International Surgery Journal
Asimi AR et al. Int Surg J. 2018 Feb;5(2):413-419
http://www.ijsurgery.com
pISSN 2349-3305 | eISSN 2349-2902

DOI: http://dx.doi.org/10.18203/2349-2902.isj20180011

Original Research Article

The safety and efficacy of nephron sparing surgery in T1N0M0 renal cell carcinoma

Athar R. Asimi[1]*, Mohammad S. Wani[1], Mohammad I. Lone[2]

[1]Department of Surgery, [2]Department of Pathology, Sher-I-Kashmir Institute of Medical Sciences, Soura, Srinagar, Jammu and Kashmir, India

Received: 08 November 2017
Accepted: 09 December 2017

***Correspondence:**
Dr. Athar R. Asimi,
E-mail: dratharasimi@gmail.com

ABSTRACT

Background: Renal cell carcinoma (RCC) accounts for approximately 3% of adult malignancies and 90-95% of neoplasm arising from the kidney. Objective was to explore the safety and efficacy of nephron sparing surgery (NSS) for T1N0M0 renal cell carcinomas (RCC) and to assess the oncological outcome of NSS in T1N0M0 RCC.
Methods: A total of 31 cases were enrolled for the study of which 11 (35.5%) underwent NSS and 20 (64.5%) underwent radical nephrectomy (RN). The clinical results were followed up and comparatively analyzed.
Results: NSS was performed using a margin of 1cm, no positive surgical margin was detected. The mean blood loss and mean duration of surgery in NSS and RN was comparable. Among all one patient from NSS group experienced urinary leak which was managed by placement of DJ stent. The overall complication rate was 9.1% in NSS. Lab. tests before surgery and after surgery at 6month was done in the both groups and results obtained was within normal limits. Only one patient developed metastasis from NSS group and died at 14th month of fallow-up, whereas neither metastasis nor mortality were recorded in RN group.
Conclusions: Nephron sparing SURGERY has proven to be a safe and effective approach for Renal cell carcinoma with comparable clinical results to radical nephrectomy especially in tumour ≤4cm.

Keywords: Cell carcinoma, Nephron, Nephron sparing surgery, Radical nephrectomy

INTRODUCTION

Renal cell carcinoma (RCC) accounts for approximately 3% of adult malignancies and 90-95% of neoplasm arising from the kidney. This disease is characterized by a lack of early warning signs, diverse clinical manifestations, and resistance to radiation and chemotherapy.[1-3] During the last 30 years the incidence of RCC has increased by about 3% per year, primarily reflecting an increase in the incidental detection of small renal masses with non-invasive abdominal imaging.[4,5] Consultation for patients with small renal masses is now a relatively common occurrence and given recent controversies about the management of these lesions, the term small renal mass has entered the urological lexicon. Although early detection has increased during the last decade, cancer specific mortality has not decreased, calling into question the current paradigm of aggressive surgical treatment of small renal masses, predominantly by radical nephrectomy.[6-9]

Risk factors

Established: Tobacco exposure, Obesity, Hypertension

Putative

Lead compounds, Various chemicals (e.g., aromatic hydrocarbons), Trichloroethylene exposure, Occupational exposure (metal, chemical, rubber, and printing

industries), Asbestos or cadmium exposure, Radiation therapy, Dietary (high fat/protein and low fruits/vegetables)

Genetic and hereditary risk factors

Some people inherit a tendency to develop certain types of cancer. The DNA that inherit from parents may have certain changes that give tendency to develop cancer are Von Hippel-Lindau disease, Hereditary papillary renal cell carcinoma, Hereditary leiomyoma-renal cell carcinoma, Birt-Hogg-Dube (BHD) syndrome, Familial renal cancer, Hereditary renal oncocytomas.[10-13]

Signs and symptoms of kidney cancer

Incidental

- Local Tumour Growth
- Hematuria
- Flank pain
- Abdominal mass
- Perirenal hematoma
- Metastases
- Persistent cough
- Bone pain
- Cervical lymphadenopathy

Constitutional symptoms

- Weight loss/fever/malaise
- Obstruction of the Inferior Vena Cava
- Bilateral lower extremity oedema
- Nonreducing or right-sided varicocele
- Paraneoplastic Syndromes
- Hypercalcemia
- Hypertension
- Polycythemia
- Stauffer's syndrome

Surgery for kidney cancer

Radical nephrectomy

In this operation, the whole kidney along with contents of Gerota's are removed, along with the removal of involved Hilar Nodes. The objective of surgical therapy is to excise all tumours with an adequate surgical margin.

Partial nephrectomy (nephron-sparing surgery-NSS)

Nephron-sparing surgery (NSS) for the treatment of a renal tumour was first described by Czerny in 1890 (reviewed in Herr, 2005). However, high morbidity limited its application. In 1950, Vermooten suggested that peripheral encapsulated renal neoplasm could be excised locally while leaving a margin of normal parenchyma around the tumour. In this procedure only the part of the kidney containing cancer is removed, leaving the rest of the organ behind. This type of surgery is now the preferred treatment for patients with early stage kidney cancer. It is often done to remove single small tumours (those less than 4 cm across), and can be done in patients with larger tumours (up to 7 cm across). Studies have shown the long-term results to be about the same as those when the whole kidney is removed. The obvious benefit is that the patient keeps more of their kidney function. A partial nephrectomy may not be an option if the tumour is in the middle of the kidney or is very large, if there is more than one tumour in the same kidney, or if the cancer has spread to the lymph nodes or distant organs.

Nephron-sparing surgery (NSS) with resection of the tumour only was usually reserved for patients with solitary kidney, bilateral tumours or chronic kidney disease (imperative indication).[14,15]

When prospectively analyzing the renal function of more than 1 million people in Northern California, Go et al. showed that any loss of renal function increases the risk for cardiovascular events and reduces life expectancy.[16] A large series of NSS in patients presenting with a small renal tumour (cT1a) in the presence of a healthy contralateral kidney (elective indication) showed good oncological long-term outcomes with a moderate perioperative complication rate.[17-19]

Documented the oncologic outcome of elective nephron-sparing surgery and radical nephrectomy for low-stage renal cell carcinoma. Nephron-sparing surgery (NSS) can safely be performed with slightly higher complication rates than radical nephrectomy (RN).[20]

A study on Mini-Margin Nephron Sparing Surgery for Renal Cell Carcinoma 4 cm or less and reported Mini-margin NSS is as safe and effective as RN in treating early localized RCC 4 cm or less.[21]

In Comparison to radical nephrectomy, partial nephrectomy better preserves renal parenchyma and function.[22]

The excellent cancer control and outcomes can be achieved with NSS in carefully selected patients with tumours >4 cm.[23]

The elective nephron-sparing surgery (NSS) for renal cell carcinoma (RCC) < 4 cm has been accepted as alternative to radical nephrectomy (RN).[24]

METHODS

The present study was conducted in the department of urology and department of pathology Sher-i-Kashmir Institute of Medical Sciences, Soura Srinagar after clearance from the ethical committee.

Our study includes only prospective cases. Only patients with RCC 4 cm or less, without lymph node or distant metastasis detected before and during the operation, and clinically Stage T1aN0M0 were included in the study and all cases were confirmed by histopathological evaluation to be RCC. Pathologic Stage T1aN0M0 was included in the study. After doing base line investigations high quality cross sectional imaging study (CECT or MRI, in the presence of adequate renal function) was done to assess the contrast enhancement, exclude angiomyolipomas, assess for locally invasive features, define the relevant anatomy and evaluate the status of the contralateral kidney. All cases were staged, classified, and graded according to TNM criteria. On postoperative histopathological examination those with benign or other type of malignancies rather than RCC were excluded from the study. Patients with nodal or distant metastasis and tumour >4cm in size detected before or during operation were excluded from the study. Patients with renal impairment, bilateral or multiple RCCs were excluded. Preoperatively, all the patients were informed of the surgery and asked to sign the permission paper.

Procedure

The kidney capsule was sharply incised approximately 1cm away from tumour pseudocapsule and the tumour will be enucleated with an anticipated margin of 1cm. To prevent renal ischemic damage, all patients were vigorously hydrated few minutes before vessel occlusion. After removing the tumour, the samples were meticulously checked for gross margin status. When no renal parenchyma was present outside the pseudocapsule, additional thin layer of renal parenchyma will be respected for margin pathological evaluation. Surgical procedure for RN was performed as standard technique.

Duration of surgical procedure, estimated blood loss, renal function (before and after surgery) and local recurrence or distant metastasis (seen in the follow up period) was compared between two groups (NSS and RN).

Follow up

The first time follow-up was at 3months after NSS or RN. The regular follow-up afterward for both groups of patients was conducted every 3 to 6 months in reference to recurrence of tumour in the kidney. The renal function, urine routine test, kidney ultrasound and chest X-ray, CT scan or MRI of the abdomen and chest will be performed annually, or at any time in cases of clinical suspicion by ultrasonography or X-ray.

Statistical analyses

Comparisons of features between patients treated with NSS and RN were evaluated using the chi-square, Fisher's exact and t-test. Overall and cancer-specific survivals were estimated using Kaplan-Meier method. Statistical analyses will be performed using SPSS.

RESULTS

Gender distribution

A total of 31 cases were enrolled for the study of which 21 (67.7%) were males and 10(32.3%) were females. Male to female ratio was 2.1:1.

Age distribution

The mean age was 51.7 years. The age ranged from 18-70 years.

Mode of presentation

Majority (N=20) of the cases (67.7%) were detected incidentally while being evaluated for an unrelated cause. Ten (32.3%) cases were symptomatic, 7 (22.6%) presenting with hematuria and 3(09.7%) with loin pain.

Risk factors

Of the 31 patients, 15 had obesity (48.4%), 14 was smoker (45.2) and 8 had hypertension (25.8).

Radiological characteristics

Side

13 (41.9%) patients had tumour on their right side while 18 (58.1%) had on their left side.

Tumour location

9 (29%) tumours were located in Upper pole, 10 (32.3%) in mid-pole and 12 (38.7%) in Lower pole.

Mode of surgery

Of the 31 patients, 11(35.5%) underwent Nephron Sparing surgery and 20(64.5%) underwent radical nephrectomy.

Ischemia was used in Nephron Sparing surgery, we have clamped main vascular pedicle during NSS. The mean clamping time was 18.8 minutes (range: 15-25min.). We have used V-loc suture for renorrhaphy during Nephron Sparing Surgeries and the results indicate a promising development in reducing ischemia time.

Perioperative study variables of this study

Blood loss: Mean blood loss was 55.7 ml (Range: 40-80ml). The mean blood loss in NSS was 56.4 ml and in RN was 55 ml. So intra-operative blood loss was almost similar in the NSS and RN groups (P=0.73).

Table 1: Comparison of blood loss in two groups.

Blood loss (ml)	Mean	SD	Range	P-value
Group 1 (NSS) (n=11)	56.4	11.20	40-80	0.730#
Group 2 (RN) (n=20)	55.0	10.0	40-70	

Operative duration

Mean duration of surgery was 127 min. (Range: 105-150 min.). The mean duration of surgery in NSS was 125min. and in RN was 127min. So, the duration was similar in the NSS and RN (P=0.447).

Table 2: Comparison of duration of surgery in two groups.

Duration of surgery (minutes)	Mean	SD	Range	P-value
Group 1(NSS) (n=11)	125	12.65	105-150	0.447#
Group 2 (RN) (n=20)	129	14.38	105-150	

Statistically Non-significant difference (P-value>0.05).

Complication post-operatively

Among all patients only one patient from Nephron Sparing surgery group experienced urinary leak in 1st weeks after surgery. This patient was managed by placement of DJ stent installation which was removed at 6weeks.

The overall complication rate was (9.1%) in NSS. There was no complication post-operatively in RN group. No serious haemorrhage requiring reoperation occurred. Blood transfusion, bladder recatheterization, angioembolization, and temporary hemodialysis complications had not encountered during the postoperative course of patients. None of the patients died within the first 30 days after surgery.

Table 3: Comparison of complications in two groups.

Complications	Group 1 (NSS) n=11		Group 2 (RN) n=20		P-value
	No.	%	No.	%	
Urinary fistula	1	9.1	0	0	0.355#

Statistically Non-significant difference (P-value>0.05)

Hospital stay

The mean hospital stay was 6.4 days (Range: 6-10 days). The mean hospital stay for RN was 6.3 and in NSS was 6.5. So, the duration of hospital stay was almost same for both groups. (p=0.425).

Table 4: Comparison of hospital stay in two groups.

Hospital stay (days)	Mean	SD	Range	P-value
Group 1 (NSS) n=11	6.5	1.21	6-10	0.425#
Group 2 (RN) n=20	6.3	0.47	6-7	

Statistically Non-significant Difference (P-value>0.05)

Lab investigations

Renal functions (Serum urea and Serum creatinine) before surgery and after surgery at 6month were done in the both groups (NSS and RN). The results obtained were statistically non-significant.

The mean S. Creat. Pre-op was 0.85 in PN and 0.94 in RN and the mean S. Creat. at 6 month post-op was 1.01 in PN and 1.06 in RN. The mean S. urea pre-op was 13.11 in PN and 12.85 in RN and the mean S. urea at 6 month post-op was 13.27 in PN and 12.89 in RN. So, the results were non-significant in both groups as the parameters were within normal limits in both groups.

Table 5: Comparison of renal function in two groups.

Group	Variable	Preop		Postop		P-value
		Mean	SD	Mean	SD	
1 (NSS)	Urea	25.27	7.42	23.91	6.04	0.136#
	Creat.	0.85	0.34	1.01	0.18	0.198#
2 (RN)	Urea	27.50	5.63	28.60	4.30	0.503#
	Creat.	0.94	0.40	1.06	0.57	0.195#

Statistically Non-significant Difference (P-value>0.05)

Urine examination was done in both groups pre-operatively and post-operatively at 6 months. In total 31 cases hematuria (RBC+) was present in 7(22.6%) pre-operatively and it was observed that there was normal urine examination in both groups at 6 months of fallow-up.

Table 6: Comparison of urine examination in two groups.

Urine examination		Group 1(NSS) n=11	Group 2(RN) n=20	Total
Pre-op	N	8 (72.7%)	16 (80%)	24 (77.4%)
	RBC +	3 (27.3%)	4 (20%)	7 (22.6%)
Post-op	N	11 (100%)	20 (100%)	31 (100%)

Mean haemoglobin, mean serum total protein and Mean Serum Albumin pre and post surgery were compared in both groups (NSS and RN) and it was observed that the parameters were within normal in both groups. So, the difference was statistically non-significant.

Recurrence /metastasis post-operatively

Only one patient developed metastasis in our study which was from NSS group, whereas none from RN group developed metastasis.

Table 7: Comparison of lab. investigations in two groups.

Group	Variable	Pre-op		Post-op		P-value
		Mean	SD	Mean	SD	
1 (NSS)	HB	13.11	1.83	13.27	1.33	0.535#
	Protein	7.48	0.32	7.76	0.26	0.483#
	Albumin	4.41	0.27	3.92	1.33	0.235#
2 (RN)	HB	12.85	2.49	12.89	1.54	0.851#
	Protein	7.73	0.60	7.41	0.44	0.086#
	Albumin	4.12	0.56	4.17	0.37	0.560#

Statistically Non-significant Difference (P-value>0.05)

Histology of Renal cell carcinomas in this study

Clear cell type (N=24) was the most common subtype of RCC, followed by Papillary type (N=7). Margins were negative in all cases.

Mortality

In our study one patient died in NSS group at 14th month of fallow-up because of metastasis, whereas no mortality was recorded in RN group.

Table 8: Comparison of mortality of surgery in two groups.

Mortality	Group 1 (NSS) n=11		Group 2 (RN) n=20		P-value
	No.	%	No.	%	
Yes	1	9.1	0	0	0.355#
No	10	90.9	20	100	

Statistically Non-significant Difference (P-value>0.05)

DISCUSSION

In recent decades, multiple studies have shown excellent cancer specific survival in patients subjected to NSS. There are extensive reports to support elective NSS for renal masses 4 cm or smaller in greatest dimension. (25-27). Cancer-specific and metastases-free survival are comparative between patients treated with NSS and RN for small early RCC and complication rates, morbidity and mortality are similar for NSS and RN.[28-31] NSS provides better preservation of renal function than RN.[28] It has been suggested that at least some local recurrence after partial nephrectomy may be due to residual tumour cells on the tumour bed. Based on the assumption, resection of the tumour with a 1-cm margin of normal-appearing parenchyma around the tumour had been considered the standard surgical technique for NSS for many years.[32,33] However, the size of the surgical margin that should be removed with the tumour remains controversial. An optimal margin will guarantee complete tumour removal as well as keep local recurrence rates to a minimum. An over-resected margin could increase the surgical difficulty and compromise residual renal function, especially in the case of a solitary kidney. It could also increase the morbidity of any surgical complications.

In the present study, NSS was performed using a margin of 1cm, no positive surgical margin was detected. Also, the follow-up showed a comparative overall survival with 1cm NSS and radical nephrectomy. Only one patient in NSS groups died of cancer-related causes (metastasis) detected during follow-up. Only one patient in NSS group developed urinary leak. Our study also shows a significant lower complication rate in 1cm NSS. These data show that NSS with 1cm margin can effectively achieve local tumour resection with excellent long-term patient survival for those with RCC of 4 cm or less (T1aN0M0), while not increasing the local recurrence rate. Moreover, further potential advantages of NSS are in favour of preservation of renal parenchyma and with a

lower incidence of major blood supply vessel and collecting system damage.

The study is limited by the small (N=31) number of cases, hence a larger sample size obtained by extending this study period would help describe our experience further with more definite conclusions.

CONCLUSION

Nephron Sparing Surgery has proven to be a safe and effective approach for Renal cell carcinoma with comparable clinical results to Radical nephrectomy especially tumour ≤4 cm. Nephron Sparing Surgery provides excellent renal function preservation, favourable long-term progression-free survival, lower complication rate, and is not associated with an increased risk of local recurrence. Nephron Sparing Surgery preserves nephrons and the renal function remains stable at 6 months. Nephron Sparing Surgery for tumour ≤4 cm has shown promising out-come. The increased risk of chronic renal insufficiency and proteinuria after Radical nephrectomy supports use of Nephron Sparing Surgery.

Present study was limited by the small sample size and short follow-up given the study period. A larger sample size and longer follow-up will provide better insight and understanding of the long term outcomes of Nephron sparing surgery.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Asimi AR, Wani MS, Lone MI. The safety and efficacy of nephron sparing surgery in T1N0M0 renal cell carcinoma. Int Surg J 2018;5:413-9.