

# Nomogram for predicting the likelihood of postoperative surgical complications in patients treated with partial nephrectomy: a prospective multicentre observational study (the RECORD 2 project)

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## Objective

To identify meaningful predictors and to develop a nomogram of postoperative surgical complications in patients treated with partial nephrectomy (PN).

## Patients and Methods

We prospectively evaluated 4308 consecutive patients who had surgical treatment for renal tumours, between 2013 and 2016, at 26 Italian urological centres (RECORD 2 project). A multivariable logistic regression for surgical complications was performed. A nomogram was created from the multivariable model. Internal validation processes were performed using bootstrapping with 1000 repetitions.

## Results

Overall, 2584 patients who underwent PN were evaluated for the final analyses. The median (interquartile [IQR]) American Society of Anesthesiologists (ASA) score was 2 (2–3). In all, 72.4% of patients had clinical T1a (cT1a) stage tumours. The median (IQR) Preoperative Aspects and Dimensions Used for an Anatomical (PADUA) score was 7 (6–8). Overall, 34.3%, 27.7%, 38% of patients underwent open PN (OPN), laparoscopic PN (LPN), and robot-assisted PN (RAPN). Overall and major postoperative surgical complications were recorded in 10.2% and 2.5% of patients, respectively. At multivariable analysis, age, ASA score, cT2 vs cT1a stage, PADUA score, preoperative anaemia, OPN and LPN vs RAPN, were significant predictive factors of postoperative surgical complications. We used these variables to construct a

nomogram for predicting the risk of postoperative surgical complications. At decision curve analysis, the nomogram led to superior outcomes for any decision associated with a threshold probability of >5%.

## Conclusion

Several clinical predictors have been associated with postoperative surgical complications after PN. We used this

information to develop and internally validate a nomogram to predict such risk.

## Keywords

complications, nephron-sparing surgery, nomogram, partial nephrectomy, renal cell carcinoma, robot-assisted partial nephrectomy

## Introduction

According to the latest AUA guidelines, partial nephrectomy (PN) should be preferred over radical nephrectomy (RN) for localised tumours, regardless of the surgical approach [1]. In fact, PN has comparable oncological outcomes with better preservation of renal function and a lower rate of long-term cardiovascular events compared to RN [2,3]. Nevertheless, PN is a technical challenging procedure. Surgical complications are a prominent concern of PN, as they have been reported in up to 30% of cases [4,5]. Major surgical complications are also frequent (3–6% of cases) and can be potentially life-threatening [6].

Although the urological community expresses a general consensus that the perioperative surgical risks are justified by the theoretical long-term favourable outcome compared to RN, the risk/benefit ratio of PN is not only related to the patients' and tumour's clinical characteristics, but also with the surgeon's experience with different approaches [7]. A careful assessment of these features is paramount and should drive treatment decision-making for patients with renal tumours. A personalised counselling tool predicting surgical complications in patients suitable for PN has not been developed to date.

The aims of the present study were as follows: (i) to define the incidence, severity and predictors of postoperative surgical complications after PN relying on a rigorous prospectively recorded web-based database from a national collaborative project, and (ii) to generate a surgical nomogram to predict the likelihood of postoperative surgical complications after PN.

## Patients and Methods

The Italian REgistry of COnservative and Radical surgery for cortical renal tumour Disease (RECORD 2 project) is a prospective observational multicentre project promoted by the Italian Society of Urology (SIU). Overall, 4325 consecutive patients who underwent renal surgery for cortical renal tumours at 26 Italian urological centres, between 1 January 2013 and 31 December 2016, were included. Of these, 2584 patients underwent PN and 1712 RN, whilst 29 patients had

missing data. Only the 2584 patients who underwent PN were included in the study and formed the analytical cohort.

An online central data server was generated and centrally controlled to limit missing or wrong data inputs. All data of patients undergoing surgery were prospectively recorded by medical doctors. The database includes six main folders: (i) anthropometric and preoperative data; (ii) imaging, indications (elective, relative and absolute) and comorbidities; (iii) intraoperative data; (iv) postoperative data; (v) histological analysis; and (vi) follow-up. Comorbidity status was evaluated using the Charlson Comorbidity Index (CCI), physical status by the American Society of Anesthesiologists (ASA) classification system, and performance status by the Eastern Cooperative Oncology Group (ECOG) score. Surgical indications were defined as elective (unilateral lesion with healthy contralateral kidney), relative (presence of diabetes, hypertension or lithiasis that could potentially affect kidney function in the future), and absolute (bilateral tumours, multiple tumours, moderate-to-severe chronic kidney disease or tumours involving an anatomically or functionally solitary kidney). The Preoperative Aspects and Dimensions Used for an Anatomical (PADUA) score was calculated to assess the nephrometry complexity of each case [8]. Centre caseload was defined as the number of PNs per year.

Surgical postoperative complications were defined as any postoperative event caused by surgery until the 30th postoperative day, altering the normal postoperative course and/or delaying discharge. The severity of complications was graded according to the modified Clavien–Dindo classification [9]. Acute kidney injury (AKI) was defined as an increase in serum creatinine to  $\geq 1.5$ -times baseline. The recommendations for the development and implementation of reporting and grading of complications after PN of the European Association of Urology (EAU) panel were applied [10].

## Statistical Analysis

A univariate and multivariable logistic regression for postoperative surgical complications were performed. The

area under the receiving operator characteristic (ROC) curves (AUC) was used to quantify predictive discrimination. Different ROC curves using the same set of observations were compared to assess how comorbidities, nephrometry and surgical parameters could affect the outcome within the multivariable model (*roccomp* function) [11]. A nomogram was generated from the statistically significant variables at multivariable logistic regression. Internal validation processes were performed using bootstrapping with 1000 repetitions. Calibration was assessed by comparing the predicted probabilities with the actual observed proportions on 1000 bootstrap resamples. A decision curve analysis was applied to determine whether the clinical value of the newly derived model increased the net benefit over a realistic range of threshold probabilities [12]. Statistical significance was set at  $P < 0.05$ . All tests were two-sided. Analyses were carried out using STATA, version 14.1 (StataCorp LP, College Station, TX, USA).

## Results

### Patient Characteristics and Surgical Features

The preoperative clinical characteristics and the univariate analysis of postoperative surgical complications are summarised in Table 1. The cohort comprised 64.7% males. The median (interquartile range [IQR]) age was 64.6 (55–72) years. The median (IQR) CCI score was 1 (0–2). A clinical T1a (cT1a), cT1b and cT2 stage was reported in 72.4%, 24.3% and 3.3% of the patients, respectively. The median (IQR) PADUA score was 7 (6–8), and scores  $\geq 10$  were registered in 15.9% of patients. Patients had relative and absolute indication for surgery in 12.1% and 3.4% of patients, respectively. The surgical features are summarised in Table 2. Patients were treated in centres performing a median (IQR) of 63 (41–84) PNs/year: 1876 (72.6%), 468 (18.1%) and 240 (9.3%) patients were treated in centres performing  $>50$ , 25–50 and  $<25$  PNs/year, respectively. Open PN (OPN), laparoscopic PN (LPN) and robot-assisted PN (RAPN) were planned in 886 (34.3%), 717 (27.7%) and 981 (38%) patients, respectively. Off-clamp procedures were performed in 47.6% of the patients, and an enucleative strategy of resection was adopted in 36.1%. Conversion to an open approach was registered in seven of 717 (0.9%) LPNs and three of 981 (0.3%) RAPNs.

### Postoperative Surgical Complications

Postoperative surgical complications were reported in 264 (10.2%) patients. Of these, 1.9% were Clavien–Dindo Grade I, 5.9% Grade II, 1.1% Grade IIIa, 1.2% Grade IIIb, and 0.2% Grade IVa. Overall, 8.5% of the patients required postoperative treatment for bleeding: 7.1% were treated

with transfusions [median (IQR) units transfused 2 (1–2)], 0.9% with superselective embolisation, and 0.5% with surgical re-intervention. Persistent urinary leakage was diagnosed in 1.1% of patients requiring prolonged maintenance of the drain and its manipulation in 0.2%, whilst 0.9% required urinary stenting or nephrostomy tube insertion. Two (0.1%) patients who underwent OPN required re-intervention for bowel obstruction. Four (0.2%) patients who underwent OPN required drain positioning for postoperative pneumothorax. Postoperative AKI managed with pharmacological treatment was recorded in 2.2% of patients.

### Multivariable Models for Postoperative Surgical Complications

At the full multivariable model, age (odds ratio [OR] 1.01, 95% CI 1.00–1.03;  $P = 0.03$ ), ASA score (OR 1.28, 95% CI 1.00–1.62;  $P = 0.046$ ), cT2 vs cT1a stage (OR 2.03, 95% CI 1.13–3.67;  $P = 0.01$ ), PADUA score (OR 1.16, 95% CI 1.05–1.25;  $P = 0.001$ ), preoperative anaemia (OR 2.20, 95% CI 1.58–3.05;  $P < 0.001$ ), OPN (OR 2.87, 95% CI 1.94–4.27;  $P < 0.001$ ) and LPN (OR 1.73, 95% CI 1.13–2.64;  $P = 0.01$ ) vs RAPN, were significant predictive factors of postoperative surgical complications, whilst CCI and ECOG scores, surgical indication, baseline creatinine, centre caseload, and enucleoresective strategy were not (Table 3). The full model had an ROC AUC of 73.1%.

The ROC AUC slightly decreased if the comorbidity and performance status scores (72.4%,  $P = 0.15$ ) and if the cT stage and PADUA score (71.1%,  $P = 0.09$ ) were removed from the full model (Fig. 1a,b). In comparison with the full model, a reduced model without surgical approach and resection strategy reduced the ROC AUC to 69.6% ( $P < 0.001$ ) and decreased it to 68.7% ( $P < 0.001$ ) if centre caseload was also removed (Fig. 1c,d).

### Surgical Nomogram

The final nomogram included age, ASA score, preoperative anaemia, surgical indication, cT stage, PADUA score, and surgical approach (Fig. 2a). The ROC AUC of the model was 72.4%. After a bootstrapping with 1000 repetitions, the model reported a bias of  $-0.05$  and a standard error of 0.607 (95% CI  $-7.13$ ,  $-4.75$ ). Calibration plot focusing on nomogram performance characteristics exhibited a slight underestimation when predicted postoperative surgical complication risk was compared to  $>50\%$  observed events (Fig. 2b). At the decision curve analysis, the nomogram led to superior outcomes for any decision associated with a threshold probability of  $>5\%$  and showed a meaningful net benefit of the model compared to PADUA score in threshold probabilities between 5% and 30% (Fig. 2c).

**Table 1** Preoperative characteristics of the 2584 patients treated with PN for renal tumours and univariate analysis of postoperative surgical complications.

Preoperative characteristics (n = 2584)	Descriptive analysis		Univariate analysis for postoperative complications	
	Value		OR (95% CI)	P
Gender, n (%)				
Male	1671 (64.7)		1.27 (0.97–1.65)	0.08
Female	913 (35.3)		1.00 (reference)	–
Age, years, median (IQR)	64.6 (54.9–72.2)		1.03 (1.02–1.04)	<0.001
BMI, kg/m <sup>2</sup> , median (IQR)	25.8 (23.7–28.7)		0.98 (0.95–1.01)	0.19
ECOG score				
Median (IQR)	0 (0–1)		1.14 (1.08–1.13)	<0.001
≥1, n (%)	737 (28.5)		1.73 (1.33–2.27)	<0.001
ASA score				
Median (IQR)	2 (2–3)		1.97 (1.61–2.42)	<0.001
≥3, n (%)	700 (27.1)			
CCI score, median (IQR)	1 (0–2)		1.19 (1.10–1.29)	<0.001
AA-CCI score,	4 (2.5–5)		1.18 (1.11–1.26)	<0.001
Surgical indication, n (%)				<b>0.02</b>
Elective	2122 (82.1)		1.00 (reference)	
Relative	372 (14.4)		1.12 (0.78–1.60)	0.55
Imperative	90 (3.5)		2.27 (1.27–4.07)	<b>0.006</b>
Tumour side, n (%)				
Right	1316 (50.9)		1.12 (0.87–1.45)	0.39
Left	1268 (49.1)		1.00 (reference)	
cT stage, n (%)				<b>0.001</b>
T1a	1872 (72.4)		1.00 (reference)	
T1b	628 (24.3)		1.17 (0.87–1.58)	0.29
T2	84 (3.3)		2.78 (1.61–4.81)	<0.001
Multiple ipsilateral lesions, n (%)	152 (5.9)		1.61 (0.94–2.73)	0.08
Tumour growth pattern, n (%)				0.54
≥50% Exophytic	1444 (55.9)		1.00 (reference)	
<50% Exophytic	933 (36.1)		1.14 (0.87–1.50)	0.34
Entirely endophytic	207 (8.0)		1.21 (0.76–1.94)	0.42
Tumour location relative to the polar line (PL), n (%)				<b>0.009</b>
Entirely above PL	1505 (58.2)		1.00 (reference)	
≤50% crosses PL	616 (23.8)		1.32 (0.90–1.95)	0.15
>50% crosses PL	463 (17.9)		1.55 (1.17–2.05)	<b>0.002</b>
Nearness to the collecting system, n (%)				<0.001
≥7	1332 (51.5)		1.00 (reference)	
>4 but <7	884 (34.2)		2.16 (1.57–2.96)	<0.001
≤4	368 (14.2)		1.58 (1.10–2.27)	<b>0.01</b>
PADUA score, median (IQR)	7.0 (6.0–8.0)		1.16 (1.07–1.26)	<0.001
R.E.N.A.L. score, median (IQR)	6.0 (5.0–7.0)		1.18 (1.09–1.26)	<0.001
PADUA score complexity index, n (%)				<b>0.001</b>
6–7	1274 (49.3)		1.00 (reference)	
8–9	900 (34.8)		1.37 (1.02–1.84)	<b>0.035</b>
≥10	410 (15.9)		1.91 (1.35–2.69)	<0.001
Baseline haemoglobin, g/dL, median (IQR)	14.2 (13.2–15.1)		0.72 (0.66–0.78)	<0.001
Preoperative anaemia <sup>†</sup> , n (%)	326 (12.0)		3.06 (2.28–4.13)	<0.001
Baseline creatinine, mg/dL, median (IQR)	0.9 (0.8–1.0)		1.81 (1.39–2.39)	<0.001
Baseline eGFR, mL/min/1.73 m <sup>2</sup> , median (IQR)	85.8 (69.9–100.4)		0.99 (0.98–0.99)	<0.001

AA-CCI, age-adjusted CCI; BMI, body mass index; eGFR, estimated GFR; R.E.N.A.L. nephrometry score, consists of (R)adius (tumour size as maximal diameter), (E)xophytic/endophytic properties of the tumour, (N)earness of tumour deepest portion to the collecting system or sinus, (A)nterior (a)/posterior (p) descriptor and the (L)ocation relative to the polar line. <sup>†</sup>Anaemia was defined as haemoglobin concentration under the threshold of 12 and 13 g/dL in women and men, respectively. Values in bold are statistically significant.

## Discussion

PN is a complex surgical intervention and the prediction of surgical complication rate, in addition to the oncological and functional outcomes, is paramount to assess the risk/benefit ratio of PN compared to RN [13,14]. In our present study, the overall postoperative surgical complication rate was 10.2% and the major surgical postoperative complication rate was

2.5%. These results represent a further demonstration of the increasing safety of this procedure over time and slightly exceed the perioperative results of the Italian registry of conservative surgery for renal tumours (RECORD 1 project) from 2008 to 2012, which reported an overall and major complication rate of 13.1% and 3.5%, respectively [4]. The overall and Clavien–Dindo Grade III complication rate reported in the present study was also lower compared to

**Table 2** Intraoperative characteristics of the 2584 patients treated with PN for renal tumours and univariable analysis for postoperative surgical complications.

Intraoperative characteristics( <i>n</i> = 2584)	Descriptive analysis		Univariate analysis for postoperative complications	
	Value		OR (95% CI)	<i>P</i>
OPN, <i>n</i> (%)	886 (34.3)		3.74 (2.67–5.23)	<b>&lt;0.001</b>
Transperitoneal	146 (16.5)			
Retroperitoneal	740 (83.5)			
LPN, <i>n</i> (%)	717 (27.7)		1.71 (1.16–2.52)	<b>0.01</b>
Transperitoneal	443 (61.8)			
Retroperitoneal	274 (38.2)			
RAPN, <i>n</i> (%)	981 (38.0)		1.0 (reference)	
Transperitoneal	847 (86.3)			
Retroperitoneal	134 (13.7)			
Centre caseload, <i>n</i> , median (IQR)	63 (41–84)		1.02 (1.01–1.03)	<b>&lt;0.001</b>
Type of resection, <i>n</i> (%)				
Enucleation	934 (36.1)		1.00 (reference)	
Standard PN	1650 (63.9)		1.95 (1.45–2.64)	<b>&lt;0.001</b>
Haemostatics on tumour renal bed, <i>n</i> (%)				
Application	2176 (84.2)		1.00 (reference)	0.55
No application	408 (15.8)		1.10 (0.79–1.56)	
Renorrhaphy on tumour renal bed, <i>n</i> (%)				
Used	2191 (84.8)		1.00 (reference)	0.09
Not used	393 (15.2)		1.39 (0.94–2.06)	
Pedicle clamping, <i>n</i> (%)				
On-clamp	1353 (52.4)		1.00 (reference)	
<i>En bloc</i>	301 (22.2)			
Arterial	1052 (87.8)			
Off-clamp	1231 (47.6)		1.11 (0.85–1.43)	0.45

*P* values in bold statistically significant.

those of the national database of the BAUS reporting an overall complication rate of 17.8% and a Clavien–Dindo Grade  $\geq$  IIIa complication rate of 5% in 1044 patients treated with PN at 10 institutions from 2001 to 2012 [15]. Indeed, the higher rate of complications in that series could be related to the different era of patients' accrual and to the lower rate of minimally invasive PNs compared to our present study (41.5% vs 65.7%). Larcher et al. [5] reported from the Surveillance, Epidemiology, and End Results (SEER) Medicare registry an overall complication rate of 37%, a transfusion rate of 11%, and AKI in 5.8% of the cases in almost 2000 patients treated with PN. The older age and the higher rate of comorbidities of Medicare beneficiaries together with the different characteristics of the healthcare providers tracked in a population-based dataset and the different surgical era can explain such a discrepancy.

We constructed a multivariable model to predict the risk of developing postoperative surgical complications after PN. Age, baseline haemoglobin, cT stage, PADUA score and planned surgical approach were significant predictive factors of postoperative surgical complications, and therefore included in the model. As for patients performance status and its impact on the safety of PN, three different scores were included in the full multivariable model, but, interestingly, there was a trend towards significance only for two of them (ASA score [ $P = 0.046$ ] and ECOG score

[ $P = 0.07$ ]), whilst the most accurate CCI failed to reach significance at multivariable analysis. Indeed, the development of a new proper comorbidity scale to specifically predict the outcomes after renal surgery would be helpful for patient counselling.

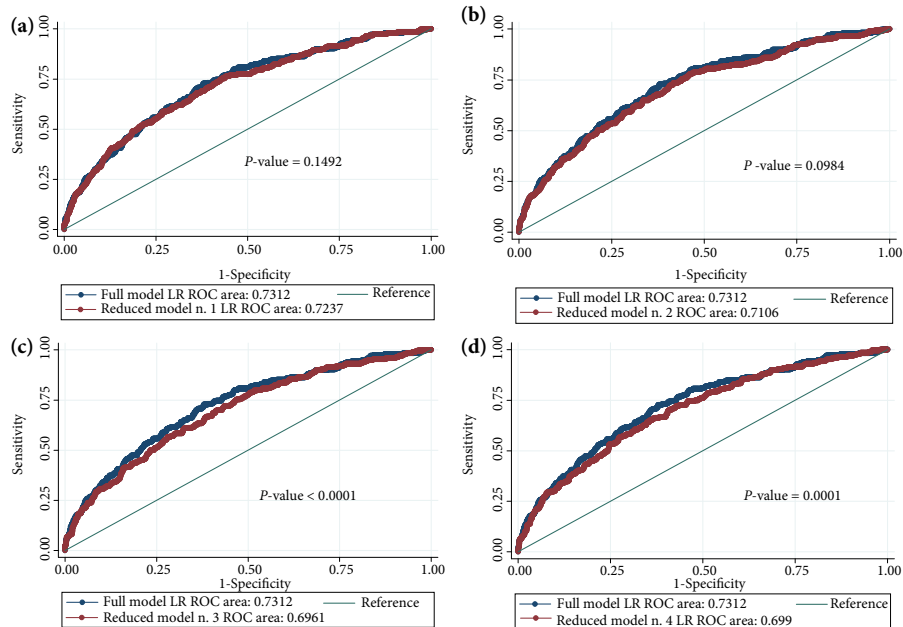
Patients with cT2 tumours had more than double the risk of developing surgical complications compared to those with cT1a tumours, whilst cT1a and cT1b tumours had a comparable rate of surgical complications ( $P = 0.76$ ). Indeed, the surgical feasibility of PN in patients with cT1b disease has been reported by several authors [16,17]. A recent report suggests that PN should not compromise the oncological outcome in patients with  $>7$  cm renal tumours even when performed with a robot-assisted approach [18]. However, most of the surgical series comparing PN with RN reported a significantly higher blood loss and complication rate in patients treated by PN [19–22]. The cT stage should be carefully considered together with the nephrometry features of the tumour: in our present study, each point increase in the PADUA score determined a significant increase risk of 13% of developing surgical postoperative complications. The PADUA score has been shown to predict the risk of perioperative complications in patients who underwent OPN in series including mostly patients with  $<4$  cm renal tumours [8,23]. This was confirmed also in the present more comprehensive study including patients treated with

**Table 3** Multivariable logistic regression analyses of postoperative surgical complications adjusting for preoperative and surgical variables in the 2584 patients treated with PN for renal tumours.

Multivariate logistic regression analysis for postoperative surgical complications															
	Full model			Reduced model no. 1			Reduced model no. 2			Reduced model no. 3			Reduced model no. 4		
	OR (95% CI)	P		OR (95% CI)	P		OR (95% CI)	P		OR (95% CI)	P		OR (95% CI)	P	
Age (continuous)	1.01 (1.00–1.03)	0.034		1.02 (1.01–1.03)	0.001		1.01 (0.99–1.02)	0.11		1.01 (1.00–1.02)	0.02		1.01 (1.00–1.03)	0.02	
ASA score (continuous)	1.28 (1.00–1.62)	0.046					1.28 (1.00–1.62)	0.04		1.48 (1.17–1.86)	<0.001		1.44 (1.13–1.81)	0.002	
ECOG score (continuous)	1.21 (0.98–1.47)	0.071					1.21 (0.99–1.47)	0.07		1.13 (0.93–1.38)	0.19		1.15 (0.94–1.41)	0.15	
CCI score (continuous)	1.01 (0.92–1.12)	0.733					1.02 (0.92–1.11)	0.80		1.03 (0.93–1.14)	0.59		1.03 (0.93–1.13)	0.56	
Surgical indication		0.66						0.68			0.47			0.36	
Elective	1.00 (ref.)			1.00 (ref.)			1.00 (ref.)			1.00 (ref.)			1.00 (ref.)		
Relative	0.79 (0.51–1.21)	0.28		0.82 (0.54–1.25)	0.36		0.87 (0.57–1.32)	0.52		0.70 (0.47–1.07)	0.11		0.74 (0.52–1.14)	0.17	
Absolute	1.48 (0.80–2.73)	0.22		2.11 (1.18–3.78)	0.01		1.49 (0.81–2.75)	0.19		1.56 (0.85–2.87)	0.15		1.59 (0.86–2.93)	0.13	
cT stage		0.04			0.03						0.04			0.02	
T1a	1.00 (ref.)			1.00 (ref.)						1.00 (ref.)			1.00 (ref.)		
T1b	1.17 (0.85–1.58)	0.33		1.18 (0.86–1.60)	0.30					1.16 (0.85–1.58)	0.76		1.17 (0.86–1.60)	0.30	
T2	2.03 (1.13–3.67)	0.01		2.12 (1.18–3.79)	0.01					2.23 (1.24–4.00)	0.01		2.22 (1.24–3.98)	0.01	
PADUA score (continuous)	1.16 (1.05–1.25)	0.001		1.15 (1.03–1.25)	0.002					1.18 (1.08–1.28)	<0.001		1.17 (1.07–1.27)	<0.001	
Preoperative anaemia	2.20 (1.58–3.05)	<0.001		2.34 (1.69–3.24)	<0.001		2.29 (1.66–3.16)	<0.001		2.29 (1.66–3.16)	<0.001		2.27 (1.64–3.14)	<0.001	
Baseline creatinine (continuous)	1.26 (0.92–1.72)	0.14		1.36 (1.00–1.83)	0.04		1.23 (0.90–1.67)	0.19		1.19 (0.87–1.61)	0.27		1.28 (0.87–1.75)	0.12	
Centre caseload (PNs/year)	0.993 (0.98–0.997)	0.278		0.99 (0.99–1.00)	0.27		0.99 (0.99–1.00)	0.57		0.99 (0.99–1.00)	0.001				
Surgical approach		<0.001			<0.001			<0.001			<0.001				
OPN	2.87 (1.94–4.27)	<0.001		3.10 (1.20–2.76)	<0.001		3.08 (2.07–4.58)	<0.001							
LPN	1.73 (1.13–2.64)	0.011		1.81 (1.20–2.75)	0.005		1.72 (1.12–2.63)	0.01							
RAPN	1.00 (ref.)			1.00 (ref.)			1.00 (ref.)								
Standard PN vs SE	1.02 (0.72–1.45)	0.91		1.04 (0.73–1.47)	0.53		1.12 (0.79–1.60)	0.52							

The reduced model no. 1 excludes the comorbidity and physical status scores from the regression analysis. The reduced model no. 2 excludes the PADUA score and cT stage from the regression analysis. The reduced model no. 3 excludes the surgical approach and technique from the regression analysis. The reduced model no. 4 excludes the surgical approach and technique from the regression analysis. SE, simple enucleation.

**Fig. 1 (a–d)** Comparison of ROC AUCs of full vs reduced logistic regression (LR) models. **(a)** Comparison of the full model vs the reduced model no. 1 excluding the CCI, ASA and ECOG scores from the regression analysis. **(b)** Comparison of the full model vs the reduced model no. 2 excluding the PADUA score and cT stage from the regression analysis. **(c)** Comparison of the full model vs the reduced model no. 3 excludes the surgical approach from the regression analysis. **(d)** Comparison of the full model vs the reduced model no. 4 excludes the surgical approach and technique from the regression analysis.



minimally invasive approaches and for cT1b–T2 renal tumours.

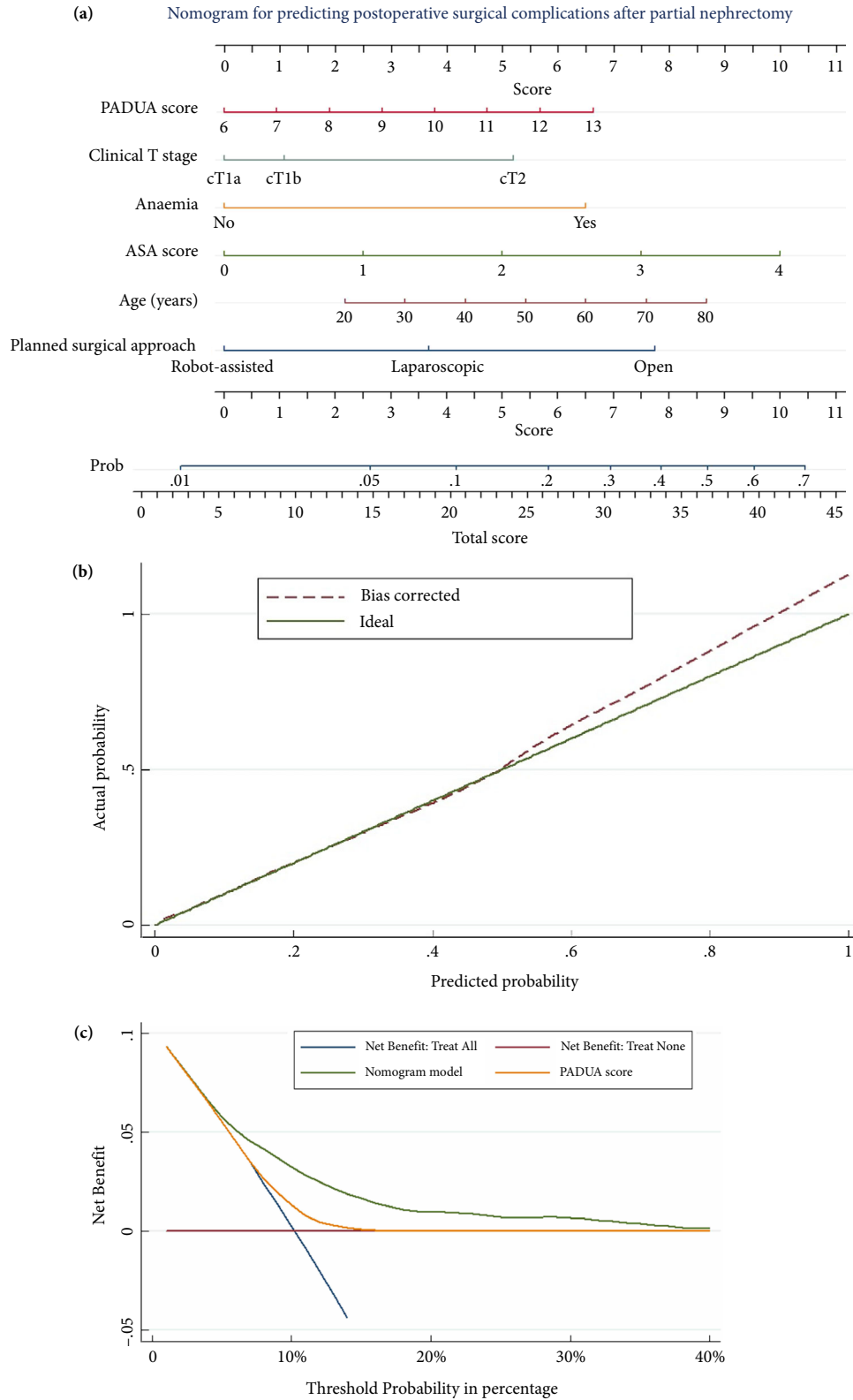
As for centre expertise and the ways in which surgery can be performed, it was not the centre caseload, but the surgical approach that independently correlated with a reduction of surgical complications. In fact, OPN and LPN compared to RAPN were the most meaningful surgical predictors of postoperative surgical complications. However, centre expertise and surgical approach are tightly interconnected in our present study: amongst the 16 of 26 centres where the robotic system was available, 12 conducted >50 PNs/year. Conversely, the surgical technique of tumour resection lost significance at multivariable analysis. Nevertheless, the surgical variables had the strongest impact on postoperative surgical complications in our multivariable model. Their exclusion led to a loss of clinical significance of the model (AUC 73.1% vs 68.7%;  $P < 0.001$ ). A possible explanation of these results is attributable to the benefits of minimally invasive surgery and the improved dexterity and vision of the robotic system, which allows a more precise dissection, careful haemostasis, and renal reconstruction with a shorter learning curve compared to laparoscopy [24]. Therefore, the surgical approach might have a greater impact on predicting the likelihood of surgical complications than the surgical technique and centre caseload.

Interestingly, the absolute indication was not a significant predictor of postoperative surgical complications in the full

model. This finding is consistent also with other multicentre [4] and high-volume centre [25] series. Indeed, surgeons are also often enticed to treat complex renal masses with a conservative strategy in patients with imperative indications. However, this highly challenging procedure is often performed in high-volume centres by very experienced surgeons: this might explain why the surgical indication was not a significant predictor of surgical complications at multivariable analysis in our present series. However, surgical indication did not reach significance even in the multivariable reduced model no. 4, which excluded surgical parameters and centre volume, but it did in the multivariable model no. 2, which excluded comorbidity and performance status scores. This could be related to the not uncommon presence of comorbidities in patients with impaired renal function due to medical reasons. Indeed, further studies are needed to better address this point and PN in patients with absolute indications remains an extremely challenging procedure.

Nomograms provide a numerical estimation of risk in the form of a probability based on several patient, tumour and surgical characteristics, and they are currently considered the most accurate tool to predict outcomes after surgical treatment. Numerous similar models have been published for urological malignancies to predict oncological outcomes [26–28], for specific treatment decision-making [24,29], and to assess the risk of surgical complications [30,31]. Internal bootstrapping was then performed to assess whether the

**Fig. 2** (a) Surgical nomogram for predicting postoperative surgical complications in patients undergoing PN for renal tumours. (b) Calibration plot of the actual vs predicted probability of the surgical nomogram for predicting postoperative surgical complications evaluated by 1000 bootstrap resamples. (c) Decision curve analysis for the evaluation of the clinical net benefit using the surgical nomogram and PADUA score for detecting postoperative surgical complications.





observed probability in 1000 resamples of the cohort was consistent with the prediction of the nomogram constructed using the entire cohort. The calibration plot showed an overlap of the predicted and observed probability of the surgical nomogram revealing a clinical meaningfulness of the nomogram when the observed/predicted risk was <50%. Furthermore, the decision curve analysis showed that the statistical model would improve the clinical decision-making when the predicted risk was >5%.

Despite a nomogram having been previously developed to assess the risk of complications after PN [5], the present study adds a nephrometry score to the model and describes carefully all postoperative complications including their grade. A predictive tool, such as this, can enable clinicians to evaluate the risk of postoperative surgical complications and might allow more accurate risk stratification on each individual case before treatment.

Despite the strengths, the present study is not devoid of limitations. First, we could not determine the experience and the learning curve of each surgeon therefore the centre caseload of PNs per year, was chosen as a surgical experience surrogate. Thus, our nomogram should be interpreted in light of the lack of specific knowledge on the treating surgeon's experience and skills in PN, and future studies considering this variable as a predictor of surgical complications are warranted to confirm its impact on key PN outcomes. A conservative vs radical treatment and an enucleative vs standard PN resection were performed according to the surgeons' preference. Minimally invasive approaches were performed according to the centre availability and to the preference of the surgeons that might prefer an open approach for the management of complex renal masses despite the availability of a robotic platform. Another potential drawback of the present study is the lack of external validity of the constructed nomogram. The nomogram should also be tested on other multicentre international cohorts, as our present findings might not be entirely generalisable to all patients undergoing PN. However, the internal validation was performed on the largest nation-based prospective database on PN available to date. Indeed, the high-quality report of outcomes was guaranteed by the rigorous control of data prospectively inserted on the Internet-based platform only by medical doctors from the participating centres. Finally, the present nomogram is not meant to guide the decision to perform PN vs RN in individual patients with localised renal masses but rather to provide an estimate of the likelihood of postoperative surgical complications according to specific patient-, tumour- and surgery-related variables to assist clinical decision-making in everyday practice.

The present study offers several opportunities for future research in this field. Indeed, multicentre prospective studies should (i) provide external validation of our nomogram in

different clinical scenarios; (ii) develop a novel physical status score specific for PN to assess the real impact of those comorbidities that affect perioperative outcome in patients treated with conservative surgery; and (iii) integrate our nomogram in a more comprehensive decision-making tool to individualise selection strategy of PN vs RN in patients eligible for surgical treatment with PN.

## Conclusions

Surgical complications are a not-negligible aspect to consider in the treatment decision-making for patients with localised renal tumours undergoing PN, with a 10.2% and 2.5% rate of overall and major postoperative surgical complications, respectively. We developed a surgical nomogram including: age, ASA score, ECOG score, preoperative anaemia and creatinine, surgical indication, cT stage, PADUA score, and surgical approach, to accurately predict the risk of postoperative surgical complications in patients with localised renal tumours after PN.

## Conflict of Interest

None declared.

## Funding

None.

## Ethical Approval

The study was first approved by the Ethics Committee of the leading Centre of the RECORD project (Department of Urology, University of Florence, Careggi Hospital, Florence, Italy) and then by all Ethics Committees of all Centres participating in the project.

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**Abbreviations:** AKI, Acute kidney injury; ASA, American Society of Anesthesiologists; AUC, area under the curve; CCI, Charlson Comorbidity Index; EAU, European Association of Urology; ECOG, Eastern Cooperative Oncology Group; IQR, interquartile range; PADUA, Preoperative Aspects and Dimensions Used for an Anatomical (score); (L)(O)(RA)PN, (laparoscopic) (open) (robot-assisted) partial nephrectomy; RECORD, Registry of Conservative and Radical surgery for cortical renal tumour disease; ROC, receiving operator characteristic; RN, radical nephrectomy.