

Did we take physical therapy serious after lithotripsy: a meta-analysis of prospective studies

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Abstract

Background Stone-free rate (SFR) after lithotripsy was one of the most frequent concerned issue, especially in patients following extracorporeal shockwave lithotripsy (ESWL) and flexible ureteroscopy (retrograde intrarenal surgery, RIRS). Physical therapy including percussion, inversion, physical vibration and their combinations was administrated to improve the SFR, but there was no conclusive evidence to support this theory. To conclude the effectiveness and safety of physical therapy on the SFR in patients received ESWL/RIRS. Methods We systematically reviewed the literature focused on physical therapy in patients after ESWL/RIRS on PubMed, Scopus, Cochrane library and Embase from 2000 to 2019 April. We mainly focused on stone-free rate and complications rate. Results Nine prospective studies including 8 randomized control trials and 1 non-randomized study were enrolled, and 1747 subjects were analyzed. All the physical therapy we enrolled was finally concluded into EPVL (external physical vibration lithocbole) and PDI (percussion, diuresis and inversion). Compared to conventional group, physical therapy provided a higher SFR (OR: 2.68; 95% CI: 1.74–4.12; P = 0.0001), especially SFR in lower calyx stones (OR: 3.60; 95% CI: 2.26–5.73; P= 0.0001). In subgroup analysis, EPVL (OR: 2.28; 95% CI: 1.27–4.07; P =0.005) and PDI (OR: 3.51; 95% CI: 1.96–6.26; P = 0.0001) were both effective. Drinking enough water before treatment was supposed to increase the SFR (OR: 3.31; 95% CI: 2.39–4.60; p = 0.0001). Otherwise, medical intervention such as furosemide (OR: 5.21; 95% CI: 0.53–50.72; P = 0.156) and tamsulosin (OR: 1.05; 95% CI: 0.61–1.82; P = 0.855) did not improve the SFR. No significant difference was detected in terms of complications rates (OR: 0.83; 95% CI: 0.61–1.14; P = 0.25). Conclusions EPVL or PDI were both effective and safe in increasing the SFR after ESWL/RIRS, but its effectiveness was limited in LCS. Drinking enough water before physical therapy helped to improve the SFR. The role of furosemide and tamsulosin in physical therapy or surgery need to be testified by large-scale, high-quality studies.

Background

Urolithiasis was one of the most frequent noted diseases in urology. The incidence of urolithiasis varies from 1% to 13% in different area, and is still increasing^{1,2}. Without medical intervention, the recurrence rate following the operation will 50% within 5 years and 80-90% within 10 years, brought great challenge to urologists³.

Percutaneous nephrolithotomy (PCNL) was well established procedure for the management of upper urinary tract stone larger than 2 cm, while extracorporeal shockwave lithotripsy (ESWL) and retrograde intrarenal surgery (RIRS) were regarded as the first line choice for moderate size stones ranged from 1cm to 2 cm⁴⁻⁶. Exactly, the PCNL had a higher stone free rate when compared to ESWL and RIRS for a large burden stone, but also associated with a higher complication rate, especially the percutaneous tract related hemorrhage following PCNL, destined that ESWL and RIRS had their certain position in the management of upper urinary tract stones^{7,8}.

With the improved lithotripsy efficiency in ESWL and the dusting technique in RIRS, RIRS and ESWL were more and more popular in small burden stones while the fragments following ESWL and RIRS became much more concerned, especially the lower caliceal stones (LCS)⁹. It was reported that the SFR following ESWL was about 23.1%-91.5%, and ranged from 45.6% to 96.7% in patients with RIRS¹⁰. The residual fragments would influence the SFR undoubtedly, and was prone to bring stone recurrence. Residual fragments' related complications

following ESWL and RIRS were also foreseeable, renal colic, urinary tract infection (UTI), and sometimes ureteral steinstrasse required additional surgical interventions.^{11,12}

Auxiliary procedures were introduced to facilitate stone fragments passage, we summarized two aspects and their combinations. Firstly, medical expulsive therapy (MET), such as diuretics, sometimes Chinese patent medicine, α receptor blockers (**Tamsulosin**), and so on¹³. Secondly, physical therapy like increasing physical activity, body inversion, percussion on renal region, sleeping on the healthy side, and so on¹⁴⁻¹⁶.

Tamsulosin was widely used in clinic to expel SF even its function efficacy is still under great suspicion. Some multi-center RCTs showed there was no significance in the stone passage when compared to the placebo group¹⁷⁻¹⁹. Exactly, the stone fragments in lower pole were much more prone to stay since the gravity and the influence of lower calyceal anatomy. Roller coaster and intercourse were reported to promote renal stone passage^{20,21}. Thus, the physical treatment was theoretically effective to accelerate the stone fragments passage, when changing the body position and rolling the stone fragments into ureteral pelvic junction. More recently, new technique like external physical vibration lithotripsy (EPVL) was designed to facilitate stone fragments Passage.

However, there was no conclusive evidences on physical therapy facilitating SF passage, nor clear guidelines in introducing standard physical therapy to facilitate stone fragment passage after lithotripsy. The present systematic review and meta-analysis was aimed to evaluate the overall therapeutic effect of physical therapy and its complications compared to patients without physical interventions. And provide a higher evidence to support the effectiveness and safety of physical therapy. Hopefully, urologists may take more physical therapy into consideration when patient receiving RIRS or ESWL.

Methods

1.1 Literature Search and article selection

A systematic literature review was performed in March 2019 utilizing PubMed, Scopus, Cochrane library and Embase. A comprehensive literature search was done separately with the following search terms: “physical or mechanical percussion”, “inversion”, “vibration”, “External physical vibration lithotripsy”, “(EPVL), “extracorporeal shockwave lithotripsy”, (ESWL) and “flexible ureteroscopy” (RIRS) “for urinary tract stone”. Selection of relevant studies was in accordance with protocol items of PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines (<http://www.prisma-statement.org>). All potentially eligible studies from cited references from the selected articles retrieved in the search were also assessed as significant papers.

All the process as showed in Figure 1 (Figure legends - Flow of studies selection for systematic review and meta-analysis.) was completed by two reviewers Peng and Wen, and disagreements were resolved by consensus after consulting W.Z.

1.2 Selection criteria

Studies were included in the present analysis if met the following inclusion criteria: (1) Prospective studies published in English either randomized controlled trials (RCTs) or non-RCTs; (2) with more than 30 cases; (3) The study subjects compare physical therapy (external physical vibration lithocbole, mechanical percussion, inversion, position change or other similar means) with other interventions; (4) Ureteral or renal stones whose size were was less than 20mm, without abnormal ureteral or renal anatomy; (4) Patients received surgery like ESWL or RIRS before physical therapy or not; (5) Patients demographics, such as age, gender, body mass index (BMI), stone location, stone size and comorbidities were in the list. (6) Adult patients, aged from 16 to70.

On the other hand, exclusion criteria were: (1) Retrospective studies, conference abstracts or repeated publications; (2) Non-published materials, reviews or editorials. (3) Studies published in other language rather than English.

1.3 Statistical analysis

Meta-analysis of comparable data was conducted using Review Manager Version 5.3 software and Stata Edition 14.2.

The level of evidence (LE) was assessed using GRADE system to assess the methodological quality of the studies, non-randomized controlled trials (N-RCTs) using the Newcastle-Ottawa Scale (NOS) and the Jadad scale were applied for RCTs.

Since the categorical variables of SFR and complications rate were our primary study subjects, statistical analysis was carried out using odds risk (OR) and 95% confidence intervals (CIs). Heterogeneity was assessed using chi-squared test and the Higgins I^2 statistic. No matter the significant heterogeneity ($P > 0.1$, $I^2 > 50\%$) exist or not, the random effect model was used for pooled analysis at first, and would be testified later. Additionally, the source of heterogeneity, analysis publish bias and subgroup pooled analysis was administrated.

To analysis the influence of physical therapy, stone location, medical interventions and drinking water. Stone fragments location was classficated into lower calyx stone (LCS), upper calyx stone (UCS), middle calyx stone (MCS), renal pelvic stone (RPS) and upper ureteral stone (UUS). Medical interventions contained tamsulosin and furosemide. All the useful results would be available for the subgroup analysis.

Results

1. Study characteristics

Table 1 listed a total of 9 prospective studies published from 2001 to 2018 were finally included in the present analysis, including 8 RCTs²²⁻²⁹ and 1 prospective case control study³⁰. There were 3 multi-center studies (NCT02645708²⁴, NCT02643134²⁵, one not registered²⁷). There were 8a two-arm studies and 1a threearmstudy²⁹. A total of 1959 subjects were included in the present study, 978 in the physical therapy group and 981 in control group, respectively.

All the physical therapy, we enrolled, was finally concluded into EPVL and PDI. As it demonstrated in the Table 2, 5 studies^{22-25, 29} focus on EPVL, 1²⁹ of which involved tamsulosin. In 4 studies of PDI group, 1 study²⁷ investigated only the mechanical percussion but was classified into a PDI group and the rest of 3² are all PDI, but 1²⁸ did not describe the application of diuresis. And LE of all the RCTs was 1b and the score of methodological quality are from 3 to 5. Risk of bias assessment is described in figure 2 (Figure legends - Results of bias assessment.).

2. Meta-analysis results

2.1 Stone-Free Rate

A total of 9 eligible studies reported the SFR referred to physical percussion, EPVL and PDI after ESWL, RIRS or not. A higher SFR was provided by physical therapy (OR= 2.72, 95% CI: 1.79–4.14, p = 0.000, figure. 3 (Figure legends - Meta-analysis of stone-free rate and subgroup analysis of different techniques.)). Heterogeneity test showed that $I^2 = 55\%$ and p = 0.018, which supported random effect used in our meta-analysis.

The funnel plot (figure 4 (Figure legends - Funnel plot of publish bias.)) revealed an symmetry and begg`s test revealed Z = 1.79 and p = 0.074, both of which suggested no presence of a publication bias in our study.

2.2 SFR changed with time

With time after treatment moved on, SFR was also changing. Specifically, the first week (OR: 2.44; 95% CI: 1.00–5.93; p = 0.050), Week 2 (OR: 1.98; 95% CI: 1.34–2.92; p = 0.001), month 1 (OR: 3.49; 95% CI: 1.94–6.28; p = 0.000) and month 3 (OR: 3.62; 95% CI: 1.71–7.66; p = 0.001, figure 5 (Figure legends - Meta-analysis of stone-free rate in week 1, week 2, month 1 and month 3.))

2.3 First two day stone expulsion

In figure 6 (Figure legends - Meta-analysis of stone expulsion in the first two days.), first two day stone expulsion rate was higher in physical therapy group than control group (OR= 1.58, 95% CI: 1.07–2.32, p = 0.021)

2.4 Complication rate

Overall complication rate was higher in the control group as showed in figure 7 (Figure legends - Meta-analysis of overall complication rate and subgroup analysis of specific complications.), but there was no significant difference (OR: 0.84; 95% CI: 0.61–1.14; p = 0.25). There was also no significance in hematuria (OR: 0.79; 95% CI: 0.42–1.48; p = 0.462), dizziness (OR: 2.87; 95% CI: 0.89–9.32; P = 0.079), lumbago (OR: 0.62; 95% CI: 0.32–1.22; P = 0.164) and urinary infection (OR: 0.75; 95% CI: 0.40–1.41; P= 0.372), respectively.

3. Sub-group meta-analysis

3.1 Influence of different physical therapy

As demonstrated in figure 3 (Figure legends - Meta-analysis of stone-free rate and subgroup analysis of different techniques.), when we classified treatment into EPVL and PDI, SFR no matter in EPVL (OR: 2.28; 95% CI: 1.27–

4.07; $p = 0.005$) or in PDI (OR: 3.54; 95% CI: 2.22–5.64; $p = 0.000$) was higher than in the control group.

3.2 Influence of stone location to SFR

In the subgroup analysis (figure 8 (Figure legends - Subgroup analysis of different stone locations in SFR.)), physical intervention group had a higher SFR in LCS (OR: 3.75; 95% CI: 2.39–5.89; $p = 0.000$). However, there were no significant difference in other groups, UCS (OR: 1.70; 95% CI: 0.14–21.12; $p = 0.678$), MCS (OR: 5.51; 95% CI: 0.32–94.90; $p = 0.240$), RPS (OR: 5.08; 95% CI: 0.24–107.94; $p = 0.297$) and UUS (OR: 1.63; 95% CI: 0.97–2.74; $p = 0.064$) respectively.

3.3 Influence of medical interventions to SFR

According to the analysis result (figure 9 (Figure legends - Subgroup analysis of medical intervention in SFR.)), patients who received no medicines like furosemide and tamsulosin during the physical therapy owned significantly higher SFR (OR: 3.48; 95% CI: 2.48–4.91; $p = 0.000$). However, in tamsulosin group, physical therapy combined tamsulosin or not showed no significant difference compared to tamsulosin group (OR: 1.05; 95% CI: 0.61–1.82; $p = 0.855$). Similarly, furosemide was also insignificant (OR: 5.69; 95% CI: 0.86–37.78; $p = 0.072$) to the blank group.

3.4 Influence of drinking water before therapy

When the studies were divided according to whether patients drink enough water before receiving physical therapy as it was showed in Figure 10 (Figure legends - Subgroup analysis of drinking water before physical therapy in SFR.), enough water before therapy was helpful to increase the stone-free rate (OR: 3.31; 95% CI: 2.39–4.60; $p = 0.0001$). Otherwise, there was no statistical difference (OR: 1.83; 95% CI: 0.57–5.85; $p = 0.308$) between the studies where no recommends on water before the treatment.

Discussion

Since our study were based on prospective studies, our study was a high level evidence to support what we found and concluded. But in sub-group analysis, we realized that in some area, large-scale RCTs were supposed to testified our findings as we described below.

Physical interventions, used to aid fragments discharge, had become a relatively long history. Honey et al³¹ in 2000 reported PDI can effectively mobilize SF out of the lower pole calyces and help in the passage of fragments. Further, a meta-analysis published in 2013 from Liu et al.³², limited evidence from two small studies indicated that PDI may be safe and effective to assist clearance of LCS after ESWL (RR 0.62, 95% CI: 0.47-0.82). Based on this research, we included 2 more prospective studies including one RCT. In a total of 4 prospective studies, 3 were RCTs and 1 was prospective case control study. Three of them were only focused on the LCS, except one contained upper urinary stone. We identified that percussion can facilitate the SF passage, mainly the LCS, which is Consistent with the result of Liu et al... We wondered if the PDI therapy or physical percussion would work in other urinary locations.

Based on the similarly physical principle, a new device called EPVL made in China have been widely used. In 2016, Zhang et al.³³ conducted a meta-analysis in Chinese enrolling Five randomized or Quasi-randomized controlled trials and suggested that EPVL had been effective in promoting upper urinary tract residual stone expulsion (OR = 4.50, 95% CI 2.02-10.00, P = 0.0002). From standing point of our study, we searched related item EPVL and finally enrolled 5 RCTs and 3 of them were multi-center studies. According to our subgroup analysis, the application of EPVL provided a higher SFR after ESWL or RRIS (OR: 2.28; 95% CI: 1.27–4.07; p = 0.005).

As mentioned i before, the role of tamsulosin in ureteral stone was uncertain even systematic reviews came to a conclusion that tamsulosin can facilitate the stone passage in distal ureter in our study, Liu et al focused on EPVL combined with tamsulosin to promote a higher SFR for an upper ureteral stone fragment. But this three-arm study found a significant difference in the first week between EPVL combined with tamsulosin and tamsulosin alone. The stone free rate was much higher in EPVL+ tamsulosin (91.1%, P < 0.05), but it hard to tell whether single EPVL (50%) or single tamsulosin (50%) was more helpful. Interestingly, the SFR (94.5%, 93.6% and 93.5%, p > 0.05) showed no significant difference in the second week. We supposed that may be all of the methods above were working and one can increase the efficacy of other. It still needs further research to prove their function.

From guideline, one of suggestions to prevent urolithiasis formation or recurrence is drinking water. Whether drinking water and when to drink water will help stone fragments expulsion. We divided the studies into a water group and a blank group based on patients received enough water before therapy, we surprisingly found that enough water before the therapy is essential to improve the SFR for both of the treatment and control groups, and it was suggested to drink more than 1500ml water per day (OR: 3.31; 95% CI: 2.39–4.60; P = 0.0001).

Even though we analyzed the efficacy of PDI before, but when we considered the effect of diuresis alone, we found only 2 of 4 PDI studies had specified description on the use of furosemide, and the use of furosemide did not improve the SFR (OR: 5.21; 95% CI: 0.53–50.72; P = 0.156). But we had to admit the limitation of studies enrolled. The same situation happen in tamsulosin group, which confused us was the tamsulosin and EPVL seemed to enhance each other when they combined together. But when they used separately, they showed no difference in SFR.

When it comes to the complications of physical therapy, we did not found any significant difference in terms of hematuria, dizziness, lumbago and urinary infection. As EPVL and PDI are working through facilitating the stone passage, it did not increase the risk of renal colic or strainstress formation. Therefore, the physical therapy does not have the risk of increasing complication with the transient increase of stone fragments. Conversely, complications rate seemed higher in the interventional group not statistically significant (OR: 0.83; 95% CI: 0.61–1.14; P = 0.25).

Conclusions

This review indicates that physical therapy, no matter EPVL or PDI, is both a safe and an effective way to improve the SFR in LCS with no invasion or side effects. Furthermore, drinking enough amount of water may facilitate this process. But there was a lack of relevant and very limited evidences to support medical interventions like tamsulosin or furosemide influence effect Physical therapy does not promote the SF passage in other positions rather than LCS, which is supposed to be testified by further investigations and higher evidence such as RCTs.

Abbreviations

SFR: Stone-free rate,

SF: stone fragment,

RIRS: retrograde intrarenal surgery,

ESWL: extracorporeal shockwave lithotripsy,

EPVL: external physical vibration lithotripsy,

PDI: percussion, diuresis and inversion,

LCS: lower caliceal stones,

MET: medical expulsive therapy.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Availability of data and material

All data generated or analysed during this study are included in this published article and its supplementary information files.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

L.P. owned the idea, designed the study and wrote the manuscript. J.W. performed the searching under the strategy and collected data. W.Z. and G.Z. revised methodology and manuscript and offered advice during the whole process. All authors mentioned above read and approved the final manuscript.

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Tables

Table 1 summary of comparative studies included.

Study	Year	Period	Type	Location	Surgery	Size	Treat	Control	LE	Quality
Wu1	2017	2016-2016	RCT	Kidney	RIRS	<17	EPVL	N	1b	5
Wu2	2017	2015-2016	RCT	upper urinary	ESWL	<15	EPVL	N	1b	5
Tao	2018	2017-2017	RCT	upper ureter	ESWL	1--20	EPVL	N	1b	5
long	2016	2014-2014	RCT	LCS	ESWL	6—20	EPVL	Tansulozin	1b	3
Liu	2018	2013-2014	RCT	upper ureter	NA	3-10	EPVL	Tansulozin	1b	3
Jing	2018	2015-2016	RCT	Ureter, kidney	ESWL	NA	MP	N	1b	4
Albanis	2009	28 months	Pro	LCS	ESWL	20	HDI	N	2b	8#
Chiong	2005	Since 2001	RCT	LCS	ESWL	4,-20	PDI	N	1b	4
Pace	2001	1999-2000	RCT	LCS	ESWL	4	MPI	N	1b	3

NA: not available, N: blank. #: nos score.

Table 2 Information of different physical treatments.

Study	Technique	Brand	First	Percusioon	Inversion	Drinking	Furosemide	Tamsulosin	Times	Follow UP
Wu1	EPVL	Friend I	1W	16~20	26□	1000-2000	NA	NA	□1-2	2,3,5W
Wu2	EPVL	Friend I	1W	16-20	26□	1500-2000	NA	NA	□1-2	1,2,4W
Tao	EPVL	Friend I	30	15-20	26□	1000	NA	NA	1	1,2,4W
Long	EPVL	Friend I	IM	6_12	26□	1000-1500	NA	NA	□1-4	0.1,1,3W
Liu#	EPVL	Friend I	-	12	NA	Na	NA	0.4mg/2w	2	0.2,1,2W
Liu	EPVL	Friend I	-	12	NA	Na	NA	0.4mg/2w	2	0.2,1,2W
Jing	MP	VT300	IM	15-20	35□	1000-3000	NA	NA	2/2d	0.1,1,2W
Albanis	HDI	MPL 9000	IM	NA	12□	1000	40mg	NA	4	1□3M
Chiong	PDI	NA	1W	15	45□	□500	NA	NA	4/1-2w	3M
Pace	PDI	NA	IM	10	60□	NA	20mg	NA	3/3w	3M

NA: not available, N: blank, IM: immediate, W:week, M: month.

Figures

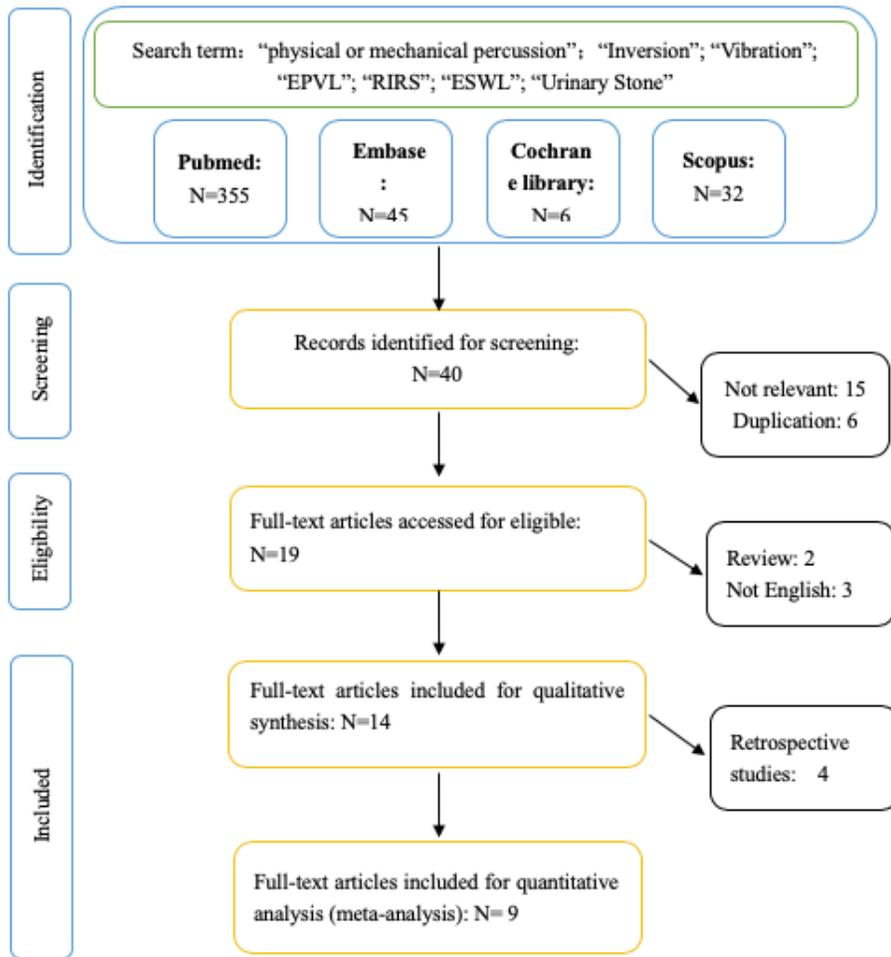


Figure 1

Flow of studies selection for systematic review and meta-analysis.

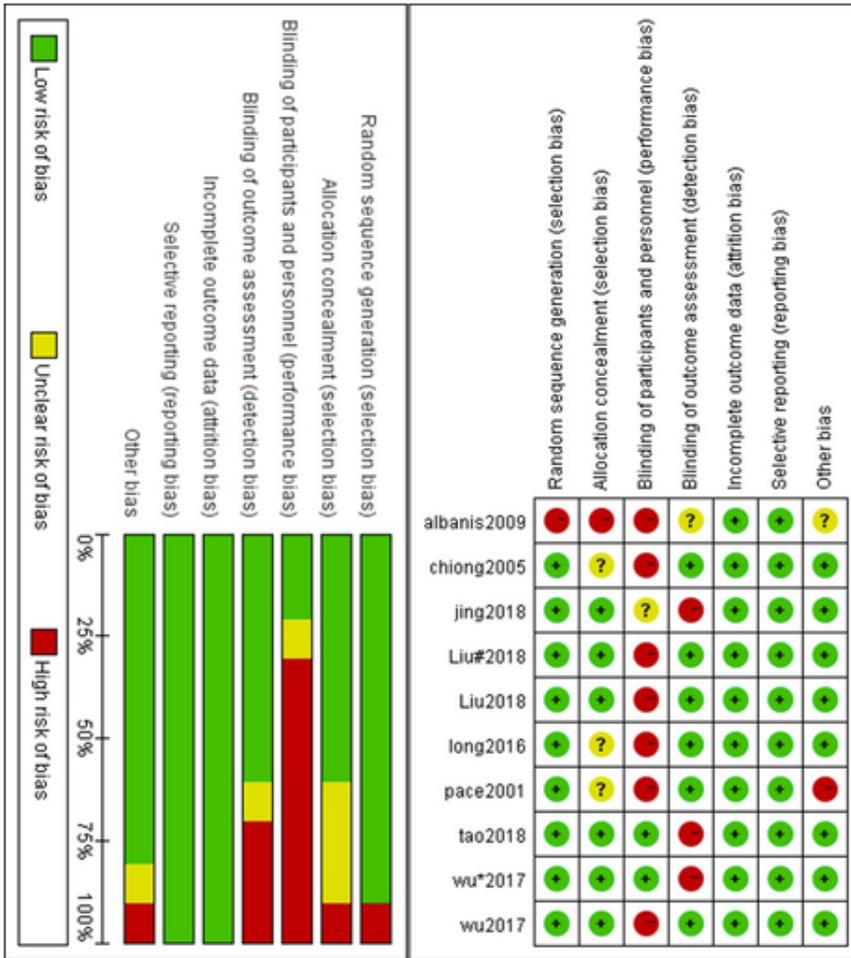


Figure 2

Results of bias assessment.

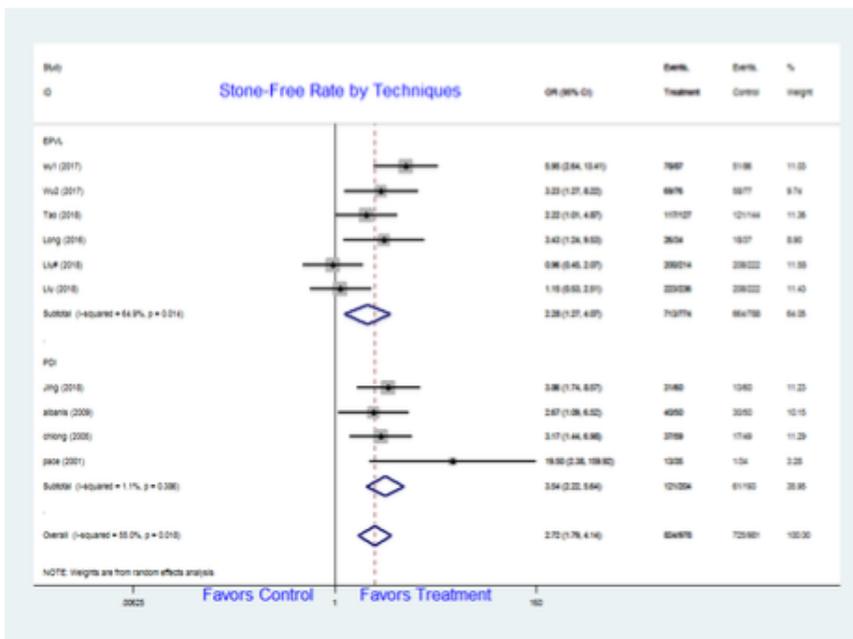


Figure 3

Meta-analysis of stone-free rate and subgroup analysis of different techniques.

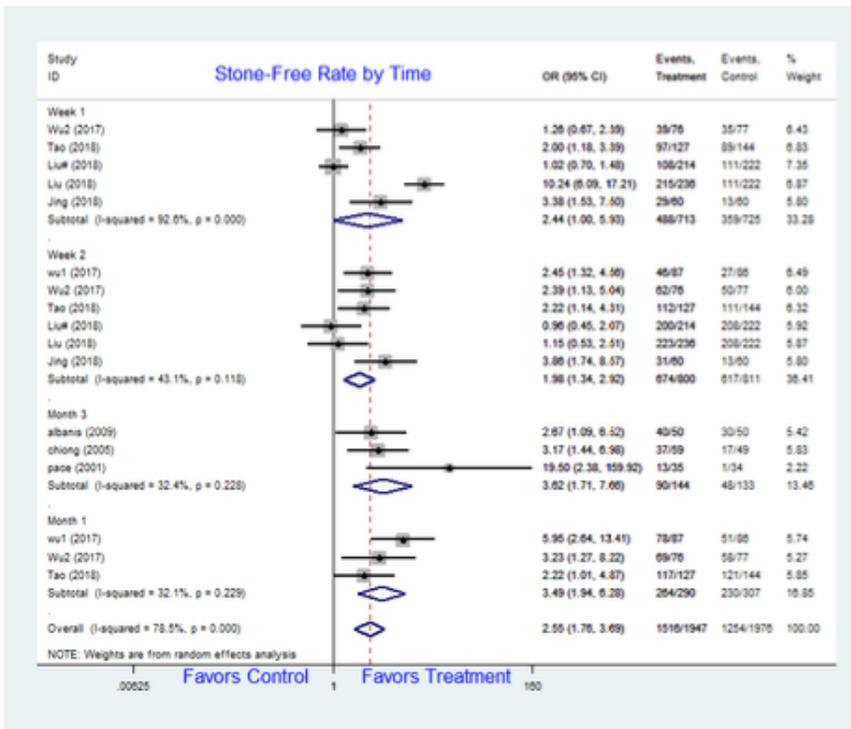


Figure 4

Meta-analysis of stone-free rate in week 1, week 2, month 1 and month 3.

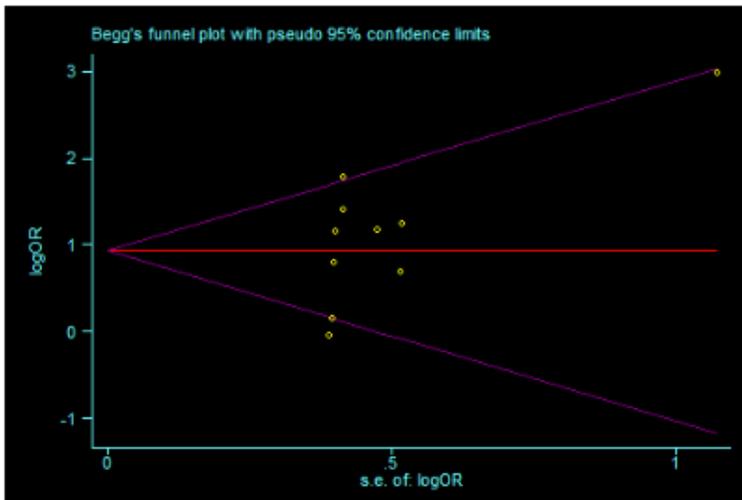


Figure 5

Funnel plot of publish bias.



Figure 6

Meta-analysis of stone expulsion in the first two days.

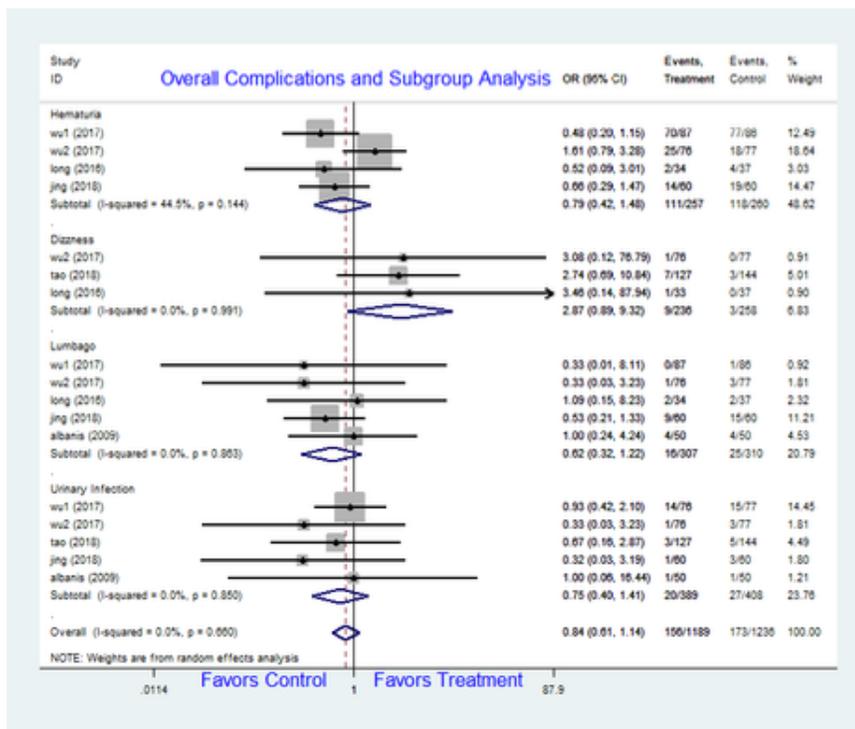


Figure 7

Meta-analysis of overall complication rate and subgroup analysis of specific complications.

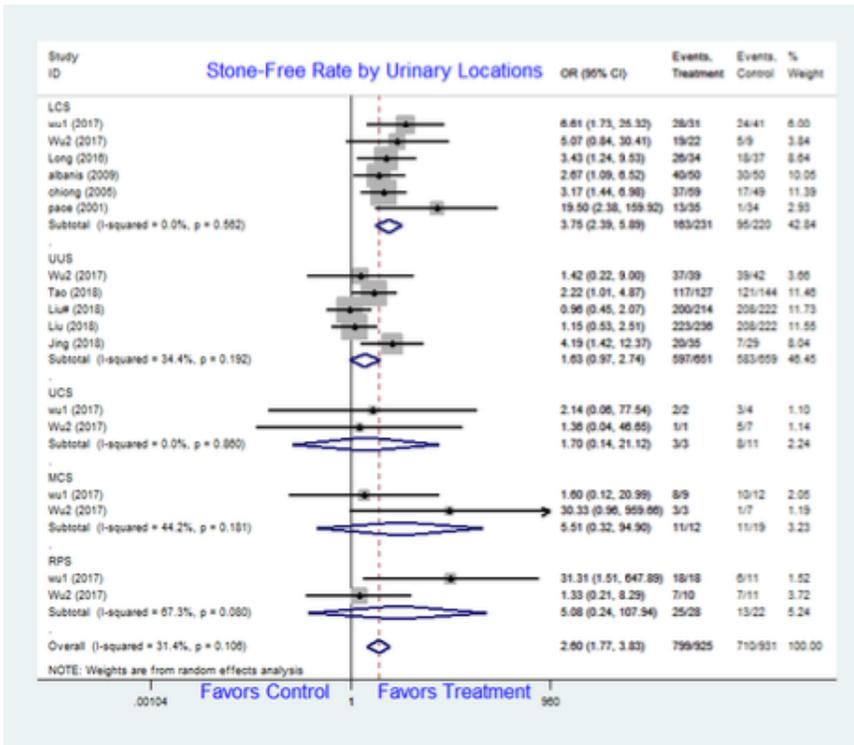


Figure 8

Subgroup analysis of different stone locations in SFR.

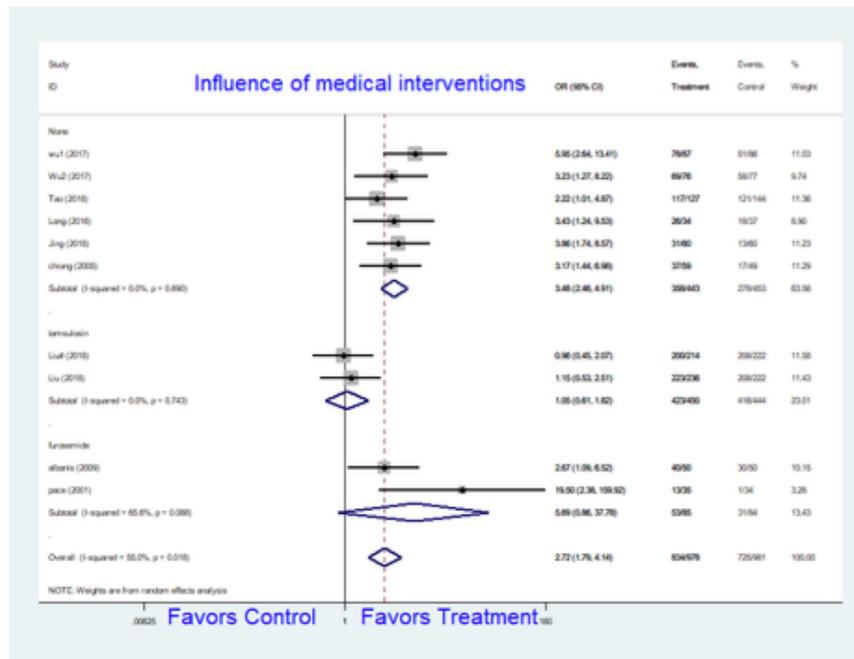


Figure 9

Subgroup analysis of medical intervention in SFR.

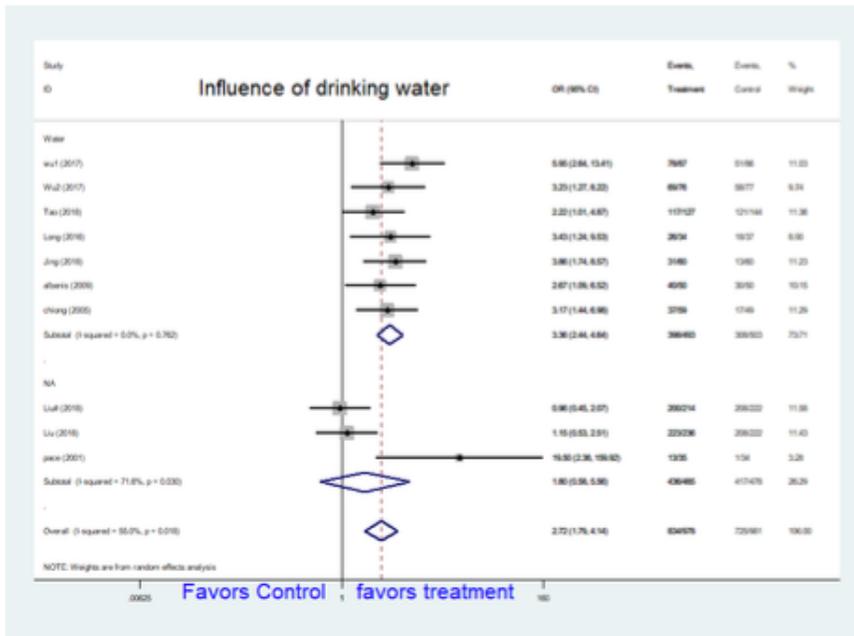


Figure 10

Subgroup analysis of drinking water before physical therapy in SFR.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [supplement1.doc](#)