

# Differentiation of Small Renal Masses of 4cm or less between Renal Cell Carcinoma and Cysts using Attenuation Values on Unenhanced Computerized Tomography



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## Abstract

**Purpose:** To retrospectively investigate the feasibility of distinguishing small renal masses of 4cm or less between renal cell carcinoma (RCC) and cysts using attenuation values with unenhanced computerized tomography (CT).

**Materials and Methods:** Patients who had pathologically confirmed RCC with a maximum diameter of 4cm or less were selected as patients with RCC. Patients who satisfied the eligibility criteria for renal cysts in this study were enrolled as patients with cysts. CT values [Hounsfield units (HU)] were measured for each lesion and compared between RCC and cysts.

**Results:** Sixty-one patients with a total of 62 RCCs and 70 patients with a total of 114 cysts satisfied the eligibility criteria of patients with RCC and renal cysts, respectively. Median values of lowest CT attenuation for RCC and cysts were 1.0HU and -17HU, those of highest CT attenuation were 59HU and 36HU, and those of mean CT attenuations were 30HU and 10HU, respectively. The differences in these values between RCC and cysts were statistically significant ( $p < 0.0001$ ). The area under the curves for the diagnostic efficacy of the lowest, highest, and mean CT attenuation values were 0.871, 0.963, and 0.984, respectively. Regarding mean CT attenuation, the sensitivities and specificities of differentiation between RCC and renal cysts with 15HU were 98% and 90%, and those with 20HU were 94% and 96%, respectively.

**Conclusion:** It is possible to clearly differentiate small renal masses between RCC and renal cysts using the mean attenuation with unenhanced CT.

**Keywords:** CT Attenuation value; Diagnostic efficacy; Renal cell carcinoma; Renal cyst; unenhanced CT

**Abbreviations:** RCC: Renal Cell Carcinoma; Ct: Computerized Tomography; Hu: Hounsfield Units; Hipaa: Health Insurance Portability and Accountability Act; Pacs: Picture Archiving and Communication Systems; Mdct: Multidetector Ct; Roi: Region of Interest; Sd: Standard Deviation; Roc: Receiver Operating Characteristic; Auc: Area Under the Curve; Ci: Confidence Interval; Mri: Magnetic Resonance Imaging

## Introduction

Incidental detection of renal masses by unenhanced computerized tomography (CT) has increased in recent years, owing to technical advancements as well as improvements in the processing of CT images. Although the most common renal masses are renal cysts, the number of cases of renal cell carcinoma (RCC) that are incidentally detected by unenhanced CT is not rare [1,2]. In particular, in older people, the frequency of detection of RCC and renal cysts is increasing because the prevalence of these lesions is increased in older people [3, 4]. It is important to distinguish renal cysts from RCC because the management for these lesions is different. However, there are occasional cases in which differentiation of renal masses

between RCC and renal cysts is difficult, particularly for small renal masses. The shape of small RCC is often similar to that of renal cysts. The Bosniak system [5] has been used as the accepted method of classifying renal masses for distinction between malignancy and benign tumors with CT. In this system, renal masses with a hairline-thin wall and water attenuation, and without septa, calcification, or solid components are considered as benign cysts. However, the visual appearance of small RCC is often homogeneous, and the septa, the thickness of the wall, and mural nodules in small RCC are not detected on unenhanced CT. Additionally, small RCC rarely displays calcification, and often displays low density. Thus, there is a high risk of misdiagnosis of small RCC as cysts.

Several studies have been performed to distinguish small renal masses between benign and malignant tumors using enhanced CT [6-10] and investigated renal masses with unenhanced CT [11-14]. However, to our knowledges, there are very few reports in the literature on the distinction of renal masses, particularly regarding small renal masses, using unenhanced CT. Therefore, the purposes of this study are to retrospectively investigate the feasibility of distinguishing small renal masses of 4 cm or less between RCC and renal cysts using CT attenuation values of unenhanced CT.

## Materials and Methods

### Patient selection

This study was approved by Ethical Review Board of the authors' institution and is compliant with Health Insurance Portability and Accountability Act (HIPAA). The requirement for informed consent was waived because of the retrospective nature of the study. To search for patients with RCC, we retrospectively reviewed the data of the medical records and diagnostic studies in our institution from March 2002, because the data of CT images were remained in the Picture Archiving and Communication Systems (PACS) from this time. The patients who had a pathologically confirmed renal malignant tumor of 4cm or less in maximum diameter and preoperative unenhanced CT series were chosen as patients with RCC. In terms of renal cysts, we retrospectively searched the data of diagnostic reporting system from October 2004, which was the time the reporting system was established at our institution. Patients with renal cysts who were enrolled in this study satisfied the following eligibility criteria:

- I. Had a tumor of 4cm or less in maximal diameter.
- II. Was diagnosed as having a cyst by unenhanced, arterial, and nephrographic CT examinations by an experienced radiologist.
- III. Fulfill the condition for class I on the Bosniak classification system.
- IV. No enhancement in arterial and nephrographic phase (except where considering technical limits [15], the lesion had a less than 10HU enhancement.
- V. No changes in diameter at the comparison CT performed 1 year or more before or after the initial CT data.

### CT technique

All CT examinations were performed with a 16-multidetector CT (MDCT) scanner (LightSpeed Ultra 16, GE Medical Systems, Milwaukee, Wisconsin) and 64-MDCT scanner (LightSpeed VCT, GE Medical Systems). The voltage was 120kVp with modulated tube currents ranging from 50 to 400mA and the noise index was set at 16. The slice thickness of the source data was a 1.25mm at non-intervals, and images were reconstructed at 5mm slice thickness at non-intervals for review. The matrix

was 512 × 512, and all images were viewed in an abdominal window (width: 300HU, level: 45HU). The same parameters were used for all phases and the scans were reconstructed in slice thickness. The unenhanced, arterial, and nephrographic phases were performed in accordance with the renal mass protocol. The contrast-enhanced images were obtained after intravenous administration of contrast material. The dose of contrast material was 1.5mL/kg body weight at a rate of 3.0mL per second to a maximum of 100mL and scan delays of 30 and 180 seconds for arterial and nephrographic phases. The density of contrast material was altered according to the body weight of the patients, as follows: < 45kg, iohexol 300 (Omnipaque 300, GE Healthcare); ≥ 45kg to 50kg, ioversol 320 (Optiray 320, FujiPharma); ≥ 50kg to 60kg, iohexol 350 (Omnipaque, Daiichi Sankyo Company); ≥ 60kg, iopamidol 370 (Iopamiron 370, Bayer Yakuhin).

### Image analysis

The unenhanced CT scans in standard PACS were reviewed for both RCC and renal cysts measuring 4cm or less in maximal diameter. Identified RCC and renal cysts were measured at the approximate center of the lesion in the 5mm transverse images, and maximum diameter of the lesion was noted. Corresponding circular or ellipsoid region of interest (ROI) measurements were obtained for each RCC and renal cysts. Attenuation values of each RCC and renal cyst were obtained using a large ROI, of at least 50% or more of the lesion, in maximum diameter. The lowest, highest, mean, and standard deviation (SD) attenuation of CT values within ROI were measured for each lesion in Hounsfield units (HU).

### Statistical analysis

The lowest, highest, mean, and SD attenuation values in HU were compared between RCC and renal cysts using the Mann-Whitney U test. To analyze the diagnostic efficacy between RCC and renal cysts, the receiver operating characteristic (ROC) curves for the lowest, highest and mean CT attenuation values were generated. The curves were analyzed to determine the cutoff CT attenuation value with the highest diagnostic accuracy for differentiating between RCC and renal cysts. Associations among the diagnostic efficacy and cutoff attenuation values were calculated using the Fisher's exact probability test. All analyses were performed with IBM SPSS Statistics 20.0 software (SPSS, Armonk, New York). P-values of less than 0.05 were considered to indicate a statistically significant difference between 2 groups.

## Results

### Patient and tumor characteristics

From March 2002 to December 2016, we identified a total of 276 consecutive patients diagnosed as RCC at Tokyo Medical University Hachioji Medical Center. Of these 276 patients, 215 were excluded because of the size of their RCC (larger than 4cm), lack of unenhanced CT, or pathological evidence. Thus,

this study was formed with the remaining 61 patients with a total of 62 pathologically proven RCC 4cm or less in maximum diameter. Thirty-nine patients were men and 22 were women. The median age of the patients was 69 years (range, 39-86 years). The median size of tumors was 2.7cm (range, 1.1-4.0 cm). The partial nephrectomy was performed for 31 tumors and the radical nephrectomy was performed for remaining 31 tumors. All 62 tumors were histologically identified, as follows: clear cell renal cell carcinoma, 49 tumors; papillary renal cell carcinoma, 4 tumors; chromophobe renal cell carcinoma, 8 tumors; and mucinous tubular and spindle cell carcinoma, 1 tumor. Regarding patients with a renal cyst, a total of 4,728 patients were diagnosed as having a renal cyst by CT examination at our institution from October 2004 to December 2016. Of these patients, 70 patients with a total of 114 renal cysts satisfied the eligibility for renal cysts in this study. Forty-seven patients were men and 23 were women. The median age of the patients was 57 years (range, 48-89 years). The median size of tumors was 1.9cm (range, 0.8-4.0cm). Patient and tumor characteristics are summarized in (Table 1).

**Table 1:** Patient and tumor characteristics.

|   | RCC           | Cyst          |
|---|---------------|---------------|
| No. of patients (tumors)                              | 61 (62)       | 70 (114)      |
| <b>Sex (percentage)</b>                               |               |               |
| Male  | 39 (64)       | 47 (67)       |
| Female  | 22 (36)       | 23 (33)       |
| Age (years), median (range)                           | 69 (39-86)    | 57 (48-89)    |
| Tumor size (cm), median (range)                       | 2.7 (1.1-4.0) | 1.9 (0.8-4.0) |
| <b>operation (percentage)</b>                         |               |               |
| Partial nephrectomy                                   | 31(50)        |               |
| Radical nephrectomy                                   | 31(50)        |               |
| <b>Pathology of renal cell carcinoma (percentage)</b> |               |               |
| Clear cell renal cell carcinoma                       | 49 (79)       |               |
| Papillary renal cell carcinoma                        | 4 (6)         |               |
| Chromophobe renal cell carcinoma                      | 8 (13)        |               |
| Mucinous tubular and spindle cell carcinoma           | 1 (2)         |               |

**Evaluation of CT values within a ROI**

The comparison of unenhanced CT attenuation values between RCC and renal cysts within the ROI is summarized in (Table 2). The median values of lowest CT attenuation for RCC and renal cysts were 1.0 HU (range, -31-25HU) and -17HU (-41-7HU), those of highest CT attenuation were 59HU (29-109HU) and 36HU (17-57HU), and those of mean CT attenuation were 30 HU (10-47HU) and 10HU (0-27HU), respectively. The differences in these values between RCC and renal cysts were statistically significant (p<0.0001). The median SD values of CT attenuation for RCC and renal cysts were 10HU (6-15HU) and 10HU (5-16HU), respectively, without a significant difference (p= 0.261). The median values of the lowest, highest and mean

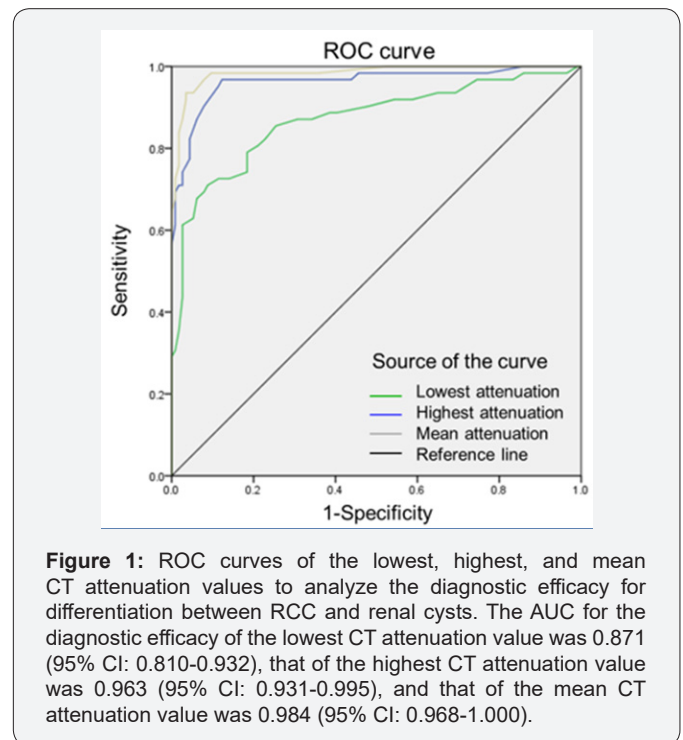
CT attenuation for RCC misdiagnosed as simple renal cysts in our institution were 2HU (-11-20HU), 57HU (49-83HU), and 34HU (23-41HU), respectively.

**Table 2:** Comparison of CT attenuation values between RCC and cyst.

| Median Value (range)   | RCC              | Cyst            | p       |
|------------------------|------------------|-----------------|---------|
| Lowest CT attenuation  | 1.0HU (-31-25HU) | -17HU (-41-7HU) | <0.0001 |
| Highest CT attenuation | 59HU(29-109HU)   | 36HU (17-57HU)  | <0.0001 |
| Mean CT attenuation    | 30HU (10-7HU)    | 10HU (0-7HU)    | <0.0001 |
| SD of CT attenuation   | 10HU (6-5HU)     | 10HU (5-6HU)    | 0.261   |

RCC: Renal Cell Carcinoma; HU:Hounsfield Units; SD:Standard Deviation.

Figure 1 shows the ROC curve of the lowest, highest, and mean CT attenuation values for the diagnostic efficacy of differentiating between RCC and renal cysts. The area under the curve (AUC) for the diagnostic efficacy of the lowest, highest, and mean CT attenuation values were 0.871 [95% confidence interval (CI): 0.810-0.932], 0.963 (95% CI: 0.931-0.995), and 0.984 (95% CI: 0.968-1.000), respectively. Among these values, the AUC of the mean CT attenuation value was the highest. Associations between the diagnostic efficacy and the cutoff value of the mean CT attenuation are summarized in (Table 3). Regarding the mean CT attenuation, sensitivities and specificities for differentiation between RCC and renal cysts with 10HU were 98% and 55%, those with 15HU were 98% and 90%, and those with 20 HU were 94% and 96%, respectively.



**Figure 1:** ROC curves of the lowest, highest, and mean CT attenuation values to analyze the diagnostic efficacy for differentiation between RCC and renal cysts. The AUC for the diagnostic efficacy of the lowest CT attenuation value was 0.871 (95% CI: 0.810-0.932), that of the highest CT attenuation value was 0.963 (95% CI: 0.931-0.995), and that of the mean CT attenuation value was 0.984 (95% CI: 0.968-1.000).

**Table 3:** Relationships among the diagnostic efficacy and the cutoff value for the mean CT attenuation.

**Table 3 (a):** The cutoff CT value, 10 HU.

| Cutoff Value        | RCC n=62 tumors | Cyst n=114 tumors | p        |
|---------------------|-----------------|-------------------|----------|
| ≤ 10 HU n=64 tumors | 1 tumor (2%)    | 63 tumors (55%)   |          |
| >10 HU n=112 tumors | 61 tumors (98%) | 51 tumors (45%)   | < 0.0001 |

**Table 3 (b):** The cutoff CT value, 15 HU.

| Cutoff value         | RCC n=62 tumors | Cyst n=114 tumors | p        |
|----------------------|-----------------|-------------------|----------|
| ≤ 15 HU n=104 tumors | 1 tumor (2%)    | 103 tumors (90%)  |          |
| > 15 HU n=72 tumors  | 61 tumors (98%) | 11 tumors (10%)   | < 0.0001 |

**Table 3 (c):** The cutoff CT value, 20HU.

| Cutoff Value         | RCC n=62 tumors | Cyst n=114 tumors | p       |
|----------------------|-----------------|-------------------|---------|
| ≤ 20 HU n=114 tumors | 4 tumors (6%)   | 110 tumors (96%)  |         |
| > 20 HU n=62 tumors  | 58 tumors (94%) | 4 tumors (4%)     | <0.0001 |

**Discussion**

In the present study, it was possible to clearly differentiate small renal masses between RCC and renal cysts using 15HU or 20HU in mean attenuation taken with unenhanced CT. The method used in this study to measure CT attenuation values is simple and reproducible. Unenhanced CT is being used more frequently to examine patients for a variety of conditions, including flank pain [16], the monitoring of urolithiasis [17], and CT colonography [18], and so forth. This has led to an increase in the incidental detection of small renal masses. As a result, there has been an increase in the need for the diagnostic differentiation of small renal masses between malignant and benign tumors by unenhanced CT. It is known that the patients with a small RCC have good prognosis and can be effectively treated by laparoscopic surgery or partial nephrectomy [19-22]. However, the prognosis worsens with progression of disease. The current 5-year survival rate is 74% overall, decreasing to 67% among patients with locoregional disease and 12% among patients with metastatic disease [23,24]. It is important to detect the RCC before advanced stages. Small renal masses with high attenuation on unenhanced CT may be diagnosed as complicated cysts and often require follow-up or additional image analyses by enhanced CT, ultrasonography, or magnetic resonance imaging (MRI). Thus, renal masses on unenhanced CT can be prevented from increasing in size, even if these lesions are malignant. However, small RCC with low attenuation on unenhanced CT is often similar to and have the risk of being misdiagnosed as simple renal cysts.

For the imaging diagnosis of renal masses, enhanced CT is considered to produce images of highest precision and is therefore recommended. Diagnoses of small RCC with enhanced

CT were reported in several studies [6-10,25-28]. Song et al. reported that a corticomedullary phase minus precontrast phase value of greater than 42HU with enhanced CT was predictive with 97.1% sensitivity and 85.7% specificity for differentiated RCC [28]. These studies in the literature reported that no other examination for diagnosing renal masses is necessary if the lesion is diagnosed as RCC by enhanced CT [27]. The differentiation of small renal masses using enhanced CT has been considered relatively straightforward. On the other hand, the management of renal masses incidentally detected with unenhanced CT is controversial [29]. A few investigators have reported the success of unenhanced CT for differentiating RCC from benign renal masses [11-14].

These studies have suggested that renal masses with mean unenhanced CT value of less than 20HU generally indicate benignity and no further examinations are required. The results of our present study were similar to that of these previously studies. However, the previous studies analyzed RCCs of all sizes, and these studies did not take the size of the tumors into consideration. Pooler et al. reported that the mean diameter and unenhanced CT attenuation values of homogeneous RCC were statistically significantly lower than those of heterogeneous RCC [11], and hence, there is the possibility that unenhanced CT attenuation values of RCC may change according to tumor size. With regard to small renal masses, it may be possible to set the mean unenhanced CT value to be used as a threshold for differentiating RCC from renal cysts not only at 20HU but also at 15HU. Our present study was not intended to establish the absolute threshold for distinguishing small renal masses between RCC and renal cysts, which would be more appropriately addressed using ultrasonography, enhanced CT, or MRI. The limitation of this study is that the possibility of selection bias with regard to prediction cannot be ruled out owing to the fact that the current study was a retrospective series. Further prospective studies are hence required to confirm our findings.

**Conclusion**

Our study indicates that it is possible to clearly differentiate small renal masses between RCC and renal cysts using a mean attenuation value of 15HU or 20HU on unenhanced CT. We recommend that small renal masses on unenhanced CT that contain areas of ROI with an attenuation value of 15HU or more should be further analyzed for accurate diagnosis.

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