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Robotic Partial *vs* Radical Nephrectomy for Clinical T3a Tumors: A Narrative Review

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Abstract

Introduction: T3a renal masses include a diverse group of tumors that invade the perirenal and/or sinus fat, pelvicaliceal system, or renal vein. The majority of cT3a renal masses represent renal cell carcinoma (RCC) and have historically been treated with radical nephrectomy (RN) given their aggressive nature. With the adoption of minimally invasive approaches to renal surgery, the combination of improved observation, pneumoperitoneum, and robotic articulation has allowed urologists to consider partial nephrectomy (PN) for more complex tumors. Herein, we review the existing literature regarding robot-assisted PN (RAPN) and robot-assisted RN (RARN) in the management of T3a renal masses.
Methods: A literature search was performed using PubMed for articles evaluating the role of RARN and RAPN for T3a renal masses. Search parameters were limited to English language studies. Applicable studies were abstracted and included in this narrative review.
Results: T3a RCC caused by renal sinus fat or venous involvement is associated with $\sim$50% lower cancer-specific survival than those with perinephric fat invasion alone. CT and MRI can both be used to stage cT3a tumors, however, MRI is more accurate when assessing venous involvement. Upstaging to pT3a RCC during RAPN does not confer a worse prognosis than pT3a tumors treated with RARN; however, patients who undergo RAPN for T3a RCC with venous involvement have relatively higher rates of recurrence and metastasis. Intraoperative tools including drop-in ultrasound, near-infrared fluorescence, and 3D virtual models improve the ability to perform RAPN for T3a tumors. In well-selected cases, warm ischemia times remain reasonable.
Conclusions: cT3a renal masses represent a diverse group of tumors. Depending on substratification of cT3a, RARN or RAPN can be employed for treatment of such masses.

Keywords: renal cancer, robotics, partial nephrectomy, renal mass, T3 renal cell carcinoma, radical nephrectomy

Introduction

Renal masses comprise a diverse group of tumors ranging from benign tumors to aggressive malignancies. The majority of renal masses will be malignant, even at small sizes, with clear cell histology analysis being the most common type. When intervention is indicated, the management of localized renal cell carcinoma (RCC) is predominantly surgical, either through partial nephrectomy (PN) or through radical nephrectomy (RN). In the case of small renal masses, PN is strongly preferred given excellent oncologic outcomes with the added benefit of nephron preservation.[1,2]

Although there are many considerations in how to perform PN including modality (open, laparoscopic, and robot-assisted) and approach (transperitoneal and retroperitoneal), robot-assisted partial nephrectomy (RAPN) is now the most common surgical approach in the United States.[3]

Although clinical T1 (cT1) and cT2 RCC, by definition, are only differentiated by size, cT3 RCC comprises a more heterogeneous group of renal masses. Although organ-

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confined RCC carries a 5-year cancer-specific survival (CSS) of up to 90% (cT1–T2), this decreases to 75% to 80% for tumors involving perinephric fat[4] and, even worse, approaches 50% with venous involvement.[5] As such, most cT3 renal masses have been classically managed with RN. Oncologic outcomes, however, must be carefully weighed against functional outcomes, as RN increases the risk of chronic kidney disease (CKD) and may exclude some patients from necessary systemic therapy.

In select patients with T3a renal masses and pre-existing proteinuria or CKD, or an anatomic or functional solitary kidney, PN is more imperative and should be considered. RAPN of these more complex tumors can be challenging and associated with a higher risk of perioperative complications.[6] In this article, we aim to review the existing literature regarding the use of RAPN and robot-assisted radical nephrectomy (RARN) in the treatment of cT3a renal masses.

Staging of cT3a Renal Tumors

cT3a renal masses are defined by invasion into the perinephric fat, renal sinus fat, pelvicaliceal system, and/or renal veinous system (Fig. 1). In earlier classification systems, tumors with direction extension into the ipsilateral adrenal gland were also considered cT3a renal tumors, but this was later changed to T4 disease in the seventh edition American Joint Committee on Cancer TNM Staging System given significantly worse oncologic outcomes in this population.[7] This underscores the critical nature of accurate clinical staging given the impact it has on surgical decision making.

Although all patients with solid renal masses require multiphase cross-sectional imaging, either with CT or with MRI, there are some differences in the diagnostic accuracy of CT and MRI when assessing T3a tumors, specifically. The specificity and sensitivity of CT in detecting perinephric fat invasion are 32% to 96% and 85% to 93%, respectively.[8] MRI is slightly more sensitive in detecting perinephric invasion than CT because of a more visible capsule on fat-subtraction images, but similarly lacks specificity.[9] CT has a sensitivity of 71% to 88% in detecting renal sinus fat invasion, whereas its ability to detect renal vein involvement ranges from 59% to 69%.[10] Large right-sided tumors can distort the short right renal vein and make clear delineation of the renal vein–vena cava interface difficult on CT. Conversely, MRI offers superior soft tissue resolution using T2-weighted and diffusion-weighted imaging sequences, which improves the sensitivity to 64% to 89% in detecting tumor thrombi.[11] MRI is also better able to differentiate between bland and tumor thrombus. For these reasons, it is generally prudent to obtain an MRI when there is suspicion for renal vein invasion.

Oncologic Outcomes Based on Subclassification of T3a Renal Tumors

In contrast to the size-driven designation of T1 and T2 RCC, T3 classification is based on anatomic extension alone, as mentioned above. Yet, there is still evidence to support tumor size as an important prognostic factor in T3a disease. Patients with resected T3a RCC ≤7 cm have a 5-year disease-specific survival (DSS) of 63%, whereas DSS decreases to only 46% when tumor size is >7 cm.[12] In patients with T3a RCC secondary to fat invasion only, each 1 cm increase in tumor size is associated with a 9% decrease in DSS.[12]

In light of the homogeneous categorization, quite heterogeneous outcomes are noted among the various cT3a subtypes. Patients with sinus fat involvement are at 1.47 times higher risk of RCC-related death than those with perinephric fat invasion alone,[13] which may be because of increased access to the venous system. Venous involvement was historically thought to be a poor prognosticator, with main renal vein involvement carrying a worse prognosis than segmental vein invasion alone.[14] However, recent reports have demonstrated acceptable outcomes assuming the primary tumor is confined to the kidney and negative surgical margins are obtained.[5]

This supports other work that has demonstrated that the metastatic potential of RCC with tumor thrombi is quite heterogeneous and invasion not universally driven by the most aggressive clone.[15] The metastatic potential of RCC remains incompletely understood and further research may provide insight into subpopulations that may derive maximal benefit from RAPN as compared with RARN. Unsurprisingly, T3a tumors with multiple patterns of extension (i.e., renal vein thrombus and perinephric fat invasion) are associated with an increased risk of disease progression and

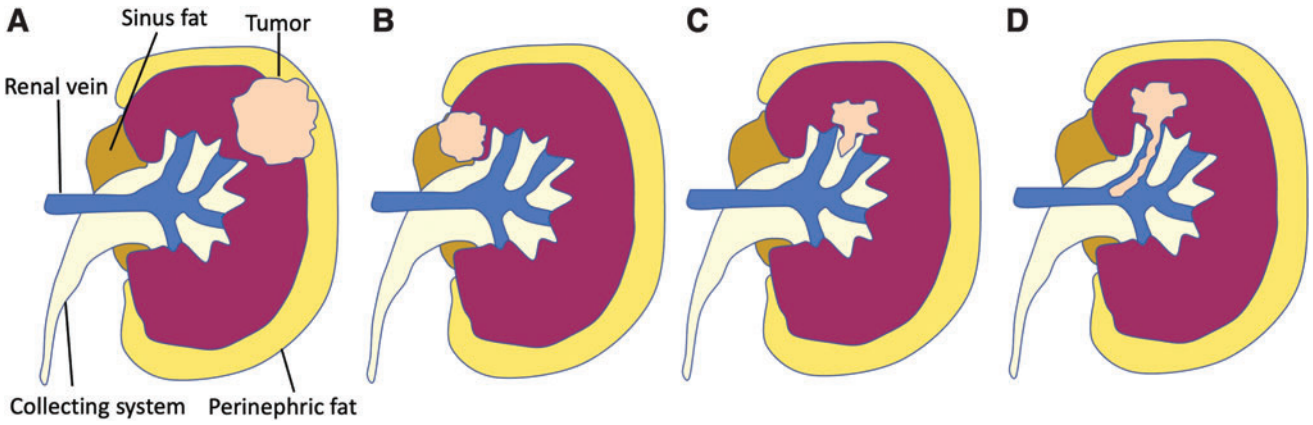

FIG. 1. Subclassification of T3a renal tumors. **(A)** Perinephric fat invasion, **(B)** renal sinus fat invasion, **(C)** collecting system invasion, **(D)** segmental or main renal vein invasion. Color images are available online.

cancer-related death after surgery, and, therefore, should be managed more aggressively.[16]

Given the diversity of cT3a renal masses, it is critical that physicians consider anatomic patterns of extension and the ability to achieve a negative margin when counseling patients on surgical options (RAPN or RARN).

Oncologic Outcomes After RN and PN for cT3a Tumors

Open RN has traditionally been the preferred treatment for most patients with cT3 renal masses with an average 5-year CSS of 80% in a large review of >18,000 patients with T3a, T3b, and T3c tumors.[17] Beginning in the 1990s, laparoscopic radical nephrectomy (LRN) was adopted as an acceptable alternative to open RN, demonstrating equivalent oncologic outcomes for T3 RCC.[18] Although there was some initial concern that minimally invasive RN could result in port site metastases, these are quite rare and felt to be an indicator of overall disease progression rather than an isolated result of surgical technique.[19]

The use of RARN in the United States has been increasing 11.8% annually since 2004, whereas the use of LRN has been decreasing 5.5% annually.[20] In a study comparing 941 patients with ≥cT2 renal masses undergoing RARN or LRN, of whom 18% were cT3 specifically, RARN and LRN were associated with equivalent overall survival (OS) and recurrence-free survival (RFS). More patients who underwent RARN *vs* LRN had hilar tumors (28% *vs* 10%) and ≥cT3 tumors (21% *vs* 16%), suggesting that surgeons prefer the robotic approach for more complex and high-risk tumors.[20]

Much of our knowledge regarding the oncologic efficacy of PN for T3a RCC stems from patients with pathologic upstaging from T1/T2 to T3, which ranges from 6% to 13%.[21,22] Factors associated with upstaging to T3a including patient age, tumor size, central tumor location, and Fuhrman grade.[23] OS is 13% to 26% lower in patients who have cT3a renal tumors compared with those who are upstaged from cT1 to pT3a renal tumors at the time of surgery,[24] likely because of the grossly more advanced nature of disease visible on preoperative imaging.

Compared with RN, PN does not jeopardize cancer control in those with upstaged pT3a RCC.[25–28] In fact, two studies have suggested that PN may confer an RFS advantage.[26,27] This may be because of selection bias or increased opportunity to receive adjuvant therapy caused by preserved renal function. Although the data support the safety of RAPN in T3a tumors, it should be interpreted with caution as tumor size, location, type of T3a disease (vascular *vs* sinus invasion *vs* perinephric invasion *vs* multiple), and surgeon comfort/ability should drive surgical decision making. Ultimately, complete resection with negative margins is the most important outcome to achieve.

Several studies specifically assessing the role of RAPN for T3a tumors have been published (Table 1).[29–34] A large single-institution retrospective series compared 140 patients who underwent RAPN or RN in a matched-control manner.[30] At a median follow-up duration of 20 months, there was no difference in OS, CSS, or RFS, and the only factor associated with increased mortality on multivariable analysis was ≥2 aggressive tumor features (positive margin, necrosis, lymphovascular invasion, Grade ≥3, or presence of sarcomatoid elements). Another study retrospectively compared patients who underwent RAPN or open PN for pT2 or pT3 RCC.

Of the 35 patients reviewed, 26 had pT3a renal tumors.[33] There was no difference in the positive margin rate or local RFS between RAPN and open PN, though ischemia time, complication rates, and length of stay all favored RAPN. Yim et al. recently published a multi-institutional study from the Robotic Surgery for Large Renal Mass (ROSULA) collaborative group of 157 patients undergoing RAPN for cT3a renal masses.[32]

In this group, the median tumor size was 7 cm and 66% of tumors were cT3a because of extension into the renal sinus or perinephric fat. Ninety-six percent of patients achieved negative margins, and 5-year RFS, CSS, and OS rates were 82%, 93%, and 91%, respectively. These survival rates are similar to those in studies evaluating upstaged pT3a RCC, and suggest that with adequate surgical planning, outcomes are acceptable despite clinically evident aggressive growth patterns of cT3a tumors.

Given the diversity of cT3a tumors, researchers have investigated the role of RAPN specifically in patients with T3a tumors secondary to venous involvement. Abaza and colleagues first reported on RAPN for T3a tumors with venous involvement in 2013.[29] This included three patients with only T3a disease and one patient who was pT4 because of liver involvement. Despite negative margins in all patients, two of the four patients developed metastatic disease within 6 months. A more recent study by Morgan and colleagues evaluated 45 patients who underwent RAPN for pT3a tumors secondary to venous involvement, of whom only 25% had suspected T3a disease based on preoperative imaging.[34]

The positive margin rate was 6.7% and after a median follow-up duration of 29 months, two patients developed a local recurrence and four developed distant metastases. Two years local RFS and metastasis-free survival was 95.4% and 95.3%, respectively. The relatively high rate of both local and distant recurrence in patients with pT3a RCC secondary to renal vein involvement undergoing PN is not surprising given the potential for hematogenous spread.

Renal Function Preservation After PN and RN for T3a Tumors

The implications of developing CKD are broad and severe. Risk factors for CKD, such as hypertension and diabetes, are common in patients with RCC, and thus, many patients before intervention already have some level of nephron impairment. Preoperative CKD stage 3 and above has been shown to be an independent risk factor for survival in patients undergoing renal surgery.[35] Nevertheless, although several retrospective studies have shown a lower incidence of CKD and overall mortality in patients with renal masses undergoing PN compared with RN, the landmark EORTC 30904 trial, in which patients with T1–T2 tumors ≤5 cm were prospectively randomized to RN or PN, showed that 10-year OS was 5% higher in the RN group and cardiovascular deaths were also less common.[36–38]

Although the EORTC study had multiple limitations, including low accrual, no information on the quality/extent of parenchyma resected in the PN group, and high rate of crossover (15% planned PN received RN), we did learn that PN reduced the incidence of moderate CKD (stage 3) but had

TABLE 1. REPORTS OF ROBOT-ASSISTED PARTIAL NEPHRECTOMY FOR cT3a MASSES OVER THE PAST 10 YEARS (SINCE 2012)

Reference	*Total number/ number with cT3a*	*Pathologic staging details*	*Treatment*	*Tumor size*	*Survival/recurrence*	*Change in renal function*	*Follow-up, months*
Abaza and Angell (2013)	4/3	4 (100%) pT3a (all with venous involvement)	4 (100%) underwent RAPN	7.8 cm[a]	2 (50%) developed metastases	ΔeGFR 6 months postoperatively: −21.5 mL/min/m^2	9.4[b]
Andrade et al. (2017)[30]	140/NR	140 (100%) pT3a	70 (50%) underwent RAPN 70 (50%) underwent RN	3.8 cm[b] (RAPN) 4.7[b] (RN)	3-years OS 90% (RAPN) *vs* 84% (RN), $p=0.4$ 3-years CSS 94% (RAPN) *vs* 95% (RN), $p=0.8$ 3-years RFS 95% (RAPN) *vs* 100% (RN), $p=0.03$	Renal preservation 86% (RAPN) *vs* 70% RN, $p<0.001$	20[b]
Marra et al. (2018)[31]	2549/NR	821 (3.2%) pT3a	42 (1.6%) underwent PN 2507 (98.4%) underwent RN	5.3 cm[a] (PN) 7.3 cm[a] (RN)	5-years OS 57% (PN) *vs* 46% (RN), $p=0.19$ 5-years CSS 71% (PN) *vs* 52% (RN), $p=0.02$[c]	ΔeGFR 9 months postoperatively: −27% (PN) *vs* −41% (RN), $p=0.13$	27.3[b]
Yim et al. (2021)[32]	157/157	157 (100%) cT3a	157 (100%) underwent RAPN	7.0 cm[b]	5-years OS 91.3% 5-years CSS 92.3% 5-years RFS 82.1%	ΔeGFR 12 months postoperatively: −7 mL/min/m^2	26[b]
Beksac et al. (2022)[33]	35/NR	26 (74%) pT3a	20 (57.1%) underwent RAPN 15 (42.9%) underwent OPN	5.8 cm[b] (RAPN) 6.0 cm[b] (OPN)	3 (8.6%) developed local recurrence 4 (11.4%) developed metastases	79% eGFR preservation at 1 year in RAPN group	21.1[b]
Morgan et al. (2022)[34]	45/11	43 (100%) pT3a (all with venous involvement)	45 (100%) underwent RAPN	4.3 cm[a]	2 years local RFS 95.4% 2 years MFS 95.3%	ΔeGFR 25 months postoperatively: −6.6 mL/min per m^2	28.5[b]

[a]Values reported as mean.
[b]Values reported as median.
[c]Results not significant after matching.
CSS = cancer-specific survival; eGFR = estimated glomerular filtration rate; MFS = metastasis-free survival; NR = not recorded; OPN = open partial nephrectomy; OS = overall survival; PN = partial nephrectomy; RAPN = robot-assisted partial nephrectomy; RFS = recurrence-free survival; RN = radical nephrectomy.

similar rates of severe CKD (stages 4 and 5) as RN. Taken together, although most healthy patients with a functional contralateral kidney will have acceptable renal function after RN, nephron-sparing approaches should be considered when feasible and oncologically sound for those with pre-existing CKD or risk factors for development of CKD.

With that said, CKD caused by surgical removal of nephrons has been shown to be different than CKD caused by medical causes and is associated with less CKD progression and improved survival.[39] This conceptually makes sense given that surgical CKD results in fewer but functional filtration units as compared with more numerous, but diseased, filtration units. A recent meta-analysis assessed renal functional outcomes in T3a tumors and found that renal function, as assessed through estimated glomerular filtration rate (eGFR), was improved in patients undergoing PN for T3a renal tumors as compared with RN (weight mean difference 12.48 mL/min).[40]

In patients wherein there is concern for significant postoperative renal dysfunction, validated equations can be used to predict postnephrectomy GFR.[41] In the case of asymmetric kidneys on preoperative cross-sectional imaging, a renogram may be useful in determining differential function. Patients with a high risk of CKD progression after surgery, as evidenced by a preoperative GFR <45, proteinuria, CKD in the setting of diabetes, or if postoperative GFR is expected to be <30, should be referred to nephrology preoperatively to assess risk of CKD progression and address any modifiable risk factors.[42]

Surgical determinants of renal function after PN include the number of nephrons spared (maximal parenchymal preservation) and the duration of warm ischemia time (WIT). The use of enucleation for complex tumors has been associated with greater renal function preservation compared with a wide margin resection.[43] Furthermore, more peripherally located and lower complexity tumors have also been associated with improved postoperative renal function.[44] This may stem from the potential for ischemia-related parenchymal loss as part of the renorrhaphy.

With regard to ischemia, WIT is recommended to be limited to 25 to 30 minutes if possible.[45] Although performing an off-clamp or selectively clamped RAPN is possible in certain situations, T3a tumors are often centrally located and may be best excised under complete ischemia. This allows for a relatively bloodless field and optimized observation during resection (optimizing the potential for negative margins), as well as guards against the possibility of tumor thrombus embolism.

Although laparoscopic PN for central tumors is associated with a longer WIT than for peripheral tumors, a multicenter study of 157 RAPNs for cT3a renal masses, of which 22% had venous involvement, reported a median WIT of 19 minutes.[32] There was only a 7 mL/min per 1.72 m^2 median decrease in eGFR, and 55% of patients had a ≥90% preservation of eGFR. Additional studies on RAPN for T3a tumors secondary to venous invasion report WITs of 9 to 30 minutes.[29,34] These data support the notion that RAPN for T3a tumors can be performed without prolonged ischemia or significant postoperative compromise of renal function.

Technical Considerations of RAPN for T3a Tumors

RAPN for complex T3a renal masses can be challenging and surgeons should be aware of the techniques and tools available when attempting such cases. First and foremost, a thorough review of preoperative imaging is essential to understanding the anatomic relationship of the tumor and other structures. Tumors can be approached transperitoneally or retroperitoneally based on patient and tumor factors and surgeon preference. A transperitoneal approach is likely more familiar to most surgeons and allows increased working space and better access to the renal vein for tumors with venous involvement. Multiple adjunctive tools, including intraoperative ultrasound with small drop-in probes, virtual 3D anatomic models, near-infrared fluorescence (NIRF), and TilePro™,[46–49] can better facilitate RAPN for complex tumors.

Early and frequent use of intraoperative ultrasound is critical to delineate the location of the tumor and characterize the tumor's interface with perinephric fat, renal sinus fat, and renal vasculature. Both laparoscopic and drop-in robotic ultrasound probes exist, however, the smaller drop-in probes allow greater rotational mobility and improved surgeon autonomy.[46] When there is concern for perinephric fat involvement on preoperative imaging, ultrasound is helpful in determining the tumor location before incising Gerota's fascia to leave some of the perinephric fat on top of the tumor in the case of RAPN.

Intraoperative ultrasound is also useful in identifying the extent of tumor thrombus in the renal vein either for clamping in the case of RAPN or for ligation in the case of RARN. The operating room team should be well versed in using the ultrasound machine, as often, the overall gain or time-gain compensation need to be adjusted to better observe deeper structures such as renal sinus fat.

There is an increasing interest in the use of 3D virtual models (VMs) in augmenting intraoperative ultrasound, improving preoperative surgical planning/counseling, and assisting in intraoperative navigation and decision making. Three-dimensional VMs utilize the preoperative CT or MRI to generate a 3D virtual reconstruction of the kidney, tumor, kidney vasculature, and collecting system. The VM can then be viewed and manipulated by the surgeon at the console intraoperatively and the transparency of the anatomic structures can be adjusted to provide cognitive fusion.

Surgeons report better spatial orientation and understanding of the anatomy when using a 3D VM, and it impacts the decision to perform an RAPN or RARN in 20% of cases.[47] A randomized controlled trial showed that the use of an intraoperative 3D VM decreased intraoperative blood loss, but not operative or clamp times when performing RAPN.[50] The utility of 3D VMs in cT3a tumors remains to be defined.

NIRF utilizes an NIR camera specific to a wavelength of 700 to 1000 nm and a fluorescent dye such as indocyanine green (ICG) that allows preferential fluorescence of well-vascularized structures. NIRF can be used to confirm complete ischemia if the main renal artery is clamped or to guide selective clamping by confirming that the tumor to be excised is not fed by any other arterial branches aside from the one being clamped.[51] Although many cT3a tumors are centrally located and not typically amenable to selective clamping, NIRF may prove useful in intraoperative assessment of margin status during resection.

As ICG binds the transmembrane protein bilitranslocase, which is expressed in normal proximal convoluted tubules but not malignant tissue, normal renal parenchyma fluoresces

under NIR, but malignant tissue does not.[52] Differential fluorescence is noted in 90% of RCC and 72% of oncocytomas.[53] To use differential fluorescence for this purpose, 0.25 to 0.5 mL of ICG is administered before clamping the artery. During resection, one can use NIRF to help confirm that the tumor margin fluoresces green, and, therefore, represents nonmalignant renal parenchyma. In one single-surgeon series of 361 RAPNs, the use of NIRF resulted in a 0.33% positive margin rate.[53] When using NIRF to confirm ischemia, a larger dose of ICG (1.5–2.5 mL) is administered after clamping the artery.

RAPN for T3a tumors because of venous involvement provides a unique challenge given the vascular involvement. Small tumor thrombi in intraparenchymal veins can often simply be excised with the tumor and the vein closed as part of the renorrhaphy. If there is invasion into a subsegmental or segmental vein, the main renal vein is dissected out to the segmental branches, and the tumor-containing vein branch is clipped, cut and oversewn, or stapled. Thrombus extending into the main renal vein necessitates a more complex resection and reconstruction.

Intraoperative ultrasound should be used to delineate the distal extend of the thrombus and the vein should be clamped distal to this point with enough space between the clamp and thrombus to allow for reconstruction. Clamping the renal vein also helps avoid a CO_2 embolism while the tumor-containing venous branch is open. When opening the main renal vein, all additional nonrenal venous branches should be controlled before opening the vein. For a left renal vein thrombus, the left adrenal and gonadal vein should be ligated or clamped to avoid blood loss during thrombectomy. In addition, the renal vein should be incised longitudinally and the tumor thrombus removed en bloc with the tumor.[29] The renal vein can then be repaired with a fine nonabsorbable monofilament suture such as polypropylene.

Conclusions

T3a renal masses represent a diverse group of tumors that should be approached on an individual basis, taking into account clinical characteristics and surgeon experience/expertise. Although MRI does not provide much benefit over CT in detecting perinephric or sinus fat invasion, it is preferred when evaluating for a tumor thrombus. Oncologic outcomes for T3a RCC treated with RAPN are acceptable provided a negative margin can be obtained, however, cT3a RCC secondary to renal vein invasion carries a higher recurrence risk. Improved stratification of these diverse tumors using clinical parameters or biomarkers will hopefully further improve our ability to counsel patients in the role of RARN and RAPN in T3a renal masses.

Authors' Contributions

T.E.S. contributed to conceptualization, methodology, investigation, data curation, writing—original draft, writing—review and editing, and project administration.

P.T.G. was involved in investigation, writing—original draft, and writing—review and editing.

C.R.T. carried out investigation, writing—original draft, and writing—review and editing.

R.L.S. was in charge of conceptualization, methodology, writing—original draft, writing—review and editing, and supervision.

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Abbreviations Used

CKD = chronic kidney disease
CSS = cancer-specific survival
CT = computed tomography
cT1 = clinical T1
DSS = disease-specific survival
eGFR = estimated glomerular filtration rate
ICG = indocyanine green
LRN = laparoscopic radical nephrectomy
MFS = metastasis-free survival
MRI = magnetic resonance imaging
NIRF = near-infrared fluorescence
NR = not recorded
OPN = open partial nephrectomy
OS = overall survival
PN = partial nephrectomy
RAPN = robot-assisted partial nephrectomy
RARN = robot-assisted radical nephrectomy
RCC = renal cell carcinoma
RFS = recurrence-free survival
RN = radical nephrectomy
VM = virtual model
WIT = warm ischemia time