INTRODUCTION

Multidetector computed tomography (MDCT) of the abdominal solid organs, including the liver and kidney, is an essential imaging modality of routine clinical practice for the diagnosis, treatment planning, and follow-up of many diseases. The diagnostic accuracy of CT examination is highly dependent on the imaging protocols and, in particular, on contrast media (CM) in...
Effects of Different Iodine Concentrations on the Characterization of Small Renal Lesions

Injection protocols, including the concentration of CM and injection speed (1-3).

With recent improvements in the temporal and spatial resolutions in MDCT, the need for a more efficient approach in the use of iodinated CM has increased (4). Several studies investigated the influence of CM with different iodine concentration on parenchymal and vascular enhancement in body imaging (1, 5-7).

Although the choice of contrast agent concentration and administration techniques are still controversial, many authors have shown that enhancement of the abdominal arteries directly correlates to the amount of iodine per second (8, 9), which is also known as the “iodine flux” (10). With greater iodine flux, the region of interest (ROI) will be higher in density. Conversely, because a lower amount of total iodine lowers the risk of contrast-induced nephropathy (11-13), CT protocols should always find a compromise between the required contrast enhancement and the amount of iodine injected (10).

Small renal masses (SRM) are usually defined by a diameter of up to 4 cm, and they constitute 48% to 66% of all newly diagnosed renal tumors and 38% of all excised renal masses (14-16). However, most incidental renal masses now detected on cross-sectional imaging are less than 2.5 cm in size (17). With increasing utilization of diagnostic imaging modalities, detection of smaller renal lesions has increased. Furthermore, the need for greater characterization of the detected small renal lesions, including contrast enhancement after the injection of CM, has increased. It has become critical for planning further treatment or evaluation. There have been several articles comparing the qualities of images derived from different iodine concentrations in the upper abdomen or renal arteries using 240, 300, or 370 mgI/mL (18, 19). However, no reports have characterized small renal lesions using these different iodine concentrations.

The purpose of this study is to compare the effects of two different iodine concentrations on the characterization of small renal lesions that are detected via MDCT and are less than 2 cm in diameter.

MATERIALS AND METHODS

Patient Population

This study was approved by the Institutional Review Board, and informed consents were obtained from each patient. Between September 2009 and February 2012, 38 patients who underwent both nephrectomy due to renal tumor and postoperative follow-up CT were enrolled in this study. Thirty-seven of 38 patients were confirmed to have renal cell carcinoma. One patient had oncocytoma. Patients consisted of 25 men and 13 women, with a mean age \[ \pm \text{standard deviation (SD)} \] of 61 \( \pm 9.5 \) years. On both the initial and follow-up CT, the small renal lesions with a maximum diameter of less than 2 cm were evaluated. These small lesions were thought to be mostly benign. Among the 38 patients, 27 patients had 43 small renal lesions in either the contralateral kidney \((n = 29)\) or the postoperatively remaining kidney \((n = 14)\). Out of 43 small renal lesions, seven lesions showed high attenuation \([> 20 \text{ Hounsfield unit (HU)}]\) on precontrast CT imaging, suggesting hemorrhagic cysts. And one high attenuation lesion showed a decreased HU value upon follow-up precontrast CT, which suggested that the hemorrhage was resolved.

Multidetector Row CT Protocol

A contrast-enhanced CT was performed using multidetector row helical CT systems (Somatom Definition, Siemens, Munich, Germany; Sensation 16, Siemens; Mx 8000, Philips Medical Systems, Best, the Netherlands; Brilliance 64, Philips Medical Systems). The CT parameters used were 120 kVp, a slice thickness of 5 mm, a rotation time of either 0.5 or 0.75 seconds, and pitches ranging from 0.89 to 1.35. The milliamperage ranged from 137 to 303 mA as a result of automatic tube current modulation. CT images were obtained with the subject in a supine position with the arms above the head in the cephalocaudal direction, imaging from the base of the lungs to the upper border of the pelvic bones.

Contrast Injection Protocol

All patients underwent CT scanning after injection of 370 mgI/mL iodinated CM (Iopamidol, Pamiray 370, DongKook Pharm. Co., Seoul, Korea) on the initial CT. Patients were then randomized into two groups. Group A \((n = 19)\) underwent a follow-up CT scan after injection of 250 mgI/mL iodinated CM (Iopamidol, Pamiray 250, DongKook Pharm. Co.), and group B \((n = 19)\) underwent a follow-up CT scan with 300 mgI/mL (Iopamidol, Pamiray 300, DongKook Pharm. Co.). In group A, 17 patients had 30 small renal lesions; and in group B, 10 patients had 13 small renal lesions (Fig. 1). The injection rate was fixed.
at 3 mL/sec, and the total amount of CM was variable according to each patient's body weight (2 cc/kg), ranging from 70 cc to 120 cc. All patients underwent biphasic contrast-enhanced CT that included unenhanced, corticomedullary phase, and excretory phase scans. Corticomedullary phase images were acquired 30–40 seconds following injection. Excretory phase images were acquired 3 minutes following injection. Due to the difficulties in renal lesion evaluation in the corticomedullary phase, the excretory phase images from 3 minutes after CM injection were evaluated. The mean time interval between the initial CT examination and second CT examination was 406.2 ± 149.4 days (range: 175–772 days).

Image Analysis

Quantitative Evaluation

Quantitative evaluation was performed by measuring the HU values of small renal lesions. Patient data was anonymized by an independent radiologist not involved in this imaging analysis. Quantitative analysis was performed by a consensus of two experienced uroradiologists (blinded S.Y.K., S.I.H.), who were blinded to the CM protocol. In all examinations, attenuation values were measured by placing circular ROIs, which were approximately 1 cm in diameter, on small renal lesions, renal parenchyma adjacent to small renal lesions, and outside the image of the patient’s body. The size of each ROI was kept smaller than that of renal lesions to avoid differential diagnostic influence of proximity to the adjacent renal parenchyma. If the diameter of the lesion was less than 1 cm, the size of the ROI was modified to 75% of the lesion's dimension. The attenuation measurements were performed three times and then averaged. HU values of the small renal lesions were compared in each group. To investigate the influence of acquisition parameters on image homogeneity attenuation values, signal to noise ratio (SNR) values for all measurements were calculated. SNR was calculated by dividing the average HU value by the SD of ROI, located outside the patient’s body (1, 20-22).

Qualitative Evaluation

Three uroradiologists (blinded S.I.H., J.Y.C., M.H.M.), who had over 20 years of experience in analyzing body CT scans and

Table 1. Mean and SD of Each Small Renal Lesions and Surrounding Tissues

<table>
<thead>
<tr>
<th></th>
<th>Group A (n = 30)</th>
<th>Group B (n = 13)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>370 mgI/mL</td>
<td>250 mgI/mL</td>
</tr>
<tr>
<td>Renal lesion HU</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>44.9</td>
<td>32.3</td>
</tr>
<tr>
<td>SD</td>
<td>26.0</td>
<td>24.4</td>
</tr>
<tr>
<td>p-value</td>
<td>0.002</td>
<td>0.552</td>
</tr>
<tr>
<td>Surrounding parenchyma HU</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>197.6</td>
<td>160.5</td>
</tr>
<tr>
<td>SD</td>
<td>29.9</td>
<td>24.8</td>
</tr>
<tr>
<td>p-value</td>
<td>&lt; 0.001</td>
<td>0.279</td>
</tr>
<tr>
<td>Signal to noise</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>34.4</td>
<td>29.0</td>
</tr>
<tr>
<td>SD</td>
<td>16.6</td>
<td>15.3</td>
</tr>
<tr>
<td>p-value</td>
<td>0.144</td>
<td>0.382</td>
</tr>
</tbody>
</table>

HU = Hounsfield unit, SD = standard deviation
who were blinded to the concentration of CM used, analyzed the qualities of the MDCT images. They were asked to evaluate the lesion’s conspicuity and diagnostic influence of the artifact’s adjacency to the renal parenchyma.

For the evaluation of lesion conspicuity phase, 43 small renal lesions from both groups were evaluated. A subjective 5-point scale was used for qualitative assessment: 1 = unacceptable, 2 = poor, 3 = fair, 4 = good, and 5 = excellent. The 5-point scale method has been widely used in the evaluation of image quality in different iodine concentrations (23, 24). The images were graded as unacceptable if the margins of the small renal lesions were indistinguishable on all images. The images with an indistinct margin between the lesion and the renal parenchyma on most images were graded as poor. Images were graded as fair if the lesion margin and renal parenchyma were present only in some images while not distinct in others. Images in which the margin of the lesion and the parenchyma were present in all of the images at the proper level were graded as good. Images were graded as excellent if the margins of the lesion and the parenchyma were definite, leading to clear and easy evaluation.

In addition, the influence of each artifact’s proximity to the adjacent renal parenchyma in differentiating between both was also evaluated in both groups. The images were graded as 1 if the lesion was influenced by the artifact from CM in the collecting system. If not, the images were graded as 0.

**Statistical Analysis**

For quantitative assessment, a paired \( t \)-test was used to compare the HU values of small renal lesions and SNR. For qualitative assessment, a Wilcoxon signed rank test was used. A \( p \)-value of less than 0.05 was considered to indicate a statistically significant difference. For evaluation of interobserver agreement, weighted kappa values and overall proportion of agreements were analyzed (25).

**RESULTS**

**Quantitative Evaluation**

Table 1 shows the mean and SD of attenuation in small renal lesions and surrounding parenchyma in both groups. The mean HU of group A and group B was 44.9 (± 26.0) and 32.6 (± 28.6), respectively, when 370 mgI/mL of CM was injected. In group A, where 250 mgI/mL of CM was used on a follow-up CT, the mean HU was 32.3 (± 24.4). The mean HU was 31.8 (± 28.1) in the follow-up CT of group B, where 300 mgI/mL of CM was used. In group A, a comparison between 370 mgI/mL and 250 mgI/mL yielded significant differences in the HUs of small renal lesions (\( p = 0.002 \)) and those of the adjacent renal parenchyma (\( p < 0.001 \)) (Fig. 2). In group B, with a comparison between 370 mgI/mL and 300 mgI/mL, there was no significant difference in the HUs of small renal lesions (\( p = 0.552 \)) and those of the adjacent renal parenchyma (\( p = 0.279 \)) (Fig. 3).

The quantitative assessment of image homogeneity, based on the comparison of SNR with different iodine concentrations, revealed that no significant statistical differences were found to be in evidence either in group A (370 mgI/mL vs. 250 mgI/mL, \( p =

![Fig. 2. Small renal lesion of a 54-year-old male patient; imaged using 370 mgI/mL (A) and 250 mgI/mL contrast medium (B).](image-url)
0.144) or in group B (370 mgI/mL vs. 300 mgI/mL, \( p = 0.382 \)).

**Qualitative Evaluation**

Table 2 shows the results of lesion conspicuity in both groups. In group A, where the concentrations of CM were 370 mgI/mL and 250 mgI/mL, readers 1 and 2 reported that there was no significant difference between images derived from 370 mgI/mL and 250 mgI/mL CM (\( p = 0.573 \) and 0.224), although reader 3 reported a significant difference (\( p = 0.032 \)) between both. In group B, where the concentrations of CM were 370 mgI/mL and 300 mgI/mL, all three readers showed no statistical differences with respect to lesion conspicuity (\( p = 0.132, 0.086, \) and 0.380, respectively).

Table 3 shows the influence of the artifact’s proximity to the adjacent parenchyma. The Wilcoxon signed rank test revealed that there was no statistical difference in the number of cases that showed an influence of the proximity of the artifact on diagnostic differentiation from the adjacent renal parenchyma (\( p < 0.05 \)). The overall proportion of agreement among three reviewers was 94.7% in group A and ranged from 78.9% to 89.5% in group B.

**DISCUSSION**

The principal factors affecting the enhancement of CM in CT

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**Table 2. Qualitative Evaluation of Lesion Conspicuity in Both Groups**

<table>
<thead>
<tr>
<th>Lesion Conspicuity</th>
<th>Group A (n = 30) (370 mgI/mL vs. 250 mgI/mL)</th>
<th>Group B (n = 13) (370 mgI/mL vs. 300 mgI/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Average Weighted Kappa (370 mgI/mL)*</td>
<td>Average Weighted Kappa (370 mgI/mL)*</td>
</tr>
<tr>
<td></td>
<td>Average Weighted Kappa (250 mgI/mL)*</td>
<td>Average Weighted Kappa (300 mgI/mL)*</td>
</tr>
<tr>
<td></td>
<td>( p )-Value</td>
<td>( p )-Value</td>
</tr>
<tr>
<td>Reader 1</td>
<td>0.573</td>
<td>0.132</td>
</tr>
<tr>
<td>Reader 2</td>
<td>0.224</td>
<td>0.086</td>
</tr>
<tr>
<td>Reader 3</td>
<td>0.032</td>
<td>0.380</td>
</tr>
</tbody>
</table>

*Average weighted kappa: average weighted kappa value for reader 1 versus 2, reader 2 versus 3, and reader 1 versus 3.

**Table 3. Influence of the Artifact to Adjacent Parenchyma**

<table>
<thead>
<tr>
<th>Group A (n = 19) (370 mgI/mL vs. 250 mgI/mL)</th>
<th>Group B (n = 19) (370 mgI/mL vs. 300 mgI/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>370 mgI/mL</td>
<td>370 mgI/mL</td>
</tr>
<tr>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>( p )-Value</td>
<td>( p )-Value</td>
</tr>
<tr>
<td>Reader 1</td>
<td>0.000</td>
</tr>
<tr>
<td>Reader 2</td>
<td>1.000</td>
</tr>
<tr>
<td>Reader 3</td>
<td>0.317</td>
</tr>
<tr>
<td>Proportion of agreements (%)</td>
<td>Proportion of agreements (%)</td>
</tr>
<tr>
<td>94.7</td>
<td>89.5</td>
</tr>
</tbody>
</table>
imaging include patients, the CT scan, and CM (26). Patient-related factors including body weight, body surface area, cardiac output, and cardiovascular circulation affect the magnitude or timing of contrast enhancement (26).

Advancements in MDCT technology have revolutionized scanning and contrast administration protocols in body imaging (23). To take full advantage of MDCT, contrast enhancement protocols and scan timing must be modified for each clinical imaging application. CT scanning parameters which critically affect the contrast enhancement include scan duration, scan direction, multiphasic acquisitions during different phases of contrast enhancement, and scan delay after CM injection.

CM injection protocols are determined by a combination of several factors, including CM volume (27-31), CM concentration, rate of injection, and type of injection (27, 32). The rationale of any injection protocol is to deliver an adequate amount of CM in order to obtain optimal parenchymal and vascular enhancement. In the liver, the parenchymal enhancement is directly dependent on the total amount of iodine injected. Thus, it is affected by the total volume of CM. It can be modulated on the basis of iodine concentration: The higher the iodine concentration, the lower the volume of injected CM (1, 5, 31). For example, to achieve optimal parenchymal enhancement of the liver (around 50–60 HU), it is necessary to deliver around 500–750 mgI per kg of body weight (1). Conversely, vascular enhancement is directly dependent on the iodine delivery rate, which is the iodine load given per unit of time (1, 5).

Intravenous CM are available commercially in a wide range of concentrations (from 240 to 370 mgI/mL). When the volume, injection rate, and duration of CM are fixed, a higher concentration CM will deliver a larger dose of iodine faster. This results in a higher magnitude of peak contrast enhancement and a wider temporal window for CT imaging at a given level of enhancement.

Recently, CM with a high iodine concentration (350 mgI/mL) have been commonly reported as being widely used with MDCT (26). This trend reflects a consensus that a high rate of iodine delivery is a desirable pairing with a fast MDCT scan to maximize arterial enhancement for CT angiography and improve depiction of hypervascular tumors (26). However, an increased concentration of iodine can exacerbate the adverse effects of contrast materials.

There are a few reports regarding the concentration of CM in evaluating either the upper abdomen, aorta, or chest (4, 19, 23). Sandstede et al. (19) compared the effectiveness of six contrast injection protocols (including iodine concentrations of 240, 300, and 370 mgI/mL) and different injection rates (ranging between 3.3 and 5 mL/sec) in evaluating the upper abdomen (including the liver, pancreas, and spleen). They concluded that there was no significant difference between each methodology (19). Rengo et al. (1) made a comparison between high concentration iodine (400 mgI/mL) and low concentration iodine (320 mgI/mL) in vascular and parenchymal CT enhancement of the liver. They concluded that the same iodine delivery rate and total iodine load did not provide statistically significant differences in liver parenchymal and vascular contrast enhancement.

There are also other reports regarding vascular enhancement evaluation with different iodine concentrations in body imaging (10, 24, 33). Loewe et al. (10) compared the diagnostic efficacy of 350 mgI/mL and 400 mgI/mL CM in the evaluation of the abdominal aorta and abdominal arteries in a prospective, randomized, double-blind, multi-center trial. They demonstrated the non-inferiority of the 350 mgI/mL versus the 400 mgI/mL iodine concentration in the evaluation of abdominal MDCT angiography.

A small renal mass corresponds to the clinical staging of a T1a renal tumor according to the American Joint Committee on Cancer—and such a tumor is generally defined as a mass within the kidney, with a maximum size of 4 cm (34, 35). With the advancement of CT technology and screening programs, incidentally-discovered renal masses currently comprise 48–66% of tumors as compared with 3–13% in the 1970s (34, 36), showing a markedly increased ratio. The evaluation of enhancement of the small renal lesion (including SRM or cysts) after CM injection is critical for the characterization of the lesion—i.e., whether the lesion needs treatment or just follow-up.

We quantitatively and qualitatively evaluated the small renal lesions of less than 2 cm in size as detected on CT images with different CM concentrations. In the quantitative evaluation, the HUs of small renal lesions imaged through usage of either 370 mgI/mL and 250 mgI/mL of iodinated CM were found to be significantly different. In contrast, the HUs of small renal lesions imaged through usage of either 370 mgI/mL or 300 mgI/mL of iodinated CM were found to be no different from each other.
Thus, when evaluating small renal lesions, the use of 300 mgI/mL instead of 370 mgI/mL iodine CM would not change the results. However, the use of 250 mgI/mL instead of 370 mgI/mL CM could reveal different results in the evaluation of small renal lesions. In qualitative evaluations regarding the conspicuity of small renal lesions, all three reviewers reported no significant difference in group B, where we compared the results of 370 mgI/mL and 300 mgI/mL CM. However, in group A, where we compared the results of 370 mgI/mL and 250 mgI/mL CM, one reviewer reported a significant difference between both. Our results suggest that a CM of 300 mgI/mL can replace 370 mgI/mL–but that a CM of 250 mgI/mL has limitations in replacing 370 mgI/mL (even though the diagnostic influence of the proximity of the artifact to the adjacent parenchyma was found to have been negligible).

The main limitation of our study is that small renal lesions we evaluated were not pathologically confirmed, although we assume that most renal lesions were benign cysts. However, regarding the most common clinical situation, our results proved to be helpful in evaluating incidentally-detected small renal lesions found in post-contrast CT study. The second limitation of our study is that the qualitative evaluation was subjective, despite the attempted quantitative evaluation by measuring the HUs of small renal lesions. However, it is also true that (as seen in other publications) subjective assessment by experienced radiologists is a common method for image quality analysis (23, 24). The third limitation is that the number of cases in each group was small. Another limitation is that we used different CT machines, which might contribute to the confounding factors in this study. These biases could not be controlled, and the comparison of enhancement is limited. Because the renal lesions are quite small, the measurement errors due to pseudoenhancement and/or the location of the renal lesions could affect the results.

In spite of these limitations, our results revealed that for the characterization of small renal lesions with less than 2 cm in diameter, 300 mgI/mL CM can be used instead of 370 mgI/mL. However, our findings also showed that the use of 250 mgI/mL CM may reveal insufficient results as compared with the better CM of 370 mgI/mL. Lastly, because the quality of enhancement of renal mass has been shown to be variable based on how much iodine is used, more detailed renal mass evaluation follow-up studies are needed to more precisely identify the amount optimal for quality renal parenchymal enhancement.

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33. Ramgren B, Björkman–Burtscher IM, Holtås S, Siemund R.
CT에서 발견된 작은 신장 병변의 분석에 있어서 조영제의 요오드 농도에 따른 효과 분석

이학종1,2,3,4 · 김상윤1,2,3,5,6 · 조정연1,2,3,5,6 · 황성일1,2,3,4 · 문민환1,2,3,7 · 김승협1,2,3,5,6*

목적: 작은 신장 병변의 CT 분석에 있어서 조영제의 요오드의 농도의 차이에 따른 효과를 분석하고자 한다.

대상과 방법: 38명의 환자를 대상으로 하여 370 mgI/mL의 요오드화 조영제를 사용하여 CT를 촬영하였다. 이후 환자들 을 두 군으로 나누어서, A군(𝑛= 19)의 경우에는 이후 추적 검사 시 250 mgI/mL를 주입하였고, B군(𝑛= 19)의 경우에는 300 mgI/mL의 조영제를 주입하였다. 각 검사에서 2 cm 이하의 신장 병변의 Hounsfield unit (이하 HU)과 신호 대 잡음 비율(signal to noise ratios; 이하 SNR)을 측정하였다. 병변의 영상성과 주위 신실질에 대한 허상의 영향 등도 평가하였다.

결과: A군의 경우, 초기와 추적 검사의 CT에서 작은 신장 병변의 HU 값은 유의한 차이를 보였지만, B군의 경우에는 큰 차이를 보이지 않았다. SNR은 두 군 모두 유의한 차이를 보이지 않았고, 인공물의 영향도 유의한 차이는 없었다.

결론: 작은 신장 병변을 평가할 때, 300 mgI/mL의 조영제는 370 mgI/mL 대신 사용될 수 있을 것으로 사료되나, 250 mgI/mL의 조영제는 370 mgI/mL 조영제 사용 때와 다른 결과를 보여줄 수 있으므로 신중하게 고려되어야 한다.

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