Did we take physical therapy serious after ESWL and retrograde intrarenal surgery

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Linjie Peng
the first affiliated hospital of Guangzhou Medical University
ORCiD: https://orcid.org/0000-0003-1400-4611

Junjun Wen
the first affiliated hospital of Guangzhou medical university

Guohua Zeng
the first affiliated hospital of Guangzhou medical university
ORCiD: https://orcid.org/0000-0002-3110-8933

Wen Zhong
gzgyzhongwen@163.com Corresponding Author
ORCiD: https://orcid.org/0000-0003-0540-7195

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Abstract

**Background:** Physical therapy, including percussion, inversion, vibration and combinations, was clinically administrated to improve the stone-free rate (SFR). The present study aimed to investigate the role of physical after ESWL and retrograde intrarenal surgery (RIRS).

**Methods:** Systematic review of literature from PubMed, Scopus, Cochrane library and Embase which focused on physical therapy after ESWL and RIRS was administrated, meta-analysis was performed, SFR and complications was investigated.

**Results:** A total of 8 prospective studies with 1065 patients were enrolled, including 7 randomized control trials and 1 prospective study. 1 study was designed on RIRS and the rest 7 studies were on ESWL. Compared to observation group, physical therapy provided a higher SFR (OR= 3.38, 95% CI: 2.45-4.66, p< 0.0001) at any time point (week1, week2 and month1), especially the SFR in lower calyceal stone (OR: 3.51; 95%CI: 2.21-5.55; p<0.0001) and upper ureteral stone (OR:2.79; 95%CI:1.62-4.81; p=0.0002). In subgroup analysis, EPVL (external physical vibration lithecbole, OR:3.47; 95%CI:2.24-5.37; p<0.0001) and PDI (percussion, diuresis and inversion, OR:3.24; 95%CI:2.01-5.21; p<0.0001) were both effective. Complications such as hematuria, lumbago, dizziness and urinary tract infection were all comparable (OR: 0.84; 95% CI: 0.62-1.13; p = 0.237).

**Conclusions:** Physical therapy was effective and safe in increasing the SFR after ESWL and RIRS without significant side effects, especially for lower calyceal stone and upper ureteral or renal pelvic stone. A consistent protocol for physical therapy after lithotripsy was needed to be built, which would promote a better final stone-free. And the role of drinking enough water, furosemide and tamsulosin in physical therapy required further test.

**Review Registration:** PROSPERO 2019 CRD42019130228.

Background

Urolithiasis was one of the most frequently noted diseases in urology. The incidence of urolithiasis varied from 1% to 13% in different area, and was still increasing [1, 2]. Percutaneous nephrolithotomy (PCNL) was well established procedure for calculi larger than 2 cm, while extracorporeal shockwave lithotripsy (ESWL) and retrograde intrarenal surgery (RIRS) were first line choice for moderate size
stones ranged from 1cm to 2 cm [3-5]. The essential characteristics of PCNL, ESWL and RIRS destined different SFR and complication. Accordingly, PCNL, ESWL and RIRS had their inherent position in the management of upper urinary tract stones [6-11].

It was reported that SFR was 23.1%-91.5% with ESWL, and 45.6%-96.7% with RIRS [12]. The fate of residual fragments was getting more and more concerned, given that spontaneous passage was needed after ESWL or RIRS. Residual fragments related complications was foreseeable, renal colic, urinary tract infection (UTI), and steinstrasse was most common and might require additional operations [13, 14]. Furthermore, with a recurrence rate of 50% within 5 years and 80-90% within 10 years, residual fragments are more prone to recurrence and cause great economic burden [15].

Medical expulsive therapy (MET), including diuretics, Chinese patent medicine, α receptor blockers (tamsulosin) had been used as auxiliary method to improve SFR [16]. But medicine effect of tamsulosin in dilate ureteral luminal are still controversial [17-19], as well as other medicines.

Theoretically, lower calyceal stones (LCS) more prone to stay in situ owing to the renal collecting system anatomy and gravity, especially when patients keep a vertical position most of the time [20]. Stone fragments rolling into ureteral pelvic junction or upper ureter through body position change would increase the possibility of expulsion [21]. Based on which, self-help position therapy was performed to improve SFR after lithotripsy [22, 23]. Interestingly, physical activities like roller coaster and intercourse were proved to promote renal stone expulsion, indicating a potential modality to attain stone-free [21, 24-28]. Later, the physical therapies including percussion and inversion was tried in clinical practice [29]. More recently, external physical vibration lithecbole (EPVL) was designed to facilitate stone fragments passage, which combined the vibration and inversion by a precise manipulation from a machine [30].

However, there was no conclusive evidences of physical therapy facilitating stone fragments passage after lithotripsy, nor widely accepted or uniformed protocols. The present systematic review and meta-analysis was aimed to evaluate the role of physical therapy following ESWL and RIRS, and provide a higher level evidence for urologists to take physical therapy into serious consideration after lithotripsy to improve SFR.
Methods

1.1 Literature Search and article selection

The protocol of this study had been registered in PROSPERO (CRD42019130228). Systematic literature review in PubMed, Scopus, Cochrane library and Embase was performed in March 2019. A comprehensive literature search was conducted separately with following search strategy: (“physical or mechanical percussion”, OR “inversion”, OR “vibration”, OR “external physical vibration lithocbole”, OR “EPVL”), and (“extracorporeal shockwave lithotripsy”, OR “ESWL”, OR “flexible ureteroscopy”, OR “RIRS”), and (“residual stone”, OR “stone fragment”, OR “urinary stone”). The selection of relevant studies was in accordance with protocol items of PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines. The potentially eligible studies from the cited references in the enrolled papers were also assessed as significant papers. All the process was completed by two reviewers LJP and JJW, and disagreements were resolved by consensus after consulting WZ and GHZ.

1.2 Selection criteria

Studies were enrolled 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 compared physical therapies (external physical vibration lithocbole, mechanical percussion, inversion, position change or other similar means) with other interventions/conservative observations; (4) Patients received ESWL or RIRS within 3 months before physical therapy; (5) Patients demographics, such as age, gender, body mass index (BMI), stone location, stone size and comorbidities were provided; (6) Adult patients. Studies as below would be excluded: (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

Methodology was performed using Review Manager Version 5.3 software and R software, version R 3.6.1 (https://www.r-project.org/). The level of evidence (LE) was assessed using GRADE system to assess the methodological quality of the studies, Newcastle-Ottawa Scale (NOS) in non-randomized
controlled trials (N-RCTs), while Jadad scale in RCTs. Since the categorical variables of SFR and complications rate was our primary study subject, statistical analysis was carried out using odds risk (OR) and 95% confidence intervals (CIs).

Heterogeneity was assessed using the Higgins $I^2$ statistic (minimal heterogeneity: 0-30%, moderate heterogeneity: 31-50%, significant heterogeneity: >50%) [31]. When significant heterogeneity exists ($I^2 >50$%), the random effect model would be used for pooled analysis, otherwise fixed model would be performed. Furthermore, contour-enhanced funnel plots, sensitivity analysis and subgroup pooled analysis was performed to test the potential publish bias and heterogeneity.

In subgroup analysis, available residual stone fragments location would be classified into lower calyx stone (LCS), upper calyx stone (UCS), middle calyx stone (MCS), upper ureteral stone and renal pelvic stone (UPS), or else stone locations prior to lithotripsy was used instead. To analysis SFR alteration following time change, the SFR in first two weeks (week 1 and week 2) and first month (month 1) would be analyzed. As a medical equipment applied in larger spread, EPVL would also be enrolled into subgroup analysis by comparing to those without the use of EPVL (PDI, percussion, diuresis and inversion).

Results

1. Characteristics and quality of the included studies

As listed in Table 1, a total of 8 prospective studies published from 2001 to 2019 were finally included in the present analysis [29, 32-38], including 7 RCTs and 1 prospective case control study, and 3 of which were multi-center studies (NCT02645708, NCT02643134, one not registered). 1 study was after RIRS and the rest 8 studies were after ESWL, no eligible studies focused on physical therapies for residual stone fragments after PCNL. A total of 1065 subjects were included in the present study, 528 in the physical therapy group and 537 in control group, respectively. The baseline information of gender (OR= 0.96, 95% CI: 0.71-1.28, p=0.76), age (MD= 0.17, 95% CI: -0.11–0.46, p=0.24) and BMI (MD= 0.17, 95% CI: -0.26–0.60, p=0.45) was comparable in over population, details were showed in Table 1. The stone sizes were all less than 2cm prior to lithotripsy, except not available in one studies. The details of stone location and stone fragment numbers after lithotripsy were not available in all the
Risk of bias assessment was described in Figure 2.

Details of different physical techniques was presented in the Table 2, which included the techniques applied, machine used, time to first session physical therapy, time for each session of percussion, inversion angle, water drinking, whether medicine applied and the follow-up. 4 studies used EPVL (external physical vibration lithocbole), 2 with PDI (percussion, diuresis and inversion), 1 with MP (mechanical percussion), and 1 with HDI (hydration diuresis and inversion), respectively. Discrepancies was noticed in different techniques, but EPVL had a similar protocol. Drinking 500-3000ml water was advised in 7 studies prior to the physical therapy to provide promote stone expulsion by diuresis. As for the time to perform the first session physical therapy, 4 studies taken physical therapy immediately after ESWL, 3 within postoperative first week, and 1 in at least 3 months after ESWL. 1 to 4 sessions of physical therapy in total were given among overall studies, based on the last therapy outcomes or previous study design. Combined with percussion, an inversion angle of 12-60° tilt was selected. Percussion parameter was definite in EPVL, with a power of 40W, vibration frequency of 2800-3500 blows per minute, amplitude of 5mm, while there was not available in other physical therapy procedure. The percussion lasted 10-20 minutes in each session. The definition of stone-free was no observation of stone fragments under radiography (KUB, CT or ultrasound).

2. Meta-analysis results

2.1 Stone-Free Rate

A total of 8 eligible studies reported the SFR following physical therapy, and all the cases received medical interventions (7 ESWL and 1 RIRS prior to physical therapy). As shown in Figure. 3.A, a higher SFR was noted in physical therapy group (OR= 3.50, 95% CI: 2.55–4.81, p<0.0001). Heterogeneity test showed no significant heterogeneity ($I^2 = 0\%$, $p = 0.54$), and sensitivity analysis in Figure. 3.C showed that omitting each studies would not change final results or cause large elevation of quantitative difference. But minimal publication bias was detected in contour-enhanced funnel plots.
(t=1.85, p=0.113, Figure. 3.B), as the study of Pace et.al showed a marked deviation compared with other studies. Given that the study of Pace et.al was performed in 2000, which was much earlier than the others, and the results was far abnormal when compared with others, we decided to remove it from the final pool analysis. After excluding this study from final analysis, SFR in physical therapy group was still higher when compared to non-intervention group (OR= 3.38, 95% CI: 2.45–4.66, p<0.0001), and there was no significant heterogeneity was detected (I² = 0%, p = 0.76, Figure. 4). Additionally, higher rate of first two-day stone expulsion was observed in physical therapy group than non-intervention group (OR= 2.07, 95% CI: 1.36-3.16, p = 0.0007), as showed in Figure 5.A.

2.2 Complication
Overall complication rate was comparable as showed in Figure 6 (OR: 0.84; 95% CI: 0.62-1.13; p = 0.237), there was no significant difference in terms of hematuria (OR: 0.84; 95% CI: 0.54-1.29; p = 0.423), dizziness (OR: 2.88; 95% CI: 0.89-9.39; P = 0.078), lumbago (OR: 0.61; 95% CI: 0.31–1.19; P = 0.146) and urinary infection (OR: 0.73; 95% CI: 0.39-1.36; P= 0.328), respectively.

3. Subgroup meta-analysis
3.1 SFR in different physical therapy
As demonstrated in Figure 4, when we classified treatment into EPVL and PDI, SFR no matter in EPVL (OR: 3.47; 95% CI: 2.24-5.37; p < 0.0001) or in PDI (OR: 3.24; 95% CI: 2.01-5.21; p < 0.0001) was higher than in the non-intervention group.

3.2 SFR in different time
As depicted in Figure 5.B, comparisons of SFR in all time points (week1, week2 and month1) presented a statistically higher SFR in physical therapy group (OR: 2.48; 95% CI: 1.99–3.10; p < 0.0001), as was that, in the first week (OR: 1.93; 95% CI: 1.35–2.76; p =0.0003), in second week (OR: 2.59; 95% CI: 1.83-3.66; p < 0.0001), and in first month (OR: 3.51; 95% CI: 2.17-3.10; p < 0.0001).

3.3 Influence of stone location to SFR
A higher SFR in physical therapy group was noted in the overall analysis (OR: 3.19; 95% CI: 2.27-4.50; p < 0.0001). In the subgroup meta-analysis in term of the stone fragments location (Figure 7),
physical intervention group had a higher SFR in LCS (OR: 3.51; 95% CI: 2.21-5.55; p < 0.0001) and UPS (OR: 2.79; 95% CI: 1.62-4.81; p= 0.0002). However, there were no significant difference in other locations (UCS and MCS were mixed into pooled analysis due to few information) (OR:3.39; 95% CI: 0.77-15.03; p=0.108).

Discussion

Based on the present meta-analysis, physical therapy following RIRS and ESWL did improved the SFR at different time points, especially the stone location in lower calyx (OR: 3.51; 95% CI: 2.21-5.55; p < 0.0001) and renal pelvis/upper ureter (OR: 2.79; 95% CI: 1.62-4.81; p = 0.0002) benefit much more from the physical therapy than the stone in other locations (upper calyx and middle calyx).

Furthermore, the physical therapy did not bring more complication (all P> 0.05).

Currently, with popular of minimal invasive or non-invasive techniques, the stone clearance has become the first consideration after lithotripsy, especially spontaneous passage was needed in ESWL and RIRS. A better way to facilitate the residual stone fragment passage and improve SFR was worldwide discussed. As was known, a serial of factors would influence the spontaneous passage of the stone fragments following RIRS and ESWL, for example, lower pole stones, multiple calyceal stones, large stone burden and stone density parameters were reported to affect the SFR significantly [39, 40]. Others factors such as ureter condition, washing of urine, and ureteral smooth muscle movement should also be taken into consideration [41].

After the ESWL and RIRS, what we can do to improve the SFR was that, facilitate the stone fragments into the ureter, pushing the fragments passage from the dilated ureter, thus self-help position therapy, diuresis, relaxation ureteral smooth muscle was tried [17, 25].

In 2000, Honey et.al [42] reported PDI (percussion diuresis and inversion) can effectively mobilize residual stones out of the lower pole calyces, and eventually assist passage of fragments. In the meta-analysis published in 2013 from Liu et.al, limited evidence from two small studies indicated that PDI was safe and effective to assist clearance of LCS after ESWL (RR: 0.62, 95% CI: 0.47-0.82). Owing to the limited number of studies enrolled and rapid development of techniques, a pooled analysis based on this were required to discuss the clinical prospect of physical therapies. Fortunately, the
present meta-analysis enrolled more studies and again testified the effectiveness of PDI in improving SFR following ESWL and RIRS, especially the LCS and UPS, indicating that physical therapy for such special location stones would work.

With the increasing experience and regeneration of equipment, a new device called EPVL was invented in China, which can provide a well-controlled inversion and changing body position from a rotating couch, and also a circled mechanical percussion [32]. It was reported to improve the SFR following ESWL and RIRS. With multiple approaches for mechanical percussion, effective percussion could be performed. In 2016, Zhang et.al [43] performed a meta-analysis in Chinese enrolling Five randomized or Quasi-randomized controlled trials and demonstrated that EPVL was effective in promoting upper urinary tract residual stones expulsion (OR = 4.50, 95% CI 2.02-10.00, p=0.0002). According to subgroup analysis in present meta-analysis, the application of EPVL provided a higher SFR after ESWL and RRIS (OR: 3.47; 95% CI: 2.24-5.37; p < 0.0001), as well as PDI (OR: 3.24; 95% CI: 2.01-5.21; p < 0.0001). Given that there were no standard protocol for physical therapy, EPVL might provide a relative uniformed and repeatable protocol for clinical practice, thus more practical than other physical therapy.

Zhang et.al [44] investigated the potential ideal time to perform EPVL after RIRS, in which 3 days, 7 days, 14 days after RIRS were compared. They found that, the best time to perform EPVL was 3 days after RIRS, with a high SFR (final SFR: 91.11%) at any time points. However, the appropriate time point to performed the first session physical therapy was still not conclusive, since the present study did not get enough information from the enrolled studies.

Medical expulsive therapy (MET), including diuretics, Chinese patent medicine, α-receptor blockers (tamsulosin) had been used as auxiliary procedure to improve SFR. But the role of tamsulosin in dilation ureteral luminal was still controversial, as well as other medicines. In a three-arm study, Liu et.al [30] compared EPVL combined with tamsulosin, EPVL alone and tamsulosin alone, and found that, EPVL combined with tamsulosin could promote a higher SFR for distal ureteral stone fragments when compared the other two groups in the first week (91.1% vs. 50.5% vs.50%, P < 0.05). However, there was no significant difference in final SFR (94.5%, 93.5% and 93.6%, p > 0.05). Diuresis was
supposed to help stone fragments expulsion through urine washing, studies enrolled in present meta-analysis recommended enough water drinking before physical therapy (1000-3000ml). However, the volume of drinking water, when to drink, and the role of furosemide was still inconclusive, since limited information was got from the enrolled studies. Thus, further investigations were required to testify the role of combined physical therapy and MET.

When it came to the complications of physical therapy, we did not found any significant difference in terms of hematuria, lumbago and urinary infection between physical therapy and observation group, but inversion during physical therapy might cause dizziness even though with no statistical significance (OR: 2.88; 95% CI: 0.89-9.39; p= 0.078). EPVL and PDI facilitated the stone fragments passage, but did not increase the risk of renal colic and strainstrass formation in the present meta-analysis.

To be noticed, there was several limitations about this meta-analysis. The primary limitation was the small number of eligible studies and sample sizes. In addition, the appropriate time point to performed the first session physical therapy, and the role of tamsulosin and diuresis in physical therapy was still inconclusive, which need further investigations. With growing need of physical therapy, a standard protocol for mechanical percussion and inversion was required to be built in the near future. well-designed and large sample RCTs was still demanded to assess details of physical therapy.

Conclusions
Physical therapy was effective and safe in increasing the SFR after ESWL and RIRS without significant side effects, especially for lower calyceal stone and upper ureteral or renal pelvic stone. A consistent protocol for physical therapy after lithotripsy was needed to be built, which would promote a better final stone-free. And the role of drinking enough water, furosemide and tamsulosin in physical therapy required further test.

Declarations

Ethics approval and consent to participate

Not applicable.
Consent for publication

Not applicable.

Availability of data and mate

All data generated or analyzed 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

LJP carried out the study design, the literature search, quality assessment and data extraction, participated in the data analysis, drafted the manuscript. JJW performed the literature search, quality assessment and data extraction. WZ participated in the study design and supervised the project, and helped draft the manuscript, is corresponding author for this manuscript. GHZ is also the corresponding author for this manuscript, participated in study design and manuscript revision. All authors have read and approved the manuscript.

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Not applicable.

Abbreviations

SFR: Stone-free rate,
RIRS: retrograde intrarenal surgery,
ESWL: extracorporeal shockwave lithotripsy,
EPVL: external physical vibration lithocbole,
PDI: percussion, diuresis and inversion,
LCS: lower caliceal stones,
UCS: upper calical stones,
MCS: middle caliceal stones,
UPS: upper ureter and renal pelvic stone,

MET: medical expulsive therapy.

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## Tables

Table 1 summary of comparative studies included.

| Study+ years | Period | Type  | Location | Surgery | Stone Size | Gender | Age  | BMI   | LE    | Quality |
|--------------|--------|-------|----------|---------|------------|--------|------|-------|-------|---------|
| Wu 1         | 2016-  | RCT   | Kidney   | RIRS    | <17        | 66/21: 66/24 | 64.9+1. | 2     | 23.6  | +0.3  | 1       |
| Wu 2         | 2015-  | RCT   | upper urinary | ESWL | <15        | 56/20: 52/25 | 42.7+1. | 3     | 23.8  | +0.3  | 1       |
| Tao 2        | 2017-  | RCT   | upper ureter | ESWL | 1-20       | 83/44: 96/48 | 50.4+5.7 | 0.6   | 25.2  | +3.4  | 1       |
| Long 2       | 2014-  | RCT   | LCS      | ESWL    | 6-20       | 20/14: 22/15 | 44+9.5: 45.8+9.9 | 25.6 | 1     |
| Jin 2        | 2015-  | RCT   | Ureter, kidney | ESWL | NA         | 43/17: 49/11 | 38.2+1 | 0.6   | 25.8  | +2.7  | 1       |
| Albanisz 2   | 2009-  | Pro   | LCS      | ESWL    | 20         | 37/13: 39/11 | 36(16-69) | 2     | 25.2  | +4.2  | 1       |
| Chion 2      | 2000-  | RCT   | LCS      | ESWL    | 4-20       | 50/9: 30/19 | 45(23-72) | 1     | 25.2  | +4.2  | 1       |
| Pace 2       | 1999-  | RCT   | LCS      | ESWL    | <4         | 23/12: 29/5 | 40.6+2 | 1     | 25.2  | +4.2  | 1       |

NA: not available, N: blank, #: nos score, LCS: lower calyceal stone, Pro: prospective study. stone size
Table 2 Information of different physical treatments.

| Study | Technique | Machine | First treat | Percussion Time(min) | Inversion (degree) | Drinking (ml) | Medicine | SF | Treat session | Follow Up |
|-------|-----------|---------|-------------|----------------------|-------------------|---------------|----------|----|---------------|-----------|
| Wu1   | EPVL      | Friend I| 1 W         | 16~20                | 26                | 1000-2000     | No       | 0  | 1-2           | 2,3,5 W   |
| Wu2   | EPVL      | Friend I| 1 W         | 16-20                | 26                | 1500-2000     | No       | 0  | 1-2           | 1,2,4 W   |
| Tao   | EPVL      | Friend I| 1 W         | 15-20                | 26                | 1000          | NA       | 0  | 1             | 1,2,4 W   |
| Long  | EPVL      | Friend I| IM          | 6-12                 | 26                | 1000-1500     | NA       | 0  | 1-4           | 1,3W      |
| Jing  | MP        | VT300 MPL| IM         | 15-20                | 35                | 1000-3000     | NA       | 0  | 2/2d          | 1,2W      |
| Albani| HDI       | 9000    | IM          | NA                   | 12                | 1000          | F 40mg   | 0  | 4            | 13M       |
| Chion | PDI       | NA      | 1W          | 10                   | 45                | 500           | NA       | 0  | 4/1-2w        | 3M        |
| Pace  | PDI       | NA      | >3M         | 10                   | 60                | NA           | F 20mg   | 0  | 4/4w          | 3M        |

NA: not available, N: blank, IM: immediate, W: week, M: month, F: Furosemide, SF: definition of stone-free(mm)

Figures
Flow of studies selection for systematic review and meta-analysis.
Risk of bias summary.

Figure 2
### A Meta-analysis of stone-free rate among overall included studies

**Figure 3.B** Contour-enhanced funnel plots. **Figure 3.C** Results of sensitivity analysis.
| Study       | Experimental Events | Control Events | Odds Ratio | OR   | 95%-CI | Weight |
|------------|---------------------|----------------|------------|------|--------|--------|
|            | Total               | Total          |            |      |        |        |
| Wu1 2017   | 78                  | 87             |            | 5.95 | [2.64; 13.41] | 12.4%  |
| Wu2 2017   | 69                  | 76             |            | 3.23 | [1.27; 8.22]  | 12.4%  |
| Tao 2018   | 117                 | 127            |            | 2.22 | [1.01; 4.87]  | 20.9%  |
| Long 2016  | 26                  | 34             |            | 3.43 | [1.24; 9.53]  | 9.5%   |
| Fixed effect model | 324            | 344            |            | 3.49 | [2.26; 5.39]  | 55.1%  |
|            |                     |                | Heterogeneity: $i^2 = 0\%$, $\tau^2 = 0$, $p = 0.40$ |
|            |                     |                |            |      |        |        |
| technique = PDI |                   |                |            |      |        |        |
| Jing 2018  | 31                  | 60             |            | 3.86 | [1.74; 8.57]  | 14.7%  |
| Albanis 2009 | 40               | 50             |            | 2.67 | [1.09; 6.52]  | 14.0%  |
| Chiong 2005 | 37                 | 59             |            | 3.17 | [1.44; 6.98]  | 16.2%  |
| Fixed effect model | 169            | 159            |            | 3.24 | [2.01; 5.21]  | 44.9%  |
|            |                     |                | Heterogeneity: $i^2 = 0\%$, $\tau^2 = 0$, $p = 0.83$ |
|            |                     |                |            |      |        |        |
| Fixed effect model | 493            | 503            | 3.38 [2.45; 4.66] | 100.0% |
|            |                     |                | Residual heterogeneity: $i^2 = 0\%$, $p = 0.65$ |

Figure 4

Meta-analysis of stone-free rate after excluding studies in bias and subgroup analysis of EPVL and PDI.
Figure 5

A Meta-analysis of first two-day stone expulsion. Figure 5.B Subgroup analysis of stone-free rate in first two weeks and first month
### Figure 6

Meta-analysis of related complications.
| Location          | Study   | Experimental Events Total | Control Events Total | Odds Ratio | OR    | 95%-CI   | Weight |
|-------------------|---------|---------------------------|----------------------|------------|-------|---------|--------|
| LCS               | Wu1 2017 | 28 31                     | 24 41                | 6.61       | 5.2%  | [1.73; 25.32] |        |
|                   | Wu2 2017 | 19 22                     | 5 9                  | 5.07       | 2.5%  | [0.84; 30.41] |        |
|                   | Long 2016 | 26 34                     | 18 37                | 3.43       | 10.6% | [1.24; 9.53]  |        |
|                   | Albanis 2009 | 40 50                     | 30 50                | 2.67       | 15.6% | [1.09; 6.52]  |        |
|                   | Chiong 2005 | 37 59                     | 17 49                | 3.17       | 18.1% | [1.44; 6.98]  |        |
| Fixed effect model|         | 196 186                   |                      | 3.51       | 52.0% | [2.21; 5.55]  |        |
|                   | Heterogeneity: $I^2 = 0\%, \tau^2 = 0, p = 0.84$ |
| UPS               | Wu2 2017 | 37 39                     | 39 42                | 1.42       | 5.0%  | [0.22; 9.00]  |        |
|                   | Tao 2018 | 117 127                   | 121 144              | 2.22       | 23.3% | [1.01; 4.87]  |        |
|                   | Jing 2018 | 20 35                     | 7 29                 | 4.19       | 8.6%  | [1.42; 12.37] |        |
|                   | Wu1 2017 | 18 18                     | 6 11                 | 31.31      | 0.5%  | [1.51; 647.89]|        |
|                   | Wu2 2017 | 7 10                      | 7 11                 | 1.33       | 5.2%  | [0.21; 8.29]  |        |
| Fixed effect model|         | 229 237                   |                      | 2.79       | 42.6% | [1.62; 4.81]  |        |
|                   | Heterogeneity: $I^2 = 10\%, \tau^2 = 0.0565, p = 0.35$ |
| Others            | Wu1 2017 | 2 2                       | 3 4                  | 2.14       | 1.1%  | [0.06; 77.54] |        |
|                   | Wu2 2017 | 1 1                       | 5 7                  | 1.36       | 1.4%  | [0.04; 46.65] |        |
|                   | Wu1 2017 | 8 9                       | 10 12                | 1.60       | 2.5%  | [0.12; 20.99] |        |
|                   | Wu2 2017 | 3 3                       | 1 7                  | 30.33      | 0.3%  | [0.96; 959.66]|        |
| Fixed effect model|         | 15 30                     |                      | 3.39       | 5.4%  | [0.77; 15.03] |        |
|                   | Heterogeneity: $I^2 = 0\%, \tau^2 = 0, p = 0.53$ |

**Figure 7**

Subgroup analysis of influence of different stone fragment locations. LCS = lower calyx stone, UPS = upper ureter and renal pelvic stone, Others = upper calyx and middle calyx stone.

**Supplementary Files**

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