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Review Article

Management of small renal masses: An interventional radiologist's perspective

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ABSTRACT

Renal cell carcinoma is relatively common malignancy. Its imaging features are often non-specific and can present a diagnostic dilemma for clinicians. Historically, all patients with a renal mass underwent radical nephrectomy. Advances in technology have allowed for an increase in partial nephrectomies and percutaneous ablations. This essay briefly describes some of the imaging findings of renal cell carcinoma and several of its mimics followed by an in-depth review of procedural management with a particular focus on recent advancements.

1. Introduction

Renal cell carcinomas (RCC) are the eighth most common cancer in 2017 and the most common renal malignancy [1]. Most RCC's are sporadic; however, several autosomal dominant genetic disorders predispose patients including Von Hippel-Lindau syndrome, hereditary clear cell carcinoma, and hereditary papillary carcinoma [2–4]. Known modifiable risk factors for RCC smoking, obesity, and hypertension [5]. There is also a growing body of evidence suggesting a connection between RCC and physical inactivity, obesity, alcohol exposure, and several industrial cleaners (i.e. trichloroethylene) [6].

The worldwide incidence has continued to rise over the last several decades and varies based on geography [7,8]. The incidence appears to be highest in North America and Europe and lowest in South America and Asia [9]. Approximately 65,000 new cases of RCC are diagnosed in the United States, which accounts for between 3 and 5% of all newly diagnosed neoplasms [10]. The rising incidence of RCC has been largely attributed to the increasing use of ultrasound and cross-sectional imaging [11].

Despite the increasing incidence of RCC, the mortality has remained essentially unchanged over the last 50 years. The 5-year overall survival rate in 1954 was 34% [12]. Since then the 5-year overall survival rate has steadily risen by 1–2% per year to approximately 74%. This is partially due to early incidental detection resulting in lead-time bias, as the annual death per 100,000 people from renal cell carcinoma has been approximately 4 since 1975 [1]. However, improved procedural treatment technique and advances in medical therapy have made a dramatic improvement in many patients overall survival and quality of life [13].

2. Diagnosis

Most renal masses are asymptomatic due to their retroperitoneal location. The classic presentation of RCC of flank pain, hematuria, and palpable abdominal mass represents locally advanced disease and is now rarely found [14]. Other possible symptoms include fevers, weight loss, night sweats, anemia, liver dysfunction, non-reducing varicocele, bilateral lower extremity edema, paraneoplastic syndromes, and perirenal hemorrhage [15,16]. Because of the variable presentation RCC has been historically been referred to as the “Internist's tumor.” [17] However, some sources are now referring to it as the “Radiologist's tumor” due to the increased incidental detection on cross-sectional imaging [18,19].

Unfortunately, the imaging findings of renal cell carcinoma are seldom pathognomonic. More often than not they are described as enhancing renal masses that are indistinguishable from renal oncocytomas or lipid-poor angiomylolipomas (Fig. 1) [20,21]. They may also be confused with infiltrative transitional cell carcinoma, renal lymphoma, or pseudo-tumors [22]. Because of this imaging ambiguity, surgical resection has been the main tool to definitively diagnose renal cell carcinoma.

CT has been the most common imaging modality to evaluate renal masses. Renal cell carcinomas have a variable appearance on CT. Most are solid renal masses; however, up to 14% may be cystic [23]. Non-

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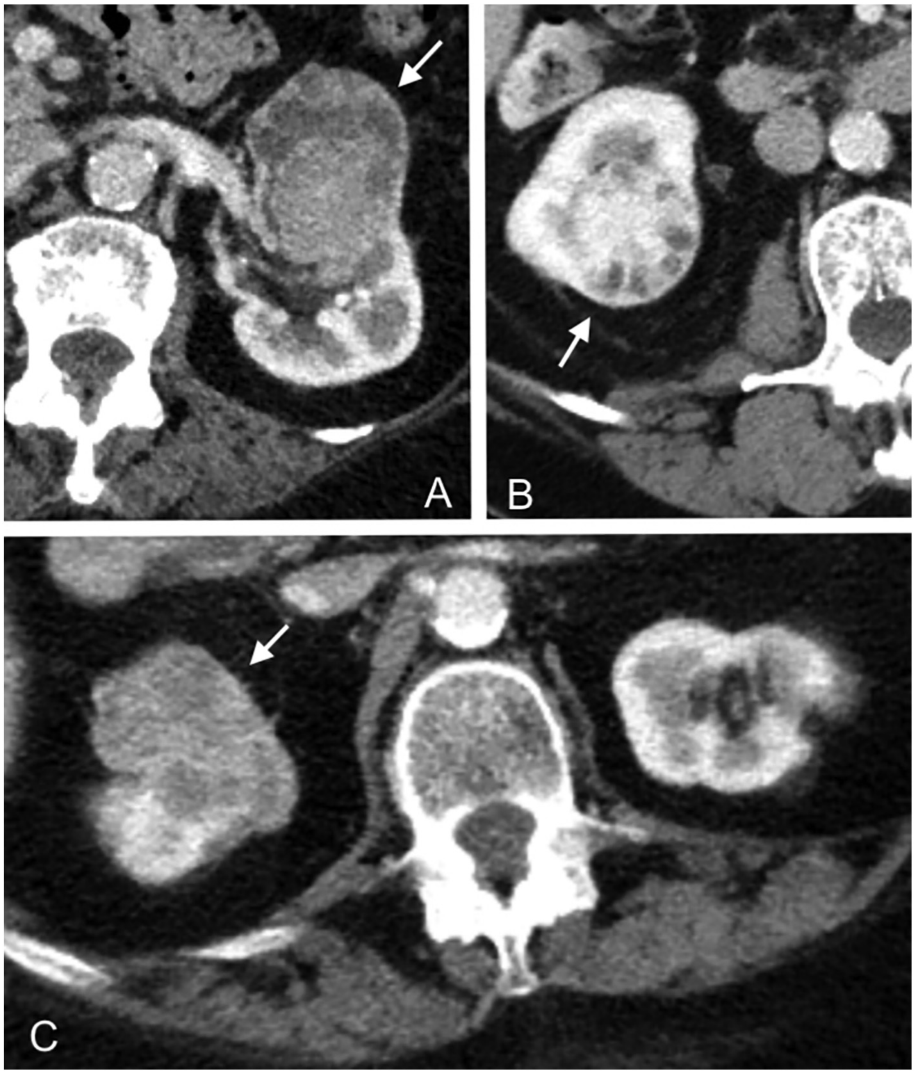

Fig. 1. Renal masses - CT. Three similar appearing renal masses. Image A was proven to be a renal cell carcinoma, image B was proven to be a renal oncocytoma, and image C was proven to be a lipid-poor angiomylolipoma.

contrast images most often demonstrate a hypo-attenuating, iso-attenuating, or hyper-attenuating solid mass. Post-contrast images demonstrate an enhancing mass, which is hypo-attenuating relative to the normal renal parenchyma. MRI and ultrasound are reasonable alternatives to CT in patients that cannot tolerate iodinated contrast or should not be exposed to ionizing radiation and has similar sensitivity to CT [24].

3. Staging

The original Robson's staging system was developed from a 10 year case series of patients receiving radical nephrectomy [25]. This staging system relied on tumor location relative to anatomic landmarks including Gerota's fascia, renal vasculature, lymph nodes, and local organs (Table 1). This system was replaced a more complex TNM staging system. A major drawback to the Robson's system was the combination of two heterogeneous groups. Patients with local vascular involvement benefit from surgical treatment, whereas patients with local lymph node invasion have a poorer prognosis and should undergo medical therapy [26]. The modern TNM staging system avoids this by being a more granular system (Table 2) [27].

Table 1
Original Robson's renal cell carcinoma staging system.

Stage	Definition
Stage I	Confined to renal parenchyma
Stage II	Involved in perinephric fat, but confined within Gerota's fascia
Stage III	A) Tumor involves main renal vein or IVC
	B) Involves regional lymph nodes
	C) Involves both regional vessels and lymph nodes
Stave IV	A) Involves adjacent organ other than adrenal glands
	B) Distant metastasis

4. Management

4.1. Active surveillance

Active surveillance is the least invasive approach to managing a small renal mass. This may be the only option for patients with an unacceptably high surgical mortality risk. Other patients may choose to forgo surgery to avoid permanent post-operative renal replacement therapy. Finally, some otherwise healthy patients may opt for active surveillance after a thorough discussion and informed consent, which clearly explains the calculated risk inovled [28].

There is currently limited evidence comparing active surveillance to

Table 2
Current renal cell carcinoma T.N.M. staging system.

T.N.M.	Stage: definition
Primary tumor (T)	**T0:** No evidence of a primary tumor.
	T1: The tumor is only in the kidney and is no larger than 7 cm (cm), or a little < 3 in., across.
	T1a: The tumor is 4 cm (about 1½ inches) across or smaller and is only in the kidney.
	T1b: The tumor is larger than 4 cm but not larger than 7 cm across and is only in the kidney.
	T2: The tumor is larger than 7 cm across but is still only in the kidney.
	T2a: The tumor is > 7 cm but not > 10 cm (about 4 in.) across and is only in the kidney.
	T2b: The tumor is > 10 cm across and is only in the kidney.
	T3: The tumor is growing into a major vein or into tissue around the kidney, but it is not growing into the adrenal gland (on top of the kidney) or beyond Gerota's fascia (the fibrous layer that surrounds the kidney and nearby fatty tissue).
	T3a: The tumor is growing into the main vein leading out of the kidney (renal vein) or into fatty tissue around the kidney.
	T3b: The tumor is growing into the part of the large vein leading into the heart (vena cava) that is within the abdomen.
	T3c: The tumor has grown into the part of the vena cava that is within the chest or it is growing into the wall of the vena cava.
	T4: The tumor has spread beyond Gerota's fascia (the fibrous layer that surrounds the kidney and nearby fatty tissue). The tumor may have grown into the adrenal gland (on top of the kidney).
Regional lymph nodes (N)	**NX:** Regional (nearby) lymph nodes cannot be assessed (information not available).
	N0: No spread to nearby lymph nodes.
	N1: Tumor has spread to nearby lymph nodes.
Distant metastasis (M)	**M0:** There is no spread to distant lymph nodes or other organs.
	M1: Distant metastasis is present; includes spread to distant lymph nodes and/or to other organs.

surgical excision or ablation therapy. The majority of the literature is observational and suffers from a lack of standardized surveillance protocols and reported oncologic outcomes may be inaccurate due to possible intrinsic bias, such as active surveillance for patients with benign small renal masses [29]. However, several well-designed prospective clinical trials have demonstrated that active surveillance is a reasonable option for well-selected patients [30,31].

4.2. Radical nephrectomy

Radical nephrectomy has historically been the standard treatment for renal masses. It includes en bloc resection of the entire kidney, the perinephric fat, ipsilateral adrenal gland, and local lymphadenectomy from the crus of the diaphragm to the aortic bifurcation. This procedure may be performed open, laparoscopic, or robotically. Multiple studies have demonstrated equivalent cancer free survival rates between open and laparoscopic radical nephrectomies [32,33].

4.3. Partial nephrectomy

Partial nephrectomy was originally reserved for patients at high risk of developing renal failure [34]. Over the years, several studies have shown similar oncologic outcomes between partial and radical nephrectomy when appropriately stage matched [35,36]. Population studies have correlated radical nephrectomy with increased risk of chronic renal disease, cardiovascular morbidity and mortality, and increased overall mortality [37–40]. For these reasons, partial nephrectomy has become an increasingly popular choice for T1 renal masses when possible [41].

Originally introduced in 2009, the RENAL nephrometry scoring system has been a helpful tool to aid surgeons in deciding between a radical nephrectomy and partial nephrectomy [42]. The scoring system utilizes lesion size and location to characterize them into low (4–6), intermediate (7–9), or high (10 − 12) complexity lesions (Table 3). This has been shown to correspond to increased rates of complication after partial nephrectomy as the score increases [43]. Additionally, this score has been shown that higher complexity lesions are more likely to correspond to higher grade histopathology [44].

The basic principles of partial nephrectomy include mobilization of the kidney with early vascular control via hilar clamping, limiting ischemia time by reducing hilar clamp time, negative margins, hemostasis, creating a water tight closure for the collecting system, and closing the renal defect. Partial nephrectomy may be done open, laparoscopic, or robotic with similar oncologic outcomes [45,46]. The kidney may be accessed by a transperitoneal or retroperitoneal approach.

Tumor resection traditionally includes a 2–3 mm margin of normal parenchyma as well as the overlying perinephric fat [47]. However, there has been a recent trend to minimize margin size and enucleate small tumors in an attempt to reduce ischemic time and preserve functional renal tissue [48]. Current evidence suggests similar oncologic outcomes for enucleation compared to resection with wider margins [49]. Occasionally intraoperative ultrasound may assist with tumor localization if necessary. It can give real-time information about tumor margins and can be particularly useful in cases where the tumor is not easily visible or palpable on the surface of the kidney [50,51].

Partial nephrectomy may also be performed open, laparoscopic, or robotically. Historically, laparotomy has been preferred due to the increased visibility and access of the surgical field. However, improvements in intracorporeal suturing techniques, hemostatic agents, and laparoscopic technology have helped flattened a previously steep learning curve [52]. Oncologic outcomes between the open and laparoscopic techniques appear to be similar [53].

3-D visualization, increase instrument range of motion, and

Table 3
RENAL nephrometry scoring system.

	Score		
Components	1 Point	2 Points	3 Points
R (radius)	≤4 cm	> 4 cm but < 7 cm	≥7 cm
E (exophytic/endophytic)	≥50% exophytic	< 50% exophytic	Completely endophytic
N (nearness to collecting system/ sinus)	≥7 mm	> 4 mm but < 7 mm	≤4 mm
A (anterior/posterior)	No points given. "a" for anterior, "p" for posterior, and "x" for neither.		
L (location relative to polar lines)	Entirely above upper polar line or below lower polar line	Mass crosses polar line	50% of mass is across polar line, mass is entirely in between polar lines, or mass cross axial midline

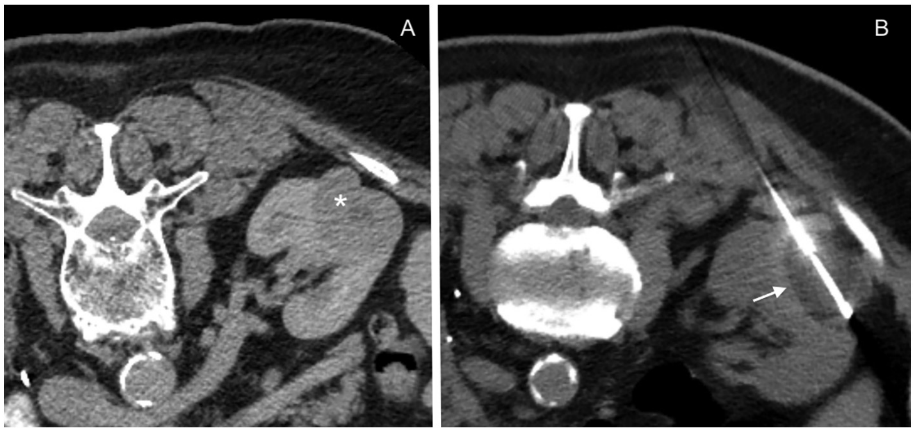

Fig. 2. Ablation images. Image A demonstrates a solid renal mass (white asterisk). Image B demonstrates a cryoablation probe with the renal mass. An ice ball is forming around the end of the probe (white arrow) and ablating the tumor.

improved dexterity have made robotic partial nephrectomy increasingly popular approach with a decreased learning curve [54]. However, long-term oncologic outcomes have not been verified with robotic partial nephrectomy. While several meta-analyses support similar outcomes, there are no published randomized trials [55,56].

4.4. Ablation

Ablative techniques are a relatively established treatment for RCC, though the indications have yet to be fully defined. It is generally reserved for patients who have multiple comorbidities and would be poor surgical candidates. The American Urologic Association recommends the use of radiofrequency ablation or cryoablation [57]. Radiofrequency ablation utilizes an alternating current that passes through an electrode probe, which vibrates ions in the tissue and generates heat. The current safely disperses through a large grounding pad placed on the patients' thigh [58]. The probe maintains tissue temperatures between 50 °C and 100 °C, resulting in cell death and eventually coagulative necrosis [59]. Cryoablation probes cool surrounding temperatures to approximately −40 °C which causes enzymatic damage and intracellular ice crystal formation, resulting in cell damage and death (Fig. 2). Additionally, cryoablation causes thrombosis of local blood vessels resulting in a hypoxic environment [60].

Microwave ablation is an additional technique utilized for percutaneous management of renal cell carcinoma. Microwaves radiate through tissue and cause polar molecules, such as water, to oscillate as they continually re-align with the microwave field. As these molecule oscillate they generate thermal energy which results cell damage and death [60]. Microwaves transmit through different tissues relatively consistently, regardless of electrical impedance. This allows for more even heating of larger volumes of tissues compared to radiofrequency ablation [61].

The ideal ablative candidate would have an exophytic tumor that is < 3 cm and is easily accessed percutaneously [62]. Larger tumors may be treated percutaneously; however, there is a higher risk of incomplete ablation, local recurrence, and complications [62]. Non-target structures such as small bowel, large bowel, iliofemoral nerve, or psoas muscle may be displaced through hydro-dissection, gas-insufflation, or angioplasty balloon interposition [63]. Once the estimated ablative zone is free from non-target structures a probe is placed into the tumor. If the tumor is large enough it may require multiple probes with overlapping ablative zones.

Complications from renal ablation are related to probe placement and thermal injury and can be categorized into urologic and non-urologic. Urologic complications include hemorrhage, urine leak, urinary tract infection, and ureteral stricture. Non-urologic complications include pneumothorax, skin burns, nerve injury, bowel injury, and tract seeding [64]. In general, procedural complications increase as the size of the tumor increases [65].

Functional outcomes after thermal ablation of renal cell carcinomas appear to be good. One retrospective study demonstrated decreased decline in eGFR and decreased progression to chronic kidney disease when comparing thermal ablation patients to similarly matched patients who underwent radical or partial nephrectomy [66,67]. Another retrospective study showed minimal decrease in eGFR for patients with a solitary kidney who underwent renal thermal ablation [68].

Unfortunately, oncologic outcomes are not as well described in post ablation patients compared to surgical patients. Most early studies were small, had short follow-up, and lacked biopsy proven diagnosis [69]. To confound this even more, there is very little standardization within the literature regarding technical success or reporting local recurrence [70].

Several recent long-term studies have demonstrated more durable oncologic outcomes [71]. A meta-analysis by Pieroazio et al. demonstrated lower local recurrence-free survival rates for single session ablation therapy compared to surgical resection. However, this effect was negated after accounting for multiple treatments [29]. Tracy et al. demonstrated 93% metastasis free and 99% cancer-specific 5-year survival rates for patients with solitary renal cell carcinoma < 4 cm [72]. Olweny et al. demonstrated a 5-year cancer-specific survival of 97.2% in patients with T1a renal cell carcinoma [73]. A population-base analysis by Talenfeld et al. followed patients who underwent percutaneous thermal ablation, partial nephrectomy, and radical nephrectomy for T1a renal cancer for 4 years. All three groups had similar overall survival and local recurrence rates, while the ablation group had lower rates of procedural complications and progression to chronic kidney disease [74].

Additionally, renal mass ablation has been demonstrated to be a cost effective treatment. In 2013, Castle et al. reported the median total cost (which included procedural cost, hospital stay, and a 6-month post-procedure period) of a CT-guided percutaneous radiofrequency ablation for clinical T1a renal cell carcinoma was $6475. The median total cost of open partial nephrectomy, robotic partial nephrectomy, and laparoscopic radiofrequency ablation were $17,018, $20,314, and $13,965, respectively [75]. In 2016, Xing et al. reported the average direct procedural cost of percutaneous ablation for T1a renal cell carcinoma was $7988 compared to $18,359 for partial nephrectomy [76].

5. Conclusion

While the incidence of renal cell carcinoma has increased over the last 50 year, the mortality has remained stable. This is primarily due to earlier detection and improvements in treatment. Active surveillance is the least invasive approach to managing small renal masses and is typically utilized for patients who would not tolerate surgery. Radical nephrectomy was once the mainstay of treatment. However, this has been replaced by partial nephrectomy when appropriate. Percutaneous thermal ablation has mainly been reserved for patients who are poor surgical candidates.

Oncologic and functional outcomes have been well established for radical and partial nephrectomies for renal cell carcinoma. Outcomes for renal cell carcinoma ablation are less well defined, however recent evidence is promising. While surgical resection is the gold standard of treatment, ablative therapies may be a safe and cost-effective treatment for small renal masses for appropriately selected patients with similar oncologic outcomes.

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