Predictive factors of bleeding and fever after percutaneous nephrolithotomy

Les facteurs prédictifs de la survenue de fièvre et des complications hémorragiques post néphrolithotomie percutanée

Mohamed Amri [1,2], *Sahbi Naouar* [1,3], *Badreddine Ben Khalifa* [1,3], *Nahla Hmidi* [4,1], *Braiek Salem* [4,2], *Rafik ElKamel* [4,2]

1- *Hôpital Ibn Aljazzar- Kairouan*
2- *Faculté de médecine de Monastir*
3- *Faculté de Médecine de Sousse*
4- *Hôpital Fattouma Bourguiba- Monastir*

RÉSUMÉ

Objectif: La NLPC est le traitement standard des lithiases rénales de gros volume (≥2 CM). Cependant, elle est pourvoyeuse de complications touchant environ un quart des patients. L'objectif principal était de déterminer les facteurs prédictifs de la survenue de fiévre et des complications hémorragiques post- NLPC.

Méthodes: Il s'agit d'une étude épidémiologique observationnelle analytique transversale à visée étiologique portant 170 cas de NLPC réalisées dans notre service d'urologie entre Janvier 2012 et Janvier 2016. On a réalisé une analyse univariée suivie d'une analyse multivariée afin de déterminer les facteurs prédictifs indépendants de la survenue de fiévre et des complications hémorragiques.

Résultats: L'âge moyen de nos patients a été de 49,41 ± 15,07 ans (14-83). Le taux de stone free était de 83,5%. On a enregistré 48 cas de complications postopératoires (28,2%): 34 cas de fièvre; 14 cas de complications hémorragiques. Après analyse univariée, le diabète était associé à la survenue des complications hémorragiques après NLPC (p=0,002). Le caractère coralliforme du calcul (p=0,0001), la position de décubitus ventral (p=0,009) , la durée opératoire (p=0,0001) et la présence de calculs résiduels ≥ 7mm (p=0,01) étaient associés à la survenue de fièvre postopératoire. Après analyse multivariée, le diabète était le seul facteur prédictif indépendant de la survenue des complications hémorragiques en postopératoire (OR=7,6). Les facteurs prédictifs indépendants de fièvre après NLPC étaient le caractère coralliforme du calcul (OR=5,9) , la position ventrale du malade (OR=3,7) et une durée opératoire > 95 minutes (OR=6,2).

Conclusion: A nos connaissances, notre série est la première qui rapporte une association statistiquement significative entre la position ventrale du malade et la survenue de fièvre post NLPC. Ceci doit être verifié ultérieurement par des séries à effectif plus important.

Mots-clés

Néphrolithotomie percutanée ,complications hémorragiques, fièvre, facteurs prédectifs.

SUMMARY

Aim: Percutaneous nephrolithotomy (PCNL) remains the standard procedure for large (≥2 cm) renal calculi; however, up to one quarter of PCNL patients experience some perioperative complications. The aim of the present study was to investigate the factors that may influence bleeding and fever following percutaneous nephrolithotomy.

Methods: In total, 170 patients, who underwent percutaneous nephrolithotomy between January 2012 and January 2016 in our Urology department, were retrospectively evaluated for postoperative bleeding and fever. Preoperative, operative and postoperative factors were assessed using univariate followed by multivariate regression.

Results: The mean patient age was 49.41 ± 15.07 years (14-83). The overall stone-free rate was 83.5%. We recorded 48 postoperative complications (28.2%): 34 cases of fever and 14 cases of bleeding. Univariate analyses showed an association between diabetes and postoperative bleeding (p=0.002). Staghorn calculus (p=0.0001), prone position (p=0.009), operative time (p=0.0001) and presence of residual stones ≥ 7 mm were associated to postoperative fever (p=0.01). Multivariate stepwise regression analyses showed that diabetes was the only independent predictive factor of postoperative bleeding (OR=7.6). Staghorn lithiasis (OR=5.9), prone position (OR=3.7) and operative time > 95 minutes (OR=6.2) were the predictive factors of postoperative fever.

Conclusions: To our knowledge, this study is the first to report that prone position was significantly associated with fever after percutaneous nephrolithotomy. Further studies are necessary to confirm our results in a greater number of patients.

Key-words

Percutaneous nephrolithotomy, Bleeding, Fever, Predictors.

INTRODUCTION

Currently, percutaneous nephrolithotomy (PCNL) is the treatment of choice of large (> 2 cm) or complex renal stones, extracorporeal shock wave lithotripsy (SWL) failure stones and cases accompanied by anatomical malformation, with stone-free rates exceeding 90% (1). However, up to one quarter of PCNL patients experience some perioperative complications including bleeding, acute collecting system injuries, adjacent structure injuries, infectious complications and prolonged urine (2). Determining which patients are at greatest risk is extremely important to reduce the occurrence of these complications.

In this study, our objective was to investigate the factors that may influence postoperative bleeding and fever following PCNL, focusing on the experience of a single surgeon.

METHODS

Study population

In a cross-sectional study, between January 2012 and January 2016, the data of 170 patients who underwent procedures performed by the same surgeon were assessed to exclude the possible bias of surgical experience. Patients with incomplete records were excluded from the study.

Preoperative data were obtained retrospectively, including pre-existing comorbidities with Charlson Comorbidity Index (CCI) score (3), history of previous SWL or stone surgery (PCNL or open), preoperative white blood count (WBC), serum creatinine and urine culture, the stone location, size (stone burden and surface) and density, the complexity of stone and the presence of hydronephrosis. Intraoperative data, including the PCNL position (prone or supine), operative time and the use of nephrostomy tube were entered in the database. Postoperative data included early postoperative complications, need for blood transfusion, hospital stay and stone-free rate at 1 month follow-up.

Definition of variables

The size of stone was determined by using its largest and smallest diameter on coronal reconstruction of computed tomography (CT). In order to calculate the surface area (SA) of calculi, the following equation formulated by Tiselius (4) was used, where *L* is length (the largest diameter) and *w* corresponds to width (the smallest diameter): SA = Lwт0.25.

In order to carry out the statistical analysis, stones were classified into “simple “ and complex ones. Kidney stones localized either in calyx or in pelvis were called as simple stones; stones filling one or more calices in addition to pelvis and staghorn stones were termed as complex stones.

Postoperative radiological evaluation was based on KUB radiography or ultrasonography depending on the radiopacity of the stone. We defined success as completely stone-free status or clinically insignificant residual fragments (< 4 mm).

Postoperative hemorrhage was defined as a persistent immediate or delayed gross haematuria needing blood transfusion and/or radiologic selective angioembolization. Fever was defined as a temperature ≥ 38.5°C documented during, at least, 48 hours postoperatively.

Statistical analysis

All statistical analyses were performed using the statistical package SPSS (IBM Corp. Released 2011. IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY: IBM Corp.). Categorical variables, expressed as the numbers or percentages, were compared using the Chi-square or Fisher’s exact test. Continuous variables, shown as the mean ± standard deviation (SD), were analyzed using Student’s *t* test or Mann–Whitney *U* test. Comparative differences were considered statistically significant when $p < 0.05$.

A multivariate analysis was performed using logistic regression to establish the predictive factors for the development of complications. An univariate analysis was previously conducted, where the relations between the dependent variables (occurrence of complications) and each of the independent variables were analyzed, in order to include in the model those variables which a priori could be highly predictive ones. The cut-off values of quantitative variables was determined using the receiver operating characteristic (ROC) curves; the area under the ROC curve (AUC) values of 0.7 or higher were considered significant.

RESULTS

The patient, stone, operative and postoperative characteristics of the 170 cases included in this series, are

detailed in Table 1. The mean age was 49.4 ± 15.07 (range: 14-83) and 30 patients (17.6%) were 65 years old or older. CCI score was calculated as < 2 for 125 patients (73.5%) and as ≥ 2 for 45 patients (26.5%). A history of ipsilateral open surgery and SWL was present in 26 (15.3%) and 20 (11.3%) patients, respectively. Mean stone size was 545.9 ± 337.9 mm2 (range 106-2967). Stones were complex in 66% (n=112) of the patients and staghorn stone was detected in 41% (n=70).

Table 1. Patient, stone, operative and postoperative characteristics.

Characteristic	
Age (yr)	49.4 ± 15.07
Gender, n (%)	
Male	109 (64.1)
Female	61 (35.9)
CCI score, n (%)	
< 2	125 (73.5)
≥ 2	45 (26.5)
Previous treatment lithiasis, n (%)	
ESWL	26 (15.3)
Open surgery	20 (11.8)
Preoperative Creatinine serum (umol/ml)	82.9 ± 33.2 (30-375)
Preoperative blood white (elements 10^3/ml)	7.71 ± 2.51 (0.96-18.6)
Preoperative positive urine culture, n (%)	12 (7)
Kidney location, n (%)	
Right	76 (44.7)
Left	92 (54.3)
Bilateral	2 (1)
Location, n (%)	
Single calyx	11 (6.4)
Renal pelvis	47 (27.6)
Pelvis + 1 calyx	94 (55.2)
Pelvis + 2 calices	8 (4.7)
Pelvis + 3 calices	10 (5.8)
Size	
Burden (mm)	31.8 ± 10.3 (13-70)
Surface (mm^2)	545.9 ± 337.9 (106-2967)
Complexity, n (%)	
Simple	58 (34)
Complex	112 (66)
Stone density (HU)	837.4 ± 276.5 (299-1502)
Presence of hydronephrosis, n (%)	63 (37)
PCNL position, n (%)	
Prone	33 (19.4)
Supine	137 (80.6)
Mean operative time (min)	92.9 ± 30.4 (40-180)
Postoperative complications	48 (28.2)
Bleeding	14 (8.2)
Fever	34 (20)

CCI: Charlson Comorbidity Index; PCNL: Percutaneous Nephrolithotomy; HU: Hounsfield Unit.

Prone position was favored by the surgeon at the beginning of his experience. Then, the majority of PCNL procedures were performed in supine position (n=137, 80.6%). Percutaneous nephrostomy tract was created using metal telescopic dilators (Alken) which fit tightly to the 30Fr Amplatz sheath, in all the cases; balloon dilators were not available in our institution. A total of 164 (96.5%) patients were treated with single-access PCNLs, and the remaining patients (3.5%) underwent multiple-access procedures. The mean operative time was 92.94 ± 30.47 min (range 40-180 min). Six patients (5.7%) underwent tubeless and stentless PCNL. An overall success rate of 83.5% (n=142) was achieved after one session PCNL.

Postoperative complications occurred in 48 procedures (28.2%). Postoperative bleeding occurred in 14 cases (8.2%), among them 2 cases (1.2%) required radiologic selective embolization for arteriovenous fistula and pseudoaneurysm. Postoperative fever occurred in 28 cases (16.4%). Only 4 patients had postoperative bleeding and fever at the same time.

In univariate analysis, the factor that affected postoperative bleeding was diabetes (p=0.0001) (Table 2). Postoperative fever was affected by staghorn stone (p=0.0001), prone position (p=0.009), operative time (p=0.0001) and the presence of residual stones ≥ 7 mm (p=0.01) (Table 3). In the ROC curve, the best cutoff point of operative time was 95 minutes with sensitivity of 79 % and specificity of 64% (area under the curve [AUC]=0.75, p=0.02, CI 95% [0.65-0.84]).

According to stepwise multivariate binary regression analysis, diabetes was the only independent predictive factor of postoperative bleeding (OR=7.6, p=0.001, CI 95% [2.3-25.06]). Staghorn lithiasis (OR=5.9, p=0.0001, CI 95% [2.3-15.3]), prone position PCNL (OR=3.7, p=0.02, CI 95% [1.1-9.3]) and operative time ≥ 95 min (OR=6.2, p=0.0001, CI 95% [2.3-16.2]) were the independent predictive factors of fever after PCNL.

DISCUSSION

In this study, 48 cases of postoperative PCNL complication were recorded, including 34 cases of fever and 14 cases of bleeding. Multivariate analyses showed that diabetes was the only independent predictive factor of postoperative bleeding (OR=7.6). Staghorn lithiasis (OR=5.9), prone position (OR=3.7) and operative time > 95 minutes (OR=6.2) were the predictive factors of postoperative fever. Although PCNL is recognized as a safe technique to

Table 2. Univariate and multivariate determinants for bleeding after PCNL.

	Univariate analysis			Multivariate analysis		
	Bleeding (n=14)	**No bleeding** (n=156)	***P* value**	***P* value**	**OR**	**CI 95%**
Age (yr)	54.2±10.9	48.9±15.3	0.3			
Gender, n (%)						
Male	6 (5.5)	103 (94.5)	0.08			
Female	8 (13)	53 (87)				
Diabetes mellitus, n (%)	6 (30)	14 (70)	**0.002**	**0.001**	**7.6**	**2.3-25.06**
Hypertension, n (%)	3 (9.7)	28 (90.3)	0.7			
CCI score						
< 2	8 (6.4)	117 (93.6)	0.2			
≥ 2	6 (13.3)	39 (86.7)				
Previous open surgery, n (%)	1 (5)	19 (95)	1.0			
Previous SWL, n (%)	2 (7.7)	24 (92.3)	1.0			
Creatinine serum (umol/l)	68.8±15.6	84.1±34.1	0.17			
Stone laterality, n(%)						
Right	5 (6.5)	71 (93.5)	0.45			
Left	9 (9.8)	83 (90.2)				
Stone complexity, n (%)						
Simple	5 (8.8)	52 (91.2)	1.00			
Complex	9 (8)	104 (92)				
Staghorn stone, n (%)	8 (11.4)	62 (88.6)	0.2			
Stone size						
Stone burden (mm)	35.1±11.9	31.5±10.2	0.81			
Stone surface (mm^2)	639.2±344.8	537.6±337.1	0.78			
Stone density (HU), n (%)						
< 1000	6 (42.8)	110 (70.6)	0.07			
≥ 1000	8 (57.2)	46 (29.4)				
Presence of hydronephrosis, n(%)	5 (7.4)	63 (92.6)	0.73			
PCNL position, n (%)						
Prone	4 (12)	29 (88)	0.47			
Supine	10 (7.3)	127 (92.7)				
Mean operative time (min)	107.1±40.4	91.6±29.2	0.9			

CCI: Charlson Comorbidity Index; SWL: Shock Wave Lithotripsy; PCNL: Percutaneous Nephrolithotomy; HU: Hounsfield Unit; OR: Odds Ratio; CI: Confidence Interval

treat renal stones, especially large and multiple calculi, it can still results in some specific complications. Total complication rates after PCNL vary widely, with reported rates of between 10.9% and 83% (5-7). Major or significant complications are, however, generally rare. The Clinical Research Office of the Endourological Society (CROES) collected prospective data for 5803 consecutive patients who were treated with PCNL at centres around the world for 1 year; the overall perioperative complication rate was 20.5%, with 11.1% of them being of grade I, 5.3% of grade II, 3.6% of grade III, 0.5% of grade IV and 0.03% of them being of grade V (6).

The incidence of bleeding during or after PCNL has been reported to vary between 1% and 23% in the literature (8-11). Although most bleeding can be managed conservatively, 0.3% to 1.4% of patients require intervention such as angioembolization to control severe bleeding (11). The incidence of blood transfusion after percutaneous procedures has been 2% to 45% among different series(8). In our series, postoperative bleeding occurred in 14 cases (8.2%), among them 2 cases (1.2%) required radiologic selective embolization for arteriovenous fistula and pseudoaneurysm.

Predictive factors of bleeding after PCNL are still

Table 3. Univariate and multivariate determinants for fever after PCNL.

	Univariate analysis			Multivariate analysis		
	Fever (n=34)	**No fever** (n=136)	***P* value**	***P* value**	**OR**	**CI 95%**
Age (yr)	49.5±15.8	49.3±14.9	0.9			
Gender, n (%)						
Male	20 (18.3)	89 (81.7)	0.47			
Female	14 (23)	47 (77)				
Diabetes mellitus, n (%)	3 (15)	17 (85)				
CCI score						
< 2	24 (19.2)	101 (80.8)	0.66			
≥ 2	10 (22.2)	35 (77.8)				
Creatinine serum (umol/l)	91.8±58.4	80.7±22.9	0.08			
WBC (x10^6/mm3)	78.4±27.5	76.8±24.56	0.33			
Preoperative positive culture, n (%)	4 (33.3)	8 (66.7)	0.26			
Stone laterality, n(%)						
Right	16 (21)	60 (79)	0.81			
Left	18 (19.5)	60 (79)				
Stone complexity, n (%)						
Simple	10 (17.5)	47 (82.5)	0.5			
Complex	24 (21.2)	89 (78.8)				
Staghorn stone, n (%)	23 (32.8)	47 (67.2)	**0.0001**	**0.0001**	**5.9**	2.3 -15.3
Stone size						
Stone burden (mm)	30.9±10	32.02±10.4				
Stone surface (mm^2)	532.3±268	549.3±354				
Stone density, n (%)						
< 1000	22 (64.7)	108 (79.4)	0.44			
≥ 1000	12 (35.3)	28 (20.6)				
Presence of hydronephrosis, n (%)	16 (21.6)	58 (78.4)	0.87			
PCNL position, n (%)						
Prone	12 (36.4)	21 (63.6)	**0.009**	**0.02**	**3.7**	1.1-9.3
Supine	22 (16)	115 (84)				
Operative time (min)						
< 95	7 (7.5)	86 (92.5)	**0.0001**			
≥ 95	27 (35)	50 (65)		**0.0001**	**6.2**	2.3-16.2
Residual stones ≥ 7 mm, n (%)	20 (29.4)	48 (70.6)	**0.01**			

CCI: Charlson Comorbidity Index; PCNL: Percutaneous nephrolithotomy; OR: Odds Ratio; CI: Confidence Interval

controversial because of the lack of homogeneity among studies and consensus on classifying complications. The correlation between diabetes and complications after PCNL remains uncertain. Numerous studies have shown diabetes as a risk factor of hemorrhagic complications after PCNL (8,12-14). Diabetes was the only independent predictive factor for bleeding after PCNL in our study. The relationship between diabetes and bleeding after the initial trauma of tract formation was explained with arteriosclerosis (13). In addition, diabetes affects the whole vascular system, resulting in microangiopathies, which are highly vulnerable to bleeding (14). Additional clinical factors, shown to increase the risk of bleeding during or after PCNL, include previous open renal surgery and previous unsuccessful SWL treatment (15,16). However, the reverse have been reported by other studies (17,18). The development of severe damage at the microvascular level and the interstitium in nephrons after SWL has been incriminated in bleeding after PCNL in this group (15). Solitary kidney was also defined as a significant risk factor of hemorrhage during or after PCNL because of compensatory renal hypertrophy;

puncture and dilation through thick renal parenchyma may increase the possibility of bleeding damage to more renal tissue and its vascular supply (9,19). The influence of stone size, hydronephrosis and parenchyma thickness on postoperative bleeding is still controversial (9,11-13). However, the influence of stone complexity has been well-documented in the literature (6,8-10,14). The number of punctures has also been incriminated in vascular injuries in many series (5,7-9,13). Sheath size has been shown as a predictive factor of bleeding, while method of tract nephrostomy dilation remains controversial (5,8). Nalbant et al.(20) showed no difference between dilation methods (Alken, Amplatz and balloon dilators) in term of bleeding in a series of 487 PCNLs. It is well-recognized that perforation of the pelvicaliceal system during dilation or stone disintegration and forceful manipulation of the rigid nephroscope to access stones in different calices may damage adjacent blood vessels (9,10,13). The influence of operative time on bleeding has been demonstrated by several studies (10,12).

Patients undergoing PCNL face a high risk of developing fever, systemic inflammatory response syndrome and to a lesser degree bacteremia and urosepsis. Indeed, 4 out of 1000 patients will die following PCNL (21). Previous studies have reported that, despite careful preoperative preparation, post-PCNL fever and SRIS occur in 21-39.8% (1) and 11%-35% of patients (22), respectively, with progression to sepsis in 2.5% of patients (22).

Previous studies reported that, the key risk factors for SIRS following PCNL were: stone size (1,23-26), stone culture (25,27), pelvic urine culture (25,27), while bladder urine culture has been found to correlate poorly with infection (25). Other factors including stone complexity (22-26), hydronephrosis (27), paraplegia, neurogenic bladder (22,23), the preoperative urine WBC count (24) and the number of punctures have been shown to be significant predictive factors of infectious complications after PCNL (22,26). The influence of diabetes remains controversial. Gutierrez et al. (1) showed, in a large series of 5803 procedures, that diabetes was significantly associated to post PCNL-fever (OR=1.23; p=0.02); however, other authors have demonstrated the reverse (23,24). Concerning patient position, it has been suggested that PCNL in supine position reduce postoperative fever and sepsis by the theoretical decrease in pyelovenous back flow resulting from the improved drainage of irrigation fluid around the nephroscope in the supine position. However, no statistically significant difference in the rates of postoperative pyrexia or sepsis has been found in the prone and supine positions (28). To our knowledge, this study is the first to report prone position as a significant independent factor of postoperative fever with an OR of 3.7. The influence of prolonged operative duration has been demonstrated as a significant risk factor of infectious complications following PCNL (26). In this study, operative time > 95 min was significantly associated to post-PCNL fever (sensibility=79%, specificity=64%). Recently, new risk factors for SRIS and fever following PCNL have been reported, which are preoperative neutrophile-lymphocyte count ratio ≥ 2.5 (29) and high intraoperative irrigation pressures (22,30). It has been demonstrated that systemic fluid absorption during PCNL can occur due to increased intrapelvic pressure leading to pyelovenous-lymphatic backflow, pyelotubular backflow, and forniceal rupture. SRIS and fever may be attributed to absorption of irrigation fluid containing endotoxin released during manipulation of infection calculi (30).

Limitations of our study: it is a retrospective study from single institute, which might lead to selection bias. Some parameters were not studied such as stone culture and renal pelvis urine culture because they were not routinely analysed.

CONCLUSIONS

In the present study, several factors appear to affect postoperative bleeding and fever after PCNL. It is also the first to report that prone position was significantly associated with post-PCNL fever. Further studies are necessary to confirm our results in a greater number of patients.

Abbreviations

PCNL = percutaneous nephrolithotomy ; SWL = extracorporeal shock wave lithotripsy; CCI = Charlson Comorbidity Index ; WBC = white blood count; CT = computed tomography; HU = Hounsfield Unit; KUB = Kidney, ureter, bladder; SA = surface area ; SIRS = Systemic inflammatory response syndrome; SD = standard deviation; ROC = receiver operating characteristic; AUC = area under curve; OR = odds ratio; CROES = Clinical Research Office of the Endourological Society.

Ethics approval and consent to participate

This study was performed in accordance with the ethical standards of the Declaration of Helsinki. Pursuant to the provisions of the ethic guideline in Tunisia, written consent was not required in exchange for public disclosure of study information in the case of retrospective study.

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competent interests

The authors declare that they have no competing interests.

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