Tumor Necrosis on Magnetic Resonance Imaging Correlates With Aggressive Histology and Disease Progression in Clear Cell Renal Cell Carcinoma

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Abstract

Magnetic resonance imaging (MRI) has been shown to successfully differentiate renal cell carcinoma subtypes. The purpose of this study was to assess whether (1) the morphologic features of clear cell renal cell carcinoma on MRI correlated with its histologic pattern and (2) MRI findings correlate with disease progression. We demonstrate that MRI evidence of necrosis, renal vein thrombosis, and retroperitoneal collaterals correlate with tumor clear cell percentage and disease progression.

Objective: The study objective was to correlate the magnetic resonance imaging (MRI) features of clear cell renal cell carcinoma (ccRCC) with the histopathologic features and disease progression. **Methods:** Institutional review board approval for this retrospective study was obtained; patient consent was not required. The initial staging MRI scans of 75 patients with histologically confirmed ccRCC were retrospectively reviewed. The imaging was assessed by 2 radiologists for the presence of tumor necrosis, cystic degeneration, intracellular fat, hemorrhage, retroperitoneal collaterals, and renal vein thrombosis. Quantitative analysis for the MRI presence of intracellular lipid within tumors was performed. MRI findings were correlated with histopathologic findings of clear cell percentage, alveolar and tubular growth pattern, and disease progression. Statistical associations were evaluated with nonparametric univariable analyses and multivariable logistic regression models. **Results:** Correlation between MRI and histopathologic features was performed in 75 patients, whereas follow-up data were available for progression analysis in 68 patients. The presence of tumor necrosis, retroperitoneal collaterals, and renal vein thrombosis on MRI was significantly associated with a low percentage of tumor cells with clear cytoplasm ($P < .01$) and metastatic disease at presentation or disease progression ($P < .01$). At multivariable analysis, necrosis remained the only feature statistically associated with disease progression ($P = .03$; adjusted odds ratio, 27.7; 95% confidence interval, 1.4-554.7 for reader 1 and $P = .02$; adjusted odds ratio, 29.3; 95% confidence interval, 1.7-520.8 for reader 2). **Conclusions:** Necrosis in ccRCC on MRI correlates with the histopathologic finding of lower percentage of tumor cells with clear cytoplasm and is a poor prognostic indicator irrespective of tumor size.

Clinical Genitourinary Cancer, Vol. 12, No. 1, 55-62
Keywords: carcinoma, clear cell metastatic renal cell carcinoma, clear cell percentage, kidney neoplasms, MRI

Introduction

In 2010, an estimated 59,000 Americans were diagnosed with renal cell carcinoma (RCC) and approximately 13,000 died of the disease.[1] The different subtypes of RCC and their distinct molecular characteristics[2] have led to improved treatment and therapy directed by tumor subtype.[3,4] Although cytokine therapy with interferon alfa or interleukin (IL)-2 was considered to be the standard treatment for metastatic RCC before the introduction of targeted therapies, the latter are now considered the standard of care for most patients with metastatic RCC.

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Submitted: May 19, 2012; Revised: Jul 20, 2013; Accepted: Jul 31, 2013; Epub: Oct 19, 2013

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1558-7673/$ - see frontmatter
http://dx.doi.org/10.1016/j.clgc.2013.07.006

It has been shown that magnetic resonance imaging (MRI) can accurately differentiate RCC histologic subtypes based on the dynamic contrast enhancement pattern and the morphologic appearance.[5,6] A feature analysis of the appearance of renal masses on conventional T1-weighted (T1W) and T2-weighted (T2W) MRI combined with contrast-kinetics on gadolinium-enhanced MRI allows for distinction among the 3 most common histologic subtypes (ie, clear cell, papillary, and chromophobe)[5,6] and angiomyolipomas without visible fat[7] with a high degree of diagnostic accuracy. Furthermore, certain MRI characteristics or "imaging phenotype" is predictive of the growth kinetics among different renal masses, which could help predict their aggressiveness.[8]

MRI also provides information about the tumor characteristics (eg, the presence of necrosis or hemorrhage), can detect intracellular lipids, and delineate intracystic architecture (eg, nodules or septations).[9-11] These morphologic MRI features may correlate with the histologic appearance of clear cell renal cell carcinoma (ccRCC) and give useful prognostic information about the tumor subtype. The aim of this study was to correlate the MRI features of ccRCC with the pathologic features and to assess whether the MRI features correlate with disease progression/metastatic disease.

Material and Methods

Study Population

This was a single-institution, Health Insurance Portability and Accountability Act–compliant, institutional review board–approved retrospective study with waiver of informed consent. A computerized MRI database was retrospectively searched from January 2001 to September 2006 for patients with pre-surgical MRI for assessment of a renal mass and histologically confirmed diagnosis of ccRCC. First, the study correlated the MRI features of ccRCC with the histologic appearance. Patients were excluded if the imaging or pathologic specimen was unavailable for review. Then, MRI tumor features were correlated with time to disease progression. Patients were excluded if follow-up survival data were unavailable.

Imaging Technique

All patients were imaged using a 1.5T clinical scanner (Vision or Symphony; Siemens Medical Systems, Erlangen, Germany; Excite TwinSpeed or Excite HD; GE Healthcare, Waukesha, WI) with the following sequences: chemical shift imaging with axial dual-echo T1W gradient echo (GRE) in phase (IP) and opposed phase (OP) images (repetition time/echo time; 180-205/2.2 [OP] − 4.4 [IP] msec, flip angle 80°, 160 × 256 matrix, 1 acquired signal, 35- to 40-cm field of view, section thickness of 6-8 mm with a 1-mm gap and ±62 kHz bandwidth). Coronal T2W half-Fourier single shot fast spin echo (SSFSE) or half-Fourier acquisition with single-shot turbo spin echo (HASTE) was then performed (repetition time/echo time; infinite/60 msec, flip angle 130-155°, 192 × 256 matrix, 35-40 cm field of view, section thickness of 4-5 mm with a 1-mm gap and ±62 kHz bandwidth).

Coronal and sagittal 3-dimensional T1W GRE images (repetition time/echo time; 3.8-4.5/1.8-2.0 msec, flip angle 12°, 35-45 cm field of view, section thickness of 3-4 mm and a ±62 kHz bandwidth) were obtained before and after administration of a bolus of 0.1 mmol/kg body weight of gadopentetate dimeglumine (Magnevist; Berlex Laboratories, Wayne, NJ) at a rate of 2 mL/sec and followed by a 20-mL saline flush. Post-contrast coronal images were acquired dynamically in the corticomedullary and nephrographic phases with a first pass timed to the corticomedullary phase using a 2-mL test bolus of gadolinium. The nephrographic phase was initiated 20 seconds after the corticomedullary phase. Post-contrast sagittal 3-dimensional T1-W GRE images were acquired during the excretory phase immediately after completion of the dynamic coronal acquisitions.

Quantitative Analysis

Region of interest (ROI) analysis was performed on all lesions to assess for the presence of intracellular lipids in the tumor on the basis of a previously validated technique.[11-13] Briefly, the technique involved calculation of the change in signal intensity (SI) in the tumor between IP and OP images. The SI index was then calculated as follows: $[(tIP - tOP)/(tIP)] \times 100$, where tIP is tumor SI on IP images, and tOP is tumor SI on OP images. On the basis of prior experience in adrenal adenomas, intracellular lipid was considered to be present if the SI index was greater than 16.5%.[11-13] The ROI analysis were performed by 1 radiologist (N.H.) with 1-year fellowship training in abdominal MRI, 7 months before performing the qualitative imaging analysis to avoid recall bias. A circular ROI was placed in the center of the tumor, encompassing at least two thirds of its solid component (average and minimum area size of 9.7 cm^2 and 1.7 cm^2, respectively). The area, location, and size of the ROI were constant between IP and OP images. Care was taken to avoid the edge of the tumor, near its interface with the adjacent perirenal fat, so that phase cancellation artifact could be avoided.[14,15]

Qualitative Analysis

MRI scans were analyzed independently by 2 radiologists (N.H., J.W., each with 1 year fellowship training in abdominal MRI) to assess for the following attributes in the renal mass: (1) necrosis: high SI on T2W images (but not as high as fluid), low SI on T1W images, lack of enhancement, and central location within the tumor; (2) cystic degeneration: areas with high SI on T2W images (similar to that of fluid elsewhere), low SI on T1W images, lack of enhancement, and lobulated cystic morphology; (3) the presence or absence of intravoxel fat (subjective loss of SI on OP images relative to IP images); (4) hemorrhage: nonenhancing areas of high SI on T1W and variable signal on T2W; (5) retroperitoneal collateral vessels; (6) renal vein thrombosis.[9,16] Tumor size was also measured for each tumor, and the longest dimension was recorded.

Progression Analysis

A retrospective review of the electronic medical record was performed on all patients by a single reviewer (A.B.) who was unaware of the MRI findings. Data collected included standard patient and disease characteristics, baseline laboratory and biochemical parameters, disease stage at presentation, and time to progression. The presence of disease progression was defined as radiologic evidence of tumor recurrence or metastases after nephrectomy or metastatic disease at presentation.

Pathology Analysis

All slides for each tumor were reviewed to confirm the clear cell histology by a single uropathologist with 11 years of experience