ORIGINAL ARTICLE

Comparing Extracorporeal Shock Wave Lithotripsy and Ureteroscopy for Treatment of Proximal Ureteric Calculi: A Cost-Effectiveness Study

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SUMMARY

Extracorporeal shockwave lithotripsy (ESWL) and ureteroscopy (URS) are two main methods of treating proximal ureteric stones. Success rates and cost-effectiveness of the two methods were compared. A total of 67 patients who underwent treatment between January 2007 and July 2007 at a state general hospital were included in the study. The success rate for ESWL group was 81.8% and for URS group was 84.6%. ESWL technique produced a significant higher overall cost per patient than URS (RM930.02 versus RM621.95 respectively). There was no significant difference in quality of patient's life. Cost-effectiveness ratio was lower for URS. The analysis suggested that URS was more cost-effective than ESWL.

KEY WORDS:
Cost-effectiveness analysis, Shock wave lithotripsy, Ureteroscopy, Ureteric calculi

INTRODUCTION

ESWL and URS are two main methods of treating proximal ureteric stones. Surgeons perform less open surgery nowadays because the procedure is invasive and often results in more major complications compared to ESWL and URS[1]. Success rate of ESWL treatment is between 55-70%[1,2]. The success of URS treatment depends on the skill of the surgeons but, in general, it is able to produce 'stone-free status' in shorter time. The success rate for this method is between 91-100%[3,4]. URS treatment is available in almost all public general hospital but only a few hospitals in Malaysia have ESWL machine because of its high cost.

The best method of treatment for ureteric stones is still debatable[15,35]. Choice of treatment relies on patient's condition, surgeon's experience, patient's preference and available technology. Patients who stay far from hospital would choose URS to avoid excessive visits because of its high success rate for single treatment[2]. Other important aspects that must be considered are stone size, location, composition as well as anatomy of the ureter.

The use of medical technology inevitably leads to higher cost due to purchase and maintenance of the equipment. The presence of a variety of medical technology in the health market further complicates the matter. Thus, evidence-based evaluation is necessary to justify the acquisition of such technology. Most studies found that the cost of treating ureteric stone with URS is much cheaper than using ESWL[2,6,7]. However, Bierkens *et al*. concluded otherwise[8].

This study evaluated ESWL and URS according to their cost-effectiveness and quality of life produced. We focused on proximal ureteric stone because its spontaneous passage is less common compared to distal and mid-ureteric stones. Galvin *et al*. found that spontaneous stone passage rate of proximal ureteric stone is only 12% compared to mid-ureteric and distal stones (22% and 45% respectively)[9]. Most cost-effectiveness analysis (CEA) involved institutions from developed countries. It is necessary to see the cost-effectiveness aspect from the perspective of developing country.

Ureteric stones

Ureteric stones are any calcification present along urinary tract. They are formed in the renal papilla where they grow and migrate into the urine[10]. Urinary tract stones are categorized by their composition (uric acid, cystine, struvite or mixed). The categorization would help to assist in metabolic evaluation and treatment [11]. Most ureteric stones migrated from renal calyces or pelvis but some stones form in the ureteric tract itself when there is urinary flow obstruction[12]. Stones or calculi are formed when the urine is oversaturated with calcium, magnesium, ammonium or phosphate salts or there are insufficient normal inhibitors of stone formation in the urine[13,14].

Epidemiology

Lotan *et al*. found that the prevalence of urinary tract stone disease was 13% for adult male and 7% among the female[15]. The risk of having urinary tract stones in the developed country populations is between 10-15%. This risk is even higher in Middle East countries due to development, industrialization and dietary habits[9,16].

The expenditure to treat urinary tract stones had increased from 1.83 billion USD in 1993 to 2.01 USD in 2000[15]. The figures could also reflect the increasing trend of the disease burden and its expenditure in other countries. In Malaysia, urinary stone disease contributed about 12.4% to the total number of surgical ward admissions[17].

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Almost 80% of urinary stones are formed from calcium salts while 15% are struvite stones[18]. Patients with high body mass index (BMI), glucose intolerance and Type 2 diabetes have higher risk to develop uric acid stones[19]. Size and location of ureteric stones are the most important factors that help to predict whether spontaneous stone passage is possible[9].

Treatment of ureteric stones

Watchful waiting, medicine, open surgery, laparoscopic surgery, ESWL and endoscopic techniques URS are among the methods used in treatment of proximal ureteric stone. Ureteric stones that persist after two months might not pass out spontaneously[5]. Most ureteric stones that require definitive treatment are successfully removed with either ESWL or URS[20].

Since its introduction in 1980, ESWL has dramatically changed the treatment of ureteric stone. The method, originally designed to examine supersonic jet parts, has become one of the main method of treating renal and ureteric stones. In 1997, American Urological Association Stone Guidelines Panel recommended the use of ESWL as the main treatment method for stones less than 2cm in size[3]. The components of ESWL include shockwave source, focusing tool, coupling device and stone imaging unit[21]. There are many variations of ESWL machine in the market. Each has different specifications and efficacy. Dornier HM3 is said to be the most efficacious lithotripter and has become the benchmark for other machines[22].

ESWL fragments the stones by focusing high-energy shockwave to the stones. Fragmentation could occur via direct pressure, erosion or cavitations when the energy surpasses the tension within the stone. The success of ESWL relies on the size, number, composition and location of ureteric stones. Other factors are skill and experience of the operator, high quality ESWL machine and patient selection.

ESWL is less effective on cystine and calcium oxalate monohydrate stones[3]. It is also less effective when the ureter is complex. Complications of ESWL treatment are temporary hematuria, 'steinstrasse', renal colic, internal hematoma and hypertension. (Steinstrasse literally means stone street; caused by stone fragments that accumulate in the ureter in a linear fashion). The complications are more frequent when high number of shockwaves and high energy are used and after two or more sessions of ESWL[23].

URS involves the introduction of endoscope through urethral meatus into the urethra, bladder, ureter and kidney. Lithotrite is inserted through the sheath and break the stone into smaller fragments which can be removed with forceps or basket. URS is often used to treat stones larger than 2cm in size and impacted stones[3]. Upon contact with lithotrites, stones can migrate to the proximal ureter or renal pelvis and reduce the effectiveness of the procedure. The use of laser lithotrite could minimize this problem. Jeon *et al*. found that holmium:YAG laser lithotripter could reduce procedure time and hospital stay when compared to Lithoclast lithotripter (EMS, Switzerland)[24].

URS does not only break urinary stones but it is also being used to treat urinary tract cancer, repair ureteric strictures and ureteropelvic junction obstruction[25]. Its versatility should be considered in more general cost analyses. URS needs normal saline irrigation to ensure good operating vision. The equipments of URS usually warrant repair after being used for 20-25 times.

Pre-operative antibiotics are given for all URS procedures. The operation could traumatize ureteric wall causing it to be edematous. Hence, it is a common practice to put ureteric stent after URS to ensure good urine passage and facilitate healing of ureteric wall. It can also reduce the risk of urinoma and ureteric stricture[3]. Stents need to be removed six to eight weeks after URS. Routine use of antibiotics and ureteric stent will increase cost of URS.

URS has a better success rate than ESWL for first treatment[26]. ESWL often requires repeated sessions and additional procedures including ureteric stent insertion and even URS. The situation will add to the existing high cost of ESWL. Nevertheless, URS could initiate urosepsis, penetrate ureteric wall, cause bleeding, stricture and avulsion of ureteric wall[11].

Cost Effectiveness Analysis (CEA)

CEA is a form of economic evaluation that compares cost and outcome of a health program[27]. CEA and cost-utility analysis (CUA) have dominated health care journals compared to cost-benefit analysis (CBA) due to the difficulty of tagging life and health with monetary values.

Different programs or treatments for the same health problem usually produce different results. However, if the outcome of two or more competing programs could be measured in the same dimension, CEA could determine the most cost-effective program. ESWL and URS are two different medical technologies that treat ureteric stone and the outcome of treatment can be stated in quality of life. Thus, CEA is the most suitable method to compare the two methods of treatment. It is a very useful way to assess effectiveness to maximize output for an allocated budget[28].

All calculations of input and output in economic evaluation are affected by uncertainties which are created by imperfect knowledge about disease and effects of interventions. Uncertainties also exist in discounting process and during generalization of results in different situations. Sensitivity analysis is a method used to assess the robustness of results. The analysis makes a few assumptions for every uncertain parameter[27]. Confidence in results is strengthened when the initial conclusion remains despite using different assumptions.

Success Rate

Most of previous studies used success rate or efficiency quotient as the outcome for competing programs or interventions[2]. Patients who are stone-free (based on radiological examination) and symptom-free are considered to have successful treatment[1]. The standard criterion for a successful ESWL treatment is to achieve stone-free status at three months after treatment[3].

The study intended to compare effectiveness of ESWL and URS in term of cost-effectiveness ratio (CER).

MATERIALS AND METHODS

The Research Ethics Committee of Universiti Kebangsaan Malaysia (UKM) approved the study before data collection. All patients treated between January 2007 and July 2007 for proximal ureteric stones either with ESWL or URS were included in this cross-sectional study. The study analyzed and compared the ESWL and URS groups in terms of effectiveness of treatment method and costs. We adopted the societal view for assessment of costs.

Inclusion criteria included patients with radio-opaque stones located between ureteropelvic junction and sacroiliac joint. Patients who had previous operation to the abdomen or had recent treatment with ESWL or URS six months before the study were excluded. Universal sampling was used. Sixty-seven patients who gave their written consent were included in the study. Thirty patients had their stone disease treated with ESWL while 37 others were in the URS group. Determination of treatment modality relied on discussion between surgeons and patients.

Patients were interviewed with socio-demographic, costing and SF-36 questionnaires during follow-up in the specialist out-patient clinic six weeks after the treatment. Patients' medical record, charges, radiographs and operative notes were examined. Hospital's administrative and financial reports were also examined. The study utilized various sources for information to strengthen the reliability of data. Co-morbidities are chronic diseases such as diabetes, hypertension, respiratory and cardiovascular diseases that would affect selection of treatment modality. Stone free-status was determined six weeks after treatment with ESWL or URS[2].

Patients underwent ESWL treatment with EDAP LT-02 at intensity of 80-90% for 100-120 minutes depending on patient comfort and pain. Most patients required oral non-steroidal anti-inflammatory drugs though some would need injectable diclofenac, ketoprofen, tramadol or pethidine for pain relief. URS was performed with a rigid 7F ureteroscope in combination with electrohydraulic probe (EHL). All patients had stents inserted after URS.

Dependent variables were stone-free status and quality of life scores. Independent variables were sosiodemographic data, size of proximal ureteric stones ureter and costs borne by patients, patients' relatives and hospital.

Hospital and patient costs were considered in the analysis. Hospital costs were categorized into capital and recurrent costs. The costs were compiled after reviewing hospital financial and administrative report for 2006. Capital costs included hospital building, furniture, ESWL machine and URS instruments[42]. Clinic fees ward charges and day-care centre charges were not included in the calculation of cost-effectiveness ratio to avoid double-counting. Success rates of each method of treatment were calculated. Quality of life scores were calculated based on PCS scores derived from SF-36. SF-36 has been used to study health status in Medical Outcome Study (MOS). It is designed for use in clinical practice, health policy evaluation and population study. SF-36 utilizes rating scale to calculate values given by patients to their health status. The questionnaire has 36 items that assess eight health concepts: limitation in physical activities due to health problem; limitation in social activities due to physical or emotional problems; limitation daily activities due to health problem; limitation in daily activities due to emotional problem; bodily pain; general mental health; vitality and general perception of health[27].

Scores in all dimensions are stated on scale 0-100. Higher scores suggest better health and well-being. Generally, chronic diseases, medical consultation within two weeks and female gender showed lower score in all variables[28]. Syntax is used to calculate scores from SF-36 questionnaire. The initial scores are coded prior to calculation of each dimension. Scores will be calibrated according to given weights.

SF-36 questionnaire is easy to use and fulfills the reliability and validity criteria[27]. Brazier *et al*. found that it was able to generate Cronbach's alpha of 0.85 with coefficient reliability of more than 0.75 for all dimensions except social function[29]. SF-36 has been validated for Malaysian population (Sararaks 2005, Azman 2003)[30,31]. Sararaks (2005) stated that the Malay version of SF-36 is consistent and valid for use in Malaysia.

Student's t test, chi square, Fischer's exact test and Mann-Whitney U tests were used where appropriate. Logistic regression analysis was done to look for factors influencing stone-free status. Univariate analysis of General Linear Model (GLM) was used to compare scores before-after treatment and between the two treatment methods.

RESULTS

ESWL group had 30 patients and URS group had 37 patients. The patient demographics are shown in Table I and II. No statistically significant difference was found between ESWL and URS groups with respect to the age, sex, race, formal education level, monthly income and co-morbidity problems. Common co-morbidities among patients in both groups were diabetes mellitus, hypertension, gout and tuberculosis.

Ureteric stone sizes showed significant difference between the two groups (Mann-Whitney U test, p=0.004). Patients in ESWL group had larger stones. Stone size was stratified according to the size of ureteric stone ($\leq$1.0cm and > 1.0cm) because it is more meaningful to analyze as it corresponds to stone management. For stones with size of less or equal to 1.0cm, eleven patients (29.7%) were treated with ESWL while 26 patients (70.3%) had URS procedure performed on them. ESWL was used to treat 19 patients (63.3%) for larger stones while eleven patients (36.7%) were treated with URS. Chi square test showed a significant difference between the two groups with respect to the size of ureteric stones (p=0.006). It appears that URS was the preferred treatment for smaller stones while ESWL was used to treat much larger ureteric stones.

Stone-free status

The overall success for the ESWL and URS were 46.7% and 32.4% respectively. Chi square test did not reveal significant any difference (p=0.314). When stratified to stone size, the success rates were higher in both groups with smaller stones, as shown in Table III. Stone-free rates were 81.8% (9 subjects) for ESWL and 84.6% (22 subjects) for URS group. For larger stones, the success rates were 36.8% for ESWL and 27.3% for

URS. Fischer exact test did not show any significant difference between treatment methods and success rates for different sizes of ureteric stones (p=1.000 and 0.702).

Factors related to stone-free status
Logistic regression analysis (Table IV) showed that ureteric stone size before treatment is a very important factor to predict the stone-free status after treatment. Stones with size less or equal to 1.0cm have more than 12 times probabilities to achieve stone-free status after treatments as compared to bigger stones. The logistic model could explain about 35% of the variation in the outcome variable (stone-free status).

Cost analysis
Treatment cost calculation included those incurred by the hospital (provider) and patients and their relatives.

Hospital costs
HSNZ was built in 1983 with a cost of RM80,037,167.00. Based on annuitization procedure, the equivalent annual cost for the hospital building was RM6,422,394.68. The building cost for all the facilities involved in treatment of ureteric stones (ESWL room, surgical clinic, surgical wards and operation theatre) was calculated according to their floor space and compared to the total hospital floor space. The building cost for each patient was calculated by dividing these costs with the number of patients utilizing each facility. The building costs for each patient who had ESWL and URS treatments were RM17.11 and RM40.91 respectively.

Cost for acquiring hospital furniture was RM1,245,688.80. The costs for each building facilities were also calculated according to their floor spaces and divided by the number of patients utilizing them. The cost of hospital furniture for each patient who had ESWL treatment was RM0.79 and URS treatment was RM1.83. Similar method of calculation was used for utility cost. Utility cost for each patient treated with ESWL was RM10.57 and for URS, the cost was RM25.29. Table V displays the costs of hospital equipment. Cost of hospital equipment for ESWL treatment was RM666.14 and for URS was RM51.57 for each patients.

The recurrent costs for hospital were personnel, laboratory and radiological investigations, drugs, administrative cost, utility and additional procedures. Cost of personnel summed up the costs of all personnel involved in the treatment activities. Costs of each personnel were calculated according to their monthly income with 9600 (minutes at work) and multiplied with time spent in treatment activities[42]. Monthly income for each personnel was based on salary received during their fifth year of service.

Total administrative cost for the year 2005 was RM12,632,306.00. It was assumed that one-third of the cost was used to manage outpatients and management of inpatients used up the other two-third of the total cost. The number of outpatients in 2005 was 179,079. Inpatient administrative cost for each patient was calculated according to their average length of stay, which was 4.01 days. The number of inpatient in 2005 was 241,762. Hence, total inpatient days were 949,465.62 days. On average, ESWL treatment required 2.19 days and patients for URS treatment stayed for 3.63 days. Administrative cost for each patient having ESWL treatment was RM19.42 and for URS treatment, the cost was RM32.19.

Procedure cost was derived from additional procedures such as insertion and removal of ureteric stent and urinary catheter. Means (and standard deviations) of procedure cost for ESWL group was RM0.00 and for URS group RM33.37 (10.05). None of the patient treated with ESWL had additional procedure.

Patients' costs
Clinic fee was imposed on patients during their visit to surgical clinic and day care center. Most patients who had URS treatment would attend day care center, instead of surgical clinic for follow-up, to have ureteric stents removed. Means (standard deviations) of clinic fee was RM10.00 (0.00) for ESWL group and RM38.49 (11.37) for URS group. Transportation cost was derived from patient's estimation of their expenses from their home to hospital and back. Means (standard deviations) of transportation cost for ESWL and URS group were RM63.43 (41.90) and RM54.35 (30.31) respectively. Means (standard deviations) of ward charges for ESWL group was RM29.83 (77.36) and for URS group was RM141.49 (14.31). Patient's monthly income was divided with 9600 and multiplied with total waiting time. Housewives and unemployed patients were assumed to have no income. Means (standard deviations) of waiting cost for ESWL group was RM12.28 (12.87) and URS group was RM7.47 (10.94). Household cost was cost of waiting for patients' relatives and friends accompanying them to get treatment in the hospital. Means (standard deviations) of household cost for ESWL and URS groups were RM12.95 (42.94) and RM47.88 (108.85) respectively.

Total costs
Means (standard deviations) of total hospital cost was RM841.34 (25.86) for ESWL group and RM512.30 (103.88) for URS group. Student's t test showed that the difference was significant ($p<0.05$). Means (standard deviations) of total patient cost for ESWL group was RM128.50 (106.33) and URS group was RM289.62 (116.01). The difference was significant statistically (Student t test, $p<0.05$). Cost profile for each group is shown in Table VI.

As the analysis adopted societal view, both hospital and patient costs were considered. However, the sum of these costs had to subtract ward charges, clinic fees and day-care charges to avoid double counting. Means (standard deviations) of total cost for ESWL group was RM930.02 (62.24) and for URS group was RM621.95 (160.91). The difference was significant statistically (Student's t test, $p<0.05$).

Measurement of effectiveness with SF-36
The SF-36 measures eight concepts: physical functioning, role limitations due to physical health, bodily pain, general health perceptions, vitality, social functioning, role limitations due to emotional problems, and general mental health. Two summary measures of physical (PCS) and mental (MCS) health are constructed from the eight scales. The study used PCS scores to measure effectiveness of treatment because SF-36

did not produce a single composite index. The measurement is responsive to treatments that alter physical morbidity[32]. MCS is more appropriate to use when treatment or medications studied focus on mental health.

Univariate analysis in General Linear Model (GLM) found that there were significant score differences before and after treatment in all scales except Mental Health. However, the score differences between the two groups were only significant for Physical Role, Emotional Role and Mental Health scales where scores for URS group were higher than ESWL group. There were significant score difference before and after treatment in PCS and MCS but the differences were not significant when the univariate analysis compared the two treatment groups. Table VII displayed the mean scores for SF-36 summary measures.

CEA

The study examined the costs from a societal view. Effectiveness measures were the differences in SF-36 scores for PCS. Method of treatment that produces less cost over the increment of one unit quality of life is more cost-effective. Table VIII shows the comparison of cost-effectiveness ratio (CER) between ESWL and URS methods. CER at five percent discounts was 86.18 for URS and 247.02 for ESWL. This resulted from a lower treatment costs and higher PCS score increment for URS. The analysis suggested that URS was more cost-effective than ESWL.

Sensitivity analysis

Uncertainties existed in the estimation of costs. Hence, sensitivity analysis was performed by varying the discount rates from five percent to zero percent and ten percent. Costs that changed when discount rate changed were building cost, hospital furniture cost and cost of hospital equipment. CER at zero percent discounts was 174.39 for ESWL and 82.25 for URS. At ten percent discount, cost per PCS score increment was 335.29 for ESWL and 90.85 for URS. Therefore, URS was also found to be more cost-effective than ESWL at different discount rates.

Table I: Sociodemographic distribution of patients who had either ESWL or URS treatment for proximal ureteric stones.

	Treatment methods				p value
	ESWL		URS		
	Frequency	%	Frequency	%	
Gender					
Male	17	56.7	13	43.3	0.078*
Female	13	35.1	24	64.9	
Race					
Malay	29	44.6	36	55.4	1.000^
Non-Malay	1	50.0	1	50.0	
Formal education					
None	4	30.8	9	69.2	0.376^
Primary	4	44.4	5	55.6	
Secondary	7	36.8	12	63.2	
Certificate/Diploma/Degree	15	57.7	11	42.3	
Co-morbidity					
Present	8	33.3	16	66.7	0.159*
Absent	22	51.2	21	48.8	
Stone size					
≤ 1.0 cm	11	29.7	26	70.3	0.006*
> 1.0 cm	19	63.3	11	36.7	

*Chi square test, significant at p<0.05
^Fisher's exact test, significant at p<0.05

Table II: Patient distribution according to age, monthly income and proximal ureteric stone size

	Treatment methods		p value
	ESWL Mean (S.D.)	URS Mean (S.D.)	
Age (years)	52.67 (10.56)	48.73 (12.46)	0.174*
Monthly income (RM)	961.26 (870.45)	860.54 (1036.34)	0.673*
Stone size (cm)	1.42 (0.67)	0.95 (0.41)	0.004^

*Student's t test, significant at p<0.05
^Mann-Whitney U test, significant at p<0.05
S.D. – standard deviation

Table III: Stone-free status after six weeks of treatment with ESWL and URS

Stone size		Stone-free status		p value
		Yes Frequency (%)	No Frequency (%)	
≤ 1.0 cm	ESWL	9 (81.8%)	2 (18.2%)	1.000*
	URS	22 (84.6%)	4 (15.4%)	
	Total	31 (83.8%)	6 (16.2%)	
> 1.0 cm	ESWL	7 (36.8%)	12 (63.2%)	0.702*
	URS	3 (27.3%)	8 (72.7%)	
	Total	10 (33.3%)	20 (66.7%)	

* Fischer exact test, significant at p<0.05

Table IV: Estimates of logistic regression model showing the association between variables and stone-free status six weeks after treatment with ESWL and URS

	B	S.E.	Wald	df	Sig.	OR	95.0% C.I. for EXP(B)	
							Lower	Upper
Treatment methods	0.121	0.686	0.031	1	0.859	1.129	0.295	4.329
Age	0.017	0.032	0.271	1	0.603	1.017	0.955	1.083
Gender	0.710	0.652	1.186	1	0.276	2.035	0.567	7.305
Co-morbidity	-0.125	0.754	0.028	1	0.868	0.882	0.201	3.865
Stone size	2.515	0.666	14.254	1	<0.05*	12.372	3.352	45.664
Constant	-3.000	1.797	2.787	1	0.095	0.050		

*significant at p<0.05, Nagelkerke R square 0.353
S.E – standard error
OR – odds ratio
C.I. – confidence interval

Table V: Costs of equipment used in treatment of proximal ureteric stones with ESWL and URS

	Purchasing price (RM)	Life expectancy (years)	Cost/year* (RM)	Cost/patient (RM)
ESWL machine	3 162 911.80	20	253 800.44	666.14
Operating table	171 832.00	10	22 253.13	2.15
URS instruments	27 582.00	10	3572.01	44.09
Operating lights	27 348.96	10	3541.83	0.34
TV monitor	1200.00	5	277.17	3.38
Patient's trolley	66 000.00	15	6358.56	0.61
Physiological monitoring device	44 995.50	5	10 392.77	1.00

Table VI: Cost profile for each patient treated with ESWL and URS for proximal ureteric stone

	Treatment methods		p value
	ESWL Mean (S.D.)	URS Mean (S.D.)	
Hospital cost			
Capital cost			
Building	17.11	40.91	-
Furniture	0.79	1.83	-
Equipment	666.14	51.57	-
Recurrent cost			
Personnel	53.40 (18.36)	70.24 (35.60)	0.016*
Laboratory examination	15.50 (6.73)	32.38 (10.86)	<0.05*
Diagnostic imaging	49.17 (12.12)	55.03 (18.46)	0.139
Medications	9.24 (16.85)	169.51 (93.28)	<0.05*
Auxiliary procedures	0.00	33.37 (10.05)	<0.05*
Administration	19.42	32.19	-
Utilities and maintenance	10.57	25.29	-
Total hospital cost	841.34 (25.86)	512.30 (103.88)	<0.05*
Patient's cost			
Clinic fee	10.00	38.49 (11.37)	<0.05*
Transportation	63.43 (41.90)	54.35 (30.31)	0.325
Waiting time	12.28 (12.87)	7.42 (10.94)	0.099
Household	12.95 (42.94)	47.88 (108.85)	0.080
Ward charges	29.83 (77.36)	141.49 (14.31)	<0.05*
Total patient's cost	128.50 (106.33)	289.62 (116.01)	<0.05*
Total cost^	930.02 (62.24)	621.95 (160.91)	<0.05*

^total cost from societal view
S.D. – standard deviation
*Student's t test, significant at p<0.05

Table VII: Summary measures for SF-36 scores before treatment and six weeks after treatment with ESWL and URS (GLM analysis)

	Treatment methods				p value
	ESWL Mean (S.D.)		URS Mean (S.D.)		
	Before	After	Before	After	
PCS	39.91	43.56	36.19	44.06	a 0.003*
	(5.54)	(6.23)	(5.04)	(8.01)	b 0.256
MCS	38.76	44.62	35.89	46.59	a 0.006*
	(5.23)	(5.59)	(4.81)	(6.59)	b 0.680

* Significant at p<0.05
S.D. – standard deviation
PCS - Physical component scale
MCS - Mental component scale
p value:
a - mean difference before and six weeks after treatment
b - mean difference between ESWL and URS treatment

Table VIII: Cost-effectiveness ratio (CER) for ESWL and URS in treatment of proximal ureteric stone

	Treatment methods		p value
	ESWL Mean (S.D.)	URS Mean (S.D.)	
Treatment cost	930.02 (62.24)	621.95 (160.91)	<0.05
PCS score difference	4.77 (4.26)	7.96 (5.63)	0.021*
CER	247.02	86.18	<0.05*

S.D. – standard deviation
*Mann-Whitney U test, significant at p<0.05

DISCUSSION

Choice for treatment

The treatment of choice for patients with ureteric stones is still being debated.[15,35]. ESWL and URS are two major methods of treatment which are quite similar in term of their effectiveness. In 1997, American Urological Association (AUA) recommended ESWL as the first line treatment for ureteric stones[36]. However, newer findings suggested that both methods have similar effectiveness based on their success rates[37]. Hence, both methods could serve as first line treatment. Inevitably, the other important factor which has to be considered in deciding the choice of treatment is cost. Cost-effectiveness analysis is a useful economic evaluation that is able to make comparison between different methods of treatment. A number of studies adopted success rate of treatment as the outcome but Painter *et al*. recommended that quality of patient's lives should be included to make it more meaningful[5]. The choice of treatment of ureteric stones varies in different institutions. It also depends on size and location of ureteric stones, available technologies, cost, surgeon's experience and patient's preference[4,8].

ESWL has not changed much since its introduction in 1980s as compared to URS. The effectiveness of new generation ESWL lithotripters is quite similar to older generation machines. It is often quoted that the old HM3 lithotripter is the most effective in terms of success rate and serves as a benchmark for other lithotripters[22]. The success rate of any ESWL machine also depends on how it is being used and who use it. A study found that the highest success rate was achieved by surgeons who treated the most number of patients, used the highest number of shockwaves and had the longest fluoroscopic time[5]. However, the technology and success rate of URS improves a step forward compared to ESWL. New generation ureteroscopes are smaller and more flexible compared to the previous batches which were rigid and bigger in size. Furthermore, the incorporation of laser in treatment results in better success rates. The presence of various ESWL and URS models in the market and subsequently their use in numerous cost analysis studies could result in different conclusions.

Sampling and demographic factors

Universal sampling was used because it was anticipated that randomization would produce a smaller number of samples. Sixty seven patients who fulfilled the inclusion and exclusion criteria were enrolled for the study. Thirty patients were treated with ESWL while 37 others were subjected to treatment with URS. Both groups did not differ in terms of age, sex, race, formal education level, income and co-morbidities. The study found significant difference between treatment groups and stone sizes. ESWL technique was more often used to treat stones more than 1.0cm in their longest diameter but URS method was used in the treatment of smaller stones (less than 1.0cm diameter). Gettmann suggested that ESWL should be used to treat stones smaller than 1.0cm while URS is the choice for larger stones for better success rates[20].

Stone-free rates

Our overall success rates for both ESWL and URS methods were low (46.7% and 32.4%), compared to other studies which were 55-89% for ESWL and 80-92% for URS[2,7,8,15,20]. It is imperative to state that similar studies on ureteric stones will be influenced by the categorization of stone sizes and their locations. Pearle *et al*. only included ureteric stones which were less than 15mm in size while Bierkens *et al*. studied stones in middle and distal ureter only[7,8]. Categorization of stone size in this study followed the methodology used by Parker *et al* [2].

Stratification of stone size produced higher success rates for stones size of less than 1cm (ESWL 81.8% and URS 84.6%). However, the success rates for bigger stones were 36.8% and 27.3% for ESWL and URS respectively. Success of treatment was observed six week after the first treatment because of time factor. Other studies made the observation at three months and after additional treatment such repetition of procedures or other suitable methods[1,2,6,7,8]. Logistic regression analysis supported the notion that stone size is a very important factor influencing the success of ESWL or URS treatment. Demographic factors and methods of treatment did not show significant importance.

Hospital cost analysis

The cost data was positively skewed. Briggs (1997) argued that it is inappropriate to use median costs in cost analysis because the interest is on the average per patient cost for a particular treatment and medians are usually smaller than means[42]. Hence, means were used to describe data costs.

The hospital spent RM837.22 for each patient who had ESWL treatment and RM494.76 each patient in URS group. The most obvious difference was the costs of equipment. ESWL machine contributed almost 80% of hospital cost for ESWL group (RM666.14) while the cost of URS equipment was only slightly more than ten percent of total hospital cost for URS group (RM51.57). It cost about RM2 millions to buy and assemble one ESWL machine and an additional of RM160,000.00 per year for maintenance. One URS machine cost about RM20,000.00 and the maintenance cost is lower. Bierkens *et al*. found that the cost of ESWL machine was the major contributor to overall cost[8]. The high cost of ESWL machine could be reduced by increasing its use to achieve economies of scale. HSNZ treated 381 patients with the machine every year compared with 82 patients from URS group. While the surgeons could use ESWL more frequently to treat patients; the clinical indications, patient's preference and the number of trained personnel could be the limiting factors. Most studies did not include its use in treatment of other conditions such as renal stones and bladder stones which would further reduce the cost for each patient.

The most substantial cost for URS group was cost of medications which contributed more than 33% of the total hospital cost for URS group. Cost of medications for each patient in ESWL group was only RM9.15. URS is a more invasive procedure and all patients in the group required anesthesia. Patients were given intravenous antibiotics, anesthetic drugs and pain killers. Large standard deviation for URS group suggested that wide varieties of medications were used. There is a potential to reduce the cost by complying with the clinical pathway and adhering to antibiotic guideline, hence reducing variation in selection of medications.

The costs of personnel and laboratory examination were also higher in the URS group. This is expected because any procedures to be performed under anesthesia would require a more thorough assessment. Compliance to clinical pathway could reduce these costs. Administrative cost was higher in the URS group because patients stayed in hospital wards. There was no significant difference between costs of personnel in both groups.

Hospital cost for URS group could be further reduced if the procedure was performed as day-care surgery and thus, avoiding ward charges and less household cost. Chan et al. found that day-care URS performed in Hospital Universiti Kebangsaan Malaysia (HUKM) were safe and effective[38]. Nevertheless, not all patients in URS group were eligible for day-care surgery. It was limited by day-care surgical criteria such as ASA classification II or less. They must live near the hospital and have easy access to hospital should complications occurred.

Patients' cost analysis

ESWL treatment incurred a significant lower cost to the patients and relatives than URS. The cost was RM128.50 for ESWL and RM289.62 for URS. The cost for ESWL was cheaper from patient's perspective because patients in URS group needed hospital admission and subsequent visit to day-care center for removal of ureteric stent. They also had to put up with ward and day-care charges. Comparatively, patients in ESWL group only spent on clinic fees. Patients' cost could be reduced if URS became a day-care procedure[8,38]. Costs of transportation, waiting time and household did not show any significant difference.

Cost analysis from societal view

Cost variables tend to have skewed distribution[43]. Despite positive skewness of most cost data, the analysis used the robust Student's t test to measure the differences.

Overall cost included both hospital and patients' cost. However, transfer payments such as clinic fees, ward charges and day-care charges were not included to prevent double counting. ESWL technique produced a significant higher overall cost than URS which was RM930.02 for every patient. URS cost was RM621.95 per patient. Although Bierkens et al. found that URS incurred higher cost due to high hospitalization cost; other studies agreed that ESWL cost were much higher mainly due to high purchasing and maintenance costs[2,5,6,8].

Effectiveness measurement

SF-36 is a generic measurement tool to assess quality of life of a patient. It was the only tool validated for the Malaysian population[32,33]. Its use in economic evaluation is very significant despite the presence of a few shortcomings. SF-36, like Nottingham Health Profile, does not produce a single index of quality of life. Instead, it generates two summary measures (PCS and MCS) to enable comparison between different treatment methods [35,39].

ESWL and URS are two important methods to treat ureteric stones. This is reflected by the study findings that there were significantly higher SF-36 scores, except for Mental Health domain, after both treatments. PCS and MCS also showed significant differences before and after treatment but not between the two treatment methods. The results suggested that both treatment methods were equally effective in terms of quality of life and producing stone-free status.

Use of ureteric stent could possibly fabricate a negative impact to quality of life. All patients with stent fell in the URS group. Gettman *et al*. found that urinary symptoms and pain caused by ureteric stent reduced the quality of life in

almost 80% of patients[20]. Hence, we could expect higher PCS scores for patients in URS group if the stent were not used. Some authors recommended that routine use of ureteric stent was unnecessary[20].

Quality-adjusted life year (QALY) might provide a much more meaningful interpretation of patient's life because it includes the quality and quantity aspects of life. However, the calculation of QALY must combine these two aspects and SF-36 is not calibrated to the scale where death=0 and full health=1 [27].

CEA

This cost-effectiveness analysis found that URS method was more effective than ESWL. Total cost per increment in quality of life score for URS was lower (866.18) than ESWL (247.02). This situation resulted from a lower overall cost for URS and higher increment in PCS score. Even if the increments in quality score were similar, a substantially higher cost of ESWL would produce a higher cost-effectiveness ratio for ESWL. Previous comparisons found that the cost of treatment with URS was much cheaper than ESWL at all ureteric stone locations[6,15]. Parker *et al*. made comparison between ESWL and a more expensive form of URS which utilized holmium:YAG laser[2]. The result was also in favor of URS as a more effective method. It is necessary to consider that direct comparison between studies on ureteric stone treatment might not be possible because they used different definitions and technologies.

Apart from cost, technical effectiveness of treatment methods, the need for accessory procedures such as stenting, ward admission, treatment complications and treatment failures should have been considered to determine the most cost-effective method of treatment. Other issues such as price control, subsidy and the nature of health care system (private or public) could also have an impact on costs.

Selection of suitable technologies must also take into account the availability of urologist, epidemiology of stone disease in a given locality and the need assessment of the community. Untrained manpower could not produce the desired output or achieve efficacy. Need assessment would ensure that the technology is necessary and accepted by the community. An important factor that has to be considered while acquiring the technology is the package offered by vendors such as training of staffs, maintenance of machine and spare parts.

Sensitivity analysis changed the discount rate of five percent to zero and ten percents in order to address the issue of uncertainty. The results still showed that URS was more cost-effective than ESWL.

ESWL machine in HSNZ is not exclusively used for the treatment of ureteric stones. Other urinary tract stones such as renal and urinary bladder stones are being treated with the same machine. Similarly, URS is also being used in treatment of urinary tract strictures and diagnostic tissue biopsy for urinary tract growths. Thus, selection of medical technologies must also consider the prevalence of disease in the local population.

In health market, the use of advanced medical technologies is usually associated with higher treatment quality; and higher treatment cost[40]. Cost-effectiveness of competing treatment methods should be included in the discussion between doctor and patient before deciding on the most suitable methods.

Study limitation

The sample size was rather small because of a relatively short study period (seven months) and the need for follow-up for every patient. The combination of small sample size and early follow-up could have resulted in smaller increment in SF-36 scores.

Information bias might exist due to the nature of a retrospective study where respondents had to recall their past experiences. Efforts were made to reduce this bias by including only the patients that had treatment at least six months before the study begun. Relatives were also interviewed to validate the information on cost given by patients. Charges were used for costs borne by patients such as clinic fees, ward charges and day-care visits because many patients could not provide reliable information regarding these costs.

Calculation of cost for unemployed patients and housewives remained as a dilemma. The study assumed that they did not have any income. Cost of treatment complication was hard to determine because of incomplete documentation and patients were unable to provide detailed explanation. The study could not include the cost of re-treatment and failed treatment due to limited time.

Quality of life assessment should be based on QALY[5,25,39]. The three major health status classification systems are Quality of Well-Being (QWB), Health Utilities Index (HUI) and EuroQol (EQ-5D) but none has been validated for Malaysian population. Thus, their use was avoided despite being attractive options.

CONCLUSION

Ureteric stone is a burden to patient and society. ESWL and URS are major treatment methods besides observation, medications and open surgery. It is worth to assess cost-effectiveness of the treatment to justify the methods used in treatment. The main purpose of any economic evaluation is to assist in decision making. This study compares cost-effectiveness for each treatment method by calculating total cost for one unit increment in PCS score. Major cost for ESWL is equipment cost which includes purchasing, installation and maintenance costs. Antibiotics use is the main cost for URS. This CEA (societal view) found that URS is significantly more cost-effective than ESWL in treating proximal ureteric stones. Adhering to clinical guidelines and clinical pathways would ensure less variation and thus could reduce cost. Day-care URS could further reduce cost but a cost analysis is required for evidence. A more comprehensive study should include treatment failures and treatment of complications.

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