Bilateral simultaneous ureteroscopy for bilateral stone disease: a systematic review

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Introduction: *The treatment of bilateral renal and/or ureteric stones can be challenging due to concerns about its safety and efficacy compared to staged ureteroscopy. This review evaluates the current evidence to look at the outcomes of bilateral simultaneous ureteroscopy (BS-URS) for urinary stone disease.*

Material and methods: *A systematic review using studies identified by a literature search between January 1990 and August 2013. All English language articles reporting on outcomes of BS-URS for urolithiasis were included. Two reviewers independently extracted the data from each study.*

Results: *A total of seven studies (312 patients) were identified with a mean age of 40 years. Of the reported stone location, two thirds of the stones were in the ureter. With a mean operative time of 58 minutes, stone free status was achieved in 87.1% after the first look and 91.6% after a re-look for pure ureteric stones. Nearly 86% of patients had a postoperative stent inserted with a mean hospital stay of 2 days.*

In the pure ureteric stone cohort a total of 134 (50.8%) complications were reported. Around three quarters of the complications were Clavien I grading (hematuria, lower urinary symptoms and flank pain) and under a quarter were Clavien III complications.

Conclusion: *Although BS-URS achieved a high overall stone free rate; the complication rate seemed to be high. The quality of included studies in this review was weak and future research with good methodology is required to evaluate the feasibility and safety of BS-URS procedure.*

Key Words: review, bilateral, calculi, laser, stone, ureteroscopy

Introduction

Recent endoscopic advancement and evolution has positively impacted contemporary ureteroscopic management of ureteric and renal calculi. Ureteroscopy (URS) has been effectively employed in a number of complex settings such as obese patients,[1] pregnant patients,[2] and patients with bleeding diathesis[3] in both adult and pediatric populations. Both the American Urological Association (AUA)[4] and the European Association of Urology (EAU)[5] advocate the use of URS in the above mentioned clinical settings.

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Despite the availability of sophisticated ureteroscopes and laser technology the uptake of bilateral simultaneous URS (BS-URS) has been rather slow. This is primarily due to concerns of serious complications such as bilateral ureteric or renal injuries. Simultaneous URS (BS-URS) for bilateral renal tract stone disease has been recommended in selected cases by the AUA, although its efficacy and safety is poorly documented. The first reported BS-URS was by Camilleri et al[6] in 1994. Since then, many authors have reported their case series of BS-URS for ureteral and/or renal calculi with varying conclusions on the safety and efficacy of the approach. The potential benefits of BS-URS are a single anesthetic session, shorter combined hospital stay and reduced cost compared with a staged procedure.

This systematic review aims to review the world literature on BS-URS for both ureteral and renal calculi and to analyze the feasibility and safety of this approach.

Material and methods

Evidence acquisition: criteria for considering studies for this review

Inclusion criteria: 1) All articles written in the English language; 2) Studies reporting on outcomes following BS-URS for urolithiasis; 3) Patients of any age

Exclusion criteria: Studies reporting on outcomes of BS-URS for non-urolithiasis indication such as malignancy

Search strategy

The search involved finding relevant studies from MEDLINE, EMBASE, the Cochrane Central Register of Controlled Trials, CINAHL, Google Scholar and individual urological journals between January 1990 and August 2013. The terms used in the search included the following: 'bilateral', 'simultaneous', 'synchronous', 'ureteroscopy', 'ureterorenoscopy', 'calculi', 'stones' and 'urolithiasis'. Boolean operators (AND, OR) were used to refine the search, Figure 1.

Data extraction and analysis

Two reviewers independently identified all studies that appeared to fit the inclusion criteria for full review. The references of the searched studies were evaluated for potential inclusion into the review. Where possible, contact was attempted with authors to verify data if the study was unclear or if the data was unavailable from the study. The following data was extracted from the studies: 1) Country of origin; 2) Study type; 3) Ureteroscope type; 4) Method of stone extraction; 5) Population demographics (age and gender); 6) Stone size and location.

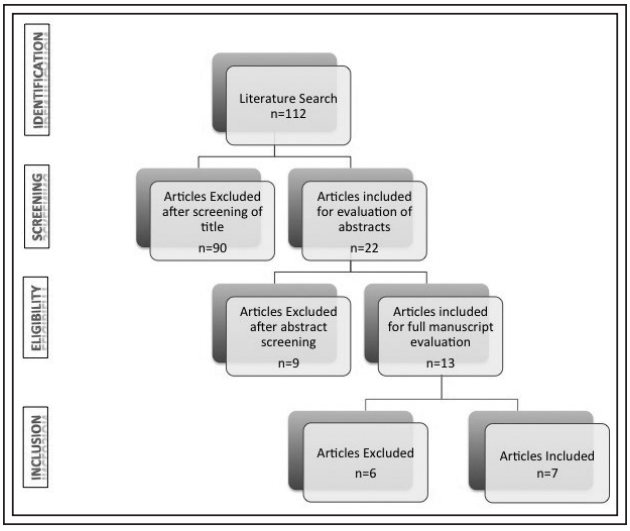

Figure 1. PRISMA flow chart for article selection process of review. Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. *PLoS Med* 2009;6(7):e1000097.

Outcome measures

Primary outcomes: 1) Operative time; 2) Proportion of patient requiring insertion of ureteric stent; 3) Stone free rates (SFR); 4) Hospital stay.

Secondary outcomes: complication rates.

Evidence level of included studies

The levels of evidence and recommendation were based on the Centre For Evidence Based Medicine.[7]

Results

Literature search and included studies

The literature search yielded 112 studies, of which seven studies met the inclusion criteria, Table 1. All the studies were observational cohort studies. Two of the studies[10,13] were retrospective studies. The remaining studies did not clearly document the study method. The earliest study was published in 2003, whilst the majority (four studies) was published in 2012. There were two studies from Turkey and one each from China, Egypt, India, Iran and USA.

Patient, stone and operative characteristics

There were a total of 312 patients. Six studies[6-11] reported on the male to female ratio. Overall there was a slight male preponderance (1.7:1). The overall mean age (40 years, range 4-78) was calculated from five studies. The mean stone size and stone burden were poorly reported across all the studies and has been summarized in Table 1.

The methods of URS and stone retrieval varied across all the studies; the most popular methods being the semi-rigid URS and pneumatic lithotripsy utilized in three of the studies.[11,12,14] Four studies clearly document the use of semi-rigid ureteroscopes.[10-12,14] In one study it does appear that the authors employed a rigid ureteroscope, although not clearly documented.[9] Huang et al used only flexible ureteroscopes and Hollenbeck et al used both flexible and semi-rigid ureteroscopes.[8] Huang et al is the only study that used access sheaths for their procedures.[13] The distribution of stones is summarized in Table 2. Two studies reported on stone composition.[13,14] Only Huang et al reported the use of access sheaths. None of the studies reported preoperative stenting. Gunlusoy et al[12] explicitly reported excluding patients who had preoperative stents or nephrostomy insertion. Two studies clearly reported threshold stone size to

TABLE 1. **Overview of included studies**

	Studies						
	Hollenbeck 2003[8]	**Darabi 2005[9]**	**El-Hefnawy 2011[10]**	**Mushtaque 2012[11]**	**Gunlusoy 2012[12]**	**Huang 2012[13]**	**Isen 2012[14]**
Study type	Unclear	Unclear	Retrospective	Unclear	Unclear	Retrospective	Unclear
LOE	3	3	3	3	3	3	3
URS	Semi (6.9 F)/ flexi (7.5F) + HL	Rigid (unclear) + lithotripsy ND (8F Wolf or 10.5F Storz)	Semi rigid + PL + HL (8F/10F Wolf)	Semi rigid + PL (7.8F)	Semi rigid (8F/10F) + PL	Flexi + HL (URF-P5 Olympus)	Semi rigid + PL (8F/ 9.8Fr Wolf)
N	23	19	89	60	55	25	41
M:F	ND	10:13	68:21	38:22	37:18	13:12	17:24
Mean age yrs (SD/range)	52 (± 14.9)	ND (4-78)	49 (13-74)	ND (11-60)	46.1 (22-81)	49.8 (28-69)	41.2 (28-76)
Mean stone size, mm (SD/range)	ND	ND	ND	ND (5-20)	10.7 (± 4.2, 5-21)	ND	8.8 (7-16)
Mean stone burden, mm (SD/range)	16.1 (± 11.7)	ND	ND	ND	ND	24 (± 5, 17-37)	ND
SFR definition	ND	ND	ND	Unclear	No stones	< 1 mm	< 4 mm
Follow up imaging to evaluate stone free status	Plain x-ray (KUB)	ND	Plain x-ray (KUB) and NCCT	Plain x-ray (KUB)	Plain x-ray (KUB), USS and IVU (in case of pelvicalyceal dilation)	CT	Plain x-ray (KUB) and USS or NCCT
Time between surgery and imaging	1 month	ND	After procedure and before discharge and 3 months	1, 5 and 28 days	1 day and 6 weeks	7 days	7 days

LOE = level of evidence; URS = ureteroscopy; HL = holmium laser, PL = pneumatic lithotripsy, SD = standard deviation, ND = not documented)

define stone free status.[13,14] Huang et al[13] defined residual stone size < 1 mm as stone free and Isen et al[14] defined stone size < 4 mm as stone free. The imaging modality and duration between intervention and imaging to evaluate stone free status for each individual study is demonstrated in Table 1. Two studies reported stone composition.[13,14] In the Huang et al series 64%, 28% and 8% of the patients had calcium oxalate stone, mixed and magnesium ammonium phosphate stones respectively.[13] In Isen et al series stone analysis results were available in 8 (19.5%) patients: calcium oxalate in 7, calcium phosphate in 2 and uric acid in 1.[14]

Primary outcomes

Operative time: Five studies[8,11-14] reported operative time. The overall mean operative time was 57.7 minutes (range 21-175 minutes), Table 3.

Ureteric stent insertion: Six studies[8,10-14] reported on postoperative ureteric stents insertion. A total of 85.8% of all patients had postoperative ureteric stents inserted.

TABLE 2. **Number of stones by location**

	Studies							
	Hollenbeck 2003[8]	**Darabi 2005[9]**	**El-Hefnawy 2011[10]**	**Mushtaque 2012[11]**	**Gunlusoy 2012[12]**	**Huang 2012[13]**	**Isen 2012[14]**	**Totals**
Ureteric	4	38	178	120	110	ND	82	354
Renal	15	ND	ND	ND	ND	128	ND	143
Renal + ureteric	4	ND	ND	ND	ND	ND	ND	4
UP	ND	ND	ND	ND	ND	26	ND	26
MP	ND	ND	ND	ND	ND	31	ND	31
LP	ND	ND	ND	ND	ND	42	ND	42
RP	ND	ND	ND	ND	ND	29	ND	29
UU	ND	ND	ND	16	21	ND	16	53
MU	ND	ND	ND	50	28	ND	11	89
DU	ND	ND	ND	54	61	ND	55	170
Above pelvic brim	ND	ND	154	ND	ND	ND	ND	154
Below pelvic brim	ND	ND	24	ND	ND	ND	ND	24

ND = not documented; U/M/LP = upper/mid/lower pole; RP = renal pelvis; U/M/DU = upper/mid/distal ureter

Mushtaque et al had the lowest rate at 65%. Huang and Isen stented all their patients post procedure,[13,14] Table 3. Stone free rates (SFR): All seven studies reported on SFR, Table 3. Five studies reported purely on ureteral stones,[9-12,14] Table 4. After first look URS, the overall mean SFR for ureteral stones was 87.1%. On second look the SFR improved to 91.6%, Table 4.

Huang et al reported only on renal calculi using a flexible ureteroscope.[13] Their reported first and second look SFR was 56% and 88.5% respectively.[13]

TABLE 3. **Summary of primary outcomes**

	Studies						
	Hollenbeck 2003[8]	**Darabi 2005[9]**	**El-Hefnawy 2011[10]**	**Mushtaque 2012[11]**	**Gunlusoy 2012[12]**	**Huang 2012[13]**	**Isen 2012[14]**
Op time (min)	90 ± 46	ND	ND	40-120	59 ± 21 (21-100)	81.2 ± 25 (42-137)	58.4 (36-81)
Stent insertion, n (%)	18 (75)	Unclear	78 (87.6)	39 (65)	96/110 units (87.3)	25 (100)	41 (100)
Ureteric SFR (%)	100	84.2	95.5	85	94.5	ND	98.7
Renal SFR (%)	63	ND	ND	ND	ND	88.5	ND
Overall SFR (%)	88	84.2	95.5	85	94.5	88.5	98.7
Hospital stay (days)	ND	ND	2.3 ± 1 (1.5-7)	2.35 (1-5)	2.4 ± 0.9 (1-5)	ND	1.2 (1-3)

ND = not documented

TABLE 4. **Stone free rates (SFR)**

Studies	Ureteral stones	
	1st SFR (%)	2nd SFR (%)
Darabi 2005[9]	84.2	84.2
El-Hefnawy 2011[10]	86	95.5
Mushtaque 2012[11]	85	85
Gunlusoy2012[12]	90	94.5
Huang 2012[13]	NA	NA
Isen 2012[14]	90.2	98.7
Overall	**87.1**	**91.6**

NA = not applicable

Hollenbeck at al used both semi rigid and flexible ureteroscopes to treat both ureteral and renal calculi. First look SFR for only renal, renal and ureter and only ureteric stones was 42%, 50% and 80% respectively.[8] Second look SFR for only renal, renal and ureter and only ureteric stones was 63%, 67% and 100% respectively.[8]
Hospital stay: Four studies[10-12,14] reported on hospital stay. The overall mean hospital stay was 2 days (range 1-7 days), Table 3.

Secondary outcomes

All seven studies reported on complications. In the pure ureteric stone cohort (5 studies,[9-12,14] all used semi-rigid/rigid scopes) a total of 134 complications were reported with a overall mean complication rate of 50.8%. The most common complication was "hematuria that did not require blood transfusion" (n = 31), followed by "lower urinary track symptoms" (n = 27) and "abdominal/flank/pelvic pain requiring analgesia" (n = 18). The complications ranged from Clavien I to Clavien III, Table 5. There were 99 Clavien I complications, accounting for about three-quarters of all complications and 31 Clavien III complications, making up just under a quarter, Figure 3. Eleven and 13 cases of mucosal injury and ureteric perforation/laceration were reported respectively. None of the studies adopted the Post-Ureteroscopic Lesion Scale (PULS) for describing these injuries. The assumed PULS classification for mucosal injury was PULS 1&2 and for uretereric perforation/laceration was PULS 3&4. Isen et al reported the most complications, with the most severe complications being mucosal injury and ureteral perforation (PULS 3&4, Clavien III), both of which were managed with ureteric stenting for 3 weeks.

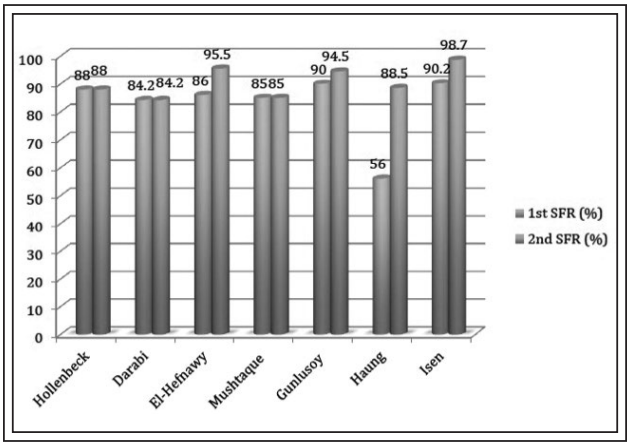

Figure 2. First and second look stone free rate (SFR) by study.

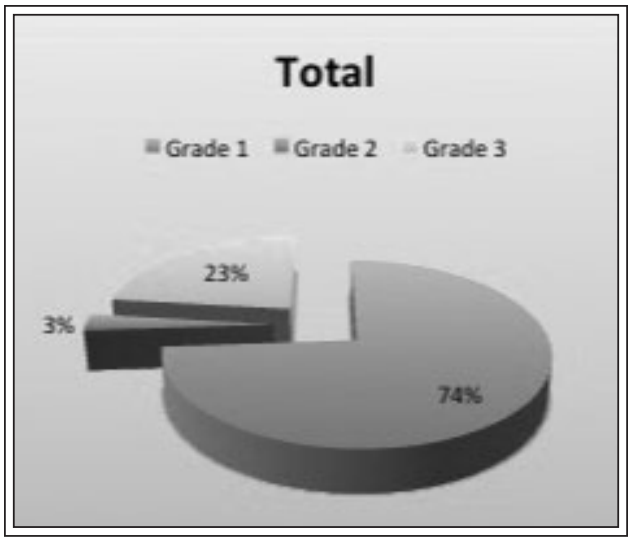

Figure 3. Number of complications (%) categorized by Clavien classification for the five studies 9-12,14 reporting on ureteric stones only.

Hollenbeck at al[8] used both semi rigid and flexible ureteroscopes to treat pure ureteral, pure renal and ureter and renal calculi. The study reported one death (Clavien V); the patient developed a pulmonary embolus leading to death after a procedure that lasted 175 minutes. Additionally they reported four patients with pain (Clavien I), one with UTI/urosepsis (Clavien II), one with urinoma (Clavien III) and one with a small ureteral perforations (PULS 3, Clavien III) managed with a ureteral stent following the procedures. They however did not report individual cohort complications for pure ureteral, pure renal and ureter and renal calculi cohorts.

Huang et al[13] (renal calculi using a flexible ureteroscope) reported two cases of hematuria (Clavien I) and two cases of urinary tract infection (Clavien II).

TABLE 5. **Complications reporting on pure ureteric stones only**

Nature of complication	Frequency	Clavien classification
Hematuria not requiring blood transfusion	31 (25%)	I
Lower urinary tract symptoms (LUTS)	27 (20%)	I
Abdominal/flank/pelvic pain requiring analgesia	18 (13.4%)	I
Fever	18 (13.4%)	I
Ureteral perforation/laceration (Grade 3 and 4 on PULS)	13 (10%)	III
Mucosal injury (Grade 1 and 2 on PULS)	11 (8%)	III
UTI/urosepsis/pyelonephritis	2 (1.5%)	II
Stone migration	5 (3.7%)	III
Post-obstructive diuresis	3 (2.2%)	I
Pain requiring readmission	2 (1.5%)	I
Pain requiring early stent removal	2 (1.5%)	III
Pyrogenic infection	2 (1.5%)	II

PULS = post-ureteroscopic lesion scale

Discussion

All the studies were of level-3 evidence. This review suggests BS-URS has the potential to be an effective strategy for the management of bilateral urolithiasis achieving an overall SFR of close to 90%. As expected the SFRs for ureteric calculi were superior in comparison with renal calculi. This is likely to be due to the longer retrograde access, more complex calyceal anatomy and other technical challenges associated with renal calculi. The average operative time was close to an hour, which is comparable with contemporary outcomes of other techniques of large stones.[1-5] The majority of patients had postoperative ureteric stents (85.8%). Concerns of acute kidney injury due to transient bilateral ureteric spasms, apart from other causes are the likely rationale behind this trend. The AUA and EAU guidelines suggest post ureteroscopy only following complicated URS.[4,5] Although there aren't any clear recommendations for postoperative ureteric stenting in a BS-URS setting, the authors recommend regular stenting to keep morbidity to a minimum. The mean hospital stay was prolonged at 2 days, however, this may be comparable to the cumulative hospital stay for a staged procedure.

The primary argument against BS-URS has been the postoperative complication associated with it. Predictably the complication rate in this review was relatively high. The majority of the complications were Clavien III or less. There was one reported death from a pulmonary embolism following a prolonged procedure (175 minutes). These complications are significantly higher than unilateral URS. It has to be however borne in mind that in BS-URS the stone burden is obviously higher than contemporary series outcomes on unilateral URS on single sided calculi. Hence the outcomes of BS-URS should be compared with the cumulative outcomes of a staged URS in patients with bilateral urolithiasis. Hollenbeck et al compared staged URS with BS-URS for bilateral urolithiasis in a retrospective series. They reported that BS-URS was associated with added morbidity; however, the cumulative risk with staged procedures (14% per procedure) was similar to BS-URS (29%).

With the advent of miniature low-caliber ureterscopes, flexible ureteroscopes, laser technology (holmium YAG), the availability of a plethora of gadgetry and increasing experience there has been a significant paradigm shift in the management of renal tract stones. There is increasing employment of URS in the management of larger and more complex stones previously only in the realm of PCNL. Aboumarzouk et al's[15] systematic review of nine studies reported a mean SFR of 93.7% in patients with a mean renal stone size of 2.5 cm when dealt with flexible ureteroscopy and lasertripsy. The overall complication rate was 10.1% of which 5.3% were deemed major complications. Observing theses trends it is therefore entirely plausible that BS-URS in more contemporary series is likely to have better outcomes as well. BS-URS has potential advantages of a single anesthetic and theatre time and reduced cumulative hospital stay. With decreasing resources and increasing costs these benefits could prove to be invaluable for healthcare institutions.

Although the reported literature is sparse, bilateral single session strategy has been employed by other

techniques such as PCNL and SWL for bilateral urolithiasis as well. The reported SFR for bilateral PCNL ranges between 87% to 96%, hospital stay between 2.9 days to 4.3 days and complication rates range between 17.5 % to 36%.[16-18] The reported SFR for bilateral-SWL ranged between 60%-80%.[19,20]

One of the limitations of this review is the poor level of available evidence. The authors would therefore suggest interpreting this data with caution due to poor quality of currently available evidence and heterogeneity. All the evidence in this review was from observational cohort studies of data, which involved both ureteric and renal stones (Level 3). For dissemination of widespread standardized practice there is a requirement for high quality evidence. Further research in the form of prospective collaborative studies or large volume single series are required to establish: 1) Safety and feasibility of BS-URS; 2) Cost-analysis to evaluate benefit over staged URS for bilateral urolithiasis; 3) Learning curves required to perform BS-URS.

Furthermore comparison of BL-URS with single session-URS and other treatment options such as BL-ESWL and BL-PCNL will be required in a randomized control trial setting. Additionally there is a requirement for standardization of entry criteria into studies, definition of pre-intervention parameters and post-intervention outcomes in order to compare various interventions. Somani et al[21] have recently suggested the use of "stone free level" as an outcome measure of intervention for renal tract calculi. This is simple model, however requires acceptability and validation before widespread use. More effort and research is required to design similar models.

The outcomes of ureteroscopy are also influenced by factors such as diameter of the scopes and type of manufacturer. The low numbers of studies and heterogeneity of the data in this review made it impossible to evaluate the influence of these factors.

Conclusion

The evidence from this systematic review suggest that BS-URS is an effective procedure with overall SFR close to 90%. However, operating on both urinary systems does come at a cost, namely a slightly higher than expected complication rate, although a significant proportion of these were Clavien III or less. However it remains unclear how this compares to the cumulative morbidity associated with staged procedures. The authors would however suggest interpreting this data with caution due to poor quality of currently available evidence. More research is required to assess the safety and feasibility of BS-URS in management of bilateral urolithiasis. □

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