COMPARISON OF EFFICACY BETWEEN LASER AND PNEUMATIC LITHOTRIPSY FOR URETERAL STONE MANAGEMENT: A SYSTEMATIC REVIEW AND META-ANALYSIS

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ABSTRACT

Objective: *This study aimed to evaluate the efficacy of ureteroscopy lithotripsy (URS) using laser lithotripsy compared to pneumatic lithotripsy for ureteral stone management.* ***Material & Methods:*** *A systematic search was conducted in PubMed and ScienceDirect. The search and screening process in this study followed the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) guideline to include relevant RCTs. The included studies were assessed for their risks of bias using the Cochrane risk of bias tool 2 (RoB 2). The comparison of outcomes, which includes stone-free rate, DJ-Stent use, and mean fragmentation time between laser and pneumatic lithotripsy was analyzed using Review Manager 5.4.* ***Results:*** *A total of 11 RCTs evaluating a total of 235 patients with ureteral stone were analyzed in this review. Compared to pneumatic lithotripsy, laser lithotripsy has a significantly higher stone-free rate (OR 2.39, 95% CI 1.78-3.21, p < 0.001), longer mean fragmentation time (MD 4.11, 95% CI 3.17-5.04, p < 0.001), and lower DJ stent use rate (OR 0.53, 95% CI 0.36-0.76) based on the forest plot analysis.* ***Conclusion:*** *Patients undergoing laser lithotripsy have a higher stone-free rate, a lower DJ stent use rate, and albeit a longer mean fragmentation time compared to pneumatic lithotripsy.*

Keywords: *Ureteroscopy lithotripsy, laser lithotripsy, pneumatic lithotripsy.*

ABSTRAK

Tujuan: *Penelitian ini bertujuan untuk mengetahui efikasi URS dengan menggunakan litotripsi laser dibandingkan dengan litotripsi pneumatik pada pasien batu ureter.* ***Bahan & Cara:*** *Penelitian sistematis dilakukan dari database elektronik yaitu PubMed, dan Science-direct. Pencarian dan pemilihan studi pada penelitian ini mengikuti pedoman PRISMA. Seluruh studi yang digunakan pada penelitian ini berupa randomized controlled trial (RCT). Studi yang telah tersaring pada penelitian ini dinilai validitasnya menggunakan cochrane risk of bias tools 2 (ROB 2). Perbandingan tingkat bebas batu, tingkat penggunaan DJ stent, dan waktu fragmentasi antara litotripsi laser dan litotripsi pneumatik dianalisis menggunakan Review Manager 5.4.* ***Hasil:*** *Sebanyak 11 RCT, dengan jumlah pasien total sebanyak 235 orang dengan diagnosa batu ureter dianalisis pada penelitian ini. Analisis gabungan menunjukkan bahwa dibandingkan litotripsi pneumatik, litotripsi laser memiliki tingkat bebas batu yang lebih tinggi secara signifikan (OR) 2.39 (IK 95% 1.78-3.21, p < 0.001), waktu fragmentasi lebih lama (IK 95%, 3.17-5.04 dengan p < 0.001)), dan memiliki tingkat penggunaan DJ stent lebih rendah (OR 0.53 (IK 95%, 0.36 – 0.76).* ***Simpulan:*** *Pasien yang menjalani litotripsi laser memiliki tingkat bebas batu yang lebih tinggi, tingkat penggunaan DJ stent yang lebih rendah, dan waktu fragmentasi yang lebih lama dibandingkan pasien litotripsi pneumatik.*

Kata Kunci: *Litotripsi ureteroskopi, litotripsi laser, litotripsi pneumatik.*

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INTRODUCTION

Urolithiasis is one of the most common causes of morbidity in the field of urology.[1] Ureter is the most common urinary organ affected by the formation of stone (76.4%) followed by the kidney (15.8%).[2] Ureterolithiasis occurred in a variety of age groups. Among adults, anatomical abnormalities, and other external factors are believed to have a major role in the formation of ureterolithiasis. The prevalence of ureterolithiasis varies among age, sex, and race.[3] Men are more prone to urolithiasis compared to women with a prevalence ratio of 2:1.

Most patients came with complaints of colicky flank pain felt spreading to the scrotal area. The management of patients with ureterolithiasis varies from oral pharmacotherapy to surgical interventions. Approximately 75 to 90% of ureteral stones can be expulsed spontaneously. This phenomenon relies on the diameter of the stone.[4] Education regarding lifestyle changes to patients with stones less than 4 mm in diameter and without complications, such as fever, hydronephrosis, and unbearable pain may help the spontaneous process of expulsion. In cases where the size of the stone is more than 5 mm, medical expulsion therapy (MET) may help spontaneous expulsion in 40% of cases.[5]

The active act of stone removal is one of the possible alternatives that need to be performed if there is a complication or failure of therapy using METs. There are several modalities of operative treatment, such as open surgery, extracorporeal shock wave lithotripsy (ESWL), laparoscopic ureterolithotomy, and ureteroscopy (URS).[6] Currently, minimally invasive surgeries like URS or laparoscopy are commonly used. The reason between URS or laparoscopic use is the few amounts of complications that may arise compared to the open alternative. The trend of operative interventions for stone management is increasing as there are consequences for conservative management failure, including potential persistent pain during the therapy. The main risk for intervention is the potential risks from anesthesia, upper urinary tract infection, and ureteral injury, which could be reduced by state of the art techniques with certain triptors.[7]

There are several alternatives of energy that can be used to fragment ureteral stones, such as ultrasonic wave, electrohydraulic, pneumatic, and laser. However, pneumatic lithotriptor is the most commonly used compared to other alternatives due to its efficacy for many types of stones.[8] The current improvement of technology generates new alternatives like laser. Laser has several modes to fragment stones. Laser Ho YAG is reported to have good outcomes. The use of Laser is recently reported to have several advantages compared to pneumatic lithotriptors.[9] However, there are also other publications that highlighted the efficacy of pneumatic lithotriptors over other alternatives including laser.

OBJECTIVE

This study aimed to evaluate the efficacy of ureteroscopy lithotripsy (URS) using laser lithotripsy compared to pneumatic lithotripsy for ureteral stone management.

MATERIAL & METHODS

We performed a systematic search in the PUBMED and Science Direct databases. The search and screening process was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA). The main keywords used during the search were lithotriptor, laser, and pneumatic. The measured dependent variables were: stone-free rate, mean fragmentation time, and the use of DJ stent after every procedure.

This meta-analysis included only randomized controlled trial design studies which compare laser to pneumatic lithotripsy. Case-control, cross-sectional, cohort, and non-randomized controlled trials were excluded. The inclusion and exclusion criteria are presented in table 1.

Data were independently extracted from each study applying a standardized form by all reviewers and all the disparency of the reviewers was solved by discussion. If the reviewers could not reach a consensus, another author was consulted to resolve the dispute and a final decision was made by the majority of votes.

The risk of bias of the studies was performed to determine the quality of each included study. The

Table 1. Inclusion and exclusion criteria of the research.

Inclusion	Exclusion
Randomized controlled trials (RCTs)	Research in the form of abstract only
Studies comparing pneumatic and laser lithotripsy for ureteral stone management	Studies evaluating patients with kidney stone undergoing a laser and pneumatic lithotripsy combination
Studies with 2 arms or more	Studies evaluating pediatric patients
Patients undergoing URS	

studies were evaluated using the Cochrane risk of bias tools (RoB) for randomized trial, which assessed several parameters: selection bias, performance bias, detection bias, reporting bias, and incomplete outcomes. This review did not use other tools as the included studies were all RCTs.

Every included article was presented in the baseline characteristics table. The studies' authors, year, sample size in each arm, age, design, stone size in centimeters (cm), stone-free rate, DJ stent use rate, and mean fragmentation time (MFT) are reported for each study. Quantitative analysis was performed using a pooled analysis comparing variables for each study. The samples were divided into the laser lithotripsy (LL) and pneumatic lithotripsy (PL) groups.

The visualization of each study result was presented in forest plot. Continuous data were presented as mean and standard deviation, in which the difference was compared between each study. Dichotomous data from the proportion and sample size were analyzed as odds ratio. The analysis was performed using Review Manager 5.4.

RESULTS

A total of 11 studies were included in this meta-analysis. The data from each study was analyzed and presented in the forest plot. Heterogenous research data was analyzed using a random-effects model, whereas homogenous data was analyzed using a fixed-effects model. The flow of this research is briefly described in the prism flowchart in figure 1.

Every included study was analyzed both qualitatively and quantitatively as well as presented as a tabulation in Table 2. There are 2033 patients from 11 studies with an average age of 41.6 + 3.8 years old.

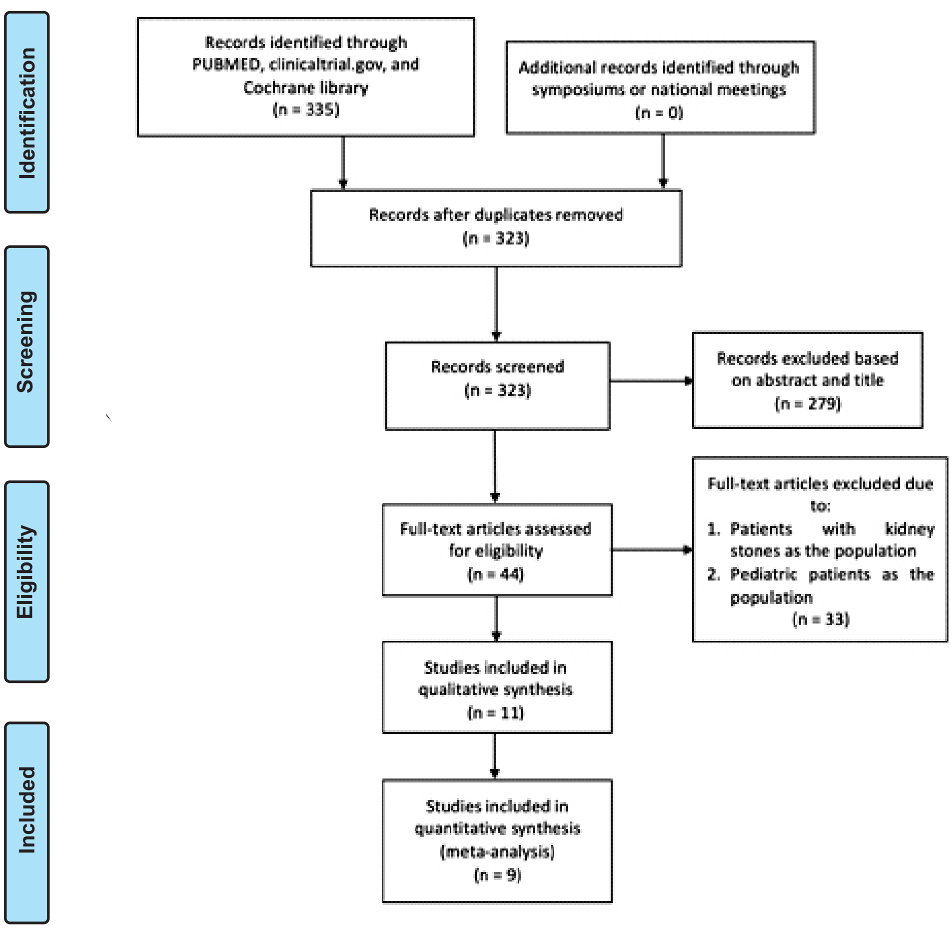

Figure 1. PRISMA diagram describing the systematic search and screening process.

The 2035 samples in this study were divided into the laser lithotripsy group consisting of 1021 samples and pneumatic lithotripsy consisting of 1014 samples. From the overall meta-analysis, the data is quite homogeneous based on the results from I2, so the analysis uses a fixed effect model. The components assessed in this meta-analysis were SFR, DJ stent usage rates, and MFT.

There are 8 studies evaluating the SFR results of the groups. Pooled analysis showed that the studies were homogenous (I2 = 34%, p = 0.16). Analysis was therefore performed using the fixed-effects model. LL group had a higher SFR compared to the PL group (OR: 2.39 95% CI 1.78-2.31, $p < 0.001$) as shown in figure 2.

Table 2. Studies' Baseline Characteristics.

No	Author	Year	Intervention	Samples	Age (years)	Stone size (mm)	Follow-Up (months)	Early SFR (n)	Stone Migration (%)	Stent (n)	MFT (minutes± SD)
1	Razaghi	2013	Laser	56	35.9	11.7	3	56	-	-	
			Pneumatic	56	36.4	10	3	46	-	-	7.9 ± 4.2
2	Binbay	2011	Laser	40	40.2	11	16	39	2.5	13	-
			Pneumatic	40	39.6	11.8	15.3	32	10	40	-
3	Bagbanci	2016	Laser	128	44	1.12	11.3	120	9.4	79	16.48±4.74
			Pneumatic	130	44	1.17	11.52	112	18.5	25	12.24±3.95
4	Cimino	2014	Laser	60	48	11	-	-	1.66	-	-
			Pneumatic	57	51	10.2	-	-	10.53	-	-
5	Garg	2009	Laser	34	44	11.1	11.35	33	0	22	24.03 ± 9.51
			Pneumatic	25	43	11.1	7.92	21	16	19	19.80 ± 4.44
6	Kassem	2012	Laser	40	43.9	12.8	-	32	12.50	5	44.5 ± 28.2
			Pneumatic	40	46.1	1.31	-	32	30	12	53.5 ± 29.2
7	Li	2015	Laser	493	40.3	8.5	12	450	4.30	493	-
			Pneumatic	489	43.5	8.8	12	395	4.90	489	-
8	Maghsoudi	2008	Laser	39	42.5	12.07	-	-	2.40	-	-
			Pneumatic	40	38.5	10.2	-	-	7.30	-	-
9	Manohar	2008	Laser	25	35.7	9.63	3	-	24	25	9.82 ± 7.58
			Pneumatic	25	37.6	10.17	3	-	16	25	7.86 ± 3.25
10	Rabani	2019	Laser	58	41.7	9.29	-	46	8.55	-	-
			Pneumatic	59	41.1	9.77	-	46	8.55	-	-
11	Nour	2020	Laser	48	36.72	113.6	3	47	4.20	40	-
			Pneumatic	53	41 54	13 22	3	51	3 70	40	-

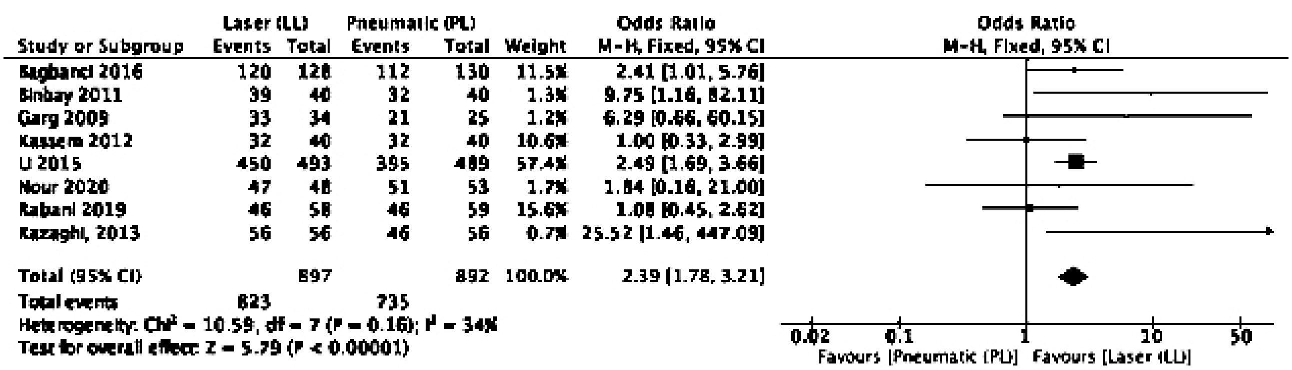

Figure 2. The SFR results analysis presented in the forest plot indicating a favorable tendency towards the LL group.

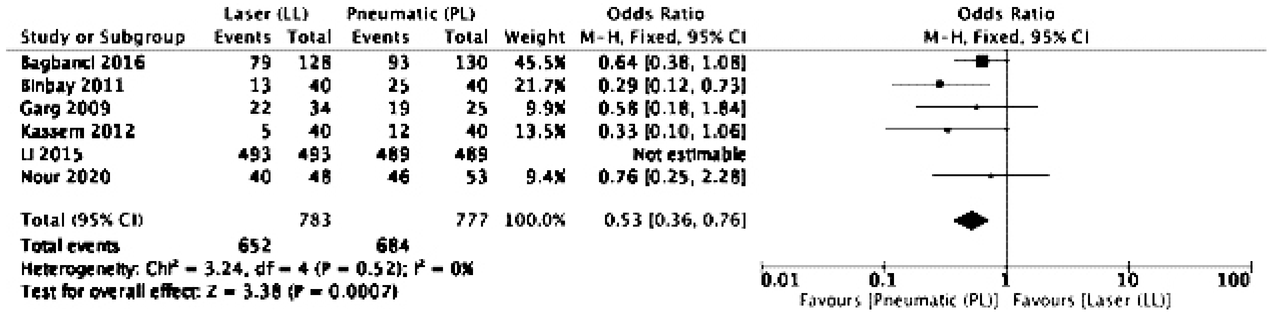

Figure 3. Forest plot analysis showing a significantly higher DJ Stent use among the PL Group compared to the LL group.

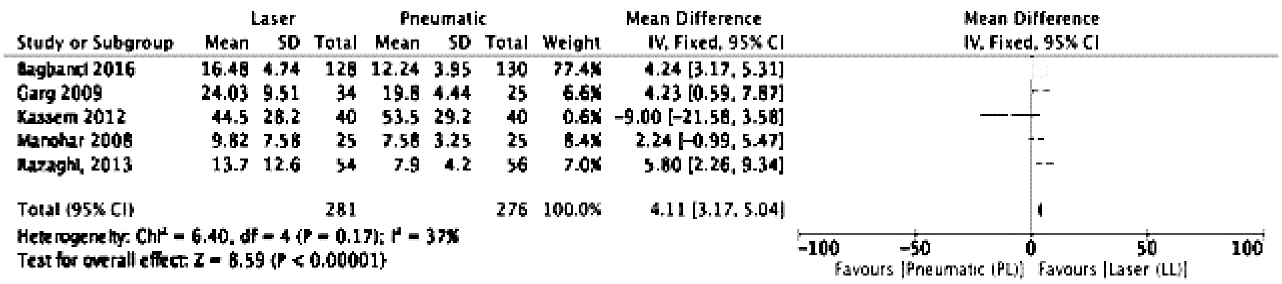

Figure 4. Forest plot analysis showing a significantly lower MFT among the PL group compared to the LL group.

There are 6 studies evaluating DJ-stent use after both procedures. The pooled analysis results showed homogeneity (I2 = 0%, p = 0.52). As the samples were homogeneous, a fixed-effects model was used. The forest plot analysis in figure 3 showed a significantly higher DJ Stent use among the PL group compared to the LL group (OR 0.53, 95% CI 0.36-0.71, p = 0.0007).

There are 5 studies evaluating stone fragmentation time results between the groups. Pooled analysis results showed a low level of heterogeneity (I2 = 37%, p = 0.17), leading to fixed-effects model analysis. The MFT of the PL group was significantly 4.11 minutes lower compared to the LL group (MD 4.11, 95% CI 3.17-5.04, p = 0.0007) as shown in figure 4.

DISCUSSION

Ureteral colic is a common complaint among patients found daily in the practice of general practitioners. The pathogenesis of this condition is due to an obstruction of urinary flow leading to urinary tract distention. The increase of pressure of the urinary tract will cause a release of inflammatory mediators perceived as a painful sensation by the body.[10] There are several causes of ureteral obstruction, including ureteral stone, blood clot, tumor, and trauma. Ureteral stone is the most common etiology for ureteral obstruction.[11] Stones with more than 5 mm in size are usually treated with medical expulsive therapy (MET), such as alpha-blockers, calcium channel inhibitors, or PDE5 inhibitors to reduce colicky pain episodes as well as increasing the chance for spontaneous expulsion.[12] Failure of METs is usually followed by surgical interventions. One of the most common surgical procedures is Ureterorenoscopy (URS). Innovations in URS have led to better optical use and the utilization of new energies to increase efficacy in ureteral stone management.[13]

Among all energy alternatives in URS, pneumatic and laser energies are the most commonly used.[9] Currently, the efficacy between laser and pneumatic lithotripsy is still being debated. Laser is considered better in terms of fragmentation time and flexibility, however, pneumatic is considered better in terms of cost and application.[6] Previous meta-analysis attempted to compare laser and pneumatic URS, however, the review had not analyzed the parameters of MFT and DJ stent use rate in great detail.[14] Moreover, there were three published RCTs after the publication of said review comparing the efficacy and safety between the two methods.

One of the variables for efficacy is SFR, which was explained in 8 studies: Bagbanci et al, Binbay et al., Garg et al., Kassem et al., Li et al., Nour et al., Rabani et al., and Razaghi et al.[15-23] The meta-analysis in this study showed a higher SFR among the LL group, except the result by Kassem et al. The difference shown in the study by Kassem et al is possibly due to the relatively small sample size in the two arms of the study.[18] The pooled analysis showed a 2.39 fold increase of SFR of the LL group compared to the PL group.

There is a difference in mechanism between the pneumatic and laser groups affecting the efficacy of both modalities to reach stone fragmentation.[24] Pneumatic lithotripsy works by generating mechanical energy similar to how a hammer breaks a stone by transmitting an air projectile with a frequency up to 12 times per minute.[25-26] Stone fragmentation occurs due to the transmission of repeated kinetic energy towards the stone.[27] The main problem that may occur due to pneumatic lithotripsy is retrograde expulsion of the stone. Laser lithotripsy (Holmium: YAG) uses photothermal energy as a source for stone fragmentation. The released energy would lead to gradual stone fragmentation.[20,28]

This review also discussed the rate of DJ stent use among the two groups. There are 6 studies evaluating DJ stent use, Bagbanci et al., Binbay et al., Garg et al., Kassem et al., Li et al., and Nour et al.[15-18,20-21,29] Quantitative analysis showed that the patients in the PL group underwent DJ stent placement more frequently compared to the LL group. There is a variety of indications for DJ stent use after URS, several of which are to reduce the possibility of post-procedural obstruction and pain. The majority of DJ stent use is to reduce obstruction due to residual stones.[20] This study showed that the LL group has a higher SFR which may be related to lower DJ stent use rate. Laser is known to be able to fragment stone into smaller pieces compared to the pneumatic alternative. Smaller fragments have a higher probability of spontaneous expulsion compared to larger ones.[30] Most URS use semi-rigid scopes which could lead to larger fragments that are more difficult to be extracted.[28] The use of ballistic energy lead to a possibility of retropulsion during the procedure. These factors lead to a higher DJ stent use rate among the PL group compared to the LL group.

One of the important outcomes for efficacy is MFT. There are 5 included studies evaluating MFT as an outcome: Bagbanci et al., Garg et al., Kassem et al., Manohar et al., dan Razzaghi et al.[15,17-18,23,31] The analysis of the studies showed that, on average, LL is 4.11 minutes slower compared to PL. The MFT results in this review implied that PL is more effective compared to LL in terms of procedure duration. The direct mechanism of PL to fragment stone plays a huge role in effectiveness in duration compared to LL.[32] This finding is different compared to the previous meta-analysis which showed a longer operating time in the PL group compared to the LL group.[14] The difference in results is due to the difference in duration parameters evaluated. This review evaluated the duration of MFT without taking into account other factors that may affect the operating time during the entire procedure. Other additional factors may increase the overall time of the PL procedure.

CONCLUSION

Patients undergoing URS with LL have a higher SFR and lower DJ stent use rate compared to the PL group, however, LL requires more time to fragment stones compared to PL. Further studies should focus on the comparison between the procedures with the same amount of energy used, using a larger sample size to evaluate potential adverse events during and after both procedures.

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