Warm ischemia time length during on-clamp partial nephrectomy: does it really matter?

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ABSTRACT

BACKGROUND: The impact of warm ischemia time (WIT) on renal functional recovery remains controversial. We examined the length of WIT>30 min on the long-term renal function following on-clamp partial nephrectomy (PN).
METHODS: Data from 23 centers for patients undergoing on-clamp PN between 2000 and 2018 were analyzed. We included patients with two kidneys, single tumor, cT1, minimum 1-year follow-up, and preoperative eGFR≥60 mL/

min/1.73m^2. Patients were divided into two groups according to WIT length: group I "WIT≤30 min" and group II "WIT>30 min." A propensity-score matched analysis (1:1 match) was performed to eliminate potential confounding factors between groups. We compared eGFR values, eGFR (%) preservation, eGFR decline, events of chronic kidney disease (CKD) upgrading, and CKD-free progression rates between both groups. Cox regression analysis evaluated WIT impact on upgrading of CKD stages.
RESULTS: The primary cohort consisted of 3526 patients: group I (N.=2868) and group II (N.=658). After matching the final cohort consisted of 344 patients in each group. At last follow-up, there were no significant differences in median eGFR values at 1, 3, 5, and 10 years (P>0.05) between the matched groups. In addition, the median eGFR (%) preservation and absolute eGFR change were similar (89% in group I *vs*. 87% in group II, P=0.638) and (-10 in group I *vs*. -11 in group II, P=0.577), respectively. The 5 years new-onset CKD-free progression rates were comparable in the non-matched groups (79% in group I *vs*. 81% in group II, log-rank, P=0.763) and the matched groups (78.8% in group I *vs*. 76.3% in group II, log-rank, P=0.905). Univariable Cox regression analysis showed that WIT>30 min was not a predictor of overall CKD upgrading (HR:0.953, 95%CI 0.829-1.094, P=0.764) nor upgrading into CKD stage ≥III (HR:0.972, 95%CI 0.805-1.173, P=0.764). Retrospective design is a limitation of our study.
CONCLUSIONS: Our analysis based on a large multicenter international cohort study suggests that WIT length during PN has no effect on the long-term renal function outcomes in patients having two kidneys and preoperative eGFR≥60 mL/min/1.73m^2.

KEY WORDS: Nephrectomy; Warm ischemia; Delayed graft function.

Renal function preservation is one of the main goals following partial nephrectomy (PN), while maintaining the perioperative and oncological safety. PN provides better renal function outcomes,[1, 2] but its and similar oncological outcomes compared to radical nephrectomy (RN).[3] Therefore, most urological guidelines recommend PN as the first line-treatment option for cT1 renal masses whenever feasible, regardless of the surgical approach that surgeons are familiar with.[4, 5] Factors affecting renal function after PN have been extensively evaluated in literature. Several non-modifiable factors are associated with poor postoperative renal function including aging, male gender, medical comorbidities "*e.g.*, diabetes mellitus (DM) and hypertension (HTN)," large tumors, presence of solitary kidney, and poor preoperative renal function.[6-8] While modifiable factors are usually related the surgical approach (*i.e.*, open, laparoscopic, and robotic), ischemia technique (*i.e.*, warm, cold, and zero ischemia), the length of warm ischemia time (WIT), and the volume of preserved renal parenchyma after surgery. Recently, several multicenter studies have shown similar short-[9, 10] and long-term[11] renal function outcomes following open PN (OPN), laparoscopic PN (LPN), and robotic-assisted PN (RAPN). In addition, Greco *et al.* reported that none of ischemia technique (*i.e.*, warm, cold, or zero ischemia) outperforms the other in term of renal function preservation.[12] Furthermore, it is worth noting that the quality and quantity of preserved renal parenchyma is strongly associated with postoperative renal function after PN.[13, 14] Regarding WIT, controversy exists regarding the cut-off WIT length that should not be exceeded during PN. WIT values of 20 min,[15] 25 min,[16] and 30 min have been suggested to maintain renal function.[17] On the other hand, other clinical studies have shown that WIT>30 min has no effect on the long-term renal function.[18, 19] In addition, some research pointed out that kidney tissues can tolerate up to 60 min. of controlled clamp ischemia without acute renal functional loss, with only mild renal structural tissue changes.[20] Obviously, for single kidneys and/or in patients with poor preoperative renal function, every minute of warm ischemia counts,[21] thereby minimizing WIT or using zero ischemia PN are strongly recommended to preserve kidney function as much as possible. In this study, we used a large multi-institutional international database to evaluate the actual impact of WIT length during PN on the long-term renal function outcomes in patients with two kidneys and adequate preoperative kidney function.

Materials and methods

Patients

This study is a retrospective multi-institution study. We have received ethical approval for

this study from the institutional review board (IBR number: H1R1-01-Oct19-02). Data for patients who underwent PN for management of renal masses between 2000 and 2018 were collected. Twenty-three centers from 10 countries/regions participated in our research: USA, UK, Germany, Italy, Spain, Belgium, South Korea, the Philippines, Saudi Arabia, and Egypt. We included patients with a cT1 single kidney mass (*i.e.*, ≤7 cm), two kidneys, baseline eGFR≥60 mL/min/1.73 m^2, and at least one year of follow-up in the analysis. Regarding the ischemic technique during PN, we only included warm ischemia. Patients with cold ischemia or zero ischemia and patients with incomplete data or who did not meet the inclusion criteria were excluded.

Baseline characteristics

Patients' demographic and pathologic parameters were obtained including age, gender, Body Mass Index, DM, HTN, cardiac diseases, tumor size, tumor complexity, preoperative renal function, length of WIT, and surgical approaches (*i.e.*, OPN, LPN, and RAPN). Tumor complexity was defined according to R.E.N.A.L. nephromerty score. Baseline renal function was measured by eGFR using the Modification Diet in Renal Disease (MDRD) formula.[22] Patients were divided according to the length of WIT in two groups: group I "WIT≤30 min." and group II "WIT>30 min."

Renal function and follow-up

Postoperative eGFR measurements were obtained yearly until the latest follow-up. eGFR percentage preservation was calculated using the formula: (latest measured eGFR / preoperative eGFR×100). Absolute eGFR percentage (%) change was estimated using the formula: (latest measured eGFR – preoperative eGFR×100). We used the National Kidney Foundation definition to classify chronic kidney disease (CKD).[23] Overall CKD upstaging was defined as any increase in CKD stage, while new-onset CKD was defined as upstaging of CKD stage I or stage II to ≥ stage III at longest follow-up.

Study outcome measurements

Primary endpoint was to compare eGFR values, eGFR (%) preservation, absolute eGFR (%) change, events of overall CKD upstaging and new-onset CKD, and the CKD-free progression rates between both groups at longest follow-up. Secondary endpoint was to evaluate predictors of overall and new-onset CKD upstaging.

Propensity-score matching

Selection bias and confounding factors are the main shortcomings of retrospective comparative studies. In this case, we used propensity-score matching (PSM) analysis to match patients in group I and patients in group II to reduce the impact of these shortcomings. Based on the following variables, a multiple logistic regression model was used to evaluate the propensity score of each patient; age, BMI, gender, DM, HTN, tumor size, clinical stage, preoperative eGFR, RENAL score, proteinuria, and surgical technique.According to the propensity score, the patients in group I were matched with the closest patients in group II using a predefined matching tolerance of 0.002. Finally, after a 1:1 match, each group included 344 patients, and the preoperative variables in the PSM identification group were compared again.

Statistical analysis

Continuous variables were presented as mean±standard deviation (SD) or as median and interquartile range (IQR). We used the Student's *t*-test to compare normally distributed data and the Mann–Whitney test to compare nonparametric data. Categorical variables were presented as frequency and percent (%). We used the χ^2 test or Fisher's Exact Test to compare categorical data. The Kaplan-Meier Test was used to estimate for 1, 3, and 5 CKD-free progression rates and the differences between groups were assessed with a log-rank test. A multivariable Cox regression analysis were used to examine the predictors of overall and new-onset CKD upstaging. All statistical analyses were two-sided, and P value of less than 0.05 was considered statistically significant. The IBM SPSS version 23 statistical package (SPSS Inc., Chicago, IL, USA) was used to perform all tests.

Results

Table I summarized baseline demographics of unmatched and matched cohorts. The number of

TABLE I.—*Comparison of renal functional outcomes between both groups at last follow-up.*

Variables	before PSM Whole cohort			After PSM (1:1 match)		
	WIT≤30 (N.=2867)	WIT>30 (N.=658)	P value	WIT≤30 (N.=344)	WIT>30b (N.=344)	P value
eGFR follow-up, median (IQR)						
at 1-year	82 (69-94)	84 (71-96)	0.072	80 (65-90)	83 (68-96)	0.064
at 3-year	80 (68-92)	80 (70-94)	0.584	78 (67-90)	78 (67-94)	0.986
at 5-year	79 (65-92)	76 (64-93)	0.320	80 (65-91)	77 (60-94)	0.786
at 10-year	82 (66-93)	67 (57-90)	0.085	66 (67-84)	64 (54-89)	0.935
Last eGFR, median (IQR) ††	79 (65-91)	79 (65-94)	0.420	77 (62-89)	77 (63-93)	0.274
eGFR (%) preservation, median (IQR) ††	90 (78-99)	88 (74-100)	0.246	89 (77-99)	87 (74-100)	0.638
Absolute eGFR change, median (IQR) ††	-8 (-1 to -19)	-11 (-24 to 0)	0.282	-10 (-1 to -21)	-11 (0 to -23)	0.577
Postoperative CKD, N. (%) ††						
Stage 1	809 (28.2)	208 (31.6)	0.115	91 (26.5)	103 (29.9)	0.060
Stage 2	1511 (52.7)	315 (47.9)		173 (50.3)	158 (45.7)	
Stage 3	510 (17.8)	130 (19.8)		73 (21.2)	83 (24.1)	
Stage 4	28 (1)	3 (0.5)		5 (1.5)	0 (0)	
Stage 5	10 (0.3)	2 (0.3)		2 (0.6)	0 (0)	
Overall CKD upgrading, N. (%) ††	1030 (35.9)	250 (38)	0.323	137 (39.8)	130 (37.8)	0.584
New-onset CKD upgrading, N. (%) ††	548 (19.1)	135 (20.5)	0.412	80 (23.3)	83 (24.1)	0.788
Follow-up, months, median (IQR)	45 (26-64)	49 (31-71)	0.003*	48 (29-65)	47 (29-70)	0.944

PSM: propensity score matching, WIT: warm ischemia time, CKD: chronic kidney disease, eGFR: estimated glomerular filtration rate.
†† eGFR value or CKD stage at longest follow-up; *statistically significant.

patients in group I and group II were 2868 and 658, respectively. Median follow-up period was 46 (IQR: 27-65) months. Six-hundred eighty-three patients (19.3%) were upstaged into CKD stage ≥III. Before matching, patients in group I had significantly higher mean age (59.3 *vs.* 54.8, P<0.001), higher incidence of male gender (69.1% *vs.* 61.4%, P<0.001), proteinuria (12.2% *vs.* 8.7%, P=0.010), and RPN (44.4% *vs.* 38.1%, P=0.013) compared to patients in group II. There were no significant differences in terms of mean BMI, median preoperative eGFR, mean RENAL score, mean tumor size, incidence of DM and HTN (P=0.389, P=0.058, P=0.143, P=0.310, P=0.144, and P=965, respectively). After 1:1 PSM, 344 patients were included in each group. When comparing both matched groups, there were no significant differences in all baselines' demographic variables (P>0.05) (Supplementary Digital Material 1: Supplementary Table I). Table I summarized the renal functional outcomes between unmatched and matched cohorts. In unmatched groups, the median eGFR values at 1, 3, 5 and 10 years did not show significant difference (P>0.05). In addition, the median eGFR (%) preservation and absolute eGFR change were similar between both groups at longest follow-up (89% in group I *vs.* 87% in group II, P=0.638) and (-10 in group I *vs.* -11 in group II, P=0.577), respectively. Similarly, the incidence of overall CKD upgrading in group I was 35.9% compared to 38% in group II (P=0.323), and new-onset CKD upgrading ≥3 was 19.1% in group I compared to 20.5% in group II (P=0.412). After 1:1 PSM, there were no significant differences in all renal function outcomes parameters including median eGFR values (P>0.05), median eGFR (%) preservation (P=0.638), median absolute eGFR change (P=0.577), events of overall CKD upgrading (P=0.584) and new-onset CKD (P=0.788). The overall 1, 3, and 5 years new-onset CKD free-progression rates were 98.4%, 90%, and 79.4%, respectively. The 5 years new-onset CKD-free progression rates were comparable in the non-matched groups (79% in group I *vs.* 81% in group II, log-rank, P=0.763) (Figure 1) and the matched groups (78.8% in group I *vs.* 76.3% in group II, log-rank, P=0.905) (Figure 2). Further subgroup analysis of new-onset CKD free-progression rates were stratified into four groups according to the length of WIT: group A (<15 min), group B (16-30 min), group C (31-45 min). and group D (≥46 min). Of note, the 5 years new-onset CKD free-progression rates were 80.3%, 78.4%, 81.5%, and 79.4% in group A, B, C, and D, respectively (log-rank, P=0.675). Table II showed the univariable and multivariable Cox regression analysis of risk factors as-

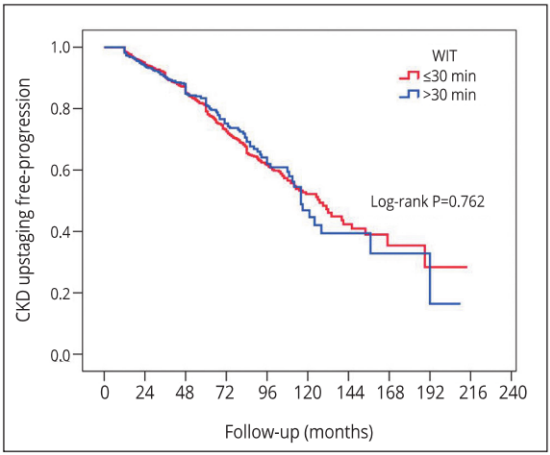

Figure 1.—Kaplan-Meier new-onset CKD free-progression in unmatched cohorts stratified according to the length of WIT.

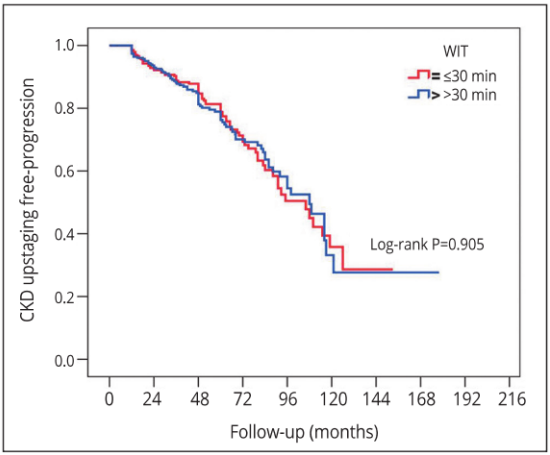

Figure 2.—Kaplan-Meier new-onset CKD free-progression in matched cohorts stratified according to the length of WIT.

TABLE II.—*Univariable and multivariable analysis of factors associated with events of overall CKD upgrading (N.=360/3525) and new-onset CKD (N.=674/3525).*

Variables	Univariable analysis		Multivariable analysis	
	HR (95% CI)	P value	HR (95% CI)	P value
Overall CKD upstaging				
Age (continues)	1.016 (1.011-1.020)	<0.001*	1.009 (1.005-1.014)	<0.001*
BMI (continues)	1.017 (1.007-1.027)	0.001*		
Male gender	0.999 (0.887-1.125)	0.988		
DM (yes)	1.577 (1.381-1.800)	<0.001*	1.369 (1.191-1.575)	<0.001*
HTN (yes)	1.358 (1.217-1.516)	<0.001*	1.185 (1.055-1.330)	0.004*
Tumor size (continues)	1.097 (1.058-1.137)	<0.001*	1.072 (1.032-1.114)	<0.001*
R.E.N.A.L. Score	1.067 (1.035-1.100)	<0.001*	1.044 (1.011-1.078)	0.009*
WIT (continues)	0.997 (0.992-1.001)	0.172		
WIT (>30 min)	0.953 (0.829-1.094)	0.491		
Baseline eGFR	0.991 (0.988-0.995)	<0.001*	0.995 (0.992-0.999)	0.007*
Proteinuria (yes)	1.072 (0.905-1.269)	0.422		
New-onset CKD				
Age (continues)	1.050 (1.043-1.057)	<0.001*	1.021 (1.014-1.029)	<0.001*
BMI (continues)	1.036 (1.022-1.049)	<0.001*	1.016 (1.001-1.030)	0.034*
Male gender	1.198 (1.012-1.417)	0.036*		
DM (yes)	2.645 (2.252-3.108)	<0.001*	1.611 (1.353-1.919)	<0.001*
HTN (yes)	1.952 (1.678-2.270)	<0.001*	1.283 (1.092-1.507)	0.002*
Tumor size (continues)	1.211 (1.155-1.270)	<0.001*	1.176 (1.120-1.235)	<0.001*
R.E.N.A.L. Score	1.091 (1.047-1.137)	<0.001*		
WIT (continues)	0.997 (0.991-1.004)	0.436		
WIT (>30 min)	0.972 (0.805-1.173)	0.764		
Baseline eGFR	0.939 (0.933-0.944)	<0.001*	0.948 (0.943-0.954)	<0.001*
Proteinuria (yes)	1.482 (1.207-1.820)	<0.001*		

BMI: Body Mass Index, ASA: American Society of Anesthesiologists, DM: diabetes mellitus, HTN: hypertension, CVD: coronary vascular disease, eGFR: estimated glomerular filtration rate, CAD: chronic kidney disease, WIT: warm ischemia time, PN: partial nephrectomy.
*Statistically significant.

sociated with overall CKD and new-onset CKD upgrading. On univariable analysis WIT>30 min was not a predictor of overall CKD upgrading (HR: 0.953, 95%CI 0.829-1.094, P=0.764) nor upgrading into CKD stage ≥III (HR: 0.972, 95%CI 0.805-1.173, P=0.764). Multivariable analysis revealed that DM (HR 1.611, 95%CI 1.353-1.919; P<0.001), HTN (HR: 1.283, 95%CI 1.092-1.507; P=0.002), tumor size (HR: 1.176, 95%CI 1.120-1.235; P<0.001), BMI (HR: 1.016,

95%CI 1.001-1.030; P=0.034), age (HR: 1.021, 95%CI 1.014-1.029; P<0.001), and lower preoperative eGFR (HR: 0.948, 95%CI 0.943-0.954; P<0.001) were independent predictors of new-onset CKD upgrading.

Discussion

In the current multi-center international study, we evaluated the effect of WIT length during PN on the long-term renal function prognosis. We selected for this study many patients (N.=3526) with two kidney and preoperative eGFR of ≥60 mL/min/1.73 m^2, to give an actual representation of the typical patients undergoing PN surgery for the treatment of cT1 renal tumors. At last follow-up, WIT>30 min was not associated with overall CKD upgrading or CKD upgrading ≥ stage III. In addition, all renal function parameters including median eGFR values at 1, 3, 5, and 10 years, eGFR (%) preservation and absolute eGFR change in the unmatched and matched groups were comparable. Aging, high BMI, DM, HTN, larger tumors, and lower preoperative eGFR were predictors of new-onset CKD upgrading. Literature data regarding the impact of WIT length and renal function outcomes remains controversial.[7, 8, 16, 18-20, 24, 25] Our data and several studies[7, 8, 18-20, 24] found that long WIT does not affect long-term renal function recovery, while other studies showed that prolonged WIT>25 min. could lead to an irreversible ischemic insult to the kidney and might have deleterious long-term effects.[16, 25] We believe that WIT length is a critical parameter in patients with solitary kidney[13, 21, 26] and poor preoperative renal function due to increased risk of acute kidney injury (AKI) in the early postoperative period. In patients with solitary kidneys, on-clamp RPN had a higher risk of progression to CKD 3b,4,5 stages (P=0.034) compared to those underwent of-clamp RPN, in addition, WIT was as independent predictor of progression to CKD (HR:1.09, P<0.001) at median follow-up of 13 months.[26] In the setting of two kidneys, a recent study by Dong *et al.* found that renal functional recovery after on-clamp PN is primarily dependent on nephron mass preservation and use of hypothermia. Each additional 10 min. of warm ischemia was associated with only a 2.5% decline in renal function that may not be clinically significant in patients with a normal contralateral kidney, where compensatory hypertrophy of the healthy contralateral kidney can mask ipsilateral renal damage.[27] Furthermore, in a large multicenter study of 668 patients, each with two kidneys, undergoing RPN for cT1 tumor, WIT threshold of 20 min. was significantly associated with an increased risk of AKI at discharge (OR=6.23; CI 1.52,30.39, P=0.015), nevertheless, extended WIT was not found to be significantly associated with eGFR decline at 1 year (P>0.05).[28] Interestingly, Parekh *et al*. studied the structural and functional changes in 40 patients undergoing on-clamp PN. The mean duration of warm ischemia and cold ischemia were 32.3 and 48 min., respectively. Their data suggested greater tolerance of human kidneys to clamp ischemia of 30-60 min. with only mild structural changes and no acute functional loss.[20] Recently, a systematic reviews and meta-analysis evaluating ischemia techniques (*i.e.,* warm, cold, or zero ischemia) during PN found that none of the available ischemia techniques is universally superior to the others, and other factors play a role in the surgical outcome.[12] In the contrary, Lane *et al*. suggested that WIT length is the strongest modifiable surgical risk factor for poor renal function after PN and efforts to minimize it should be pursued.[7] Literature data showed that non-modifiable factors have great impact on long-term renal function together with the volume of preserved parenchymal after PN.[6-8, 13, 14, 29] Our results showed that age, DM, HTN, large tumors, high BMI, and low preoperative eGFR are risk factors for new-onset CKD upgrading at longest follow-up. In their recent analysis, Brassetti *et al*. have proposed a new tool named ROMe's (defined as the concomitant lack of cancer-recurrences, death, and new-onset CKD development), and found that young age and high preoperative eGFR were independent predictors of ROMe's achievement.[29] The inevitable impact of aging and medical comorbidities such as DM and HTN may lead to decrease of renal blood flow, development of tubular interstitial fibrosis and glomerular sclerosis, rendering the kidney highly vulnerable to AKI and CKD development.[30, 31] In addition, high BMI is associated with increased risk of CKD and/or ESRD develop-

ment.[32] Several studies have shown that the volume and quality of preserved renal parenchyma after PN is considered an important factor in renal function preservation rather than WIT.[8, 13, 14, 33] Recently, Wu *et al.* evaluated the predictors of percentage parenchymal mass preserved (PPMP) in 464 patients underwent PN. They found that, PPMP correlated strongly with eGFR preservation (P<0.001) and lower PPMP is the most common and important source of functional decline after PN. Larger tumors, greater tumor complexity, and prolonged ischemia time were associated with lower PPMP probably reflecting the complexity of the surgery.[33] In patients with a solitary kidney, PPMP was significantly higher than for patients with two kidneys (median 89% *vs.* 82%; P<0.001), confirming that PPMP is a modifiable factor and the need to preserve more nephrons led to optimization of intraoperative surgical strategy such as such as ischemia type, tumor resection and reconstruction that will determine the quantity as well as the quality of PPMP.[33, 34] Unfortunately, we did not evaluate the effect of retained nephron mass volume, as data was not available. Nevertheless, our multivariable analysis revealed that large tumors are associated with poor long-term renal function. The resection of large tumors is greatly detrimental to the volume of nephron mass loss; in addition, deep and excess renorrhaphy sutures to close the large parenchymal defect may lead to more renal ischemia and nephrons loss. To minimize the ischemic effect of renorrhaphy on the renal tissue, Porpiglia *et al.* suggested that the suture should be oriented at right angles with respect to the line of the arcuate arteries, avoid including the arcuate arteries to preserve the medullar blood supply, avoid excessive compression of the parenchymal tissue during suturing of the cortex, and avoid calyceal involvement by using precise sutures perpendicular and superficial to the collecting system defect.[35] It is recommended to use 3/0 monofilament running absorbable suture that is cinched with surgical clips (*i.e.,* a sliding-clip renorrhaphy). Of note, the different types of surgical clips used during renorrhaphy had similar operative and surgical outcomes.[36] Furthermore, the type of renorrhaphy (*i.e.*, single-layer *versus* double-layer suture) also might influence the healthy parenchyma incorporated in the renorrhaphy but literature is still lacking about the best suture technique after PN.[35] Rather than renorrhaphy technique, there are other intraoperative factors should be taken in consideration as they might affect the postoperative renal functional outcomes such as: the type of hilar clamping (*i.e.*, global, selective, or super-selective) and the type of tumor resection (*i.e.*, enucleation, enucleoresection, or wedge resection).[37-39] A recent systematic review and cumulative meta-analysis evaluated the impact of various hilar control techniques on functional outcomes of RPN and showed that the off-clamp, selective/super-selective clamp, and early hilar unclamping techniques are safe and feasible approaches, with potentially superior functional outcomes when compared with the on-clamp RPN cohort.[37] Regarding the different types of tumor resection, tumor enucleation is oncologically safe, maximizes the preservation of vascularized parenchyma, and helps to expand the indications of kidney-sparing surgery to more complex cases.[38] In their systematic review and meta-analysis, Xu *et al.* suggested that tumor enucleation has faster recovery, better renal function protection, without evidence of an increase relapse rate or mortality rate when compared with PN.[39] Unfortunately, the evaluation of these intraoperative factors was not feasible in our study, because many these variables were missed in our data and not included in the analysis, which is a limitation of the study. Recently, several studies have shown that the use of three-dimensional (3D) virtual reconstruction of standard bi-dimensional (2D) imaging can be used for preoperative planning before PN, surgeon training, and patient counselling.[40] Compared with 2D imaging, 3D virtual reconstruction and augmented reality can be attributed to a better perception of tumor depth and its relationships with intrarenal structures, and higher accuracy in predicting overall and major postoperative complications.[41] We believe that this new technology can provide precise tumor resection, increase the volume of parenchymal preservation, and improve renal functional outcomes.

Limitations of the study

The present study does not devoid of limitations. First, risk of selection bias cannot be excluded due to its retrospective design. Second,

the impact of parenchymal volume preservation after PN was not examined due to lack of data; however, we believe that it is associated with the tumor size, which was an important predictor of poor renal function on multivariable analysis. Third, other intraoperative factors such the type of hilar clamping, renorrhaphy and tumor resection techniques were not included in the analysis due to insufficient data, however, we believe that these factors are of utmost important in patients with solitary kidneys and/or poor preoperative renal function, and we need to optimize the intraoperative surgical strategy for each patient to maximize the preservation of renal parenchyma and minimize the ischemia time. Fourth, estimation of functional status of both the operated and contralateral kidney was not available due to absence of renal isotope scan data. In this setting, renal function assessment was based on repeated eGFR measurements which is a reliable and simple tool. Nevertheless, our study has several strength points. Our study is largest one that evaluate WIT impact on the long-term renal functional outcomes. The median follow-up time was 46 months, and all participants had a minimum of 1-year renal function assessment. To minimize the influence of confounding factors between WIT groups, a PSM (1:1 match) analysis was carried out. In addition, it is a multicenter multiethnicity study represents a real-world cohort.

Conclusions

In conclusion, in patients with two normal nephrons and adequate preoperative renal function, our large multicenter international cohort study suggests that the length of warm ischemia during PN has no effect on the long-term renal function outcomes. It is worth noting that other non-modifiable factors such as age, DM, HTN, BMI, tumor size, and preoperative eGFR are considered powerful determinants of poor renal function.

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