

Perioperative complications and postoperative outcomes of partial nephrectomy for renal cell carcinoma: Does indication matter?

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ABSTRACT

Introduction: The aim of the study was to determine whether perioperative complications and postoperative outcomes varied with the indication of partial nephrectomy (PN).

Materials and Methods: We reviewed data of 184 consecutive PN for suspected renal cell carcinoma operated between January 2004 and December 2013. Complications using the Clavien-Dindo classification were compared between surgeries for absolute indications (chronic renal failure, bilateral tumors, or solitary kidney), those for relative indications (comorbid illnesses with the potential to affect renal function) and elective indications (patients without risk factors). Complex tumors were defined as size >7 cm, multiple, hilar, and endophytic tumors.

Results: Patients with an absolute indication had larger tumors ($P = 0.001$) and tumors of a higher pathological T-stage ($P = 0.03$). Minor complications (Clavien 1 and 2) occurred in 25.4% patients in the elective arm versus over 40% in the other arms ($P = 0.049$). Major complications (Clavien 3+) were less common in the elective arm (3.2% cases vs. 12.7% in the relative arm and 13.8% in the absolute arm) with a trend to significance ($P = 0.09$). On multivariate analysis, absolute indication (odds ratio [OR] = 2.4, $P = 0.04$) and surgery for a complex renal mass (OR = 2.5 times, $P = 0.03$) remained significant predictors of minor complications. Major complications were more common in the relative (OR = 5.5, $P = 0.057$) and absolute indication arm (OR = 5.231, $P = 0.051$) with a trend toward significance.

Conclusions: Elective indication was associated with fewer complications than PN for relative or absolute indications.

INTRODUCTION

Partial nephrectomy (PN) was initially described as a surgical alternative in patients with renal cell carcinoma (RCC) in solitary kidneys or those with bilateral tumors, in whom radical nephrectomy (RN) would lead to dialysis dependence.^[1] Once the oncological safety and efficacy of PN were established and it became clear that RN was associated with long-term morbidity and mortality, PN became the standard of care for all patients with T1a renal masses.^[2,3] The indications for PN are expanding to include T1b tumors, even in patients with no absolute indication to preserve renal parenchyma.^[4]

Earlier studies found that patients undergoing PN for absolute indications tended to have higher complication rates and poorer oncological outcomes when compared with patients who had elective indications.^[5-7] We reviewed our data to determine whether the perioperative outcome of PN differed with the indication for which the surgery was performed.

MATERIALS AND METHODS

We undertook a retrospective review of electronic medical records (EMR) from 2004 to 2013. All PNs for preoperatively suspected RCC were included in the study. Indications were

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classified as (1) absolute (patients in whom preservation of renal parenchyma was imperative such as bilateral renal masses, solitary kidney, chronic kidney disease (CKD) with serum creatinine >1.4 mg%); (2) relative (patients with a comorbid illness with the potential to compromise renal function in the future such as diabetes mellitus, hypertension, urolithiasis, and pelviureteric junction obstruction); and (3) elective (patients with no risk factors for renal function deterioration).

Data on patient demographics, tumor variables, intraoperative events, and postoperative complications were collected. Glomerular filtration rate (GFR) was calculated using the Modification of Diet in Renal Disease (MDRD) formula, and the patients were stratified into CKD stages using the National Kidney Foundation classification.^[8,9] Preoperative radiological imaging was reviewed in all cases. Due to variability in the source, quality, and modalities of imaging, it was impossible to reliably apply standard nephrometry scoring systems and therefore we defined complex renal masses as masses of size >7 cm, multiple tumors, endophytic position, or hilar location.

Operative events (ischemia time, intraoperative stenting, blood loss, etc.) and data regarding complications were obtained from the electronic operative records. All complications were recorded in the EMR, either in the discharge summary, operative notes, or in the follow-up notes. For this study, all complications were reported using the Clavien-Dindo classification system.^[10] Minor complications included Clavien grades 1 and 2, and major complications were Clavien 3–5. Urine leak that was managed conservatively was classified as Clavien 2, while that requiring intervention was classified as Clavien 3. In patients with multiple complications, the Clavien grade assigned was that of the highest complication.

Statistical analysis was performed using SPSS version 16 (SPSS Inc., Chicago USA). The Pearson's Chi-square test was used for qualitative variables, and analysis of variance test was used for quantitative data. Multivariate analysis was performed using logistic regression.

RESULTS

A total of 184 patients with 222 tumors (range 1–10) were included in our study. The mean age was 51 years (range 22–83 years) with a male:female ratio of 4:1. 12 patients had bilateral tumors and 9 had von Hippel–Lindau disease. The median follow-up was 17 months (range 3–100 months). Laparoscopic PN was performed in 25 cases and the rest were done by an open approach. The eligible cases were then classified into three groups by indication – absolute (58 patients), relative (63 patients), and elective (63 patients).

Baseline variables for the 3 groups are given in Table 1. Patients in the absolute indication arm had larger tumors

($P = 0.001$) with a higher pathological T-stage ($P = 0.032$), while patients in the elective arm were younger ($P = 0.001$). Complications between the three arms are detailed in Table 2. Minor complications (Clavien 1 and 2) occurred in 25.4% patients in the elective arm versus over 40% in each of the other arms. This result was statistically significant ($P = 0.049$). Similarly, Clavien 3 or higher complications were less common in the elective arm (3.2% cases vs. 12.7% in the relative arm and 13.8% in the absolute arm) with a trend to significance ($P = 0.09$). There was a trend toward significance ($P = 0.06$) for urine leak needing intervention, which was more common in the absolute arm (4 cases vs. 1 case in the relative arm and none in the elective arm). Similarly, a higher blood transfusion rate was also observed in the absolute arm (33% vs. 18.03% and 17.5%, $P = 0.07$). There was no significant difference in the creatinine levels between the three groups at 6 and 12 months.

On multivariate analysis [Table 3], absolute indication (odds ratio [OR] = 2.4, 95% confidence interval [CI]: 1.056–5.525, $P = 0.04$) and surgery for a complex renal mass (OR = 2.5, 95% CI: 1.072–5.958, $P = 0.03$) remained statistically significant predictors of minor complications. Major complications were more common in the relative (OR = 5.5, 95% CI: 0.95–32.025, $P = 0.057$) and absolute indication arms (OR = 5.231, 95% CI: 0.993–27.54, $P = 0.051$). Laparoscopic PN was the only significant predictor of major complications (OR = 4.814, 95% CI: 1.335–17.367, $P = 0.016$), probably reflecting our early learning curve with this procedure. There was only one case with a positive margin, who had no recurrence at 48 months of follow-up.

DISCUSSION

PN is now established as the standard of care for clinically localized small renal masses, whether or not preservation of renal parenchyma is imperative.^[2] However, PN is a technically challenging procedure with a perioperative complication rate that has been shown to be significantly higher than that of RN.^[11–13] A British nephrectomy audit revealed that PN had the highest complication rate (5.4%), with a larger risk of Clavien 3b complications, among all types of nephrectomies.^[14]

Early studies showed that complications of PN were highest among those with absolute indications.^[6,7] In a study of 76 patients (50 elective cases and 26 imperative cases), major complications were significantly higher in patients in the absolute arm ($P = 0.000$).^[6] In a review of 155 cases of open PN between 1980 and 2005, Coffin *et al.* reported that elective cases were associated with better perioperative outcomes ($P = 0.01$).^[7] A recent study by Long *et al.* described the perioperative complications of 381 robotic PN, of which 98 were for an imperative indication and 283 were for an elective indication.^[5] Complications of Clavien grade 3 and above were significantly more common in the imperative

Table 1: Baseline demographic and pathologic variables

Variable	Absolute (n=58)	Relative (n=63)	Elective (n=63)	P
Mean age (years)*	53.14 (±13.38)	53.44 (±8.23)	46.95 (±10.31)	0.001
Tumor size (cm)*	5.46 (±2.95)	4.29 (±1.6)	3.99 (±1.92)	0.001
Ischemia time (min)*	25.3 (±10.7)	31.7 (±8.6)	27.9 (±12.2)	0.21
Complex renal mass (%)†	27.6	19.04	20.6	0.49
Laparoscopic PN (n)†	3	11	11	0.08
pT-stage (%)†				
1a	43.1	54	69.1	0.03
1b	32.8	33.3	16.2	
2a	1.7	3.2	2.9	
2b	3.4	1.6	0	
3a	3.4	4.8	0	
Multifocal	10.2	1.6	1.5	
Benign	5.1	1.6	3.2	
Histology (%)†				
Clear cell	79.3	87.3	76.5	0.84
Papillary	8.6	7.9	8.8	
Chromophobe	5.2	1.6	4.4	
Collecting duct	1.7	1.6	0	
Benign	5.2	1.6	3.2	
Grade (%)†				
I	16.4	11.5	13.3	0.39
II	60	73.8	75	
III	23.6	13.1	10	
IV	0	1.6	1.7	

*By ANOVA analysis, †By Pearson's Chi-square test. PN=Partial nephrectomy, ANOVA=Analysis of variance

Table 2: Comparison of perioperative complications and renal functional outcomes

Variable	Absolute (n=58)	Relative (n=63)	Elective (n=63)	P
Mean estimated blood loss (ml, SD)*	522.22 (±286.97)	584.3 (±546.4)	531.4 (±347.9)	0.78
Transfusion rate (%)†	33.3	18.03	17.5	0.07
Postoperative hemorrhage (n)†	3	4	1	0.39
Angioembolization (n)†	0	1	1	0.63
Surgical re-exploration (n)†	2	1	0	0.33
Urine leak (n)†	6	4	3	0.47
Urine leak needing intervention (n)†	4	1	0	0.06
Death within 30 days (n)†	1	1	0	0.56
Incidence of Clavien I-II (%)†	44.8	42.9	25.4	0.049
Incidence of Clavien III-V (%)†	13.8	12.7	3.2	0.09
Rise in creatinine at 6 months (mg, %)*	0.08 (±0.26)	0.03 (±0.16)	0.04 (±0.15)	0.37
Rise in creatinine at 12 months (mg, %)*	0.04 (±0.37)	0.04 (±0.27)	0.002 (±0.16)	0.78

*By ANOVA analysis, †By Pearson's Chi-square test. ANOVA=Analysis of variance, SD=Standard deviation

indication group (7.15 vs. 2.47%, $P < 0.001$).^[5] However, on multivariate analysis, only body mass index ($P = 0.032$) and R.E.N.A.L. score ($P = 0.006$) were significant predictors of the overall complication rate.^[5] In our study, minor complications were significantly lower in the elective arm, and this remained true on multivariate analysis. We also found a trend toward lower major complications in the elective arm. Overall, this seems in agreement with prior studies and suggests that PN in patients with an absolute indication is likely to carry a higher risk of complications.

Complexity of the renal mass, as measured by nephrometric systems, is an important factor that can affect the complication rate.^[11] The R.E.N.A.L. scoring system appears to correlate well with the degree of complexity of the tumor and helps predict the complication rate especially for minimally invasive PN.^[11] In the study by Long *et al.*, the R.E.N.A.L. score was a significant predictor of overall complications

during robotic PN.^[5] In our study, patients often underwent radiological imaging before referral to our center, thereby making it impossible to accurately compare nephrometric scores. Furthermore, the vast majority of our cases were done by the open approach. To achieve some grading of complexity for the purposes of the study, we defined complex renal masses using standard technical characteristics such as size, endophytic nature, and hilar location. We found that complex renal masses were a significant predictor of minor (Clavien 1–2) surgical complications on multivariate analysis but not major complications.

In our study, the change in serum creatinine from preoperative to postoperative levels (at both 6 and 12 months) was not significantly different between the three arms and this is in agreement with previously reported data. In the study by Kural *et al.*, there was no significant change in serum creatinine levels between preoperative and postoperative

Table 3: Logistic regression analysis for minor (Clavien 1-2) and major (Clavien 3-5) complications

Outcome	Variable	Contrast	Multivariable OR (95% CI)	P
Clavien 1-2 complications	Age	1 unit increase	0.996 (0.965, 1.029)	0.82
	Indication	Elective	Reference	
		Relative	1.997 (0.808, 4.932)	0.13
		Absolute	2.415 (1.056, 5.525)	0.037
	Number of tumors	1 unit increase	5.978 (0.481, 74.327)	0.16
	CT size	1 cm increase	1.209 (0.991, 1.474)	0.06
	Complex mass	No	Reference	
		Yes	2.527 (1.072, 5.958)	0.034
	Surgical approach	Open	Reference	
		Lap	1.607 (0.571, 4.516)	0.37
Clavien 3-5 complications	Age	1 unit increase	0.983 (0.930, 1.039)	0.55
	Indication	Elective	Reference	
		Relative	5.514 (0.95, 32.025)	0.06
		Absolute	5.231 (0.993, 27.54)	0.051
	Number of tumors	1 unit increase	0.788 (0.205, 3.036)	0.79
	CT size	1 cm increase	1.082 (0.851, 1.375)	0.52
	Complex mass	No	Reference	
		Yes	2.246 (0.614, 8.214)	0.22
	Surgical approach	Open	Reference	
		Lap	4.814 (1.335, 17.367)	0.016

CI=Confidence interval, OR=Odds ratio, CT=Computed tomography

levels between the two arms.^[6] Long *et al.* showed no difference in CKD upstaging between the two arms and the percentage change in GFR was actually lower in the imperative arm.^[5] They attributed this to efforts to preserve as much renal parenchyma as possible in the imperative arm.^[5]

Our study has certain limitations. It is a retrospective analysis, and the relatively short follow-up prevents meaningful oncological conclusions being drawn. Furthermore, the absence of nephrometry scores has been discussed. Despite these limitations, our study provides the first data on this subject from India and will be of significant utility in preoperative patient counseling. It is the only study to date that has classified the indications for PN into absolute, relative, and elective. This was done in an effort to make the groups more homogeneous and comparable, and we believe this adds considerably to the validity of results obtained. Furthermore, the use of the Clavien-Dindo system for reporting complications simplifies the data and allows for easy comparison.

CONCLUSIONS

Patients undergoing partial nephrectomy for elective indications at our institution had fewer complications than those for relative or absolute indications. On multivariate

analysis, indication remained a significant predictor of minor complications, and there was a trend toward lower major complications in the elective arm.

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