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"Percutaneous Nephrolithotomy (PCNL) versus other treatments for stone management in horseshoe kidneys: A systematic review"

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ABSTRACT
Urolithiasis represents the most frequent complication of horseshoe kidneys. All known approaches for stone disease management have been reported in these patients, including Extracorporeal Shockwave Lithotripsy, ureteroscopy, Percutaneous Nephrolithotomy, open surgery and laparoscopy. The purpose of this systematic review is to compare Percutaneous Nephrolithotomy with other least-invasive procedures in patients with horseshoe kidneys. Following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Guidelines, PubMed®, Scopus® and Cochrane® primary databases were systematically screened, from inception to 29 May 2023. Both prospective and retrospective comparative studies including patients with horseshoe kidneys and urolithiasis, who underwent Percutaneous Nephrolithotomy and other treatments for stones management, were eligible. Non comparative studies and case series were also included. A total of 10 studies met inclusion criteria and were included in final qualitative synthesis. In total 583 patient underwent Percutaneous Nephrolithotomy and other treatments for stone management in included studies. Stone free rates ranged from 57.1% to 88% for Percutaneous Nephrolithotomy, from 55.6% to 100% for ureteroscopy, from 27.3% to 83.3% for Extracorporeal Shockwave Lithotripsy and was 100% for pyelolithotomy and 71.4% for Percutaneous Nephrolithotomy in combination with ureteroscopy. Although percutaneous Nephrolithotomy was associated with more complications when compared to other treatment modalities, most of them were Grade I or Grade II ones, according to the Clavien-Dindo Classification System. Management of urolithiasis can be efficiently and safely accomplished in almost all cases of horseshoe kidneys. Extracorporeal Shockwave Lithotripsy, ureteroscopy, Percutaneous Nephrolithotomy and pyelolithotomy all represent excellent choices for the treatment of stones in these patients, being feasible, efficient and safe. Percutaneous Nephrolithotomy was associated with the highest stone-free rates, but also with the highest complication rates. Access should be ideally performed via the upper poles. Optimal stone management in patients with horseshoe kidneys depends on stone burden, stone location and surgeon's preference.

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Introduction

Horseshoe kidney (HSK) is the most frequently reported renal fusion anomaly with an estimated prevalence of around 1 in 400 to 1 in 666 newborns [1,2] and is caused by the abnormal migration of the metanephric blastema during embryogenesis [3]. HSKs are characterized by a triad of position (ectopia), rotation (malrotation) and vascularity anomalies [4,5]. As a result, the collecting systems are displaced anteriorly, the ureters merge into the renal pelvises more superiorly and laterally and ureteropelvic junction obstruction (UPJO) often coexists [6,7]. All these anatomical variations impede drainage of the collecting systems and predispose HSKs to stasis, recurrent urinary tract infections (UTIs) and stone formation [8]. Indeed, urolithiasis has been found to represent the most frequent complication of HSKs, with an incidence of around 20–60% [8,9]. Except anatomic abnormalities, evidence arising from recent studies supports a multifactorial etiology of stone disease in patients with HSKs, with various metabolic abnormalities met in almost 100% of them [10].

Irregular calyceal positioning and orientation, immobility, anomalous vasculature and altered proximity with surrounding viscera render management of stone disease in anomalous kidneys a challenge for endourologists [11]. Optimal treatment of urolithiasis in these cases aims for total stone clearance and utilization of the least invasive modalities [12]. All known approaches for stone disease management have been reported in patients with HSKs, including Extracorporeal Shockwave Lithotripsy (SWL), ureteroscopy (URS), Percutaneous Nephrolithotomy (PCNL), open surgery and laparoscopy (laparoscopic pyelolithotomy or laparoscopically assisted PCNL) [13]. Nevertheless, current urolithiasis guidelines do not reach a consensus regarding the selection of the optimal approach in patients with HSKs and stone disease

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[14,15]. According to several reports, PCNL has been widely considered as the treatment of choice for stones larger than 2 cm or after SWL failure in HSKs [8,13,16,17]. Indeed, several studies have proved the feasibility, safety and efficacy of PCNL in patients with HSKs, reporting high stone-free rates [10,13,18–21]. However, PCNL has been associated with high complication rates [22]. SWL is frequently performed for stone management in HSKs as a useful and well tolerated approach [23]. Utilization of Retrograde Intrarenal Surgery (RIRS) for stone management is HSKs has shown a gradual increase being characterized by high stone-free and low complication rates [24]. The purpose of this systematic review is to report different approaches for stone management in patients with HSKs, with an emphasis given into comparison of PCNL with other least-invasive procedures such as SWL, URS and laparoscopic pyelolithotomy (LP).

Methodology

Search strategy

Following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Guidelines and after establishing an a priori protocol (which was registered to https://osf.io on 13 May 2023), PubMed®, Scopus® and Cochrane® primary databases were systematically screened, from inception to 29 May 2023. Other potentially eligible studies were retrieved using the reference list of included studies. Only human studies and articles in English were accepted. The following search string was used: 'horseshoe kidney' OR 'renal fusion' AND (percutaneous OR PCNL). The search strategy used the PICO (Patients, Intervention, Comparison, Outcome) criteria.

Selection criteria and data extraction

The search strategy used the PICO (Patients, Intervention, Comparison, Outcome) criteria. Patients (P) with urolithiasis, undergoing PCNL and other treatments for stone disease management were included. The Intervention (I) should be PCNL and other treatments for stone management such as RIRS and SWL. Comparison (C) was between PCNL and other treatments for stones in Horseshoe Kidneys, including RIRS and SWL. Regarding the Outcomes (O), the primary endpoints were stone free rates, residual stone and complications according to Clavien-Dindo Classification, while the secondary endpoints were operative time, hospital stay, hemoglobin drop, postoperative creatinine and secondary treatments. Included studies were comparative prospective studies (randomized, quasi randomized and non-randomized) including patients with horseshoe kidneys and urolithiasis undergoing PCNL compared to other treatment modalities for stones management. Non comparative studies including more than one treatment modalities for stone management in horseshoe kidneys were also included. Retrospective studies and case series were included, while ex vivo studies and case reports were excluded. Studies reporting PCNL and other treatment modalities for stone management in anomalous kidneys in general were included only if separate detailed data for horseshoe kidneys were provided.

Article selection

Two of the authors (T.S. and V.T.) independently reviewed the literature according to the inclusion and exclusion criteria. Disagreements about eligibility were resolved in conjunction with a third reviewer (P.K.) until consensus was reached. In total, 449 articles matched initial search (PubMed: 144, Scopus: 285, Cochrane: 20). After removing duplicates ($n = 130$), 319 records were screened by title and abstract. A total of 250 records were excluded and 69 full-text articles were assessed for eligibility. Further, SQR3 (Survey, Question, Read, Recite, and Review) technique was used and 10 relevant articles were selected and included in qualitative synthesis, while 59 were excluded. Reasons for exclusion included review and meta-analyses ($n = 1$), case-reports or videos ($n = 7$) and irrelevant data (outcomes or techniques not related to this study, $n = 51$). Figure 1 represents the PRISMA Flow chart.

Results

Studies characteristics

Ten studies met inclusion criteria and were included in final qualitative synthesis [12,23,25–32]. Seven studies were retrospective and non-comparative in nature [12,25,27,29–32]. Two studies were retrospective and comparative (PCNL vs RIRS) [23,26]. One study was a case-series [28]. In total 583 patients underwent PCNL and other treatments for stone management in included studies [12,23,25–32]. PCNL was reported in all studies [12,23,25–32]. SWL was reported in seven studies [12,25,27–29,31,32]. URS (RIRS/URS/Flexible URS) was reported in eight studies [12,23,25–27,29–31]. Pyelolithotomy was reported in three studies [12,28,29], 2 of which laparoscopic [12,29]. One study reported mini PCNL (MPCNL) in combination with Flexible URS [27].

Preoperative characteristics

Patient preoperative characteristics are presented in Table 1. The number of patients who were included in selected studies ranged from 25 [31] to 96 [30], while the number of renal units ranged

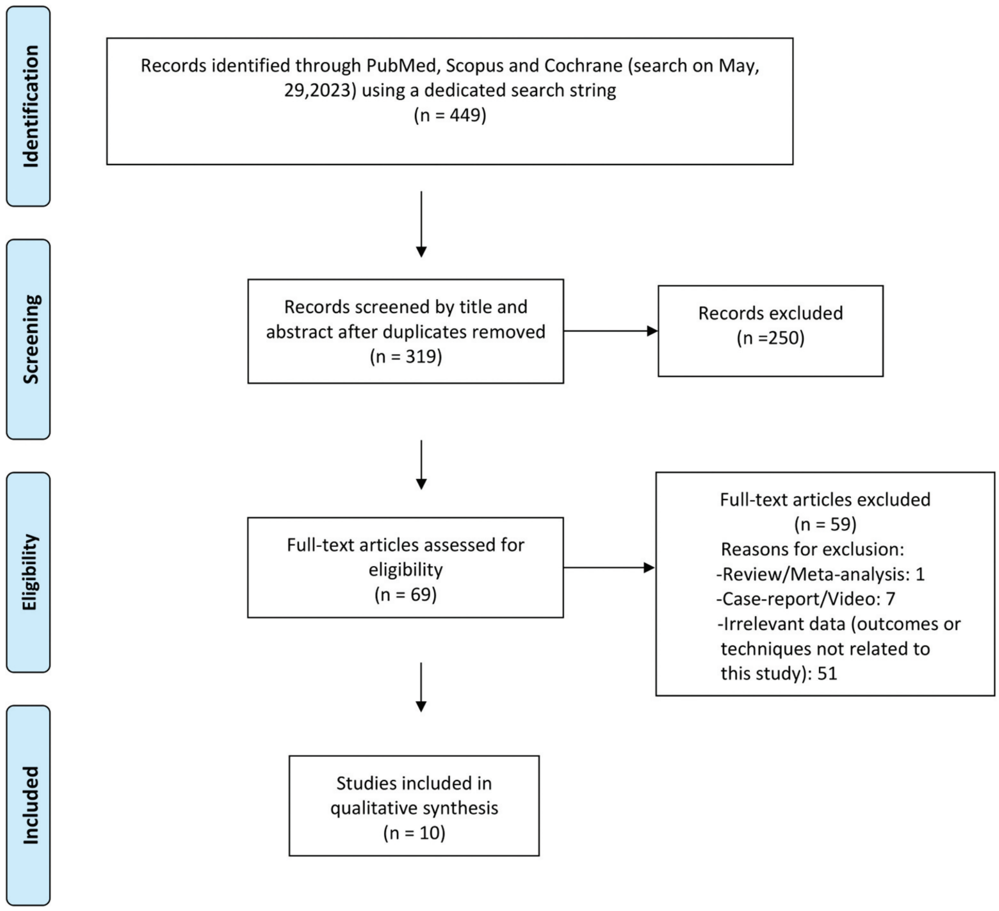

Figure 1. Preferred reporting items for systematic reviews and meta-analyses (PRISMA) flow chart for the selection of included studies.

from 29 [31] to 103 [12]. Mean patient age did not exceed 51 years-old in none of the included studies and the male to female rate ranged from 56:32 [23] to 49:6 [29], tending toward a slight male predominance. Mean stone size and mean digitized surface area were heterogenous for different treatment modalities in selected studies and are presented in Table 1. Most stones were located in renal calyces, followed by the renal pelvis and the ureter, respectively, while most stones were unilateral and most frequently present on the left side [12,23,25–32]. Presence of hydronephrosis was not reported by all studies and ranged from 26/49 [26] to 38/62 [27] of patients. The mean preoperative creatinine value was normal in most patients [12,26,28,29,31]. The most frequently reported symptom during presentation was pain, followed by haematuria and recurrent urinary tract infections [12,26,29,32]. Staghorn stones represented only the minority in the studies which provided data about stone characteristics [12,29,31,32]. In total, PCNL was used in 339 cases, URS in 172 cases, SWL in 58 cases,PCNL combined with URS in 14 cases, pyelolithotomy in 8 cases (2 laparoscopic ones) and nephrectomy in 2 cases [12,23,25–32].

Intraoperative characteristics

Table 2 provides a detailed description of included studies' intraoperative parameters. Mean operative time ranged from 74.5 ± 19.3 [30] to 106.4 ± 16.6 [27] minutes for PCNL, from 40.5 ± 11.2 [30] to 93.1 ± 11.5 for URS [27], from 44.8 ± 5.3 [27] to 88 (60–130) [12] for SWL and was 180 minutes for laparoscopic pyelolithotomy [12,29] and 124.4 ± 15.1 minutes for PCNL in combination with URS [27]. Mean number of sessions ranged from 1.29 [31] to 2.9 [32] for SWL, from 1 [23] to 1.4 ± 0.6 for PCNL [27], from 1.22 ± 0.07 [23] to 1.4 ± 0.5 [27] for URS and was 1.3 ± 0.6 for PCNL in combination with URS [27]. Mean hemoglobin drop fluctuated from 1.27 (0.2–5.0) [12] to 1.83 ± 0.51 [27] for PCNL, from 0.13 ± 0.07 [23] to 0.20 (0.0–0.4) [12] for URS and was 0.03 (0.0–0.2) [12] for SWL and 2 [12] for LP, respectively. In most studies a calyceal puncture was selected for establishing access in PCNL, while a single access point was used in most cases [12,23,25–32]. The equipment which was used for different treatment modalities is presented in Table 2. The Flex-X2 flexible ureteroscope with holmium laser was most frequently reported for URS in selected studies, the Dornier Compact Delta was the most commonly reported

Table 1. Patients' baseline characteristics.

Study Name	Number of Patients	Age (years-old)	Male to Female Rate	Stone size (mm)/DSA (mm^2)	Stone Location/Side	Presence of Hydronephrosis	Preoperative Cr (mg/dl)	Presentation/Staghorn number	Procedure
Blackburne et al. (mean) [25]	n = 45 (64 renal units)	**Overall**: 49.4 (23–78), **PCNL**: 51.2 (23–75), **URS**: 48.1 (29–78), **SWL**: 32.5 (23–42)	**PCNL**: 19:7, **URS**: 13:7, **SWL**: 0:2	**PCNL**: 22.4 (10–57), **URS**: 8.4 (2–25), **SWL**: 4.5 (4–5)/NA	NA/**PCNL**: 3 bilateral, **URS**: 3 bilateral	NA	NA	NA/NA	**PCNL** (*n* = 37), **URS** (*n* = 25), **SWL** (*n* = 2)
Kartal et al. (mean) [26]	n = 49	**RIRS**: 43.2 ± 8.4, **PCNL**: 41.5 ± 9.9	**RIRS**: 23:5, **PCNL**: 18:3	**RIRS**: 22.3 ± 9.1, **PCNL**: 24.5 ± 8.1/NA	n = 15 (renal pelvis), *n* = 34 calyces/n = 26 (right), *n* = 23 (left)	**RIRS**: *n* = 12, **PCNL**: *n* = 14	**RIRS**: 0.98 ± 0.30, **PCNL**: 0.95 ± 0.37	Pain (**PCNL**: 52.4%, **RIRS**: 60,7%)/NA	**RIRS** (*n* = 28), **PCNL** (*n* = 21)
Ding et al. (mean) [27]	n = 62	43.4± 10.4	49:13	22.3 ± 7.7/511.3 ± 355.4	NA/n = 51 unilateral, *n* = 11 bilateral	n = 38	NA	NA/NA	**SWL** (*n* = 11), **Retrograde FURS** (*n* = 18), **MPCNL** (*n* = 19), **MPCNL/Antegrade FURS** (*n* = 14)
Eryildirim et al. (mean) [23]	n = 88	41.161.25*	56:32	20.590.75*/NA	n = 30 (renal pelvis), *n* = 58 (calyces)/NA	1.720.11*	NA	NA/NA	**PCNL** (*n* = 38), **RIRS** (*n* = 50)
Singh et al. (mean) [12]	n = 85 (*n* = 103 renal units)	38.2 (7–67)	65:20	NA/**PCNL**: 595.5 (99–3850), **RIRS/URS**: 142.4 (28–290), **SWL**: 145 (50–225), **LP**: 1662	n = 42 (renal pelvis), *n* = 32 (calyces), *n* = 18 (pelvis +calyces), *n* = 2 ureter/NA	NA	1.05	Pain (*n* = 75), hematuria (*n* = 12)/ **PCNL**: (*n* = 8), **LP**: (*n* = 1)	**PCNL** (*n* = 67), **RIRS/Flexible URS** (*n* = 10), **SWL** (*n* = 7), **LP** (*n* = 1)
Goel at al. (mean) [28]	n = 34 (*n* = 36 renal units)	38 (11–56) (median)	28:6	39.27 (21–70)/NA	n = 17 (renal pelvis), *n* = 17 (calyces)/n = 22 (left), *n* = 10 (right), *n* = 2 (bilateral)	NA	1.08 (0.7–1.7)	NA/NA	**PCNL** (*n* = 24), **pyelolithotomy** (*n* = 6), **nephrectomy** (*n* = 2), **SWL** (*n* = 2)
Symons et al. (mean) [29]	n = 55 (*n* = 69 renal units)	36.5 (7–60)	49:6	NA/**PCNL**: 614.3 (99–3850), **SWL**: 149.2 (50–225), **Flexible URS**: 172 (63–281), **Rigid URS**: 44 (28–60), **LP**: 1662	NA/NA	NA	0.97	Pain (*n* = 40), hematuria (*n* = 4), both (*n* = 6), other (*n* = 5)/n = 6	**PCNL** (*n* = 47), **SWL** (*n* = 5), **Rigid and Flexible URS** (*n* = 3), **LP** (*n* = 1)
Ergin et al. (mean) [30]	n = 96	**Overall**:39 (range:1–72), **RIRS**: 40.9± 15.9, **PCNL**: 46.3 ± 18.6	**RIRS**: 24:12, **PCNL**: 39:21	**RIRS**: 17.8 ± 4.5, **PCNL**: 27.9 ± 8.6/NA	n = 26 (renal pelvis), *n* = 98 (calyces)/n = 72 (left), *n* = 52 (right)	NA	NA	NA/NA	**PCNL** (*n* = 60), **RIRS** (*n* = 36)
Al Otay et al. (mean) [31]	n = 25 (*n* = 29 renal units)	37 (2–78)	16:9	NA/NA	n = 16 (calyces), *n* = 3 (UPJ), *n* = 1 (ureter), *n* = 4 (multiple)/n = 14 (left), *n* = 7 (right), *n* = 4 (bilateral)	NA	66 mmol/L	NA/n = 1	**SWL** (*n* = 6), **PCNL** (*n* = 7), **Flexible URS** (*n* = 1), **Semi-rigid URS** (*n* = 1)
Viola et al. (mean) [32]	n = 44 (*n* = 49 renal units)	50 (3–83)	36:13	NA/**SWL**: 91 (10–1600), **PCNL**: 197 (6–2400)	NA/Equally located on the right and left side	NA	NA	hematuria, recur- rent urinary tract infections, and loin pain/n = 1	**PCNL** (*n* = 19), **SWL** (*n* = 25)

DSA: Digitized Surface Area (mm^2), **Cr**: Creatinine (mg/dl), **PCNL**: Percutaneous Nephrolithotomy, **URS**: Ureteroscopy/Ureterorenoscopy, **SWL**: Shockwave Lithotripsy, **RIRS**: Retrograde Intrarenal Surgery, **FURS**: Flexible Ureterorenoscopy, **MPCNL**: Mini-Percutaneous Nephrolithotomy, **LP**: Laparoscopic Pyelolithotomy, **UPJ**: Ureteropelvic Junction.
*These are the exact values as they were presented by the authors.

device for SWL and finally the prone position, a 18 G needle and fluoroscopy were the most frequently reported settings for PCNL, while regarding the energy device there was not a clear preference and holmium laser, pneumatic and ultrasonic lithotripters were almost equally reported during PCNL in selected studies [12,23,25–32].

Postoperative characteristics

Postoperative characteristics and outcomes of PCNL along with other treatment modalities for stone management in horseshoe kidneys are presented in Table 3. Mean hospital stay ranged from 1.58 ± 0.20 [23] to 6.9 ± 1.4 days [27] for PCNL, from 1.1 ± 1.4 [27] to 3.15 ± 0.24 days [23] for ureteroscopy, from 0 [27] to 1.5 (1–2.5) days [12] for SWL, from 4 [29] to 5.5 days [12] for laparoscopic pyelolithotomy and was 6.6 ± 0.8 days for PCNL in combination with ureteroscopy [27]. Unfortunately, stone free rates and secondary procedures rates were not uniformly defined in all studies. We tried to report these rates after the first session and thus most data reported in Table 3 refer to rates after the first session in cases where multiple sessions were used. Nevertheless, in some studies it is not clearly stated what these rates refer to. Stone free rates ranged from 57,14% [31] to 88% [12,29] for PCNL, from 55,6% [27] to 100% [29] for ureteroscopy, from 27.3% [27] to 83,3% [28] for SWL and was 100% for pyelolithotomy [12,28,29] and 71,4% for PCNL in combination with ureteroscopy [27]. Mean postoperative creatinine was only reported in one study and was 0.95 ± 0.32 for RIRS and 0.89 ± 0.33 for PCNL [26]. Complications according to Clavien-Dindo classification system [33] are shown in detail in Table 3. As expected from its more interventional nature, PCNL was associated with more complications when compared to other treatment modalities [12,23,25–32]. Nevertheless, most of them were Grade I or Grade II ones, according to the Clavien-Dindo Classification System. Regarding the stones' composition, most of them were calcium oxalate ones or contained predominantly calcium oxalate. However, information about stone composition was not provided by all studies.

Discussion

In a systematic review and meta-analysis of five studies comparing SWL with Flexible URS for treating stones in HSKs, the authors concluded that both options are effective and safe for stones <2 cm. However, they reported that Flexible URS was associated with greater initial and overall stone-free rates, while complication rates were also lower in comparison with SWL [34]. To our knowledge, this is the first systematic-review reporting the outcomes, safety and efficacy of PCNL versus other treatments for stone management in HSKs. Stone-free rates of SWL for management of urolithiasis in HSKs have been reported to range from 31% to 100% [32,35–37]. Reported stone-free rates for PCNL in HSKs range from 66% to 89% [9,18,38–43]. Stone-free rates for Flexible URS have been reported to range from 70 to 88.2% [44–46]. In the articles included in our systematic review, stone free rates ranged from 57,14% [31] to 88% [12,29] for PCNL, from 55,6% [27] to 100% [29] for URS, from 27.3% [27] to 83,3% [28] for SWL and was 100% for pyelolithotomy [12,28,29] and 71,4% for PCNL in combination with URS [27].

Blackburne et al.. (Urology, 2016) reported that although all surgical approaches (SWL, URS and PCNL) can be associated with excellent outcomes in HSKs, overall stone-free rates can be confined by increased stone burden. The authors emphasized that anatomical variations in patients with HSKs (orientation of the renal pelvis and course of the ureter) can impede the passage of fragments after SWL. They also noted that their study represents one of the biggest studies regarding URS in patients with HSKs. They thus recommended to inform patients with horseshoe kidneys undergoing URS, that lower pole stones can be sometimes associated with residual fragments, due to inability to access the stone with the ureteroscope and thus a conversion to PCNL cannot be excluded. Finally, they emphasized on that anomalous anatomy and aberrant vasculature of HSKs represent a challenge for the urologist who wants to proceed with PCNL in these patients. However, they declared that PCNL should represent the treatment of choice for large stone burdens and the development of flexible nephroscopes has helped in that direction [25].

Kartal et al.. (Central European Journal of Urology, 2019) compared RIRS and PCNL for the treatment of urolithiasis in HSKs. RIRS was associated with a higher retreatment rate and a shorter hospital stay, while PCNL was associated with more serious complications. They suggested considering RIRS for some cases of large stones in these patients so as to avoid complications related to PCNL. In the discussion section of their paper, they summarized all the difficulties encountered during RIRS in these patients. According to them, manipulations with the flexible ureteroscope are difficult due to the flat pelvises and the narrow intrarenal spaces of these patients. Their anomalous anatomy and the long length of the flexible ureteroscope that remains outside of the urethra are all factors that result in lower stone-free rates and higher need for a second session. They noted that this has an effect on the cost for healthcare systems and they suggested using a ureteral access sheath (UAS) but judiciously, so

Table 2. Included studies' intraoperative characteristics.

Study Name	Operative Time (min)	Number of Sessions	Hemoglobin Drop (g/dL)	Access	Equipment
Blackburne et al.. (mean) [25]	NA	NA	NA	Single upper pole (*n* = 31), two access points (*n* = 2)	NA
Kartal et al. (mean) [26]	RIRS: 65.7 ± 29.9, PCNL: 86.6 ± 40.8	NA	NA	On the appropriate calyx and/or directly on the stone, multiple accesses (*n* = 3)	RIRS: FLEX-X2 flexible ureteroscope (UAS and basket for some cases), PCNL: prone position, 18 G needle, fluoroscopy, 0.035-inch j tip guidewire, up to 30 F dilatation, amplatz sheath, nephrostomy.
Ding et al. (mean) [27]	SWL: 44.8 ± 5.3, Retrograde FURS: 93.1 ± 11.5, MPCNL: 106.4 ± 16.6, MPCNL with Retrograde FURS: 124.4 ± 15.1	SWL: 1.7 ± 0.5, Retrograde FURS: 1.4 ± 0.5, MPCNL: 1.4 ± 0.6, MPCNL with Retrograde URS: 1.3 ± 0.6	MPCNL: 1.83 ± 0.51, MPCNL with Retrograde FURS: 1.43 ± 0.42	Mean number of tracts: MPCNL: 1.6 ± 0.5, MPCNL with Retrograde FURS: 1.1 ± 0.3	SWL: Dornier Compact Delta lithotripter (1400 kV), FURS: 12/14 F Flexor UAS, URF *p*-3 or *p*-5 ureteroscope, 200 μm holmium laser fiber (0.8–1.2 J, Lumenis), MPCNL: supine position, 18 G needle, 8–16 F dilator and Peel-away sheath, ultrasonography, 8/9.8 F rigid renoscope, 550 μm holmium laser fiber (2–3 J, Lumenis).
Eryildirim et al. (mean) [23]	PCNL: 75.8± 42.64, RIRS: 80.2 ± 65.13	PCNL: 1, RIRS: 1.22 ± 0.07	PCNL: 1.55 ± 0.15, RIRS: 0.13 ± 0.07	NA	RIRS: lithotomy position, holmium laser, PCNL: prone position, pneumatic lithotripter.
Singh et al. (mean) [12]	PCNL: 87 (30–180), RIRS/Flexible URS: 42 (30–110), SWL: 88(60–130), LP: 180.	NA	PCNL: 1.27 (0.2–5.0), RIRS/Flexible URS: 0.20 (0.0–0.4), SWL: 0.03 (0.0–0.2), LP: 2	Either the stone bearing calyx or the calyx from which the stone could be reached	SWL: Dornier Compact Delta lithotripter (13 kV), LP: transperitoneal approach, Semi-Rigid URS: 6/7.5-Fr or 8/9.8-Fr semi rigid uretero-renoscope, holmium laser (1.2 J fragmentation, 0.4J dusting), Flexible URS: 12/14-Fr UAS, Flex-X2 URS, holmium laser (1.2 J fragmentation, 0.4J dusting), PCNL: prone position, ultrasound, 12–14 or 20 or 24-Fr scope, laser or pneumatic lithoclast.
Goel at al. (mean) [28]	NA	NA	NA	Infra-costal approach superior calyceal (*n* = 16), middle calyceal (*n* = 8) and inferior calyceal (*n* = 2)	NA
Symons et al. (mean) [29]	1 stage PCNL: 63.0 (30–120), 2 stages PCNL: 97.3 (40–195), 3 stages PCNL: 180, 4 stages PCNL: NA, LP: 180	1 (*n* = 46), 2 (*n* = 12), 3 (*n* = 1), 4 (*n* = 1)	1 stage PCNL: 1.2 (0–2.3), 2 stages PCNL: 1.4 (0.2–3), 3 stages PCNL: 2, 4 stages PCNL: 5	Upper calyceal access (*n* = 29), solitary upper calyceal tract (*n* = 21) upper-pole with mid- or lower-pole access in a multi-tract procedure (*n* = 8).	SWL: 13 kV
Ergin et al. (mean) [30]	RIRS: 40.5 ± 11.2, PCNL: 74.5 ± 19.3	NA	NA	Selected calyx	RIRS: 9.5–11.5F UAS, Flex X2 flexible ureteroscope, 170–200 μm holmium laser (Medilash), PCNL: prone position, fluoroscopy, 18 G needle, Teflon Amplatz dilator, 24 F semi rigid ureteroscope, ultrasonic and pneumatic lithotripter, grasping forceps, 14 F nephrostomy tube.
Al Otay et al. (mean) [31]	NA	SWL: 1.29	NA	NA	NA
Viola et al. (mean) [32]	NA	SWL: 2.9 (1–3)	NA	Upper pole posterior calix (*n* = 7), middle pole posterior calix (*n* = 7), lower pole posterior calix (*n* = 3) two tracts (*n* = 3)	SWL: Dornier MPL 2000, Wolf Piezolith 2300, Dornier Compact Delta (17–22 kV), PCNL: fluoroscopy, dilation up to 30 Fr, 26 Fr Amplatz sheath, rigid nephroscope, ultrasound energy (holmium laser for only 1 case), 10.2 Fr nephrostomy.

PCNL: Percutaneous Nephrolithotomy, URS: Ureteroscopy/Ureterorenoscopy, SWL: Shockwave Lithotripsy, RIRS: Retrograde Intrarenal Surgery, FURS: Flexible Ureterorenoscopy, MPCNL: Mini-Percutaneous Nephrolithotomy, LP: Laparoscopic Pyelolithotomy, UAS: Ureteral Access Sheath.

Table 3. Included studies' postoperative characteristics.

Study Name	Hospital Stay (days)	Stone Free Rates	Secondary Procedures	Postoperative Cr (mg/dL)	Complications	Stone Type
Blackburne et al. (mean) [25]	NA	PCNL: 81.1%, URS: 84%, SWL: 50%	PCNL: 27%, URS: 0%, SWL: 0%	NA	PCNL: *n* = 3 (*n* = 1 Grade I, *n* = 1 Grade II, *n* = 1 Grade III), URS: *n* = 0, SWL: *n* = 0	Calcium oxalate 52.9%
Kartal et al. (mean) [26]	RIRS: 2.07 ± 1.9, PCNL: 4.1 ± 2.2	RIRS: 71.4%, PCNL (single session): 81%	RIRS: 14.3%, PCNL: 19%	RIRS: 0.95 ± 0.32, PCNL: 0.89 ± 0.33	RIRS: *n* = 7 (*n* = 4 Grade I, *n* = 2 Grade II, *n* = 1 Grade IIIa) PCNL: *n* = 8 (*n* = 1 Grade I, *n* = 4 Grade II, *n* = 2 Grade IIIa, *n* = 1 Grade IVb)	NA
Ding et al. (mean) [27]	SWL: 0, Retrograde FURS: 1.1 ± 1.4, MPCNL: 6.9 ± 1.4, MPCNL with Retrograde FURS: 6.6 ± 0.8	SWL: 27.3%, Retrograde FURS: 55.6%, MPCNL: 68.4%, MPCNL with Retrograde FURS (single session): 71.4%	NA	NA	SWL: *n* = 1, Retrograde FURS: *n* = 3, MPCNL: *n* = 3, MPCNL with Retrograde FURS (major complications): *n* = 2	n = 22/45 calcium oxalate
Eryildirim et al. (mean) [23]	RIRS: 3.15 ± 0.24, PCNL: 1.58 ± 0.20	PCNL: 84.2% 3 months, RIRS: 82.0% 3 months	PCNL: 7.9%, RIRS: 6.0%	NA	PCNL: *n* = 19 (*n* = 11 Grade I, *n* = 3 Grade II, *n* = 2 Grade IIIa, *n* = 3 Grade IIIb), RIRS: *n* = 16 (*n* = 11 Grade I, *n* = 1 Grade II, *n* = 1 Grade IIIa, *n* = 3 Grade IIIb)	NA
Singh et al. (mean) [12]	PCNL: 4.7 (2–12), RIRS/Flexible URS: 1.5 (1–3.5), SWL: 1.5 (1–2.5), LP: 5.5	PCNL: 88%, RIRS/Flexible URS: 80%, SWL: 50%, LP: 100%	PCNL: *n* = 2, RIRS/Flexible URS: *n* = 2, SWL: *n* = 1, LP: *n* = 0	NA	PCNL: *n* = 13 (*n* = 9 Grade I, *n* = 2 Grade II, *n* = 3 Grade III), RIRS/Flexible URS: *n* = 2 (Grade I), SWL: *n* = 2 (Grade I), LP: *n* = 1 (Grade I)	NA
Goel at al. (mean) [28]	NA	Pyelolithotomy: 100%, SWL: 50% %, PCNL superior calyceal: 75%, PCNL middle calyceal: 25%, PCNL inferior calyceal: 100%	Pyelolithotomy: *n* = 0, SWL: *n* = 1, PCNL: *n* = 4	NA	n = 8 (none was Grade III or more)	NA
Symons et al. (mean) [29]	LP: 4	PCNL: 88%, SWL: 80%, URS: 100%, LP: 100%	PCNL: *n* = 1, SWL: *n* = 0, URS: *n* = 0, LP: *n* = 0	NA	LP: *n* = 0	All stones were predominantly calcium oxalate dihydrate
Ergin et al. (mean) [30]	RIRS: 1.4 ± 0.7, PCNL: 2.2 ± 1.4	RIRS: 72.2%, PCNL (single session): *n* = 66.6%	PCNL: *n* = 14	NA	RIRS: *n* = 5 (all minor), PCNL: only minor complications	NA
Al Otay et al. (mean) [31]	NA	PCNL (single session): 57.14%	PCNL: *n* = 3	NA	NA	NA
Viola et al. (mean) [32]	NA	PCNL: 75%, SWL: 31%	PCNL: *n* = 2, SWL: *n* = 7	NA	PCNL: *n* = 9 (*n* = 2 major, *n* = 7 minor), SWL: *n* = 0	n = 10/32 calcium oxalate

Cr: Creatinine (mg/dl), PCNL: Percutaneous Nephrolithotomy, URS: Ureteroscopy/Ureterorenoscopy, SWL: Shockwave Lithotripsy, RIRS: Retrograde Intrarenal Surgery, MPCNL: Mini-Percutaneous Nephrolithotomy, LP: Laparoscopic Pyelolithotomy.

as to avoid mucosal injury and hemorrhage in these patients. Finally, they once again emphasized the difficulty of spontaneous passage of fragments in these patients. They thus suggested fragmenting the stones as much as possible and removing small fragments with baskets. They also recommended fragmentation of stones located in lower poles after their transportation in a more appropriate area [26]. Eryildirim et al.. (Archivio Italiano di Urologia E Andrologia, 2018) once again compared the safety and the efficacy of RIRS versus PCNL for the management of urolithiasis in HSKs. Complications were comparable between the two groups, while RIRS was associated with a higher number sessions and operative time. Interestingly, the authors made some useful comments on PCNL for horseshoe kidneys. According to them, a supracostal approach which is frequently useful for access to upper poles but associated with a high risk of pleural injury, is safe in these patients. In their opinion, upper pole access in patients with horseshoe kidneys enables total stone burden removal in a single session, while a lower pole access should be avoided, due to the more posterior location of these calyces [23].

Ding et al. (Journal of X-Ray Science and Technology (2012) presented their practice for stone management in HSKs. They reported that MPCNL is efficient for stones ≥2 cm, while MPCNL in combination with Flexible URS is a safe and efficient tailored approach for complex or multiple stones, improving stone-free rates and minimizing access tract numbers and blood loss, with the disadvantage of increased operative time, though. Retrograde Flexible URS represents for them a both feasible and efficient approach for stones ≤2–3 cm but may be associated with repeat sessions and residual stone fragments. They also encountered difficulty in bending the flexible ureteroscope and fragmenting and repositioning lower pole stones in the narrow intrarenal space of horseshoe kidneys. Interestingly, they noted that the stone location had a more significant impact on stone-free rates of ureteroscopy, than the stone burden. They thus proposed that in cases of small residual fragments in lower poles, patients are followed-up with imaging and MPCNL is offered to them, if necessary. Finally, they considered SWL as an acceptable non-invasive option for small solitary stones [27].

Singh et al. (BJU International, 2018) studied the changing trend of stones management in anomalous kidneys in general. The authors described in a detailed manner, technical peculiarities, encountered during PCNL in patients with HSKs. According to them the pelvicalyceal system is more easily accessible in horseshoe kidneys, due to the lower position of the superior calyces, which can be accessed subcostally. Moreover, the special anatomy of these kidneys requires a more medial entry site and thus the posterior calyces can be directly accessed. Although abnormal vasculature of these kidneys has been traditionally considered as a source of worry for performing PCNL in these patients, the authors note that the majority of this vasculature lies anteriorly and the area posteriorly to the superior calyces is usually vascular-free. They also mentioned that the tract may be longer in these kidneys, necessitating sometimes a longer nephroscope. They suggested accessing the pelvicalyceal system via the upper pole, which is more superficially and posteriorly placed, while the subcostal lower pole calyces are not accessible percutaneously. In that way, both the upper and the lower poles, the pelvis and the proximal ureter can be accessed. Furthermore, the longitudinal axis of the nephroscope is aligned with the longitudinal axis of the kidney, minimizing pressure and bleeding risk. They noted that a supracostal access is rarely need and if necessary, it should be performed through a posterior calyx, more medially and it may pass through the paraspinal muscles. In their opinion, a flexible nephroscope can avoid unnecessary lower calyces' punctures. Finally, they recommended considering SWL only in low-density stones and in promptly excreting kidneys, while they suggested use of laparoscopic-guided PCNL in cases where an acoustic window cannot be detected or the bowel cannot be displaced [12].

Symons et al.. (BJU International, 2008) declared in their study a preference for PCNL in patients with HSKs, and their stone-clearance rate of 88% along with the minimal complications which were reported, confirmed the safety and the efficacy of their statement. In their opinion, SWL and Flexible URS also represent possible approaches for smaller stone burdens with acceptable stone-clearance rates. Finally, they suggested considering laparoscopic pyelolithotomy in some cases, especially in cases with a large stone burden in the isthmus of the horseshoe kidney [29]. Al Otay et al.. (Urology Annals, 2018) presented their strategy for stone management in HSKs. Patients with stones >2 cm were considered as ideal candidates for PCNL, while patients with stones <2 cm were considered as ideal candidates for SWL and all underwent the placement of a pigtail catheter before SWL. Interestingly, they managed expectantly patients with small asymptomatic nonobstructing stones <8 mm with hydration and medical treatment. An intervention (URS) was only needed for only 1 patient (9%) during follow-up [31]. Finally, Viola et al.. (Urologia Internationalis, 2007) stated that the SWL stone-free rate in their series was disappointing, while the altered orientation of the calyces in HSKs offer an ideal environment for access during PCNL [32].

This systematic review has certain limitations. The presented data were heterogenous and thus a meta-analysis was not possible. Furthermore, a thorough comparative analysis for each treatment modality was not feasible due to the heterogenous data and the non-comparative design of must studies included in this systematic review. Although we included only the latest articles, included articles publication year ranged from 2006 to 2022. It is thus possible that the lower stone-free rates and higher complication rates presented in some of the older articles can be attributed to the older equipment used at the time of the study. Moreover, all articles are retrospective. The implementation of larger prospective studies or even randomized-controlled trials is necessary for drawing safer conclusions. Another important limitation was that stone-free, success and secondary procedure rates were not uniformly defined in included studies. Furthermore, procedures were performed by different surgeons in several different Centres and thus differences in outcomes between different studies can be associated with the surgeon's experience and the availability of the equipment. Nonetheless, these results present the common practice. Finally, indications for preference of one technique over the other, for management of urolithiasis in HSKs, ranged among Centres and it was frequently based on surgeon's preference.

Conclusion

Management of urolithiasis in patients with HSKs can be efficiently and safely accomplished in almost all cases. SWL, URS, PCNL and pyelolithotomy all represent excellent choices for the treatment of stones in these patients, being feasible, efficient and safe. Other approaches such as conservative management and combined PCNL with URS have also been reported. In general, PCNL has been associated with the highest stone-free rates, but also with the highest complication rates. Nevertheless, in highly experienced surgeons and Centers the complication rates are low. Access should be ideally performed via the upper poles. SWL represents a good option for smaller stones, but patients should be informed regarding the high possibility of secondary and auxiliary procedures. Flexible URS is also an excellent choice, with stone-free rates between those reported for SWL and PCNL, but presents some technical difficulties. Pyelolithotomy, which is more often performed in a laparoscopic way, should be preserved for the most complicated cases. It becomes clear that optimal stone management in patients with HSKs depends on stone burden, stone location and surgeon's preference. Larger prospective studies and, if possible, randomized-controlled trials comparing PCNL with other treatments in horseshoe kidneys, should be performed in order to draw safer conclusions.

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List of abbreviations

PCNL	Percutaneous Nephrolithotomy.
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses.
SWL	Shockwave Lithotripsy.
HSK	Horseshoe Kidney.
UPJO	Ureteropelvic Junction Obstruction.
UTI	Urinary Tract Infection.
URS	Ureteroscopy.
RIRS	Retrograde Intrarenal Surgery.
PICO	Patients, Intervention, Comparison, Outcome.
SQR3	Survey, Question, Read, Recite, and Review.
MPCNL	Mini Percutaneous Nephrolithotomy.
LP	Laparoscopic Pyelolithotomy.
UAS	Ureteral Access Sheath.
DSA	Digitized Surface Area.
Cr	Creatinine.
FURS	Flexible Ureterorenoscopy.
UPJ	Ureteropelvic Junction.

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