

Open partial nephrectomy for T1a-b solid renal masses: A developing country perspective

Harris H. Qureshi, Gohar Sultan, Rehan Mohsin, Asad Shehzad, Muhammed Mubarak, Syed Anwer Naqvi, Syed Adeeb ul Hassan Rizvi, Altaf Hashmi

Abstract:

Background: Partial nephrectomy (PN) is a viable treatment option for patients with T1a-b solid renal masses. We herein aim to describe our experience on the use of open partial nephrectomy (OPN) and its outcome.

Material and Methods: All patients who underwent open partial nephrectomy at Sindh Institute of Urology and Transplantation (SIUT), between January 2009 and December 2015 were included in this study. Data items were collected and analyzed.

Results: A total of 55 OPN procedures were undertaken on 55 patients between 2009 and 2015. The mean age of patients was 48.9 ± 11.7 years with majority of males (65.5%). The mean maximum tumor dimension was 4.3 ± 0.8 cm. The mean operation time was 139 ± 29.7 min. Warm ischemia time was 13.19 ± 5.3 min. The median R.E.N.A.L ((R)adius (size at the maximal diameter), (E)xophytic/ endophytic properties, (N)earness of tumour to the collecting system or sinus, (A)nterior/posterior descriptor, and (L)ocation relative to polar lines) and P.A.D.U.A. (pre-operative aspects and dimensions used for an anatomical) scores were 8 (IQR:7 - 8) and 5 (IQR: 4.5 - 7), respectively. The mean pre- and post-operative creatinine levels were 7.3 mmol/L and 7.4 mmol/L. Estimated blood loss was 217 ± 143 ml. No intra-operative and post-operative complications were documented. The mean length of stay was 4 days. The majority of patients showed clear cell carcinoma (80%), followed by papillary tumors (12.8 %) and one oncocytoma. There were no positive oncological surgical margins. Patients were followed up for a median of 40 months. There were no recurrences.

Conclusion: In conclusion, open partial nephrectomy is a safe and effective method of treatment for localized solid renal tumors of less than 7cm with contralateral normal kidney.

Keywords: Partial nephrectomy, radical nephrectomy, renal masses, clear cell carcinoma, papillary tumors.

Introduction:

Renal cell carcinomas (RCCs) account for about 85% of solid renal masses. With widespread use of imaging facilities for non-specific abdominal complains, RCCs are being detected at early stage and smaller size which leads to excellent oncological outcomes.¹ Due to earlier detection, their incidence has risen to more than 2% per year.²

Radical nephrectomy (RN) was initially performed for the treatment of small renal masses

(SRMs) but was associated with deterioration of chronic kidney disease (CKD), cardiovascular morbidity and decreased patient survival. Previously, partial nephrectomy (PN) was only considered in patients with renal tumor in solitary kidney, tumors in both kidneys or in patients with CKD. With increased understanding that most of these masses are indolent and have similar oncological outcomes irrespective of radical nephrectomy or partial nephrectomy, led to partial nephrectomy becoming a recommended treatment option for patients with SRMs.³

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Sindh Institute of Urology and Transplantation (SIUT), Karachi.

HH Qureshi

G Sultan

R Mohsin

A Shehzad

M Mubarak

SA Naqvi

SAH Rizvi

A Hashmi

Correspondence:

Prof Muhammed

Mubarak, Department of

Histopathology, Sindh

Institute of Urology and

Transplantation (SIUT),

Karachi.

Cell: (009221) 99215752

Email: drmubaraksiut@

yahoo.com

Although open partial nephrectomy (OPN) is commonly performed worldwide, it is still not widely performed in our country. Even no published data is available from Pakistan. We aim to share our institutional experience on OPN.

Materials and Methods:

All patients who underwent PN at Sindh Institute of Urology and Transplantation (SIUT), Karachi, Pakistan between January 2009 and December 2015 were included in this study. The study was conducted in accordance with ethical principles as laid down in the Declaration of Helsinki. Written informed consent was obtained from all patients prior to the surgical procedure. Data were collected prospectively and entered into predesigned proforma.

Patients' demographics and clinical characteristics like age, gender and presence of co-morbidities, were recorded. Serum creatinine and estimated glomerular filtration rate (eGFR) were recorded on the day of operation and one day post-operatively. The eGFR was calculated using the modification of diet in renal disease (MDRD) formula.⁴ Abdominal triphasic computed tomography (CT) was performed to evaluate details about tumor location, depth, and proximity to collecting system and sinuses. CT scan was also used to assess renal arterial and venous anatomy.

Pre-operatively, radiologic tumor characteristics were scored by a senior radiologist and consultant urologist using R.E.N.A.L. (radius, exophytic/endophytic, nearness, anterior/posterior, location) Nephrometry score and pre-operative aspects and dimensions used for anatomic (P.A.D.U.A.) classification.¹ The total operative time, estimated blood loss (EBL), warm-ischemia time (WIT) and adverse events were recorded in each patient. Urine leak was defined as continued Jackson-Pratt drain output for 1 week with a creatinine level of drainage more than twice that of serum creatinine.⁵

Surgical procedures: All patients received intercostal incision above the 12th rib ranging from 7 to 11 cm. The latissimus dorsi, external oblique and internal oblique muscles were transected

and the transverses abdominis was divided, while preserving the intercostal neurovascular bundle. The transverses abdominis and transversalis fascia near the distal tip of the 12th rib were divided and pleura was displaced away with the finger by blunt dissection. Then, the retroperitoneal fat, Gerota's fascia and the perinephric fat were incised to expose the kidney and the tumor. Then, renal artery was identified and isolated with blunt dissection followed by clamping with bulldog clamp. Afterwards, the renal tumor was sharply incised, leaving 1-2 cm of grossly normal parenchyma around the tumor with forceps clamping. After resection, the remaining normal renal parenchyma (around 2-3 mm strip) was shave-excised from areas with suspicious gross residual tumor and sent to histopathologist as frozen section for presence of tumor in estimated time of 10-15 min. If frozen section was found positive for tumor, the operation was converted into radical nephrectomy.

All transected blood vessels on the renal incised surface were sutured with 3-0 Vicryl sutures, the collecting system was continuously closed with 4-0 Vicryl sutures and renal parenchyma was closed by 2-0 Vicryl sutures. The bulldog clamps were then removed.

Statistical analysis: Statistical analyses were performed with SPSS software (SPSS, version 20.0, IBM Corporation, Armonk, NY, USA). Results are presented as means±standard deviation (SD) for quantitative data or as numbers with percentages for qualitative data. Statistical differences in quantitative data were determined using t test or Mann-Whitney U test. The Fisher exact test or chi-square test was used for qualitative data. $P < 0.05$ was considered statistically significant.

Results:

A total of 55 open partial nephrectomy (OPN) (28 right, and 17 left) operations were undertaken between 2009 and 2015. Two patients' data was excluded from analysis, as they were converted into RN. Laproscopic or robotic partial nephrectomy was not available at our institution over the duration of this study. Majority of

Table-1: The main patient and tumor characteristics and oncological outcomes

Clinical characteristics	
Age, years; mean \pm SD (range)	48.9 \pm 11.7 (28 – 68)
Males. n (%)	35 (65.5)
BMI, kg/m ² mean \pm SD (range)	26.7 \pm 6.5 (13.9 – 35.9)
Presenting complains, n (%)	
Hematuria	31 (56.4)
Abdominal pain	12 (21.8)
Incidental finding	8 (14.5)
Mass	4 (7.3)
R.E.N.A.L Score, median (IQR)	8 (7 - 8)
P.A.D.U.A score, median (IQR)	5 (4.5 - 7)
Tumor characteristics	
Tumour size in cm, mean \pm SD (range)	4.3 \pm 0.89 (2.2 – 5.9)
Lateral location, n (%)	39 (71 %)
Medial location, n (%)	16 (29)
Exophytic, n (%)	53 (96.3)
Sinus invasion, n (%)	18 (32.7)
Collecting system, n (%)	20 (36.3)
Histopathology, n (%)	
Clear cell carcinoma	44 (80)
Papillary	7 (12.8)
Chromophobe	3 (5.4)
Oncocytoma	1 (1.8)
Surgical features	
Operation time min, mean \pm SD (range)	139 \pm 29.7 (90 -175)
Warm ischemia time, min mean \pm SD (range)	13.19 \pm 5.3 (range:6 - 25 min)
Estimated blood loss in ml, mean \pm SD (range)	217 \pm 143 ml (102 – 345 ml)

BMI :Body mass index, P.A.D.U.A :preoperative aspects and dimensions used for an anatomical, R.E.N.A.L: (R)adius (size at the maximal diameter), (E)xophytic/ endophytic properties, (N)earness of tumour to the collecting system or sinus, (A)nterior/posterior descriptor, and (L)ocation relative to polar lines.

patients presented with complains of haematuria, which was found in 31(56.4%) cases. Only 8 (14.5 %) patients were detected on imaging studies.

Patient demographics: The patient demographics are shown in Table-1. The study population had a mean age of 48.9 \pm 11.7 years (range: 28 – 68 years) with the majority of patients being males (65.5%). The mean body mass index (BMI) was 26.7 \pm 6.5 kg/m² (range: 13.9 – 35.9).

Tumor characteristics and surgical outcomes: We only included single solid renal tumors with a mean tumour size of 4.3 \pm 0.89 cm (range: 2.2 – 5.9 cm). Clinical TNM staging showed 26(47.2%) tumors to be T1a and 29(52.8 %)

T1b. The mean operation time was 139 \pm 29.7 min (range:90 -175 min). Warm ischemia was used in all patients and the mean ischemia time was 13.19 \pm 5.3 min (range:6 - 25 min). The median R.E.N.A.L and P.A.D.U.A. scores were 8 (IQR:7 - 8) and 5 (IQR:4.5 - 7), respectively.

Majority of tumors were located laterally (71%) and exophytic (96.3 %). Sinus invasion was observed in 32.7% while collecting system was involved in 36.3 % of the study population.

The average pre-and post-operative creatinine levels were nearly similar (7.37 mmol/L and 7.40 mmol/L). Estimated blood loss was 217 \pm 143 ml (range:102 – 345 ml), and no patient required blood transfusion. No intra-operative and post-operative complications were documented. The mean length of stay was 4 days

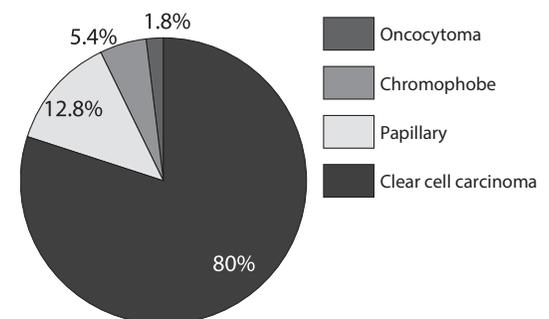


Figure-1: Histopathology

(range:3 – 8 days).

The oncological outcomes are summarized in Table 1. The majority of patients on histological analysis showed clear cell carcinoma 44(80%), followed by papillary tumours 7(12.8%), Chromophobe tumor 3(5.4%) and 1(1.8%) oncocytoma. The intra-operative frozen section analysis of normal renal parenchyma was found positive in two patients. There were no positive oncological surgical margins. No patient in the study had nodal or metastatic disease. Patients were followed up for a median of 40 months (range:4 – 61 months). There have been no recurrences to date, but one patient was lost to follow-up.

Discussion:

Globally, there is a gradual rise in utilization of partial nephrectomy for the treatment of kidney tumors due to benefit of renal function preservation.^{1,3,5} Keeping in view the associated morbidity and mortality of radical nephrectomy, American Urology Association (AUA) guideline committee has recommended partial nephrectomy as preferred treatment option for T1 renal masses, whenever technically possible.^{6,7} Similarly, European Association of Urology (EAU) guidelines also advocate partial nephrectomy over radical nephrectomy, whenever feasible.⁸ According to recent prospective randomized control trials, both procedures have excellent oncological outcomes.⁹⁻¹¹

Due to widespread availability of imaging facilities and use for non-specific symptoms, there has been increased detection of asymptomatic small renal tumors.^{3,12,13} The incidental diagnosis of renal tumor in our study was seen in only 14.5% patients, in contrast to about 70% in the west.³ Our study population belongs to developing country where easy accessibility to resources is not available, which can be the factor for discrepancy in results.

Partial nephrectomy is a favorable treatment option for young and healthy patients with renal cell carcinoma (RCC). Mean age in our study population is comparable to other studies conducted in Pakistan and South Koreans with male predominance.^{14,15} Studies conducted in western population showed that RCC was predominant in older patients.^{13,14,16} Our study also demonstrated clear cell carcinoma as a predominant type of RCC, similar to other studies.¹⁵

Flank incision is preferred for open partial nephrectomy, not only because it is safe but also provides excellent kidney exposure.¹⁷ Wang et al,⁵ recently demonstrated successful partial nephrectomy with supra 12 mini flank incision with shorter ischemia time and minimal blood loss. No tumor recurrence, metastasis, or deterioration in renal function was observed in mean follow up of 19 months by the author. Larger incision in traditional open partial nephrectomy

is associated with prolonged admission stay and mostly flank bulge.¹⁴ We also utilized small incision which may be contributing factor in shorter hospital stay and no flank bulge.

To minimize the risk of intraoperative bleed, renal artery clamping and renal cooling is utilized during renal tumor resection.¹ Studies has demonstrated that this has no impact on post-operative kidney function.^{18,19} A retrospective series in patients with solitary kidney demonstrated that severe chronic renal insufficiency occurs more in patients with warm and cold ischemia as compared to patients in whom no renal artery clamping was performed.²⁰ In our study, mean WIT was 13.19 ± 5.3 min and none of our patients underwent renal deterioration in mean follow up of 24 months. This may be because all our patients had normal contralateral kidney.

It has been suggested in studies that few millimeters of resection margin is adequate for partial nephrectomy to avoid tumor recurrence, provided that the biopsy of renal bed intraoperatively is tumor free.²¹⁻²³ In our study population, frozen section of renal parenchyma was performed in all patients and 1cm of tumor-free margin was utilized as part of institutional policy. In two cases, frozen sections showed presence of tumor which were treated with RN. Although, studies have demonstrated equivalent tumor recurrence with positive or negative surgical margins,^{24,25} we followed during this study period our institutional protocol and converted partial nephrectomy to RN procedure. Even, simple enucleation has been found to have equivalent oncological outcomes as compared to standard partial nephrectomy.²⁶

Studies have demonstrated equal cancer outcome of RN and partial nephrectomy for renal tumors ≤ 7 cm.³ Lerner et al.²⁷ documented a 95% 5-year tumor free survival in partial nephrectomy patients with tumors < 3 cm but 80% with tumors > 6 cm. Ramany et al.²⁸ demonstrated that patients with tumour size of < 4 cm and tumor size of 4 to 7 cm have comparable 5-year tumor free survival.

Due to minimal invasion, laparoscopic partial nephrectomy (LPN) is becoming an alternative to open partial nephrectomy but not only it is a complex procedure and specialized training is required but also its associated with 18 to 28% complications, even in highly experienced medical centers.^{29,30} partial nephrectomy related major complications includes; bleeding, urinary fistula and infection. Memorial Sloan Kettering Cancer Center (MSKCC) investigators demonstrated that operative time and solitary kidney were significant factor associated with operation related complications of partial nephrectomy.³¹ In a larger study of 1118 partial nephrectomy patients, urinary leaks were reported in only 0.4% patients. Authors observed that large tumor, more blood loss and longer ischemia time was associated with urine leaks.³² A multi-center study also demonstrated that with higher R.E.N.A.L score there is increasing odds of urine leak in patient with partial nephrectomy.³³

It has been observed that formation of urinary fistula post-partial nephrectomy ranges from 1.8 to 21% but it is lower with small, asymptomatic tumors.²³ Campbell et al.³³ reported a 13% acute renal failure in patients with open partial nephrectomy. In which, 3.9% were operated for elective indication. Factors that were found associated with post operative acute renal failure were tumor size more than 7cm, more than 50 % excision of renal tissue and ischemia time of more than 60 min. In our study, the mean operation time was 139 ± 29.7 min and the mean ischemia time was 13.19 ± 5.3 min. None of our patient required blood transfusion with estimated intraoperative blood loss 217 ± 143 ml. All of the above mentioned factors may be the reason for no intraoperative and post-operative complications in our study population.

In order to standardize reporting of renal tumors, three renal tumour scoring systems have been proposed: R.E.N.A.L., the pre-operative aspects and dimensions used for an anatomical (P.A.D.U.A) classification and C index indicating either a smaller tumour and/or a tumour more distant from the centre of the kidney. In various studies, these scoring system has been

utilized in PN and has not only guided in surgical decision making i.e., RN vs. partial nephrectomy but also suggested to predict post-operative complications and renal functional outcomes. The correlation of RENAL score with tumor grade and histology has also been demonstrated, suggesting that with the increase of tumor size there would be greater probability of high grade and clear cell histology.³⁴ Lavallée et al.³⁵ speculated that less ischemia time shall be required in less complex tumors. The author demonstrated that increase in score of P.A.D.U.A, R.E.N.A.L and C-index was associated with more ischemia time.

The median score of R.E.N.A.L and P.A.U.D.A in our study was 8 and 5, respectively. A low score was observed in our study, with consequent low complications and low ischemia time as compared to other studies.

This is first study conducted in Pakistani population who underwent open partial nephrectomy with mean follow up of 40 months and its results are consistent with western studies. We did not collect post-operative pain score and effect on creatinine months after operation but in mean follow-up of 24 months none of our patient required dialysis or renal transplantation. There are some other limitations in the study too. These include the wide margin of healthy parenchyma that was excised as per our policy. This was because this was our early experience and learning phase. Now, our practice complies with the latest standards in the field. The practice of frozen sections is also being used less and less and we are moving to less and less removal of healthy parenchyma. The high prevalence of haematuria in our patients for the size of tumors also needs further study. Despite the above limitations, we believe that this study is a significant contribution to the existing literature on this topic from a developing country.

Conclusion:

Open partial nephrectomy (OPN) is a safe and effective method of treatment for localized solid renal tumors of less than 7 cm with contralateral normal kidney. It is not only associated

with short hospital stay and operation time, and limited blood loss, but also with low rate of perioperative complications.

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Role and contribution of authors:

Dr Harris H. Qureshi, MBBS, FCPS, Assistant Professor, Urology Department, SIUT, conception, designing, collection, analysis of data and primary drafting of the paper.

Dr Gohar Sultan, MBBS, FCPS, Professor, Urology Department, SIUT, conception, designing, collection, analysis of data and primary drafting of the paper.

Dr Rehan Mohsin, MBBS, FCPS, Professor, Urology Department, SIUT, acquisition of data, and critical review of the paper

Dr Asad Shehzad, MBBS, FCPS, Professor, Urology Department, SIUT, acquisition of data, and critical review of the paper

Dr Muhammed Mubarak, MBBS, DCP (London), MCPS, FCPS, Professor, Pathology Department, SIUT, conception, designing, collection, analysis of data and primary drafting of the paper

Dr Altaf Hashmi, MBBS, MS, Professor, Urology Department, SIUT, critical review and final approval of the manuscript

Dr Syed Anwer Naqvi, MBBS, MS, FCPS, Professor, Urology Department, SIUT, critical review and final approval of the manuscript

Dr Syed Adeebul Hassan Rizvi, MBBS, FCPS, FRCS, Professor, Urology Department, SIUT, critical review and final approval of the manuscript

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