THE EFFECTIVENESS OF ULTRASONIC LITHOTRIPTOR COMPARED TO COMBINED ULTRASONIC AND PNEUMATIC LITHOTRIPTOR IN PERCUTANEOUS NEPHROLITHOTOMY (PCNL) SURGERY: A SYSTEMATIC REVIEW AND META-ANALYSIS

[1]Anggana Suryatmana, [1]Doddy M. Soebadi, [1]Tarmono Djojodimedjo.

[1] Department of Urology, Faculty of Medicine/Universitas Airlangga, Soetomo General Hospital, Surabaya.

ABSTRACT

Objective: *To evaluate the effectiveness of the ultrasonic lithotriptor compared to the combined ultrasonic-pneumatic lithotriptor in percutaneous nephrolithotomy (PCNL).* ***Material & Methods:*** *A systematic search was conducted focusing on studies evaluating nephrolithiasis patients who underwent PCNL using pneumatic, ultrasonic, ultrasonic-pneumatic, or laser lithotriptor. The search was conducted in the PUBMED and Science-direct databases from early to September 2020.* ***Results:*** *There were 406 journals in the initial search. On further selection, 3 randomized controlled trials (RCT) were obtained, with a total of 251 patients. The stone-free rate of three studies had low heterogeneity, I2=0% (P=0.34), so a fixed effect statistical model was used. There was no significant difference (P=0.44) between the stone-free rates from the ultrasonic lithotriptor group and the combination with an odds ratio of 1.26 (95% CI = 0.70-2.26). High heterogeneity was obtained with I2=71% (P=0.03) for the mean fragmentation time, so random effect statistical model was used. There was no significant difference (P=0.56) between the mean fragmentation time of the ultrasonic lithotriptor and combination group with a mean difference of -3.69 (95% CI = -16.09-8.71).* ***Conclusion:*** *The ultrasonic lithotriptor did not have a significant difference in stone-free rate, and mean fragmentation time compared to the combined ultrasonic-pneumatic lithotriptor in PCNL. More RCT studies are needed.*

Keywords: *Lithotriptor, percutaneous nephrolithotomy, PCNL, pneumatic, ultrasonic.*

ABSTRAK

Tujuan: *Mengkaji perbedaan efektifitas litotriptor ultrasonik dibandingkan dengan litotriptor kombinasi ultrasonik dan pneumatik pada operasi percutaneous nephrolithotomy (PCNL).* ***Bahan & Cara:*** *Penelitian ini merupakan telaah sistematik dan meta analisis, dengan subjek pasien batu ginjal yang menjalani tindakan PCNL menggunakan litotriptor pneumatik, ultrasonik, kombinasi ultrasonik, pneumatik, atau laser. Dilakukan pencarian jurnal berbahasa inggris dengan topik terkait yang terpublikasi melalui database search engine PUBMED dan SCIENCE-DIRECT dari awal hingga September 2020.* ***Hasil:*** *Terdapat 406 jurnal pada seleksi awal. Pada tahap seleksi lebih lanjut, didapatkan 3 studi randomized controlled trial (RCT), dengan total 251 pasien. Pada stone-free rate, ketiga studi memiliki heterogenitas rendah dengan I2 0% (P=0.34), sehingga digunakan model statistik fixed effect. Pada analisis didapatkan perbedaan yang tidak signifikan (P=0.44) antara jumlah stone-free rate dari kelompok litotriptor ultrasonik dan kombinasi dengan rasio odds 1.26 (95% CI = 0.70-2.26). Pada mean fragmentation time, didapatkan heterogenitas tinggi dengan I2=71% (P=0.03), sehingga digunakan model statistik random effect. Selanjutnya didapatkan perbedaan yang tidak signifikan (P=0.56) antara mean fragmentation time dari kelompok litotriptor ultrasonik dan litotriptor kombinasi dengan perbedaan rerata -3.69 (95% CI = -16.09-8.71).* ***Simpulan:*** *Litotriptor ultrasonik tidak memiliki perbedaan yang signifikan dalam hal stone-free rate, dan mean fragmentation time dibandingkan litotriptor kombinasi ultrasonik dan pneumatik pada PCNL. Diperlukan studi RCT yang lebih banyak.*

Kata Kunci: *Litotriptor, percutaneous nephrolithotomy, PCNL, pneumatik, ultrasonik.*

Correspondence: Doddy M. Soebadi; c/o: Department of Urology, Faculty of Medicine/Universitas Airlangga, Soetomo General Hospital, Surabaya. Jl. Mayjen. Prof. Dr. Moestopo 6-8 Surabaya 60286. Phone: +62315501318; Fax: +62315024971. Mobile phone: +62816500755. Email: dmsoebadi@yahoo.com.

INTRODUCTION

The prevalence of kidney stones (nephrolithiasis) is reported to be increasing worldwide. The incidence of nephrolithiasis has doubled within 40 years in both men and women in Japan. This increase has been most pronounced in the last 10 to 20 years.[1] In Indonesia, based on the Riset Kesehatan Dasar (Riskesdas) in 2013, the prevalence of kidney stones showed an increasing trend with the highest incidence in the 55 to 64 years age group, and a higher incidence in men, namely 0.8%.[2]

Percutaneous Nephrolithotomy (PCNL) is an operative procedure to remove stones in the renal tract through an endoscopic intervention-based approach to the calyx system with small skin incisions. PCNL involves retrograde percutaneous access and endoscopic assistance via flexible ureterorenoscopy.[3] Stone removed by broke the stone up into small fragments, initially.[4] Possible risks are bleeding, infection, tissue or organ damage, stones removal failure, and radiation exposure when using the C-arm.

PCNL has become the choice of therapy for large or complex upper urinary tract stones. However, the limitation of this procedure is the relatively high radiation exposure of the patient and the urologist. On the other hand, the advantages of PCNL are the lower rate of transfusion requirements, the need for fewer access, and a lower risk of procedure failure due to bleeding and shorter operative time. Recently, a new PCNL based on ultrasonography (USG) had developed, which can reduce radiation exposure when the procedure is performed.[5]

The PCNL procedure method requires a lithotriptor as a stone breaker. There are various approaches related to the energy sources needed by the lithotriptor in the purpose of breaking stones, for example ultrasonic, pneumatic, a combination of ultrasonic-pneumatic, and laser.[6] Traditional lithotriptors such as ultrasonic and pneumatic have good results in breaking stones in the urinary tract, but complications of bleeding or trauma to the urinary tract are also higher than the latest technology. The use of lasers has given good results and reduced the number of complications and side effects. However, laser lithotriptor requires higher power, special maintenance, and expensive.[7]

To date, several studies directly compare the effectiveness and safety of various lithotriptors in patients undergoing kidney stone surgery and upper urinary tract surgery who underwent PCNL procedure. However, no one has ever conducted a systematic review and meta-analysis study in this field.

OBJECTIVE

This study aimed to systematically evaluate the difference in the effectiveness of ultrasonic lithotriptor compared to combined ultrasonic-pneumatic lithotriptor in PCNL procedure.

MATERIAL & METHODS

This research is a systematic analysis and meta-analysis. This study's subjects were patients with kidney stones who underwent PCNL using pneumatic, ultrasonic, combined ultrasonic-pneumatic, or laser lithotriptor. All authors searched for independent correlated studies of published English journals via the PUBMED and Science-direct search engine databases from early to September 2020. Relevant references from all articles were retrieved and searched manually. The keywords used in the literature search are described in table 1.

This study used the protocol writing guidelines for The Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA). In this study, the lithotriptor variables (pneumatic, ultrasonic, combination, and laser) were determined as independent variables to be compared with one another. The dependent variable of this research is the stone-free rate and the length of operation. Selection of study results based on reading the title, abstract, keywords, and the selected journal's full text. The journal was selected based on predetermined inclusion and exclusion criteria (Table 2).

Data were extracted independently from each study based on the criteria in a standardized form by all authors and then cross-checked. Any disagreements will be resolved by discussion between the authors. If the authors cannot reach an agreement, other experts are included to resolve differences, and a majority vote makes the final decision.

In this study, an assessment of the research bias and the quality of each selected journal article was conducted. For RCT research, this study uses the Cochrane Risk of Bias Tools In For Randomized

Table 1. Keyword on the PubMed/Science-direct database searching.

Database	Keywords
PubMed	("ultrasonically"[All Fields] OR "ultrasonicated"[All Fields] OR "ultrasonication"[All Fields] OR "ultrasonicator"[All Fields] OR "ultrasonics"[MeSH Terms] OR " ultrasonics"[All Fields] OR "ultrasonic"[All Fields] OR ("pneumatic"[All Fields] OR "pneumatically"[All Fields] OR "pneumatics"[All Fields]) OR ("lithotriptor"[All Fields] OR "lithotriptors"[All Fields])) AND ("nephrolithotomy, percutaneous" [MeSH Terms] O R ("nephrolithotomy" [All Fields] AND "percutaneous"[All Fields]) OR "percutaneous nephrolithotomy"[All Fields] OR ("percutaneous"[All Fields] AND "nephrolithotomy"[All Fields]) OR (("percutaneous"[All Fields] OR "percutaneously"[All Fields] OR "percutanous"[All Fields]) AND "nephrolithotripsy"[All Fields]) OR "PCNL"[All Fields]) (257)
Science Direct	1. Ultrasonic AND Pneumatic Ultrasonic Percutaneous nephrolithotomy (93) 2. Ultrasonic and pneumatic PCNL (56)

Table 2. Inclusion and exclusion criteria of the research.

Inclusion	Exclusion
Randomized controlled trial, cohort, retrospective, case-control, and cross-sectional studies	Case reports, and case series
The study had 2 or more arms	Animal model studies
A study comparing ultrasonic lithotriptor with combined ultrasonic-pneumatic lithotriptor in PCNL procedure.	In-vitro study
Patients diagnosed with kidney stones > 2 cm	Review study
Patients with > 18 years of age	Single-arm study
Patients undergoing PCNL.	Studies comparing lithotriptor to placebo

Trials. This study uses the scoring method from The Newcastle-Ottawa Scale (NOS) for observational journal articles.[8-9]

In this study, the data from each selected journal article will be presented descriptively and a comparison analysis between variables is carried out. Basic data in the form of the name of the author, the year of study, the location of the study, the number of samples, the mean age of the patient, the study design, the size of the stone, the type of stone, and the follow-up were reported as descriptive data.

Meta-analysis statistical analysis is used to see the differences between the variables studied. In this study, a forest plot was used to see the differences in each variable for the particular study. In continuous data, the analysis used the mean and standard deviation of variables to determine the mean differences. In the dichotomous data, the number of proportions and the total sample were used to see the difference in odds ratios of each study. This study uses the Review Manager (RevMan) version 5.4 for Windows as a data analysis processing software. All data obtained will initially be collected in tabulations that are integrated into one data system.

RESULTS

A systematic search for published journal articles was performed using the PUBMED and Science-direct databases. There are 406 journal articles obtained using the initial selection keywords. There were 3 studies with a randomized controlled trial (RCT) design in the further selection stage and no study with an observational design that met the study inclusion criteria. The author's name and year, the study design, the inclusion criteria, the number of samples, the type of stone, the size of the stone were included in the tabulation of the basic characteristics of this study.

The form of intervention/treatment, stone-free rate and mean fragmentation time were included in the research results' tabulation stage. There is one study comparing ultrasonic, pneumatic, and combined lithotriptor, then two studies are comparing ultrasonic and combined lithotriptor. The data presented by each study then analyzed and presented in the forest plot. Heterogeneous research data will be analyzed using a random-effect model, while homogeneous data will be analyzed using a fixed-effect model. The flow of this research is briefly described in the PRISMA Flowchart in Figure 1.

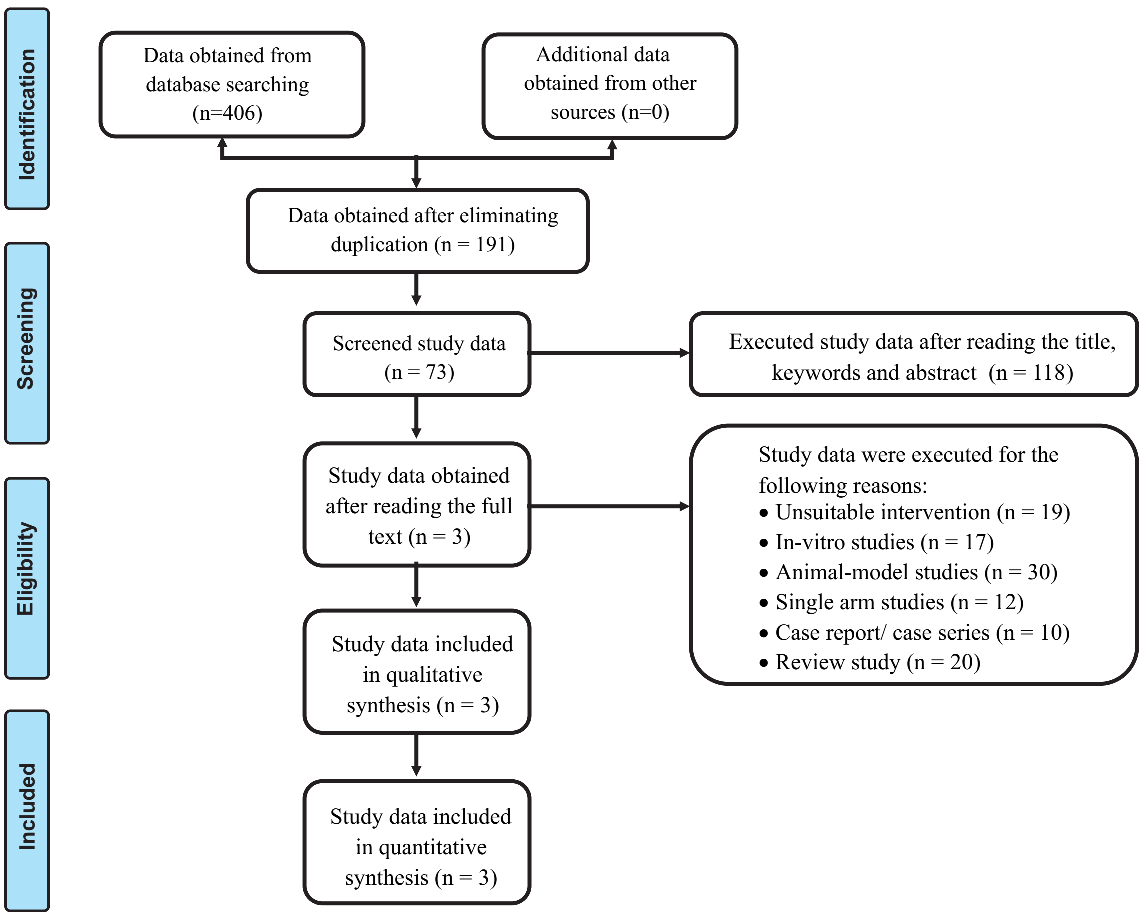

Figure 1. PRISMA flowchart.

Table 3. Basic characteristics of research articles.

Author	Country	Design	Sample	Intervention	Stone size
Nadya 2017	United States	RCT	201	Ultrasonic (71) vs Pneumatic (64) vs Combination (66)	(mm^2): 627.9/407.8/ 577.5
Pietrow 2003	United States	RCT	20	Ultrasonic (10) vs Combination (10)	(mm^2): 795.5/809.2
Lehman 2008	United States	RCT	30	Ultrasonic (17) vs Combination (13)	(mm): 18.5/21

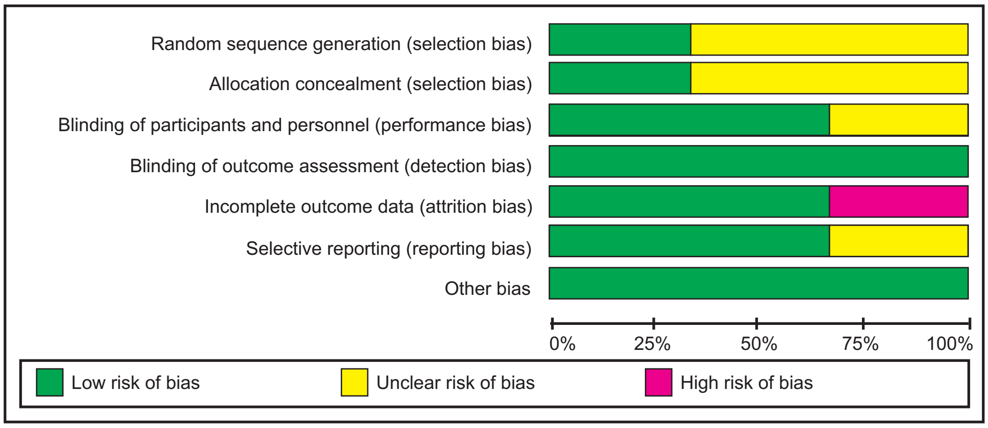

Figure 2. Research risk of bias chart.

The total sample of all studies that met the inclusion criteria of this study was 251 patients. The number of each sample from each intervention group was divided equally. There were differences in stone size between studies, and the study by Lehman et al. 2008 did not include burden sizes (mm2). The types of stones from each study were uric acid stones, calcium oxalate monohydrate, dihydrate stones, cystine stones, and struvite stones.

All studies selected for this study had an RCT design. Therefore, the measurement of the risk of research bias used the method of the Cochrane Risk Of Bias Tools In For Randomized Trials (Figure 2). There were 2 studies that included in the research inclusion criteria that did not adequately describe the randomization process of the samples that entered each intervention group. One study described the allocation concealment mode clearly and the other two studies had an unclear research bias in this section. Both studies carried out the blinding process of research samples as well as health workers, and one study did not describe the blinding process. The three studies did not describe whether the blinding process was carried out on the research results, but the author argued that the absence of a blinding process in the study results did not affect the measurement of the research results.

The study conducted by Pietrow et. al in 2003 has a high risk of bias for the incomplete study results. The study did not attach the standard deviation of mean fragmentation time data. However, to be analyzed, the researcher used the standard deviation estimation using the application available in the Review Manager. None of the studies had high risk in reporting bias and all studies were free from another risk of bias. The study conducted by Nadya et.al, conducted in 2017 had a low risk of research bias in all aspects of research bias.

This study aims to differentiate the stone-free rate and the mean fragmentation time in patients with kidney stones treated with PCNL using an

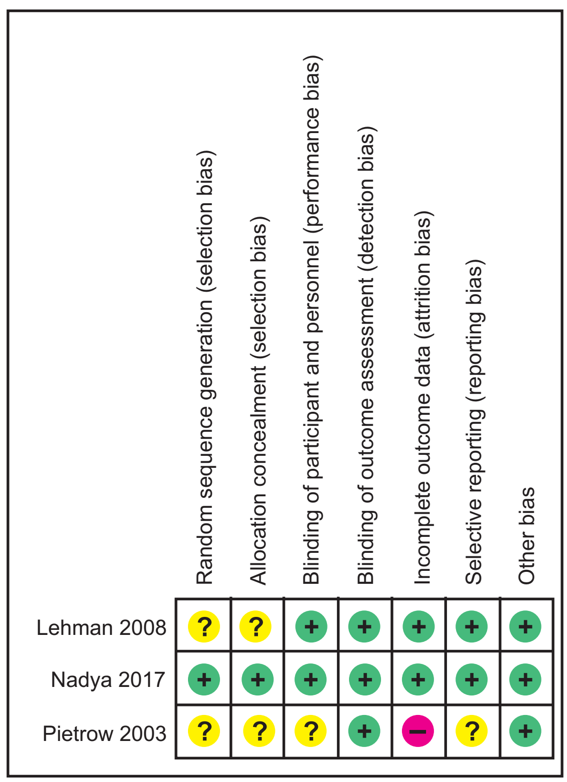

Figure 3. Summary of risk of bias. The green color indicates a low risk of bias, the red color indicates a high risk of bias and the yellow color indicates an unclear risk of research bias.

ultrasonic lithotriptor and a combination of pneumatic-ultrasonic lithotriptor.

Stone-free rate is the number of stone-free events after the PCNL procedure. In Nadya et al's study conducted in 2017, 43 patients (65.1%) from the ultrasonic lithotriptor group were declared stone-free, while 39 patients (54.9%) from the combination lithotriptor group. There was the same number of stone-free rates between the 2 intervention groups in the study conducted by Pietrow et. al 2003. However, there was a higher stone-free rate in the combined lithotriptor intervention group (58.8%) than in the ultrasonic lithotriptor (46.1%).

In the forest plot analysis, the combination of the three studies had statistically low heterogeneity with I2=0% (P=0.34). Therefore, a fixed effect statistical model is used to determine the results of the study. Furthermore, there was no significant difference (P=0.44) between the number of stone-free rates from the ultrasonic lithotriptor group and the combination with an odds ratio of 1.26 (95% CI = 0.70-2.26).

The mean fragmentation time is the time it takes from the lithotriptor contact to the stone breaking/ removal of the stone from the kidney. There are 2 studies that stated a long time in the ultrasonic lithotriptor group and 1 study which stated that the combined lithotriptor was longer for stone fragmentation.

In this study, a forest plot analysis was conducted to determine the significance and heterogeneity of the difference in mean

Table 4. Stone-free rate of each group.

Author	Sample	Stone-free Rate	
		Ultrasonic	Combination
Nadya 2017	Ultrasonic (71) vs Pneumatic (64) vs combination (66)	43 (65.1%)	39 (54.9%)
Pietrow 2003	Ultrasonic (10) vs combination (10)	7 (70.0%)	7 (70.0%)
Lehman 2008	Ultrasonic (17) vs combination (13)	6 (46.1%)	10 (58.8%)

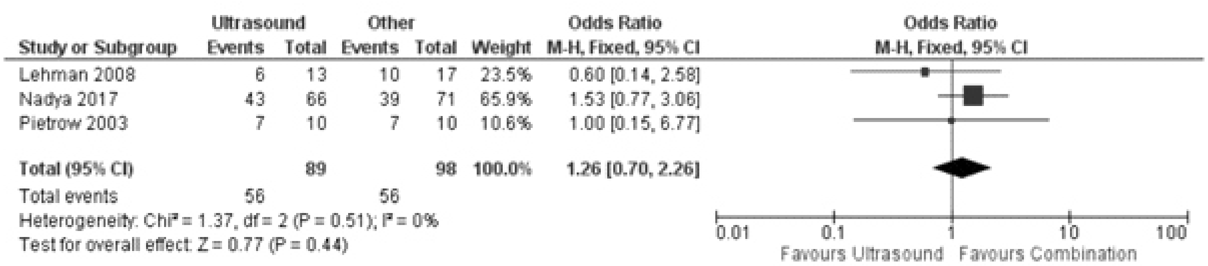

Figure 4. Forest plot the difference in stone-free rate between ultrasonic and combination lithotripsy.

Table 5. Mean fragmentation time of each group.

Author	Sample	Mean Fragmentation time	
		Ultrasonic	Combination
Nadya 2017	Ultrasonic (71) vs Pneumatic (64) vs Combination (66)	28.9 minutes (29.9)	26.6 minutes (26.9)
Pietrow 2003	Ultrasonic (10) vs Combination (10)	43.7 minutes	21.1 minutes
Lehman 2008	Ultrasonic (17) vs Combination (13)	31.5 minutes	37 minutes

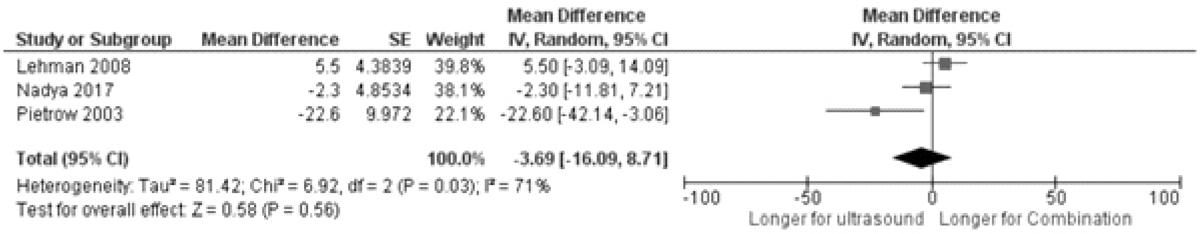

Figure 5. Forest plot the difference in mean fragmentation time between ultrasonic and combination lithotripsy.

fragmentation time between the ultrasonic lithotriptor and combination lithotriptor groups. After combining all studies, there was a statistically high heterogeneity with I2=71% (P=0.03). Therefore, a random effect statistical model is used to determine the results of the study. Furthermore, there was no significant difference (P=0.56) between the mean fragmentation time of the ultrasonic lithotriptor and combination lithotriptor groups with a mean difference of -3.69 (95% CI = -16.09-8.71).

DISCUSSION

Ultrasonic lithotriptor was first used in the early 1950s and was only used as an experimental laboratory.[10] Early human use was first used to destroy stones in the bladder.[11] Ultrasonic lithotriptor can work best with a rigid endoscope. Stone breaking occurs using vibrational energy generated by ultrasonic waves with an average wave speed of 20 kHz. The stone fragments particles will form after the initial contact of the stone with the ultrasonic probe. The tip of the ultrasonic probe will produce high-frequency resonances in the stone which will result in the stone fragmentation process. However, the ultrasonic lithotriptor does not perform well with all types of stones. Ultrasonic lithotriptor has proven successful in small, low-density stone with rough surfaces. The ultrasonic lithotriptor has a hole in the middle that can function to suck up stone fragments.[6,12]

One of the challenges of ultrasonic lithotriptors is the need to be in direct contact with the stone to create stone fragmentation. It is important not to put excessive pressure on the stone, where it will push against the mucosa. The lithotriptor can also create larger stone fragments as manual compression of the stone increases, therefore it requires minimal manipulation. The operator is not allowed to bend the probe as this will cause it to overheat. Ultrasonic probes are very prone to clogging and this can increase overheating, especially in small diameter probes. Ultrasonic lithotriptor has minimal risk of causing tissue perforation, and in general, it only causes minimal damage to surrounding tissue.[13-14]

The most recently developed rigid lithotriptor is a combination model that combines two modes of therapy to increase the efficiency of stone fragmentation. Currently, there are two models: one combines ultrasonic and pneumatic-ballistic probes; and some combine two ultrasonic probes, one is fixed and the second is movable.

Using two systems, the combined pneumatic and ultrasonic lithotriptor is expected to have higher effectiveness compared to ultrasonic lithotriptor. However, there was no significant difference in the stone-free rate between the two lithotriptors (P=0.44). There can be seen a trend towards a combination of pneumatic and ultrasonic lithotriptor in terms of stone-free rate when compared to ultrasonic lithotriptor (OR = 1.26, 95% CI = 0.70-2.26). This is still possible because there are differences in stone size and stone type from each study. The results of this study have low statistical heterogeneity (P = 0.51, I2 = 0%). Therefore statistical tests can be performed using a fixed-effect model.

The ultra lithoclast (Electro Medical Systems, Nyon, Switzerland) was the first combination model to be introduced. The design uses a pneumatic ballistic probe that is placed through a hollow metal ultrasound probe with the tip of the pneumatic probe extending 1 mm beyond the perforated probe. This lithotriptor allows the use of each component singly or in combination. The mechanism of action is identical to each component when individually activated. Several studies have compared this combination device with individual ultrasonic lithotriptors or pneumatic lithotriptors, and have shown superior results.[15]

In this study, there was no difference in the mean fragmentation time between the two lithotriptors (P=0.56), but it can still be seen that the ultrasonic lithotriptor system has a longer trend for fragmentation time with a mean difference of -3.69 (95% CI = -16.09-8.71). However, the stone size and stone type of each study were different. This may affect the length of the fragmentation time. Only the research by Pietrow et al. 2003 had a significant difference in fragmentation time between the ultrasonic lithotriptor (43.7 minutes), and the ultrasonic-pneumatic combination (21.1 minutes). In the results of this study, 2 studies did not attach a standard deviation of continuous data, therefore researchers used standard error estimates using the Review Manager application. The statistical heterogeneity of this study was quite large (P = 0.03, I2 = 71%), so a random effect statistical model was used.

This study has several limitations, including the total number of studies obtained in this study was only 3 RCTs. There were 2 studies with small sample size and 1 study with an unclear risk of research bias due to incomplete methods and research results. However, all studies have varied renal stone sizes, as well as different types of stones. There are 2 studies that do not include the standard deviation of continuous data (mean fragmentation time). The researcher estimated the standard deviation using the tools provided by the Review Manager application so that the data could be analyzed on the forest plot. The mean fragmentation time parameter has high heterogeneity; thus, the authors used a random effect statistical model.

CONCLUSION

It can be concluded that the ultrasonic lithotriptor did not have a significant difference in stone-free rate, and mean fragmentation time, compared to the combined ultrasonic-pneumatic lithotriptor in patients with kidney stones who were treated with PCNL. A greater number of RCT studies is needed, especially with a large sample size and good methodology.

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