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ORIGINAL INVESTIGATION

Is percutaneous nephrolithotomy effective and safe in elderly patients? Outcomes of a case-control study

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Background and aims. Percutaneous nephrolithotomy is the recommended treatment option for large or otherwise complex renal or proximal ureteral stones. Being a challenging procedure, its efficacy and safety in elderly patients is questioned. The present study aimed to determine the impact of age on percutaneous nephrolithotomy outcome, comparing patients < 70y with those ≥ 70y.
Methods. We analysed our prospectively maintained Internal Review Board approved database on percutaneous nephrolithotomy to compare demographics, perioperative outcomes and postoperative complications of patients < 70y with those of patients ≥ 70y.
Result. Among 638 patients treated between April 2005 and March 2018, 553 were < 70y and 85 were ≥ 70y. There was no difference between the two populations in all preoperative characteristics but American Society of Anaesthesiologists score, which was significantly worse in elderly patients. Operative outcomes were similar in the 2 populations but elderly patients had a greater complications rate (54.1 *vs* 42%; p = 0.005) and a higher rate (9.4 *vs* 4.2%; p = 0.0525) of infective complications. Indeed, multivariate analysis showed that age > 70y and positive stone culture were associated with a significantly higher rate of clinically-significant complications.
Conclusions. Percutaneous nephrolithotomy proved to be effective in consecutive/unselected elderly (≥ 70y) candidates to such procedure but at the price of a greater risk of, mainly minor, complications. The higher incidence of infective complications speaks for potentially reduced immune response of such patients and sets the rationale for further addressing this issue.

Key words: PCNL, Percutaneous nephrolithotomy, Elderly, Urolithiasis

INTRODUCTION

Percutaneous nephrolithotomy (PCNL) is the recommended treatment option for large or otherwise complex renal or proximal ureteral stones. The procedure involves creating a narrow percutaneous access to the kidney and the formation of a working tract connecting the flank surface with the intrarenal collecting system through which nephroscopy is performed. This allows endoscopic stone disintegration and removal of the stone fragments. Though effective, this procedure is considered challenging as serious and even lethal complications may occur. Most life-threatening situations are due to postoperative infection, systemic inflammatory response syndrome (SIRS) and sepsis [1 2].
Even if the age itself is not considered a contraindication to PCNL, decreased functional reserve, comorbid conditions [3] and the reduced efficiency of the immune

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system, also known as immunosenescence [4], may expose to a greater risk of complications, thereby influencing the surgeon's decision-making process. On the other hand, the incidence of nephrolithiasis in elderly people is growing; because of the high risk of urinary tract infection and renal dysfunction with untreated large kidney stones, a conservative approach may not always be wise [5 6].

To date, a few studies addressed the issue of PCNL efficacy and safety in the elderly. Moreover, quite different age cut-offs, ranging from 60 to 80 years, have been used to define elderly patients. The present study aimed to determine the impact of age on PCNL outcome, comparing patients < 70y with those ≥ 70y.

MATERIAL AND METHODS

Data of patients scheduled for PCNL at our Department were prospectively entered into our Internal Review Board approved dedicated database.

Preoperatively, all patients underwent abdominal computed tomography scanning and urine culture. Antibiotic prophylaxis was carried out according to current recommendations [7]. All procedures were carried out in our supine antero-lateral position or in the Galdakao-modified supine position [8-10]. Until the end of 2014, standard anesthesia was general whereas, from the beginning of 2015, it was spinal. Renal collecting system was punctured under fluoroscopic guidance using an 18G needle. The percutaneous tract was dilated to 17.5F (mini-PCNL) or to 26-30F (standard PCNL). Following stone/s fragmentation/extraction, flexible ureteroscopy and/or nephroscopy was carried out to check for stone clearance. Whenever possible, the procedure was closed placing a mono-J ureteral stent and a Foley catheter, thus were tubeless or Tachosil-sealed tubeless procedures [11 12]. Whenever deemed necessary, we used a double-J stent instead of the mono-J ureteral catheter or a nephrostomy tube [13]. All procedures were carried out by one of us (LC).

All patients underwent abdomen X-ray and renal ultrasound (US) at 1 month postoperatively to assess stone free rate (SFR). Abdominal CT was used as needed. Patients with residual fragments ≤ 4mm were considered stone-free [14]. Perioperative complications were assessed using the Clavien classification system adjusted for PCNL [2]. Infective complications were defined fever or SIRS lasting > 24h, and/or infection.

Statistical analysis

The Mann-Whitney U-test was used for continuous variables, whereas the Chi-square test was used for categorical variables. Univariate and multivariate analysis were used to test the impact of clinical factors on complications Clavien > 1. Data were analysed by Stata 14 (StataCorp LP, College Station, TX, USA). All tests were 2-sided with a significance level set at $p < 0.05$.

RESULTS

A total of 638 patients treated between April 2005 and March 2018 were eligible for the present study; of them, 553 (86.7%) were < 70y and 85 (13.3%) were ≥ 70y. Their descriptive characteristics are reported in Table I. There was no difference between the two populations in most baseline characteristics, specifically gender, body mass index (BMI), positive preoperative urine culture and stone size. However, as expected, elderly patients had a significantly greater ASA score due to their comorbidities. Specifically, elderly patients were more likely to have cardiovascular comorbidities, worsened renal function, and to be on anticoagulant and antiplatelet therapy. Elderly patients were more likely to have spinal anesthesia; otherwise, there was no difference in the operative characteristics of the two populations, including Amplatz sheath size, operative time, tubeless procedure and positive stone culture rates (Tab. I).

Table II reports outcomes in the two populations. There was no difference in median Hb loss, blood transfusion rate and SFR. Elderly patients had an overall greater complication rate (54.1 *vs* 42%, respectively; $p = 0.005$) and longer postoperative hospital stay. However, most complications were minor (Clavien 1) and there was a difference between the two populations for Clavien grade 3 complications due to the higher rate of infective complications (9.4 *vs* 4.2%, respectively) seen in elderly patients.

Finally, Table III reports univariate and multivariate analyses of factors predicting complications Clavien > 1. Univariate analysis showed that age > 70y, operative time, and positive stone culture rates were associated with a significantly higher risk of Clavien > 1 complications. At multivariate analysis however only age > 70y and positive stone culture confirmed to be significant predictors of Clavien > 1 complications.

DISCUSSION

The present study pointed out that elderly patients suffered more complications than their younger counterpart in spite of the two populations being similar for most preoperative, operative and also postoperative outcomes. Indeed, there was a significant difference in infective complications, which was likely due to the

Table I. Patients preoperative and operative characteristics.

	< 70 years n = 553	> 70 years n = 85	P-value
Age* (years)	52.0 (41.5, 59.8)	74.4 (72.0, 77.9)	< **0.0001**
Female gender, n (%)	300 (54.2%)	42 (49.4%)	0.4
BMI*	26.0 (24.0, 30.0)	26.1 (24.5, 29.0)	0.8
Positive preoperative urine culture, n (%)	56 (10.1%)	12 (13.6%)	0.3
Stone size* (mm)	23.0 (18.0, 30.0)	25.0 (18.0, 30.0)	0.8
Stone features, n (%) Single Multiple Stanghorn	 274 (49.5%) 179 (32.4%) 100 (18.1%)	 45 (52.9%) 26 (30.6%) 14 (16.5%)	0.8
ASA score, n (%) 1 2 3 4	 58 (10.5%) 448 (81.0%) 46 (8.3%) 1 (0.2%)	 5 (5.9%) 62 (72.9%) 18 (21.2%) 0 (0.0%)	0.002
General Anesthesia, n (%)	275 (49.7%)	33 (38.8%)	0.06
"Mini" Amplatz sheath, n (%)	275 (49.7%)	49 (57.6%)	0.27
Surgical time*, min	75.0 (60.0, 100.0)	75.0 (60.0, 100.0)	0.9
Tubeless, n (%)	424 (76.6%)	70 (82.4%)	0.2
Positive stone culture, n (%)	46 (13.0%)	11 (19.0%)	0.2

*Data expressed as medians (interquartile range).

Table II. Outcome data.

	< 70 years n = 553	> 70 years n = 85	P-value
Infective complications, n (%)	23 (4.2%)	8 (9.4%)	0.0525
HB loss* (g/dl)	1.00 (0.00-2.10)	0.90 (-0.10-2.00)	0.5
Blood Transfusion, n (%)	25 (5%)	6 (7%)	0.3
Clavien, n (%) 0 1 2 3 4 5	 321 (58.0%) 160 (28.9%) 37 (6.7%) 31 (5.6%) 4 (0.7%) 0 (0.0%)	 39 (45.9%) 25 (29.4%) 7 (8.2%) 11 (12.9%) 2 (2.4%) 1 (1.2%)	0.005
Post-operative hospital stay* (days),	3.0 (2.0, 4.0)	3.0 (2.0, 5.0)	0.015
Stone free, n (%)	392 (71.9%)	63 (75.0%)	0.6

*Data expressed as medians (interquartile range).

significant difference in the preoperative ASA score, a known indicator of patients comorbidities and consequent frailty.

Fulop et al. [15] reported that frailty in elderly people is an evolving concept defining a complex phenomenon that leads to dysregulation of several physiological systems, including the neuroendocrine, metabolic and immune inflammatory system. The latter determines how an organism is able to face different extrinsic and intrinsic challenges. Age-related changes of the immune system are defined as 'immunosenescence' and involve alterations in both the innate and adaptive immune systems that lead to a disequilibrium of the immune response resulting in low-grade efficacy [16 17]. As a consequence, elderly people are more susceptible to infections, cancers and autoimmune disorders. Though several attempts have been made to create algorithms and strategies that can assess frailty syndrome, an universally accepted definition still lacks.

The correlation between age and infective complications was further supported by multivariate analysis showing that age > 70y and positive stone culture were significant predictors of Clavien > 1 complications, including infective complications. Again, these findings

Table III. Univariate and multivariate analysis predicting Clavien > 1 complications.

	Univariate analysis		Multivariate analysis	
	O.R. (95% CI)	**P-value**	**O.R. (95% CI)**	**P-value**
Age > 70	2.19 (1.26 to 3.80)	0.005	2.46 (1.15 to 5.29)	0.020
Female gender	1.06 (0.68 to 1.64)	0.79		
BMI, per unit	0.98 (0.93 to 1.04)	0.56		
Positive preoperative urine culture	1.00 (0.46 to 2.21)	0.98		
Stone size, per unit	1.02 (1.00 to 1.04)	0.36	1.00 (0.97 to 1.03)	0.967
Stone features				
Single	ref.			
Multiple	1.33 (0.80 to 2.19)	0.27		
Stanghorn	1.72 (0.96 to 3.04)	0.065		
ASA score				
1	ref.			
2	0.83 (0.41 to 1.66)	0.594		
3	0.49 (0.17 to 1.41)	0.187		
Spinal Anesthesia	0.54 (0.35 to 0.86)	0.009	0.53 (0.13 to 2.25)	0.391
"Mini" Amplatz sheath	0.50 (0.32 to 0.79)	0.003	0.92 (0.22 to 3.88)	0.916
Surgical time, per unit	1.01 (1.00 to 1.01)	0.001	1.00 (0.99 to 1.01)	0.369
Tubeless	0.45 (0.28 to 0.72)	0.001	0.77 (0.37 to 1.63)	0.498
Positive stone culture	3.71 (1.96 to 7.03)	< **0.001**	3.67 (1.83 to 7.38)	< **0.001**

would provide further evidence for a less efficient immune system in our elderly population. Though such hypothesis could be supported by the elderly having greater ASA scores, no specific frailty or immunity assessment was made.

Our data are not that different from those reported in literature. Sahin et al. [18] compared data of 28 PCNL performed in patients > 60y with those of 178 procedures performed in patients ≤ 60y. Though elderly people had a significantly higher incidence of solitary kidney, outcomes in the 2 populations were reported to be similar. Elderly patients however had a greater rate (14 *vs* 10%) of fever without bacteremia.

Okeke et al. [19] analysed data of the PCNL Global Study conducted by the Clinical Research Office of the Endourological Society (CROES) to assess the impact of age on PCNL outcome. In this prospective observational study collecting data of 5803 patients treated at 96 centers worldwide between November 2007 and December 2009, elderly (≥ 70y) patients were found to have, in a matched analysis, a statistically significant higher rate of overall complications.

Morganstern et al. [20] retrospectively reviewed perioperative data of octogenarians who underwent PCNL at a high-volume stone center (36 renal units) and matched them to patients < 65 years of age by stone burden and sex (72 renal units). Though octogenarians had a higher mean ASA score, more comorbidities, and worse renal function, no difference in length of hospital stay or stone free rates were seen. Octogenarians did not experience more minor Clavien (1 e 2) or major Clavien (3a e 4b) complications. The authors concluded that, in spite of risk factors, PCNL can be safely and successfully performed in appropriately selected octogenarians without increased perioperative complications.

A strong point of our study was having included consecutive patients providing their cardiovascular status allowed to undergo PCNL. These are somehow different from the concept of "appropriately-selected" population and somehow explain the large number of patients we included. Case volume is a relevant factor in determining outcome in endourological procedures [21].

Limitations include being a retrospective analysis, but data were prospectively collected, and absence of a control group managed by observation or by retrograde intrarenal surgery (RIRS); however, the first would have been unethical in symptomatic patients, the latter would have probably exposed elderly patients to a higher risk of potentially serious infective complications [22].

To conclude, PCNL proved to be effective in consecutive/unselected elderly (≥ 70y) candidates to such procedure but, somehow expectedly, to be associated with a higher incidence of infective complications. These data suggest that great attention should be paid to such potentially serious complications, setting the rationale for well-designed prospective studies addressing this issue.

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Conflict of Interest

The authors declare no conflict of interest.

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