

## Supine is Superior to Prone Position in Treating the Distal Ureteral Calculi During Extracorporeal Shockwave Lithotripsy: An Updated Meta-Analysis

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**Purpose:** Although extracorporeal shockwave lithotripsy (SWL) has been confirmed to be effective in treating ureteral stone, a definitive conclusion on which patient's position is the optimal option during SWL treatment remains unclear. We, therefore, performed this updated meta-analysis to further clarify it.

**Materials and Methods:** PubMed, Embase, and Cochrane library were performed to capture all potentially eligible studies from their inception to October 2020. After screening eligible studies, extracting essential data, and assessing the risk of bias, we used STATA 14.0 to complete all statistical analyses.

**Results:** We included 7 studies involving 8 cohorts in the final analysis. Our meta-analysis suggested that the prone position was inferior to the supine position in terms of stone fragmentation and stone clearance rate after completing the first treatment (95% CI: 0.30-0.63; OR = 0.44;), however, subgroup analysis indicated that the difference between supine and prone positions for stone fragmentation and the stone clearance rate was only getting statistical significance for distal ureteral stone (95% CI: 0.23-0.53; OR = 0.35). Moreover, subgroup analysis of two eligible randomized controlled trials suggested that the mean number of sessions per patient in the supine group was less than that in the prone group (95% CI: 0.11-0.48; WMD = 0.294). No major and severe complication was detected to be done with the association with positions.

**Conclusion:** SWL of the supine position may be the preferred option because this strategy can increase the distal ureteral stone-free rate compared to the prone position.

**Keywords:** lithotripsy; meta-analysis; prone position; shockwave lithotripsy; supine position; ureteral stone

### INTRODUCTION

There is no optimal strategy for the management of ureteral stone, especially distal ureteral stone so far.<sup>(1)</sup> Although extracorporeal shockwave lithotripsy (SWL) and ureteroscopy are all considered as acceptable treatments for ureteral stones, SWL is considered the first-line therapeutic option and has been extensively used to treat ureteral stones, especially distal ureteral stones<sup>(2,3)</sup> because it has several advantages, compared to ureteroscopy, such as characteristics of noninvasive management, ambulatory procedure, and lack of severe undesirable side effects.<sup>(4)</sup> However, the clinical value of SWL is associated with several aspects such as basic characteristics of stones including size, location and specified composition and the type of the lithotripter used.<sup>(1)</sup> For the purpose of improving the treatment effects of SWL, several regimes including sedation, a slow shock wave firing rate, ramping up the voltage, sufficient transmission media for optimal coupling, a wider focal zone, the application of a belt, and adequate pain relief have been developed and introduced.<sup>(5)</sup> Unfortunately, the optimal strategy of ureteral stone especially distal location has not yet been obtained.

Evidence suggested that the position of patients during SWL will directly affect the treatment effects of SWL because the bony structure of the pelvis will interfere with the effective transmission of the shock waves to the target stone.<sup>(6,7)</sup> Although the prone position has been widely used for the treatment of distal ureteral stone in order to reduce the negative effect of the pelvis,<sup>(8)</sup> several drawbacks such as large skin-to-stone distance limits the application of prone position.<sup>(9)</sup> Therefore, modifications to patient positioning during SWL have been proposed in order to improve the efficacy of the treatment.<sup>(10)</sup> As an alternative option, supine position has been introduced previously into clinical practice to address the issues faced by conventional prone position during SWL because it can effectively avoid the negative impact of pelvic bone through passing the greater sciatic foramen along the gluteus maximus muscle to deliver the shock waves.<sup>(11)</sup>

To date, several clinical trials have been performed to investigate the comparative efficacy and safety of conventional prone position and modified supine position during SWL for the treatment of ureteral calculi and found that SWL via the supine position is more effective and safer than that via the prone position. Moreover, a

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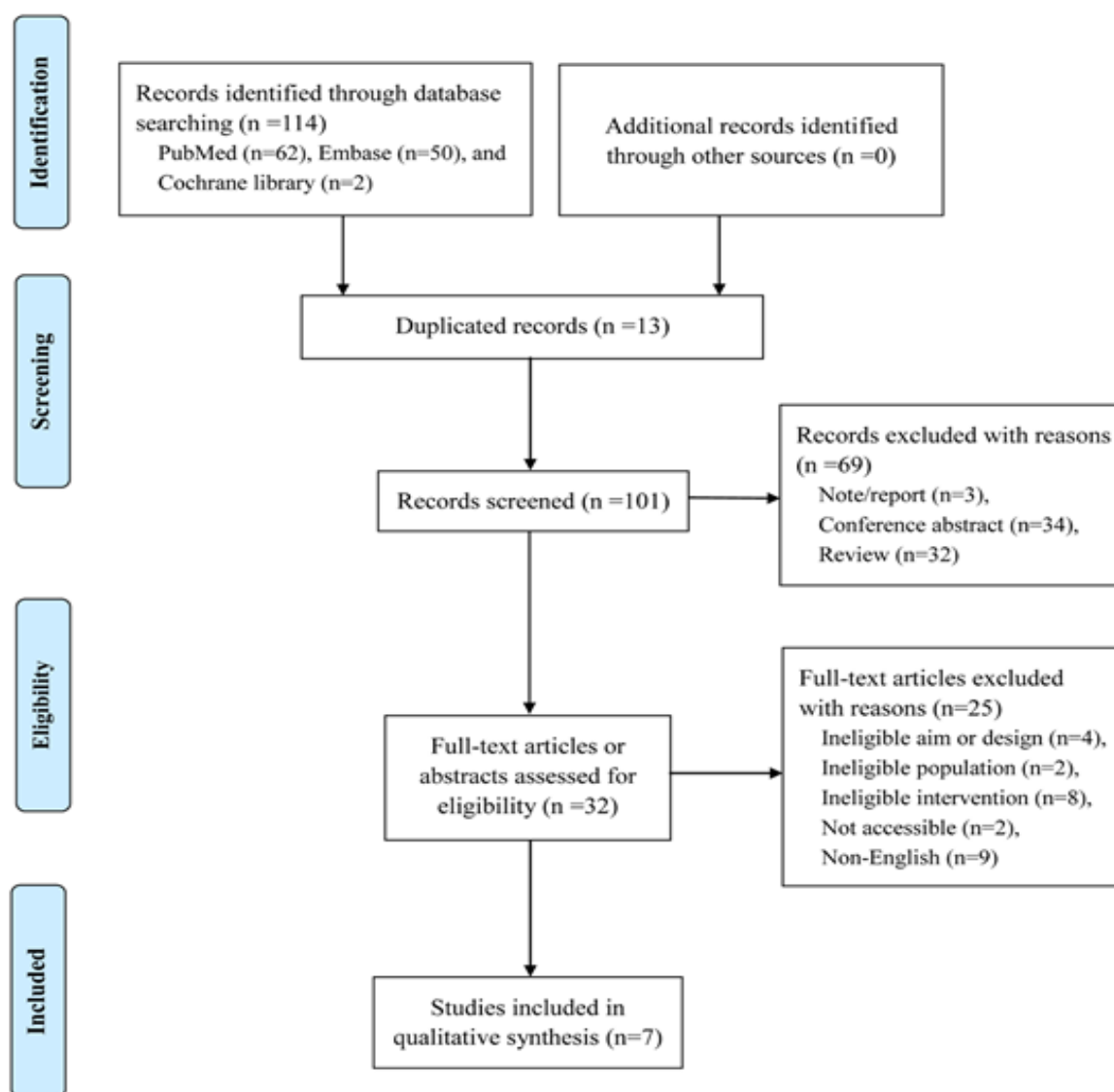
**Table 1.** Basic characteristics of 7 included studies

Study, Year	Country	Design	Location of Ureteral Stone	Stone Size, Mm; Mean $\pm$ SD (Range)		Sample Size		Age, Year; Mean $\pm$ SD (Range)	
				Prone	Supine	Prone	Supine	Prone	Supine
Choo, 2018	Korea	RCT	Distal	6.73 $\pm$ 1.67	6.40 $\pm$ 1.54	75	73	44.95 $\pm$ 11.5	44.5 $\pm$ 12.2
Göktaş, 2000	Turkey	RCT	Proximal	7.85 $\pm$ 0.94	8.10 $\pm$ 0.83	48	48	NA	NA
Kamel, 2015	Egypt	RCT	Distal	8.4 $\pm$ 0.65	8.6 $\pm$ 0.5	49	49	47.6 $\pm$ 3.5	44.3 $\pm$ 4.3
Hara, 2006a	Japan	RSC	Both	7.3 (3-11)	9.1 (3-28)	110	248	NA	NA
Hara, 2006b	Japan	RSC	Both	7.7 (3-18)	9.1 (3-24)	98	156	NA	NA
Istanbulluoglu, 2011	Turkey	RSC	Distal	61.32 (16-204) <sup>a</sup>	59.04 (10-238) <sup>a</sup>	194	148	41.12 (2-81)	50.16 (10-84)
Phipps, 2013	UK	RSC	Distal	7.9 $\pm$ 0.4	7.6 $\pm$ 0.3	38	72	48.3 $\pm$ 2.2	51.3 $\pm$ 1.8
Zomorrodi, 2007	Iran	RSC	Proximal	13.6	12.8	35	33	43.6	46

**Abbreviations:** RCT, randomized controlled trial; RSC, retrospective cohort; the unit of number is mm<sup>2</sup>; NA, not available.

previous meta-analysis<sup>(12)</sup> also suggested that supine SWL is more effective than prone SWL for achieving a stone-free status. However, there are limited studies providing a high level of evidence. So, a definitive conclusion about the optimal position during SWL

remains conflicting. Moreover, previous meta-analysis simultaneously incorporated studies with different designs into individual analysis which will cause to estimate biased results because of bias resulting from studies with different designs can not be eliminated,



**Figure 1.** Flow diagram of identification and screening of eligible studies. Other sources are defined as reference lists of included studies.

**Table 2.** Parameters of ESWL

Study, Year	Type of Sedation	Rate of Shocks	Mean No. of Shock Waves		Mean Powera, %	
			Prone	Supine	Prone	Supine
Choo, 2018	general or regional anesthesia	90 pulses/min, with a maximum of 4000 shock waves/session	NA	NA	NA	NA
Göktas, 2000	no analgesics or anesthetics	NA	4863.54 ± 2114.85	3704.16 ± 1726.75	NA	NA
Kamel, 2015	sedoanalgesia	maximum of 4000 shocks/session	3667±187	3634 ± 156	78.7 ± 3.1	75.6 ± 2.9
Hara, 2006 <sup>a</sup>	diclofenac sodium or intramuscular pentazocine	3000 waves shocks/session	NA	NA	NA	NA
Hara, 2006 <sup>b</sup>	NA	NA	NA	NA	NA	NA
Istanbulluoglu, 2011	midazolam and fentanyl	NA	3960 (1940-7000)	2953 (1250-5500)	NA	NA
Phipps, 2013	oral/rectal diclofenac	NA	3997.9 ± 225	5043.2 ± 154.7	71.4 ± 1.9	70.7 ± 1.6
Zomorodi, 2007	NA	NA	3148.5 ± 621.0	3066.1 ± 346.3	NA	NA

<sup>a</sup>Data are presented as mean ± SD (range). ESWL, extracorporeal shock wave lithotripsy; NA, not applicable.

which greatly comprises the robustness and reliability of findings. We, therefore, performed this updated systematic review and meta-analysis to further determine the comparative efficacy of SWL for treating ureteral stone including distal and proximal location performed in the supine related to the prone position.

## MATERIALS AND METHODS

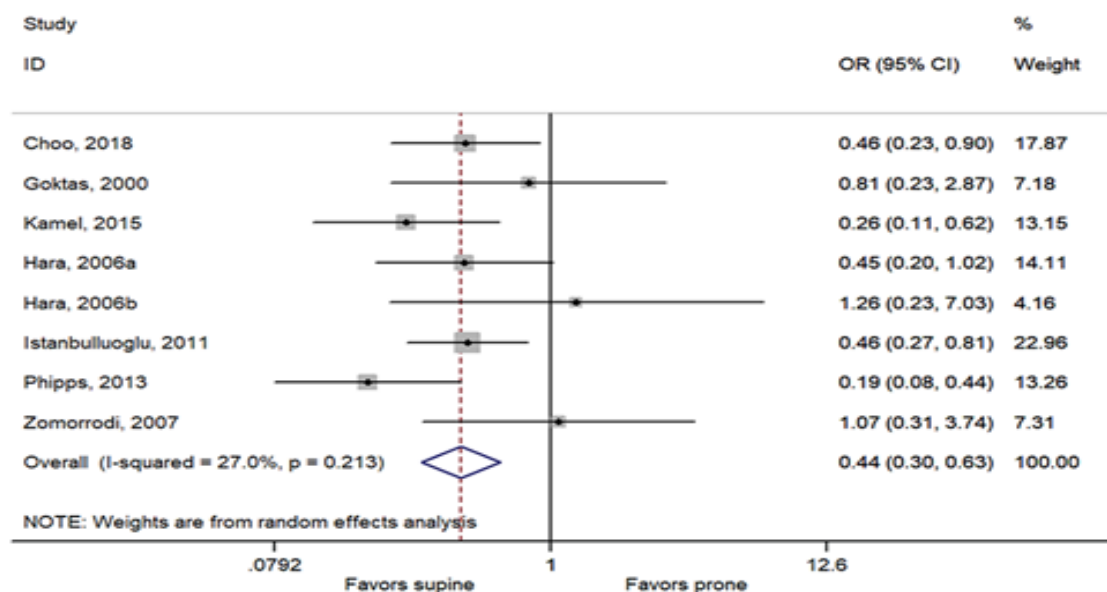
We developed the framework of the current systematic review and meta-analysis according to the recommendations issued by the Cochrane Collaboration<sup>(13)</sup> for the purpose of ensuring the methodological quality because we did not register formal protocol. Moreover, all results were reported based on the framework recommended by the preferred reporting items for systematic reviews and meta-analyses (PRISMA) statement.<sup>(14)</sup> We did not impose ethical approval and patients' informed consent because all essential data in the current systematic review and meta-analysis was extracted from published studies.

## Eligibility criteria

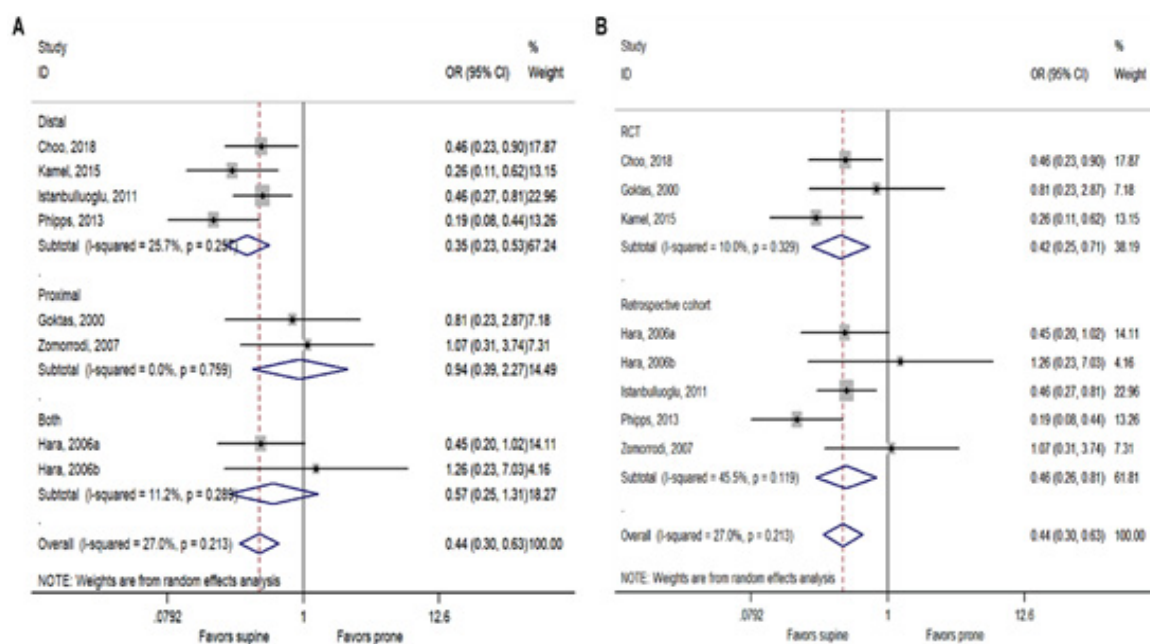
We mainly designed our selection criteria according to the previous meta-analysis.<sup>(12)</sup> The inclusion criteria were as follows: (a) adult patients who underwent lithotripsy for ureteral stone; (b) trials investigating the comparative efficacy and safety of supine SWL with prone SWL for treating ureteral stone; and (c) studies that discuss at least one of the following outcomes including stone-free rate after the first and the final SWL session and the mean number of SWL sessions per patient. Studies were excluded if they met the following criteria: (a) a preliminary study group and another updated study with comprehensive information has been reported by the same study, (b) studies without sufficient information, and (c) reviews, editorials, letters, case reports, conference abstracts, and cell and animal studies. No ethical consent was required because this study was prepared on the basis of previous data.

## Information sources and search strategy

According to the recommendation proposed by the



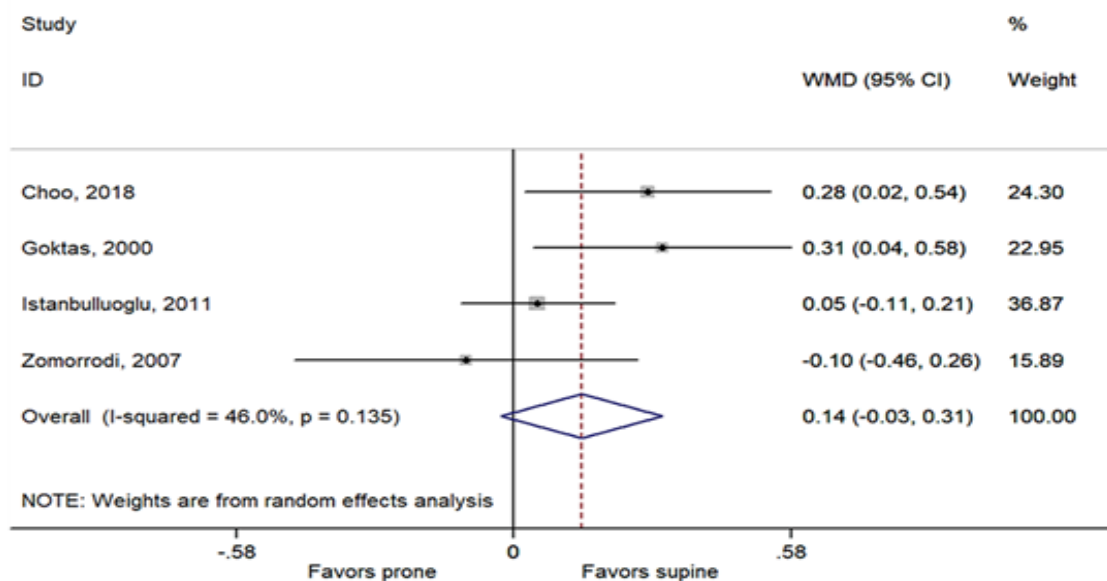
**Figure 2.** Forest plot of stone-free rate after the first session. OR, odds ratio. The black horizontal line and diamond presents 95% confidence interval (CI) of individual study respectively, and grey square represents weight of each study. Moreover, the blue diamond refers to pooled estimate.



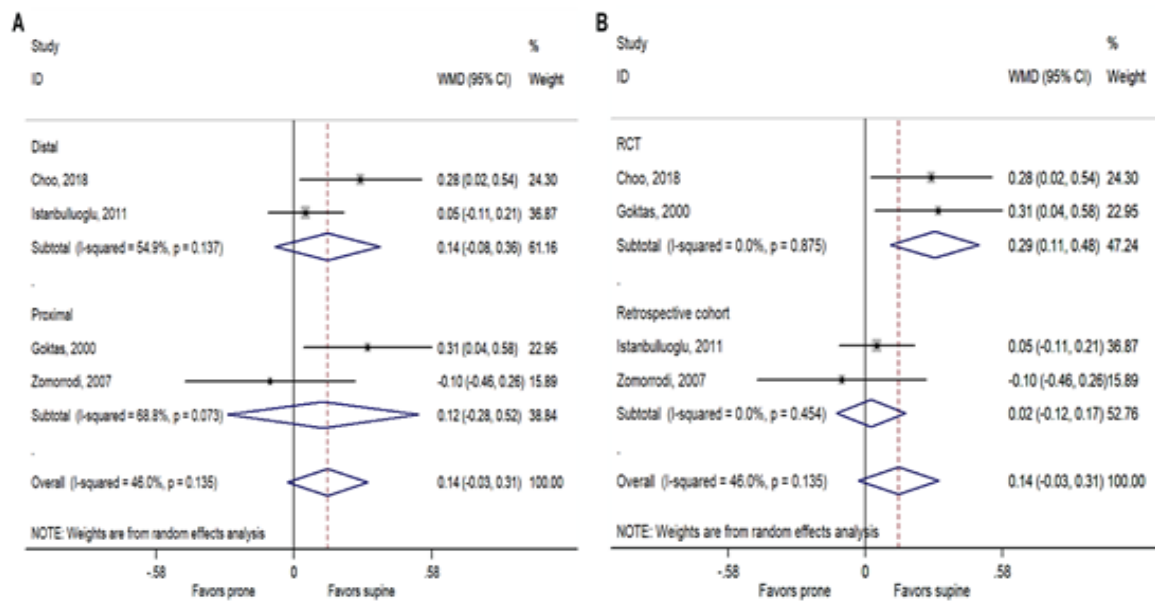
**Figure 3.** Subgroup analysis of stone-free rate after the first session. OR, odds ratio; RCT, randomized controlled trial. The black horizontal line and diamond presents 95% confidence interval (CI) of individual study respectively, and grey square represents weight of each study. Moreover, the blue diamond refers to pooled estimate.

Cochrane handbook, a systematic search was conducted in three electronic databases including PubMed, Embase and the Cochrane library in order to identify relevant studies. The time of search was limited from their inception until to October 2020. We used medi-

cal subject heading (MeSH) of ‘Lithotripsy’, ‘Ureteral’, ‘Prone position’ and ‘Supine position’ as well as relevant keywords to develop the search strategy, and modification was made according to the unique requirements of each database. We only considered studies



**Figure 4.** Forest plot of the number of sessions. OR, odds ratio. The black horizontal line and diamond presents 95% confidence interval (CI) of individual study respectively, and grey square represents weight of each study. Moreover, the blue diamond refers to pooled estimate.



**Figure 5.** Subgroup analysis of the number of sessions. OR, odds ratio; RCT, randomized controlled trial. The black horizontal line and diamond presents 95% confidence interval (CI) of individual study respectively, and grey square represents weight of each study. Moreover, the blue diamond refers to pooled estimate.

published in the English language for inclusion because no translator who has expertise in other languages was enrolled. Meanwhile, we also manually the references list of all included studies and topic-related reviews to help identify any potential studies. Any disagreements about identification of studies were resolved by discussion or consulting a third senior reviewer.

### Study selection

Two independent investigators selected eligible studies according to our selection criteria. We firstly removed duplicate studies based on literature management software. Then, we excluded ineligible studies through screening titles and abstracts of unique studies. Finally, we retrieved the full-texts of the remaining studies to check their eligibility for inclusion.

### Data collection

Two investigators independently extracted the following items using the pre-designed data extraction sheet: basic characteristics of the study including first author, publication year, and country, patients' characteristics including sample size, the number and age of the patients, location of the ureteral stone, and stone size, and clinical characteristics of study including outcomes, and sources of risk of bias. Stone-free rate after the first SWL treatment session was included as the primary outcome, and the mean number of SWL sessions per patient was regarded as the secondary outcome. Stone-free status was defined as having either no or only clinically insignificant residual stone fragments (< 3 mm), evaluated by kidney-ureter-bladder radiography or ultrasonography performed at the third month or longer after the last SWL session.<sup>(12)</sup> If an included study was designed to have more than two groups, then the methods recommended by the Cochrane Handbook for Systematic Reviews of Interventions were used to divide the individual study into two unique RCTs or combine

groups to create a single pair-wise comparison.<sup>(15)</sup> If essential information was missed from the original study, then the leading author was contacted for additional information. Any inconsistencies in data extraction were solved based on the consensus principle.

### Quality of the evidence

At the end of our research, a total of 8 cohorts of patients from 7 studies entered our analysis. Level of evidence of all articles was assessed independently by two authors according to the Cochrane Handbook<sup>(16)</sup> and modified the Newcastle-Ottawa Quality Assessment Scale.<sup>(17)</sup> In Cochrane risk of bias assessment tool, the quality of all eligible studies was assessed from the following six domains: random sequence, allocation concealment, blinding, incomplete data, selective reporting, and other sources. In the modified Newcastle-Ottawa Scale, a score of 1-9 stars were assigned to all controlled studies. Discrepancy in the assessment were resolved through discussion until a consensus was achieved.

### Statistical analysis

All of the analyses were performed using STATA SE 14.0 software (StataCorp, College Station, Texas, USA). The number of stone-free patients after the first session and the average number of treatment sessions under each position was extracted. Dichotomous data and continuous data were expressed as odds ratio (OR) and weighted mean difference (WMD) with 95% confidence interval (CI), respectively. Statistical heterogeneity among these studies was qualitatively assessed using Cochran's Q and estimated quantitatively using  $I^2$  statistic (> 50%, and  $P < .1$ , high heterogeneity).<sup>(18)</sup> Considered the potential heterogeneity from variabilities of study region and patients, we adopted random-effect model in all of the combined effects to avoid the overestimation of the pooled results.<sup>(19)</sup> Moreover, we also performed subgroup analysis of stone-free after

the first session and number of sessions based on location of ureteral stone and type of study design. We didn't assess possible publication bias by funnel plots and Egger's test due to the number of studies included in each quantitative analysis was less than 10, in which case the funnel plots and Egger's test could yield misleading results.<sup>(20,21)</sup>

## RESULTS

### Search results

A total of 114 studies were identified at the initial search stage for PubMed, Embase, and Cochrane Library. We excluded 13 duplicate studies with the EndNote software. A total of 32 studies were retained after excluding 69 ineligible studies through verifying the title and abstract. We included 7 eligible studies for the final analysis after excluding 25 ineligible studies as the following reasons through full-text check: ineligible aim or study design ( $n = 4$ ), ineligible participants ( $n = 2$ ), ineligible intervention regime ( $n = 8$ ), not accessible ( $n = 2$ ), and ineligible language ( $n = 9$ ). The process of searching and screening literature was shown in **Figure 1**.

Basic characteristics of all included studies

A total of 7 eligible studies involving 8 cohorts were enrolled finally. Of 7 studies, three were randomized controlled trial<sup>(9,22,23)</sup> and four were retrospective cohort.<sup>(6,8,24,25)</sup> These studies were undertaken in Korea,<sup>(22)</sup> Turkey,<sup>(23,24)</sup> Egypt,<sup>(9)</sup> Japan,<sup>(6)</sup> UK,<sup>(8)</sup> and Iran,<sup>(25)</sup> respectively. The publication year of all included studies were between 2006 and 2018. The sample size of individual eligible study was between 68 and 358, with the total sample size of 1474. Of these 7 eligible studies, one study<sup>(6)</sup> was divided into two unique cohorts. Four studies<sup>(8,9,22,24)</sup> focused on distal ureteral stone, two<sup>(23,25)</sup> focused on proximal ureteral stone, and one<sup>(6)</sup> focused on both ureteral stone. We documented the basic characteristics of all 7 studies were in Table 1. Meanwhile, parameters of SWL and characteristics of stone were summarized in **Table 2**.

### Quality of all included studies

Among the three randomized controlled trials, only one study<sup>(22)</sup> was graded as low risk of bias in random sequence generation and allocation concealment, all were high risk of bias in blinding of participants and personnel and low risk of bias in incomplete outcome data, selective reporting, and other bias. Among four retrospective cohorts,<sup>(6,8,24,25)</sup> the total quality score of individual study was all more than 7. We summarized the results of appraising quality of all included studies in Table S1.

Stone-free rate after the first session

Seven studies<sup>(6,8,9,22-25)</sup> involving 8 cohorts reported stone-free rate for SWL in the supine and prone positions after the first SWL session. Heterogeneity in pooled analysis was not significant ( $P = .21$ ;  $I^2 = 27\%$ ). Based on a meta-analysis of data from these 8 cohorts, the stone-free rate in the prone group was significantly lower than that in the supine group (95% CI: 0.30-0.63; OR = 0.44; **Figure 2**), and the sensitivity analysis through omitting individual study with one by one further confirmed the robustness of pooled result (**Figure S1**). Subgroup analysis based on location of stone indicated that the difference between supine and prone positions was only statistical significance in distal ureteral stone (95% CI: 0.23-0.53; OR = 0.35; **Figure 3A**). Subgroup analysis based on study design includ-

ing randomized controlled trial (95% CI: 0.25-0.71; OR = 0.42; **Figure 3B**) and retrospective cohort (95% CI: 0.26-0.81; OR = 0.46; **Figure 3B**) further confirmed the difference between supine and prone positions.

### Number of sessions per patient

Among 7 eligible studies, four<sup>(22-25)</sup> reported the number of sessions per patient. Meta-analysis suggested no statistical difference (95% CI: -0.03-0.31; WMD = 0.14; **Figure 4**) between prone and supine positions during SWL, which was further confirmed by sensitivity analysis through omitting individual study with one by one (**Figure S2**). Subgroup analysis depending on the location of the stone (**Figure 5A**) obtained consistent pooled results with overall pooled result. However, subgroup analysis based on study design found that the mean number of sessions per patient in the supine group was lower than that in the prone group when calculated pooled estimates based on two eligible randomized controlled trials (95% CI: 0.11-0.48; WMD = 0.294; **Figure 5B**).

### Complications during treatment

Of seven included studies, five studies reported complications during SWL treatment. Istanbulluoglu and colleagues reported that patients experienced petechiae with various degrees and early hematuria.<sup>(24)</sup> Göktas and colleagues reported that patients in the prone position experienced discomfort on inspiration and expiration and pain localized to the lumbar vertebrae.<sup>(23)</sup> However, no serious complications were reported by Phipps et al.,<sup>(8)</sup> Kamel et al.,<sup>(9)</sup> and Choo et al.<sup>(22)</sup> We could not quantitatively estimate the pooled effects about complications because data were not suitable for meta-analysis. However, most importantly, available evidence suggested that no major or severe complications were observed in any of these trials.

## DISCUSSION

To date, the optimal strategy of ureteral stone is not still unclear, especially for distal ureteral stone.<sup>(26)</sup> Whereas, SWL and ureteroscopy were considered as the acceptable therapeutic methods for distal ureteral stones by both the American Urological Association (AUA) and European Association of Urology (EAU) guidelines.<sup>(27,28)</sup> However, compared to ureteroscopy, extracorporeal shockwave lithotripsy has been extensively used to treat distal ureteral stones as first-line treatment due to several advantages such as minimal invasion and lack of major or severe undesirable side effects.<sup>(4)</sup> To date, however, the optimal strategy of SWL has not yet been obtained despite several advances in technology.<sup>(29)</sup> Considering the fact that the efficiency of transmission of shockwave during SWL is deeply associated with bony structure of pelvis, modifications of patient's position during SWL treatment was introduced, and then several studies have also investigated the impact of various patient's positions on the efficiency of SWL.<sup>(6,8,23-25)</sup> Meanwhile, one meta-analysis has also further investigated the comparative efficacy and safety between supine and prone positions during SWL, and initially suggested that supine SWL is more effective than prone SWL for achieving a stone-free status.<sup>(12)</sup> Nevertheless, a definitive conclusion has not yet been generated. After completing the current updated systematic review and meta-analysis, we found that the supine position was made in association with increased the stone-free

rate compared to prone position, which was also confirmed by sensitivity analysis and subgroup analysis based on study design. Moreover, subgroup analysis based on location of ureteral stone further suggested that supine position during SWL significantly increased the distal ureteral stone-free rate. Although we did not find significant difference between supine and prone positions in terms of the number of sessions per patient when we incorporated all studies with various designs into individual analysis, subgroup results based on two randomized controlled trials indicated that supine position may be associated with decreased number of sessions compared to prone position during SWL treatment. However, urologists must firstly identify whether SWL should be adopted through comprehensively evaluating several factors such as stone size, stone location, patient medical status, patient age, and body mass index.

To date, only one meta-analysis<sup>(12)</sup> focused on comparative efficacy and safety between supine and prone positions during SWL has been published, and concluded a superior comparison of supine position compared to prone position from the stone-free rate after treatment. It must be pointed out that, however, the conclusion was generated from pooled estimate based on 4 clinical studies, of which 3 studies were retrospective design. Moreover, the previous meta-analysis only focused on patients with distal ureteral stone although our present study found that the supine position only associated with increased distal ureteral stone-free rate after performing subgroup analysis. Compared to the previous meta-analysis, our meta-analysis obtained more reliable and robust pooled results because our study has major two advantages including more eligible studies and detailed clarification of ureteral stone.

We also must acknowledge some limitations in our systematic review and meta-analysis. Firstly, we included the observational study in our analysis simultaneously owing to the paucity number of RCTs in the specific topic. However, we performed subgroup analysis being dependent on the study design to further test the robustness of all pooled results. Secondly, we failed to quantitatively obtain the pooled estimate of the safety profile of each position since only one study has reported numerical data.<sup>(22)</sup> Thirdly, the stone free rate in the included studies was evaluated by the plain x-ray of kidney, ureter, and bladder (KUB) and/or ultrasonography (US), however those both are inefficient for detection of ureteral stones. Fourthly, we did not perform subgroup analysis to further explore the impact of several important features including stone composition and density and radiographic characteristics on pooled results due to limited data. Fifthly, another one limitation with the present systematic review was the language restriction and that only three major databases were searched and therefore, relevant studies may have been missed.

## CONCLUSIONS

Our study further confirmed the supine approach is superior in stone fragmentation and clearance than prone approach. Stone-free rate of the supine position after the first treatment session is significantly higher compared to prone position for patients who underwent SWL. However, research that compared the safety profile of each position is still destitute. Future research can focus on the long-term benefit and patients report outcomes

regarding the safety of supine and prone position.

## CONFLICT OF INTEREST

The authors declare that the submitted work was conducted with no conflict of interest.

## APPENDIX

<https://journals.sbm.ac.ir/uroj/index.php/uj/libraryFiles/downloadPublic/35>

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