Impact of Ureteral Stent Size on Stone-Free Rates in Ureteroscopic Lithotripsy for Ureteral Stones: Randomized Controlled Trial

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Objective: *To determine the stone-free rates after ureteroscopic lithotripsy (URSL) between patients who had large and small ureteral stent.*

Material and Method: *A prospectively randomized controlled study. Patients who underwent URSL between January 2014 and April 2015 were enrolled. Sixty eligible patients were randomized into 3 groups: non-stented as a control group (n = 20), 4.7 Fr stented (n = 20), and 6 Fr stented groups (n = 20). The lithotripsy technique was stone fragmentation using Holmium: YAG laser (Lumenismodel™) until the fragment was smaller than 2 mm. The stone fragments were left in situ without extraction. Primary outcome was stone-free rates detected by non-contrast-enhanced computed tomography (NCCT). Secondary outcomes were irritative symptoms evaluated by overactive bladder symptoms score (OABSS), flank pain, hematuria, urinary tract infection (UTI), auxiliary procedure, and readmission.*

Results: *The pre-operative characteristics of each group were similar. A stone-free rate in non-stented, 4.7 Fr stented, and 6 Fr stented groups was 95%, 85%, and 85% (p = 0.524), respectively. There was no statistically differences between 4.7 Fr and 6 Fr stented groups for irritative symptoms (25% vs. 45%, p = 0.185), flank pain (10% vs. 5%, p = 0.548), asymptomatic pyuria (35% vs. 25%, p = 0.288), febrile UTI (5% vs. 10%, p = 0.151) and hematuria (45% vs. 30%, p = 0.327). The operative time, postoperative pain, analgesic requirement, length of hospital stay, auxiliary procedures, and readmission were not different.*

Conclusion: *There was no difference in stone-free rates and stent-related adverse effects between small and large size ureteral stent after URSL. The irritative symptoms and febrile UTI tended to be less in small stented.*

Keywords: *Ureteric calculi, Ureteroscopic lithotripsy, Ureteral stent, Stone-free rate*

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Advancement of instrumentation, including small caliber semi-rigid ureteroscope and the introduction of Holmium: YAG laser, ureteroscopic lithotripsy (URSL) has evolved into a safe and efficacious modality for treatment of ureteral stones in upper and lower ureter. Although the major advantage of stenting is to prevent ureteral obstruction and may facilitate the passage of stone fragments[1-4]. Several prospective randomized trials have found that routine ureteral stenting after uncomplicated URSL is not necessary[5-8]. Avoiding stent lowers costs and gives less irritative symptoms[5-8]. A meta-analysis revealed no difference in stone-free rate between non-stented and stented groups[8]. However, there is no prior study on the impact of ureteral stent size on stone-free rate. Therefore, if stent is considered, we questioned that the small caliber of ureteral stent is able to prevent postoperative ureteric obstruction, allows passage of stone fragments, or to have minimal stent related adverse effects?

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Materials and Method

We prospectively enrolled the patients who underwent URSL for ureteral stones between January 2014 and May 2015 in Siriraj Hospital, Mahidol University. The indications for URSL were stone larger than 6 mm, renal deterioration, no progression of stone location after 6 weeks of medical expulsion therapy, intractable pain, and recurrent UTI (Table 1). Patient who was younger than 18 years old, pregnant, or had

Table 1. Indication for URSL

	No stent (n = 20)	4.7 Fr stent (n = 20)	6 Fr stent (n = 20)	*p*-value
Unlikely to pass spontaneously	14 (70%)	17 (85%)	17 (85%)	0.392
Renal deterioration	11 (55%)	6 (30%)	11 (55%)	0.187
Failed conservative	9 (45%)	7 (35%)	9 (45%)	0.760
Intractable pain	8 (40%)	9 (45%)	3 (35%)	0.098
Recurrent UTI	5 (25%)	4 (20%)	7 (35%)	0.551
Others	2 (10%)	0	1 (5%)	0.349

clear indication for postoperative stenting such as ureteral perforation, solitary kidney, and infection were excluded from this study.

A total of 69 potential patients were enrolled in this study. Informed consents were obtained for all patients before participation. Of these, nine patients were excluded (five patients had concomitant ureteric stricture, two patients had ureteral perforation, and two patients had stone migration into renal pelvis). Therefore, 60 eligible patients were simple randomized by computer into three groups; non-stented, 4.7 Fr stented, and 6 Fr stented groups.

The surgery was performed under general anesthesia. The semi-rigid ureteroscope (Wolf® 6.0/7.5 Fr) was used with Holmium: YAG laser and laser fiber 365 or 550 micron (Lumenis™). The power was set at 5 to 10 Watt (0.5 to 1.0 J, 10 to 15 Hz). Stone was fragmented until there was no fragments larger than 2 mm.The fragments were left in situ without extraction. At the end of the procedure, non-stented or ureteral stent 4.7 Fr/21-32 cm (Sof-Flex®) or 6 Fr/22 to 30 cm (Stretch™ VL) was obtained regarding to the randomization. Stent removal was scheduled in next two weeks.

Primary outcome was stone-free rates which detected by non-contrast-enhanced computed tomography (NCCT) (1.25 mm thickness per slice) after stent removal. This was evaluated at 4 weeks postoperatively. Stone-free was defined as an absence of stone fragments along the ureter. Secondary outcomes were irritative symptom scores, flank pain, hematuria, urinary tract infection (UTI), auxiliary procedures, and readmission.

Patient demographic data included age, gender, body mass index (BMI), Glomerular filtration rate (GFR), and comorbidity were recorded. All patients were requested to answer the questionnaires which evaluate pre-operative and two weeks postoperative irritative voiding symptoms by using overactive bladder symptom score (OABSS)[8]. Pain was evaluated by visual analogue scale. Urinalysis was obtained to evaluate hematuria.

Statistical analysis was obtained using SPSS version 22. Chi-square test, one-way ANOVA, and Kruskal-Wallis test were utilized for group comparison. All tests were 2-sided with p-value <0.05 to consider statistically significant.

Results

Patient demographic data was well balanced between groups as shown in Table 2. The mean size of ureteral stone was 7.7±2.5, 8.8±3.6, and 8.5±2.7 mm (p = 0.563) in non-stented, 4.7 Fr stented, and 6 Fr stented groups, respectively. The number of patients who had stones located in upper ureter was 4 (20%) in non-stented, 12 (60%) in 4.7 Fr stented, and 14 (70%) in 6 Fr stented groups (p = 0.004).

Clinical outcomes were shown in Table 3. A stone-free rate in non-stented, 4.7 Fr stented, and 6 Fr stented groups was 95%, 85%, and 85% (p = 0.524), respectively. There was no statistically difference in operative times (35, 32.5, 32.5, p = 0.793) and length of hospital stay (2, 2, 2, p = 0.232). In group of 6 Fr stented, two patients had readmission for auxiliary procedure. One patient had distal ureter obstruction after stent removal. In this case the ureteral stent was placed again. Another patient had acute pyelonephritis required readmission for intravenous antibiotic.

The residual stone was detected in seven patients: one patient of non-stented group and three patients for each group of 4.7 Fr and 6 Fr ureteral stent. Size of residual stone was 2.0 mm in all groups. The data were shown in Table 4.

Early postoperative outcomes (24-hour after URSL) were shown in Table 5. There was no difference of postoperative pain (0.5±0.9, 0.3±0.5, 0.4±0.8, p = 0.855), analgesic usage (3.4±4.9, 2.3±3.9, 2.6±3.2, p = 0.800), and fever (20%, 20%, 25%, p = 0.906) among three groups of non-stented, 4.7 Fr stented, and 6 Fr stented, respectively.

Table 2. Demographic data

	No stent (n = 20)	4.7 Fr stent (n = 20)	6 Fr stent (n = 20)	*p*-value
Age (years), mean ± SD	59.7±10.7	57.4±10.4	54.7±11.3	0.348
Sex				0.934
Female	12 (60%)	11 (55%)	1 (55%)	
Male	8 (40%)	9 (45%)	19 (45%)	
BMI (kg/m^2), mean ± SD	25.7±3.8	26.3±3.7	25.8±6.1	0.895
GFR (mL/min/1.73 m^2), mean ± SD	72.5±18.9	72.5±17.3	76.1±23.9	0.804
CKD				
Stage 2	12 (60%)	14 (70%)	8 (40%)	0.362
Stage 3	4 (20%)	4 (20%)	4 (20%)	
Stage 4	0	0	1 (5%)	
ASA				
1	8 (40%)	7 (35%)	6 (30%)	
2	11 (55%)	11 (55%)	9 (45%)	
3	1 (5%)	2 (10%)	5 (25%)	0.435
Stone side				
Right	10 (50%)	10 (50%)	13 (65%)	
Left	10 (50%)	10 (50%)	7 (35%)	0.545
Stone site				
Lower	16 (80%)	8 (40%)	6 (30%)	
Upper	4 (20%)	12 (60%)	14 (70%)	0.004
Stone size (mm), mean ± SD	7.7±2.5	8.8±3.6	8.5±2.7	0.563
Degree of hydronephrosis				
No	2 (5%)	4 (20%)	5 (25%)	0.420
Mild	7 (35%)	11 (55%)	5 (25%)	
Moderate	8 (40%)	4 (20%)	9 (45%)	
Severe	3 (15%)	1 (5%)	1 (5%)	

Table 3. Clinical outcomes

	No stent (n = 20)	4.7 Fr stent (n = 20)	6 Fr stent (n = 20)	*p*-value
Stone-free rates	19 (95%)	17 (85%)	17 (85%)	0.524
Operative time (min) median (min, max)	35 (10, 70)	32.5 (15, 65)	32.5 (15, 150)	0.793
Length of hospital stay (days) median (min, max)	2 (1,15)	2 (1,8)	2 (1,8)	0.232
Readmission	0	0	1 (5%)	0.362
Auxiliary procedure	0	0	1 (5%)	0.362

Stent-related adverse outcomes were shown in Table 6. Irritative symptoms, flank pain, asymptomatic pyuria, febrile UTI, and hematuria were significantly higher in stented groups. Whereas, there was no statistically difference between 4.7 Fr and 6 Fr stented for those irritative symptoms (25% vs. 45%, $p = 0.185$), flank pain (10% vs. 5%, $p = 0.548$), asymptomatic pyuria (35% vs. 25%, $p = 0.288$), febrile UTI (5% vs. 10%, $p = 0.151$), and hematuria (45% vs. 30%, $p = 0.327$). The data were shown in Table 7.

Discussion

Stenting after uncomplicated URSL is not necessary and stone-free rate is not different between non-stented and stented groups. However, in case the ureteral stent is considered, such as to divert urine for obstructive cases or to prevent obstruction due to ureteral mucosal edema the impact of ureteral stent size

Table 4. Residual stone data

	No stent (n = 20)	4.7 Fr stent (n = 20)	6 Fr stent (n = 20)	Total (n = 60)
Residual stone	1 (5%)	3 (15%)	3 (15%)	7 (11.7%)
Stone site				
Lower	1 (5%)	3 (15%)	2 (15%)	6 (10%)
Upper	0	0	1 (5%)	1 (1.7%)
Mean initial stone size (mm)	7.0	8	11.3	9.2
Residual stone size (mm)	2.0	2.0	2.0	2.0

Table 5. Early post operative outcomes (24-hour after URSL)

	No stent (n = 20)	4.7 Fr stent (n = 20)	6 Fr stent (n = 20)	*p*-value
Pain score mean $\pm$ SD	0.5$\pm$0.9	0.3$\pm$0.5	0.4$\pm$0.8	0.855
Analgesic requirement mean $\pm$ SD	3.4$\pm$4.9	2.3$\pm$3.9	2.6$\pm$3.2	0.800
Fever	4 (20%)	4 (20%)	5 (25%)	0.906

Table 6. Stent-related adverse outcomes

	No stent (n = 20)	4.7 Fr stent (n = 20)	6 Fr stent (n = 20)	*p*-value
Increased OABSS	0	5 (25%)	9 (45%)	0.004
Increased flank pain	0	2 (10 %)	1 (5%)	0.624
Asymptomatic pyuria	2 (10%)	7 (35%)	4 (25%)	0.155
Febrile UTI	0	1 (5%)	4 (25%)	0.059
Hematuria	1 (5%)	9 (45%)	6 (30%)	<0.001

Table 7. Adverse outcomes between 4.7Fr stent and 6Fr stent groups

	4.7 Fr stent (n = 20)	6 Fr stent (n = 20)	*p*-value
Increased OABSS	5 (25%)	9 (45%)	0.185
Increased flank pain	2 (10%)	1 (5%)	0.548
Asymptomatic pyuria	7 (35%)	4 (25%)	0.288
Febrile UTI	1 (5%)	4 (25%)	0.151
Hematuria	9 (45%)	6 (30%)	0.327

on stone-free rates have not been established. Therefore, this study aimed to compare the stone-free rate between small and large size ureteral stent. Other purpose was to compare the undesirable side effects of the two different sizes of ureteral stents.

In this study, there was no statistically difference of stone-free rate between patient who had 4.7 Fr and 6 Fr ureteral stent (85% vs. 85%). Stone-free rate in non-stented group (95%) tended to be higher than both of thestented groups (85%), nevertheless, this was not statistically significant. Goktas C et al[9] studied the technique of stone fragmentation without

extraction in 238 patients. 15% (36/238) of cases had upper ureteric calculi while 75% had no ureteral stent. The mean of stone diameter was 8.7 mm. The overall stone-free rate was 95%. Stone-free was defined as no fragment larger than 3 mm and detected by multimodality of imaging (plain film, ultrasonography, and CT scan), mostly was plain film. This figure was similar to our study, but we utilized CT scan in all cases to detect smaller residual stone.

Our study included both of upper and lower ureteric calculi. According to simple randomization, there were more patients who had lower ureteric calculi in non-stented group than others. However, there were no differences in stone-free rates of any group. There were seven patients who had residual stone. In six of these, the stone was initially in lower ureter and the mean size was 9.2 mm; in another, the stone was 7 mm in upper ureter. Therefore, stone size is more important than location for stone-free rate.

The perioperative outcomes included operative time, postoperative pain, analgesic requirement, postoperative fever, length of hospital stay, auxiliary procedures, and readmission were not different among these three groups. The overall readmission rate was 1.67% and auxiliary procedures were 1.67% in our study. This was different from previous studies from Goktas C et al[9], which utilized the larger ureteroscope and both of pneumatic and laser lithotripsy. They revealed 25% of readmission and 11% of auxiliary procedure.

Patients in stented groups, both of small and large size experienced more irritative symptoms (35%) than non-stented group (0%). Likewise, meta-analysis from Liang Tang et al revealed similar results with significantly higher rate of urinary frequency and urgency in stented group[10]. Erturk E et al[11] and Rocco Damiano et al[12] reported no differences in terms of pain or irritative symptoms between small and large size stented. Nevertheless, our study revealed less irritative symptoms in small stent than large stent (25% vs. 45%, $p = 0.001$).

Nabi G et al reported that patients who had ureteral stent after ureteroscopy experienced more irritative symptoms and infectious complications than non-stented[5]. Our study also had the similar result of these complications. While the large stent tended to have more incidence of febrile UTI than the small stent, but this was not statistically significant (25% vs. 5%, $p = 0.151$). Hematuria was less in non-stented than both of large and small stented (5% vs. 30% vs. 45%, $p<0.001$); whereas, there was no difference in this complication between large and small stented (30% vs. 45%, $p = 0.327$).

Conclusion

This study is a randomized controlled trial to determine the association between size of ureteral stent and stone-free rates after URSL. There was no difference in stone-free rates between small and large size ureteral stent. Perioperative outcomes were similar. Irritative symptoms and febrile UTI were fewer in smaller stented; however, they were not statistically significant.

Compliance with ethical standards

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. The study was approved by Siriraj Institutional Ethical Review Board, protocol number 599/2556 (EC2).

What is already known on this topic?

Ureteral stent is an indication after ureteroscopy for cases which have ureter obstruction or ureter injury. However, stent size does not impact drainage of urine while drainage of stone fragments has not been established.

What this study adds?

The study was carried out to establish the impact of ureteral stent size on stone-free after ureteroscopic lithotripsy.

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Potential conflicts of interest

None.

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การศึกษาผลของขนาดสายระบายท่อไตต่ออัตราการกำจัดเศษในผู้ป่วยนิ่วท่อไตที่รักษาด้วยการส่องกล้องสลายนิ่วโดยการทดลองแบบสุ่มและมีกลุ่มควบคุม

พรเพ็ญ ประสารชัยมนตรี, ไชยยงค์ นวลยง, ธวัชชัย ทวีมั่นคงทรัพย์, เอกรินทร์ โชติกวาณิชย์

__วัตถุประสงค์:__ เพื่อศึกษาเปรียบเทียบอัตราการกำจัดเศษนิ่วในผู้ป่วยนิ่วท่อไตที่รักษาโดยการส่องกล้องสลายนิ่วระหว่างการใส่สายระบายท่อไตขนาดเล็กและขนาดใหญ่

__วัสดุและวิธีการ:__ ผู้ป่วยที่เข้ารับการรักษาโดยการส่องกล้องสลายนิ่วท่อไตที่โรงพยาบาลศิริราชระหว่างเดือนมกราคม พ.ศ. 2557 ถึงพฤษภาคม พ.ศ. 2558 โดยแบ่งผู้ป่วยแบบสุ่มเป็น 3 กลุ่ม คือ กลุ่มที่ไม่ใส่สายระบายท่อไต (กลุ่มควบคุม), กลุ่มที่ใส่สายระบายท่อไตขนาดเล็ก (4.8 Fr) และกลุ่มที่ใส่สายระบายท่อไตขนาดใหญ่ (6 Fr) โดยผู้ป่วยทุกรายได้รับการส่องกล้องสลายนิ่วด้วยเลเซอร์เพื่อให้แตกเป็นเศษนิ่วขนาดเล็กกว่า 2 มิลลิเมตร และทิ้งไว้ให้หลุดออกมาเองอัตราการกำจัดเศษนิ่วถูกตรวจสอบด้วยการทำเอกซเรย์คอมพิวเตอร์แบบไม่ฉีดสารทึบรังสี

__ผลการศึกษา:__ อัตราการกำจัดเศษนิ่วในผู้ป่วยกลุ่มที่ไม่ใส่สายระบายท่อไต กลุ่มที่ใส่สายระบายขนาดเล็ก และกลุ่มที่ใส่สายระบายขนาดใหญ่ คือร้อยละ 95, ร้อยละ 85 และร้อยละ 85 ตามลำดับ โดยไม่มีความแตกต่าง อย่างมีนัยสำคัญทางสถิติ (p = 0.524) อาการไม่พึงประสงค์จากสายระบายท่อไตขนาดเล็กและขนาดใหญ่ ได้แก่ อาการระคายเคืองทางเดินปัสสาวะ (ร้อยละ 25 และ 45, p = 0.185) อาการปวดหลัง (ร้อยละ 10 และ 5, p = 0.548) การติดเชื้อทางเดินปัสสาวะ (ร้อยละ 5 และ 10, p = 0.151) และอาการปัสสาวะเป็นเลือด (ร้อยละ 45 และ 30, p = 0.327) ไม่พบว่ามีความแตกต่างกันอย่างมีนัยสำคัญทางสถิติ

__สรุป:__ ไม่พบความแตกต่างของอัตราการกำจัดเศษนิ่วและอาการไม่พึงประสงค์จากสายระบายท่อไตระหว่างสายขนาดเล็กและขนาดใหญ่ อย่างไรก็ตาม อาการระคายเคืองและการติดเชื้อทางเดินปัสสาวะมีแนวโน้มน้อยกว่าในกลุ่มที่ใส่สายระบายท่อไตขนาดเล็ก