Multiple approaches are available to manage small renal tumors.

Current Management Considerations for the Incidentally Detected Small Renal Mass

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Background: Nephron-sparing treatments remain underutilized for the management of small renal masses despite a rise in incidentally detected renal cell carcinoma and a downward stage migration.

Methods: Historical publications representative of currently accepted paradigms were reviewed, and the results of a contemporary scientific literature search conducted in PubMed focusing on studies involving humans, published in English, and inclusive of clinical trials, meta-analyses, randomized controlled trials, and practice guidelines are included. Results from contemporary retrospective trials augment the data when level I or II evidence is absent.

Results: Phase III clinical trial results substantiate the long-held tenet that partial nephrectomy is equivalent to radical nephrectomy with respect to safety and oncologic efficacy. Further, minimally invasive techniques using laparoscopy and robotic assistance to achieve partial nephrectomy appear equally effective to traditional open techniques. Although no prospective randomized studies are available, large retrospective studies support the notion that active surveillance and thermal ablative techniques are viable options for carefully selected patients.

Conclusions: The management of small renal masses encompasses a host of therapeutic options, all of which must be considered and discussed with the individual patient.

Introduction

Despite a downward stage migration, smaller tumor size at time of diagnosis, and a rise in the incidental discovery of renal masses, renal cell carcinoma (RCC) still accounts for an estimated 3% to 4% of newly diagnosed adult malignancies and a rising cancer-specific death rate.1,5 Although the utilization of extirpative surgery has kept pace with the rising incidence of RCC, nephron-sparing surgery (NSS) remains underutilized despite becoming a standard of care for the management of small renal masses (SRMs).6,7 Using contemporary literature, we present current treatment modalities for the management of SRMs.

Methods

We verified background information, inclusive of widely accepted treatment paradigms and sentinel

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and core biopsies, respectively. No false positives were noted; therefore, a positive predictive value of 100% was achieved. The specificity and sensitivity of core biopsies was 100% and 95.2%, respectively.

Beyond the classification of either malignant or benign, acquiring tissue at the time of percutaneous renal mass biopsy allows for the identification of tumor subtype and grade. However, available studies examining the concordance between preoperative biopsies and the pathology obtained at the time of extirpative intervention are limited, and those that do exist include fewer than 100 patients in any one study.11,13,14 Schmidbauer et al13 found the concordance to be 91% and 76% for RCC subtype and Fuhrman grade, respectively, when comparing the specimens obtained at the time of biopsy with those at the time of surgery. Subtype discrepancies are rare when the clear-cell variety is identified, but they arise more frequently with the papillary or chromophobe histologies.11,13,14 Specifically, the ability to discriminate between benign oncocytoma and RCC of the chromophobe subtype remains unproven.14 Further, biopsy specimens are prone to underestimate the true nuclear grade of a specimen.13,14

Given the aforementioned data, together with an exceedingly rare incidence of biopsy tract seeding and a low complication rate (with < 2% necessitating intervention), current American Urology Association guidelines8 support percutaneous biopsy for a clinical stage I renal mass in patients considering an array of management options. However, biopsy is not advocated in healthy patients unwilling to accept the uncertainty.7

**Preoperative Nomograms**

Nomograms based on preoperative parameters created using retrospectively evaluated outcomes provide probabilities for the presence of a malignancy or high-grade tumor at the time of extirpative surgery.15,16 Although an accurate nomogram could obviate the need for percutaneous biopsy and reduce the number of extirpative procedures performed to discover benign disease, currently available nomograms can neither prospectively validate nor replace histological diagnosis.

**Radical Nephrectomy**

Initially, the modality of choice for the management of all renal masses was open radical nephrectomy, which involves removal of the kidney (the ipsilateral adrenal gland still encompassed by Gerota’s fascia) and regional lymph nodes as described in 1969 by Robson.17 This procedure remains the gold standard to which all other treatments are compared due its high achievement of cancer control as measured by local tumor control, progression-free survival, recurrence-free survival, and cancer-specific survival rates.
Ipsilateral Adrenalectomy
The necessity for ipsilateral adrenalectomy has been scrutinized in recent years. Findings within large cohorts, inclusive of tumors 7 cm in diameter or above and tumors involving the upper pole, suggest that the rates of synchronous adrenal involvement are 1% to 5%.18-20 Further, when assessing for adrenal involvement using current imaging modalities, the negative predictive value is nearly 100%,19 and no improvements in overall survival rates have been demonstrated in those undergoing concomitant ipsilateral adrenalectomy without clinical or radiological suspicion of adrenal involvement.18-20 Therefore, ipsilateral adrenalectomy at the time of extirpative surgery for RCC is not advocated in those without radiological and operative findings suggestive of adrenal involvement.9

Regional Lymphadenectomy
Performing regional lymph node dissection (LND) at the time of radical nephrectomy (RN) or PN has recently gained some clarity, although this approach is still debated within the urologic oncology community. In 2009, Blom et al21 first published results regarding a prospective randomized European Organization for Research and Treatment of Cancer (EORTC) intergroup phase III study comparing the outcomes of patients assigned to RN with those assigned to both RN and regional lymphadenectomy. A total of 732 lesions amenable to inclusion and defined as clinical stage T1 to T3 tumors (using the 1978 TNM staging system22) without radiological or clinical findings of regional or distant metastasis were included in the study. As part of that study, all patients in the cohort undergoing LND underwent a dissection extending from the crus of the diaphragm inferiorly toward the bifurcation of the aorta or vena cava. The median follow-up was 12.6 years with no statistical difference noted with regard to overall survival, locoregional disease progression, or distant metastatic spread between those undergoing and not undergoing LND at the time of RN. Only 14 (3%) of the patients undergoing LND had confirmed regional nodal metastasis.21

By 2011, Whitson et al23 used Surveillance, Epidemiology and End Results data to retrospectively evaluate treatment patterns and outcomes among those undergoing LND in the context of RCC. Of the 9,586 patients without evidence of distant metastatic disease managed with extirpative measures inclusive of LND, the data clearly demonstrate a significant positive correlation between lymph node metastasis with increasing tumor size, tumor stage, higher nuclear grade, older age, and male sex. In this cohort, 1,265 patients (13.2%) exhibited node-positive disease. At a median follow-up of 3.5 years, the cancer-specific survival rates were significantly different for those with node-negative disease compared with node-positive disease (58% and 20%, respectively). The authors also examined the effects of more extensive LND. In those with a negative lymph node status, no benefit to harvesting more nodes was found. By contrast, the opposite was found in those with positive nodes, suggesting that performing LND in those with positive nodes was beneficial. Supporting this assertion, among 112 patients with node-positive disease who underwent LND compared with 17 who did not, a significant median overall survival benefit of 5 months ($P = .0002$) was found on univariate analysis, and this benefit remained on multivariate analysis for those undergoing LND who were 3 times less likely to die of RCC.22 The multivariate analysis also demonstrated a significant overall survival benefit to those undergoing LND in terms of their subsequent response to immuno therapy.24

Laparoscopic Radical Nephrectomy
Despite the diverse surgical approaches for RCC, they all remained invasive prior to the acceptance of laparoscopic techniques. Clayman et al25 first described laparoscopic radical nephrectomy (LRN) in 1991 and, since that time, safety26 and efficacy with respect to cancer control27 between open radical nephrectomy and LRN have been deemed equivalent. In a large meta-analysis evaluating the complications of laparoscopic renal surgery, 20 studies described complication rates attributed to LRN.26 The most common complication was the need to convert to an open surgical procedure (2.5% of cases). Venous and arterial bleeding (1.8% and 1.0%) were both noted as common complications, with transfusion being necessary 0.7% of the time. Colonic injury was the only other complication noted in more than 1% of the procedures (1.5% of cases). Luo et al27 noted mean cancer-specific survival rates of 82.3 months and 81.6 months for pT1 lesions managed by LRN or open radical nephrectomy, respectively, while the cancer-specific survival rates related to pT2 lesions were 69.0 months and 72.1 months for the same aforementioned procedures. No significant differences were demonstrated between these two surgical approaches in this regard.

Interestingly, a recent Cochrane Review28 conducted to assess the differences between the various surgical techniques currently used to manage RCC identified only three randomized studies. Thus, currently accepted standards are mostly based on retrospective or prospective studies without randomization.

Partial Nephrectomy
The role of PN was actively evaluated in the 1990s. Open PN (OPN) as we know it today was first described by Licht and Novick29 in 1993, and the first report of a laparoscopic partial nephrectomy (LPN) was reported that same year by Winfield et al.30 By
the end of the following decade, multiple studies illuminated the inverse relationship between estimated glomerular filtration rate and the incidence of hospitalizations, cardiac events, and overall death, thus touting the benefits of performing NSS.\textsuperscript{31-33} PN has since become the standard of care for uncomplicated SRMs.\textsuperscript{7,9} Furthermore, its utilization is imperative in those with an anatomically or functionally solitary kidney, bilaterally afflicted kidneys, genetic predispositions for future renal malignancies, and chronic renal insufficiency. Despite general consensus regarding the appropriate utilization of PN, Hollenbeck et al\textsuperscript{6} reported a gross underutilization of NSS for the management of RCC.

**Immediate Outcomes and Safety**

Although the clinical safety and oncologic efficacy of NSS were previously reported in retrospective studies (Tables 1 and 2),\textsuperscript{34-44} it was not until 2007 that results from a prospective randomized clinical trial highlighted the immediate perioperative outcomes of PN compared with RN.\textsuperscript{43} It was at this time that the EORTC Data Center reported the results of the first phase III clinical trial examining the immediate outcomes of RN compared with PN for the management of SRMs. Specifically, 541 patients with sporadic solitary renal tumors (≥ 5 cm in diameter) without evidence of regional or distant metastasis were randomized to undergo either OPN or RN.\textsuperscript{43} Due to some crossover between the randomly assigned treatment and the received treatment, the analysis was reported with respect to patients who actually received the respective treatment. Perioperative blood loss was significantly less for those undergoing RN compared with PN ($P < 0.001$). However, RN resulted in a significantly larger rise in serum creatinine ($P < 0.0001$). No major complications were attributed to either treatment modality, and no differences were noted in the rates of pleural injury: 9.3% and 11.5% for RN and PN, respectively. Urinary fistulas were discovered only in those managed by PN, with a reported rate of 4.4%. Postoperative imaging abnormalities were identified in 21 patients (inclusive of 9 hematomas, 3 urinomas, 1 renal infarction, 1 lymphoceles, and 1 bowel obstruction). However, the distribution was not significantly different between the two treatment groups. Further, reoperation rates were similar between the two groups: 4.4% and 2.4% for PN and RN, respectively.

**Oncologic Efficacy and Survival**

Four years later, Van Poppel et al\textsuperscript{44} revisited the same EORTC cohort\textsuperscript{43} to evaluate the oncologic efficacy of PN compared with RN when addressing SRMs, representing the first phase III clinical trial prospectively evaluating the outcomes of PN. All outcomes were reported based on the intention-to-treat principle as 5.9% of those randomized to RN underwent PN and 14.6% of those randomized to PN underwent RN. At the time of reporting, the median follow-up was 9.3 years and the 10-year overall survival rates were 75.7% (95% confidence interval [CI], 69.4–81.0) and 81.1% (95% CI, 75–85.9) for all newcomers undergoing PN and RN, respectively. The rates were similar when evaluating patients with pathologically confirmed RCC. Further, the number of cancer-specific deaths and the progression rate were not significantly different between the two treatment modalities. Cancer-specific death occurred in only 12 patients (3%), and 10-year progression rates were 4.1% (95% CI, 1.7–6.5) and 3.3% (95% CI, 1.2–5.4) for PN and RN, respectively. Although no definitive equivalence between PN and RN was demonstrated due to the lack of sufficient accrual, no significant differences were demonstrated between the two treatment modalities with respect to overall survival, cancer-specific survival, or disease progression rates. Also, these results did not substantiate the paradigm that NSS is associated with fewer cardiac events and deaths due to the preservation of renal function. However, renal function was not a targeted endpoint of this investigation.

**Robot-Assisted Laparoscopic Partial Nephrectomy**

First reported in 2004 by Gettman et al,\textsuperscript{45} robot-assisted laparoscopic PN (RALPN) has garnered growing attention due to the potential advantages of 6 degrees of distal instrumental articulation, three-dimensional stereoscopic optics, improved ergonomics for the surgeon, and computer elimination of tremor. Given the relatively recent implementation of this evolving technology, long-term data regarding its use are limited. However, a recent retrospective study by Benway et al\textsuperscript{46} failed to demonstrate differences between standard LPN and RALPN with respect to operative time, breach of the collecting system, margin status, and complication rates. The researchers did note that the mean volume of intraoperative hemorrhage, warm ischemia time, and perioperative duration of hospitalization were significantly less when performing RALPN compared with LPN. Further, more complex tumors did not alter perioperative outcomes of RALPN. This was not true when performing LPN. Pierorazio et al\textsuperscript{46} also reported shorter operative and ischemia times as well as less intraoperative bleeding when using robotic-assisted compared with conventional laparoscopic techniques to perform PN.

**Single-Port Laparoscopic Partial Nephrectomy and Single-Port Robot-Assisted Partial Nephrectomy**

First described in 2009 by Aron et al,\textsuperscript{46} single-port NSS is feasible in well-selected cases with respect to its ability to achieve negative margins, limit intraoperative hemorrhage, and minimize renal ischemia,
### Table 1. Selected Trials of Partial Nephrectomy Outcomes When Targeting Small Renal Masses

<table>
<thead>
<tr>
<th>Study (yr)</th>
<th>Study Type</th>
<th>No. of Patients</th>
<th>Approach</th>
<th>Conversion to RN (%)</th>
<th>Ischemia Time (min)</th>
<th>Operative Time (min)</th>
<th>EBL (mL)</th>
<th>Positive Margin (%)</th>
<th>Overall Rate of Complications (%)</th>
<th>Transfusion Rate (%)</th>
<th>Urinary Leak (%)</th>
<th>Delayed Bleed (%)</th>
<th>Length of Stay (days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patard³⁴ (2007)</td>
<td>Retro</td>
<td>600</td>
<td>OPN</td>
<td>—</td>
<td>19.3</td>
<td>147</td>
<td>386</td>
<td>1.5</td>
<td>10.8</td>
<td>6.3</td>
<td>1.7</td>
<td>—</td>
<td>7.7</td>
</tr>
<tr>
<td>Gill³⁶ (2007)</td>
<td>Retro</td>
<td>1,028</td>
<td>OPN</td>
<td>0</td>
<td>20.1</td>
<td>266</td>
<td>376</td>
<td>0</td>
<td>20.2</td>
<td>5.1</td>
<td>2.4</td>
<td>1.6</td>
<td>5.8</td>
</tr>
<tr>
<td></td>
<td></td>
<td>771</td>
<td>LPN</td>
<td>0.1</td>
<td>30.7</td>
<td>201</td>
<td>300</td>
<td>0.9</td>
<td>26.7</td>
<td>4.5</td>
<td>3.1</td>
<td>4.2</td>
<td>3.3</td>
</tr>
<tr>
<td>Pierozzii³⁷ (2011)</td>
<td>Retro</td>
<td>102</td>
<td>LPN</td>
<td>—</td>
<td>18</td>
<td>193</td>
<td>245</td>
<td>1</td>
<td>16.7</td>
<td>4.9</td>
<td>5.9</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Marszalek³⁸ (2011)</td>
<td>Retro</td>
<td>105</td>
<td>LPN</td>
<td>3.8</td>
<td>23.2</td>
<td>102</td>
<td>—</td>
<td>—</td>
<td>12.3</td>
<td>—</td>
<td>1.9</td>
<td>6.6</td>
<td>5.7</td>
</tr>
<tr>
<td>Benway³⁹ (2009)</td>
<td>Retro</td>
<td>118</td>
<td>LPN</td>
<td>0.8</td>
<td>28.4</td>
<td>174</td>
<td>196</td>
<td>1</td>
<td>10.2</td>
<td>—</td>
<td>3.4</td>
<td>—</td>
<td>2.7</td>
</tr>
<tr>
<td></td>
<td></td>
<td>129</td>
<td>RALPN</td>
<td>0</td>
<td>19.7</td>
<td>189</td>
<td>155</td>
<td>3.9</td>
<td>8.5</td>
<td>—</td>
<td>2.3</td>
<td>—</td>
<td>2.4</td>
</tr>
<tr>
<td>Spana⁴⁰ (2011)</td>
<td>Retro</td>
<td>450</td>
<td>RALPN</td>
<td>1.1</td>
<td>20.2</td>
<td>188</td>
<td>206</td>
<td>—</td>
<td>15.8</td>
<td>4</td>
<td>1.6</td>
<td>0.4</td>
<td>—</td>
</tr>
<tr>
<td>Dulabon⁴¹ (2011)</td>
<td>Retro</td>
<td>446</td>
<td>RALPN</td>
<td>1.5</td>
<td>20.21</td>
<td>188</td>
<td>213</td>
<td>1.6</td>
<td>5.1</td>
<td>4</td>
<td>1.6</td>
<td>—</td>
<td>2.9</td>
</tr>
</tbody>
</table>

*Perioperative outcomes from studies with > 100 patients and published within the last 5 years prior to closure of literature review.

EBL = estimated blood loss (intraoperative), LPN = laparoscopic partial nephrectomy, OPN = open partial nephrectomy, Prosp = prospective, RALPN = robot-assisted laparoscopic partial nephrectomy, RCT = randomized controlled trial, Retro = retrospective, RN = radical nephrectomy.

### Table 2. Selected Trials of Long-term Oncologic Outcomes of Partial Nephrectomy

<table>
<thead>
<tr>
<th>Study (yr)</th>
<th>Study Type</th>
<th>No. of Patients</th>
<th>Median Age (yrs)</th>
<th>Median Tumor Size (cm)</th>
<th>Median Follow-up (yrs)</th>
<th>Progression (%)</th>
<th>CSS (%)</th>
<th>OS (%)</th>
<th>10-yr Rates (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Overall</td>
<td>Local</td>
<td>Distant</td>
<td>Local and Distant</td>
</tr>
<tr>
<td>Herr³¹ (1999)</td>
<td>Retro</td>
<td>70</td>
<td>57</td>
<td>3</td>
<td>10</td>
<td>3</td>
<td>1.5</td>
<td>1.5</td>
<td>—</td>
</tr>
<tr>
<td>Fergany³² (2000)</td>
<td>Retro</td>
<td>107</td>
<td>73³³</td>
<td>4.7³³</td>
<td>8.7</td>
<td>32</td>
<td>4</td>
<td>21.5</td>
<td>6.5</td>
</tr>
<tr>
<td>Van Poppel³³ (2011)</td>
<td>Prosp RCT</td>
<td>268</td>
<td>62</td>
<td>3</td>
<td>9.3</td>
<td>4.5</td>
<td>4</td>
<td>—</td>
<td>—</td>
</tr>
</tbody>
</table>

³³Value is actually a mean.

CSS = cancer-specific survival, OS = overall survival, Prosp = prospective, RCT = randomized controlled trial, Retro = retrospective.
albeit in small numbers with both standard LPN and robot-assisted techniques. Both transperitoneal transumbilical and retroperitoneal approaches just below of the tip of the 12th rib have been described, and the first video-recorded single-port retroperitoneal LPN was published in 2011.

Cost Analysis
With the continually rising costs of health care and diminished national funding, interest in cost comparisons between equivalent techniques (with respect to oncologic efficacy and patient safety) is paramount and may dictate the future direction of health care. Mir et al presented a meta-analysis cost comparison of RALPN, LPN, and OPN that included more than 5,000 procedures. The study accounted for costs associated with operating room time, professional fees, equipment use, length of hospital stay, pharmacy costs, and ancillary services. LPN was the most cost effective ($10,311/case) for performing NSS compared with OPN ($11,427/case) and RALPN ($11,962/case). These discrepancies stem from the longer length of hospital stay associated with OPN and the high capital and maintenance costs required to perform RALPN.

Ischemia
Although renal ischemia is often not a necessity when addressing small, largely exophytic lesions, it provides a means for minimizing intraoperative renal hemorrhage, improving the visualization of the extent of the tumor, precisely excising the tumor, and offering an unobstructed field at the time of renal reconstruction.

To balance these benefits of applying renal ischemia with the potential detrimental effect of exposing residual normal renal parenchyma to ischemic conditions, significant efforts have been suggested to develop novel means to limit or omit the use of renal ischemia. However, isolated arterial occlusion, selective segmental renal artery clamping, early unclamping, and “zero ischemia” are not generally accepted and remain investigational because validation through randomized prospective studies remains scarce.

As opposed to hilar clamping of the renal vein and artery, which allows for venous backflow perfusion, a small, prospective porcine solitary kidney model investigated arterial occlusion and demonstrated a protective effect with respect to renal functional loss when instituted during OPN. However, no protective effect was demonstrated when performing LPN, potentially due to the presence of a pneumoperitoneum, which may negate venous backflow. A follow-up retrospective study involving humans offered no strong substantiation of these findings.

Smaller reductions in estimated glomerular filtration rates were attributed to NSS when using selective segmental renal artery clamping compared with renal artery occlusion. Prerequisite computed-tomographic angiography for arterial mapping was performed and operative times, intraoperative hemorrhage volume, and warm ischemia times were significantly longer in those two studies.

Nguyen and Gill discussed early unclamping involving the release of the hilar clamp after controlling exposed intrarenal blood vessels and performing off-clamp renal reconstruction. Significantly less warm ischemia time was required, and an associated smaller reduction in estimated glomerular filtration rates attributed to the extirpative surgery. However, the width of the median surgical margin was shorter for the cohort managed by early unclamping, thus leaving more functional renal parenchyma intact.

Seeking to maintain the benefits of applying traditional renal ischemia without exposing the targeted renal moiety to a truly anoxic environment, Eisenberg et al introduced the novel concept of “zero ischemia,” which was achieved by using pharmacological agents (eg, isoflurane, nitroglycerin, esmolol) to reduce the mean arterial pressure of patients to between 50 to 80 mmHg at the time of deep resection. Extensive invasive cardiovascular monitoring was required to closely monitor the systemic effects of the induced hypotension; such monitoring included the use of electrocardiographic leads, a bispectral index brain monitor, a cerebral oximeter, a central venous catheter, an arterial line, a pulmonary artery catheter, and transesophageal echocardiography, all of which were placed at the outset of the procedure. The first 15 cases had no associated cardiac or neurological events. However, the authors suggested potential risks from the procedure and noted that the selection of patients at low risk for these catastrophic events would be necessary.

Further, this approach seems paradoxical because alternative approaches have limited ischemia only to the kidneys or the tumor-containing portion of the kidneys, while “zero ischemia” potentially threatens multiple organ systems.

Renal Cooling
Achieving an organ temperature of 15°C was considered the most beneficial method to protect renal function during renal ischemia in 1975. Historically, this was achieved by immersing the organ within externally applied ice slush at the time of OPN. As minimally invasive surgical techniques evolved, multiple methods of instituting renal cooling were described. Gill et al described entrapping the fully mobilized kidney within a specimen retrieval bag along with infused ice slush before exposing the tumor for excision, and Weld et al simultaneously used two standard suction irrigators to infuse nearly frozen saline irrigation to achieve hypothermia. Arterial perfusion with cold Ringer’s lactate solution using either
a percutaneous femoral artery access or laparoscopic insertion of a 21-gauge butterfly needle directly into the renal artery was also investigated. Cold perfusion of the renal collecting system using either retrograde perfusion via transurethral ureteral access or laparoscopic cannulation of the renal pelvis has also been described. However, intrarenal temperatures of 15°C were not achieved and the minimal invasive application of renal cooling remains cumbersome.

Renal Nephrometry

The effects of ischemia and hypothermia use are well studied (benefits exist for omitting ischemia and limiting warm ischemia times to < 20–30 minutes); however, a recent multicenter study of 660 patients discovered the true tenet of postpartial nephrectomy renal function is the reality that the more viable tissue is left behind, the better the postoperative renal function of the remaining ipsilateral kidney. Thus, multiple scoring systems (e.g., Padua, C-index, R.E.N.A.L. nephrometry) characterize renal lesions with respect to the perceived potential to spare renal parenchyma uninvolved by the tumor at the time of PN. These descriptive tools account for the size of a tumor, its intrarenal position, its nearness to the collecting system or renal hilum, and the degree to which it is exophytic (as demonstrated on preoperative imaging). Although small retrospective studies have examined interobserver reliability and the prognostic value of nephrometry scoring with respect to surgical approach and perioperative complications, their capacity to accurately predict outcomes with respect to preserving glomerular filtration capacity remains controversial. However, a clear subjective value to nephrometry scoring exists to provide a concise anatomical description of renal lesions when reporting renal surgery outcomes.

Positive Surgical Margins

By contrast to performing RN in which a substantial buffer of Gerota’s fascia and unaffected renal parenchyma often surrounds the targeted lesion, PN does not afford this luxury and the potential for a positive surgical margin (PSM) must be addressed. To address this issue, Bensalah et al retrospectively reviewed matched cohorts, each containing approximately 100 patients. Participants underwent NSS and were partitioned into those demonstrating a PSM and those with a negative surgical margin. No differences were demonstrated in cancer-specific or overall survival rates, with a mean follow-up of 38.5 and 31 months, respectively. However, the local recurrence rate of 11% was significantly higher in those with a PSM. A total of 39% of specimens from patients with a PSM harbored residual tumor following repeat NSS or ipsilateral RN. Marszalek et al reviewed instances of PSMs associated with NSS, reporting an overall rate of PSMs ranging from 0% to 7%. When comparing OPN, LPN, and RALPN outcomes, the rates of a PSM were 0% to 7%, 0.7% to 4%, and 3.9% to 5.7%, respectively. This is consistent with a PSM rate of 1.5% demonstrated in a multicenter cohort examining the outcomes of 809 NSS procedures. For those with a PSM and a median follow-up of 32 months, a local recurrence rate of 33% was demonstrated as opposed to a significantly lower rate of 2.9% in patients with a negative surgical margin at the time of surgery (P = .0001). Thus, when using a multivariate analysis inclusive of bilateral tumor size, a PSM was the largest contributor (with a hazard ratio of 11.5) for predicting future local recurrence.

Thermal Ablative Techniques

Although cryoablation and RFA were originally employed to manage SRMs found in those with significant comorbidities, advanced age, and/or personal preferences prohibitive of extirpative management, these techniques have garnered increasing acceptance as an option for initial therapy in well-selected cases in which nonaction is not acceptable to the patient. Cryoablation and RFA rely on extreme focal cold or heat application, respectively, to destroy targeted tissues. Lesions can be visualized through ultrasonography, computed tomography, or magnetic resonance imaging prior to inserting thermal ablative probes into the mass either percutaneously or through laparoscopy.

When addressing treatment options for an SRM, extirpative measures are the gold standard in healthy individuals without confounding comorbidities or circumstances. However, thermal ablative techniques may be recommended as a treatment modality in those with stage T1a lesions and significant competing comorbidities.

Cryoablation

SRM management was first described in 1995. However, automated cryoablation technology and its use in tissue destruction have been evolving since the 1960s. Current cryoablation probes capitalize on the Joule-Thomson effect by using pressurized argon and helium gases to rapidly freeze and thaw targeted lesions. Adjusting the rate of gas flow or adding additional probes tailors the ice ball to treat each individual lesion. The effects of cryoablation are many, but they may not be fully realized until hours after the procedure has terminated. Extracellular freezing, targeted tissue desiccation, intracellular pH alterations, and protein denaturation can occur during active cooling. Intracellular ice crystal formation accounts for the mechanical destruction of the intracellular organelles as well as the cell membrane when temperatures ap-
because urologists may be overtreating lesions when applied to appropriately selected candidates. This practice has been endorsed by the American Urology Association and the European Urological Association when applied to appropriately selected candidates because urologists may be overtreating lesions of potential insignificance. Table 4 provides a review of contemporary publications addressing cohorts actively surveyed renal masses.

In 2011, 178 patients with 209 incidentally discovered SRMs were prospectively enrolled in a phase II clinical trial of active surveillance with treatment delayed until the time of progression. Eligible patients were diagnosed with an SRM within the last 12 months without any evidence of metastasis or history of systemic therapy. Patients had a life expectancy of more than 2 years and received a percutaneously acquired needle core biopsy of the lesion. Thirty-four (22.5%) of the 151 lesions with at least 1 year of follow-up and at least two sets of imaging demonstrated local progression; only 2 (1.6%) of the patients exhibited distant metastasis at a median follow-up of 28 months from the time of initial diagnostic imaging. The mean overall growth rate was 0.13 cm/year with no discernible difference in growth rates between those lesions proven by biopsy as malignant compared with those histologically defined as benign. A second prospective study from 2011 involving 82 patients examined the growth kinetics of renal masses. However, due to the multicenter nature of the two aforementioned studies and their overlap of authorship, they were unable to validate whether these were two completely distinct cohorts. A study by Mason et al included patients with lesions up to 7 cm with a minimum radiographic follow-up of only 6 months. However, the median follow-up time was 36 months. Larger masses were allowed and included in the study and stratified by size. Lesions of ≥2.45 cm in diameter were associated with a more rapid growth rate (0.4 cm/year) compared with lesions of <2.45 cm in diameter (0.13 cm/year), with an overall rate of 0.25 cm/year. These values are consistent with a meta-analysis of 8 retrospectively examined cohorts involving 234 renal lesions with no evidence of local and/or distant metastases that exhibited a mean annual growth rate of 0.28 cm/year, with only 3 (1%) of the patients progressing to metastatic disease at a mean follow-up time of 34 months. Of note, tumor size at the initial diagnosis was not predictive of the growth rate of the mass within this meta-analysis. However, of those lesions pathologically confirmed as malignant, the growth rate was 0.4 cm/year.

Recently, a rise in the utilization abdominal cross-sectional imaging has been associated with a rising incidence of RCC, an increasing prevalence of incidentally discovered renal masses, and a downward stage migration over the same time period. These findings, along with a paradoxical concomitant rise in rates of cancer-specific mortality, increasing life expectancy, and an increasing cumulative burden of comorbidities, have led urologists to offer active surveillance as a form of management to their patients when addressing a newly diagnosed SRM and determining the most suitable therapeutic choice. This practice has been endorsed by the American Urology Association and the European Urological Association when applied to appropriately selected candidates because urologists may be overtreating lesions of potential insignificance. Table 4 provides a review of contemporary publications addressing cohorts actively surveyed renal masses.

Radiofrequency Ablation
RFA uses alternating radiofrequency energy delivered by a probe, generating heat from the impedance of targeted cells to achieve cell death and coagulation necrosis. Temperatures can reach up to 105°C, but tissue is destroyed at temperatures exceeding 70°C, leaving behind a necrotic lesion after 24 to 48 hours and reaching maximal size within 7 days. RFA was first applied to renal tumor management in 1997.88

Outcomes
To date, there remains a paucity of prospective randomized studies reporting the outcomes of thermal ablative techniques (Table 3). However, in 2008, Kunkle and Uzzo provided a meta-analysis of 47 studies inclusive of 1,375 SRMs with a mean tumor diameter of 2.6 cm treated with cryoablation or RFA. At a median follow-up of 18.7 months, 5.2% and 12.9% of lesions managed with cryoablation and RFA, respectively, had local progression, representing a significant difference between the two cohorts (P < .001). Further, metastatic progression rates were noted in 1% of patients treated with cryoablation and 2.5% of patients treated with RFA. However, these rates were not significantly different. The combined rates of local progression and distant metastasis were 1.8% and 1%, respectively, which is similar to the rate of distant metastasis reported after nearly 3 years of follow-up in the active surveillance studies described below.

Active Surveillance
Recently, a rise in the utilization abdominal cross-sectional imaging has been associated with a rising incidence of RCC, an increasing prevalence of incidentally discovered renal masses, and a downward stage migration over the same time period. These findings, along with a paradoxical concomitant rise in rates of cancer-specific mortality, increasing life expectancy, and an increasing cumulative burden of comorbidities, have led urologists to offer active surveillance as a form of management to their patients when addressing a newly diagnosed SRM and determining the most suitable therapeutic choice. This practice has been endorsed by the American Urology Association and the European Urological Association when applied to appropriately selected candidates because urologists may be overtreating lesions of potential insignificance. Table 4 provides a review of contemporary publications addressing cohorts actively surveyed renal masses.

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### Table 3. — Selected Trials of Outcomes of Renal Mass Thermoablation

<table>
<thead>
<tr>
<th>Study (yr)</th>
<th>Study Type</th>
<th>No. of Patients</th>
<th>Approach</th>
<th>Modality</th>
<th>Age (yrs)</th>
<th>Tumor Size (cm)</th>
<th>Follow-up (yrs)</th>
<th>Rate of Local Recurrence (%)</th>
<th>Metastasis Rate (%)</th>
<th>CSS (%)</th>
<th>OS (%)</th>
<th>Complication Rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>del Cura77 (2010)</td>
<td>Retro</td>
<td>65</td>
<td>Perc</td>
<td>RFA</td>
<td>68.0</td>
<td>3.1</td>
<td>2.2</td>
<td>7.7</td>
<td>—</td>
<td>89.7</td>
<td>13</td>
<td></td>
</tr>
<tr>
<td>Ferakis88 (2010)</td>
<td>Retro</td>
<td>39</td>
<td>Perc</td>
<td>RFA</td>
<td>61.4</td>
<td>3.1</td>
<td>5.1</td>
<td>10.2</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td></td>
</tr>
<tr>
<td>Tracy89 (2010)</td>
<td>Retro</td>
<td>208</td>
<td>Perc/Lap/Open</td>
<td>RFA</td>
<td>64.0</td>
<td>2.4</td>
<td>2.3</td>
<td>4.4</td>
<td>1.4</td>
<td>99.5</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Zagoria90 (2011)</td>
<td>Retro</td>
<td>41</td>
<td>Perc</td>
<td>RFA</td>
<td>—</td>
<td>72</td>
<td>2.6</td>
<td>4.7</td>
<td>12.2</td>
<td>7</td>
<td>97.6</td>
<td>59</td>
</tr>
<tr>
<td>Ji91 (2011)</td>
<td>Retro</td>
<td>106</td>
<td>Lap</td>
<td>RFA</td>
<td>58.1</td>
<td>—</td>
<td>2.7</td>
<td>0.9</td>
<td>100</td>
<td>—</td>
<td>100</td>
<td>6.6</td>
</tr>
<tr>
<td>Chalasani92 (2010)</td>
<td>Retro</td>
<td>19</td>
<td>Lap/Open</td>
<td>Cryo</td>
<td>56.7</td>
<td>2.6</td>
<td>3.5</td>
<td>21</td>
<td>—</td>
<td>94.7</td>
<td>89.5</td>
<td>0</td>
</tr>
<tr>
<td>Strom80 (2011)</td>
<td>Retro</td>
<td>61</td>
<td>Perc</td>
<td>Cryo</td>
<td>68.6</td>
<td>2.7</td>
<td>2.6</td>
<td>16.4</td>
<td>—</td>
<td>93.7</td>
<td>88.9</td>
<td>14.8</td>
</tr>
<tr>
<td></td>
<td>Retro</td>
<td>84</td>
<td>Lap</td>
<td>Cryo</td>
<td>65.7</td>
<td>2.5</td>
<td>3.5</td>
<td>5.9</td>
<td>—</td>
<td>91.7</td>
<td>89.3</td>
<td>15.5</td>
</tr>
</tbody>
</table>

Cryo = cryoablation, CSS = cancer-specific survival, Lap = laparoscopic, OS = overall survival, Perc = percutaneous, Retro = retrospective, RFA = radiofrequency ablation.

### Table 4. — Selected Trials of Outcomes for the Active Surveillance of Renal Masses

<table>
<thead>
<tr>
<th>Study (yr)</th>
<th>Study Type</th>
<th>No. of Patients</th>
<th>Age (yrs)</th>
<th>Tumor Size (cm)</th>
<th>Follow-up (yrs)</th>
<th>Growth Rate (cm/yr)</th>
<th>Progression&lt;sup&gt;a&lt;/sup&gt; Rate (%)</th>
<th>Metastasis Rate (%)</th>
<th>CSS (%)</th>
<th>OS (%)</th>
<th>Received Definitive Management (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abou Youssif94 (2007)</td>
<td>Retro</td>
<td>35</td>
<td>71.8</td>
<td>2.2</td>
<td>4.0</td>
<td>0.21</td>
<td>0.17</td>
<td>5.7</td>
<td>100</td>
<td>74.3</td>
<td>22.9</td>
</tr>
<tr>
<td>Kouba95 (2007)</td>
<td>Retro</td>
<td>43</td>
<td>67.0</td>
<td>2.9</td>
<td>3.0</td>
<td>0.7</td>
<td>0.35</td>
<td>0</td>
<td>—</td>
<td>100</td>
<td>90.7</td>
</tr>
<tr>
<td>Abouassaly96 (2008)</td>
<td>Retro</td>
<td>110</td>
<td>81.0</td>
<td>2.5</td>
<td>2.0</td>
<td>0.26</td>
<td>0.08</td>
<td>3.6</td>
<td>—</td>
<td>100</td>
<td>69</td>
</tr>
<tr>
<td>Crispen96 (2008)</td>
<td>Retro</td>
<td>109</td>
<td>69.8</td>
<td>2.6</td>
<td>2.0</td>
<td>0.28</td>
<td>0.21</td>
<td>4.3</td>
<td>1.4</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Haramis97 (2011)</td>
<td>Retro</td>
<td>44</td>
<td>71.7</td>
<td>2.7</td>
<td>6.4</td>
<td>0.15</td>
<td>0</td>
<td>0</td>
<td>100</td>
<td>97.7</td>
<td>4.5</td>
</tr>
<tr>
<td>Jewett98 (2011)</td>
<td>Prosp</td>
<td>178</td>
<td>73.0</td>
<td>2.1</td>
<td>0.13</td>
<td>13.1</td>
<td>1.1</td>
<td>100</td>
<td>94.4</td>
<td>5.1</td>
<td></td>
</tr>
<tr>
<td>Mason99 (2011)</td>
<td>Prosp</td>
<td>82</td>
<td>74.0</td>
<td>2.3</td>
<td>3.0</td>
<td>0.25</td>
<td>—</td>
<td>—</td>
<td>1.2</td>
<td>98.8</td>
<td>91.4</td>
</tr>
</tbody>
</table>

<sup>a</sup>Total progression inclusive of local and distant disease; however, there is no consistent definition of local progression.

CSS = cancer-specific survival, OS = overall survival, Prosp = prospective, Retro = retrospective.
local cancer control.\textsuperscript{98,99} Although our knowledge of the natural history of renal masses is growing, it remains unclear — and without validation — as to what size or histological criteria are indicative of rapid progression or metastasis. Further, percutaneous renal biopsy is warranted when a renal lesion is suspicious for a distant metastasis or presents in the clinical context of a prior malignancy or minimally enhancing renal mass of < 3 cm at its largest diameter.

Conclusions

Significant advances have been made in our therapeutically armamentarium for small renal masses. Patients currently presenting with a suspicious renal lesion have several treatment options to consider, including partial or radical nephrectomy (open, laparoscopic, robotic-assisted), percutaneous ablation (eg, radiofrequency ablation, cryoablation), and active surveillance. The treatment choice recommended to individual patients must take into account physician experience and training, patient expectations and comorbidities, and tumor-specific characteristics (ie, size and location). As we embark on a new era of personalized medicine, treating urologists and health care professionals alike must become familiar with these treatment options and understand their merits and pitfalls, thereby providing patients with realistic expectations and treatment outcomes.

References


