Angiomyolipoma with Minimal Fat: Can It Be Differentiated from Clear Cell Renal Cell Carcinoma by Using Standard MR Techniques?¹

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Purpose:

To retrospectively assess whether magnetic resonance (MR) imaging with opposed-phase and in-phase gradient-echo (GRE) sequences and MR feature analysis can differentiate angiomyolipomas (AMLs) that contain minimal fat from clear cell renal cell carcinomas (RCCs), with particular emphasis on small (<3-cm) masses.

Materials and Methods:

Institutional review board approval and a waiver of informed consent were obtained for this HIPAA-compliant study. MR images from 108 pathologically proved renal masses (88 clear cell RCCs and 20 minimal fat AMLs from 64 men and 44 women) at two academic institutions were evaluated. The signal intensity (SI) of each renal mass and spleen on opposed-phase and in-phase GRE images was used to calculate an SI index and tumor-to-spleen SI ratio. Two radiologists who were blinded to the pathologic results independently assessed the subjective presence of intravoxel fat (ie, decreased SI on opposed-phase images compared with that on in-phase images), SI on T1-weighted and T2-weighted images, cystic degeneration, necrosis, hemorrhage, retroperitoneal collaterals, and renal vein thrombosis. Results were analyzed by using the Wilcoxon rank sum test, two-tailed Fisher exact test, and multivariate logistic regression analysis for all renal masses and for small masses. A *P* value of less than .05 was considered to indicate a statistically significant difference.

Results:

There were no differences between minimal fat AMLs and clear cell RCCs for the SI index ($8.05\% \pm 14.46$ vs $14.99\% \pm 19.9$; *P* = .146) or tumor-to-spleen ratio ($-8.96\% \pm 16.6$ and $-15.8\% \pm 22.4$; *P* = .227) when all masses or small masses were analyzed. Diagnostic accuracy (area under receiver operating characteristic curve) for the SI index and tumor-to-spleen ratio was 0.59. Intratumoral necrosis and larger size were predictive of clear cell RCC (*P* < .001) for all lesions, whereas low SI (relative to renal parenchyma SI) on T2-weighted images, smaller size, and female sex correlated with minimal fat AML (*P* < .001) for all lesions.

Conclusion:

The diagnostic accuracy of opposed-phase and in-phase GRE MR imaging for the differentiation of minimal fat AML and clear cell RCC is poor. In this cohort, low SI on T2-weighted images relative to renal parenchyma and small size suggested minimal fat AML, whereas intratumoral necrosis and large size argued against this diagnosis.

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Preoperative characterization of benign and malignant renal masses is imperfect, and approximately 10%–17% of renal masses that are surgically excised are benign (1–3). Approximately 2%–6% of the benign solid masses excised from the kidney in surgical series are angiomyolipomas (AMLs) (1,4).

The use of computed tomography (CT) and magnetic resonance (MR) imaging for the diagnosis of AML relies on the detection of adipose tissue (ie, bulk fat) within a renal mass (5–9). At the histopathologic level, AMLs contain various proportions of adipose tissue, smooth muscle, and thick-walled blood vessels (10). The amount of intratumoral fat in AMLs can affect the diagnosis of these lesions; with scant amounts of fat, an imaging diagnosis of AML may be impossible (4,6). Characterization of AML based on the presence of intratumoral fat is more challenging in small (<3-cm) renal masses (11).

Fat content of 25% or less per high-power field has been described in AMLs that contain minimal amounts of fat at the histopathologic level (4).

However, the term *minimal fat AML* is used inconsistently in the radiology literature, and it is often applied to masses with a histopathologic description of little or no fat (12,13) or to masses that do not show obvious fat from cross-sectional imaging (12,14). On CT images, the presence of multiple adjacent negative attenuation values within a renal mass is typical of a classic AML that contains bulk fat, but those values may be subtle or completely absent in a minimal fat AML (5). While minimal fat AMLs can be homogeneous and may be hyperattenuating compared with the surrounding renal parenchyma on unenhanced CT images (and isoechoic to the renal parenchyma on sonography), these findings are not specific (15).

The appearance of bulk intratumoral fat on an MR image indicates AML (16). This can be achieved by comparing images obtained with the same sequence parameters before and after application of a chemically selective fat-suppression pulse or when fat-water separation techniques are used (17,18). The presence of a dark rim at the renal mass–kidney interface or

within a renal mass on opposed-phase and in-phase gradient echo (GRE) MR images is indicative of bulk fat, which is indicative of an AML (7,9,19). While these findings reliably lead to a diagnosis of lipid-rich AML, in our experience these findings were absent in minimal fat AMLs because of the scant amount of fat.

Opposed-phase and in-phase GRE imaging was recently proposed as a method to help reliably distinguish minimal fat AML from renal cell carcinoma (RCC) (14). Kim et al (14) found that minimal fat AMLs demonstrated greater decrease in signal intensity (SI) on opposed-phase images compared with in-phase images than did RCCs, possibly due to a higher intracellular lipid content in the minimal fat AMLs. However, in that study, characterizations did not include RCC subtypes (14). When examined with electron microscopy, the clear cell subtype of RCC contained substantially more intracytoplasmic lipids than did other histologic subtypes (20), which may explain the characteristic loss of SI

Advances in Knowledge

- Minimal fat angiomyolipoma (AML) and clear cell renal cell carcinoma (RCC) can demonstrate intravoxel fat on opposed-phase and in-phase gradient-echo MR images, but they cannot be distinguished from each other on the basis of this finding.
- Low signal intensity (SI) on T2-weighted images (relative to SI of renal cortex) and small size were predictive of minimal fat AML, whereas high SI on T2-weighted images and larger size were predictive of clear cell RCC, regardless of the presence of intravoxel fat in the mass.
- The presence of intratumoral necrosis within a renal mass virtually excludes the diagnosis of AML.

Implications for Patient Care

- When evaluating renal masses, the presence of decreased SI of a mass on opposed-phase T1-weighted images compared with in-phase images is a non-specific finding that does not allow for accurate distinction between minimal fat AML and clear cell RCC.
- A small renal mass with intravoxel fat and homogeneous low SI on T2-weighted images is highly suggestive of a minimal fat AML.
- Necrotic renal masses should be managed by assuming a malignant histology, regardless of the demonstration of microscopic fat within the mass on opposed-phase and in-phase gradient-echo MR images.

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Abbreviations:

AML = angiomyolipoma
GRE = gradient echo
RCC = renal cell carcinoma
SI = signal intensity
SI_{in} = SI on in-phase images
SI_{opp} = SI on opposed-phase images

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Conflicts of interest are listed at the end of this article.

on opposed-phase MR images of clear cell RCC (6,16,21). However, only moderate amounts of intratumoral lipids (limited to that in the clear cell component) have been shown in papillary RCC, and only small amounts have been shown in chromophobe RCC (20).

To the best of our knowledge, the diagnostic accuracy of chemical shift imaging to help differentiate pathologically confirmed minimal fat AMLs, specifically from clear cell RCC and particularly in small renal tumors, has not been previously tested. Furthermore, the MR imaging features that may help to differentiate minimal fat AML from clear cell RCC have not been reported. Therefore, the purpose of our study was to retrospectively evaluate the ability of MR imaging to differentiate minimal fat AML from clear cell RCC by using opposed-phase and in-phase GRE imaging and MR feature analysis, including a subset analysis of small tumors.

Materials and Methods

Study Patients

This dual-institution (Beth Israel Deaconess Medical Center, Boston, Mass; New York University Langone Medical Center, New York, NY) retrospective study was conducted in accordance with the Health Insurance Portability and Accountability Act and was approved by each institution's institutional review board committees with waivers of informed consent. A computerized MR imaging database at each institution was retrospectively searched for records of patients with renal masses from January 2001 to September 2009 by using the indication and the diagnosis fields. This yielded records from 553 MR imaging examinations; from these, 311 patients had been pathologically confirmed to have AML or clear cell RCC. These patients were cross referenced with those that had pathologic slides available for review, and those who had AMLs with less than 25% fat content at the histopathologic level were identified. Two hundred three lesions

were excluded for the following reasons: intratumoral bulk fat was visible on the MR image ($n = 26$; these were removed either secondary to the prospective lack of recognition of the presence of bulk fat [$n = 4$] or because their removal was a clinical necessity [$n = 22$]); there was more than 25% fat content at the histopathologic level ($n = 37$); pathologic slides were not available for review ($n = 93$); single-shot fast spin-echo or longitudinal T1-weighted opposed-phase or in-phase GRE images were not obtained ($n = 6$); and images were obtained with a 3-T magnet ($n = 6$) or parallel imaging was utilized ($n = 35$). Patients who underwent MR imaging with a 3-T magnet were not included because the later echo was out of phase (22). Parallel imaging was excluded to avoid the confounding effects of noise propagation in SI determinations and the subsequent controversies when obtaining signal-to-noise measurements (23,24). Our study cohort consisted of 108 patients with 108 lesions (88 clear cell RCC and 20 minimal fat AML lesions; 62 men and 26 women had clear cell RCC [age, 25–89 years; mean age, 59 years]; and three men and 17 women had minimal fat AML [age, 30–81 years; mean age, 54 years]).

MR Imaging Technique

All patients were examined with a phased-array coil (four to six elements) and 1.5-T systems (Vision, Symphony, or Avanto, Siemens Medical Systems, Erlangen, Germany; Excite TwinSpeed or Excite HD, GE Healthcare, Waukesha, Wis) with the following sequences: (a) axial T1-weighted opposed-phase and in-phase GRE imaging (repetition time of 180–205 msec and an echo time of 2.1–2.8 msec for opposed-phase and 4.4–5.3 msec for in-phase imaging; 80° flip angle, one signal acquired; bandwidth, ± 62 kHz; field of view, 35–40 cm; section thickness, 6–8 mm; gap, 1 mm; 160×256 matrix); (b) coronal T2-weighted half-Fourier single-shot fast spin echo without fat saturation (repetition time msec [effective]/echo time msec, $\infty/60$; 130°–155° flip angle; bandwidth, ± 62 kHz; field of view, 35–40 cm;

section thickness, 4–5 mm; gap, 1 mm; 192×256 matrix); (c) three-dimensional fat-saturated T1-weighted GRE images (3.8–4.5/1.8–2.0; 12° flip angle; section thickness, 3–4 mm [preinterpolation]; bandwidth, ± 62 kHz; field of view, 35–45 cm; $128\text{--}256 \times 256 \times 512$ matrix) obtained before and after administration of an intravenous bolus of 0.1 mmol/kg of gadopentetate dimeglumine (Magnevist; Berlex Laboratories, Wayne, NJ) at a rate of 2 mL/sec, and followed by a 20-mL saline flush based on a previously described three-dimensional strategy (25). Contrast agent-enhanced images were acquired in the corticomedullary and nephrographic phases, with a first pass timed to the corticomedullary phase by using a 1- or 2-mL bolus test dose of gadolinium chelate (26). At Beth Israel Deaconess Medical Center, early and late nephrographic phases were respectively initiated 20 and 70 seconds after the corticomedullary phase. At New York University Langone Medical Center, the nephrographic phase was initiated 30–40 seconds after the corticomedullary phase (with slight timing differences based on the time to peak and the length of acquisition of the three-dimensional T1-weighted GRE sequences).

Quantitative MR Image Analysis

To prevent recall bias, SI in the renal lesions and spleen was measured 7 months prior to the qualitative imaging analysis by one radiologist (N.H., 5 years of experience). A circular region of interest was placed in the center of the tumor, encompassing at least two-thirds of its solid component. The SI of the spleen was measured by using a region of interest that was identical in size to that used to measure the renal tumor. The area, location, and size of the region of interest were constant between in-phase and opposed-phase images. Care was taken to avoid the edge of the tumor, near where it interfaced with the adjacent perirenal fat, so that a phase cancellation artifact would be avoided (27,28).

Mean SI measurements were recorded in arbitrary units. The SI index was calculated as $[(\text{tumor SI}_{\text{in}} - \text{tumor SI}_{\text{opp}})/(\text{SI}_{\text{in}})]$, where SI_{in} represents the

SI on in-phase images and SI_{opp} represents the SI on opposed-phase images. The tumor-to-spleen ratio was calculated as $\{[(\text{tumor } SI_{opp}/\text{spleen } SI_{opp})/(\text{tumor } SI_{in}/\text{spleen } SI_{in})] - 1\} \times 100$. The SI index and tumor-to-spleen ratio of clear cell RCC and minimal fat AMLs were compared.

Qualitative MR Image Analysis

Before and after administration of the contrast agent, opposed-phase and in-phase GRE, single-shot fast spin-echo, and three-dimensional GRE images were independently analyzed by two radiologists (N.H.; J.W., 5 years of experience) to assess the following characteristics of the renal mass: (a) the presence of intravoxel fat, represented by subjective loss of SI on opposed-phase images relative to in-phase images; (b) predominant SI in the tumor on T2-weighted single-shot fast spin-echo images that was lower than, the same as, or higher than SI of the cortex; (c) predominant SI in the tumor on T1-weighted in-phase and opposed-phase images that was lower than, the same as, or higher than SI of cortex; (d) cystic degeneration, represented by areas with SI equal to that of cerebrospinal fluid on T2-weighted images; low SI on T1-weighted images; lack of enhancement; and lobulated morphology; (e) necrosis, represented by high SI on T2-weighted images, although not as high as SI of cerebrospinal fluid; low SI on T1-weighted images; lack of enhancement; and central location within the tumor; (f) hemorrhage, represented by nonenhanced areas of high SI on T1-weighted images with variable SI on T2-weighted images, which did not suppress on fat-saturated sequences; (g) renal vein thrombosis; and (h) retroperitoneal collateral vessels.

Pathologic Analysis

To confirm the diagnosis of either clear cell RCC or minimal fat AML in all patients, pathologic specimens were retrospectively reviewed by each institution's uropathologist (B.G., 9 years of experience; J.M., 20 years of experience), who were both blinded to the MR findings. The amount of intratumoral fat was quantified for all minimal fat AMLs by reviewing all histopathologic

slices and by subjectively estimating the percentage of the neoplasm that was composed of adipocytes. AMLs were only included if they had estimated fat contents that were less than 25% at the histopathologic level. By indication of the interpreting uropathologist, immunohistochemical analysis (ie, analysis of HMB-45 or melan-A) was retrospectively performed to confirm the diagnosis of AML in selected cases.

Statistical Analysis

The mean, standard deviation, and median were evaluated for the distribution of the quantitative continuous variables for the 20 minimal fat AMLs and 88 clear cell RCCs. The nonparametric Wilcoxon rank sum test was used to compare the central tendency of the distributions between the two groups of lesions. For the qualitative variables, the Fisher exact test was used to compare the sample proportions of the two groups. κ Values with 95% confidence intervals were calculated to assess interreader agreement for the following qualitative variables: 0 = no agreement, 0.01–0.20 = slight agreement, 0.21–0.40 = fair agreement, 0.41–0.60 = moderate agreement, 0.61–0.80 = substantial agreement, and 0.81–1 = almost perfect agreement. A univariate analysis determined the statistically significant variables ($P < .05$) to model the probability of minimal fat AML versus clear cell RCC, which were then used to fit a multivariate logistic regression model. Due to the relatively small sample size of the minimal fat AMLs, the Firth correction factor (29) was utilized to obtain convergence and estimate the multivariate model. Statistical significance was indicated by a type I error of .05. The diagnostic accuracy of SI index and tumor-to-spleen ratio for the diagnosis of AML was calculated by fitting a logistic regression model and by obtaining the c statistic. Additionally, we compared the distributions of the analysis variables in the tables and in the multivariate logistic regression analysis to assess for institutional and scanner effects. All analyses were performed with SAS software (version 9.2 for Windows; SAS Institute, Cary, NC).

Results

Pathologic Diagnosis

Pathologic diagnosis was achieved by means of partial nephrectomy ($n = 19$) or radical nephrectomy ($n = 1$) in the 20 patients with minimal fat AML and by means of radical nephrectomy ($n = 52$), partial nephrectomy ($n = 32$), or percutaneous core biopsy ($n = 4$) in the 88 patients with clear cell RCCs. The size of clear cell RCC (mean, 5.6 cm; median, 4.1 cm; range 1.2–19.7 cm) was larger than that of minimal fat AMLs (mean, 2.1 cm; median, 1.5 cm; range, 1.2–4.9 cm) ($P = .001$). A total of 40 masses measured less than 3 cm in size (14 minimal fat AMLs and 26 clear cell RCCs). The average estimated histopathologic fat content of the 20 patients with minimal fat AML was $5.3\% \pm 7.08$ (median, 5%).

Quantitative Analysis

The mean patient age was $53.9 \text{ years} \pm 13.4$ in the AML cohort and $58.7 \text{ years} \pm 14.49$ in the clear cell RCC cohort ($P = .23$). The ratio of men to women was 2.26:1 in the clear cell RCC cohort and 1:5.7 in the minimal fat AML cohort ($P < .001$).

There was no statistically significant difference in the percentage of decrease in SI between minimal fat AMLs and clear cell RCCs when the SI index or the tumor-to-spleen ratio was used (Table 1). The SI index and tumor-to-spleen ratio were not different between minimal fat AMLs ($8.05\% \pm 14.46$ for SI index, $-8.96\% \pm 16.6$ for tumor-to-spleen ratio; $P = .146$) and clear cell RCC ($14.99\% \pm 19.9$ for SI index, $-15.8\% \pm 22.4$ for tumor-to-spleen ratio; $P = .227$), (Figs 1, 2). Similarly, no significant difference was found between the SI index and tumor-to-spleen ratio for small clear cell RCCs and minimal fat AMLs (Table 2). The diagnostic accuracy of SI index and tumor-to-spleen ratio for the diagnosis of AML was 0.59.

Smaller size correlated with minimal fat AML, and the larger area under receiver operating characteristic curve ($A_z = 0.76$) used 2 cm as a cutoff for a sensitivity of 89% and specificity of 65%.

Figure 1

Figure 1: Box-and-whisker plot of SI index for clear cell RCC (*ccRCC*) and minimal fat AML (*mfAML*) groups. These two data sets had no statistically significant difference between them, and there was no threshold for the SI index that would allow accurate differentiation between clear cell RCC and minimal fat AML.

Figure 2

Figure 2: Box-and-whisker plot of the tumor-to-spleen ratio for clear cell RCC (*ccRCC*) and minimal fat AML (*mfAML*) groups. These two data sets had no statistically significant difference between them, and there was no threshold for the tumor-to-spleen ratio that would allow accurate differentiation between clear cell RCC and minimal fat AML.

Qualitative Analysis

Tumor sizes and six qualitative variables (SI on T2-weighted images, cystic degeneration, necrosis, hemorrhage, retroperitoneal collaterals, renal vein thrombosis) were statistically significant and associated with pathologic diagnosis in the univariate analysis of all masses in our study (Table 3) (Fig 3). Subjective detection of intravoxel fat on opposed-phase and in-phase GRE images did not correlate with the diagnosis of minimal fat AML (Table 3). Although none of the minimal fat AMLs demonstrated cystic degeneration or necrosis, up to 36% (33 of 88) and 39% (34 of 88) of clear cell RCCs demonstrated cystic degeneration or necrosis ($P < .001$) (Fig 4). For the qualitative analysis, the two radiologists estimated that κ was greater than 0.7 (ie, substantial agreement) (Table 4). Only two features remained statistically significant in the multivariate model: SI on T2-weighted images and size of the lesion. The combination of a low SI on T2-weighted images with small lesion size (< 2 cm) increased the probability that a renal mass would represent a minimal fat AML versus a clear cell RCC (Table 5) with the diagnostic accuracy (c statistic) of 0.98.

Table 1

Quantitative Characteristics of All Clear Cell RCCs and Minimal Fat AMLs

Quantitative Variables	Minimal Fat AML ($n = 20$)*	Clear Cell RCC ($n = 88$)*	P Value†
Mean age (y)	53.9 ± 13.4 (54.5)	58.7 ± 14.5 (59)	.233
Size (cm)	2.1 ± 0.9 (1.5)	5.6 ± 3.9 (4.1)	.001
Tumor-to-spleen ratio (%)	-8.96 ± 16.6 (-7.92)	-15.8 ± 22.4 (-11.1)	.227
SI index	8.05 ± 14.46 (3.85)	14.99 ± 19.90 (8.75)	.146

* Number in parentheses is the median

† Wilcoxon rank sum test.

Table 2

Quantitative Characteristics of Small (< 3 -cm) Renal Masses

Quantitative Variables	Minimal Fat AML ($n = 14$)	Clear Cell RCC ($n = 26$)	P Value*
Tumor-to-spleen ratio (%)	-12.46 ± 16.2 (-12.4)	-10.67 ± 16.6 (-9.1)	.623
SI index (%)	12.0 ± 15.4 (5.72)	10.8 ± 17.3 (6.92)	.922

Note.—Number in parentheses is the median. P values from Wilcoxon rank sum test.

When evaluating small renal masses, only SI on T2-weighted images and cystic degeneration remained statistically associated with the diagnosis of minimal fat AML and clear cell RCC, respectively (Table 6).

No statistically significant differences regarding the distribution of analysis variables, other than the outcome (minimal fat AML vs clear cell RCC), were noted between the two institutions. Six of the 20 minimal fat

Table 3

Univariate Analysis of Qualitative Characteristics of Clear Cell RCC and Minimal Fat AML

	Minimal Fat AML (<i>n</i> = 20)		Clear Cell RCC (<i>n</i> = 88)		
Qualitative Variable	Reader 1	Reader 2	Reader 1	Reader 2	<i>P</i> Value*
T1-weighted in-phase SI					
Lower than cortex	2 (10)*	2 (10)	22 (25)	25 (28)	.198
Same as cortex	16 (80)	16 (80)	62 (70)	59 (67)	.151
Higher than cortex	2 (10)	2 (10)	4 (5)	4 (5)	
T1-weighted opposed phase SI					
Lower than cortex	5 (25)	5 (25)	37 (42)	36 (41)	.306
Same as cortex	15 (75)	15 (75)	49 (56)	50 (57)	.355
Higher than cortex	0 (0)	0 (0)	2 (2)	2 (2)	
Subjective assessment for intravoxel fat					
Yes	4 (20)	3 (15)	36 (41)	43 (49)	.123
No	16 (80)	17 (85)	52 (59)	45 (52)	.006
T2-weighted SI					
Lower than cortex	17 (85)	16 (80)	11 (13)	6 (7)	.001
Same as cortex	3 (15)	3 (15)	19 (22)	21 (24)	.001
Higher than cortex	0 (0)	1 (5)	58 (66)	61 (69)	
Cystic degeneration					
Yes	0 (0)	0 (0)	32 (36)	30 (34)	.001
No	20 (100)	20 (100)	56 (64)	58 (66)	.001
Necrosis					
Yes	0 (0)	0 (0)	34 (39)	34 (39)	.001
No	20 (100)	20 (100)	54 (61)	54 (61)	.001
Hemorrhage					
Yes	0 (0)	0 (0)	21 (24)	20 (23)	.011
No	20 (100)	20 (100)	67 (76)	68 (77)	.022
Renal vein thrombosis					
Yes	0 (0)	1 (5)	11 (13)	8 (9)	.121
No	20 (100)	19 (95)	77 (87)	80 (91)	1.00
Collaterals					
Yes	2 (10)	2 (10)	32 (36)	32 (36)	.031
No	18 (90)	18 (90)	56 (64)	56 (64)	.031

Note.—Data are the number of lesions. Numbers in parentheses are percentages.

* Fisher exact test for comparison between readers 1 and 2.

AMLs were from Beth Israel Deaconess Medical Center and 14 were from New York University Langone Medical Center (Fisher exact test, $P < .001$). The center effect was included in the multivariate logistic regression analysis and was not found to be statistically significant ($P = .288$). It was not included in the model.

Discussion

Limited ability to characterize minimal fat AMLs accurately and preoperatively is supported by the consistent presence of these tumors in recent

surgical series (4,30,31). Various imaging strategies have served as attempts to recognize AMLs by detecting small amounts of fat in imaged lesions. AMLs that contain minimal amounts of fat have been defined at the histopathologic level as containing less than 25% fat content per high-power field (4), although less than 5% fat content is commonly present in monophasic AMLs (31). Lane et al (33) recently found levels of fat that were substantially lower in the estimated percentage volume of intratumoral fat for surgical minimal fat AMLs as compared with surgically removed “classic”

AMLs. This was consistent with our results, and revealed an average 5% fat content in the AMLs from our study. Therefore, it is not surprising that the standard imaging techniques may fail to demonstrate intratumoral fat in these lesions and have limited sensitivity for this diagnosis. A limited specificity is not surprising because of the predisposition of certain histologic subtypes of RCC (eg, clear cell RCC) to accumulate intracellular fat (16,21,32). Our study confirmed the limited use of opposed-phase and in-phase GRE imaging for the differentiation of minimal fat AML and clear cell

RCC, including those representing the subset of small renal masses.

Kim et al (14) reported excellent sensitivity and specificity (96% and 93%, respectively) for differentiating AMLs with minimal fat from other renal neoplasms by using MR imaging, whereby an SI index of 25% and a tumor-to-spleen ratio of -32% yielded excellent sensitivity and specificity (88% and 97%, respectively) for this differentiation. There are important considerations that explain our inability to achieve the same distinction by using similar analyses.

First, we applied strict inclusion criteria for minimal fat AMLs in our series that were based on the findings of Milner et al (4). The minimal fat AMLs in our series were restricted to lesions with less than 25% fat content at the histopathologic examination. Kim et al found that only nine of 26 AMLs had pathologic confirmation, and 17 of the 18 masses examined with serial imaging were categorized as minimal fat AMLs—without pathologic confirmation—which makes alternate histologic characteristics possible in those 17 cases. The high overall prevalence of minimal fat AMLs in that series (47% [26 of 55]) suggests that at least some of the masses that were not resected may not have met the proposed pathologic criteria for minimal fat AML ($<25\%$ fat content) (4,12).

Second, in the study by Kim et al (14), a variety of tumors (23 RCCs with unspecified subtypes, two oncocytomas, two lymphomas, and one reninoma) were included in the non-AML group. We compared minimal fat AMLs to a confined group of histologically proved clear cell RCCs. Clear cell RCC is a subtype that contains increased levels of intracellular lipids, as demonstrated with both in vitro electron microscopy and in vivo MR imaging (8,20,21,32). To the best of our knowledge, intratumoral fat has not been described in renal oncocytoma, lymphoma, or reninoma. Therefore, we suspected that a lower proportion of fat-containing tumors in the non-AML group masked the effect that clear cell RCCs had in the study by Kim et al, thereby enabling a distinction between the two groups.

Figure 3: (a) Coronal T2-weighted half-Fourier single-shot turbo spin-echo MR image (5/62; 256×104 matrix; thickness, 5 mm) of 62-year-old woman with right lower pole AML shows well-defined cortical mass (arrow) of homogeneous low SI relative to renal cortex SI. Axial T1-weighted (b) in-phase (160/2.7) and (c) opposed-phase (160/5.3) GRE MR images (256×106 matrix; thickness, 8 mm) at level of the mass (arrow) show no appreciable decrease in SI on c. SI index was -0.9 and tumor-to-spleen ratio was 3.4.

Third, another explanation is that there were differences in the region of interest analyses between the two studies. In the study by Kim et al, the region of interest encompassed the entire tumor, whereas, in our study, areas of cystic degeneration, necrosis, and hemorrhage were purposely avoided. By restricting the region of interest to the solid component of the tumor, partial volume effects can be minimized, which offers an improved potential to quantify and compare the fat content. It can be argued that a large necrotic clear cell RCC is not a diagnostic dilemma for a minimal fat AML in clinical practice. Therefore, we subdivided the analysis to focus on the more clinically challenging small lesions. In this subset, there was no statistically significant difference ($P = .623$) in the percentage of intravoxel fat as determined with opposed-phase and in-phase GRE imaging in the minimal fat AMLs versus the clear cell RCCs. Given the relatively small size of this subgroup in our cohort ($n = 40$; 14 minimal fat AMLs, 26 clear cell RCCs),

it is recommended that larger studies of pathologically confirmed minimal fat AMLs be conducted.

In our study, two imaging features allowed differentiation of minimal fat AML from clear cell RCC for large (>3 -cm) and small lesions: Low SI on T2-weighted images was predictive of minimal fat AML, and necrosis correlated with clear cell RCC. Furthermore, the combination of small size with low SI on T2-weighted images provided an excellent diagnostic accuracy.

Certain MR imaging features can be used for noninvasive differentiation of the most common subtypes of RCC (16,33,34). In addition, low SI on T2-weighted images and small size provided a diagnostic accuracy that was 0.98 for the diagnosis of minimal fat AML in our series, which is concordant with previous observations in small series (13). In our experience, low SI on T2-weighted images in a mass that contains small amounts of fat (ie, decreased SI on opposed-phase images compared with that on in-phase

Figure 4

Figure 4: (a) Coronal T2-weighted half Fourier single-shot turbo spin-echo MR image (5/62; 256×104 matrix; thickness, 5 mm) of 78-year-old man with clear cell RCC and a simple cyst in left kidney (K) shows large heterogeneous mass (arrow) in upper pole, with predominantly high SI relative to that of kidney. Axial T1-weighted (b) in-phase (160/2.7) and (c) opposed-phase (160/5.3) GRE MR images (256×106 matrix; thickness, 8 mm) show marked decrease in SI in the mass (arrow) on c compared with the b, indicative of intravoxel fat. SI index was 62.9 and tumor-to-spleen ratio was -67.8 . A simple cyst is also present laterally (*). (d) Coronal subtracted (unenhanced from enhanced) three-dimensional T1-weighted spoiled-GRE MR image (4.5/1.9; 256×128 matrix; preinterpolation thickness, 3.75 mm) obtained during nephrographic phase shows heterogeneous enhancement of the mass with central irregular nonenhanced area (arrow), consistent with necrosis.

images) is highly suggestive of minimal fat AML. However, given the overlap with the appearance on the MR image of papillary RCC on T2-weighted images (ie, low SI), this finding alone does not have sufficient specificity to allow for the accurate characterization of

minimal fat AMLs when small amounts of fat are not evident (11). Although not assessed in this study, the coexistence of low SI on T2-weighted images and avid enhancement should help to differentiate minimal fat AML from the typically hypoenhanced papillary RCC (35).

Table 4

Interreader Variability Analysis

Variables	κ Value*
SI on T2-weighted images	.74 (0.64, 0.84)
Cystic degeneration	.86 (0.76, 0.97)
Necrosis	.93 (0.86, 1.00)
Hemorrhage	.79 (0.84, 0.94)
Collaterals	.91 (0.83, 0.99)

*Numbers in parentheses are 95% confidence intervals.

Table 5

Multivariate Logistic Regression Analysis Relating Statistically Significant MR Imaging Features to AML

Reader and Feature	Adjusted Odds Ratio
Radiologist 1	
SI on T2-weighted images	
Lower than cortex	328.9 (15.2, 999)
Same as cortex	25.5 (1.1, 577.9)
Higher than cortex	1
Size	0.41 (0.20, 0.81)
Radiologist 2	
SI on T2-weighted images	
Lower than cortex	145.1 (17.1, 999)
Same as cortex	11.8 (1.4, 100.2)
Higher than cortex	1
Size	0.47 (0.27, 0.84)

Note.—The model c statistic was 0.98. Numbers in parentheses are 95% confidence intervals.

While intratumoral necrosis was good for helping differentiate between minimal fat AML and clear cell RCC in our series, a larger series would provide a more definitive conclusion regarding the true sensitivity and specificity, because this finding was not present in any of the small clear cell RCCs in our study.

Our study had limitations. First, as with all retrospective studies, the prospect of unintended selection bias exists. Second, the quantitative values were obtained by the same radiologist who participated in the qualitative imaging analysis; however, the 7-month period between each collection of these separate

Table 6

Univariate Analysis of Quantitative Characteristics of Small (<3-cm) Renal Lesions

	Minimal Fat AML (<i>n</i> = 14)		Clear Cell RCC (<i>n</i> = 26)		
Quantitative Variables	Reader 1	Reader 2	Reader 1	Reader 2	<i>P</i> Value*
T2-weighted SI					
Lower than cortex	11 (79)	11 (79)	2 (8)	2 (8)	.001
Same as cortex	3 (21)	2 (14)	3 (12)	3 (12)	.001
Higher than cortex	0 (0)	1 (7)	21 (80)	21 (80)	.001
Cystic degeneration					
Yes	0 (0)	0 (0)	9 (100)	8 (100)	.016
No	14 (100)	14 (100)	17 (0)	18 (0)	.036
Necrosis					
Yes	0 (0)	0 (0)	0 (0)	1 (4)	1.000
No	14 (100)	14 (100)	26 (100)	25 (96)	1.000

Note.—Numbers in parentheses are percentages.

* Fisher exact test for comparisons between readers 1 and 2.

data pools minimized potential for recall bias. Finally, the number of minimal fat AMLs was small but consistent with their low prevalence, as reported in surgical series (4,30,31). Furthermore, all AMLs in our series had pathologic confirmation and fulfilled the histopathologic criteria of minimal fat AML (ie, <25% fat content per high-power field) (4).

In summary, opposed-phase and in-phase GRE MR imaging cannot be used to accurately distinguish minimal fat AMLs from clear cell RCCs; the presence of necrosis virtually excludes the diagnosis of AML, whereas low SI on T2-weighted images and small size favors the diagnosis of minimal fat AML over that of clear cell RCC.

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