A comparison of kidney oxygenation profiles between partial and complete renal artery clamping during nephron sparing surgery in a porcine model

Karim Bensalah, MD,[1] Jay D. Raman, MD,[1,3] Ilia S. Zeltser, MD,[1]
Aditya Bagrodia, MD,[1] Steven M. Lucas, MD,[1] Wareef Kabbani, MD,[2]
Jeffrey A. Cadeddu, MD[1]

[1]Department of Urology, University of Texas Southwestern Medical Center, Dallas, Texas, USA
[2]Department of Pathology, University of Texas Southwestern Medical Center, Dallas, Texas, USA
[3]Division of Urology, Penn State Milton S. Hershey Medical Center, Hershey, Pennsylvania, USA

BENSALAH K, RAMAN JD, ZELTSER IS, BAGRODIA A, LUCAS SM, KABBANI W, CADEDDU JA. A comparison of kidney oxygenation profiles between partial and complete renal artery clamping during nephron sparing surgery in a porcine model. The Canadian Journal of Urology. 2009;16(3):4632-4638.

Objective: *To compare kidney oxygenation profiles between partial and complete renal artery clamping during nephron sparing surgery (NSS) in a porcine model.*

Materials and methods: *Twelve female farm pigs underwent a laparoscopic nephrectomy. Subsequently, an open partial nephrectomy was performed on the remaining kidney using either total (n = 6, TC) or partial (n = 6, PC) clamping of the renal artery. Real time renal partial oxygen pressure (rPO_2) was monitored using a Licox probe (Integra, San Diego, CA). Creatinine levels were measured prior to open partial nephrectomy and on POD #3 and #7. The remaining kidney was harvested for pathologic evaluation.*

Results: *Compared to TC, the PC group demonstrated a more favorable renal oxygenation profile during the NSS. Specifically, rPO_2 decreased less from baseline (58% versus 84%, p = 0.03), took a longer interval to nadir (23.1 min versus 8.7 min, p = 0.04), and experienced a more rapid recovery to maximal or baseline values (4.8 min versus 10.4 min, p = 0.03) in the PC group. Furthermore animals undergoing TC had significantly higher creatinine levels at POD #3 (2.2 mg/dl versus 1.6 mg/dl, p = 0.03) and POD #7 (2.5 mg/dl versus 1.7 mg/dl, p = 0.009). Histological analysis demonstrated varying levels of acute inflammation in the two groups. Finally, the intraoperative blood loss was greater in the PC versus TC group (40 cc versus 10 cc, p = 0.04).*

Conclusions: *In this porcine model, partial clamping of the renal artery during NSS was feasible and demonstrated a favorable renal oxygenation profile. Theoretically, intraoperative rPO_2 monitoring may provide a novel means to allow real time assessment and titration of kidney perfusion during partial nephrectomy.*

Key Words: partial nephrectomy, renal ischemia, renal oxygenation, Licox probe

Accepted for publication April 2009

Acknowledgements
The authors are grateful to Dr. Ahmed Idris for his technical assistance with the Licox probe, and to Stephanie Shaffer for her assistance with intraoperative and postoperative animal care. Karim Bensalah is funded by the Association Francaise d'Urologie.

Address correspondence to Dr. Jeffrey A. Cadeddu, Dept. of Urology, University of Texas Southwestern Medical Center, 5323 Harry Hines Boulevard J8-106, Dallas, TX 75204 USA

Introduction

Radical nephrectomy has historically been the gold standard therapy for the management of renal masses. More recently, the increased diagnosis of small kidney tumors coupled with good oncologic and kidney preservation outcomes have propelled nephron sparing surgery (NSS) to the forefront of therapy.[1-3] The technique of open partial nephrectomy (OPN) is well established.[4] With improvements in minimally invasive surgery, laparoscopic partial nephrectomy

(LPN) has increasingly become a safe and effective alternative to OPN in centers of excellence.[5-7]

Adequate tumor resection typically requires clamping of the renal vascular pedicle to ensure a bloodless field. This, however, is at the expense of subjecting the kidney to anoxia and resultant ischemic injury. Furthermore, laparoscopic reconstruction of the kidney is typically more challenging, leading to a longer ischemic time and potentially increased nephron injury.[8,9] While kidney cooling increases ischemic tolerance, it is not routinely employed during minimally invasive surgery.[10]

As more renal masses are managed by NSS, particularly by laparoscopic modalities, it is imperative to investigate technical refinements that may reduce ischemic damage and offer better renal protection. In theory, partial renal arterial occlusion, and thereby partial kidney perfusion, may be an attractive concept to decrease renal hypoxia and thus prolong the relative ischemic interval while maintaining an adequate operative field. To better address this issue, we compared the impact of partial versus complete renal artery clamping on intraoperative renal oxygenation profiles and acute postoperative renal function outcomes during nephron sparing surgery in a solitary kidney porcine model.

Materials and methods

Study design

The study was performed following approval by our Institutional Animal Care and Use Committee (IACUC). Thirteen female farm pigs were included in this study, with one pig used to develop a reproducible model for intraoperative renal oxygenation monitoring. The remaining 12 pigs underwent two surgical procedures. The initial operation was a right laparoscopic nephrectomy to create a solitary kidney model. The second procedure was a contralateral open partial nephrectomy (OPN) performed 7 days thereafter. The pigs were randomized into two groups; six underwent a partial nephrectomy with total clamping (TC) of the renal artery, while the remaining six underwent the same procedure with partial renal arterial clamping (PC). Intraoperative hemodynamic parameters (blood pressure, heart rate, and core temperature) were monitored during all cases.

Laparoscopic nephrectomy

All laparoscopic nephrectomies were performed via a transperitoneal approach. Briefly, following induction of general anesthesia, the pigs were placed in a left lateral decubitus position and three trocars were utilized (12 mm lateral to the rectus muscle, 12 mm in the right lower quadrant, and a 5 mm below the costal margin). The hilum was dissected and transected en bloc with an endovascular stapler. The ureter was clipped and divided and the kidney mobilized from its remaining peritoneal attachments. The specimen was extracted in a laparoscopic sac by extending one of the trocar incisions.

Figure 1. Licox brain tissue oxygen monitoring system (Integra, San Diego, CA) consisting of one oxygen catheter probe and one temperature probe.

Licox measurements and open partial nephrectomy

Renal tissue oxygen partial pressure (rPO_2) was monitored in real time using the Licox brain tissue oxygen monitoring system (Integra, San Diego, CA), Figure 1. The system consists of one oxygen catheter probe and one temperature probe that was inserted through a double lumen bolt into the cortex of the kidney, Figure 2. The oxygen catheter has a diameter

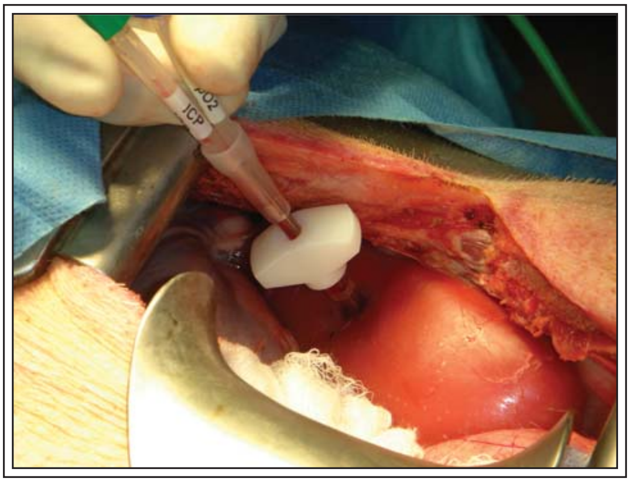

Figure 2. Licox oxygen monitoring probe inserted into renal cortex.

of 0.5 mm with a measurement area of 5 mm. Both probes are linked to a monitoring device that displays both rPO_2 and temperature curves in real time. Reproducible Licox oxygenation measurements were obtained in one pig that only underwent an open renal exploration and not a partial nephrectomy operative procedure. The probe was inserted 1 cm through the kidney capsule into the renal cortex and confirmation of probe depth in this pig was obtained by bivalving the kidney. Steady state oxygenation levels were achieved within 2-3 minutes and remained constant for a 30 minute observation period.

Partial nephrectomy was performed through an extraperitoneal flank incision. The kidney was mobilized with careful dissection of the renal artery to minimize vasospasm. In all 12 cases, only a single renal artery was identified. The Licox probe was inserted into the upper pole of the renal cortex at a site distinct from surgical resection. The rPO_2 was allowed to reach a steady state baseline prior to initiating vascular clamping. Thereafter, either complete or partial renal arterial clamping was performed using a conventional curved Satinsky vascular clamp. In all cases, the Satinsky was placed entirely across the renal artery and was fully clamped in pigs undergoing TC. For PC, the renal artery was clamped by approximately 50% of its outer diameter as measured by an electronic microcaliper. The renal vein was not clamped in either of the surgical arms. The renal artery was clamped (PC or TC) for a period of 10 minutes prior to initiating partial nephrectomy. Subsequently, a lower pole partial nephrectomy was performed and the base of the resection was oversewn with a 2-0 vicryl suture for hemostasis and closure of the collecting system. The parenchyma was closed with interrupted sutures over a gauze bolster. The artery remained totally or partially occluded for a set period of 30 minutes in each pig, even though the partial nephrectomy was completed in less time. The abdominal wall was then closed without drainage.

Licox monitoring started when the renal artery was initially dissected and concluded after renal artery unclamping when the rPO_2 reached its preocclusion baseline or after 10 minutes of stable unchanged values, Figures 3 and 4. Given the profound decrease in rPO2 levels within a few minutes of arterial clamping, a total clamping interval of 30 minutes seemed reasonable for a surgical endpoint in this acute phase study. The following parameters were recorded: percentage decrease from baseline rPO_2, interval to nadir rPO_2 after arterial clamping, percentage of rPO_2 recovery after unclamping, interval to recover to baseline rPO_2 or maximum rPO_2 after unclamping. Nadir was defined as the lowest rPO_2 value monitored during the clamping period. Because of potential interanimal variability, results are expressed as percentage change from baseline values observed for each pig.

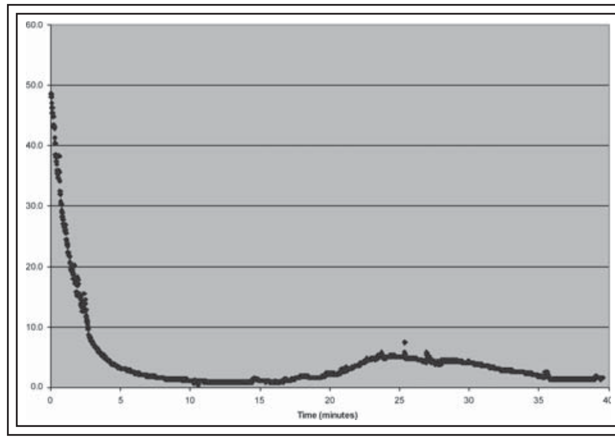

Figure 3. Licox tissue oxygenation profile during a partial nephrectomy with total clamping (TC) of the renal artery. Following clamping (t = 0 min), rPO_2 drops rapidly to a nadir value of less than 10% of baseline measurement. Following unclamping (t = 30), rPO_2 remains unchanged and fails to increase to baseline while measured for an additional 10 minutes.

Postoperative care

The animals were observed for a 7 day period after the OPN. Serum creatinine measurements were obtained

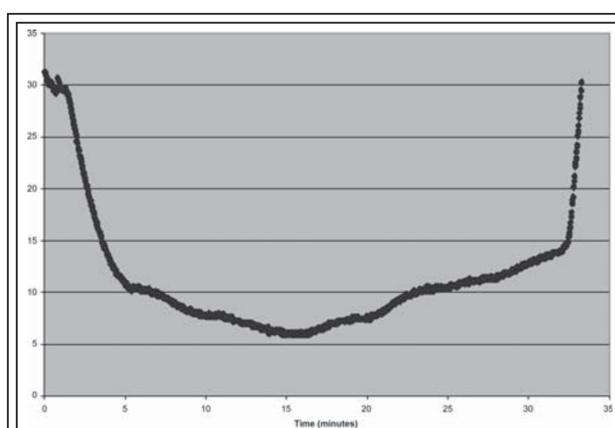

Figure 4. Licox oxygenation profile during a partial nephrectomy with partial clamping (PC) of the renal artery. Following clamping, rPO_2 promptly decreases to a nadir value of 20% of the baseline measurement. However, following unclamping (t = 30 min), the rPO_2 rapidly recovers to baseline values.

on day 0 just prior to OPN, on POD #3 following the partial nephrectomy, and on POD #7 prior to euthanasia. At day 7, the pigs were euthanized and the remaining kidney specimen was harvested and submitted for pathologic evaluation. Histological analysis was completed by a uropathologist blinded to clinical outcomes and study design.

Statistical analysis

Results between groups were compared using the non parametric Mann-U-Whitney test. All statistics were completed with SPSS version 13.0 (SPSS Inc., Chicago, IL) with $p < 0.05$ considered statistically significant.

Results

Animal characteristics

Mean animal weight was 35 kg in the TC group and 33 kg in the PC group. All laparoscopic nephrectomies were performed successfully with an uneventful postoperative recovery, and all pigs survived the OPN without complications. Table 1 summarizes the operative parameters. The mean percentage of resected kidney tissue (calculated by the ratio weight of the partial specimen/total weight of the kidney) was similar between the PC (mean 13.1%, range 7-17) and TC specimens (mean 12.2%, range 9.5-15). The mean reduction in renal artery diameter during partial clamping was 50% (range, 35% to 65%). There was no difference in operative duration, although estimated blood loss (EBL) was higher in the PC group (10 cc versus 40 cc, p = 0.04).

rPO_2 measurements

rPO_2 profiles are summarized in Table 1. Following arterial clamping, mean rPO_2 decrease from baseline was greater in the TC group compared to the PC group (84% versus 58%, p = 0.03). Furthermore, in one case of PC, we did not observe any decline of rPO_2 during the clamping interval. The mean interval to reach the nadir rPO_2 was longer in the animals that underwent PC than in the animals with TC (23.1 min versus 8.7 min, p = 0.04). Following unclamping, rPO_2 returned to baseline value in 50% of the cases from PC compared to 20% of the cases in the TC group. Finally, the interval to recover baseline rPO_2 or reach the maximum postclamping value was shorter in the PC group (mean, 4.8 min versus 10.4 min, p = 0.03).

Serum creatinine levels, Figure 5

Baseline serum creatinine measured 7 days after the laparoscopic nephrectomy and just prior to the partial nephrectomy was comparable in both groups (mean, 1.6 mg/dl versus 1.5 mg/dl, p = 0.24). At day 3 following partial nephrectomy, mean serum creatinine was higher in the TC group (2.2 mg/dl versus 1.6 mg/dl, p = 0.03). By day 7, while the mean serum creatinine continued to increase in the TC group to 2.5 mg/dl, the creatinine remained stable in the PC group at 1.7 mg/dl (p = 0.009). Changes in serum creatinine from day 0 to 3 and day 0 to 7 were both higher in the TC group compared to the PC group (mean, 0.5 mg/dl versus 0.07 mg/dl and 0.86 mg/dl versus 0.16 mg/dl, respectively, p = 0.01 and p = 0.009).

TABLE 1. **Summary of operative parameters and rPO_2 profiles**

Operative parameters	Total clamping	Partial clamping	p value
OR duration (min) Mean (range)	94 (63-117)	81 (48-131)	0.94
EBL (cc) Mean (range)	10 (5-20)	40 (20-110)	0.04
Decline from baseline rPO_2 (%) Mean (range)	84% (26%-98%)	58% (0%-84%)	0.03
Interval to nadir rPO_2 (min) Mean (range)	8.7 (2.4-24.8)	23.1 (14.7-28.4)	0.04
Recovery of baseline rPO_2 (%) Mean (range)	57% (23-100)	83% (53-100)	0.24
Interval to recover baseline or maximal rPO_2 (min) Mean (range)	10.4 (4.9-15.7)	4.8 (1.2-7.9)	0.03

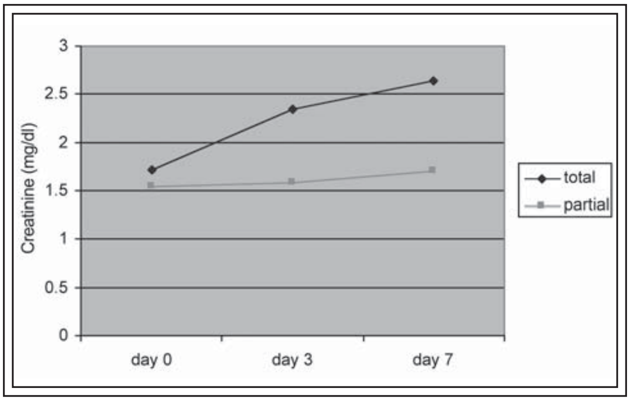

Figure 5. Mean serum creatinine changes in pigs undergoing nephron sparing surgery using either partial or total renal arterial clamping.

Histological analysis, Table 2.
There was no histological evidence of tubular necrosis in either groups. All harvested kidneys showed patterns of acute inflammation except for two pigs in the PC group and one in the TC group. Overall, histology demonstrated varying levels of acute inflammation (ranging from none to significant) with no clear difference between the two groups. There was no evidence of intimal damage of the renal artery from either of the clamping procedures.

TABLE 2. **Summary of histological analyses for harvested kidney specimens**

Pig	Type of clamping	Extension of inflammation	Inflammation intensity
1	Total	Patchy	Moderate
2		Patchy	Moderate
3		Patchy	Mild
4		Patchy	Mild
5		Focal	Mild
6		None	None
7	Partial	Patchy	Moderate
8		None	None
9		Patchy	Mild
10		None	None
11		Patchy	Marked
12		Patchy	Moderate

Discussion

Limiting warm ischemic interval during NSS has always been a paramount clinical concern, especially as LPN has become a reliable option for the management of small renal tumors.[5,6,8] Although it duplicates the open technique,[11] the laparoscopic procedure is more challenging and harbors a higher morbidity.[8] Moreover, even when accomplished by the most experienced surgeons, ischemic duration of laparoscopic partial nephrectomy is still 50% longer than that of OPN.[8] Therefore, there is a need for technical refinements and novel approaches to improve intraoperative ischemic monitoring that may improve kidney preservation during NSS.

Our study demonstrated that compared to total arterial clamping with resultant kidney anoxia, partial renal arterial clamping may decrease acute ischemic insults to the kidney during nephron sparing surgery in a porcine model. Indeed, both the improved oxygenation confirmed by intraoperative tissue oxygen tension monitoring (by Licox) and postoperative serum creatinine measurements support this potential benefit of partial clamping. Pathologic results, however, were less conclusive. No animals displayed patterns of tubular necrosis, although the majority demonstrated histological signs of acute inflammation. This may be explained by the fact that the clamping time was limited to 30 minutes, which is well under the 120 minutes warm ischemia tolerance of a porcine kidney.[12] Given our focus on renal oxygenation measurements and the profound decrease in rPO_2 levels observed within a few minutes of arterial clamping, a total clamping interval of 30 minutes seemed reasonable for a surgical endpoint in this acute phase study. Indeed, future work with longer ischemic intervals would better address this histological endpoint.

Renal perfusion has an important impact on the ischemic injury to the kidney. Specifically, metabolic activities in the kidney occur predominantly in an aerobic environment, and therefore the kidney is highly sensitive to hypoxia and anoxia. Determinants such as hypotension, dehydration and arterial spasm can increase ischemic insult.[13] Clamping of the renal artery results in severe hypoperfusion of the kidney which responds by arteriolar vasoconstriction to limit filtration and maintain tubular function.[14] If this blood flow reduction is sustained, it can lead to acute tubular necrosis with severe ischemic damage secondary to intracellular accumulation of calcium, generation of oxygen species, depletion of adenosine triphosphate and apoptosis.[15] The impact of acute tubular necrosis on long term renal function outcomes, however, is not clearly understood. Renal cells can undergo repair, regeneration and proliferation after ischemic damage, but there are no precise prognostic factors that can predict the degree of recovery, although it is well known that a longer ischemia time is deleterious.[9,16] As all of these mechanisms are initiated by the absence of perfusion, the concept of partial occlusion of the renal artery to maintain some blood flow through the kidney is an attractive refinement.

In fact, many technical modifications have been reported to minimize the consequences of total clamping of the renal pedicle. The majority involve avoiding hilar control. Initially, most laparoscopic surgeons performed the operation without pedicle clamping, limiting their indications to small exophytic tumors. Others have advocated renal parenchymal clamping either in the open[17] or laparoscopic[18] setting. However, these techniques are limited to polar peripheral lesions. We have also reported our experience with radiofrequency assisted laparoscopic partial nephrectomy to preclude clamping of the renal artery for select renal tumors though this is limited to small exophytic tumors.[19] Recently, Baumert suggested that early arterial unclamping diminishes warm ischemia time without increasing blood loss.[20] Nguyen et al have similarly shown that in experienced hands early unclamping laparoscopic partial nephrectomy technique significantly decreases ischemia time by more than 50% and also trends toward decreased complications.[21] Our concept of partial clamping is different in that it avoids any anoxic insult by permitting a continuous low level of renal perfusion. Furthermore, by maintaining a consistent reduced blood flow rate, adverse intraoperative events that can occur by early unclamping as described by Baumert et al are avoided. We found that with partial renal arterial occlusion, the EBL was higher in the PC group, though this subjectively did not affect resection visualization or technique or objectively impact operative duration.

This study is among the first, to our knowledge, to utilize the Licox monitoring system to evaluate renal oxygenation in real time during partial nephrectomy.[22] Tissue oxygen tension reflects the balance between oxygen supply and demand. Currently, clinical experience with such monitoring is only available in the neurological domain. Measurement of brain oxygen tension affords the possibility for continuous monitoring of cerebral oxygenation and early detection of ischemia. Although measurements detect local tissue oxygen tension, such values accurately reflect the global cerebral oxygenation if the catheter is positioned in a relatively undamaged part of the brain.[23] Depth and duration of tissue hypoxia after traumatic brain injury have been shown to predict unfavorable outcome and death, with the likelihood of death increasing when brain oxygen tension drops below 15 mmHg.[24] With similar techniques, oxygen tension can be measured in all human tissues. We hypothesize that rPO_2 profiles in the renal cortex would correlate with ischemic damage. We observed a corresponding significant difference in both rPO_2 profiles and renal function outcome between PC and TC groups, suggesting that percentage change from baseline rPO_2 values and longer recovery time following unclamping may be reliable markers of ischemic kidney damage. Of course, further work in a larger scale study is necessary before we can further extrapolate that the rPO_2 profile can predict ischemic insults to the kidney.

There are several avenues for future direction. With regards to type of ischemia, we elected to utilize warm ischemia in this model for two reasons. Firstly, data from Schuler and colleagues suggests that in a porcine renal ischemia model, pigs that were treated with retrograde renal cooling had a slower recovery of pO_2 to baseline values (by Licox monitoring) following hilar unclamping.[22] These authors postulated hypothermic vasospasm. Due to this potential confounding variable, we elected not to use cold ischemia in the initial model. Furthermore, as laparoscopic partial nephrectomy is almost universally performed under warm ischemia, we felt that this may be a more applicable starting point for ischemia studies. However, undoubtedly, the role of cold ischemia must be better elucidated. In addition, our study evaluates oxygenation and serum creatinine changes following a fixed ischemic interval of 30 minutes. We elected for this duration based upon contemporary data from human series. However, it will be necessary to evaluate this longitudinally over a longer ischemic interval. Longer time points will allow us to ascertain the true amount of time "gained" by partial clamping.

Finally, there are several limitations in our study. Firstly, tissue oxygenation is by definition heterogeneous and can be influenced by many vascular parameters such as the number, diameter, and spatial distribution of the renal vasculature. While all of our cases only had a single renal artery, rPO_2 can also be affected by the presence of functional shunting resulting from microcirculatory disruption. Furthermore, renal blood flow is not uniformly distributed within the kidney. Most of the renal blood supply is directed to the cortex. By contrast, in the outer medulla, countercurrent oxygen exchange occur leading to a progressive fall in pO_2 from cortex to medulla.[15] For this reason, we systematically placed the probe in the cortical region of the kidney. Secondly, as with most animal studies, there is also concern regarding the translation of results to human care. During our resection, we did not have to take into account the location of the tumor and the proximity of vascular or collecting system structures all of which are very important in the clinical setting. Moreover, although the porcine kidney is a close model of the human organ, physiological differences remain and the response to renal injury may differ. Thirdly, future work will require more precise measurements of blood flow regulation through a partially clamped renal artery. Indeed, Doppler ultrasound would better quantify flow through the artery and would offer better precision than measurements of renal arterial diameter. Finally, although there was more blood loss with partial clamping, the subjective level of operative difficulty was the same in cases of PC or TC. However, we cannot extrapolate that such conditions would similarly exist in the human.

Conclusion

In this acute recovery porcine model, partial clamping of the renal artery during nephron sparing surgery was feasible and demonstrated a favorable renal oxygenation profile when compared to total clamping. Theoretically, intraoperative rPO_2 monitoring may provide a novel means to allow real time assessment and titration of kidney perfusion during partial nephrectomy. Future studies with larger numbers of animals, longer warm ischemia times, and subsequently human phase I investigations are warranted to better address this issue. □

References

1. Hollingsworth JM, Miller DC, Daignault S, Hollenbeck BK. Rising incidence of small renal masses: a need to reassess treatment effect. *J Natl Cancer Inst* 2006;98(18):1331-1334.
2. Fergany AF, Hafez KS, Novick AC. Long-term results of nephron sparing surgery for localized renal cell carcinoma: 10-year followup. *J Urol* 2000;163(2):442-445.
3. Huang WC, Levey AS, Serio AM, et al. Chronic kidney disease after nephrectomy in patients with renal cortical tumours: a retrospective cohort study. *Lancet Oncol* 2006;7(9):735-740.
4. Uzzo RG, Novick AC. Nephron sparing surgery for renal tumors: indications, techniques and outcomes. *J Urol* 2001;166(1):6-18.
5. Aron M, Gill IS. Minimally invasive nephron-sparing surgery (MINSS) for renal tumours part I: laparoscopic partial nephrectomy. *Eur Urol* 2007;51(2):337-346; discussion 46-47.
6. Hacker A, Albadour A, Jauker W et al. Nephron-sparing surgery for renal tumours: acceleration and facilitation of the laparoscopic technique. *Eur Urol* 2007;51(2):358-365.
7. Gill IS, Kavoussi LR, Lane BR et al. Comparison of 1,800 laparoscopic and open partial nephrectomies for single renal tumors. *J Urol* 2007;178(1):41-46.
8. Gill IS, Matin SF, Desai MM et al. Comparative analysis of laparoscopic versus open partial nephrectomy for renal tumors in 200 patients. *J Urol* 2003;170(1):64-68.
9. Porpiglia F, Renard J, Billia M et al. Is renal warm ischemia over 30 minutes during laparoscopic partial nephrectomy possible? One-year results of a prospective study. *Eur Urol* 2007;52(4):1170-1178.
10. Janetschek G. Laparoscopic nephron sparing surgery: ischemic renal damage. *Curr Opin Urol* 2006;16(2):45-46.
11. Gill IS, Desai MM, Kaouk JH et al. Laparoscopic partial nephrectomy for renal tumor: duplicating open surgical techniques. *J Urol* 2002;167(2 Pt 1):469-467; discussion 75-76.
12. Orvieto MA, Tolhurst SR, Chuang MS et al. Defining maximal renal tolerance to warm ischemia in porcine laparoscopic and open surgery model. *Urology* 2005;66(5):1111-1115.
13. De Maeyer P, Oosterlinck W, De Sy W. Prevention of vasospasms during extensive renal surgery. An experimental study in rats. *Eur Urol* 1981;7(4):224-226.
14. Thadhani R, Pascual M, Bonventre JV. Acute renal failure. *N Engl J Med* 1996;334(22):1448-1460.
15. Lameire N, Van Biesen W, Vanholder R. Acute renal failure. *Lancet* 2005;365(9457):417-430.
16. Thompson RH, Blute ML. At what point does warm ischemia cause permanent renal damage during partial nephrectomy? *Eur Urol* 2007;52(4):961-963.
17. Mejean A, Vogt B, Cazin S, Balian C, Poisson JF, Dufour B. Nephron sparing surgery for renal cell carcinoma using selective renal parenchymal clamping. *J Urol* 2002;167(1):234-235.
18. Verhoest G, Manunta A, Bensalah K et al. Laparoscopic partial nephrectomy with clamping of the renal parenchyma: initial experience. *Eur Urol* 2007;52(5):1340-1346.
19. Zeltser IS, Moonat S, Park S, Anderson JK, Cadeddu JA. Intermediate-term prospective results of radiofrequency-assisted laparoscopic partial nephrectomy: a non-ischaemic coagulative technique. *BJU Int* 2008;101(1):36-38.
20. Baumert H, Ballaro A, Shah N et al. Reducing warm ischaemia time during laparoscopic partial nephrectomy: a prospective comparison of two renal closure techniques. *Eur Urol* 2007;52(4):1164-1169.
21. Nguyen MM, Gill IS. Halving ischemia time during laparoscopic partial nephrectomy. *J Urol* 2008;179(2):627-632; discussion 32.
22. Schuler TD, Perks AE, Fazio LM et al. Impact of arterial and arteriovenous renal clamping with and without intrarenal cooling on renal oxygenation and temperature in a porcine model. *J Endourol* 2008;22(10):2367-2372
23. Haitsma IK, Maas AI. Advanced monitoring in the intensive care unit: brain tissue oxygen tension. *Curr Opin Crit Care* 2002;8(2):115-120.
24. van den Brink WA, van Santbrink H, Steyerberg EW et al. Brain oxygen tension in severe head injury. *Neurosurgery* 2000;46(4):868-876; discussion 76-78.