Urolithiasis (2021) 49:351–358
https://doi.org/10.1007/s00240-020-01232-4

ORIGINAL PAPER

Association between time to lithotripsy and stone-free rate in patients with ureteral stones undergoing shock wave lithotripsy

Satoshi Washino[1,2] · Takanori Hayase[2] · Tomoaki Miyagawa[2] · Yoshiaki Arai[1]

Received: 26 July 2020 / Accepted: 18 November 2020 / Published online: 2 January 2021

Abstract

Early shock wave lithotripsy is associated with higher stone-free rate compared to delayed treatment of ureteral stones, but may constitute overtreatment because ureteral stones can pass spontaneously. We studied the association between time to treatment and stone-free rate in patients with ureteral stones to determine optimal shock wave lithotripsy timing. We retrospectively analyzed 537 patients undergoing shock wave lithotripsy for ureteral stones. Patients were divided into five groups according to time from onset of symptoms to lithotripsy—urgent (0–3 days), early (4–30 days), late (31–60 days), long-delayed lithotripsy (≥ 61 days), and asymptomatic. Stone-free rates were compared among groups. Mean age and stone size were 55.6 ± 13.1 years and 7.48 ± 3.29 mm, respectively. Mean number of shock wave lithotripsy sessions and stone-free rate were 1.37 and 91.6%, respectively, in the overall population. Stone-free rates were 95.2%, 96.8%, 91.3%, 86.3%, and 82.7% in urgent, early, late, long-delayed lithotripsy, and asymptomatic groups, respectively. Long-delayed lithotripsy and asymptomatic groups had significantly more lithotripsy sessions and lower stone-free rate, compared to urgent and early lithotripsy groups. In multivariate analysis, time to lithotripsy [long-delayed lithotripsy (odds ratio: 0.273, $p = 0.004$) and asymptomatic nature (odds ratio: 0.236, $p = 0.002$)] and age (odds ratio: 0.959, $p = 0.003$) independently affected stone-free rate. In conclusion, time to lithotripsy is a strong predictive factor for stone-free status following shock wave lithotripsy. Urgent shock wave lithotripsy did not improve stone-free rate if performed within 1 month. However, time to shock wave lithotripsy > 2 months reduced likelihood of stone-free status.

Keywords Shock wave lithotripsy · Stone-free rate · Time to lithotripsy · Ureteral stones

Introduction

Urinary tract stones are among the most common urological conditions worldwide with estimated prevalence rates of 1–5% in Asia, 5–9% in Europe, and 13% in the USA [1]. Most small stones pass spontaneously or by medical expulsive therapy [2]. The passage rate and spontaneous passage time are affected by the size and position of the stones [3]. Shock wave lithotripsy (SWL) and ureteroscopy lithotripsy (URS) are the main treatments for unpassed ureteral stones [4]. SWL is recommended for proximal and middle ureteral stones, as well as distal stones < 10 mm; URS is recommended for all ureteral stones [5, 6]. SWL can be performed without general or regional anesthesia on an outpatient basis, while URS requires hospitalization and general or regional anesthesia.

In the era of the novel coronavirus disease (COVID-19) pandemic, some patients with ureteral stones may have the virus and medical resources are limited. General anesthesia,

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s00240-020-01232-4.

✉ Satoshi Washino
suwajiisan@yahoo.co.jp

Takanori Hayase
hayase-t@jichi.ac.jp

Tomoaki Miyagawa
sh2-miya@jichi.ac.jp

Yoshiaki Arai
neoneoarai1220@icloud.com

[1] The Department of Urology, Nishi-Omiya Hospital, Saitama, Japan

[2] The Department of Urology, Jichi Medical University Saitama Medical Center, 1-847 Amanuma-cho, Omiya-ku, Saitama 330-8503, Japan

especially intubation and extubation, is associated with a high risk of COVID-19 transmission [7, 8]; therefore, it is essential to avoid general anesthesia as much as possible. SWL requires fewer medical resources and might pose a lower risk of COVID-19 transmission, compared to URS. Therefore, SWL is becoming increasingly important for the treatment of unpassed ureteral stones.

Early SWL has been reported to yield a higher stone-free rate (SFR), compared to delayed SWL [9]. However, early SWL may constitute overtreatment because some stones pass spontaneously or with medical expulsive therapy. It remains unknown whether urgent SWL is feasible and how long conservative therapies can be continued without compromising SWL outcomes. Here, we studied the association between time to SWL and SFR in patients with ureteral stones undergoing SWL to determine the optimal timing for SWL.

Materials and methods

Patients

Patients undergoing SWL for ureteric calculi in Nishi-Omiya Hospital, Japan, between January 1, 2013 and June 30, 2019, were screened for inclusion in this retrospective study. This study was approved by the Internal Review Board of Nishi-Omiya Hospital (approval no. #20191206-1). In total, 588 patients were initially included; 51 were excluded for the following reasons: ureteral stent or nephrostomy ($n=24$); lack of follow-up ($n=13$); multiple stones in 1 ureter ($n=9$); and previous URS and/or SWL for the target stone ($n=5$) (Fig. 1). Thus, 537 patients were included in the analysis. In total, 491 patients (91.4%) underwent computed tomography (CT) prior to SWL, but 46 patients did not.

The locations of ureteral stones were classified as proximal (U1), middle (U2), and distal ureter (U3). Patients were grouped according to the time to SWL as urgent (0–3 days), early (4–30 days), late (31–60 days), long-delayed (≥61 days), and asymptomatic (unknown). Ureteral wall thickness was measured at the stone site on preoperative non-contrast CT scans, as described previously [10].

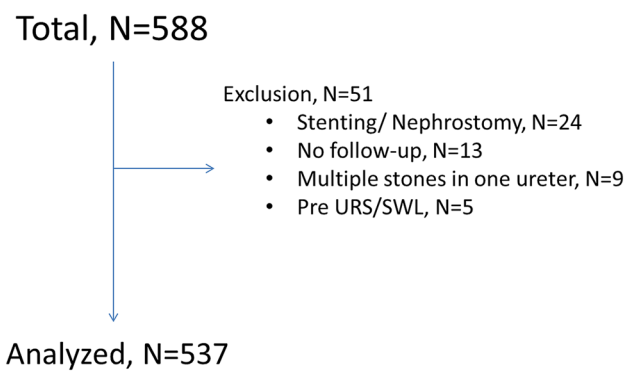

Fig. 1 Flow diagram outlining patient selection. *URS* ureteroscopy lithotripsy, *SWL* shock wave lithotripsy

SWL methods

SWL was performed using a Dornier Delta II lithotripter (Dornier MedTech, Munich, Germany). Most patients underwent SWL on an outpatient basis, although older patients or those with one or more severe comorbidities were admitted for SWL. Pain control was achieved using diclofenac sodium (50 mg, suppository) and/or pentazocine hydrochloride (15 mg, intramuscular injection). All SWLs were performed with stepwise power and a shock wave rate of 90–100 per minute by a single experienced surgeon (Y. A.). Stone fragmentation was determined by X-ray examination. Medical expulsive therapy following SWL was not routinely performed.

Endpoints

The primary endpoint was SFR, stratified according to time to SWL. The secondary endpoint was SFR following one session of SWL, stratified according to time to SWL. Factors associated with stone-free status were also assessed. Stone-free status was defined as an absence of the target stone on plain X-rays of the kidney, ureter, and bladder. Patients were followed-up every 2–4 weeks by X-ray until stone-free status was achieved; some patients who did not achieve a stone-free status underwent additional SWL sessions. Comorbidities were graded using the Clavien–Dindo classification [11].

Statistical analysis

Variables were compared using the *t* test or Mann–Whitney *U* test, as well as the χ^2 test or Fisher's exact test, as appropriate. Comparisons among three or more groups were performed by one-way ANOVA followed by the Dunnett multiple comparison test or the Kruskal–Wallis test followed by the Dunn multiple comparison test. Binary logistic regression analysis was performed to identify factors independently associated with stone-free status following SWL. Statistical analyses were performed using GraphPad Prism (ver. 7.0; GraphPad, La Jolla, CA, USA) and SPSS Statistics for Windows (ver. 19.0; IBM Corp., Armonk, NY, USA).

Table 1 Patients' characteristics ($N = 537$)

	N	(%)
Age, mean (SD)	55.5	(13.1)
Gender		
Male	402	(74.9)
Female	135	(25.1)
Symptoms		
Pain	416	(77.5)
Hematuria	67	(12.5)
Fever	18	(3.4)
Nothing	75	(14.0)
Unknown	1	(0.2)
Initial/recurrent		
Initial	347	(64.6)
Second Rec	115	(21.4)
Third or more	69	(12.9)
Unknown	6	(1.1)

SD standard deviation

Table 2 Stone characteristics

	N	(%)
Laterality		
Rt	247	(46.0)
Lt	290	(54.0)
Location		
U1	310	(57.7)
U2	120	(22.4)
U3	107	(19.9)
Hydronephrosis		
Yes	411	(76.4)
No	50	(9.3)
Unknown	46	(8.6)
Stone size, mm, mean (SD)		
U1	7.77	(3.58)
U2	7.37	(3.12)
U3	6.76	(2.41)
Total	7.48	(3.29)
Stone density, CT values (HU), mean (SD)		
U1	849	(310)
U2	784	(278)
U3	755	(267)
Total	816	(297)

SD standard deviation, *CT* computed tomography, *HU* Hounsfield unit

Results

Patient characteristics

Patient characteristics are shown in Table 1. The patients consisted of 402 men (74.9%) and 135 women (25.1%), with a mean ± SD age of 55.5 ± 13.1 years. Pain, hematuria, and fever occurred in 77.5%, 12.5%, and 3.4% of patients, respectively; 14.0% were asymptomatic patients, in whom the finding of ureteral stones was incidental. There had been no prior urolithiasis in 64.6% of patients, while 35.6% had at least one previous episode of urolithiasis (Table 1). Stones were present in the right ureter in 46.0% of patients, whereas they were present in the left ureter in the remaining 54.0% of patients. Stones were located in U1, U2, and U3 in 57.7%, 22.4%, and 19.9% of patients, respectively (Table 2). Hydronephrosis was present in 76.4% of patients. The mean ± SD stone size was 7.48 ± 3.29 mm. U1 stones (7.77 ± 3.58 mm) were the largest, followed by U2 (7.37 ± 3.12 mm) and U3 stones (6.76 ± 2.41 mm) (Table 2). Mean ± SD CT values were 816 ± 297 Hounsfield units in the overall population. In total, 28.8%, 10.2%, and 31.1% of all patients were treated with non-steroidal anti-inflammatory drugs, butyl scopolamine, and both drugs in combination to control colic pain before SWL; 29.2% of the patients were not prescribed any painkiller. For pain control during SWL, 83.7% and 14.2% of patients were treated with diclofenac sodium alone or diclofenac sodium plus pentazocine. The mean ± SD number of shock waves per patient was $2.83 \times 10^3 \pm 0.40 \times 10^3$. The maximum power of lithotripsy was ≤ 2 kV in 12.5% of patients, 3–4 kV in 57.2% of patients, 5–6 kV in 30.2% of patients, and unknown in 0.2% of patients.

Associations between time to SWL and outcomes

The mean ± SD number of SWL sessions was 1.37 ± 0.92 in the overall population. Patients in the long-delayed and asymptomatic groups required significantly more SWL sessions, compared to patients in the urgent and early groups (1.55 ± 1.10 and 1.79 ± 1.08 vs. 1.24 ± 0.82, $p = 0.0002$ and $p < 0.0001$, respectively) (Table 3).

SFR was 91.6% in the overall population. SFRs in urgent and early groups were similar (95.2% and 95.8%) and decreased with increasing time to SWL. SFRs in long-delayed and asymptomatic groups were significantly lower, compared to urgent and early groups (86.3% and 82.7% vs. 95.6%, $p = 0.0033$ and $p = 0.0008$, respectively), while SFR in the late group (91.3%) was not significantly different from SFR in urgent and early groups ($p = 0.14$) (Table 4). Long-delayed and asymptomatic groups also had lower SFR following one session of SWL, compared to urgent and early groups (65.3% and 48.0% vs. 83.2%; $p = 0.0004$ and $p < 0.0001$, respectively) (Table 4).

The mean ± SD time to stone-free status in patients who became stone-free was 24.1 ± 34.4 days; this did not significantly differ between urgent and early groups

Table 3 The number of SWL sessions stratified with time to SWL and stone location

The number of SWL sessions												
	Urgent (0–3 days)		Early (4–30 days)		Late (31–60 days)		Long delayed (≥61 days)		Asymptomatic (unknown)		Total	
	Mean	(SD)	Mean	(SD)	Mean	(SD)	Mean	(SD)	Mean	(SD)	Mean	(SD)
U1	1.33	(1.08)	1.23	(0.87)	1.31	(0.87)	1.60*	(1.37)	1.66**	(0.94)	1.36	(0.99)
U2	1.21	(0.58)	1.18	(0.58)	1.23	(0.44)	1.26	(0.55)	1.96**	(1.34)	1.37	(0.83)
U3	1.25	(0.55)	1.25	(0.53)	1.24	(0.54)	1.69*	(1.06)	1.83**	(0.94)	1.44	(0.80)
Total	1.29	(0.91)	1.22	(0.78)	1.28	(0.71)	1.55*	(1.10)	1.79**	(1.08)	1.37	(0.92)

SD standard deviation

*$p < 0.05$, **$p < 0.01$ vs urgent to early SWL (0–30 days)

Table 4 Stone-free rate stratified with time to SWL and stone location

	Urgent (0–3 days)		Early (4–30 days)		Late (31–60 days)		Long delayed (≥61 days)		Asymptomatic (unknown)		Total	
	SFR (%)	*N*	SFR (%)	*N*	SFR (%)	*N*	SFR (%)	*N*	SFR (%)	*N*	SFR (%)	*N*
Stone-free rate (%)												
U1	96.2	52	95.9	145	94.3	35	92.5	40	84.2*	38	93.9	310
U2	92.9	14	97.8	45	92.3	13	82.6*	23	84.0	25	90.8	120
U3	94.4	18	91.7	24	85.7	21	81.3	32	75.0	12	86.0	107
Total	95.2	84	95.8	214	91.3	69	86.3*	95	82.7*	75	91.6	537
Stone-free rate (%) following one session of SWL												
U1	82.7	52	84.1	145	80.0	35	72.5	40	52.6**	38	78.1	310
U2	78.6	14	88.9	45	69.2	13	73.9	23	44.0**	25	73.3	120
U3	77.8	18	75.0	24	76.2	21	50.0*	32	41.7*	12	64.5	107
Total	81.0	84	84.1	214	76.8	69	65.3*	95	48.0**	75	74.3	537

SFR stone-free rate, *N* number of patients

*$p < 0.05$, **$p < 0.01$ vs urgent to early SWL (0–30 days)

(17.6 ± 19.4 vs. 22.0 ± 33.5 days, respectively, $p = 0.512$) (Supplementary Table 1). Asymptomatic patients required significantly greater time to achieve stone-free status, compared to patients in the urgent and early groups, while patients in the long-delayed group tended to require more time (40.8 ± 60.3 and 28.1 ± 35.8 days in asymptomatic and long-delayed groups vs. 20.0 ± 28.2 days in urgent and early groups, $p = 0.0012$ and $p = 0.080$, respectively).

Associations between other factors and outcomes

The SFR, and that following one SWL session, were lower for stones ≥ 10 mm in diameter than for stones < 10 mm in diameter (86.4% vs. 92.9% and 55.3% vs. 78.8%; $p = 0.043$ and $p < 0.0001$, respectively); these results were associated with more SWL sessions and a longer time to stone-free status for patients with larger stones (1.94 ± 1.61 vs. 1.24 ± 0.58 and 42.0 ± 55.3 vs. 20.1 ± 27.0 days; $p < 0.0001$ and $p < 0.0001$, respectively) (Table 5). The SFR, and that following one SWL session, were lower for U3 compared to U1 stones (86.0% vs. 93.9% and 64.5% vs. 78.1%; $p = 0.014$ and $p = 0.0068$, respectively). We found no significant difference in the SFR, number of SWL sessions, or time to stone-free status between patients with and without hydronephrosis (92.5% vs. 86.0%, 1.34 ± 0.87 vs. 1.53 ± 0.74, and 23.6 ± 34.3 vs. 30.5 ± 41.7 days; $p = 0.17$, $p = 0.11$, and $p = 0.16$) but the SFR following one SWL session was higher in patients with than without hydronephrosis (76.8% vs. 55.3%, $p = 0.0055$).

Factors associated with stone-free status in multivariate analysis

In univariate analysis, factors associated with stone-free status were age (odds ratio [OR], 0.964; 95% confidence interval [CI], 0.941–0.988; $p = 0.004$), stone size (OR 0.910; 95% CI 0.843–0.982; $p = 0.015$), stone location in U3 (OR 0.400; 95% CI 0.196–0.820; $p = 0.012$), and time to SWL (long delayed: OR 0.288; 95% CI 0.128–0.645; $p = 0.002$, and asymptomatic: OR 0.218;

Table 5 Association between stone size, stone location, and hydronephrosis with outcomes

		SFR		SFR following one SWL		The number of SWL, times		Time to stone-free, days	
	N	%	*p* value	%	*p* value	Mean (SD)	*p* value	Mean (SD)	*p* value
Stone size									
< 10 mm	434	92.9	0.043	78.8	< 0.0001	1.24 (0.58)	< 0.0001	20.1 (27.0)	< 0.0001
≥ 10 mm	103	86.4		55.3		1.94 (1.61)		42.0 (53.3)	
Stone location									
U1	310	93.9	ref	78.1	ref	1.36 (0.99)	ref	22.5 (29.2)	ref
U2	120	90.8	0.29[#]	73.3	0.31[#]	1.37 (0.84)	ns	29.0 (49.8)	ns
U3	107	86.0	0.014[#]	64.5	0.0068[#]	1.44 (0.80)	ns	23.1 (26.1)	ns
Hydronephrosis									
(+)	441	92.5	0.17	76.8	0.0055	1.34 (0.87)	0.11	23.6 ± 34.3	0.16
(−)	50	86.0		55.3		1.53 (0.74)		30.5 (41.7)	

SFR stone-free rate, *SWL* shockwave lithotripsy, *ref* reference, *ns* not significant

[#]*p* values versus U1

Table 6 Univariate and multivariate analyses to analyze factors associated with stone-free status

	Univariate analysis			Multivariate analysis		
	OR	95% CI	*p* value	OR	95% CI	*p* value
Age						
Years	0.964	0.941–0.988	0.004	0.959	0.933–0.986	0.003
Sex						
Male	ref	ref		ref	ref	
Female	(−)	(−)	0.911	(−)	(−)	0.480
Laterality						
Rt	ref	ref		ref	ref	
Lt	(−)	(−)	0.302	(−)	(−)	0.599
Hydronephrosis						
No	ref	ref		ref	ref	
Yes	(−)	(−)	0.110	(−)	(−)	0.779
Stone size						
mm	0.910	0.843–0.982	0.015	(−)	(−)	0.551
Stone location						
U1	ref	ref		ref	ref	
U2	0.647	0.298–1.404	0.270	(−)	(−)	0.650
U3	0.400	0.196–0.820	0.012	(−)	(−)	0.049
Stone density						
CT value (HU)	(−)	(−)	0.647	(−)	(−)	0.352
Distance of skin to stone						
mm	(−)	(−)	0.630	(−)	(−)	0.959
Time to SWL						
≤ 30 days	ref	ref		ref	ref	
31–60 days	0.479	0.175–1.309	0.151	0.417	0.146–1.186	0.417
≥ 61 days	0.288	0.128–0.645	0.002	0.273	0.112–0.680	0.004
Asymptomatic	0.218	0.096–0.492	< 0.001	0.246	0.192–0.593	0.002

SWL shock wave lithotripsy, *OR* odds ratio, *CI* confidence interval, *ref* reference, *Hydro* hydronephrosis, *CT* computed tomography, *HU* Hounsfield unit

95% CI 0.096–0.492; $p < 0.001$) (Table 5). In multivariate analysis, age (OR 0.959; 95% CI 0.933–0.986; $p = 0.003$) and time to SWL (long-delayed: OR 0.273; 95% CI 0.112–0.680; $p < 0.004$, and asymptomatic: OR 0.218; 95% CI 0.192–0.593; $p = 0.002$) were independently associated with stone-free status. Sex, stone laterality, presence of hydronephrosis, stone size, stone location, stone density, and the distance between the skin and the stone showed no significant associations (Table 6).

Association between time from complaint onset and increased ureteral wall thickness on CT

Ureteral wall thickness was measurable in 454 patients, and was greater in patients with an interval between complaint onset and CT of ≥ 31 days, and in asymptomatic cases, compared to those within 3 days (1.98 ± 0.68, 2.41 ± 0.61, 2.30 ± 1.19, and 3.43 ± 1.49 mm vs. 1.78 ± 0.79 mm in cases with intervals of 4–30, 31–60, and ≥ 61 days, and asymptomatic cases vs. those of 0–3 days; $p = 0.26$, $p = 0.0042$ $p = 0.0031$, and $p < 0.0001$, respectively) (Fig. 2). The SFR did not differ significantly by ureteral wall thickness (92.8% for a wall thickness < 2.5 mm vs. 89.6% for a thickness ≥ 2.5 mm, $p = 0.26$) but a thicker wall was associated with a lower SFR following one SWL session, an increase in the number of SWL sessions required, and a longer time to stone-free status (79.1% vs. 62.8%, 1.31 ± 0.82 vs. 1.52 ± 0.97, and 23.4 ± 35.8 vs. 29.2 ± 37.0 days for wall thicknesses of < 2.5 mm vs. ≥ 2.5 mm; $p = 0.0004$, $p = 0.0006$ and $p = 0.0044$, respectively).

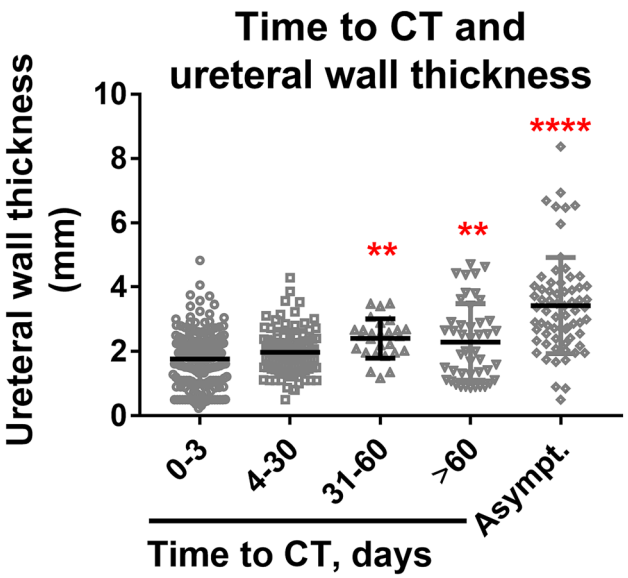

Fig. 2 Association between time from onset to CT and ureteral wall thickness. Ureteral wall thickness increased after 31 days or more from onset, or asymptomatic cases compared to that in 3 days from onset. $^{**}p < 0.01$, $^{****}p < 0.0001$ vs. 0 to 3 days. *Asympt.* asymptomatic cases

Comorbidities

Twenty-three patients (4.3%) experienced comorbidities in the overall population; grade 3 or higher comorbidities occurred in only 10 patients (1.9%), all of which constituted pyelonephritis (Supplemental Table 2). In all 10 patients, pyelonephritis was resolved by antibiotics with or without ureteral stenting.

Discussion

In the present study, time to SWL was strongly and independently associated with stone-free status following SWL. SFR reached 95% for patients with ≤ 30 days to SWL, and then gradually decreased. Patients in the long-delayed (> 60 days) and asymptomatic groups required significantly more SWL sessions and showed lower SFR.

The success of SWL reportedly depends on best clinical practices, including clinician experience level and shock wave rate, lithotripter efficacy, stone size, location, and hardness [6]. In the present study, SWL was performed by a single experienced surgeon; therefore, the degree of variation in surgical procedures was low. We explored factors related to stone-free status, following SWL. The results indicated that time to SWL and age were independently negatively associated with stone-free status, while stone size, stone density (CT value), the distance from the skin to the stone, and stone location showed no associations in multivariate analysis (Table 6). Ichiyanagi reported that older age tended to be associated with delayed stone clearance following SWL [12]. There have been no studies regarding the association between time to SWL and SFR; the outcomes of SWL in patients with asymptomatic ureteral stones have not yet been determined, although patients with urgent SWL have a higher SFR, compared to patients with delayed SWL [9]. The present study demonstrated that longer time to SWL and asymptomatic ureteral stones were negatively associated with SFR. Therefore, time to SWL and age should be considered with respect to SWL for the treatment of ureteral stones.

The aim of emergent treatment in patients with acute renal colic is relief of symptoms, unless there are indications for immediate intervention (e.g., renal function impairment and signs of urinary tract infection or sepsis) [13]. Kumar et al. [14] reported that the time needed for stone clearance, the retreatment rate, and the requirement of auxiliary procedures were significantly higher when treatment was performed beyond 48 h after onset of pain. In a meta-analysis, emergent SWL was found to

be more effective than delayed SWL in terms of SFR; it also required fewer ancillary procedures [9]. However, most small ureteral stones passed spontaneously or with medical expulsive therapy. An estimated 95% of stones up to 4 mm pass in ≤ 40 days with conservative treatment; medical expulsive therapy seems to be efficacious for treatment of patients with ureteral stones, especially distal stones > 5 mm [2]. Choi et al. [15] reported significantly better treatment outcomes in the emergent group only for patients with stone size < 10 mm and proximal stones. In a randomized controlled trial, Kumar et al. [14] found no significant difference in SFR between patients with delayed SWL and those with early SWL, although the numbers of auxiliary procedures and SWL sessions were significantly lower in patients with early SWL. The usefulness of emergent SWL remains controversial with respect to SFR. In the present study, SFR remained up to 95% for ≤ 30 days and we found no difference in the time to stone-free status between patients in the urgent (0–3 days) and early groups (4–30 days) (Table 4 and Supplementary Table 1). These results indicate that it is feasible to continue conservative therapy or medical expulsive therapy for up to 30 days in patients without severe pain and/or infection.

Patients in the long-delayed (time to SWL > 60 days) and asymptomatic groups had significantly lower SFR and required more SWL sessions, compared to patients in the urgent and early groups (Tables 3 and 4). Especially in patients with distal stones (U3 stones), SFR could decline to ~ 80%; SFR following one session of SWL was only 40–50% (Table 4). Ureteral stones cause ureteral edema that develops gradually after 24–48 h, progressing over time; these stones ultimately impact the ureteral wall, resulting in impaired stone clearance [16]. We found that ureteral wall thickness, as revealed by CT, increased significantly more than 1 month after onset (Fig. 2), which compromised stone clearance following SWL. It is feasible to avoid continued use of conservative therapy or medical expulsive therapy for more than 2 months if SWL is considered as an alternative approach. If time to surgical treatment is expected to be > 2 months, URS may be preferable; notably, SFR is less affected by time to surgical procedure in patients undergoing URS [9].

This study had some limitations. In particular, the retrospective nature of this study increased the patient selection bias and the number of patients in some groups was small, especially those in the late and asymptomatic groups. Furthermore, this study did not assess the retreatment rate.

Conclusion

Time to lithotripsy is strongly associated with SFR following SWL. SWL in an urgent care setting does not improve SFR if it is performed within 1 month, while time to SWL > 2 months reduces the likelihood of stone-free status.

Author contributions SW and YA contributed to the study conception and design. Material preparation, data collection and analysis were performed by SW and TH. The first draft of the manuscript was written by SW, TM and YA and all the authors commented on previous versions of the manuscript. SW edited this manuscript. All the authors read and approved the final manuscript.

Funding Non-applicable.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Human and animal rights This article does not contain any studies with human participants or animals performed by any of the authors.

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