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Renal cell carcinoma subtype differentiation using single-phase corticomedullary contrast-enhanced CT

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ABSTRACT

Objective: To compare multiphase and single-phase corticomedullary contrast-enhanced computed tomographic (CT) imaging in the differentiation of renal cell carcinoma (RCC) subtype.
Material and methods: Pathology records were reviewed from January 2008 to March 2013. The final cohort consisted of 79 patients (57 men, 22 women; mean age: 64±13). Quantitative tumor percentage enhancement (TE), cortical enhancement, and tumor-to-cortex enhancement (TCI) indexes were calculated.
Results: Single-phase evaluations showed significantly lower mean TE and TCI for papillary tumors when compared with clear cell and cromophobe tumors ($P<.01$). Comparison of receiver operating characteristic curve analyses did not show significant differences between both evaluation methods.
Conclusion: Accuracy of RCC subtype differentiation with single-phase corticomedullary contrast-enhanced CT is comparable to multiphasic imaging.

1. Introduction

In the last decades, a steady increase in renal cancer rates, mostly renal cell carcinomas (RCCs), has been observed [1]. This is explained by early diagnosis of asymptomatic cancers, particularly incidental diagnosis during imaging for other purposes, in up to 61% of cases [2], owing to the widespread use of abdominal computed tomography (CT) and magnetic resonance imaging (MRI) [3]. Routine CT examinations are frequently performed after the administration of intravenous iodinated contrast but without the acquisition of unenhanced images [4]. However, dedicated CT imaging of known renal masses is nearly universally performed with an initial unenhanced phase prior to one or more postcontrast phases [3,5].

Several reports have demonstrated the feasibility of RCC subtype differentiation using dynamic multiphasic imaging CT (and MRI) studies [6–14], using the unenhanced images for the baseline CT attenuation measurements of renal masses [6,8–10,12–15]. However, a recent study showed no significant differences of the attenuation values between pathologically proven RCC subtypes on unenhanced CT [16].

To our knowledge, no study has been performed demonstrating that measurement of enhancement for tumor subtype analysis does not require unenhanced images. Thus, the aim of the present study was to intraindividually compare the ability to differentiate RCC subtype between classic multiphasic imaging and single-phase corticomedullary contrast-enhanced CT, based on both previously described and novel indices, using the psoas muscle as a surrogate.

2. Material and methods

The ethics committees of the four institutions involved approved the present study, and patient consent was waived.

2.1. Patient population

A retrospective review of pathology records, from January 2008 to March 2013, was conducted in the four institutions involved. A total of 275 postnephrectomy RCC specimens including the three most common subtypes, namely, clear cell, papillary, and cromophobe, were considered. One hundred sixty-three specimens were excluded because preoperative CT scans had been performed outside the participating institutions or they had undergone MRI only. Out of the 112 remaining, there were further exclusions due to inadequate protocols for image acquisition (absence of unenhanced phase or inadequate arterial/corticomedullary phase) and/or no contrast administration, resulting in a final cohort of 79 patients, all with unilateral tumors (53 clear cell, 11 papillary, 15 cromophobe).

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The mean patient age was 64±13 years, with a male (n=57) to female (n=22) predominance (2.6:1). The average size of the tumors was 50.1±30.4 mm.

2.2. Pathological diagnosis

Senior pathologists from each institution reviewed surgical specimens. RCCs were classified according to the World Health Organization classification (2004). Histopathological analysis was performed on surgically removed masses from either total or partial nephrectomy.

2.3. CT technique

All CT scans were performed with either a 4-detector row (LightSpeed Qx/I; GE Healthcare, USA) (n=25), a 6-detector row (Somatom 6; Siemens, Erlangen, Germany) (n=16), a 16-detector row (Emotion 16; Siemens, Erlangen, Germany) (n=13), or a dual-source scanner (SOMATOM Definition; Siemens, Erlangen, Germany) (n=25). CT images were obtained during breath holding with the following parameters: 120 kVp, variable tube current (between 150 and 400 mA), and section thickness interval of 3–5 mm, depending on the protocol used.

All patients received 500–900 ml of oral contrast material [E-Z CAT (2% barium sulfate suspension); E-Z EM, Westbury, NY] 30–50 min before CT.

Contrast-enhanced CT images were obtained after the injection of 100–120 ml of nonionic iohexol (Omnipaque 350; GE Healthcare) or iopromide (Ultravist 370) at a rate of 3–3.5 ml/s. All studies were at least dual-phase studies, including unenhanced images and at least one of the following: arterial/corticomedullary phase (n=79), nephrographic phase (n=54), or excretory phase (n=41) images.

On the basis of the appearance of the normal kidney parenchyma, images were classified as unenhanced if no contrast agent had been administered and as arterial/corticomedullary if there was differential enhancement between the renal cortex and medulla.

The term optimal arterial/corticomedullary phase requires definition, and timing of the arterial phase is affected by many variables; some are related to the injection, such as rate and volume, and others are related to the patient, such as cardiac output and weight. Thus, in order to establish greater consistency for the arterial phase, the inclusion criteria for an adequate arterial/corticomedullary phase (which was used for measurements) represented images acquired during an imaging window starting in the late hepatic arterial phase (predefined as the presence of contrast in the renal arteries and renal veins) and ending in the hepatic arterial dominant phase (predefined as the presence of contrast in the portal vein and the absence of contrast in the hepatic veins) [17].

2.4. Data collection and image analysis

Four investigators participated in data collection in their own institutions, gathering patient lists and pathological reports and cross-referencing with picture archiving and communication system. Imaging studies were then recorded in digital DICOM format and copied to OsiriX image processing software (v 5.x 64-bit).

All quantitative measurements were performed by the same investigator, with 10 years of experience of abdominal CT. The density measurements [Hounsfield units (HU)] were obtained by placing region-of-interest (ROI) areas over the renal cortex and the most enhancing part of the tumor mass in the corticomedullary phase. ROI measurements were placed at the most vascularized region of the tumor, devoid of vessels, calcifications, and cystic/necrotic tissue. The reviewer used a copy-and-paste feature available on the software to measure densities on the unenhanced images. Occasionally, minor manual adjustments were needed to tune the location and the area of the ROI on the corticomedullary phase. An ROI area was also placed over the ipsilateral psoas muscle in the corticomedullary phase, and the value obtained was used as surrogate for substitution of the precontrast cortical and tumor densities.

The calculated ROI measurements within tumor, uninvolved renal cortex, and the ipsilateral psoas muscle on unenhanced and corticomedullary phases were used to calculate the three indices used: tumor percentage enhancement (TE), cortical enhancement (CE), and tumor-to-cortex enhancement index (TCI).

The term “multiphase” contemplated the use of unenhanced and corticomedullary images. Conversely, the term “single phase” was used to term isolated corticomedullary image evaluation.

Multiphase TE and CE were calculated using the following formulas [11]:

$$TE = \left(HU_{\text{tumor postcontrast}} - HU_{\text{tumor precontrast}}\right) / HU_{\text{tumor precontrast}} \times 100\%;$$
$$CE = \left(HU_{\text{cortex postcontrast}} - HU_{\text{cortex precontrast}}\right) / HU_{\text{tumor precontrast}} \times 100\%.$$

The single-phase TE and CE were calculated using the following formulas:

$$TE = \left(HU_{\text{tumor postcontrast}} - HU_{\text{psoas postcontrast*}}\right) / HU_{\text{psoas postcontrast*}} \times 100\%;$$
$$CE = \left(HU_{\text{cortex postcontrast}} - HU_{\text{psoas postcontrast*}}\right) / HU_{\text{psoas postcontrast*}} \times 100\%.$$

The TCI was then estimated based on the following formula: TCI= TE/CE for both multiphase and single phase, and the CE was only used for that purpose. Fig. 1 demonstrates the method of ROI placement used to calculate the TE and TCI.

2.5. Statistical analysis

One-way analysis of variance (ANOVA) for independent samples was used to determine if there were differences in the mean attenuation values of the tumor and cortex in the unenhanced phase, and of the mean attenuation of the psoas muscle in the arterial phase, across all three subtypes. The Tukey honest significant difference test was used to identify which groups were different from each other, where applicable.

The mean, standard deviation, and medians of the TE and the TCI for all three subtypes in both multi- and single-phase CTs were determined.

One-way ANOVA was also used to test for mean differences in TE and TCI between the three tumor subtypes.

The diagnostic performance in differentiating subtypes of RCC was evaluated by performing receiver operating characteristic (ROC) curve analysis for the comparison of clear cell and papillary RCCs. The area under curve (AUC) was calculated to determine an optimal cutoff for differentiating the subtypes with the best accuracy possible. Comparisons of ROC curves were performed.

All statistical analyses were performed with MedCalc for Microsoft Windows software (version 11.3.0.0, MedCalc Software).

3. Results

There were no significant differences between the precontrast densities of the three tumor subtypes or between the densities of the respective healthy renal cortices.

There were no significant differences between the arterial/corticomedullary densities of the psoas muscles (Table 1).

Clear cell RCCs showed the highest percentage tumor enhancement (Fig. 1), both in multiphase CT, with a mean of 264%, and also in the single-phase CT, using the psoas muscle as the basis for comparison, with a mean of 106%. The TCI was also highest in this group, with mean values of 0.75 for both the multiphase and single-phase images (Table 2).