Determinants of renal functional decline after open partial nephrectomy: a comparison of warm, cold, and non-ischemic modalities

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Introduction: *Renal functional decline after partial nephrectomy (PN) may be related to a variety of nonmodifiable and modifiable factors, including ischemia time (IT) and modality. We sought to determine the impact of these factors on renal functional degeneration after PN.*
Materials and methods: *Multicenter retrospective analysis (n = 347) was performed, identifying patients who underwent open PN using warm, cold, and non-ischemic techniques. Primary outcome was development of de novo chronic kidney disease (CKD), (estimated glomerular filtration rate (eGFR) < 60 mL/min/1.73 m^2), at 1 year follow up. Univariate and multivariable analysis (MVA) were performed examining factors associated with ischemia technique and the development of de novo CKD.*
Results: *Median follow up 34.7 months. Two hundred and forty-one patients underwent warm ischemic, 31 cold ischemic, and 75 clampless PN. Patient characteristics were similar between groups. Clampless group had lower mean RENAL scores (6.4) than cold (7.9, p = 0.005) and warm (7, p = 0.037) ischemia groups. Cold ischemia cohort had longer median IT than the warm cohort (50min versus 25 min, p = 0.001). There were no significant differences in proportion of patients developing de novo CKD (warm 14.9%, cold 15%, clampless 8.7%, p = 0.422). MVA demonstrated that neither ischemic modality nor IT ≥ 30 minutes was associated with development of de novo CKD, while RENAL scores of increasing complexity (RENAL score 7-9 OR 4.32, p = 0.003; RENAL score ≥ 10 OR 15.42, p < 0.001) were independently associated with de novo CKD.*
Conclusions: *Increasing tumor complexity, as indicated by the RENAL score, was an overriding determinant of post PN renal functional outcome. Prospective investigation is requisite to elucidate risk and protective factors for renal functional degeneration after PN.*

Key Words: carcinoma, renal cell, partial nephrectomy, ischemia, chronic kidney disease, glomerular filtration rate, RENAL nephrometry

Introduction

Partial nephrectomy (PN) is considered to be the reference standard in patients with clinical T1a renal masses, providing equivalent oncologic outcomes to radical nephrectomy.[1-3] PN offers the advantage of superior long term renal functional outcomes with lower rates of chronic kidney disease (CKD) and metabolic sequelae.[4-6] Renal functional decline after PN may be related to a variety of factors, including percent of renal parenchyma spared, patient age, body mass index (BMI), and RENAL nephrometry scores. Duration and modality of ischemia utilized during partial nephrectomy remain the only modifiable factors associated with CKD.[7-11]

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Efforts have been made to minimize the effects of ischemia on renal function by refining ischemic technique. Cold ischemia allows for longer ischemia time (IT) by reducing oxygen demand of the kidney while clamped.[12] Clampless techniques and regional ischemic techniques are being investigated in hopes of further improving renal functional outcomes.[8,13-16] Questions remain about optimal technique of ischemia during PN and its effects on renal functional outcome. We sought to examine factors related to renal functional degeneration after PN in a cohort of patients which underwent warm, cold and non-ischemic approaches to tumor excision.

Materials and methods

Study design and clinical management

After obtaining Institutional Review Board approval, a multicenter retrospective study was performed evaluating the effect of different ischemic modalities on postoperative renal functional outcomes in patients undergoing warm (WI), cold (CI), and clampless (CL) open PN. Patients who underwent surgery from January 2003 to April 2011 at the University of Tennessee Health Science Center (Memphis, TN, USA), Naval Medical Center San Diego, VA San Diego Medical Center, and the University of California San Diego Health System were included in the study. Preoperative evaluation of patients included a physical exam, serum creatinine and other laboratory measurements, confirmatory imaging using computed tomography (CT) or magnetic resonance imaging (MRI) as dictated by renal function, and chest imaging (radiography or CT). Additional staging was obtained as indicated.

Open PN was offered for elective, relative (estimated glomerular filtration rate (eGFR) < 70 with presence of drivers for medical kidney disease), and imperative indications (solitary kidneys, bilateral tumors, eGFR < 60). Patients who underwent PN for solitary kidney or those with bilateral tumors or urothelial malignancy, as well as those with incomplete records or less than 1 year months of follow up, were excluded from the study. Selection of modality of ischemic or clampless approach was determined by the surgeon utilizing preoperative imaging and intraoperative examination. Patients with tumors felt to require greater than 30 minutes of resection and renorrhaphy time underwent cold ischemia, those who were felt to be doable within a 30 minute span were managed by warm ischemia, and patients whose tumors were felt to be amenable to a clampless approach did not undergo clamping of the renal artery during surgery.

Operative procedure

Our technique has been described previously.[8,17] All PN were performed by two fellowship trained, high volume renal surgeons. Initial surgical approach was identical for all three groups: an extraperitoneal flank or subcostal transperitoneal incision, kidney mobilization, renal hilar dissection and control followed by tumor isolation. During WI and CI surgeries, Bulldog or Satinsky clamps were used to occlude the renal artery. Ice slush was placed on the kidney for cold ischemic cases. When performing clampless partial nephrectomy, blood loss was controlled using either direct manual compression on the renal parenchyma or a focal radiofrequency bipolar resection device (Habib 4X, Angiodynamics, Queensbury, NY, USA). This was followed by excision of the tumor with surrounding margin of normal by scalpel or hydro-jet dissector (ERBEJET, ERBE USA, Marietta, GA, USA). Renorrhaphy was then performed using absorbable suture closure of collecting system and segmental blood vessels, followed by parenchymal closure. Closed suction (Jackson-Pratt) drains were placed in all patients prior to closure.

Data collection and analysis

Patient clinicopathological characteristics and perioperative data were compared between groups (WI, CI and CL). Preoperative imaging was used to determine complexity of tumors using RENAL nephrometry scores, based on diameter of renal mass, endophytic/exophytic quality, nearness to collecting system or sinus, anterior/posterior location, as well as location relative to polar lines.[8,17,18] Clinical data included age, sex, race, BMI, history of hypertension, smoking, and diabetes. Renal function was evaluated using serum creatinine levels (mg/dL) and estimated glomerular filtration rate (eGFR), which was calculated using the MDRD equation.[19] Pathological data included tumor characteristics (size, location, histological diagnosis), surgical margin status, and AJCC stage.[20] Perioperative data, including operative time, estimated blood loss (EBL; mL), ischemia time (IT; min), collecting system entry, blood transfusion, length of stay, postoperative renal function, urine leak, and other complications (Clavien grading),[21] was also included in the final analysis.

Primary outcome was development of de novo eGFR < 60 mL/min/1.73 m^2 at 1 year follow up. Secondary outcomes included change in eGFR between preoperative and 1 year follow up (IQR) and median % change in eGFR between preoperative and 1 year follow up (IQR). Values were compared between groups using Chi,[2] Fisher's exact test, ANOVA, Kruskal-Wallis test, and Mann-Whitney U test. Multivariate analysis (MVA) was performed to examine factors associated with the development of de novo eGFR < 60 which were clinically relevant or significant at the univariate level. All p values were based on two-sided tests of significance, with

TABLE 1. **Patient demographics and tumor characteristics**

	Warm ischemia (n = 241)	Cold ischemia (n = 31)	No ischemia (n = 75)	p value
Mean age ± SD (years)	57 ± 17.3	56 ± 11.9	55 ± 14.6	0.385
Sex				0.876
Male	153 (63.5%)	21 (67.7%)	49 (65.3%)	
Female	88 (46.5%)	10 (33.3%)	26 (34.7%)	
Race				0.536
Caucasian	144 (60%)	14 (53.8%)	40 (53.3%)	
Other	97 (40%)	17 (46.2%)	35 (46.7%)	
Mean BMI ± SD, kg/m²	28.5 ± 5.3	26.1 ± 3.8	28.2 ± 7.6	0.322
Hypertension	159 (66%)	13 (50%)	53 (70.7%)	0.159
Smoking	133 (58.8%)	11 (50%)	48 (67.6%)	0.253
Diabetes	60 (24.9%)	8 (30.8%)	23 (30.7%)	0.542
Central tumor location	82 (34%)	14 (50%)	25 (33.3%)	0.229
Median tumor size, cm (IQR)	3.3 (2.4-4.3)	3 (2-5.2)	3.9 (2.5-5.5)	0.188
Clinical T-stage				0.274
T1	204 (84.6%)	23 (74.2%)	60 (80.0%)	
T2+	37 (15.4%)	8 (25.8%)	15 (20.0%)	
Central tumor location	82 (34.0%)	14 (45.2%)	25 (33.3%)	0.449

BMI = body mass index

statistical significance set a priori at $p < 0.05$. Statistical analysis was performed using SPSS software, version 17.0 (Chicago, IL, USA).

Results

Table 1 shows patient demographics and tumor characteristics of those who underwent open PN (n = 347) between 2003 and 2011 [241 underwent WI, 31 underwent CI, and 75 underwent CL PN]. Median follow up (IQR) was 34.7 months (18.8-64.2). The three groups were similar in mean age (p = 0.385), sex (p = 0.876), race (p = 0.536), BMI (p = 0.322), and proportion of patients with history of hypertension (p = 0.159), smoking (p = 0.253), and diabetes (0.542). All three cohorts also had similar median tumor size (p = 0.188), and proportion of clinical T1/T2+ tumors (p = 0.274), and tumors in central locations (p = 0.449).

TABLE 2. **RENAL nephrometry scores**

	Warm ischemia (n = 218)	Cold ischemia (n = 18)	No ischemia (n = 71)	p value
Mean total RENAL score ± SD	7 ± 1.8	7.9 ± 1.7	6.4 ± 1.6	0.003
Nephrometry				0.011
Simple (4-6)	105 (48.2%)	3 (16.7%)	36 (50.7%)	
Intermediate (7-9)	90 (41.3%)	13 (72.2%)	34 (47.9%)	
Complex (10+)	23 (10.6%)	2 (11.1%)	1 (1.4%)	
Nephrometry				0.041
< 9	163 (74.8%)	13 (72.2%)	63 (88.7%)	
≥ 9	55 (25.2%)	5 (27.8%)	8 (11.3%)	

Table 2 demonstrates RENAL scores in the different ischemia groups. The clampless cohort had lower mean RENAL scores (6.4 ± 1.6) than warm (7 ± 1.8, p = 0.037) and cold (7.9 ± 1.7, p = 0.005) ischemia groups. Patients who underwent clampless surgery also had fewer complex nephrometry scores when stratified by simple (4-6), intermediate (7-9), and complex (10+) scores (p = 0.011), and a greater proportion of RENAL scores < 9 (p = 0.041). When breaking down the nephrometry score by its individual components, no differences were observed between the three groups.

Perioperative variables, complications, and outcomes are shown in Table 3. There were no differences between the three cohorts in terms of median EBL (p = 0.169) or

TABLE 3. **Perioperative variables, complications and outcomes**

	Warm ischemia (n = 241)	**Cold ischemia (n = 31)**	**No ischemia (n = 75)**	**p value**
Perioperative variables				
Mean OR time ± SD, mins	194 ± 53	245 ± 76	239 ± 59	0.009
Median EBL, mL (IQR)	300 (150-400)	250 (200-500)	250 (150-400)	0.169
Median ischemia time, min (IQR)	25 (22-28)	50 (43-65)	-	0.001
Collecting system entry	129 (53.9%)	15 (57.7%)	42 (56%)	0.876
Patient(s) transfused	20 (8.3%)	6 (19.4%)	8 (10.7%)	0.147
Complications (≤ 30 day)	34 (14.1%)	9 (29%)	9 (12%)	0.065
Low grade	19 (7.9%)	7 (22.6%)	4 (5.3%)	0.012
High grade	18 (7.5%)	4 (12.9%)	7 (9.3%)	0.555
Urine leak	19 (7.9%)	3 (9.7%)	5 (6.7%)	0.866
Positive margins	4 (1.7%)	1 (3.3%)	1 (1.3%)	0.773
Median LOS, days (IQR)	6 (5-7)	5 (4-6)	8 (7-10)	< 0.001
Pathological findings				
Pathology				0.711
Malignant	196 (81.3%)	26 (83.9%)	64 (85.3%)	
Benign	45 (18.7%)	5 (16.1%)	11 (14.7%)	
Malignant tumors				0.628
Clear cell	142 (72.4%)	15 (71.4%)	53 (82.8%)	
Papillary	40 (20.4%)	4 (19%)	9 (14.1%)	
Chromophobe	11 (5.6%)	2 (9.5%)	2 (3.1%)	
Other	3 (1.5%)	0	0	
Benign tumors				0.111
Oncocytoma	20 (44.4%)	2 (40%)	8 (72.7%)	
Angiomyolipoma	20 (44.4%)	1 (20%)	3 (27.3%)	
Other	5 (11.1%)	2 (40%)	0	
Renal function outcomes				
Mean preoperative eGFR ± SD	91 ± 27.3	87.4 ± 36.7	95.1 ± 25	0.377
Mean eGFR at 1 year FU ± SD	72.7 ± 22.8	70.5 ± 29.2	78 ± 21.2	0.164
Median delta eGFR (IQR)	-15.1 (-23.8 to -7.2)	-12.7 (-23.4 to 0)	-13.2 (-20.8 to -6.9)	0.364
Median % eGFR change (IQR)	-17.1% (-26.3 to -10.4)	-17.2% (-32.6 to 0)	-14.4% (-22.4 to -8.8)	0.319
Preoperative GFR < 60	30 (12.4%)	6 (19.4%)	5 (6.7%)	0.146
eGFR < 60 at 1 year follow up	58 (24.1%)	9 (29%)	11 (14.7%)	0.197
de novo eGFR < 60	28 (11.6%)	3 (9.7%)	6 (8%)	0.542

EBL = estimated blood loss; LOS = length of stay; eGFR = estimated glomerular filtration rate

TABLE 4. **Multivariable analysis for factors associated with development of de novo chronic kidney disease**

Variable	OR	95% CI Lower	95% CI Upper	p value
Model 1 – Ischemia type				
Ischemia group (non = ref)				0.593
Warm	1.71	0.60	4.84	0.312
Cold	1.73	0.34	8.86	0.508
Nephrometry (simple 4-6 = ref)				< 0.001
Intermediate 7-9	4.32	1.66	11.25	0.003
Complex 10-12	15.42	4.57	51.99	< 0.001
Model 2 – Ischemia time				
Ischemia time ≥ 30 mins	0.938	0.279	3.15	0.918
Nephrometry (simple 4-6 = ref)				< 0.001
Intermediate 7-9	4.28	1.65	11.10	0.003
Complex 10-12	14.27	4.16	48.92	< 0.001

rates of collecting system entry (p = 0.876), transfusion (p = 0.147), or positive margins (0.773). Rates of low grade complications were significantly higher in the CI group (22.6% versus warm 7.9% versus clampless 5.3%, p = 0.012), although all three cohorts had similar rates of high grade complications (p = 0.555). Rates of urine leak were similar among the three groups as well (p = 0.866). The cold ischemia cohort had longer mean OR times (245 min ± 76 min) than the WI (194 ± 53) or CL (239 ± 59) groups (p = 0.009). Patients who underwent cold ischemic PN also had longer median ischemia times than the warm ischemia cohort (50 min versus 25 min, p = 0.001). Median length of stay was longer in the CL patients (8 days) compared to the WI (6) and CI (5) groups (p < 0.001).

There was no difference between the groups for mean preoperative eGFR (p = 0.377), and mean eGFR 1 year postoperative (p = 0.164). Change in eGFR, in terms of both absolute (delta eGFR: WI -15.1, CI -12.7, CL -13.2, p = 0.364) and relative (% delta eGFR: WI -17.1%, CI -17.2%, CL -14.4%, p = 0.319), was also similar between groups. There was no significant difference between the groups for preoperative CKD (WI 12.8%, CI 19.4%, CL 6.7%, p = 0.146) or 1 year postoperative CKD (WI 24.1% versus CI 29% versus CL 14.7% p = 0.197). Rate of de novo CKD was not significantly different between the groups (WI 11.6%, CI 9.7%, CL 6%, p = 0.542).

Table 4 shows multivariable analyses for de novo eGFR < 60. Variables that were significant on univariate testing or of clinical interest were tried in the MVA model, including: ischemia technique, ischemia time (< 30 min versus ≥ 30 min), BMI, diabetes, hypertension, pathology (benign/malignant), estimated blood loss (< 100 mL versus ≥ 100mL), 30 day complication, and RENAL nephrometry score grouping; only variables that remained significant in the multivariate model were included in the final model. Two MVA models were performed, one analyzing ischemic modality and one with ischemia time ≥ 30 minutes. In the first model, none of the three different ischemic cohorts (warm, cold, clampless) was associated with development of de novo stage III CKD (p = 0.565). Further analysis comparing the clampless cohort to clamped (WI + CI) revealed that clamping of the renal artery during surgery was not associated with development of de novo CKD (p = 0.313; results not shown). Compared to those with simple nephrometry scores (4-6), intermediate RENAL scores (7-9) had an odds ratio of 4.3 for development of de novo CKD (p = 0.001), while complex scores (10-12) had an even stronger association with de novo CKD following PN (OR 15.4, p < 0.001). In the second model, ischemia time ≥ 30 minutes was not associated with development of renal insufficiency (p = 0.918), nor was IT ≥ 20 minutes associated with de novo CKD in a subanalysis of the warm ischemia cohort (p = 0.651; results not shown). Intermediate and complex RENAL scores had very similar associations with development of de novo eGFR < 60 as in the first model.

Discussion

A body of literature suggests a variety of nonmodifiable and modifiable clinicopathological factors may play a role in influencing renal functional recovery following nephron-sparing surgery, including patient demographics, pre-existing medical conditions,

RENAL nephrometry score, percent renal parenchyma spared, and modality of ischemia utilized during surgery.[8,11,12,22] Indeed, degree of impact of the major modifiable factors, ischemia time and modality, has been questioned. Most studies on the topic have focused on single kidney systems and have not compared all three approaches (warm, cold, and non-ischemic). We evaluated the impact of a variety of nonmodifiable factors in the setting of the different categories of ischemic approach to tumor resection and repair in a two-kidney system. To our knowledge, this study represents the first such investigation. Our investigation revealed no significant difference in rates of de novo CKD in the three groups.

Indeed, RENAL score, a surrogate for tumor size and complexity, represents an overarching variable associated with renal functional outcome—by inversely correlating with parenchyma spared (a result of nonmodifiable factors), and also potentially impacting ischemia duration, a modifiable factor.[12,22-24] In our MVA, intermediate RENAL nephrometry scores were associated with de novo CKD compared to 'simple' scores with an odds ratio of greater than 4, while an even stronger association was noted with complex RENAL scores (odds ratio > 14 in both MVA models, Table 4). Simmons et al analyzed impact of renal volume preservation on renal functional outcome in 39 patients undergoing open or laparoscopic PN and found that percent functional renal volume preserved (utilizing a cylindrical volume ratio method to estimate percent of functional volume preservation on CT images obtained before and after PN, $p = 0.04$) as well as preoperative renal function ($p < 0.001$), are primary determinants of long term renal function following PN.[22] In a follow up investigation, Simmons et al compared the RENAL and C-index scoring systems in 299 patients with a contralateral normal kidney who underwent open, laparoscopic or robotic PN. They noted that on MVA that RENAL score "R": and "N" domains correlated with percent functional volume preservation, and "N" and "L" domains correlated with warm ischemia time and estimated blood loss. Furthermore, they noted that diameter and overall RENAL scores also significantly correlated with long term percent GFR preservation.[24] Long et al analyzed 177 patients who underwent open or laparoscopic PN and noted that increasing RENAL nephrometry score was the only independent factor which correlated with increasing warm ischemia time (OR 5.89, $p = 0.03$). Bylund et al analyzed 162 patients who underwent minimally invasive partial nephrectomy, and noted a statistically significant association between increasing RENAL score and warm ischemia time as well ($p < 0.001$).[25] Initial tumor volume and complexity as described by the RENAL score, and in turn functional volume preserved during surgery, appears to be an overriding determinant of postoperative renal function when compared to other perioperative factors, in these studies as well as our own analysis.

Questions remain regarding an acceptable limit of ischemia time. Thompson et al analyzed 362 patients with a solitary kidney who underwent open or laparoscopic partial nephrectomy and demonstrated an increased odds ratio for developing CKD of 1.05 for each additional minute of warm IT ($p < 0.001$), with a cut point of 25 minutes as the best distinction between outcomes.[23] Funahashi et al investigated impact of renal ischemia on effective renal plasma flow (ERPF) and found that warm IT > 25 minutes was associated with significantly lower ERPF at 6 months postoperatively.[26] Other studies have suggested that clinical sequelae of warm IT < 30 minutes are minimal.[27]

Non-ischemic partial nephrectomy offers the potential benefit of eliminating clamping of the renal artery, yet there still exists uncertainty regarding its clinical application, alongside of the real risk of significant hemorrhage during resection and repair. Direct manual compression on the renal parenchyma, as well as bipolar dissectors such as the HABIB 4X radio frequency device, help to minimize blood loss, though our clampless cohort did not have statistically significant differences in EBL or operative time when individually compared to the other groups. Kaczmarek et al performed a multicenter analysis of 886 robotic partial nephrectomies, 66 of which were clampless, and found that clampless PN was associated with a smaller decrease in eGFR at last follow up compared to matched clamped controls (delta GFR 1.6 versus -6.2, $p = 0.008$).[28] White et al conducted a prospective randomized control study of 90 patients undergoing open PN (45 with versus 45 without radio frequency ablation) and demonstrated improvement in blood loss with the HABIB 4X device; however, they did not demonstrate a significant improvement in renal functional outcomes.[29] Similarly, our clampless cohort failed to demonstrate significantly lower rate of novo CKD, Table 3, compared to the other groups, even with more favorable RENAL scores, Table 2. In a previous investigation of factors affecting postoperative renal function in 228 patients with two kidneys undergoing either WI or CL open PN by our own group, neither ischemic modality (WI versus CL) nor ischemia time (≥ 20 min versus < 20 min) were associated with development of de novo CKD.[8] Findings from recent studies comparing warm

and non-ischemic partial nephrectomy suggest that clampless technique should be used when technically feasible, though the majority of renal tumors are not amenable to CL partial nephrectomy.[30] Attempts to expand utilization of clampless technique for more complex tumors by segmental tertiary arterial ischemia have had mixed results.[16] Further investigation will be required to determine the exact benefits of and limits to performing clampless NSS.

Conversely, in our current MVA and analysis of CI, WI and non-ischemic technique, ischemia time ≥30 minutes did not correlate with de novo CKD (p = 0.918), which suggests that cold ischemia is an effective strategy of minimizing renal functional decline by allowing for longer ischemia times. Our cold ischemia cohort had a median IT of 50 minutes, twice that of the WI cohort (25 minutes, p = 0.001), while rates of de novo CKD were similar between the two groups (11.6% WI versus 9.7% CI). Ischemic modality was not found to be significantly associated with de novo CKD in our MVA, as well as when comparing patients who underwent clampless versus clamped (including both WI and CI) surgery, Table 3 and Table 4. Our study suggests that our application of cold ischemic technique, in appropriately selected patients, has allowed for patients with more complex tumors and longer planned ischemia times to have comparable renal functional outcomes to patients with more favorable preoperative characteristics.

While most of the perioperative outcomes were similar among our three cohorts, we found that overall 30 day complication rates in our CI cohort were more than twice that of the other groups, approaching statistical significance (p = 0.065). The cold ischemia cohort had significantly higher rates of low grade complications (p = 0.012), again more than double that of the other cohorts. This could be related to factors other than the cold ischemic technique itself. The CI cohort had longer operative times, which have been shown to independently correlate with increased risk of complications in procedures such as laparoscopic colectomy and robotic and open PN.[31,32] Furthermore, the higher RENAL scores in the CI group may also contribute to this finding. Simhan et al examined 390 patients undergoing open and robotic PN and found that increasing tumor complexity, as measured by RENAL score, is associated with the development of major complications after PN (OR 5.4, p = 0.03).[32] Ficarra et al performed a multi-institutional analysis of 347 robotic PN which showed that increasing complexity of renal tumors, as measured by the Preoperative Aspects and Dimensions Used for Anatomical (PADUA) classification score system, was independently associated with both increasing ischemia time (OR 1.3, p = 0.005) and overall complication rate (OR 1.4, p < 0.001).[33] Nonetheless, presence of perioperative complications was not an independent risk factor for the development of de novo CKD in our MVA.

Limitations to our study include its retrospective nature, and the inherent limitations with respect to data acquisition and selection bias. Furthermore, we examined only patients with two kidneys and did not examine patients who underwent minimally invasive partial nephrectomy. In a two kidney system, differences in warm ischemia time < 30 minutes may not be of significant consequence,[9] no matter what the approach may be.[8,34,35] We did not analyze proportion of renal parenchyma spared,[24] and also used serum creatinine to estimate GFR. Furthermore, although RENAL score has been shown to be highly reproducible, reviewers at each institution may have differed in how they calculated these values – leading to some variation in scores between sites that may have affected our results.[36,37] We demonstrate that RENAL score may be a useful surrogate whose increase is associated with renal functional degeneration after partial nephrectomy, regardless of ischemic modality. Our analysis is strengthened by its multicenter nature, as well as the fact that our three cohorts were similar in terms of preoperative characteristics. To our knowledge, this represents the first report in the literature to examine determinants of renal functional degeneration in a cohort of patients who undergo warm, cold and non-ischemic technique. Further follow up and prospective investigation is requisite to assess impact of each ischemic modality and to precisely quantify renal functional recovery and identify risk and protective factors for renal functional degeneration after partial nephrectomy.

Conclusions

Our study suggests that increasing complexity of RENAL score is an over-arching and independent risk factor associated with renal functional decline following partial nephrectomy. RENAL score may be a useful surrogate marker of nonmodifiable factors such as tumor complexity or percent parenchyma spared, as well as modifiable factors such as ischemia time. Questions remain regarding the exact benefits and applicability of each ischemia modality, and further prospective investigation is requisite to elucidate the utility and role of clampless technique for partial nephrectomy.

Disclaimer

The views expressed in this article are those of the authors and do not necessarily reflect those of the U.S. Navy or Department of Defense. □

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