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Research Article

Cost-Effectiveness Analysis of Ureteroscopy vs. Extracorporeal Shockwave Lithotripsy in the Management of Distal Ureteral Stones in Adults Using Propensity Score Matching Analysis

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Abstract

Introduction: To compare cost-effectiveness between Ureteroscopy (URS) and Extracorporeal Shockwave Lithotripsy (ESWL) in the management of distal ureteral stones. **Materials and Methods:** We retrospectively analyzed the clinical demographic features, stone burden, education level, and comorbidities. Propensity score matching was used to reduce the bias of confounding variables. A decision tree to project costs and outcomes associated with the management of distal ureteral stones was developed. Sensitivity analysis was based on Tornado diagram by analyzing the correlation between managements in model inputs and the distribution of the outcomes. Scatter plots from the Monte Carlo simulation was performed to demonstrate the distribution of incremental cost-effectiveness. **Results:** A total of 720 patients (345 underwent URS and 375 underwent ESWL) were enrolled from our database. There was a significant difference (p<0.001) between the incidence of gender, Body Mass Index (BMI), education level, diabetes mellitus, hypertension, and stone size. Patients who are male, with lower BMI, higher education level, without diabetes mellitus, with hypertension, and with smaller stone size are willing to undergo ESWL as first-line therapy for distal ureteral stones. After propensity score matching (URS: ESWL, 1:1), 366 patients were included (183 underwent URS and 183 underwent ESWL). The one-way sensitivity analysis on the probability of a successful stone-free rate demonstrated that URS always has the highest net monetary benefits value without the influence of stone size. **Discussion/ Conclusion:** We concluded URS is a cost-effective strategy compared with ESWL after adjusting to the confounding factors, irrespective of stone size.

Keywords: Cost-effectiveness; Extracorporeal shockwave lithotripsy; Ureteroscopy

Introduction

Urolithiasis is an important public health issue with a substantial health burden and considerable global economic consequences [1-3]. Although urolithiasis is rarely fatal, it does have a profound impact on the quality of life. Moreover, >5% of the US population has been diagnosed with nephrolithiasis, and about one-half of (first-time) stone formers will have a recurrence within five years. The age-adjusted prevalence of urolithiasis in 2010 in Taiwan was 9.01%, 5.79%, and 7.38% in males, females, and all subjects, respectively [4]. The direct and indirect costs of stone diseases are substantial among working-age adults [3]. The cost of stone management reflects the cost of healthcare services required to treat stone diseases and utilization rates. Although the care of individuals with urolithiasis has changed from the inpatient to the outpatient setting and the hospital length of stay has decreased, the costs continue to rise because of increases in kidney stones prevalence [5]. Thus, reducing physician fees for decreasing treatment-related costs is not practical. There were no significant improvements in surgical technique or machine development. One area of cost savings could be to develop better guidelines for acute management, optimizing timing for surgery in acute settings [5]. Innes et al. [6] suggested that patients with >7-mm ureteral stones or 5-7 mm proximal ureteral stones should undergo early intervention to improve outcomes. Consequently, early intervention may increase morbidity for patients with smaller stones (<5 mm). The current guideline [7] indicated that Ureteroscopy (URS) or Extracorporeal Shockwave Lithotripsy (ESWL) is the main treatment option in patients with mild or distal ureteral stones. Thus, this intervention relieves the obstruction and achieves a stone-free status. Furthermore, URS is more effective than ESWL. However, the EWSL has the advantage of being noninvasive and a less costly alternative. A higher probability of repeating the procedure is sometimes needed, raising the overall cost since the ESWL is less effective. The treatment-related adverse events are also different between interventions. Another important factor for treatment selection is the cost for patients suitable for both modalities. A cost-effectiveness analysis comparing URS and ESWL is needed, taking these factors into account. Moreover, a recent meta-analysis study comparing the cost-effectiveness between URS and ESWL showed limited evidence to suggest that URS is less expensive than ESWL [8]. Another study [9] from the UK demonstrated that the magnitude of the cost difference means that URS is unlikely to be a cost-effective intervention at a population level for first-line treatment, implying that EWSL should be the first treatment of choice. Due to the lack of standardization in patient profile, the healthcare insurance system and the studies seem contradictory. In Taiwan, >98% of the population is covered by the national health insurance system. Therefore, the cost is uniform in the study. Other basic social demographic data (e.g., age, gender, education level, and selected comorbidities) were considered factors for treatment choices. Therefore, these potential confounders were adjusted in the current study cohort. This is the most standardized study comparing cost-effectiveness between URS and ESWL.

Materials and Methods

Patients

Data came from consecutive patients with a distal ureteral stone between 2017 and 2019 at the Kaohsiung Medical University Hospital, Taiwan. Moreover, clinical data were retrospectively collected. The present study was supervised by the Institutional Review Board of the Kaohsiung Medical University Hospital (KMUHIRB-E(II)-20180159). All patients had radiological evidence of urinary stones.

Model Structure

A decision tree to project costs and outcomes associated with the management of distal ureteral stones was developed to evaluate clinical outcomes and costs associated with the management of uncomplicated distal ureteral stones. We defined complicated stones as those with sings of sepsis or acute renal failure, solitary kidney and bilateral obstructive uropathy. Complicated stones were excluded in the current cohort. We compared two strageies, (1) ESWL, and (2) URS. Gender, age, Body Mass Index (BMI), education level, hypertension, diabetes mellitus, and fever were included as selected comorbidities due to the potential influence of treatment choice. Therefore, these potential confounders were adjusted in the current study cohort. Furthermore, propensity score matching reduced the bias of confounding variables found in the treatment effect obtained from simply comparing outcomes. The initial treatment and total costs within one month were recorded. The cost-effectiveness was analyzed according to stone size.

ESWL

Patients who underwent ESWL were evaluated by serum creatinine level and coagulation profile. ESWL was performed using the third-generation Dornier lithotripter (Dorneier, Gernamy) as the outpatient procedure. Voltage was set at 10-12 Kv and shockwave was set at 3000-3500 shocks for each treatment. Patients were discharged after 1-2 hours surveillance with routine pain relief medications and evaluated one or two weeks later by radiologic exam to assess stone passage.

URS

Patients who underwent URS were by routine pre-operation survey (including urine analysis, renal function, liver function, coagulation profile, chest radiograph, electrocardiography and electrolyte data. Ureteroscopy was performed using 4.5/8-Fr, 5° semi-rigid ureteroscope (Richard Wolf, Germany) under geneal anesthesia. For ureteroscopic lithotripsy, a pneumatic lithotripter (Swiss Litho Clast®) was used and stones were fragmented down to pieces smaller than 2 mm in diameter. A 6Fr double J was indwelled after the procedure. Patients were discharged at the second day after catheter removal. The stent were removed 2 weeks later after the operation.

Key Assumptions

Some of the basic assumptions in this model included the following:

- There were no kidney stones in the current status.
- Ancillary treatment is a different treatment to the primary treatment.
- If the patient did not pass the stone after ESWL, we did not recommend second ESWL treatment within 28 days.
- The urologist always successfully finished the retrograse access for URS and always placed a ureteral stent after the procedure.
- All patients removed the ureteral stent 2 weeks after the operation.

Statistics

Differences between categorical parameters were assessed using c^2 or Fisher's exact test. Continuous parameters were assessed by using a t-test or Mann-Whitney-Wilcoxon test. The threshold for statistical significance was set at $p < 0.05$. The Statistical Package for Social Sciences, version 20.0 (SPSS Inc., Chicago, IL, USA), was used for all statistical analyses. Furthermore, TreeAge Pro 2017 was used for cost-effectiveness and sensitivity analyses. Sensitivity analysis was based on the Tornado diagram by analyzing the correlation between managements in model inputs and the outcomes' distribution. Consequently, scatter plots from the Monte Carlo simulation were performed to demonstrate the distribution of incremental cost-effectiveness.

Results

Between 2017 and 2019, 772 consecutive patients with a distal ureteral stone were sampled at the Kaohsiung Medical University Hospital in Kaohsiung, Taiwan. Bilateral stones, multiple stones, stone-related pyelonephritis, ESWL-related stonestreet, coagulation disorders, incomplete medical records, and loss of follow-up patients were excluded (N = 52). Moreover, 720 patients underwent either URS or ESWL and were included in the current study (Table 1). Furthermore, Table 1 shows a significant difference between the incidence of gender, BMI, education level, diabetes mellitus, hypertension, and stone size. Patients who are male, with lower BMI, higher education level, without diabetes mellitus, with hypertension, and with smaller stone size are willing to undergo ESWL as first-line therapy for distal ureteral stones (Figure 1). There was no significant difference between the two groups except for the stone size. The decision tree with initial branches is shown in Figure. 2. The initial treatment and total costs between URS and ESWL were US 991±260, US 1,127±287, and US 1,039, US 1,148±140, respectively (Table 2). For patients with a smaller stone (<1 cm), the initial treatment cost and total cost between URS and ESWL were US 1,016±323, US 1,134±343, and US 1,039, US 1,153±148, respectively (The average exchange rate in 2020 was US$1 to New Taiwan (NT)$ 28**)**. Similar trends exist for patients with larger stones (>1 cm) (URS: ESWL, US 975±205, US 1,124±241, and US 1,039, US 1,125±82, respectively). The one-way sensitivity analysis on the probability of a successful stone-free rate demonstrated that URS always has the highest net monetary benefits value without the influence of stone size. The scatter plots from the Monte Carlo simulation (Supplemental Figure 1) and the Tornado diagram (Supplemental Figure 2) are shown in the supplementary files. The incremental cost-effectiveness ratio between URS and ESWL was US 136.1. The present study showed that URS had a higher stone-free rate and lower overall costs.

Parameter	**Category**	Before propensity score match (N=720)			After propensity score match (N=366)		
		URS	ESWL	p-value	URS	ESWL	p-value
		N=345	N=375		N=183	N=183	
Gender[&]	Male	183(53.0)	271(72.3)	**<0.001***	126(68.9)	117(63.9)	0.376
	Female	162(47.0)	104(27.7)		57(31.1)	66(36.1)	
Age (years) [#]		53.6+/-12.1	52.1+/-11.9	0.087	52.6+/-11.9	52.1+/-12.7	0.711
BMI[#]		30.7+/-2.8	29.6+/-3.5	**<0.001***	30.5+/-2.8	30.3+/-4.1-	0.575
Education level[#]		9.6+/-4.0	12.4+/-3.9	**<0.001***	11.1+/-3.3	11.1+/-4.6	0.99
Diabetes mellitus[&]	Yes	68(19.7)	41(10.9)	**0.001***	28(15.3)	26(14.2)	0.883
	No	277(80.3)	334(89.1)		155(84.7)	157(85.8)	

Hypertension&	Yes	76(22.0)	159(42.4)	**<0.001***	56(30.6)	58(31.7)	0.91
	No	269(78.0)	216(57.6)		127(69.4)	125(68.3)	
Fever episode&	Yes	7(2.0)	11(2.9)	0.591	3(1.6)	5(2.7)	0.721
	No	338(98.0)	364(97.1)		180(98.4)	178(97.3)	
Stone size&	<1cm	160(46.4)	333(88.8)	**<0.001***	75(41.0)	152(83.1)	**<0.001***
	>1cm	185(53.6)	42(11.2)		108(59.0)	31(16.9)	
&: Chi-Square test; #: Student's T-test; *Statistically significant							

Table 1: Comparisons between propensity score match and other important demographic parameters in distal ureteral stones.

Parameters	Total	URS	ESWL	Incremental Difference	ICER
	N=366	N=183	N=183		
Initial treatment cost (US)	1,015±185	991±260	1,039	-48	-136.054
Other treatment cost (US)	122±115	136±81	108±139	27	
Total cost within one month (US)	1,138±225	1,127±287	1,148±140	-20	-136.1
Stone free (rate)	311(84.9)	169(92.3)	142(77.6)	14.70%	
Stone < 1cm					
Initial treatment cost (US)	1,032±185	1,016±323	1,039	-23	-171.171
Other treatment cost (US)	115±124	118±49	114±148	4	
Total cost within one month (US)	1,147±231	1,134±343	1,153±148	-19	-171.2
Stone free (rate)	198(87.2)	71(94.7)	127(83.6)	11.10%	
Stone > 1cm					
Initial treatment cost (US)	989±183	975±205	1,039	-65	-2.38095
Other treatment cost (US)	135±97	149±96	85±82	64	
Total cost within one month (US)	1,124±216	1,124±241	1,125±82	-1	-2.9
Stone free (rate)	113(81.3)	98(90.4)	15(48.4)	42.00%	
ICER, Incremental Cost-Effectiveness Ratio; The average exchange rate in 2020 was US$1 to New Taiwan (NT)$ 28					

Table 2: Comparisons of marginal cost benefits ratio between different treatment modality in distal ureteral stones.

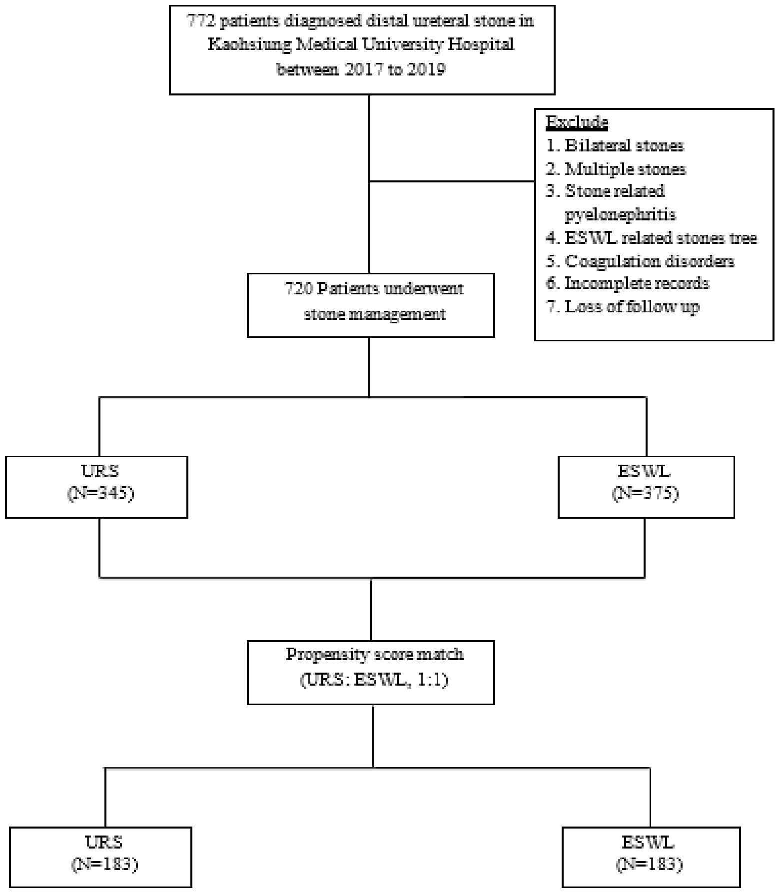


Figure 1: Patient enrollment for patients with distal ureteral stone underwent either Extracorporeal Shockwave Lithotripsy (ESWL) or Ureteroscopy (URS).

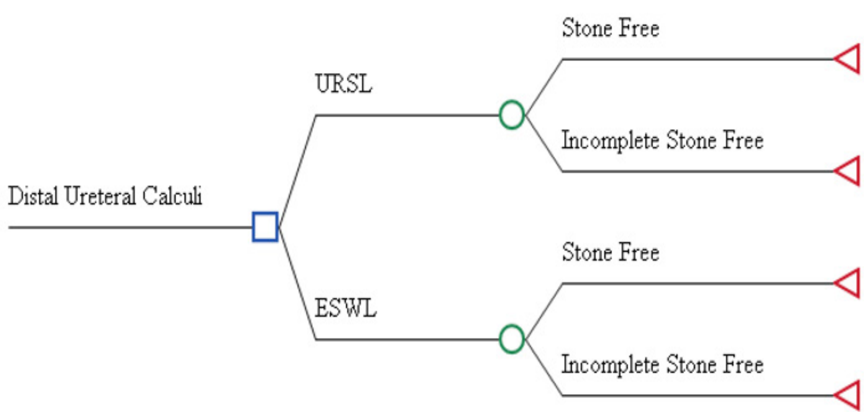
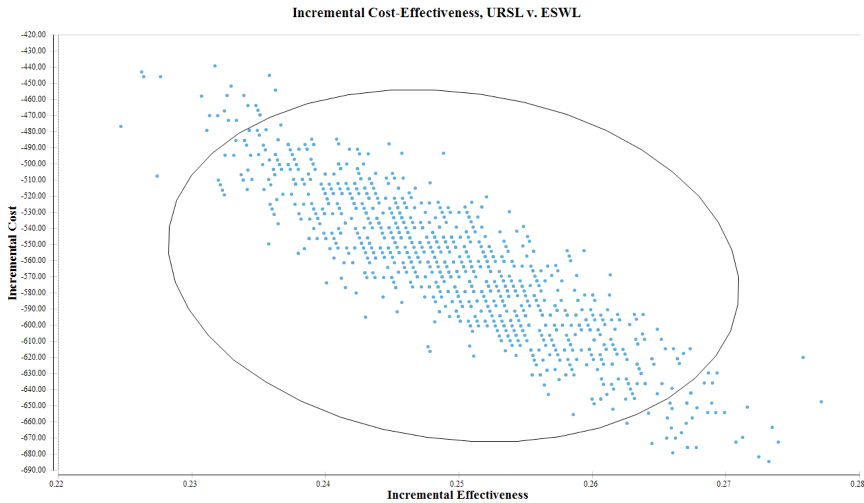
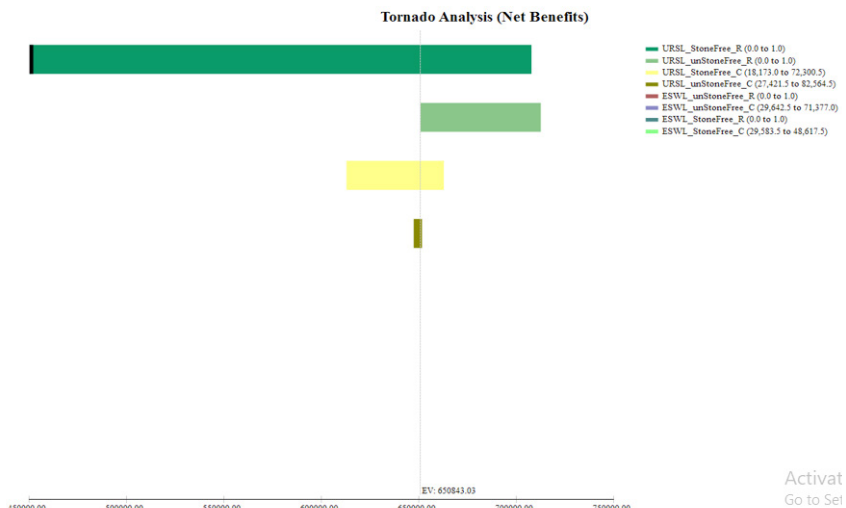


Figure 2: The decision tree with initial branches.



Supplementary Figure 1: Scatter plots from the Monte Carlo simulation.



Supplementary Figure 2: The Tornado diagram.

Discussion

Most ureter stones were amenable for either URS or ESWL. Considering that the health resources are already maximum, the treatment for stone diseases should be selected because of cost-effectiveness. The first meta-analysis [8] showed that URS seems to be more cost-effective for treating all sizes of stones. However, limited evidence suggests that URS is less expensive than ESWL due to a lack of standardization. Furthermore, the Cochrane database [10] included seven RCTs showing that stone-free rates were lower in patients who underwent ESWL. However, retreatment rates were lower in the URS group. Thus, URS achieves a greater stone-free rate but with a higher complication rate and a longer hospital stay than ESWL. The cost-effectiveness study comparing URS and ESWL was still limited. The cost can be different among the different countries. The equipment purchase price, maintenance cost, and repair cost were also of great difference. Furthermore, Patel et al. [11] showed that socioeconomic status impacts the urolithiasis surgical management, underscoring disparity recognition importance in endourologic care and ensuring appropriate surgical care regardless of socioeconomic status. The different insurance systems also impact treatment choices. Moreover, private insurance payers were more likely to undergo ESWL than public insurance payers. The heterogeneity of data makes the comparison for cost-effectiveness from URS and ESWL difficult. Another issue for cost-effectiveness when dealing with stone diseases is the stone burden. For stone size >1 cm, URS seems to be more cost-effective and ESWL was viewed as a treatment choice in patients with stone size <1 cm in some reports [12-17]. Also, some reports suggested that ESWL should remain the first-line therapy for all ureteral stones [15-17]. Consequently, URS was more cost-effective than ESWL for ureteral stone treatment irrespective of stone size [8, 18-20] (Table 3).

Study	Nation	Total	ESWL	URSL	Cost effectiveness
Huang et al. 2009 [18]	Taiwan	448	360	88	URS
Salem et al. 2009 [12]	Egypt	200	100	100	>1cm URS, <1cm ESWL
Verze et al. 2010 [13]	Italy	273	137	136	>1cm URS, <1cm ESWL
Zhang et al. 2011 [15]	China	526	257	269	ESWL
Cone et al. 2014 [19]	USA	158	78	80	URS
Cui et al. 2014 [16]	China	160	80	80	ESWL
Kumar et al. 2015 [14]	India	180	90	90	>1cm URS, <1cm ESWL
Budia et al. 2016 [17]	Spain	180	95	85	ESWL
Cone et al. 2017 [20]	USA	113	51	62	URS
Current study	Taiwan	366	183	183	URS

Table 3: Collected reports of cost-effectiveness study within 10 years.

Several factors influence decision-making when dealing with ureteral stones. For example, gender-based differences may exist in underlying urinary risk factors, presentation, and treatment response [21]. Other operation fields demonstrated that gender might influence patient selection for interventions, especially when multiple treatment options exist [22]. However, such diversity in surgical choice has not been identified in ureteral calculi. In this series, before the propensity score matching, over 60% of women choose URS for first-line therapy. Women were reported [21] to have a higher preponderance of infection-related stone, sometimes concomitant infection, needing more urgent intervention. Thus, the gender impact of decision-making biases should not be underestimated when assessing cost-effectiveness. Another important reason is the estimations of the successful ESWL rate.

The failure of the ESWL results in an increase in medical costs and complications (e.g., acute kidney injury, hematuria, and obstructive symptoms). Therefore, evaluating the clinical outcome predictors of ESWL is important. Higher abdominal fat quantities, especially visceral fat, were previously shown to be associated with a lower calculus-free rate following ESWL treatment [23]. URS in obese and overweight patients is an acceptable treatment modality, with success rates similar to non-obese patients [24]. The raw data of this study showed that obese patients were prone to undergo URS than ESWL. Therefore, adjusting these confounding factors may reveal the true cost-effectiveness of treating ureteral calculi. Patients with hypertension and diabetes were significantly different from those without it. In the last two decades, the current urinary stone treatment trends are increasing for URS and decreasing for ESWL and open surgery [25]. Patients with hypertension have a higher rate of using ESWL than URS. The data regarding whether ESWL is associated with a long-term elevation in blood pressure were controversial. Some reports still demonstrated an association between nephrolithiasis patients treated with ESWL and subsequent hypertension diagnosis [26,27]. Patients who undergo ESWL may need regular blood pressure follow-up. Doctors performed more URS in diabetic patients compared with those without it. A population-based study suggested that diabetes is associated with stone disease, and diabetes may be a factor in the development of uric acid stones [28]. Due to its radiolucent properties, undergoing more URS is reasonable for patients. Thus, no report compared the cost-effectiveness of URS and ESWL in adjusting to these confounding factors.

URS is a cost-effective strategy compared with ESWL after adjusting to the confounding factors in patients with distal ureteral stones, irrespective of stone size. Further studies are needed to determine patients' preferences and help doctors make personalized decisions when dealing with ureteric stone diseases. This study has several limitations. First, this was a retrospective analysis. As with most retrospective studies, data may be subject to incomplete, missing, or inaccurate reporting of events. Second, other predisposing factors (e.g., smoking, family history, and dietary habits) were not adjusted in this study. Third, selection bias may occur during the identification of the study population. Despite these limitations, this is the first study based on propensity score matching analysis in the world.

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