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European Association of Urology

Review – Stone Disease

Treatment of Bladder Stones in Adults and Children: A Systematic Review and Meta-analysis on Behalf of the European Association of Urology Urolithiasis Guideline Panel

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Abstract

Context: Bladder stones (BS) constitute 5% of urinary stones. Currently, there is no systematic review of their treatment.
Objective: To assess the efficacy (primary outcome: stone-free rate [SFR]) and morbidity of BS treatments.
Evidence acquisition: This systematic review was conducted in accordance with the European Association of Urology Guidelines Office. Database searches (1970–2019) were screened, abstracted, and assessed for risk of bias for comparative randomised controlled trials (RCTs) and nonrandomised studies (NRSs) with ≥10 patients per group. Quality of evidence (QoE) was assessed using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) tool.
Evidence synthesis: A total of 2742 abstracts and 59 full-text articles were assessed, and 25 studies (2340 patients) were included. In adults, one RCT found a lower SFR following shock wave lithotripsy (SWL) than transurethral cystolithotripsy (TUCL; risk ratio 0.88, $p = 0.03$; low QoE). Four RCTs compared TUCL versus percutaneous cystolithotripsy (PCCL): meta-analyses demonstrated no difference in SFR, but hospital stay (mean difference [MD] 0.82 d, $p < 0.00001$) and procedure duration (MD 9.83 min, $p < 0.00001$) favoured TUCL (moderate QoE). Four NRSs comparing open cystolithotomy (CL) versus TUCL or PCCL found no difference in SFR; hospital stay and procedure duration favoured endoscopic surgery (very low QoE). Four RCTs compared TUCL using a nephroscope versus a cystoscope: meta-analyses demonstrated no difference in SFR; procedure duration favoured the use of a nephroscope (MD 22.74 min, $p < 0.00001$; moderate QoE). In children, one NRS showed a lower SFR following SWL than TUCL or CL. Two NRSs comparing CL versus TUCL/PCCL found similar SFRs; catheterisation time and hospital stay favoured endoscopic treatments. One RCT comparing laser versus

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pneumatic TUCL found no difference in SFR. One large NRS comparing CL techniques found a shorter hospital stay after tubeless CL in selected cases; QoE was very low.
Conclusions: Current available evidence indicates that TUCL is the intervention of choice for BSs in adults and children, where feasible. Further high-quality research on the topic is required.
Patient summary: We examined the literature to determine the most effective and least harmful procedures for bladder stones in adults and children. The results suggest that endoscopic surgery is equally effective as open surgery. It is unclear whether stone size affects outcomes. Shock wave lithotripsy appears to be less effective. Endoscopic treatments appear to have shorter catheterisation time and convalescence compared with open surgery in adults and children. Transurethral surgery, where feasible, appears to have a shorter hospital stay than percutaneous surgery. Further research is required to clarify the efficacy of minimally invasive treatments for larger stones and in young children.

1. Introduction

Despite constituting only approximately 5% of all urinary tract stones [1], bladder stones (BSs) are responsible for 14% of hospital admissions [2] and 8% of urolithiasis-related deaths in developed nations [3]. BSs are more prevalent in men and in developing countries [4–6]. BSs have a bimodal age distribution: incidence peaks at 3 [5,7] and 60 yr [4]. BSs may cause lower urinary tract symptoms, infections, pain, and haematuria, and have been associated with bladder cancer [8].

BSs can be classified as primary, secondary, and migratory [9]. Primary or endemic BSs occur in the absence of other urinary tract pathologies, typically seen in children in areas with a diet lacking animal protein, poor hydration, and recurrent diarrhoea [10]. Secondary BSs occur in the presence of other urinary tract abnormalities, including bladder outlet obstruction, neurogenic bladder dysfunction, chronic bacteriuria, foreign bodies including catheters, bladder diverticulae, and bladder augmentation or urinary diversion. Migratory BSs form in the upper urinary tract [9].

Although open cystolithotomy (CL) is the traditionally accepted treatment modality [8], minimally invasive treatments have widely been adopted to reduce hospital stay and convalescence. However, it is unclear whether these treatments may compromise stone-free rates (SFRs) and what morbidity they may expose patients to [8,9]. We present the first systematic review that addresses benefits and harms of procedures used to remove BSs in either adults or children.

2. Evidence acquisition

2.1. Search strategy

We conducted a systematic review in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) statement [11] and the Cochrane Handbook for Systematic Reviews of Interventions [12]. Medline, Embase, and Cochrane controlled trials databases and clinicaltrial.gov were searched between January 1970 and February 2019 for relevant English-language publications.

The published a priori protocol includes the search strategy [13]. Following deduplication, two review authors (J.D. and Y.R.) independently screened the abstracts for eligibility. The full-text articles were retrieved and scrutinised independently by two review authors. For any incompletely reported data, study authors were contacted. Disagreements were resolved by discussion or by consulting a third author (A.N. or C.T.).

2.2. Types of study design included

All randomised controlled trials (RCTs) and comparative nonrandomised studies (NRSs) comparing any treatments of BSs with ≥10 patients per arm were included. Conference abstracts were excluded.

2.3. Types of participants included

Male and female adults and children of any ethnicity with single BS or multiple BSs were included. Recurrent or first-time stone formers, and patients with all stone sizes and compositions were eligible. Patients with pre-existing bladder augmentation or diversion were excluded. Mixed populations which accounted for <10% of the cohort were accepted.

2.4. Types of interventions included

Open CL, transurethral cystolithotripsy (TUCL), percutaneous cystolithotripsy (PCCL), shock wave lithotripsy (SWL), and laparoscopic removal were evaluated. Any technique or lithotripsy modality was accepted for all interventions [9].

2.5. Types of outcome measures included

The primary benefit outcome was SFR, measured at any time point up to 1 mo postoperatively using any modality. Any definition of stone free used by trialists was accepted. The primary harm outcome was unplanned procedures (including intra- and postoperative ones).

Secondary outcomes were complications of treatment (intraoperative, postoperative, and late). Postoperative complications were classified by the review team using the Clavien-Dindo (CD) classification [14] where sufficiently reported, or details were obtained by contacting the authors. Postoperative complications were defined as complications occurring up to 4 wk and late complications as those occurring after 4 wk, or as defined by the trialists.

Other included outcomes were retreatment rate (including second-session SWL), recurrence rate (≥1 mo), duration of procedure, catheterisation and hospital stay, pain, quality of life, patient satisfaction, and ionising radiation exposure. All reported definitions or measures were accepted.

2.6. *Assessment of risks of bias*

The risk of bias for RCTs was assessed in accordance with Cochrane guidance [12]. Extra domains were used to assess confounders in NRSs: a pragmatic approach informed by methodological literature [15]. We assessed whether each prognostic confounder was considered, whether the confounder was balanced between the intervention and the control group, and whether, if necessary, the confounder was controlled for in the analysis. A list of the most important potential confounders for harm and benefit outcomes was developed a priori with clinical content experts (the European Association of Urology Urolithiasis Guideline Panel): stone size, aetiology, gender, preoperative catheterisation, and previous open surgery.

2.7. *Quality of evidence assessment*

The Grading of Recommendations Assessment, Development, and Evaluation (GRADE) tool [16] was used to assess the quality of evidence (QoE) for critical and important outcomes for decision making, including assessment of study design, risk of bias, directness, consistency, and precision [16]. The outcomes that were assessed included SFR, unplanned procedures, major postoperative complications, late complications, length of hospital stay (all rated as critical for decision making), duration of procedure, and retreatment (rated as important).

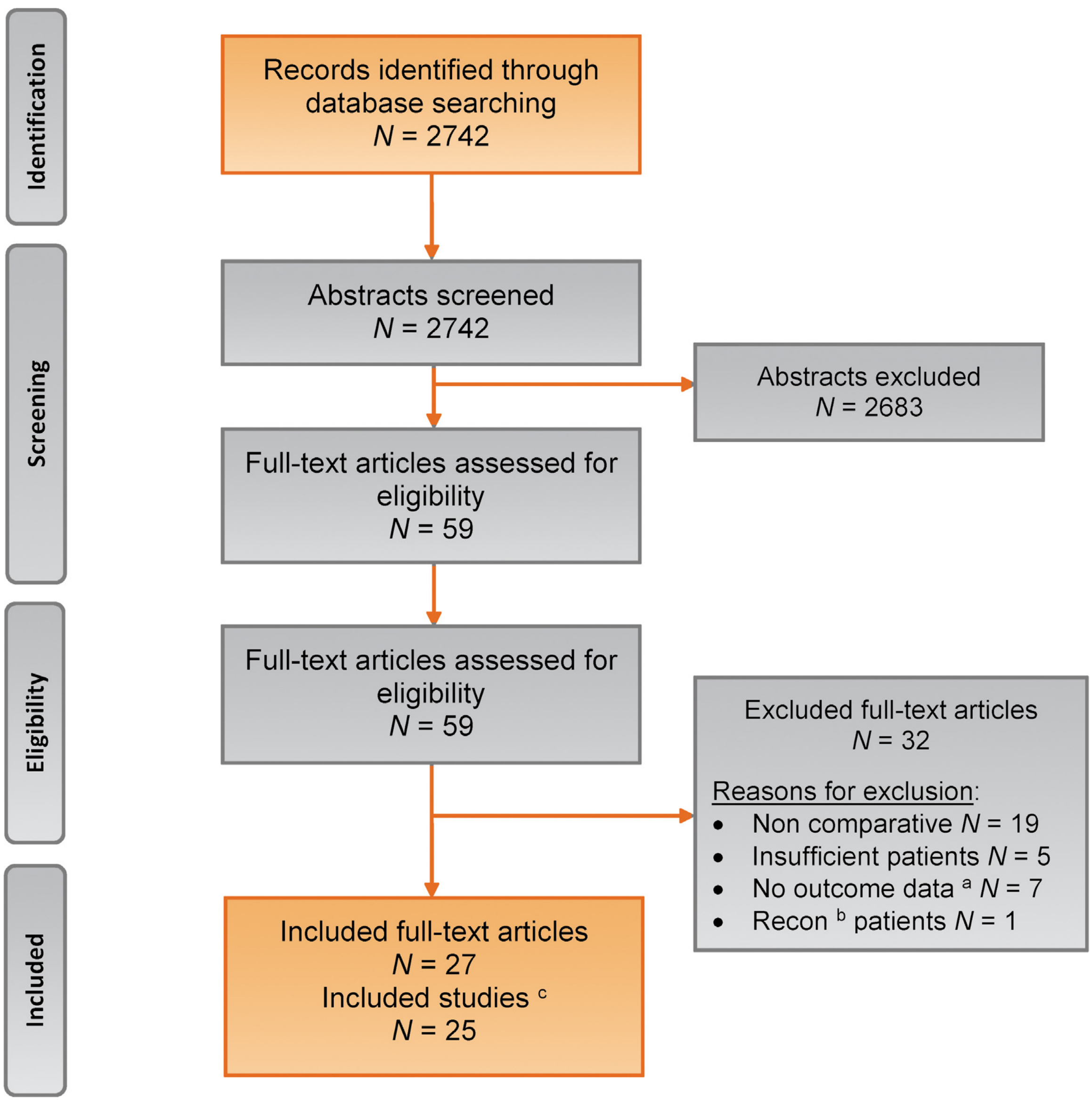

Fig. 1 – Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram of studies identified, excluded and included. NRS = nonrandomised study. [a] Despite contacting authors (Rizvi et al. [20], Ercil et al. [22], Turkan et al. [49], Aegukkatajit et al. [50], Smith et al. [51], and Bapat [52]). [b] Stone(s) in augmented bladder or urinary diversion (eg, neobladder). [c] Communication with authors (Bhatia et al. [25,53], Al-Marhoon et al. [39], and Mahran et al. [54]) confirmed that two NRSs were reported in two articles each. Data were extracted from both articles.

2.8. Data analysis

We report data at available time points and reported *p* values where available, or if unavailable, we calculated these using RevMan. We conducted an intention-to-treat analysis, if data were available; otherwise, an available case analysis was performed. We did not impute missing data. In the case of incompletely reported data, we contacted the authors.

For dichotomous outcomes, we report risk ratios (RRs) and 95% confidence intervals (CIs) in forest plots: odds risks are less robust when data include 100% [17]. Where deemed clinically appropriate, a meta-analysis was performed using a random-effect model due to heterogeneity in study design, intervention schedule, outcome definition, and time point or modality of measurement.

For continuous outcomes, we report the mean difference (MD) with standard deviation and/or range and corresponding 95% CIs and *p* values, where available.

3. Evidence synthesis

3.1. Description of the included studies

A total of 2742 abstracts were screened and 59 full-text articles were assessed: 27 articles on 25 studies were included with 2340 patients: 1526 adults and 814 children. Reasons for exclusion are listed in Fig. 1.

3.2. Study characteristics

Characteristics of the included studies are listed in Supplementary Table 1. Twenty studies on adults were included: nine RCTs and 11 NRSs; two studies compared four interventions, and four studies compared three interventions. Five studies in children were included: one RCT and four NRSs; two studies compared three interventions.

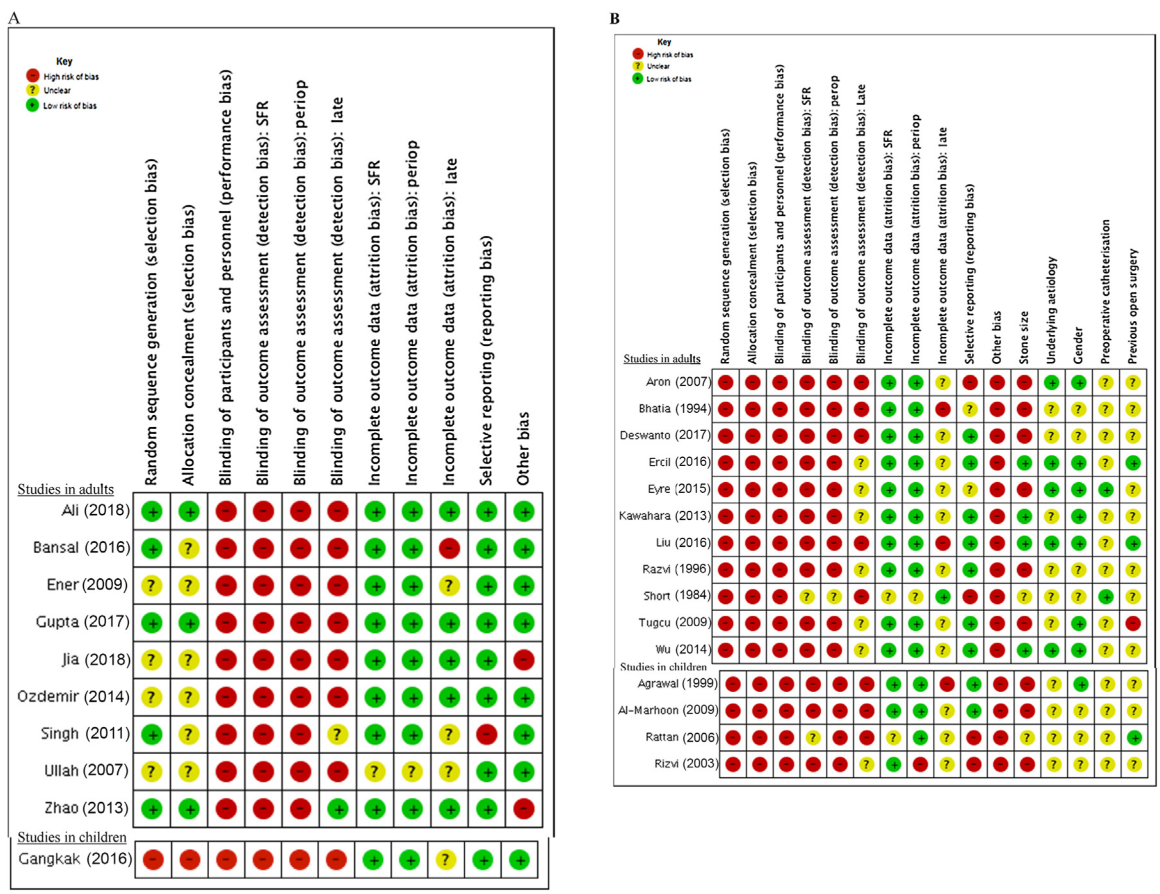

Fig. 2 – Risk of bias for included studies: (A) RCTs and (B) NRSs. Note boxes without a risk of bias assessment summary icons indicate studies from which data for this outcome category were unavailable, despite contacting authors. In adults, only Zhao et al. [31] reported any blinding, which was employed for investigators assessing late complications; Bansal et al. [32] reported high attrition rates for late outcomes without explanation. Ullah et al. [26] excluded patients with <12-mo follow-up and so was assessed as an unclear risk of attrition bias. Singh et al. [29] did not report complications and was assessed as a high risk of reporting bias. Zhao et al. [31] used blocked randomisation without blinding for SFR and perioperative outcomes, and so was assessed as a high risk of other bias. Stone sizes were well matched in all RCTs. For NRS, Liu et al. [28] did not report follow-up per group; overall follow-up ranged from 6 to 12 mo and so was assessed as a high risk of attrition bias for late outcomes. Reporting bias was assessed as a high risk in Aron et al.'s [34] and Short et al.'s [27] study, as no harm data were reported. Stone size determined which intervention patients underwent in the study of Bhatia et al. [53], and was significantly different from that in the studies by Aron et al. [34], Eyre et al. [36], Deswanto et al. [24], Razvi et al. [37], Tugcu et al. [33], and Wu et al. [35]. Tugcu et al. [33] excluded patients with previous open surgery from PCCL but not from TUCL. In children, the RCT used alternating consecutive patient allocation Gangkak et al. [19]. Rizvi et al. [20] reported perioperative outcomes for TUCL and CL, but not for SWL. Stone size was not reported by Rattan et al. [38], but was unmatched in all other NRSs: stone size and age determined intervention in Al-Marhoon et al.'s [39] study [20,40]. CL = cystolithotripsy; NRS = nonrandomised study; PCCL = percutaneous cystolithotripsy; RCT = randomised controlled trial; SFR = stone-free rate; SWL = shock wave lithotripsy; TUCL = transurethral cystolithotripsy.

3.3. Risk of bias in included studies

The risk of bias assessment of included studies are summarised in Fig. 2. GRADE QoE assessments are reported in Supplementary Tables 2 and 3. Stone sizes were well matched in all RCTs.

3.4. Outcome data

Outcome data are summarised in Tables 1 and 2. SFR was defined only by three RCTs in adults [18,19] and one NRS in children [20]. SFR was assessed using direct visualisation, X-ray, ultrasound (US), or a combination of X-ray and US (Supplementary Table 1). Postoperative complications were graded using the CD classification by one RCT and two NRSs in adults [21–23]. There were no reported CD 4–5 complications. No study reported quality of life, satisfaction, cost, or ionising radiation exposure outcomes. Minor postoperative complications were not defined or reported separately in any study; hence, a meta-analysis was not deemed appropriate (Supplementary Tables 3 and 4).

3.5. Studies in adults

3.5.1. SWL versus TUCL

One RCT ($n = 100$) found a lower SFR following SWL versus TUCL (RR 0.88, $p = 0.03$; Supplementary Fig. 1A–C) [23]. Retreatment appeared to favour TUCL ($p = 0.06$). Multiple SWL sessions were performed: after three SWL sessions, SFRs were not significantly different from the sessions with one TUCL (94% vs 98%, $p = 0.3$). There were no unplanned procedures or major complications. Length of hospital stay favoured SWL (MD 1 d). These outcomes were assessed as low QoE.

Two NRSs in 226 adults [24,25] found a slightly higher SFR for TUCL than for SWL (97.7% vs 89.7%; $p = 0.07$ and 97.0% vs 93.9%; $p = 0.50$). Urethral strictures were events with a very low incidence (1.5% overall) and were not significantly different in either study. Duration of procedure was shorter for SWL in one study (MD 50 min). Very low QoE supported these outcomes. One NRS reported a higher rate of unplanned procedures following SWL (5.2% vs 1.2%, $p = 0.19$) in 144 patients despite SWL including continuous irrigation in all patients and fragment evacuation in 15.9% [25].

3.5.2. TUCL versus CL

One RCT and two NRSs ($n = 160$) compared TUCL versus CL [24,26]. Meta-analysis was not deemed appropriate (Supplementary Fig. 2A–D). SFR was similar in all studies. The duration of the procedure ($p = 0.016$), catheterisation time ($p = 0.023$), and the duration of hospital stay favoured TUCL (MD 6.10 d, $p = 0.02$, 5.0 d) [26]. No unplanned procedures or major postoperative/late complications were reported. Retreatment was not significantly different except in one NRS conducted in 1973–1980, which reported lower recurrence rates following CL ($p < 0.005$) [27]. The QoE was very low for all outcomes.

Table 1 – Outcomes for included studies in adults

Study ID	Treat 1	Treat 2	Treat 3	Com	Outcome	No. of pts for this outcome: Treat 1	Treat 2	Treat 3	Com	Outcome data: Treat 1	Treat 2	Treat 3	Com	p value[a]
Gupta (2017) [55] (RCT)	PCCL			TUCL nephro	SFR	32			30	100% (32)			100% (30)	1.00[a]
					Retreatment	32			30	0% (0)			0% (0)	
					Recurrence	32			30	0% (0)			0% (0)	
					Duration of stone proc. (min)	32			30	34.31 ± 7.00			32.73 ± 8.71	0.428
Zhao (2013) [31] (RCT)	PCCL + TURP			TUCL nephro + TURP	SFR	38			34	100% (38)			94.1% (32)	0.22[a]
					Retreatment	38			34	0% (0)			5.9% (2)	0.26[a]
					Recurrence	38			34	0% (0)			0% (0)	NA
					Duration of stone proc. (min)	38			34	30.1 ± 10.3			72.7 ± 20.2	<0.001
Bansal (2016) [32] (RCT)	TUCL nephro	PCCL		TUCL Cysto	SFR	70	70		70	100% (70)	100% (70)		100% (70)	1.00, 1.00, 1.00[a]
					Unplanned procedure	70	70		70	0% (0)	0% (0)		0% (0)	NA
					Major postop comp.	70	70		70	0% (0)	0% (0)		0% (0)	NA
					Urethral stricture	64	65		62	7.8% (5)	0% (0)		3.2% (2)	0.28[a], 0.28[a], 0.10[a]
					Length of hospital stay (d)	64	65		62	1.3 ± 0.7, 1–2	2.12 ± 0.6, 1–3		1.15 ± 0.8, 1–2	0.240, 0.001, 0.001
					Pain score (VAS)	64	65		62	4.2 ± 1.7, 2–6	5.3 ± 2.1, 3–7		3.1 ± 1.3, 1–5	0.001, 0.001, 0.001

Table 1 (*Continued*)

Study ID	Treat 1	Treat 2	Treat 3	Com	Outcome	No. of pts for this outcome				Outcome data				*p* value[a]
						Treat 1	Treat 2	Treat 3	Com	Treat 1	Treat 2	Treat 3	Com	
					Duration of stone proc (min)	70	70		70	33.6 ± 7.0, 22–48	47.8 ± 17.6, 29–77		51.2 ± 23.2, 30–90	0.001, 0.33, 0.001
					Convalescence (d)	64	65		62	6.2 ± 1.9, 3–7	8.1 ± 3.2, 4–10		5.6 ± 2.3, 2–7	0.095, 0.001, 0.001
Singh (2011) [29] (RCT)	TUCL nephro	PCCL		TUCL cysto	SFR	22	23		20	100% (22)	100% (23)		100% (20)	1.00, 1.00, 1.00[a]
					Duration of stone procedure (min)	22	23		20	32.1 ± 8.5	46 ± 7.3		69.2 ± 16.3	0.005
Ener (2009) [30] (RCT)	TUCL nephro			TUCL cysto	SFR	22			21	100% (22)			100% (21)	1.00 a
					Retreatment	18			18	0% (0)			0% (0)	NA
					Recurrence	18			18	0% (0)			0% (0)	NA
					Unplanned procedure	22			21	0% (0)			0% (0)	NA
					Intraop complications	13			8	0% (0)			0% (0)	NA
					Duration of proc (min)	22			21	48.2 ± 13.2			68.1 ± 22.7	<0.01
Ozdemir (2014) [44] (RCT)	TUCL nephro			TUCL cysto	SFR	24			22	100% (24)			100% (22)	1.00[a]
					Retreatment	24			22	0%			0%	NA
					Recurrence	24			22	0%			0%	NA
					Duration of proc. (min)	24			22	42.00 ± 7.30			59.14 ± 10.62	<0.0001
Jia (2018) [18] (RCT)	TUCL (JQL sheath)			TUCL (URS)	SFR	45			41	97.8% (44)			90.2% (37)	<0.05
					Retreatment	45			41	2.2% (1)			9.8% (4)	0.18[a]
					Duration of proc. (min)	45			41	25.8 ± 12.5			46.6 ± 26.3	<0.05
Ullah (2007) [26] (RCT)	TUCL mech			CL	SFR	20			20	100% (20)			100% (20)	1.00[a]
					Retreatment	20			20	5% (1)			0% (0)	0.49[a]
					Recurrence	20			20	5% (1)			0% (0)	0.49[a]
					Unplanned procedure	20			20	0% (0)			0% (0)	NA
					Intraop comp.[b]	20			20	5% (1)			0% (0)	0.49[a]
					Major postop comp.	20			20	0% (0)			0% (0)	NA
					Urethral stricture	20			20	0% (0)			0% (0)	NA
					Duration of cath (d)	20			20	2.2 ± NR, 1–5			7.3 ± NR, 5–11	NR
					Length of hosp stay (d)	20			20	2.9 ± NR, 2–6			7.9 ± NR, 6–12	NR
					Duration of proc. (min)	20			20	30			70	NR
Ali (2019) [23] (RCT)	SWL			TUCL	SFR	50			50	86% (43)			98% (49)	0.03[a]
					Retreatment	50			50	14% (7)			2% (1)	0.06[a]
					Unplanned procedure	50			50	0% (0)			0% (0)	
					Intraop comp.	50			50	0% (0)			8% (4)	0.50
					Major postop comp.	50			50	0% (0)			0% (0)	
					Length of hosp stay (d)	50			50	0			1	NR
					Duration of proc. (min)	50			NR	44 ± 11			NR	

Table 1 (*Continued*)

Study ID	Treat 1	Treat 2	Treat 3	Com	Outcome	No. of pts for this outcome: Treat 1	Treat 2	Treat 3	Com	Outcome data: Treat 1	Treat 2	Treat 3	Com	p value[a]
Aron (2007) [34] (NRS)	PCCL + TURP			TUCL nephro + TURP	SFR	35			19	100% (35)			84.2% (16)	0.09[a]
					Retreatment	35			19	0% (0)			15.8% (3)	0.09[a]
					Recurrence	35			19	0% (0)			0% (0)	NA
					Duration of stone procedure (min)	35			19	20.0 ± 5.9 (15–38)			43.2 ± 10.6 (30–64)	<0.001
Tugcu (2009) [33] (NRS)	PCCL + TURP			TUCL cysto + TURP	SFR	25			38	100% (25)			92% (35)	0.19[a]
					Retreatment	25			38	0% (0)			7.9% (3)	0.30[a]
					Duration of proc. (min)	25			38	22.7 ± 4.99			39.9 ± 11.61	0.001
Bhatia (1994) [25,53] (NRS)	SWL			TUCL mech	SFR	58			86	89.7% (52)			97.7% (84)	0.07
					Retreatment	58			86	10.3% (6)			7.0% (6)	0.48[a]
					Recurrence	22			28	0% (0)			10.7% (3)	0.25[a]
					Intraop comp.[c]	58			86	0% (0)			7.0% (6)	0.14
					Major postop comp.[d]	58			86	5.2% (3)			1.2% (1)	0.19[a]
					Unplanned proc.[d]	58			86	13.6% (3)			3.6% (1)	0.19[a]
					Urethral stricture	22			28	0% (0)			7.1% (2)	0.37[a]
					Duration of cath (d)	58			86	0.6, NR, NR			2.0, NR, NR	NR
					Length of hosp stay (d)	43			80	0.8, NR, NR			2.4, NR, NR	NR
					Duration of proc. (min)	58			86	40 ± NR (16–78)			90 ± NR (NR)	NR
Deswanto (2017) [24] (NRS)	TUCL pneum	SWL		CL	SFR	33	49		10	97.0% (32)	93.9% (46)		100% (10)	0.99[a], 0.73[a], 0.50
					Retreatment	33	49		10	3.0% (1)	6.1% (3)		0% (0)	0.99, 0.77, 0.53
					Intraop complications	33	49		10	0% (0)	0% (0)		0% (0)	NA
					Major postop comp.	33	49		10	0% (0)	0% (0)		0% (0)	NA
					Unplanned procedure	33	49		10	0% (0)	0% (0)		0% (0)	NA
					Urethral stricture	33	49		10	0% (0)	0% (0)		0% (0)	NA
					Length of hosp stay (d)	33	49		10	4.8 ± 3.3 (NR)	0		10.9 ± 8.2 (NR)	0.02, [a]40
Ercil (2016) [22] (NRS)	TUCL las resecto + TURP			TUCL pneum cysto + TURP	SFR	33			29	97.0% (32)			96.6% (28)	0.93[a]
					Duration of stone procedure (min)	33			29	40.3 ± 13.7 (NR)			56.9 ± 14.0 (NR)	<0.0001
Eyre (2015) [36] (NRS)	TUCL EHL	TUCL wash	TUCL combo EHL + mech	TUCL mech	SFR	15	11	36	49	100% (15)	100% (11)	100% (36)	100% (49)	1.00[a], 1.00[a], 1.00[a], 1.00[a], 1.00[a]
					Intraop com.[e]	15	11	36	49	0% (0)	0% (0)	0% (0)	2.0% (1)	NR
					Unplanned proc.[e]	15	11	36	49	0% (0)	0% (0)	0% (0)	2.0% (1)	NR
					Major postop comp.	15	11	36	49	0% (0)	0% (0)	0% (0)	0% (0)	NA
					Length of hosp stay (d)	94.6% (106 of 112)				2.1 ± 0.86	1.2 ± 0.87	2.5 ± 2.34	1.4 ± 1.2	0.029, 0.51, 0.018, NR
Razvi (1996) [37] (NRS)	TUCL USL	TUCL pneum	TUCL EHL	TUCL mech	SFR	17	20	16	53	88% (15)	85% (17)	63% (10)	90% (48)	
					Retreatment	NR	20	16	NR	NR	15% (3)	37.5% (6)	NR	
					Intraop complications	9	14	12	29	0% (0)	7.1% (1)	0% (0)	3.4% (1)	
					Unplanned procedure	9	14	12	29	0% (0)	0% (0)	8.3% (1)	10.3% (3)	

Table 1 (*Continued*)

Study ID	Treat 1	Treat 2	Treat 3	Com	Outcome	No. of pts for this outcome				Outcome data				*p* value[a]
						Treat 1	Treat 2	Treat 3	Com	Treat 1	Treat 2	Treat 3	Com	
					Major postop comp.	9	14	12	29	0% (0)	0% (0)	8.3% (1)	10.3% (3)	
					Duration of cath (d)	9	14	12	29	2	3	6	4	
					Length of hosp stay (d)	9	14	12	29	6	3	9	7	
					Duration of proc. (min)	9	14	12	29	56	57	85	48	
Short (1984)	TUCL EHL	TUCL mech		oCL	Recurrence	16	34		27	50% (8)	44.1% (15)		7.4% (2)	<0.005
[27] (NRS)					Stone-free interval (mo):	10	19		9	13.8	18.4		70.8	<0.01, <0.01, NS
Liu (2016)	PCCL			oCL	SFR	21			16	100% (21)			100% (16)	1.00[a]
[28] (NRS)					Retreatment	21			16	0% (0)			0% (0)	NA
					Recurrence	21			16	0% (0)			0% (0)	NA
					Unplanned procedure	21			16	0% (0)			0% (0)	NA
					Major postop comp.	21			16	0% (0)			0% (0)	NA
					Duration of cath (d)	21			16	2.5 ± NR, 2–3			8.6 ± NR, 6–11	0.016
					Length of hosp stay (d)	21			16	2.6 ± NR, 2–4			3.5 ± NR, 2–5	0.643
					Duration of proc. (min)	21			16	18.2 ± NR, 11–35			32.3, 23–52	0.023
Kawahara (2013)	TUCL las 30 W			TUCL las 100 W	SFR	31			25	100% (31)			100% (25)	1.00[a]
[21] (NRS)					Intraop complications	31			25	0% (0)			0% (0)	NA
					Unplanned procedure	31			25	0% (0)			0% (0)	NA
					Major postop comp.	31			25	0% (0)			0% (0)	NA
					Duration of proc. (min)	31			25	32.6 ± 36.5			44.4 ± 38.8	0.25[a]
Wu (2014)	TUCL resecto + TURP			TUCL cysto + TURP	SFR	55			54	100% (55)			100% (54)	1.00[a]
[35] (NRS)					Duration of proc. (min)	55			54	25.8 ± 15.6			36.4 ± 19.3	<0.01

Cath = catheterisation; CL = cystolithotripsy; com = comparator; comp. = complications; cysto = cystoscope; duration of stone proc. = duration of stone procedure only (including access); EHL = electrohydraulic lithotripsy; intraop = intraoperative; hosp = hospital; JQL sheath = water sealing cap allowing seal when a URS is used through a resectoscope sheath; las = laser; NA = not available; nephron = nephroscope; NR = not reported; NRS = nonrandomised study; oCL = open cystolithotripsy; PCCL = percutaneous cystolithotripsy; pneum = pneumatic lithotripsy; postop = postoperative; proc = procedure (stone procedure only); pts = patients; RCT = randomised controlled trial; resecto = resectoscope; SD = standard deviation; SFR = stone-free rate; SWL = shock wave lithotripsy; treat = treatment; TUCL = transurethral cystolithotripsy; TURP = transurethral resection of the prostate; URS = ureteroscope; USL = ultrasonic lithotripsy; VAS = visual analogue scale (0–10).

p values are listed as follows: treat 1 versus comp, treat 2 versus comp, and treat 1 versus treat 2. Dichotomous outcomes (SFR, retreatment, recurrence, and complications) are reported as percentage (n). Continuous outcomes (pain score, length of hospital stay, procedure, and catheterisation) are reported as mean ± SD, range where reported. Major postoperative complications are Clavien-Dindo grade ≥ 3; further details are reported in Table 6. The only late complications reported were urethral strictures.

[a] *p* value was calculated by the review team for dichotomous outcomes where it was not reported.
[b] Urethral injury—managed conservatively.
[c] Two urethral injuries, three bladder trauma, and one bladder perforation—all managed conservatively.
[d] Urethral fragment impaction—urethroscopy.
[e] Bladder perforation—repaired.

Table 2 – Outcomes for included studies in children

Study ID	Treat 1	Treat 2	Com	Outcome	No. of pts. for this outcome			Outcome data			*p* value[a]	Other
					Treat 1	Treat 2	Com	Treat 1	Treat 2	Com		
Gangkak (2016) [19] (RCT)	TUCL las		TUCL pneum	SFR	12		13	100% (12)		100% (13)	1.00[a]	
				Retreatment	12		13	0 (0%)		0 (0%)	NA	
				Recurrence	12		13	0 (0%)		0 (0%)	NA	
				Intraop complications	12		13	0 (0%)		0 (0%)	NA	
				Unplanned procedures	12		13	0 (0%)		1 (7.7%)	0.52[a]	Impacted
				Major postop complications	12		13	0 (0%)		1 (7.7%)	0.52[a]	urethral
				Urethral stricture	12		13	0 (0%)		0 (0%)	NA	fragment
				Length of hospital stay (d)	12		13	1.2 ± 0.7		1.8 ± 0.8	0.05	
				Duration of procedure (min)								
				All	12		13	35.5 ± 14.0		36.6 ± 8.7	0.81	
				<1.5 cm	7		7	25.6 ± 4.9		31.6 ± 5.9	0.04	
				1.5–3 cm	5		6	49.4 ± 9.8		44.6 ± 7.8	0.40	
Agrawal (1999) [40,43] (NRS)	PCCL USL		oCL	SFR	38		21	100% (38)		100% (21)	1.00[a]	
				Retreatment	38		21	0% (0)		0% (0)	NA	
				Recurrence	38		21	0% (0)		0% (0)	NA	
				Intraop complications	38		21	0% (0)		0% (0)	NA	
				Unplanned procedures	38		21	0% (0)		0% (0)	NA	
				Major postop complications	38		21	0% (0)		0% (0)	NA	
				Urethral stricture	38		21	0% (0)		0% (0)	NA	
				Duration of catheterisation (d)	38		21	2 ± NR, NR		10 ± NR, 7–14	NR	
				Length of hospital stay (d)	38		21	3 ± NR, 2–5		9 ± NR, 7–12	NR	
				Duration of procedure (min)	38		21	25 ± NR, 15–50		45 ± NR, 30–65	NR	
Al-Marhoon (2009) [39] (NRS)	PCCL pneum or USL	TUCL pneum or las	oCL	SFR	27	27	53	100% (27)	100% (27)	100% (53)	1.00[a]	
				Retreatment	16	11	25	0% (0)	0% (0)	0% (0)	NA	
				Recurrence	16	11	25	0% (0)	0% (0)	0% (0)	NA	
				Intraop complications	27	27	53	3.7% (1)	3.7% (1)	1.9% (1)	0.53[a], 0.53[a], 1.00[a]	PCCL: bladder
				Unplanned procedures	27	27	53	14.8% (4)	3.7% (1)	1.9% (1)	0.05[a], 0.53[a], 0.19[a]	perf.; TUCL: SPC
				Major postop complications	27	27	53	11.1% (3)	0% (0)	0% (0)	0.08[a], NA, 0.19[a]	for urethral
				Urethral stricture	27	27	53	0% (0)	3.7% (1)	0% (0)	NA, 0.28, 0.50[a]	rupture; CL: SB
				Length of hospital stay (d)	54		53	2.6		4.8	<0.05	injury
				Duration of procedure (min)	54		53	46 ± 14		38 ± 12	NS	
Rattan (2006) [38] (NRS)	Tubeless oCL		Traditional oCL	Intraop complications	136		40	0% (0)		0% (0)	NA	
				Catheter insertion	136		40	5.8% (8)		0% (0)	0.26[a]	
				Unplanned procedures	136		40	6.6% (9)		0% (0)	0.22[a]	
				Major postop complications	136		40	6.6% (9)		0% (0)	0.22[a]	
				Urethral stricture	136		40	0% (0)		2.5% (1)	0.16[a]	
				Length of hospital stay (d), median	136		40	2.0		6.0	<0.01	

Table 2 (*Continued*)

Study ID	Treat 1	Treat 2	Com	Outcome	No. of pts. for this outcome			Outcome data			p value[a]	Other
					Treat 1	Treat 2	Com	Treat 1	Treat 2	Com		
Rizvi (2003) [20] (NRS)	ESWL (<1 cm)	TUCL pneum (1–3 cm)	oCL (>3 cm)	SFR	63	77	307	47.6% (30)	93.5% (72)	100% (307)	<0.00001, 0.02,	
				"Complications" (not defined)[b]		77	307		11.5% (9)	29% (89)	NR, 0.0003[a], NR	
				Length of hospital stay (d)	63	77	307	0	0	NR, 5–7	NR	
				Duration of procedure (min)	63	77	307	40	45–70	20–30	NR	

CD = Clavien-Dindo; CL/oCL = open cystolithotripsy; Com = comparator; comp = complications; ESWL = extracorporeal shock wave lithotripsy; intraop = intraoperative; las = laser lithotripsy; PCCL = percutaneous cystolithotripsy; perf = perforation (bladder injury: immediate repair); pneum = pneumatic lithotripsy; postop = post-operative; pts = patients; NA = not available; NR = not reported; NRS = nonrandomised study; NS = not significant; RCT = randomised controlled trial; SB = small bowel (injured during drain suturing: immediate repair); SD = standard deviation; SFR = stone-free rate; SPC = suprapubic bladder catheter; SWL = shock wave lithotripsy; treat = treatment; TUCL = transurethral cystolithotripsy; USL = ultrasonic lithotripsy.

p values listed are as follows: treat 1 versus comp, treat 2 versus comp, and treat 1 versus treat 2. Dichotomous outcomes (SFR, retreatment, recurrence, and complications) are reported as percentage (*n*). Continuous outcomes (pain score, length of hospital stay, procedure, and catheterisation) are reported as mean ± SD, range unless otherwise stated. Major complications are CD ≥3 postoperative complications. More detailed complications are reported in Table 6. The only late complications reported were urethral strictures. Tubeless CL indicates no drain and no catheter, and traditional CL: indicates retropubic drain and urethral catheter.

[a] *p* value was calculated by the review team where authors did not state it in their report.

[b] "Complications" were not defined or described in any detail by Rizvi et al. [20]. Complications following SWL were not reported.

3.5.3. PCCL versus CL

One NRS compared PCCL versus CL in patients with urethral strictures ($n = 37$), and found no difference in outcomes except for duration of catheterisation ($p = 0.016$), procedure ($p = 0.023$), and estimated blood loss ($p = 0.035$), which favoured PCCL [28].

3.5.4. PCCL versus TUCL

Four RCTs compared PCCL versus TUCL in 409 adults. All used pneumatic lithotripsy. Stone free was not defined and was assessed using X-ray or US on day 1 [29,30] or the day of discharge [31], or the modality and timing of assessment were unclear [32]. The meta-analysis demonstrated no difference in SFR when using either a nephroscope (RR 1.00, CI 0.98–1.03, $p = 0.77$) or a cystoscope (RR 1.00, CI 0.97–1.03, $p = 1.00$; QoE was moderate; see Fig. 3.

The meta-analysis demonstrated that compared with PCCL, TUCL was quicker using a nephroscope (MD 9.83 min, range 1.32–18.34, $p < 0.00001$) but slower when using a cystoscope (MD 13.21 min, CI −32.61 to 6.19, $p = 0.002$; moderate QoE).

Convalescence and pain score favoured TUCL with either nephroscope (RR 1.90, CI 0.99–2.81, $p < 0.0001$ and RR 1.10, CI 0.44–1.76, $p = 0.001$) or cystoscope (RR 2.50, CI 1.53–3.47, $p < 0.00001$ and RR 2.20, CI 1.60–2.80, $p < 0.00001$; Supplementary Fig. 3) [32]. Similarly, the meta-analysis demonstrated a shorter hospital stay for TUCL using both nephroscope (MD 0.82 d, CI 0.59–1.05, $p < 0.00001$) and cystoscope (MD 0.97 d, CI 0.72–1.22, $p < 0.00001$; moderate QoE).

There were no differences in unplanned procedures or major postoperative complications (low QoE) [32]. For late complications, one RCT reported a low event rate (3.6% overall) at 24-mo follow-up, suggesting a small nonsignificant benefit for PCCL compared with both TUCL nephroscope (RR 0.09, CI 0.01–1.61, $p = 0.10$) or TUCL cystoscope (RR 0.19, CI 0.01–3.90, $p = 0.28$; very low QoE).

There was no significant difference for retreatment rate: QoE was low for TUCL nephroscope (with two RCTs; meta-analysis found RR 1.02 [0.96–1.09], $p = 0.53$) and very low for TUCL cystoscope (with two NRSs; $p = 0.09$ and $p = 0.30$) [33,34].

3.5.5. TUCL: nephroscope, cystoscope, or resectoscope?

Four RCTs compared TUCL using a nephroscope versus a cystoscope ($n = 271$) using pneumatic ± ultrasonic lithotripsy. Stone-free assessment was with X-ray or US on day 1 [29,30] or the day of discharge [31], or was not stated [32]. The meta-analysis revealed no difference in SFR (RR 1.00; CI 0.98–1.02, $p = 1.00$; Fig. 4) as all patients were rendered stone free (moderate QoE).

Using a nephroscope was significantly quicker (MD 22.74 min, CI 31.64–13.84, $p < 0.00001$; moderate QoE). Hospital stay was similar (MD 0.15 d, CI 0.13–0.43, $p = 0.30$; low QoE). Bansal et al. [32] reported a benefit for using a cystoscope in postoperative visual analogue scale for pain (MD 1.10, CI 0.57–1.63, $p < 0.0001$) and a benefit for using a nephroscope in convalescence (MD 1.90 d, CI 2.82–0.98, $p < 0.0001$; Supplementary Fig. 4). There were no

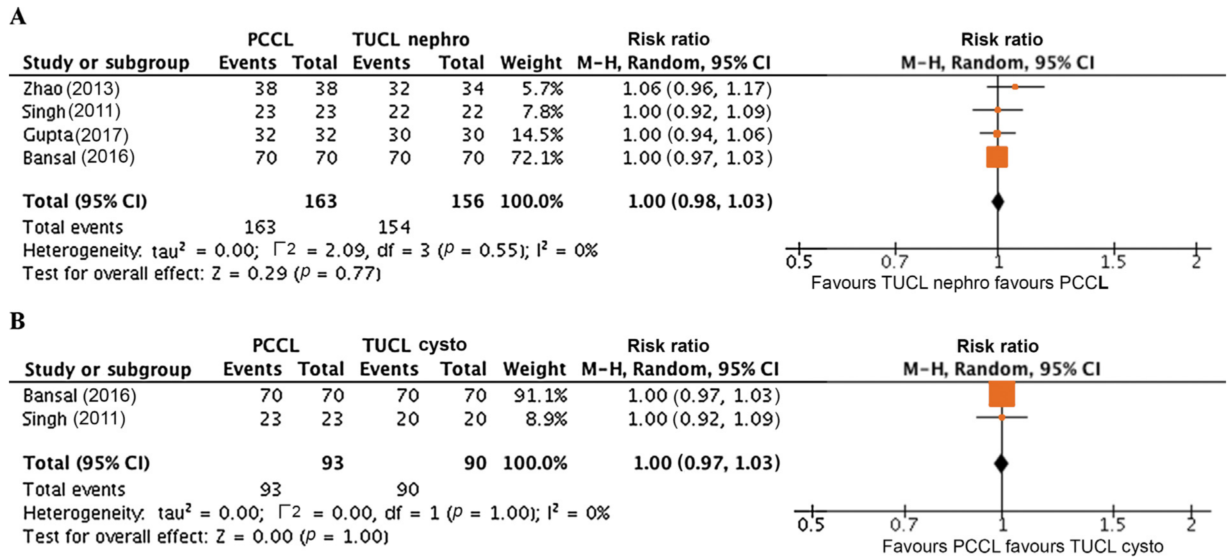

Fig. 3 – Forest plots for stone-free rate (SFR) for the comparison of percutaneous cystolithotripsy (PCCL) versus transurethral cystolithotripsy (TUCL) using a nephroscope (TUCL nephro) or cystoscope (TUCL cysto) using pneumatic lithotripsy for the treatment of bladder stones in adults: (A) PCCL versus TUCL nephro, and (B) PCCL versus TUCL cysto. CI = confidence interval; M-H = Mantel-Haenszel.

unplanned procedures or major complications. A low late-complication event rate was reported (3.4% overall) and no difference (RR 0.97, CI 0.91–1.04, $p = 0.38$; low QoE). No patient received retreatment (low QoE).

Two NRSs compared TUCL using resectoscope versus cystoscope ($n = 171$). Outcomes were similar except for procedure duration: using a resectoscope was significantly quicker (MD 10.6 min, CI 17.2–4.0, $p < 0.01$, and MD 16.6 min, CI 23.51–9.69, $p < 0.0001$) [22,35]. One NRS used laser in both cases [22], whilst the other used laser with a resectoscope and pneumatic with a cystoscope [35].

3.5.6. *TUCL lithotripsy modalities*

Five NRSs compared TUCL lithotripsy modalities ($n = 385$; Supplementary Fig. 5) [21,22,27,36,37]. No difference in SFR was found between any lithotripsy modality (mechanical, laser, pneumatic, ultrasonic, electrohydraulic lithotripsy [EHL], or washout alone).

Laser lithotripsy was faster than pneumatic lithotripsy (MD 16.6 min, CI 23.51–9.69, $p < 0.0001$) in one NRS ($n = 62$); however, laser used a resectoscope and pneumatic used a cystoscope [22]. High-power (100 W; 3.5 J, 5 Hz) laser was not significantly faster than low-power (30 W;

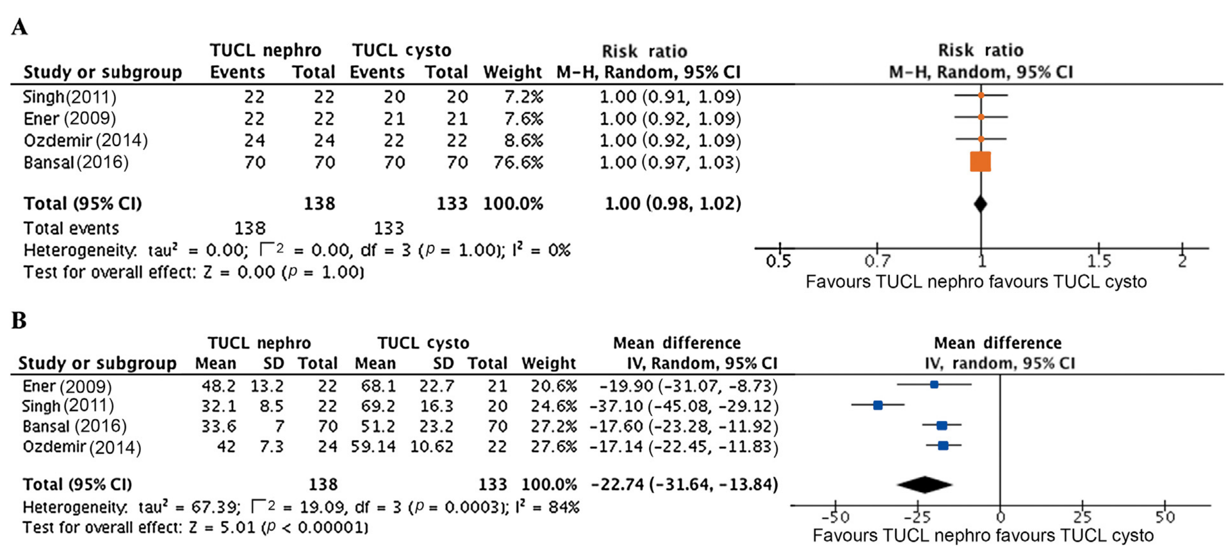

Fig. 4 – Forest plots for the comparison of transurethral cystolithotripsy (TUCL) using a nephroscope versus a cystoscope (TUCL nephro vs TUCL cysto) for the treatment of bladder stones in adults: (A) SFR and (B) Duration of procedure. CI = confidence interval; M-H = Mantel-Haenszel; SD = standard deviation; SFR = stone-free rate.

2.5 J, 5 Hz) laser (MD 11.8 min, CI −8.1 to 31.7, p = 0.25) in an NRS (n = 56) [21].

Unplanned procedures and major postoperative complications were low rate events, and were not significantly different between lithotripsy modalities, although one NRS suggested that they might be higher with EHL or mechanical lithotripsy than with pneumatic or ultrasonic lithotripsy [37]. All outcomes had very low QoE (Figs. 5 and 6).

3.6. Studies in children

The QoE was assessed as very low for all outcomes for all comparisons. Forest plots are available in Supplementary Figs. 6–10.

3.6.1. SWL versus CL and SWL versus TUCL

One large NRS (n = 447) compared SWL (for <1 cm stones), TUCL (1.1–3 cm stones), and CL (>3 cm stones or previously failed SWL or TUCL) [38]. SFR was lower in SWL than in CL or TUCL ($p < 0.00001$ and $p < 0.00001$). Length of hospital stay appeared to favour SWL and TUCL over CL, but detailed descriptors were not reported [20]. No other outcomes were reported for SWL.

3.6.2. TUCL versus CL

Two NRSs compared TUCL and CL: cohorts had unmatched stone sizes; a meta-analysis was not deemed appropriate [20,39]. TUCL had a significantly lower SFR (93.5% vs 100%, p = 0.02) in one study [20] and equal in the other (100% vs 100%). Length of hospital stay and duration of procedure

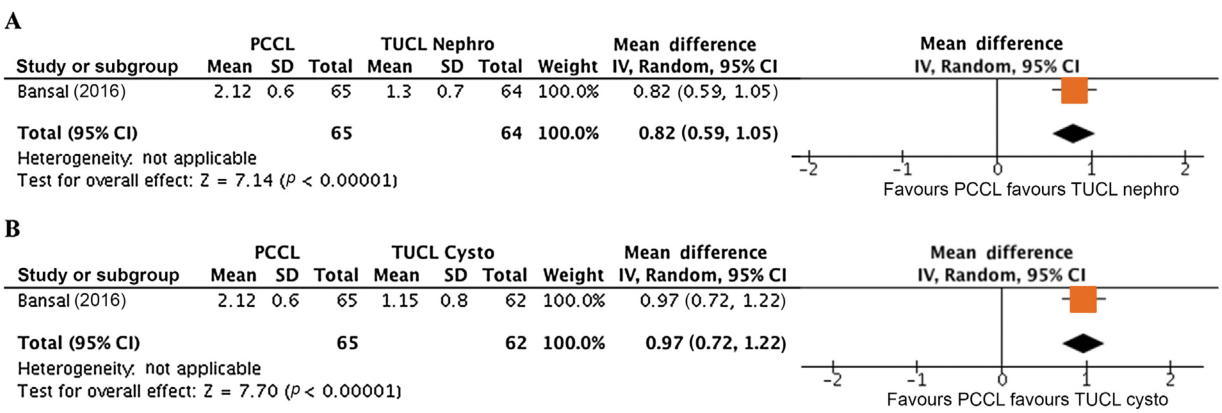

Fig. 5 – Forest plots for duration of hospital stay (in days) for the comparison of percutaneous cystolithotripsy (PCCL) versus transurethral cystolithotripsy (TUCL) using a nephroscope (TUCL nephro) or a cystoscope (TUCL cysto) using pneumatic lithotripsy for the treatment of bladder stones in adults: (A) PCCL versus TUCL nephro, and (B) PCCL versus TUCL cysto. CI = confidence interval; SD = standard deviation.

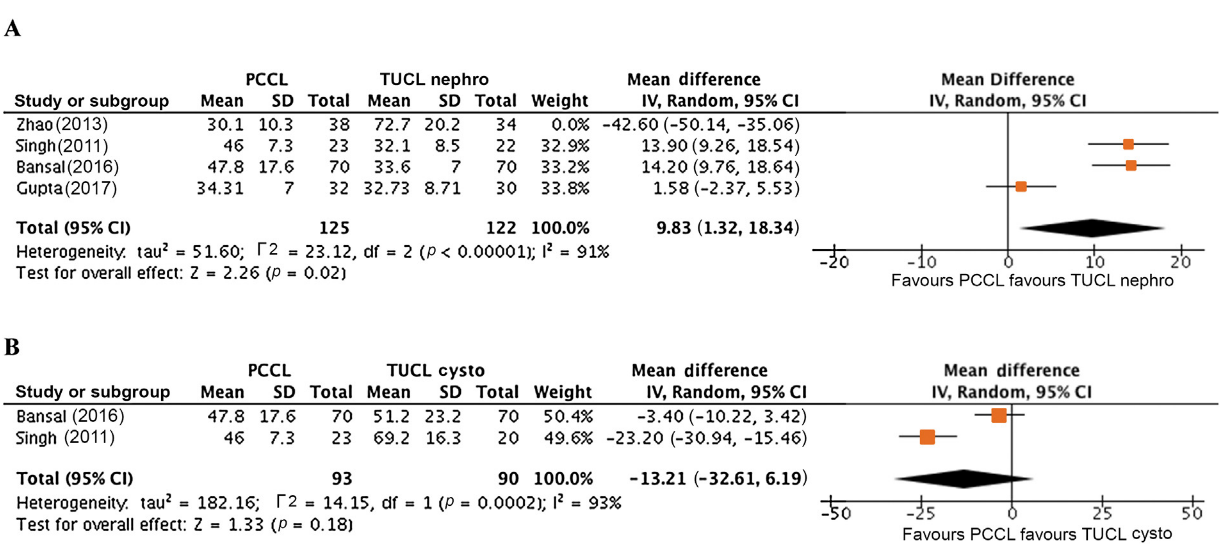

Fig. 6 – Forest plots for duration of procedure (in minutes) for the comparison of percutaneous cystolithotripsy (PCCL) versus transurethral cystolithotripsy (TUCL) using a nephroscope (TUCL nephro) or a cystoscope (TUCL cysto) using pneumatic lithotripsy for the treatment of bladder stones in adults: (A) PCCL versus TUCL nephro, and (B) PCCL versus TUCL cysto. Zhao et al.'s [31] study was excluded from the meta-analysis. Although they reported "operative time for stone management" in a table, the text suggested that this did not include the time taken to obtain percutaneous access (cystoscopy, wire insertion, dilatation, and sheath insertion) and trap the stone in a bag for lithotripsy. They reported significantly shorter "operative time for stone management" than the TUCL group. All patients had >6 cm stones and underwent simultaneous TURP. We were unable to obtain further details despite contacting the authors. CI = confidence interval; SD = standard deviation; TURP = transurethral resection of the prostate.

appeared to favour TUCL [20]. Unplanned procedures and late complications were not significantly different in one NRS, which reported no major postoperative complications, recurrences, or retreatments [39]. "Complications" were reported without further details (despite contacting the authors) in the other NRS that favoured TUCL (11.5% vs 29%, $p = 0.003$) [20].

3.6.3. PCCL versus CL

Two NRSs compared PCCL and CL ($n = 139$): cohorts had unmatched stone sizes; a meta-analysis was not deemed appropriate [39,40]. There was no significant difference in SFR (100% in all), unplanned procedures (6.2% vs 1.4%), or major postoperative complications (4.6% vs 0%).

A benefit for PCCL was suggested for the length of hospital stay (MD 6 d), procedure (MD 20 min), and catheterisation (8 d) in one study; however, other descriptors (standard deviation and p values) were not reported [40]. There were no late complications, recurrence, or retreatment.

3.6.4. PCCL versus TUCL

One NRS compared PCCL versus TUCL ($n = 54$): age and stone size determined intervention choice [39]. All patients were rendered stone free. PCCL appeared to have a clinically significantly higher rate of unplanned procedures (14.8% vs 3.7%, $p = 0.19$) and major postoperative complications (11.1% vs 0%, $p = 0.19$). One urethral stricture occurred in the TUCL group ($p = 0.50$). There was no difference in intraoperative complications [39].

3.6.5. TUCL with laser versus pneumatic lithotripsy

One small quasi-RCT compared TUCL with laser versus pneumatic lithotripsy: all 25 children were stone free ($p = 1.00$; defined as <3 mm fragments on X-ray and ultrasound at 3 wk) [19]. There was no significant difference in unplanned procedures or major complications (RR 0.36, CI 0.02–8.05, $p = 0.52$) for both. There were no late complications or retreatments. Length of hospital stay (MD 0.60 d, CI 1.19–0.01, $p = 0.05$) and procedure (MD 1.10, CI -10.33 to 8.13, $p = 0.82$) were similar overall. However, for <1.5 cm stones, there was a suggestion of a slightly quicker procedure using laser (MD 6.0 min (11.68–0.32, $p = 0.04$) [19].

3.6.6. Tubeless CL versus traditional CL

One large NRS ($n = 176$) compared tubeless CL (no catheter or drain) and traditional CL [38]. SFR was not available, despite contacting authors. Unplanned procedures and major complications both suggested a clinically significant benefit for traditional CL (6.6% vs 0%, $p = 0.22$). However, all patients requiring an unplanned postoperative procedure had had a previous surgery or urine infection. Hospital stay was shorter with tubeless CL (2.0 vs 6.0 d, $p < 0.01$). Urethral strictures were a very low rate event (0.56% overall) and so were not robustly compared, although appeared lower with tubeless CL (0% vs 2.5%, $p = 0.16$).

4. Discussion

This study provides the first ever systematic review and meta-analyses on the treatment of BSs, and has informed the first national or international guideline on BSs [41]. Complete removal of a stone constitutes the most important outcome when evaluating the efficacy of any stone treatment. Our results indicate that SWL was less effective than endoscopic or open surgery in both adults and children in terms of SFR, although the QoE was low or very low. An RCT on small (<2 cm) BSs in adults found that ≤ 3 SWL sessions were required to equal the SFR achieved in one TUCL treatment [42]. It remains unclear whether SWL technique optimisation might improve SFR.

Our results also suggest that the adoption of endoscopic treatments (TUCL and PCCL) has reduced the morbidity of BS procedures, in terms of hospital stay, convalescence, and catheterisation time, compared with CL, whilst providing comparable SFR for both adults and children. However, overall QoE for SFR ranged from moderate to very low. Included studies reported inconsistent timing and modality of stone-free status assessment. Only three RCTs [18,19] and one NRS [20] defined stone-free status. It is unclear whether higher-quality studies would be likely to find different outcomes.

Interventions were not robustly compared for differing stone size or, in children, age. It is unclear whether SFRs are impaired for larger stones in endoscopic treatments or whether TUCL is less effective and/or more morbid in infants. However, one RCT on endoscopic surgery in adults included >4 cm stones, with an average of 6 cm BSs; yet an overall SFR of 97% was achieved [31]. Higher-quality RCTs stratified by stone size and patient characteristics are required.

SFRs were not significantly different for endoscopic techniques. However, the results on secondary outcomes from this systematic review and meta-analyses were informative. TUCL is superior to PCCL in terms of procedure duration and hospital stay (from meta-analyses) and also pain and convalescence (from a single RCT) [32] in adults. Higher-quality trials are likely to strengthen these findings.

Our meta-analysis of four RCTs and the results of two NRSs [22,35] demonstrated that TUCL is quicker when a nephroscope or a resectoscope, respectively, were used in adults compared with a cystoscope. This suggests that using a scope with continuous flow shortens TUCL procedure time, with equal SFRs.

The type and rate of complications related to different therapeutic approaches are important in treatment decision making. Complications were only classified or defined by three included studies [21–23], although we were able to apply CD classification using published data or by contacting authors. However, major postoperative complications, unplanned procedures, and late complications (urethral strictures) are low incidence events, and therefore the included studies are likely to have been underpowered to detect a difference between procedures, and so could not be robustly assessed in this systematic review.

Overall, there were no differences in unplanned procedures and major postoperative complications (low QoE) between PCCL and TUCL in adults. PCCL appeared to have a higher rate of major postoperative complications (14.8%) and unplanned procedures (11.1%) than TUCL in a small NRS in children [39], although this event rate was not replicated in a larger NRS comparing PCCL and CL in children (0% and 0%) [43].

Major postoperative complications, including bladder perforation and bleeding, may be higher when using mechanical lithotripsy (eg, Mauermeyer, Lithotrite) or EHL compared with pneumatic or laser lithotripsy in adults [21,37]. SFRs were not significantly different between lithotripsy modalities. We therefore concluded that the optimum lithotripsy modality is the modality with which the individual surgeon has the most experience.

Major postoperative complications and unplanned procedures were clinically significantly increased in tubeless (no catheter or drain) versus traditional CL in a large NRS in children [38]. However, only patients with a previous infection or surgery developed major complications. Furthermore, tubeless CL reduced hospital stay and catheterisation time, and is therefore preferable in carefully selected children with endemic BSs [38].

The most important long-term complication of BS treatments is urethral stricture formation, which was the only reported late complication. Follow-up was typically ≥1 yr in RCTs, many of which included routine uroflowmetry screening, suggesting that urethral strictures would be detected. However, the incidence of urethral strictures among adults included in RCTs was very low (overall 2.8% with TUCL) and was not significantly different for TUCL versus PCCL [26,30,44]. This incidence is similar to that reported following transurethral resection of the prostate (2.2–9.8%) [45,46].

Urethral stricture formation rates were not affected by whether PCCL or TUCL (using a cystoscope or nephroscope) was performed; however, included studies were underpowered for this outcome. Therefore, the risk of urethral stricture formation should be considered for individual patients.

This systematic review did not consider conservative or medical management of BSs, BSs in patients with augmented or reconstructed bladders or the concomitant treatment of benign prostatic hyperplasia (BPH). The literature supports concomitant BS and BPH treatment, without increasing major complications compared with BPH treatment alone [41,47,48]. We found no studies comparing conservative or medical BS management with procedural intervention. Asymptomatic migratory BSs in adults may be left untreated, especially if <1 cm [41]. However, primary and secondary BSs are usually symptomatic, unlikely to pass spontaneously, and thus active treatment is typically required [13].

Our systematic review indicates that further research comparing the benefits and harms of treatments for BSs in adults and children is required, particularly comparing minimally invasive treatments with CL, which should stratify patients by stone size and characteristics (including age), as well as define and robustly measure outcomes.

5. Conclusions

This systematic review demonstrates that endoscopic, transurethral, and percutaneous BS treatments are associated with comparable SFRs, but with a shorter operation and catheterisation duration as well as a shorter length of hospital stay, compared with open CL, in both adults and children. SWL appears to offer an inferior SFR when compared with other procedures, but offers the shortest duration of hospital stay. In adults, TUCL using an instrument with continuous flow (eg, a nephroscope or a resectoscope) is quicker than when using a cystoscope. Mechanical, pneumatic, and laser lithotripsy appear to be equivalent for endoscopic BS treatments in adults and children, although there is a lack of robust evidence comparing modalities. Tubeless CL (without a drain or a catheter) can safely be performed in children with endemic BSs and no prior bladder surgery or infections. There is an urgent need for high-quality research comparing treatment modalities for differing stone sizes and in very young children.

Author contributions: James F. Donaldson had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Türk, Donaldson, Ruhayel, Neisius, MacLennan.
Acquisition of data: Donaldson, Ruhayel, Yuan.
Analysis and interpretation of data: Ruhayel, Donaldson, Türk, Neisius.
Drafting of the manuscript: Donaldson, Ruhayel, Türk, Neisius, Skolarikos.
Critical revision of the manuscript for important intellectual content: Türk, Ruhayel, Petrik, Skolarikos, Seitz, Thomas, Neisius, Donaldson.
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prostate cancer prior to curative-intent surgery or radiotherapy. Princess Alexandra Hospital, Brisbane, Australia. Patient recruitment only. (5) PVS trial: A Prospective, Randomized, Controlled, Multi-Center Evaluation of a Powered Vascular Stapler in Laparoscopic Nephrectomies and Nephroureterectomies: ESC-15-002. Ethicon, Western General Hospital, Edinburgh, Scotland UK. Aleš Petrik has received speaker honoraria from Olympus Czech Group, S.R.O., and Cook Medical Europe Ltd.; fellowship and travel grants from Astellas; and consultant fees from Olympus and Cook Medical. Christian Seitz has received consultant fees from Astellas and speaker honoraria from Rowa Wagner. Andreas Neisius has received fellowships/travel grants from Storz, Wolf, Astellas, Astellas, Boston Scientific, Novartis, Janssen, Eichard Wolf, and Karl Storz; consultant fees from Novartis, MSD, and Roche; speaker honorarium from Siemens Healthcare, Pfizer, Astellas, Ferring, Boston Scientific Europe, Pfizer, MSD, and Boston Scientific; and has participated in trials for Bayer, Kendle, Merck, Astellas, and MSD. Kay Thomas has participated in trials for TISU. Christian Türk, Andreas Skolarikos, Cathy Yuhong Yuan, Yasir Ruhayel, Steven MacLennan, and Robert Shepherd have nothing to disclose.

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Appendix A. Supplementary data

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