Treatment modalities for small-sized urolithiases and their impact on health-related quality of life

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ABSTRACT

Introduction: Health-related quality of life (HRQoL) is often reduced in patients with urolithiasis. The objective of this study was to perform a systematic review to describe impact on HRQoL based on different modalities of treatment for small urolithiases with a diameter smaller or equal to 10 mm.

Methods: Electronic databases were searched with no language or date restrictions to identify studies which were included if they reported: adult patients (≥18 years old), renal or ureteral stone(s) confirmed on imagery, validated reporting of HRQoL, and stone diameter equal or smaller than 10 mm undergoing active surveillance, medical expulsive therapy (MET), shockwave lithotripsy (SWL), or ureteroscopy (URS).

Results: Of 672 citations, nine articles were eligible. Five studies (all ureteral) reported HRQoL according to medical stone management. Three of them found that HRQoL in MET patients was

KEY MESSAGES

- Literature shows that patients with urinary stones ≤10 mm have better HRQoL when treated with MET vs. AS, when treated with SWL vs. URS for renal stones, and when treated with URS vs. SWL for ureteral stones.
- In addition to stone location, other factors, such as stone size and postoperative stenting, should be considered for optimal HRQoL.
- There is a need for prospective, multicenter, observational studies with long-term followup using a standardized, disease-specific instrument, such as the WISQoL.

better than in active surveillance patients and two studies found no difference in HRQoL between MET and active surveillance groups. Four studies (three ureteral, one renal) reported HRQoL according to surgical stone management. Of the ureteral stone studies, two reported better HRQoL in URS patients than in SWL patients, while one study found no difference between URS and SWL groups. In the renal stone study, SWL patients had better HRQoL than URS patients.
Conclusions: Patients with urinary stones 10 mm or smaller have better HRQoL when treated with MET vs. active surveillance, when treated with SWL vs. URS for renal stones, and when treated with URS vs. SWL for ureteral stones. There is an important need for more studies on this topic.

INTRODUCTION

Kidney stones, causing intense pain and frequent recurrence, significantly impact Health-Related Quality of Life (HRQOL).[1] Various therapeutic options, from active surveillance to surgical interventions like shock wave lithotripsy (SWL) and ureteroscopy (URS), are available based on stone size.[2] While the role of medical expulsive therapy (MET) remains controversial, existing literature suggests potential benefits for larger (5-10mm) distal ureteral stones.[3] HRQOL measurement tools, influenced by variables like stone location and ureteral stent presence, are essential for kidney stone patients.[4-5] Despite this, and to our knowledge, there are no systematic reviews in the current literature regarding the management of small urolithiases measuring ≤10mm.

METHODS

This study was registered a priori on PROSPERO (registration ID CRD42023454869). No funding was received.

Search strategy

In order to conduct this systematic review, we performed an electronic search for relevant literature on 4 databases (Medline, Embase, Cochrane Central Register of Controlled Trials, Web of Science). The advanced search on these databases included articles from inception to July 2023, and our search terms were made up of 3 main categories: terms associated with "urolithiasis", terms associated with "therapeutic options", and terms associated with "quality of life". Articles written in a language other than English were retained and translated, and once all the literature was gathered from the databases, duplicates were identified and discarded using EndNote (version 20), a reference management software (Clarivate, London).

Study selection

Study selection was performed by two authors (N.L., P.N.). Reviewers first independently screened titles and abstracts for potentially relevant articles and then independently performed

full-text review according to predefined eligibility criteria. References of included articles were cross searched to identify any articles missed during the initial search. Disagreements were resolved by consulting the senior authors (M.B).

Eligibility criteria

All case reports, case series, case-control, cohort and randomized-control studies were included if they included (1) Adult patients (18 years and older), (2) presence of renal or ureteral stone(s) confirmed on imagery, (3) validated reporting of HRQOL and (3) stone diameter equal or smaller than 10mm. The exclusion criteria for the study were as follows: review studies, studies done on a pediatric population, studies not reporting HRQOL, studies not reporting outcome on patients with stones ≤10mm, studies not comparing treatment modalities, and studies where the full text was not available. An abstract review and a full-text review were conducted on all compiled articles independently by two reviewers (N.L., P.N.) to filter relevant articles. Any discordance was resolved with the help of a third reviewer (M.B.).

Data items

One reviewer (N.L.) performed data abstraction, which another reviewer (P.N.) verified independently. Corresponding authors were not contacted when the outcome was unavailable. We extracted the following when available: study design, study year, number of participants, objective of the study, main inclusion criteria, therapeutic option comparators, distribution of participants in each therapeutic option, post-operative stenting, stone size, stone density, stone location, age, sex, body mass index (BMI), HRQOL measurement tool, HRQOL measurement timing, and reported HRQOL outcome.

Assessment of risk bias

Information on the authors, affiliations, date, and source of each study included in this review was hidden to avoid bias in the assessment of the methodological quality of the articles. Assessment of the quality of included studies was performed independently by two authors (N.L., P.N.) using the Risk of Bias in Non-Randomized Studies – of Interventions (ROBINS-I) tool.[6] The possible levels of risk of bias were as follows: low risk, moderate risk, serious risk, and critical risk. Any discordance was resolved with the help of a third reviewer (M.B.).

RESULTS

From a total of 672 studies, we identified 9 relevant articles based on our inclusion and exclusion criteria (Figure 1, Table 1).

Medical management

Five studies have been reported since 2014, offering an up-to-date perspective on the reported HRQOL according to the medical management of stones 10mm or smaller.[8,9,10,11,13] Eryildirim et al. (2015) studied 120 patients with single ureteral stones between 5 and 10mm who received either MET via tamsulosin or underwent active surveillance with pain management only, and concluded that after 4 weeks, the first group had significantly better mean HRQOL scores on the

EuroQOL scale (0.80 vs 0.72; $p < 0.05$), comprised of 5 subsets: mobility, self-care, usual activities, pain or discomfort, and anxiety or depression. None of the patients had stents inserted. Stone passage rates and conversion to stone removal procedures were 36.7% and 16.7% in the active surveillance group versus 43.3% and 11.7% in the MET group. In the following year, Eryilidirim et al. also looked at 80 patients who had undergone SWL for single ureteral stones between 5 and 10mm in any segment of the ureter, and who subsequently underwent either MET or conservative management only. Once again, they concluded that the MET group had significantly better mean HRQOL scores on the EuroQOL scale, comprised of the same 5 subsets, after 4 weeks (0.82 vs 0.78; $p < 0.05$). The primary outcomes for this study included analgesic requirements, number of colic renal attacks, number of emergency department (ED) visits, and HRQOL.

Ju et al. (2020) studied 165 patients who had undergone URS for single distal ureteral stones 10mm or smaller, and who subsequently received terazosin and nifedipine, terazosin only, or conservative management only. Patients who received terazosin and nifedipine after URS had significantly better mean Quality of Life Scores (QOLS) than patients who received terazosin only or conservative management only after URS, at 1-week post-intervention ($p < 0.05$). All patients had stents inserted following the URS procedure. Stone passage rates were 94.5% in the combination group, 81.8% in the terazosin group, and 65.5% in the conservative management group. The primary outcomes of this study included stone passage rates and times.

Lee et al. (2014) looked at 108 patients with single proximal ureteral stones 6mm or smaller who received either tamsulosin or underwent active surveillance, and concluded that after 4 weeks, there was no significant difference noted in mean HRQOL scores on the EuroQOL scale. None of the patients had stents inserted. The stone passage rate was significantly higher in the MET group as opposed to the active surveillance group (74.1% vs 46.3%; $p<0.05$) and the active surveillance group tended to be more likely to convert to SWL or URS as opposed to the MET group, although this was not significant.

Pickard et al. (2015) studied 1150 patients with single ureteral stones 10mm or smaller who were treated with either tamsulosin, nifedipine, or underwent active surveillance. They found no significant difference noted in mean HRQOL scores on the EuroQOL scale at 4 weeks and 12 weeks, or on the 36-Item Short Form Survey (SF-36) physical and mental components at 4 weeks and 12 weeks. Stone passage rates were 81.2% in the tamsulosin group, 80.2% in the nifedipine group, and 79.9% in the active surveillance group.

In all 5 studies, there was a single stone, and the location of the stone was in the ureter. One study[10] looked at distal segment stones, one study[11] looked at proximal segment stones, and 3 studies[8,9,13] looked at all ureteral segments. In 3 studies,[8,11,13] the patients were not stented between the beginning of the intervention and the measurement of HRQOL. In one study,[10] stents were routinely inserted in all patients following the URS procedure and were removed 4 weeks post-operatively. In one study,[9] the presence or absence of stents was not described. When

described, stone passage rates and avoidance rates of conversion to procedural management were always higher in groups with better HRQOL. Other study characteristics are detailed in Table 2.

Surgical or procedural management

Four studies studying HRQOL according to the surgical management of urinary stones 10mm or smaller were reported since 2005.[7,12,14,15] Ceylan et al. (2018) looked at 111 patients with single proximal ureteral stones 10mm or smaller who underwent either SWL or URS, and concluded that at 4 weeks post-intervention, there was no significant difference noted in the mean HRQOL scores on any of the subsets of the SF-36, which include physical functioning, mental health, role limitation due to physical health or emotional health, bodily pain, general health, vitality, and social functioning. No data on procedural success rates were available.

Pearle et al. (2005) looked at 78 patients with single lower pole renal stones 10mm or smaller who underwent either SWL or URS, and concluded that at 4 weeks post-intervention, patients who underwent SWL had significantly better mean HRQOL scores on the SF-36 than patients who underwent URS, and 90% of patients who underwent SWL vs 63% of those who underwent URS would choose to undergo the same procedure again ($p < 0.05$). Secondary treatments were necessary in 15.6% of SWL cases (6.3% SWL and 9.4% URS), while 2.9% of URS patients underwent URS again.

Sarica et al. (2016) looked at 80 patients with single upper ureteral stones between 5 and 10mm who underwent either SWL or URS, and concluded that at 4 weeks post-intervention, patients who underwent URS had significantly better mean HRQOL scores on the EuroQOL scale than patients who underwent SWL (0.87 vs 0.77; $p < 0.05$). Stone passage rates were 83.9% in the URS group, and 16.1% required removal of residual fragments by flexible URS. Stone passage rates were 70.6% in the SWL group and 26.5% required secondary treatment with URS. The primary outcomes in this study included stone passage rate and complication rates.

Finally, Sonmez et al. (2021) looked at 153 patients with middle and upper ureteral stones 10mm or smaller who underwent either SWL, URS without stenting, URS with 4.8 French stenting, or URS with 6 French stenting. It was found that at 2 weeks post-intervention, patients who underwent URS with no stent placement had significantly better mean HRQOL scores on the SF-36 when compared to patients who underwent SWL or URS with 4.8 French or 6 French stenting (69.9 vs 61.1 vs 59.9 vs 56.3; $p < 0.05$). No data on procedural success rates were available.

In all 4 studies, included patients had a single stone. In 3 of the 4 studies,[7,14,15] the location of the stone was in the ureter and in one study[12], the location of the stone was renal. In one study,[12] patients were not post-operatively stented. In the 3 other studies, some of the patients were post-operatively stented. In the study presented by Ceylan et al., the proportion of patients who had stents inserted post-operatively was not specified. In the study presented by Pearle et al., 3.1% of SWL patients received stents while 88.6% of URS patients received stents. In the study presented by Sonmez et al., 28.1% and 27.5% of total patients received a 4.8 French and 6 French stents respectively. When described, stone passage rates and rates of avoidance of

secondary procedures for ureteral stones were always higher in groups with better HRQOL. In the study on renal stones, HRQOL in the SWL group was higher despite higher rates in secondary procedure. Other study characteristics are detailed in Table 3.

DISCUSSION

Multiple treatment options for urolithiasis exist, with treatment modality selection dependent on factors like stone size, location, complexity, and patient-specific symptoms and comorbidities.[16] The choice of treatment significantly influences the patient's HRQOL, reflecting their freedom from impairment, handicap, or disability.[17] Validated HRQOL measurement tools, such as the widely used EuroQOL scale and SF-36, were prevalent in our study, along with the disease-specific WISQOL designed for kidney stone patients.[18] Variables impacting HRQOL in these patients encompass age, stone location, and the presence of a ureteral stent.[5]

Quality of life in medical management

The qualitative outcomes of our systematic review reveal that, in the current literature, a majority of studies suggest that patients with ureteral stones of 10mm or less generally experience improved HRQOL when treated with MET compared to conservative pain management. This aligns with findings from studies like that of Hollingsworth et al., where patients receiving alpha-blockers or calcium channel blockers for ureteral stones, irrespective of size, demonstrated better stone passage rates than those under active surveillance.[19] Consistently, groups reporting enhanced HRQOL in our study exhibited higher stone passage rates and lower conversion rates to procedural management (SWL, URS).

Additional factors, including stone location and the presence of ureteral stents, can influence HRQOL.[5] All five studies focusing on patients undergoing medical management examined ureteral stones, where the impact on HRQOL is notable due to potential urinary obstruction and severe colic pain.[8] As expected, the threshold for active intervention in ureteral stones (5mm) was smaller than that for renal stones.[8] Stone passage rates for proximal ureteral stones are generally lower than for distal calculi, as they must traverse the entire length of the ureter before passing spontaneously, likely impacting HRQOL.[11] This mechanism may elucidate the differing findings observed in the studies conducted by Ju et al. and Lee et al. in one of the studies,[10] patients had a post-URS stent inserted. Despite their clinical significance, previous research indicates that ureteral stents can diminish HRQOL in patients with stones.[6] Nonetheless, since all participants in the study had stents during the HRQOL assessment, the likelihood of its role as a confounding factor is minimal. Plausible factors affecting HRQOL in stone patients include advanced age and female gender.[6,20] Most studies evaluated HRQOL four weeks post-stone event, with one reporting measures at one week and another including a second assessment at 12 weeks. A randomized control trial focusing on ureteral stones 10mm or smaller found that, regardless of the management choice, HRQOL gradually improved, returning to the level of the general population after 12 weeks.[13] This progressive improvement over time may account for differences in HRQOL measurements at various time points across studies.

HRQOL in surgical or procedural management

Our findings indicate that, in the majority of studies, patients undergoing URS for stones measuring 10mm or smaller tend to experience better HRQOL compared to those treated with SWL. While one study focused on renal stones, while three other studies examined ureteral stones.[7,14,15] In the study on renal stones, patients subjected to SWL demonstrated significantly superior HRQOL compared to those undergoing URS, aligning with similar observations reported in the literature for renal stones of varying sizes. Thompson et al. reported more favorable patient-reported outcome measures after SWL compared to URS, potentially attributed to the non-invasive nature of SWL, requiring minimal anesthesia and lacking instrumentation compared to URS. Additionally, the common practice of leaving a post-operative stent after URS may contribute to less positive outcomes.[6] Nevertheless, considering anatomical challenges in lower pole calyces, further improvements in URS could enhance stone-free rates compared to SWL.[12] In studies focusing on ureteral stones, patients undergoing URS demonstrated significantly better HRQOL than those treated with SWL, likely due to the obstructive nature of stones pre-intervention and improved stone-free rates following URS compared to SWL. In Drake et al.'s investigation of upper ureteral stones, regardless of size, URS demonstrated superior stone-free rates at 1 month and lower retreatment rates compared to SWL.[22] Across all studies, groups exhibiting better HRQOL consistently had higher stone passage rates and lower rates of secondary procedures for ureteral stones.

Among the three studies focusing on ureteral stones, one examined upper ureteral stones[7] and observed no discernible difference in HRQOL between URS and SWL. However, two other studies,[14,15] encompassing upper and upper/middle stones, reported superior HRQOL in URS patients compared to those undergoing SWL. Notably, URS is typically favored for ureteral stones in the middle or distal segments, while SWL is the preferred choice for proximal ureteral stones.[23] Various variables associated with each procedure, such as the post-operative placement of a ureteral stent following URS, may also impact HRQOL.[21] Sonmez et al.'s study distinctly indicated that patients who uderwent URS without post-operative stenting had notably superior HRQOL compared to those with post-operative stenting. In individuals undergoing SWL, the presence of residual fragments, particularly those exceeding 2mm, can also exert significant effects on HRQOL.[24]

Encouraging patients to actively participate in decisions regarding stone treatment is crucial. Patient decision-making aids have proven to enhance patients' understanding of various surgical options for ureteral stone removal. Additionally, considering the influence of patient characteristics on HRQOL outcomes, such as comorbidities and socio-demographic status, is essential.[26] For instance, comorbidities such as obesity and diabetes mellitus (type 2), advanced age, and socioeconomic vulnerability are all associated with significantly reduced scores on both the SF-36 and WISQOL scales.[26,27]

Limitations

This review offers insight into the effect of urinary stones on patients' HRQOL, and the treatment-related differences that exist within it. The heterogeneity of included studies in terms of study design, patient populations, interventions, and reporting of results rendered the possibility of a meta-analysis impossible and presented a limitation regarding the interpretation of the evidence and generalized conclusions of our study. Furthermore, the nature of the included studies brought about several limitations. 1) As the outcomes of HRQOL were self-reported by the participants, they are vulnerable to response bias and recall bias; 2) Although our search method was robust, there may have been some studies that were not identified due to screening error; 3) lack of the use of a homogenous, standardized, disease-specific scale such as the WISQOL led to heterogeneous reporting of the primary outcome; 4) If there is a tendency for authors to publish studies with positive or significative results, there is the possibility of publication bias.

Risk of study bias

Two studies[10,13] were deemed to have low risk of bias, especially for bias due to confounding, bias in classification of interventions, and bias in measurement of outcomes. The remaining 7 studies[7,8,9,11,12,14,15] were deemed to have moderate risk of bias, with most of these studies having potential sources of either selection bias, bias due to missing data or bias due to confounding.

CONCLUSION

Current evidence suggests that individuals with small urolithiasis (≤10mm) experience enhanced HRQOL when treated with MET instead of conservative pain management, SWL instead of URS for renal stones, and URS instead of SWL for ureteral stones. Alongside stone location, factors like stone size, post-operative stenting, predicted stone-free rates, and the likelihood of secondary procedures play pivotal roles in optimizing HRQOL when selecting a treatment approach. There is a pressing need for further investigations in this realm, particularly prospective, multi-center, observational studies featuring standardized long-term follow-up and employing a disease-specific instrument like the WISQOL.

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FIGURES AND TABLES

Table 1. Summary of included studies with key findings

Author, year	Level of evidence	Sample size	Key findings	QoL tool	Followup timing	Primary outcomes
Ceylan et al, 2018[7]	IIb	111	No significant difference in HRQOL between patients who underwent SWL or URS, at 4 weeks post-intervention for ureteral stones	SF-36	4 weeks post-intervention	HRQOL
Eryildirim et al, 2015[8]	IIb	120	Patients who received tamsulosin had significantly better HRQOL than patients who underwent active surveillance, at 4 weeks for ureteral stones	EuroQOL	4 weeks after beginning of treatment or active surveillance	Stone passage rate
Eryildirim et al, 2016[9]	IIb	80	Patients who received MET after SWL had significantly better HRQOL than patients who received conservative management only after SWL, at 4 weeks post-intervention for ureteral stones	EuroQOL	4 weeks after beginning of treatment or active surveillance	Analgesic requirements, number of colic renal attacks, number of ED visits, HRQOL
Ju et al, 2020[10]	IIb	165	Patients who received terazosin and nifedipine combination therapy after URS had significantly better HRQOL	Quality of Life scale	1 week after beginning of treatment or active surveillance	Stone passage rate and time

			than patients who received terazosin only or conservative management only after URS, at 1 week post-intervention for ureteral stones			
Lee et al, 2014[11]	IIb	108	No significant difference in HRQOL between patients who received tamsulosin or underwent active surveillance, at 4 weeks for ureteral stones	EuroQOL	4 weeks after beginning of treatment or active surveillance	Stone passage rate
Pearle et al, 2005[12]	IIb	78	Patients who underwent SWL had significantly better HRQOL than patients who underwent URS, at 4 weeks post-intervention for renal stones	SF-36	4 weeks post-intervention	Stone passage rate
Pickard et al, 2015[13]	IIb	1150	No significant difference in HRQOL between patients who received tamsulosin, nifedipine, or placebo, at 4 and 12 weeks for ureteral stones	EuroQOL and SF-36	4 and 12 weeks after beginning of treatment or active surveillance	Stone passage rate
Sarica et al, 2016[14]	IIb	80	Patients who underwent URS had significantly better HRQOL than patients who underwent SWL, at 4 weeks post-	EuroQOL	4 weeks post-intervention	Stone passage rate, complication rate

			intervention for ureteral stones			
Sonmez et al, 2021[15]	IIb	183	Patients who underwent URS with no stent placement had significantly better HRQOL than patients who underwent SWL or URS with stent, at 2 weeks post-intervention for ureteral stones	SF-36	2 weeks post-intervention	HRQOL

HRQoL: health-related quality of life; SWL: shockwave lithotripsy; URS: ureteroscopy.

Table 2. Summary of included articles on medical management

Author, year	Stone location	Post-operative stenting	HRQOL tool and measure timing	Comparators	Age (SD)	Sex (male)	Conversion rate to SWL or URS (%)	Stone passage rate (%)
Eryildirim et al, 2015[8]		No	EuroQOL, 4 weeks	Active surveillance	37.23 (1.56)	NA	16.7%	36.7%
				MET	37.07 (2.26)	NA	11.7%	43.3%
Eryildirim et al, 2016[9]		NA	EuroQOL, 4 weeks	Active surveillance	39.81 (14.21)	NA	NA	NA
				MET	39.04 (12.00)	NA	NA	NA
Ju et al, 2020[10]	Ureter	Yes	Quality of Life scale, 1 week	Active surveillance	44.2 (12.2)	63.6%	NA	65.5%
				Terazosin:	42.8 (12.2)	69.1%	NA	81.8%
				Terazosin + nifedipine	43.6 (12.9)	65.5%	NA	94.5%
Lee et al, 2014[11]		No	EuroQOL, 4 weeks	Active surveillance	47.9 (11.4)	61.1%	20.4%	46.3%
				MET	43.6 (12.4)	64.8%	7.4%	74.1%

Pickard et al, 2015[13]		No	EuroQOL and SF-36, 4 and 12 weeks	Active surveillance	42.8 (12.3)	77.9%	NA	79.9%
				Tamsulosin	43.1 (11.5)	82.2%	NA	81.2%
				Nifedipine	42.3 (11.0)	82.8%	NA	80.2%

HRQoL: health-related quality of life; SWL: shockwave lithotripsy; URS: ureteroscopy.

Table 3. Summary of included articles on surgical or procedural management

Author, year	**Stone location**	**Post-operative stenting**	**HRQOL tool and measure timing**	**Comparators**	**Age (SD)**	**Sex (male)**	**Secondary treatment rate (%)**	**Stone passage rate (%)**
Ceylan et al, 2018[7]	Ureter	No	SF-36, 4 weeks	SWL	41.3 (12.6)	45.3%	NA	NA
				URS	40.4 (11.0)	46.6%	NA	NA
Pearle et al, 2005[12]	Renal	SWL 3.1%	SF-36, 4 weeks	SWL	52.5 (12.3)	59.4%	15.6%	65.4%
		URS 88.6%		URS	49.3 (14.2)	48.6%	2,9%	50.0%
Sarica et al, 2016[14]	Ureter	No	EuroQOL, 4 weeks	SWL	38.73 (2.48)	NA	26.5%	70.6%
				URS	42.27 (2.41)	NA	16.1%	83.9%
Sonmez et al, 2021[15]	Ureter	SWL No	SF-36, 2 weeks	SWL	33.0 (7.8)	34.5%	NA	NA
		URS no		URS	29.2 (7.6)	41.0%	NA	NA
		URS + 4.8 French Yes		URS + 4.8 French	30.3 (7.8)	32.6%	NA	NA
		URS + 6 French Yes		URS + 6 French	32.3 (8.9)	26.2%	NA	NA

HRQoL: health-related quality of life; SWL: shockwave lithotripsy; URS: ureteroscopy.