Robotic Partial Nephrectomy for Renal Cell Carcinomas With Venous Tumor Thrombus

Ronney Abaza and Jordan Angell

OBJECTIVE To describe the first report of robotic partial nephrectomies (RPNs) for renal cell carcinoma (RCC) with venous tumor thrombus (VTT).

METHODS Partial nephrectomy for RCC extending into the renal vein has been described in limited fashion, but such a complex procedure has not previously been reported in minimally-invasive fashion. We demonstrate the feasibility of robotic nephron-sparing surgery despite vein thrombi and the results of the initial four highly-selected patients to have undergone this novel procedure. Two patients underwent RPN for RCC with VTT involving intraparenchymal vein branches, and 2 others had VTT involving the main renal vein. Mean patient age was 65 years (range 50-74 years). Mean tumor size was 7.75 cm (range 4.3-12.8 cm) with mean RENAL (radius, exophytic/endophytic, nearness to collecting system, anterior/posterior, and location) nephrometry score of 9.75 (range 8-12).

RESULTS Mean warm ischemia time was 24.2 minutes (range 19-27 minutes) and mean estimated blood loss was 168.8 mL (range 100-300 mL). No patients required transfusion, and there were no intraoperative complications. No patients required conversion to open or standard laparoscopic surgery. All 4 patients were discharged home on the first postoperative day. A single postoperative complication occurred in 1 patient who was readmitted with an ileus that resolved spontaneously. All patients had negative surgical margins. Two patients developed metastatic disease on surveillance imaging.

CONCLUSION RPN in patients with VTT is safe and feasible in selected patients. Given the risk of metastatic disease in patients with pathologic stage T3a RCC, the role of nephron sparing requires further evaluation such that radical nephrectomy remains the standard of care. UROLOGY 81: 1362–1368, 2013. © 2013 Elsevier Inc.

Nephron-sparing surgery (NSS) has become the standard of care for small renal masses.[1] Given the advantages of renal preservation without loss of oncologic efficacy when compared to radical nephrectomy, NSS has been extended beyond traditional indications to larger and more complex tumors. Although originally designed for small tumors and imperative indications, such as solitary kidneys or pre-existing renal insufficiency, more recent studies have demonstrated that NSS can be performed for tumors >4 cm, in purely elective cases, and for complex tumors safely and with oncologic success.[2]

Furthermore, NSS has even been reported in very limited fashion for patients with venous tumor thrombus (VTT) found either before partial nephrectomy or during excision, which may represent the most challenging of NSS procedures. Although radical nephrectomy is considered the standard of care for such tumors, imperative NSS has caused some investigators to extend the limitations of NSS to situations in which VTT is present, similar to the extension of NSS beyond the original indications for tumors <4 cm only. Sengupta et al[3] reported open partial nephrectomy in the setting of VTT involving the renal vein or vena cava in 7 patients with solitary kidneys. Three other recent series of open partial nephrectomy for VTT confined to the renal vein in 2, 6, and 8 patients each confirm the feasibility of NSS in such patients.[4-6]

Robotic partial nephrectomy (RPN) has been increasingly applied to complex tumors with outcomes comparable to open partial nephrectomy,[7] but it has not previously been shown to be feasible for patients with VTT. We describe the initial patient series of minimally invasive NSS in the setting of VTT, which was performed with robotic assistance.

TECHNICAL CONSIDERATIONS

RPN was performed in 4 patients with renal tumors with VTT between October 2010 and February 2012 by a single surgeon (R.A.). Feasibility of NSS was evaluated

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based upon extent of VTT on preoperative imaging studies and ability to preserve adequate venous drainage of the renal remnant after excision. Two patients had VTT involving intraparenchymal branches of the renal vein, of which 1 was unsuspected on imaging and identified intraoperatively, and 2 patients had VTT involving the main renal vein.

Mean patient age was 65 years (range 50-74 years) with mean body mass index of 24.3 kg/m^2 (range 20-28). Mean tumor size was 7.75 cm (range 4.3-12.8 cm) with mean RENAL (radius, exophytic/endophytic, nearness to collecting system, anterior/posterior, and location) nephrometry score of 9.75 (range 8-12). Given the nature of the procedure, a detailed patient consent process was used in addition to all patients undergoing surgery under an institutional review board approved prospective protocol. All patients were given the choice of partial vs radical nephrectomy and consented to partial vs radical nephrectomy with the explanation that radical nephrectomy would be performed if the ability to resect the tumor completely was felt to be compromised. The only exception was in the 1 patient in which the venous thrombus was identified intraoperatively. In this patient, RPN consent did not include specific discussion of VTT. Last, all patients consented to the possibility of conversion to open surgery if felt by the surgeon to be safer for the patient for any reason (oncologic or otherwise).

All procedures were performed transperitoneally with patients in the flank position using the da Vinci Surgical System (Intuitive Surgical Inc., Sunnyvale, CA). A 4-port approach was used in all cases, including 2 8-mm ports for robotic instruments and 2 12-mm ports with 1 for the robotic camera and 1 for the assistant. The renal artery and vein were dissected circumferentially with care not to dislodge the tumor thrombus, and vessel loops were placed on each before tumor localization with laparoscopic ultrasonography. The extent of the tumor thrombus was carefully delineated with intraoperative ultrasonography as well.

Intravenous mannitol was given for renal protection before clamping the renal artery. The renal vein was clamped distal to the VTT in cases of main renal vein tumor thrombus, whereas for intraparenchymal VTT, the renal vein was not clamped and the pneumoperitoneum was increased to 20 mm of Hg until the renorrhaphy was completed. Excision of the tumor was performed strategically with the goal of addressing the tumor thrombus last or leaving only a small portion of attached parenchyma for stability before extracting the VTT.

In cases of intraparenchymal VTT, the resection was performed along the length of the involved vein branch into the renal sinus fat until the end of the thrombus was identified (Fig. 1). The vein was then amputated with the entire VTT still attached to the main renal tumor. In cases of VTT involving the main renal vein (Fig. 2), the excision of the tumor was performed along with the involved vein branch until reaching the main renal vein. The renal vein was then incised along its long axis to allow thrombus removal intact while still attached to the renal mass, after which the vein was repaired with nonabsorbable suture to restore its ability to drain the renal remnant (Fig. 3). Renorrhaphy was then performed with running sutures to oversew the extraction bed followed by capsular reconstruction sutures without a bolster. Tumors with their attached VTT were removed in an extraction bag. No surgical drains were placed despite collecting system entry in all 4 patients.

Lymphadenectomy was not performed as no patients had clinically positive nodes on imaging studies or found at the time of surgery. Postoperative care included diet as tolerated and ambulation the same day as surgery. On the first postoperative day, serum studies were obtained, Foley catheters were removed, and patients were discharged home. Pathologic analysis of specimens was performed per routine at our institution, including margin assessment with 1 or more malignant cells at the plane of excision constituting a positive margin.

RESULTS

Individual preoperative, postoperative, and pathologic results for each of the 4 patients are listed in Table 1. Mean warm ischemia time was 24.2 minutes (range 19-27 minutes), and mean estimated blood loss was 168.8 mL (range 100-300 mL) with no transfusions. Mean operative time was 274.8 minutes (range 227-392 minutes). Although all patients were discharged home on the first postoperative day, 1 patient was readmitted for ileus that resolved spontaneously after 2 days with no other postoperative complications in any patients. All patients had negative surgical margins, including at the renal vein edges, as defined by standard pathologic criteria for T3a/T3b tumors, whereby no adherence/invasion of the vein wall was identified at the margin. Pathology included clear cell renal cell carcinoma (RCC) in 3 patients, papillary RCC in 1 patient, and mean Fuhrman grade of 3.5 (range 2-4).

Mean preoperative serum creatinine level was 0.89 mg/dL (range 0.65-1.32 mg/dL), with mean immediate postoperative creatinine of 1.26 mg/dL (range 0.85-1.96 mg/dL) and mean 6-month postoperative creatinine of 1.01 mg/dL (range 0.77-1.31 mg/dL).

Median follow-up was 9.4 months (range 2.0-17.6 months). On follow-up imaging, 2 patients developed metastatic disease, including isolated pulmonary metastasis in 1 patient after 6 months and pulmonary and liver metastasis 2 months after surgery in another patient who had T4 disease and resection of a portion of liver at the time of RPN. The other 2 patients remain free of disease on surveillance imaging at 1 year and 2 years postoperatively without additional therapy as no patients were treated adjuvantly. The liver involvement in the 1 patient with T4 was not identified until the time of surgery and was addressed at the outset of the procedure as soon as it was identified to determine whether continuation robotically would be possible. Upon

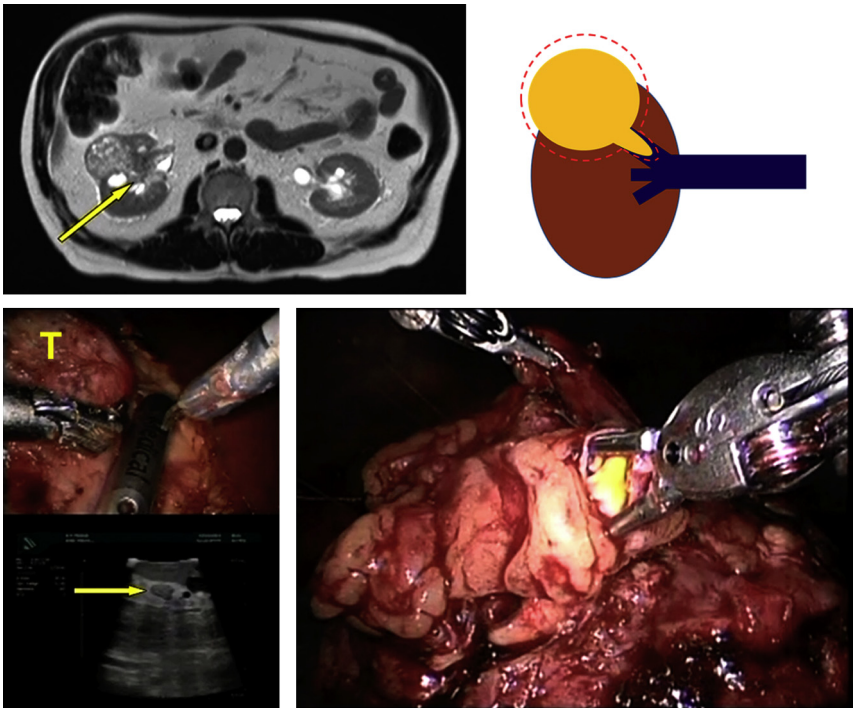

Figure 1. Images of representative robotic partial nephrectomy for renal tumor with intraparenchymal vein tumor thrombus including preoperative magnetic resonance imaging (MRI) with arrow indicating venous thrombus (upper left), schematic diagram of planned tumor resection (upper right), laparoscopic ultrasound identification of tumor in vein within renal sinus (lower left), and completely excised tumor with inspection of vein margin (lower right). (Color version available online.)

successfully accomplishing the resection of liver with an adequately wide margin and with minimal blood loss, the RPN procedure was then performed.

COMMENT

As implementation of NSS has grown among urologists in the management of small renal masses, its role in larger tumors continues to evolve.[2] Recent reports, although small in patient number, have shown feasibility and acceptable outcomes for open NSS in the setting of renal masses with VTT,[3-6] primarily for patients with imperative indications for NSS, such as solitary kidney. The current series is the first description in the literature of minimally invasive NSS for tumors with VTT and represents an initial patient experience demonstrating feasibility of a robotic technique.

Although our experience with RPN for VTT in a limited number of patients suggests feasibility and safety with results comparable to open series, the role of NSS for VTT in an elective setting (whether robotic or open) is yet uncertain and should be approached with caution. Clearly, this procedure, whether performed with open or robotic surgery, is highly complex and requires a level of expertise in NSS, such that it should not be embarked upon lightly. It is our belief that excision of renal tumors, even when VTT is present, as long as a negative surgical margins and respect of oncologic principles can be preserved, is reasonable in selected patients who would otherwise be candidates for NSS if not for the VTT. Nevertheless, this is yet unproven and remains controversial even when performed by experienced NSS surgeons with low complication rates.

Of note, during this time period, 9 patients with renal vein tumor thrombi underwent robotic radical nephrectomy, reflecting the highly selected nature of the patients and tumors undergoing this procedure. Additionally, the surgeon performing all 4 procedures in this series had previously performed robotic radical nephrectomy with vena caval tumor thrombectomy,[8] allowing an experience that likely aided in these cases and may not be shared by most surgeons.

The results of EORTC 30904 (European Organization for Research and Treatment of Cancer) found no survival benefit for NSS over radical nephrectomy,[9] which has caused re-evaluation of NSS in the urologic community. Although the findings of this randomized study should not lead to abandonment of NSS in favor of radical nephrectomy for all renal tumors, whether NSS is adequately beneficial for the most complicated or largest tumors to justify the additional potential complications is questionable and worthy of careful consideration. Although the oncologic equivalence of NSS with radical nephrectomy has been demonstrated in European Organization for Research and Treatment of Cancer 30904 and other nonrandomized studies, whether this applies to tumors with VTT specifically is uncertain.

Radical nephrectomy would have been sound in any of our 4 patients and remains the standard of care until larger experiences and longer follow-up are reported.

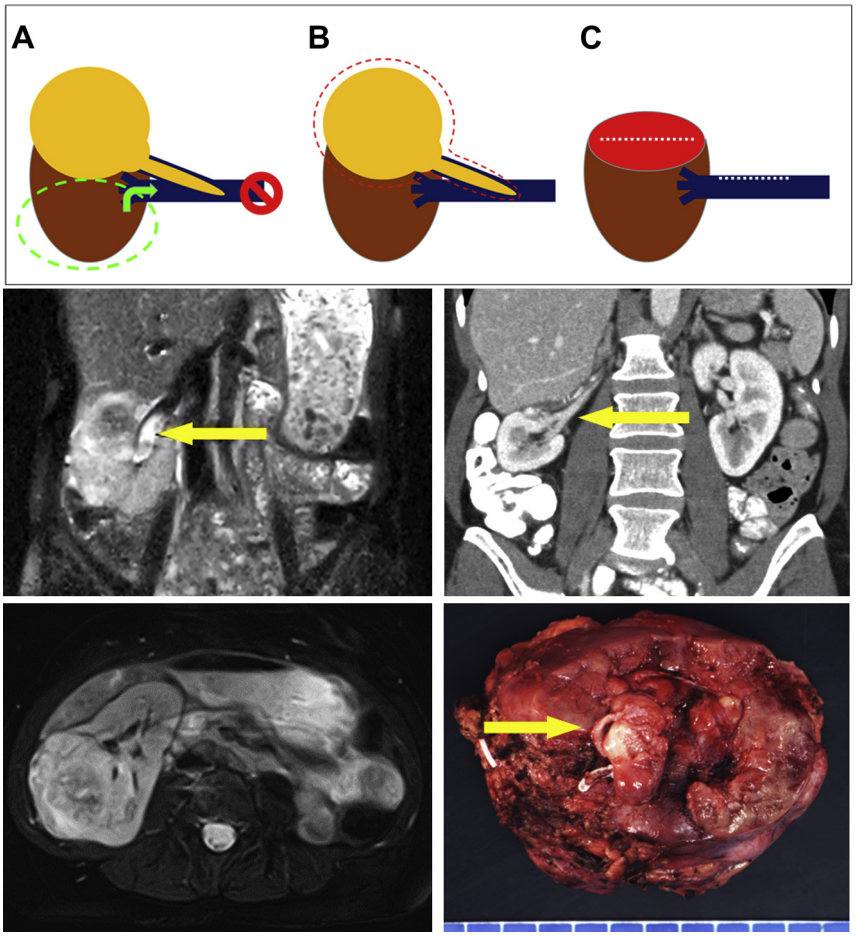

Figure 2. Schematic diagram of renal tumors with venous extension into main renal vein (upper panel) with strategy for addressing tumor thrombus to allow drainage of renal remnant **(A)** by excising tumor and thrombus intact **(B)** with renorrhaphy and reconstruction of vein **(C)** and example of right upper pole renal tumor with venous tumor thrombus, including preoperative magnetic resonance imaging (MRI) with arrow showing vein thrombus (center left and lower left), postoperative computed tomography (CT) scan at 6 months with arrow showing patent vein (center right) and specimen with arrow showing resected vein branch with tumor thrombus that was protruding into main renal vein attached (lower right). (Color version available online.)

Although performing NSS in these patients with T3a is less likely to benefit patients when elective because of the risk of systemic recurrence, whether partial or radical nephrectomy is performed may not have an impact on the development of systemic recurrence. Patients with venous extension of RCC may be at greater risk of systemic rather than local recurrence because of hematogenous spread. If this is true, then if NSS can be achieved with negative margins and low complications, partial nephrectomy may not be irrational although certainly not a guarantee of cure.

In our series, 2 of 4 patients unfortunately developed systemic recurrence, not unlike the findings of Sengupta et al[3] in which 5 of 7 patients experienced systemic recurrence or died of metastatic recurrence of RCC. This reflects the severity of RCC with VTT in which the majority of patients will recur within 5 years with nearly half of recurrences within the first year after surgery.[10] Although this might discourage NSS in patients with VTT, it is impossible to predict which will recur systemically and which will not at the time of surgical decision-making. Nephrectomy remains the standard approach, but giving patients the option of NSS when possible and certainly when imperative for renal function, gives patients the "benefit of the doubt" rather than the more nihilistic approach of assuming they will all recur systemically and therefore may be worth considering.

Our study is limited by a small number of patients and short follow-up and is, therefore, unable to answer the question of whether NSS is preferred in VTT patients when elective. We endeavored only to demonstrate feasibility of a robotic technique in selected patients and not to prove that it should be done. It has been suggested that in locally advanced tumors, the resulting worse prognosis from the metastatic potential of the tumor is exclusive of whether or not the patient undergoes radical or partial nephrectomy.[11] If this suggestion is correct, the benefit of sparing the healthy portion of the kidney is the same as in any other patient with RCC, although with a higher risk that systemic recurrence and death from disease may obviate such benefit. Regardless

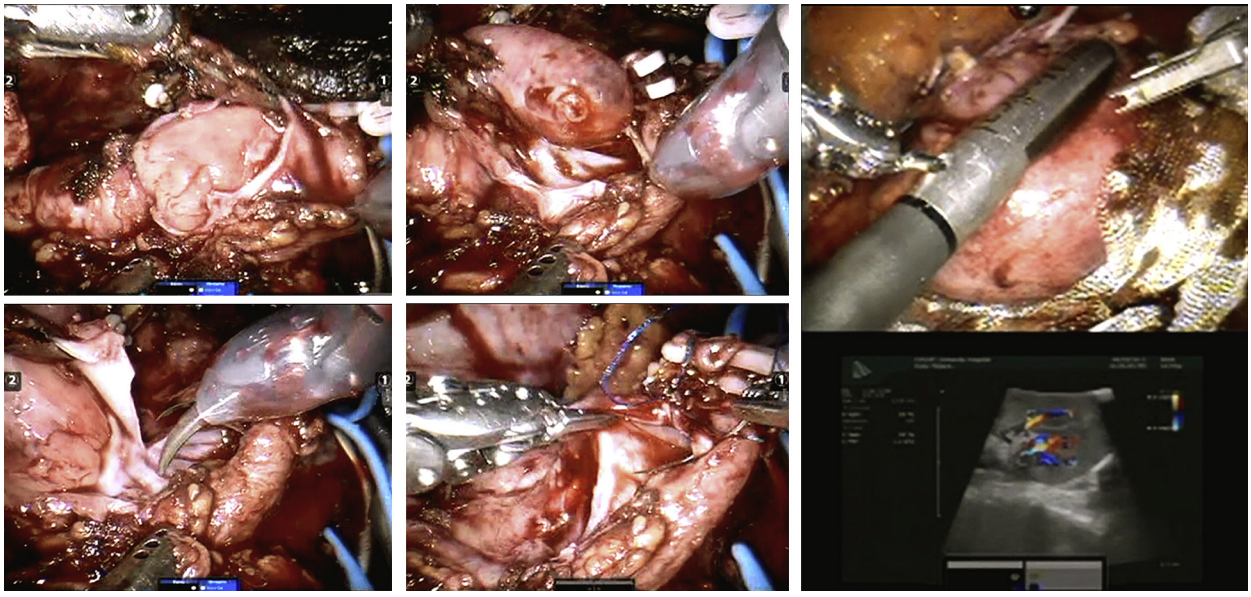

Figure 3. Intraoperative images of tumor thrombus in main renal vein, including incision in renal vein (upper left) to allow extraction of tumor thrombus intact (upper middle), excision of upper pole vein branch containing thrombus (lower left) to allow reconstruction of main renal vein (lower center), and Doppler ultrasound confirming vascular in and outflow in renal remnant (far right). (Color version available online.)

Table 1. Preoperative, postoperative, and pathologic results for each of 4 patients undergoing robotic partial nephrectomy with venous tumor thrombectomy

Variables	Patient #1	Patient #2	Patient #3	Patient #4
Age (y)	70	74	50	66
Body mass index (kg/m^2)	27	22	20	28
ASA score	3	3	3	2
Tumor size on imaging (cm)	3.9	4.9	8.5	11.0
RENAL nephrometry score	8a	9x	12h	10x
Venous thrombus extent	Vein branch	Vein branch	Main renal vein	Main renal vein
Preoperative serum creatinine (mg/dL)	0.77	0.83	0.65	1.32
Preoperative estimated GFR	106	96	103	58
Operative time (min)	230	227	250	392
Estimated blood loss (mL)	150	100	125	300
Warm ischemia time (min)	27.3	19.0	26.3	24.5
Closest resection margin (cm)	NR	0.2	0.1	<0.1
Postoperative serum creatinine (mg/dL)	1.31	0.94	0.85	1.96
Postoperative estimated GFR	57	83	75	37
6-mo serum creatinine (mg/dL)	1.25	1.10	0.74	1.31
6-mo estimated GFR	61	70	88	58
Length of stay (d)	1	1	1	1
Complications	Ileus	None	None	None
Maximum tumor dimension (cm)	4.3	4.6	9.3	12.8
Histology	Clear cell RCC	Clear cell RCC	Clear cell RCC	Papillary RCC
Fuhrman grade	2	4	4	4
Pathologic stage	pT3a	pT3a	pT3a	pT4

ASA, American Society of Anesthesiologists; GFR, glomerular filtration rate; NR, not reported; RCC, renal cell carcinoma; RENAL, radius, endophytic, nearness to collecting system, anterior/posterior, and location.

of whether or not further study will support the role of NSS in the setting of VTT, our novel series demonstrates the safety and feasibility of RPN for such patients as compared with the previously-described open approach.

CONCLUSION

NSS in the setting of RCC with venous tumor thrombi involving intraparenchymal veins or the main renal vein is feasible robotically in select patients. Given the higher likelihood of systemic recurrence in such patients with T3a disease, the role of nephron-sparing in elective situations is of uncertain benefit and remains controversial.

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EDITORIAL COMMENT

As utilization and experience with partial nephrectomy (PN) increases, expert surgeons find themselves offering nephron-sparing surgery for larger and potentially more aggressive tumors. This is relatively uncharted territory, as most oncological data on PN is derived from series of small renal masses.[1,2] In the current report, the authors document their early experience performing robot-assisted laparoscopic partial nephrectomy (RALPN) for 4 cases of renal cell carcinoma (RCC) with venous extension (2 cases with main renal vein and 2 with branch involvement).

The authors are to be congratulated for this report which clearly demonstrates the safety and feasibility of RALPN for RCC with renal vein involvement. It is important to note, however, that this report must be viewed only as a feasibility study and not as justification for the routine use of PN in this setting. As the authors mention, no study to date has rigorously studied the oncologic outcomes of PN for RCC with venous extension. Based on this report, we are left to question the efficacy of PN for such tumors. Notably, the authors found that 2 patients (50%) developed metastatic disease within just 1 year of surgery. One wonders how these patients would have fared had they received treatment with radical nephrectomy (RN) and lymphadenectomy. As a counterargument to this point, the authors hypothesize that PN with negative margins served as an adequate resection because of the fact that RCC with tumor thrombus is felt to spread predominantly by a hematogenous route. However, we feel this assertion is conjecture at best, as 1 large study (n = 537) found that 18% of patients with renal vein involvement harbored positive lymph nodes.[3] Given this finding, we suspect that a more radical approach may confer an oncologic advantage.

An interesting observation from this report is that the patients studied had normal renal function and therefore the indication for RALPN was elective. It is unclear why the authors would choose an oncologically untested technique in lieu of RN. This is especially relevant today in light of the findings of European Organization for Research and Treatment of Cancer (EORTC) 30904, which showed no survival advantage of PN over RN.[4]

In summary, this report demonstrates the safety and feasibility of RALPN for the resection of RCC with venous extension. Increasingly faced with more challenging renal tumors and patients enamored with the idea of saving nephrons, kidney cancer surgeons find themselves asking the question "just because I can, should I?" The answer to this question is not simple and warrants additional study. Until such studies are performed, RN remains the standard of care for locally advanced tumors.

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REPLY

While we admit that it is conjecture and have no evidence to support or refute it, we do not believe that patients who already have occult hematogenous micrometastatic disease (eg, lung) at the time of surgery would be cured by radical nephrectomy with or without node dissection. Therefore, the more pertinent question that should be raised by those who would advocate for nephrectomy even if partial nephrectomy can be performed adequately to achieve local control, is whether the additional manipulation of the tumor for nephron sparing might potentiate hematogenous dissemination.

In other words, is the tumor and/or thrombus manipulated more during partial nephrectomy as compared with radical nephrectomy, even though in nephrectomy the vein still has to be dissected completely for division? Could this lead to a higher risk of spread, even though the tumor thrombus has already been exposed to venous circulation sometimes for years before detection? We do not know, but it is certainly possible.

Although the question "just because I can, should I?" is wise and absolutely appropriate in this setting, we will not know if we should until we try. Our report only demonstrates feasibility. Oncologic efficacy or lack thereof cannot be determined from 4 patients. As in the early days of partial nephrectomy or even breast lumpectomy before robust data was available, patients

should be carefully counseled with open discussion of the current standard of care when other untested but feasible options exist. Most patients with renal vein thrombi during the time period reported were either not offered partial nephrectomy because they were not felt to be appropriate candidates or chose radical nephrectomy, as all 13 patients had normal renal function. Radical nephrectomy remains the standard of care.

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