# Robotic cold ischemia achieves comparable functional outcomes to open cold ischemia during partial nephrectomy for complex kidney tumors

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## Abstract

**Objectives:** To compare the perioperative and functional outcomes after open and robotic partial nephrectomy performed with cold ischemia.

**Methods:** A retrospective chart review was completed of consecutive patients who underwent partial nephrectomy with renal hypothermia between January 2011 and September 2016. The study cohort included both open (Open Cold Ischemia, OCI; n=170) and robotic (Robotic Cold Ischemia, RCI; n=31) patients with complex renal masses (R.E.N.A.L. score >7) who did not meet exclusion criteria. A modified intracorporeal technique 1 was utilized for the introduction of ice slush at the time of hilar clamping in the RCI group. Statistical testing was performed to compare key perioperative and functional outcomes after ensuring equilibration of both groups by clinicodemographic criteria.

**Results:** Both groups were statistically equivalent with respect to baseline characteristics. Median GFR preservation postoperatively was 86.7% for the open group and 86.6% in the robotic group (p=0.49). Cold ischemia time (CIT) in the open group was 35 minutes compared to 28 minutes (p = 0.03) in the robotic group. LOS was significantly shorter by 2 days (p < 0.01) in the robotic group. Positive margins was noted to be 17 (10%) in the open group and 2 (6.5%) patients in the robotic group (p=0.48).

**Conclusions:** We demonstrate an effective and simplified method of intracorporeal ice cooling during robotic partial nephrectomy. Our data suggests that results with this approach compare favorably to open cold ischemia technique. Intracorporeal ice cooling can be considered when performing complex partial nephrectomies with ischemia times expected to exceed 25 minutes.

**Keywords:** Nephron-sparing surgery, renal cold ischemia, robotic partial nephrectomy, robotic surgery

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## INTRODUCTION

One of the conventional advantages of open surgery in the management of renal masses has been in facilitating the routine employment of cold ischemia that allows for prolonged hilar clamping of up to 3 h without permanent injury to the kidney.[1,2] This has been especially advantageous for larger or more complex tumors in which prolonged ischemia is generally required. However, over

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the past 10–15 years, there have been increasing efforts to incorporate intracorporeal hypothermia into minimally invasive surgery, allowing one to combine the benefits of the decreased morbidity profile of minimally invasive surgery with the optimization of renal functional outcomes.

We originally published our methods for implementing cold ischemia in laparoscopic partial nephrectomy in 2003.[3] However, the technique was cumbersome due to the need to introduce a specimen bag around the kidney to contain the ice slush. Since then, additional methods for renal intracorporeal cooling have been described including retrograde ice-cold fluid injection through a ureteral catheter and renal artery infusion.[4-10] Recently, a robotic technique was defined which required a large midline incision, expensive gel port, and a custom-made ice plunger.[11]

We previously published our technique for robotic intracorporeal renal hypothermia which established its ease and feasibility and demonstrated a short-term benefit on renal function compared to warm ischemia.[12,13] In the interim, we have continued to gain experience and fine-tune its application. However, to establish its utility compared to conventional open icing, we wished to conduct the present study with the goal of comparing the two techniques and demonstrating the noninferiority of robotic intracorporeal renal hypothermia in terms of key perioperative and functional outcomes.

## MATERIALS AND METHODS

### Study population and design

After obtaining institutional review board approval, we queried our departmental partial nephrectomy database for patients who had undergone clamped partial nephrectomy under cold ischemia between January 2011 and September 2016. OCI was routinely used throughout the study period, but RCI was first implemented in September 2013. The choice between open and robotic technique was made at the discretion of the operating surgeon. In patients in whom robotic partial nephrectomy was being planned, preoperative imaging was reviewed to assess tumor complexity and decide on the utility of employing RCI. If the R. E. N. A. L. scores were >7 and if warm ischemia time was anticipated to exceed 25 min, RCI, as opposed to warm ischemia, was chosen as the preferred technique. Patients with missing ischemia times were excluded ($n$ = 34°CI patients). This yielded the final study cohort.

### Surgical technique

All cases in the RCI group were performed through a transperitoneal approach by a single surgeon (JHK) using

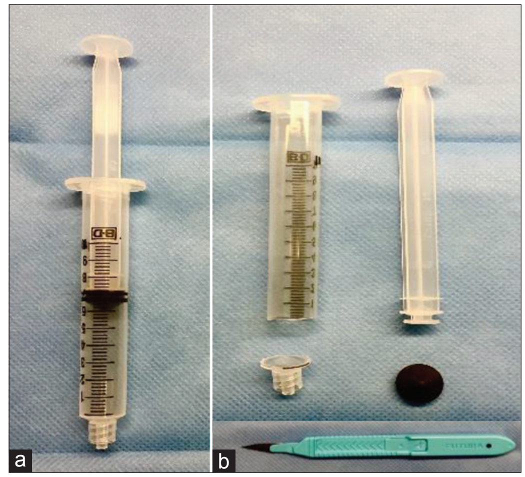


**Figure 1:** (a) Unmodified 10cc syringe. (b) Modified 10cc syringe with removed stopper

a standardized technique, as previously described.[12] Preoperative planning with the surgical team addressed such issues as operative suite arrangement. Since the initial paper, we have switched to using ten 10 cc syringes for ease of ice slush introduction, as shown in Figure 1. We have also limited the total amount of ice slush to 400–500 cc, which we have found to be sufficient to achieve desirable temperatures of <20°C.

In the OCI group, all cases were performed through a conventional retroperitoneal flank approach by 13 surgeons, all with at least 1 year of staff experience. Renal hypothermia was achieved by packing ice slush around the defatted kidney immediately following hilar clamping. The duration of time that the kidney was iced tumor excision was variable (ranging from 0 to 10 min) and was dictated by surgeon preference.

### Study variables

Study variables for matched comparison of OCI and RCI included patient age, gender, race, non-age-adjusted Charlson-Deyo comorbidity index (CCI), body mass index (BMI), solitary kidney status, presence of preoperative chronic kidney disease (CKD) stage 3 or greater, clinical tumor size, R. E. N. A. L. nephrometry score,[14] and histology.

### Study outcomes

The primary study outcome was glomerular filtration rate (GFR) preservation at last follow-up. GFR was estimated using the modification of diet in renal disease formula. GFR preservation was calculated by dividing the GFR at last follow-up by the preoperative GFR (within 1 month before surgery) and was expressed as a percentage. Secondary outcomes included ischemia time, estimated blood loss (EBL), surgical margin status, intraoperative complications, postoperative complications, and inpatient length of stay (LOS). Postoperative complications were graded using the Clavien classification system, including minor (Clavien 1–2) and major (Clavien 3–5) complications.

### Statistical analysis

Nonnormally distributed data were expressed by the median and interquartile range (IQR). The OCI and RCI groups were compared in terms of the primary and secondary outcomes using the Pearson Chi-square and Fisher's exact tests for categorical variables and the Mann-Whitney U test for ordinal and continuous variables. Statistical tests were performed using SAS University Edition (SAS Institute Inc., Cary, NC, USA). All *P* values were two-sided, and values <0.05 were considered statistically significant.

## RESULTS

A total of 201 partial nephrectomy cases were included in our study, 170 utilizing OCI and 31 utilizing RCI. The median age of our cohort was 62 years (IQR 54–70) and median tumor size was 4.6 cm (IQR 3.3–5.8). Median BMI and CCI were 30 kg/m2 (IQR 27.0–32.2) and 1 (IQR 0–2), respectively. No statistically significant differences were seen between OCI and RCI groups regarding age, gender, BMI, CCI, the presence of preoperative CKD, R. E. N. A. L. score, and tumor size [Table 1]. There was no difference in average preoperative estimated GFR (eGFR) (OCI 73.8 [range 49.1–98.5] vs. RCI 80.5 [range 50.4–110.6], $P = 0.18$) between cohorts.

For the RCI group, adequate cooling was confirmed, with a mean nadir temperature during icing of 15.3°C, which occurred an average of 13.4 min after ice application. Body temperature remained stable with a mean drop of 0.43°C noted during lowest kidney temperature.

Median operative times between groups were similar (OCI 218 [IQR 179–253] vs. RCI 223 [IQR 201–264], $P = 0.28$). Median EBL was significantly lower in the RCI cohort (300 mL [IQR 200–400] vs. 100 mL [IQR 50–150], $P < 0.01$). Positive surgical margin rates (OCI 10.2% vs. RCI 6.5%, $P = 0.48$) were similar between groups as were transfusion rates (OCI 12.9% vs. RCI 6.5%, $P = 0.48$). Robotic approach was associated with a shorter median LOS (5 days [IRQ 4–6] vs. 3 days [IQR 2-4], $P < 0.01$). The OCI group experienced a greater overall complication

**Table 1: Case characteristics by approach**

| Variables | Total (*n*=201) | Open (*n*=170) | Robotic (*n*=31) | *P* |
|---|---|---|---|---|
| Median age, years (IQR) | 62 (54–70) | 63 (56–70) | 55 (46–69) | 0.1317 |
| Male, *n* (%) | 126 (64.6) | 110 (64.7) | 16 (64.0) | 0.9451 |
| Race, *n* (%) | | | | |
| White | 163 (83.6) | 141 (82.9) | 22 (88.0) | 0.5237 |
| Nonwhite | 32 (16.4) | 29 (17.1) | 3 (12.0) | 0.423 |
| Median CCI (IQR) | 1 (0–2) | 1 (0–2) | 1 (0–2) | 0.8156 |
| Median BMI (kg/m$^2$), IQR | 30.0 (27.0–32.2) | 30.1 (27.1–33.2) | 29.3 (26.7–31.7) | 0.2371 |
| Solitary kidney, *n* (%) | 37 (12.6) | 25 (14.7) | 2 (8.0) | 0.5388 |
| CKD, *n* (%) | 27 (13.9) | 50 (29.4) | 8 (32.0) | 0.7915 |
| Median nephrometry score (IQR) | 9 (8–10) | 9 (8–10) | 9 (8–10) | 0.669 |
| Median tumor size (cm), (IQR) | 4.6 (3.3–5.8) | 4.8 (3.5–5.8) | 3.7 (3.1–5.2) | 0.0628 |

IQR: Inter quartile range, CCI: Charlson-Deyo comorbidity index, BMI: Body mass index, CKD: Chronic kidney disease

**Table 2: Surgical and functional outcomes by approach**

| | Total (*n*=201) | Open (*n*=170) | Robotic (*n*=31) | *P* |
|---|---|---|---|---|
| Median operative time, min (IQR) | 218 (180–256) | 218 (179–253) | 223 (201–264) | 0.28 |
| Median ischemia time, min (IQR) | 32 (26–48) | 35 (26–50) | 28 (24–35) | <0.01 |
| Median EBL, (mL) (IQR) | 250 (150–400) | 300 (200–400) | 100 (50–150) | <0.01 |
| Positive surgical margins, *n* (%) | 18 (9.4) | 17 (10.2) | 2 (6.5) | 0.48 |
| Blood transfusion, *n* (%) | 22 (11.3) | 22 (12.9) | 2 (6.5) | 0.22 |
| Operative complications, *n* (%) | 8 (4.1) | 8 (4.7) | 0 | 0.6 |
| Postoperative complications, *n* (%) | | | | |
| Minor | 45 (22.3) | 42 (24.7) | 3 (9.7) | 0.02 |
| Major | 26 (12.9) | 25 (14.7) | 1 (3.2) | |
| Median LOS, day (IQR) | 4 (4–5) | 5 (4–6) | 3 (2–4) | <0.01 |
| Mean preoperative GFR±SD | 74.6±25.3 | 73.8±24.7 | 78.8±28.6 | 0.25 |
| Mean latest GFR±SD | 64.0±22.3 | 63.7±21.7 | 65.2±25.2 | 0.48 |
| Median GFR preservation, % (IQR) | 86.6 (75.0–97.2) | 86.7 (74.6–99.6) | 86.6 (75.2–94.1) | 0.49 |
| Median GFR follow-up (months) | 7.7 (1.4–25.3) | 9.8 (1.6–29.0) | 6.1 (0.3–14.5) | <0.01 |
| Median overall follow-up (months) | 19.4 (7.4–35.6) | 24.1 (12.3–40.6) | 6.1 (0.3–17.3) | <0.01 |

IQR: Inter quartile range, EBL: Estimated blood loss, LOS: Length of stay, GFR: Glomerular filtration rate, SD: Standard deviation rate (39.4% vs. 16.0%, $P = 0.02$). When complications were stratified between minor (OCI 24.7% vs. 9.7%, $P = 0.16$) and major (OCI 14.7% vs. 3.2%, $P = 0.21$), no differences were seen, although rates of complications trended to lower levels in the RCI group. Rates of intraoperative complications were not statistically different between groups (OCI 4.7% vs. RCI 0%, $P = 0.60$) [Table 2].

The median duration of GFR follow-up between both groups was dissimilar (OCI 9.8 months [IQR 1.6–29.0] vs. RCI 6.1 months [IQR 20.3–14.5], $P = 0.01$). Mean latest eGFR (OCI 63.7 [standard deviation [SD] 21.7], vs. 65.2 [SD 25.2], $P = 0.48$) and median percent preserved eGFR (OCI 86.7% [IQR 74.9–99.6] vs. RCI 86.6% [IQR 75.2–94.1], $P = 0.49$) were no different between OCI and RCI cohorts [Table 2].

## DISCUSSION

Over the years, urologists have continued to expand the indications for partial nephrectomy to tumors of increasing complexity in the name of preservation of renal function. With increasingly complex tumors comes the challenge of maintaining acceptable durations of ischemic time to mitigate the risk of injury to kidney function. Given the benefits afforded by renal cooling,[1,2] hypothermia has conventionally been implemented through open techniques when faced with challenging situations such as hilar tumors, infiltrating masses, or multiple tumors in solitary kidneys. Over the years, the incorporation of renal hypothermia in minimally invasive surgery has been refined into a method that can now be widely employed in a reliable and reproducible manner. However, for RCI to gain additional traction in the urologic community, it would need to be demonstrated that it improves outcomes in a similar manner.

Herein, we present our early experience with RCI and demonstrate that it achieves perioperative outcomes that compare very favorably with traditional open techniques.

Among equally matched groups undergoing partial nephrectomy for complex tumors, we have found that RCI achieves equivalent rates of GFR preservation of 87% compared to OCI. Furthermore, we found that median ischemia time, EBL, postoperative complications, and LOS were all reduced in the RCI group. Many of these benefits can be attributed to the decreased morbidity associated with robotic surgery. Findings of decreased convalescence and blood loss have previously been demonstrated in a comparable group of patients undergoing robotic vs. open partial nephrectomy for higher complexity tumors.[15]

If our hypothermia technique is chosen for robotic partial nephrectomy, we suggest preoperative surgical team-based planning to outline the operative steps we have described. Room organization is also key in smaller operating suites due to the addition of the surgical ice unit, and the need to access and transfer the ice from the modified 10cc syringes to the bedside promptly. To best prepare the syringes, heavy scissors can be used on some syringe brands that are not made of brittle plastic; alternatively, an 11 blade can be used. Custom-made syringes may be a good solution for this technical issue. We use the 10cc syringes instead of other sizes because of the similar diameter of the 10cc syringe and the 12 mm laparoscopic port, which maximizes the efficiency of the introduction of the ice slush. Finally, it is important to have appropriate surgeon expectations with this technique. Longer ischemic times should be anticipated compared to noncooled techniques due to the time required to introduce the ice slush. However, the benefits in renal function appear worthwhile. Furthermore, slightly extended operative times may be anticipated in RCI since both artery and vein should be clamped to cool the kidney, which adds more time to the hilar dissection.

In our previous publication from 2003,[3] we made two erroneous assumptions; (i) that the kidney needed to be placed in an endocatch bag to protect the bowel from cold ischemia; (ii) that the use of 30 cc syringes would be required for ice slush delivery. In this study, we observed that abandoning the endocatch bag simplified the procedure without any additional risk of ileus due from contact with bowel. Simply surrounding the kidney with 4 × 18 inch sponges was enough to contain ice around the kidney. Use of smaller syringes minimized the risk of ice impaction and improved delivery though a 12 mm port.

There are several limitations with this paper. As with any retrospective design, some unmeasured and residual confounders that can account for differences in outcomes may exist. We did not have temperature data for the open cohort, and so it remains possible, although unlikely given the experience of the involved surgeons, that desirable cooling temperatures were not reached. The cohort volume was low, especially in the robotic arm, and with larger volumes, the baseline differences in tumor size between open and robotic groups may reach statistical significance. Significant differences were seen in the median duration of GFR follow-up, with 6 months in the RCI group compared to 9 months in the OCI group; however, it is likely that GFR had stabilized by this time interval and hence, it remains unlikely that this would have produced differences in GFR preservation. Finally, a quarter of patients undergoing RCI had ischemic durations <24 min, and so the presence of these cases may have diluted the beneficial effects attributable to hypothermia. Nonetheless, RCI was no worse than OCI in terms of renal functional outcomes.

## CONCLUSIONS

Intracorporeal ice-slush kidney cooling during robotic partial nephrectomy appears to generate comparable functional results and favorable perioperative outcomes to open cold ischemia for higher complexity tumors. Our technique is simple to implement with proper planning and is cost-effective, and it may be further popularized in the future with custom-made syringes. This may allow further dissemination of this technique, which we recommend be employed in cases in which ischemic durations are anticipated to be prolonged.

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Nil.

### Conflicts of interest
Jihad H. Kaouk certifies that all conflicts of interest, including specific financial interests and relationships and affiliations relevant to the subject matter or materials discussed in the manuscript (e.g., employment/affiliation, grants or funding, consultancies, honoraria, stock ownership or options, expert testimony, royalties, or patents filed, received, or pending), are the following: Endocare, Inc., Intuitive. - J.H. Kaouk (consultant). Nothing to disclose for Dr. Nelson, Dagenais, Maurice, Ramirez, Caputo, Babbar, and Yerram.

## REFERENCES

1. Wickham JE. Regional renal hypothermia. Ann R Coll Surg Engl 1971;48:99-113.
2. Ward JP. Determination of the optimum temperature for regional renal hypothermia during temporary renal ischaemia. Br J Urol 1975;47:17-24.
3. Gill IS, Abreu SC, Desai MM, Steinberg AP, Ramani AP, Ng C, *et al.* Laparoscopic ice slush renal hypothermia for partial nephrectomy: The initial experience. J Urol 2003;170:52-6.
4. Colli J, Cotter K, Dorsey P, Mitchell G, Lee BR. Intrarenal pressures remain low with placement of a dual lumen catheter for retrograde irrigation to induce renal hypothermia. Int Urol Nephrol 2012;44:1425-9.
5. Saitz TR, Dorsey PJ, Colli J, Lee BR. Induction of cold ischemia in patients with solitary kidney using retrograde intrarenal cooling: 2-year functional outcomes. Int Urol Nephrol 2013;45:313-20.
6. Colli JL, Dorsey P, Grossman L, Lee BR. Retrograde renal cooling to minimize ischemia. Int Braz J Urol 2013;39:37-45.
7. Crain DS, Spencer CR, Favata MA, Amling CL. Transureteral saline perfusion to obtain renal hypothermia: Potential application in laparoscopic partial nephrectomy. JSLS 2004;8:217-22.
8. Schoeppler GM, Klippstein E, Hell J, Häcker A, Trojan L, Alken P, *et al.* Prolonged cold ischemia time for laparoscopic partial nephrectomy with a new cooling material: Freka-gelice-a comparison of four cooling methods. J Endourol 2010;24:1151-4.
9. Hruby S, Lusuardi L, Jeschke S, Janetschek G. Cooling mechanisms in laparoscopic partial nephrectomy: Are really necessary? Arch Esp Urol 2013;66:139-45.
10. Kijvikai K, Viprakasit DP, Milhoua P, Clark PE, Herrell SD. A simple, effective method to create laparoscopic renal protective hypothermia with cold saline surface irrigation: Clinical application and assessment. J Urol 2010;184:1861-6.
11. Rogers CG, Ghani KR, Kumar RK, Jeong W, Menon M. Robotic partial nephrectomy with cold ischemia and on-clamp tumor extraction: Recapitulating the open approach. Eur Urol 2013;63:573-8.
12. Ramirez D, Caputo PA, Krishnan J, Zargar H, Kaouk JH. Robot-assisted partial nephrectomy with intracorporeal renal hypothermia using ice slush: Step-by-step technique and matched comparison with warm ischaemia. BJU Int 2016;117:531-6.
13. Kaouk JH, Samarasekera D, Krishnan J, Autorino R, Acka O, Brando LF, *et al.* Robotic partial nephrectomy with intracorporeal renal hypothermia using ice slush. Urology 2014;84:712-8.
14. Kutikov A, Uzzo RG. The R.E.N.A.L. nephrometry score: A comprehensive standardized system for quantitating renal tumor size, location and depth. J Urol 2009;182:844-53.
15. Simhan J, Smaldone MC, Tsai KJ, Li T, Reyes JM, Canter D, *et al.* Perioperative outcomes of robotic and open partial nephrectomy for moderately and highly complex renal lesions. J Urol 2012;187:2000-4.