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Does Aging Affect the Efficiency of Extracorporeal Shock Wave Lithotripsy (ESWL) on Ureter Stones?

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ABSTRACT

Objective
Current evidence concerning the effect of aging on the treatment outcome of extracorporeal shock wave lithotripsy (ESWL) is still conflicting. We performed a retrospective analysis to investigate the effect of age on the treatment outcome of ESWL for ureteric stones.

Materials and Methods
Our study was a pair-matched analysis comparing the three month stone free rate (SFR) after primary ESWL. Between March 1st, 2013 and December 31st, 2015, a total of 1204 patients received ESWL in our facility. We recruited 131 patients who were above or equal to 65 years old, 72 of whom met our inclusion criteria. These patients were stratified into Group A. To compare differences in treatment outcome between age groups, patients in Group A were matched 1:1 to patients aged less than 65 years by their stone size, stone location and gender. These matched patients were sorted into Group B. We compared the three-month SFR and the effect of co-morbidities on the three-month SFR between the two groups using the Pearson's chi-square test and multivariate analysis.

Results
Seventy-two patients were included with a male-to-female ratio of 1:1 in each group. The average stone size was 6.74 mm (95% confidence interval, CI: 7.51-5.96) and 6.61 mm (95% CI: 7.25-5.96) in Group A and B, respectively (p=0.799). There were no differences in the three month SFR between Group A and B (63.9% *vs.* 66.7%, p=0.726). Univariate analysis suggested that stone location and diameter were related to SFR. However, multivariate analysis failed to show any statistically significant factors affecting SFR, including age.

Conclusion
In our study, age did not affect the three month SFR of ESWL. Therefore, ESWL could be an effective treatment modality for older patients. However, prospective studies with detailed data collection are required to validate these findings.

Keywords
Age; Extracorporeal Shock Wave Lithotripsy (ESWL); Urolithiasis; Stone free rate.

INTRODUCTION

Extracorporeal shock wave lithotripsy (ESWL) has been one of the choices for ureteric calculi since its invention in the 1980s.[1] For years, many investigators have been attempting to identify predictive factors associated with treatment outcome of ESWL. Stone size, location, composition and the performance of ESWL have been acknowledged as predictive factors of treatment success,[1] but the effect of aging is still under debate.

Previous evidence concerning the effect of age on ESWL is conflicting. In an early study of prognostic factors of ESWL success rate, patients between 40 and 60 years had the best outcomes among different age groups.[2] In a prospective study of 2954 patients with renal stones treated by ESWL, patients older than 40 years had inferior success rates than their younger counterparts.[3] Meanwhile, a retrospective analysis of 2192 patients with solitary urolithiasis revealed that aging was related to the stone-free rate (SFR) of renal stones, but not of ureteric stones.[4] On the other hand, in a retrospective review of 688 patients, age was not related to the treatment failure rate of ESWL.[5] Furthermore, Gomha et al[6] developed an algorithm to predict the treatment success rate of ESWL, and using their model, age was not associated with treatment outcome. The proposed hypothesis regarding the effect of age on treatment outcome of ESWL is that aging decreases lean body mass and bone density but increases body fat,[7] which is suggested to hamper stone targeting and dampen shockwave transmission, thereby leading to treatment failure.[8]

As the ageing population increases in Taiwan, the incidence of elderly patients with urolithiasis is also expected to increase. For clinicians facing the challenge of choosing an optimal treatment for these patients, treatment efficiency is the most important issue which influences overall decision-making. To clarify whether age has an effect on three month SFR of patients receiving ESWL, we performed a retrospective chart review of patients in different age groups who underwent ESWL treatment, and evaluated differences in treatment outcome between groups.

MATERIALS AND METHODS

This was a retrospective study that utilized data obtained from a review of patient medical records. We established a database from our electronic medical record system containing images, laboratory data, and clinical information of all patients who received ESWL between March 1st, 2013 and December 31st, 2015. A total of 1204 patients were identified, 131 of whom were above 65 years old. Patients were included if they received ESWL for ureteric stones and did not have a previous record of ESWL. Patients were excluded if they underwent 1) ESWL as adjuvant treatment within 6 months of ureteroscopic lithotripsy (URSL), or 2) percutaneous nephrolithotomy (PCNL); 3) if they had double J stent placement while receiving ESWL; 4) if they did not attend follow-up appointments; 5) if they had unknown follow-up status; or 6) if they had ureteric stones diagnosed within 3 months of primary ESWL that was performed for the treatment of renal stones, as these were considered residual fragments from previous treatment. Seventy-two patients met our inclusion criteria and were stratified into Group A.

To compare the influence of age on ESWL efficiency, we selected 72 patients as the control group (Group A). The patients from Group A were matched 1:1 by their maximum stone diameter, gender, side, and location of the stone. If the maximum stone diameter was not matched, the criterion was then extended to ±2 mm. If there were no identical stone locations to match, a stone located within 1 cm above or below the position was selected. All of the inclusion criteria were applied to the matched group as well as to Group A. When more than one match was identified, random selection was performed by computer software. The matched patients were included in Group B.

Diagnosis of ureteric stones was based on clinical evidence on abdominal pain, a kidney-ureter-bladder (KUB) radiograph, and a renal ultrasound demonstrating hydronephrosis. If additional imaging was available, namely an abdominal computer tomography (CT) focusing on the ureters or an intravenous pyelography (IVP), then this was also reviewed. Recognition of comorbidities was based upon prescribed medication with diagnosis written in the charts. Blood urea nitrogen (BUN) and creatinine (Cr) levels within 30 days prior to ESWL were recorded. The success of primary ESWL was defined as no evidence of stone fragment either on KUB, CT, or IVP and no hydronephrosis on renal ultrasonography within 3 months after the procedure. Treatment failure was defined as either one of the following: 1) the presence of a residual ureteric stone on imaging, or 2) hydronephrosis on renal ultrasound discovered after 3 months following the procedure; or 3) need for more than one ESWL procedure or adjuvant treatment such as URSL or PCNL targeting the same ureteric stone.

All patients were treated by electromagnetic lithotripter Dornier Compact Delta II® (Dornier Medtech, Munich, Germany). No anesthesia was administered before or during the procedure. A single dose of intramuscular non-steroidal anti-inflammatory drugs (NSAID) was given to patients if pain was complaint during the procedure with numeric rating scale score ≥2. All patients were placed in the supine position regardless of stone location. Medical expulsive therapy (MET) with a combination of oral NSAID and α-blocker was prescribed for seven days after the procedure. Our ESWL protocol included targeting of the stone under fluoroscopic guidance with or without the aid of renal ultrasound. A shockwave was administered in 60-80 waves per minute with a charging voltage of 8-12 kV. A total of 2500-3000 shockwaves were delivered in one treatment session by means of step-wise power ramping. All patients were surveyed at one week, one month and three months after the procedure with a combination of KUB, renal ultrasound and, in some cases, CT or IVP.

We compared treatment efficacy, co-morbidities and adjuvant treatments between groups. Statistical comparison was performed using Pearson's chi-square test for categorical data and Fisher's exact test for small sample size. Student's *t*-test was applied for continuous variables.

Multiple logistic regressions were applied to further analyze the relationship between co morbidities and treatment efficacy. Univariate logistic regression was first applied to identify possible confounders of SFR, and multivariate analysis was than performed for those factors with a p value <0.3 in univariate analysis. We set two tail, $\alpha=0.05$ as our level of significance. Statistical analysis was performed using Microsoft Excel 2011 package (Microsoft Crop., Seattle, WA, USA). The study has been approved by the institutional review board of Taipei Medical University.

RESULTS

Matching was achieved in all 72 patients. Thirty-six male and female patients were included in each group. The mean age of Group A was 70.2 years (range 82-65) and that of Group B was 44.9 years (range 63-21) (p<0.001). The average stone size was 6.74 mm (95% confidence interval, CI, 7.51-5.96) in Group A and 6.61 mm (95% CI 7.25-5.96) in Group B (p=0.8). Forty-two patients had ureteric stones on the left side and 30 patients on the right.

Subsequent analysis of stone location revealed 33 proximal and distal ureteric stones and 6 ureter-pelvic junction (UPJ) stones in Group A. Group B had identical stone distribution, but one of the patients with a UPJ stone was unmatched; therefore, a proximal ureteric stone located 6 mm from the location of the UPJ stone was randomly selected.

In the co-morbidity analysis, there were significant differences in renal function measurements between groups. The BUN was 18.9 mg/dL and 16.2 mg/dL in group A and B (p=0.004), respectively. Serum Cr was 1.13 mg/dL in Group A and 1.01 mg/dL in Group B (p=0.034). Compared to group B, group A had more patients with hypertension (36 *vs.* 11, respectively, $p<0.001$), type 2 diabetes mellitus (15 *vs.* 5, respectively, $p=0.016$), coronary artery disease (12 *vs.* 1, respectively, $p=0.002$) and hyperuricemia (9 *vs.* 2, respectively, $p=0.028$) (Table 1).

The 3 month SFR was 2.78% higher in Group B compared to group A (63.9% *vs.* 66.7%, respectively, $p=0.726$), but no statistical significance was reached. We further classified the patients into 3 subgroups according to their stone location. Compared to Group A, the SFR in Group B was higher for distal ureteric stones (66.7% *vs.* 75.8%, respectively, $p=0.415$) and UPJ stones (16.7% *vs.* 40.0%, respectively, $p=0.545$), but lower for proximal ureteric stones (69.4% *vs.* 61.8%, respectively, $p=0.494$).

Statistical significance was not seen in subgroup analysis by stone location (Table 2). Univariate logistic regressions were used to investigate possible confounders of SFR. Stone location ($p=0.01$) and diameter ($p=0.02$) were shown to be related to SFR. However, there was no significant relationship between any of the potential confounders and SFR in multivariate analysis (Table 3).

Twenty-three patients in Group A and 24 in Group B received adjuvant treatment. In Group A, 12 patients received URSL, 9 patients received more than one ESWL, and two received both URSL and ESWL. In Group B, 17 patients received URSL, 5 received more than one ESWL, and one received both URSL and ESWL. One patient in Group B underwent PCNL targeting a UPJ stone. Table 4 summarizes the adjuvant therapies received by patients in both groups.

DISCUSSION

Our study was designed to investigate the effect of age on the 3-month SFR of ESWL in a cohort of Taiwanese patients. In our research, there was no significant difference in the 3-month SFR between group A (≥65 years-old) and group B (<65 years-old) (63.9% *vs.* 66.7%, respectively, $p=0.726$). Subsequent analysis of co-morbidities and stone characteristics (location, diameter) by means of univariate and multivariate logistic regressions further demonstrated that these underlying factors also did not affect the treatment outcome of ESWL.

Our study result is in accordance with several prior studies that investigated the effect of age on the outcome of ESWL. Philippou et al[9] conducted a retrospective, pair-matched analysis of 230 patients above and below 70-years-old and

Table 1. *Demographic analysis of group A and group B*

	Group A		Group B		*p* value
Patient demographics	n	95% *CI*[g]	n	95% *CI*[g]	
Total patients	72		72		
Male	36		36		
Female	36		36		
Mean age[h]	70.2	[82, 65]a	44.9	[63, 21][a]	***< 0.001
Stone character					
Stone size (mm)[h]	6.74	95% *CI*[g]	n	95% *CI*[g]	
Left	42		72		
Right	30		36		
Distal ureter	33		36		
Proximal ureter	70.2	[82, 65]a	44.9	[63, 21][a]	***< 0.001
Ureteropelvic junction	6		5		
Laboratory data[h]					
BUNb (mg/dl)	18.9	[17.5, 20.3]	16.2	[14.9, 17.4]	**0.004
Crc (mg/dl)	1.13	[1.04, 1.22]	1.01	[0.94, 1.07]	*0.034
Co-morbidities					
Diabetes mellitus, type 2[i]	15		15		*0.016
Hypertension[i]	36		11		***< 0.001
Hyperuricemia[j]	9		2		*0.028
CAD[f,j]	9		1		**0.002

Note. [a][oldest age, youngest age]; [b]Blood urea nitrogen; [c]Serum creatinine; [d]Activated partial thromboplastin time; [e]International normalized ratio; [f]Coronary artery disease; [g]Confidence interval; [h]Student's *t*-test; [i]Pearson's chi-square; [j]Fisher's exact test

Table 2. *Three month stone free rate (SFR) after Extracorporeal Shock Wave Lithotripsy*

	Group A		Group B		*p* value
SFR[a,b]	n	(%)	n	(%)	
Overall	46	63.9	48	66.7	0.726
Distal ureter	22	66.7	25	75.8	0.415
Proximal ureter	23	69.7	21	61.8	0.494
Ureteropelvic junction	1	16.7	2	40.0	0.545

Note. [a]Three month stone free rate; [b]Pearson's chi-square

Table 3. *Univariate and multivariate analysis of confounders on stone free rate*

	Univariate analysis			Multivariate analysis		
	CE.[g]	SE.[h]	*p* value	CE	SE	*p* value
Age	-0.02	0.01	0.22	-0.01	-0.01	0.33
Proximal stone	0.03	0.35	0.93	-0.15	0.40	0.70
UPJ[a] stone	-1.75	0.70	*0.01	-1.42	0.83	0.09
Diameter	-0.16	0.07	*0.02	-0.09	0.07	0.23
HTN[b]	-0.50	0.37	0.17	-0.07	0.44	0.87
Gender	-0.50	0.35	0.73			
BUN[c]	-0.12	0.03	0.70			
Cr[d]	0.001	0.52	1.00			
CAD[e]	-0.18	0.60	0.77			
DMf	-0.26	0.49	0.59			
Hyperuricemia	-0.08	0.65	0.90			

Note. [a]ureteropelvic junction stone; [b]Hypertension; [c]Blood urea nitrogen; [d]Serum creatinine; [e]Coronary artery disease; [f]Diabetes mellitus, type 2; [g]Coefficient; [h]Standard error

Table 4. *Adjuvant treatment after primary Extracorporeal Shock Wave Lithotripsy (ESWL)*

	Group A	Group B	
	n	n	*p* value
URSLa	12	17	
ESWLb	9	5	
Combinedc	2	1	
PCNLd	0	1	
Totalf (percentagee)	23(31.9 %)	24(33.3 %)	0.861

Note. [a]ureteroscopic lithotripsy; [b]received more than one ESWL focusing on the same stone ; [c]combination treatment of URSL and ESWL on the same stone; [d]percutaneous nephrolithotomy; [e]percentage of patients receiving adjuvant treatment in each group; [f]Pearson's chi-square.

found no significant difference in SFR between the different age groups. In a study evaluating the prognostic factors related to ESWL success, Abdel-Khalek et al[3] demonstrated that age was not a significant prognostic factor. Furthermore, a retrospective review of 238 patients who underwent shock wave lithotripsy in Israel revealed that age itself had no significant impact on the success rate of ESWL, and that this procedure was associated with a minimal morbidity rate regardless of patient age.[10] The above two studies both compared patients older than 70 years to those younger. On the other hand, Ng et al[4] divided patients into three arms: above 60-years-old, below 40-years-old and those in between. His investigation indicated that SFR after ESWL is lower in older patients with renal stones, but no differences were discovered in patients with ureteric stones. Ikegaya et al[11] stratified patients in 10 year intervals from 30- to 70-years-old and revealed that the efficacy of ESWL decreased with age. Since each of the studies described above were conducted using different patient populations stratified according to different age cut-off points, there is at present no consensus regarding the effect of age on SFR.

To our knowledge, this study was the first attempt to investigate the effect of age on the success rate of ESWL among Taiwanese patients. Unlike prior studies,[4,9-11] we stratified patients into those older than 65-years-old and those younger. We chose this cut-off in order to meet the commonly accepted definition of 'elderly' and also to meet the age criterion of social welfare in Taiwan. Nevertheless, multiple logistic regression analysis further confirmed that age was not related to SFR in our study, regardless of stratification. Through matching the patients by their gender, location, and diameter of stones, we minimized the effect of confounding factors and focused on the effect of age. However, several limitations should be mentioned. First, not all patients underwent non-contrast computer tomography (NCCT) imaging during follow-up after ESWL. Given that the sensitivity and specificity of NCCT to diagnose urolithiasis is much higher than that of KUB radiography and ultrasound,[1,12] we may have overestimated the SFR in both groups. However, since our primary objective was to investigate the effect of age on ESWL, the absolute value of SFR was not our major concern. Furthermore, most patients received a combination of KUB radiography and ultrasound for treatment outcome evaluation, which are commonly used in routine clinical practice in Taiwan, and therefore we believe that these methods were sufficient to minimize the rates of missed diagnoses. Second, our male-to-female ratio was 1:1, which was different from the ratio reported in a previous epidemiological analysis in Taiwanese patients, cited at 1:1.56.[13] Since we only included patients that received primary ESWL on ureteric stones, those treated with other modalities or those with renal stones were not investigated.

Therefore, it is reasonable that our gender proportion was different from that of other studies. Third, this is a retrospective study that so many variables we did not taking into account that can have a big influence in the renal function as co-morbidities and presence or absence of obstruction. We should take it into consideration if we will do more study of ESWL.

Although we did not directly evaluate the effect of body composition on ESWL success rates, our results challenge the hypothesis that as patients age their lean body mass decreases and body fat increases, thereby reducing the efficiency of ESWL treatment. There are two possible explanations for this. First, the differences in body composition leading to altered ESWL efficiency may be more prominent for renal stones than for ureteric stones.[4] Since renal stones are encapsulated by the renal parenchyma and Gerota's fascia, the effect of shockwave elimination by body composition may be more prominent than for ureteric stones. However, it has been reported that age does not affect SFR regardless of stone location.[9] Additional data is required to support this hypothesis, but this is beyond the scope of the present study. Second, it is suggested that aging increases body fat and decreases lean body mass,[7] thereby leading to a decreased SFR.[8] The effect of body composition on ESWL efficiency may be minor.

A much larger study population is required to discover the impact of body composition affecting SFR.

In conclusion, the treatment efficacy of ESWL in elderly population is no inferior to that of younger population in our study. However, this recommendation should be considered in light of the limitations cited above. To further investigate the issue, further prospective studies are required that also evaluate patients' complete BMI and body composition measurements.

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CONFLICTS OF INTEREST

The authors confirm that there are no conflicts of interest to disclose.

REFERENCES

1. Türk C, Petřík A, Sarica K, Seitz C, Skolarikos A, Straub M, et al. EAU guidelines on Interventional treatment for Urolithiasis. *Eur Urol*.2015; 69(3): 475-82. doi: 10.1016/j.eururo.2015.07.041

2. Ackermann DK, Fuhrimann R, Pfluger D, Studer UE, Zingg EJ. Prognosis after extracorporeal shock wave lithotripsy of radiopaque renal calculi: a multivariate analysis. *Eur Urol*. 1994; 25(2):105-109. doi: 10.1159/000475261

3. Abdel-Khalek M, Sheir KZ, Mokhtar AA, Eraky I, Kenawy M, Bazeed M. Prediction of success rate after extracorporeal shock-wave lithotripsy of renal stones--a multivariate analysis model. *Scand J Urol Nephrol*. 2004; 38(2): 161-7. doi: 10.1080/00365590310022626

4. Ng CF, Wong A, Tolley D. Is extracorporeal shock wave lithotripsy the preferred treatment option for elderly patients with urinary stone? A multivariate analysis of the effect of patient age on treatment outcome. *BJU Int*. 2007; 100(2): 392-395. doi: 10.1111/j.1464-410X.2007.06909.x

5. Delakas D, Karyotis I, Daskalopoulos G, Lianos E, Mavromanolakis E. Independent predictors of failure of shockwave lithotripsy for ureteral stones employing a second generation lithotripter. *J Endourol*. 2003; 17: 201-5. doi: 10.1089/089277903765444302

6. Gomha MA, Sheir KZ, Showky S, Abdel-Khalek M, Mokhtar AA, Madbouly K. Can we improve the prediction of stone-free status after extracorporeal shock wave lithotripsy for ureteral stones? A neural network or a statistical model? *J Urol*. 2004; 172: 175-179. doi: 10.1097/01.ju.0000128646.20349.27

7. St-Onge MP, Gallagher D. Body composition changes with aging: the cause or the result of alterations in metabolic rate and macronutrient oxidation? *Nutrition*. 2010; 26(2): 152-5. doi: 10.1016/j.nut.2009.07.004

8. El-Nahas AR, El-Assmy AM, Mansour O, Sheir KZ. A prospective multivariate analysis of factors predicting stone disintegration by extracorporeal shock wave lithotripsy: the value of high-resolution noncontrast computed tomography. *Eur Urol* 2007; 51(6): 1688-1693; discussion 1693-1694. doi: 10.1016/j.eururo.2006.11.048

9. Philippou P, Lamrani D, Moraitis K, Bach C, Masood J, Buchholz N. Is shock wave lithotripsy efficient for the elderly stone formers? Results of a matched-pair analysis. *Urol Res*. 2011; 40(4): 299-304. doi: 10.1007/s00240-011-0424-4

10. Halachmi S, Meretyk S. Shock wave lithotripsy for ureteral stones in elderly male patients. *Aging Male*. 2006; 9(3): 171-174. doi: 10.1080/13685530600907985

11. Ikegaya H, Kato A, Kumano S, Tominaga T. Correlation between age and the efficacy of ESWL. *BJU Int*. 2005; 96(7): 1145. doi: 10.1111/j.1464-410X.2005.05924_2.x

12. Poletti PA, Platon A, Rutschmann OT, Schmidlin FR, Iselin CE, Becker CD. Low-dose versus standard-dose CT protocol in patients with clinically suspected renal colic. AJR AmJ Roentgenol 2007; 188(4): 927-933. doi: 10.2214/AJR.06.0793

13. Huang W-Y, Chen Y-F, Carter S, Chang H-C, Lan C-F, Huang K-H. Epidemiology of upper urinary tract stone disease in a Taiwanese population: A nationwide, population based study. *J Urol*. 2013; 189(6): 2158-2163. doi: 10.1016/j.juro.2012.12.105