Meta-analysis of Optimal Management of Lower Pole Stone of 10 - 20 mm: Flexible Ureteroscopy (FURS) versus Extracorporeal Shock Wave Lithotripsy (ESWL) versus Percutaneus Nephrolithotomy (PCNL)

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ABSTRAK

Latar belakang: *pengelolaan optimal batu kaliks inferior masih kontroversial, karena tidak ada suatu metode tunggal yang sesuai untuk menghilangkan semua batu kaliks inferior. Prosedur invasif (fURS) minimal seperti extracorporeal shock wave lithotripsy (ESWL), percutaneous nephrolithotomy (PCNL) dan flexible ureteroscopy adalah pilihan terapi untuk batu kaliks inferior. Tujuan penelitian ini adalah untuk mengetahui manajemen optimal batu kaliks inferior ukuran 10 - 20 mm.* ***Metode:*** *studi meta-analisis dari penelitian kohort sebelum Juli 2016 dengan menggunakan database Medline dan Cochrane dilakukan. Batu kaliks inferior ukuran 10-20 mm ditatalaksana dengan fURS, ESWL dan PCNL dengan follow up 1-3 bulan setelah tindakan merupakan kriteria inklusi, sedangkan batu saluran kemih di lokasi lain dan dengan ukuran yang berbeda di eksklusi. Data dianalisis dengan* fixed-effects model *menggunakan metode Mantzel-Haenzel untuk menghitung pooled Risk Ratio (RR) dan 95% Confidence Interval (CI). Heterogenitas dinilai dengan menghitung statistik I^2. Semua analisis dilakukan dengan* Review manager *5.3.* ***Hasil:*** *kami menganalisis 8 penelitian kohort. Angka bebas batu dari 958 pasien (271 PCNL, 174 fURS dan 513 ESWL), 3 bulan pasca operasi, adalah 90,8% (246/271) setelah PCNL, 75,3% (131/174) setelah fURS dan 64,7 % (332/513) setelah ESWL. Berdasarkan angka bebas batu, PCNL lebih baik dari fURS (overall RR 4,12 (95% CI 2,09 – 8,09); p<0,001 dan I2=0%) dan ESWL (overall RR 0,23 (95% CI 0,16 – 0,35); p = <0,001 dan I^2 = 32,8%). Namun, bila dibandingkan antara fURS dan ESWL, fURS lebih baik dari pada ESWL dengan overall RR 0,66 (95% CI0,47 - 0,92; p = 0.015 dan I^2 = 45,5%).* ***Kesimpulan:*** *PCNL memberikan angka bebas batu yang lebih tinggi dibandingkan dengan fURS dan ESWL. Studi meta-analisis ini diharapkan dapat membantu ahli urologi sebelum melakukan tindakan intervensi pada batu kaliks inferior ukuran 10-20 mm.*

Kata kunci: *batu kaliks inferior, flexible ureteroscopy, extracorporeal shock wave lithotripsy, percutaneus nephrolithotomy.*

ABSTRACT

Background: *the optimal management of lower calyceal stones is still controversial, because no single method is suitable for the removal of all lower calyceal stones. Minimally invasive procedures such as extracorporeal shock wave lithotripsy (ESWL), percutaneous nephrolithotomy (PCNL) and flexible ureteroscopy (fURS) are the therapeutic methods for lower calyceal stones. The aim of this study was to identify the optimal management of 10-20 mm lower pole stones.* ***Methods:*** *a meta-analysis of cohort studies published before July 2016 was performed from Medline and Cochrane databases. Management of 10-20 mm lower pole stone treated by fURS, ESWL and PCNL with follow-up of residual stones in 1-3 months after procedure were include and urinary stone in other location and size were excluded. A fixed-effects model with Mantzel-Haenzel method was used to calculate the pooled Risk Ratio (RRs) and 95% Confidence Interval (CIs). We assessed the heterogeneity by calculating the I^2 statistic. All analyses were performed with Review manager 5.3.* ***Results:*** *we analized 8 cohort studies. The stone free rate from 958 patients (271 PCNL, 174 fURS and 513 ESWL), 3 months after operation, was 90.8% (246/271) after PCNL; 75.3% (131/174) after fURS; and 64.7% (332/513) after ESWL. Base on stone free rate in 10-20 mm lower pole stone following management, PCNL is better than fURS (overall RR was 1.32 (95% CI 1.13 – 1.55); p<0.001 and I^2=57%) and ESWL (overall risk ratio 1.42 (95% CI 1.30 – 1.55); p=<0.001 and I2 = 85%). But, if we compare between fURS and ESWL, fURS is better than ESWL base on stone free rate in 10-20 mm lower pole stone management with overall RR 1.16 (95% CI 1.04 – 1.30; p=0.01 and I^2=40%).* ***Conclusion:*** *percutaneus nephrolithotomy provided a higher stone free rate than fURS and ESWL. This meta-analysis may help urologist in making decision of intervention in 10-20 mm lower pole stone management.*

Keywords: *lower pole stone, flexible ureteroscopy, extracorporeal shock wave lithotripsy, percutaneus nephrolithotomy.*

INTRODUCTION

The optimal management of lower calyceal stones is still in debate controversial and a dilemmatic for urologist.[1–5] No single method is suitable for the removal of all lower calyceal stones. The goal of lower calyceal stone management is to achieve maximal stone clearance with minimal morbidity. Newly developed minimally invasive procedures have displaced open stone surgery.[1,6] Extracorporeal shock wave lithotripsy (ESWL), percutaneous nephrolithotomy (PCNL), and flexible ureteroscopy are the currently used therapeutic methods.[5,7]

To date, guidelines have confirmed ESWL as the method of first choice for small and mid-sized urinary calculi. However, currently urologists and patients are more critical about ESWL when considering the best treatment for a stone. The limited results of ESWL, even after repeated treatment sessions for stones, in the lower pole, or for difficult stone compositions (e.g. calcium oxalate monohydrate, brushite or cystine), might explain stone development.[8,9]

Advances in distal-tip deflection and scope durability have expanded the role of fURS from a diagnostic to a therapeutic procedure. This improvement in technology has built on existing experience to expand the potential indications of flexible ureteroscopy including intrarenal stones, ESWL failure, infundibular stenosis, morbid obesity, musculoskeletal deformities, and bleeding diathesis. Endourological techniques and skills, especially for fURS have been improved significantly, making fURS both very efficient and safe.[8]

Fernstrom and Johansen in 1976 first described the technique of removing a kidney stone percutaneously. Since then advances in technology, technical skill, and understanding of physiological principles have allowed percutaneous stone retrieval with increasing efficiency.[10] It has a confirmed efficacy for managing lower-pole renal calculi, with a constantly high stone free rate (SFR) independent of stone size. The Lower Pole I Study showed SFRs of 100%, 93% and 86% for stones of <10 mm, 10–20 mm and larger stones, respectively. Other studies have confirmed these excellent results.[8]

Patients prefer a noninvasive procedure and accept that long-term follow-up will be managed

by shockwave lithotripsy (ESWL) if other factors allow. The impact of stone size on the results of ESWL is more pronounced in lower pole (LP) stones than others. The recent advances in renal endoscopies and the development of percutaneous nephrolithotomy (PCNL) have provided the urologist with a safe and effective method for the treatment of 10 - 20 mm stones in the lower calyx.[1] Therefore, we did a systematic review to compare the outcome of ESWL, fURS and PCNL as different modalities of management of midsize (10–20 mm) lower calyceal stones.

METHODS

We searched the Medline and Cochrane databases for publications before July 2016. (lower pole) AND urinary calculi) AND flexible ureteroscopy) AND extracorporeal shock wave lithotripsy) AND percutaneus nephrolithotomy) OR lower pole) OR urinary calculi) OR flexible ureteroscopy) OR extracorporeal shock wave lithotripsy) OR percutaneus nephrolithotomy were used as search strategy. Finally, we checked references from relevant publications and review articles.

Eligibility Criteria

Prospective study were included if treatment was done in adult patient (>18 years old), patient with lower pole stone (10-20 mm) who is treated by flexible ureteroscopy (FURS) and/or extracorporeal shock wave lithotripsy (ESWL) and/or percutaneus nephrolithotomy (PCNL) with follow-up of the stone free rate for 1-3 months after procedure. Patients with urinary stone in other locations, non-English articles, case reports or case series were excluded.

Methodological Quality

Quality of study was assessed by reviewing paper titles and abstracts. In the first screening, authors assessed all of the abstracts retrieved from the search and then obtained the full-text version of the articles that met the inclusion criteria. These authors evaluated the studies' eligibility and quality, and they subsequently extracted the data. The process of identifying eligible studies is summarized in **Figure 1**.

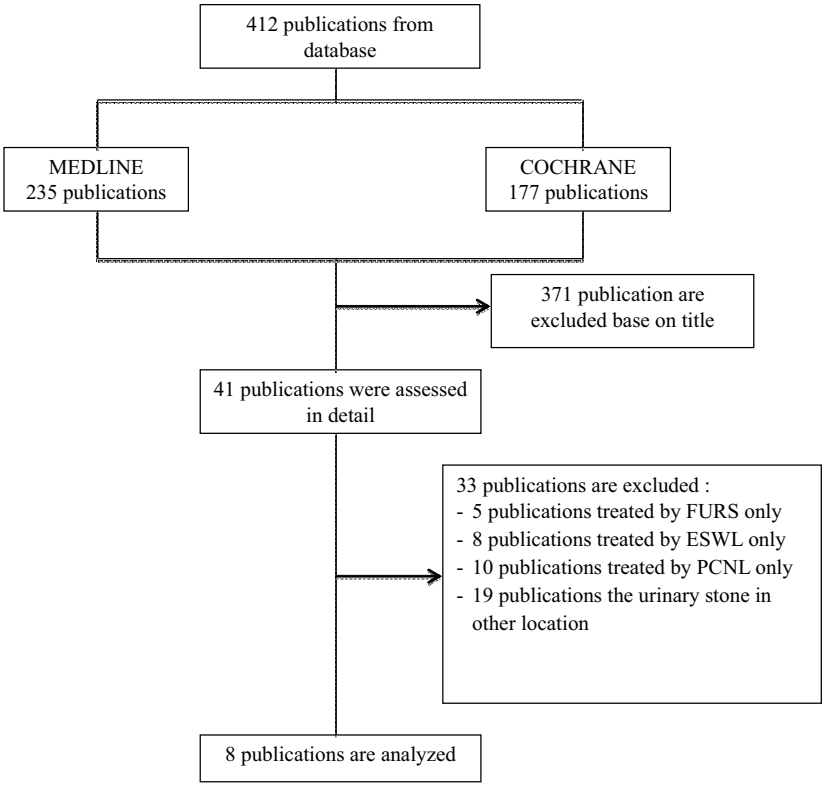

Figure 1. Literature search

Statistical Analysis

A fixed-effects model with Mantzel-Haenzel method was used to calculate the pooled Risk Ratio (RRs) and 95% Confidence Interval (CIs) by comparing fURS, ESWL and PCNL in management of 10-20 mm lower pole stone. We assessed the heterogeneity by calculating the I^2 statistic. The heterogeneity was classified as low (I^2 25%-50%), moderate (I^2 50%-75%) and high (I^2>75%). All analyses were performed with Review manager 5.3.

RESULTS

As presented in **Figure 1**, 412 publications were identified from the database, out of which 371 publications were excluded based on the screening of the title and abstract. Forty one potentially eligible publications were assessed in detail, and 8 publications met the eligibility criteria and analyzed (2 studies compare of all managements, 3 studies compare ESWL and fURS, 3 studies compare ESWL and PCNL and a study compare fURS and PCNL. (**Table 1**) summarize the characteristics of the eligible studies.

Flexible Ureteroscopy versus Extracorporeal Shock Wave Lithotripsy

We obtained data from 705 patients from 5 literatures, comprises of 174 patients in fURS and 531 patients in ESWL group. We found 43 patient with residual stone from 174 patients treated with fURS (follow-up 3 month, 75.3%) and 187 patients from 531 patients treated with ESWL (follow-up 3 month, stone free rate 64.8%).

Figure 2 shows that FURS is better than ESWL based on the stone free rate in following ≤20 mm lower pole stone management with overall RR 1.16 (95% CI 1.04 – 1.30); p = 0.01 and I^2 = 40%.

Flexible Ureteroscopy versus Percutaneous Nephrolithotomy

We obtained data from 463 patients from 5 literatures, comprises of 174 patients in fURS and 289 patients in PCNL group. We found 43 patient with residual stone from 174 patients treated with fURS (follow-up 3 month, 75.3%) and 25 patients from 289 patients treated with PCNL (follow-up 3 month, stone free rate 91.3%). (**Table 1**)

Table 1. Summary of findings table: stone free rate in management of lower pole stone

Outcome	Comparative Risks (95% CI)		Risk Ratio (95% CI)	Comparative Risks (95% CI)		Risk Ratio (95% CI)	Comparative Risks (95% CI)		Risk Ratio (95% CI)	Quality of Evidence (GRADE)
	ESWL	FURS		ESWL	PCNL		FURS	PCNL		
Stone Free rate	286/406, stone free rate 70.4%.	122/155, stone free rate 78.7%	1.16 (1.04–1.30)	229/352, stone free rate 65.1%.	228/251, stone free rate 90.8%	1.42 (1.30-1.55)	48/70, stone free rate 68.5%	171/183, stone free rate 93.4%	1.32 (1.13-1.55)	moderate
			(5 studies with 561 participants)			(4 studies with 603 participants)			(3 studies with 253 participants)	

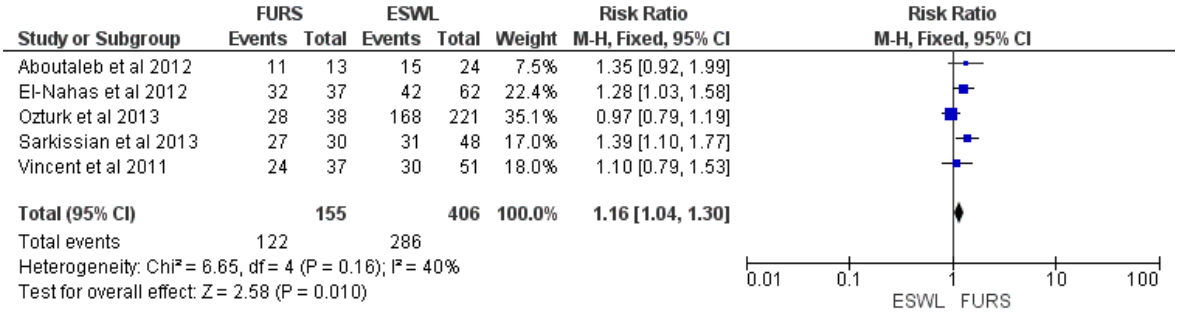

Figure 2. Forest plot comparison between FURS and ESWL stone free rate in lower pole stone ≤20 mm management.

Figure 3 shows PCNL is better than fURS based on the stone free rate in ≤ 20 mm lower pole stone management with overall RR 1.32 (95% CI 1.13 – 1.55); p<0.001 and I^2=57%.

Percutaneous Nephrolithotomy versus Extracorporeal Shock Wave Lithotripsy

We obtained data from 820 patients from 4 literatures, comprised of 289 patients in PCNL and 531 patients in ESWL group. We found 25 patient with residual stone from 289 patients treated with PCNL (follow-up 3 month, 91.3%) and 187 patients from 531 patients treated with ESWL (follow-up 3 month, stone free rate 64.8%).

Figure 4 shows PCNL is better than ESWL based on the stone free rate in ≤ 20 mm lower pole stone following management with overall RR 1.42 (95% CI 1.30 – 1.55); p = <0.001 and I^2 = 85%.

DISCUSSION

Lower pole (LP) renal stones provide a unique challenge when considering their management.[11] The issues are mostly around the presence of one or more lower pole anatomical variations, an increased infundibular (IF) length and a decreased IF width and angle.[12] LP stones that are symptomatic, locally obstructing, infection related, or increasing in size require intervention.[13,14] Methods for treatment of LPSs 10 – 20 mm in length represent a major controversy in the urological literature.[1,15,16] Smaller, asymptomatic stones can be managed expectantly, though with periodic follow-up a significant number will exhibit increasing size or become symptomatic.[17,18]

For most stones smaller than 10 mm, SWL is the treatment of choice, while for stones greater than 20 mm, percutaneous management is generally indicated.[19,20] Stones in the range of 10 - 20 mm represent an area of ongoing controversy regarding respective roles of SWL, PCNL and ureteroscopy.[1,13–15,17] In such cases, consideration should also be given to intrarenal anatomy and stone fragility in determining appropriate therapeutic intervention.[17,21]

Based on this meta-analysis, it shows that PCNL is better than fURS and ESWL (p=<0.001). Then, fURS is better than ESWL base on stone free rate in ≤20 mm lower pole stone management (p=0.01). With the minimal morbidity and widespread availability of ESWL, PCNL had assumed a diminished role in stone management over the past two decades. Several

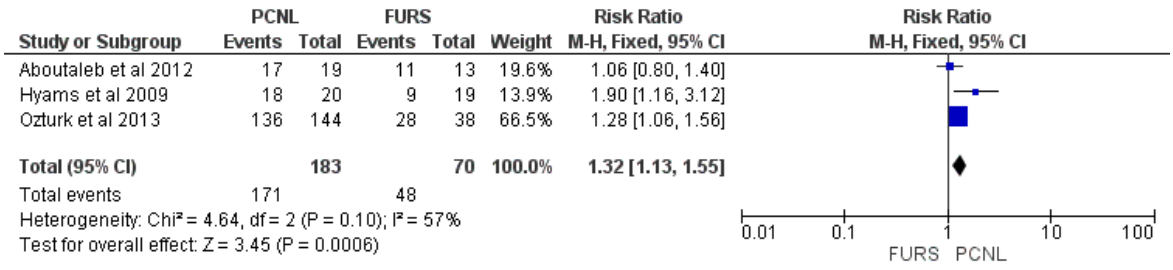

Figure 3. Forest plot comparison between FURS and PCNL stone free rate in lower pole stone ≤ 20 mm management.

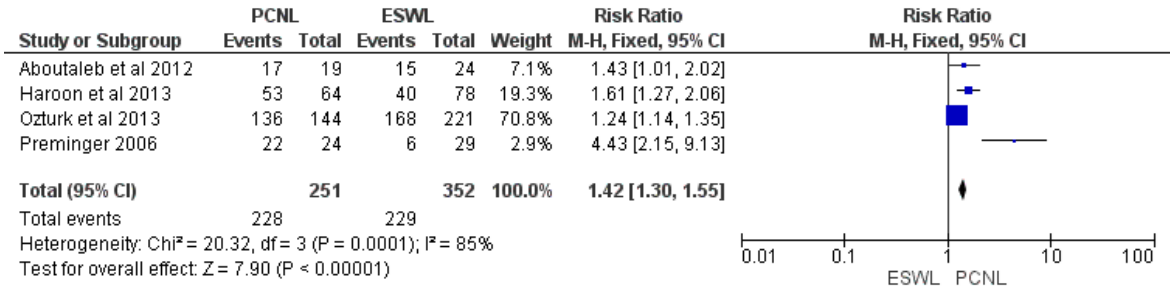

Figure 4. Forest plot comparison between PCNL and ESWL stone free rate in lower pole stone ≤ 20 mm management.

indications remain well accepted, however, including stones failing SWL, stones associated with distal obstruction, and the occasional patient in whom SWL is contraindicated for factors such as body habitus or proximate calcified aneurysm. Additionally virtually all studies to date comparing SWL and PCNL demonstrate an inverse relationship between stone burden and stone free rates after SWL, particularly in the lower pole calyx. In contrast, the success of PCNL is almost independent of stone size. Stone burden, therefore, is a well recognized factor in the decision for SWL or PCNL.[17,21]

A multicentre lower pole study group, conducted the first prospective randomized trial with the aim of determining the optimal treatment of lower pole calculi. The group compared stone-free rates in 52 patients undergoing SWL and 55 randomized to PCNL. Overall stone free rates for PCNL were far superior to that of SWL (95% v. 37%), retreatments were more common in the SWL group (16% v. 9%) and auxillary procedures were more frequent with SWL patients (16% v. 2%). Stratification by stone size was also consistent with prior studies, demonstrating SWL stone-free rates of 68% for stones smaller than 10 mm in diameter, 55% for 10–20 mm stones and 29% for stones larger than 20 mm. The corresponding stone-free rates for PCNL were 100%, 93% and 86%, demonstrating that, for PCNL, stone-free rates are largely independent of stone size.[4] The comparison of stone clearance rate between ESWL and more invasive treatments such as PCNL or ureteroscopy was also done by many authors, however, overall complication rates in the Lower Pole Study were not significantly different.[4,20]

In the treatment of lower calices stone of less than 20 mm, El-Nahas et al.[2] reported the matched groups which included 37 patients who underwent fURS and 62 patients who underwent ESWL. Retreatment rate was significantly higher for ESWL (60% vs 8%, $p<0.001$). Preminger found that stone-free rates for calculi between 11 and 20 mm were 21% and 92% for SWL and PNL, respectively.[15] Similarly, Haroon et al[3] reported the proportion of patients who were stone-free after 4 weeks was significantly higher in the PCNL group than in the SWL group (83% vs. 51%, $p<0.001$). The cause of the higher retreatment and stone free rate in ESWL may be the use of a second generation electromagnetic lithotripsy machine with a small focal area and lower shock energy in comparison with the original HM3. Thus a stone larger than 10 mm is expected to require multiple sessions of ESWL. On the other hand, the causes of retreatment in the fURS group had unexpected incidents such as malfunction of the ureteroscope or laser machine and development of complications (e.g. perforation of the ureter).[2,22]

Of the patients with nephrolithiasis in the United States who received commercial healthcare in 2000, the overall distribution of procedures was approximately 54% for ESWL, 40% for URS, 5% for PCNL, and 1% for open surgery. Although it is accepted that the selection criteria for PCNL (e.g. large and/or complex stone disease) will lead to lower usage rates, the factors affecting the disparity between the rates of ESWL and URS are not as clear. Understanding the trends in treatment choice requires accounting for numerous considerations through the perspective of hospitals, physicians, and patients.[17,19,21]

Flexible ureteroscopy (fURS) offers advantages in certain patient populations such as those with bleeding diathesis, those taking anticoagulants, those with renal anomalies such as a calyceal diverticulum, morbidly obese patients and those with orthopedic or other abnormalities with body habitus that may make ESWL or PCNL challenging to perform.[4] Ozturk et al[14] reported that success rates were 76, 94, and 73% respectively in ESWL, PCNL, and fURS. The highest stone-free rate was in the PNL group ($p<0.05$). For treatment of lower pole stones 10 – 20 mm in length, fURS provide a significantly higher stone free rate and lower retreatment compared with ESWL. The incidence of complications after fURS was not significantly higher than after ESWL and the severity of complications was comparable. These results support the increasing role of fURS in the treatment of 10–20 mm lower pole stones.[1,23,24]

Renal stones of less than 10 mm are usually treated successfully with ESWL; larger stones, especially within the lower pole, are

more efficiently treated by PCNL. FURS is recommended as a second-line treatment for smaller lower-pole stones and an as alternative for stones of moderate size if there are negative predictors for the success of ESWL.[16,25,26] In 10 – 20 mm renal stone, PCNL seem to be the most successful but most invasive method. Despite this recommendation, fURS is already used as the method of choice for such stones by many urologists, although individual factors and preferences must be considered.[8,14]

In this study, we are not considering individual factors and types of lithotriptors that may influence stone free rate. The rate of symptomatic episodes and stone growth can be low depending on disease factors and the patient population, and systematic re-treatment in the short term is not justified. Further study is needed to improve our understanding of the risk of stone recurrence or progression after surgery using consistent definitions of small residual fragments and uniform treatment protocols.

CONCLUSION

Percutaneus Nephrolithotomy (PCNL) provides a higher stone free rate than fURS and ESWL and may help urologist making decision of an intervention in 10-20 mm lower pole stone management.

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