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Renal Function after Partial Nephrectomy Versus Radical Nephrectomy for Renal Cell Carcinoma: A Comparative Study

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Keywords: Demographic Characteristics; BMI; Radical nephrectomy; Renal cell carcinoma; Post-operative symptoms.

Abstract

Background: Renal Cell Carcinoma (RCC) is the third most common malignancy of the genitourinary system characterized by lack of early warning clinical manifestations (asymptomatic) and late triad of symptoms (flank pain, hematuria, and palpable renal mass). It accounts for approximately 2-3 % of the adult malignancy and 90% to 95% of neoplasms arising from the kidney. With the improvement in imaging technique, small and asymptomatic RCC is easily diagnosed and treated but advanced RCC is difficult to trat because its inherent resistance to conventional chemotherapy and radiotherapy.

Objective: To compare the time-dependent changes of estimated Glomerular Filtration Rate (eGFR) after Partial Nephrectomy (PN) and Radical Nephrectomy (RN) for Renal Cell Carcinoma (RCC).

Type of study: Randomized controlled clinical trial.

Place of Study: Department of Urology, BSMMU and Comfort Nursing Home (Pvt.) Ltd. Dhaka, during the period of January, 2017 to September, 2018.

Method and Procedure: This prospective randomized controlled clinical trial study is conducted in the Department of Urology, BSMMU andComfort Nursing Home (Pvt.) Ltd, Dhaka, from January, 20178 to September, 2018. Total 52 patients having renal cell carcinoma (<7cm) and normal

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contralateral kidney, available preoperative and postoperative serum creatinine and MDRD-eGFR measurements are included in this study, Preoperative MDRD-eGFR<30 ml/min/1.73m^2 or serum creatinine level >1.5 mg/dl before surgery is excluded from this study. After detailed explanting about the nature of the study to the participants and with written consent, 52 patients are randomly allocated into two groups by lottery method. In group-A 26 patients are enrolled for Partial Nephrectomy (PN) and in group-B, 26 patients are enrolled for Radical Nephrectomy (RN). The enrolled patients are evaluated after surgical intervention under general anesthesia with different surgeons in multiple institutes by measuring serum creatinine and MDRD-eGFR postoperatively 1, 3, 7 days, and 3 monthlies for one year. MDRD-eGFR declining is assessed from the preoperative value to the lst post-operative value at the end of follow up. During follow up period, out of total 52 patients in both groups 2 patients in group-A and one patient in group-B did not come in regular follow up, one patient missing in each group and one patient died in group-B did not come in regular follow up, one patient missing in each group and one patient died in group-B. So total 23 patients in each group are followed up after operation.

Results: Demographic characteristics, BMI, pre- and post-operative symptoms and sign of the patients, most of the tumor characteristics (location, hydronephrosis and enhancement) are not statistically. Significant in both groups but statistically significant changes are found in tumor size (p=0.004) and tumor type (p=0.013). There is no significant difference in preoperative serum creatinine and eGFR in both groups but the time-dependent changes of eGFR after RN show plateau form initially and then gradually declining form the first post-operative day to the 12 post-operative months. In case of Partial Nephrectomy (PN), a lowest eGFR is observing in postoperative day 1 and gradually recovered to near preoperative level for 12 months. The mean (+SD) eGFR decreased more significantly in RN (group-B 18.56 ml/min) than PN patients (group- A 6.31 ml/min) from preoperative 4 to 12 months after operation and show statistically significant differences between and within both groups (p<0.001, <0.001 respectively).

Conclusion: Time dependent changes of estimated Glomerular Filtration Rate (eGFR) after Partial Nephrectomy (PN) is better than Radical Nephrectomy (RN) for Renal Cell Carcinoma (RCC). Partial Nephrectomy (PN) is therefore the better procedure for preservation of renal function.

Introduction

Renal Cell Carcinoma (RCC) is the most common malignancy of the kidney and accounts for about 2-3 % of all adult neoplasms [1]. Overall, approximately 12 new cases are diagnosed per 100,000 population per year, with a male-to-female predominance of 3:2. This is primarliy a disease of older adults, with typical presentation between 50 and 70 years of age [2]. The incidence of renal tumors has risen over the last decades. Due to the progress in radiological imaging, the majority of renal tumors are detected incidentally (<50%) during diagnostic work-up for other patient comlaints. The triad of symptom-flank pain, gross hematuria, and palpable mass only occur in the minority of patients (7-10 %) and are usually a sing of locally advanced disease [3]. Radical Nephrectomy (RN) has been the standard treatment for any Renal Cell Carcinoma (RCC) during the last 30 years. The role of open raidcal nerhrectomy in the management of RCC has changed somewhat over the last decade [1]. Although radical nephrectomy (RN0 has long been the standard treatment for renal cell carcinoma (RCC), many studies have recently been documented the improved overall survival, better preservation of renal function, the safety and oncological efficacy of Nephron-sparing surgery (NSS) for RCC [3]. The curren guidelines form the European Urology Association (EUA) and American Urology Association (AUA) have recommended NSS for RCCs smaller than 4cm. Despite these recommendatins, RN is still wideley performed for small tumors in individuals with a normal contralaeral kidney [4]. Nephron-Sparing Surgery (NSS) with reseciton of the tumor only was usually reserved for patinets with solitary kidney, bilateral tumors or chronic kidney disease. It has become the standard of surgery for patients with solitary kidney, bilateral tumors or chronic kidney disease. It has become the standard of surgery for patients presenting with renal tumors <4 cm in size (cTla) with a healthy contralateral kidney due to good oncological long-term outcomes with a moderate perioperative complication rate. In selected cases NSS is considered as alternative treatment for 4-7 cm sized renal tumors (cTlb). For renal tumors >7 cm in size (cT2a), NSS can also be performed safely in properly selected patients with good short-term functional and oncologic outcomes. Both RN and NSS are therefore considered standard treatments for RCC and the main difference in outcome between these procedures is the preservatin of renal funciton [3]. Renal function after surgfery for RCC has usually been assessed by using serum creatinine (SCr.0) level alone but SCr. is affected by factors affecting generation, including muscle mass and dietary intake. As a result, renal function tends to be overestimate in patients who are elderly or for some other reason have decreased muscle mass. Furthermore, it is difficult to evaluate SCr. level in both male and female patients because the normal ranges of serum creatinine difer between men and women. So e GFR is the most accurate index for assessing renal function ans the National Kidney Foundation Kidney Disease Outcome Quality Initiative (NKF KEOQI) guidelines recommened using estimate glomerular with age, diabetes and hypertension [5]. In a study of 253 patients with RCC by Miyamoto et al. [6]. Have assessedthe renal function usung the eGRR and investigate the time dependent chanes of the eGFR after the operation and found postoperative eGFR<60 ml /min is 23% and 57.6% in radial nerephrectomy and nephron sparing surgery.The aim of this study is to evaluate the time-dependent changes or renal function of the patents after RN and PN for RCC by using MDRD equations for estimating eGFR from measuring creatinine level preoperatively and postoperatively 1,3,7 days, and 3 monthly for one year in the Bangladeshi population and the result of this study will emphasize more in renal preserving procedure for eligible patients with RCC.

Objective

General objective

- To compare renal functional status after partial nephrectomy and radical nephrectomy for renal cell carcinoma.

Specific objectives:

- To estimate serum creatinine among the patients undergoing partial nephrectomy and radical nephrectomy before operation.

- To estimate serum creatinineamong the patients undergoing partial nephrectomy and radical nephrectomy after operation at different interval.
- To estimate eGFR among the patents undergoing partial nephrectomy and radical nephrectomy before operation.
- To estimate eGFR among the patients undergoing partial nephrectomy and radical nephrectomy after operation at different interval.
- To compare eGFR among the patients undergoing partial nephrectomy and radical nephrectomy after operation at different interval.
- To compare eGFR between partial nephrectomy and radical nephrectomy patients.

Materials and Methods

Type of study: Randomized controlled clinical trail.

Study period: January to September-2018.

Study place: Department of Urology Bangabandhu Sheikh Mujib Medical University (BSMMU) and Comfort Nursing Home (Pvt.) Ltd. Dhaka.

Study population: Patients having renal cell carcinoma (≤7cm) attending in the outpatient department of BSMMU hospital and Comfort Nursing Home (Pvt.) Ltd, Dhaka from January to September-2018, is included in this study and surgical intervention is done.

Inclusion criteria

- ✓ Age (35-75 years)
- ✓ A solitary renal mass, size ≤ 7cm (cT1a, cT1b)
- ✓ A radiographically normal contralateral Kidney

Exclusion criteria

- ✓ Patient with a preoperative serum creatinine level> 1.5 mg/dl
- ✓ Patient with a preoperative glomerular filtration rate <30 ml/min/1.73 m^2
- ✓ Patient with a tumor in solitary kidney.
- ✓ Patient with bilateral or multiple renal tumors.
- ✓ Contralateral unhealthy kidney.
- ✓ Obese patients (BMI>30 Kg/M^2)
- ✓ Pregnant patient
- ✓ Patient refusing consent
- ✓ Patient missing or dead during follow up

Sample size: Thus, 23 patients will be needed in each group (52).

Sampling technique: Purposive sampling technique will be applied to collect the sample for this study who are admitted with the diagnosis of renal cell carcinoma in the department of urology, BSMMU and Comfort nursing home (Pvt.) Ltdin Dhaka are selected as per inclusion and exclusion criteria for the present study. After written informed consent, total 52 patients are recruited and divided into two groups by lottery method.

Study groups: There are two groups of study subjects.

Group-A: Patients who were undergone partial nephrectomy by open method.

Group-B: Patients who were undergone radical nephrectomy by open method.

- ✓ Preoperative variable:BMI of the patient
- ✓ Chronic disease/co-morbid disease-cardiovascular (HTN), DM.
- ✓ Serum creatinine (mg/dl)
- ✓ eGFR (ml/min/1.93$m^{2)}$

Postoperative Variable (outcome Variable)

- ✓ Serum creatinine (mg/dl)
- ✓ eGFR (ml/min/1.73 m^2)

Investigation

Diagnostic purpose

- ➢ USG of whole abdomen.
- ➢ Computed tomography scan with urogram and angiogram

Evaluation purpose

- ➢ Blood Hemoglobin level
- ➢ Urine R/M/E and C/S
- ➢ Serum electrolytes
- ➢ RBS
- ➢ CXR-P/A
- ➢ Serum Creatinine
- ➢ eGFR

Key steps of the procedure

- ➢ Patient was included in the study after fulfilling the selection criteria (inclusion and exclusion criteria).
- ➢ Informed written consent was taken by all patients after explaining about the study, different management options, the possibility of response and the complications related to the procedure.
- ➢ Preoperative general fitness of the patients was checked by physical examinations and investigations.
- ➢ Under standard procedure, partial nephrectomy in group-A patients and radical nephrectomy in group-B patients were performed.

Immediate postoperative follow up

In this study, patients were followed up early 1,3,7 days postoperatively by evaluating-

- ✓ Subjective complaints (History)
- ✓ Clinical examination
- ✓ Investigation
  - ○ Urine R/M/E and C/S

- Hemoglobin level
- Serum creatinine
- eGFR

Subsequent follow up: 3 monthly for 1 year.

- ✓ History
- ✓ Clinical examination
- ✓ Investigation
  - Urine R/M/E and C/S
  - Hemoglobin level
  - Serum creatinine
  - eGFR

Date collection

- The study subjects were selected on the basis of inclusion criteria from the patients who underwent partial nephrectomy or radical nephrectomy in the Department of Urology, BSMMU and Comfort nursing home (Pvt.) Ltd in Dhaka.
- The demographic information, relevant medical history, examination findings and investigation reports of all the study subjects were recorded in the data collection sheet.
- Any patient facing complications during the procedure was excluded from study.
- Any patient who died during follow up was excluded.
- All patients were conducted over telephone as scheduled for follow up after initial treatment.
- The data sheet was filled up after taking brief history, review of records and variable documents form patients.

Data analysis

After compilation, the data was presented in the form of tables, figures and graphs, as necessary.

- Statistical analysis of the results was done by using computer based statistical software SPSS 20.0 version for windows operating system.
- Results are expressed as mean (±SD) and compared by Student's unpaired (independent) and paired (dependent) t-test for continous variables and Chi square test for categorical variables.
- A `p' value of < 0.05 was considered as significant.

Operational definition

Renal cell carcinoma: Renal Cell Carcinoma (RCC) is a kidney cancer that originates in the lining of the proximal convoluted tubule, a part of the very small tubes in the kidney that transport waste molecules from the blood to the urine.

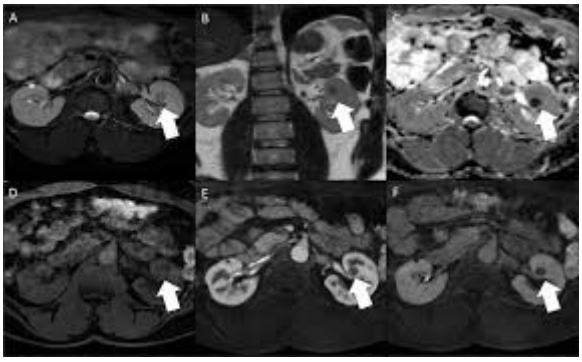

Figure 1: CT finding of right renal mass (RCC) in coronal and axial view (Source: case no-24, 2017).

Radical nephrectomy: The prototypical concept of RN encompasses the basic principles of early ligation of the renal artery and vein, removal of the kidney with primary dissection extremely to the Gerota fascia, excision of the ipsilateral adrenal gland, and performance of an extended lymphadenectomy form the crus of the diaphragm to the aortic bifurcation.

Nephron sparing surgery: An operation to remove a kidney tumor by removing only part of the kidney leaving healthy tissue.

Creatinine: It is a breakdown product of creatinine phosphate in muscle and is usually produced at a fairly constant rate by the body and excreted by kinnys in urine. The normal serum creatinine range for men is 0.6-1.3 mg/dL. The normal range for women is 0.5-1.2 mg/dl (Source: BSMMU biochemistry report, 2018).

Chronic kidney disease: Chronic Kidney Disease (CKD) is a progressive loss in kidney function over a period of months of years.

Figure 2: CTP finding of right renal ass (RCC)-coronal and axial view (Source case no-17, 2017).

Endophytic tumor: An endophytic tumor was defined as less than 40% of the lesion extending off the surface of the kidney.

Exophytic tumor: Tumor that intending to grow outward beyond the surface epithelium from which it orginates:

Hypertension: Medical guidelines define hypertension as a blood pressure higher than 130 over 80 millimeters of mercury (mmHg), according to guidelines issued by the American Heart Association (AHA) in November 2017.

Diabetes: A disease in which the body's ability to produce or respond to the hormone insulin is impaired, resulting in abnormal metabolism of carbohydrates and elevated levels of glucose in when fasting. Less than 7.8 mmol/ (140mg/dl) 2 hours after eating. In diabetes patient, blood sugar level in fasting condition- ≤7.0 mmol/1.2 hours after eating ≥11.1 mmol/(≥7.0 mmol/1,2 hours after eating ≥11.1 mmol/1 (≥mg/dl) (Source: BSMMU biochemistry report, 2018).

Kidney tumor: Renal cell carcinoma is the commonest solid lesion within the kidney which originates form the proximal renal tubular epithelium and comprises different RCC types with specific histopathological and genetic characteristics [7], From a clinical point of view. Three main types of RCC are important: clear cell (cRCC) 65%, papillary (pRCC-type 1 and II) 15% and chromophobe (chRCC) 10% generally, in all RCC types, prognosis worsens with stage and histopathological grade. Etiological factors include lifestyle such as smoking, obesity, hypertension and occupational exposure to specific carcinogens [8]. The 5-year overall survival for all types of RCC is 49%, which has further improved since 2006 probably due to an increase in incidentally detected RCCs as well as by the introduction of tyrosine kinase inhibitors. Sarcomatoid changes can be found in all RCC types and they are equivalent of high grade and very aggressive tumors [9].

Radical nephrectomy: Radical nephrectomy refers to complete removal of the kidney outside the Gerota fascia together with the ipsilateral adrenal gland and complete regional lymphadenectomy from the crus of the diaphragm to the aortic bifurcation [10]**.** Radical nephrectomy is reserved for renal tumors that are not amenable to partial nephrectomy. Indication for radical nephrectomy include tumors in nonfunctional kidneys, large tumours replacing the majority of renal parenchyma, tumours associated with detectable regional lymphadenopathy, or tumors associated with renal vein thrombus. Complication relating to RN includes damage during Suprahilar and Retrocrural lymphadenectomy-duodenum, pancreas, liver, spleen, superior mesenteric artery, celiac trunk, superior mesenteric autonomic plexus, and cisterna chili, Injury to the vasculature of the Gut. There are two surgical approach for radical surgery-Flank Approaches (Subcostal Flank Approach, Supracostal Flank Approach, Dorsal Lumbotomy Approach, Thoracoabdominal Approach), Anterior Approaches (Anterior Midline Approach, Anterior Subcostal Approach, Chevron Incision-Bilateral Anterior Subcostal Approach [2].

Partial Nephrectomy: Partial nephrectomy is the surgical removal of a kidney tumor along with a thin rim of normal kidney, with the aims of curing the cancer and preserving as much normal kidney as possible. Whenever preservation of functioning renal parenchyma is important, partial nephrectomy substitutes for radical nephrectomy. The first partial nephrectomy was performed in 1884 by Wells for the removal of a perirenal fibro-lipoma [11]. Partial nephrectomy to treat renal malignancy was first described in 1890 by Czerny [12]. In 1950, Vermooten reported that peripherally located, encapsulated renal tumors could be removed by partial excision of renal tissue Partial nephrectomy has now become a standard procedure for appropriately selected patients with renal cell carcinoma (RCC). Partial nephrectomy is indicated for cases in which a radical nephrectomy would render the patient a nephric with a subsequent immediate need for dialysis. Such cases include Synchronous bilateral RCC, Tumors in a solitary kidney, Unilateral tumor with a poorly functioning opposite kidney(imperative indications), Unilateral RCC and those with a functioning opposite kidney with an uncertain future function in artery stenosis, hydronephrosis, chronic pyelonephritis and systemic diseases such as diabetes and hypertension that result in arteriosclerosis and nephron-affecting impairment, elective indication patients with small (4 cm or less in diameter) unilateral tumors with a healthy contralateral organ[13]. Several surgical techniques are available for performing partial nephrectomy in patients with renal tumors. Description of these techniques, including performing the incision, exposing the Kidneys, and closing the situs, are described in detail elsewhere [14]. The five main surgical processes include performing the incision, exposing the kidney, and closing the situs, are described in detail elsewhere (Monite JE and Novick AC, 1998). The five main surgical processes include enucleation of tissue, polar segmental nephrectomy, wedge resection, major transverse resection, and extracorporeal partial nephrectomy followed by renal auto-transplantation [13], All of these techniques require steady vascular control and thorough hemostasis, avoidance of renal ischemia, complete tumour removal with free margins, and efficient closure of the intrarenal collecting system. Finally, an adequate postoperative renal function must be maintained since a functioning renal remnant of at least 20% of one normal kidney is necessary to avoid end-stage renal failure [15]. However, it is important not to compromise the extent of the surgical procedure to preserve renal function at the expense of an incomplete resection.

Estimated GFR: Glomerular Filtration Rate (GFR) is accepted as the best overall measure of kidney function. Measuring GFR directly is considered the most accurate way to detect changes in kidney status, but measuring the GFR directly is complicated, requires experienced personnel, and is typically performed only in research settings and transplant centers [16]. The GFR can be estimated from serum creatinine concentration and demographic and clinical variables such as age, sex, ethnicity, and body size. Creatinine is a muscle waste product that is filtered form the blood by the Kidneys and released into the urine at a relatively steady rate. When kidney function decreases, less creatinine is eliminated and concentrations increases in the blood. With the creatinine test, a reasonable estimate of the actual GFR can be determined but not the accurate result. The normal mean value for GFR in healthy young men and women is approximately 130mL/min per 1.73 m^2, and 120mL/min per 1.73m^2 respectively, and declines by approximately 1 mL/min per 1.73m^2 per year after 40 years of age [17]. For men, the equation of eGFR (ml/min/1.73m^2)= 194 x (SCr) $^{1.094}$ X (age) $^{0.287}$ and for women it is multiplied by 0.739. GFR is related to Chronic Kidney Disease (CKD). Current guidelines define chronic kidney disease as kidney damage or a Glomerular Filtration Rate (GFR) less than 60 mL/min per 1.73 m^2 for 3 months or more, regardless of cause [18]. To facilitate detection of chronic kidney disease, guidelines recommend different equations to calculate eGFR. The following two are most common and require a person's blood creatinine result, age, and assigned values based

upon sex and race. Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) creatinine equation (2009) recommended by the National Kidney Foundation for calculating eGFR in adults. Modification of Diet in Renal disease Study (MDRD) equation which is now widely accepted and many clinical laboratories are using it to report GFR estimates [19,20].

Results & observations

Distribution of patients by gender show (table-I), most of the patients in both groups are male. In group A 14 (60.9%) patients are male and 09 (39.1%) patients are female. In group-B, 15(65.2%) patients are male and 8(34.8%) patients are female (table-I), Mean (± SD) and range of age distribution of the patients in group -A is 48.91 ± 8.79 years, (35-65) years and in group-B is 50.70 ± 12.23 years, (35-74) years (table-1), Mean (±SD) BMI in group-A is 20.70±2.36 kg/m^2 and in group-B is 21.22 ± 6.36 kg/m^2 (table-I). There are no statistically significant differences in demographic characteristic (sex, age) and BMI between two groups (p= 0.760, 0.573, 0.714 respectively: table-I).

Table 1: Patients characteristics in both groups (n= 46).

	Group-A	Group-B	P-Value
	(Nephron-Sparing Surgery) (n= 23)	(Radical Nephretomy) (n= 23)	
Sex			
Male	14 (60.9)	15 (65.2)	0.760
Female	9 (39.1)	8 (34.8)	
Age (years)			
(mean ± SD)	48.91 ± 8.79	5.70 ± 12.23	0.573
Range (years)	35-65	35-74	
BMI (kg/m2) (mean±SD)	20.70 ± 2.36	21.22 ± 6.36	0.714

Chi square test and independent't test was done to measure the level of significance.

Table 2: Pre and post-operative symptoms & sign of the patients in both groups (n= 46).

	Group-A	Group-B	P-Value
	(Nephron-Sparing Surgery) (n= 23)	(Radical Nephretomy) (n= 23)	
Pre-operative			
Flank pain			
Yes	18(78.3)	16(69.6)	0.502
No	5 (21.7)	7 (30.4)	
Hematuria			
Yes	5 (21.7)	7 (30.4)	0.502
No	18 (78.3)	16 (69.6)	
Diabetes			
Yes	6 (26.1)	5 (21.7)	0.730
No	17 (73.9)	18 (78.3)	
Hypertension			
Yes	10 (43.5)	10 (43.5)	1,000
No	13 (56.5)	13 (56.5)	
Post-Operative			
Fever			
Yes	3 (13.0)	2 (8.69)	1,000
No	20 (87.0)	21 (91.30)	

Chi-square test was done to measure the level of significance.

Pre and post-operative symptoms & sign of the patients in both groups shows (Table II), 18 (78.3%) and 16 (69.6%) of the patients are presented with flank pain at presentation in group-A group-B respectively and rest of the patients have no flank pain (Table II). 5 (21.7%) and 7 (30.4%) of the patients present with hematuria at presentation in group-A and group-B respectively and rest of the patients have no hematuria (Table II). Most of the patients are free from diabetes which are 17 (73.9%) in group-A and 18 (78.3%) in group-B and rest of the patients have no diabetes (Table II). Hypertension in present in 10 (43.5%) of the patients in both groups and rest of the patients have no hypertensions (Table II). During post-operative period, most of the patients had no post-operative fever which are 20 (87.00%) in group-A, 21 (91.3%) in group-B and minorities of the patients have post-operative fever in both groups (Table II). There are no statistically significant differences in pre and post-operative clinical symptoms andsigns of the patients between two groups (p= 0.502, 0.502, 0.730, 1,000, 1.000 respectively: Table II).

Table 3: Distribution of the patients according to tumor characteristics in both groups (n= 46).

	Group-A	Group-B	P-Value
	(Nephron-Sparing Surgery) (n= 23)	(Radical Nephretomy) (n= 23)	
Tumor size (cm)	4.28 ± 0.91	5.08 ± 0.89	0.004
Ranger (cm)	(2.60 - 6.30)	(2.90-6.90)	
Tumor location			
Upper pole	9 (39.1)	12 (52.2)	0.563
Lower pole	10 (43.5)	9 (39.1)	
Interpolar	4 (17.4)	2 (8.7)	
Tumor type			
Exophytic	19 (82.6)	5 (51.7)	0.013
Endophytic	4 (17.4)	13 (78.3)	
Hydronephrosis			
Yes	1 (4.3)	2 (8.6)	0.187
No	22 (95.7)	21 (91.3)	
Enhancement			
Yes	23 (100.0)	21 (91.3)	0.489
No	0 (0.0)	2 (8.7)	

Independent' t' test and Chi-square test was done to measure the level of significance

Tumor size of kidney of the patients shows (Table III), mean (±SD) tumor size in group-A 4.28 (±0.91), cm, range 2.6-6.30 cm and in group-B 5.08 (± 0.89) cm, range 2.9-6.9cm (Table V). Most

of the renal tumors are exophytic 19 (82.6%) and rest of the tumors are endophytic 4 (17.4%) In Group-A (Table III), and in group-B, 5(21.7%) of renal tumors are exophytic and 18 (78.3%) are endophytic (Table V). There are statistically significant differences in tumor size and in tumor type between two groups (p= 0.004, 0.013 respectively). In group-A, renal tumors are located in 9 (39.1%) of the patients in the upper pole, 10 (43.5%) in lower pole and 4 (17.4%) in the interpolar (Table III), in group-B, tumors located in 12 (52.2%) of the patients in the upper pole, 9 (39.1%) in the lower pole and 2 (8.7%) in the interpolar (table-III). In majority of the patients had no hydronephrosis in the kidney a diagnosis which are group-A 22 (95.7%) group-B 21 (91.3%) and minorities of the patients have hydronephrosis (Table III) in group-A all the tumors have contrast enhancement and in group-B 21 (91.3%) had contrast enhancement and 2 (8.7%) had no contrast enhancement (Table III). There are no statistically significant differences in tumor location, hydronephrosis and in tumor contrast enhancement between two groups (p= 0.563., 0.187, 0.489 respectively, Table III).

Table 4: Serum creatinine status before and time depended changes after operation (at different follow up) in both groups (n= 46).

Serum creatnine	Group-A	Group-B	P-Value
	(Nephron-Sparing Surgery) (n= 23)	(Radical Nephretomy) (n= 23)	
Before operation	1.02 ± 0.24	1.07 ± 0.22	0.432
After Operation			
At 1st POD	1.23 ± 0.28	1.34 ± 0.35	0.236
At 3rd POD	1.17 ± 0.25	1.32 ± 0.29	0.067
At 7th POD	1.16 ± 0.19	1.29 ± 0.29	0.087
After 3 months of POD	1.11 ± 0.23	1.35 ± 0.27	0.002
After 6 months of POD	1.14 ± 0.17	1.33 ± 0.21	0.225
After 9 months of POD	1.13 ± 0.16	1.37 ± 0.20	<0.001
After 12 months of POD	1.13 ± 0.16	1.38 ± 0.18	<0.001
Serum creatinine changes (before op *vs* after 12 months of POD)	0.11 ± 0.08	.31 ± 0.04	<0.001
p-value (before op *vs* after 12 months of pOD)	0.002	0.003	

Independent ' t' test was done between groups and dependent' t' test was done within group to measure the level of significance.

During evaluation of patient's serum creatinine status before operation shows (table-IV), mean (±SD) serum creatinine in group-A 1.02 ± 0.24 mg/dl and in group-B 1.07 ± 0.22 mg/dl (Table IV) but there is no significant difference preoperatively (p= 0.432). After operation, time depended changes of serum creatinine status of the patients at 1st, 3rd and 7th POD in group-A, 1.23 ± 0.28, 1.17 ± 0.25, 1.16 ± 0.19 mg/dl and in group-B, 1.34 ± 0.35, 1.32 ± 0.29, 1.29 ± 0.29 mg/dl respectively (table-IV) but there are no significant differences in serum creatinine status at 1st, 3rd and 7th POD between two groups (p= 0.236, 0.067, 0.087 respectively; Table IV)). At 3, 6, 9 and 12 months follow up period after operation, time depended mean (±SD) serum creatinine status changes in group-A, 1.11 ± 0.23, 1.14±0.17, 1.13 ± 0.16 mg/dl and in group-B, 1.35 ± 0.27, 1.33 ± 0.21, 1.37 ± 0.20, 1.38 ± 0.18 mg/dl respectively (table-IV) but statistically significant differences present in serum creatinine status in 3,6,9 and 12 months POD between significant differences present in serum creatinine status in 3, 6, 9 and 12 months POD between significant differences present in serum creatinine status in 3,6,9 and 12 months POD between two groups p= 0.002, 0.002, <0.001, <0.001 respectively, (Table IV). The mean (± SD) serum-creatinine status changes from preoperative to 12 months after operation in group-A, 0.11 ± 0.08 mg/dl and in group-B 0.31 ± 0.04 mg/dl which shows statistically significant differences is serum creatinine status between and within the groups (p<0.001, 0.002, 0.003 respectively, Table IV).

Table 5: eGFR status before and time depended changes after operation (at different follow up) in both groups (n=46).

eGFR	Group-A	Group-B	P-Value
	(Nephron-Sparing Surgery) (n= 23)	(Radical Nephretomy) (n= 23)	
Before operation	7.22 ± 14.48	73.17±17.74	0.671
After operation			
At 1st POD	64.39 ± 16.05	57.78 ± 11.50	0.116
At 3rd POD	67.52 ± 15.24	57.43 ± 10.23	0.012
At 7th POD	67.96 ± 13.66	60.13 ± 13.08	0.053
After 3 months of POD	69.65 ± 14.81	56.61 ± 11.58	0.002
After 6 months of POD	68.39 ± 13.61	55.91 ± 9.49	0.001
After 9 months of POD	68.52 ±12.52	54.83 ± 10.44	<0.001
After 12 months of POD	68.91 ± 12.86	54.61 ±10.86	<0.001
Decrease in eGFR (ml/min)	6.31 ± 1.62	18.56 ± 6.88	<0.001
p-value (before op *vs* after 12 Months of POD	<0.001	0.001	<0.001

Independent' t test was done between groups and dependent' t' test was done within group to measure the level of significance.

During evaluation of patient's eGFR status before operation shows (Table V) mean (±SD) eGFR in group-A, 75.22 ± 14.48 ml/min and in group-B, 73.17 ± 17.74 ml/min (table-V) but there are no significant differences preoperatively (p=0.671). After operation, the time depended changes of eGFR status of the patients at 1st POD in group-A, 64.39±16.05 ml/min and in group-B, 57.78 ± 11.50 ml/min (Table V) but there are no significant differences in eGFR status at 1st POD between two groups (p=0.116, table-V). At 3rd, 7th POD and 3,6,9,12 months follow up period after operation, time depended mean (± SD) eGFR status changes in group-A, 67.52 ± 15.24, 67.96 ± 13.66, 69.65 ±14.81, 68.39 ± 13.61, 68.91 ± 12.86 ml/min and in group-B, 57.43 ± 10.23, 60.13 ± 13.08, 56.61 ± 11.58, 55.91 ± 9.49, 54.83 ± 10.44, 54.61 ± 10.86 ml/min respectively; Table V) but statistically significant differences present in eGFR status in 3rd, 7th POD and 3,6,9,12 moths follow up between two groups (`p' value in 3rd, 7th, 3,6,9 and 12 months POD= 0.012, 0.053, 0.002, 0.001, <0.001 respectively; table-V). The mean (±SD) eGFR status decreased from preoperative to 12 months after operation in group-A 6.31±1.62 ml/min and in group-B 18.56±6.88 ml/min which shows statistically significant differences in eGFR status from pre-operative to 12 months follow up between and within

the groups (p<0.001, <0.001, 0.001 respectively; Table V).

Discussion

With evolution of imaging modalities (USG, CT/MRI), small and asymptomatic RCC is early diagnosed and the fucnitnal and oncological outcome of NSS have incresed. Currently, therer is contorversy regarding the clinical efficacy of NSS and RN in reating localized RCC. According to EAU gudileine (2014), nephron sparing surgery is the first treatment option for cTla tumor (<4 cm) and a viable option for cTlb lesion (>4cm) when technically feasible [21]. In this prospective study, preoperative and postoperative time dependent changes of renal function up to 12 months after NSS (Group-A) and RN (Group-B) are assessed by measuring eGFR using MDRD formula as renal function tends to be overestimated by using seru creatinine which is affected by several factors affecting creatinine generation. Is this study, the risk factors for the development of new onset of CKD (eGDFR<60 ml/min) after operation are observed but univaritate or multivariate logistic regression analysis to predict association with renal function is not done. With regard to patient baseline characteristics (age, sex, BMI) in the current study, no significant differences (p= 0.760, 0.573, 0.714 respectgively) are noted that can affect renal function, An interesting finding is that the age ranges in gorup-A, (35-65) years and in group B, (35-74) yeasrs but classically renal tumors occur in sixth and seventh decades of Life. The early occurrence of tumors in the current study perhaps due to easier access or exposure to carcinogen ()smoking, industrial chemicals) and more rapid diagnostic and therapeutic methods available currently; additionally, many patients are diagnostic and therapeutic methods available currently; adddditionally, many patients are diagnosed indidentally during medical evaluation for other symptoms [22]. Although compensatory hypertrophy occurs in ll age groups after nephrectomy due to increased renal plasma flow and more pronounce in <30 years of age, effective renal plasma flow is known to decrease with patient age resulting in decreased compensatory hypertrophy with increased age and progressive deterioration of renal function. Most of the patients in both groups are male (NSS= 60.9%, RN= 65.2%) that indicates renal cell carcinoma is more prevalence in male and similar result (NSS= 67.5%, RN+66%) was also reported by scosyrev et al. [23]. The male predominance in our country may be due to presence of inccreased ris factors n male (cigarette smoking, job profession in various chemical industries and exposure to toxins). Male patients had a significantly greater increase in effective renal plasma flow as well creatnine clearance than female patients at 1 week (p<0.005) and at I year (p<0.0001) after nephrectomy due to more compensatory hypertrophy than female [24]. In case of BMI, obese patients (>30kg/m^2) are excluded from this tudy and the result is slightly differ (average 21 *vs* 23 kg/m^2) from study noted by Miyamotot er al. [6], because majority of study population are low income group and most of them are note overweight. In pre and postoperative sympthoms & sign (flank pain, hematuria, diabetes, hypertension , post-operative fever) of the patients in both groups have no significant differences (p= 0.502, 0.502 0.730, 1.00 1.00 respectively) and do not influence renal fucniton, Diffecent results were observed by Ptel et al. [35], in which flank pain 48% in Ochsner clinic and 50% in UCLA hospital that were lower than present study (in group-A 78.3%, group-B 69.6% respectively) because they are mroe diagnosed incidentally and may get immediate management for pain. Though heamtuira is the late presentation but within this study. heamturia is higher in group-B than group-A (21.7% *vs.* 30.4%) because most of the tumors are larger and endophytic in group-B which may invlolve the PCS and may causes hematuria 35% in St. Luke's Hospital, 40% n Ochsner clinic and in Mayo clinic 32%. Minorities of the patients in this study have hypertension and diabetes that are well controlled preoperatively, introoperatively and postoeratively up to follow up period by measuring regular blood pressure with getting anti-hypertensive drugs, measuring blood sugar level with giving short acting insulin, oral hypoglycemic agents and adive is given to control hypertension was reported 44% in NSS, 60.8% in RN by Liss et al. [25], compared to 43.5% in both groups of current study due to their sedentary life styles and consumption of lipid rich food. Serveral conflicing studies examined the long-term effects for renal donation on the contraleteral kidney. Anderson et al. [10], noted that renal donors might be at slightly increased risk for the development of heypertension decondary to chronic hyperfiltariton after unlilateral nephrectomy. Miller et al. [26], reported that 31% of the patients develop hypertension after donor nephrectomy but has no significant impact on renal function (p<0.05). In baseline tumor characteristicsk, eman tumor size differs according to type of surgery in which lagger tumor in group - (5.8 cm) than group-A (4.28cm) which influence the renal function in the present study (p= 0.004) because larger tumor reduce more functional renal parenchyma. Leivovich et al. [21], reported that 4 cm or smaller RCC showed better quality of life and less renal impairment for NSS than for RN. Comparable result is observed from the study by Simon et al. [27], which reported that mean tumors size in NSS was 3.63 cm and in RN 5.54 cm and there was statistically significant difference (p<0.001). Different results were also observed in several studies due to large sample size and early incidental diagnosis of tumors in which mean (SD) tumor type () central *vs* peripheral) had no impact no renal function (serum creatinine 1.43 mg/dl in both groups) although NSS in technically more difficult in centrally located lesions leading to longer ischemia times and increased incidence of collecting system injuries. Other tumor characteristics (tumor location, contrast enhancement, hydronphrosis) have been examined for their association with outcomes in patients with RCC but there are no statistically significant differences (p<0.05). In group-A, lower polar tumors are more (43.5%) and in group-B, upper polar tumors are more (52.2%) There is minimal difference in the current study from another study by Patel et al. [28], which showed that tumors were located 34% in upper pole, 34% in the lower pole and 9% in the mid portion, In general, it is accepted that renal tumor enchancement of >15 Hounsfield unties (HU) in CT is suggestive of a malignancy [29]. The CT enhances have shown a significant association with histological subtypes of renal cell cancer in which heterogeneous enhancement pattern is seen in clear-cell RCC compared with chromophobe and papillary RCCs [30]. In this study, all the tumors in group-A and 91.3% tumors in gorup-B have contrast enhancement and rest of the tumors have USG features of RCC but statistically no significant difference is present (p= 0.489). In majority of the patients had no hydronephrosis in the kidney during diagnoses which are 95.7% in group-A and 91.3% in group-B. No study was reported relating to contrast enhancement, hydronephrosis and renal function. In preoperative period, mean serum creatinine status in lower in gorup-A than in group-B (1.02 *vs* 1.07 mg/dl; table-IV) and have no significant difference (p= 0.4320). Different mean serum creatinine results (NSS= 0.83 mg/dl, RN= 1.7 mg/dl; p<0.001) in the study by krebs et al. [31], were seen due to large sample size. The lower serum creatinine level in the current study may be due to more functioning renal parenchyma and small tumor size in affected kidney of group-A than group-B.

After operation, time-dependent changes of serum creatinine status of the patients at 1st, 3rd and 7th POD are less pronouced in gorup-A than group-B (figure-I) and have no significant differences in both groups (p>0.05) but At 3,6,9 and 12 months, the changes remain stable up to 12 months in group-A but increases gradually in gorup-B (figure-I) and have no significant differences in both groups (p>0.002). Similar result was documented by Miyamoto et al. [6], in post-operative serum creatinine level between two groups (Nss= 96 mg/dl, RN= 1.24 mg/dl; p<0.001). From preoperative to 12 Months after operation, mean creatinine status changes is less in group-A (.11 mg/dl) than in group-B (.31 iomg*/dl) and hvae statisically significant differences in between and within the groups (p= 0.002, 0.003 respectively). Comparable result found by Clark et al. [32], in a Prospective study in which creatinine clearance dropped more RN (0.56 ml/min, 31.6%) than NSS (0.09 ml/min, 6.1%) and p<0.001. Hakim and Ringden et al. [33], documented that the removal of one kidney from a patient with two normally functioning kidneys results in functional adapatation and compensatory hypertrophy of the remaining kidney. Creatinine clearance increases to 70 to 75% of the preoperative creatinine clearance within several weeeks post operatively. Serveral studies have followed patineets for more than 10 oyears after door nephrectomy and found than cratinine clearance remined stable. In preoperative period, mean eGFR is more in group-A (75.22 ml/min) than in group-B (73.17 ml/min) due to small tumor size and more functioning renal parenchyma and have no significant difference (p>0.671.) Similar eGFR results were observed in the studies (71.4 *vs* 71.3 ml/min, p>0.05) by Miyanmoto et al. (2012) and (80.2 *vs*. 78.2 *vs.* 78.2 ml/min; P>0.05) by pignot et al (2014 The time depended changes mean eGFR status at 1st POD is not significant (P= 0.116) but at 3rd, 7th POD and 3,6,9,12 months, it becomes signficant in both groups (P<0.001)) because of more residual functioning renal parenchyma present after NSS. Comparable result are noted by Mariusdottir et al. [4], in which significant differences was observed postoperatively and after 60 months (56 *vs.* 44 ml/min, p< 0.001; 59 *vs.* 45 ml/min; p<0.001). The mean eGFR decreased more significantly in gorup-B (18.56 ml/min) than group-A (6.31 ml/min) from preoperative to 12 months after operation and have significant difference (p<0.001; Table V). The current results differ from the study by miyamoto et al. [6], in which eGFR decrease by 9.27 ml/min in NSS and 25.1 ml/min (p<0.0002) in RN due to large tumor size is NSS and large smaple size (152 patients). The time-dependent changes of eGFR after RN show plateau from initially and then gradually declining form the first postoperative day to the 12 postoperative months. In case of NSS, a lowest eGFR is observing in postoperative day 1 and gradually recovered to near preoperative level for 12 months (Anderson et al. [24], reported that compensatory hypertrophy was completed I week after donor nephrectomy and Tanaka et al. [34], reported 2 to 4 weeks after RN. Krebs et al. [31], reported that eGFR in NSS patients were higher than RN in postoperatively. The compensatory hypertrophy after donor nepherectomy has previously been believed to be beneficial but compensatory hyperfiltration due to arterial vasodilatation with increased flow and eventually proteinuria, azotemia and hypertension but does not lead to long term decrease in renal function [24]. At the end of diccussion, the present study suggested than although compensatory hypertrophy occurs in the early postoperative day in RN than NS, renal functional outcome is more stable in NSS than RN due to functioning residual renal parenchyma.

Conclusion

Time dependent changes of estimated Glomerular Filtration Rate (eGFR) after partial nephrectomy is better than Radical Nephrectomy (RN) for Renal Cell Carcinoma (RCC) in 12 months follow up period. PN has minimal impact on post-operative renal function measured by eGFR whereas RN is associated with significantly greater renal function decline. PN is therefore the better procedure for preservation of renal function.

Limitations of the study

1. Small sample size
2. Lack of longer follow up (only 12 months)
3. Surgery is performed by multiples surgeons.
4. Associated risk factors are not evaluated by logistic regression analysis.
5. Patients with renal failure (eGFR<30ml/min), obese patients and pregnant women are not included in the present study.

Recommendations

Observing time depended changes of eGFR of the present study. It can be said that partial nephrectomy has preserved renal function more than radical nephrectomy. With this view in mind following recommendation are put for consideration of future researchers as well as relevant authority.

1. Regular practice of partial nephrectomy in patients with localized RCC in our country.
2. Large sample size should be taken for further study.
3. Longer follow up should be given.
4. Intervention should be done by single surgeon.
5. Meta-analysis for further evaluation of renal function.

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