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Percutaneous Nephrolithotomy Versus Retrograde Intrarenal Surgery: A Systematic Review and Meta-analysis

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Abstract

Context: Recent advances in technology have led to the implementation of mini– and micro–percutaneous nephrolithotomy (PCNL) as well as retrograde intrarenal surgery (RIRS) in the management of kidney stones.
Objective: To provide a systematic review and meta-analysis of studies comparing RIRS with PCNL techniques for the treatment of kidney stones.
Evidence acquisition: A systematic literature review was performed in March 2014 using the PubMed, Scopus, and Web of Science databases to identify relevant studies. Article selection proceeded according to the search strategy based on Preferred Reporting Items for Systematic Reviews and Meta-analysis criteria. A subgroup analysis was performed comparing standard PCNL and minimally invasive percutaneous procedures (MIPPs) including mini-PCNL and micro-PCNL with RIRS, separately.
Evidence synthesis: Two randomised and eight nonrandomised studies were analysed. PCNL techniques provided a significantly higher stone-free rate (weighted mean difference [WMD]: 2.19; 95% confidence interval [CI], 1.53–3.13; $p < 0.00001$) but also higher complication rates (odds ratio [OR]: 1.61; 95% CI, 1.11–2.35; $p < 0.01$) and a larger postoperative decrease in haemoglobin levels (WMD: 0.87; 95% CI, 0.51–1.22; $p < 0.00001$). In contrast, RIRS led to a shorter hospital stay (WMD: 1.28; 95% CI, 0.79–1.77; $p < 0.0001$). At subgroup analysis, RIRS provided a significantly higher stone-free rate than MIPPs (WMD: 1.70; 95% CI, 1.07–2.70; $p = 0.03$) but less than standard PCNL (OR: 4.32; 95% CI, 1.99–9.37; $p = 0.0002$). Hospital stay was shorter for RIRS compared with both MIPPs (WMD: 1.11; 95% CI, 0.39–1.83; $p = 0.003$) and standard PCNL (WMD: 1.84 d; 95% CI, 0.64–3.04; $p = 0.003$).
Conclusions: PCNL is associated with higher stone-free rates at the expense of higher complication rates, blood loss, and admission times. Standard PCNL offers stone-free rates superior to those of RIRS, whereas RIRS provides higher stone free rates than MIPPs. Given the added morbidity and lower efficacy of MIPPs, RIRS should be considered standard therapy for stones <2 cm until appropriate randomised studies are performed. When flexible instruments are not available, standard PCNL should be considered due to the lower efficacy of MIPPs.
Patient summary: We searched the literature for studies comparing new minimally invasive techniques for the treatment of kidney stones. The analysis of 10 available studies shows that treatment can be tailored to the patient by balancing the advantages and disadvantages of each technique.

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1. Introduction

Minimally invasive procedures have almost completely replaced open surgery in patients with kidney stones over the past two decades [1]. Percutaneous nephrolithotomy (PCNL) is now the standard of care for the treatment of large (>2 cm) stones [2]. However, its higher stone-free rates are counterbalanced by the risk of complications [3]. Recent advances in technology have led to a reduction in nephroscope diameter with the goal of minimising the surgical morbidity of PCNL. Thus *miniperc* and *microperc* have been implemented [4,5].

An alternative to the percutaneous approaches is provided by flexible ureteroscopy, also referred to as retrograde intrarenal surgery (RIRS). Originally proposed in the treatment of a lower pole stone resistant to shockwave lithotripsy (SWL) [6], studies have shown its utility in the management of larger renal stones throughout the entire pelvicalyceal system [1].

The 2013 European Association of Urology (EAU) guidelines recommend PCNL and RIRS as first-line treatment for lower pole stones when anatomic factors make SWL unfavourable [2]. The role of RIRS in the renal pelvis and remaining calyces, although technically feasible, is under investigation for stones >1.5 cm [1].

The main drawbacks of retrograde access include the requirement of flexible scopes, limited visualisation, reduced size of fragment removal, and the need for flexible lithotrites and baskets [7]. Cost is a major deterrent to RIRS, particularly in developing countries [8]. However, percutaneous approaches have traditionally provided enhanced capacity for stone removal, given the use of large-sheath diameters. This paradigm has recently changed with the progressive miniaturisation of devices for percutaneous access. PCNL techniques offer significant economic advantages due to the decreased reliance on disposable instrumentation.

The aim of this study was to perform a meta-analysis of available studies comparing RIRS with percutaneous surgery (including standard PCNL, miniperc, and microperc) in the management of kidney stones.

2. Evidence acquisition

2.1. Literature search and article selection

A systematic literature review was performed in March 2014 using PubMed, Scopus, and Web of Science databases to identify relevant studies. Searches were restricted to publications in English and in the adult population. Separate searches were done with the following search terms: *percutaneous nephrolithotomy, retrograde intrarenal surgery, percutaneous lithotripsy, RIRS, miniPCNL, micropercutaneous nephrolithtomy*, and *flexible ureteroscopy*.

Article selection proceeded according to the search strategy based on Preferred Reporting Items for Systematic Reviews and Meta-analysis criteria (www.prismastatement. org) (Fig. 1). Only studies comparing PCNL and RIRS were included for further screening. Cited references from the selected articles retrieved in the search were also assessed for significant papers. Conference abstracts were not included because they were not deemed to be methodologically appropriate. Two independent reviewers completed this process, and all disagreements were resolved by their consensus.

2.2. Assessment of study quality

The level of evidence (LE) was rated for each included study according to the criteria provided by the Oxford Centre for Evidence-based Medicine [9]. The methodological quality of the studies was assessed using the Newcastle-Ottawa Scale (NOS) for nonrandomised controlled trials (RCTs) [10] and the Jadad scale for RCTs [11]. Two reviewers reviewed the full texts of the included studies. Preoperative demographic characteristics as well as perioperative and postoperative outcomes between the two procedures were compared.

2.3. Statistical analysis

A meta-analysis was performed to assess the overall outcomes of PCNL compared with RIRS. A subgroup analysis was performed considering standard PCNL (sheath size ≥24F) only versus RIRS and minimally invasive percutaneous procedures (MIPPs; ie, mini- and microperc) only versus RIRS.

In one study a combination of mini and standard PCNL was used, and this study was included in the overall analysis but not in the subgroup analysis [12]. Of 10 studies, 2 were multi-institutional [12,13].

Extracted data for the analysis included operative time, estimated blood loss, length of hospital stay, need for auxiliary procedures, and postoperative complication rate. Odds ratio (OR) was used for binary variables, and mean difference or standardised mean difference was used for the continuous parameters. For studies presenting continuous data as means and range, standard deviations were calculated using the methodology described by Hozo and associates [14]. Pooled estimates were calculated with the fixed-effect model (Mantel-Haenszel method) if no significant heterogeneity was detected; otherwise, the random-effect model (DerSimonian-Laird method) was used. The pooled effects were determined by the z test, and $p < 0.05$ was considered statistically significant. The Cochrane chi-square test and inconsistency (I^2) were used to evaluate the heterogeneity among studies. Data analysis was performed with Review Manager software (RevMan v.5.1, Cochrane Collaboration, Oxford, UK).

3. Evidence synthesis

3.1. Study characteristics

Ten studies were selected for the analysis including 727 PCNL cases (61.55%) and 454 RIRS cases (38.44%) (Table 1). There were no differences between PCNL and RIRS study populations in terms of mean age (44.8 vs 45.07 yr, respectively) and body mass index (24 kg/m^2 vs 24.1 kg/m^2, respectively).

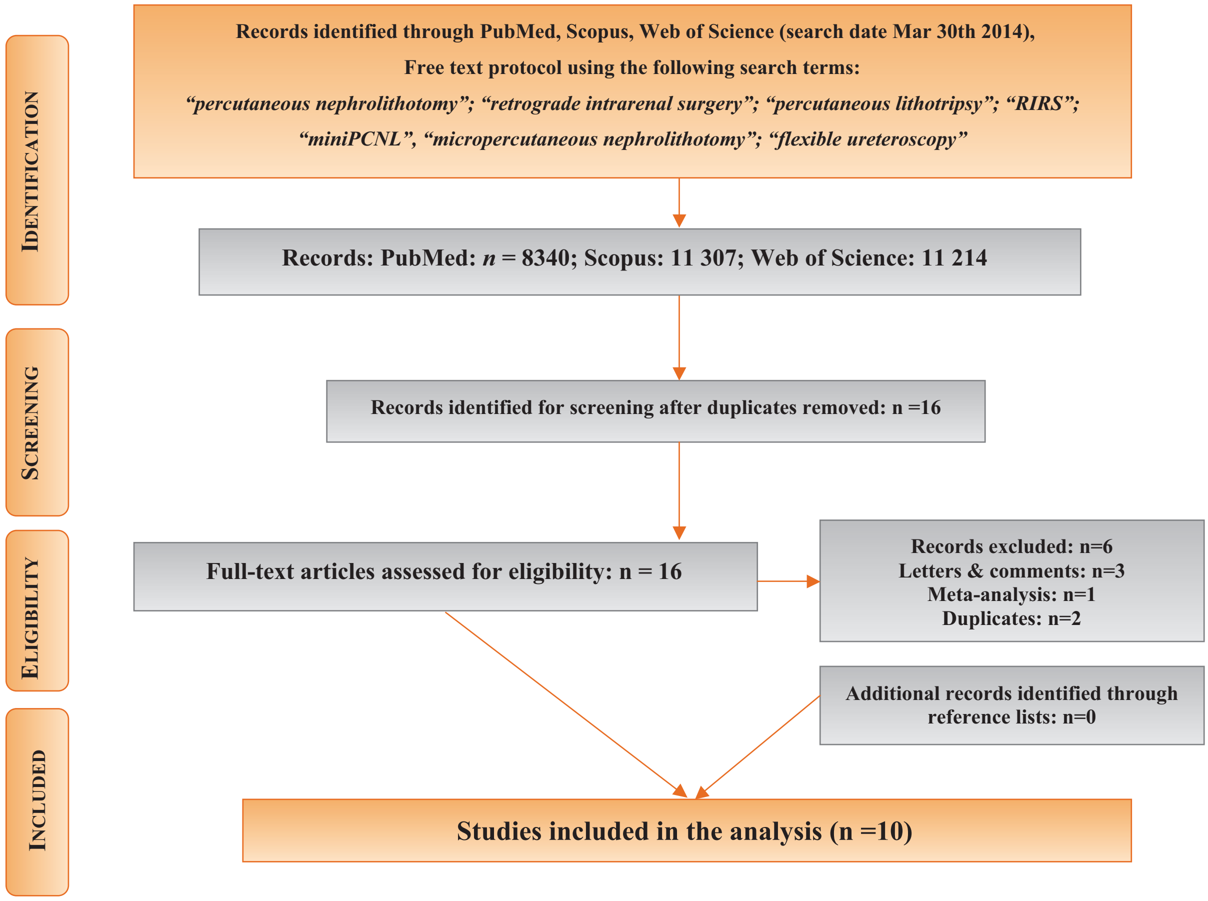

Fig. 1 – Preferred Reporting Items for Systematic Reviews and Meta-analysis flow of study selection.

RIRS was compared with standard PCNL in four studies [15–18], miniperc in four [13,19–21], and microperc in one [22].

Six studies were retrospective case-control studies (LE: 3b) [12,13,15,16,18,20] including one matched-pair analysis [15], two prospective case controls (LE: 3b) [19,21], and two RCTs (LE: 2b) [17,22]. The methodological quality of included studies was relatively high for six of the nonrandomised studies (NOS: 6 of 9 points) [12,15,16, 19–21] and medium for two (NOS: 5 of 9 points and 4 of 9 points) [13,18], whereas the two RCTs were medium quality (Jadad scale: 3 of 5 points) [17,22].

Indications for surgery were different between standard PCNL and MIPPs (Table 2). Only one MIPP study [18] and one PCNL study [15] included multiple stones. Surgical technique for PCNL varied in terms of image guidance, access, use of flexible nephroscopy, and type of lithotripsy (Table 3). Regarding the RIRS technique, less variation among studies was observed. Major differences included ureteric dilation, access sheaths, and stenting (Table 3). Routine stenting was reported by three studies [15,17,21], whereas the rest either selectively used stents [12,16, 19,20,22] or failed to mention their use [13,18]. Most stents were left in for 1–2 wk, although selective stenting up to 21 d was used in one study [20].

3.2. *Outcomes*

3.2.1. *Overall analysis*

There was no significant difference between PCNL and RIRS in terms of operative time (weighted mean difference [WMD]: −4.81 min; 95% CI, −14.05 to 4.43; $p = 0.31$). PCNL provided a significantly higher stone-free rate (OR: 2.19; 95% CI, 1.53–3.13; $p < 0.001$), higher complication rates (OR: 1.61; 95% CI, 1.11–2.35; $p < 0.001$), and a larger decrease in haemoglobin (WMD: 0.87 g/dl; 95% CI, 0.51–1.22; $p < 0.001$) (Fig. 2a–2e). RIRS led to a shorter hospital stay (WMD: 1.28 d; 95% CI, 0.79–1.77; $p < 0.001$).

3.2.2. *Subgroup analysis: standard percutaneous nephrolithotomy*

Standard PCNL provided a significantly higher stone-free rate (OR: 4.32; 95% CI, 1.99–9.37; $p = 0.0002$), whereas no statistically significant difference was found in terms of operative time (WMD: −9.21 min; 95% CI, −28.80 to 10.38; $p = 0.36$) and complication rate (OR: 1.59; 95% CI, 0.84–3.02; $p = 0.16$) (Fig. 3a–3d). Length of hospital stay was shorter for RIRS (WMD: 1.84 d; 95% CI, 0.64–3.04; $p = 0.003$). There was no difference in the rate of auxiliary procedures (OR: 0.61; 95% CI, 0.16–2.27; $p = 0.46$).

Table 1 – Percutaneous nephrolithotomy versus retrograde intrarenal surgery: summary of comparative studies

Study	Institution (country)	Study period	Study design	LE	Inclusion criteria	PCNL technique (access sheath size)	Cases, *n*		Study quality
							PCNL	RIRS	
Akman et al. [15]	Haseki Hospital (Turkey)	2008–2011	Matched-pair analysis	3b	2–4 cm, single or multiple stones, any location	Standard (30F)	34	34	6*
Bozkurt et al. [16]	Kecioren Hospital (Turkey)		Retrospective case control	3b	1.5–2 cm, no previous treatment	Standard (24F)	42	37	6*
Bryniarski et al. [17]	Silesia Medical University (Poland)	2008–2010	RCT	2b	>2 cm, single stone, renal pelvis location, no previous treatment	Standard (30F)	32	32	3°
Sabnis et al. [19]	Muljibhai Patel Hospital(India)	2009–2011	Prospective case control	3b	1–2 cm, single or multiple stones, any location	Mini (16–19F)	32	32	6*
Ozturk et al. [18]	Diskapi Yildirim Beyazit Hospital (Turkey)	2007–2012	Retrospective case control	3b	1–2 cm, lower pole	Standard (30F)	144	38	5*
Kirac et al. [20]	Koru Hospital (Turkey)	2009–2012	Retrospective case control	3b	<1.5 cm, lower pole	Mini (16–18F)	37	36	6*
Sabnis et al. [22]	Muljibhai Patel Hospital (India)	2011–2012	RCT	2b	<1.5 cm, single stone or multiple stones accessible via single tract	Micro (16 g)	35	35	3°
Kruck et al. [13]	Multiple institutions (Germany)	2001–2007	Retrospective case control	3b	Any size, any location	Mini (16–18F)	172	108	4*
Resorlu et al. [12]	Multiple institutions (Turkey)		Retrospective case control	3b	1–2 cm radiolucent stones, any location	Mixed (12–30F)	140	46	6*
Pan et al. [21]	Renji Hospital (China)	2005–2011	Prospective case control	3b	2–3 cm, single stone, any location	Mini (18F)	59	56	6*

LE = level of evidence; PCNL = percutaneous nephrolithotomy; RCT = randomised controlled trial; RIRS = retrograde intrarenal surgery.
* Using Newcastle-Ottawa Scale (score from 0 to 9).
° Using Jadad scale (score from 0 to 5).

Table 2 – Stone size, multiplicity, and renal location

Study	Stone size		Multiple stone, %		Stone location, %							
					Upper pole		Middle pole		Lower pole		Renal pelvis	
	PCNL	RIRS	PCNL	RIRS	PCNL	RIRS	PCNL	RIRS	PCNL	RIRS	PCNL	RIRS
Akman et al. [15]	270*	286*	32.4	17.6	17.6	17.6	5.8	5.8	41.2	44.1	35.3	32.4
Bozkurt et al. [16]	170*	165*	40.4	51.3	–	–	–	–	–	–	–	–
Bryniarski et al. [17]	352*	414*	–	–	–	–	–	–	–	–	–	–
Sabnis et al. [19]	15.2	14.2	21.8	34.4	3.1	9.4	0	3.1	31.2	28.1	43.7	25
Ozturk et al. [18]	17.4	17.3	–	–	–	–	–	–	100	100	–	–
Kirac et al. [20]	10.5	10.2	23.4	27.0	–	–	–	–	100	100	–	–
Sabnis et al. [22]	1.1	1	–	–	8.5	5.78	8.57	8.57	42.8	48.6	40	37.1
Kruck et al. [13]	12.6	6.8	–	–	–	–	–	–	42.7	76.8	–	–
Resorlu et al. [12]	17.3	15.6	15.7	21.7	12.1#	15.2#	–	–	38.6	30.4	33.6	32.6
Pan et al. [21]	22.4	22.3	–	–	8.5	12.5	18.6	12.5	53	51.8	19.9	23.2

PCNL = percutaneous nephrolithotomy; RIRS = retrograde intrarenal surgery.
* mm^2; all other units are in millimetres.
\# Upper and middle pole stones.

3.2.3. Subgroup analysis: minimally invasive percutaneous procedures

MIPPs had significantly shorter operative time than RIRS (WMD −6.75 min; 95% CI, −12.97 to −0.52; $p = 0.03$), whereas RIRS had improved stone-free rates over MIPP (OR: 1.70; 95% CI, 1.07–2.70; $p = 0.03$) (Fig. 4a–4d). RIRS patients also had a shorter hospital (WMD: 1.11 d; 95% CI, 0.39–1.83; $p = 0.003$). No statistical significant difference was found when RIRS was compared with MIPPs for complication rate (OR: 1.46; 95% CI, 0.87–2.45; $p = 0.15$) and rate of auxiliary procedures (OR: 1.68; 95% CI, 0.39–5.15; $p = 0.49$).

3.3. *Interpretation of data*

The assessment of studies involving endourologic procedures is in general a challenging task because a variety of instrumentation, techniques, and perioperative care pathways are used. The present analysis was conducted with the aim of systematically identifying and critically analysing all available studies comparing the outcomes of PCNL with those of RIRS in the management of kidney stones.

Percutaneous surgery originated in the 1980s, and it traditionally uses a large (28–30F) working sheath, facilitating irrigation during the procedure and debris to drain freely, and direct removal of large stone fragments. These features enabled PCNL to achieve very high stone-free rates while reducing surgical morbidity compared with open stone surgery [23]. Over the last decade, there has been increasing interest in mini and micro percutaneous techniques. However, technological advances in the field of flexible ureteroscopy, coupled with the availability of novel endoscopic basket devices and flexible lithotrites, have allowed RIRS to flourish, expanding its indications to stones with a kidney location. Thus many recent publications have reported successful treatment of larger and larger stones using single or staged ureteroscopic procedures [1,24,25].

Meta-analysis of extractable data in the present study was performed by running first an overall analysis considering all studies together, regardless of the PCNL technique (standard, mini, and micro); then, by running two subgroup analyses, one including only studies on standard PCNL and the other considering only studies on MIPPs (miniperc and microperc).

Operative times were not found to vary between PCNL and RIRS. Five studies showed PCNL having shorter procedure times [15,16,19–21], whereas two favoured RIRS [17–22]. A statistically significant difference in favour of PCNL was noted when only studies on MIPPs were included (WMD: −6.75 min; 95% CI, −12.97 to −0.52; $p = 0.03$). However, this difference is unlikely to translate into any clinical significance in terms of benefit to patient and/or reduced costs.

Operative times are strictly related to nuances in the surgical technique, and many technical differences were noted in this regard. Not including differences between MIPPs versus standard PCNL, percutaneous methods showed variations in intraoperative imaging, dilation technique, sheath size, lithotripters, nephrostomy tube type/placement, ureteric stent placement, and tract closures.

Of those studies favouring RIRS for operative times, Bryniarski et al. reported that standard PCNL performed by a single surgeon took 20 min longer using an access obtained by the urologist, telescopic dilators, and ultrasonic lithotripsy [17]. It was not reported whether larger fragments were only fragmented or removed using graspers. The second study identifying shorter operative times for RIRS used a variety of sheath sizes (12–30F) and only dealt with radiolucent stones [22].

Only three studies explicitly reported that urologists performed renal punctures [17,20,22]. One study only used 30F balloon dilators inflated to 18 atm [15], whereas three used a combination of Amplatz with or without metal telescopic with or without balloon dilators [12,16,20], and the rest used metal telescopic dilators. All standard PCNL studies reported prone positioning, with most using ureteric catheter insertion for contrast instillation. All studies used intraoperative fluoroscopy, and in two of them flexible nephroscopy was also used [12,16]. Lithotriptor types

Table 3 – Variations in percutaneous nephrolithotomy and retrograde intrarenal surgery techniques, as stated in the Methods section: an overview

	Studies									
	Akman et al. [15]	Bozkurt et al. [16]	Bryniarski et al. [17]	Sabnis et al. [19]	Ozturk et al. [18]	Kirac et al. [20]	Sabnis et al. [22]	Kruck et al. [13]	Resorlu et al. [12]	Pan et al. [21]
PCNL technique										
Imaging	F		F	US	F	F	F/US	F/US	F	US
Access			Urologist			Urologist	Urologist			
Sheath size, F	30	24	30	16–19	30	16–18	4.5	16–18	12–30	18
Dilator										
Balloon	X	X				X			X	
Metal			X		X			X	X	X
Amplatz		X				X				
Lithotripsy technique										
Pneumatic		X			X	X			X	
Ultrasonic		X	X	X		X	X		X	X
Laser		X		X						X
Grasper removal		X				X			X	
NT	R	S		S		S	None (JJ used)	None (JJ used)	S	R
RIRS technique										
Safety wire	X	X				X			X	
UAS	S	S		S	R	R	R		S	R
Dilator										
Fascial				X		X	X	X	X	X
Semirigid URS	X		X							X
Technique										
Dust		X	X	X		X	X		X	X
Basket				X			X			
Relocation of LP				X			X			X
Laser setting, W	8–10		15	15			5–15			10–15
Stent	R	S	R	S		S	S		S	R

F = fluoroscopy; JJ = double J ureteric stent; LP = lower pole (stone), NT = nephrostomy tube, PCNL = percutaneous nephrolithotomy; R = routine use, RIRS = retrograde intrarenal surgery; S = selective use; UAS = ureteral access sheath placement; URS = ureteroscopy; US = ultrasound.

included pneumatic [15,16,18], ultrasonic [16,17], or laser [16]. None of the studies mentioned combined pneumatic/ultrasonic modalities. In all MIPP studies, laser lithotripsy was used, as well as graspers for stone extraction. Three studies also selectively used pneumatic and ultrasonic lithotripters [13,20,21]. Only one study used routine 16F nephrostomy tube placement for 2 wk [21], two selectively placed 12–14F tubes [16,20], and one used double J stents and haemostatic gel for tract closure [13]. In one microperc study, the authors used a 16-g needle through which visualisation and laser fragmentation was conducted using a tubeless technique [22]. Regarding the RIRS technique, less variation among studies was observed. Major differences included ureteric dilation, access sheaths, and stenting. Four studies used routine access sheath placement between 11.5 and 14F [18,20–22], and four used selectively placed sheaths

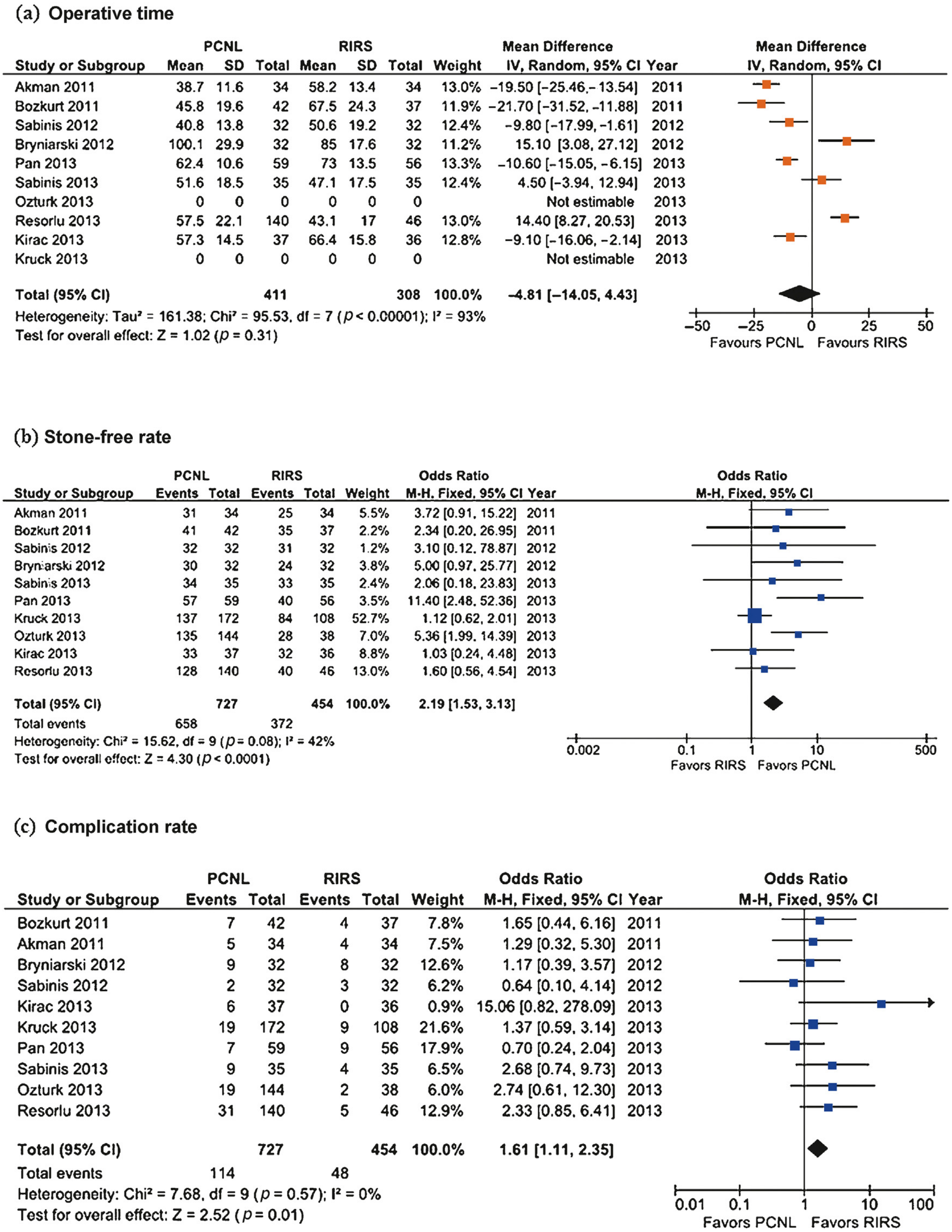

Fig. 2 – Forest plots for the overall analysis: (a) operative time; (b) stone-free rate; (c) complication rate; (d) hemoglobin drop; (e) hospital stay. CI = confidence interval; M-H = Mantel-Haenszel; PCNL = percutaneous nephrolithotomy; RIRS = retrograde intrarenal surgery; SD = standard deviation.

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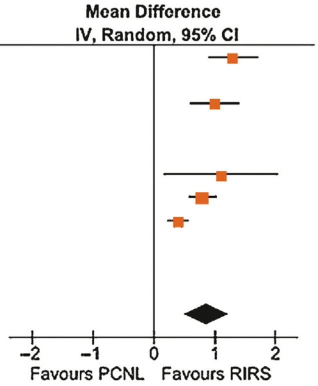
(d) Hb drop

Study or Subgroup	PCNL Mean	PCNL SD	PCNL Total	RIRS Mean	RIRS SD	RIRS Total	Weight	Mean Difference IV, Random, 95% CI	Year
Akman 2011	1.6	1.2	34	0.3	0.1	34	20.2%	1.30 [0.90, 1.70]	2011
Bozkurt 2011	0	0	0	0	0	0		Not estimable	2011
Sabinis 2012	1.4	1	32	0.4	0.6	32	20.2%	1.00 [0.60, 1.40]	2012
Bryniarski 2012	0	0	0	0	0	0		Not estimable	2012
Kruck 2013	0	0	0	0	0	0		Not estimable	2013
Kirac 2013	1.5	0.7	37	0.4	2.8	36	9.4%	1.10 [0.16, 2.04]	2013
Pan 2013	1.3	0.8	59	0.5	0.4	56	24.5%	0.80 [0.57, 1.03]	2013
Sabinis 2013	0.96	0.4	35	0.56	0.3	35	25.8%	0.40 [0.23, 0.57]	2013
Ozturk 2013	0	0	0	0	0	0		Not estimable	2013
Resorlu 2013	0	0	0	0	0	0		Not estimable	2013
Total (95% CI)			**197**			**193**	**100.0%**	**0.87 [0.51, 1.22]**	

Heterogeneity: Tau² = 0.12; Chi² = 24.05, df = 4 ($p < 0.0001$); I² = 83%
Test for overall effect: Z = 4.77 ($p < 0.00001$)



(e) Hospital stay

Study or Subgroup	PCNL Mean	PCNL SD	PCNL Total	RIRS Mean	RIRS SD	RIRS Total	Weight	Mean Difference IV, Random, 95% CI	Year
Akman 2011	2.5	1.4	34	1.2	1.5	34	10.6%	1.30 [0.61, 1.99]	2011
Bozkurt 2011	2.3	1.6	42	1.3	0.7	37	11.6%	1.00 [0.47, 1.53]	2011
Sabinis 2012	2	0.6	32	1.9	0.7	32	12.7%	0.10 [−0.22, 0.42]	2012
Bryniarski 2012	11.3	4.4	32	6.8	3.4	32	4.3%	4.50 [2.57, 6.43]	2012
Ozturk 2013	0	0	0	0	0	0		Not estimable	2013
Pan 2013	4.4	1.4	59	1.9	1.3	56	11.8%	2.50 [2.01, 2.99]	2013
Kirac 2013	1.7	0.5	37	1	0.2	36	13.2%	0.70 [0.53, 0.87]	2013
Kruck 2013	7.3	3.4	172	5.1	3	108	10.1%	2.20 [1.44, 2.96]	2013
Sabinis 2013	2.3	0.9	35	2	0.7	35	12.5%	0.30 [−0.08, 0.68]	2013
Resorlu 2013	2.6	0.9	140	1.3	0.5	46	13.1%	1.30 [1.09, 1.51]	2013
Total (95% CI)			**583**			**416**	**100.0%**	**1.28 [0.79, 1.77]**	

Heterogeneity: Tau² = 0.46; Chi² = 119.46, df = 8 ($p < 0.00001$); I² = 93%
Test for overall effect: Z = 5.16 ($p < 0.00001$)

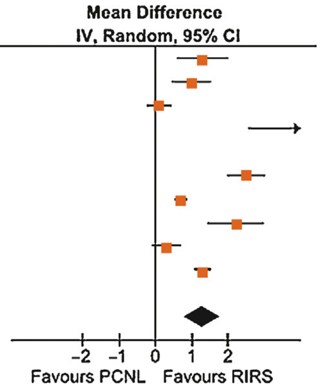


Fig. 2. (***Continued***).

[12,15,16,19]. Five studies used routine semirigid ureteroscopy for visualisation and ureteric dilation [13,15,17,20,21], and in three fascial dilators were used [12,19,22]. All studies used laser lithotripsy (200- to 272-µm fibres), between 5 and 15 W, using a dusting technique (reducing fragments to easily passible sandlike pieces), with only the two studies by Sabnis et al. reporting basket extraction of larger fragments [19,22].

Included in the MIPP group, one study included the three-piece 4.85F micro-nephroscope (All-Seeing Needle) [22]. Because microperc eliminates tract dilation and sheath placement, improvements in complications should be expected. Due to the inability to remove fragments manually, laser lithotripsy and pressure irrigation are used to dust stones, clearing debris through the collecting system. Even more than miniperc, the capability of fragment removal is reduced, and both techniques demand meticulous fragmentation and stenting to prevent a subsequent *steinstrasse* (ie, "street of stones"). These evolving techniques offer exciting additions to the endourologist's armamentarium; however, their indications remain to be explored.

Stone-free rate represents a key parameter when evaluating the efficacy of a stone surgical procedure. The overall analysis showed significantly higher stone-free rates for PCNL (OR: 2.19; 95% CI, 1.53–3.13; $p < 0.00001$). Opposite findings were obtained when looking at subgroup analyses. Standard PCNL had better results than RIRS (OR: 3.07; 95% CI, 1.69–5.61; $p = 0.0003$), whereas RIRS was better than MIPPs (OR: 1.70; 95% CI, 1.07–2.70; $p = 0.03$).

Stone-free rates are directly correlated with the types of treated stone. Only one MIPP study [19] and one standard PCNL study [15] included multiple stones. All standard PCNL studies, excluding the one from Ozturk et al. [18], assessed stones >2 cm, whereas only one MIPP study looked at this stone size [21]. Lower pole stone position favours a percutaneous approach in stones >1.5 cm, due to technical challenges in reaching and performing extensive lithotripsies at maximal ureteroscopic deflection. Two studies assessed lower pole stones only [18,20], whereas others included between 20% and 43% lower pole stone burdens. Because percutaneous access can be achieved directly in line with the stone burden, position does not tend to affect stone removal. However, with an increased reliance on laser dusting in MIPPs, challenges to fragment clearance are similar to those seen in SWL (eg, lower pole infundibular diameter/length/angle, urine output). Accordingly, stone-free rates should improve over weeks as debris

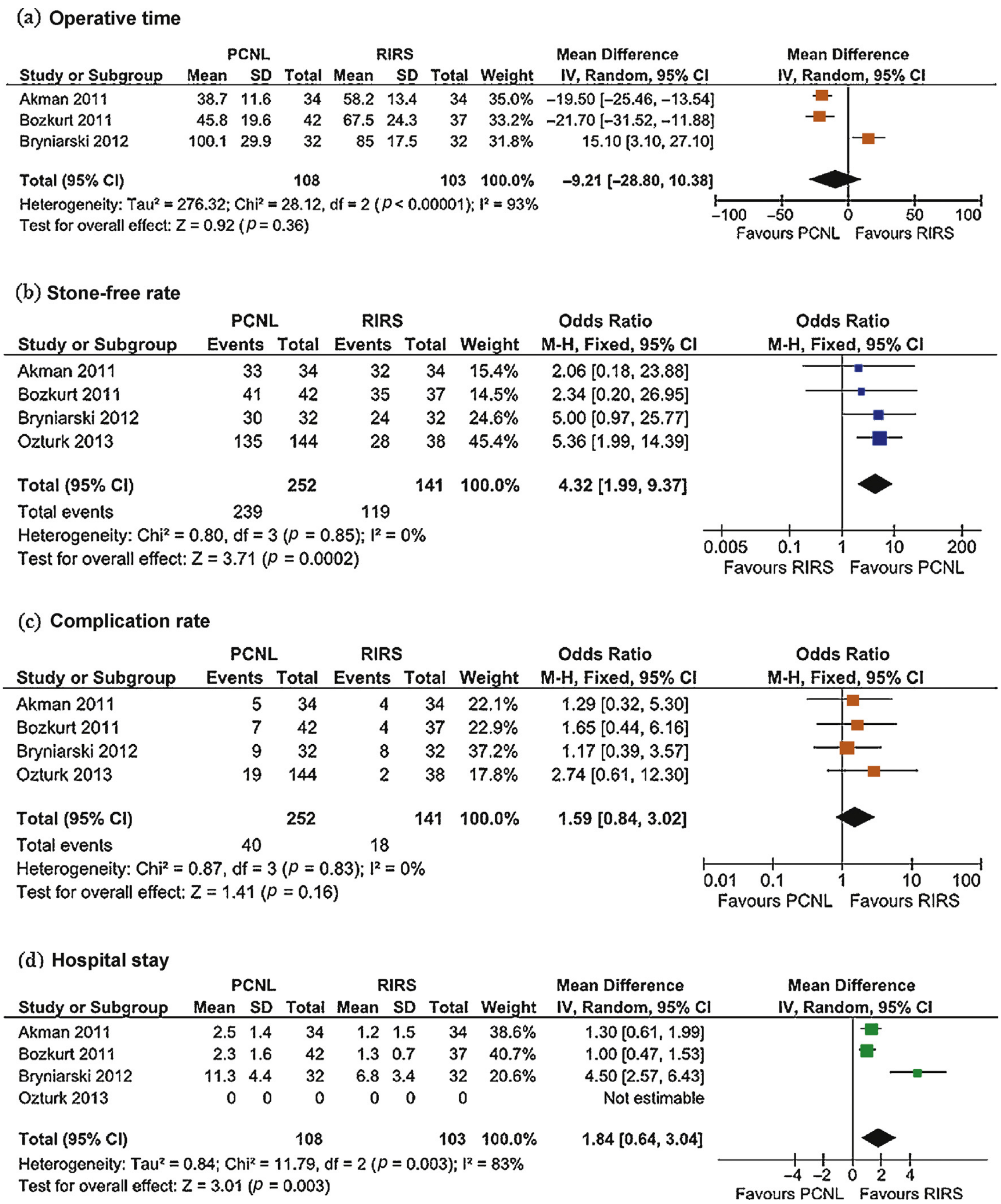


Fig. 3 – Forest plots for the standard percutaneous nephrolithotomy subgroup analysis: (a) operative time; (b) stone-free rate; (c) complication rate; (d) hospital stay.
CI = confidence interval; M-H = Mantel-Haenszel; PCNL = percutaneous nephrolithotomy; RIRS = retrograde intrarenal surgery; SD = standard deviation.

is cleared with the passage of urine. Theoretically, because miniperes allow fragments to be grasped, results should be more in keeping with standard PCNL. However from our subgroup analysis, this was not the case.

Moreover, the "stone-free status" was assessed in a different way in each study. Postoperative imaging spanned from postoperative day 1 [15] to the third postoperative month [12,13,15]. Most studies used a combination of x-ray and ultrasound, with two using routine computed tomography (CT) imaging [12,21]. Studies on standard PCNL used 3 mm as the cut-off for insignificant fragments, with the study by Akman et al. omitting the definition of fragment size [15]. Miniperc studies used a combination of imagining at 1–3 mo, with size cut-offs of 0 mm [22], 2 mm [21], and 3 mm [19,20]. Microperc studies defined stone free as "no residual fragments on any imaging," although imaging modalities used were not elaborated on.

There were no significant differences in secondary procedure rates, regardless of the PCNL technique. No second-look PCNLs was reported, and ureteroscopy

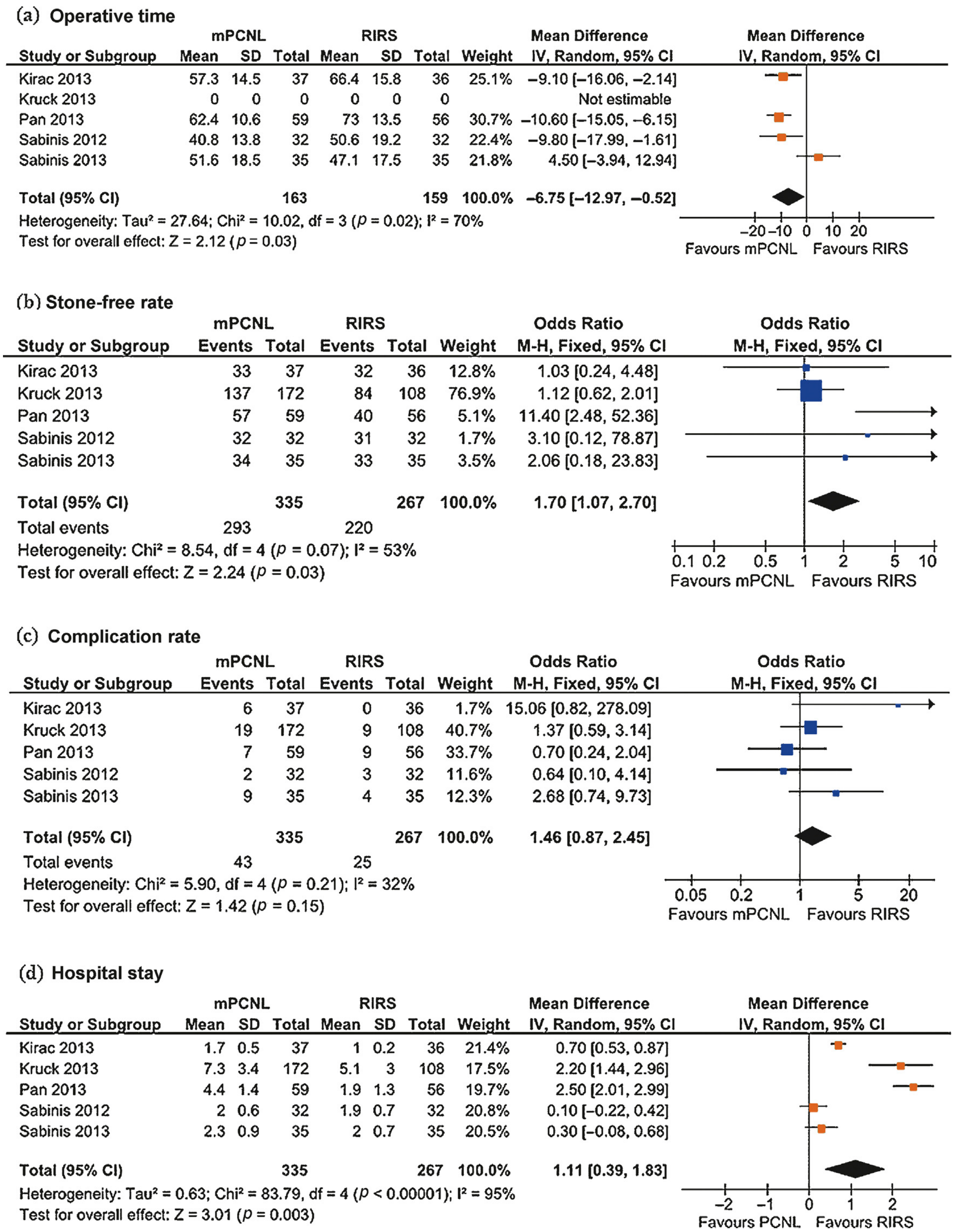


Fig. 4 – Forest plots for the minimally invasive percutaneous procedure subgroup analysis: (a) operative time; (b) stone-free rate; (c) complication rate; (d) hospital stay.
CI = confidence interval; M-H = Mantel-Haenszel; mPCNL = minimally invasive percutaneous nephrolithotomy; RIRS = retrograde intrarenal surgery; SD = standard deviation.

made up most of the secondary procedures for residual fragments. Indications for secondary procedures were only described by two studies [17,21], using residual fragment size criteria as guidelines. As secondary procedure rates for RIRS increase with stone size, of three studies including stones <2 cm, only Bryniarski et al. reported secondary procedure rates and showed a 12.5% secondary procedure rate for RIRS compared with 6.25% for PCNL for these larger stones [17].

Given that the stone-free rates for RIRS are lower then PCNL, and there were no significant differences in secondary procedures, RIRS patients may be at higher risk for future stone-related events (eg, symptoms, recurrence, intervention). However, because no included studies addressed recurrence, we cannot confirm whether this is the case.

At the overall analysis it was found that PCNL carries higher complication rates (OR: 1.61; 95% CI, 1.11–2.35; $p < 0.01$) compared with RIRS. Rates of fever (PCNL: 3–25%; RIRS: 2–28%), prolonged antibiotic use (PCNL: 2–8%; RIRS: 4–5%), and sepsis (PCNL: 0.5–2%; RIRS: 3–5%) were varied and not included in every study. Bleeding issues composed most of the PCNL complications, as suggested by the larger decrease in haemoglobin values (WMD: 0.87 g/dl; 95% CI, 0.51–1.22; $p < 0.00001$). This translated into a more frequent use of transfusions in patients undergoing PCNL (5.5% overall). Unique to PCNL were prolonged urine leaks ($n = 4$), embolisation ($n = 1$), pleural injury ($n = 1$), and pelvic perforation ($n = 2$), whereas *steinstrasse* ($n = 1$), ureteral injuries ($n = 2$) requiring open reconstruction ($n = 1$) were unique to RIRS.

Complication rates were not significantly different when comparing RIRS with MIPPs or standard PCNL. Because the study by Resorlu et al. was removed from the subgroup analysis, due to including both MIPPs and standard PCNL [12], it likely accounts for why percutaneous procedures had higher overall complication rates. Interpreting complications proved to be challenging because key information regarding transfusion threshold, antibiotic indications, and definitions for sepsis were not clearly stated.

The UK Health Episode Statistics database reviewed >5700 PCNL patients over 6 yr and identified rates for haemorrhage (1.4%), urinary tract infection (3.8%), fever (1.7%), sepsis (0.7%), and 30-d readmission rates (9%) [26]. Because diagnostic codes were used to identify clinical variables, it is difficult to understand the severity of these complications. Using data from the Clinical Research Office of the Endourological Society database, de la Rosette et al. found that Clavien score is strongly associated with duration of hospital stay [3]. Tyson et al. reported that insurance status was associated with increased complication rates. Multivariate analysis identified that the differences may actually be attributed to higher rates of medical comorbidities in those on Medicare and Medicaid compared with private insurance. Pulmonary disorders (OR: 7.77), coagulopathies (OR: 6.16), anaemias (OR: 3.82), and paralysis (OR: 2.16) were the strongest predictors of multiple perioperative complications [27].

Although practices for hospital admission vary globally, patients are routinely admitted after PCNL, whereas patients undergoing RIRS can be observed or discharged the same day. This disparity is highlighted by the range of mean admission times, with a Polish group admitting PCNL patients for 11.3 d and RIRS patients for 6.8 d [17], compared with a Turkish group (PCNL: 1.7 d; RIRS: 1 d) [20]. In many countries, such as the United States, RIRS is mostly performed as an outpatient procedure, and average length of stay is <24 h. Not surprisingly, RIRS showed an overall shorter length of stay as compared with PCNL in our analysis (WMD: 1.28 d; 95% CI, 0.79–1.77; $p < 0.0001$), which can be regarded as an important feature in terms of cost reduction. RIRS also had the significantly shorter hospital stay at subgroups analyses, compared with both MIPPs and standard PCNL.

Because these procedures share overlapping indications, the increased morbidity of PCNL needs to be considered when comparing it with less invasive RIRS. Although a size threshold of 2 cm is a commonly cited reason for choosing PCNL over RIRS, many other factors (eg, stone position, anatomic abnormalities, obesity, coagulopathies) influence the decision [2]. In this analysis all but one study [21] comparing MIPPs with RIRS used stones <2 cm as their inclusion criteria. Mean stone sizes were difficult to compare because standard PCNL studies reported mean area, whereas MIPPs used maximum diameter. If we assumed all MIPPs-treated stones were perfect spheres (area = diameter squared), this hypothetical overestimate still shows these stones were 50 mm^2 smaller than those treated by standard PCNL. As such, innovations in percutaneous surgery are challenging current dogma, diverging from the EAU recommendation for PCNL to be used in stones >2 cm [2].

Because current evidence shows RIRS to have superior stone-free rates, shorter hospital admission rates, and reduced bleeding when compared with MIPPs, with no differences in auxiliary procedures or complication rates, one must question the utility of MIPPs. With the evolution in both flexible ureteroscopes and miniaturised nephroscopes, perhaps these trends will change as the technologies and indications mature. However, based on pooled results from these studies, MIPPs show relatively few benefits over flexible ureteroscopy for stones <2 cm. Stones >2 cm have yet to be adequately tested in comparative trials.

The present analysis was conducted using the currently available comparative studies. However, most of the studies were nonrandomised comparisons, and only two (medium quality) RCTs were available for inclusion. Overall, only 10 studies comparing PCNL with RIRS could be identified thorough a systematic review of the literature and therefore included in the meta-analysis. Such a small number of studies can be interpreted as representing a remote area of clinical research. However, these procedures are widely performed on a large scale in daily clinical practice worldwide. Thus this increases the relevance of this analysis while stressing the need for further efforts in conducting well-designed clinical studies in this field.

Heterogeneity among studies was found to be high for several parameters. This heterogeneity can be explained by the difference in surgical practices, follow-up imaging, scheduling, and outcome definitions. Studies comparing MIPPs with RIRS were more uniform in how RIRS was performed, with almost all using ureteric access sheaths, semirigid ureteroscopy (to survey and dilate ureter), relocation of lower pole stones, and selective stent insertion. For percutaneous procedures, these studies were more likely to use intraoperative ultrasound imaging, tubeless techniques, and follow-up CT imaging. This may signify a potential bias in that those reporting MIPP techniques represent a population of surgeons whose uniform experience with endourology generates a dissimilar comparison group as compared with standard PCNL.

These limitations complicate interpreting our findings; nevertheless, the present meta-analysis captures the breadth of current practices and attempts to fill a gap in the current literature, providing the most up-to-date information in this area.

4. Conclusions

Meta-analysis of available comparative studies suggests that PCNL provides overall significantly higher stone-free rates than RIRS, at the expense of higher complication rates, blood loss, and longer length of stay, with no differences in surgical time and secondary procedures.

Nevertheless, RIRS can provide higher stone-free rates compared with MIPPs. Given the added morbidity and reduced efficacy in MIPPs for stones <2 cm, RIRS should be considered standard therapy in these patients. However, MIPPs may play a role in these patients when instrumentation and/or expertise in RIRS are lacking. Strong consideration should be given to standard PCNL in this situation due to the inferior efficacy of MIPPs.

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Study concept and design: Autorino, De Sio.
Acquisition of data: Balsamo, Di Palma, Torricelli.
Analysis and interpretation of data: Autorino, De, De Sio.
Drafting of the manuscript: De, De Sio.
Critical revision of the manuscript for important intellectual content: Autorino, Kim, Laydner, Molina, Monga, Zargar.
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