Stone-free rate predictors at first flexible ureteroscopy and laser fragmentation

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Abstract

Introduction: Flexible ureteroscopy and laser fragmentation (FURSL) is a minimally invasive modality for surgical treatment of renal stones. Inadequate selection of patients for this treatment generates a cost-effectiveness unbalance. **Objective:** To know the stone-free rate predictors in a single surgical time in patients undergoing FURSL. **Method:** Retrospective cohort of patients undergoing FURSL. Global and gender-categorized univariate and multivariate (logistic regression) analyses were performed to identify stone-free predictors at first FURSL. **Results:** Stone-free rate at first FURSL was 73.62%. Predictors in males were patient age and stone size, density and multiplicity; in females, body mass index and multiplicity of stones. **Conclusions:** Stone-free rate predictors at first FURSL are different in males and females. Women with overweight and obesity probably have easy-to-fragment and easy-to-extract stones associated with uric acid.

KEY WORDS: Ureteroscopy. Kidney stones. Obesity. Costs and cost analysis.

Introduction

Flexible ureteroscopy and laser fragmentation (FURSL) is the minimally invasive treatment most frequently used in patients with kidney stones who have poor prognostic factors for extracorporeal lithotripsy or who failed this treatment. In addition, it is useful in patients with blood dyscrasias or comorbidities that prevent percutaneous nephrolithotripsy for bulky calculi.

The primary objective in any surgical procedure for kidney stones should be complete elimination of the lithiasic load at first attempt; the degree at which the procedure achieves this goal is an important criterion to guide patient decision and expectations.¹

Being a woundless procedure that is technically less demanding than percutaneous nephrolithotripsy, FURSL

is directly requested by the patient or suggested by the doctor in an attempt to generalize surgical treatment for all types of calculi, which causes that not all kidney stones are resolved at first surgery and that even in some cases three or four procedures of this type are necessary to solve them, which translates into high and unnecessary surgical costs that would have been avoided if a different surgical procedure had been chosen from the beginning.

In an attempt to adequately select patients for FURSL, several studies have sought factors that predict a stone-free rate (SFR) status, but without taking into account the number of procedures required for kidney stones resolution.²

The factors most frequently identified as SFR predictors in FURSL include stone location, multiplicity and volume.²

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Date of reception: 15-08-2018
Date of acceptance: 05-01-2019
DOI: 10.24875/GMM.M19000249

Gac Med Mex. 2019;155:148-153
Contents available at PubMed
www.gacetamedicademexico.com

Figure 1. Flow-chart of the cohort of patients undergoing FURSL.

There are no studies specifically evaluating these factors by gender, and hence the results are a mixture of prognostic factors assuming that they are the same for men and women, without taking into account that there are different characteristics between both genders, such as the composition and thus the hardness of the stone, the size of the kidney and the distinctive structural characteristics of genitals in both genders.

Therefore, knowing the predictive factors of SFR in a single surgical time in patients undergoing FURSL will help to make better therapeutic decisions based on cost-effectiveness.

Method

A retrospective cohort of consecutive patients undergoing FURSL at the Mexican Institute of Social Security National Medical Center Siglo XXI Specialty Hospital from October 2014 to January 2017 was studied. The cohort included men and women older than 18 years with kidney stones who had preoperative abdominopelvic computed tomography and abdominal simple X-ray and radiological control studies to evaluate the resolution of stones. Patients who had previously undergone FURSL for the same stone, those with non-observable stones in preoperative abdominal plain X-ray and those with incomplete follow-up data were excluded. In all of

them, transoperative fluoroscopy and Holmium laser (200-micron fiber) were used for fragmentation and a JJ catheter was placed at the end of the procedure at the surgeon's discretion, which was left at least until the radiological control evaluation.

The variables assessed as potential predictors were age, gender, body mass index, history of urinary infection, history of endoscopic or open urological surgeries for stones in the same kidney, history of urinary strictures or upper urinary tract obstructive malformations, stone size (sum of the largest diameter of all calculi), density (highest value in Hounsfield units), location and multiplicity of the stones, and length and infundibular diameter of the lower calyx and pyelocalycial angle.

The primary outcome measure was SFR, defined as absent or non-significant stones (< 4 mm) in the control imaging study (Somani level 4C and 4x), three weeks after the first FURSL procedure.³

Statistical analysis was carried out with SPSS, version 20. Patients were divided by gender. In the univariate analysis, success versus failure was contrasted for SFR by means of Student's t-test or Mann-Whitney U-test according to data distribution. For categorical or stratified variables, the hypothesis was contrasted using the chi-square test.

A multivariate analysis was performed by means of logistic regression with the Wald method, with the

Table 1. Characteristics of patients undergoing flexible ureteroscopy and laser fragmentation (n = 158)

Characteristic	n	%
Demographics		
Women	93	58.9
Obesity or overweight	114	72.2
Left side	85	53.8
Single stone	98	62
Stone localization		
Upper calyx	9	5.7
Middle calyx	7	4.4
Lower calyx	64	40.5
Pyelic	14	8.9
Ureteral	10	6.3
Multiple not including lower calyx	8	5.1
Multiple including lower calyx	46	29.1
Preoperative clinical characteristics		
History of urinary tract infection	29	18.4
History of open surgery	33	20.9
History of endoscopic surgery	78	49.4
Ureteral stricture or malformations	29	18.4
Use of aspirin or anticoagulants	7	4.4
Liver cirrhosis	3	1.9
Hypertension	38	24.1
Preoperative hematuria	114	72.2
Urine culture		
Negative	109	69
Non-ESBL <i>Escherichia coli</i>	16	10.1
ESBL <i>Escherichia coli</i>	26	16.5
<i>Enterococcus sp.</i>	2	1.3
<i>Klebsiella sp.</i>	1	0.6
<i>Pseudomonas sp.</i>	4	2.5
JJ catheter bearer	65	41.1
Transoperative characteristics		
Use of ureteral access sheath	132	83.5
Type of anesthesia		
Block	7	4.4
Block plus general	5	3.2
General	146	92.4
Transoperative hypertension	10	6.3
JJ catheter placement at the end	149	94.3
	Mean	SD
Age (years)	50.52	11.68
Body mass index	28.55	5.34
Creatinine	0.98	0.42

Table 1. Characteristics of patients undergoing flexible ureteroscopy and laser fragmentation (n = 158) (Continued)

Characteristic	Mean	%
Stone size (mm)	16.04	10.15
Stone density (HU)	1106.03	347.78
Pyelocalyceal angle (degrees)	82.78	14.92
Lower infundibulum diameter (mm)	10.51	9.80
Lower infundibulum length (mm)	19.25	6.17

ESBL = extended spectrum betalactamase; HU = Hounsfield units.

Note: Stone size is the sum of all stones longest diameters.

predictive variables found in the univariate analysis to identify interactions and adjust each one. Odds ratios (ORs) and confidence intervals were obtained for variables that remained as predictors.

There were no maneuvers, procedures or risk conditions additional to the treatment that was previously assigned to the patient, and thus the study was considered as an investigation with lower than minimal risk, which was approved by the Local Committee of Ethics and Research of the Hospital with registry number R-2016-3601-93.

Results

One-hundred and fifty-eight evaluable patients were obtained (Figure 1), out of which 93 (58.9 %) were females. Population age was 50.5 years on average. Mean weight was 73.7 kg, height was 1.60 m and body mass index was 28.5; 114 patients were overweight or obese, 85 (53.2 %) stones were left sided and 98 (62.02 %) were single. The stones were located at the upper calyx in nine (5.7 %), middle calyx in seven (4.4 %), lower calyx in 64 (40.5 %), renal pelvis in 14 (8.9 %), ureter in 10 (6.3 %), multiple stones that did not include the lower calyx in eight (5.1 %) and multiple stones that included the lower calyx in 46 (29.1 %). Mean size of the calculi was 16.04 mm (Table 1). Ureteral access sheath was used in 132 (83.5%) and a JJ catheter was left in 149 (94.3 %). Overall SFR was 73.62 %.

In the univariate global analysis (both genders), the number (single versus multiple) and volume of the stones were found to be predictors of SFR. In the gender-categorized analysis, prognostic factors were different for men and women. In the multivariate analysis, age and stone location, size and density remained as predictors for residual lithiasis after the first procedure in men; in women, normal or low body mass index and multiple lithiasis predicted residual lithiasis (Table 2).

(Continue)

Discussion

At National Medical Center Siglo XXI Specialty Hospital, FURSL is not usual for stones at the upper third of the ureter; most are treated without the need for flexible instruments and, for this reason, our results might be better applied to patients who only have kidney stones. The Clinical Research Office of the Endourological Society multicenter study recorded 73 % of patients with stones that only involved the ureter and recorded rigid and flexible ureteroscopy procedures pooled results,⁴ which makes it difficult for conclusions that are generalizable to the kidney to be obtained.

Resorlu et al. described that stone size, composition and multiplicity, as well as infundibulopyelic angle and the presence of renal malformations were prognostic factors for SFR in FURSL,² with hydronephrosis being added by Ito et al.⁵ In the patient global analysis, only volume and multiplicity had an influence on SFR; however, in a multivariate analysis separating patients by gender, we found that the factors that predict SFR in the first FURSL are different for men and women. Age younger than 50 years, location in the ureter or renal poles, and stone lower density and size are favorable prognostic factors for men. Surprisingly, only body mass index ≥ 25 and single stones had a positive influence in women.

It is possible that the larger proportion of men in the cohorts of other studies⁴ have an influence on the results of global analyses (not categorized by gender), making for the prognostic factors of greater weight to be the ones that are important in men and hiding those that are significant in women.

FURSL is an adequate treatment option in patients with obesity,⁶ but body mass index influence on SFR is conflicting.⁷⁻¹⁰ Doizi et al. found that a higher body mass index was associated with higher resolution of stones at first procedure, which was even more evident when the comparison was made with patients with high body mass index.⁸ Similarly, in our study, women with a body mass index ≥ 25 had a favorable prognosis for SFR.

The frequency of urinary lithiasis increases with body mass index, regardless of age, which is more evident in women.¹¹ As body mass index increases, the proportion of uric acid stones also increases in both genders,¹² which has been more evident in women in the last two decades.¹³ We believe that calculi in women with obesity and overweight are softer, which would translate into a better prognosis with endoscopic

resolution due to a higher fragmentation-extraction rate of these stones when compared with calculi with calcium content.^{12,14-16}

Daudon et al. recorded that the frequency of uric acid stones in women with normal weight increased from 6.1 to 17.1 % in women with obesity, in addition to decreasing the proportion of patients with calcium phosphate stones.¹⁷ Siener et al. also found that as women's body mass index increased, the proportion of calcium oxalate stones decreased and urinary urate excretion increased.¹⁸

Regarding the cutoff point for SFR to be considered, Ghani et al. suggest that the threshold should be 2 mm; however, it has also been referred that the study to discriminate such a fine threshold would have to be a computed tomography due to the decrease in plain abdominal X-ray sensitivity as stones are smaller.¹

Subjecting all patients to control computed tomography is not usual in international studies, where there is a valid mixture, at least in practice, of ultrasound, plain abdominal X-rays and computed tomography, which are heterogeneous studies Ghani obtains his conclusions from and issues his recommendations.¹

Despite its sensitivity, the use of computed tomography has been limited by the need to maintain exposure to radiation as low as possible (the ALARA concept) and by the probability that in the future other lithiasis events occur or several surgeries are required in these patients to resolve the same calculus.¹⁹

Discrimination of < 4 mm fragments in a plain abdominal X-ray is complicated, and, therefore, reducing the cutoff point to 2 mm or less would only add subjectivity and would not modify the treatment to be followed for residual calculi, which essentially it is the same if the stone measures 2 or 3 mm, as shown by international guidelines, which indicate that > 5 mm is the cutoff point from which the probability of requiring an additional invasive treatment for residual non-infected calculi increases. This is based on the natural history of these fragments and their likelihood of spontaneous expulsion.^{20,21}

We intend for our study with the 4 mm cutoff point to have external validity, i.e. that it can be generalized to urological usual practice for decision-making according to the international guidelines in force up to this moment, with a cost-effectiveness-safety balance being maintained.

Our research is the first to demonstrate that SFR prognostic factors are different in men and women and, thus, we believe that generalizing the prognostic factors in patients with lithiasis without taking gender

Table 2. Residual lithiasis predictors at first flexible ureteroscopy and laser fragmentation, categorized by gender (n = 158)

Variables	Males (n = 65)							Females (n = 93)						
	Univariate*					Multivariate**		Univariate*					Multivariate**	
	Solved		Persistent		p	Adjusted OR	p	Solved		Persistent		p	Adjusted OR	p
	n	%	n	%				n	%	n	%			
Age (years)														
≤ 50	17	44.7	4	14.8	0.015	1	0.009	28	52.8	19	47.5	0.611		
> 50	21	55.3	23	85.2				25	47.2	21	52.5			
						39.80								
						(2.52-627.16)								
Body mass index														
< 25	10	26.3	6	22.2	0.706			10	18.9	18	45.0	0.007	4.72	0.004
≥ 25	28	73.7	21	77.8				43	81.1	22	55.0			
													(1.63-13.66)	
													1	
Multiplicity														
Single	21	55.3	16	59.3	0.749			43	81.1	18	45.0	0.000	1	0.000
Multiple	17	44.7	11	40.7				10	18.9	22	55.0			
													9.06	
													(1.95-27.83)	
Location (single stones)														
Ureteral	6	15.8	1	3.7	0.115	1	0.018	2	3.8	1	2.5	0.002		
Calyceal (polar)	15	39.5	11	40.7				32	60.4	15	37.5			
Calyceal (interpolar or pelvic)	2	5.3	6	22.2				10	18.9	3	7.5			
						71.32								
						(2.09-2428.57)								
						1525.72								
						(10.10-230297.25)								
Stone size (mm)														
≤ 10	17	44.7	5	18.5	0.088	1	0.03	21	39.6	19	25.0	0.04		
11-20	11	28.9	11	40.7				24	45.3	15	37.5			
> 20	10	26.3	11	40.7				8	15.1	15	37.5			
						26.70								
						(1.37-518.36)								
						38.35								
						(2.35-624.07)								
History of urinary tract infection														
No	37	97.4	26	96.3	1.00			41	77.4	25	62.5	0.118		
Yes	1	2.6	1	3.7				12	22.6	15	37.5			
History of open surgery														
No	31	81.6	19	70.4	0.291			41	77.4	34	85.0	0.356		
Yes	7	18.4	8	29.6				12	22.6	6	15.0			
History of endoscopic surgery														
No	20	52.6	21	77.8	0.038			22	41.5	17	42.5	0.924		
Yes	18	47.4	6	22.2				31	58.5	23	57.5			
Pyelocalyceal angle (degrees)														
≤ 100	36	94.7	23	85.2	0.224			49	92.5	38	95.0	0.696		
> 100	2	5.3	4	14.8				4	7.5	2	5.0			
Hounsfield Units														
≤ 850	13	34.2	3	11.1		1	0.044	12	22.6	8	20.0	0.488		
851-1450	23	60.5	17	63.0				33	62.3	22	55.0			
> 1450	2	5.3	7	25.9				8	15.1	10	25.0			
						12.07								
						(1.06-136.57)								
						22.66								
						(1.16-442.20)								

*Chi-square test, **Logistic regression (Backward Wald), with significance at p ≤ 0.05. Empty boxes in the multivariate analysis mean non-significant results.

into consideration is a mistake. We suggest that our findings should be validated with other clinical studies in order to be able to generalize them.

New technologies should be evaluated in the context of cost-effectiveness and not according to personal preferences. The objective in any surgical procedure

should be the resolution of the problem at first attempt, and therefore it should be standardized as the outcome to be assessed in future studies.

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