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Rapid Communication

Chronic Renal Insufficiency after Laparoscopic Partial Nephrectomy and Radical Nephrectomy for Pathologic T_{1a} Lesions

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ABSTRACT

Purpose: **To report the prevalence of new-onset renal insufficiency in patients undergoing laparoscopic partial nephrectomy (LPN) as compared to laparoscopic radical nephrectomy (LRN) for pathologic T_{1a} lesions.**

Patients and Methods: **Forty-eight patients and 37 patients with a normal contralateral kidney, preoperative creatinine (Cr) concentration <2 mg/dL, and tumors <4 cm in size underwent LPN and LRN, respectively. Glomerular filtration rate (GFR) was estimated using an abbreviated Modification of Diet in Renal Disease (MDRD) equation. Cr concentrations and GFR values were analyzed in patients undergoing LPN or LRN. Statistical analysis was performed with two-tailed *t*-test assuming unequal variances, to establish significance by $P < 0.05$.**

Results: **Preoperative Cr and GFR was equivalent in the LPN and LRN groups (0.9 mg/dL and 90 mL/min). At last follow-up (mean 205 and 233 days in the LPN and LRN groups, respectively) mean creatinine was 1.03 ± 0.3 mg/dL *v* 1.4 mg/dL ± 0.3 ($P = 0.0002$). Estimated GFR was 79 ± 22 mL/min per 1.73 m^2 *v* 55 ± 14 mL/min per 1.73 m^2 (range 31–91 mL/min per 1.73 m^2; $P < .0001$) in the LPN and LRN groups, respectively. One patient in the LPN group and three patients in the LRN group had clinical renal insufficiency as defined by Cr >2.0 mg/dL. Subclinical renal insufficiency (Cr < 2.0, but calculated GFR <60 mL/min per 1.73 m^2) was present in 57% of the LRN patients *v* 15% of the LPN patients.**

Conclusions: **LPN preserves renal function more effectively than LRN for pathologic T_{1a} lesions. Subclinical renal insufficiency (GFR <60 mL/min per 1.73 m^2) was present in the majority of patients undergoing radical nephrectomy in our series. Importantly, this series included the use of warm ischemia in all cases.**

INTRODUCTION

CHRONIC RENAL INSUFFICIENCY (CRI) has become a major public health concern, with 336,000 people on dialysis in 2004.[1] The independent and graded association between estimated glomerular filtration rate (GFR) below 60 mL/min per 1.73 m^2 and cardiovascular morbidity and mortality,[2] accounts in part for the fact that patients with CRI are five to ten times more likely to die before being classified as having end-stage renal disease (ESRD).[1] Thus, CRI is an important factor in the decision to perform radical nephrectomy (RN) versus nephron-sparing surgery for small suspicious renal lesions.

Historically, for patients with renal tumors, open radical nephrectomy (ORN) was considered the standard of care. However, after pioneering studies demonstrating the safety and efficacy of open partial nephrectomy (OPN), the indications for OPN have expanded to the elective setting. OPN has now been shown to have equivalent cancer control to ORN for tumors less than 4 cm in size, and investigations are being performed for appropriately-selected tumors 4 to 7 cm in size.[3–6] Impor-

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tantly, besides cancer control, patients undergoing elective OPN have the benefit of long-term prevention of renal insufficiency. Studies have shown improved glomerular filtration rates (GFR) and creatinine concentrations in patients undergoing OPN as opposed to ORN for small renal lesions.[7,8]

Laparoscopic partial nephrectomy (LPN) is a newer technique that may serve as an alternative to OPN for selected lesions. One disadvantage of LPN is warm ischemia, as renal hypothermia may be difficult to perform via laparoscopic means. Certain novel methods have been developed,[9,10] but the majority of cases are still performed with warm ischemia. It is unknown if LPN will produce the same advantages as OPN with regard to prevention of long-term renal insufficiency.[7,8] Few studies of long-term renal function after LPN have been reported in the literature. Cleveland Clinic surgeons reported their experience in 200 patients undergoing LPN, and initially four patients required dialysis after surgery for acute renal failure, and although an analysis of the effect of warm ischemia was presented with 4 months' mean follow-up, no comparison to either OPN or RN was made.[13,14] Cornell urologists compared LPN to OPN, and reported that 1 to 2 days' postoperative creatinine (Cr) concentrations showed no significant difference before or after surgery.[15] A group from Johns Hopkins compared patients undergoing laparoscopic radical nephrectomy (LRN) to those receiving LPN, and found a significantly higher postoperative creatinine concentration in the LRN group (1.51 ± 0.22 mg/dL *v* 1.18 ± 0.37 mg/dL; $P = 0.02$).[16]

Although the advantages of open partial nephrectomy *v* radical nephrectomy are clear with regard to deterrence of renal insufficiency, similar studies have not been well documented with LPN. The goal of this communication is to retrospectively evaluate the effects on renal function of LPN *v* RN in patients with pathologic T_{1a} tumors (or benign pathology <4 cm in size) with all LPN patients undergoing warm ischemia.

METHODS

Patient selection

Institutional review board approval was obtained to retrospectively review the outcomes of renal surgery. All consecutive patients undergoing laparoscopic renal surgery by one surgeon were screened. Patients were selected for inclusion if they had a suspicious renal mass, with final pathology of pT_{1a} or benign pathology <4 cm in size, a normal functioning contralateral kidney (kidneys with radiographically diagnosed simple cysts were included), and no pre-existing chronic renal insufficiency (CRI) as defined by creatinine <2.0 mg/dL. Preoperative characteristics including gender, ethnic origin, age, body mass index (BMI), American Society of Anesthesiologists (ASA) score, hypertension, diabetes mellitus, and current or past tobacco use were recorded. The ASA score was analyzed because it has been found to be associated with CRI after both partial and radical nephrectomy.[12] GFR was estimated for patients LPN or LRN using an abbreviated Modification of Diet in Renal Disease (MDRD) equation: GFR (mL/min per 1.73 m^2) = $32788/1.73 \times (\text{serum Cr})^{-1.164} \times (\text{age})^{-0.203} \times 0.742$ if female, and × 1.21 if African-American.[17] Statistical analysis was performed with two-tailed *t*-test assuming unequal variances, to establish significance by $P < 0.05$. A Fisher's exact test was used when indicated.

RESULTS

Demographic data

A total of 48 patients in the LPN and 37 patients in the LRN group met inclusion criteria for analysis. The mean ages of those in the LPN group and the LRN group were 59 years (range 35–80 years) and 67 years (range 37–85 years), respectively ($P = 0.01$). In all other demographic categories (gender, race, BMI, comorbidities, percentage with hypertension, percentage with diabetes mellitus, and percentage of tobacco users), the differences between the groups were not significant ($P > 0.05$). Males were slightly over-represented in both groups with 28/48 (58%) and 21/37 (57%) in the LPN and LRN groups, respectively. African-Americans were in the minority in both groups, 4/48 (8%) of LPN patients and 4/37 (11%) of LRN patients. Mean BMI was 30 kg/m^2 (range 20.9–46.3 kg/m^2) in the LPN group versus 29 kg/m^2 (range 21.8–55.9 kg/m^2) in the LRN group; 33/48 (69%) of LPN patients and 20/37 (54%) of LRN patients had hypertension. The average ASA score was 2.4 for both groups. Regarding tobacco use, 4/48 (8%) and 5/37 (14%) in the LPN and LRN groups, respectively, currently used tobacco, and 10/48 (21%) in the LPN group and 12/37 (32%) in the LRN group had used tobacco in the past.

Operative and pathologic data

Mean tumor size was significantly larger ($P = 0.0001$) in the LRN group, with a mean size of 2.8 ± 0.8 cm, *v* 2.0 ± 1.0 cm in the LPN group. Pathology revealed renal cell carcinoma (all subtypes) in 63% of LPN patients and 92% of LRN patients. Oncocytoma was present in 11/48 (23%) of LPN patients and no LRN patients. Other benign entities were present in 3/48 (6%) of the LPN patients and 3/37 (8%) of the LRN patients (most commonly, benign complex cystic lesions). Mean warm ischemia times were 26 ± 8 minutes. Operative times were significantly shorter in the LRN group, with mean times of 113 minutes (range 35–221 minutes) *v* 155 minutes (range 82–253 minutes) in the LPN group ($P = 0.0001$).

Preoperative renal function

Preoperative Cr and GFR were not significantly different between the two groups, with a mean creatinine of 0.9 mg/dL and 90 mL/min in both groups (Table 1). Mean follow-up was 211 days or 7 months in the LPN group *v* 233 days or 7.8 months in the LRN group.

Postoperative renal function

Mean postoperative creatinine was 1.03 ± 0.34 mg/dL *v* 1.4 ± 0.32 mg/dL ($P = 0.0002$) in the LPN and LRN groups, respectively. Mean GFRs were 79 ± 22 mL/min per 1.73 m^2 *v* 55 ± 14 mL/min per 1.73 m^2 ($P = .000001$) in the LPN and LRN groups, respectively (Table 1). Postoperative clinical renal insufficiency (defined as creatinine ≥2.0 mg/dL) was present in one patient (2%) in the LPN group, and three patients in the LRN group (8%) at last follow-up ($P = 0.32$, using Fisher's

TABLE 1. PREOPERATIVE AND LAST FOLLOW-UP CREATININE AND ESTIMATED GFR

	LPN		*LRN*		
	Mean	*SD*	*Mean*	*SD*	P *value*
Preoperative creatinine (mg/dL)	0.9	0.2	0.9	0.2	0.30
Preoperative GFR (mL/min per 1.73 m^2)	89.5	22.1	90	16.7	0.91
Follow-up days post-surgery	211	214	233	214	0.64
Last follow-up creatinine (mg/dL)	1.03	0.34	1.4	0.32	0.0002
Last follow-up GFR (mL/min per 1.73 m^2)	79	22	55	14	1×10^{-6}

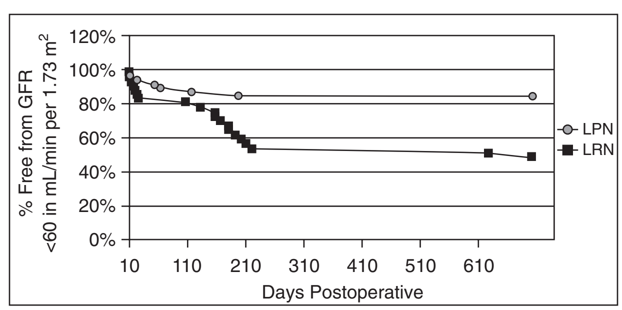
exact test). Subclinical renal insufficiency, defined by GFR <60 mL/min per 1.73 m^2, but Cr <2.0 mg/dL, was present in 7/48 (15%) in the LPN group *v* 21/37 (57%) in the LRN group (*P* = .004, using Fisher's exact test). The cumulative incidence of freedom from renal insufficiency, defined as a GFR <60 mL/min per 1.73 m^2, starting at >10 days postoperatively, showed a marked difference in LRN *v* LPN patients (49% *v* 85%) (Fig. 1). (Note that in Figure 1, the downward slope at days 110 to 210 is indicative of the surgeon's routine practice to check creatinine concentrations at 4 to 6 months postoperatively, depending on scheduling concerns, and it is not indicative of a nephron-losing event at the 100-day mark. Creatinine concentrations were generally checked 1 to 2 weeks postoperatively, and 4 to 6 months postoperatively, then every 6 months.)

DISCUSSION

This study demonstrates that patients with small renal tumors have better renal function when undergoing laparoscopic partial nephrectomy compared to radical nephrectomy. These results, which are already established in open partial nephrectomy studies, have not been well documented in laparoscopic partial nephrectomy series with warm ischemia. Our study is consistent with results of historic open partial nephrectomy series, but it also suffers from several limitations, many of which are also limitations of other open partial nephrectomy series.

When compared to other studies of OPN, our mean preoperative creatinine concentration (0.9 mg/dL) was similar to those previously reported (1.0 *v* .98 mg/dL for OPN *v* ORN), and the creatinine concentration at last follow-up for LPN of 1.0 mg/dL was the same as that reported for OPN.[11] In other series, the average mean time to develop renal insufficiency has been reported at 14 to 18 months; thus it is therefore likely that our mean follow-up of 7 months was too short to capture the eventual rate of CRI.[7,12] This could explain why, though our perioperative data are similar to those of OPN, we report only one (2%) LPN and three (8%) LRN patients (*P* = 0.32) with Cr >2 mg/dL throughout the follow-up period, Lau and colleagues reported 11.6% of OPN and 22.4% of ORN patients with Cr >2 mg/dL at some point during 10 years' follow-up.[8] This weakness in our communication is likely because the follow-up period is not yet mature enough to obtain statistical differences, and 10-year outcomes are certainly the reference standard. However, despite the shorter follow-up period, there is a striking difference in the number of patients with subclinical renal insufficiency in the LRN group compared to the LPN group. Subclinical CRI, defined as a creatinine <2.0 mg/dL, but still with a GFR <60 mL/min per 1.73 m^2, was present in 57% of the LRN group, and only 15% of the LPN group (*P* = .004). Several of these patients will likely progress to clinical renal insufficiency over time, mirroring the results of other similar studies. This concept is critical, as patients undergoing radical nephrectomy may appear to have a "normal creatinine" in the middle-to-high 1's, but in reality, calculation of GFR uncovers chronic renal insufficiency that may manifest over several years post-nephrectomy. It is likely that over longer periods of time, deterioration of renal function in all patients in this series will result in similar CRI rates to those reported in OPN/ORN series, but until 10-year follow-up data are generated, this remains a presumption.

Because of the nature of a retrospective analysis, we are aware that the two groups (LPN and LRN) are not completely matched. Nevertheless, the preoperative GFR and creatinine values were not statistically different, so the impact of such bias may be limited. These biases are not unique to our series, as another series reported a similar and significant trend toward younger patients (57 *v* 63 years old)[11] with smaller tumors (2.4 *v* 3.0 cm)[7] undergoing OPN *v* RN. Another large series found similarly significant differences with mean ages of 56.2 *v* 67.3 years for OPN *v* LRN.[18] Differences in tumor types have also been reported,[11,15] and this series certainly had differences in histology in the LPN group *v* the radical nephrectomy group, as outlined in the results section. It is unclear how this would impact renal function.



Patients with follow-up	Day 30	Day 60	Day 90	Day 120	Day 200	Day 300	Day 400	Day 500	Day 600
LPN	33/48	28/48	26/48	25/48	24/48	13/48	9/48	6/48	3/48
LRN	27/37	25/37	25/37	25/37	16/37	12/37	8/37	6/37	3/37

FIG. 1. Cumulative freedom from GFR <60 mL/min per 1.73 m^2.

It would be ideal to perform this study as a prospective randomized trial, but unfortunately this may not be possible on a practical concentration, as patients made treatment decisions for these options. There are no randomized trials on this topic in the literature. The decision to proceed with LPN *v* OPN *v* LRN *v* ORN was decided by the patients after counseling, and the surgeon felt comfortable with all four techniques and counseled patients on all four techniques. The specific reasons that certain patients choose LRN over LPN or OPN are complex, and their analysis is beyond the scope of this paper; we examined it, but it was difficult to confidently analyze retrospectively. The most common reasons that were subjectively identifiable included patient preference as the overwhelming indicator of surgical type. Preoperative counseling was based on preoperative imaging, which in several cases revealed the mass to be $>$4 cm in size, which may have influenced patient preference. In some cases, a hilar mass was present and patients elected laparoscopic radical nephrectomy over a complex partial nephrectomy. This communication does attempt to show preference or superiority of any of the procedures, except to show that renal function is better preserved with LPN compared to LRN.

Arguments that organ preservation is unnecessary with regard to the kidneys have centered around early studies involving kidney donors.[19] Patients with renal neoplasia are, on average, older and thus more likely to have comorbidities (62% hypertension and 19% diabetes mellitus in this series). Renal insufficiency is defined by current guidelines to be an estimated GFR $<$60 mL/min per 1.73 m^2, or evidence of kidney damage for a total of 3 months.[20] Historically, creatinine has often been used as a substitute measure of renal function, but the importance of using GFR to identify renal insufficiency is illustrated in this cohort, in whom estimation of GFR demonstrated that 21/37 (57%) of LRN *v* 7/48 (7%) of LPN patients exhibited subclinical renal insufficiency at last follow-up. This is comparable to the 3-year follow-up data reported by Huang and associates, which showed that 70% of RN *v* 17% of OPN patients developed new onset of GFR $<$60 mL/min per 1.73 m^2.[7] Again, it appears that in our study, LPN is somewhat consistent with OPN (and is superior to total renal excision) with respect to preservation of renal function. Differential pre- and postoperative renal scintigrams were not performed, and neither were 24-hour urine assays for creatinine clearances. These weaknesses are likely uniform across all similar studies and their effects are difficult to define.

Lastly, the results herein were obtained with a reasonably short warm ischemic time, and certainly if these times were longer, there would likely be more deterioration of renal function. Thus, these results are reflective of an experienced renal surgeon with laparoscopic intracorporeal suturing skills, and may not be applicable to all surgeons. Even accounting for all of these weaknesses, this study identifies LPN as an advantageous option in preserving renal function, when compared to total renal excision. Similarly to OPN, there are great benefits in nephron sparing with regard to prevention of renal insufficiency. However, renal function is but one variable in a patient's complex decision-making process of choosing between total excision, partial excision, or ablation of a small renal mass via the laparoscopic, open, or percutaneous approaches.

CONCLUSION

Overall, we conclude that LPN (with warm ischemia) offers a distinct advantage over radical nephrectomy with regard to the effects on renal function. This conclusion is consistent with those of prior groundbreaking studies that scrutinized the advantages of OPN.[7,8,11,12,21] Further work needs to be performed to train surgeons in nephron-sparing procedures, educate patients on their benefits, and examine the long-term effects of nephron-sparing surgery on downstream quality and quantity of life.

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ABBREVIATIONS USED

ASA = American Society of Anesthesiologists; BMI = body mass index; Cr = creatinine; CRI = chronic renal insufficiency; ESRD = end-stage renal disease; GFR = glomerular filtration rate; LRN = laparoscopic radical nephrectomy; LPN = laparoscopic partial nephrectomy; MDRD = Modification of Diet in Renal Disease; OPN = open partial nephrectomy; ORN = open radical nephrectomy; RN = radical nephrectomy.