Retrograde Intrarenal Surgery vs. Percutaneous Nephrolithotomy vs. Extracorporeal Shock Wave Lithotripsy for Lower Pole Renal Stones 20-10 mm : A Meta-analysis and Systematic Review

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Purpose: To conduct a comprehensive meta-analysis of existing evidence to quantify and compare the safety and efficacy of PCNL (percutaneous nephrolithotomy), RIRS (retrograde intrarenal surgery) and ESWL (extracorporeal shockwave liithotrispy) for lower pole renal stones 10-20mm.

Materials and Methods: We conducted a systematic literature search in the EMBASE, MEDLINE, Cochrane databases and Google Scholar to identify relevant studies published in English up to May 2018. Literature reviewed included meta-analyses, and randomized and nonrandomized studies. The subject in the management of PCNL, RIRS and ESWL of studies which included patients with lower pole renal stones 10-20mm. The odd ratio (OR) and mean difference(MD) with its 95% confidence interval (CI) using fixed-or-random-model were calculated to estimate the safety and efficacy of PCNL, RIRS and ESWL for lower pole renal stones 10-20mm. Two reviewers independently assessed the quality of all included studies, and the RevMan 5.3 software was used to analyze the included studies.

Results: Three randomized controlled trials and five retrospective case control studies were included, involving a total of 1615 patients in our meta-analysis. Our results suggest that, for lower pole renal stones 10-20mm, PCNL has a great advantage to RIRS(OR=1.95, 95% CI: 1.22-3.12, P = .005, I^2 = 39%) and ESWL(OR=0.22, 95% CI: 0.15-0.34, P < .00001, I^2 = 0%) in stone-free rate. Comparing PCNL(MD=-24.97, 95% CI: -40.90--9.04, P = .002; I^2 = 76%) (MD=-2.43, 95% CI:-4.70--0.17, P = .04, I^2 = 99%) and RIRS(MD= -15.39, 95% CI: -25.54--5.25, P = .003, I^2 = 99%) (MD=-0.95, 95% CI: -1.29--0.61, P < .00001, I^2 = 96%), ESWL owns some advantages in shorter operative time and hospital stay. Both of PCNL (OR=70.21,95%CI:25.01-197.11, P < .00001) (OR=4.01,95%CI:2.04-7.89, P < .0001) and RIRS (OR=32.31,95%CI:18.39-56.76, P < .00001, I^2=0%) (OR=3.06, 95%CI:1.94-4.84, P < .00001, I^2=19%) have some strong points in lower retreatment rate and auxiliary procedure rate comparing ESWL, but no statistical significant difference is found between them(OR=0.46,95% CI:0.15-1.42, P =.18, I^2=0%)(OR=0.75,95% CI:0.35-1.59,P =.45). About complication rate, there's no statistical significant difference found in PCNL(OR=1.42, 95%CI:0.91-2.21,P=.12, I^2=0%), RIRS (OR=0.74,95%CI:0.51-1.07,P = .11, I^2=30%) and ESWL(OR=0.41,95% CI:0.16-1.09, P = .07,I2=70%).

Conclusion: Both of PCNL and RIRS offer a longer operative time, the lower retreatment rate and auxiliary procedure rate while PCNL has the longest hospital stay and the highest SFR. However, ESWL is confirmed to have the lowest SFR, the higher retreatment rate and auxiliary procedure rate, but a shorter operative time and the shortest hospital stay. The overall complication rates among the three therapies are comparable.

Keywords: retrograde intrarenal surgery; percutaneous nephrolithotomy; extracorporeal shock wave lithotripsy; lower pole renal stones; meta-analysis.

INTRODUCTION

There is chronically a huge controversy about which is the best treatment option for intermediate size (10-20 mm) lower pole renal stones. Although many treatments can be chosen to remove the stones, it is also extremely difficult to choose the best way from these treatments, because many factors such as patient body habitus, cost and patient preference, local renal anatomy, must be taken into account when determining the treatment for lower pole renal stones[1-4]. According to the current EAU Guidelines[5], PCNL (percutaneous nephrolithotomy), RIRS (retrograde intrarenal surgery) and ESWL (extracorporeal shockwave liithotrispy) are recommend as the treatment options for lower pole (LP) renal stones between 10 and 20 mm, moreover, current guidelines also indicate both ESWL and endourology (PCNL, RIRS) can be chosen to treat lower pole renal stones between 10 and 20 mm when there is no unfavourable factors including shock wave-resistant stones (calcium oxalate monohydrate, brushite, or cystine), steep infundibular-pelvic angle, long lower pole calyx

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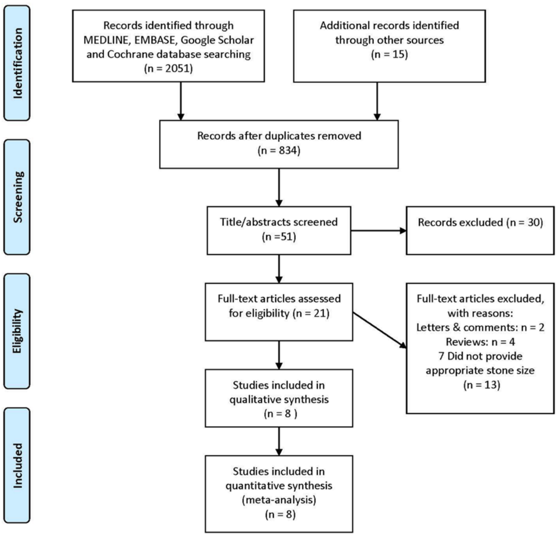

Figure 1. Flowchart for records selection process of the meta-analysis (according to PRISMA template: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097).

(> 10mm), narrow infundibulum (< 5mm) and long skin-to-stone distance (> 10cm), but if there are some unfavourable factors, endourology is the preferred option comparing ESWL. There is no exact answer about which is the best treatment option for intermediate size (10-20 mm) lower pole renal stones till the present moment.

Although there are some meta-analysis or reviews[6-10] comparing the treatment efficacy of PCNL, RIRS and ESWL for renal calculi, so far there is only one meta-analysis[10] comparing the treatment efficacy of PCNL, RIRS and ESWL for lower pole renal stones between 10 and 20 mm, but the meta-analysis[10] only evaluated the stone-free rate of the three treatments and its included studies was retrospective case control. Therefore, the present study focused on a comprehensive meta-analysis of existing evidence to quantify and compare the safety and efficacy, which was evaluated by stone-free rate, operative time, hospital stay, complication rate, retreatment rate and auxiliary procedure rate, of PCNL, RIRS and ESWL for lower pole renal stones 10-20mm.

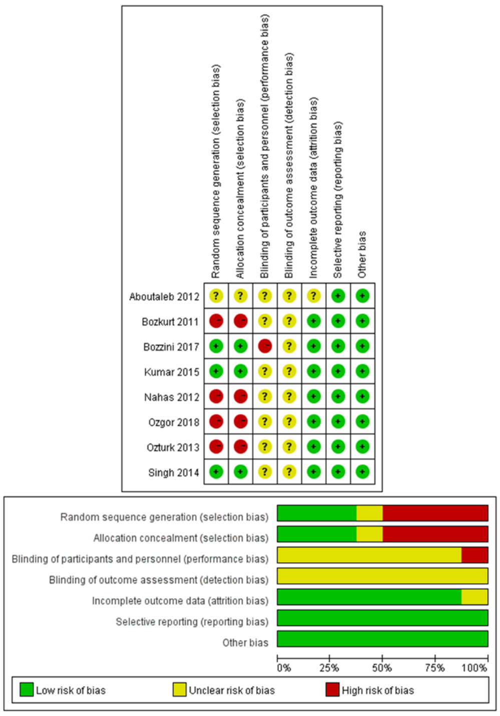

Figure 2. Risk of bias graph and risk of bias summary.

MATERIALS AND METHODS

The meta-analysis was conducted and reported according to Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) statement[11].

Data sources and searches

We conducted a systematic literature search in the EMBASE, MEDLINE, Cochrane databases and Google Scholar to identify relevant studies which reported retrograde intrarenal surgery vs. percutaneous nephrolithotomy vs. extracorporeal shock wave lithotripsy for lower pole renal stones 10-20mm published in English up to May 2018. The Medical Subject Heading (MeSH) terms and/or key words and/or free words were (flexible ureterorenoscopy / retrograde intrarenal surgery / flexible ureteroscopy / RIRS OR percutaneous lithotripsy / percutaneous nephrolithotomy / PCNL OR extracorporeal shock wave lithotripsy / ESWL) AND inferior / lower AND calices / calyceal / calyx. Then we made additional manual searches using the reference lists from key studies to retrieve other papers relevant to our topic. We contacted corresponding authors to obtain some missing data from selected studies.

Study selection

Two reviewers (G J. and J H.) reviewed all the full texts of the identified studies. The studies were included in the meta-analysis if the following inclusion criteria were met: 1. The study had a retrospective case control design or randomized control design; 2. The subject in the management of PCNL, RIRS and ESWL of the recruited studies must be patients who had lower pole renal stones 10-20mm; 3. The study evaluated the efficacy of RIRS, PCNL and ESWL in management of lower pole renal stones 10-20mm, and reported at least 3 outcomes of the following: stone-free rate, operative time, hospital stay, complication rate, retreatment rate and auxiliary procedure rate. 4. The language of the study was in English. All studies that did not meet the above criteria were excluded.

Data extraction and quality assessment

A standardized data extraction form collecting information on the year of study period, country, the levels of evidence (LE), study design, inclusion criteria, number of cases and controls, age, sex, side, stone size, stone-free rate, operative time, hospital stay, complication rate, retreatment rate and auxiliary procedure rate, was used to extract data. The levels of evidence (LE) for all included studies were estimated independently by two reviewers (G J. and J H.) according to the criteria provided by the Oxford Centre for Evidence Based Medicine[12]. Two independent reviewers (G J.

Table 1. Characteristics of the included studies

Author, year	Country	Study period	Study design	LE quality	Study criteria	Inclusion	Cases,n PCNL	RIRS	ESWL
Bozkurt et al ,2011	Turkey	2009-2010	Retrospective case control	3b	6*	1.5-2cm	42	37	-
Aboutaleb et al, 2012	Egypt	2007-2011	Retrospective case control	3b	5*	1-2cm	19	13	24
El-Nahas et al ,2012	Egypt	2007-2010	Retrospective case control	3b	7*	1-2cm, symptomatic	-	37	62
Ozturk et al ,2013	Turkey	2007-2012	Retrospective case control	3b	5*	1-2cm	144	28	221
Ozgor et al ,2018	Turkey	2011-2013	Retrospective case control	3b	7*	1-2cm	-	128	113
Singh et al, 2014	India	2011-2013	RCT	2b	3#	1-2cm, radio-opaque	-	35	35
Kumar et al ,2015	India	2012-2013	RCT	2b	3#	1-2cm	-	43	42
Bozzini et al, 2017	Italy;Austria; UK;Russia	2010-2014	RCT	2b	3#	1-2cm	181	207	194

LE =level of evidence; RCT=randomized controlled trial; RIRS=retrograde intrarenal surgery; PCNL=percutaneous nephrolithotomy; ESWL=extracorporeal shock wave lithotripsy; *Using Newcastle-Ottawa scale (score from 0 to 10);# Jadad scale (score from 0 to 5)

and J H.) appraised and determined the methodological quality of each included study according to the Newcastle-Ottawa Scale (NOS) for nonrandomized controlled trials[13] and the Jadad Scale for randomized controlled trials (RCTs)[14]. The NOS was assessed according to selection, comparability and exposure. And the Jadad Scale was evaluated according to randomization double blinding, withdrawals and dropouts. We defined the NOS scores as 6-9 being high methodological quality, 4-5 being medium quality and < 4 being low quality. We also defined the Jadad scores as > 2 being high methodological quality and ≤ 2 being low quality. The NOS quality scores and the Jadad scores presented did not influence decisions to pool studies in the meta-analysis, it was only as part of descriptive summaries for each study. The Cochrane Collaboration's tool for assessing risk of bias was also used to assess all included studies according to random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting, and other biases. "Low bias" "High bias" or "Uncertain" was used to show the evaluate results. When there were different opinions of the 2 reviewers for a study, we found a solution by discussing or inviting the third researcher to assist in.

Data synthesis and meta-analysis

The results of our data analysis are presented in forest plots. The heterogeneity was classified as low ($I2 \leq 50\%$) and high ($I2 > 50\%$). According to that the homogeneity was low or high, we used the fixed or the random effect model in our meta-analysis. If high heterogeneity ($I2 > 50$) was still found, we conducted subgroup analysis or sensitivity analysis. The Odd Ratio (OR) and Mean Difference (MD) with its 95% Confidence Interval (CI) using fixed-or-random-model were calculated to estimate the stone-free rate, operative time, hospital stay, complication rate, retreatment rate, auxiliary procedure rate of PCNL, RIRS and ESWL for lower pole renal stones 10-20mm. The funnel plot was used to estimate the publication bias. For all statistical analyses, a two-sided $p < 0.05$ was considered statistically significant. We used Review Manager Software (RevMan v.5.3, Cochrane Collaboration, Oxford, UK) to conduct data analysis.

RESULTS

Literature search and study election

A PRISMA[11]) flow chart of screening and selection results is shown in **Figure 1**. After a systematic literature search, we retrieved 2051 extracts and obtained 15 additional citations by other sources. From 51 studies initially identified, 21 were considered potentially suitable. After a full-text review, 8 studies[15-22], including three RCTs[20-22] and five retrospective case controls[15-19], with 1615 lower pole renal stones 10-20mm patients met the inclusion criteria and were included in the final analysis. NOS quality scores of one retrospective case control was six, two retrospective case controls were scored seven revealing high quality, and remaining two retrospective case controls are scored five as medium quality. The Jadad scores of all RCTs are three revealing high quality. **Figure 2** shows the risk of bias for all the 8 studies assessed and summary results for the domains. NOS quality scores and Jadad scores are showed in **Table** 1.

A total of 1615 patients including 538 RIRS cases (33.3%), 386 PCNL cases (23.9%) and 691 ESWL cases (42.8%) were compared in our meta-analysis. In all included studies, there were three studies comparing all the three treatment techniques, whereas one comparing RIRS and PCNL, and four comparing ESWL and RIRS. **Table 1** provides a description of the 8 studies which were published between 2011 and 2018. In addition, most studies showed the preoperative demographic characteristics such as patients' mean age, sex ratio, stone size and stone location. **Table 2** provides the summary of baseline patient characteristics and the operative effect of included studies.

Results of Meta-analyses

Stone-free Rate

In terms of the stone-free rate (SFR), PCNL provided a significantly higher SFR compared with RIRS (OR=1.95,95% CI:1.22-3.12, P =.005, $I^2 = 39\%$) (**Figure. 3a**) and ESWL (OR = 0.22, 95% CI: 0.15-0.34, $P <$ .00001, $I^2 = 0\%$) (**Figure. 3c**). On the other hand, RIRS also provided a significantly higher SFR compared with ESWL (OR=0.42, 95% CI:0.31-0.56, $P <$.00001, $I^2 =$

Table 2. Summary of baseline patient characteristics and the operative effect of included studies.

Author, year	Treatment	Age, year	Sex		Side		Stone size (cm)	Stone-free Rate(%)	Operative Time (minutes)	Hospital Stay (days)	Complication Rate(%)	Retreatment	Auxiliary Procedure Rate(%) Rate(%)
			Male	Female	Left	Right							
Bozkurt et al 2011	PCNL	47.4 ±15.5	25	17	22	20	1.70 ± 0.12	97.6 (41/42)	45.8 ± 19.6	2.3 ± 1.6	16.7 (7/42)	0 (0/42)	-
	RIRS	41.2 ± 13.6	21	16	18	19	1.65 ± 0.69	94.6 (35/37)	67.5 ± 24.3	1.3 ± 0.7	18.9 (7/37)	2.7 (1/37)	-
Aboutaleb et al 2012	RIRS	47.2 ±15.2	7	6	-	-	1.45 ± 0.32	84.6 (11/13)	76 ± 34	1 ± 0.56	46.2 (6/13)	-	-
	PCNL	45.3 ± 14.3	14	5	-	-	1.73 ± 0.33	89.5 (17/19)	63 ± 32	2 ± 0.9	31.6 (6/19)	-	-
	ESWL	53.2 ± 19.0	19	5	-	-	1.56 ± 0.43	62.5 (15/24)	48.3 ± 16.7	0.73 ± 0.21	41.7 (10/24)	-	-
El-Nahas et al 2012	RIRS	47.8 ± 10.7	26	11	19	18	1.31 ± 0.24	86.5 (32/37)	73 ± 29	-	13.5 (5/37)	8.1 (3/37)	10.8 (4/37)
	ESWL	45.4 ± 11.3	41	21	32	30	1.30 ± 0.23	67.7 (42/62)	92 ± 41	-	4.8 (3/62)	59.7 (37/62)	16.1 (10/62)
Ozturk et al 2013	RIRS	52	22	16	21	17	1.73 ± 0.15	73.7 (28/38)	-	-	5.3 (2/38)	-	-
	PCNL	41.1	88	56	85	59	1.74 ± 0.15	93.8 (135/144)	-	-	13.2 (19/144)	-	-
	ESWL	44.2	123	98	142	79	1.70 ± 0.16	76.0 (168/221)	-	-	3.2 (7/221)	-	-
Ozgor et al 2018	RIRS	45.9 ± 14.7	63	65	-	-	12.1 ± 5.0	89.0 (114/128)	52.3 ± 16.2	0.88 ± 0.69	15.6 (20/128)	-	-
	ESWL	48.6 ± 14.9	65	48	-	-	11.3 ± 3.1	77.9 (88/113)	25.9 ± 2.5	0. 09 ± 0.04	15.0 (17/113)	-	-
Singh et al 2014	RIRS	37.7 ± 11.8	22	13	18	17	1.51 ± 0.36	82.9 (29/35)	78.8 ± 20.03	2 ± 0.64	31.4 (11/35)	5.7 (2/35)	8.6 (3/35)
	ESWL	34.5±13.1	20	15	16	19	1.65±0.23	48.6 (17/35)	42.25 ± 6.34	0.51±0.22	48.6 (17/35)	65.7 (23/35)	45.7 (16/35)
Kumar et al 2015	RIRS	33.4±1.4	20	23	-	-	1.31 ± 0.11	86.0 (37/43)	47.1±1.1	1.3	9.3 (4/43)	2.3 (1/43)	9.3 (4/43)
	ESWL	33.1±1.3	21	21	-	-	1.32 ± 0.12	73.8 (31/42)	43.6 ± 1.4	0.13	7.1 (3/42)	64.3 (27/42)	19.0(8/42)
Bozzini et al 2017	RIRS	55.8±16.1	101	106	104	103	1.48 ± 0.27	82.1 (170/207)	55.8 ± 11.4	1.3 ± 0.4	14.5 (30/207)	4.3 (9/207)	8.7 (18/207)
	PCNL	54.8±17.2	87	94	98	83	1.52±0.33	87.3 (158/181)	72.3 ± 13.8	3.7±1.5	19.1 (35/181)	2.2 (4/181)	6.6 (12/181)
	ESWL	53.3±14.8	97	97	101	93	1.38±0.31	61.9 (120/194)	40.9±7.7	0.12 ± 0.1	6.7 (13/194)	61.3 (119/194)	22.1 (43/194)

RIRS=retrograde intrarenal surgery; PCNL=percutaneous nephrolithotomy; ESWL=extracorporeal shock wave lithotripsy

33%) (**Figure. 3b**).

Operative Time

As for the operative time, ESWL provided a significantly shorter operative time compared with RIRS (MD=-15.39, 95% CI: -25.54--5.25, P = .003, I2 = 99%) (**Figure. 4b**) and PCNL(MD=-24.97, 95% CI: -40.90--9.04, P = .002; I^2 = 76%, respectively) (**Figure. 4c**), whereas no statistical significant difference of operative time was found between PCNL and RIRS (MD=-5.43, 95% CI: -35.54-24.67, P =.72, I2 = 97%) (**Figure. 4a**).

Hospital Stay

Referring to the hospital stay, ESWL offered a significantly shorter hospital stay compared with RIRS (MD=-0.95, 95% CI: -1.29--0.61, P < .00001, I2 = 96%) (**Figure. 5b**) and PCNL (MD=-2.43, 95% CI:-4.70--0.17, P = .04, I^2 = 99%) (**Figure. 5c**). Furthermore, RIRS also provided a significantly shorter hospital stay compared with PCNL (MD=1.49, 95% CI: 0.41-2.56, P = .007, I^2 = 95%) (**Figure. 5a**).

Complication Rate

When comes to the complication rate, PCNL provided no significantly higher or lower complication rate compared with RIRS(OR=1.42,95%CI:0.91-2.21,P =.12, I^2 = 0%) (**Figure. 6a**) and ESWL(OR=0.41,95% CI:0.16-1.09,P=.07,I2=70%) (Figure. 6c). Furthermore, no statistical significant difference of complication rate was found between RIRS and ESWL(OR=0.74,95% CI:0.51-1.07,P =.11, I^2 = 30%) (**Figure. 6b**).

Retreatment Rate

For the retreatment rate, ESWL provided a significantly higher retreatment rate compared with RIRS (OR=32.31, 95%CI:18.39-56.76, P <.00001, I^2 = 0%) (Figure. 7b) and PCNL(OR=70.21,95%-CI:25.01-197.11, P < .00001) (**Figure. 7c**). whereas no statistical significant difference of retreatment rate was found between PCNL and RIRS(OR=0.46,95% CI:0.15-1.42,P =.18, I2 = 0%) (**Figure. 7a**).

Auxiliary Procedure Rate

Speaking of auxiliary procedure rate, both of RIRS(OR=3.06, 95%CI:1.94-4.84, P < .00001, I^2 = 19%) (**Figure. 8b**) and PCNL(OR=4.01,95% CI:2.04-7.89, P < .0001) (**Figure. 8c**) showed a significantly lower auxiliary procedure rate compared with ESWL. Whereas no statistical significant difference of auxiliary procedure rate was found between PCNL and RIRS(OR=0.75,95%CI:0.35-1.59, P = .45) (**Figure. 8a**).

Sensitivity analysis and Publication Bias

The reasons that caused the heterogeneity among studies were extremely complex, in order to explain the high heterogeneity, a sensitivity analysis was performed. Each included study was deleted every time to verify whether the individual data influenced the heterogeneity. If the heterogeneity dropped sharply following one or two studies being removed, it indicated the study had a great influence on the heterogeneity. But when we got rid one or two studies every time from the meta-analysis whose result still had a high heterogeneity such as operative time(ESWL vs. RIRS,MD=-15.26,95% CI:-30.86--0.33, P = 0.06,I2 = 99%) , hospital stay (ESWL vs. RIRS,MD=-0.86,95%CI:-1.43--0.28, P = 0.003,I2 = 96%) , the high heterogeneity could not descend to the degree that we could accept. After analyzing the existing data, we finally attributed the high heterogeneity to the difference in patient inclusion criteria, outcome definitions and standards, surgical experience, follow-up imaging and duration. The funnel plots did

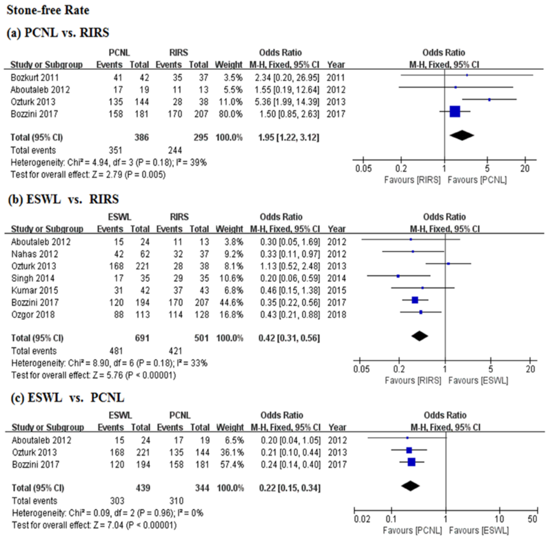

Figure 3. Forest plot comparing stone-free rate between (a) PCNL and RIRS, (b) ESWL and RIRS, (c) ESWL and PCNL. PCNL = percutaneous nephrolithotomy; RIRS = retrograde intrarenal surgery; ESWL = extracorporeal shock wave lithotripsy; M-H = Mantel-Haenszel; IV= inverse variance; CI = confidence interval.

not show any obvious asymmetry, further indicating that there was no publication bias in our meta-analysis (**Figure 9**).

DISCUSSION

The present meta-analysis results demonstrated that each of the three treatments for lower pole renal stones between 10 and 20 mm has its own advantages. Our study is the first meta-analysis which, in many aspects,

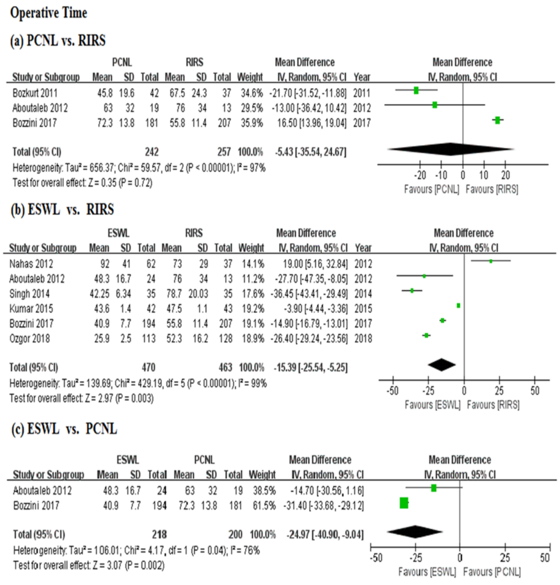

Figure 4. Forest plot comparing operative time between (a) PCNL and RIRS, (b) ESWL and RIRS, (c) ESWL and PCNL. PCNL = percutaneous nephrolithotomy; RIRS = retrograde intrarenal surgery; ESWL = extracorporeal shock wave lithotripsy; M-H = Mantel-Haenszel; IV = inverse variance; CI = confidence interval; SD = standard deviation.

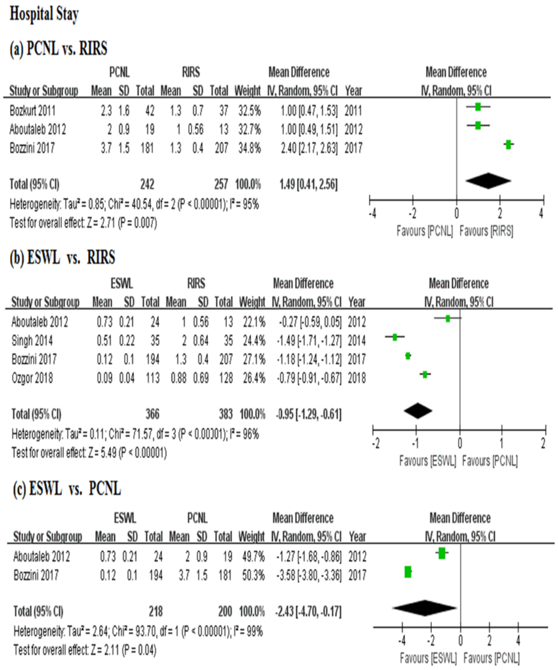

Figure 5. Forest plot comparing hospital stay between (a) PCNL and RIRS, (b) ESWL and RIRS, (c) ESWL and PCNL. PCNL = percutaneous nephrolithotomy; RIRS = retrograde intrarenal surgery; ESWL = extracorporeal shock wave lithotripsy; M-H = Mantel-Haenszel; IV = inverse variance; CI = confidence interval; SD = standard deviation.

examined the safety and efficacy of PCNL, RIRS and ESWL for lower pole renal stones 10-20mm. Although there are 8 included studies whose quality scores, evaluated by the NOS and the Jadad Scale, were high or medium, the quality of the studies did not influence decisions to pool studies in the meta-analysis. According to the meta-analysis results of synthesizing 8 included studies involving 1615 patients, we know that: when you choose a treatment for lower pole renal stones 10-20mm, PCNL has a great advantage to RIRS and ESWL in stone-free rate. Comparing PCNL and RIRS, ESWL owns some advantages in shorter operative time and hospital stay. Both of PCNL and RIRS have some strong points in lower retreatment rate and auxiliary procedure rate comparing ESWL, but no statistical significant difference is found between them. About complication rate, there's no statistical significant difference found in PCNL, RIRS and ESWL.

Open renal stone surgery was formerly used to treat renal stones, but by now it has been abandoned in most cases, and indicated only in some special conditions[18]. Extracorporeal shock wave lithotripsy (ESWL) was recommend as the first-line therapy for management of intrarenal calculi < 20 mm by the American Urological Association guidelines and European Association of Urology (EAU) many years ago[23,24]. After that, ESWL, by right of the advantages such as being an outpatient procedure, better patient acceptance and minimal anesthesia requirement, has been the most preferred treatment measure for lower pole renal stones < 20 mm for a while[16,18]. But with fiber optics and the availability of small-sized instrumentation developing, retrograde

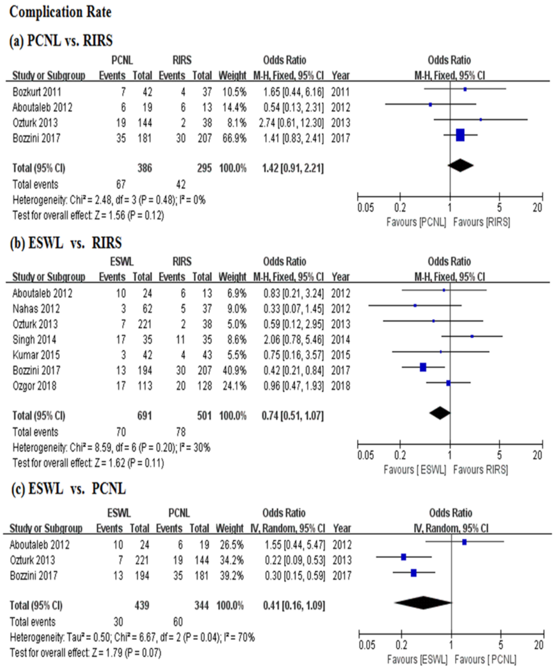

Figure 6. Forest plot comparing complication rate between (a) PCNL and RIRS, (b) ESWL and RIRS, (c) ESWL and PCNL. PCNL = percutaneous nephrolithotomy; RIRS = retrograde intrarenal surgery; ESWL = extracorporeal shock wave lithotripsy; M-H = Mantel-Haenszel; IV = inverse variance; CI = confidence interval.

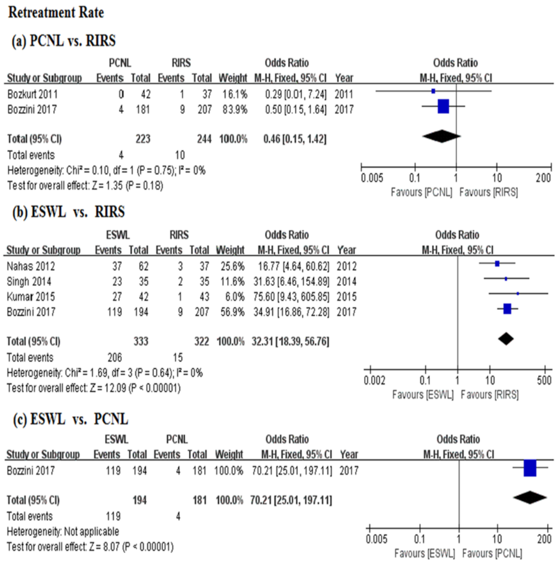

Figure 7. Forest plot comparing retreatment rate between (a) PCNL and RIRS, (b) ESWL and RIRS, (c) ESWL and PCNL. PCNL=percutaneous nephrolithotomy; RIRS = retrograde intrarenal surgery; ESWL = extracorporeal shock wave lithotripsy; M-H = Mantel-Haenszel; IV = inverse variance; CI = confidence interval.

intrarenal surgery (RIRS), relying on the advantages of higher stone-free rate (SFR) with less bleeding and lower risk of renal damage, for renal calculi smaller than 20 mm has gained more and more supports from the urologists[16,19,25,26]. In addition, as the renal endoscopies and percutaneous nephrolithotomy (PCNL) are developing, a safe and effective therapy has been offered to larger lower pole kidney stones in recent years[27]. Therefore, we has compared the treatment efficacy of PCNL, RIRS and ESWL for lower pole renal stones between 10 and 20 mm.

SFR occupies a key parameter in the process of estimating the efficacy of stone operation procedure[9]. Some studies considered that the highest SFR in the renal pelvis or ureteropelvic junction for single calculi was 80% to 88%[28,29], and when stones were located in the lower pole, it dropped below 50% to 70%[30-32], so some people pointed out that when applying ESWL treated the lower pole renal stones, the SFR was dependent on anatomic features[33]. However, the SFR, from the results of our study, ranged from 48.6% to 77.9%. And some people held a view that PCNL had the advantage of achieving the highest SFR for these stones, but it was a technique of the most invasive among three treatment procedures[34-36]. And some other studies[37-39] also revealed PCNL owned a high success rate for all stone sizes in lower pole renal stones because of its high SFR. But there was an opinion that when PNCL couldn't been chosen such as for patients with high surgical risks or challenges, RIRS became a more feasible alternative comparing to ESWL in term of SFR[17,18,20,21,40,41]. The

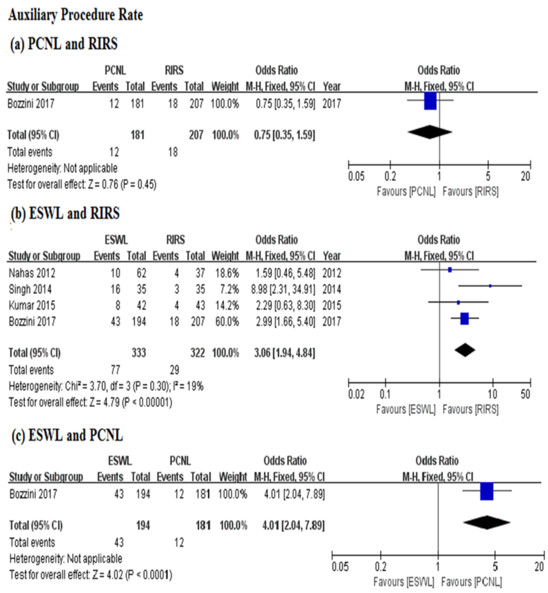

Figure 8. Forest plot comparing auxiliary procedure rate between (a) PCNL and RIRS, (b) ESWL and RIRS, (c) ESWL and PCNL. PCNL = percutaneous nephrolithotomy; RIRS = retrograde intrarenal surgery; ESWL = extracorporeal shock wave lithotripsy; M-H = Mantel-Haenszel; IV = inverse variance; CI = confidence interval.

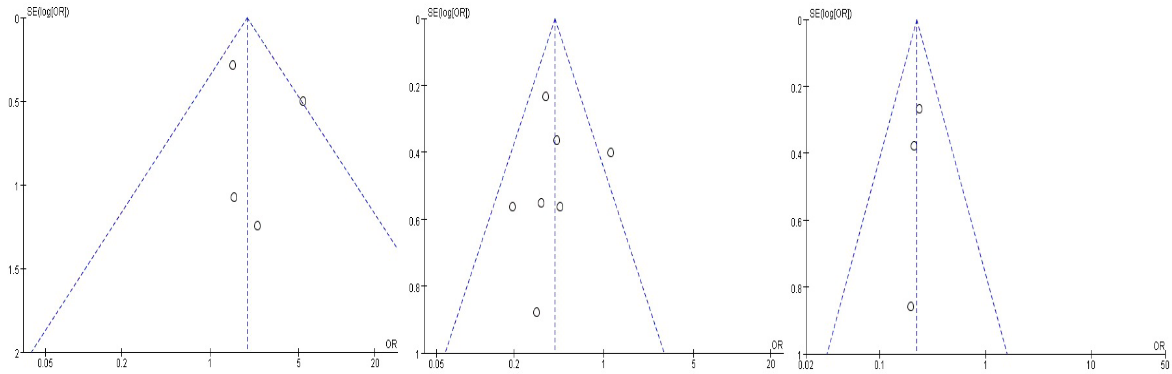

Figure 9. Funnel plot analysis to detect publication bias.(Each point represents a separate study)

result of our meta-analysis also, definitely, showed that PCNL provided a significantly higher SFR comparing with RIRS and ESWL, furthermore, RIRS owned a higher SFR than ESWL.

There was a review[8] that indicated the operative time of PCNL was shorter than RIRS, and the study by Schuster et al.[42] also deemed that the difference may bring damnification to patients in a sense because of the longer duration of ureteroscopic procedure strongly relating to postoperative complications, especially the perforation of ureter. It, on the one hand , suggested the operative time of RIRS should been strictly limited, on the other hand, surgical technics in this respect should be advanced[8,9]. More studies[16,22] reported that ESWL offered the shortest operative time among the three therapies because of its noninvasive. Our meta-analysis also proved that ESWL had the shortest operative time among the three therapies, but there was no statistical significant difference of operative time to be found between PCNL and RIRS. The variation of the results may be generated because of the factors that the included studies had small sample size or that the size of the stones of subjects investigated were different. In addition, our study indicated that there was no statistical significant difference of complication rates to be found among the three treatments. This result was different comparing to other studies[9,43-45] which thought PCNL provided a higher complication rate than RIRS, at the expense of higher blood loss and longer hospital stay. But Zhang et al.[8] in their review gained a conclusion which thought the overall complication rates were comparable among the three treatment techniques, the conclusion was same as ours. This pointed out that ESWL was not noninvasive as same as we thought in the past. As for hospital stay, some people[8,9,43,44] expressed the viewpoint that PCNL had the longest hospital stay, RIRS offered a longer hospital stay and ESWL possessed the shortest hospital stay. They indicated PCNL was the most invasive because of making more damages and bleeding more blood. Furthermore they also deemed that in many countries RIRS was increasingly performed as an outpatient procedure, which made RIRS have more advantages than PCNL in hospital stay, but it had some disadvantages such as the possible need for staged procedures, the costs of acquisition and maintenance of the complex endourological instruments, and risk of ureteral injuries[46]. They also showed many patients had a preference for ESWL profiting from its minimal anesthesia requirement[18], being more efficacious and cost-effective, the noninvasive and low morbidity outpatient procedure[32,47,48]. But when ESWL was applied to treat stones of kidney, it was limited because of stone composition, size and location of stones[6]. In addition, some people held a view that PCNL was associated with low morbidity (a lower incidence of septic shock and less bleeding) in experienced hands[49]. It suggests that urologist should promote themselves to study in order to master the skills of surgery and allay suffering of patients. In our study, we also demonstrably obtained a result that PCNL had the longest hospital stay, RIRS provided a longer hospital stay and ESWL offered the shortest hospital stay.

On the other hand, our study indicated PCNL and RIRS provided a lower retreatment rate and auxiliary procedure rate while ESWL had a higher retreatment rate and auxiliary procedure rate, the result was accepted by many authors[8,17,20-22]. Some studies revealed when urologists or patients chose ESWL to treat stones, various factors such as obesity, stone density, chemical composition and unfavorable lower pole anatomy would influence effects on fragmentation or clearance[50,51]. ESWL had many advantages, but the disadvantages of ESWL had long bedeviled urologists and made some surgeons who preferred to choose ESWL to treat renal calculus change their ideas and turn to PCNL and RIRS in order to get a disposable treatment.

There were several limitations to be addressed in our meta-analysis. First, some missing data was not obtained despite repeated attempts to contact the authors. Second, over half of the included studies were retrospective case control studies which had some limitations because of being susceptible to recall bias or information bias and difficult to validate information[52]. Third, there was bias in the country of the authors of included studies, although we used some measures to minimize it , it did not abolish them. In addition, although we performed a sensitivity analysis to explain the high heterogeneity, it could not descend to the degree that we could accept. After analyzing the existing data, we found several logical reasons to explain the high heterogeneity among some studies, but inevitably, the accuracy of our study was partly influenced. Future, better well-designed retrospective case controls and RCTs with high quality are needed. The interpretation of our findings might be influenced by the above limitations, but as the first meta-analysis which, in many aspects, typically focused on the management of lower pole renal stones 10-20mm and simultaneously included PCNL, RIRS and ESWL, our study would offer the most up-to-date information in this field.

CONCLUSIONS

Our results suggest that, for lower pole renal stones 10-20mm, both of PCNL and RIRS offer a longer operative time, the lower retreatment rate and auxiliary procedure rate while PCNL has the longest hospital stay and the highest SFR. However, ESWL is confirmed to have the lowest SFR, the higher retreatment rate and auxiliary procedure rate, but a shorter operative time and the shortest hospital stay. The overall complication rates among the three therapies are comparable. When urologists choose these treatments, urologists must synthesize the individual characteristics of patients and unique advantages of the therapies. Furthermore, more RCTs and retrospective case control studies are needed to certify these conclusions and to advance knowledge in this area.

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CONFLICT OF INTEREST

The authors report no conflict of interest.

REFERENCES

1. Schoenthaler M, Wilhelm K, Hein S, et al. Ultra-mini PCNL versus flexible ureteroscopy: a matched analysis of treatment costs (endoscopes and disposables) in patients with renal stones 10-20 mm. World J Urol. 2015;33:1601-5.
2. Knoll T, Jessen JP, Honeck P, Wendt-Nordahl G. Flexible ureterorenoscopy versus miniaturized PNL for solitary renal calculi of 10-30 mm size. World J Urol. 2011;29:755-9.
3. Jessen JP, Honeck P, Knoll T, Wendt-Nordahl G. Flexible Ureterorenoscopy for Lower Pole Stones: Influence of the Collecting System's Anatomy. J Endourol. 2014;28:146-51.
4. Skolarikos A, Gross AJ, Krebs A, et al. Outcomes of Flexible Ureterorenoscopy for Solitary Renal Stones in the CROES URS Global Study. J Urol. 2015;194:137-43.
5. Türk C, Knoll T, Petrik A, et al. EAU guidelines on urolithiasis. Eur Urol 2014.258-89
6. Srisubat A, Potisat S, Lojanapiwat B, Setthawong V, Laopaiboon M. Extracorporeal shock wave lithotripsy (eswl) versus percutaneous nephrolithotomy (pcnl) or retrograde intrarenal surgery (rirs) for kidney stones (review). Cochrane Database Syst Rev. 2009;4:CD007044.
7. Mi Y, Ren K, Pan H, et al. Flexible ureterorenoscopy (F-URS) with holmium laser versus extracorporeal shock wave lithotripsy (ESWL) for treatment of renal stone <2 cm: a meta-analysis. Urolithiasis. 2016;44:353-65.
8. Zhang W, Zhou T, Wu T, et al. Retrograde Intrarenal Surgery Versus Percutaneous Nephrolithotomy Versus Extracorporeal Shockwave Lithotripsy for Treatment of Lower Pole Renal Stones: A Meta-Analysis and Systematic Review. J Endourol. 2015;29:745-59.
9. De S, Autorino R, Kim FJ, et al. Percutaneous nephrolithotomy versus retrograde intrarenal surgery: a systematic review and meta-analysis. Eur Urol. 2015;67:125-37.
10. Yuri P, Hariwibowo R, Soeroharjo I, et al. Meta-analysis of Optimal Management of Lower Pole Stone of 10 - 20 mm: Flexible Ureteroscopy (FURS) versus Extracorporeal Shock Wave Lithotripsy (ESWL) versus Percutaneus Nephrolit. Acta Med Indones. 2018;50:18-25.
11. Moher D, Liberati A, Tetzlaff J, Altman DG, Group P. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. J Clin Epidemiol. 2009;62:1006-12.
12. Phillips B, Ball C, Sackett D. Oxford Centre for Evidence-based Medicine—levels of evidence. Centre for Evidence-Based Medicine. Web site: http://www.cebm.net/index.aspx?o=1025. 2009.
13. Wells G, Shea B, O'connell D, et al. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomized studies in meta-analysis.Ottawa Health Research Institute web site. Available at: http://www.ohri.ca/programs/clinical_epidemiology/oxford.htm. 2011.
14. Clark HD, Wells GA, Huet C, et al. Assessing the quality of randomized trials: reliability of the Jadad scale. Control Clin Trials. 1999;20:448-52.
15. Bozkurt OF, Resorlu B, Yildiz Y, Can CE, Unsal A. Retrograde intrarenal surgery versus percutaneous nephrolithotomy in the management of lower-pole renal stones with a diameter of 15 to 20 mm. J Endourol. 2011;25:1131-5.
16. Aboutaleb H, El-Shazly M, Badr Eldin M. Lower pole midsize (1-2 cm) calyceal stones: outcome analysis of 56 cases. Urol Int. 2012;89:348-54.
17. El-Nahas AR, Ibrahim HM, Youssef RF, Sheir KZ. Flexible ureterorenoscopy versus extracorporeal shock wave lithotripsy for

treatment of lower pole stones of 10-20 mm. BJU Int. 2012;110:898-902.

18. Ozgor F, Sahan M, Yanaral F, Savun M, Sarilar O. Flexible ureterorenoscopy is associated with less stone recurrence rates over Shockwave lithotripsy in the management of 10-20 millimeter lower pole renal stone: medium follow-up results. Int Braz J Urol. 2018;44:314-22.
19. Ozturk U, Sener NC, Goktug HN, Nalbant I, Gucuk A, Imamoglu MA. Comparison of percutaneous nephrolithotomy, shock wave lithotripsy, and retrograde intrarenal surgery for lower pole renal calculi 10-20 mm. Urol Int. 2013;91:345-9.
20. Singh BP, Prakash J, Sankhwar SN, et al. Retrograde intrarenal surgery vs extracorporeal shock wave lithotripsy for intermediate size inferior pole calculi: a prospective assessment of objective and subjective outcomes. Urology. 2014;83:1016-22.
21. Kumar A, Kumar N, Vasudeva P, Kumar Jha S, Kumar R, Singh H. A prospective, randomized comparison of shock wave lithotripsy, retrograde intrarenal surgery and miniperc for treatment of 1 to 2 cm radiolucent lower calyceal renal calculi: a single center experience. J Urol. 2015;193:160-4.
22. Bozzini G, Verze P, Arcaniolo D, et al. A prospective randomized comparison among SWL, PCNL and RIRS for lower calyceal stones less than 2 cm: a multicenter experience : A better understanding on the treatment options for lower pole stones. World J Urol. 2017;35:1967-75.
23. Preminger GM, Assimos DG, Lingeman JE, et al. Chapter 1:AUA guideline on management of staghorn calculi: Diagnosis and treatment recommendations. J Urol. 2005;173:1991-2000.
24. Tiselius HG. Prospective, Randomized Trial Comparing Shock Wave Lithotripsy and Ureteroscopy for Lower Pole Caliceal calculi 1cm or Smaller. Eur Urol. 2006;49:586-7.
25. Sener NC, Bas O, Sener E, et al. Asymptomatic lower pole small renal stones: shock wave lithotripsy, flexible ureteroscopy, or observation? A prospective randomized trial. Urology. 2015;85:33-7.
26. Shah HN. Retrograde intrarenal surgery for lower pole renal calculi smaller than one centimeter. Indian J Urol. 2008;24:544-50.
27. May DJ, Chandhoke PS. Efficacy and cost-effectiveness of extracorporeal shock wave lithotripsy for solitary lower pole renal calculi. J Urol. 1998;159:24–7.
28. Galvin DJ, Pearle MS. The contemporary management of renal and ureteric calculi. BJU Int. 2006;98:1283-8.
29. Breda A, Ogunyemi O, Leppert JT, Schulam PG. Flexible ureteroscopy and laser lithotripsy for multiple unilateral intrarenal stones. Eur Urol. 2009;55:1190-6.
30. Cass AS. Comparison of first generation (Dornier HM3) and second generation (Medstone STS) lithotriptors: Treatment results with 13,864 renal and ureteral calculi. J Urol. 1995;153:588–92.
31. Kijvikai K, Haleblian GE, Preminger GM, de la Rosette J. Shock wave lithotripsy or ureteroscopy for the management of proximal ureteral calculi: an old discussion revisited. J Urol. 2007;178:1157-63.
32. Pearle MS, Lingeman JE, Leveillee R, et al. Prospective randomized trial comparing shock wave lithotripsy and ureteroscopy for lower pole caliceal calculi 1 cm or less. J Urol. 2005;173:2005-9.
33. Sumino Y, Mimata H, Tasaki Y, et al. Predictors of lower pole renal stone clearance after extracorporeal shock wave lithotripsy. J Urol 2003;168:1344-7.
34. Yuruk E, Binbay M, Sari E, et al. A prospective, randomized trial of management for asymptomatic lower pole calculi. J Urol. 2010;183:1424-8.
35. Atis G, Culpan M, Pelit ES, et al. Comparison of Percutaneous Nephrolithotomy and Retrograde Intrarenal Surgery in Treating 20-40 mm Renal Stones. Urol J. 2017;14:2995-9.
36. Sari S, Ozok HU, Cakici MC, et al. A Comparison of Retrograde Intrarenal Surgery and Percutaneous Nephrolithotomy for Management of Renal Stones ≥ 2 CM. Urol J. 2017;14:2949-54.
37. Resorlu B, Kara C, Senocak C, Cicekbilek I, Unsal A. Effect of previous open renal surgery and failed extracorporeal shockwave lithotripsy on the performance and outcomes of percutaneous nephrolithotomy. J Endourol. 2010;24:13–6.
38. Lingeman JE, Siegel YI, Steele B, Nyhuis AW, Woods JR. Management of Lower Pole Nephrolithiasis: A Critical Analysis. J Urol. 1994;151:663-7.
39. Basiri A, Nouralizadeh A, Kashi AH, et al. X-Ray Free Minimally Invasive Surgery for Urolithiasis in Pregnancy. Urol J. 2016;13:2496-501.
40. Preminger GM. Management of lower pole renal calculi: shock wave lithotripsy versus percutaneous nephrolithotomy versus flexible ureteroscopy. Urol Res. 2006;34:108-11.
41. Javanmard B, Kashi AH, Mazloomfard MM, Jafari AA, Arefanian S. Retrograde Intrarenal Surgery Versus Shock Wave Lithotripsy for Renal Stones Smaller Than 2 cm: A Randomized Clinical Trial. Urol J. 2016;13:2823-8.
42. Schuster TG, Hollenbeck BK, Faerber GJ, Wolf JS, Jr. Complications of ureteroscopy: analysis of predictive factors. J Urol.

2001;166:538-40.

43. Kuo RL, Lingeman JE, Leveillee R. Lower pole II: Initial results from a comparison of shock wave lithotripsy (SWL), ureteroscopy (URS), and percutaneous nephrostolithotomy (PNL) for lower pole nephrolithiasis. J Urol.2003;169(Suppl.): 486

44. Albala DM, Assimos DG, Clayman RV, et al. Lower pole I: a prospective randomized trial of extracorporeal shock wave lithotripsy and percutaneous nephrostolithotomy for lower pole nephrolithiasis-initial results. J Urol. 2001;166:2072-80.

45. Maghsoudi R, Etemadian M, Kashi AH, Ranjbaran A. The Association of Stone Opacity in Plain Radiography with Percutaneous Nephrolithotomy Outcomes and Complications. Urol J. 2016;13:2899-902.

46. Karaolides T, Bach C, Kachrilas S, Goyal A, Masood J, Buchholz N. Improving the durability of digital flexible ureteroscopes. Urology. 2013;81:717–22.

47. Gerber GS. Management of lower-pole caliceal stones. J Endourol. 2003;17:501-3.

48. Koo V, Young M, Thompson T, Duggan B. Cost-effectiveness and efficiency of shockwave lithotripsy vs flexible ureteroscopic holmium:yttrium-aluminium-garnet laser lithotripsy in the treatment of lower pole renal calculi. BJU Int. 2011;108:1913-6.

49. Wang Y, Jiang F, Wang Y, et al. Post-percutaneous nephrolithotomy septic shock and severe hemorrhage: a study of risk factors. Urol Int. 2012;88:307-10.

50. El-Assmy AM, El-Nahas AR, Mansour O, et al. A prospective multivariate analysis of factors predicting stone disintegration by extracorporeal shock wave lithotripsy: the value of high-resolution noncontrast computed tomography. Eur Urol. 2007;51:1688-94.

51. Sampaio FJ, Aragao AH. Limitations of extracorporeal shockwave lithotripsy for lower caliceal stones: anatomic insight. J Endourol. 1994;8:241-7.

52. Song JW, Chung KC. Observational studies: cohort and case-control studies. Plast Reconstr Surg. 2010;126:2234-42.