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The characterization of small hypoattenuating renal masses on contrast-enhanced CT[☆]

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Abstract

Purpose—To determine if small hypoattenuating renal masses can be characterized as simple cysts or renal cell carcinomas on contrast-enhanced computed tomography (CT).

Materials and methods—We retrospectively identified 20 small (≤ 1.5 cm) hypoattenuating renal masses seen on contrast enhanced CT, consisting of 14 simple cysts and six renal cell carcinomas. Three independent readers recorded subjective visual impression (five-point scale from 1=definitely fluid to 5=definitely solid), CT attenuation, border (well circumscribed or ill defined), and shape (ovoid or irregular) for each lesion.

Results—The overall area under the receiver operator characteristic curves for subjective visual impression, CT attenuation, border, and shape were 0.97, 0.82, 0.59, and 0.55, respectively. Using dichotomized ratings (1–2=cyst and 3–5=carcinoma), subjective impression had a sensitivity and specificity of 100% and 79–100%, respectively, for the diagnosis of renal cell carcinoma. Using a threshold of 50 Hounsfield Units (HU) or more, CT attenuation had a sensitivity and specificity of 100% and 43–64%, respectively.

Conclusion—Small hypoattenuating renal masses can be characterized with reasonable accuracy by subjective impression and CT attenuation; lesions that appear solid on visual inspection or have an attenuation value of 50 HU or more are likely to be renal cell carcinoma. © 2009 Elsevier Inc. All rights reserved.

Keywords

Kidney neoplasms; CT; Kidney; Cysts; Computed tomography; Contrast enhancement

1. Introduction

Most small renal masses, including simple cysts and renal cell carcinomas, are asymptomatic and discovered on abdominal CT or other imaging performed for unrelated reasons [1–5]. CT is the most sensitive technique for the detection of small renal masses [1,2,6]. In larger masses, measurement of CT attenuation is central to the distinction of simple cysts from renal cell carcinomas, but measurement of CT attenuation is known to be unreliable in lesions under 1.5 cm in diameter due to partial volume effects and pseudoenhancement [2,7–12]. As a result, the management of such lesions is problematic

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[1,2,4,13,14]. Radiological options include surveillance or further evaluation by thin section multiphase CT, ultrasound, or magnetic resonance (MR) imaging [9,15–18]. However, additional imaging is burdensome for the patient and may not yield a definitive result, and referring physicians may not always follow recommendations for additional imaging. Any CT finding that might help distinguish small cystic and solid lesions would clearly be helpful. Therefore, we undertook this study to determine if small (1.5 cm or less in diameter) hypoattenuating renal masses can be characterized as simple cysts or renal cell carcinomas on contrast-enhanced CT.

2. Materials and methods

2.1. Subjects

This was a retrospective single-institutional study and was approved by our Committee on Human Research. Written informed consent was not required. We identified patients with small simple renal cysts by first using a computerized search of our radiology departmental information system (IDXrad, software version 9.7.1, IDX Systems, Burlington, VT, USA) to find patients with contemporaneous (within 6 months) abdominal MR imaging and contrast-enhanced CT performed between 1998 and 2003. The median time difference between the CT and MR scans was 42 days (range, 1–150). An experienced radiologist reviewed the CT and MR images in these patients and identified 14 patients with proven small simple renal cysts, based on the presence of a hypoattenuating renal lesion less than 1.5 cm in maximal axial diameter on contrast-enhanced CT and corresponding MR images showing the lesion to be of fluid signal-intensity on T2-weighted images and nonenhancing after intravenous gadolinium administration [19] (Fig. 1). In order to avoid potential weighting of data, only one lesion was chosen in each patient, even if multiple lesions were present. The 14 patients with small simple cysts consisted of 7 men and 7 women with a mean age of 57 years (range, 27–86). The mean cyst diameter was 0.9 cm (range, 0.4–1.3). We next identified all patients with a surgically proven diagnosis of renal cell carcinoma based on a computerized search of pathology reports generated between 1997 and 2001. Six patients who had renal cell carcinomas that were less than 1.5 cm in maximum diameter and who had a preoperative contrast-enhanced CT performed at our institution (Fig. 2) were found. The six patients with small renal cell carcinomas consisted of 4 men and 2 women with a mean age of 64 years (range, 55–74). The mean renal cell carcinoma diameter was 1.2 cm (range, 1.0–1.4).

2.2. CT technique

CT scans were performed using helical CT scanners (Lightspeed, $n=8$; HiSpeed CT/i, $n=9$; HiSpeed Advantage, $n=3$; General Electric, Milwaukee, WI, USA). All patients received 150 ml intravenous iohexol (Omnipaque 350, Nycomed Amersham, Princeton, NJ, USA) and 800 ml oral diatrizoate meglumine (Hypaque, Nycomed Amersham, Princeton, NJ, USA). All patients were imaged during the portal venous phase with image acquisition after a scan delay of 70 s. Slice collimation was 2.5 mm ($n=3$), 5 mm ($n=9$), or 7 mm ($n=8$). In addition, three patients were also imaged prior to intravenous contrast administration, six were imaged during the arterial phase of enhancement (scan delay of 45 seconds), and 11 were imaged during delayed phase (scan delay of 3–5 min). All images were contiguous.

2.3. MR technique

Abdominal MR imaging was performed on a 1.5-T whole-body MR scanner (Signa; GE Medical Systems, Milwaukee, WI, USA). Patients were examined in the supine position, using the body coil for excitation and a torso phased array surface coil (GE Medical Systems) for signal reception. MR sequences included in-phase and opposed-phase T1-weighted axial spoiled gradient echo (TR/TE, 90–150/4.2 and 2.1; flip angle, 75°; slice

thickness, 8 mm; gap, 1 mm; field of view, 25–40 cm; number of acquisitions, 1; matrix, 256×128–192), fat-saturated T2-weighted axial fast spin echo (TR/TE_{eff}, 4000–5000/100; slice thickness, 8 mm; gap, 1 mm; field of view, 25–40 cm; number of acquisitions, 1; matrix, 256×160), T2-weighted coronal single shot fast spin echo (TR/TE_{eff}, ∞/100; slice thickness, 6 mm; gap, 1 mm; field of view, 25–40 cm; number of acquisitions, 1; matrix, 256×160–192), and dynamically enhanced T1-weighted axial 3-dimensional time-of-flight spoiled gradient echo (TR/TE, 6.7/2.7; flip angle 20°; slice thickness, 6 mm with zero-filled interpolation to 3-mm intervals; field of view, 25–40 cm; number of acquisitions, 0.75; matrix, 256×128–160) after bolus intravenous administration of 0.1 mmol/kg gadolinium chelate (gadodiamide, Omniscan; Nycomed).

2.4. CT interpretation

Three attending radiologists with subspecialty experience in abdominal imaging independently reviewed the randomized contrast-enhanced images of all 20 lesions on a picture archiving and communications system (Impax, Agfa, Mortsel, Belgium) workstation. To prevent confusion with other lesions, readers were aware of the location of the lesions of interest. Readers were unaware of all other clinical and radiological information. Readers recorded subjective impression on visual inspection, CT attenuation, border, and shape for each lesion. Subjective impression was rated on a five-point scale of 1 (definitely fluid), 2 (probably fluid), 3 (indeterminate), 4 (probably solid), or 5 (definitely solid). CT attenuation was measured in Hounsfield Units (HU) by placing a region of interest in the center of the lesion on the portal venous phase images. Border was rated as well circumscribed or ill defined. Shape was rated as ovoid or irregular.

2.5. Statistical analysis

Statistical analysis was performed using Stata software package version 7.0 (Stata, College Station, TX, USA). Interobserver agreement was evaluated by intraclass correlation coefficient for the continuous variable of objective CT attenuation [20] and was evaluated by the weighted kappa statistic for the ordinal categorical variables of subjective impression, border, and shape. The weighted kappa statistic was interpreted as follows: 0–0.2=slight agreement, 0.21–0.4=fair agreement, 0.41–0.6 moderate agreement, 0.61–0.8 substantial agreement, and 0.81–1 almost perfect agreement [21]. The sensitivity, specificity, positive predictive value, and negative predictive value in the distinction of simple cyst and renal cell carcinomas were calculated for each of the variables studied. Dichotomised ratings (1–2=cyst and 3–5=carcinoma) were used for analysis of subjective impression. Based on preliminary data review, a threshold of 50 HU was used for subsequent analysis of CT attenuation. The relationship between subjective impression, border, shape, and objective CT attenuation and the final diagnosis was analyzed for each reader using Fisher's Exact test. The mean objective CT attenuation between benign cysts and renal cell carcinomas were compared using Student's *t* test. For all tests, *P* values less than .05 were considered statistically significant. Nonparametric receiver operator characteristic curves were calculated for the ordinal categorical variables of subjective impression, border, and shape [22]. Receiver operator characteristic curves using maximum-likelihood models were calculated for the continuous variable of CT attenuation [23].

3. Results

Interobserver agreement for CT findings is summarized in Table 1. Readers demonstrated excellent agreement for measurement of CT attenuation. Only fair to moderate interobserver agreement was found for assessment of subjective impression, border, and shape. The sensitivity, specificity, positive predictive value, negative predictive value, and statistical significance of the CT findings studied in the distinction of small simple renal cysts and

renal cell carcinomas are shown in Table 2. A significant difference in mean CT attenuation measurements was seen between simple cysts and renal cell carcinomas ($P<.01$ for readers 1 and 3, $P<.05$ for reader 2). For all readers, lesions with a CT attenuation less than 50 HU were simple cysts, while lesions with a higher attenuation were either cysts or carcinomas (Fig. 3). Renal cell carcinomas could be distinguished from simple cysts by subjective impression, but could not be distinguished by shape or border. Receiver operator characteristic curves for the distinction of small simple renal cysts and renal cell carcinomas using the CT findings studied are shown in Table 3 and Fig. 4. The overall area under the receiver operator characteristic curves for subjective impression, CT attenuation, border, and shape were 0.97, 0.82, 0.59, and 0.55, respectively.

4. Discussion

Our study suggests that the frequent description of small (1.5 cm or less in diameter) hypoattenuating renal lesions on portal venous phase contrast enhanced CT as “too small to accurately characterize” or “indeterminate” is not entirely correct, because both subjective impression and CT attenuation can help distinguish small cysts from renal cell carcinomas. In this study, lesions that appeared possibly to definitely solid on visual inspection were likely to be renal cell carcinomas, with a sensitivity of 100% and a positive predictive value of 67–100%, although this sign was somewhat subjective, with paired kappa values of 0.33 to 0.69 for comparisons between the three readers. Subjective criteria may be better suited for evaluating some renal masses than objective attenuation measurements. For example, a recent study documented the utility of assessing lesion heterogeneity as a marker of malignancy in the distinction of high-density cysts from renal cell carcinoma on portal venous phase contrast-enhanced CT (27), so it is not surprising that this finding is also valid in the evaluation of small hypoattenuating lesions. In addition, we found small lesions with a CT attenuation of 50 HU or more were likely to be renal cell carcinomas, with a sensitivity of 100% and a positive predictive value of 43–55%. This sign demonstrated greater interobserver agreement, with paired intraclass correlation coefficients of 0.90–0.93. The threshold attenuation of 50 HU for the identification of small renal cysts is higher than the normal upper limit of simple fluid attenuation, usually considered to be 20 HU (10). This higher threshold is presumably due to the effects of partial volume averaging and pseudoenhancement, which are known to result in higher computer generated attenuation measurements in small lesions [2,7–12].

Currently, the recommendation for indeterminate small renal masses is follow-up imaging studies [4] because it is thought that most of these lesions are cysts, and that even if the lesions are malignant, there is little risk of advancement of tumor stage [24]. However, it is also known that small renal malignancies can metastasize if left untreated [25], and earlier treatment may improve prognosis [26], since the tumor stage at the start of treatment is the most important prognostic factor for primary renal malignancy [27]. Our findings should not be interpreted as replacing these recommendations or indicating that definitive characterization of small hypoattenuating renal lesions is possible; rather, we are suggesting that our findings may influence the strength of recommendations for additional evaluation of these lesions, whether by ultrasound or MR imaging. Incidental small hypoattenuating renal lesions are encountered every day in routine practice, and aggressive follow-up of all such lesions is not practical, feasible, or commonly performed. Our findings may help stratify patients with small hypoattenuating renal lesions and identify the subgroup most needing additional imaging for possible renal cell carcinoma. Such a selective approach to these lesions may also improve the likelihood that a referring physician will request the additional imaging studies suggested. This could, in turn, lead to an earlier diagnosis of renal cell carcinoma and potentially contribute to improved survival.

Our study has a number of limitations. The sample size ($n=20$) was small, which was partially a reflection of the limited number of surgically resected renal cell carcinomas under 1.5 cm at our institution. We identified patients with renal cell carcinoma by review of histopathological findings. This is a possible source of selection bias, since lesions that are more obviously malignant on imaging may be more likely to undergo surgery. Unfortunately, there is no method that allows us to identify cases of clinically unrecognized renal cell carcinoma. Subjective impression of small renal lesions is not amenable to objective definition and demonstrated greater interobserver variability than CT attenuation measurement. CT attenuation measurements may be dependant on CT scanner model and CT technique [7,8,28]. Notwithstanding this caveat, lesions measuring less than 50 HU in our series were all benign cysts rather than renal cell carcinomas. Finally, our study could be criticized for not including small high-density cysts. However, given that CT density measurement is critical to the diagnosis of high-density cysts and that CT density measurements are unreliable for small lesions, it would be difficult to construct a methodology that would identify such cysts. It is even possible that our study did include such lesions, since we cannot reliably make the distinction of small simple cysts from small high-density cysts.

In conclusion, small hypoattenuating renal masses can be characterized at contrast-enhanced CT with reasonable accuracy by subjective impression and CT attenuation; lesions that appear possibly to definitely solid on visual inspection or have an attenuation value of 50 HU or more are likely to be renal cell carcinomas.

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Fig. 1.

A 50-year-old man with simple renal cyst. A, Portal venous phase contrast-enhanced CT scan with 2.5 mm collimation demonstrates a 1.2 cm hypoattenuating lesion. B, Axial T2 weighted fast spin echo MR image shows the lesion is of uniformly high T2 signal. C, Axial T1-weighted spoiled gradient echo MR image after intravenous gadolinium shows the lesion is non-enhancing.

Fig. 2.

A 58-year-old woman with renal cell carcinoma. A, Portal venous phase contrast-enhanced CT scan with 7 mm collimation demonstrates a 1.1 cm hypoattenuating lesion in the left kidney. Subsequent resection demonstrated a renal cell carcinoma.

Fig. 3.

Plot of CT attenuation measurements (HU) for cyst and renal cell carcinomas by reader. The mean CT attenuation for the simple cysts was significantly less than that of the renal cell carcinomas ($P < .01$, $P < .05$, and $P < .01$ for Readers 1, 2, and 3 respectively). The horizontal line drawn at 50 HU denotes the level below which only cysts are found.

Fig. 4. Overall receiver operator characteristic curves for CT criteria and prediction of malignancy. Az indicates area under the receiver operator characteristic curve.

Table 1

Interobserver agreement (and 95% confidence intervals) for CT findings, by reader pairs

CT finding (parameter)	Reader 1 vs. 2	Reader 2 vs. 3	Reader 1 vs. 3
Subjective impression (weighted kappa)	0.69 (0.54–0.85)	0.33 (0.21–0.45)	0.38 (0.27–0.49)
CT attenuation (intraclass correlation coefficient)	0.93 (0.87–0.99)	0.90 (0.82–0.98)	0.93 (0.88–0.99)
Border (weighted kappa)	0.29 (0.08–0.51)	0.56 (0.34–0.79)	0.13 (–0.08 to 0.34)
Shape (weighted kappa)	NA	0.46 (0.26–0.65)	NA

NA=statistic could not be calculated since all shapes for reader 1 were the same (ovoid).

Table 2

Distinction of small simple cysts from renal cell carcinomas based on CT findings

CT finding	Parameter	Reader 1	Reader 2	Reader 3
Subjective impression 1–2=cyst and 3–5=cancer)	Sensitivity	100% (6/6)	100% (6/6)	100% (6/6)
	Specificity	100% (14/14)	79% (11/14)	79% (11/14)
	Positive predictive value	100% (6/6)	67% (6/9)	67% (6/9)
	Negative predictive value	100% (14/14)	100% (11/11)	100% (11/11)
	<i>P</i> value	<.001	<.005	<.005
CT attenuation (<50=cyst and ≥50=cancer)	Sensitivity	100% (6/6)	100% (6/6)	100% (6/6)
	Specificity	64% (9/14)	57% (8/14)	43% (6/14)
	Positive predictive value	55% (6/11)	50% (6/12)	43% (6/14)
	Negative predictive value	100% (9/9)	100% (8/8)	100% (6/6)
	<i>P</i> value	<.05	<.05	.115
Border (well circumscribed=cyst and ill-defined=cancer)	Sensitivity	83% (5/6)	17% (1/6)	17% (1/6)
	Specificity	86% (12/14)	71% (10/14)	21% (3/14)
	Positive predictive value	71% (5/7)	20% (1/5)	8% (1/12)
	Negative predictive value	92% (12/13)	67% (10/15)	38% (3/8)
	<i>P</i> value	<.01	.52	.63
Shape (Ovoid=cyst and irregular=cancer)	Sensitivity	0% (0/6)	0% (0/6)	0% (0/6)
	Specificity	100% (14/14)	79% (11/14)	93% (13/14)
	Positive predictive value	0% (0/6)	0% (0/3)	0% (0/1)
	Negative predictive value	70% (14/20)	65% (11/17)	68% (13/19)
	<i>P</i> value	1.00	.52	1.00

Table 3

Per reader and overall areas under the receiver operator characteristic curve (with 95% confidence intervals) for each of the CT findings studied in the distinction of small simple cysts and renal cell carcinomas

CT finding	Reader 1	Reader 2	Reader 3	Overall
Subjective impression	1.00 (1.00–1.00)	0.96 (0.89–1.00)	0.90 (0.80–1.00)	0.97 (0.93–1.00)
CT attenuation	0.85 (0.68–1.00)	0.80 (0.60–1.00)	0.90 (0.76–1.00)	0.82 (0.72–0.93)
Border	0.85 (0.66–1.00)	0.56 (0.36–0.76)	0.53 (0.23–0.73)	0.59 (0.50–0.72)
Shape	0.50 (0.50–0.50)	0.61 (0.50–0.72)	0.54 (0.46–0.61)	0.55 (0.50–0.59)