

Early clamp release during laparoscopic partial nephrectomy: Implications for preservation of renal function

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Abstract

Introduction: Intraoperative warm ischemic time (WIT), associated with hilar clamping during partial nephrectomy (PN), is an established modifiable risk factor for renal dysfunction. We assessed early clamp release (ECR) as a strategy to reduce WIT and assess its impact on renal function and bleeding.

Methods: We retrospectively assessed patients who underwent minimally invasive PN by a single surgeon at our centre since December 2011. Comparing the standard technique to an ECR modification, WIT, complications, change in estimated glomerular filtration rate (eGFR), and change in differential function as demonstrated by MAG-3 nuclear renography were assessed. Followup blood work and renograms were performed at 6–12 weeks postoperatively and compared to baseline in 70 patients (35 ECR: 35 control).

Results: The ECR and control groups were similar in age, sex, and tumour size, with only patient weight being higher in the ECR group (91.6 vs. 81.6 kg; $p < 0.05$). WIT was significantly lower in ECR group compared to control (18.8 vs. 31.5 minutes; $p < 0.05$). Although there was no significant difference in change from baseline eGFR in the early postoperative period (Day 3) or in followup (6–12 weeks), the control group had a significantly greater loss of ipsilateral renal function from baseline compared to the ECR group (9 vs. 4% change; $p < 0.05$). Blood loss and complication rate were similar between groups.

Conclusions: The ECR technique offers a safe, reproducible alternative that reduces WIT during laparoscopic PN. ECR demonstrates a reduction in overall ipsilateral renal dysfunction, without increasing complication or intraoperative bleeding risk.

Introduction

Kidney cancer is a common malignancy, with almost 6000 new cases each year in Canada.^{1,2} The incidence of renal

cell carcinoma has been rising due to the frequent use of imaging modalities.³ Most recently, the standard of care for small renal masses has been partial nephrectomy (PN). The oncological outcomes with PN are comparable to those of radical nephrectomy and demonstrate over 90% disease-specific survival for T1a disease.⁴ Minimally invasive surgical approaches, including laparoscopic, hand-assisted, and robot-assisted, have become progressively more common over the past decade and are considered excellent alternatives to open PN.⁵⁻⁷

Vascular clamping is performed to prevent hemorrhage and allow visualization of the renal bed during the excision of renal tumours. The interruption and re-establishment of blood flow during clamping results in ischemia reperfusion injury, which has been shown to be associated with acute kidney injury and chronic renal damage. Accordingly, the degree of renal recovery postoperatively has been shown to be associated with warm ischemic time (WIT) during resection. Studies used to compare WIT have traditionally used markers like serum creatinine and estimated glomerular filtration rate (eGFR) as indicators of renal function;⁸ however, these measures are believed to lack sensitivity due to the contralateral kidney compensation for renal functional loss. Although the quantification of acceptable WIT is controversial,^{9,10} one analysis in patients with solitary kidneys undergoing PN revealed that WIT greater than 20 minutes is associated with increased risk of acute and chronic renal insufficiency.¹¹

Many surgeons have investigated alternative options to reduce this risk of renal loss. Surgical techniques, such as “off-clamp,” “zero-ischemia,” and “segmental clamping,” have been used to reduce WIT.¹²⁻¹⁵ Although they have typically been demonstrated to be safe, these studies are limited by patient selection bias, small tumours, crude tests used to analyze renal function, and small patient populations.¹⁶⁻¹⁸

In effort to reduce our WIT, we used an early clamp release (ECR) technique during laparoscopic partial nephrectomy (LPN). As a measure for quality assessment for this modification in surgical technique, we reviewed prospectively collected data to evaluate the safety of this technique

and assessed pre- and post-partial nephrectomy ipsilateral renal function with nuclear renography, serum creatinine, and eGFR.

Methods

The data collection for this study was approved by the ethics board at Western University in London, Ontario. A retrospective chart review was carried out using prospective data from patients who have undergone either robot-assisted, hand-assisted, or traditional LPN between December 2011 and December 2015 at our centre by a single surgeon. Patients selected were consecutive patients undergoing ECR LPN (n=35) and the equivalent number of patients who had a LPN immediately preceding the initiation of the new technique. All patients were evaluated preoperatively with routine bloodwork and nuclear renography to assess split differential function and eGFR. Exclusion criteria included patients with bilateral renal masses, patients converted to complete nephrectomy, patients who did not receive preoperative renograms, and one patient who was too obese to undergo nuclear renography testing.

We evaluated intraoperative WIT and surgical factors, such as estimated blood loss (EBL), operative time, and 90-day complication rate, in order to assess efficacy and safety of our ECR technique. Our primary outcomes were short and long-term renal dysfunction. We evaluated changes in serum creatinine and eGFR immediately postoperatively and at the three-month followup appointment. We also examined MAG-3 nuclear renogram split differential function at 6–12 weeks postoperatively compared to preoperative values.

Statistical analysis was carried out to compare patient factors between groups (student's t-test and chi-square test) with $p < 0.05$ considered statistically significant.

Technical description of ECR

Standard positioning and port placement were carried out for da Vinci robotic-assisted and standard LPN as previously described.^{19,20} The renal hilum and the vessels were identified and isolated. Intraoperative ultrasound was used to identify the borders of the mass, rule out other renal lesions, and assess renal vascular flow, as previously described by our group.²¹

Prior to resection, 0.5 mg/kg IV mannitol was administered and both renal arteries and veins were clamped. Doppler ultrasound was used to confirm there was no flow throughout the kidney. The tumour was then resected sharply. Visible vessels were ligated or controlled with bipolar cautery. A running 2.0 PDS 'whipstitch' was used to reapproximate the collecting system and the inner aspect of the renal parenchyma. Our closure was tested using an injection of

methylene blue through the 5 French, open-ended catheter placed preoperatively. If a collecting system leak was identified, it was closed with another layer of 2.0 PDS. Once the first layer closure was complete, Floseal® (Baxter, IL, U.S.) was applied to the surgical bed and clamps were released. A second external layer of closure was then carried out using interrupted 0 PDS with the sliding locking clip technique described by Benway et al.²² Hemostatic agents were applied as necessary after the reconstruction. The perinephric fat was closed over our reconstruction and a drain was placed.

By comparison, with the standard clamp release technique, the vascular clamps were released after the completion of the second layer closure using interrupted 0 PDS suture.

Results

Patient demographics

The patient demographics were similar between ECR and standard clamp release groups (Table 1); however, the ECR group had a mean weight of 91.6 kg, which was significantly heavier compared to standard clamp release group (81.6 kg). As well, the ECR group was associated with more robotic-assisted operations vs. control.

Tumour characteristics

Tumour size was smaller in the ECR vs. control group (36 cm³, range 1–133 cm³ vs. 55.4 cm³, range 1–170 cm³, respectively), but was not statistically significant (Table 2). Nephrometry scores were blindly calculated by a third party in a retrospective fashion and confirmed by one author (GC). Mean nephrometry scores were 6.8 and 7.7 in the ECR and control groups, respectively. There was not a significant difference between scores. In both groups, most tumours were pathologically T1, with only two ECR and three control group patients having T2 tumours. Both groups had seven patients with positive or indeterminate surgical margins. None of the specimen had multifocal positive margins. Most

Table 1. Patient characteristics of the ECR and control groups.

	ECR (n=35)	Standard (n=35)
Mean age, years	58.8	59.5
Gender		
Male	25	19
Female	10	16
Weight, kg	91.6	81.6*
Method		
Robotic	22	11*
Laparoscopic	13	24*

*Statistically significant with $p < 0.05$. ECR: early clamp release.

Table 2: Tumour pathological characteristics comparing ECR and control group

	ECR (n=35)	Standard (n=35)
Size, cm ³ (range)	36.1 (1–133)	55.4 (1–170)
Nephrometry score, mean	6.8	7.7
Stage		
T1a	23	19
T1b	10	13
>T2	2	3
Pathology		
ccRCC	18	21
Chromophobe	6	3
Papillary	4	3
Oncocytoma	6	4
Other*	1	4
Positive margin status	7	7

*Oncocytoma, metanephric adenoma, or unclassified. ccRCC: clear-cell renal cell carcinoma; ECR: early clamp release.

tumours were clear-cell renal cell carcinomas (ccRCC), with an equally small distribution of other variants.

Operative outcomes

To determine the safety and efficacy of the ECR procedure, surgical factors were compared between the two groups (Table 3). WIT is represented by the “on-clamp time.” Clamp time in the ECR group was significantly lower vs. standard technique (18.8 vs. 31.5 minutes; $p<0.05$). This included one patient in the ECR group who needed to go back on clamp for bleeding and had a total clamp time of 31 minutes. Although there was a higher percentage of robotic vs. laparoscopic PNs in the ECR vs. standard group, there was no difference in clamp times between laparoscopic vs. robotic operations (mean 17.6 vs. 19.5 minutes, respectively). Importantly, there were no significant differences in EBL, transfusion rates, operating time, length of stay in hospital, or the 90-day complication rate between ECR and standard LPN groups. One Clavien IV and three Clavien III complications were seen in each group. Postoperative complications in the ECR group includ-

ed: delayed bleeding requiring transfusion and embolization, urine leak, aspiration pneumonitis requiring reintubation and intensive care unit admission, perinephric abscess requiring insertion of a drain, and a postoperative splenectomy. Similar complications arose in the standard approach and included urine leak, pseudoaneurysm bleeding requiring transfusion and embolization, and respiratory distress requiring intensive care admission and ventilation.

Functional outcomes

The primary intent of this study was to evaluate the impact of ECR on renal function. Renal function was compared using standard serum creatinine and eGFR measures (Table 4). Preoperative serum creatinine was similar between groups (mean of 81.2 and 78.4 $\mu\text{mol/L}$ in the ECR and control groups, respectively). Three months postoperatively, the decline in renal function was similar and both groups showed an increase in mean creatinine (ECR 4.9 $\mu\text{mol/L}$ vs. control 8.9 $\mu\text{mol/L}$). Accordingly, the calculated reduction of eGFR in both groups was similar (12.0 vs. 10.7 mL/min/1.73 m^2).

In addition to biochemical analysis of renal function, comparison of renal function/excretion using MAG3 nuclear renograms preoperatively and 6–12 weeks postoperatively was performed. Preoperative split function of the affected kidney was similar between groups (48 and 49% in the ECR and standard groups, respectively). Importantly, the decline in split function was significantly greater in the standard technique group (9%) compared to the ECR group (4%) (Table 4).

Discussion

WIT is a well-documented risk factor for postoperative renal impairment and a number of studies have been published

Table 4. Changes in renal function comparing ECR and control groups

	ECR (n=35)	Standard (n=35)
sCR, $\mu\text{mol/L}$		
Preoperative	81.2	78.4
6–12-week postoperative	86.1	87.3
Change	+4.9	+8.9
eGFR, mL/min/1.73 m^2		
Preoperative	112.1	94.3
6–12-week postoperative	100.1	83.6
Change	-12	-10.7
% change	-8.5%	-11.0%
Differential function, %		
Preoperative	48	49
6–12-week postoperative	44	40
Change	-4	-9*

* $p<0.05$. ECR: early clamp release; eGFR: estimated glomerular filtration rate; sCR: serum creatinine.

Table 3. Surgical factors comparing ECR and control group

	ECR (n=35)	Standard (n=35)
Clamp time, min (range)	18.8 (10–31)	31.5* (22–68)
EBL, ml	301	284
OR time, min	234	243
LOS (days)	4.6	5.3
90-day complication rate, n	7	5
Clavien score		
II	3	1
III	3	3
IV	1	1
V	0	0

*Statistically significant value, $p<0.05$. EBL: estimated blood loss; ECR: early clamp release; LOS: length of stay; OR: operating room (time from start of procedure to completion).

recently evaluating efficacy of different techniques.^{11,23-25} Since it was adopted in 2013, we have performed ECR exclusively for both laparoscopic and robotic PN, which reduced WIT by nearly 14 minutes. Although there have been previous studies describing the ECR technique, this is the first study to assess its impact on WIT and renal damage compared with the standard technique.²⁶ As a matter of quality assurance, we also wanted to ensure that the ECR technique did not lead to a higher rate of bleeding, complications, or length of stay.

Other groups have assessed LPN techniques using crude tests, such as serum creatinine and eGFR, which are often inaccurate and subject to day-to-day variability.¹⁵ In addition, in patients with a normal contralateral kidney, serum creatinine (and derived eGFR) does not accurately assess renal damage due to compensation by the contralateral kidney. Uniquely, our study used MAG-3 nuclear renography to assess the change in renal function (via assessment of tubular secretion and glomerular filtration) in the ipsilateral unit. Using renography, loss of renal function in the affected kidney was assessed by comparing renographic changes with the unaffected unit. Accordingly, when preoperative to postoperative renal function were assessed by creatinine and eGFR in our patient population, no difference was noted between ECR and standard LPN. It is only when assessment of ipsilateral renal damage was assessed by renography that the impact of ECR and shorter WIT was noted.

The safety and efficacy of ECR was assessed by comparing operative and postoperative factors. There was no difference in blood loss, length of operative time, length of stay in hospital, or complication rate between ECR and standard LPN groups. Our outcomes are reassuring, as complication rates are similar to other LPN series.¹⁶ By comparison, off-clamp or selective clamping PNs have been reported to be associated with higher EBL and complication rates.^{11,17,27} In the past, techniques permitting reduced clamp time were performed in selected patients with smaller tumours and lower nephrometry scores, whereas in our study, no selection bias occurred, since the technique was applied to all LPN cases in succession.

Limitations of our study include a relatively small patient population, owing from a single surgeon experience. Although this was a retrospective study, data was collected within a long-standing LPN database that prospectively assessed preoperative and postoperative renal function at precise time points. Aside from a higher body mass index in the ECR group, the two groups were similar demographically. As well, there were more robotic PNs performed in the ECR group, but WIT between robotic and standard LPN groups were similar, indicating that a higher percentage of robotic PNs did not affect the difference in WIT between ECR and standard LPN groups.

Before universal use of the described ECR technique, careful multicentre assessment of the technique should be

performed. We believe that this technique can be performed by experienced surgeons who are currently performing robotic or standard LPN. Unlike a technically demanding off-clamp or selective clamping technique that may be associated with higher bleeding and positive margin rates (owing to a wet renal resection bed), the ECR technique is technically simple, requiring only that the clamps be released prior to the second closure layer. If excessive bleeding occurs as a result of the ECR technique, the clamp need only be reapplied, as it did in one of our procedures.

Conclusion

ECR is a safe method of LPN that significantly reduced WIT and renal damage vs. standard LPN according to assessment by nuclear renography. Intraoperative and postoperative complication rate and blood loss was not affected by ECR.

Competing interests: The authors report no competing personal or financial interests.

This paper has been peer-reviewed.

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