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ORIGINAL PAPER

Development and internal validation of El-Shazly-Buchholz's nomogram to predict postoperative complications after PCNL: A multicenter study

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Summary

***Introduction:** A model to predict the risk of surgical complications following percutaneous nephrolithotomy (PCNL) could be a useful tool to guide clinical decision-making. The aim of this study was to develop a simple and widely applicable stratification tool to be used for patient counseling, surgical planning, evaluation of outcomes, and academic reporting.*
***Methods:** Data of patients who underwent PCNL were retrieved from the database of the collaborating centers including demographics of patients, characteristics of their stones and urinary tracts, and perioperative data. The primary outcome was the development of postoperative complications. Data were randomly split into a training dataset (85%) and a validation dataset (15%). A univariate and multivariate logistic regression analysis of the training dataset was performed to identify independent predictors of postoperative complications. Model variables were used to construct a nomogram that was internally validated on the testing dataset by measuring calibration, discrimination, and plotting the decision curve.*
***Results:** Six hundred thirty one patients (245 Males) with a median (IQR) age of 49 (37-56) years were included. Postoperative complications occurred in 147 (23.3%) patients. Significant predictors of complications included preoperative urine culture ($p < 0.001$), largest stone diameter ($p = 0.02$), and intraoperative blood loss ($p = 0.002$). A nomogram was developed from the predictors and applied to the validation dataset showing an area under the curve (95%CI) of 66.4% (52.2;80.6).*
***Conclusions:** This new scoring system emphasized patient characteristics and operative details rather than stone characters to predict the morbidity of PCNL. Furthermore, it should facilitate risk adjustment, enabling physicians to better define the nephrolithiasis disease continuum and identify patients who should be referred to tertiary care centers.*

KEY WORDS: *Percutaneous nephrolithotomy; Complications; Urine culture; Stone diameter; Intraoperative blood loss.*

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INTRODUCTION

Percutaneous nephrolithotomy (PCNL) is the gold standard procedure to treat relatively large renal stones (> 2 cm) with a high success rate but still with significant morbidity despite technical advances. There is no consensus on an ideal predictive model of morbidity outcomes following PCNL. Available predictive tools aim at assessing the kidney stone complexity to predict the stone-free rate. They include the Guy's Stone Score, the CROES nomogram, S.T.O.N.E. nephrolithometry, *Seoul National University Renal Stone Complexity* (S-ReSC) score, and the *Simple Stone Score* (SSS) (1-5). In our opinion, the risk of surgical complications is an important variable that should guide clinical decision-making. In comparative studies, none of the available scoring systems was fully satisfactory in predicting surgical complications (6). Considering the deficient literature in assessing post-PCNL morbidity, this study was conducted to develop a widely applicable, simple disease stratification tool that will greatly improve patient counseling, surgical planning, evaluation of outcomes, and academic reporting.

METHODS

Patient data

A total of 631 patients who underwent PCNL at the collaborating centers were retrospectively analyzed. The procedures used in this study adhere to the tenets of the Declaration of Helsinki (as revised in 2013). Approval was obtained from the *Research Ethics Committees of Medical Research Center HMC* (MRC-01-20-385). Because of its retrospective nature, the consent was waived from the participants. All the information collected during the research project remained confidential to the extent required and provided by law. Patient data were anonymized, coded, and kept by the principal investigator.

The preoperative clinical data included age, gender, *body mass index* (BMI), recurrent stone status, previous renal surgery in the ipsilateral kidney, associated comorbidities, the *American Society of Anesthesia* (ASA) score, preoperative urine culture, and diagnostic imaging (modality). Stone characteristics were the stone diameter, burden, density (*Hounsfield Unit*), and the number of involved calyces.

Intraoperative documented data included PCNL position, operative time, number of tracts, size of the tract, intraoperative blood loss (Hb loss > 2 gr/dl), pus on the puncture, residual fragments size and number, exit strategy, combination with *retrograde intrarenal surgery* (RIRS), and the caseload of surgeon per year. Postoperatively, collected data were fever, urine culture, sepsis, bleeding, postoperative transfusion, length of hospital stay, and stone-free status/residual fragments.

Study outcome

The primary outcome was the development of postoperative complications by Clavien-Dindo system (7). A secondary outcome was the development of postoperative infectious complications.

Statistical analysis

The data were randomly split into a training dataset (85%) and a validation dataset (15%). In the training dataset, a univariate and multivariate logistic regression analysis was performed to identify independent predictors of the occurrence of any postoperative complication. Statistical significance was determined using the Chi-square or Fischer's exact tests for categorical variables whenever appropriate. Mann-Whitney U or Student t-tests were used for non-parametric and parametric variables, respectively. Model variables were used to construct a nomogram. The nomogram was internally validated by measuring calibration, discrimination, and plotting the decision curve. A calibration plot was generated to identify how much predicted nomogram probabilities match the actual post-operative complications values. The discrimination was evaluated by calculating the area under the curve (desired when more than 50%). Decision curve analysis reveals the net benefit of using the model to detect postoperative complications.

The decision curve compares the ability of the nomogram to distinguish the occurrence or absence of complications according to a range of threshold probabilities. If the decision curve shows a higher net benefit, it is clinically beneficial.

Statistical analysis was performed using R programming language version 4.1.2. with p-value less than 0.05 was considered statistically significant.

Results

Patients' demographics

A total of 631 patients with a median (IQR) age of 49 (37:56) years were included. Female patients constituted 38.83% while obese patients (> 30 BMI) accounted for 43.26%. Four institutions contributed to the current study [J: 100 (15.85%), M: 99 (15.69%), R: 332 (52.61%), and U: 100 (15.85%) patients].

Postoperative complications occurred in 147 (23.3%) patients. After random splitting, there was no significant difference between both groups. The difference between both groups is shown in Table 1.

Table 1.
Comparison between training and validating datasets for patients who underwent percutaneous nephrolithotomy in 4 institutions.

Parameter		Train	Validate	p-value
Institutions				0.3
	J	79 (14.74%)	21 (22.11%)	
	M	83 (15.49%)	16 (16.84%)	
	R	287 (53.54%)	45 (47.37%)	
	U	87 (16.23%)	13 (13.68%)	
Age median (IQR)		50 (38:56)	47 (34.5:55)	0.09
Gender				0.6
	Female	205 (38.25%)	40 (42.11%)	
	Male	331 (61.75%)	55 (57.89%)	
BMI, median (IQR)		29.31(26.1:32.1)	28.5 (26.7:32.8)	0.9
Obesity				0.2
	Non-obese	298 (55.6%)	60 (63.16%)	
	Obese	238 (44.4%)	35 (36.84%)	
Recurrent one				0.7
	No	375 (69.96%)	64 (67.37%)	
	Yes	161 (30.04%)	31 (32.63%)	
Previous one surgery				0.6
	No	380 (70.9%)	64 (67.37%)	
	Yes	156 (29.1%)	31 (32.63%)	
Diabetes Mellitus				0.7
	No	474 (88.43%)	86 (90.53%)	
	Yes	62 (11.57%)	9 (9.47%)	
Hypertension				0.3
	No	444 (82.84%)	83 (87.37%)	
	Yes	92 (17.16%)	12 (12.63%)	
ASA score				0.5
	I	310 (57.84%)	54 (56.84%)	
	II	194 (36.19%)	38 (40%)	
	III	32 (5.97%)	3 (3.16%)	
Preoperative urine culture				0.7
	Negative	490 (91.42%)	85 (89.47%)	
	Positive	46 (8.58%)	10 (10.53%)	
LSD, mm, median (IQR)		30 (20:41)	32 (25:40)	0.2
Number of involved calyces				0.5
	0	103 (19.22%)	16 (16.84%)	
	1	196 (36.57%)	31 (32.63%)	
	2	102 (19.03%)	24 (25.26%)	
	3	135 (25.19%)	24 (25.26%)	
HU, mean (SD)		1037 (312.9)	971.2 (325.5)	0.07
Sheath size				0.1
	Mini	164 (30.6%)	21 (22.11%)	
	Standard	372 (69.4%)	74 (77.89%)	
OR time, min, median (IQR)		70 (35:120)	80 (45:130)	0.07
Intraoperative blood loss				0.5
	No	494 (92.16%)	90 (94.74%)	
	Yes	42 (7.84%)	5 (5.26%)	
Residual fragment				0.1
	No	424 (79.1%)	68 (71.58%)	
	Yes	112 (20.9%)	27 (28.42%)	
LOS, days, median (IQR)		1 (1:2)	1 (1:3)	0.2

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Parameter		Train	Validate	P-value
Stone free status				0.2
	No	106 (19.78%)	25 (26.32%)	
	Yes	430 (80.22%)	70 (73.68%)	
No. of punctures				0.07
	Single	464 (86.57%)	75 (78.95%)	
	Multiple	72 (13.43%)	20 (21.05%)	
RF number, median (IQR)		1 (1:2)	1 (1:2)	0.9
PCN only *				0.3 F
	No	21 (4.36%)	1 (1.32%)	
	Yes	461 (95.64%)	75 (98.68%)	
JJ only *				0.6
	Yes	405 (84.02%)	66 (86.84%)	
	No	77 (15.98%)	10 (13.16%)	
PCN and JJ *				0.3
	No	97 (20.12%)	11 (14.47%)	
	Yes	385 (79.88%)	65 (85.53%)	
Postoperative Complications				0.4
	No	415 (77.43%)	69 (72.63%)	
	Yes	121 (22.57%)	26 (27.37%)	
Infectious Complications				0.3
	No	432 (80.6%)	72 (75.79%)	
	Yes	104 (19.4%)	23 (24.21%)	

BMI: Body mass index; ASA: American society of anesthesiology; LSD: Largest stone diameter; HU: Hounsfield units; OR: Operation; LOS: Length of stay.
** Mode of drainage after the procedures.*

Predictors of complications in the training dataset

Significant variables include preoperative urine culture [positive: 24 (5.78%) versus 22 (18.18%), p < 0.001], median (IQR) largest stone diameter [30 (20:40) *versus* 35 (22:48), p = 0.02], intraoperative blood loss [24 (5.78%) *versus* 18 (14.88%), p = 0.002]. Data are displayed in Table 2. On multivariate logistic regression analysis, independent predictors were intra-operative blood loss [odds ratio (OR) and 95% confidence interval (CI): 2.5 (1.2:4.9), p = 0.007], preoperative urine culture [OR (95%CI): 3.2 (1.6:6), p < 0.001] (Table 3).

Nomogram development and validation

A nomogram was developed from the predictors and is displayed in Figure 1. The nomogram is applied to the validation dataset. The area under the curve (95%CI) was 66.4 (52.2; 80.6). Regarding calibration, the nomogram's predicted probabilities slightly overestimated the post-operative complications' actual occurrence. The Calibration plot is displayed in Figure 2A. The decision curve shows a higher net benefit of the model in a wide range of thresholds (25%-75%). Therefore, the model is performing better in this range of thresholds than if treatment of complications is considered in all patients or in none of the patients. Results are displayed in Figure 2B.

Figure 1.
Nomogram for the evaluation of the risk of complications after PCNL.

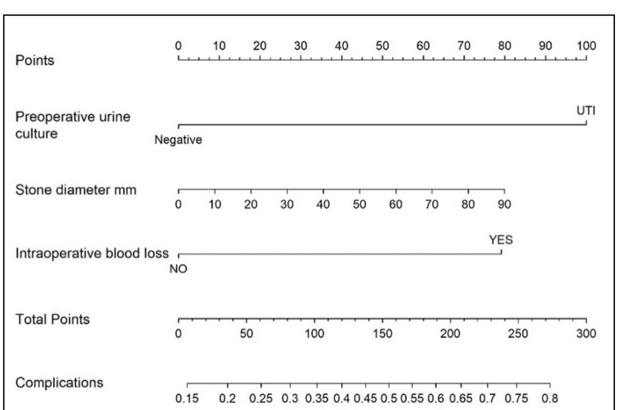


Table 2.
Univariate and logistic regression analysis for predictors of post-PCNL complications.

Parameter		Complications		P-value
		No	Yes	
Age median (IQR)		49 (38:56)	51 (37:62)	0.2
Gender				1
	Female	158 (38.07%)	47 (38.84%)	
	Male	257 (61.93%)	74 (61.16%)	
BMI median (IQR)		29.3 (26.1:32.1)	29.3 (25.3:31.9)	0.5
Recurrent stone				0.5
	No	294 (70.84%)	81 (66.94%)	
	Yes	121 (29.16%)	40 (33.06%)	
Diabetes Mellitus				0.3
	No	363 (87.47%)	111 (91.74%)	
	Yes	52 (12.53%)	10 (8.26%)	
Hypertension				0.05
	No	336 (80.96%)	108 (89.26%)	
	Yes	79 (19.04%)	13 (10.74%)	
Preoperative urine culture				< 0.001
	Negative	391 (94.22%)	99 (81.82%)	
	UTI	24 (5.78%)	22 (18.18%)	
LSD, mm, median (IQR)		30 (20:40)	35 (22:48)	0.02
Number of involved calyces				0.07
	0	89 (21.45%)	14 (11.57%)	
	1	150 (36.14%)	46 (38.02%)	
	2	73 (17.59%)	29 (23.97%)	
	3	103 (24.82%)	32 (26.45%)	
HU, mean (SD)		1038.7 (319.3)	1031(291)	0.8
Sheath size				1
	Mini	127 (30.6%)	37 (30.58%)	
	Standard	288 (69.4%)	84 (69.42%)	
Intraoperative blood loss				0.002
	No	391 (94.22%)	103 (85.12%)	
	Yes	24 (5.78%)	18 (14.88%)	
No. of punctures				0.5
	Single	362 (87.23%)	102 (84.3%)	
	Multiple	53 (12.77%)	19 (15.7%)	
RF number, median (IQR)		1 (1:2)	1 (1:2)	0.3
Drainage				0.08
	JJ	11 (2.65%)	9 (7.44%)	
	JJ and PCN	304 (73.25%)	81 (66.94%)	
	PCN	60 (14.46%)	16 (13.22%)	
	Tubeless	40 (9.64%)	15 (12.4%)	

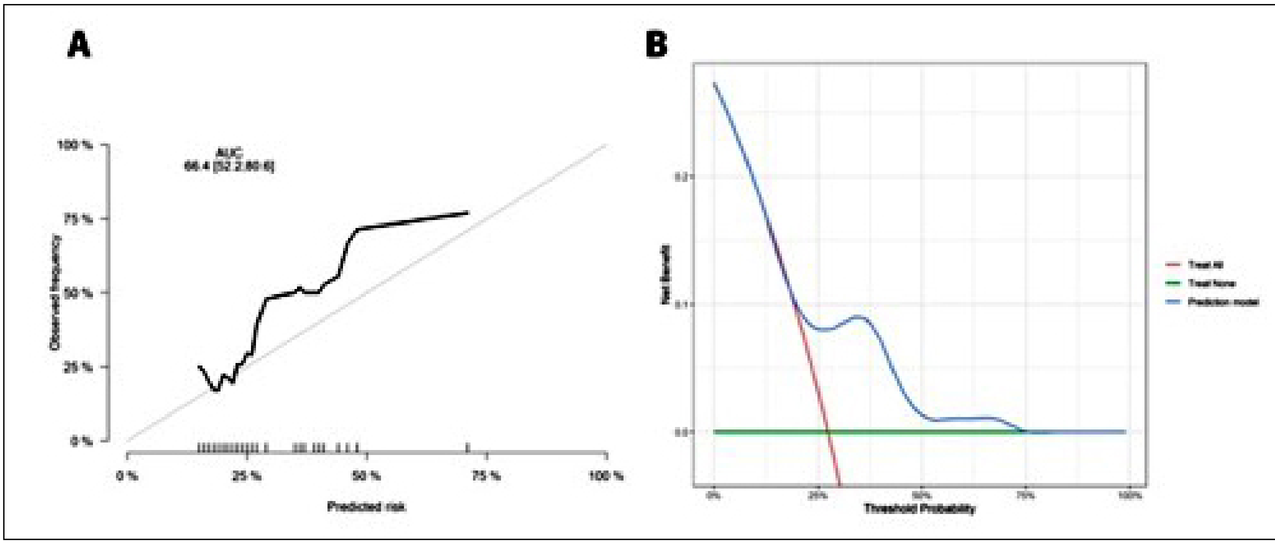
BMI: Body mass index; LSD: Largest stone diameter; HU: Hounsfield units; OR: Operation; LOS: Length of stay.
** Mode of drainage after the procedures.*

Table 3.
Multivariate logistic regression analysis for predictors of postoperative complications after percutaneous nephrolithotomy.

	B	OR (95% CI)	p-value
(Intercept)	-1.807	0.164 (0.09:0.2)	< 0.001
Intraoperative blood loss (yes)	0.925	2.521 (1.2:4.9)	0.007
Preoperative urine culture (positive)	1.168	3.215 (1.6:6.1)	< 0.001
Largest stone diameter, mm	0.01	1.01 (0.9:1.02)	0.1

B: Regression coefficient; OR: Odds ratio; CI: Confidence interval.

Figure 2.
Calibration plot (A) and Range of Threshold.



Discussion

Literature exhibits multiple stone scoring systems for evaluating outcomes of percutaneous nephrolithotomy including the Guy's stone score, the *Clinical Research Office of the Endourological Society* (CROES) nomogram, the S.T.O.N.E. score, and the S-ReSC score (1-5). The pivotal variables in all the scoring systems are stone location, stone number, and the presence of staghorn calculi. The Guy's stone score stratifies patients into four grades, where grade I indicates a solitary stone with simple anatomy (mid-lower pole or renal pelvis), grade II a solitary stone in the upper pole or multiple stones with simple anatomy or a solitary stone with abnormal anatomy, grade III multiple stones with abnormal anatomy or stones in a calyceal diverticulum or partial staghorn stone, and grade IV staghorn stone or any stone in a patient with spina bifida or spinal injury. The S.T.O.N.E. score classifies patients into low-, moderate-, and high-risk groups according to stone size (S), tract length (T), obstruction (O), number of involved calyces (N), and essence (E) (composition or stone density). The CROES nomogram grades risk across a continuous scale considering the stone burden, location, number, and surgical volume. The S-ReSC scoring system subdivides the pelvicaliceal system in nine locations and the score is the cumulative sum of the locations involved by the stone.

Several studies evaluated the efficacy of these stone-scoring systems in predicting the stone-free status and the incidence of complications after percutaneous nephrolithotomy. A systematic review (6) of ten studies (8-17) with metanalysis compared the efficacy of the stone scoring systems in predicting stone-free rate after PCNL most of them confirming their equal predictive efficacy of the stone-free rate.

Stone free status was negatively related to Guy's (WMD = -0.64, p < 0.0001) and S.T.O.N.E. score (WMD = -1.23, p < 0.0001) and positively to the score of CROES nomogram (WMD = 29.48, p = 0.003). No significant difference between the three stone scoring nomogram was found at comparison of *area under curves* (AUC) of predicting stone free rate.

A secondary outcome of the systematic review of *Jiang et al.* (6) was the comparison of the efficacy of the stone score systems in predicting complications after PCNL. *Tailly et al.* (16) and *Sfoungaristos et al.* (15) did not find correlation between stone scores and complication rates. Similarly, *Noureldin et al.* (14) and *Kocaaslan et al.* (12) observed no significant correlation of Guy score and S.T.O.N.E. score with complications after PCNL. Only *Bozkurt et al.* (8) observed a correlation of Guy's score and the CROES nomogram with complication rates after PCNL. In addition, *Choi et al.* (10) compared the predictability of the outcomes of tubeless PCNL using the Guy score, CROES nomogram, and S.T.O.N.E. score showing that only the Guy score was able to predict the complication rate after PCNL. The metanalysis showed that only the Guy's score was able to predict complications after PCNL (WMD = -0.29, 95% CI: -0.57 to -0.02, p = 0.03).

A systematic review (18) specifically focused on the correlation between stone scoring systems and postoperative complications after PCNL in adult patients adding six studies (19-24) to the 5 studies (9, 10, 13, 16, 17) previously considered by the systematic review of *Jiang et al.* (6). A significant correlation with complications was obtained with Guy's stone score in 6 out 9 studies, with S.T.O.N.E. nephrolithometry score in 4 out 11 studies, with CROES score in 3 out 9 studies and with S-ReSC score in one of two studies, respectively. Other studies (16, 19-21) showed no correlation between nomograms and post-surgical complications graded using the *Clavien-Dindo* (CD) classification system modified for PCNL (8).

Biswas et al. (22) found significative correlations between GSS, S.T.O.N.E. nephrolithometry score, and CROES score with post-operative complications including EBL. *Labadie et al.* (13) reported no significant correlation at logistic regression analysis of GSS, S.T.O.N.E. nephrolithometry score and CROES score with most post-operative complications, although GSS and S.T.O.N.E. nephrolithometry were correlated with EBL. *Choi et al.* (9) found a correlation between GSS and post-operative complications, while S.T.O.N.E. nephrolithometry score and CROES score were not correlated. Similar results were obtained by the same authors in a cohort of tubeless PCNL (10). *Al Adl et al.* (23) evaluated the correlation between all four nomograms and complications observing a modest correlation of S.T.O.N.E. nephrolithometry score, GSS, S-ReSC score, and CROES score with complications according to CD, although only GSS, S-ReSC score and CROES score correlated with EBL. *Khan et al.* (24) reported significant correlation between both S.T.O.N.E. nephrolithometry score and GSS with overall complication rates at multivariate analysis. Overall results demonstrated that stone morphology, as accurately described by the stone scoring systems, seemed to be not sufficient by itself to accurately predict the risk of complications after PCNL.

Our nomogram adds to a measure of stone size, as stone diameter, other two easily obtained measures as positivity of preoperative urine culture and intraoperative blood loss. Preoperative urine culture is mandatory before PCNL although it was well demonstrated that a negative midstream urine culture cannot exclude the presence of infection in the stone or the urinary tract upstream of the stone (25).

A systematic review of 19 studies demonstrated that positivity of stone culture was associated with higher odds of developing a *Systemic Inflammatory Response Syndrome* (SIRS) after PCNL in comparison with *preoperative midstream urine culture* (PMUC), although the odds of developing sepsis were not significantly different between positivity of stone culture or PMUC (26).

In another study, high *procalcitonin* (PCT) values, IL-6 (> 264 pg/ml), SIRS score (> 2.5), *National Early Warning Score* (NEWS) (> 2.5), *quick Sequential Organ Failure Assessment* (qSOFA) (> 0.50) and surgical time were independent risk factors for septic shock (27). Finally, at multivariate analysis, renal pelvic pressure ≥ 30 mmHg during PCNL procedure was included among the more relevant risk factors for urosepsis together with operative time, bladder urine culture and hydronephrosis (28).

Intraoperative blood loss is a parameter that can be only obtained at the end of the procedure therefore it cannot be used in the choice and the planning of the treatment although it can be useful to identify those patients that are at higher risk of complications requiring a strict follow-up for prevention and early treatment of complication.

The strength of this study is the homogeneity of the series that was analyzed, which comes from only 4 centres that contributed at least 100 cases each. The number of cases studied is relatively high although for the prediction of less frequent and more serious complications it could be even too small. Furthermore, the retrospective design constitutes another limitation.

Finally, for the prediction of infectious complications, some microbiological parameters were not available (culture of the pelvic urine and of the stone) as well as some laboratory tests (C-reactive protein, procalcitonin) and symptomatic scores predictive of the systemic inflammatory response or sepsis. For these reasons, the efficacy of the nomogram will have to be confirmed by prospective studies of larger series.

Conclusions

This new scoring system (the *El-Shazly-Buchholz's* nomogram) emphasized on patient characteristics and operative details rather than stone features as in previous scores. It should allow reliable and accurate comparisons of treatment efficacy and quality of surgical care by predicting the morbidity of PCNL. Furthermore, it should facilitate risk adjustment, enabling physicians to better define the nephrolithiasis disease continuum and identify patients who should be referred to tertiary care centers.

Acknowledgments

This study was designed by *Noor Buchholz* who organized its initial phase and contributed an important surgical case series. After he passed away on February 13, 2024, his collaborators and friends wanted to complete his work so that the memory of his enthusiastic activity in the study and treatment of kidney stones is maintained over time.

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