

Original Research Article

Comparison of glomerular filtration rate (GFR) changes in radical nephrectomy versus nephron sparing surgery (NSS) for pT1 renal cell carcinoma (RCC)

*Phukan C, Venkatramani V, Banerji JS, Kekre NS and Devasia A

Abstract

Department of Urology, Christian
Medical College, Vellore

*Corresponding Author's Email:
Email: drchandanph@yahoo.com
Tel - +91-416-2282055; +91-
9442152347

To determine the impact of nephron sparing surgery (NSS) versus radical nephrectomy (RN) on the glomerular filtration rate (GFR) in pT1 renal cell carcinoma (RCC). All patients with renal tumors (pT1) who underwent either NSS or RN between 2004 and 2011 were studied retrospectively. GFR, chronic kidney disease (CKD) stage and serum creatinine were studied pre-operatively, and post-operatively. Of 341 patients, 77 underwent NSS and 264 underwent RN. Mean GFR was 75 and 76 ml/min/1.73m² pre-operatively in the NSS and RN group. There was a statistically significant reduction in GFR in the RN versus NSS group in the immediate postoperative period (p=0.008), at three months (p=0.001) and at one year (p=0.001). On multivariate analysis it was seen that hypertension and radical nephrectomy were predictors of significant worsening of GFR at one year. There was a significant change of CKD stage from stage I/II to CKD III-V at one year in the RN versus NSS group (p=0.043). Radical nephrectomy was associated with a significant fall in GFR when compared to NSS even on multivariate analysis. Nephron sparing surgery is important in the treatment of pT1RCC to preserve renal function.

Keywords: Glomerular Filtration Rate, Nephron sparing surgery, Radical nephrectomy, Renal Cell Carcinoma,

INTRODUCTION

Nephron sparing surgery(NSS) is an established option for renal cell carcinoma (RCC) in patients with compromised renal function (Licht and Novick, 1993; Morgan and Zincke, 1990). Large series have demonstrated equivalent survival with minimal differences in perioperative morbidity (Kowalczyk et al., 2013). The impact of chronic kidney disease on life span in those who undergo radical nephrectomy (RN) has been documented to be more significant than oncological outcome, especially since diseases like diabetes mellitus and hypertension have a potential to compound renal dysfunction (Lau et al., 2000). In those with a threat to contralateral renal function from conditions such as calculus disease, renal artery stenosis, diabetes or hypertension, NSS has a potential to minimize the impact

of nephron loss. Ever since its oncological safety was established, NSS began to be offered to patients with a normal contralateral kidney as well (Steinbach et al., 1995; Herr, 1999). This is of particular relevance considering the increasing incidental detection of small renal masses (SRMs) on imaging.

Hence we sought to review our experience with NSS and RN in pT1 renal masses to determine the effect of each on GFR.

MATERIALS AND METHODS

In this retrospective electronic chart review spanning a period of 8 years from 2004 to 2011, all patients with

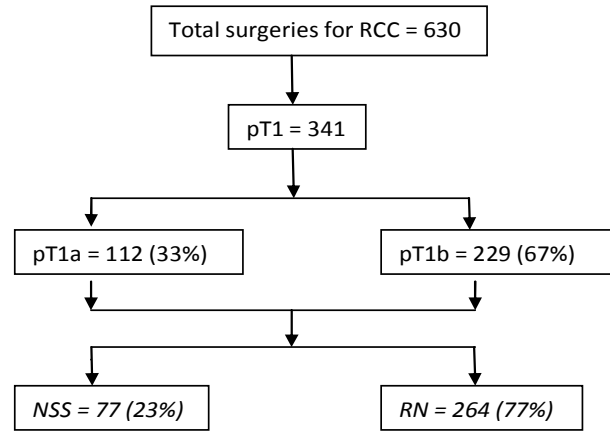


Figure 1. Showing the distribution of arms:

Table 1. Baseline distribution of patient characteristics

Characteristics		NSS arm	RN arm	p
N		77	264	
Sex	Male	59	192	0.495
	Female	18	71	
Age	<50	37	107	0.301
	50-60	27	97	
	61-70	13	51	
	>71	0	9	
Creatinine (mg%)		1.13 ± 0.29 (SE = 0.03)	1.09±0.26 (SE = 0.02)	0.323
Diabetes (%)		25 (32.5)	68 (25.8)	0.111
Hypertension (%)		34 (44.2)	92 (34.8)	0.156
Obesity (%)		27 (35.1)	86 (32.6)	0.449

tumors less than or equal to 7cm on final histopathology were included. Those with normal renal function were evaluated with triphasic contrast enhanced computed tomography (CECT). Magnetic resonance imaging (MRI) was performed in patients with pre-existing renal insufficiency.

The tumor was staged according to the 2009 American Joint Committee on Cancer revision of the TNM system:

- T1: ≤7.0 cm and confined to the kidney
 - T1a: ≤4.0 cm and confined to the kidney,
 - T1b: Tumor>4.0 and ≤7.0 cm and confined to the kidney (AJCC cancer staging manual, 2010).

GFR was calculated using the abbreviated Modification of Diet in Renal Disease formula:

$$\bullet \text{ GFR (ml/min/1.73m}^2\text{)} = 186 \times (\text{Creatinine}/88.4)^{-1.154} \times (\text{Age})^{-0.203} \times (0.742 \text{ if female}).$$

CKD was staged into 5 groups according to National kidney foundation, Kidney disease outcome and quality

initiative.

The decision for NSS or RN was based on size and location of the tumor, patient or surgeon's preference or potential compliance for follow up. Follow-up information was available for patients through a computerized registry. Patients were recommended follow-up as per standard guidelines for the relevant tumour stage.

Statistical method: SPSS-16 was used for statistical analysis. Standard tests of significance were used.

RESULTS

A total of 630 cases of RCC underwent surgery during the study period (Figure 1). Of these, 341 were pT1 and were included in our study. Seventy-seven (23%) underwent NSS and 264 (77%) underwent RN. 22% of T1a and 23% of T1b tumours underwent NSS. The mean

Table 2. Comparison of GFR values at various points in time between the NSS and RN arms

GFR(ml/min/1.73m ²)	NSS	RN	p
Pre-operative	75±22.64 (SE = 2.58)	76.1±20.32 (SE = 1.25)	
Immediate post-operative	63.97±16.33 (SE = 1.86)	57.1±18.89 (SE = 1.18)	0.008
3 months	70.65±20.25 (SE = 3.20)	60.17±14.43 (SE = 1.18)	0.001
1 year	71.61±19.05 (SE = 3.22)	57.97±(15.97) (SE = 1.38)	0.001

Table 3. Multivariate analysis of factors contributing to fall in GFR

Factor	Co-efficient	p
NSS or RN	4.44	0.029
Age	-0.28	0.077
Diabetes mellitus	-3.35	0.388
Hypertension	-8.49	0.024
Obesity	1.77	0.372

Table 4. Comparison of the worsening of CKD stage and change in serum creatinine between NSS and RN arms

Worsening of CKD stage	NSS	RN	p
• Immediate post-operative	14.28%	34.56%	0.0136
• 1 year	3.33%	23.33%	0.0433
Change in serum creatinine	NSS	RN	p
• Immediate post-operative	+1.161	+1.281	0.086
• 3 months	+1.232	+1.009	0.165
• 1 year	+0.458	+0.539	0.702

age of patients in the NSS group was 51 years (Range 24-70years) whereas it was 52 years (range 15-81years) in the RN group. The incidence of risk factors for the development of renal insufficiency such as hypertension, diabetes, obesity was similar in the two groups (Table 1).

The pre operative GFR in both the NSS and RN groups was comparable (Table 2). The GFR in the NSS arm didn't change much post-operatively, especially on the three-month and one-year follow up. However there was a significant drop in GFR in the RN group at all these points (immediate post-operative, 3 months and 1 year). (Table 2)

Multivariate analysis was performed comparing the pre-operative GFR to that at one year of follow-up. It showed that hypertension and undergoing radical nephrectomy were significant contributors to renal impairment (Table 3).

Worsening of the CKD stage (as defined previously) was also significantly more in the RN group compared to the NSS group. This was noted in the immediate post-operative period as well as at one year of follow-up. (Table 4)

The baseline creatinine value in both groups was comparable. In addition, there was no significant

difference in the increase in creatinine values between the partial and radical nephrectomy groups at any time post-operatively. (Table 4)

DISCUSSION

In our study there was a significant decrease in the GFR of those undergoing radical nephrectomy, when compared to a similar cohort undergoing NSS. The changes were appreciated at all points in time viz. immediate post operatively, at three months and at one year. To evaluate the possibility of any selection bias, due to the retrospective nature of the study, we did a subgroup analysis for those above 60 years of age. In the partial nephrectomy group there were 16.7% (13/77); those in the radical nephrectomy group were slightly larger at 22.2% (60/264). It is possible that the slightly larger cohort of older patients in the radical nephrectomy group may have contributed to the lower mean GFR in this subset. However, statistically there seemed to be no difference with a p-value of 0.301.

Though oncological outcome in organ confined RCC is excellent, patients often suffer from morbidity and mortality related to renal failure. There have been several studies, including animal models, showing that there is accelerated hypertension and worsening of pre-existing renal failure after nephrectomy (Chapman et al., 2010; Satasivam et al., 2011). Moreover, as RCC is a disease of the middle aged and older population, the prevalence of coexisting diseases like diabetes and hypertension is greater and the onset of renal failure brings with it a very substantial cardiovascular risk (Weight et al., 2010). It should be noted that the overall chance of dying while on dialysis is about 6.3% per year (Meier-Kriesche et al., 2000). Patients with pT1 tumors have been found to have greater than a 90% 5-year survival rate. Thus the prerogative is to concentrate on better "renal" outcomes in this patient population.

Huang et al showed that 29% of a study population of 662 patients developed new onset of GFR lower than 60 ml/min/1.73m², and a further 16% developed new onset CKD with GFR < 45 ml/min/1.73m² following nephrectomy (Huang et al., 2006). This supports the notion that patients who undergo radical nephrectomy have a significantly higher risk of developing moderate-severe CKD and therefore may experience negative effects on life span and quality of life.

Using the SEER database, Sun and colleagues concluded that patients treated with radical nephrectomy, were in all probability, likely to die of other cause mortality (cardiovascular and CKD related causes) after surgery (Weight et al., 2010; Sun et al., 2011). This remained true even after adjusting for cancer specific mortality.

Interestingly, in our study the difference in serum creatinine in both populations was not statistically significant. This indicates that serum creatinine is not

sensitive enough to determine significant changes in renal function and routine GFR measurement should be performed (Huang et al., 2006).

Being retrospective, our study has inherent limitations. Follow-up data is variable in both arms and only patients with all required data were used in the calculations. The indications for NSS and RN were variable in our population, depending upon feasibility of follow up and surgeon preference.

Similar reports from the Indian subcontinent also showed comparable results (Agrawal et al., 2007; Gupta et al., 2007). However, ours remains the largest such study from the subcontinent. In the study by Agarwal et al, none of the 26 patients in their series required renal replacement therapy after the NSS (Agrawal et al., 2007). Gupta et al too in their series of 36 patients undergoing NSS showed that none of their patients progressed to renal failure (defined as increase in serum creatinine > 20 mg/dl) at a mean follow-up of 52.1 months (Gupta et al., 2007). They compared their study with Lau et al and McKiernan et al, who had shown that RN resulted in more cases of renal insufficiency (defined as increase in serum creatinine > 20 mg/L), in comparison to NSS (Lau et al., 2000; McKiernan et al., 2002).

CONCLUSIONS

A significant drop in GFR was observed in patients undergoing RN compared with NSS. This was true in immediate post-operative period as well as at three months and one year follow-up. Multivariate analysis indicated that hypertension and undergoing RN were significant contributors to developing renal impairment.

There was significant worsening of GFR to a higher CKD stage in those undergoing radical nephrectomy. This difference was significant in the immediate post op and after one year. Creatinine level by itself did not show a significant drop, indicating the need for GFR monitoring in this cohort.

ACKNOWLEDGEMENT

There was no potential conflict of interest including financial and non-financial in this paper. All the data obtained were from the MRD section in the institution.

REFERENCES

- Agrawal S, Jha MS, Khurana N, Ansari MS, Dubey D, Srivastava A, Kapoor R, Kumar A, Jain M, Mandhani A. (2007). Nephron sparing surgery: A single institution experience. *Indian J Urol*;23:23-27.
- AJCC cancer staging manual (2010). 7th Ed. New York: Springer.
- Chapman D, Moore R, Klarenbach S (2010). Residual renal function after partial or radical nephrectomy for renal cell carcinoma. *Can Urol Assoc J*;4(5):337-343.
- Gupta NP, Kumar A, Hemal AK, Dogra PN, Seth A, Kumar R. (2007). Open nephron-sparing surgery in renal tumors with normal

- contralateral kidney: A single centre experience of 8 years. *Indian J Urol*;23:18-22.
- Herr HW (1999). Partial nephrectomy for unilateral renal carcinoma and a normal contralateral kidney: 10-year follow-up. *J Urol*;161(1):33-34.
- Huang WC, Levey AS, Serio AM, Snyder M, Vickers AJ, Raj GV, Scardino PT, Russo P (2006). Chronic kidney disease after nephrectomy in patients with renal cortical tumours: a retrospective cohort study. *Lancet Oncol*;7(9):735-740.
- Kowalczyk KJ, Choueiri TK, Hevelone ND, Trinh QD, Lipsitz SR, Nguyen PL, Lynch JH, Hu JC (2013). Comparative effectiveness, costs and trends in treatment of small renal masses from 2005 to 2007. *BJU Int*;112(4):E273-280.
- Lau WK, Blute ML, Weaver AL, Torres VE, Zincke H. (2000). Matched comparison of radical nephrectomy vs. nephron-sparing surgery in patients with unilateral renal cell carcinoma and a normal contralateral kidney. *Mayo Clin Proc*;75:1236-1242.
- Licht MR, Novick, AC (1993). Nephron sparing surgery for renal cell carcinoma. *J Urol*;149(1):1-7.
- McKiernan J, Simmons R, Katz J, Russo P. (2002). Natural history of chronicrenal insufficiency after partial and radical nephrectomy. *Urology*;59:816-820.
- Meier-Kriesche HU, Port FK, Ojo AO, Rudich SM, Hanson JA, Cibrik DM, Leichtman AB, Kaplan B (2000). Effect of waiting time on renal transplant outcome. *Kidney Int*;58:1311-1317.
- Morgan WR, Zincke H (1990). Progression and survival after renal-conserving surgery for renal cell carcinoma: experience in 104 patients and extended follow-up. *J Urol*;144(4):852-857.
- Satasivam P, Rao K, Guggenheimer K (2011). The effect of hypertension and diabetes on the degree of renal function deterioration after unilateral nephrectomy *BJU Int* ;108(9):1508-1512.
- Steinbach F, Stoćkle M, Hohenfellner R (1995). Clinical experience with nephron-sparing surgery in the presence of a normal contralateral kidney. *SeminUrolOncol*;13(4):288-291.
- Sun M, Abdollah F, Bianchi M, Trinh QD, Jeldres C, Tian Z, Shariat SF, Widmer H, Zorn K, Menon M, Montorsi F, Perrotte P, Karakiewicz PI. (2011). A stage-for-stage and grade-forgrade analysis of cancer-specific mortality rates in renal cell carcinoma according to age: a competing-risks regression analysis. *EurUrol*;60:1152-1159.
- Weight CJ, Larson BT, Fergany AF (2010). Nephrectomy induced chronic renal insufficiency is associated with increased risk of cardiovascular death and death from any cause in patients with localized cT1b renal masses. *J Urol*;183(4):1317-1323.