


# Recent Advances in the Management of Localized and Locally Advanced Renal Cell Carcinoma: A Narrative Review

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**Purpose:** To review the current status of surgical and procedural treatments for renal cell carcinoma (RCC), focusing on oncological and functional outcomes, and the use of techniques for advanced disease over the last 10 years.

**Findings:** Partial nephrectomy (PN) has become the reference standard for most T1 and T2 masses. In cT2 RCC, PN exhibits oncological equivalence and improved functional outcomes compared to radical nephrectomy (RN). Additionally, emerging data suggest that PN may be used to treat cT3a RCC. The robot-assisted platform is increasingly used to treat locally advanced RCC. Studies suggest safety and feasibility of robotic RN and robotic inferior vena cava tumor thrombectomy. Additionally, single-port robot-assisted laparoscopic approaches are comparable to multiport approaches in select patients. Long-term data show that cryoablation, radiofrequency ablation, and microwave ablation are equipotent in management of small renal masses. Emerging data suggest that microwave may effectively treat cT1b masses.

**Keywords:** renal cell carcinoma, cryoablation, nephrectomy, microwave ablation, partial nephrectomy, radiofrequency ablation

## Introduction

According to the World Health Organization (WHO), 431,288 new cases of renal cell carcinoma (RCC) were diagnosed in 2020. This makes RCC the 14th–most commonly diagnosed cancer and third amongst urological malignancies.<sup>1</sup> Historically, radical nephrectomy (RN) has been the cornerstone and standard of care for treating localized RCC. Emerging data increasingly suggest that partial nephrectomy (PN) is oncologically equivalent to RN in most localized RCC and may provide benefit from nephron preservation.<sup>2–7</sup> Furthermore, ablative strategies have emerged as a robust alternative to surgical excision in small renal masses.<sup>8–10</sup> This review discusses advances in surgery, ablation, and minimally invasive surgery (MIS).

## Methodology

We performed PubMed (<http://www.ncbi.nlm.nih.gov/pubmed>) searches with the keywords “partial nephrectomy”, “radical nephrectomy”, “T2”, “T3a”, “minimally invasive surgery”, “open”, “IVC tumor thrombectomy”, “nephrometry”, “single-port”, “multi-port”, “radiofrequency ablation”, “cryoablation”, “T1a”, “microwave ablation”, “T1b”, and “tumor histology” over the last 10 years. Due to limited data, we expanded our search to the past 20 years for robotic inferior vena cava (IVC) tumor thrombectomies. We selected articles that discussed oncological outcomes, functional outcomes, complication rates, and patient-satisfaction outcomes. We excluded case reports and articles not meeting these selection criteria.

## Surgical Advances

### Emergence of Minimally Invasive Partial Nephrectomy as Reference Standard for cT2 Tumors [Table 1]

PN has become established as the preferred definitive method of management for T1a and T1b tumors using both minimally invasive and open approaches. In recent years, emerging reports have shown that in T2 RCC, PN is equivalent to RN in oncological outcomes and superior in functional outcomes. Nonetheless, historical series and meta-analyses utilizing historical data have demonstrated significantly increased risk of complications or PN in the T2 setting when compared to RN. These data were based on primary open-approach PN.<sup>2,11–14</sup> Contemporary analyses with robot-assisted PN (RAPN), however, suggest a decreased morbidity profile while maintaining oncological equipoise and functional benefit for PN. Bertolo et al compiled a series of 298 patients with cT2a tumors who underwent PN with a median follow-up of 12 months. They reported all-cause mortality (ACM) of 3.3%, cancer-specific mortality (CSM) of 0.8%, and a recurrence rate of 10%. Functionally, these patients did have a statistically significant decrease in estimated glomerular filtration rate (eGFR) at discharge (17.5%,  $p<0.001$ ). However, by 1 year, their eGFR had recovered such that there was no significant difference from the original preoperative values ( $p=0.2$ ).<sup>15</sup> Bradshaw et al performed the first study examining outcomes in a pure MIS series, performing a propensity score–matched comparison of 648 patients with cT2a tumors who underwent either RAPN (216 patients) or MIS-RN (432 patients). The authors noted that surgery type was not an independent predictor of ACM ( $p=0.601$ ) or recurrence ( $p=0.555$ ). Furthermore, type of surgery was not associated with a significant difference in 5-year overall survival (OS; PN 76.3% vs RN 88.0%,  $p=0.2221$ ) or 5-year disease-free survival (DFS; PN 78.6% vs RN 85.3%,  $p=0.630$ ) for those who had pT2 masses. Nonetheless, while the authors noted that PN had a higher rate of positive surgical margins (PSMs) than RN (8.3% vs 2.6%,  $p=0.001$ ), the presence of PSM was not a predictor of ACM ( $p=0.423$ ) or recurrence ( $p=0.831$ ). RAPN did not result in a significantly higher rate of intraoperative complications (6.9% vs 5.3%,  $p=0.478$ ), major (Clavien–Dindo grade  $\geq$ III) complications (5.3% vs 2.3%,  $p=0.063$ ), or 30-day readmissions (0.9% vs 2.5%,  $p=0.238$ ).<sup>16</sup> Amparore et al examined 116 patients with cT2 RCC who underwent PN (52 patients) or RN (64 patients). They found 5-year other-cause mortality (OCM) rates of 5.1% (PN) vs 6.6% (RN;  $p=0.9$ ), 5-year CSM rates of 7.7% (PN) vs 16.7% (RN;  $p=0.08$ ), and 5-year progression-free survival (PFS) rates of 92.2% (PN) vs 72.8% (RN;  $p=0.02$ ). Surgery type was not independently associated with OCM ( $p=0.6$ ), CSM ( $p=0.9$ ), or PFS ( $p=0.7$ ). There was no significant difference in the rates of PSM between the PN and RN cohorts (1.9% vs 3.1%,  $p=0.5$ ). Furthermore, RAPN was not associated with a significantly higher rate of intraoperative transfusion (5.8% vs 4.7%,  $p=0.9$ ) or major (Clavien–Dindo grade  $\geq$ III) complications (1.9% vs 0,  $p=0.07$ ).<sup>17</sup> Overall, these studies show that PN is equivalent to RN for cT2 tumors in terms of oncological outcomes and superior in terms of preserving renal function.

### Partial Nephrectomy for T3a Renal Masses [Table 1]

Extracortical extension of renal malignancy into the venous or collecting systems or perinephric or renal sinus fat (T3 RCC) have historically been viewed as a definitive indication for RN. Recent reports have examined feasibility and short-term outcomes of PN in T3a RCC. Yim et al analyzed 157 patients who underwent PN for cT3a renal masses. A total of 150 patients (95.5%) had negative margins. The 5-year recurrence-free survival (RFS), cancer-specific survival (CSS), and OS were 82.1%, 93.3%, and 91.3%, respectively. The median change in eGFR was 7 mL/min/1.72 m<sup>2</sup>, and 55.4% of patients preserved  $\geq$ 90% of their eGFR. Failure to achieve the optimal outcome of negative surgical margins, warm ischemia time  $<$ 25 minutes, no perioperative complications, and  $\geq$ 90% eGFR preservation was associated with increasing age (OR 1.05,  $p<0.001$ ), increasing BMI (OR 1.07,  $p=0.035$ ), diabetes (OR 2.55,  $p=0.025$ ), increasing RENAL nephrometry score (RNS) (OR 1.25,  $p=0.018$ ), decreasing preoperative eGFR (OR 1.03,  $p=0.001$ ), increasing operative time (OR 1.01,  $p=0.012$ ), and estimated blood loss (EBL)  $>$ 300 mL (OR 5.04,  $p=0.005$ ).<sup>18</sup> Additionally, Andrade et al compared patients with pT3a RCC who underwent RAPN or RARN. There were 70 patients in each cohort. Renal function preservation was significantly higher in the PN cohort (86% vs 70%,  $p<0.001$ ). The estimated 3-year OS (90% vs 84%,  $p=0.42$ ), CSS (94% vs 95%,  $p=0.78$ ), and RFS (95% vs 100%,  $p=0.06$ ) were similar in the PN and RN cohorts.<sup>19</sup>

**Table 1** Advances in minimally invasive partial nephrectomy

Authors	Patient population	Tumor stage/RNS	Follow-up	OS/ACM/perioperative complication rate	CSS/CSM/postoperative complication rate	RFS/Recurrence	Functional outcomes
Bradshaw et al <sup>16</sup>	648 (216 PN, 432 RN)	cT2a	34 months (median)	ACM at last follow-up: HR 0.78, $p=0.601$ (RN/PN reference)	—	Recurrence at last follow-up: HR 1.28, $p=0.555$ (RN/PN reference)	De novo eGFR <60: HR 2.35, $p<0.001$ (RN/PN reference)
Amparore et al <sup>17</sup>	116 (52 PN, 64 RN)	cT2	46 months (median)	5-year OCM: HR 0.6, $p=0.6$ (PN/RN reference)	5-year CSM: HR 0.9, $p=0.9$ (PN/RN reference)	5-year PFS: HR 0.7, $p=0.7$ (RN/PN reference)	Median $\Delta$ eGFR 1 year: $-6.2$ (PN) vs $-24.2$ (RN), $p=0.001$
Bertolo et al <sup>15</sup>	298 (all PN)	cT2a	12 months (median)	ACM at last follow-up: 10 cases (3.3%)	CSM at last follow-up: 2 cases (0.8%)	Recurrence at last follow-up: 25 cases (10%)	Median $\Delta$ eGFR at discharge: $-17.5\%$ , $p<0.001$
Yim et al <sup>18</sup>	157 patients (all PN)	cT3a	26 months (median)	5-year OS: 91.3%	5-year CSS: 93.3%	5-year RFS: 82.1%	$\Delta$ eGFR 12 months postoperative: $-7$ mL/min/m <sup>2</sup>
Andrade et al <sup>19</sup>	140 (70 PN, 70 RN)	pT3	20 months (median)	3-year ACM: HR 2.48, $p=0.27$ (RN/PN reference)	3-year CSS: 94% (PN) vs 95% (RN), $p=0.78$	3-year RFS: 95% (PN) vs 100% (RN), $p=0.06$	Postoperative to preoperative eGFR: 86.0% (PN) vs 70% (RN), $p<0.001$
Patel et al <sup>20</sup>	929 (686 RN, 243 PN)	pT3	48 months (mean)	ACM at last follow-up: HR 0.84, $p=0.041$ (PN/RN reference)	—	Recurrence at last follow-up: HR 0.31, $p=0.076$ (PN/RN reference)	$\Delta$ eGFR at last follow-up: $-6.1$ (PN) vs $-19.4$ (RN), $p<0.001$
Shvero et al <sup>21</sup>	134 (48 PN, 86 RN)	pT3a	Median: 50.1 months	5-year ACM: $p=0.974$	5-year CSM: $p=0.626$	5-year local recurrence: $p=0.978$	5-year $\Delta$ creatinine: 0.37 mg/dL (RN) vs 0.06 mg/dL (PN), $p=0.107$
Maurice et al <sup>22</sup>	276 (138 RN, 138 PN)	pT3a	Median: 68 months	5-year ACM: HR 0.54, $p=0.01$ , (PN/RN reference)	—	—	—
Ghali et al <sup>23</sup>	150 PNs (59 robotic, 91 open)	cT2a	Median: 35 months	Median EBL (mL): 100 (MIS) vs 200 (O), $p=0.015$ Median warm IT (mins): 26 (MIS) vs 21 (O), $p=0.512$	30-day Clavien $\geq 3$ CR: 5.1% (MIS) vs 16.2% (O), $p=0.041$	—	Median $\Delta$ eGFR at last follow-up $-6.2$ (MIS) vs $-7.8$ (O), $p=0.543$
Malkoc et al <sup>24</sup>	110 PNs (54 robotic, 56 open)	cT2a or greater	—	Median EBL (mL): 250 (MIS) vs 300 (O), $p=0.014$ Median IT (mins): 31.5 (MIS) vs 35 (O), $p=0.02$	30-day Clavien grade $\geq 3$ CR: 3.7% (MIS) vs 12.5% (O) ( $p=0.16$ )	—	Median eGFR preservation: 82.7% (MIS) vs 82.2% (O) ( $p=0.83$ )
Kim et al <sup>25</sup>	149 (64 open, 85 robotic)	R.E.N.A. L. $\geq 10$	Median: 30 months	Median EBL (mL): 200 (MIS) vs 200 (O), $p=0.888$ Median IT (mins): 24 (MIS) vs 21 (O), $p=0.147$	90-day Clavien grade $\geq 3$ CR: 11.8% (MIS) vs 18.8% (O), $p=0.438$	—	Mean $\Delta$ eGFR $-6.5$ (MIS) vs $-3.8$ (O), $p=0.351$

**Abbreviations:** RNS, RENAL nephrometry score; OS, overall survival; ACM, all-cause mortality; CSS, cancer-specific survival; CSM, cancer-specific mortality; RFS, recurrence-free survival; PFS, progression-free survival; PN, partial nephrectomy; RN, radical nephrectomy; eGFR, estimated glomerular filtration rate (mL/min/1.73 m<sup>2</sup>); MIS, minimally invasive surgery; O, open; CR, complication rate; IT, ischemia time; TR, transfusion rate.

Several studies have analyzed outcomes of patients who were pathologically upstaged from cT1–2 to pT3a. Patel et al analyzed 929 such patients who underwent either RN (n=686) or PN (n=243). Multivariate analysis showed that surgery type was not a significant predictor of recurrence. Kaplan–Meier analysis showed 5-year RFS for cT1-upstaged PN, cT1-upstaged RN, cT2-upstaged PN, and cT2-upstaged RN of 79%, 74%, 70%, and 51%, respectively (log-rank  $p<0.001$ ). Five-year OS for cT1-upstaged PN, cT1-upstaged RN, cT2-upstaged PN, and cT2-upstaged RN was 64%, 65.2%, 56.4%, and 55.2%, respectively (log-rank  $p=0.059$ ). Additionally, eGFR decreased less with PN than RN (6.1 vs 19.4 mL/min/1.73 m<sup>2</sup>,  $p<0.001$ ).<sup>20</sup> Shvero et al performed a similar study with 134 patients who were pathologically upstaged from cT1–2 to pT3 after PN or RN. Their multivariate analysis showed that surgery type was not a predictor of local recurrence ( $p=0.978$ ), metastatic progression ( $p=0.972$ ), CSM ( $p=0.626$ ), or ACM ( $p=0.974$ ) at 5-year follow-up. It is important to note that there was a significant difference in median tumor size between the PN and RN cohorts (4 cm vs 7 cm,  $p<0.001$ ).<sup>21</sup> Finally, Maurice et al analyzed 276 patients with tumors that were pathologically upstaged to T3a who underwent PN (138 patients) or RN (138 patients). With a median follow-up of 68 months, they found that PN was associated with significantly less risk of ACM (HR 0.54,  $p=0.01$ ).<sup>22</sup> The findings from the aforementioned studies suggest that patients with cT3 RCC with indication for PN may have acceptable short- to intermediate-term outcomes, and that PN is an appropriate option in patients with T3 tumors and with indication for nephron preservation.

## Open PN vs MIS PN for Large (T2+) and Complex Renal Masses [Table 1]

While emerging reports suggest the feasibility of MIS-PN for large and complex masses, direct comparisons of open and MIS approaches have been few. Ghali et al examined 150 patients with cT2a RCC who underwent open PN (91) or MIS PN (59). They found no significant difference in the perioperative complication rate, postoperative Clavien grade  $\leq 2$  complication rate, or median change in eGFR at follow-up. However, there was a higher rate of Clavien grade 3 or higher complications in those who underwent open PN (16.2%) than those who underwent MIS PN (5.1%;  $p=0.041$ ).<sup>23</sup> Malkoc et al reported a similar study of 110 patients with tumors  $\geq 7$  cm who underwent open PN (56) or MIS PN (54). The MIS PN cohort demonstrated lower EBL (250 mL vs 300 mL,  $p=0.014$ ), median ischemia time (31.5 min vs 35 min,  $p=0.02$ ), median hospitalization time (3.5 days vs 5.3 days,  $p<0.001$ ), and intraoperative transfusion rate (9.4% vs 30.4%,  $p=0.008$ ). However, there was no significant difference between the cohorts in intraoperative complication rate, postoperative complication rate, or eGFR preservation.<sup>24</sup> Taken together, these reports suggest that MIS-PN has similar functional outcomes to open PN for large masses and may be associated with benefit with respect to decreased blood loss and morbidity.

Utilization of nephron-sparing surgery has historically been limited in patients with complex renal masses, with concerns about increased risk of complications and oncological risk. One method of measuring tumor complexity is through RNSs. Kim et al examined 149 patients with RNSs  $\geq 10$  who underwent open PN (64) or MIS PN (85). They found only lower median hospital stay for their MIS PN patients (5 days vs 7 days,  $p<0.001$ ). They found no significant difference between the two cohorts in median EBL, median ischemia time, intraoperative complications, intraoperative transfusions, postoperative complication rates, or mean eGFR decrease.<sup>25</sup> Although retrospective studies comparing surgical techniques are inherently susceptible to selection bias, these studies together suggest that in certain scenarios, MIS PN may confer a lower risk of intraoperative complications in patients undergoing PN for cT2 masses and those with complex renal mass. However, it remains to be determined if MIS confers a lower rate of postoperative complications for these patients and whether it is beneficial for those with RNSs  $\geq 10$  in elective circumstances.

## Evolution of Robotic RN for Inferior Vena Cava Tumor Thrombi (TT) [Table 2]

RCCs may invade the renal vein and extend into the IVC cephalad into the right atrium. Tumor thrombi (TT) such as these occur in roughly 5%–15% of all RCC.<sup>26</sup> These operations carry significant risk of major operative and postoperative complications and mortality and are considered high-risk procedures that often require an interdisciplinary team with urological oncologists, hepatobiliary surgeons, and cardiothoracic surgeons for optimal management, which has historically been an extensive multichambered abdominal and sometimes thoracic operation. However, in the last 15–20 years, minimally invasive techniques and platforms have been increasingly applied to this challenging oncological phenomenon. Abaza et al performed five robot-assisted, right-sided RNs with IVC thrombectomy (IVCTE). Two of the patients had Mayo level I ( $\leq 2$  cm from the confluence of the renal vein and IVC) TT and three patients had level II ( $>2$  cm from the confluence of the renal

**Table 2** Evolution of robotic radical nephrectomy with inferior vena cava tumor thrombectomy

Authors	Number of patients	Tumor side	Perioperative results	Complications	Outcomes
Abaza et al <sup>27</sup> Wang et al <sup>28</sup>	5 (2 level I, 3 level II) 17 (4 level I, 13 level II)	All right-sided 13 right-sided, 4 left-sided	— Median OT (min): 131 (R), 250 (L) Median EBL: 240 mL Median IVC blocking time: 17 min	No complications Perioperative Clavien grade II: 1 Perioperative Clavien grade IV: 1	— —
Abaza et al <sup>29</sup> Chopra et al <sup>30</sup>	32 (30 level I, 2 level II) 24 (13 level II, 11 level III)	27 right-sided, 5 left-sided 16 right-sided, 7 left-sided	— Median OT: 4.5 hours Median EBL: 240 mL	TR = 9.4% Intraoperative TR: 5/24 pts (20.8%) Clavien II within 1 year: 2 pts. Clavien III within 1 year: 2 pts	7/32 (21.9%) cases of recurrence All Pts alive (follow-up 16 mo)
Wang et al <sup>31</sup>	13 (7 level III, 6 level IV)	9 right-sided, 4 left-sided	Median OT: 465 min Median EBL: 2000 mL Median first porta hepatis blocking time: 40 min Median Cardiopulmonary bypass time: 72 min	TR: 92.3% (12/13) Perioperative Clavien IV: 3 pts Mortality Rate: 7% (1/13)	Progression: 1 death, 2 (median follow-up 18 mo)

**Abbreviations:** R, right; L, left; EBL, estimated blood loss; IVC, inferior vena cava; OT, operative time; TR, transfusion rate; pts, patients; mo, months.

vein and IVC but below the hepatic veins) TT. There were no complications, transfusions, or readmissions.<sup>27</sup> Wang et al also reported a series of 17 RARNs with IVCTE. Thirteen cases were right-sided and four left-sided. Median operating times were 131 min and 250 mins for the right and left sides, respectively. For left-sided procedures, the median warm ischemia time was 18 minutes.<sup>28</sup> Abaza et al went on to combine his results with others in a multi-institutional case series examining 32 cases of RARN with IVCTE. Thirty of these cases were level I TT and two level II TT, and 27 were right-sided and five left-sided. All of the procedures were performed without open conversion. Three patients required 1–3 units of blood. After mean follow-up of 15.4 months, seven patients' had tumors recurred. However, of these seven, four had node-positive disease on postlymphadenectomy pathological examination.<sup>29</sup> Chopra et al analyzed operative success and 1-year outcomes in 24 patients with Mayo level II and III (above the hepatic veins, but below the diaphragm) IVC TT who underwent RARN with IVCTE. Sixteen cases were right-sided and seven left-sided. MIS was successful in all but one patient, who required open conversion. All tumors were excised with negative surgical margins. Five patients required intraoperative blood transfusion, and four had complications (two Clavien 2, one Clavien 3a, and one Clavien 3b). Of the 24 patients who underwent successful MIS, three had positive lymph nodes. At 1-year follow-up, eleven patients had metastatic disease and ten had received adjuvant therapy.<sup>30</sup> Wang et al performed a similar study with 13 patients who underwent RARN with Mayo level III–IV (above the diaphragm) IVCTE. Nine cases were right-sided and four left-sided. They performed all surgeries without needing to convert to an open approach. Three patients had grade IV complications. The perioperative mortality rate was 7.7%. In the following 18 months, two patients died and one had disease progression.<sup>31</sup> These case series have demonstrated that a minimally invasive approach is feasible for patients with RCC and level I–IV TT. However, further clinical investigations are required to delineate the role of minimally invasive versus open IVCTE in terms of short- and long-term oncological outcomes and complication rates.

### Single-Port vs Multiport MIS PN [Table 3]

Single-port (SP) laparoscopic surgery emerged in the last 15 years as a potential minimally invasive alternative to traditional multiport approaches that may further reduce incisional morbidity and promote improved cosmesis.<sup>32</sup> Patients undergoing SP nephrectomy have similar operative outcomes with higher cosmetic satisfaction than those who underwent a multiport (MP)

nephrectomy, with cosmetic benefit derived by consolidation of working ports and extraction incision into a discrete periumbilical or Pfannenstiel incision.<sup>33,34</sup> Nonetheless, adoption of pure laparoscopic platforms has been hindered by a technology gap with respect to robust and wristed instrumentation and the difficulty of training surgeons in this approach.<sup>35</sup> Development of the DaVinci SP robotic platform (Intuitive, Sunnyvale, USA) has led to renewed interest in and application of SP robotic approaches for a variety of procedures, including PN and RN. Harrison et al set out to determine if there was a tangible benefit to either technology using propensity score–matched cohorts of 48 patients who underwent SP or MP MIS PN for renal tumors  $\leq 4$  cm. They found no significant difference in median operative time, median EBL, intraoperative complications, or postoperative complications. However, they did find that those who underwent SP PN had significantly shorter median hospital stay (1.4 days vs 1.6 days,  $p=0.0045$ ) and lower median opioid use on postoperative day 1 (4.6 MME vs 9.8 MME,  $p=0.0209$ ).<sup>36</sup> Glaser et al also attempted to establish whether one technique was preferable when they examined 78 patients who underwent either SP PN (26) or MP PN (52). They found no significant differences between the two cohorts in mean operative time, rate of EBL  $>500$  mL, complication rates, rate of discharge on postoperative day 1, or rates of opioid prescriptions being filled.<sup>37</sup> Currently, there seems to be little tangible benefit to using an SP in lieu of MP technique when performing PN. SP PN may lead to shorter hospital stays and less opioid dependence, but further investigation is warranted.

## Advances in Thermal Ablation

### Long-Term Functional and Oncological Outcomes for Cryoablation and Radiofrequency Ablation [Table 4]

In recent years, ablative techniques, including radiofrequency ablation (RFA) and cryoablation (CA), have become established options for patients with select small renal masses who are not optimal surgical candidates or who prefer a minimally invasive nonsurgical approach, with reports demonstrating oncological efficacy. Psutka et al examined 185 patients (143 T1a and 42 T1b) treated with RFA. On follow-up, there were 12 cases of recurrence (6.5%) with a median time to recurrence of 2.5 years. T1b masses were significantly more likely to recur than T1a masses (14.3% vs 4.2%,  $p=0.0196$ ).<sup>38</sup> Takaki et al analyzed 60 patients with T1b renal masses treated with RFA (21) or RN (39). The patients in the RFA cohort had significantly higher age, rate of chronic kidney disease, and American Society of Anesthesiologists scores, while the RN cohort had significantly larger tumors. Despite this, there was no significant difference between the two cohorts in 10-year RFS or 10-year CSS. In the RFA cohort, there was no significant difference between baseline eGFR and eGFR at last follow-up. In the RN cohort, there was a significant decrease in eGFR (88.4 mL/min/1.73 m<sup>2</sup> vs 59.6 mL/min/1.73 m<sup>2</sup>,  $p<0.001$ ). It is important to note that the RFA cohort had significantly lower 10-year OS (48% vs 97%,  $p<0.009$ ), although it is unclear how much of that difference was due to patient selection bias.<sup>39</sup> Ma et al analyzed 58 T1a renal tumors treated with RFA, and 5- and 10-year RFS was 94.2%. Three (5.1%) patients died during the follow-

**Table 3** Emergence of robotic single-port partial nephrectomy

Authors	Sample size	Perioperative outcomes	Postoperative outcomes
Harrison et al <sup>36</sup>	96 (48 SP PN propensity score matched with 48 MP PN)	Median OT (min): 102 (SP) vs 96.5 (MP), $p=0.8796$ Median EBL (mL): 50 (SP) vs 60 (MP), $p=0.4923$ Intraoperative minor CR: 0 (SP) vs 0 (MP) Intraoperative major CR: 0 (SP) vs 4.2 (MP), $p=0.5$	Median length of stay (days): 1.4 (SP) vs 1.6 (MP), $p=0.0045$ Median opioid use postoperative day 1: 0 (SP) vs 5.0 (MP), $p=0.0209$ 30-day postoperative minor CR: 0 (SP) vs 4.2% (MP), $p=0.5$ 30-day postoperative major CR: 2.1% (SP) vs 0 (MP), $p=1.0$ 30-day Mortality: 0 (SP) vs 0 (MP)
Glaser et al <sup>37</sup>	78 (26 SP, 52 MP)	Mean OT(min): 183.9 (SP) vs 208.6 (MP), $p=0.12$ EBL $>500$ mL: 30.8% (SP) vs 15.4% (MP), $p=0.11$ CR: 11.5% (SP) vs 5.8% (MP), $p=0.36$	Discharged on postoperative day 1: 73.1% (SP) vs 65.4% (MP), $p=0.6$ Opioid prescription filled: 76.9% (SP) vs 80.8% (MP), $p=0.69$

**Abbreviations:** SP, single port; MP, multiport; PN, partial nephrectomy; EBL, estimated blood loss; CR, complication rate; OT, operative time.

**Table 4** Advances in ablation

Authors	Patient population	Tumor stage	Median/mean tumor size	Modality	Recurrence	Survival outcomes	Functional outcomes
Psutka et al <sup>38</sup>	185 (all RFA)	T1a 143 T1b, 42	3 cm (median)	RFA	Last follow-up: 6 (4.2%) T1a, 6 (14.3%) T1b, $p=0.0196$	—	—
Takaki et al <sup>39</sup>	60 (21 RFA, 39 RN)	T1b	4.6 cm (RFA), 5.2 (RN, mean)	RFA	10-year RFS: 84% (RN) vs 88% (RFA), $p=0.99$	10-year OS: 97% (RN) vs 48% (RFA), $p<0.009$ 10-year CSS: 100% (RN) vs 94% (RFA)	RFA eGFR: 63.2 (baseline), 56.8 (last follow-up, $p=0.08$ ) RN eGFR: 88.4 (baseline), 59.6 (last follow-up, $p<0.001$ )
Ma et al <sup>40</sup>	58 (all RFA)	T1a	2.2 cm (mean)	RFA	10-year RFS: 94.2%	10-year OS: 91.1%	—
Knox et al <sup>41</sup>	234 (all CA)	T1a and T1b	2.5 cm (mean)	CA	Local recurrence last follow-up: 1.5% Metastases last follow-up: 5.2%	10-year ACM: 2.7%	eGFR 70.32 (preprocedure), 67.92 (3-month postprocedure, $p=0.01$ )
Pecoraro et al <sup>42</sup>	5763 (5521 PN and 242 CA)	T1b	46.9 mm (CA), 51.0 mm (PN, median)	CA	CSM: HR 2.50, $p=0.03$ (CA/PN reference) OCM: HR 1.45, $p=0.12$ (CA/PN reference)	—	—
Klapperich et al <sup>43</sup>	100	cT1a	2.6 cm (median)	MWA	—	3-year PFS: 88% 3-year CSS: 100% 3-year OS: 91%	eGFR: 57.9 (preablation), 44 (6-month postablation), $p=0.5$
Guo and Arellano <sup>44</sup>	119	cT1a	2.4 cm (mean)	MWA	PFS at 1, 2, and 3 years: 100%, 92.8%, and 90.6%	OS at 1, 2, and 3 years: 99.0%, 97.7%, and 94.6%	—
Guo and Arellano <sup>45</sup>	23	cT1b	5.2 cm (mean)	MWA	PFS at 1, 2 and 3 years: 100%, 90.9%, and 90.9%	OS at 1, 2, and 3 years: 95.2%, 85.7%, and 71.4%	—
Shapiro et al <sup>46</sup>	325 (40 MWA, 74 PN, 211 RN)	T1b	4.4 cm (MWA), 4.7 cm (PN), 5 cm (RN)	MWA	5-year RFS: 94.5% (MWA), 97.9% (PN, $p=0.58$ ) and 99.2% (RN, $p=0.02$ )	5-year CSS: 100% (MWA), 97.6% (PN, $p=0.45$ ) and 95.5% (RN, $p=0.32$ )	Median $\Delta$ eGFR at 3 months: -4.5% (MWA), -3.2% (PN, $p=0.65$ ), and -29% (RN, $p<0.001$ )

**Abbreviations:** RFA, radiofrequency ablation; RN, radical nephrectomy; RFS, recurrence-free survival; OS, overall survival; CSS, cancer-specific survival; eGFR, estimated glomerular filtration rate; CA, cryoablation; ACM, all-cause mortality; PN, partial nephrectomy; CSM, cancer-specific mortality; OCM, other-cause mortality; MWA, microwave ablation; PFS, progression-free survival.

up, which translates to 5- and 10-year OS of 95.7% and 91.1%.<sup>40</sup> Knox et al analyzed 234 biopsy-proven T1a/T1b RCCs that were treated with CA. Complete response to CA occurred following one session in 195 of 204 tumors and following two sessions in 200 of 204 tumors. There were three cases of recurrence in the 200 cases followed up (1.5%) and ten cases of metastatic progression out of the 193 eligible cases (5.2%). Variables associated with metastatic progression were tumor size, prior kidney surgery, and clear-cell histology. The ACM rate was 2.7%. With regard to functional preservation, there was a significant difference in eGFR at baseline and follow-up (70.32 vs 68.17 mL/min/1.73 m<sup>2</sup>,  $p=0.01$ ).<sup>41</sup> Pecoraro et al utilized the SEER (Surveillance, Epidemiology, and End Results) database to analyze 5763 patients with T1b RCC, 5521 of whom were treated with PN and 242 with CA. They found that CA was a significant predictor of CSM (HR 2.50,  $p=0.03$ ) and a relative risk factor of OCM (HR 1.45,  $p=0.12$ ).<sup>42</sup> The current state of the literature supports utilization of CA and RFA for management of T1a tumors with durable outcomes in patients with tumors <3.5 cm in size that are comparable with surgical excision; however, outcomes in T1b RCC are significantly worse with ablative modalities and utilization of CA, and RFA for T1b tumors should only be considered in circumstances where excisional therapy is contraindicated due to significant systemic risk to the patient.

## Emergence of Microwave Therapy [Table 4]

Microwave ablation (MWA) has emerged as an alternative ablative platform to RFA and CA, with promising short- and intermediate-term outcomes in T1 RCC. Klapperich et al analyzed 100 patients with T1a masses who underwent MWA. Technical success was achieved in all patients, and 3-year RFS was 99%. Three-year PFS, CSS, and OS was 88%, 100, and 91%, respectively. Additionally, there was no significant difference in eGFR at baseline and postablation (57.9 mL/min/1.73 m<sup>2</sup> vs 44 mL/min/1.73 m<sup>2</sup>,  $p=0.5$ ).<sup>43</sup> Guo and Arellano performed two studies that analyzed the outcomes of patients with T1a and T1b masses following MWA. In their first study, they analyzed 119 patients with cT1a masses and found a complete response to MWA in 95.3% of cases. Additionally, they reported PFS of 100%, 92.8%, and 90.6% at 1, 2, and 3 years and OS of 99.0%,

97.7% and 94.6% at 1, 2, and 3 years, respectively.<sup>44</sup> In their second study, they analyzed 23 patients with cT1b masses. Complete response was achieved in 87% of patients on the first attempt and 100% of patients on the second attempt. At 1, 2, and 3 years, PFS was 100%, 90.9%, and 90.9% and OS 95.2%, 85.7%, and 71.4%, respectively.<sup>45</sup> Shapiro et al analyzed a group of 325 patients with T1b RCC who underwent RN (211), PN (74), or MWA (40). The 5-year RFS for MWA (94.5%) was noninferior when compared to PN (97.9%,  $p=0.58$ ), but significantly lower than RN (99.2%,  $p=0.02$ ). Nonetheless, the 5-year CSS for the MWA cohort (100%) was not significantly different from the PN (97.6%,  $p=0.45$ ) or RN one (95.5%,  $p=0.32$ ).<sup>46</sup> Taken together, the current state of the literature reflects short- to intermediate-term outcomes in MWA that are promising for T1 RCC, suggesting efficacy in the T1b and T1a cohorts of patients. Nonetheless, longer-term follow-up data are required to confirm durability of outcomes.

## Conclusion

In this review, we discussed advances in the surgical and ablative treatment of RCC. RAPN has become the reference standard for most T2 masses because of its oncological equipoise and functional preservation when compared to RN. PN may also be utilized for selected clinical T3a renal masses with imperative indication for functional preservation. Additionally, a robotic approach to PN has been shown to have improved morbidity when compared to open PN, which is comparable to the morbidity profile of RN for large and complex masses. Emerging reports suggest that RARN with IVC TT is feasible for select patients, with benefits of MIS and acceptable short-term oncological outcomes. Robotic SP PN has been shown to demonstrate improved cosmesis with the possibility of shorter hospital stays and improved postoperative pain, although this must be confirmed with further investigation. In the field of thermal ablation, different energy approaches, such as CA, RFA, and MWA, have demonstrated acceptable efficacy for tumors <3 cm, while only MWA has shown acceptable short-term outcomes in larger (T1b) masses. Further investigation is necessary to establish the role of MWA for management for T1b masses. These data reflect the current state of the art of the field, though the analyses are limited by their retrospective nature and selection bias, and in the case of the surgical series, the analyses were conducted in high-volume centers of excellence by experienced surgeons, and as such, the applicability of the data may be limited, but serve as the starting point for further investigation.

## Summary

Nephron-sparing and minimally invasive surgery has become increasingly effective for management of large renal masses. Ablative techniques are now feasible alternatives in select patients.

## Future Directions

Future studies should be aimed at establishing the extent of disease that can be sufficiently treated with PN vs RN, which is best carried out via a randomized clinical trial.<sup>47</sup> It remains unclear whether PN for patients beyond T2 disease confers a functional and mortality benefit compared to RN. Additionally, it is unclear whether an MIS approach for tumors with IVC extension is adoptable beyond centers of excellence. SP MIS for RCC should be further investigated to examine any potential differences in complication rates and satisfaction outcomes. With regard to ablation, MWA must be further explored before being deemed a safe alternative treatment for T1b RCC. Further investigation is needed to establish how tumor histology and complexity affects response to different ablation techniques.

## Disclosure

The authors report no conflicts of interest in this work.

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