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Review

Recurrent renal cell carcinoma following nephrectomy and ablation therapy: Radiology perspective

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ABSTRACT

Renal cell carcinoma (RCC) is the most common renal malignancy, accounting for approximately 2% of adult malignancies and 4% of new cancer cases in the United States every year. Imaging guided ablative therapy, including radiofrequency (RF) ablation, cryotherapy and microwave has gained popularity over the last decade in treatment of small tumors. Antiangiogenic therapy has set itself to be the standard of care for many patients with metastasis these days. With hope for more research, survival rates of metastatic RCC may increase from a current 2-year survival rate of approximately 20%. Variation in imaging surveillance protocol in terms of frequency, modality, and duration is noted among guidelines developed by several organizations.

In this review article, we will discuss follow-up imaging protocols, patterns of RCC recurrence following different modalities of treatment, imaging appearance, as well as usual and unusual sites of metastatic disease.

1. Introduction

Renal cell carcinoma (RCC) is the most common renal malignancy, accounting for approximately 2% of adult malignancies and 4% of new cancer cases in the United States every year [1]. There has been a dramatic increase in incidence of incidentally detected RCC in recent decades, largely due to increased utilization of cross-sectional imaging for various indications [2–5].

Local recurrence of RCC, defined as relapse within the renal fossa in case of radical nephrectomy or at the resection margin in case of partial nephrectomy, occurs in about 5% of patients [6]. Up to 30% of patients have distant metastatic disease on initial presentation [7]. Among patients with localized diseased, who subsequently undergo radical nephrectomy, 20–30% will eventually develop metastatic disease [7].

2. Follow-up imaging

2.1. CT protocol

Computed Tomography (CT) of the thorax and abdomen is most frequently used for imaging follow-up of RCC. However, Magnetic Resonance Imaging (MRI) is an adequate substitute for imaging of the abdomen [8].

Follow-up CT protocols used for surveillance imaging varies from one institution to the other. At our institution, unenhanced images of the abdomen only are performed in post-partial nephrectomy and post-ablation patients, while not for patients following radical nephrectomy. A multiphase scan is performed after the injection of iodinated contrast (320 mg/ml of iso-osmolar contrast with volume ranging between 70 and 120 ml, according to patient's renal function) similar to the protocol used for detection, characterization, and staging of renal masses [9]. Arterial phase images (bolus triggered) are performed from the diaphragm to the symphysis pubis, using bolus trigger technique, with 3-mm slice thickness, with reconstruction at 3-mm interval. Venous phase (60 s) performed from the diaphragm to the iliac crests and delayed (5 min) imaging is also performed from the kidneys through the bladder using same parameters. Additionally, thin slice data (0.75 mm) are provided to aid in interpretation [9].

For patients following radical nephrectomy, unenhanced images are not performed. Unenhanced images through the kidneys are only performed in post-partial nephrectomy and post-ablation patients at the initial baseline exam. If initial baseline exam is negative, unenhanced images can be omitted for subsequent follow-up exams, unless a suspicious finding is found during follow-up.

RCC has a propensity to produce hypervascular metastases, which may be visualized on one phase of contrast enhancement only, particularly on arterial phase [9,10]. A study by Jain et al. evaluated the detection of RCC metastases in dual phase abdominal CT reported that 14 of 62 (21%) patients with metastatic lesions in the liver, pancreas or kidney were detected on arterial phase only, whereas 9 of 62 (14.5%)

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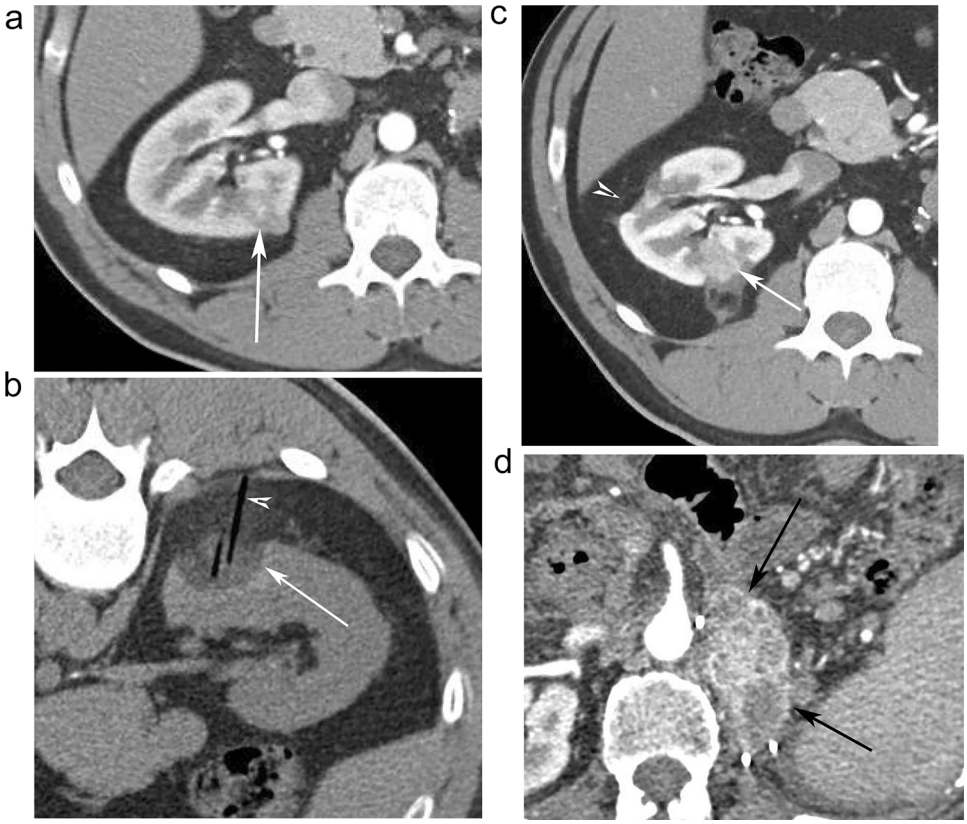

Fig. 1. RCC recurrence post-ablation and local recurrence in the nephrectomy bed. (a) 43-year-old male with clear cell RCC of the left kidney, status post radical left nephrectomy, now with metastatic lesion in the right kidney. Axial CT image of the abdomen shows an enhancing mass in the mid-pole of the right kidney (arrow). (b) Axial CT image of the abdomen in the same patient during cyroablation for the mass in (a). Note the cryoablation probes (arrowhead) within the mass (arrow). (c) Axial CT image of the abdomen 9 months following cryoablation shows enhancing nodule in the ablation zone (arrow), consistent with local recurrence. Incidental note of cortical scarring in the anterolateral aspect of the kidney (arrow head), not present on the pre-procedure scans (not shown), likely sequela of cryoablation. (d) 69-year-old male with clear cell RCC of the left kidney, status post radical left nephrectomy. Axial CT image shows heterogeneously enhancing mass in the left nephrectomy bed, consistent with local recurrence.

Table 1
Frequency of and Time to Recurrent Disease Following Nephrectomy for RCC According to Pathologic Stage.

Stage	Recurrence Rate (%)	Time of Recurrence (mos.)
T1	0–7	35–48
T2	14–27	25–30
T3	26–54	11–22

Note——Adapted from Patel et al. [12].

patients with metastatic lesions in these solid organs were detected on venous phase only [10].

2.2. Post-ablation magnetic resonance imaging (MRI) protocol

The follow-up imaging protocol at our institution includes axial unenhanced, non-fat saturation three-dimensional (3D) T1 weighted images (T1WI), axial T2 weighted (T2WI), axial diffusion weighted images (DWI), and apparent diffusion coefficient (ADC) images. Post-contrast imaging is performed following an injection of 0.1 mmol/kg of gadolinium chelate (Gadavist®, Bayer, Leverkusen, Germany) at a rate of 2 ml/s. Axial and coronal T1 weighted images with fat saturation are typically obtained, with addition of subtraction images to avoid any influence of high signal on T1WI.

2.3. Follow-up strategy

To date, there is no clear consensus in the literature for follow-up of patients after different interventions for RCC in terms of frequency and timing of follow-up. However, several international guidelines are available in the literature. These include the National Comprehensive Cancer Network (NCCN), American Urological Association (AUA) [11], European Association of Urology (EAU), and Canadian Urological Association (CUA). The follow-up strategy is mostly stage dependent; the higher the stage and the more aggressive the tumor, the more intense and frequent the follow-up will be [12]. These recommendations vary in frequency and type of recommended follow-up study (CT, MRI, ultrasound, or chest x-ray), and duration of surveillance.

In general, the aforementioned fact applies to patients who undergone nephrectomy, with clear confidence of absence of positive surgical margins. For clinically localized T1 stage disease, many guidelines suggest less frequent follow-up given the low risk of recurrence. Patients with prior ablation or those with positive surgical margins, clearly require more aggressive follow-up strategy to detect recurrence at an early stage. For example, the NCCN and AUA provide specific surveillance recommendations up to 3 years for pT1 patient, up to 5 years for post-ablation patients, and greater or equal for pT2 patients. Continued surveillance beyond these time frames is left up to the discretion of the provider. Some institutions developed a follow-up strategy based on initial tumor stage, Fuhrman grade, and patient's performance status [12].

3. RCC recurrence

3.1. Radical nephrectomy versus partial nephrectomy

Radical nephrectomy involves removal of the kidney, excision of perirenal fat, ipsilateral adrenal gland, and lymph node dissection; in other words, en bloc removal of all contents of Gerota's fascia. Despite the fact that ipsilateral adrenal metastasis occurs in only 1–10% of patients, ipsilateral adrenalectomy is a part of the classical radical nephrectomy [13].

Partial nephrectomy has been adopted increasingly in recent years in place of radical nephrectomy, taking the advantage of preservation of healthy renal tissue, and therefore the overall renal function. Nephron-sparing surgery is getting popularity since the reported outcome in terms of survival rates is comparable to those of radical nephrectomy [13].