



Comparison of Off-Clamp and On-Clamp Partial Nephrectomy and Its Impact on the Renal Functional Outcome: A Single Institute Experience in South Indian Patients

Sivakumar Mahalingam¹, Anand Raja^{2*}, Kathiresan Narayanaswamy³, Krishna Kumar Rathinam⁴

¹Department of Surgical Oncology, Cancer Institute (WIA), Adyar, Chennai, India

³Cancer Institute (WIA), Dr. S.Krishnamurthy Campus, Apollo Speciality Hospitals, Chennai, India

⁴Department of Nuclear medicine, Cancer Institute (WIA), Adyar, Chennai, India

Abstract

Introduction: Partial nephrectomy (PN) or nephron sparing surgery is the standard of care for all feasible renal tumors < 4cm. Multiple partial nephrectomy techniques have evolved to reduce the ischemic injury to the renal parenchyma with variable effects on renal function. Off clamp technique avoid ischemic injury to the renal parenchymal altogether and better preserves the long term renal function, delaying or avoiding the development of chronic kidney disease. The aim of the study is to compare off-clamp and on-clamp techniques of partial nephrectomy and its impact on the renal functional outcome.

Methods: Patient who underwent partial nephrectomy from January 2007 to December 2016 were analyzed retrospectively. The partial nephrectomy renal units were grouped into off-clamp and on-clamp (warm and cold ischemia) group. The demographic data, clinico-pathological factors, pre-operative and post-operative glomerular filtration rate (GFR) as measured by radioisotope renography Tc99m-DTPA (diethylenetriaminepentacetate) scan, surgical margin, complications (Clavien Dindo classification), hospital stay, blood loss and blood transfusion rate were compared and analyzed between the two group.

Results: Twenty three eligible renal units who underwent partial nephrectomy between January 2007 and December 2016 were included for analysis. The mean age was 46 years. One was a pediatric patient with bilateral wilms tumor aged 2 years and he underwent staged bilateral partial nephrectomy. Majority had clear cell histology 78% (18/23), papillary histology 13% (3/23) and two wilms tumor. All had open partial nephrectomy except two had laparoscopic assisted procedure. Ten (43%) underwent on-clamp technique out of which one had warm ischemic and nine had cold ischemic clamping technique. The mean clamping time was 35 minutes for the available six renal units in the on-clamp group. Thirteen (57%) patients underwent off-clamp technique. There is no difference in the age, sex, tumor site, size, grade, margins, histology type, overall complications, blood loss, blood transfusion and hospital stay among the two groups. All surgical margins were negative in both groups. The preoperative mean GFR (Tc99m-DTPA scan) was comparable 70.13 and 67.78 ml/min/1.73m² (p=0.765) between the on-clamp and off-clamp group. The percentage GFR decrease in the postoperative period (>3 months) was 0.28 % in the off-clamp group compared to 8 % in the on-clamp group.

Conclusion: Off-clamp partial nephrectomy is a feasible and oncologically safe technique. It is a promising technique which avoids the ischemic renal parenchymal injury after partial nephrectomy. The renal functional outcome is better with off-clamp technique compared to on-clamp partial nephrectomy. The limitation is the non-availability of standardization of techniques and prospective randomized trials.

Keywords: Nephrectomy; Chronic kidney disease; Glomerular filtration rate; Radioisotope renography

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*Correspondence:

Anand Raja, Cancer Institute (WIA),
Dr. S.Krishnamurthy Campus, No.18,
Sardar Patel Road, Guindy, India,
Tel:+91-44-22209150;

E-mail: dr_anand@yahoo.com

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Introduction

Partial nephrectomy is the standard of care for all feasible renal tumors < 4cm with proven long term outcomes [1]. Pedicle clamping technique is done to ensure blood-less surgical field and ease the resection. Prolonged renal ischemia time is associated with high risk of adverse renal function outcomes even after partial nephrectomy [2-4]. To reduce or avoid the ischemia time and maximize the functional outcomes various techniques are being practiced [5]. No guidelines or recommendations are available on the optimal technique to maximize the renal functional outcomes. The data on long-term renal functional outcomes after partial nephrectomy or comparison between off-clamp and on-clamp partial nephrectomy is not available from India.

Methods

Between January 2007 and December 2016, the case records of all patients who underwent partial nephrectomy were taken up for the study. Patient who underwent partial nephrectomy and final histopathology report with malignancy was included for the study. Patient who had benign histology were excluded from the study.

Study design: Retrospective observation study

Statistical method: Frequency tables describe the clinico-pathological factors and outcomes. The student t-test and Pearson Chi-square test compares the clinico-pathological variables, short-term outcomes and preoperative renal functional (Tc99m-DTPA scan) between the off-clamp and on-clamp partial nephrectomy group. Overall survival outcome was calculated by Kaplan meier test.

Preoperative evaluation: Hemogram, renal function test- GFR, creatinine clearance, blood urea and creatinine, liver function

test, coagulation profile, chest x ray, contrast enhanced computer tomography (CECT) abdomen and pelvis. The GFR measurement was performed using radioisotope renography Tc99m-DTPA scan. CT angiogram with renal vessel reconstruction was done based on the complexity of the lesion.

Surgical technique: Midline transperitoneal or retroperitoneal flank approach. Preoperative ureteric stenting was routinely used during the initial periods. But after 2014 ureteric stenting was selectively used for complex lesions located near the collecting system. Kidney was mobilized and renal vessels were separately dissected out. For on-clamp technique vascular clamps were applied to both vein and artery and unclamped once resection and renorrhaphy is completed. Sterile ice slush was packed all around the kidney in case of cold ischemia technique. The renal vessels are not clamped in off-clamp technique. Tumor is excised enbloc with the perinephric fat and gerota fascia covering the tumor with target margin of 5 mm to 10 mm. Renorrhaphy is done using 2-0 absorbable vicryl sutures and then renopexy completes the procedure.

Follow up: Follow up visits was done every three months for first 3 years, every six months for the 4th and 5th year and then annually thereafter. At each visit a detailed clinical history, physical examination and blood urea & creatinine was done. Tc99m-DTPA renal scan was done after 3 to 6 months. Annual investigation with chest x-ray, CECT abdomen & pelvis.

Results

A total of twenty five renal units underwent partial nephrectomy. Twenty three units met the inclusion criteria. Two were excluded because of benign histology. All had open partial nephrectomy except two who had laparoscopic assisted procedure. Ten (43%) underwent

Table 1: Clinico-pathological variables comparable between the two groups.

Variables	Off-clamp n=13	On-clamp n= 10	P value
Median Age (yr)	49 (2-65)	46.5 (16-68)	0.746
Sex			0.673
Male	8 (62%)	7 (70%)	
Female	5 (38%)	3 (30%)	
Comorbids (Diabetic and Hypertension)	-	-	0.74
Side			0.855
Right	7 (54%)	5 (50%)	
Left	6 (46%)	5 (50%)	
Site(Upper, mid, lower pole)	-	-	0.312
T1a (≤ 4cm)	9 (69%)	8 (80%)	0.286
T1b (4-7 cm)	3 (23%)	2 (20%)	
T3 (> 10 cm)	1 (8%)	-	
Histology			0.333
Clear cell	10 (77%)	8 (80%)	
Papillary	01 (8%)	2 (20%)	
Wilms tumor	02 (15%)	-	
Margins			0.4
<1 cm	02 (15%)	3 (30%)	
1 or > 1 cm	11 (85%)	7 (70%)	
Grade (1,2,3)	-	-	0.497
Preoperative ureteric stenting	5 (38%)	9 (90%)	0.01

Table 2: Short-term outcomes comparable between the two groups.

Variables	Off-clamp N=13	On-clamp N=10	P value
Mean blood loss(ml)	1004	950	0.861
Blood transfusion rate(ml)	377	300	0.715
Hospital stay (Days)	12	11	0.357
30 day mortality	Nil	Nil	-
Complications			0.811
Nil	7 (54%)	5 (50%)	
Clavien Dindo II (fever,UTI)	4	4	
IIIa	1*	Nil	
IIIb	1#	1~	

UTI = urinary tract infection

* "Urine leak managed by drain placement"

"Laparotomy for bleeding"

~ "Embolization of surgical bed pseudoaneurysm"

on-clamp technique out of which one had warm ischemic and nine had cold ischemic clamping technique. The mean clamping time was 35 minutes for the available six renal units. Thirteen (57%) patients underwent off-clamp technique. The twenty three units were divided in to two group namely on-clamp and off-clamp group. The clinico-pathological variables were comparable between both the two group and listed in the table 1. The short term outcomes like mean blood loss, blood transfusion rate, hospital stay, complications and thirty day mortality was comparable and listed in table 2. The Clavien Dindo grade II was the most common complication in both the group. Urine leak was reported in one patient after off-clamp technique which was managed conservatively by drain insertion. Re-exploration laparotomy and completion nephrectomy for bleeding on the day one postoperative day after off-clamp partial nephrectomy was done. Hematuria due to surgical bed pseudo-aneurysm on day nine for one patient in the on-clamp group was managed by embolizing it.

The preoperative mean GFR was comparable between the on-clamp (70.13 ml/min/1.73m²) and off-clamp (67.78 ml/min/1.73m²) groups (p= 0.765). The comparison of the preoperative and postoperative (> 3 months) mean GFR was available for eleven renal units in off-clamp and six renal units in on-clamp technique. The percentage decline in the GFR post partial nephrectomy was less in off-clamp group 0.28% compared to the on-clamp group 8%. The preservation of post partial nephrectomy GFR (> 3months) was better with off-clamp technique 99.72% compared to the on-clamp group 92%. The decline in the post partial nephrectomy mean GFR within the group was not statistically significant because of the low power of the study. There are no local recurrences in either group. One patient died of systemic recurrence in the on-clamp group. The five years overall survival for all the twenty three partial nephrectomy renal units was 95%.

Discussion

The incidences of small renal masses (SRM) are on a raising trend due to the increase in abdominal imaging in the modern medicine [6]. The current standard for the management of high risk suspicious small renal masses is nephron sparing surgery or partial nephrectomy [7]. Various approaches and techniques of partial nephrectomy have emerged but no consensus or guidelines exist. Minimal invasive approaches are comparable with open partial nephrectomy. Robotic approach is gaining popularity with better short-term outcomes than open and laparoscopic approach [8,9]. The concern about radical

nephrectomy is the effect on long term renal function outcomes, resulting in early CKD and then cardiac morbidity [10,11]. There is a paradigm shift to partial nephrectomy as standard of care for all feasible renal tumor < 4 cm, apart from its traditional indications. Partial nephrectomy with prolonged ischemia time will also have detrimental effect on the renal function outcomes [2-4].

The renal functional outcomes after partial nephrectomy depends on the modifiable risk factors like renal ischemia time, excisional volume loss, reconstructive methods and non-modifiable risk factors like location, size, age, comorbid conditions, preoperative GFR, previous renal disease or surgery [12]. The central dogma of the partial nephrectomy is to optimize the preservation of functioning nephrons by targeting the modifiable and non-modifiable risk factors but still remains controversial and area of active research [13]. Various technique like cold ischemia time using ice slush, selective arterial clamping, super selective clamping of higher order arteries, early unclamping of vessels, non clamping are used to reduce or avoid the renal ischemia thereby improving the preservation of renal function outcome [4,14].

Various studies has shown off-clamp partial nephrectomy is feasible, safe and avoids renal ischemia with better preservation of long-term renal function outcomes [15,16]. It is currently an emerging and good technique of partial nephrectomy which needs standardization. Open off-clamp partial nephrectomy is comparable and feasible by minimal invasive approaches [16,8]. Mearini et al from Italy compared open, laparoscopic and robotic off-clamp partial nephrectomy. They concluded the efficacy and safety of laparoscopic and robotic partial nephrectomy was comparable with the open technique with the additional benefit of reduced operative time, blood loss, on demand ischemia and rate of high grade complication [18].

Meta-analysis has compared on-clamp and off clamp partial nephrectomy and its effect on the renal function outcome. A meta-analysis in 2014 by Wentao Liu et al of ten retrospective studies comparing 728 off clamp and 1267 on-clamp technique reported superior long-term renal function preservation for the off-clamp technique [19]. Another meta-analysis in 2014 from United Kingdom that includes fourteen studies concluded improved long-term renal function for off-clamp than the on-clamp technique. A non-statistical significant trend towards increased blood loss and transfusion for off-clamp technique was reported [20].

This study is one of its kinds as there is no published Indian data exist on comparison of on-clamp and off-clamp partial nephrectomy and its impact on renal functional outcomes. Another uniqueness of the study is the utilization of the Tc99m-DTPA scan for assessment and comparison of renal function in the available literature. Most studies have reported on estimated GFR (e-GFR). The limitation of this study is the retrospective nature, small power, non-availability of nephrometry score.

Conclusion

Partial nephrectomy is an underutilized procedure in India. But, with the increase in diagnosis of incidental small renal mass and awareness about this procedure, the partial nephrectomy procedures show an uptrend in recent years. India being the capital of diabetes with associated hypertension, the chance of progression to CKD is also high in our setting following nephrectomy. The need of the hour is to maximize the utilization of partial nephrectomy technique after standardization. In this context, the off-clamp technique is a promising

one as it avoids the renal parenchymal ischemia and optimizes the renal function by minimizing or delaying the development of CKD.

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