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Original Article

Reliability of nephrolithometric nomograms in patients treated with minimally invasive percutaneous nephrolithotomy: A precision study

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Abstract *Objectives:* The study aimed to evaluate quality of nephrolithometric nomograms to predict stone-free rates (SFRs) and complication rates (CRs) in case of minimally invasive percutaneous nephrolithotomy (PNL). In the last decade, nomograms have been introduced to estimate the SFRs and CRs of PNL. However, no data are available regarding their reliability in case of utilization of miniaturized devices. Herein we present a prospective multicentric study to evaluate reliability of Guy's stone score (GSS), the stone size, tract length, obstruction, number of involved calyces, and essence of stone (S.T.O.N.E.) nephrolithometry score and Clinical Research Office of the Endourological Society (CROES) score in patients treated with minimally invasive PNL.
Methods: We evaluated SFRs and CRs of 222 adult patients treated with miniaturized PNL. Patients were considered stone-free if no residual fragments of any size at post-operative unenhanced computed tomography scan. Patients demographics, SFRs, and CRs were reported and analyzed. Performances of nomograms were evaluated with the area under the curve (AUC).
Results: We included 222 patients, the AUCs of GSS, CROES score, and S.T.O.N.E. nephrolithometry score were 0.69 (95% confidence interval [CI] 0.61–0.78), 0.64 (95% CI 0.56–0.73), and 0.62 (95% CI 0.52–0.71), respectively. Regarding SFRs, at multivariate binomial logistic

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regression, only the GSS had significance with an odds ratio of 0.53 (95% CI 0.31−0.95, p=0.04). We did not find significant correlation with complications, with only a trend for GSS.
Conclusion: This is the first study evaluating nomograms in miniaturized PNL. They still show good reliability; however, our data showed lower performances compared to standard PNL. We emphasize the need of further studies to confirm this trend. A dedicated nomogram for minimally invasive PNL may be necessary.

1. Introduction

Percutaneous nephrolithotomy (PNL) is the treatment of choice for stones larger than 20 mm and for stones between 10 mm and 20 mm under specific circumstances [1,2]. Although the stone-free rate (SFR) for standard PNL (>24 Fr) is reported to be up to 94% [3], the risk of complications raised some concerns. In fact, the Percutaneous Nephrolithotomy Global Study Database maintained by the Clinical Research Office of the Endourological Society (CROES) [4] reported an overall complication rate (CR) of 20.5%. Similar results came from the registry of British Association of Urological Surgeon, reporting an overall CR of 21.3% [5]. To reduce the morbidity, in particular bleeding and extravasation, and to improve patients' quality of life, PNL has undergone many refinements in both the operating technique and utilized instruments [6−9]. Minimally invasive PNL is associated with lower CRs and shorter hospital stay compared to standard approach [10]. However, the superiority of miniaturized treatment over standard PNL in term of SFR has not been demonstrated especially for complex stones, with minimally invasive PNL being associated with prolonged operating time compared to standard approach [11]. In the last decade, a few scoring systems have been designed to predict the chances of surgical success which are of importance during standard outcome reporting as well as patients' counselling. The Guy's stone score (GSS) divides renal stones into four sub-groups (Grades I, II, III, and IV) on the basis of their complexity and depending on patient imaging characteristics [12]. The stone size, tract length, obstruction, number of involved calyces, and essence of stone (S.T.O.N.E.) nephrolithometry score is calculated using five variables (stone size, skin-to-stone distance, degree of obstruction, number of involved calyces, and stone density), assigning a score from a minimum of 5 for simplest stones to a maximum of 13 for the more complex ones [13]. A third nomogram is CROES score utilizing surgeon and patient factors (stone volume, location, prior treatments, number of stones, and case volume per year), scoring from 0 to 350. A summary of three nomograms is reported in Table 1 [12−14]. Over the years, prospective data have been published by several authors to evaluate the reliability of these nomograms [15−17]. However, no data are available regarding their validity in the field of minimally-invasive PNL. Herein we aimed to report a multicentric prospective study to assess the prognostic reliability of these nomograms in terms of SFRs and, as secondary endpoint, the CRs, in a cohort of patients who have undergone minimally invasive PNL for renal stones.

2. Patients and methods

2.1. Study population

We conducted a prospective, observational, non-interventional, multicentric study on consecutive patients who have undergone minimally invasive PNL for renal stones and who have completed at least 3 months of follow-up. The study period was from February 2019 to April 2020. All three participating centers are nominated high-volume tertiary referral centers for stone treatments and have a high-volume of greater than 60 cases of PNL per year; all procedures have been carried out by surgeons beyond their learning curve. The three centers are located in Bassano del Grappa (Italy), London (United Kingdom), and Guangzhou (China). Each center agreed to participate in the study accordingly to local ethic committee regulations. Inclusion criteria were patients >18 years, renal stones with cumulative stone diameter >20 mm or less if not suitable for retrograde surgery (including lower pole stones with steep pyelocaliceal angle). Minimally invasive PNL was characterized by a percutaneous sheath ≤22 Fr. If an active suction device was used, the procedure was named super-mini PNL despite the sheath size, which can vary from 14 Fr to 22 Fr [18].

Exclusion criteria included pregnant patients, patients with horseshoe kidneys, and patients with stones in caliceal diverticula in urinary diversion, and secondary to pyeloureteric obstruction (confirmed by MAG3 renogram). For all patients, a non-contrast-enhanced computed tomography (NCCT) of abdomen and pelvis was performed within 3 months prior to surgery. Baseline demographic and preoperative data included age, sex, American Society of Anesthesiology score, laterality, stone size (mm^2), skin-to-stone distance (mm), number of calices involved (1, 2, 3, or staghorn), mean stone density (Hounsfield unit), stone location (pelvic, lower pole, medium pole, upper pole, or multiple sites), previous treatment (extracorporeal shock wave lithotripsy, ureteroscopy, or multiple treatment), and case volume per year of each center. The stone surface (mm^2) was calculated using formula 0.785 × length × width [19]. Intra-operative data included type of puncture (ultrasound only, X-ray only, or mixed), maximum tract diameter (Fr), utilization of a device with active suction, patient's position (prone versus supine), number of puncture performed, level of upper puncture (below 12th rib, below 11th rib, or below 10th rib), and type of utilized drainage at the end of the operation (both ureteric stent and nephrostomy, only ureteric stent named as tubeless or

Table 1 Characteristics of GSS, S.T.O.N.E. nephrolithometry score, and CROES score.

Type of nomogram	Variable evaluated	Nomogram's subgroup
GSS [12]	- Grade 1: solitary stone in the mid- or lower pole; pelvis with normal anatomy	- Grade 1
	- Grade 2: solitary stone in upper pole; multiple stones with simple anatomy; any solitary stone with abnormal anatomy	- Grade 2
	- Grade 3: multiple stones with abnormal anatomy; stone in diverticulum; partial staghorn	- Grade 3
	- Grade 4: staghorn stone; any stone in patient with spina bifida or spinal injury	- Grade 4
S.T.O.N.E. nephrolithometry score [13]	- Stone size	- Low complexity [5,6]
	- Tract length	- Medium complexity [7,8]
	- Presence of obstruction	- High complexity (>9)
	- Number of calices involved	
	- Mean stone density (essence)	
CROES score [14]	- Stone volume	- Grade 1 (0—100)
	- Stone location	- Grade 2 (101—150)
	- Prior treatments	- Grade 3 (151—200)
	- Presence of staghorn	- Grade 4 (201—350)
	- Number of stones	
	- Case volume per year of the center	

GSS, the Guy's stone score; S.T.O.N.E., the stone size, tract length, obstruction, number of involved calyces, and essence of stone; CROES, the Clinical Research Office of the Endourological Society.

avoidance of any drainage named as totally tubeless). Post-operative data included length of stay (expressed as days from treatment to decision to discharge), stone biochemistry, complications within 30 days from surgery (defined accordingly to Clavien-Dindo score modified for PNL [4]), and stone-free status. For each center, GSS, S.T.O.N.E. nephrolithometry score, and CROES score have been calculated together by two surgeons, not involved with surgeries, to reduce the risk of wrong calculation.

Cut-off for residual fragments was fixed at 0 mm. Imaging modality to assess the stone-free status was NCCT 2—3 months post-operatively. Review of NCCT for confirmation of the stone-free status was completed by a fully trained radiologist not informed of surgical results. Results were compared between sub-categories according to each nomogram definition.

2.2. Surgical technique and peri-operative assessment

Each center operated according to their preferred technique; in all three centers the preferred treatment option was super-mini PNL; the caliber of the sheath may vary on the basis of the case complexity. One center (Bassano) routinely operated in supine position while the other two (Guangzhou and London) offered prone treatment. During study period, in two (Bassano and Guangzhou) out of three centers, miniaturized PNL was offered to all cases despite complexity. In one center (London) standard PNL was still chosen in more complex cases. The decision to carry out PNL with the sheath size larger than 22 Fr rather than smaller than 22 Fr was made, taking into consideration of surgeon and patient preferences. If the stone was believed not clearable in a single session with mini-PNL, a wider caliber was chosen. In all three centers, the renal punctures were carried out using combination of X-rays and ultrasounds according to the characteristics of the case.

In the study, different combinations of nephroscopes and percutaneous sheaths have been used as follows.

(a) Procedures without active suction

-Minimally invasive percutaneous set from Karl Storz (Tagerwilen, Switzerland), specifically in the configuration with 12 Fr percutaneous nephroscope and 16 Fr sheath.

(b) Procedures with active suction

-14 Fr disposable ClearPetra© sheath (Wellead, Guangzhou, China) with 7.5 Fr and 33 cm semirigid ureteroscope (Richard Wolf, Knittlingen, Germany);

-16 Fr disposable ClearPetra© sheath with 12 Fr Karl Storz percutaneous nephroscope;

-22 Fr disposable ClearPetra© sheath with 18 Fr Karl Storz percutaneous nephroscope;

-Super-mini percutaneous set from Hawk Medical Endoscopy (Guangzhou, China), including a 14 Fr sheath and a 7.5 Fr percutaneous nephroscope;

-Enhanced super-mini percutaneous set from Hawk Medical Endoscopy, including an 18 Fr sheath and a 12 Fr percutaneous nephroscope.

In all cases, Holmium-YAG laser lithotripsy was carried out using a 365 micron fiber for 7.5 Fr scopes and 550 micron fibre for thicker scopes.

2.3. Definition of outcomes

The primary outcome was evaluating the capacity of GSS, S.T.O.N.E. nephrolithometry score, and CROES score to assess the correlation with SFR and independent factors associated with SFR. An exploratory analysis about the ability of these nomograms in estimating complications was further performed.

2.4. Statistical analysis

Descriptive analysis included frequencies and proportions for categorical variables. Median and interquartile range (IQR) were reported for continuous coded variables. The Mann-Whitney *U* test was used for comparison of the continuous data and the Chi-square or Fisher's exact test for categorical data. All tests were two sided with a level of significance set at $p<0.05$.

To determine the area under the curve (AUC) predicting SFR for each nomogram, the receiver-operating curve (ROC) analysis was performed. Cut-off values were defined by the maximum Youden index value.

Univariate and multivariate binomial logistic regression models were used to assess the odds ratio (OR) with 95% confidence interval (CI) testing the relationship between the covariates and the SFRs. Covariates included all pre-operative data: age, sex, side, stone burden (mm^2), tract length (mm), degree of renal pelvic obstruction, number of calyxes involved (as per S.T.O.N.E. nephrolithometry score including 1, 2, 3, or staghorn), stone location (as per CROES score, pelvis, lower pole, mid-pole, upper pole, multiple sites), stone density (Hounsfield unit), presence of staghorn stone (as per CROES definition), number of stone, and each nomogram. In case of missing data, analysis was carried out only with complete-cases. After univariate analysis, significant factors were entered into the multivariate model, followed by backward elimination to determine the factors most associated with the achievement of a stone-free state. To determine the discrimination of the multivariate binomial logistic regression model, the AUC was further calculated. Statistical analyses were performed using RStudio Version 1.2.5001 (RStudio: Integrated Development for R. RStudio, Inc., Boston, MA, USA; URL http://www.rstudio.com/).

3. Results

A total of 222 patients fulfilled inclusion criteria and have been enrolled in the study. The median age was 54 (IQR 42—63) years. Overall, 173 patients were rendered stone-free, corresponding to a total SFR of 77.9%. A total of 25 patients have been excluded from the study: eight out of 25 patients received >22 Fr PNL (five classified as GSS 4 and three classified as GSS 3); two patients had a horseshoe kidney; two patients had urinary diversion (ileal conduit in both cases); six patients were lost at follow-up; and seven patients did not receive NCCT but ultrasound plus X-ray post-operatively in a different local hospital; therefore, their data could not be included. Table 2 shows the demographic and pre-operative data of the included patients. The median GSS was 2 with GSS 1, 2, 3, and 4 corresponding to 32.4%, 39.6%, 17.1%, and 9.5% of all cases, respectively (Table 3). Using the S.T.O.N.E. nephrolithometry score, 56.3% of patients had low complexity stones; 29.7% and 12.6% had medium and high complexity ones (median S.T.O.N.E. nephrolithometry score: 6; IQR 6—7) (Table 2

Table 2 Demographic and pre-operative data of 222 patients who have undergone minimally invasive PNL.

Variable	Total	Stone-free case	Residual stone	*p*-Value
Patient[a]	222 (100)	173 (77.9)	49 (22.1)	NA
Age[b], year	54 (42—63)	53 (42—63)	55 (47—74)	0.47
Gender[a]				0.33
Female	93 (41.9)	69 (39.9)	24 (49.0)	
Male	129 (58.1)	104 (60.1)	25 (51.0)	
Side[a]				0.45
Right	108 (48.6)	87 (50.3)	21 (42.9)	
Left	114 (51.4)	86 (49.7)	28 (57.1)	
ASA score[a]				0.367
1	98 (44.1)	78 (45.1)	20 (40.8)	
2	111 (50.0)	87 (50.3)	24 (49.0)	
3	13 (5.9)	8 (4.6)	5 (10.2)	
4	0 (0.0)	0 (0.0)	0 (0.0)	
Stone burden[b], mm^2	157 (61—372)	125 (48—337)	324 (153—588)	<0.001
Stone density[b], HU	1032 (745—1231)	1011 (727—1217)	1093 (771—1276)	0.18
Tract length[b], mm	85 (71—100)	85 (72—102)	83 (69—96)	0.16
Renal pelvic obstruction[a]				0.22
None or mild	160 (72.1)	126 (72.8)	34 (69.4)	
Moderate or severe	62 (27.9)	47 (27.2)	15 (30.6)	
Calyxes involved[a,c]				0.16
1	125 (56.3)	102 (59.0)	23 (46.9)	
2	44 (19.8)	34 (19.7)	10 (20.4)	
3	24 (10.8)	15 (8.7)	9 (18.4)	

(*continued on next page*)

Table 2 (*continued*)

Variable	Total	Stone-free case	Residual stone	*p*-Value
Multiple (staghorn)	23 (10.4)	16 (9.2)	7 (14.3)	
Stone location[a,d]				0.03
Pelvis	45 (20.3)	40 (23.1)	5 (10.2)	
Lower calyx	59 (26.6)	50 (28.9)	9 (18.4)	
Medium calyx	15 (6.8)	10 (5.8)	5 (10.2)	
Upper calyx	15 (6.8)	13 (7.5)	2 (4.1)	
Multiple sites	86 (38.7)	58 (33.5)	28 (57.1)	
Stone[a]				0.004
Single	87 (39.2)	77 (44.5)	10 (20.4)	
Multiple	135 (60.8)	96 (55.5)	39 (79.6)	
Presence of staghorn stone[a]				<0.001
Yes	54 (24.3)	31 (17.9)	23 (46.9)	
No	168 (75.7)	142 (82.1)	26 (53.1)	
Prior treatment[a]				0.34
None	181 (81.5)	137 (79.2)	44 (89.8)	
PNL	20 (9.0)	16 (9.2)	4 (8.2)	
ESWL	6 (2.7)	6 (3.5)	0 (0.0)	
Endoscopic	5 (2.3)	5 (2.9)	0 (0.0)	
Multiple	10 (4.5)	9 (5.2)	1 (2.0)	
S.T.O.N.E. nephrolithometry score[b]	6 (6—7)	6 (6—7)	7 (6—9)	<0.001
Guy's stone score[b]	2 (1—3)	2 (1—2)	3 (2—3)	<0.001
CROES nomogram[b]	211 (156—269)	218 (160—270)	169 (131—230)	0.004
CROES grade[b]	4 (3—4)	4 (3—4)	3 (2—4)	<0.001

NA, not applicable; ASA, American Society of Anesthesia; HU, Hounsfield unit; PNL, percutaneous nephrolithotomy; ESWL, extracorporeal shock wave lithotripsy; S.T.O.N.E., the stone size, tract length, obstruction, number of involved calyces, and essence of stone; CROES, the Clinical Research Office of the Endourological Society.

[a] Values are presented as *n* (%).

[b] Values are presented as median (interquartile range).

[c] Data of six patients were missing.

[d] Data of two patients were missing.

and Table 3). The median CROES score was 211 with the IQR of 156—269. Moreover, 6.8% of patients were graded as 1; 15.3% were graded 2; 23.4% and 53.2% were graded 3 and 4, respectively (Table 3). Table 4 reports peri-operative data of patients included in the study. Overall, 196 (88.3%) of patients received a super-mini PNL (with active suction).

Table 3 GSS, S.T.O.N.E. nephrolithometry score and CROES score association with SFRs and 30-day CRs.

Nephrolithometric nomogram	Patient[a], *n* (%)	SFR		30-day CR	
		n (%)	*p*-Value	*n* (%)	*p*-Value
S.T.O.N.E. nephrolithometry score			0.005		0.59
5—6	125 (56.3)	102 (81.6)		17 (13.6)	
7—8	66 (29.7)	53 (80.3)		19 (28.8)	
9—13	28 (12.6)	15 (53.6)		10 (35.7)	
GSS			<0.001		0.04
Grade 1	72 (32.4)	67 (93.1)		9 (12.5)	
Grade 2	88 (39.6)	73 (83.0)		13 (14.8)	
Grade 3	38 (17.1)	21 (55.3)		14 (36.8)	
Grade 4	21 (9.5)	12 (57.1)		10 (47.6)	
CROES system			0.007		0.02
Grade 1 (0—100)	15 (6.8)	8 (53.3)		6 (40.0)	
Grade 2 (101—150)	34 (15.3)	23 (67.6)		16 (47.1)	
Grade 3 (151—200)	52 (23.4)	38 (73.1)		11 (21.2)	
Grade 4 (201—350)	118 (53.2)	101 (85.6)		13 (11.0)	

GSS, the Guy's stone score; S.T.O.N.E., the stone size, tract length, obstruction, number of involved calyces, and essence of stone; CROES, the Clinical Research Office of the Endourological Society; SFR, stone-free rate; CR, complication rate.

[a] Data of three patients were missing.

The median access sheath diameter was 16 (IQR 14—18) Fr; 142 (64.0%) patients underwent PNL in prone position and 80 (36.0%) patients in supine position. The numbers and percentages of tubeless operations and totally tubeless operations were 70 (31.5%) and 48 (21.6%), respectively.

Correlations between peri-operative data and achievement of a stone-free state are reported in Table 2 and Table 4. Among pre-operative data (Table 2), the factors associated with SFR were stone burden ($p<0.001$), stone location ($p=0.03$), number of stone ($p=0.004$), and presence of staghorn stone ($p<0.001$). Among peri-operative data (Table 4), the tract size was associated with SFR ($p=0.002$) as well as the level of the upper puncture ($p=0.03$), and type of drainage utilized ($p=0.02$). Furthermore, the median length of stay in stone-free patients was 3 (IQR 1—4) days versus 4 (IQR 3—5) days in patients with residual fragments ($p=0.03$). The overall CR was 20.7% (46 patients out of 222). Low-degree complications occurred in 38

Table 4 Peri-operative data of 222 patients who have undergone minimally invasive percutaneous nephrolithotomy included in the study.

Variable	Total	Stone-free case	Residual stone	*p*-Value
Patient[a]	222	173 (77.9)	49 (22.1)	NA
Maximum tract diameter[b], Fr	16 (14—18)	16 (14—18)	18 (14—18)	0.002
Maximum tract diameter[a], Fr				0.003
14	85 (38.3)	72 (41.6)	13 (26.5)	
16	42 (18.9)	37 (21.4)	5 (10.2)	
18	94 (42.3)	64 (37.0)	30 (61.2)	
22	1 (0.5)	0 (0.0)	1 (2.0)	
Puncture[a]				0.14
1	199 (89.6)	157 (90.8)	42 (85.7)	
2	22 (9.9)	16 (9.2)	6 (12.2)	
3	1 (0.5)	0 (0.0)	1 (2.0)	
Active suction[a]				0.9
Yes	196 (88.3)	152 (87.9)	44 (89.8)	
No	26 (11.7)	21 (12.1)	5 (10.2)	
Level of upper puncture[a,c]				0.03
Below 12th	134 (60.4)	112 (64.7)	22 (44.9)	
Below 11th	75 (33.8)	52 (30.1)	23 (46.9)	
Below 10th	8 (3.6)	5 (2.9)	3 (6.1)	
Patient's position[a]				0.16
Prone	142 (64.0)	106 (61.3)	36 (73.5)	
Supine	80 (36.0)	67 (38.7)	13 (26.5)	
Stone biochemistry[a,d]				0.8
Calcium oxalate	150 (67.6)	116 (67.1)	34 (69.4)	
Calcium phosphate	45 (20.3)	36 (20.8)	9 (18.4)	
Urates	9 (4.1)	8 (4.6)	1 (2.0)	
Struvite	10 (4.5)	7 (4.0)	3 (6.1)	
Cystine	5 (2.3)	3 (1.7)	2 (4.1)	
Drug-related stone	1 (0.5)	1 (0.6)	0 (0.0)	
Type of drainage[a]				0.02
Stent plus nephrostomy	101 (45.5)	72 (41.6)	29 (59.2)	
Tubeless	70 (31.5)	54 (31.2)	16 (32.7)	
Totally tubeless	48 (21.6)	44 (25.4)	4 (8.2)	
Length of stay[b], day	3 (2—4)	3 (1—4)	4 (3—5)	0.03
30-day complication[a,d]				0.83
Clavien I	34 (15.3)	21 (12.1)	13 (26.5)	
Clavien II	4 (1.8)	4 (2.3)	0 (0.0)	
Clavien IIIa	3 (1.4)	2 (1.2)	1 (2.0)	
Clavien IIIb	1 (0.5)	1 (0.6)	0 (0.0)	
Clavien IVa	4 (1.8)	3 (1.7)	1 (2.0)	

NA, not applicable.

[a] Values are presented as *n* (%).

[b] Values are presented as median (interquartile range).

[c] Data of five patients were missing.

[d] Data of two patients were missing.

(17.1%) patients with Clavien-Dindo Grade I and Grade II representing 34 (15.3%) and 4 (1.8%) cases, respectively. High-degree complications occurred in 8 (3.6%) cases. In detail, 3 (1.4%) cases were scored as Grade IIIa; 1 (0.5%) case as Grade IIIb; and 4 (1.8%) cases as Grade IVa. In Table 5, complications are reported in detail.

In Table 3, we reported correlations between investigated nomograms and endpoints including the SFRs and CRs. In univariate analysis, all three scores showed significance in estimating SFRs ($p<0.001$ for GSS, $p=0.005$ for S.T.O.N.E. nephrolithometry score, and $p=0.007$ for CROES score). Looking into complications, in univariate analysis, GSS and CROES score correlated with the overall CRs ($p=0.04$ and $p=0.02$, respectively), whereas the S.T.O.N.E. nephrolithometry score did not show the same association ($p=0.59$). Binomial logistic regression analysis is reported in Table 6. At univariate analysis, all nomograms significantly correlated with SFRs; however, in multivariate analysis, only the GSS has statistical significance with the OR of 0.53 (95% CI 0.31–0.95, $p=0.04$). The AUC of the model is 0.72 (95% CI 0.70–0.76).

Analyzing the ROC curves (Fig. 1), the GSS seemed to have the best performance with an AUC of 0.69 (95% CI 0.61–0.78) followed by the CROES score with an AUC of 0.64 (95% CI 0.56–0.73), and S.T.O.N.E. nephrolithometry score with an AUC of 0.62 (95% CI 0.52–0.71) with asymptotic significance of $p<0.001$ for each. However, 95% CI of nomograms were overlapping; therefore, we cannot find superiority of a nomogram over the others. Table 7 reported the AUC, accuracy, sensitivity and specificity of the three investigated nomograms.

Table 5 Complications occurred in our study group ($n=222$) according to Clavien-Dindo classification modified for PNL.

Modified Clavien-Dindo	*n* (%)
Grade I	34 (15.3)
Pain requiring higher analgesia	21 (9.5)
Fever	9 (4.1)
Diarrhea	1 (0.5)
Self-resolving dyspnea	1 (0.5)
Clot retention requiring prolonged catheterization	1 (0.5)
Urinoma	1 (0.5)
Grade II	4 (1.8)
Fever requiring antibiotic therapy change	4 (1.8)
Grade IIIa	3 (1.4)
Hydrothorax	1 (0.5)
Displaced stent requiring repositioning under general anesthesia	1 (0.5)
Sepsis without organ failure requiring supportive therapy	1 (0.5)
Grade IIIb	1 (0.5)
Angio-embolization	1 (0.5)
Grade IVa	4 (1.8)
Sepsis requiring ICU stay	3 (1.4)
Pulmonary embolism requiring ICU stay	1 (0.5)

PNL, percutaneous nephrolithotomy; ICU, intensive care unit.

4. Discussion

The ideal nomogram should be easily applicable in daily clinical practice, have a high ability to predict SFRs and complications, and give reproducible results with low subjectivity [20]. All scoring systems have weaknesses and strengths. To date, there is no proven superiority of a nomogram over the others. Different nomograms present different characteristics, which also are influenced by the period that they have been released. In fact, they define different cut-offs for SFRs (4 mm for GSS and CROES score, and 0 mm for S.T.O.N.E. nephrolithometry score), and different imaging modalities for follow-up have been utilized (X-ray KUB for GSS and CROES score, NCCT for S.T.O.N.E. nephrolithometry score).

In the recent years, the importance of systematic and standardized reporting of outcomes after urological surgery has become evident [14,21] as the need of higher quality studies has increased. Utilization of pre-operative prognostic tools can be useful to stratify patients in different risk groups, to offer an adequate counselling, and also for research purposes. Worldwide, we are observing an increasing interest in publishing data on PNL, with 18 published articles in 2000 and 195 in 2015, corresponding to a linear increase of 279% [22]. We are also observing a rising number of PNL performed, from 6.04% in 2007 to 7.24% in 2014 [23] of all operations for stones, with minimally invasive PNL representing 33%–45% of all percutaneous procedures [24]. Therefore, aiming for a more accurate data reporting for research purposes, nephrolithometric nomograms have to be monitored to evaluate their adequacy in light of the technology advances in the field of percutaneous surgery and in the improvement of peri-operative imaging. Nowadays, several different types of miniaturized PNL have been introduced, varying in tract size, dusting and fragmentation technologies, and stones extraction techniques [7,9]. Standard and mini-PNL seem to differ in term of SFRs and this may influence nomogram performances. Several publications tried to compare the SFRs and complication rates of the two techniques; the available data do not show clear superiority of one technique over the other. Feng et al. [25] in a meta-analysis of nine Randomized Controlled Trials showed superiority of mini-PNL over standard PNL to treat 10–20 mm stones (OR 1.43; 95% CI 1.03–1.99; $p=0.03$). In case of stones larger than 2 cm, same authors did not show clear differences between techniques (OR 1.45, 95% CI 0.95–2.20, $p=0.09$), with minimally invasive PNL group associated with longer operating time. Same trials also showed lower blood transfusion rates for mini-PNL (OR 0.33; 95% CI 0.17–0.63; $p=0.007$), and other types of complications did not show significant differences.

GSS was initially described by Thomas et al. in 2011 [12], SFRs of four sub-groups were 81%, 72.4%, 35%, and 29%, respectively; the overall SFR was 62%. Authors also reported an inter-rater agreement of 0.81.

S.T.O.N.E. nephrolithometry score was introduced by Okhunov et al. in 2013 [13]. The tool was developed on data deriving from 117 patients. SFRs for low complexity stones were 94%–100%, whereas they ranged from 83% to 88% for moderate complexity and from 27% to 64% for high complexity ones.

Table 6 Univariate and multivariate binomial logistic regression analysis to assess predictors of stone-free status.

Variable	Univariate		Multivariate	
	OR (95% CI)	*p*-Value	OR (95% CI)	*p*-Value
Age[a], years	0.99 (0.97—1.01)	0.48		
Sex				
Male	1.00 (Ref.)			
Female	0.69 (0.36—1.31)	0.26		
Side				
Left	1.00 (Ref.)			
Right	1.35 (0.71—2.58)	0.36		
Stone burden[a], mm^2	0.99 (0.99—1.00)	<0.001	1.00 (0.99—1.00)	0.04
Tract length[a]	1.01 (0.99—1.02)	0.16		
Renal pelvic obstruction				
None or mild	1.00 (Ref.)			
Moderate or severe	0.83 (0.42—1.67)	0.83		
Number of calyxes involved[a]	0.75 (0.56—1.00)	0.05	1.36 (0.98—2.65)	0.21
Stone density (HU)[a]	0.99 (0.99—1.00)	0.18		
Prior treatment				
No	1.00 (Ref.)			
PNL	1.28 (0.41—4.63)	0.67		
ESWL	1.31 (0.08—NA)	0.99		
Endoscopic	1.36 (0.24—NA)	0.99		
Multiple	1.82 (0.52—54.36)	0.33		
Presence of staghorn				
No	1.00 (Ref.)			
Yes	0.25 (0.12—0.48)	<0.001	0.30 (0.11—0.72)	0.01
Number of stones				
Single	1.00 (Ref.)			
Multiple	0.32 (0.14—0.66)	0.03	0.42 (0.18—0.91)	0.03
Guy's stone score[a]	0.47 (0.33—0.67)	<0.001	0.53 (0.31—0.95)	0.04
S.T.O.N.E. nephrolithometry score[a]	0.71 (0.57—0.86)	0.001	0.95 (0.66—1.34)	0.69
CROES score[a]	1.71 (1.24—2.37)	0.001	0.89 (0.41—1.74)	0.68
AUC of the model			0.72 (0.70—0.76)	

OR, odds ratio; CI, confidence interval; HU, Hounsfield unit; PNL, percutaneous nephrolithotomy; ESWL, extracorporeal shock wave lithotripsy; S.T.O.N.E., stone size, tract length, obstruction, number of calyces, and essence of stone; CROES, Clinical Research Office of the Endourological Society; AUC, area under the curve.
[a] As continuous variable.

CROES nomogram was presented by Smith et al. in 2013 [26]. It was developed extrapolating data from 2806 patients and showed a better accuracy when compared to GSS (AUC 0.76 *vs*. 0.69, $p<0.001$).

External validation of GSS has been previously conducted by Ingimarsson et al. [27], finding significant correlation between GSS and SFR ($p=0.03$), comparable results were subsequently demonstrated by Mandal et al. [28] ($p=0.01$). Predictive role for SFR was shown also for S.T.O.N.E. nephrolithometry score by Okhunov et al. [13] ($p=0.001$). A few studies investigated also accuracy of CROES score for PNL outcomes. In fact, Sfoungaristos et al. [29] verified its reliability in 176 patients undergoing PNL, finding a good accuracy; in this study, the AUC resulted to be 0.715.

There were few studies comparing performances of these nomograms. Labadie et al. [30] showed that all three scores were statistically significant in their association with the SFR, with $p<0.05$ in all cases. At ROC analysis, AUCs were 0.634, 0.670, and 0.671 for GSS, S.T.O.N.E. nephrolithometry score, and CROES score, respectively. The same authors found that GSS and S.T.O.N.E. nephrolithometry score significantly correlated with complications. Differently, CROES score could not achieve same result. However, in this case they utilized a different criterion to define stone-free state (cut-off of 2 mm at NCCT post-operatively). In a retrospective study by Tailly et al. [17], authors utilized the same cut-off of 2 mm and found similar results on multivariate logistic regression, with an AUC of 0.629 for GSS, 0.671 for S.T.O.N.E. nephrolithometry score, and 0.646 for CROES score. Aldaqadossi et al. [31] tested the nomograms also in the pediatric population. Of the 125 patients retrospectively analyzed, all three nomograms were associated with SFRs ($p<0.001$ for all, AUC 0.70 for GSS, 0.92 for S.T.O.N.E. nephrolithometry score, and 0.78 for CROES score, respectively), but S.T.O.N.E. nephrolithometry score and CROES score nomograms were not associated with complications. In this case, a cut-off of 4 mm at NCCT post-operatively was utilized. Moreover, in a cohort of adult obese patients, Ozgor et al. [32] showed good accuracy for GSS and CROES score (AUC 0.77 and 0.84, respectively), but none of the nomograms were statistically associated with CRs. A

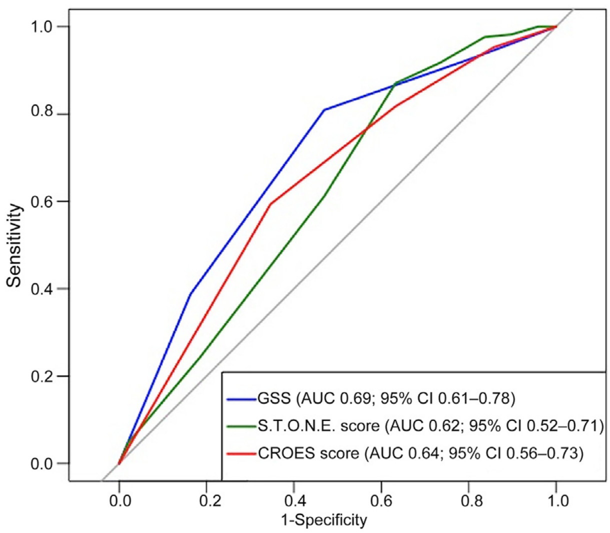

Figure 1 The receiver-operating curves for GSS, S.T.O.N.E. score and CROES score. GSS, the Guy's stone score; S.T.O.N.E., the stone size, tract length, obstruction, number of involved calyces, and essence of stone; CROES, the Clinical Research Office of the Endourological Society; AUC, the area under the curve; CI, confidence interval.

different study conducted by Choi et al. [33] evaluated the three nephrolithometric scores in tubeless PNL, and showed that only GSS was able to predict procedural success in multivariate logistic regression analysis ($p=0.001$). All these studies investigated nomograms in a standard PNL setting, but these nomograms have not been tested on miniaturized PNL before. In light of recent technological advancements, we believe these data are becoming essential. In our study, we observed similar AUCs (0.69, 0.62, and 0.64 for GSS, S.T.O.N.E. nephrolithometry score and CROES score, respectively) with those reported by aforementioned studies. However, we showed how the lower bound of AUC confidence interval remained low (0.61, 0.52, and 0.56 respectively) and this may render their accuracy not adequate. Although distribution of overall 30-day complications was significantly different considering Guy's and CROES scoring systems, since the rare occurrence, such an endpoint was not subject of investigation of the binomial logistic regression models. At the best of our knowledge, there are no studies evaluating quality of nomograms for miniaturized PNL. Our study has some limitations. This study was limited by the small sample size. One center (London) opted for standard PNL in case of very complex case; therefore, it may influence the results (although GSS 3 and GSS 4 represented 22% of all our cases). Potentially, this can limit our study's capacity of adequately assessing nomograms for more complex stones, but at the same time, it underlines the need of considering a modified nomogram for mini-PNL, if certain stones are believed not suitable for miniaturized procedures. We also acknowledge that PNL in prone and supine positions may bring different results. However, in our study, we could not observe significant differences in term of SFRs between the two techniques ($p=0.16$). Therefore, we decided to incorporate both types together. Additionally, a practical-to-use nomogram should be adaptable to PNL in all positions; these reasons determined the choice of both prone- and supine-PNL in the same study. Our aim was not to criticize the existing nomograms. However, we underline that so far, their performances for miniaturized PNL are not published, and this represents a strength of this study. We also have to underline that majority of patients included in this study were offered super-mini PNL (88.3% of all cases); therefore, results of mini-PNL without active suction devices should be potentially different and further investigations may be necessary.

We encourage further studies to confirm our data; we also believe that percutaneous surgery may need a modernized nomogram to predict SFR and complications after minimally invasive PNL. We present the first multicentric prospective study to evaluate quality of nephrolithometric nomograms in miniaturized PNL. GSS, S.T.O.N.E. nephrolithometry score and CROES score still show good reliability; however, our data seem to suggest that their performances are lower compared to standard PNL to predict SFRs and even poorer to predict

Table 7 GSS, S.T.O.N.E. nephrolithometry score and CROES score performances.

Parameter	GSS	S.T.O.N.E. nephrolithometry score	CROES score
AUC (95% CI)	0.69 (0.61—0.78)	0.62 (0.52—0.71)	0.64 (0.56—0.73)
Accuracy (95% CI)	0.75 (0.50—0.81)	0.76 (0.61—0.81)	0.61 (0.55—0.77)
Best threshold	2.5	7.5	202
Sensitivity (95% CI)	0.81 (0.75—0.88)	0.87 (0.62—0.98)	0.59 (0.53—0.86)
Specificity (95% CI)	0.53 (0.41—0.68)	0.37 (0.18—0.61)	0.65 (0.31—0.78)
NPV (95% CI)	0.44 (0.29—0.55)	0.45 (0.31—0.71)	0.32 (0.27—0.47)
PPV (95% CI)	0.86 (0.83—0.93)	0.83 (0.80—0.86)	0.86 (0.80—0.91)

GSS, the Guy's stone score; S.T.O.N.E., the stone size, tract length, obstruction, number of involved calyces, and essence of stone; CROES, the Clinical Research Office of the Endourological Society; AUC, the area under the curve; CI, confidence interval; NPV, negative predictive value; PPV, positive predictive value.

complications. Thus, different clinical prediction rules could be highlighted among these scores. We believe that further studies are required to confirm these data.

5. Conclusion

This document represents the first study evaluating reliability of nephrolithometric nomograms for minimally invasive PNL. Our data may suggest that their accuracy is slightly reduced, if compared to standard PNL. We emphasize the need of further studies to confirm this trend. A dedicated nomogram for minimally invasive PNL may be necessary.

Author contributions

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Conflicts of interest

The authors declare no conflict of interest.

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