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Original Research Article

A prospective, multi-institutional study of perioperative morbidities in the patients of renal cell carcinoma undergoing either open nephron sparing surgery or robotic nephron sparing surgery in fifty cases

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ABSTRACT

Background: Over the time, the nephron sparing surgery (NSS) has become 'gold standard' for treatment of T1a stage renal cell carcinoma (RCC) which saves precious renal tissue. We assessed and compared perioperative morbidities associated with open (ONSS) and robotic nephron sparing surgery (RNSS) in patients of T1a and T1b staged renal cell carcinoma.
Methods: This prospective study was carried out from April 2016 to March 2018. A total of fifty (n=50) RCC patients underwent open or robotic nephron sparing surgery. The demographic data and perioperative morbidities associated with both methods of NSS were recorded and comparison of parameters including warm-ischemia time (WIT), hospital stay, perioperative bleeding, impact of renal-pedicle clamping was made in T1a and T1b staged RCC patients.
Results: The most common perioperative morbidity was blood-loss and 12% patients had ≥500 ml loss. Significantly less intraoperative blood-loss was observed in RNSS compared to ONSS with decreased blood transfusion (BT), which decreased significantly after renal-pedicle clamping prior to RCC resection. Even In perioperative period, the blood loss was significantly less in RNSS patients. However, the warm ischemia time (WIT) and hospital stay was longer in patients of RNSS compared to ONSS. The WIT was prolonged in T1b compared to T1a lesions, irrespective NSS methods.
Conclusions: Although, the most common perioperative morbidity associated with NSS is blood-loss but RNSS had less perioperative morbidities compared to ONSS. The blood loss decreased significantly during intraoperative period after renal-pedicle clamping which resulted into decreased blood transfusion after NSS by either method.

Keywords: Renal, Carcinoma, Nephron, Robotic, Clamping, Morbidities

INTRODUCTION

The increased use of advanced imaging methods is resulting into incidental detection of RCC (renal cell carcinoma) in about 75% cases at early and asymptomatic stage when lesion is less than 4 cm size.[1] But, the RCC still remain one of the difficult solid malignancy cancer to treat because of its tendency to spread asymptomatically and inherent resistance to treatments using non-surgical methods e.g. chemotherapy, radiotherapy and hormone treatment.[2] To date, the only curative treatment for RCC is its complete resection with free margins irrespective of method and nephron sparing surgery (NSS) has become "the gold standard' for lesions less than 4cm (stage-T1a).[3,4] Now, NSS being increasingly used for RCC lesions measuring ≤7 cm (T1)

and all lesions in which it is technically feasibile.[5] NSS may also be used for RCC which measures >7 cm in size in context of imperative indications. In this study, we assessed various perioperative morbidities associated with open (ONSS) and robotic nephron sparing surgery (RNSS) in the RCC patients.

Aims and objectives

Primary objective was to study perioperative morbidities in RCC patients less than 7 cm size undergoing open or robotic nephron sparing surgery. The usual perioperative morbidities include blood-loss, WIT, altered Serum creatinine and hospital stays.

Secondary objective was to assess these parameters in:

- ONSS and RNSS.
- T1a and T1b staged RCC.
- Clamping of renal pedicles.

METHODS

This multi-institutional, prospective, non-randomized controlled study was carried out in fifty (n=50) patients having RCC lesion ≤7 cm (T1 lesions) who visited urology department of our institution and other from March 2016 to April 2018. All patients having RCC lesions >7 cm (>T1 stage) or metastases were excluded from this study.

The demographic profile and clinical history of each RCC patients was recorded and a standard preoperative urological evaluation was done using hematological, biochemical and urine analysis. The preoperative imaging includes a CT or MR angiography to assess anatomy of renal arteries. The blood loss during intraoperative and postoperative period was estimated by weighing blood-soaked sponges and blood-loss occurring through drainage-bag. The pleural injury, splenic damage, colonic injury, urinoma and urinary fistula formations were also assessed in perioperative and postoperative period. The renal function was calculated by measuring eGFR using MDRD formula [eGFR (ml/min/1.7m^2)=175x Serum Creatinine (µmoI/L)x0.0113)$^{-1.154}$ x Age (years)$^{-0.203}$ (x0.742, if female)]. All had their lesion excised with 2-5 mm free margins all around with renal-pedicle clamping in most patients and specimens were sent for histopathology examination. The perioperative period was defined as the period from patient's admission to discharge day following NSS.

All data was entered in Microsoft Excel Sheet under predefined variables, discrete data was presented as number (%) and continuous data as mean±SD, range or median or interquartile range whatever is appropriate. Normality of quantitative data was checked using Kolmogorov Smirnov tests and skewed data of two groups was compared using Mann-Whitney test. Student t-test was used to compare 2 groups with normally distributed data. Wilcoxon signed rank test was used for time related variables and paired t-test for normally distributed data of patient's visits (2-visits). Proportions were compared using Chi-Square or Fisher's exact test. The statistical tests were two-sided performed at a significance level of α=0.05. Data analysis was done using IBM-SPSS statistics (version-22).

RESULTS

All patients were divided into two groups, the ONSS-group underwent open nephron sparing surgery and RNSS-group underwent robotic assisted nephron sparing surgery. Twenty-two patients (44%) were between 51-70 years age group, 16 (32%) in 31-50 year and 6 (12%) each in ≤30 years and in >70 years age-groups (Table 1). Out of fifty patients, 36 (72%) were male and 14 (28%) female with M:F ratio of 2.6:1.0.

Table 1: Age distribution of patients with RCC (n=50).

Age groups (in years)	No. of patients
	N (%)
≤30	6 (12)
31-50	16 (32)
51-70	22 (44)
>70	6 (12)

In thirty four patients (68%), the lesion was detected incidentally and 16 (32%) and presented with sign or symptoms which includes haematuria (12%), fever (4%), dysuria (12%), loss of weight and appetite (8%), dizziness and sweating (4%) and rest had heaviness or discomfort in the flank (Table 2). About 10 (20%) had history of smoking and 16 (32%) hypertension. The characteristics of RCC lesions including its side, location were also recorded. Thirty-five patients (70%) had RCC measuring 4-7 cm (T1b) whereas only fifteen (30%) had <4 cm (T1a) lesion and 20 (40%) underwent open and 30 (60%) robotic procedures (Table 3 and 4). Histopathological examination of the specimens confirmed the diagnosis and evaluated nuclear grades of resected RCC lesions (Table 5).

Table 2: Clinical presentations of RCC patients (n=50).

Clinical presentations	No. of patients
	N (%)
Hematuria	6 (12)
Fever	2 (4)
Dysuria	6 (12)
Body weight loss/ appetite loss	4 (8)
Dizziness, sweating	2 (4)

Table 3: Characteristic of RCC lesions (n=50).

Characteristics of RCC lesions	No. of patients
	N (%)
Side of lesions	
Right	26 (52)
Left	24 (48)
Site of lesions	
Upper pole	22 (44)
Middle pole	14 (28)
Lower pole	14 (28)

Table 4: Procedure performed and size of RCC lesions (n=50).

	No. patients
	N (%)
Procedure performed	
ONSS	20 (40)
RNSS	15 (60)
Size of lesions	
T1a (<4 cm)	16 (32)
T1b (4-7 cm)	34 (68)

Table 5: Histopathology and grade of RCC (n=50).

Histopathology of RCC lesions	No. patients
	N (%)
Type of lesion	
Clear cell	46 (92)
Multilocular cystic	2 (4)
Papillary	2 (4)
Fuhrman grade of RCC lesions	
G-1	12 (24)
G-2	32 (64)
G-3	6 (12)

Perioperative morbidities

Blood-loss: Thirty-six patients (72%) had intraoperative blood loss more than <300 ml and 14 (28%) ≥300 ml while 44 (88%) RCC patients had postoperative blood-loss <500 ml and only 6 (12%) had blood loss ≥500 ml. In all, 72% patients had a total blood loss of less than 500ml and 16% had between 500-1000 ml and only 12% had ≥1000 ml. The RNSS group had a significantly decreased intraoperative blood-loss compared to ONSS (p-value <0.04) and postoperative blood loss was also less in RNSS but result were not significant.

Injury and fever: Eight (16%) patients had fever and none had splenic or bowel or pleural injury, significant urinoma, urinary tract infection, haematuria, urinary fistula and significant renal dysfunction.

eGFR: The change in estimated GFR (eGFR)) was statistically not significant in either group.

Warm ischemia time: Although, the warm ischemia time (WIT) was longer in RNSS group but again result were statistically not significant.

Hospital stay: The hospital stay was longer in RNSS group but results were statistically not significant (Table 6).

Blood transfusion: Overall, 12 (60%) patients required blood transfusion in the intraoperative period in ONSS-group compared to 6 (20%) in RNSS group (p<0.005) which is statistically significant. In the intraoperative period, a significantly less blood-loss occurred in the RCC patients who had renal pedicles clamping compared without clamping, which is statistically significant (p=0.009). Only, 20% patients required blood transfusion in renal pedicle clamping group compared to 80% without clamping, which is significant (p<0.012) (Table 7 and 8).

Table 6: Comparison of various perioperative morbidities in ONSS and RNSS.

	ONSS (n=20)	RNSS (n=30)	t-test	P value
Intraoperative blood loss (ml)	325±248.607	133.33±58.75	41.5	0.040
Postoperative blood loss (ml)	215.6±201.53	198.3±348.29	54.5	0.253
Overall blood loss (ml)	540±334.68	331.33±333.28	1.584	0.126
Change in eGFR	5.4±21.05	7.46±27.47	1.289	0.842
Warm ischemia time (min)	16.6±3.97	25.26±10.17	1.831	0.084
Hospital stay (days)	6.7±1.57	8.33±3.77	0.212	0.210

Table 7: Intraoperative blood transfusion in both groups.

Intraoperative blood transfusion	ONSS (n=20)	RNSS (n=30)	P value
	N (%)	N (%)	
Yes	12 (60)	6 (20)	0.005
No	08 (40)	24 (80)	

Table 8: Blood transfusion needed with and without renal-pedicle clamping.

Renal-pedicle clamping	Yes (n=40)	No (n=10)	P value
Intraoperative blood loss (ml)	145±74.16	470±272.95	0.009
Need of blood transfusion N (%)	6 (20)	8 (80)	0.012

Table 9: Comparisons of various parameters in T1a and T1b stage RCC.

Clinical Parameters	T1a (n=16) (32%)	T1b (n=34) (68%)	P value
Mean age of presentation (in year)	52.62±9.75	51.94±18.85	0.053
Mean incidental presentation	12 (75)	22 (64.7)	1.000
Mean preoperative serum creatinine (mg/dl)	0.87±0.23	1.00±0.32	0.405
Mean postoperative serum creatinine (mg/dl)	0.904±0.26	1.12±0.414	0.179
Mean total blood loss (ml)	517.5±292.22	360.64±363.27	0.126
Mean warm ischemia time (min)	16.50±1.87	25.92±10.38	0.004
Mean duration of hospital stay (days)	7.13±0.991	7.94±3.766	0.002

G. T1a and T1b lesions: The mean age of presentation was almost similar in T1a and T1b staged lesion RCC but T1a (75%) had more incidental detection compared to T1b (64.7%). WIT and hospital stay were longer for T1b lesions compared to T1a RCC which was statistically significant (p<0.004 and 0.002, respectively). There was no statistically significant difference in age, incidental presentations, serum creatinine and blood-loss (Table 9).

DISCUSSION

In our study, mean age of presentation for T1a and T1b RCC lesions were 52.62 and 51.94±18.85 years, respectively, which is similar to study by Pantuck et al who suggested that RCC is mainly a disease of older adults with typical presentation between 50-70 years.[6] The male to female ratio was 2.6:1 which is different from 3:2 as observed by Siegel et al.[7] Overall, the 68% patients had incidental detections and 32% symptomatic presentations. Three-quarters patients (75%) T1a and 64.7% T1b RCC staged had incidental presentations. Our results were similar to the study by Silverman et al, wherein 60% patients had their RCC detected incidentally due to use advanced imaging methods for evaluation of nonspecific symptoms.[8]

Parker et al in their study suggested that tobacco exposure is most common environmental risk-factor for RCC.[9] Surprisingly, in our study only 8 (16%) had history of smoking which suggest that other risk-factors may be playing more important role. Lipworth et al suggested hypertension as another risk-factor but in our study only 9 (18%) had history of hypertension.[10]

Perioperative morbidities

RCC patients undergoing NSS by either method, the hemorrhage is most common.[11] In our study, 72% patients had intraoperative hemorrhage less than 300ml and 28% ≥300 ml and overall 28% patients required intraoperative blood transfusions. Further, 88% patient had less than 500 ml and 12% ≥500 ml postoperative hemorrhage and only 12% needed blood transfusion in postoperative period. In our study, 12% patients had a total blood loss ≥1000 ml which is different from other study viz Steinbach et al (1.4%), Belldegrun et al (2.1%), Campbell et al (2.3%), Thrasher et al (2.4%), Poppel HV et al (3.1%), Moll et al (3.7%), Duque et al (4.5%).[12-18] and same may be due to different experience of surgeon or small sample size.

Campbell et al reported incidence of urinary fistula between 1.4-17.4%.[12-20] However, no such complication was seen in our study. Pleural injury can occur due to accidental opening of pleura during flank incision or rib resection for ONSS. Although, Poppel et al, reported pleural damage in about 11.5% patient.[16] but this complication was also not seen in our study. Several authors have reported various degrees of splenic injury with incidence between 0.4-0.7%.[12,14,16] Interestingly, this complication was also not encountered in any patient of our study. However, during postoperative period, 8 (16%) patients had fever in RNSS group leading to longer hospital stay.

ONSS versus RNSS: ONSS group had significantly less amount of intraoperative hemorrhage compared to RNSS group with mean intraoperative blood-loss of 325±248.607 and 133.33±58.757 ml respectively (p<0.04). But, the need for blood transfusion in intraoperative period was significantly less in RNSS group compared to ONSS (p<0.007). In our study, a significantly less blood loss occurred in RNSS group with a mean loss of 155 ml which was similar to the study by Benway et al who had similar results.[21]

Similarly, the mean postoperative blood-loss was less in RNSS group compared to ONSS with 198.33±348.290 ml and 215.60±201.531, respectively (p<0.253) suggesting less morbidity with RNSS, despite there being no statistically significant difference in the requirement of blood transfusion between both groups (p<1.00).

Overall, the mean total blood-loss was also significantly less in RNSS compared to ONSS group with 324.33±333.28 ml and 540±334.68 ml, respectively. Our results were similar to the study by several other authors viz. Boylu et al (ONSS vs. RNSS; 417 vs 268 ml: p-value <0.001), Simhan et al (256 vs. 131 ml, p<0.001), Lucas et al (250 ml vs. 100 ml, p<0.001).[22-24]

Warm ischemia time (WIT): In our study, WIT was longer in RNSS group compared to ONSS with mean value being 25.26±10.17mins and 16.60±3.97 min respectively (p-value <0.084). Over all, these results were similar to study by Boylu U (23.33min vs 18.02min with p-value <0.003) and Ficarra et al (19.2±7.3min vs 15.4±5.9 min with p-value <0.001).[22,25] However, Serni et al observed no significant difference between two groups (18.5 vs 16.4 min; p-value <0.5).[26]

eGFR: No change in eGFR preoperative and postoperative period occurred after ONSS or RNSS procedure, suggesting that renal dysfunctions may not be there after NSS, thus our result were similar to study by Boylu et al.[22]

Hospital stay: In our study, RNSS group had longer mean hospital-stay (8.33±3.77days) compared to ONSS (6.70±1.57days), which is in contrast to the study by Boylu et al, Simhan et al, Lee et al, Lucas et al, Ficarra et al and Benway et al' who observed a shorter hospital stay for RNSS group.[21-25,27] This difference may be attributed due to complains of fever in the postoperative period in 8 (16%) patients and persistent drainage in another patient.

T1a versus T1b lesions: In our study, no significant difference in total mean blood loss was seen between T1a and T1b lesions, which in contrast to the study by Patard et al, wherein mean blood loss was significantly more in T1b lesions (p<0.01).[28] WIT was longer for T1b lesions compared to T1a which is statistically significant (p<0.004). This may be attributed to increased size of RCC tumor in T1b staged lesions requiring more time for its resection along with safe free-margins.

Further, patients did not have significant change in mean preoperative and postoperative serum creatinine level and hospital-stay duration. This result is also in contrast to study by Patard et al, who observed that a significant change in mean preoperative serum creatinine occurs after NSS (more for T1b lesions). However, there was no significant difference in the mean hospital-stay, WIT and postoperative serum creatinine.[28]

Renal pedicle clamping versus unclamping

In our study, the RCC patients in both group had a significant less mean intraoperative blood loss after renal pedicle clamping compared to without clamping (p-value <0.009) which corresponds to statistically significant less intraoperative blood transfusion requirements (p-value <0.012). Thus, our study reconfirms the importance of renal pedicle clamping during NSS using any method.

CONCLUSION

Blood-loss is most common perioperative morbidity in RCC patients during nephron sparing surgery using robotic or open techniques. Renal pedicle clamping is highly desirable during resection of RCC lesions when performing NSS procedure because it is helpful in preventing intraoperative hemorrhage, thus blood transfusion. Although, RNSS is associated with less intraoperative hemorrhage compared to ONSS. Further, the large size (T1b) lesions are associated with longer warm ischemia-time compared to small size (T1a) RCC lesions.

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