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Review Article

Review of management options for localized renal cell carcinoma

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Abstract
Renal cell carcinoma (RCC) is the most common primary renal neoplasm in the United States. RCC consists of a range of kidney tumors that are distinct in histological and biological progression, wherein certain tumors have excellent prognosis due to their indolent nature and others have high metastatic potential. The majority of patients that are diagnosed with a small renal mass are found incidentally during radiology studies for other reasons. Through modern medicine and surgical advances, we understand that not all small renal masses require surgical or other procedural interventions due to the vast spectrum of biological behavior of these tumors. This article is an overview of current minimally invasive techniques utilized in the treatment of RCC including surgical interventions, ablative therapies and active surveillance.
Keywords: renal cell carcinoma; surgery; ablation; oncology; minimally invasive surgery

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Background

Renal cell carcinoma (RCC) is the most common primary renal neoplasm constituting approximately 2-3% of all adult neoplasms in the United States with an estimated 64,000 newly diagnosed cases yearly and an approximate annual mortality rate of 14,000 [1]. The highest incidences occur in those 65-75 years of age with a median age of diagnosis at 64 years. Despite advancements in diagnosis and treatment, RCC remains the most lethal of the common genitourinary malignancies. Five-year survival rates for kidney cancer, bladder cancer, and prostate cancer are 74.1%, 77.3%, and 98.6% respectively [2]. Impressive improvements have been seen with 5-year survival rates, which was 65.5% in 2000. Nonetheless, further research is needed to uncover areas for improvement and innovation.

The number of newly diagnosed RCC cases has been on the rise within the past few decades. This is largely due to incidental findings on radiologic imaging such as ultrasonography (US), computed tomography (CT), and magnetic resonance imaging (MRI) [3]. US, in particular, is a widely utilized, economically feasible, noninvasive imaging modality frequently used for a wide array of abdominal complaints. It has been well documented in the literature since 1971 that US is an accurate means of identifying malignant renal neoplasms. This is due to its fundamental capacity to differentiate cystic from solid masses [4]. A suspicious mass found incidentally on US is often further investigated, and may consequently lead to the diagnosis of RCC. A recent 2017 meta-analysis showed that in asymptomatic patients whom underwent abdominal US for screening or other abdominal symptoms unrelated to renal malignancy, 0.35% had a positive detection of at least one renal mass and 10% of those masses showed a histologically proven RCC. This translates that at least one RCC will be detected per 1000 individuals undergoing abdominal US for complaints unrelated to RCC [5].

Due to this widespread nonsystematic partial screening process, more incidental renal masses are being discovered in asymptomatic patients. Although concerning, no formal guidelines for screening are recommended at this time. High-quality randomized prospective research studies and cost-effective analyses are still needed in order to establish screening protocols.5 In addition, many incidentally discovered RCC cases are lower stage and smaller size. In fact, many are indolent localized masses with an overall better prognosis [6]. Based on the University of California Los Angeles Integrated Staging System (UISS), the 5-year survival rate for early localized RCC were 92%, 67%, and 44% for low, intermediate, and high-risk groups, respectively [7]. These survival rates are an improvement compared to earlier reports, and are likely reflective of the increase in detection of low stage (T1-T2) disease in asymptomatic patients as well as refinement in the techniques and management of RCC [2].

The focus of this review paper is on minimally invasive approaches for the management of localized RCC. Modern medicine has led us to utilize multidisciplinary approaches to solving complex disease processes. In particular, in the realm of surgery, minimally invasive surgery (MIS) has been at the forefront in redefining what it entails to undergo a surgical operation. Using MIS, surgeons are able to achieve excellent results in surgical outcomes and cancer free rates, with decreased perioperative morbidity. By utilizing the most advanced technology, and integrating radiologic guidance and histological analysis, the range of minimally invasive therapeutic options for patients with RCC has expanded drastically. This allows many patients to avoid undergoing an invasive open surgery with possible unwarranted risks with intraoperative blood loss, longer recoveries, and extended hospital stays.

This article will discuss the history of RCC treatment and compile a comprehensive review regarding modern minimally invasive techniques designed to decrease unnecessary complications and future burden on patients. Our aim is to outline the past and current RCC treatment modalities and assess their efficacy in terms of operative and oncologic outcomes.

History of Treatment

The management of RCC has evolved continuously throughout history with surgery remaining a mainstay treatment [8]. Initially, simple nephrectomy was described as the mainstay for the treatment of renal masses, however in 1962 Robson and colleagues illustrated a modification of this procedure when they reported the radical nephrectomy (RN) technique at the American Urological Association meeting [9].

Robson followed this report with a case-series in 1969 which analyzed 88 cases of patients with RCC that underwent RN between 1949 and 1964. This study showed a statistically significant improvement in survival rates at 3, 5, and 10 years when compared to other published series at that time [10]. This quickly resulted in RN becoming the standard of care for the treatment of RCC.

While RN is still widely used today, an alternative nephron-sparing surgical approach has gained popularity, as patients were experiencing significantly higher rates of cardiovascular complications and chronic renal insufficiency after undergoing RN [8, 11, 12]. The surgical principle of performing a partial nephrectomy (PN) despite a normal functioning contralateral kidney was published in 1950 by Vermooten [13]. However, at that time it was difficult for this procedure to gain traction due to concerns for uncontrolled hemorrhage, persistent urinary fistulas, and tentative outcomes. As time went on, and with the introduction of renal hypothermia to prevent ischemic damage, advancements in imaging, and refinement of techniques with improved outcomes, PN rose to acceptance as a reasonable surgical option in the late 1990's.13 Subsequently, after published results of long-term follow-ups displayed an almost 100% survival rate at 10 years with few local recurrences, PN became a well-supported means of treatment for small (T1-T2) noninvasive unilateral RCC tumors [14, 15]. When comparing PN to RN, a large multicenter prospective study in 2010 illustrated that both procedures result in comparable oncological outcomes. This study concluded that PN is the preferred choice in removing small tumors when technically feasible [16]. The 2017 AUA guidelines reflect this, stating: "Physicians should prioritize PN for the management of the cT1a renal mass when intervention is indicated. In this setting, PN minimizes the risk of chronic kidney disease (CKD) or CKD progression and is associated with favorable oncologic outcomes, including excellent local control (grade B recommendation) [17].

As with other surgical fields, the urologists managing renal malignancies embraced the integration with minimally invasive technologies and approach. The initial report of a laparoscopic nephrectomy was published in 1991, with the study suggesting that this approach be limited to benign disease of the kidney [19]. Subsequently, with advances in technology, more precise instrumentation, and improved imaging modalities, the use of laparoscopic techniques have since become widely accepted for a number of surgical procedures, achieving excellent results in many benign and malignant disease processes. In a recent meta-analysis published in 2017 comparing laparoscopic versus open radical nephrectomy, laparoscopic radical nephrectomy (LRN) was associated with improved overall mortality, lower postoperative complications, and better perioperative outcomes when compared with open radial nephrectomy (ORN) [18].

The laparoscopic approach has further expanded with the advent of hand-assisted or robotic-assisted-laparoscopic radical and partial nephrectomies, thermal ablative therapies such as cryoablation (CA) and radiofrequency ablation (RFA), and other modalities such as renal tumor enucleation, high intensity focused ultrasound (HIFU), and Cyberknife [3, 19]. At this time, additional research is still needed to provide a more comprehensive understanding of how several of minimally invasive modalities can be best utilized to yield maximum results in the clinical setting.

Minimally Invasive Surgery

Minimally invasive surgical techniques for treatments of RCC include the use of hand-assisted laparoscopic radical and partial nephrectomies as well as robotic-assisted radical and partial nephrectomies. Current 2017 AUA guidelines states that "use of minimally invasive approach in the removal of renal masses should be considered whenever possible so long it does not compromise oncological, functional or perioperative outcomes."13 This is well supported by many studies showing a significant advantage with laparoscopic techniques in reducing blood loss and length of hospital stay. In certain circumstances, laparoscopic surgery can reduce operative and warm ischemic time as well [20].

While guidelines and trends shift towards more a minimally invasive laparoscopic approach, this is not reflected on a population level. A recent population-based study evaluating the rates of open versus laparoscopic in partial and radical nephrectomy for T1a RCC showed that, between 1988 and 2005, the utilization rates for both LRN and LPN remain low with little variation over time. This likely reflects the surgical complexity, equipment requirements, and learning curve associated with use of laparoscopic and robotic devices, particularly in the context of partial nephrectomy. Furthermore, while open partial nephrectomies (OPN) are a preferred standard of care in patients with small renal masses, this resection method was often forfeited in elderly and female patients for a more minimally invasive approach with LRN. The authors expressed concerns that these patients may be denied the benefits of nephron-sparing surgery (NSS) to prioritize a minimally invasive approach [21]. Despite being limited in detailed information of tumor characteristics that impacts treatment approaches, the authors underscore an important point. It remains unclear whether NSS or minimally invasive techniques are more imperative in management of RCC. When both are not technically feasible, it is best to individualize management and advise accordingly to optimize perioperative, functional, and oncological outcomes.

Evidence for laparoscopic radical nephrectomy

Laparoscopic radical nephrectomy (LRN) has supplanted open radical nephrectomy (ORN) as a preferred standard of care for patients with RCC requiring complete removal of their kidney [13, 15]. Many studies have analyzed the outcomes of LRN versus ORN. Early on, Willie et al. reported that LRN and ORN were comparable in terms of achieving surgical objectives and early oncological outcomes [22]. These findings were consistent in a long-term follow-up study by Berger et al., which reported a 10-year cancer specific survival rate of 92% and recurrence-survival of 86% post-LRN. However, based on their data it was unknown at that time whether LRN was superior to ORN for long-term oncological control [23].

In a recent multi-institutional retrospective study comparing long-term oncological outcomes between hand-assisted LRN (HLRN) and ORN, a multivariate analysis was performed on 1098 patients who underwent radical nephrectomy. Using Cox's proportional hazards model, their data illustrated that surgical methods were not a predictive factor for disease-free survival or cancer specific survival. In terms of complications and safety, their study showed that overall perioperative complication rates were significantly higher in the ORN versus LRN. Additionally, despite having equivocal operative times for both procedures, LRN was found to have significantly less estimated blood loss and transfusion rates. They concluded that HLRN is preferential to ORN due to fewer perioperative outcomes while maintaining comparable operative time and oncological results [24]. A 2017 meta-analysis supports this conclusion. This meta-analysis reviewed similar studies that also found no significant difference in cancer-specific mortality or local tumor recurrence when comparing long-term oncologic outcomes between LRN and ORN. Therefore, LRN is recommended over ORN for its superior perioperative results, especially in small tumors <7cm [18].

On a population level, these convalescence benefits have been shown to be consistent [25]. Tan et al. showed that patients post-LRN were less likely to be admitted to the ICU and had significantly shorter hospital stays. However, an unexpected consequence of

LRN was seen in this study. Their analysis showed a significantly higher rate of inpatient mortality associated with LRN at low-volume facilities. This suggests that there may be an initial phase of increased adverse events during the early integration of laparoscopic techniques at an institution, possibly due to learning curve of surgical techniques. The authors cautioned that with the widespread adoption of minimally invasive surgeries, physicians should be more vigilant for complications and address them in a timely manner. This has implications outside of just LRN, but is ubiquitously applicable to all novel procedures including laparoscopic partial nephrectomy (LPN) and especially with the introduction of robotic assistive devices.

Evidence for laparoscopic partial nephrectomy

Despite being a technically challenging procedure with risks of hemorrhage and renal ischemia, there has been a rapid diffusion of LPN into clinical practice. Parsons et al. examined the diffusion of LPN and associated patient safety compared to OPN. Prevalence of both open and laparoscopic partial nephrectomy has increased substantially from 1998 to 2009, but the relative rate of increase for LPN has been greater. Patient safety was measured using patient safety indicators (PSI) which was formed using a published list from the Agency for Healthcare Research and Quality (AHRQ) and incidence of anesthetic complications. The PSI measured acute events concurrent with the same hospitalization as the surgery. Using a multivariate analysis, they experienced a 28% decreased probability of PSI in LPN. The study concluded that despite rapid diffusion of LPN, it has shown to be a safely adopted novel surgical technique with significantly better perioperative outcomes compared to OPN [26].

When compared with OPN, LPN patients with single small renal tumor <7cm have been shown to have shorter operative time, less estimated blood loss, and shorter hospital stays. In addition, they appear to have comparable functional and early oncological outcomes as OPN [27]. As for long-term oncological outcomes, a 10-year follow-up study showed that outcomes between OPN and LPN were comparable in patients with small cortical renal tumors. Overall survival appeared to be independent of operative technique used [28].

Evidence for Robotic Assisted Nephrectomy

An alternative to hand-assisted laparoscopic or pure laparoscopic surgery is the use of robotic platforms (RAL). In July 2000, the US Food and Drug Administration approved the use of RAL devices in surgery [29]. Since then, they have been highly integrated at many large institutes worldwide with many procedures having the option to be done robotically. From October 2008 to December 2009, the United States witnessed an increase of 18.9% of partial nephrectomies performed with RAL devices.30 When compared with OPN, RAL partial nephrectomy (RALPN) can be done without prolong warm ischemic time while offering the advantages of minimally-invasive surgery [31]. However, further studies are investigating the perceived benefits of RALPN compared to LPN.

RALPN resulted in an estimated $5,000- $11,000 increase in medical expenses compared to LRN. Despite rise in cost, there are no added benefits to perioperative outcomes or patient morbidity [32]. Therefore, assuming the availability of LRN, some suggest RAL devices should not be widely accepted as a first-line treatment approach for RN.

However, PN are more complex, requiring an additional surgical skillset and armamentarium to complete. The RAL platform allows for an improved magnification of the surgical field along with enhanced range of motion and precise movements of the robotic arms. Some suggest that these improvements make RAL devices highly attractive when performing a partial nephrectomy. Furthermore, it has been reported that training for RALPN can be successfully completed with a short learning curve allowing for, theoretically, an easy transition from LPN to RALPN [33, 34]. Although advanced RAL technology may improve operative techniques, its effects on patient outcomes are more imperative.

Recently, Choi et al. performed a large meta-analysis comparing robotic and laparoscopic partial nephrectomy for RCC. This study displayed favorable outcomes in the RALPN group with lower rates of conversion to open or radial surgery, shorter warm ischemic times, improved early renal function outcomes, and shorter hospital stays. Their analysis published no significant differences in change of serum creatinine, operative time, estimated blood loss, or positive surgical margin [35]. While this is the largest meta-analysis of its kind to date, a major limitation of this study is the poor quality of research available. At this time, randomized clinical studies with large cohorts, long-term follow-up studies, and more cost-benefit analyses are required in order to establish a comprehensive evaluation of benefits of RAL platforms during PN.

Recommendations for minimally invasive surgical management

For management of RCC using minimally invasive surgical techniques, consideration should first be given to either treating with excision or resection. Currently, NSS is the gold standard for treatment of small RCC (<4cm) due to its more favorable impact on post-surgical renal function and long-term cardiovascular effects [16]. In patients with RCC requiring radical nephrectomy, LRN is the preferred surgical intervention yielding optimal perioperative, oncological, and economical outcomes. However, for patients undergoing partial nephrectomy, a surgical approach that utilizes RAL technology should be strongly considered. Current data suggests that intraoperative and perioperative outcomes of RALPN may be superior to LPN and therefore may justify the added cost [35].

Thermal Ablative Therapies: Radiofrequency Ablation and Cryoablation

Alternatives to the above mentioned surgical techniques in the management of localized RCC include the use of thermal ablative therapies such as radiofrequency ablation (RFA) and cryoablation (CA). Historically, thermal ablative treatments have been primarily used in patients with significant comorbidity who may be poor surgical candidates. However, additional consideration is given to these minimally invasive techniques in patients with limited renal function at baseline or patients at risk to lose additional nephrons in the future. This includes patients with bilateral RCCs, a genetic predisposition to multiple tumors, chronic renal insufficiency, or a solitary kidney. Furthermore, these ablative options may be used for patients with local tumor recurrence after previous nephrectomy, distant metastases from primary RCC, or patients who require tumor debulking. Ablative techniques require a 0.5 to 1.0 cm margin to ensure that the entire tumor was treated. It is typically suggested that ablation is reserved for tumors <4 cm and that tumors between 3-4 cm may require multiple ablations for successful treatment. Contraindications to RFA or CA include tumors >5 cm or tumors near the hilum or collecting system [36].

Radiofrequency ablation (RFA)

RFA was originally utilized as an experimental treatment of small renal masses in the early 2000s, and has grown significantly as a promising treatment option. This minimally invasive technique has been widely utilized for treatment of solid tumors, particularly those involving the liver, kidneys, lungs, and musculoskeletal system [37]. In the setting of renal masses, RFA is used by both interventional radiologist and urologists, however it tends to be applied more frequently by interventional radiologists.38 The procedure uses a catheter which transmits an alternating current that produces heat. The heat is directed at the targeted tumor cells resulting in cell death at temperatures above 60°C. The procedure is guided either by CT or US and can be conducted via laparoscopic or percutaneous techniques. Prior to any ablative procedure, the patient undergoes pre-treatment imaging and biopsy to document pathologic status of the renal mass. Post-RFA, technical success is determined by the absence of contrast enhancement on contrast enhanced CT or MRI [39].

Cryoablation (CA)

CA is an additional thermal ablative technique used in the treatment of small renal masses. While RFA uses heat to destroy tumor cells, CA employs freezing temperatures. It is a procedure used by both interventional radiologists and urologists. However, unlike RFA, it is typically performed more frequently by urologists for treatment of RCC simply based on operator experience and preference [38]. CA works by utilizing liquid nitrogen or argon released from a probe to systematically freeze, thaw, and refreeze tissues. This cyclic exposure to low freezing temperatures results in the formation of intracellular ice crystals that disrupt the tumor cells' membrane, resulting in cell death. Consequently, the dead tissue around the probe becomes an "ice ball" with complete cell death achieved at 3 mm inside the "ice ball." Therefore, a 5 mm margin beyond the tumor edge is used to ensure complete tumor cell destruction.36 Cryoablation can be performed laparoscopically, percutaneously, or with an open approach. Close follow-up is required with post-procedural imaging typically performed at 1, 3, 6, 12, 18, and 24 months with 12 month intervals thereafter. Like RFA, lack of enhancement is an indication that the CA was successful [36, 40].

The current use of ablative techniques is primarily in patient populations that are poor surgical candidates, and much of the evidence relies on retrospective studies prone to selection bias. While the current evidence strongly supports the size guidelines of < 4 cm for ablation, and the superior peri-operative complication rate and renal function preservation of ablation, no randomized clinical trials have been completed to establish the use of ablation in patients with small renal tumors that are good surgical candidates.

Evidence for Radiofrequency Ablation

RFA is effective at destroying tumor, preventing recurrence, and achieving good long-term outcomes, particularly for RCC T1a tumors.38 When compared to partial nephrectomy (PN), RFA has mixed results regarding long-term outcomes, and has occasionally been shown to have more frequent local recurrence. However, RFA is associated with lower overall complication rates and is highly effective at preserving renal function.

When considering minimally invasive procedures with an emphasis on preservation of renal function, RFA is a viable treatment option in terms of technical success, survival outcomes, and limited recurrence [39, 41-45]. A study by Breen, et al. analyzed 105 renal tumors treated with ultrasound or CT guided RFA. This study displayed an overall technical success rate of 90.5% with no local recurrences on a mean follow-up of 16.7 months [41]. Additionally, Wah et al. reported a 98.5% technical success rate, with local recurrence free survival of 93.5% and cancer specific survival of 97.9% with mean follow-up of 46.1 months [39]. They also found that 98% of patients had preserved renal function when comparing pre and post-procedure GFR [39]. These studies were limited by their retrospective nature and small sample sizes but their findings are consistent. These studies support RFA as an effective, minimally invasive therapy for treatment of small renal tumors while having the added benefit of preserved renal function.

A major variable predicting efficacy of treatment is tumor size. Breen et al. determined that tumors < 3 cm are more likely to be successfully treated after 1 session [41]. Similarly, in 2011 Zagoria et al. published a 12% recurrence rate after a single ablation session. In this study tumor size predicted recurrence: recurrent tumors had an average size of 5.2 cm, compared with 2.2 cm for tumors without local recurrence [46]. Furthermore, they found no recurrence when RCC's were less than 4 cm.46 Zagoria et al. in 2001 reached similar conclusions, that RFA is reliable in eradicating RCCs 3.7 cm or smaller, and that treatment of larger tumors by RFA increases risk of residual disease [47].

Evidence for Cryoablation

Treatment of T1 renal tumors with CA has shown long-term efficacies with minimal effects on renal function. A retrospective analysis of 91 patients, with mean tumor size of 3.4 cm and mean follow-up time of 26 months, saw a technical success rate of 96% as well as a local control rate of 95%. Based on their data, they concluded that beyond 3 months' post-treatment the incidence of tumor recurrence is minimal [48]. In fact, Finley et al. found cancer specific survival of 100% over a 1 year follow-up period [49]. Longer term outcomes have also been promising at both 5 and 10 year follow up with minimal impact on kidney function [50-53]. Nielson et al. reviewed a total of 808 patients who underwent laparoscopic CA [51]. They found a 5 and 10-year survival of 90.4% and 80%, respectively, with a local recurrence rate of 3.1% and progression to metastatic disease only in 0.8% of patients. Similarly, a review article with meta-analysis in 2016 by Zondervan et al. concluded that 30-month local tumor progression rate was 8.5% with a 5-year overall RFS of 86.3%, with effective preservation of renal function [53].

The available literature for long-term outcomes CA is limited with most being non-randomized retrospective reviews. Based on current understanding, CA appears to be effective for treating small renal tumors <3 cm, with good technical success, local disease control, and good survival with preservation of renal function.

CA vs. RFA

CA and RFA are both minimally invasive methods used to treat small renal tumors in patients that are higher risk surgical candidates. Given the similar indications for the two procedures, they are often used interchangeably by practitioners based on individual preference. Data comparing the two procedures has been inconclusive, finding no significant difference between RFA and CA in recurrence free survival [54]. A review by Gervais e. al. calculated that the number of patients required to adequately assess the small (if any) differences between RFA and CA with a randomized control trial would be highly restrictive and makes such a study unlikely [54]. They went on to conclude that neither RFA nor CA have data to support a definitive answer for benefits of one ablation method over the other.

RFA and CA vs. PN

Both RFA and CA have been shown to effectively treat T1 small renal masses, however, in order to establish which NSS is best suited for patients, these thermal ablation techniques must be compared to PN.

When comparing RFA and CA to PN for small renal tumors, thermal ablative techniques have been shown to have good short term disease control, lower complication rates and better preservation of renal function. However, some studies have suggested that local recurrence of disease may be slightly higher with thermal ablation techniques versus PN, and suggest that long-term metastasis free survival may be better with PN [55-58]. Pantelidou et al. concluded that RFA produced fewer peri-operative complications and better preservation of renal function, while RALPN demonstrated an insignificantly lower recurrence rate.57 However, in a systematic review conducted by Katsanos et al., they concluded that thermal ablation via RFA produced similar oncologic outcomes to PN with significantly lower complication rates and significantly less renal function deterioration [58].

Several studies have also compared the effectiveness of CA to PN, with evidence indicating CA allows for lower peri-operative complication rates and better preservation of renal function. However, results have been mixed in regards to the oncologic outcomes of CA versus PN. Some studies suggest CA has a higher risk of local recurrence and metastatic tumor progression with lower recurrence free survival and cancer specific survival, while others have found no difference [38, 42, 59-61]. Additionally, the follow-up and long-term screening required with CA is more extensive than PN. Thus, when counseling patients it is imperative to discuss the importance of regular post-operative follow-up when considering CA. Further study is required to more definitively establish differences in oncologic outcomes between the two procedures.

These studies suggest that RFA and CA offer mixed oncologic outcomes, with fewer complications and better preservation of renal function, however some mixed results suggest that further study is needed to firmly establish thermal ablative techniques as equal to or lesser than PN in the long-term.

Current Guidelines and Our Recommendations

The most recent American Urological Association (AUA) guidelines, published in 2016, and European Association of Urology (EAU) discuss the use of thermal ablation in localized RCC. Much of the evidence quality for thermal ablation grade C, indicating that further research is needed to definitively support these recommendations. Current guidelines recommend that thermal ablation should be considered for the management of cT1a masses < 3 cm in size with prior biopsies. As previously referenced, while some believe that tumors up to 4 cm in size can be successfully treated with thermal ablation, we agree with the AUA guideline of < 3cm given that size has been shown to predict successful treatment outcomes. This size guideline could also be further modified if the patient has significant comorbidities given the lower risk of complications and better preservation of renal function. AUA guidelines also recommend that patients who undergo thermal ablation be counseled about the increased requirement for post-procedure follow-up and risk of local recurrence or tumor persistence that may require additional ablations. This was also consistent with our findings in this review.

Finally, the AUA and EAU addressed thermal ablation versus PN. They concluded that there may be a higher risk of local recurrence in thermal ablation, but that long-term oncologic outcome data is mixed. They did point out that there have been no studies that show superior oncologic outcomes in thermal ablation, while several studies have shown superior long-term outcomes of PN when the procedures have been compared. We conclude that while some data have suggested beneficial oncologic outcomes of PN when compared to thermal ablation, further study must be done to definitively establish this difference. The AUA and EAU guidelines also addressed RFA and CA compared to PN in terms of post-procedure renal function and complication rates. The AUA review concluded that there was no difference between thermal ablation and PN in renal function preservation, however our review concluded differently. We recommend that for patients who require better preservation of renal function, or are at higher risk of surgical complications, serious consider should be made for thermal ablation over partial nephrectomy.

Observation at a Minimum

Most small renal masses (SRM) are discovered incidentally, have an indolent course, and have little metastatic potential [62]. As such, there have been concerns regarding over-diagnosis and overtreatment of renal tumors found incidentally, especially in the setting of improving imaging modalities with greater anatomic detail [62, 63]. Efforts have moved towards preserving quality of life, preserving renal function, and reducing co-morbidities among this potentially complex patient population [63, 64]. In a study completed in 2008, a group designed the Charleston Comorbidity Index (CCI), which evaluated patients' comorbidities and candidacy for surgery.65 This has proven to be a useful tool for providers to help guide patients and discuss treatment options. Their results demonstrated that a Charleston index score categorized of 2 or less versus 2 or greater had significant difference in survival (*P*<0.001) [65]. Therefore, the use of this algorithm to have an objective way to identify clear clinical criteria to delineate and identify patient populations who would benefit more from observation rather than enduring more invasive procedures.

Maurice et al. conducted a study regarding non-clinical factors associated with observation for patients with renal cell carcinoma [66]. This study demonstrated that patients >75 years old, had a CCI score >1, or other pre-existing malignancies were more likely to be under observation [66]. This study utilized a national cancer registry and showed that less than 10% of patients with localized RCC were managed with active surveillance, and it's usage has remained relatively flat overtime [66]. However, observation at a minimum has been demonstrated as a viable option for many patients, including those with SRM and/or medical comorbidities or advanced renal cell carcinoma [64, 67-70]. For instance, a pooled multi-institutional analysis of 299 SRMs with median observation of 33.5 months showed a calculated mean linear growth rate of 0.31 cm/year, and 23% of the masses with zero net growth under surveillance. The majority of patients enrolled in these studies have a median age of 70 years old and some are diagnosed with stage IV RCC at the initial visit. Studies have displayed that select patients with metastatic RCC have active surveillance as a reasonable and acceptable approach, particularly in the setting of indolent, oligometastatic disease [69, 71]. In a prospective phase 2 study regarding active surveillance in patients with metastatic RCC, this showed that with a median surveillance period of 14.9 months before starting systemic therapy, a subset of patients had no observed difference in quality of life, anxiety or depression [72]. The length of active surveillance was associated with the number of organs with metastases (one versus two versus more than two; *P*=0.0239) and the location of the metastases (lung only versus other organs only versus both; *P* =0.0280) [72]. Therefore, for elderly patients with metastatic disease, active surveillance has been utilized and has been shown to effective and successful when patient populations are carefully selected.

On the contrary, in a prospective study performed by Parker et al. a cohort of 100 patients were followed for up to 2 years, showing that patients with greater illness uncertainty was associated with poorer general quality of life scores and higher distress scores [73]. This study displays that although active surveillance can be a great option for many patients due to the indolent nature of certain types of RCCs, it is also necessary to consider the patient as a whole and how their quality of life is affected with the diagnosis of a renal tumor. Overall, the idea of surveillance for patients has consistently shown to be advantageous for patients when done in a controlled trial and usually socialized countries, however, legal implications and ramifications of this approach at this time are still unknown.

Conclusion

From surgical interventions and ablative therapies to active surveillance-modernization of medical and surgical treatments has now allowed health care providers to offer patients a multitude of options regarding management of an incidentally found SRM. Based on size assessment via imaging of the renal tumor, location, and biological characteristics of the tumor, patients and providers are able to identify an individualized treatment plan to help maximize patient's quality of life and desires for their medical care. As time progresses, more and more treatment options may become available for patients such as tumor enucleation, high-intensity focused ultrasound (HIFU), and Cyberknife radiosurgery. With further research, these newer methodologies may also enhance patient's long-term survival and possibly decrease morbidity.

Conflict of interest

The authors have no potential conflicts of interest to disclose.

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