Urologia
Internationalis

Original Paper

Urol Int 2020;104:781–788
DOI: 10.1159/000508798

Received: April 14, 2020
Accepted: May 17, 2020
Published online: July 7, 2020

Assessing the Association of Surface-Intermediate-Base Margin Score with Perioperative Outcomes and Parenchymal Volume Preserved during Partial Nephrectomy

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Keywords
Nephron-sparing surgery · Scoring system · Surgical technique · SIB score

Abstract
Introduction: The present study aimed to compare the assessment of volume preservation and perioperative outcomes during partial nephrectomy (PN), according to the surface-intermediate-base (SIB) score. ***Methods:*** This prospective study included 80 patients diagnosed with renal cell carcinoma who underwent PN for a renal mass from 2014 to 2017. SIB score was macroscopically evaluated immediately after the surgery. Preoperative assessment of volume preservation (PAVP), surgeon assessment of volume preservation (SAVP), duration of ischemia, perioperative complications, pathological data, and the values of preoperative and postoperative estimated glomerular filtration rate (eGFR) were recorded. ***Results:*** A strong correlation was determined between PAVP and SAVP ($R = 0.82$, $R^2 = 0.68$, $p < 0.0001$) and between vGFR-PAVP and vGFR-SAVP calculated using the adapted eGFR (preop eGFR × [PAVP or SAVP]) ($R = 0.97$, $R^2 = 0.95$, $p < 0.001$). In multivariate analysis, preoperative tumor size, SIB score (1–2 vs. 3–5), and vGFR (PAVP and SAVP model) were significant predictors of postoperative eGFR. A low base score was associated with surgical margin positivity, and a high SIB score (≥3) was associated with perioperative complications ($p = 0.017$; $p = 0.028$). ***Conclusion:*** The SIB score can be considered a reliable surrogate for volume preservation after PN because it is strongly associated with both PAVP and SAVP. SIB score is useful in predicting functional outcomes, complications, and surgical margin positivity.

Introduction

The importance of partial nephrectomy (PN) has been shown by revealing the link between cardiovascular morbidity and chronic renal failure. Moreover, studies have demonstrated that PN improves overall survival [1, 2].

PN has become the preferred treatment option considering the negative consequences of chronic kidney disease and improved long-term survival after PN [3]. Although various techniques and outcomes of PN have been reported, they have not yet achieved standardization.

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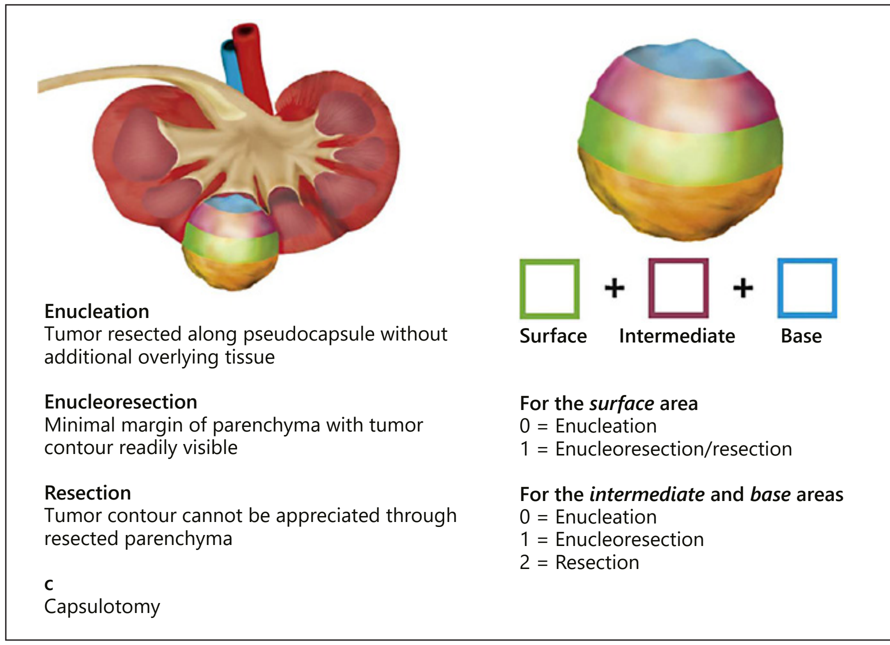

Fig. 1. Schematic view of Surface-intermediate-base (SIB) scoring system [4].

The surface-intermediate-base (SIB) margin scoring system was developed by an international consortium to evaluate the association between resection technique and complication rates, surgical margin positivity, preserved parenchymal volume, and oncologic outcomes of PN [4]. Subsequently, several updates on the SIB project have been published on the potential effect of resection techniques (assessed using the SIB score) and postoperative outcomes after PN [5–7].

Simmons et al. [8] revealed that baseline estimated glomerular filtration rate (eGFR) and preoperative assessment of volume preservation (PAVP) were primary determinants of long-term kidney function. Recent studies have demonstrated that postoperative surgeon assessment of volume preservation (SAVP) closely correlates with PAVP and postoperative eGFR [9, 10]. PAVP and SAVP play an important role in predicting postoperative renal functions and facilitating the decision to perform PN, as shown in these studies. The present study aimed to compare the assessment of volume preservation and perioperative outcomes, according to the SIB score.

Patients and Methods

This prospective study included 80 patients diagnosed with renal cell carcinoma who underwent PN for a renal mass from November 2014 and March 2017. Patients' demographic characteristics were recorded. Body mass index (BMI = weight/height^2) and preoperative eGFR (MDRD formula) were calculated [11]. The American Society of Anesthesiologists (ASA) score, the Eastern Cooperative Oncology Group (ECOG) performance scale, and the Charlson comorbidity index (CCI) were used to assess the preoperative health status [12–14].

All patients were evaluated using abdominal computed tomography. The TNM stage, tumor side, longest tumor diameter, tumor location, polar location of the renal tumor, exophytic properties, PAVP, RENAL score, collecting system invasion, and renal sinus invasion were recorded.

PAVP was calculated using the method defined by Simmons et al. [8]. A cylindrical volume ratio method was used to estimate the percent of functional volume preservation on computed tomography images obtained preoperatively. The equation, kidney volume = π × (kidney radius) r^2 × (kidney lenght) h, was used to determine preoperative cylindrical kidney volume. The kidney length was calculated by considering the uppermost and lowermost image sections. The mid polar plane was identified by averaging the uppermost and lowermost image section numbers. Kidney diameter was measured using a line passing through the center point that symmetrically divided the medial and lateral aspects of the kidney perpendicular to the hilar axis.

All patients underwent open transperitoneal PN by a single surgeon (B.A.). The surgeon assigned the SIB score immediately after surgery. The tumor resection bed was visually analyzed and divided into the following 3 circumferential areas of approximately the same length: surface, intermediate, and base (Fig. 1) [4]. Each area was visually analyzed to identify the macroscopically evident zone of minimal margin that would serve as the specific zone for score assignment. The zone used for assigning the score had to be detected visually and not microscopically. Moreover, there are no strict percentages to report. Regarding the zone of minimal margin within the surface (S) area, 0 points were assigned for enucleation (only the tumor's pseudocapsule is seen), without resection of the surrounding overlying tissue (margins less than approximately 1 mm), while 1 point was assigned for enucleoresection (wherein there was a minimal margin ≥1 mm of normal parenchyma that allowed clear visualization of the tumor's contours) or resection (removal of the tumor with substantial margin wherein the contour of the tumor could not be visualized through the resected parenchyma). The surface area scale was scored as 0 = enucleation and 1 = enucleoresection or resection. The intermediate and base scores were as follows: 0 = enucleation, 1 = enucleoresection, and 2 = resection. The sum of the SIB scores ranged from 0 to 5, where 0–1 = pure enucleation, 2 = hybrid enucleation, 3 = pure enucleoresection, 4 = hybrid enucleoresection, and 5 = resection [4].

SAVP was calculated by determining the functional volume preserved after PN, considering the amount of parenchyma replaced by the tumor (intraparenchymal portion) and the adjacent uninvolved parenchyma removed or devascularized during the procedure. Therefore, the percent preserved was calculated as follows: remaining viable parenchyma/total parenchyma + intraparenchymal tumor volume [9]. We measured the maximum tumor radius (r) and calculated tumor volume (V_{tum}) using the equation: $V_{tum} = 4/3\pi r^3$. The intraparenchymal tumor volume was estimated by taking into account the part of the tumor in the kidney.

Complete blood count and renal function tests were performed for all patients on the first postoperative day. Postoperative hospitalization time, catheter duration, and medical and surgical complications were recorded. The postoperative complications were evaluated according to the Clavien-Dindo classification [15]. On pathological examination, tumor diameter, histological type, International Society of Urological Pathology (ISUP) stage, pseudocapsule status, trifecta (warm ischemia time <25 min, no surgical complications, and negative surgical margins), peripheral and sinus fat invasion, and TNM stage were recorded.

Patients were followed up according to the European Association of Urology (EAU) guidelines, and a complete blood count and renal function tests were performed at each visit. Details of recurrence, cancer-specific survival, and overall survival were recorded. Projected kidney function based on volume preservation was calculated using the formula: vGFR = preoperative eGFR × percent of remaining parenchyma (PAVP or SAVP).

This study was approved by the local ethical committee (GO-17/71). Data were analyzed using SPSS 20.0 (IBM Corp.) software. Correlations were assessed using univariate and multivariate linear regression models with parametric statistics. Bland-Altman analysis was used to investigate the agreement between PAVP and SAVP. For univariate analysis, the χ^2 test or Fisher's exact test was used for nominal data, the *t* test was used for parametric variables, and the Mann-Whitney *U* test and the Kruskal-Wallis test were used for nonparametric variables.

Results

The mean age of the patients was 58 years (range 29–86 years). 68.8% ($n = 55$) of the patients were men, and 31.2% ($n = 25$) were women. The incidence of the right or left side was equal (40 vs. 40), and the mean tumor size was 3.69 cm (1.2–7.2 cm). The mean preoperative eGFR was 90 ± 29.1 mL/min/1.73 m^2. Patient characteristics are given in Table 1.

Table 1. Patient characteristics

Sex (*n*, %)		
Male	55	68.8%
Female	25	31.2%
Symptoms		
No	64	80%
Yes	16	20%
Surgical margin		
Positive	8	10%
Negative	72	90%
Trifecta		
Positive	62	77.5%
Negative	18	22.5%
ASA		
<3	75	93.8%
≥3	5	6.2%
CCI, median	90	0–98
SIB score		
0–1	6	7.5%
2	16	20%
3	14	17.5%
4	23	28.8%
5	21	26.2%
Exophytic rate		
>50%	55	68.8%
<50%	19	23.8%
Completely exophytic	6	7.4%

ASA, American Society of Anesthesiologists; CCI, Charlson comorbidity index; SIB score, surface-intermediate-base score.

PN was performed with ischemia in 72 (90%) patients. The mean duration of ischemia was 18.2 min (6–34 min). The mean operative time was 98.6 min (120–60 min), and the mean estimated blood loss was 136 mL (0–700 mL).

The overall rate of perioperative complications was 11.2%. Notably, intraoperative blood transfusion was administered to 2 (2.5%) patients, whereas 4 (5%) patients received a postoperative blood transfusion. Intraoperative complication (iatrogenic ureter injury) developed in 1 patient (1.25%). According to the Clavien-Dindo classification, grade 2 complications developed in 6 patients (7.5%), grade 3 complications developed in 1 patient (1.3%), and grade 4 complications in 1 patient (5%). The rate of major complications (Clavien-Dindo ≥3) was 2.5%. There was no significant difference in the overall SIB scores with age, gender, operation side, eGFR change, hospitalization time, estimated blood loss, complications, surgical margin positivity, and ischemia time (Table 2).

Table 2. Comparison of variables

	Gender (M/F)	Age, mean year	Side (right/left)	eGFR change, mean ± SD	Hospitalization time	Estimated blood loss, mL, mean ± SD	Complications, %	Surgical margin positivity, %	Duration of ischemia, mean min ± SD	Trifecta, %
p value	0.654	0.404	0.713	0.639	0.549	0.769	0.177	0.085	0.112	0.667
SIB score										
1	5/1	55±6.4	4/2	−17.8±44.5	3	133±87	0	33.3	12±9.6	66.7
2	9/7	56.2±12.3	9/7	−1.4±51.7	2.75	112±164	0	6.3	14.7±7.2	87.5
3	10/4	57.6±14.7	5/9	4.8±13.7	3	150±235	14.3	21.4	17.6±7.4	71.4
4	15/8	62±12	12/11	6.4±13.4	2.87	141±179	8.7	8.7	19.3±5	82.6
5	16/5	56.1±9.1	10/11	4.6±16.3	3.48	140±197	23.8	0	14.9±8.8	71.4

eGFR, estimated glomerular filtration rate; SIB score, surface-intermediate-base score.

The PAVP was 91.3% (62–100), while the SAVP was 82.8% (40–100). A strong correlation was determined between PAVP and SAVP ($R = 0.82$, $R^2 = 0.68$, $p < 0.0001$) and between vGFR-PAVP and vGFR-SAVP ($R = 0.975$, $R^2 = 0.95$, $p < 0.001$). Both vGFR-PAVP ($R = 0.673$, $R^2 = 0.452$, $p < 0.001$) and vGFR-SAVP ($R = 0.687$, $R^2 = 0.471$, $p < 0.001$) were correlated with postoperative eGFR (Fig. 2).

In univariate linear regression analysis, preoperative tumor size, ischemia time, SIB score (1–2 vs. 3–5), vGFR-PAVP, and vGFR-SAVP were correlated with postoperative eGFR. In multivariate analysis, preoperative tumor size, SIB score (1–2 vs. 3–5), and vGFR (PAVP and SAVP model) were significant predictors of postoperative eGFR (Tables 3 and 4).

The factors that affected the perioperative complications were as follows: ECOG score >2 ($p = 0.011$), ASA score >3 ($p = 0.022$), age >64 (according to the ROC curve, 87.5% sensitivity, 79.2% specificity, $p < 0.001$), low preoperative hemoglobin and hematocrit ($p = 0.002$; $p = 0.002$), high BMI (0.019), and a high SIB score (≥3) ($p = 0.046$). The factors that affected the surgical margin positivity were tumor size <4 cm and base score ($p = 0.035$; $p = 0.006$). A significant decrease in eGFR was observed at the 3-month visit in patients with ischemia longer than 20 min ($p = 0.048$, 38.5 vs. 27.3 mL/min/1.73 m^2).

The mean follow-up period was 14.5 months (3–29 months). At the last follow-up, the mean creatinine level was 0.99 g/dL (0.3–2.16 g/dL), and the median eGFR alteration was 3.83 mL/min/1.73 m^2. One patient developed lung and bone metastases at the 3-month follow-up, and a renal mass was detected in the contralateral kidney of 2 patients diagnosed with von Hippel-Lindau disease. Nonetheless, no patients died during the follow-up.

Discussion

The main difference between PN and radical nephrectomy is the residual renal function and the significantly reduced mortality and morbidity associated with renal failure and cardiovascular diseases [16]. Studies in the literature report that the maximum warm ischemia time should be 20 min to avoid permanent renal damage and emphasize that every minute is harmful even if below this duration [17, 18]. The mean duration of ischemia was determined as 18.2 min in the present study, and eGFR was significantly decreased at the 3-month follow-up in patients with ischemia longer than 20 min. Prolonged ischemia during PN is associated with a decrease in preserved parenchyma function and increased morbidity. Therefore, techniques and methods that could shorten the duration of ischemia should be preferred.

Various tumor resection techniques have been described for PN [3]. Simple enucleation, enucleoresection, and wedge resection are the most common techniques; however, the differences among them cannot be clearly defined. No study has determined a standardized excision methodology, and some methods are likely to be incorrectly used. Therefore, SIB scoring systems have been developed by an international consortium to evaluate the association between resection technique and complication rates, surgical margin positivity, preserved parenchymal volume, and oncologic outcomes of PN [4]. Furthermore, histological validation of the scoring system has been performed, and the clinical scoring system is amenable to histopathology methods [5]. The surgeon assigns the SIB score based on a structured, standardized assessment of the tumor specimen. This score is also validated from a pathological perspective, showing that the surgeon's judgment is reliable and mirrors the histopath-

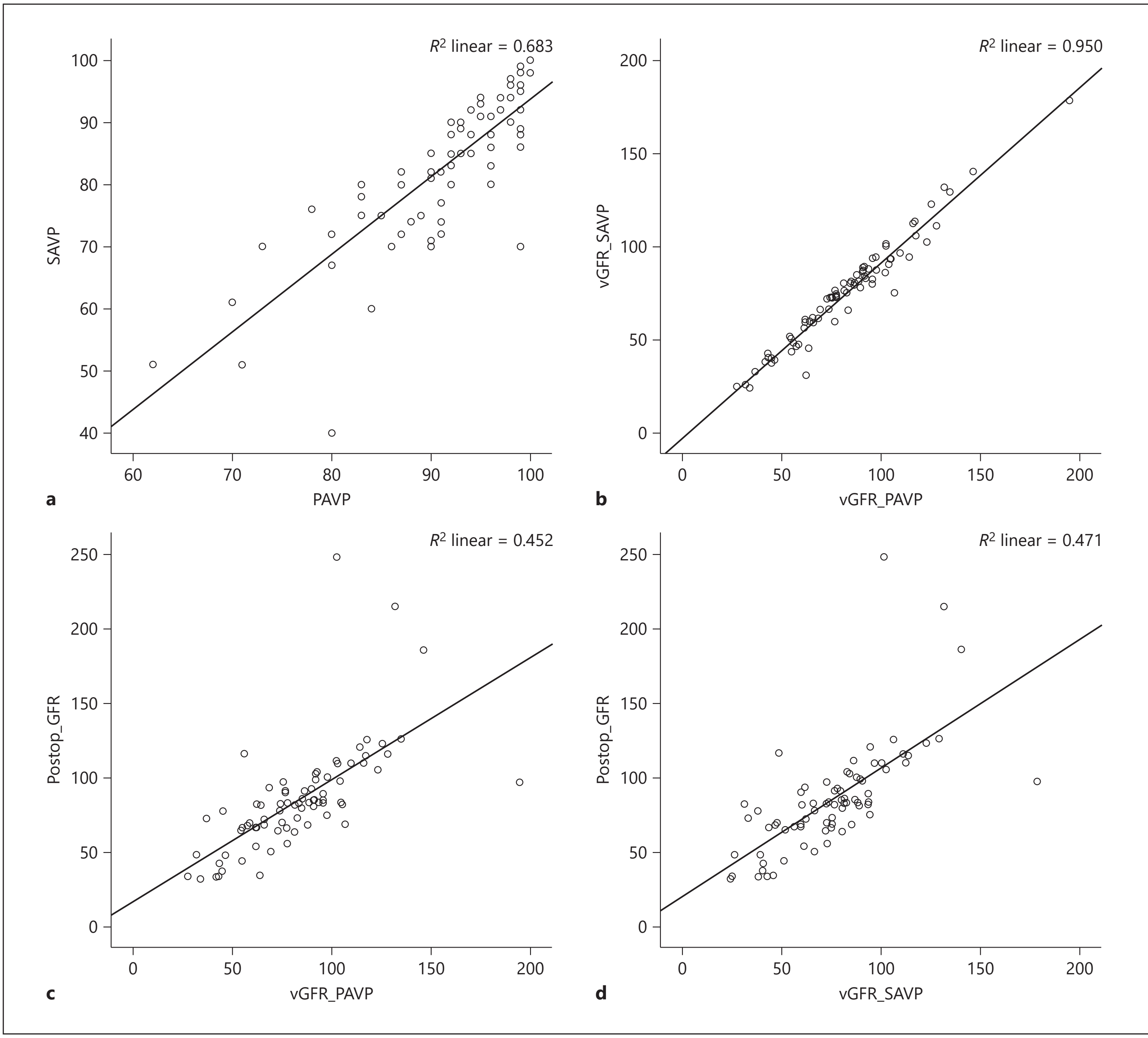

Fig. 2. Linear regression models of vGFR. **a** Comparison of PAVP and SAVP; $R = 0.826$, R^2: 0.683. **b** Comparison of vGFR-SAVP and vGFR-PAVP; $R = 0.975$, R^2: 0.950. **c** The vGFR based on PAVP compared with postoperative GFR; R: 0.673, R^2: 0.452. **d** The vGFR based on SAVP compared with postoperative GFR; R: 0.687, R^2: 0.471.

ological analysis. By objectively classifying the resection technique after PN, the SIB score can improve our understanding of PN outcomes and harmonize the PN series.

Excision of localized renal masses, while leaving peritumoral durable tissue, is a safe and acceptable technique to prevent local tumor recurrence [3]. A better understanding of the anatomy through PN and negative outcomes of renal failure has contributed to better parenchymal preservation and shorter ischemia duration. Consequently, a 10-mm surgical margin, which is considered safe, could be effectively reduced to 5 mm and below [19]. Minervini et al. [20] performed simple enucleation in 537 of 982 patients and investigated the 5- and 10-year cancer-specific and progression-free survival rates in their multicenter retrospective study. The authors demonstrated that the technique used in PN did not influence the survival rate [20]. In the present study, the overall SIB

Table 3. Factors correlated with the vGFR-PAVP-based model in the cohort

	Univariate		Multivariate	
	estimate (95% Cl)	*p* value	estimate (95% Cl)	*p* value
Age	–0.13 (–0.88, 0.22)	0.239		
Gender	–0.84 (–19.1, 8.7)	0.460		
Preoperative tumor size, cm	–0.26 (–9.1, –0.93)	**0.017**	0.95 (0.8, 2.79)	**0.001**
Ischemia time	–0.28 (–1.9, –0.26)	**0.010**	–0.01 (–0.24, 0.15)	0.679
BMI	0.177 (–0.29, 2.6)	0.115		
vGFR-SAVP	0.98 (0.95, 1)	**<0.001**	1.02 (1, 1.11)	**<0.001**
SIB score (1–2 vs. 3–5)	–0.31 (–34, –6.4)	**0.005**	0.05 (–0.01, 6.46)	**0.05**
RENAL score	–0.2 (–6.5, 0.26)	0.070		
R^2			0.979	

Bold values indicate statistical significance. PAVP, preoperative assessment of volume preservation; SAVP, surgeon assessment of volume preservation; SIB score, surface-intermediate-base score.

Table 4. Factors correlated with the vGFR-SAVP-based model in the cohort

	Univariate		Multivariate	
	estimate (95% Cl)	*p* value	estimate (95% Cl)	*p* value
Age	–0.13 (–0.85, 0.22)	0.244		
Gender	–0.06 (–17.3, 9.68)	0.572		
Preoperative tumor size, cm	–0.35 (–10.3, –2.6)	**0.001**	–0.01 (–2.7, –0.94)	**<0.001**
Ischemia time	–0.31 (–1.96, –0.37)	**0.004**	0.003 (–0.17, 0.19)	0.916
BMI	0.2 (–0.13, 2.67)	0.075		
vGFR-PAVP	0.98 (0.89, 0.99)	**<0.001**	0.92 (0.85, 0.94)	**<0.001**
SIB score (1–2 vs. 3–5)	–0.36 (–35.9, –9.6)	**0.001**	–0.05 (–6.7, –0.89)	**0.011**
RENAL score	–0.21 (–8.2, 0.2)	0.062		
R^2			0.963	

Bold values indicate statistical significance. SAVP, surgeon assessment of volume preservation; PAVP, preoperative assessment of volume preservation; SIB score, surface-intermediate-base score.

score did not affect the surgical margin, although the percentage was different. However, a low base score was found as a factor affecting surgical margin positivity. Therefore, the base of the mass should be operated with care, even if the PN begins as enucleation or resection, and wide resection of the base should be performed, if required.

Enucleation is a nephron-sparing technique in which the renal mass is dissected away from the renal parenchyma via an avascular plane along the fibrous pseudocapsule. Previous studies show that enucleation is better at preserving parenchymal volume [19]. In accordance with the literature, the present study showed that the SIB score was correlated with postoperative eGFR. One explanation for this difference may be that enucleation impairs less vascular structure and preserves more remnant kidney than resection. The fact that there were fewer complications in the enucleated group than in the resected group can also be explained with the same hypothesis.

Surgical margin negativity, a component of the trifecta, is one of the main goals of PN. However, no consensus exists regarding the influence of surgical margin positivity on recurrence and survival. The incidence of positive surgical margins after PN varies between 0 and 10.7% [21–23]. Ani et al. [23] demonstrated that surgical margin positivity was affected by tumor stage and perirenal fat invasion. Furthermore, surgical margin positivity was not an independent factor affecting survival in their study, comprising 664 patients. Tumor size of >4 cm, presence of a bilateral tumor, and positive surgical margins were shown as independent predictive factors for tumor recurrence in a multicenter study [24]. Some similar studies have also indicated an increased rate of positive surgical margins in patients with smaller tumors [25, 26]. In the present study, the predictive factors for surgical margins were determined as tumor <4 cm and low base score in the SIB scale. The small tumor size may prevent the surgical evaluation of tumor margins, leading to incomplete resection. A high positive surgical margin rate may be observed as a result of obscure, undeveloped pseudocapsule or erroneously impaired integrity of the resection margin in small tumors, and this may be more surgeon dependent in small and endophytic tumors than in large and exophytic tumors [27].

PN is a more complex operation than radical nephrectomy and has a higher complication rate, even if the tumor size is equal [28]. A randomized prospective study by Van Poppel et al. [29] reported that hemorrhage (3.1 vs. 1.2%) and reoperation rates (4.4 vs. 2.4%) were higher in the PN group. In another study comparing robot-assisted PN with open PN, Ramirez et al. [30] determined that the overall complication rates were 30.3 versus 18.2% and open surgery, race, CCI, and BMI were found as factors affecting complications. The overall complication rate was determined as 11.2% in our study, and there were no complications requiring reoperation (persistent hemorrhage or urinary fistula). These results were less than that noted in the literature. Even though the surgical experience is in the foreground, patient selection and correct technique also play a crucial role. Based on the SIB score, complications were not observed in patients who underwent pure and hybrid enucleation. In contrast, high complication rates were noted in the pure resection group, with a significant difference. Based on this difference, the enucleation method should be used more often in patients with high comorbidity scores and cardiovascular problems.

Furthermore, the postoperative preserved volume and quality of renal parenchyma are essential factors besides the ischemia duration for minimizing renal function loss. Imaging may be undertaken with preoperative and postoperative segmentation to assess the rate of parenchymal mass preservation. Some studies have indicated that SAVP assessment is closely related to postoperative eGFR and could be used to predict intraoperative renal function preservation [9, 10]. Similarly, our study observed a correlation between SAVP, PAVP, and volume-adjusted eGFR. SAVP and PAVP are useful in predicting functional outcomes after PN, and these parameters may help the surgeon to ascertain which patients would undergo PN.

Nonetheless, our study had some limitations. This was a single-center study conducted by a single surgeon (B.A.) with a small sample size. Although a single surgeon and a small sample size seem to be the weakest points of the study, the same surgical technique was used, and the high number of case experiences (>1,000 cases) may have minimized the possible variables that affect the results. All patients in the present study underwent parenchymal suturing for renorrhaphy. The technique, depth, and number of sutures may affect the remaining functional kidney volume. At the same time, the surgeon's hemostasis technique, type of surgery, and type and duration of ischemia can also affect this volume. Our study aimed to minimize these possible confounding variables by including a single surgeon's operations. The SIB score was determined by the operating surgeon, which may be accepted as a limitation for this scoring system. However, to minimize this limitation, several updates of the SIB project have been published on the potential impact of resection techniques [5, 6]. Postoperative renal function was measured at 3 months after surgery, which was a relatively short period to assess renal functional outcomes.

Conclusion

The SIB score can be considered a reliable surrogate for volume preservation after PN because it is strongly associated with both PAVP and SAVP that measure the quantity of parenchyma preserved by PN. SIB score is a useful method to predict early term functional results, surgical margin positivity, and complications. It is helpful to use these methods to preserve maximal renal function before and during PN.

Statement of Ethics

This study was approved by the local ethics committee (GO-17/71).

Conflict of Interest Statement

No potential conflicts of interest were disclosed by the authors.

Funding Sources

The authors did not receive any funding.

Author Contributions

B.Ç. and B.A.: conception or design of the work and analysis. B.Ç., H.B.H., and B.A.: interpretation of data.

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