

Systematic Review and Meta-Analysis Comparing Percutaneous Nephrolithotomy, Retrograde Intrarenal Surgery and Shock Wave Lithotripsy for Lower Pole Renal Stones Less Than 2 cm in Maximum Diameter

Panagiotis Kallidonis,* Panteleimon Ntasiotis, Bhaskar Somani, Constantinos Adamou, Esteban Emiliani, Thomas Knoll, Andreas Skolarikos and Thomas Tailly

From the Department of Urology (PK, PN, CA, TK), University of Patras, Patras, Greece, European Section of Uro-Technology (PK, BS, AS), Young Academic Urologist (PK, BS, EE, TT), Department of Urology (BS), University Hospital Southampton NHS Foundation Trust, Southampton, United Kingdom, Department of Urology (EE), Fundacion Puigvert, University Autonoma of Barcelona, Barcelona, Spain, Department of Urology (TK), Sindelfingen-Böblingen Medical Centre, University of Tübingen, Sindelfingen, Germany, 2nd Department of Urology (AS), Sismanoglio Hospital, National and Kapodistrian University of Athens, Athens, Greece, and Department of Urology (TT), Ghent University Hospital, Ghent, Belgium

Purpose: The aim of the current systematic review and meta-analysis is to provide an answer on which is the most appropriate approach for the management of the lower pole stones with a maximal dimension of 2 cm or less.

Materials and Methods: A systematic review was conducted on PubMed®, SCOPUS®, Cochrane and EMBASE®. The PRISMA guidelines and the recommendations of the EAU Guidelines office were followed. Retrograde intrarenal surgery, shock wave lithotripsy and percutaneous nephrolithotomy were considered for comparison. The primary end point was the stone-free rate.

Results: A total of 15 randomized controlled trials were eligible. Percutaneous nephrolithotripsy and retrograde intrarenal surgery have higher stone-free rates in comparison to shock wave lithotripsy and require fewer re-treatment sessions. Operative time and complications seem to favor shock wave lithotripsy in comparison to percutaneous nephrolithotripsy, but this takes place at the expense of multiple shock wave lithotripsy sessions. Retrograde intrarenal surgery seems to be the most efficient approach for the management of stones up to 1 cm in the lower pole. **Conclusions:** The pooled analysis of the eligible studies showed that the management of stones up to 1 cm in the lower pole.

agement of lower pole stones should probably be percutaneous nephrolithotripsy or retrograde intrarenal surgery to achieve stone-free status over a short period and minimal number of sessions. For stones smaller than 10 mm, retrograde intrarenal surgery is more efficient in comparison to shock wave lithotripsy. The decision between the 2 approaches (percutaneous nephrolithotripsy or retrograde intrarenal surgery) should be individual, based on the anatomical parameters, the comorbidity and the preferences of each patient.

Key Words: calculi, lithotripsy, ureteroscopy

LOWER pole stones are defined as stones located in the inferior pole calyx of the kidney. Their management usually requires some kind of active treatment since these stones are less likely to pass spontaneously.¹ The optimal treatment of LPS represents a point of debate among urologists. A variety of factors such as the anatomy of the pelvicalyceal system, patient body habitus and patient preference may influence the selection

0022-5347/20/2043-0427/0 THE JOURNAL OF UROLOGY[®] © 2020 by American Urological Association Education and Research, Inc. https://doi.org/10.1097/JU.000000000001013 Vol. 204, 427-433, September 2020 Printed in U.S.A.

Abbreviations and Acronyms

LPS = lower pole stones PCNL = percutaneous nephrolithotripsy RIRS = retrograde intrarenal surgery SFR = stone-free rate SWL = shock wave lithotripsy

Accepted for publication December 11, 2019. No direct or indirect commercial, personal, academic, political, religious or ethical incentive is associated with publishing this article.

Supplementary tables 1-7 are available from the author.

* Correspondence: University Hospital of Patras, Patras, Rion Greece (email: <u>pkallidonis@</u><u>yahoo.com</u>).

of the treatment method.^{2–5} The EAU Guidelines propose retrograde intrarenal surgery, shock wave lithotripsy and percutaneous nephrolithotomy for the management of LPS between 1 and 2 cm. Nonetheless, SWL is not considered as the treatment of choice for LPS due to its low efficacy when unfavorable factors such as steep infundibular pelvic angle and long infundibular length are present.⁶ Both PCNL and RIRS have been reported to be effective in the management of the these LPS with advantages and disadvantages associated with both approaches.^{3–8}

The aim of the current systematic review and meta-analysis is to provide an answer on which is the most appropriate approach for the management of LPS with a maximal dimension of 2 cm or less.

MATERIALS AND METHODS

Search Strategy, Eligibility Criteria and End Points A systematic review was conducted on PubMed®,

SCOPUS®, Cochrane and EMBASE® in January 2018. The PRISMA guidelines and the recommendations of the EAU Guidelines office were followed.^{9,10} The study was registered in the PROSPERO database (CRD42018086552). The search strategy and eligibility criteria for the meta-analysis are shown in supplementary table 1. Randomized controlled trials comparing SWL, RIRS and PCNL were considered. We chose to include randomized controlled trials from 2001 to 2018. We excluded all the studies that took place before 2001 because we wanted to compare the different approaches according to the newest technologies. The primary end point was the stone-free rate. A subgroup analysis based on the size of the stones that were treated was considered.

Data Extraction

Two authors (CA, PN) independently screened the studies and extracted relevant data on study characteristics and outcomes using standardized pro forma data sheets. Discrepancies were solved by a senior author (PK). Missing data were requested by email from the corresponding authors.

Statistical Analysis

The extracted data were pooled to conduct the metaanalysis. Outcomes for dichotomous/categorical variables were expressed as OR with 95% CI. The combination of these results was performed with the Mantel-Haenszel method. For continuous variables, weighted mean difference with 95% CI were combined using the inverse variance method to calculate the pooled results.¹¹ The random effects model was applied for the meta-analysis and forest plots diagrams were prepared.¹² Review Manager Version 5.3.5 was used (Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014). Variations among the studies were evaluated with the use of the chi² statistical method. The proportion of inconsistency between studies that could not be attributed to chance was measured by the calculation of the I² index. Significant heterogeneity was defined to be 50% or greater.¹³ Statistical reporting followed the recently proposed guidelines.¹⁴

Risk of Bias Assessment

The risk of bias and quality of the included studies was assessed with the Cochrane Collaboration's tool for assessing risk of bias and the GRADE Guidelines, respectively.^{15,16}

RESULTS

Selection of Studies

A total of 6,689 publications were screened and 15 randomized controlled trials published between 2001 and August 2018 were eligible. Supplementary figure 1, A (<u>https://www.jurology.com</u>) shows the selection process of the studies.

Studies Characteristics

Study design and characteristics are described in supplementary tables 2 to 4.^{17–31} The studies included patients with LPS with a size up to 2 cm in maximal diameter which were managed by SWL, RIRS or PCNL. Two corresponding authors responded to our queries to provide additional information.^{18,24}

Primary End Point

The primary endpoint was stone-free rate, and 15 studies provided data on SFR up to 3 months.^{17–31} Pooled analysis of 4 studies showed that SFR was similar for PCNL in comparison to RIRS with OR 0.67 (95% CI 0.42–1.09) (I²=0%, p=0.11) (supplementary fig. 2, *A*; <u>https://www.jurology.com</u>).^{18,19,21,25} Pooling the data from 5 and 8 studies revealed that PCNL^{17,18,23,30,31} and RIRS^{18,20,22,24,26–29} were related to higher SFR in comparison to SWL with OR 6.7 (95% CI 4.35–10.31) (I²=56%, p <0.00001) and OR 2.85 (95% CI 2.06–3.95) (I²=46%, p <0.00001), respectively (supplementary fig. 2, *B* and *C*; <u>https://www.jurology.com</u>).

Secondary End Points

Operative time. Pooled data from 3 studies each showed that the operative time was shorter for SWL in comparison to PCNL^{18,23,30} and RIRS^{18,22,24} with a mean difference of -37.17 minutes (95% CI -39.03-35.31) (I²=99%, p <0.00001) and -7.61 minutes (95% CI -8.17-7.06) (I²=100%, p <0.00001), respectively (supplementary fig. 2, D and E; <u>https://www.jurology.com</u>). After pooling the data from 4 studies, ^{18,19,21,25} the operative time was shorter for RIRS when compared with PCNL with a mean difference of 7.46 min (95% CI 5.17-9.74) (I²=99%, p <0.00001, supplementary fig. 2, F; <u>https://www.jurology.com</u>).

Hospitalization time. Five studies provided data on hospitalization.^{18,19,23,25,30} The hospitalization time was shorter in the case of RIRS in comparison to PCNL with a mean difference of 0.78 days (95% CI 0.66–0.90) (I^2 =99%, p <0.00001) (supplementary

fig. 2, *G*; <u>https://www.jurology.com</u>).^{18,19,25} SWL required shorter hospitalization in comparison to PCNL with a mean difference of -1.88 days (95% CI -1.96--1.80) (I²=100%,p <0.00001) (supplementary fig. 2, *H*; <u>https://www.jurology.com</u>).^{18,30} Sufficient data on the comparison of hospitalization between RIRS and SWL were provided by only 1 study with a significantly higher hospital stay for RIRS (p=0.01).¹⁸

Complications. When the overall complication rates were considered, the pooling of data from 3 studies showed that PCNL had a similar rate in comparison to RIRS with OR 1.41 (95% CI 0.87-2.29) (p=0.16, $I^2 = 0\%$) (supplementary fig. 3, A; https://www. jurology.com).^{18,19,25} Data from 7 studies revealed no difference in the complication rate of RIRS and SWL (OR 0.77, 95% CI 0.52–1.13) (p=0.09, $I^2 = 40\%$) (supplementary fig. 3, *B*; <u>https://www.</u>jurology.com).^{8,22,24,27-29} On the contrary, data from 3 studies comparing PCNL to SWL showed the complication rate is lower for SWL with OR 0.40 (95% CI 0.24-0.65) (p=0.0002, I²=5%) (supplementary fig. 3, C; https://www.jurology. com).^{18,23,30} Supplementary table 3 shows the complications that were observed in each of the included studies. The overall complication rates for the PCNL, RIRS and SWL groups ranged between 8.3% and 25%, 1.3% to 31.4% and 0% to 48.5%, respectively.

Re-treatment events. Only 1 study provided adequate data on the comparison of PCNL to RIRS regarding re-treatment procedures to render the patient stone-free.¹⁸ The study showed similar rates of re-treatment among the 2 approaches. PCNL had a lower number of secondary procedures when compared to SWL after pooling data from 3 studies (OR 50.67, 95% CI 22.55–113.84) (I²=0%, p <0.0001) (supplementary fig. 3, *D*; <u>https://www.jurology.com</u>).^{18,23,30} Similarly, the pooled data from 4 studies showed that SWL had significantly higher odds of secondary procedures in comparison to RIRS (OR 18.74, 95% CI 11.89–29.55) (I²=66%, p <0.00001) (supplementary fig. 3, *E*; https://www.jurology.com).^{18,22,28,29}

AUXILIARY PROCEDURES

Subgroup Analysis

RIGHTSLINKA)

Stone size up to 10 mm. None of the eligible studies reported on the treatment by PCNL of LPS with size up to 10 mm. The pooling of SFRs up to 3 months from 4 studies showed a higher rate for RIRS in comparison to SWL with OR 1.74 (95% CI 0.94–3.21) ($I^2=4\%$, p=0.08) (supplementary fig. 3, *F*; <u>https://www.jurology.com</u>).^{22,24,27,28} Data from 2 studies revealed that the operative time was shorter for SWL in comparison to RIRS for -10.76 minutes (95% CI -11.34—-10.18) (I²=94%, p <0.00001) (supplementary fig. 3, G; <u>https://www.jurology.com</u>).^{22,24} Data were insufficient for pooling to evaluate the hospitalization time differences among the approaches.¹⁸ Data from 4 studies showed that the overall complication rates were similar among the approaches with OR 0.74 (95% CI 0.36–1.52) (I²=0%, p=0.42) (supplementary fig. 3, *H*; <u>https://www.jurology.com</u>).^{22,24,27,28} Re-treatment events were more for SWL in comparison to RIRS (OR 8.46, 95% CI 3.59–19.94) (I²=3%, p <0.00001) (2 studies) (supplementary fig. 3, *I*; <u>https://www.jurology.com</u>).^{22,28}

Stone size 10 to 20 mm. Pooled data from 4 studies showed higher SFR for PCNL in comparison to SWL with OR 5.85 (95% CI 3.73–9.18) ($I^2 = 59\%$, p <0.00001) (supplementary fig. 4, A; https://www. jurology.com).^{17,18,23,30} Similarly, 3 studies revealed higher SFRs for RIRS in comparison to SWL (OR 2.96, 95% CI 1.98–4.42) ($I^2 = 0\%$, p <0.00001) (supplementary fig. 4, B; https://www.jurology.com).^{18,22,29} Only 1 study provided data on the comparison of SFRs between PCNL and RIRS and did not show any statistical significance (p=0.92).¹⁸ Pooled data from $2^{18,30}$ and $3^{18,23,30}$ studies showed that operative time was shorter for SWL in comparison to PCNL with a mean difference of -37.17 min (95% CI -39.03 - 35.31) (I²=99%, p < 0.00001) (supplementary fig. 4, C; https://www.jurology.com) and RIRS with a mean difference of 6.83 min (95% CI (6.15-7.52) (I²=100%, p < 0.00001) (supplementary) fig. 4, D; https://www.jurology.com), respectively. Pooled data analysis was not possible for the operative time of PCNL in comparison to RIRS since only 1 study provided information and did not report any significant difference (p=0.082).¹⁸ Data from 2 studies showed that the hospitalization was shorter for SWL in comparison to PCNL with a mean difference of -1.88 days (95% CI -1.96—-1.80) (I²=100%, p <0.00001) (supplementary fig. 4, E; <u>https://www.</u>jurology.com).^{18,30} Only 1 study provided data on the comparisons of hospitalization time of PCNL with RIRS and RIRS with SWL revealing a significant shorter hospital stay for PCNL (p=0.039)and SWL (p=0.001), respectively.¹⁸ The same study was the only one providing information on the overall complication rates of PCNL in comparison to RIRS. The complication rates for Clavien grades I-II and II-IV were similar among the 2 approaches (p=0.52, p=0.089).¹⁸ Pooled data from 3 studies revealed a similar complication rate for SWL and RIRS (OR 0.71, 95% CI 0.44-1.17) $(I^2 = 71\%, p = 0.18)$ (supplementary fig. 4, F; https://www.jurology.com),^{18,22,29} while data from 3 studies showed a higher complication rate for PCNL in comparison to SWL (OR 0.40, 95% CI 0.24-0.65) (I²=5%, p=0.0002) (supplementary

fig. 4, G; <u>https://www.jurology.com</u>).^{18,23,30} One study included data on the comparison of PCNL to RIRS on the need for additional procedures for stone clearance.¹⁸ After pooling the data from 3 studies, PCNL was related to less need for retreatment in comparison to SWL with OR 50.67 (95% CI 22.55–113.84) (I²=0%, p <0.00001) (supplementary fig. 4, *H*; <u>https://www.jurology.</u> <u>com</u>).^{18,23,30} Data from 3 studies showed that RIRS was associated with a lower need for re-treatment in comparison to SWL with OR 31.67 (95% CI 17.73–56.56) (I²=0%, p <0.00001) (supplementary fig. 4, *I*; https://www.jurology.com).^{18,22,29}

Risk of Bias Assessment

Selection bias. Ten studies reported the method used for random sequence generation.^{18-22,24,27,28,30} In 5 studies this was not specified.^{17,23,25,26,31} Nine studies used methods which related to low bias in the case of allocation concealment.^{18-22,24,27,28} One study was related to high risk of selection bias.²³

Performance bias. Blinding was not possible either for patients or surgeons in studies including a PCNL group. Only 1 study clearly reported the lack of blinding.¹⁸

Detection bias. Six studies stated that the followup results were reviewed by physicians blinded for the treatment.^{18–21,24,31} The remaining studies did not clarify the presence of blinding.

Attrition bias. Details on the drop-out rate or patients lost to followup were reported in 9 studies. $^{17-22,24,26,29}$

Reporting bias. Detailed outcome data by primary and secondary end points set up for this review were obtained by 13 studies.^{17-22,24,26-31} In the remaining studies relevant data were missing despite adequate followup time.

Other bias. Three studies were affected by observation bias as the evaluation method for stone-free rates was not reported.^{23,25,30} Four studies evaluated stone-free status with only plain x-ray of the kidney, ureter and bladder.^{22,26–28} Albala et al followed the patients with nephrotomogram.¹⁷ The combination of plain x-ray of the kidney, ureter and bladder and ultrasonography was performed in 2 studies.^{20,29} The remaining studies (sample size 5) used computerized tomography for the evaluation of the SFR.^{18,19,21,24,31} It should be noted that intraoperative evaluation of stone clearance is stated by Albala et al who used nephrotomogram for the evaluation of the postoperative outcome¹⁷ and Soliman et al who did not mention the imaging approach for postoperative evaluation.³⁰ The risk of bias assessment is summarized in supplementary figure 1, B and C (<u>https://www.</u>jurology.com).

Study Quality according to GRADE

The quality assessment according to GRADE is presented in detail in supplementary table 5. For the primary end point of SFR up to 3 months, the studies comparing PCNL to RIRS (5), PCNL to SWL (6) and SWL to RIRS (8) had a moderate, high and moderate quality, respectively.

DISCUSSION

A previous well conducted meta-analysis on the same topic provided pooled analysis of SFRs of SWL, RIRS and PCNL.¹ Recent high quality studies enriched the available evidence^{18–23,28,30} and set the background for a contemporary meta-analysis which currently elucidates different aspects of the efficacy of the above techniques in treating LPS.

The current study showed that PCNL and RIRS had higher SFRs in comparison to SWL. PCNL and RIRS did not have a significant difference in terms of SFRs at the same time period (p=0.11), despite higher SFRs for PCNL in 3 out of 4 studies (supplementary fig. 2, A; https://www.jurology.com). The SFR results should be interpreted with care. Twelve of the studies provided a clear definition of SFR.^{17–22,24,26–28,30,32} Specifically, the followup period was 3 months in 8 studies (supplementary table 3). This followup period could include the performance of additional sessions of each procedure to achieve stone-free status. These events were depicted in the re-treatment rates. It was the intention of the authors to present the SFRs of the procedures after the first procedure. Unfortunately, the comparative data of the SFRs after the first session were not adequate for statistical pooling and comparison of the results among the different approaches.^{25,27,30} Moreover, patients with favorable anatomical criteria in the case of the retrograde approach and SWL were selected and included in some of the studies.^{17,18,27} Cases with steep infundibular-pelvic angle (less than 30 degrees), longer calyx (more than 10 mm) and narrow infundibulum (less than 5 mm) as demonstrated by contrast enhanced computerized tomography were also excluded from the study of Bozzini et al based on the available evidence of the impact of anatomy to the outcome of SWL.^{6,18,33} This large study provided comparative data on all 3 approaches but the results were based on selected cases that could allow SWL and RIRS to provide optimal outcomes.¹⁸ The unfavorable lower calyceal anatomy was an exclusion criterion in the study by Albala et al.¹⁷ Sener et al excluded patients with steep infundibular-pelvic angle in their 2 studies.^{27,28} Similarly, Naguib et al included only

favorable calyceal anatomy cases for SWL.²³ The selection of cases with favorable anatomy may have influenced the outcomes presented for SWL and RIRS. When SWL is compared to RIRS, the use of the above exclusion criteria for both treatment modalities probably did not influence the presented comparative results.^{17,27,28} Nonetheless, Naguib et al used this criterion only for the SWL group and probably introduced a bias to the study.²³ As a result, the study was rendered as high risk for selection bias (supplementary table 5). Considering the above details in the design of the included studies, it could be advocated that a possible advantage of PCNL for managing LPS 2 cm or less without being influenced by the calyceal anatomy was probably blunted due to the selection bias, and the real-world efficacy of PCNL to treat the LPS was not appropriately appraised by the current literature and meta-analysis.

Re-treatment rates as described in the current analysis represent any procedure that was performed to render the patient stone-free after the first session. This procedure could include any endoscopic procedure or SWL. The selected approach for complete stone removal is depicted by the auxiliary procedure in supplementary table 3). SWL seemed to be more commonly used for the treatment of residual lithiasis after the performance of PCNL or RIRS. After SWL, additional SWL sessions were commonly scheduled with PCNL and RIRS also being common secondary approaches. The only study providing re-treatment rates to achieve stone-free status for the patients showed rates similar for PCNL and RIRS with the results tending to favor PCNL. Re-treatment rates were significantly higher for SWL in comparison to PCNL and RIRS. These results practically reflect the complicated anatomical relations of the lower calyceal group and the need for multiple SWL sessions to achieve stone-free status.^{33–35}

The pooled analysis showed that the operative time was longer in the case of PCNL in comparison to RIRS (supplementary fig. 2, F; https://www. jurology.com). SWL needed less operative time in comparison to PCNL and RIRS but the mean difference of 7 min between SWL and RIRS probably does not reflect any clinical significance (supplementary fig. 2, *D* and *E*; https://www.jurology.com). The included studies originated from centers with experience in endoscopy and SWL, so surgeon experience may not influence the operative time. Nonetheless, there are differences regarding the size of the nephroscopes and access sheaths which may have influenced the operative time of PCNL (supplementary table 6). The instruments for PCNL have undergone miniaturization while the flexible ureteroscopes have greatly improved in terms of visual clarity and flexibility over the years.^{36,37}

Moreover, the efficacy of laser lithotripters have improved.³⁸ Unfortunately, the impact to the operative time of the technical discrepancies is not possible to assess in a meta-analysis.

The results of the pooled analysis revealed that the hospitalization times were longer for PCNL in comparison to SWL and RIRS. The reduced hospitalization times for SWL were expected but it should be counterbalanced for 2 or 3 issues such as the retreatment rate, urgent readmissions and cost effectiveness. The discrepancies in hospitalization time may also be related to the health system of the country where the study is conducted. For example, patients could be admitted the day before surgery for endoscopy procedures while patients could be treated as day surgery cases in the case of RIRS. This information was lacking in the included studies and specific comments could not be amended.

The complication rates in the pooled analysis favored SWL in comparison to PCNL and RIRS while PCNL had a higher complication rate in comparison to RIRS. Bleeding complications requiring transfusion tended to be more common in the case of PCNL while septic complications were present in all 3 approaches (supplementary table 2). Nonetheless, the pooled results on the complications should be carefully interpreted. The definition of bleeding complication varied among the studies. For the comparison of PCNL to RIRS, 3 studies provided data for pooling. One study reported only bleeding that required blood transfusion.²¹ The other study reported that the blood loss was similar between PCNL and RIRS, despite the higher transfusion rate of PCNL.¹⁹ This separation between the hemoglobin drop and clinically significant bleeding seemed to be more accurate to represent the reality of the clinical practice. Every postoperative macroscopic hematuria does not represent a clinically significant incident. On the contrary, the study by Bozzini et al provided the largest number of patients and reported events of gross hematuria which were managed by blood transfusions or Double-J® stent.¹⁸ The number of patients who were treated by one or the other approach was not clarified. Moreover, the need for selective embolization of any bleeding was not well described in any of the included studies (supplementary table 3).

When the treated stones were up to 10 mm in maximal diameter, PCNL was never considered as an option in the eligible studies. RIRS was more efficient than SWL in rendering the patients stone-free while the complication rates were similar (supplementary fig. 3, G; <u>https://www.jurology.com</u>). This observation underlines the higher difficulty of SWL to treat the LPS in comparison to stones located in other sites of the pelvicalyceal system.

Nonetheless, a cutoff size for the selection of RIRS over SWL in these smaller stones could not be proposed with the currently available data. The selection of the approach should probably be based on patient preference and the individual characteristics of each case.

The subgroup analysis of stones ranging from 1 to 2 cm provided results with similarities with the analysis of stones up to 2 cm. The higher efficiency of PCNL or RIRS in comparison to SWL, the shorter operative time for SWL when compared to PCNL and RIRS, and any discrepancies among the approaches in hospitalization time and complications should be critically appraised under the previously mentioned scope. It is important to note that none of the studies calculated stone volume (or even stone surface). In the clinical practice, stone volumes are treated and the depiction of the stone size by the maximal diameter does not provide an accurate depiction of the stones. Thus, differences in the volume and the hardness of the stone may significantly vary and influence the outcome of the studied approaches. These issues require careful consideration for the interpretation of the current analysis as well as the subgroup analysis.

High data heterogeneity as expressed by I^2 was observed in several comparisons of the current analysis. High heterogeneity is usually related to an unreliable result. The I^2 is known to be poor in detecting the true heterogeneity.^{13,39} The calculated high level of heterogeneity can be misleading as the magnitude and directions of the effects may influence the value of I^2 . The p value, magnitude of effects, chi² and CI are useful to determine if the presented heterogeneity has significance and could render the results of a pooled analysis as unreliable.^{13,39} Supplementary table 7 explains heterogeneity results and shows that all currently presented data are statistically reliable.

The results of the current meta-analysis show that the management of LPS should probably be PCNL or RIRS when the SFR over a short period with minimal number of sessions is the priority. Patients who are willing to undergo several sessions and accept the possibility of eventually undergoing an endoscopic procedure to become stone-free could be opted for SWL. Operative time and complications seem to favor SWL especially in comparison to PCNL but this takes place at the expense of multiple SWL sessions. RIRS is the most efficient approach for the management of stones up to 1 cm in the lower pole. PCNL and RIRS are both efficient and safe approaches for treating lower stones of 1 to 2 cm, and the selection of the approach should be based on the anatomy of the patient, the bulk of the stone and experience of the surgeon.

The limitations of the current investigation included the wide time period in which the included studies were conducted (more than 15 years). Thus instruments, materials and experience with the approaches may have changed over the years. Variation in the size of instruments, such as between conventional and mini-PCNL, do not represent a limitation since the percutaneous approach remains identical. In a similar fashion, changes in the RIRS equipment took place over the above long period. Consequently, the current quantitative analysis is solid in concept and its results are reliable.

CONCLUSION

The pooled analysis of the eligible studies showed that the management of LPS should probably be PCNL or RIRS to achieve stone-free status over a short period and minimal number of sessions. SWL has a lower complication rate in comparison to PCNL. For stones smaller than 10 mm, RIRS is more efficient in comparison to SWL.

REFERENCES

- Donaldson JF, Lardas M, Scrimgeour D et al: Systematic review and meta-analysis of the clinical effectiveness of shock wave lithotripsy, retrograde intrarenal surgery, and percutaneous nephrolithotomy for lower-pole renal stones. Eur Urol 2015; 67: 612.
- Jessen JP, Honeck P, Knoll T et al: Flexible ureterorenoscopy for lower pole stones: influence of the collecting system's anatomy. J Endourol 2014; 28: 146.
- Knoll T, Jessen JP, Honeck P et al: Flexible ureterorenoscopy versus miniaturized PNL for solitary renal calculi of 10-30 mm size. World J Urol 2011; 29: 755.
- 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.
- 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.
- Türk C, Petřík A, Sarica K et al: EAU Guidelines on interventional treatment for urolithiasis. Eur Urol 2016; 69: 475.

- Ganpule AP, Bhattu AS and Desai M: PCNL in the twenty-first century: role of Microperc, Miniperc, and Ultraminiperc. World J Urol 2015; 33: 235.
- Srisubat A, Potisat S, Lojanapiwat B et al: Extracorporeal shock wave lithotripsy (ESWL) versus percutaneous nephrolithotomy (PCNL) or retrograde intrarenal surgery (RIRS) for kidney stones. Cochrane Database Syst Rev 2014; CD007044.
- Moher D, Liberati A, Tetzlaff J et al: Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. PLoS Med 2009; 6: e1000097.
- 10. Knoll T, Omar MI, Maclennan S et al: Key steps in conducting systematic reviews for underpinning

RIGHTSLINK()

clinical practice guidelines: methodology of the European Association of Urology. Eur Urol 2018; 73: 290.

- Hedges LV and Olkin I: Statistical Methods for Meta-Analysis. Orlando, Florida: Academic Press, Inc. 1985.
- 12. DerSimonian R and Laird N: Meta-analysis in clinical trials. Control Clin Trials 1986; **7:** 177.
- Higgins JP, Thompson SG, Deeks JJ et al: Measuring inconsistency in meta-analyses. BMJ 2003; **327**: 557.
- Assel M, Sjoberg D, Elders A et al: Guidelines for reporting of statistics for clinical research in urology. Eur Urol 2019; **75:** 358.
- Higgins JPT, Altman DG, Gøtzsche PC et al: The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. BMJ 2011; 343: d5928.
- Balshem H, Helfand M, Schünemann HJ et al: GRADE guidelines: 3. Rating the quality of evidence. J Clin Epidemiol 2011; 64: 401.
- 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.
- 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.
- Fayad AS, Elsheikh MG and Ghoneima W: Tubeless mini-percutaneous nephrolithotomy versus retrograde intrarenal surgery for lower calyceal stones of ≤2 cm: a prospective randomised controlled study. Arab J Urol 2017; **15:** 36.
- Javanmard B, Kashi AH, Mazloomfard MM et al: Retrograde intrarenal surgery versus shock wave lithotripsy for renal stones smaller than 2 cm: a randomized clinical trial. Urol J 2016; 13: 2823.

- Kandemir A, Guven S, Balasar M et al: A prospective randomized comparison of micropercutaneous nephrolithotomy (Microperc) and retrograde intrarenal surgery (RIRS) for the management of lower pole kidney stones. World J Urol 2017; 35: 1771.
- 22. Kumar A, Vasudeva P, Nanda B et al: Prospective randomized comparison between shock wave lithotripsy and flexible ureterorenoscopy for lower caliceal stones ≤2 cm: a single-center experience. J Endourol 2015; 29: 575.
- Naguib M, Eliwa A, Seleem M et al: Outcome of mini-PCNL versus extracorporeal shock wave lithotripsy in treatment of single lower calyceal stone 10-20mm with favorable lower calyceal anatomy: a prospective randomized study (abstract PD23-06). J Urol, suppl., 2016; **195**: e507.
- 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.
- Sabnis R, Bhattu A, Goti A et al: Management of lower calyceal (LC) stones <1.5 cm: randomised controlled trial microperc vs. RIRS. J Endourol, suppl., 2014; 28: A143, abstract MP15-23.
- Salem A, Saad I, Emran A et al: Laser lithotripsy versus ESWL for lower calyceal renal stones (abstract 1829). J Urol, suppl., 2013; 189: e751.
- Sener NC, Imamoglu MA, Bas O et al: Prospective randomized trial comparing shock wave lithotripsy and flexible ureterorenoscopy for lower pole stones smaller than 1 cm. Urolithiasis 2014; 42: 127.
- 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.
- 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.
- 30. Soliman T, Sherif H, Sebaey A et al: Miniperc vs shockwave lithotripsy for average-sized, radiopaque

lower pole calculi: a prospective randomized study. J Endourol 2016; doi: 10.1089/end.2016.0259.

- Yuruk E, Binbay M, Sari E et al: Prospective randomized trial comparing percutaneous nephrolithotomy, shock wave lithotripsy and observation for asymptomatic lower pole calculi: initial results (abstract 1383). J Urol, suppl., 2009; 181: 494.
- 32. Singh DV, Mete UK, Mandal AK et al: A comparative randomized prospective study to evaluate efficacy and safety of combination of tamsulosin and tadalafil vs. tamsulosin or tadalafil alone in patients with lower urinary tract symptoms due to benign prostatic hyperplasia. J Sex Med 2014; **11**: 187.
- Danuser H, Müller R, Descoeudres B et al: Extracorporeal shock wave lithotripsy of lower calyx calculi: how much is treatment outcome influenced by the anatomy of the collecting system? Eur Urol 2007; 52: 539.
- Elbahnasy AM, Shalhav AL, Hoenig DM et al: Lower caliceal stone clearance after shock wave lithotripsy or ureteroscopy: the impact of lower pole radiographic anatomy. J Urol 1998; 159: 676.
- Ruggera L, Beltrami P, Ballario R et al: Impact of anatomical pielocaliceal topography in the treatment of renal lower calyces stones with extracorporeal shock wave lithotripsy. Int J Urol 2005; 12: 525.
- Kamal W, Kallidonis P, Kyriazis I et al: Minituriazed percutaneous nephrolithotomy: what does it mean? Urolithiasis 2016; 44: 195.
- Sanguedolce F, Bozzini G, Chew B et al: The evolving role of retrograde intrarenal surgery in the treatment of urolithiasis. Eur Urol Focus 2017; 3: 46.
- Kronenberg P and Traxer O: Update on lasers in urology 2014: current assessment on holmium:yttrium-aluminum-garnet (Ho:YAG) laser lithotripter settings and laser fibers. World J Urol 2015; 33: 463.
- 39. Fletcher J: What is heterogeneity and is it important? BMJ 2007; **334:** 94.