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Original article

Assessment of volume preservation performed before or after partial nephrectomy accurately predicts postoperative renal function: Results from a prospective multicenter study

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Abstract

Purpose: Partial nephrectomy (PN) is standard for small renal masses, improving renal function by preserving renal parenchyma compared with radical nephrectomy. Recent work demonstrated that postoperative surgeon assessment of volume preservation (SAVP) and 3D imaging measurements agree and correlate with postoperative function. We hypothesize preoperative assessment of volume preservation (PAVP) with PN based on preoperative imaging will reliably indicate postoperative renal function.

Materials and Methods: Data were collected from 336 patients undergoing PN for suspected renal cancer by 40 surgeons at 12 centers in Europe and the United States within the Surface-Intermediate-Base International Consortium. Surgeons recorded PAVP and SAVP for individual patients; pre- and postoperative glomerular filtration rate (GFR) was estimated by Chronic Kidney Disease Epidemiology Collaboration equations. Correlations between PAVP, SAVP, and postoperative GFR were assessed with linear regression models. Bland–Altman analysis was used to assess agreement between PAVP and SAVP with a significant cutoff of 5%.

Results: Median PAVP was 90% (interquartile range [IQR] 85%–100%) and SAVP was 90% (IQR: 80%–94%). PAVP and SAVP were moderately correlated ($R^2 = 0.67$, $P < 0.0001$) and deemed "interchangeable" by Bland–Altman analysis at a 5% acceptable rate of difference (95% CI: −5.4, −3.1). Median postoperative GFR was 77.3 (IQR: 56.2, 92.0). Both PAVP ($R^2 = 0.82$, $P < 0.0001$) and SAVP ($R^2 = 0.83$,

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$P < 0.0001$) were correlated with postoperative GFR. Multivariable models utilizing volume-adjusted GFR based on PAVP or SAVP significantly and similarly predicted postoperative GFR ($R^2 = 0.72$ for each).

Conclusion: Renal function is closely linked to the amount of parenchymal volume preservation, whether estimated prior to surgery (PAVP) or afterward (SAVP). PAVP provides reasonably accurate information for decision-making in patients considering PN.

Keywords: Nephrectomy; Renal cancer; Small renal mass; Volume preservation

1. Introduction

Partial nephrectomy (PN) offers patients comparable survival to radical nephrectomy (RN) while sparing renal parenchyma, leading to a better preservation of renal function after surgery [1−8]. For this reason, PN has become the surgical standard of care for patients with amenable renal masses. Along with factors such as preoperative glomerular filtration rate (GFR), age, tumor size, and solitary kidney, the volume of preserved parenchyma appears to be an important factor determining postoperative renal function after PN [9−14] that, in turn, represents an important determinant of cancer survivorship in patients with localized renal tumors [7,8,15].

Preservation of parenchymal volume is a critical determinant of functional recovery after PN in patients without prolonged warm ischemia [12,16−22]. Preoperative and postoperative imaging with segmentation can be used to evaluate the amount of parenchymal mass preservation [13,18,23]. However, objective measurements of volume preservation (VP) by 3-dimensional imaging (3DVP) are both time and resource consuming and; therefore, not routinely performed in clinical practice [23]. Recent studies have demonstrated that postoperative surgeon assessment of volume preservation (SAVP) closely correlates with 3DVP assessment and postoperative GFR and may; therefore, be used as an estimate of renal function preservation at the time of surgery [24,25]. Estimation of renal functional loss with definitive treatment is becoming increasingly valuable with the use of both renal mass biopsy and surveillance on the rise [7,8]. In these scenarios, preoperative assessment of volume preservation (PAVP) can aid in decision-making, particularly in patients with complicated renal tumors, multiple comorbidities, or poor preoperative renal function.

However, whether surgeons may be able to adequately predict the volume of preserved parenchyma, based on preoperative imaging, has yet to be determined. The objective of this study is to determine whether PAVP may provide comparable information to SAVP as an accurate predictor of preserved renal volume and postoperative renal function after PN in a cohort of patients undergoing surgery for localized renal masses.

2. Materials and methods

Prior to study initiation, the previously published guidelines for performing PAVP and SAVP were presented to all surgeons participating in the Surface-Intermediate-Base (SIB) Margin score International Consortium (see Appendix) [24,25]. Between September 2014 and December 2015, 507 patients underwent PN for suspected renal cancer at 16 participating centers in Europe and the United States. The principles of step-by step SIB score assignment have been previously described [26]. The final resection technique was classified by the surgeon as enucleation, enucleoresection, and resection according to the SIB Margin score (enucleation, SIB score 0−2; enucleoresection, SIB score 3−4; resection, SIB 5). Data regarding PAVP and/or SAVP was recorded for 336 patients (66%) by 40 surgeons at 12 centers, which form the inclusion criteria for this study.

Each patient underwent cross-sectional CT or MRI imaging by local institutional protocols, which was used to assess PAVP. GFR was calculated using postoperative Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equations based on serum creatinine values determined immediately prior to surgery and at 3-month follow-up visit, when stabilization of renal function is complete [27]. Correlations were assessed with linear regression models using parametric statistics. Multivariable models utilizing volume-adjusted GFR (vGFR) based on either PAVP or SAVP were constructed to determine the predictive capabilities of the respective VP assessments with renal functional outcome. Bland−Altman analysis was used to assess agreement between PAVP and SAVP with a significant cutoff of 5%. All analyses and graphics were performed using the statistical software package JMP version 13 (SAS Inc., Cary, NC) with the exception of the Fisher transformation variance analyses (R statistical computing v3.4.0) [28].

3. Results

The SIB international consortium prospectively enrolled patients undergoing PN performed at high-volume surgical centers by expert surgeons using a variety of techniques, ranging from enucleation to resection. A variety of techniques were used, including open and minimally-invasive approaches, with a median estimated blood loss (EBL) of 150 ml (interquartile range [IQR]: 100, 250). According to the SIB score, enucleation was performed in 148 (44%) patients, enucleoresection in 111 (33%), and resection in 77

(23%). Ischemia was utilized in 85% ($n = 286$) of cases, including 13 (4%) with selective clamping. Median warm ischemia time (WIT) was 16 minutes (IQR: 14.0, 21.5), with only 15.4% of all patients exposed to warm ischemia for more than 25 minutes. Median length of hospital stay was 5 days (IQR: 3, 6); 3.3% of patients experienced grade 3 or 4 Clavien−Dindo complications.

SAVP was collected prospectively on 336 patients, of which PAVP was recorded for 191 (56.8%) cases, without any additional selection criteria. Patient and tumor characteristics are outlined in Table 1. A total of 40 surgeons contributed a median of 4 SAVP values each (range: 1−34). The median preoperative GFR of all patients was 85.3 (IQR: 68.9, 97.1) with 86.2% of patients having normal (GFR >60 ml/min/1.73 m^2) preoperative renal function. After surgery, renal function was preserved (<30% loss of function) in 261 cases (87%). Median postoperative GFR was 77.3 ml/min/1.73 m^2 (IQR: 56.2, 92.0). Median loss of renal function was −8.35% (IQR: −21.4%, 0.05%).

Table 1
Patient, tumor, and perioperative characteristics

Patients	336
Male gender	192 (57%)
Median age (IQR)	62 (52−70)
Median BMI (IQR)	26.1 (24.0−29.8)
Median clinical tumor size, cm (IQR)	3.0 (2.4−4.3)
Median RENAL nephrometry score (IQR)	6 (5−8)
Low (4−6)	182 (54%)
Intermediate (7−9)	133 (40%)
High (10−12)	16 (4.8%)
Resection technique	
Enucleation (SIB 0−2)	148 (44%)
Enucleoresection (SIB 3−4)	111 (33%)
Resection (SIB 5)	77 (23%)
Surgery type	
Open	92 (27.4%)
Laparoscopic	26 (7.7%)
Robotic	217 (64.7%)
Ischemia	
None	50 (15%)
Ischemia	286 (85%)
Median ischemia time, min (IQR)	16 (14−21.5)
Pathologic staging	
pT1a	159 (48.0%)
pT1b	54 (16.3%)
pT2	1 (0.3%)
pT3a	33 (9.9%)
Benign	84 (25.4%)
Median PAVP % of operative kidney (IQR)	90 (85−100)
Median SAVP % of operative kidney (IQR)	90 (80−94)
Median preoperative GFR, ml/min/1.73 m^2 (IQR)	85.3 (68.9−97.1)
Median postoperative GFR, ml/min/1.73 m^2 (IQR)	77.3 (56.2−92.0)
Median overall % loss of renal function (IQR)	−8.27 (−21.4, 0.0)
Median overall preservation of parenchyma by PAVP (IQR)	95 (93−100)
Median overall preservation of parenchyma by SAVP (IQR)	95 (90−96.75)
Solitary kidney	18 (5.4%)

Abbreviations: BMI = body mass index; GFR = glomerular filtration rate; IQR = interquartile range; PAVP = preoperative assessment of volume preservation; SAVP = surgeon assessment of volume preservation; SIB = surface-intermediate-base.

A strong correlation between vGFR-PAVP and vGFR-SAVP was observed (Fig. 1), with $R = 0.95$ ($R^2 = 0.90$, $P < 0.0001$). Median PAVP was 90% (IQR: 85%−100%) and median SAVP was 90% (IQR: 80%−94%). Moderate correlation between PAVP and SAVP was observed with $R = 0.65$ ($R^2 = 0.42$, $P < 0.0001$). Bland−Altman analysis was performed to determine the agreement between the 2 measurements. PAVP and SAVP were found to be interchangeable at a 5% acceptable rate of difference (95% CI: −5.4, −3.1) (Supplemental Fig. 1). Further variance analysis was conducted using Fisher transformation of correlations between PAVP and postoperative eGFR and SAVP and postoperative eGFR. The point estimates for PAVP and SAVP correlations to postoperative eGFR were 0.095 and 0.102 respectively, both of which fell inside the Fisher transformed 95% confidence interval of difference in correlations (−0.115, 0.128). The point estimate of difference in those correlations was 0.007.

Predictors of postoperative renal function were assessed by univariable and multivariable analysis. Age ($P < 0.0001$), preoperative tumor diameter ($P = 0.049$), robotic PN ($P = 0.0099$), EBL ($P < 0.0001$), and vGFR ($P < 0.0001$) were significant univariate predictors of postoperative GFR based on linear regression analysis. Both vGFR-PAVP ($R = 0.82$, $P < 0.001$) and vGFR-SAVP ($R = 0.83$, $P < 0.001$) were correlated with postoperative GFR (Supplementary Table 1, Fig. 1). In multivariable analysis age, tumor diameter (vGFR-PAVP model only), robotic PN (vGFR-SAVP model only), EBL (vGFR-SAVP model only), and vGFR were the significant predictors of postoperative GFR after accounting for age, gender, surgical approach, body mass index, WIT, EBL, and (radius, exophytic/endophytic properties, nearness of tumor to the collecting system or sinus in millimeters, anterior/posterior location relative to polar lines) nephrometry scoring system (RENAL) score (Table 2). Multivariable models to predict actual postoperative GFR were constructed utilizing vGFR based either on PAVP or SAVP. Each model demonstrated similar ability to predict 3-month postoperative GFR ($R^2 = 0.72$ vs. $R^2 = 0.72$ respectively; Fig. 2).

4. Discussion

The impact of surgical technique during PN on renal functional outcomes is of great interest. To this end, the SIB Margin score International Consortium is conducting a prospective clinical evaluation of PN performed by

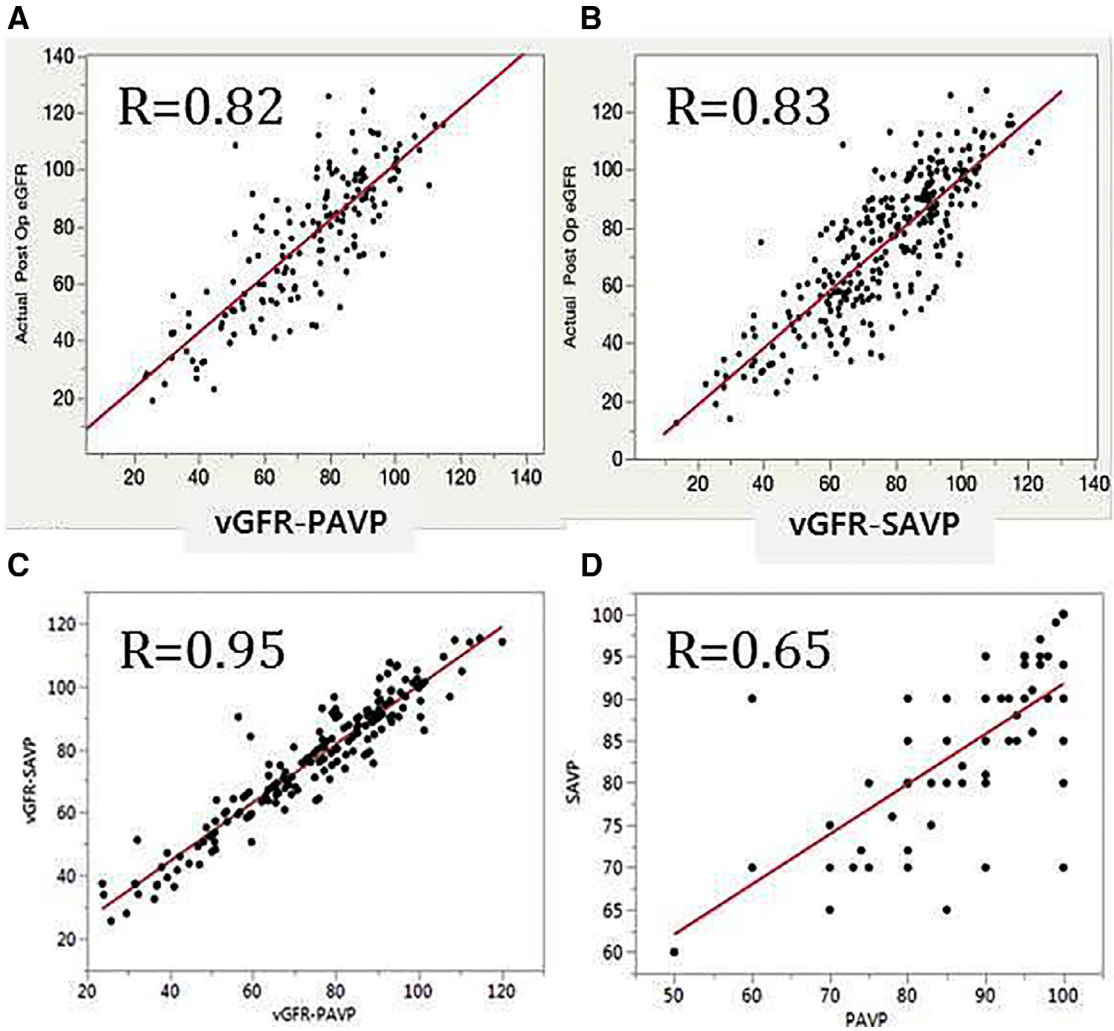

Fig. 1. Linear regression models of vGFR and actual postoperative GFR. (A) vGFR based on PAVP compared with actual postoperative GFR. There was a strong, statistically significant ($P < 0.0001$) correlation ($R = 0.82$, $R^2 = 0.67$). (B) The vGFR based on SAVP compared with actual postoperative GFR. There was again a strong correlation ($R = 0.83$, $R^2 = 0.69$) which was highly significant ($P < 0.0001$). (C) The vGFR based on PAVP compared with vGFR based on SAVP. There was a strong, statistically significant ($P < 0.0001$) correlation ($R = 0.95$, $R^2 = 0.90$). (D) PAVP correlation with SAVP. There was a strong, statistically significant ($P < 0.0001$) correlation ($R = 0.65$, $R^2 = 0.42$). Abbreviations: GFR = glomerular filtration rate; vGFR = volume-adjusted GFR; SAVP = surgeon assessment of volume preservation; PAVP = preoperative assessment of volume preservation.

surgeons at high-volume centers across Europe and United States [29,30]. The relative importance of tumor complexity, resection strategy, resection technique, and parenchymal preservation is yet to be determined. In this study, we demonstrate that both PAVP and SAVP represent reliable indicators of postoperative renal function in patients undergoing PN. Both PAVP and SAVP predicted 90% VP of the operative kidney on average and demonstrated strong agreement with each other by Bland–Altman analysis. PAVP and SAVP were shown to be interchangeable and both strongly correlated with postoperative renal function; therefore, providing the rationale to continue use of SAVP after surgery and potentially to use PAVP in the office to predict the outcome of PN or another nephron-sparing technique, and compare this with surveillance or RN. Patients could then better understand the relative risks of these options, in terms of complications, change in renal function, and most likely outcomes with each approach. Both PAVP and SAVP also correlated with postoperative GFR. Age and vGFR were the only variables significantly associated with 3-month postoperative GFR in univariable analyses and both multivariable models. Other, less significant variables in multivariable models included EBL, tumor diameter (vGFR-PAVP based model only), and robotic PN (vGFR-SAVP based model only). RENAL score, body mass index, WIT, and gender were not significant predictors of postoperative renal function in univariable or multivariable models indicating that, age and preserved volume are the most reliable indicators of postoperative GFR in this group of patients. These strongly correlative multivariable models, with $R^2 = 0.72$, are highly consistent with externally validated published models using 3DVP and preoperative GFR

Table 2
Multivariable models to predict postoperative GFR utilizing volume adjusted GFR based on PAVP or SAVP while accounting for other variables

	vGFR-PAVP based model Estimate (95% CI)	*P* value	vGFR-SAVP based model Estimate (95% CI)	*P* value
vGFR-PAVP	0.841 (0.699, 0.984)	<0.0001		
vGFR-SAVP			0.906 (0.801, 1.01)	<0.0001
Age, y	−0.450 (−0.653, −0.247)	<0.0001	−0.189 (−0.341, −0.038)	0.0146
Gender (Male vs. Female)	−0.282 (−2.84, 2.27)	0.83	0.923 (−0.878, 2.72)	0.31
Preoperative tumor diameter, cm	1.86 (0.0.176, 3.55)	0.0308	1.22 (−0.083, 2.53)	0.07
WIT, min	0.252 (−0.080, 0.585)	0.14	0.046 (−0.191, 0.284)	0.70
RENAL score	−0.659 (−2.07, 0.756)	0.29	−0.360 (−1.39, 0.666)	0.49
Estimated Blood Loss, ml	0.001 (−0.017, 0.019)	0.89	−0.012 (−0.023, −0.001)	0.029
BMI	−0.082 (−0.507, 0.342)	0.70	−0.005 (−0.337, 0.327)	0.98
Surgical approach		0.25		0.0019
Open	−0.025 (−7.70, 7.65)	0.99	0.609 (−6.57, 7.79)	0.87
Laparoscopic	6.62 (−2.89, 16.13)	0.17	5.30 (−2.94, 13.55)	0.21
Robotic	4.05 (−3.51, 11.61)	0.29	7.96 (0.951, 14.97)	0.0262
R^2		$R^2 = 0.72$		$R^2 = 0.72$

Abbreviations: vGFR = volume-adjusted glomerular filtration rate.

to predict postoperative GFR in patients undergoing both PN and RN [21,22,24]. Thus, percentage of VP during PN is indeed critical for postoperative functional outcomes and since VP might be closely linked to both resection technique and renorrhaphy technique, it will be of utmost importance to use standardized instruments of reporting VP assessments in future studies on the topic.

Renal function is generally better preserved after PN than after RN due to nephron preservation [7,8] and the amount of preserved parenchymal volume has been consistently demonstrated to be a primary indicator of postoperative renal function [12,13,15,18]. Accurate preoperative prediction of the impact of PN on renal functional outcomes can aid patient counseling, particularly in patients at significant risk for development and/or progression of chronic kidney disease after renal mass treatment. Tobert et al. demonstrated in a multicenter validation study that SAVP was highly correlated ($R^2 = 0.93$) with 3DVP measurements, and thus could act as a reliable, less time consuming, and less costly surrogate [24]. The authors suggest that the ease of obtaining PAVP (and SAVP) argue strongly for their use (rather than 3DVP) on a routine basis for postoperative planning and that time- and costintensive 3DVP should be reserved for research purposes.

Recent studies have investigated whether assessment of VP based on preoperative imaging that has been reviewed by clinical investigators ranging from attending physicians to medical students correlates with 3DVP assessment [14]. The correlation between these 2 measurements was only moderate ($R = 0.403$), with little correlation between the experience of the clinical investigators and their predictions [14]. In contrast, we found a stronger correlation between

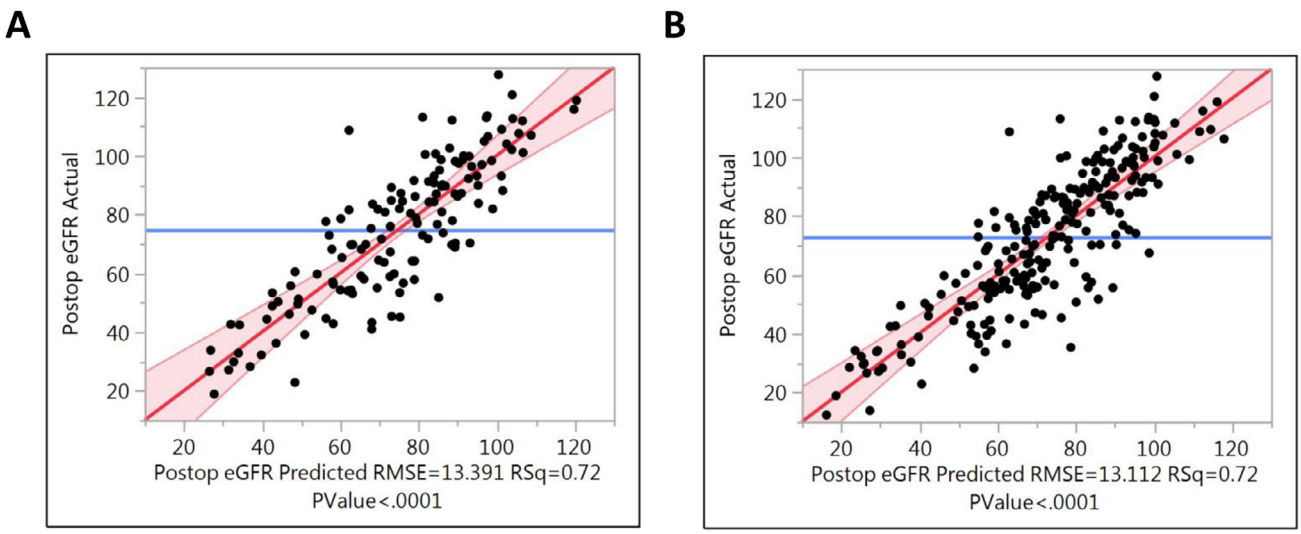

Fig. 2. Multivariable models of vGFR based models and actual postoperative GFR. (A) Multivariable model utilizing vGFR-PAVP to predict actual postoperative GFR ($R^2 = 0.72$). (B) Multivariable model utilizing vGFR-SAVP to predict actual postoperative GFR ($R^2 = 0.72$).

PAVP and SAVP (R = 0.65) performed by the operating surgeon. Incorporating preoperative GFR to calculate an estimated vGFR revealed an even stronger correlation between the 2 VP assessments (R = 0.95). Differences between the study by Zhao et al. and the present study include the timing and clinical setting of imaging review. Whereas the assessment in the earlier study was performed by a variety of reviewers after surgery; in the current study, review was performed prior to surgery and by the attending surgeon. Patients in the study by Zhao et al. also had a larger median tumor size (4.0 vs. 3.0 cm), higher median RENAL score (8 vs. 6), and lower median VP (81% vs. 90%) than the patients included in this study [14]. Finally, the 336 patients in the present study (40 surgeons, 12 centers) comprised a substantially larger dataset then the 45 patients reported by Zhao et al. (9 surgeons, 1 center).

In this study, we demonstrated a moderate correlation between PAVP and SAVP (R = 0.65) and that these values are statistically interchangeable. In addition, we demonstrated that both vGFR-PAVP (R = 0.82) and vGFR-SAVP (R = 0.83) are highly, and similarly, correlated with GFR 3 months after PN. Limitations of this study include potential interobserver bias of VP assessments. Though all surgeons had sufficient prior experience performing PN prior to study initiation, some surgeons had little prior experience estimating VP. Central review, though preferable, was infeasible due to practical concerns of obtaining Institutional Review Board and data transfer agreements in place across multiple countries and sites. Findings might also not be completely generalizable as they were collected from a multicenter collaboration of highly experienced centers and surgeons. Another limitation is the inability to assess the quality of the preserved parenchyma, either by the presence of pathology in the non-neoplastic tissue or by functional imaging assays, as these were not routinely performed at participating centers. Strengths of this study include the international, multicenter, and robust cohort of surgeons that used different techniques and approaches. Our findings are clinically important because both PAVP and SAVP may provide guidance to patients, in terms of expected postoperative functional outcomes, as well as to surgeons, in terms of appropriate selection of surgical approach and technique.

Future studies may be needed to further validate the ability of PAVP and SAVP to estimate renal function in the mid- and longterm after PN. The opportunity also exists to assess the relationship between parenchymal VP, tumor complexity metrics, and resection technique (SIB score) [26,31,32] on functional outcomes.

5. Conclusion

This large, international, multicenter collaboration demonstrates that PAVP, like SAVP, is a good predictor of postoperative renal function in patients undergoing PN. PAVP and SAVP are interchangeable in their ability to determine actual postoperative GFR. The vGFR and patient age offer additional value in counseling relative to postoperative functional outcomes. This straight-forward clinical assessment should be discussed with all patients for whom multiple options are being considered in order to facilitate communication about preservation of parenchyma and renal function.

Conflicts of interest

The authors declare no relevant potential conflicts of interest.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.urolonc.2018.11.007.

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