Running title: overnight vs standard PCNL – Basiri et al

An Overnight Stay Versus three Days Admission after uncomplicated Percutaneous Nephrolithotomy: A Randomized Clinical Trial

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Abstract

Purpose: To evaluate the safety and efficacy of discharging patients on the first postoperative day after an uncomplicated percutaneous nephrolithotomy (PCNL).

Materials and methods: after an uncomplicated successful PCNL without significant residual stone (>5mm) or any complication up to the first postoperative day, we randomly assigned patients into two groups—Group 1: overnight surgery, and Group 2: routine discharge after three days. Patients with significant residual stone on control fluoroscopy were excluded. Ninety eight and 102 patients were assigned to groups 1 and 2, respectively. Serum Hemoglobin and Cr were evaluated before the operation as well as the first postoperative day. Stone free status was evaluated using ultrasound and KUB radiography at the first postoperative day.

Results: The stone and patient characteristics were not different in two groups. The preoperative and change in the hemoglobin and creatinine levels were not significantly different between the two groups. Nine patients (9.2%) in Group 1 and five (4.9%) in Group 2 were readmitted because of complications (mainly hematuria) (p=.23). Of the readmitted patients, five in Group 1 (55%), and three in Group 2 (60%) received blood transfusion (p=.87). in these patients, group 1 received 1.6±0.51 units of blood compared with 1.93±0.25 in group 2 (p=.07). All the readmitted patients did well with conservative therapy with no need for angioembolization.

Conclusion: In uncomplicated PCNL with no significant residual stone, discharging the patient on the first postoperative day is safe. The outcome is comparable to a routine three-day hospital stay.

Trial registration: IRCT20171228038115N1**.**

INTRODUCTION

Percutaneous nephrolithotomy (PCNL) is the gold standard for surgical management of large renal stones. Since its popularization as an effective and safe modality, several modifications have been made to the original procedure[1,2] including patient positioning , choice of anesthesia [3] [4], modality for access guide [5] or tract dilation method [6]. Compared to open procedures, PCNL is associated with lower morbidity, lower post operation pain, smaller scars, shorter hospital stay, lower transfusion rate, shorter convalescence, and lower cost [7]. PCNL has become a common method and the first line of intervention for patients with a significant stone burden, because of continued improvement in safety, stone-free rate and length of hospitalization (LOH) [8,9]. The hospital stay after PCNL is much shorter than open kidney surgery; however, it has typically remained 2-5 days. A shorter hospital stay may decrease cost of PCNL, increase patients' comfort and decrease nosocomial complications. Some authors have addressed this issue by advocating tubeless outpatient PCNL in highly selected patients [10-12]. In the other hand, with recent advances in the field of retrograde intrarenal surgery (RIRS), patients are treated as outpatient or with a short hospital stay. Therefore, with reducing hospital stay in selected uncomplicated patients, PCNL may remain more economical compared with RIRS while showing superior stone free rate with a single procedure.[13,14]

This is the first randomized clinical trial that compares the safety of overnight stay with three days admission in patients undergoing uncomplicated PCNL.

MATERIALS AND METHODS

Study population

In a 6-month period from June to December 2015, 210 patients who underwent uncomplicated PCNL were included in the study according to the selection criteria (Table 1). Urinalysis and

culture, CBC and serum creatinine were conducted for all the patients. Using simple randomization method, the patients were categorized into two groups—Group 1: overnight stay after surgery, and Group 2: routine discharge after three days admission. The surgeon who visited the patients at first postoperative day, allocated patients randomly in two groups. The primary outcome was the re-admission rate. The decision about the readmission was done by another surgeon who was blind regarding the study group.

PCNL procedure

We administrated prophylactic antibiotics (first generation cephalosporin) to all the patients. In patients receiving general or spinal anesthesia, 5-French Ureteral Stent was placed on the affected side through cystoscopy. Then in prone or supine position, pyelocaliceal system and stones were determined by contrast and fluoroscopy or ultrasonography, and a Chiba needle was passed into the selected calyces of the kidney. A guidewire was passed through the needle into the pelvis over the guidewire. The dilatators and then working element (26-30F) were placed, and by using normal saline solution as irrigating solution, 24 French nephroscope was passed inside Amplatz sheaths and the stone(s) were crushed by pneumatic lithotripsy and removed with grasping forceps. Finally, a nephrostomy tube was fixed in the kidney. The size of the nephrostomy tube was 20-24F depending on the presence of bleeding during the procedure, extent of manipulation, and surgeon's preference. If a considerable amount of the stone residue (>5mm) was observed on control fluoroscopy at the end of the procedure, the patient was excluded from the study.

Post-operative care

Kidney, ureters and bladder x-ray (KUB), renal ultrasonography, hemoglobin (Hb) and creatinine (Cr), sodium and potassium were checked in all the patients on the first postoperative

day. If there was no significant residual stone and laboratory data were in normal range, and there was no fever and chill or underlying diseases such as cardiovascular disease, the patients were classified into two groups based on simple randomization method. Patients with considerable complications during or early after the surgery were excluded from the study. The patients in Group 1 were discharged after removing the Foley catheter, the ureteral stent, and the nephrostomy tube. In Group 2, the nephrostomy tube was removed on the second postoperative day. The patient was discharged on the third postoperative day after removing the Foley and the ureteral stent if no urine leakage was observed from nephrostomy site and there was no fever.

Follow-up

Before discharge, the patients were informed about symptoms such as hematuria, and the probability of having LUTS, fever and chills. They were told to refer to the emergency department in case of fever, chills, vomiting or worsening back pain. The patients were followed-up with sonography, KUB and laboratory tests one week post-operation. The patients with hematuria were readmitted and received IV fluid, and their vital signs were assessed routinely. All the patients had a complete blood count, and electrolytes and serum creatinine levels and coagulation parameters were assessed. Parenteral antibiotics were administered. If the bleeding from the nephrostomy site continued or there occurred gross hematuria with acute urine retention, then a blood transfusion plus fluid resuscitation and Foley catheterization with urinary bladder irrigation were administered.

Statistical methods

It was of interest to establish non-inferiority of discharging patients on the first postoperative day after an uncomplicated PCNL (overnight group) as compared to the patients with routine

discharge after three days regarding its complications. The primary outcome was the rate of readmission and secondary outcome was the rate of complications like sepsis and sever pain or bleeding. Considering a difference of less than 5% is of no clinical importance in calculating the sample size. Thus, the non-inferiority margin was selected to be δ=-.05. The mean complications rates of the intervention and the control groups were θ1=1% and θ2=0%, respectively. Then, by the formula: $n1 = n2 = \frac{[r\theta1(1-\theta1)+\theta2(1-\theta2)](Z\alpha+Z\beta)^2}{(\theta1-\theta2-\delta)^2}$, the required sample size with equal allocation (r=1) to achieve an 80% power (β=.2) at α=.05 was determined by n1 = n2 = 98. Adding seven participants to each group for probable loss to follow up and other reasons, 105 participants were set in each group as the sample size[15].

Descriptive statistics including means (±SDs) were calculated for the numerical variables and count and percentage were reported for the categorical or nominal ones. The Student's t-test was used for continuous variables to compare the means of both groups .The chi-squared test was used for comparing the categorical variables. The differences were considered statistically significant for P < .05. The data were analyzed using SPSS-15 software.

RESULTS

Out of a total of 300 patients who underwent PCNL, 90 patients were excluded because of not meeting the inclusion criteria, incomplete information, consent refusal or other reasons. Finally, 200 patients (98 cases in Group 1 and 102 cases in Group 2) remained in the study, and were analyzed. The CONSORT flow diagram is depicted in Figure 1.

The patients' demographic characteristics as well as preoperative and postoperative data are presented in Table 2. There were no significant differences in the patients' characteristics before and during surgery between the two groups (Table2). Only one patient in each group

needed two accesses for PCNL, and the rest underwent single-access PCNL. In the first group, patients were discharged after 14 to 20 hours.

Nine patients in Group 1 (9.1%) and five patients in Group 2 (4.9%) were re-hospitalized due to gross hematuria during the first week after surgery (P=.23). of these patients, five patients in Group 1 (55%) and three patients in Group 2 (60%) required blood transfusion after surgery (p=.87). Bleeding resolved with conservative treatment in all and no patient needed further evaluation and radiologic intervention for the treatment of bleeding. All of them were discharged after three to five days. Patients in group 2 received more blood units during admission (table 3).

The postoperative results, in terms of stone-free rate and complications, were not statistically different between the two groups.

DISCUSSION

The cost effectiveness of PCNL correlates with stone-free rate, length of hospitalization (LOH), and major complications[9]. Reducing the LOH is a key strategy to improve the cost effectiveness of PCNL[10]. The hospital stay in uncomplicated PCNL has been three days routinely. During this period, no particular healthcare is provided for these patients except removing the nephrostomy and the ureteral and urethral stents in the consecutive days. Further, based on the AUA recommendation there is no place for routine intravenous antibiotics after uncomplicated PCNL. Meanwhile, previous studies have revealed that most of the fevers after PCNL are not related to bacteremia.[16] On the other hand, we routinely do not observe severe complications during this period. The most common complications is early urine leakage and hemorrhage during and after removal of the tubes, which can be determined and managed at the same time. Nonetheless, delayed postoperative bleeding dose not have a specific time of

occurrence and we showed that 3-day hospital stay dose not reduce its risk. All these data is against routine three days admission in an uncomplicated successful PCNL. In recent years, the idea of performing PCNL as an outpatient procedure or as an overnight PCNL is considered due to the reduced hospital stay, thereby saving of attendant healthcare cost and minimizing potential nosocomial infections as well. Few case series described good outcomes with outpatient and overnight PCNL in carefully selected patients [10,17-19]. Ambulatory tubeless PCNL was first reported by Singh et al in 2005. They reported "ambulatory" PCNL in 10 patients with spinal anesthesia. The patients were kept overnight and had a mean hospital stay of 40 h. The nephrostomy tract was fulgurated with diathermy in their series[20] . The first case report of the outpatient PCNL was from Canada. They reported a patient with lower pole 11 mm stone who successfully treated with tubeless PCNL as an outpatient. She was discharged home 4 hours after leaving the operating room [18]. Shahrour and Andonian reported the median hospital stay was 1 day [21] .in their study median stone size was 2 cm. Overnight hospital stay after PCNL was reported as 1.7 days in a study by Fahad Alyami et al.[10]. The latest study by Ahmed Fahmy et al. described outpatient PCNL and the mean time to discharge home was 8.97 h. They concluded that outpatient PCNL presented several advantages, including more rapid period of recovery of the patient, minimized nosocomial infection with no additional morbidity to the patient and without compromising of the stone-free rate, and also decline in healthcare cost [19]. Another series of ambulatory PCNL on 10 patients studied by Shahrour and Andonian reported that all the patients were discharged with ureteral stent, which were removed by using flexible cystoscopy one week later[21]. Although long-term nephrostomy tube improves urinary drainage and prevents urinary extravasation as well as tract tamponade, reduces bleeding, and may facilitate a second look re-intervention as mentioned in all studies, the stone clearance rate is equal to that of conventional PCNL. Moreover, the complication rate is similar and tubeless

PCNL or early removal of the Foley catheters, nephrostomy tube, and ureteral stent make the patients feel more comfortable [22-24].

Tubeless PCNL, often with postoperative ureteral stent drainage in highly selected patients, has been shown to be a safe modification to limit the need for a long hospital stay [11,12,17]. In a report on tubeless PCNL by Bell man et al., the median hospital stay was .6 day or 14.4 hours. However, a double-J stent was placed at the end of the procedure for all the patients, and they were discharged home with an indwelling Foley catheter [18]. We inserted the nephrostomy tube in all cases. Our data shows that the rate of re-admission due to bleeding was 9% in the group one compared with 4% in the group two. Although this difference is not significant, may be due to early removal of the nephrostomy tube.

This is the first published study to access the feasibility of overnight surgery after a conventional PCNL in a randomized clinical trial**.** We evaluated the safety and outcome of overnight PCNL in selected uncomplicated patients with the placement of ureteral stent and nephrostomy tube during the operation. Our patients in the overnight group were discharged without the nephrostomy tube, Foley catheter or JJ stent. The groups were not different in sex, age, site of operation, and stone size. There were no significant differences in residual stone, hemoglobin drop and creatinine rise, transfusion rate during and after surgery, and readmission rate between the two groups. Our findings showed efficacy and safety of overnight PCNL in select patients. Nevertheless, the limitation of the present study is that the choice of the anesthesia and positioning of the patient as well as the guide for access was not constant during the study; however, these factors were distributed randomly in two groups (Table 2) and most of the patients were done in the prone position under spinal anesthesia. Nevertheless, in a bigger sample size we could perform subgroup analysis to find out whether overnight PCNL is beneficial for which patient exactly. Unfortunately, we did not evaluate the exact cost for each

individual separately in the current study. Nevertheless, we think with reducing hospital stay without increasing the complications, the cost will decrease significantly.

CONCLUSIONS

In highly selected, uncomplicated PCNL, to limit the need for hospital stay, early discharge of patients seems to be safe and do not contribute to a higher rate of complication and re-hospitalization compared with three days postoperative admission. This needs to be confirmed by studies with bigger sample size.

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CONFLICT OF INTEREST

The authors confirm there is no any conflict of interest.

ETHICAL APPROVAL

All procedures were performed in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

INFORMED CONSENT

Informed consent was obtained from all the individual participants included in the study.

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Table 1. Selection criteria.

Stones larger than 2 cm in the kidney or proximal ureter
Stones less than 2 cm with failed SWL
Acceptable anesthesia risk (ASA class< 3)
Normal coagulation status
Two functional kidneys without renal insufficiency
No active infection
≤ 2 access sites
Insignificant residual stone (<5mm)
No intra or postoperative complications
Less than or equal one unit blood transfusion during operation
Less than three unit hemoglobin decrease in the next morning
Hemoglobin more than 10mg/dl after surgery
Informed consent
No postoperative complications including fever, urinary leakage, demise, UTI and urosepsis, pneumothorax and hemothorax, colonic and GI perforation.
Normal postoperative chest X-ray (CXR)
No fever, gross hematuria or severe pain at the time of discharge

Table 2. Pre, Intra, and postoperative characteristics of the patients in two groups.

Parameters	Group1 (overnight)		Group2 (admitted three days)		P-value
	N=98		N=102		
Sex					
Male	71.4	(70)	66.7	(68)	
Female	28.6	(28)	33.3	(34)	0.46
Age (years)	44.9 ±12.8		45.97±13.49		0.57
Laterlity					
LT kidney	53.1	(52)	52	(53)	
RT kidney	46.9	(46)	48	(49)	0.87
Stone size (cm)	3.62 ±2.03		3.68±2.12		0.84
Stone size					
<1 cm	8.1	(8)	5.8	(6)	
>1 cm	91.8	(90)	96	(96)	0.53
Anesthesia type					
Spinal	92.8	(91)	90.1	(92)	
General	7.1	(7)	9.8	(10)	0.76
Guide for access					
Fluoroscopy	84.6	(83)	75.4	(77)	
Ultrasonography	15.3	(15)	24.3	(25)	0.17

Position					
Prone	100	(98)	98	(100)	
Supine	_	_	1.9	(2)	0.49
Preoperative Hb	13.85±1.53		13.84±1.62		0.94
Postoperative Hb	11.8±1.62		11.66±2		0.59
Hb drop	2.09±1.17		2.18±1.63		0.69
Preoperative Cr	1.38+_1.71		1.13+_0.31		0.16
Postoperative Cr	0.99+_0.24		1.05+_0.3		0.1
Cr rise	-0.41		-0.08		0.72
Stone free rate	71.4	(70)	70.5	(72)	0.74

Data are presented as mean (±SD) or % (n)

Table 3: Readmission and transfusion rate between two groups

Group	1 (overnight)	2 (admitted three days)	p value
Readmission	9/98 (9.2%)	5/102 (4.9%)	.23
Discharged without transfusion	4/9 (45%)	2/5 (40%)	.87
Blood transfusion	5/9 (55%)	3/5 (60%)	.87
Transfused blood units (mean±SD)	1.6±0.51	1.93±0.25	.07
Readmission duration (mean±SD)	3.8±0.9	4.0±1.0	.84
Angioembolization	0	0	-

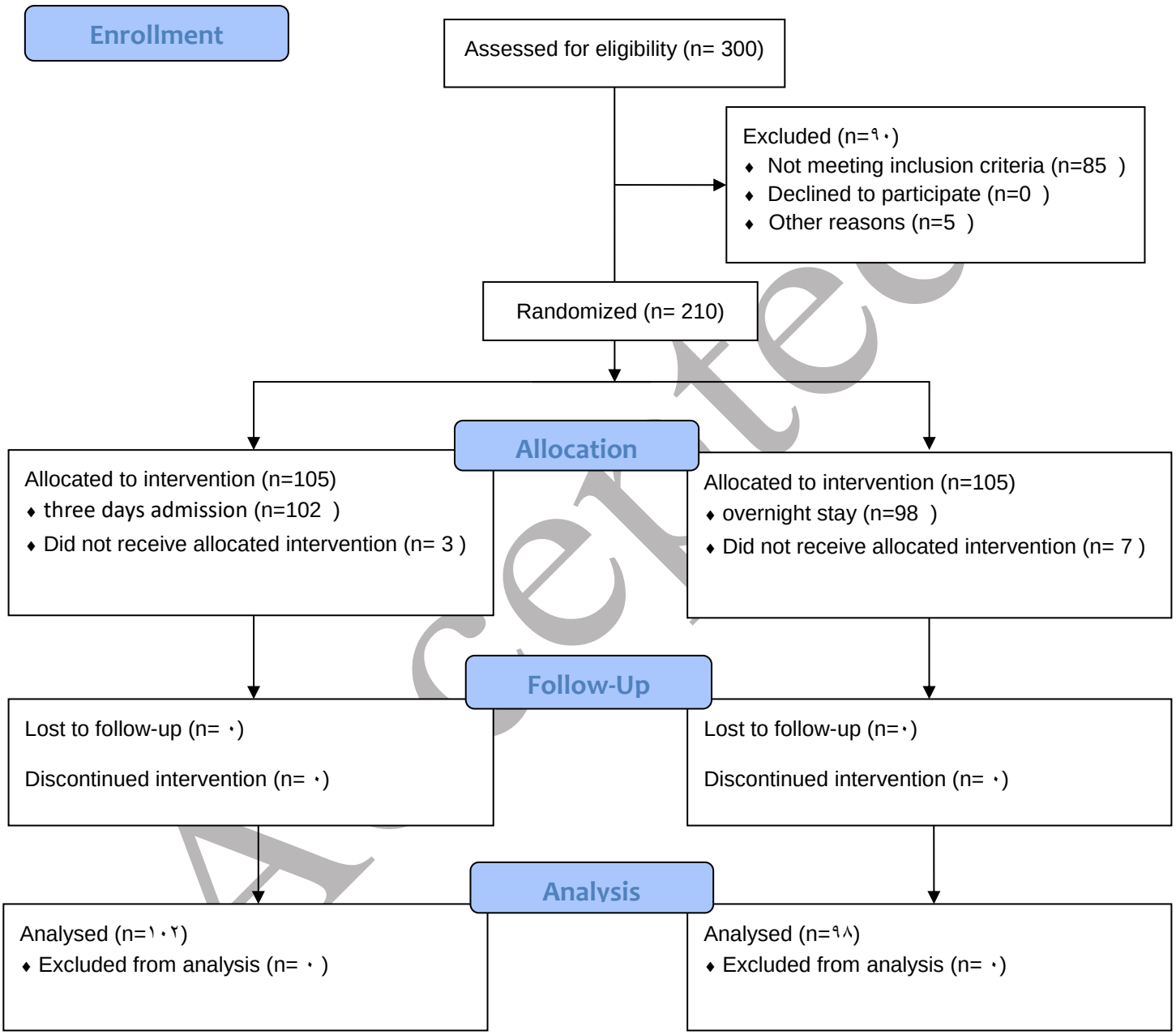

Figure 1: Flow diagram of the study