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Original Research

Surgical Delay Increases the Perioperative Blood Transfusion Rate In Percutaneous Nephrolithotomy

Yusuf Sahin,[1] Mehmet Yilmaz,[1] Enes Kilic,[2] Ahmet Yaser Muslumanoglu[1]

[1]Department of Urology, University of Health Sciences Türkiye, Bagcilar Training and Research Hospital, Istanbul, Türkiye
[2]Deparment of Urology, Zonguldak Atatürk State Hospital, Zonguldak, Türkiye

ABSTRACT

Objectives: We aimed to investigate the effect of prolonged time from diagnosis to treatment (TDT) on surgical outcomes in patients undergoing percutaneous nephrolithotomy (PNL).

Methods: This study included a total of 544 patients who underwent PNL in our clinic between November 2017 and November 2021. Clinicodemographical, radiological, and perioperative data of the patients were recorded. The stone-free rate as assessed by abdominal computed tomography at 3 months was estimated. The possible relation of the stone-free rate and perioperative complications with TDT was examined.

Results: The median age was 48 (range, 38–58) years, the median stone size was 405 (range, 250–700) mm^2, and the median stone density was 1,000 (range, 730–1,221) Hounsfield units. The median TDT was 75 (range, 42–133) days. Twenty-seven patients (5.0%) required perioperative blood transfusion (PBT). There was a statistically significant correlation between TDT and the need for PBT (p=0.022). However, there was no significant correlation between TDT and stone-free rate (p>0.05). Using a cutoff value of 90.5 days, TDT could predict the need for PBT with 59.3% sensitivity and 60% specificity.

Conclusion: Our study results suggest that the need for PBT increases in patients undergoing PNL longer than 90.5 days after the diagnosis. However, further large-scale, prospective studies are warranted to elucidate the effect of prolonged TDT on surgical outcomes in this patient population.

Keywords: Blood transfusion, percutaneous nephrolithotomy, time to treatment

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Urinary stone disease is a major health issue with an increasing prevalence worldwide and is associated with acute or chronic renal failure if left untreated.[1,2] Percutaneous nephrolithotomy (PNL) is the first-line treatment, particularly in patients with kidney stones of >2 cm, and many studies have examined the stone-free status and associated complications in this group of patients. The main factors for stone-free and complication rates after PNL include stone-related factors such as the size, location, composition, and number of stones, the presence of hydronephrosis, patient-related factors such as body mass index, comorbidities, the presence of renal abnormalities, and health-care-related factors such as annual case volume of the center.[3-6]

The novel coronavirus disease-2019 (COVID-19) pandemic had devastating consequences worldwide, as well as

Address for correspondence: Yusuf Sahin, MD. Department of Urology, University of Health Sciences Türkiye, Bagcilar Training and Research Hospital, Istanbul, Türkiye
Phone: +90 555 481 03 41 **E-mail:** dryusufsahin@hotmail.com

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post-poning elective urological surgeries. The European Association of Urology (EAU) guidelines recommended ureteral stenting or nephrostomy for obstructing and complicated urinary stones and post-poning other procedures until the pandemic was controlled.[7] In particular, the prognosis of patients who had obstructing urinary stones, but were unable to be admitted to health-care centers during the lockdowns still remains unclear.

Prolonged time from diagnosis to treatment (TDT) has been shown to decrease overall survival in certain types of cancer.[8,9] However, to the best of our knowledge, there is no study evaluating the effect of prolonged TDT on surgical outcomes in patients with urinary stones. In the present study, we hypothesized that prolonged TDT might decrease the stone-free rates and increase perioperative complications in patients undergoing PNL. We, therefore, aimed to investigate the effect of prolonged TDT on surgical outcomes in patients undergoing PNL.

Methods

Study Design and Patient Selection

This single-center, retrospective study was conducted at the department of urology, kidney stone center of a tertiary referral hospital between November 2017 and November 2021. The study was approved by the local Ethics Committee (No: 513, Date: May 20, 2021) and conducted in accordance with the principles of the Declaration of Helsinki.

Medical data of a total of 920 patients who underwent PNL during the study period were analyzed. All patients were informed about the nature of the procedure and written informed consent was obtained. Data including demographic, clinical, radiological, and perioperative characteristics of the patients were recorded. As standard, non-enhanced abdominal computed tomography (CT) was used to diagnose urinary stones and to assess stone-free status at the post-operative 3rd month. Clinically, insignificant residual stones were defined as stone fragments of <10 mm^2 on CT at the post-operative 3rd month. Patients aged <18 years (n=37), those with a solitary kidney (n=24), having pre-operative nephrostomy or ureteral stenting (n=35), undergoing endoscopic stone extraction from the same side within the past 6 months (n=23), undergoing tubeless procedures (n=150), and having missing radiological data (n=107) were excluded from the study. Finally, a total of 544 patients who met the inclusion criteria were recruited.

Statistical Analysis

Statistical analysis was performed using the Statistical Package for Social Sciences version 22.0 software (IBM Corp., Armonk, NY, USA). The Kolmogorov–Smirnov and Shapiro–Wilk tests were used to check the normality of data for quantitative variables. Continuous variables were expressed in the median and interquartile range, whereas categorical variables were expressed in number and frequency. The Mann–Whitney U and Kruskal–Wallis tests were used to determine homogeneity, independence, and the differences between related groups. The correlation coefficient and statistical significance for the relationships between TDT and perioperative stone characteristics and clinical findings were calculated using the Spearman correlation analysis. Diagnostic scanning tests including sensitivity, specificity, positive predictive value, negative predictive value, and receiver operating characteristic analysis were carried out to identify the predictive value of TDT for the need for blood transfusion. A two-sided P value of < 0.05 was considered statistically significant.

Results

A total of 544 patients who underwent PNL were included in this study. The median age was 48 (range, 38–58) years. Of the patients, 65 (11.9%) had renal abnormalities (Table 1). The median stone size was 405 (range, 250–700) mm^2, and the median stone density was 1,000 (range, 730–1,221) Hounsfield units. The median nephrostomy dwell time was 2 (range, 1–3) days, and the median length of hospital stay was 2 (range, 2–3) days. The median TDT was 75 (range, 42–133) days (Table 2). Of the patients, 28 (5.1%) had post-operative fever and 17 (3.1%) had perirenal hematoma. The median hemoglobin drop was 1.90 (range, 1.25–2.85) g/dL. Blood transfusion was applied to patients with perioperative hemoglobin level below approximately 9 g/dL. Twenty-seven (5.0%) of the patients required perioperative blood transfusion (PBT) (Table 3).

There was a statistically significant correlation between TDT and the need for PBT (p=0.022). However, there was no significant correlation between TDT and stone-free rate and other perioperative complications (p>0.05) (Tables 4 and 5). Using a cutoff value of 90.5 days, TDT could predict the need for PBT with 59.3% sensitivity and 60% specificity (Fig. 1).

Discussion

The impact of delays in elective surgeries during the COVID-19 pandemic and prolonged TDT on endourological stone management has raised many concerns. In the present study, we investigated the effect of prolonged TDT on surgical outcomes in patients undergoing PNL and to evaluate stone-free and complication rates in this group

Table 1. Demographic and clinical characteristics of patients

	Median (IQR)	n	%
Age (year)	48 (38–58)		
Sex			
Female		206	37.9
Male		338	62.1
BMI (kg/m^2)	26.3 (24.7–30.4)		
ASA Class			
ASA-1		407	74.8
ASA-2		119	21.9
ASA-3		16	2.9
ASA-4		2	0.4
Pre-operative creatinine level (mg/dL)	0.80 (0.70–0.95)		
Diabetes mellitus			
No		448	82.4
Yes		96	17.6
High blood pressure			
No		413	75.9
Yes		131	24.1
Coronary artery disease			
No		506	93.0
Yes		38	7.0
Chronic kidney disease			
No		535	98.5
Yes		8	1.5
Chronic obstructive pulmonary disease			
No		522	96.0
Yes		22	4.0
Cerebrovascular disease			
No		535	98.3
Yes		9	1.7
Renal abnormality			
No		479	88.1
Yes		65	11.9
Previous stone surgery			
No		313	57.5
Yes		231	42.5

IQR: interquartile range; BMI: body mass index; ASA: American Society of Anesthesiologists.

Table 2. Clinical, radiological, and operative data of patients

	n	%	Median (IQR)
Side			
Right	267	49.1	
Left	277	50.9	
Stone size (mm^2)			405 (250–700)
Stone CT density (HU)			1000 (730–1221)
Skin-to-stone distance (mm)			88 (74–102)
Hydronephrosis			
No	363	66.7	
Yes	181	33.3	
Staghorn calculus			
No	478	87.9	
Yes	66	12.1	
Number of stones			
Solitary	199	36.6	
Multiple	345	63.4	
Stone location			
Lower calyx	88	16.2	
Middle calyx	21	3.9	
Upper calyx	13	2.4	
Renal pelvis	143	26.3	
Multiple calyx	278	51.1	
Guy Stone Score			
GSS-1	166	30.5	
GSS-2	242	44.5	
GSS-3	93	17.1	
GSS-4	43	7.9	
CROES Score			215 (180–282)
S.T.O.N.E. Score			7 (6–8)
Surgery duration (min)			90 (70–120)
Access number			
1	514	94.7	
2	28	5.2	
3	1	0.2	
Intercostal access			
No	493	90.8	
Yes	50	9.2	
Nephrostomy duration (day)			2 (1–3)
Length of hospital stay (day)			2 (2–3)
Time from Diagnosis to Treatment (day)			75 (42–133)

IQR: Interquartile range; CT: Computed tomography; HU: Hounsfield unit; PNL: Percutaneous nephrolithotomy.

of patients. Our study results showed that a TDT of longer than 90.5 days increased the need for PBT. We believe that this study would provide an additional contribution to the literature, particularly to decrease the PBT rates in patients undergoing PNL, which is one of the main concerns for these patients.

In a study, Yamaguchi et al.[10] compared tract dilation methods of PNL in over 5,000 patients and reported that the need for PBT was significantly higher in the balloon

Table 3. Post-operative clinical information of patients

	Median (IQR)	n	%
Post-operative fever			
No		516	94.9
Yes		28	5.1
Perioperative hemoglobin drop (g/dL)	1.90 (1.25–2.85)		
Perioperative blood transfusion			
No		517	95.0
Yes		27	5.0
Post-operative hematoma			
No		527	96.9
Yes		17	3.1
Post-operative urinoma			
No		542	99.6
Yes		2	0.4
Post-operative angioembolization			
No		541	99.4
Yes		3	0.6
Post-operative ureteral stenting			
No		517	95.0
Yes		27	5.0
Perioperative complication (Clavien-Dindo)			
No		368	67.7
Clavien-Dindo-I		93	17.1
Clavien-Dindo-II		49	9.0
Clavien-Dindo-IIIA		24	4.4
Clavien-Dindo-IIIB		4	0.7
Clavien-Dindo-IVA		5	0.9
Clavien-Dindo-IVB		0	0.0
Clavien-Dindo-V		1	0.2
Emergency visit after discharge			
No		515	94.7
Yes		29	5.3
Stone-free status			
No		191	35.1
Yes		353	64.9

IQR: Interquartile range.

Table 4. Comparison of perioperative complications and stone-free status according to time from diagnosis to treatment

	Time from diagnosis to treatment (day)	
	Median (IQR)	p
Post-operative Fever		
No	74 (42–133)	0.147
Yes	94 (60–159)	
Perioperative Blood Transfusion		
No	72 (42–130)	**0.022***
Yes	113 (65–153)	
Post-operative Hematoma		
No	74 (42–133)	0.426
Yes	97 (44–148)	
Post-operative Urinoma		
No	76 (42–133)	0.595
Yes	60 (52–67)	
Post-operative Angioembolization		
No	75 (42–133)	0.903
Yes	96 (36–133)	
Post-operative Ureteral Stent Insertion		
No	74 (42–133)	0.933
Yes	81 (42–146)	
Perioperative Complication (Clavien-Dindo)		
No	64 (38–116)	0.324[b]
Clavien-Dindo-I	81 (43–134)	
Clavien-Dindo-II	98 (56–148)	
Clavien-Dindo-IIIA	82 (32–137)	
Clavien-Dindo-IIIB	62 (55–71)	
Clavien-Dindo-IVA	72 (59–74)	
Clavien-Dindo-IVB		
Clavien-Dindo-V	83 (83–83)	
Emergency Visit After Discharge		
No	75 (43–133)	0.865
Yes	77 (35–133)	
Stone-Free Status		
No	80 (45–135)	0.169
Yes	71 (42–130)	

Mann–Whitney U test; [b]: Kruskal–Wallis test; *: p<0.05; IQR: Interquartile range.

dilation group compared to the telescopic/serial dilator group. Using a 24-Fr and 30-Fr tract size in the balloon dilation group, the blood transfusion rates were 5.6% and 7.2%, respectively. In the current study, we used a 30-Fr tract size for balloon dilation. The blood transfusion rate was 5%, and the angioembolization rate was 0.6% in our study. In the study of Yamaguchi et al.[10] the transfusion rate was relatively high which can be attributed to the fact that the study was multicenter and low-volume centers (25 cases/year) were included. In our center, the annual case number was 200 in the pre-pandemic period and 90 during the

Table 5. Correlation analysis between time from diagnosis to treatment and perioperative stone characteristics and clinical findings

		Pre-operative Creatinine (mg/dL)	Hydronephrosis	Stone Size (mm^2)	Stone Density (HU)	Number of Calyx
Time From Diagnosis to Treatment (day)	Correlation Coefficient	−0.090*	−0.090*	−0.060	−0.039	0.011
	Sig. (2-tailed)	0.035	0.036	0.162	0.370	0.805
	n	544	544	544	544	544
		Stone Number	**Staghorn Calculus**	**Surgery Duration (min)**	**Hospital Stay (day)**	**Nephrostomy Duration (day)**
Time From Diagnosis to Treatment (day)	Correlation Coefficient	0.090*	−0.036	−0.003	0.003	0.053
	Sig. (2-tailed)	0.035	0.398	0.946	0.945	0.221
	n	544	544	541	544	544
		Intercostal Access	**Tract Number**	**Post-operative Fever**	**Perioperative Haemoglobin Decline (gr/dL)**	**Perioperative Blood Transfusion**
Time From Diagnosis to Treatment (day)	Correlation Coefficient	0.034	−0.004	0.062	−0.004	0.**098***
	Sig. (2-tailed)	0.429	0.932	0.147	0.929	0.**022**
	n	543	543	544	544	**544**
		Post-operative Urinoma	**Post-operative Angioembolization**	**Perioperative Complication (Clavien-Dindo)**	**Emergency Visit After Discharge**	**Stone Free Status**
Time From Diagnosis to Treatment (day)	Correlation Coefficient	−0.023	0.005	0.084*	−0.007	−0.059
	Sig. (2-tailed)	0.595	0.903	0.049	0.866	0.169
	n	544	544	544	544	544

Spearman's Correlations; *: Correlation is significant at the 0.05 level (2-tailed); HU: Hounsfield Unit.

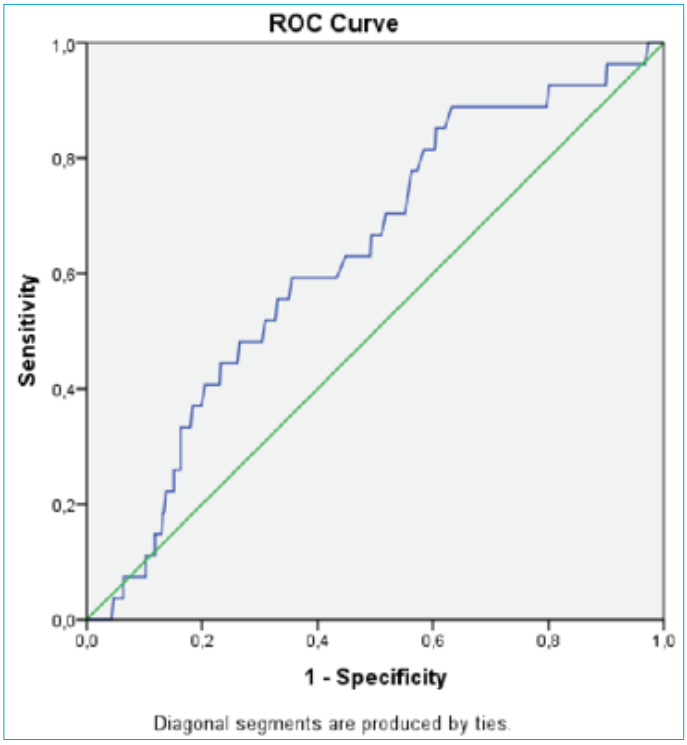

Figure 1. ROC curve analysis for time from diagnosis to treatment in patients receiving blood transfusion.

pandemic with an annual case number of more than 50 for each endourologist. In another study, Akman et al.[11] evaluated the factors affecting bleeding during PNL focusing on a single surgeon's experience. They used a 30-Fr tract size for 649 PNL procedures and the overall blood transfusion rate was 10.8% and the angioembolization rate was 1.4% which are higher than our findings. The relatively higher transfusion rate in the surgeon's first 100 cases, and the higher rates of staghorn calculus and multiple access (28% and 19.2%, respectively) may explain this difference. In addition, Srivastava et al.[12] evaluated bleeding complications of PNL and identified possible predictors. The authors reported an overall blood transfusion rate of 12.3%. The high blood transfusion rate in this study can be explained by the enrollment of patients with chronic renal failure and a high number of simultaneous bilateral PNL cases. In our study, patients with chronic renal failure and those undergoing simultaneous bilateral PNL were excluded.

One of the main concerns in PNL is the effect of prolonged TDT on the kidney. Due to the lack of adequate data on this subject, neither physicians nor patients have enough information about the adverse consequences of prolonged TDT on renal functions, stone-free rates, and complications.

As with all elective surgeries, the COVID-19 pandemic led to prolonged TDT for urinary stones. The EAU guidelines recommended urinary diversions such as ureteral stenting or nephrostomy for obstructing and complicated urinary stones.[7] However, prolonged stent or nephrostomy dwell time has been shown to be associated with bacteremia, pyelonephritis, and urosepsis.[13-15] Currently, the effects of prolonged TDT on surgical outcomes in patients scheduled for PNL for uncomplicated urinary stones still remain to be elucidated. In a systematic review, Assad et al.[16] evaluated the impact of delaying acute kidney stone surgery on the outcomes in patients with symptomatic, uncomplicated urinary stones. They found that upfront ureteroscopy instead of ureteral stenting and early (within 12–72 h) extracorporeal shockwave lithotripsy was associated with less admissions to the emergency department, medical imaging examinations, and upper urinary tract diversions. However, the main limitation was the lack of evaluation of the direct effects of post-ponement of surgical procedures on the outcomes in any of the studies included. Furthermore, none of the studies provided data regarding the timing of PNL. In our study, we excluded patients who underwent ureteral stenting or nephrostomy due to severe hydronephrosis, acute pyelonephritis, severe renal colic, or acute renal failure, which may all affect the results directly. We found a statistically significant correlation between TDT and the need for PBT. A TDT of longer than 90.5 days increased the need for PBT. However, there was no significant relationship between TDT and stone-free rates at 3 months and overall complication rates.

In the present study, the rate of patients with comorbidities that pose a risk for urolithiasis, such as diabetes, hypertension, and coronary artery disease, was high in consistent with the literature.[17] Especially during the pandemic period, these patients may have been less preferred for elective surgery, due to factors such as longer hospital stays and more need for intensive care unit, and therefore, TDT of these patients may have prolonged.[18] In addition, the relationship between perioperative hemorrhage and comorbidities such as diabetes and hypertension remains unclear.[19,20] In light of all these links, comorbidities of the patients seem to have a significant impact on surgical delay and PBT.

The relationship between urolithiasis and endothelial dysfunction has been demonstrated in various animal experiments and clinical studies. Long-term exposure to stones in the kidney may increase inflammation and consequently oxidative stress factors in the urinary system. Oxidative stress leads to an increase in pro-inflammatory cytokines in the region that may damage kidney glomeruli, tubules, and vessels. As a result, inflammation and fibrosis occur that may negatively affect kidney functions.[21] In our study, the increased rate of PBT due to prolonged TDT can be explained by this inflammatory process occurring in the renal vessels.

The main strength of this study is that it is the first study to investigate the effects of prolonged TDT on surgical outcomes in patients undergoing PNL. The main limitations include its single-center, retrospective design with a heterogeneous sample. In addition, we were unable to compare the PNL cases based on the individual experience (annual case number) of each surgeon.

Conclusion

Our study results indicate a positive, significant correlation between TDT and PBT in PNL patients. In addition, the need for PBT increases in patients undergoing PNL longer than 90.5 days after the diagnosis. However, further large-scale, prospective studies are warranted to gain a better understanding of the exact timing of PNL and to reduce the need for blood transfusion in this patient population.

Disclosures

Ethics Committee Approval: The study was approved by the Ethics Committee of Istanbul Medipol University Non-invasive Clinical Research (No: 513, dated 20.05.2021).

Patient informed consent: All patients were informed about the nature of the procedure and a written informed consent was obtained.

Peer-review: Externally peer-reviewed.

Conflict of Interest: None declared.

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