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Managing Small Ureteral Stones: A Retrospective Study on Follow-Up, Clinical Outcomes and Cost-Effectiveness of Conservative Management vs. Early Surgery

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Key Words
Conservative management • Cost-effective • Tamsulosin • Ureteral calculus • Urolithiasis

Abstract
Introduction: The management of ureteral calculi has evolved over the past decades with the advent of new surgical and medical treatments. The current guidelines support conservative management as a possible approach for ureteral stones sized = 10 mm. ***Objectives:*** We purport to follow the natural history of ureteral stones managed conservatively in this retrospective study, and attempt to ascribe an estimated health-care and cost-effectiveness, from presentation to time of being stone-free. ***Materials and methods:*** 192 male and female patients with a single ureteral stone sized = 10 mm were included in this study. The clinical and cost-related outcome was analyzed for different stone sizes (0-4, 4-6 and 6-10 mm). The effectiveness of selected follow-up (FU) scans was also analyzed. ***Results:*** Stone size was found to be related to the degree of hydronephrosis and to the likelihood of need for a surgical management. Conservative management was found to be clinically effective, as 88% of the patients did not require surgery for their stone. 96.1% of the patients with a stone 0-4mm managed to expel their ureteral stone. Bigger ureteral stones were found to be more costly. The cost-effectiveness of the single FU scans was found to be related to their efficiency, while the global cost-effectiveness of conservative management vs. early surgery was higher for smaller stones (26.8 vs. 17.32% for stones 0-4 vs. 6-10 mm). ***Conclusion:*** Conservative management is clinically effective with a significant cost-benefit, particularly for the subgroup of stones sized 0-4 mm, where a need for FU scans is in dispute. Copyright © 2015 S. Karger AG, Basel

Introduction

The management of ureteral calculi has evolved over the past decades with the advent of extracorporeal shockwave lithotripsy, the development of ureteroscopic technology and the introduction of medical expulsive therapy (MET). Patients with ureteral calculi ≤ 10mm in diameter, have a high likelihood of spontaneous stone expulsion, and the current joint EAU/AUA guidelines offer the option of an initial conservative approach with the use of MET and close follow-up [1].

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Table 1. Exclusion criteria

No.	Exclusion criteria
1	Patients with delayed (> 90 days) or suboptimal follow up
2	Patients with multiple comorbidities or on multiple medication; patients with reduced mobility
3	Patients aged < 18 years or > 80 years
4	Patients with multiple (> 1) ureteral stones or with previous surgery for ureteral stones
5	Patients admitted with obstructive urosepsis
6	Patients who changed management due to non medical reasons (social/professional etc.)
7	Patients with NSAID allergy/intolerance; patients who did not conform with given treatment

In the process of making a decision whether a patient is eligible or not for conservative management, radiologic parameters (stone size, degree of dilatation, stone position) as well as subjective parameters such as pain level, can contribute to the final decision for active treatment or surveillance. There is no strong evidence on how the stone size can be related to the pain level, while there is some evidence which correlates the type and level of pain with the stone position [2]. Larger stones understandably seem to be associated to a greater degree of hydronephrosis [3].

Hitherto, studies on MET have mainly focused on the use of α1 blockers, calcium channel antagonists and corticosteroids. The current evidence favors the α1-blockers, with tamsulosin being the most tested one [4–7]. MET seems to be mainly effective on stones 5–10 mm in size [5, 8], as stones < 5 mm have more than 65% of chances to be expelled without additional treatment [1]. The previous recommendation of MET only for distal ureteral stones, has been recently extended, with a level of evidence 1B, on the management of proximal ureteral stones [9]. Though, a recent blind randomized placebo-controlled trial debates the usefulness of Tamsulosin or nifedipine in promoting the stone passage [10].

With regards to the correct radiologic follow-up of these patients, there is a lack of consensuses in terms of timing and type of scan that should be performed [11–14]. While the recommendations from the EAU guidelines currently favor the use of non-contrast computed tomography for the diagnostic approach of the acute flank pain, there are not any current recommendations on how to follow-up ureteral stone patients, managed conservatively. There is some evidence on whether conservative management of small stones can compromise the renal function irreversibly. Most of the relevant evidence was based on animal models, and a complete reversal ureteral obstruction. Thus, the out coming evidence is controversial and biased [15–19].

Regarding the cost effectiveness of stone management, the current research has focused to the different surgical approaches [20–27].There has been surprisingly little research about the cost effectiveness of conservative management vs early surgical removal [28, 29].The out coming evidence from these studies is weak, as even patients with stones of > 10 mm were included, while in the most recent study, female patients were excluded.

Objectives

We purport to follow the natural history of ureteral stones managed conservatively in this retrospective study, and attempt to ascribe an estimated health-care and cost-effectiveness, from presentation to time of being stone-free.

Material and Methods

Data/Population

This is a retrospective analysis of our hospital's rapid access stone clinic patient register, from January 2010 until March 2012. Out of an initial pool of 924, 192 male and female patients fulfilled our inclusion criteria. All selected patients had a single ureteral stone, sized ≤ 10 mm of maximum diameter, with or without concomitant renal stones, and had opted for conservative management of their ureteral stone. The selected patients were started on MET with tamsulosin 0.4 mg once daily and regular painkillers including NSAID as required, immediately after they were diagnosed with the ureteral stone. The included patients were all diagnosed, after they had developed an episode of renal colic, and were all initially assessed in our hospital's accident & emergency (A & E) department. As per our Trust's renal colic protocol, the diagnostic assessment of all colic patients in A & E was done with an unenhanced CT kidneys ureters and bladder (KUB). If a ureteral stone was identified, MET was prescribed by the A & E team, while the patients were referred to our rapid access stone clinic, and reviewed by a urology consultant within 10 days. The pros and cons of MET vs early surgical removal or extracorporeal shockwave lithotripsy were explained to all selected patients with small ureteral stones. The patients who opted for initial conservative management were included in our sample. The exclusion criteria are summarized in table 1.

We decided that the best way to investigate on the pain perceived by the patients under the current set up was to study the number of A & E re-attendances, due to colic pain.

Follow-up

All selected patients were followed-up for their ureteral stone, with either an ultrasound scan or other scans [x-ray kidneys ureters and bladder, intravenous urogram and occasionally, where necessary, a CT KUB].

Table 2. Ureteral stone size demografics

Size (mm)	Frequency (n)	Percentage (%)	Cumulative percentage (%)
0–3.99	53	27.6	27.6
4–5.99	82	42.7	70.3
6–10	57	29.7	100
Total	192	100	–

The choice of the type of follow-up scan and the waiting intervals until this was performed were based on the stone features (position, size, radio-opaque or not, hydronephrosis). Patients with small degree of hydronephrosis, small level of pain and good renal function had usually more delayed follow-up (FU) scans, while in some cases where the stone was well evident in the x-ray KUB, this was our only follow-up scan. Occasionally, a repeat CT KUB was requested, when the pre-selected follow-up scan was not adequate.

Our target was to not postpone the follow-up scan for more than 6 weeks, even though some patients had to be re-scanned later than this. We excluded patients whose follow-up was after 180 days for whatever reason.

Surgical Procedure

Some of our patients required surgery (elective lithotripsy or stenting) during their follow-up, either because of the stone persistence on the follow-up scans, or frequent colic, or a deterioration of their renal function

Parameters Analyzed

The patients were characterized by gender, age, stone size, number of additional renal stones, and cost per single category. We divided the ureteral stones based on their size (0–4, 4–6 and 6–10 mm). The degree of dilatation due to the presence of the ureteral stone was grouped according to the radiological criteria of the CT KUB in none, mild, moderate and severe. Based on the number of stones found on the CT KUB, the patients were divided in 2 groups: a group with only one ureteral stone and a group with additional renal stones.

Statistical Analysis

All analyses were conducted using the SPSS 20 statistical software. Univariate analyses were conducted for basic statistical results such as frequencies of nominal variables and mean values of scale ones. Multivariate analyses were also conducted in order to test the relationship between different but relevant variables of interest. Depending on the variable type under investigation, these multivariate analyses included crosstabulation, bivariate correlation analysis and means-comparison with either one-way analysis of variance or independent samples t-test analysis. All results reported are statistically significant at the 0.05 level or less and can be therefore considered to be valid for the population as well.

Cost Analysis

In order to evaluate the cost-effectiveness of MET, we decided to include in our study only the individual costs of the diagnostic and follow-up scans, and those of the individual surgical operations, based on the private patient coding system. This according to our opinion managed to remove the bias of the coding defect of our Trust and provide an objective view of the cost-effectiveness of the follow-up. Even though the cost of single acts for private patients is higher than that of National Health System patients, the private patient coding is more standardized and, considering that our objective was to compare the relative costs, this offered us a trustful result.

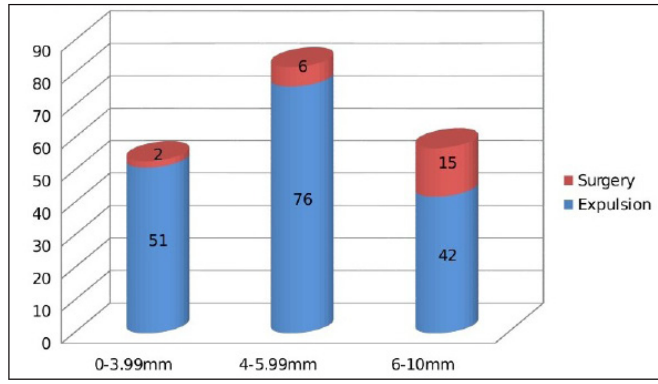

Fig. 1. Ureteral stone size*clinical outcome–crosstabulation

Table 3a. Follow up cost-Duncan[a,b]

			Subset for alpha = 0.05					
Scan method	0	0	1	2	3	4	5	6
IVU	4	0	0					
X-ray KUB	46	0	0					
US KUB	106	0		0				
X-ray KUB/US KUB	9	0			0			
CT KUB	17	0				0		
X-ray KUB/CT KUB	5	2605					0	
US KUB/CT KUB	5	2605						0
Sig.			786	1000	455	1000	1000	1000

KUB = kidneys ureters and bladder. Means for groups in homogeneous subsets are displayed. a: Uses Harmonic Mean Sample Size = 5,585; b: The group sizes are unequal. The harmonic mean of the group sizes is used. Type I error levels are not guaranteed.

Results

The final sample consisted of 192 patients with a median age of 42.72 years (range 19–79 years). Epidemiologic outcomes evidenced that 74.5% of our patients (n = 143), were male, while 25.5% (n = 49) were females. 82.3% of our patients were presented with a single ure-

Table 3b. Cost analysis per follow-up parameters–Bivariate Pearson's

		Size of ureteral stone	Delay of FU scan	Number of FU scan	FU cost	Surgical cost	Total cost	A & E re-attendance
Size of ureteral stone	Pearson Correlation	1	–0.004	0.126	–0.102	a	0.234**	0.092
	Sig. (2-tailed)		0.956	0.083	0.160	0	0.001	0.205
	N	192	192	192	192	22	192	192
Delay of FU scan	Pearson Correlation	–0.004	1	–0.010	0.047	a	–0.116	–0.038
	Sig. (2-tailed)	0.956		0.894	0.519	0	0.109	0.606
	N	192	192	192	192	22	192	192
Number of FU scans	Pearson Correlation	0.126	–0.010	1	0.438**	a	0.206**	0.239**
	Sig. (2-tailed)	0.083	0.894		0	0	0.004	0.001
	N	192	192	192	192	22	192	192
FU cost	Pearson Correlation	–0.102	0.047	0.438**	1	a	0.512**	0.067
	Sig. (2-tailed)	0.160	0.519	0		0	0	0.353
	N	192	192	192	192	22	192	192
Surgical cost	Pearson Correlation	a	a	a	a	1	a	a
	Sig. (2-tailed)	0	0	0	0		0	0
	N	22	22	22	22	22	22	22
Total cost	Pearson Correlation	0.234**	–0.116	0.206**	0.512**	a	1	0.150*
	Sig. (2-tailed)	0.001	0.109	0.004	0	0		0.038
	N	192	192	192	192	22	192	192
A & E re-attendance	Pearson Correlation	0.092	–0.038	0.239**	0.067	a	0.150*	1
	Sig. (2-tailed)	0.205	0.606	0.001	0.353	0	0.038	
	N	192	192	192	192	22	192	192

a = Cannot be computed because at least one of the variables is constant; **. Correlation is significant at the 0.01 level (2-tailed); *. Correlation is significant at the 0.05 level (2-tailed). FU = follow-up.

Table 4a. Cost analysis per outcome

Outcome	N	Subset for alpha = 0.05			
	1	2	3	4	1
Expulsion	169	764.24			
Ureteroscopy	3		986.33		
Ureteral stent	10			1245.60	
Ureterolithotripsy	8			1350.75	
ESWL	2				1604.33
Sig.		1.000	1.000	0.335	1.000

ESWL = Extracorporeal shock wave lithotripsy.

Table 4b. Cost analysis per outcome

	Outcome in 2 categories	N	Mean	Standard deviation	Std. error mean
Total Cost (£)	Expulsion	169	764,24	148,768	11,444
	Surgery	23	1317,39	352,703	73,544

teral stone, while 12% of the patients had one additional renal stone, and 5.7% had more than one additional renal stone. The mean size of the ureteral stone was 4.65 mm (1.6–9 mm, SD 1.65 mm). The majority of the ureteral stones (42.7%) were sized 4–6 mm (table 2).

Comparing male and female groups on the parameters examined (stone size, stone position, degree of dilatation, number of stones, number of re-attendances to A & E, and estimated cost), the only significant differences found were those related to the number of stones and to the degree of dilatation. Male patients had double chances (20.3 vs. 10.3%) to present additional renal stones, apart from their ureteral one, whilst female patients were more likely to have moderate (26.5 vs. 21.7%) or severe(4.1 vs. 0%) hydronephrosis.

Stone size was independently related to the degree of hydronephrosis (Pearson bivariate correlation, sig = 0.003, $p < 0.01$).

In the selected patients, 169 (88%) were successful with MET, while 23 (12%) had surgical treatment because of persistence of the ureteral stone. Patients with larger ureteral stones had a greater chance of requiring a surgical procedure (fig. 1, $p < 0.05$).

The mean delay of the follow-up scan was found to be bigger (52.77 vs. 34.7 days) for the "expulsion" group. The mean delay of follow-up scans for the entire group

Table 4c. Total costs (£) per outcome-stone size/calculation of cost benefit

	Stone size		
	0–3.99 mm (n = 53)	4–5.99 mm (n = 82)	6–10 mm (n = 57)
Expulsion (n = 169)	∑ = 38976.24 (n = 51)	∑ = 58082.24 (n = 76)	∑ = 32098.08 (n = 42)
Surgery (n = 23)	∑ = 2634.78 (n = 2)	∑ = 7904.34 (n = 6)	∑ = 19760.85 (n = 15)
Total	∑ = 41611.02	∑ = 65986.58	∑ = 51858.93
Total if early surgery	∑ = 56852.57	∑ = 87960.58	∑ = 61143.33
Cost benefit of conservative treatment	26.8%	25%	15.2%

of patients was 50.6 days, with 91.7% of the patients having 1 follow-up scan, 6.8% needing an additional one, and 3 patients (1.6%) in need of 3 different FU scans. The biggest part of the patients (55.21%), were followed up with a single ultrasound scan KUB.

The mean follow-up scan cost was 244.70 £ (99–734 £). The follow-up cost was found to be related to the type of follow-up scans used, but also to their efficiency, thus scans that may cost less as single examinations were found to be more cost-weighted if additional scans were required (table 3a, $p < 0.05$). Having performed an additional correlation of follow up parameters (follow-up scans number, follow-up scans cost, follow-up delay, A & E attendance), we demonstrated that there is a strong correlation, not only between the follow-up cost and the number of follow-up scans, but also between the total cost and the number of FU scans (table 3b, $p < 0.01$), and the number of A & E attendances (table 3b, $p < 0.05$). There was as well a correlation of the number of the A & E attendances to the number of follow-up scans (table 3b, $p < 0.01$), but not directly to the follow-up cost. The ureteral stone size was significantly correlated only to the total cost per patient (table 3b, $p < 0.01$).There was no strong correlation between the surgical cost with any of the parameters analyzed (table 3b, $p < 0.01$, $p < 0.05$).

The mean total cost per patient was 830.53 £ (515–2,064 £). Patients of the "expulsion" group had a mean cost of 764.24 £, while the patients who had to be operated, had a mean total cost of 1,317.39 £ (table 4a and 4b, $p < 0.05$). Having estimated the cost effectiveness of the conservative follow up per individual groups, the out -coming cost benefit was comparable for the first 2 stone size groups, being 26.8% and 25% for the group 0–4 mm and 4–6 mm respectively, while it was 17.32% for the group of patients with a ureteral stone 6–10 mm in size (table 4c).

Discussion

Male patients, who were the predominant sample, in concordance to the epidemiology urolithiasis [30], had also double chances for additional renal stones. Interestingly female patients scored slightly worse hydronephrosis.

Patients with ureteral stones of 6–10 mm had 22.5% greater chance of requiring surgical management, compared to the group of patients with stones of 0–4 mm. The total rate of expulsion of stones ≤ 10mm was 88%, while in the group of < 4mm, expulsion rate was 96.2%.

No stratification per stone position was made. This is a limitation of this study, though the management of proximal and distant ureteral stones shouldn't be different [9].

In our patients 90.1% were successfully followed-up with a single follow-up scan. In more than 55% of the cases this was a single USS KUB, as only 18.2% of our patients did not have any degree of dilatation on presentation. In less than 15% of our group an additional CT KUB was required. The number of follow-up scans performed was found to be related to the number of A & E re-attendances. Indeed, most of the patients who returned to A & E due to pain were re-scanned. On the contrary, the number of follow-up scans was not directly related to the stone size; the same is valid for the A & E re-attendances. Thus, patients with bigger stones do not require more scans for their follow-up, nor have more episodes of renal colic.

The mean follow-up scan delay was found to be shorter by 18 days in the group of patients that had surgical management and was shorter for patients with bigger stones, which is in concordance with their bigger chances to have surgical treatment and the need of closer monitor.

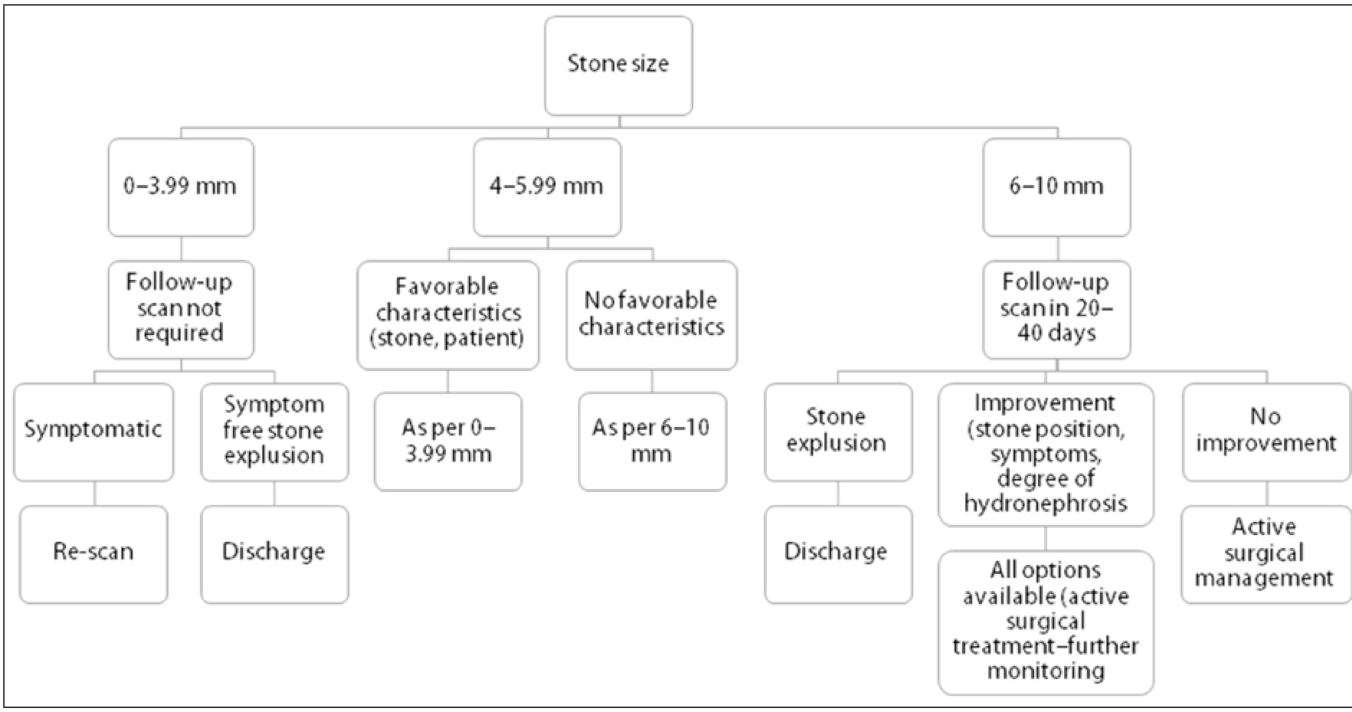

Fig. 2. Suggested algorithm for the management of single ureteric stones ≤ 10mm.

Regarding the clinical outcome of MET, the group of ureteral stones of 0–4 mm had an impressive expulsion rate of > 96%, generating doubts on the need of follow-up scans within protocol for this group. For the group of patients with stones of 6–10mm the expulsion rate was as high as 73.7%, whereas in the group of 4–6 mm this was 92.7% (fig. 1).

From our cost analysis, we saw that the cost of the follow-up was related to the number and type of scans used, but also to their efficiency. Thereby, the use of x-ray KUB as a single diagnostic instrument was less cost-effective compared to the use of the intravenous urogram, due to the bigger need for additional scans (table 3a). The total cost per patient was related to the number and cost of follow-up scans, but also to the ureteral stone size. That means that patients with bigger ureteral stones tend to cost more. The cost of surgery was not found to be related to any of the parameters.

We found that the mean total cost for the "expulsion" group patients was smaller by almost 42%, compared to the cost of the group that had surgery (764.24 vs. 1,317.39 £). The difference on the cost of the above 2 groups is generated by the cost of surgery, as all our patients were initially on a conservative protocol. Trying to investigate on the cost effectiveness of this, we compared our actual total cost to the one that would have come out if all our patients were treated with early surgery, avoiding the additional follow-up cost. We therefore divided the real total cost per stone size category with the hypothetical cost of early surgery. This way we managed to demonstrate that surveillance with follow up scans is cost effective, not only for the groups with smaller stones, but also for the group of 6–10 mm, which has 26.3% chances to end up with surgical management. In this particular group the cost benefit was 15.2%.

Conclusions

Our main findings regarding the natural history of the ureteral stone sized ≤ 10 mm are that indeed bigger stones cause bigger degree of hydronephrosis, and are less likely to be expelled with conservative management; in contrary they are not related to bigger amount of pain (A & E re-attendances). This is an outcome which hasn't been noted previously.

With regards to follow-up of our patients the single ultrasound scan KUB was found to be sufficient as a follow-up scan in more than 55% of the cases.

Considering the clinical effectiveness, patients with a stone of up to 4mm were successful with conservative management in over 96% of the cases, and this puts the usefulness of follow up scans in dispute for a particular group of these patients. Our suggestion would be that at least young, healthy and active patients within this group, could be monitored based on their symptoms. This strategy would minimize the total cost of follow-up, as well as the mean follow-up scan delay, benefiting patients in need of strict follow-up. Symptom monitoring could also be considered for some selected patients of the group of 4–6 mm, based on the stone features (position, shape), and the patient characteristics (age, mobility, co-morbidities, residence, performance status) and symptoms (fig. 2).

Another original outcome of the study was that conservative management was found to be cost-effective in all the size subgroups, scoring a cost-benefit of over 15% for the most challenging group of ureteral stones sized 6–10 mm.

The clinician though who assesses patients with ureteral stones of 6–10 mm, has to underline that they have more than 26% of chances to end up with a surgical management. Additionally, this study evidenced that patients with bigger ureteral stones, within the limits of 10mm should not suffer from more significant pain during their follow-up, compared to patients with smaller stone sizes.

Concluding, this study supports the clinical and cost-effectiveness of conservative management vs early surgery for ureteral stones ≤ 10 mm, creating also some space for modifications of the way to follow-up these patients, based on their stone size.

Limitations

There wasn't any consideration of the stone position in relation to the stone's main axis and to the ureteral axis. As known, the stone shape and position in the ureter is important in estimating the likelihood of the stone passage, particularly for stones > 6 mm. The Hounsfield units of the ureteral stones were not considered in this study, as they are not a weighting parameter in opting for conservative management or early surgery, while no stratification per stone position was made.

The use of re-admissions to A & E as a tool of measurement of pain level provides a less direct measurement, compared to pain rating systems, such as the visual analogue scale. Though, it was the most reliable tool within the current setup of this study, providing also information regarding the economic features of the pain level.

Declarations

Contributorship: A.A. and D.Z. have collected the data. M.H. and K.C. provided concept and initial design of the paper. A.P. has performed the statistical and economic analysis. A.A has written and finalized the paper.

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