

## Original Article

## A systematic review and meta-analysis on the outcomes of extracorporeal shock wave compared to ureteroscopic lithotripsy for the treatment of ureteral stones



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### المخلص

**أهداف البحث:** في هذه المراجعة النظامية والتحليل الشامل، سعى المؤلفون لمعرفة أي من الإجراءات، تفتيت الحصى بالموجات الصدمية خارج الجسم أو تفتيت الحصى بالمنظار البولي، هو الأكثر ملاءمة لعلاج حصى الحالب.

**طرق البحث:** تم إجراء الدراسة الحالية والبحث في قواعد بيانات جوجل سكو لار ويوب ميد باستخدام إرشادات بريزما. تم النظر في إجراءات تفتيت الحصى بالموجات الصدمية خارج الجسم مقابل تفتيت الحصى بالمنظار البولي لتحقيق النتائج. قمنا بتقييم مضاعفات كل طريقة، البول الدموي، التمزق، الفشل، إزالة الحصى، توقف الحصى في البداية، وقت العملية، حجم الحصى، الإجراء المساعد، والنتائج الشاملة لتوقف الحصى. تم إجراء التحليل الشامل واختبار التباين وتحليل المجموعة الفرعية والانحدار الميتا وتحليلات الحساسية واختبارات إيجر وإيجر ذو التباين الملاءم وتومسون ذو التباين الملاءم للكشف عن تحيز النشر لجميع النتائج من الإجراءات.

**النتائج:** حسب عشر دراسات مؤهلة، تم إجراء تحليل شامل لبيانات 1509 مرضى. تم علاج 677 مريضاً باستخدام تقنية الصدمات الكهربائية خارج الجسم لتفتيت الحصى، وتم علاج الباقي (عدد = 832) باستخدام إجراء تفتيت الحصى بالمنظار البولي. كانت النتائج على النحو التالي: المضاعفات (معدل الأخطار النسبية = 0.780، قيمة الاحتمال = 0.269، ك = 13.465، قيمة الاحتمال = 0.062، اي = 2، 48.011). معدل نسبة الدم في البول (معدل الأخطار النسبية = 0.782، قيمة الاحتمال = 0.657، ك = 19.056، قيمة

الاحتمال = 0.001، اي = 2، 79.01)، الثقب (معدل الأخطار النسبية = 0.13، قيمة الاحتمال = 0.003، ك = 0.159، قيمة الاحتمال = 0.997، اي = 2)، فشل العلاج (معدل الأخطار النسبية = 0.329، قيمة الاحتمال = 0.369، ك = 22.659، قيمة الاحتمال < 0.001، اي = 2، 77.934)، نسبة تفتيت الحصى (معدل الأخطار النسبية = 0.699، قيمة الاحتمال = 0.374، ك = 24.957، قيمة الاحتمال < 0.001، اي = 2، 75.959)، ونسبة الحصى الحرة بشكل عام (معدل الأخطار النسبية = 0.428، قيمة الاحتمال = 0.005، ك = 21.462، قيمة الاحتمال = 0.011، اي = 2، 58.066)، وزمن العملية الجراحية (الانحراف المعياري الموحد = 29.314، قيمة الاحتمال < 0.001، ك = 827.872، قيمة الاحتمال < 0.001، اي = 2، 99.758)، وحجم الحصى (الانحراف المعياري الموحد = 0.723، قيمة الاحتمال = 0.04، ك = 261.353، قيمة الاحتمال < 0.001، اي = 2، 96.939)، والنسبة المبدئية للحصى الحرة (معدل الأخطار النسبية = 0.236، قيمة الاحتمال < 0.001، ك = 7.446، قيمة الاحتمال < 0.059، اي = 2، 59.712)، والإجراءات البولية الإضافية (معدل الأخطار النسبية = 0.996، قيمة الاحتمال = 0.991، ك = 0.816، قيمة الاحتمال = 0.665، اي = 2، 0).

**الاستنتاجات:** أشارت هذه الدراسة إلى أن عمليات تفتيت الحصى بالموجات الصدمية خارج الجسم وتفتيت الحصى بالمنظار ضرورية في علاج حصى الحالب، على الرغم من أن معدل التفتيت أعلى في تفتيت الحصى بالمنظار مقارنة بإجراءات تفتيت الحصى بالموجات الصدمية خارج الجسم. في الواقع، تعد المعدلات الإجمالية الحالية من الحصى أفضل في إجراء تفتيت الحصى بالمنظار.

**الكلمات المفتاحية:** تفتيت الحصى بالمنظار؛ تفتيت الحصى بالموجات الصدمية خارج الجسم؛ حصى الحالب؛ المضاعفات؛ الفشل؛ التحليل التلوي

### Abstract

**Objectives:** In this systematic review and meta-analysis, we sought to identify whether extracorporeal shockwave lithotripsy (ESWL) or ureteroscopic lithotripsy (URSL)

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is the most appropriate method for treating ureteral stones.

**Methods:** We identified relevant literature by searching the Google Scholar and PubMed databases in accordance with PRISMA guidelines. We focused on the outcomes of extracorporeal shockwave lithotripsy and ureteroscopic lithotripsy. For each method, we compared complications, hematuria, perforation, failure, stone clearance, initial stone-free, operating time, stone size, auxiliary procedures, and overall stone-free outcomes. Our analysis involved meta-analysis, heterogeneity testing, subgroup analysis, meta-regression sensitivity analyses, Egger's tests, Smoothed Variance Egger's (SVE) testing, and Smoothed Variance Thomson (SVT) testing. In addition, we detected publication bias for all outcomes related to the two procedures.

**Results:** Based on ten eligible studies, we conducted a meta-analysis on a total of 1509 patients. Extracorporeal shockwave lithotripsy was used to treat 677 patients; the remaining 832 patients were treated by the ureteroscopic lithotripsy procedure. Considering the meta-analysis statistical parameters including odds ratio (OR), standardized mean difference (SMD),  $Q$ ,  $I^2$  and their  $p$ -values, the overall stone-free, operating time, stone size outcomes were identified with significant OR, SMD, and  $Q$  values. The hematuria, failure, and stone clearance outcomes were determined to have significant  $Q$  values. The perforation and initial stone free outcomes had significant OR values. And, complications and auxiliary urinary procedures were not significant in terms of OR and  $Q$  values.

**Conclusions:** Analysis indicated that ESWL and URSL procedures are essential for the treatment of ureteral stones, even though the perforation rate is higher for URSL than for ESWL. Overall stone-free rates were better for the URSL procedure.

**Keywords:** Complication; Extracorporeal shockwave lithotripsy; Failure; Meta-analysis; Ureteral stone; Ureteroscopic lithotripsy

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## Introduction

The incidence of ureteral urolithiasis in West and South Asia ranges from 5% to 20%, thus implying that this disease is quite common. The common symptoms of ureteral stones include severe pain in the lower back, renal colic, bloody urine, nausea, vomiting, fever with chills, and foul-smelling cloudy urine. When medical treatments fail, the two most commonly reported replacement treatments are Extracorporeal Shock Wave Lithotripsy (ESWL) and Ureteroscopic

Lithotripsy (URSL) which are performed with rigid-flexible and semi-flexible lithotripters.<sup>1,2</sup>

ESWL uses severe energy shock waves to break urolithiasis into small pieces that can quickly pass through the urinary tract. This procedure does not require an incision. A lithotripter generates the shock waves, and in this procedure, there is no need to insert an instrument through the urethra.<sup>3</sup>

URSL is a highly effective and minimally invasive procedure for treating urolithiasis. In this procedure, a small telescope can be used to remove ureteral stones through the urethra and from the bladder. In contrast, ESWL is a non-invasive and safe procedure that does not require anesthesia or a hospital. This procedure has a lower success rate than the URSL procedure.<sup>4,5</sup>

URSL usually requires anesthesia and is associated with a number of postoperative complications, including bleeding, infection, ureteral damage, stricture, and failure.<sup>4</sup> Several randomized clinical trials (RCTs), prospective studies, and retrospective studies, were involved in the present meta-analysis.

We conducted this systematic review and meta-analysis to compare the efficacy of each of these procedures when treating ureteral stones based on the outcomes and complications associated with each procedure.

## Methods

We applied the PRISMA method (Preferences, Recording, Items for Systematic Reviews and Meta-Analysis) to perform a systematic search of the literature between 1st, 2017 and December 10th, 2021. We searched the Google Scholar and PubMed electronic databases for relevant articles for evaluation and data.<sup>6,7</sup> Searches were performed using the following descriptive Boolean query: Comparison AND (ESWL OR URSL) AND Lithotripsy AND (Ureterolithiasis OR Ureteral stones) AND Treatment.

To determine whether articles should be included or excluded from our analysis, we searched the "All field" option. In addition to examining titles, abstracts, reviews, and meta-analyses, two investigators independently examined the extracted studies. We excluded duplicate articles and unrelated full text articles from our analyses. The inclusion criteria were as follows: English language, RCTs, prospective studies, and retrospective studies that compared ESWL and URSL procedures. We included patients with ureteral calculi who had either been treated with ESWL or URSL based on whether the authors reported the following data: initial and overall stone-free rate; complications, especially hematuria and perforations that occurred during treatment; failure, the number of stones, and stone size. The exclusion criteria were as follows: unrelated or inadequate data, studies that were not written in English language; reviews, duplicate articles, and meta-analyses. According to our checklist, reported data relating to outcomes, complications, and stone-free clearance were stored in a Microsoft Excel file. Pooled estimates of odds ratio (OR) and SMD with 95% confidence intervals (CIs) were considered as measures of effect sizes.

The mean age of patients in the ESWL group ranged from  $33.04 \pm 11.46$  years to  $55 \pm 1.2$  years; this compared to  $35.80 \pm 12.09$  years to  $55.7 \pm 1.2$  years in the URSL group.

According to the information provided in the articles, the disappearance of ureteral stones was considered as a successful clinical outcome.

This meta-analysis was carried out by MetaMUMS software.<sup>8,9</sup> This is a tool developed in MATLAB version R2013a by Mashhad University of Medical Sciences that provided the perfect environment for the current meta-analysis. An analysis of eligible studies was performed in a spreadsheet file. Odds ratios (ORs) were calculated by pooling studies. Differences between studies' standard means (SMDs) with 95% confidence intervals (CIs) were calculated as effect sizes with 95% CIs. The random effects model was used to perform Cochran Q statistical tests and to determine the  $I^2$  index. A Q test with  $p < 0.05$  and an  $I^2$  value  $> 50\%$  indicated that heterogeneity existed between studies.<sup>10–13</sup> When heterogeneity was non-significant, a fixed-effect model was applied. For moderate and considerable heterogeneity, we applied subgroup analysis, meta-regression, and sensitivity analysis. A publication bias test was performed after the generation of funnel plots, followed by trim and fill analysis.<sup>12,14</sup>

Ten published articles were selected for analysis (10 for the ESWL technique and 10 for the URSL technique). Both methods were evaluated with regards to postoperative complications (especially hemorrhage and perforations), failure, initial stone free, auxiliary procedures, overall stone-free,

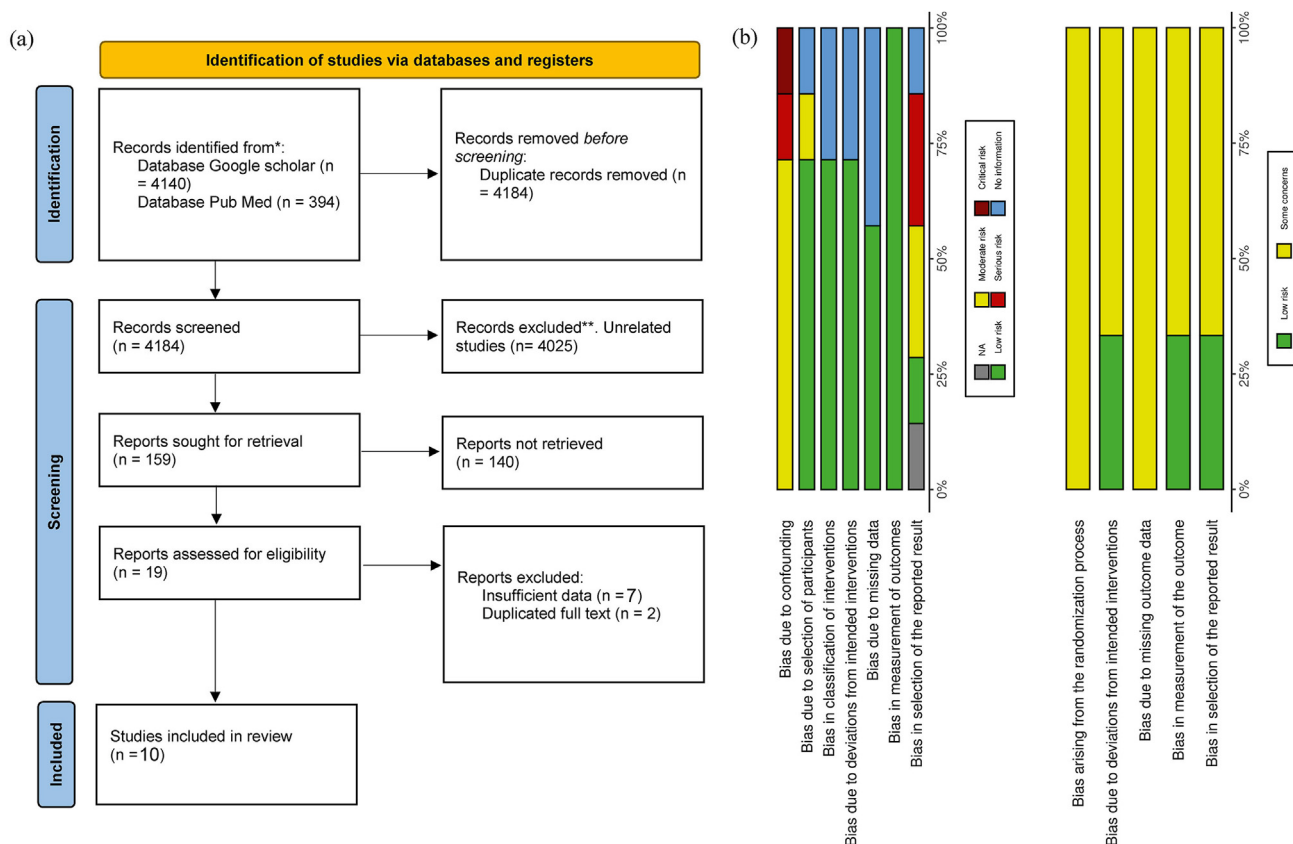
stone clearance rate, stone size, and operating time. Ten separate meta-analyses were performed in this study. A sensitivity analysis of eight complication parameters was performed to detect the sources of heterogeneity among studies. We used ROBINS-I for non-RCTs and ROB2 for RCTs and assessed the quality of the included articles.<sup>15,16</sup>

Abbreviations: OR, Odds ratio; URSL/URS, Ureteroscopic lithotripsy; ESWL, Extracorporeal shockwave lithotripsy; ISF, Initial and overall stone-free; AUP, Auxiliary procedure; RCT, Random controlled trial; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses; SMD, Standard mean difference; EML, Electromagnetic Lithotripter (Storz).

## Results

From the initial search criteria, 4534 titles were identified as being potentially relevant. Figure 1a depicts the process used to perform literature searches in accordance with the PRISMA guidelines. There were 677 ESWL patients and 832 URSL patients and the two procedures were analyzed to determine the effect of these two procedures on treatment outcomes. Of the final ten studies, five took place in Pakistan,<sup>1,2,5,17–19</sup> two in Nepal,<sup>4,20</sup> one in Japan,<sup>21</sup> and two in Egypt.<sup>22,23</sup> All of the studies reported the outcomes of both ESWL and URS lithotripsy procedures.

Three studies were RCTs (Sindhi et al.,<sup>5</sup> Jalbani et al.,<sup>17</sup> Bangash et al.<sup>1</sup>) and four were prospective studies



**Figure 1:** (a) PRISMA flowchart showing the approach taken for systematic review and meta-analysis. (b) Quality of non-RCT and RCT articles.

(Hamamoto et al.,<sup>21</sup> Rayamajhi et al.,<sup>4</sup> Joshi et al.,<sup>20</sup> Mostafa et al.<sup>23</sup>). Three studies were retrospective (Aboutaleb et al.,<sup>22</sup> Iqbal et al.,<sup>19</sup> Ur Rehman et al.<sup>18</sup>). Table 1 summarizes the characteristics, demographics, type of procedures, outcomes, complications, hematuria, perforation, failure, stone clearance, initial stone-free (ISF), operating time, stone size, auxiliary procedures, and overall stone-free outcomes for the two treatment procedures. The quality of the articles is presented in Figure 1b.

Postoperative peri renal, subcapsular and subcutaneous, false passage and urethral damage, Steinstrasse, ecchymosis, liver dysfunction, fever, sepsis, pain, skin bruises, hematoma, and subcutaneous emphysema were not considered due to the lack of sufficient data in the selected studies (Table 2). Furthermore, it is impossible to conduct a meta-analysis and meta-regression with fewer than three studies; therefore, these processes were only performed for hematuria, failure, stone clearance, ISF, AUP, stone size, and overall stone-free; subgroup analyses were not completed. Sensitivity analysis was performed in the meta-analysis of hematuria, stone clearance, ISF, and overall stone-free parameters.

To compare ESWL and URS lithotripsy procedures, we applied eleven meta-analyses on parameters, complications, hematuria, perforation, failure, stone clearance, ISF, operating time, stone size, auxiliary procedures and overall stone-free outcomes.

A meta-analysis of complications comparing ESWL and URS lithotripsy procedures obtained the following results, as reported in Figure 2a: OR = 0.780, LL = 0.501, UL = 1.212,  $p$ -value = 0.269,  $Q$  = 13.465,  $p$ -value = 0.062,  $I^2$  = 48.011.

Analysis showed that ESWL and URS lithotripsy procedures do not have any specific advantage in terms of complications since the  $p$ -value was not significant; there was no significant heterogeneity among the studies since the  $p$ -value was not significant; although the heterogeneity was moderate at 48.011%. Figure 2b shows a funnel plot for the detection of publication bias; this proved that there was no publication bias among the ten studies. Egger's tests (intercept = 0.980,  $p$ -value = 0.450) demonstrated that there was no publication bias among the studies. The SVE test (intercept = -0.831,  $p$ -value = 0.753) failed to demonstrate publication bias among the studies. The SVT test (intercept = -0.613,  $p$ -value = 0.816) also failed to demonstrate publication bias among the selected studies.

Due to moderate heterogeneity, we applied sensitivity analysis by removing the study by Aboutaleb; analysis yielded the following results: OR = 0.741, LL = 0.558, UL = 0.984,  $p$ -value = 0.038,  $Q$  = 5.689,  $p$ -value = 0.459,  $I^2$  = 0.

Analysis showed that the complications associated with URS lithotripsy were significantly more common than for ESWL. Heterogeneity tests showed that there was no significant heterogeneity among the studies (0%). Sensitivity tests showed that removing the study by Aboutaleb could explain 100% ( $R^2$ ) of heterogeneity among the studies.

Our meta-analysis of hematuria complications between ESWL and URS lithotripsy procedures yielded the following results, as shown in Figure 2c: OR = 0.782, LL = 0.263, UL = 2.320,  $p$ -value = 0.657,  $Q$  = 19.056,  $p$ -value = 0.001,  $I^2$  = 79.01.

Analysis showed that ESWL and URS lithotripsy procedures do not have any significant advantage over each

other in terms of hematuria complications. Furthermore, there was considerable heterogeneity among the studies (79.01%). This showed that sensitivity analysis should be applied when performing subgroup meta-analysis and meta-regression. However, since the source of heterogeneity was not identified, we did not report these results. Figure 2d shows a funnel plot for the detection of publication bias; no publication bias was detected between studies. Egger's test (intercept = -5.080,  $p$ -value = 0.138) failed to identify publication bias among the studies. The SVE test (intercept = 1.115,  $p$ -value = 0.677) failed to identify publication bias among the studies. The SVT test (intercept = -0.993,  $p$ -value = 0.710) failed to identify publication bias among the studies.

Due to considerable levels of heterogeneity, we applied a sensitivity test by removing studies from Aboutaleb and Iqbal; the results were as follows: OR = 0.348, LL = 0.129, UL = 0.939,  $p$ -value = 0.037,  $Q$  = 3.026,  $p$ -value = 0.220,  $I^2$  = 33.91.

Analysis showed that hematuria complications in URS lithotripsy were more significantly more common than for ESWL. Furthermore, heterogeneity tests showed no substantial heterogeneity among the studies (33.91%). Sensitivity analysis showed that removing the studies by Aboutaleb and Iqbal explained 77.04% ( $R^2$ ) of the heterogeneity.

Our meta-analysis of perforation complications compared ESWL and URS lithotripsy procedures (Figure 2e) and yielded the following data: OR = 0.13, LL = 0.034, UL = 0.494,  $p$ -value = 0.003,  $Q$  = 0.159,  $p$ -value = 0.997,  $I^2$  = 0. These results show that perforation complications are significantly more common in URS lithotripsy than in ESWL. Furthermore, there was no significant heterogeneity among studies. Figure 2f shows a funnel plot for publication bias detection and demonstrates clear bias between the published studies. Egger's test (intercept = 10.793,  $p$ -value = 0.01) proved the existence of publication bias. The SVE test (intercept = -1.1427,  $p$ -value = 0.105) did not provide evidence of publication bias. The SVT test (intercept = -1.1427,  $p$ -value = 0.105) did not provide evidence of publication bias. Due to the detection of publication bias, we applied the random Trim & fill technique. Two new studies were identified (Figure 2f); random-based meta-analysis following the addition of the two new studies yielded the following results: OR = 0.113, LL = 0.036, UL = 0.349,  $p$ -value < 0.001,  $Q$  = 0.351,  $p$ -value = 0.999,  $I^2$  = 0. These results show that complication perforation is significantly more common in URS lithotripsy than in the ESWL procedure. There was no significant heterogeneity among these studies.

Meta-analysis of procedural failure (conversion procedures or stone migration) was used to compare ESWL and URS lithotripsy procedures, yielding the following results (Figure 2g): OR = 0.329, LL = 0.029, UL = 3.712,  $p$ -value = 0.369,  $Q$  = 22.659,  $p$ -value < 0.001,  $I^2$  = 77.934. These results showed that neither the ESWL or URS lithotripsy procedure have any specific advantage over the other in terms of procedural failure. Furthermore, there was significant heterogeneity between studies (77.934%). We did not report results arising from meta-regression and subgroup analysis since the source of heterogeneity was not

**Table 1: Demographic characteristics of patients in studies treated by ESWL vs. URS lithotripsy procedures (n = 10 studies).**

Author	Design	Intervention	Method	Patients	Age	M/F	Stone size	Diagnosis	Efficacy	Stone clearance	Assessment (month)
Sindhi, 2021	RCT	ESWL	EM L	53	42.2	NA	12.6	KUB Sono	39	30	NA
		URS	Laser	53	10.2 41.9	NA	4.5 14.2	KUB Sono	50	32	NA
Joshi, 2017	Prospective	ESWL	EM L	45	10.4 33.04 11.46	M/F = 1.64	50 11.03 2.65	KUB Sono	NA	40	1 month
		URS	Laser	45	35.8 12.01	M/F = 2.46	11.41 2.90	KUB Sono	NA	37	1 month
Rayamajhi, 2020	Prospective	ESWL	EM L	50	41.28 15.3	32/18	0.96 8.58	KUB Sono	NA	28	
		URS	Laser	50	42.84 16.1	29/21	0.96 8.44	KUB Sono	NA	49	1.5 months
Mostafa, 2019	Prospective	ESWL	EM L	30	37.83 11.8	23/7	0.96 1.25	KUB Sono	NA	20	NA
Aboutaleb, 2017	Retrospective	URS	Laser	30	40.23 2.65	24/6	1.24 0.11	KUB Sono	NA	24	NA
		ESWL	EM L	66	43.6	46/20	17.9	KUB Sono	NA	NA	NA
		URS	Laser	81	2 44.3	55/26	18.2	KUB Sono	NA	NA	NA
Iqbal, 2018	Retrospective	ESWL	EM L	200	16.7 39.12 13.36	161/137	3 10.47 3.7	KUB Sono	NA	19	NA
		URS	Laser	200	43.13 13.65	39/63	13.6	KUB Sono	NA	18	NA
Hamamoto, 2018	Retrospective	ESWL	EM L	61	55 1.2	45/16	6 9.3 0.4	KUB Sono	NA	44	6 months
		URS	Laser	201	57.7 0.9	150/51	9.1 1.5	KUB Sono	NA	177	6 months
Ur Rehman, 2020	Retrospective	ESWL	EM L	75	41.21 3.15	45/30	10.51 2.31	KUB Sono	NA	71	NA
		URS	Laser	75	40.98 3.73	47/28	24.19 1.92	KUB Sono	NA	69	NA
Bangash, 2021	RCT	ESWL	EM L	50	40.78 10.2	36/14	12.57 1.67	KUB Sono	34	NA	1 week
		URS	Laser	50	38.52 10.44	19/11	12.44 1.67	KUB Sono	38	NA	1 week
Jalbani, 2019	RCT	ESWL	EM L	47	34.57 13.30	NA	NA	KUB Sono	39	NA	3 months
		URS	Laser	47	36.4 13.75	NA	NA	KUB Sono	38	NA	3 months

**Table 2: Complications of patients in studies treated by ESWL vs. URS lithotripsy procedures (n = 10 studies).**

Complications	Jalbani		Bangash		Ur Rehman		Hamamoto		Igbal		Aboutaleb	
	URSL	ESWL	URSL	ESWL	URSL	ESWL	URSL	ESWL	URSL	ESWL	URSL	ESWL
Pain	-	-	-	-	-	-	-	-	-	-	-	-
UTI	-	-	-	-	-	-	-	-	-	-	-	-
Obstruction	-	-	-	-	-	-	-	-	-	-	-	-
Ecchymosis	-	-	-	-	-	-	-	-	-	-	-	-
Fever	-	-	-	-	-	-	-	-	-	-	-	-
Hematuria	-	-	-	-	-	-	-	-	+	+	+	+
Headache	-	-	-	-	-	-	-	-	-	-	-	-
Steinstrasse	-	-	-	-	-	-	-	-	-	+	+	+
Ureteral injury	-	-	-	-	-	-	-	-	-	-	-	-
Stone migration	-	-	-	-	-	-	-	-	-	-	-	-
PR hematoma	-	-	-	-	-	-	-	-	-	-	-	-
Skin bruise	-	-	-	-	-	-	-	-	-	-	-	-
False passage	-	-	-	-	-	-	-	-	-	-	-	-
Perforation	-	-	-	-	-	-	-	-	+	-	+	+
Colic	-	-	-	-	-	-	+	+	-	-	+	+
Mucosal abrasion	-	-	-	-	-	-	-	-	+	-	-	-
SC hematoma	-	-	-	-	-	-	-	+	-	-	-	-
Sepsis	-	-	-	-	-	-	-	-	+	+	-	-
Liver dysfunction	-	-	-	-	-	-	+	-	-	-	-	-
Mild	-	-	-	-	+	+	-	-	-	-	-	-
Moderate	-	-	-	-	+	+	-	-	-	-	-	-
Severe	-	-	-	-	+	+	-	-	-	-	-	-

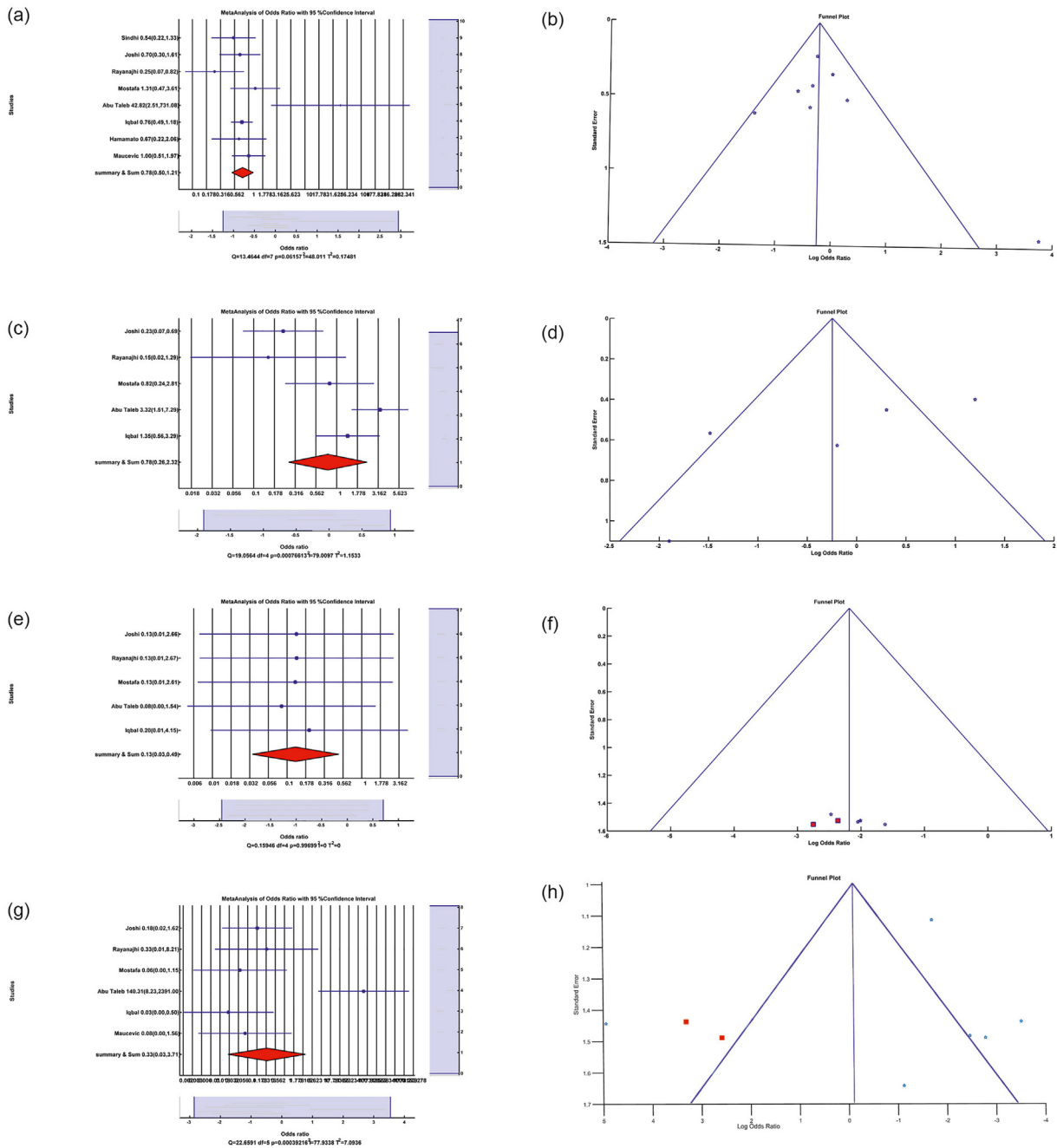
  

Complications	Mostafa		Rayamajhi		Joshi		Sindhi
	URSL	ESWL	URSL	ESWL	URSL	ESWL	URSL
Pain	-	-	-	-	+	+	+
UTI	-	-	-	-	-	-	+
Obstruction	-	-	-	-	-	-	+
Ecchymosis	-	-	-	-	+	+	-
Fever	+	-	-	-	-	-	-
Hematuria	+	+	+	+	+	-	-
Headache	-	-	-	-	+	-	-
Steinstrasse	-	+	-	+	+	-	-
Ureteral injury	-	-	-	-	-	-	-
Stone migration	-	-	+	-	-	-	-
PR hematoma	+	+	-	-	-	-	-
Skin bruise	-	+	-	-	-	-	-
False passage	+	-	-	-	-	-	-
Perforation	-	-	-	-	-	-	-
Colic	-	-	-	-	-	-	-
Mucosal abrasion	-	-	+	-	-	-	-
SC hematoma	-	-	-	-	-	-	-
Sepsis	-	-	-	-	-	-	-
Liver dysfunction	-	-	-	-	-	-	-
Mild	-	-	-	-	-	-	-
Moderate	-	-	-	-	-	-	-
Severe	-	-	-	-	-	-	-

“-” demonstrates that the study did not report any information about complications, “+” demonstrates that the study reported some information about complications.

detected. Figure 2h shows a funnel plot describing publication bias detection; this proves that there was publication bias among the studies. Egger’s test (intercept = 1.044, *p*-value = 0.899) did not identify publication bias among the studies. The SVE test (intercept = -6.619, *p*-value = 0.305) did not identify publication bias among the studies. The SVT test (intercept = -3.069, *p*-value = 0.615) did not identify publication bias among the studies. Due to the detection of publication bias on the funnel plot, we applied

the random Trim & fill technique. Two new studies were identified (Figure 2h). Random-based meta-analysis was performed after adding the two new studies; this yielded the following results: OR = 0.904, LL = 0.099, UL = 8.249, *p*-value = 0.929, Q = 34.800, *p*-value < 0.001, I<sup>2</sup> = 79.885. These results show that the two techniques were similar in terms of procedural failure with no significant difference. Furthermore, there was significant heterogeneity among studies.

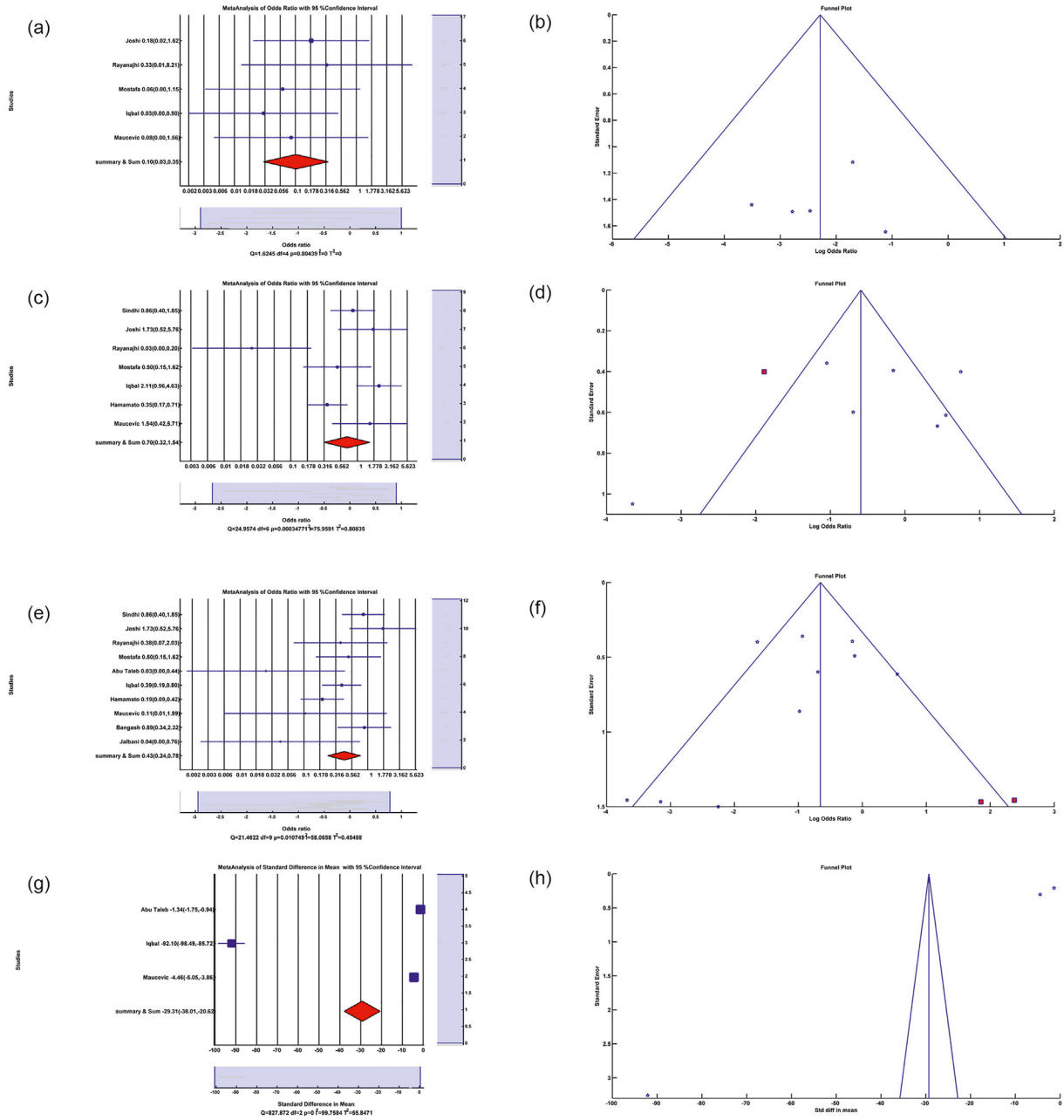


**Figure 2:** Forest plots and funnel plots for the following outcomes between ESWL and URS lithotripsy procedures; (a) complications-forest plot, (b) complications-funnel plot (c) hematuria-forest plot, (d) hematuria-funnel plot, (e) perforation-forest plot, (f) perforation-funnel plot, (g) failure-forest plot, and (h) failure-funnel plot outcomes.

With regards to sensitivity analysis, the removal of the study by Aboutaleb et al. led to the following results (Figure 3a): OR = 0.102, LL = 0.030, UL = 0.347,  $p$ -value < 0.001,  $Q = 1.625$ ,  $p$ -value = 0.804,  $I^2 = 0$ . These results showed that the study by Aboutaleb and colleagues was the source of heterogeneity and could explain the origin of heterogeneity ( $R^2 = 100\%$ ). By removing this study, analysis proved that procedural failure in the URS lithotripsy procedure was significantly more common than in the ESWL procedure. Furthermore, there was no significant heterogeneity among studies after removing the

study by Aboutaleb et al. The removal of the study by Aboutaleb (Figure 3b) showed that there was no publication bias between the studies.

Meta-analysis of stone clearance was next used to compare ESWL and URS lithotripsy and yielded the following results (Figure 3c): OR = 0.699, LL = 0.317, UL = 1.54  $p$ -value = 0.374,  $Q = 24.957$ ,  $p$ -value < 0.001,  $I^2 = 75.959$ . These results showed that ESWL and URS were similar in terms of stone clearance. Furthermore, there was significant heterogeneity between studies (75.959%). Subgroup analysis, meta-regression, and



**Figure 3:** Forest plots and funnel plots for the following outcomes between ESWL and URS lithotripsy procedures; (a) sensitivity analysis on a failure-forest plot, (b) sensitivity analysis on a failure-funnel plot (c) stone clearance-forest plot, (d) stone clearance-funnel plot, (e) overall stone-free-forest plot, (f) overall stone-free-funnel plot, (g) operating time-forest plot, and (h) operating time-funnel plot outcomes.

sensitivity analysis did not explain the source of heterogeneity; consequently, these results are not reported. Figure 3d presents a funnel plot of publication bias detection and proves the existence of publication bias between studies. Egger’s test (intercept =  $-1.721$ ,  $p$ -value =  $0.545$ ) did not identify publication bias among the studies. The SVE test (intercept =  $2.233$ ,  $p$ -value =  $0.389$ ) did not identify publication bias among the studies. The SVT test (intercept =  $1.252$ ,  $p$ -value =  $0.619$ ) did not identify publication bias among the studies. The random Trim & fill method did not identify any missed studies in terms of publication bias. One new study is shown in Figure 3d;

random-based meta-analysis after adding this new study resulted in the following data: OR =  $0.553$ , LL =  $0.245$ , UL =  $1.250$ ,  $p$ -value =  $0.154$ ,  $Q = 38.646$ ,  $p$ -value  $\leq 0.001$ ,  $I^2 = 81.887$ . These results showed that there was no significant difference between the two studies in terms of stone clearance. Furthermore, there was significant heterogeneity among studies. Due to significant heterogeneity among the studies, we applied sensitivity analysis by removing the study by Rayamajhi. The results were as follows: OR =  $0.935$ , LL =  $0.489$ , UL =  $1.788$ ,  $p$ -value =  $0.840$ ,  $Q = 14.131$ ,  $p$ -value  $\leq 0.015$ ,  $I^2 = 64.616$ . These results showed that there was no significant difference between the two studies with



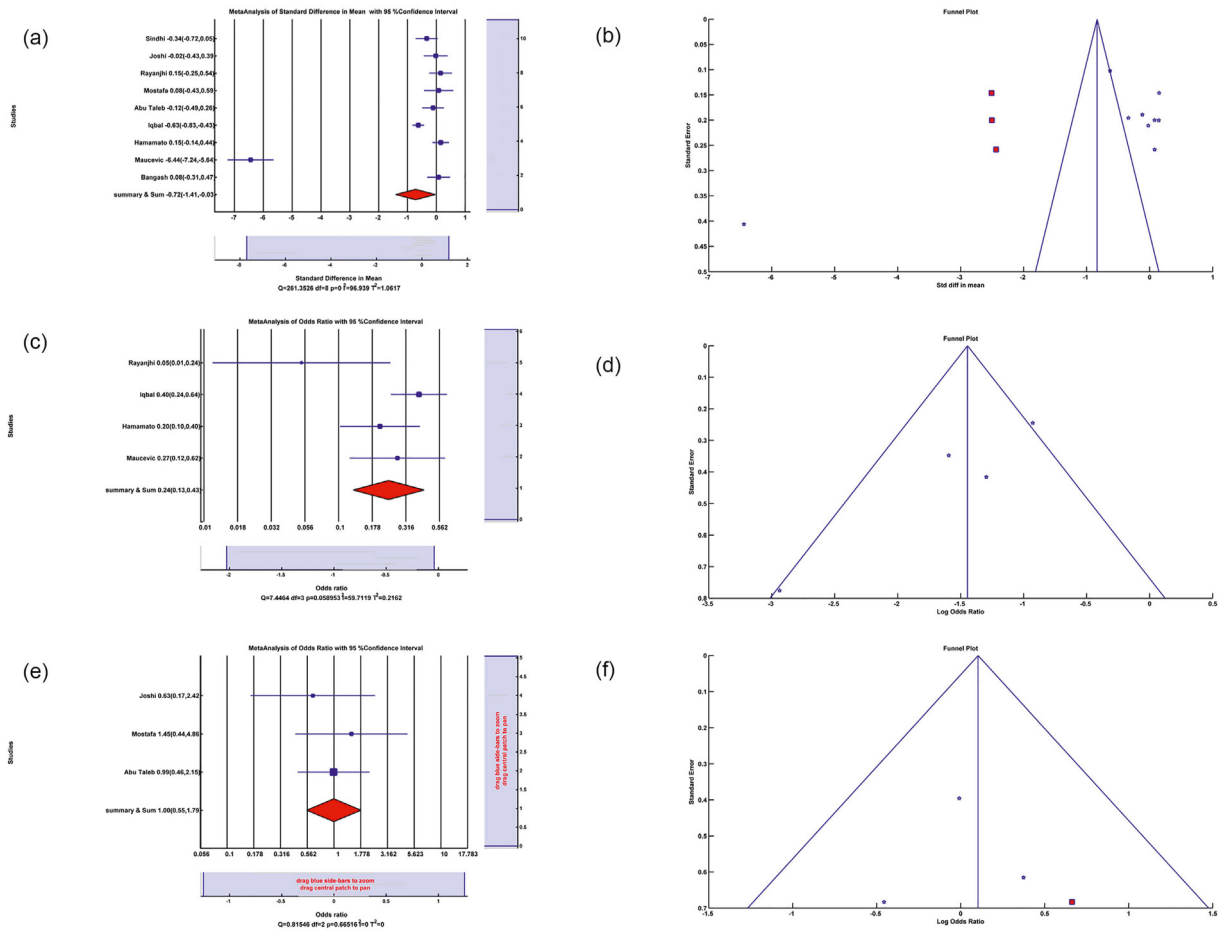
regards to stone clearance. Furthermore, there was moderate significant heterogeneity among studies. Sensitivity analysis showed that removing the study by Rayamajhi could explain (49.5%) of the heterogeneity ( $R^2$ ).

Meta-analysis of overall stone-free parameters compared ESWL and URS lithotripsy and yielded the following results (Figure 3e): OR = 0.428, LL = 0.236, UL = 0.776,  $p$ -value = 0.005,  $Q$  = 21.462,  $p$ -value = 0.011,  $I^2$  = 58.066. These results show that in terms of overall stone-free outcome, the URS lithotripsy procedure was significantly better than the ESWL procedure. Furthermore, there was significant heterogeneity (58.066%). Subgroup analysis, meta-regression, and sensitivity analysis did not explain the source of heterogeneity; therefore, we did not report these results. Figure 3f shows a funnel plot presenting publication bias detection; this demonstrated the existence of publication bias between studies. Egger's test (intercept = -1.321,  $p$ -value = 0.270) did not identify any publication bias among the studies. The SVE test (intercept = -0.633,  $p$ -value = 0.771) did not identify any publication bias among the studies. The SVT test (intercept = -1.843,  $p$ -value = 0.406) did not identify any publication bias among the studies. The random Trim & fill method identified missing studies in terms of publication bias. Two new studies were found, as shown in Figure 3f. Applying random-based meta-analysis after adding two new studies yielded the following results: OR = 0.519, LL = 0.275, UL = 0.982,  $p$ -value = 0.044,  $Q$  = 29.087,  $p$ -value  $\leq$  0.002,  $I^2$  = 62.182. These results showed that in terms of overall stone-free outcome, URS lithotripsy was significantly better than the ESWL procedure. Furthermore, there was significant considerable heterogeneity between studies. Due to the moderate heterogeneity among studies, we applied sensitivity analysis by removing the studies by Joshi, Aboutaleb, Maucevic, and Jalbani; the results were as follows: OR = 0.469, LL = 0.279, UL = 788,  $p$ -value = 0.004,  $Q$  = 9.250,  $p$ -value  $\leq$  0.015,  $I^2$  = 45.950. These results showed in terms of overall stone-free outcome, URS lithotripsy was significantly better than the ESWL procedure. Furthermore, there was moderate significant heterogeneity among studies (45.95%). Sensitivity analysis showed that removing the studies by Joshi, Abu Taleb, Maucevic, and Jalbani could explain 59.16% of the heterogeneity ( $R^2$ ).

Meta-analysis of operating time was used to compare ESWL and URS, yielding the following results (a forest plot is shown in Figure 3g): SMD = -29.314, LL = -38.008, UL = -20.619,  $p$ -value  $<$  0.001,  $Q$  = 827.872,  $p$ -value  $<$  0.001,  $I^2$  = 99.758. These showed that operating time for URS was significantly longer than for ESWL. Tests revealed significant heterogeneity (99.758%). Figure 3h shows a funnel plot depicting publication bias detection; no publication bias was detected. Egger's test (intercept = -29.945,  $p$ -value = 0.016) identified publication bias among the studies. The SVE test (intercept = -215.483,  $p$ -value = 0.100) did not identify publication bias among studies. The SVT test (intercept = -207.644,  $p$ -value = 0.104) did not identify publication bias among the studies. Furthermore, the random Trim & fill approach did not identify any missing studies in terms of publication bias. Sensitivity analysis was not applied since the number of studies was  $<$ 3.

Meta-analysis was then used to compare stone size between ESWL and URS lithotripsy, yielding the following results (a forest plot is shown in Figure 4a): SMD = -0.723, LL = -1.412, UL = -0.034,  $p$ -value = 0.04,  $Q$  = 261.353,  $p$ -value  $<$  0.001,  $I^2$  = 96.939. These results showed that the stone size for URS lithotripsy was significantly larger than for ESWL. Tests of heterogeneity were significant and proved considerable heterogeneity (96.939%). Figure 4b presents a funnel plot for publication bias detection, demonstrating publication bias between studies. Egger's test (intercept = -5.644,  $p$ -value = 0.352) did not identify publication bias among the studies. The SVE test (intercept = -0.327,  $p$ -value = 0.922) did not identify publication bias among the studies. The SVT test (intercept = -2.566,  $p$ -value = 0.452) did not identify publication bias among the studies. Furthermore, the random Trim & fill technique identified three missed studies in terms of publication bias. Three new studies were found, as shown in Figure 4b. Applying random-based meta-analysis after adding the three new studies yielded the following results: SMD = -1.182, LL = -1.931, UL = -0.432,  $p$ -value = 0.002,  $Q$  = 571.997,  $p$ -value  $<$  0.001,  $I^2$  = 98.077. These results showed that for overall stone-free analysis, the URS lithotripsy procedure was significantly better than the ESWL procedure. Furthermore, there was considerable significant heterogeneity among studies (98.077%). Due to considerable heterogeneity, we applied sensitivity random meta-analysis by removing studies by Iqbal and Maucevic, yielding the following results: SMD = 0.007, LL = -0.136, UL = 0.15,  $p$ -value = 0.925,  $Q$  = 5.164,  $p$ -value  $<$  0.523,  $I^2$  = 0. These results show that in terms of overall stone-free analysis, the URS lithotripsy and ESWL procedures were not significantly different. Furthermore, the heterogeneity was removed. Thus, removing studies by Iqbal and Maucevic explained (100%) of heterogeneity ( $R^2$ ).

Next, meta-analysis of initial stone-free (ISF) status was used to compare ESWL and URS, yielding the following results (Figure 4c): OR = 0.236, LL = 0.128, UL = 0.433,  $p$ -value  $<$  0.001,  $Q$  = 7.446,  $p$ -value  $\leq$  0.059,  $I^2$  = 59.712. These results showed that for ISF, URS lithotripsy was significantly better than ESWL. Furthermore, there was significant moderate heterogeneity (59.712%). A funnel plot is shown in Figure 4d. Meta-regression and subgroup analysis did not explain the source of heterogeneity. Egger's test (intercept = -3.588,  $p$ -value = 0.074) did not identify publication bias among the studies. The SVE test (intercept = 0.540,  $p$ -value = 0.680) did not identify publication bias among the studies. The SVT test (intercept = 0.632,  $p$ -value = 0.632, did not identify publication bias among the studies. Furthermore, the random Trim & Fill technique did not find any missed studies in terms of publication bias. Due to moderate heterogeneity, we applied sensitivity analysis by removing the article by Rayamajhi; this yielded the following results: OR = 0.300, LL = 0.199, UL = 0.454,  $p$ -value  $\leq$  0.001,  $Q$  = 2.562,  $p$ -value = 0.278,  $I^2$  = 21.938. These results showed that for ISF, URS was significantly better than ESWL. Furthermore, there was less heterogeneity (21.938%). Sensitivity analysis showed that removing the study by Rayamajhi could explain 85.83% of heterogeneity ( $R^2$ ).



**Figure 4:** Forest plots and funnel plots for the following outcomes between ESWL and URS lithotripsy procedures; (a) stone size-forest plot, (b) stone size-funnel plot, (c) initial stone-free-forest plot (d) initial stone-free-funnel plot, (e) auxiliary procedure (AUP)-forest plot, and (f) auxiliary procedure (AUP)-funnel plot.

Finally, we performed meta-analysis for auxiliary urinary procedures (AUP) to compare ESWL and URSL, yielding the following results (Figure 4e): OR = 0.996, LL = 0.555, UL = 1.791,  $p$ -value = 0.991,  $Q = 0.816$ ,  $p$ -value = 0.665,  $I^2 = 0$ . These results showed that ESWL and URS lithotripsy procedures were not significantly different in terms of AUP. Furthermore, there was no significant heterogeneity among the studies. Figure 4f shows a funnel plot demonstrating that there was no publication bias between studies. Egger’s test (intercept =  $-0.333$ ,  $p$ -value = 0.900) did not identify any publication bias among the studies. The SVE test (intercept =  $-0.944$ ,  $p$ -value = 0.719) did not identify any publication bias among the studies. The SVT test (intercept =  $-0.944$ ,  $p$ -value = 0.719) did not identify any publication bias among the studies. Furthermore, the random Trim & Fill technique found one missed study in terms of publication bias. One new study was identified, as shown in Figure 4f. The application of random-based meta-analysis after adding one new study yielded the following results: OR = 1.109, LL = 0.648, UL = 1.898,  $p$ -value = 0.705,  $Q = 1.614$ ,  $p$ -value = 0.656,  $I^2 = 0$ . These results showed that ESWL and URS lithotripsy procedures were not significantly different in terms of AUP. Furthermore, there was no significant heterogeneity among the studies.

**Discussion**

We found no evidence for differences between URSL and ESWL in terms of complications, failure, AUP, hematuria, and stone clearance with regards to treating ureteral stones. According to our results, ureteral perforation, ISF, and overall stone free status were better for the URS procedure than for the ESWL procedure. URSL, on the other hand, had a higher overall stone-free rate than the ESWL procedure, even though both techniques have high success rates. Moreover, although failures (converted procedures or migrated stones from the ureter into the calyces) were identified as sources of publication bias; removing the study by Aboutaleb<sup>22</sup> led to no publication bias between the remaining studies.

ESWL and URS lithotripsy were found to be active procedures for the treatment of ureteral stones as indicated by the findings of this study, even though perforation rates and operating times were greater for URS than for ESWL procedures. Furthermore, overall stone-free rates were also better for the URS lithotripsy procedure. Larger stone sizes are usually encountered in URS procedures.

In reviewing the history of urolithiasis treatment in the literature, the first patient was treated by extracorporeal shockwaves 35 years ago. However, surgical intervention was still required for the removal of remaining fragmented stones.

After seven years of experimental work, this procedure was developed and it became possible to treat the stones effectively by the ESWL procedure on February 7, 1980. Three years later, the ESWL Lithotripter HM3 method became accepted worldwide.<sup>24</sup> Subsequently, pneumatic or laser lithotripters were performed for urolithiasis by ureteroscopy.

While traditional treatments for urolithiasis still exist, there are several challenges for treating the disease effectively with both new and traditional methods. Some authors favor ESWL for treating urolithiasis when compared to the URS Lithotripsy procedure; other authors have the converse view.

Only three systematic reviews and meta-analyses have been published on the comparison of ESWL and URS lithotripsy.<sup>25–27</sup> Yang et al. analyzed 14 studies, Xu analyzed 13 studies, and Jung analyzed 18 studies; these authors all compared the outcomes of ESWL and URS lithotripsy procedures. The two studies failed to report failure and conversion rates. In our analysis, the two studies were not significantly different in terms of failure, stone clearance, hematuria, or AUP complications. As an initial procedure for managing urolithiasis, Yang concluded that URS lithotripsy was safe. These authors concluded that the URSL procedure was secure with a short operating time and a better stone-free rate. These researchers concluded that their study was heterogeneous; thus, meta-regression was not employed in their study.<sup>25</sup> Xu reported a reduced stone-free rate and a shorter operating time for ESWL when compared to URSL procedures, as in our study. Postoperative complications were less prevalent for the ESWL procedure in Xu's study. However, this finding did not concur with our present conclusions.<sup>26</sup>

URS lithotripsy was considered in the meta-analysis by Yang and was associated with a longer operation time and greater postoperative complications due to the invasiveness of the procedure. In contrast, ESWL is a relatively advanced procedure and is associated with significantly higher stone-free rates and a significantly lower repeat treatment rate than our results. According to Yang's study, there was a high failure rate for ESWL, particularly for large, distal stones. Furthermore, fewer complications were found to be associated with the ESWL procedure, and no significant anesthesia was required for ESWL, thus making this the treatment of choice for ureteral stones.<sup>25</sup>

Heterogeneity tests in the present meta-analysis indicated no significant differences between complication rate and the efficiency quotient, although ESWL and URSL had significantly different stone-free rates and operation times. In spite of the fact that both URSL and ESWL have their own advantages, URSL has a shorter operating time and a higher stone-free rate, making it a more efficient and safe method to treat ureteric stones.<sup>25</sup> In our study, the operation time for the URS procedure was greater than for ESWL procedures.

In a previous study, Xu et al. investigated the effectiveness of these procedures for treating ureteral calculi. Based on the meta-analysis performed by Xu et al., stone-free and repeated treatment rates, postoperative complications and operation time were significantly different between patients receiving ESWL and URS lithotripsy. There were no significant differences in the stone-free or repeated treatment rates after treatment, according to Xu et al. Postoperative stone-free rates, complication rates, and operation times were significantly lower following extracorporeal shock wave

lithotripsy than reported in Yang's study. Xu's study reported that hospital stays were shorter for URS procedures; however, we could not perform this analysis in the current study because we had a small sample size (<3).<sup>26</sup> Lower patient satisfaction, a higher repeated treatment rate, a reduced number of postoperative complications, and shorter operative times were associated with ESWL than for URSL, according to Xue et al.

A systematic review and meta-analysis was published by Jung in 2021 and analyzed the two procedures according to large ureteral stone size in RCT and non-RCT articles. These authors reported the retreatment rate for the two procedures. Stone-free rate (SFR) was high for URSL and retreatment groups. These authors performed subgroup analysis for non-RCT articles and demonstrated superior results in a group of URSL patients. Our meta-analysis was conducted on all complication parameters for the two procedures without specifically focusing on large stones. In addition, Jung's study did not report any tests for publication bias in their meta-analysis. In contrast, our study determined all complication parameters clearly and extensively, and performed different tests for publication bias (i.e., Egger's test, the SVE test, and the SVT test); we also determined heterogeneity, performed sensitivity analysis, and applied the Trim & Fill technique for reanalysis.<sup>27</sup> On the other hand, Fu et al. advised that for a subgroup variable, each subgroup should have feature more than three studies to have sufficient statistical power; we also considered this criteria.<sup>10,28</sup> However, Jung had the lowest statistical power in their subgroups, did not perform sensitivity analyses, and did not perform comprehensive statistical analysis. Moreover, we performed sensitivity analysis of eight outcome parameters to detect the heterogeneities of all types of studies in our meta-analysis that could be explained and corrected. Sensitivity analysis showed that complications associated with URS lithotripsy were more significantly more common than for ESWL. Hematuria was significantly more common for URS lithotripsy than for ESWL. Procedural failure was significantly more common for URS lithotripsy than for ESWL. Stone clearance rate was not significantly different when compared between the two techniques. Overall stone-free rate was significantly better for the URS lithotripsy procedure than for the ESWL procedure. Furthermore, in terms of ISF, the URSL procedure was significantly better than the ESWL procedure.

Meta-analysis of perforation complications showed that perforations were more significantly common in URS lithotripsy than ESWL procedures. Furthermore, there was no significant difference between the two procedures in terms of AUP.

There were some limitations to the current study that need to be considered. Considering that systematic reviews may have unavoidable publication bias, we excluded unpublished articles, non-English studies, and conference reports from our analysis. However, the trim and fill algorithm estimated that some studies were missed due to the fact that unpublished articles, non-English studies, and conference reports were excluded. This study used graphical funnel plots to analyze publication bias.

Several studies were retrospective; therefore, urological surgeons with varying surgical and treatment skills had participated in the included studies; this could have influenced the overall results of our meta-analysis. We used three RCTs in our meta-analysis. Based on ethical considerations

for future systematic reviews and meta-analyses, it is necessary to perform more RCT studies with sufficient sample sizes to produce robust results.

ESWL has been proven to be the best method for reducing operation time and minimizing perforation rate in the current meta-analysis. The URSL procedure offers better overall stone-free and stone-size results than the ESWL procedure, with equal results for ISF, failure, stone clearance, AUP, and hematuria complications.

## Conclusion

This study indicated that ESWL and URS lithotripsy procedures are essential for ureteral stone treatment, even though the perforation rate and stone size were higher in URS than for ESWL procedures. Overall stone-free rates were better for URS than for the ESWL lithotripsy procedure. However, stone clearance failure, the duration of operating times, AUP, and hematuria complications did not differ significantly between the two techniques. This study also showed that both procedures can be performed successfully to treat ureteral stones.

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## Conflict of interest

The authors have no conflict of interest to declare.

## Ethical approval

This article does not contain any studies with human participants or animals performed by any of the authors.

## Authors contributions

BS, MaS, and MoS conceived and designed the study, conducted the research, provided research materials, and collected and organized the data. MaS and MoS performed the numerical calculations and determined the experimental outcomes. BS, MaS, and MoS wrote the initial and final draft of the article. All authors discussed and aided in interpreting the results and contributed to the final manuscript. All authors have critically reviewed and approved the final draft and are responsible for the content and similarity index of the manuscript.

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