, and 0.8% incidence of colonic injury.[22,26] Studies assessing the risk of hydropneumothorax after PCNL showed that the risk was as high as 12% with percutaneous access above the twelfth rib,

Table 1 Summary comparison of SFD, SFR, repeat procedure, and failure rates per stone size reported

Author(s)	n (M/F)	BMI ≥ 30	Stone size (cm)	SFD	% SF, author definition	% SF < 4 mm after 1 stage	% underwent at least 2nd procedure	Average # stages, range	Failed URS
El-Anany et al[40]	30 (22/8)	NR	>2 cm (range NR)	≤2 mm at end of one procedure	23/30 (77%) patients	23/30 (77%) patients	0	1	3/30 (10%) PCNL 4/30 (13%) ESWL
Grasso et al[38]	51 (33/18)	NR	≥2 cm (2–6)	≤2 mm	63/66 (95%) stones after 3 stages	54/66 (81%) stones	9/66 (14%) stones	1.2/stone, 1–3	3/66 (5%) stones
Mariani[41]	59 (NR/NR)	32/59 (54%)	>2 cm (2–10)	<3 mm	60/63 (95%) stones	NR	NR	1.7/stone, range NR	NR
Mariani[42]	13 (9/4)	7/13 (54%)	2–4 cm	<3 mm	12/13 (92%) patients at 3 month f/u	10/13 (77%) patients	3/13 (23%)	1.5/patient, 1–4	NR
Mariani[43]	16 (7/9)	13/16 (81%)	>4 cm (4–10)	<3 mm	15/17 (88%) renal units after 6 stages	4/17 (23.5%) renal units	13/17 (76.5%)	2.4/renal unit, 1–6	NR
Hyams and Shah[57]	19 (11/8)	NR	2–3 cm	<4 mm	18/19 (95%) patients	17/19 (89.5%) patients	2/19 (10.5%) 1 had stone growth	1.05/patient, 1–2 (only 1 patient had 2 stages)	NR
Pevzner et al[48]	42 (16/26)	6/42 (14%)	2–9 cm	Clearance of all mobile stone fragments at 3 months, all stages	42/44 (95%) renal units	14/44 renal units (32%)	30/44 (68%)	2.07/renal unit, 1–5	2/43 (5%) ESWL
Riley et al[20]	22 (7/15)	NR	>2.5 cm (2.5–5)	No fragments larger than 2 mm on KUB	20/22 (91%) patients after 3 stages	5/22 (23%) had lower threshold for second stage	15/22 (68%)	1.82/patient, 1–3	2/22 (9%) PCNL
Breda et al[39]	15 (10/5)	NR	≥2 cm (2–2.5)	Fragments < 1 mm	14/15 (93%) patients after 4 stages	10/15 (67%) patients	5/15 (33%)	2.3/patient, 2–4 (all underwent 2nd look)	0%
Ricchiuti et al[47]	23 (12/11)	7/23 (30.4%)	≥2 cm, (2–4+)	Too small to pick up or ≤2 mm on imaging	24/32 (75%) stones	13/23 (57%) patients	10/23 (43%)	1.5/patient, 1–2	2/23 (8.7%) ESWL
Saddik et al[49]	101 (50/51)	11/101 (11%)	2–3 cm	≤3 mm	100/103 (97%) stones after 3 stages	65/103 (63%) stones	38/103 (37%)	1.49/patient, 1–3	3/103 (3%)
Hyams et al[19]	120 (72/48)	NR	2–3 cm	No stones	56/120 (47%) patients	100/120 (83%) patients	20/120 (17%)	1.2/patient, 1–3	2/120 (2%) PCNL
Prabhakar[44]	30 (NR/NR)	NR	1.6–3.5 cm	No fragments on US at 3 weeks	26/30 (87%) patients	26/30 (87%) patients	4/30 (13%)	1.1/patient, 1–2	0%
Takazawa et al[45]	20 (9/11)	NR	2–5 cm	≤4 mm	18/20 (90%) patients after 3 stages	13/20 (65%) patients	7/20 (35%)	1.4/patient, 1–3	0%
Akman et al[25]	34 (18/16)	NR	2–4 cm	<2 mm	30/34 (88%) patients after 2 stages	25/34 (74%) patients	5/34 (15%)	1.2/patient, 1–3	0%
Bryniarski et al[46]	32 (15/17)	NR	>2 cm (range NR)	<4 mm	24/32 (75%) patients	28/32 (87.5%) patients	4/32 (12.5%)	1.1/patient, 1–2	0%

Abbreviations: n, number of patients in the study; SFR, stone-free rate; NR, not reported; % SF, percentage of patients/stones/renal units that were stone-free; SFD, author's stone-free definition; URS, ureteroscopy; BMI, body mass index; ESWL, extracorporeal shock wave lithotripsy; PCNL, percutaneous nephrolithotomy; KUB, kidney-ureter-bladder x-ray; f/u, follow-up.

Table 2 Comparison of reported average OR time, ureteral access used, and complications for given stone size, and our definition of SFR

Author(s)	Mean OR time ± SD (range) minutes	Mean stone size ± SD (range) cm	Ureteral access	Scope**	Lithotripter	Complication	SFR < 4 mm after 1 stage
El-Anany et al[40]	70 ± NR (55–85); 2–3 cm, 135 ± NR (75–160); >3 cm	>2 cm (Mean, SD, range NR)	2 GW + 10 Fr D	SR up to pelvis Flex for calylx	550, 200 Ho:YAG	6.6% fever 6.6% hematuria	23/30 (77%) patients
Grasso et al[38]	NR	≥2 cm mean, SD NR (2–6)	2 GW + 10 Fr D	SR distal ureter Flex proximal	365–500, 200 Ho:YAG	3% pyelo, 3% hematuria/ transfusion 3% CVA	54/66 (81%) stones
Mariani[41]	47 ± NR (25–90) TOT	4.4 ± NR (2–10)	2 GW + 10 Fr D; balloon dilation for >3 cm stones	Dur8-Flex	EHL, 200 Ho:YAG	5% sepsis, 8% fever, 19% steinstrasse	NR
Mariani[42]	66 ± 65 (25–240) TOT	3.1 ± 6.9 (2.2–4.2)	2 GW + 10 Fr D	Flex	EHL, 200 Ho:YAG	None	10/13 (77%) patients
Mariani[43]	115 ± 89 (19–310) TOT	6.5 ± 1.5 (4–10)	2 GW + 10 Fr D	Dur8-Flex	EHL, 200 Ho:YAG	19% fever, 19% steinstrasse	4/17 (23.5%) renal units
Hyams and Shah[57]	NR	2.4 ± NR (2–3)	UAS some cases	Flex	Ho:YAG	None	18/19 (95%) patients
Pevzner et al[48]	107 ± NR (30–230) per stage	3.63 ± NR (2–9)	2 GW + some balloon dilation	Flex	365, 200 Ho:YAG	2% sepsis	14/44 (32%) renal units
Riley et al[20]	72 ± 26 (28–138) per stage	3 ± 0.62 (2.5–5)	UAS	Flex-X	600, 400, 270 Ho:YAG	4.5% sepsis, 14% stent pain, 4.5% hematoma	5/22 (23%) had lower threshold for second stage
Breda et al[39]	83 ± NR (45–140) per stage	2.2 ± 1.5 (2–2.5)	UAS all cases	Flex	200 Ho:YAG	6.6% fever, 13% hematuria	10/15 (67%) patients
Ricchiuti et al[47]	179 ± 62 (range NR) TOT; 2–3 cm 176 ± 38 (range NR) TOT; 3–4 cm 156 ± 57 (range NR) TOT; > 4 cm	3.1 ± 1.4 (2–4+)	2 GW + 10 Fr D	URF-P3 Flex	200 Ho:YAG	None	13/23 (57%) patients
Saddik et al[49]	115 ± NR (81–149) per stage	2.63 ± NR (2–3)	UAS	Dur8, Flex-X2, URF-P5, URF-V	365, 200 Ho:YAG	None	65/103 (63%) stones
Hyams et al[19]	103 ± 21 (range NR) per stage	2.4 ± 0.3 (2–3)	UAS 67% cases	Flex-X, Flex-X2, Dur8	365, 200 Ho:YAG	2% febrile UTI, 1% fever, 2% steinstrasse, 1% hematoma	100/120 (83%) patients
Prabhakar[44]	92 ± NR (45–190) per stage	2.5 ± NR (1.6–3.5)	Nottingham dilator, DUDV, UAS	Wolf or Dura-8 ACMI Flex	400 Ho:YAG	None	26/30 (87%) patients
Takazawa et al[45]	114 ± 43 (61–238) per stage	3.1 ± 1.1 (2–5)	UAS all cases	URF P-5	375, 200 Ho:YAG	5% sepsis, 15% fever	13/20 (65%) patients
Akman et al[25]	58 ± 13 (30–85) per stage	2.68 ± 6.4 cm^2 (range NR); 2–4 cm*	UAS or DUDV	SR, Flex-X2, Dur-D Gyrus	375, 200 Ho:YAG	3% sepsis, 3% fever, 3% steinstrasse, 3% ARF	25/34 (74%) patients
Bryniarski et al[46]	85 ± 18 (range NR) per stage	2.4 ± 1.1 (>2 cm, max NR)	2 GW + 12 Fr D	SR, Flex in reintervention	200 Ho:YAG	3% transfusion (15% Hct drop), 25% fever	28/32 (87.5%) patients

Notes:* surface area reported only; ** brand names listed for flexible ureteroscopes if reported.
Abbreviations: ARF, acute renal failure; CVA, cerebrovascular accident; D, dual-lumen ureteral dilator, outer diameter; DUDV, dilation ureter under direct vision; EHL, electrohydraulic lithotripsy; Flex, flexible ureteroscope; GW, guide wire; Hct, hematocrit; Ho:YAG, holmium-yttrium-aluminum-garnet laser; Pyelo, pyelonephritis; SR, semirigid ureteroscope; UAS, ureteral access sheath; UTI, urinary tract infection; TOT, total OR time.

and increased to 35% with access above the eleventh rib.[52] Noncontrast CT has been used to estimate the possibility of transgressing the pleura at the end of expiration with supracostal access. The risk was reported as 29% on the right side and 14% on the left side.[53] Taking the potential risk of these complications into account, a ureteroscopic approach to the stones should be strongly considered in some patients with significant comorbidities, where a high tract transgressing the pleural is anticipated with a PCNL.

In contrast, Aboumarzouk et al showed an overall complication rate of 10% for ureteroscopic treatment of large renal stones in a meta-analysis of 445 patients. Minor complications were reported in 4.8% of the cases and major complications in 5.3%. Major complications included steinstrasse, subcapsular hematoma, acute prostatitis, obstructive pyelonephritis, cerebrovascular accident, and hematuria with clot retention. Self-limiting hematuria occurred as a minor complication, and no transfusions were needed.[54] While this study did not classify complications into the Clavien system, minor complications generally are classified as level I, requiring only pharmaceutical intervention. In a large retrospective review of patients with coagulopathy treated with ESWL, PCNL or URS, URS had no major complications, including transfusions.[55] Bryniarski et al showed higher postoperative transfusion rate of 3% in their URS group, which may have resulted from using a 15% hematocrit drop as an indication to transfuse.[46] This was significantly less than the 16% transfusion rate in the PCNL group.[46] A systematic review of URS done on patients with bleeding diathesis had no major complications. There were 11% minor complications, including 4% with bleeding complications manifesting as transient gross hematuria that did not require continuous bladder irrigation or transfusion.[56] The lower risk of major bleeding and transfusion in URS makes it an ideal option for patients needing to avoid blood loss or at increased risk for hemorrhage.

The incidence of urosepsis appears to be similar for PCNL and URS. The risk of urosepsis after URS has been reported as 3%–5%, and is associated with an increase in stone size.[20,37,41,45] Skolarikos and de la Rosette reported the risk of urosepsis after PCNL to be approximately 4.7%.[22] Similar to URS, the risk of postoperative fever and urosepsis increases with stone size.[10] The prudent use of preoperative urine cultures and appropriate perioperative antibiotic use remains vital for this group of patients, regardless of the treatment modality.

Conclusions

The AUA guidelines indicate that PCNL is the standard of care for large renal stones because of the high SFR and low complication rates achieved. The technological advancements in both flexible ureteroscopes and the equipment used with them have resulted in improved access, visualization, fragmentation, and clearance of stones in the entire collecting system. The result has been SFR outcomes that rival PCNL in some studies, with lower overall complication rates. Obesity, staghorn stones, and increasing stone size, particularly over 4 cm, have been shown to lengthen operative time, increase the number of retreatments, and decrease SFR in both PCNL and URS. The decision to undergo URS or PCNL should be based on patient preference, relevant anatomy, surgeon experience, presence of contraindications to PCNL, and shape and size of the stone. Moderately large stones from 2 to 3 cm treated ureteroscopically have similar outcomes to PCNL.[19,57] However, SFRs with URS decrease when stone size is above 3 cm.[19,37,39,42,44,45,47]

The lack of prospective randomized trials directly comparing URS and PCNL makes comparison challenging. The numerous studies are not standardized in terms of their definition of stone-free or how stone size is reported. Follow-up imaging also varies from study to study, limiting the accuracy of direct comparison. However, taken as a whole, our interpretation of the literature suggests that a current limitation of URS is that multiple procedures for URS would be required to achieve comparable SFRs to PCNL, particularly for stones greater than 4 cm. This is an important consideration when counseling patients regarding their treatment options.[20,38,39,41,47,48] Future prospective, randomized, controlled studies are required to allow for a better comparison regarding cost, outcomes, and complications between these two surgical techniques for large (≥2 cm) renal stones.

Disclosure

Dr Bodo E Knudsen is a consultant for Boston Scientific and a hands-on course instructor for Storz and Cook.

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