学位論文（博士）

Evaluation of the renal parenchymal retention of iodinated contrast agent during follow-up computed tomography performed one day after undergoing contrast-enhanced computed tomography

（造影 CT 検査の翌日に実施したフォローアップ CT 検査におけるヨード造影剤の腎貯留の評価）

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学位論文の関連論文の研究背景及び要旨

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〔研究背景〕

造影 CT は、全身の外傷性疾患、炎症性疾患および腫瘍性疾患の診断に必要不可欠な検査である。血管内に投与されたヨード造影剤は糸球体濾過によって排泄され、腎臓に有害な影響を及ぼすと考えられており、時には造影剤腎症を引き起こすこともある。ヨード造影剤が非経口的に投与された患者の翌日の単純 CT において、患者の腎臓に造影剤が貯留していることがある。このヨード造影剤の腎貯留を評価したこれまでの研究では、主に大動脈造影や肝細胞癌に対する肝動脈化学塞栓術後などの経動脈投与を受けた患者を対象としており、これらの所見が造影剤腎症（Contrast-induced nephropathy、CIN）と関連している可能性があることが報告されている。しかしながら、造影剤の腎貯留パターンおよび腎貯留の臨床的意義は完全には理解されていない。例えば、貯留パターンは先行研究で示されている以上に多様であり、一部の患者ではパターンが重複している。さらに、動脈内投与と静脈内投与では体内での貯留パターンが異なると考えられているが、静脈内投与された患者のみにフォーカスした研究はない。そこで本研究では、経静脈的投与によって造影 CT を受けた翌日のフォローアップ CT におけるヨード造影剤の腎実質への貯留の頻度とパターンを検討し、造影 CT 前後の腎機能との関連を評価した。

〔要旨〕

方法:

2012 年 4 月から 2016 年 12 月に、当院で造影 CT を施行した翌日にフォローアップ CT を施行した 120 症例を対象とした。このうち、1)画質不良(n=2)、2)フォローアップ CT より前(3 日以内)に他の検査によりヨード造影剤が投与されていた症例(n=53)、3)大動脈解離が両側の腎動脈分岐部に及んでいた症例(n=5)、4)外傷による両側腎損傷(n=1)、5)両側の急性期の水腎症(n=2)、6)フォローアップのクレアチニン値がない症例(n=2)を除外し、55 症例を最終的な今回の研究対象とした(図 1)。腎摘出後の症例は存在しなかったが、1 症例は馬蹄腎であった。

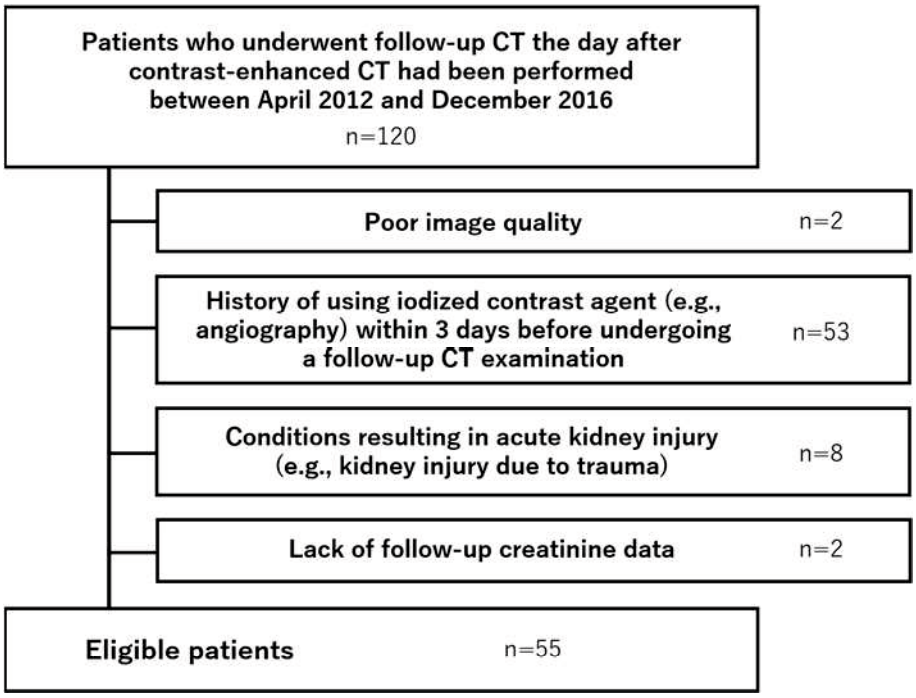

図 1　患者選択フローチャート

2 人の放射線科医が 0～6 の尺度で貯留パターンを分類した(0:貯留なし、1:びまん性実質性、2:びまん性皮質性、3:被膜下点状小結節状、4:皮質楔状、5:髄質限局性、6:腎盂)(図 2)。
パターン 1 は腸腰筋の CT 値と比較して腎実質の CT 値の比が 1 以上の場合と定義した。Region of interest(ROI)は腎門部レベルでできるだけ広く取って計測した。パターン 2-6 は視覚的評価とした。複数のパターンが認められた場合は全て評価の対象とした。

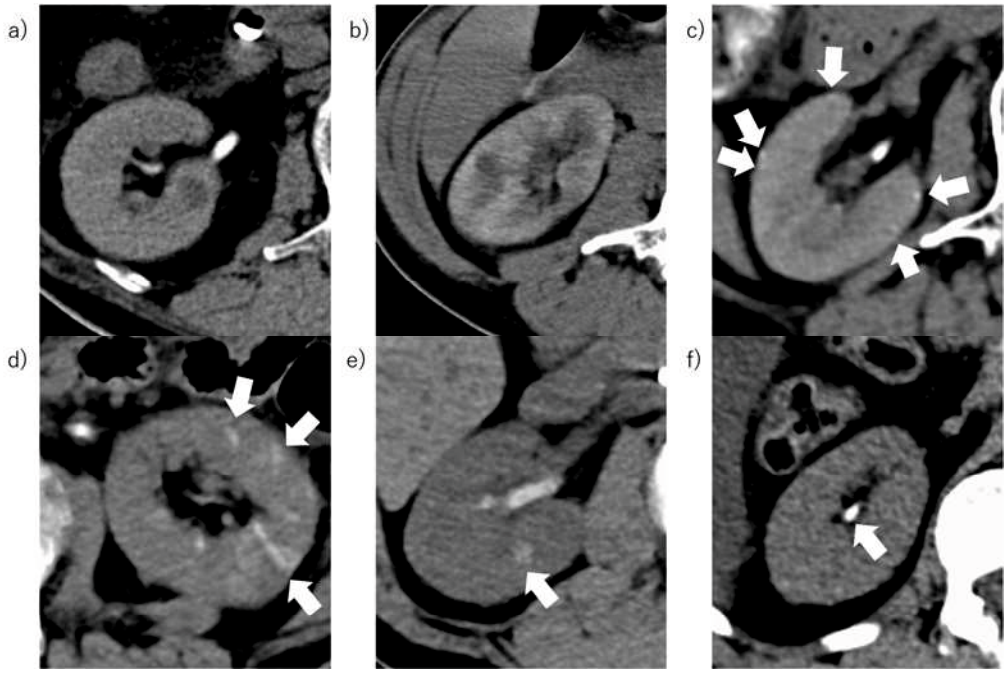

図 2　腎臓における造影剤貯留のパターン分類

a) びまん性実質性(パターン 1)。腎実質の CT 値が大腰筋よりも高値になっている。この症例ではパターン 6 も重複している。b) びまん性皮質性(パターン 2)。この症例ではパターン 1 も重複している。c) 被膜下点状小結節状(パターン 3、矢

印)。本症例ではパターン 1 も重複している。d)皮質楔状(パターン 4、矢印)。本症例ではパターン 1 も重複している。e)髄質限局性(パターン 5、矢印)。本症例はパターン 6 も重複している。f)腎盂(パターン 6、矢印)。

加えて、造影 CT 後 3 ヶ月以上後の CT が撮像されていた場合、腎の形態学的な変化や嚢胞の発生の有無も評価した。統計学的評価は 2 群間の比較に関しては Welch の t 検定を用い、カテゴリ間の比較ではカイ二乗検定や Fisher の直接確率法を用いた。
また、造影剤腎症(CIN)の発症を含む患者の臨床データを電子カルテより収集した。eGFR はクレアチニン値、体重、性別から算出した。造影剤腎症はクレアチニン値がベースラインより 25%もしくは 0.50 mg/dl 上昇した場合に診断した。
CT は 64- or 96-detector row CT scanner (SOMATOM Definition [Siemens, Forchheim, Germany] or SOMATOM Force [Siemens], Optima 660 Pro [GE Healthcare, Milwaukee, WI, USA])を用いた。画像の評価は全て 5 mm スライスの axial 画像で行った。造影 CT のプロトコールは 600 mg/I となるよう個々の患者に応じて投与量やヨード濃度、注入速度を計算して行った。

結果:
55 例中、合計 37 例(67%)で造影剤の腎貯留が認められ(貯留群), 18 例では貯留が認められなかった(非貯留群)。びまん性実質性の貯留 (パターン 1)と、腎盂の貯留(パターン 6)が最も多かった。造影 CT 前の Cre および BUN 値は、貯留群の方が非貯留群に比較して有意に高かった(それぞれ 1.26±0.22 vs. 0.70±0.04、p=0.018、20. 2±2.13 vs. 13.5±0.88、p=0.006)。AST 値と ALT 値には両群間で有意差は認められなかった。また、貯留群に対し非貯留群では CT の撮像間隔が長くなっていた(それぞれ 1244.6 ± 56.9 分 vs. 1553.1 ± 75.3 分、p = 0.002)。
CIN は 55 人中 10 人の患者で発症した。CIN の発症頻度は、非貯留群(0/18 人)よりも貯留群(10/37 人)の方が有意に高かった(p=0.021)。びまん性実質性の貯留(パターン 1)および、びまん性皮質性の貯留(パターン 2)は、CIN のある患者では、CIN のない患者に比べて有意に多かった(それぞれ p=0.003、p=0.045)。
3 ヶ月以上経過してフォローアップ CT を受けた貯留群 12 例では、造影剤の貯留は認められなかった。また、腎臓の変形や嚢胞の形成も認められなかった。

考察:
本研究では、造影 CT 翌日のフォローアップ CT での腎臓内のヨード造影剤の貯留は 67%の患者に認められた。また、造影 CT 前の血清クレアチニン値と BUN 値の上昇は腎の造影剤貯留と有意に関連していた。このことから, 造影 CT 後の造影剤の腎貯留の主な予測因子は血清 Cre 値と BUN 値の上昇であることが示唆された。
CIN の発症は臨床転帰の悪化と関連しており、造影 CT の翌日に得られた CT データを評価してハイリスク患者を特定することが重要である。我々の研究では、びまん性実質性の貯留(パターン 1)および、びまん性皮質性の貯留(パターン 2)が CIN 患者では有意に多いことが示された。逆に、CIN のある患者とない患者の間では、腎実質内の限局的な貯留(パターン 3-5)の頻度に有意な差はなく、これらのタイプの限局的な貯留は、腎障害と関連している可能性は低いと考えられた。さらに、CIN は、非貯留群(パターン 0)では発生しなかった。
ヨード造影剤の腎貯留の正確なメカニズムは完全には理解されていない。しかしながら、腎貯留はネフロ

ンを介した造影剤のゆっくりとした移行を表していると考えられている。造影剤による腎血管収縮が腎血流を遅らせるなど、ネフロンを通過する造影剤の通過時間を増加させる要因があると、より多くの造影剤が尿細管細胞内に運ばれ、虚血性傷害や尿細管損傷を引き起こす可能性がある。
本研究にはいくつかの限界がある。第一に、対象症例が比較的少なかったことである。第二に、3 種類の CT 装置を使用し、また、患者の体格に合わせてヨード濃度の異なる造影剤を使用した。第三に、1 回目と 2 回目の CT の平均撮像間隔が貯留群と非貯留群で異なっていた。更に、本研究では、eGFR を用いて腎機能を推測した。また、2 日連続で CT 検査を受けている患者の多くは、クレアチニン値の上昇を伴う重篤な全身状態であることを念頭に置いておくことが重要である。

結論:
造影 CT 前の血清 Cre 値と BUN 値の高値は翌日の腎の造影剤貯留と関連が認められた。この腎の貯留所見の中でも、特にびまん性の実質性の貯留およびびまん性皮質性の貯留パターンは、CIN 発症のバイオマーカーとなる可能性がある。

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Research article

Evaluation of the renal parenchymal retention of iodinated contrast agent during follow-up computed tomography performed one day after undergoing contrast-enhanced computed tomography

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ABSTRACT

Purpose: To examine the frequency and patterns of renal parenchymal retention of iodinated contrast agent during follow-up computed tomography (CT) performed one day after undergoing contrast-enhanced CT and to evaluate the association with the renal function before and after contrast-enhanced CT.

Materials and Methods: This retrospective study included 55 patients who underwent follow-up CT the day after contrast-enhanced CT had been performed. Two radiologists categorized the retention patterns on a scale of 0–6 (0: no retention, 1: diffuse parenchymal, 2: diffuse cortical, 3: subcapsular tiny nodular, 4: cortical wedge-shaped, 5: medullary focal, 6: renal pelvic). In addition, we collected the patients' clinical data, including the development of contrast-induced nephropathy (CIN).

Results: A total of 37 patients (67 %) showed retention of contrast agent in the kidney (retention group), while 18 did not (non-retention group). A diffuse parenchymal pattern and renal pelvis pattern were the most common. High levels of creatinine (Cre) and blood urea nitrogen (BUN) before contrast-enhanced CT were significantly associated with the retention in the kidney ($p = 0.018$, 0.006, respectively). The frequency of the development of CIN was significantly higher ($p = 0.021$) in the retention group (10/37) than in the non-retention group (0/18). A diffuse parenchymal pattern and diffuse cortical pattern were significantly more common in patients with CIN than in those without CIN ($p = 0.003$, $p = 0.045$, respectively).

Conclusion: Renal parenchymal retention of iodinated contrast agent the day after contrast-enhanced CT was a frequently recognized finding and was associated with renal dysfunction. This finding, especially diffuse parenchymal and cortical patterns, may be a potential biomarker of CIN development.

1. Introduction

Contrast-enhanced computed tomography (CE-CT) is an essential test for the diagnosis of traumatic, inflammatory and neoplastic diseases throughout the body. Iodinated contrast medium administered intravascularly is excreted by glomerular filtration, and is thought to have toxic effects on renal cells, sometimes leading to a risk of contrast-induced renal dysfunction [1]. Radiologists often see retention of contrast media in the patients' kidney when non-contrast CT is performed the day after the parenteral administration of contrast agents. Previous studies evaluating the renal retention of contrast media on CT have involved patients receiving transarterial administration, such as those after thoracic aortography or after transarterial chemoembolization (TACE) for hepatocellular carcinoma (HCC) [1–7].

Several studies have reported that these findings may be associated with contrast-induced nephropathy (CIN) [1,3,6,7]. However, the retention patterns and the clinical significance of renal retention is not fully understood. For example, retention patterns vary more than has been shown in previous studies [2,8], and some patients have overlapping patterns. Furthermore, the intra-arterial administration and intravenous administration are considered to have different retention patterns in the body [4,9,10]. Some recent studies have included groups of patients who were given intravenously at contrast CT [2,4], however, there are no studies focusing only on patients administered intravenously.

The present study therefore examined the frequency and patterns of

Abbreviations: CT, computed tomography; CIN, contrast-induced nephropathy.

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renal parenchymal retention of iodinated contrast agent during follow-up CT performed one day after undergoing contrast-enhanced CT and evaluated the association with the renal function before and after contrast-enhanced CT.

2. Materials and methods

2.1. Study population

This study project was approved by our hospital institutional review board with the waiver of written informed consent. Our hospital radiological database was searched to identify all consecutive patients who underwent follow-up CT the day after contrast-enhanced CT had been performed between April 2012 and December 2016, and 120 patients were identified. Among these, we excluded patients with 1) an image quality too poor to review (n = 2), 2) a history of using iodized contrast agent (e.g., angiography) within 3 days before undergoing a follow-up CT examination (n = 53), 3) aortic dissection extending to the bifurcation of renal arteries (n = 5), 4) bilateral kidney injury due to trauma (n = 1), 5) bilateral acute hydronephrosis (n = 2) and 6) a lack of follow-up creatinine data (n = 2). Ultimately, 55 patients with unenhanced follow-up CT obtained the day after contrast-enhanced CT (28 men, 27 women; mean age, 63.7 ± 18.2 years; age range, 15–92 years old) were included in this study (Fig. 1). Regarding the evaluation of retention, both kidneys were included, and all patients of multiple retention patterns were counted. However, in three patients (unilateral hydrated kidney due to pelvic malignancy and after previous atrophy due to one renal infarction), only the healthy kidney was evaluated. None of the patients had a post-unilateral nephrectomy, but one patient with a horseshoe kidney was included.

All clinical data, including patient demographic characteristics, such as gender, age, and body weight, and laboratory data, such as creatinine (Cre), blood urea nitrogen (BUN), alanine aminotransferase (ALT), and aspartate aminotransferase (AST), within three days before contrast-enhanced CT were extracted from our institutional electronic medical record system. In addition, the estimated glomerular filtration rate (eGFR) was calculated from the Cre, body weight, and gender data. CIN was diagnosed when the Cre levels increased by 25 % or exceeded 0.50 mg/dl within 3 days after contrast-enhanced CT [11,12]. Also, we obtained the worst BUN and Cre data within 3 days of baseline contrast CT.

No steroids or other pre-contrast CT pre-medication was administered unless there was an underlying disease and it was being administered. Regarding the status of hydration, there is no established protocol in our institute, however, the attending physician provides hydration before and after contrast-enhanced CT depending on the situation.

2.2. Imaging technique

CT studies were performed with a 64- or 96-detector row CT scanner (SOMATOM Definition [Siemens, Forchheim, Germany] or SOMATOM Force [Siemens], Optima 660 Pro [GE Healthcare, Milwaukee, WI, USA]). Unenhanced CT images were obtained in a craniocaudal direction and reconstructed every 5 mm to provide contiguous sections. For contrast-enhanced CT, 600 mg of iodine per kilogram of body weight of nonionic, iodinated contrast agents (iohexol; Omnipaque 300, Daiichi Sankyo, or iomeprol; Iomeron 300 or 350, Eisai, or iopamidol; Oypalomin 300 or 370; Fuji Pharma Co., Tokyo, Japan) was intravenously injected at 3.3–5.0 mL/s depending on the body weight of each patient, with a 30-s fixed injection duration, using a power injector (Nemoto Kyorindo Co., Tokyo, Japan). All of these contrast agents are low-osmolar contrast agents and have an osmosis and saline ratio of approximately 2:3.4. Measured osmolality is 680 mOsm/kg H2O for Omnipaque 300, 520 mOsm/kg H2O for Iomeron 300, 620 mOsm/kg H2O for Oypalomin 300 and Iomeron 350, and 800 mOsm/kg H2O for Oypalomin 370.

2.3. Imaging analyses

Unenhanced CT images obtained the day after contrast-enhanced CT were reviewed by 2 radiologists (30 and 6 years of experience) who had

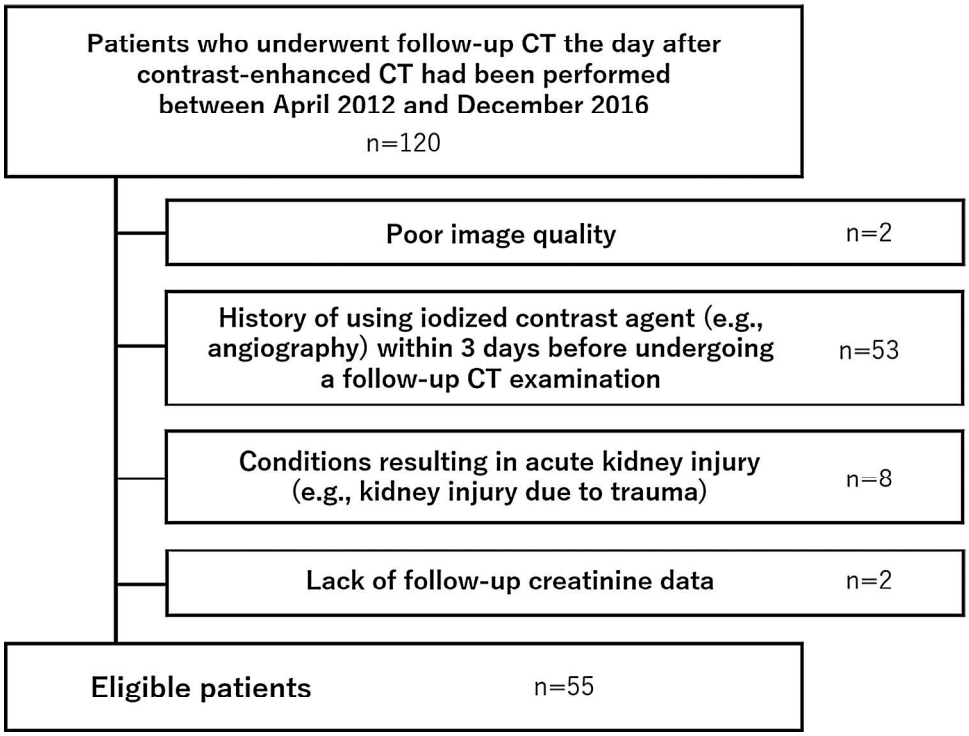

Fig. 1. The flow of selection of patients.

been blinded to the patient details and outcome data, by consensus. All of the images were investigated to categorize the retention patterns of contrast media in the kidney on a scale of 0–6 (0: no retention, 1: diffuse parenchymal, 2: diffuse cortical, 3: subcapsular tiny nodular, 4: cortical wedge-shaped, 5: medullary focal, 6: renal pelvis) (Fig. 2). Diffuse parenchymal retention (pattern 1) was defined when the renal CT attenuation value/psoas major CT attenuation value (R/P ratio) was >1.0, as the CT attenuation value of the kidney is usually lower than that of the psoas major muscle. The CT attenuation value was measured using region of interest (ROI) placement on the renal parenchyma and the psoas major muscle at the hilar level of the kidney. Other patterns (pattern 2–6) were categorized by a visual assessment. When several patterns were observed in one patient, all of them were recorded separately. In addition to this, when follow-up CT findings obtained more than three months after contrast-enhanced CT examination were available, the morphological changes in the kidney, development of small renal cysts and presence of iodine retained renal cysts were also evaluated.

Statistical testing was performed using the STATA software program (Version 15.5; StataCorp, USA). The comparison of blood sampling data, such as the Cre and BUN levels, between the two groups was carried out by Welch's *t*-test. The chi-square test and Fisher's exact test were used to compare categorical data such as gender, development of CIN. Testing was considered statistically significant with a p-value of 0.05.

3. Results

Retention of contrast agents in the kidney was observed in 37 (67 %) of 55 patients (retention group) and was not seen in 18 patients (non-retention group). The characteristics of patients with and without retention of contrast agents in the kidney are shown in Table 1. The Cre and BUN levels before contrast-enhanced CT were significantly higher in the retention group than in the non-retention group (1.26 ± 0.22 vs. 0.70 ± 0.04, $p = 0.018$, 20.2 ± 2.13 vs. 13.5 ± 0.88, $p = 0.006$, respectively). There were no significant differences in the AST or ALT levels between the two groups. CIN developed in 10 of 55 patients. The frequency of the development of CIN was significantly higher ($p = 0.021$) in the retention group (10/37 patients) than in the non-retention group (0/18 patient). The sensitivity was 1, and the specificity was 0.4. Also, the retention group had a shorter CT imaging interval (1244.6 ± 56.9 min) than the non-retention group (1553.1 ± 75.3 min) ($p = 0.002$). This difference might affect the presence of contrast retention in the renal pelvis (pattern 6) because contrast retention in the renal pelvis would be the final process of excretion.

In the retention group ($n = 37$), 9 patients had a single pattern, while 28 had a combination of 2 or more patterns. Regarding the frequency of retention patterns of contrast agent, the diffuse parenchymal pattern (25/37, 68 %) and renal pelvic pattern (25/37, 68 %) were most common, followed by the diffuse cortical pattern (13/37, 35 %). The results of the comparison of the retention patterns between patients with and without CIN development are shown in Table 2. The diffuse parenchymal pattern (pattern 1) and diffuse cortical pattern (pattern 2) were significantly more common in patients with CIN than in those without CIN (9/10 vs. 16/45; $p = 0.003$, 5/10 vs. 8/45; $p = 0.045$, respectively). Also, when comparing diffuse retention patterns (patterns 1 and 2) and other patterns (patterns 0, 3–6), there was a significant difference in the incidence of CIN ($p = 0.004$). The odds ratio for developing CIN was 14.2 (95 % confidence interval 1.71–672.3), sensitivity was 0.9, and specificity was 0.6. There were no significant differences in the frequency of localized retention (pattern 3−5) between patients with and without CIN. A comparison of patients with two or three combinations of retention patterns with other retention patterns showed no significant difference in CIN risk. No patients without retention of contrast agent (pattern 0, $n = 18$) developed CIN. Among the 10 patients who developed CIN, 6 recovered to the baseline creatinine level, while 1 retained a high level from 1 week to 1 month after contrast-enhanced CT. In the remaining 3 patients, follow-up data were not available because of death.

A total of 24 patients underwent follow-up abdominal CT after 3 months or more. Among these, 14 patients had been included in the retention group. None of these 14 showed the sustained retention of contrast agent on follow-up CT. In addition, no morphological changes in the kidney were observed, such as deformity at the site of the retention of contrast agent. The development of small renal cysts related to the retention of contrast agent was not found.

4. Discussion

In this study, retention of iodinated contrast agents in the kidney at follow-up CT obtained the day after contrast-enhanced CT was a common finding, being seen in 67 % of the patients. In addition, increased serum creatinine and BUN levels before contrast-enhanced CT were significantly associated with renal retention. This suggests that elevated serum creatinine and BUN levels are the primary predictors of renal retention of contrast agents on post-contrast CT. Furthermore, our study showed that the frequency of developing CIN in the retention group was significantly higher than in the non-retention group, suggesting that renal retention of contrast agents with increased serum creatinine and BUN levels can be a risk factor for the development of CIN.

Regarding the retention patterns, one of the most frequent pattern of retention was the diffuse parenchymal pattern, which was the same result as in previous studies [2,4]. However, among the 37 patients in the retention group, there were 28 patients (76 %) who had a combination of 2 or more patterns.

The development of CIN is associated with worsened clinical outcomes [12], so it is essential to identify high-risk patients by evaluating the CT data obtained the day after contrast-enhanced CT. Our study showed that diffuse parenchymal and diffuse cortical patterns (patterns 1–2) were significantly more common in patients with CIN than in those without CIN, suggesting that the diffuse parenchymal and/or cortical renal retention of contrast agents with increased Cre and/or BUN is likely to predispose patients to CIN and may be considered a prognostic factor of a worsened renal function. Conversely, the frequency of localized retention (patterns 3−5) between patients with and without CIN was not significantly different. Therefore, these types (patterns 3−5) of localized retention are unlikely to be associated with renal injury. In addition, CIN did not occur in the patients with no retention (pattern 0).

The precise mechanism underlying the renal retention of iodinated contrast agents is not fully understood. However, renal retention is thought to represent the slow transition of contrast agents through the nephron [13,14]. Contrast-induced renal vasoconstriction slowing the renal blood flow or other factors that increase the transit time of contrast material through the nephrons may result in a higher amount of contrast agents being transported into the tubular cell, causing ischemic injury and tubular damages [12,13,15].

In the 12 patients in the retention group who received follow-up CT after 3 months or more, the sustained retention of contrast agent was not observed. In addition, neither the deformity of the kidney nor the formation of a cyst related to the renal retention of contrast agents was found. These results suggest that renal retention of contrast agents may have little long-term influence on the renal parenchymal damage, so acute renal injury should be monitored in patients with renal retention of iodinated contrast agents after contrast-enhanced CT.

Several limitations associated with the present study warrant mention. First, the study population was relatively small. Therefore, the results obtained in this study need to be confirmed in large series. Second, we used three types of CT devices because of issues of clinical availability; however, the imaging techniques as well as the injection methods of contrast agents were based on our routine protocols. Additionally, we included three different types of contrast agents. Iodixanol, which has been previously shown to have a high retention rate [16,17],

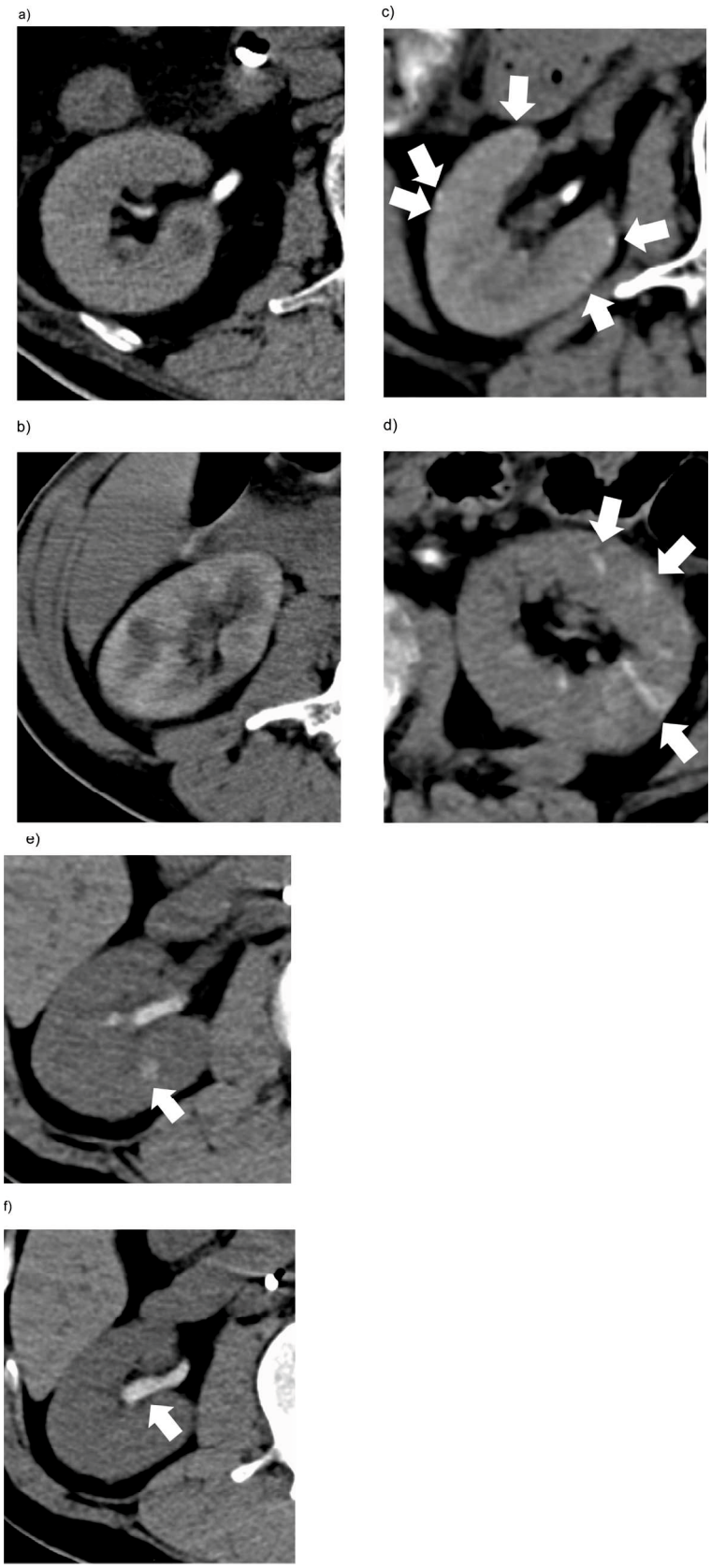

Fig. 2. Categorization of retention of iodinated contrast agent in the kidney.
a) Diffuse parenchymal retention (pattern 1). CT attenuation of the kidney is higher than that of the psoas major muscle. The patient also showed pattern 6 (renal pelvis). b) Diffuse cortical retention (pattern 2). CT attenuation of the renal cortex is higher than that of the renal medulla. c) Subcapsular tiny nodular retention (pattern 3) (arrows). The patient also showed pattern 1 (diffuse parenchymal). d) Cortical wedge-shaped retention (pattern 4) (arrows). e) Medullary focal retention (pattern 5) (arrow). The patient also showed pattern 6 (renal pelvis). f) Renal pelvis retention (pattern 6) (arrow).

Table 1
Characteristics of patients with and without retention of contrast agents in the kidney.

	Non-retention group (n = 18)	Retention group (n = 37)	p-value
age	59.94 ± 5.14	65.65 ± 2.67	0.33
female (%)	10 (56)	18 (49)	0.63
body weight	51.5 ± 4.54	50.7 ± 2.49	0.87
Baseline Clinical Data			
Serum creatinine (mg/dl)	0.70 ± 0.04	1.26 ± 0.22	0.018
BUN (mg/dl)	13.5 ± 0.88	20.2 ± 2.13	0.006
eGFR (ml/min/1.73m2)	84.8 ± 7.05	68.8 ± 7.50	0.13
AST (IU/L)	82.2 ± 41.1	83.3 ± 21.0	0.98
ALT (IU/L)	73.4 ± 33.8	55.9 ± 9.82	0.62
Development of CIN (%)	0 (0)	10 (27)	0.021
time interval from the baseline contrast CT study (minute)	1553.1 ± 75.3	1244.6 ± 56.9	0.002
Post contrast Clinical Data			
Serum creatinine (mg/dl)	0.71 ± 0.04	1.45 ± 0.25	0.006
BUN (mg/dl)	14.6 ± 1.93	24.9 ± 2.94	0.005

Table 2
Patterns of retention of patients who developed CIN or without CIN.

	without CIN (n = 45)	with CIN (n = 10)	p-value
Pattern 0: no retention	18	0	0.021
Pattern 1: diffuse parenchymal	16	9	0.003
Pattern 2: diffuse cortical	8	5	0.045
Pattern 3: subcapsular tiny nodular	6	0	0.58
Pattern 4: cortical wedge-shaped	8	3	0.40
Pattern 5: medullary focal	6	0	0.58
Pattern 6: renal pelvis	19	6	0.48
Combination of two or more patterns	21	7	0.30
Combination of three or more patterns	12	5	0.25
Pattern 1 + 2 (diffuse)	17	9	0.004
Pattern 3–5 (localized retention within the renal parenchyma)	15	3	1.00

was not included in this study. However, more data need to be accumulated regarding the retention patterns according to the different types of contrast medium. Third, the mean interval between the first and second CT was different between the retention and non-retention groups. Although this fact might affect the presence of contrast retention in the renal pelvis (pattern 6), the validity of the results of this study regarding the occurrence of CIN will not be reduced. Finally, in this study, renal function was evaluated by using the eGFR. However, the eGFR may not have accurately reflected renal function because it is affected by several factors such as patients' habitus and nourishment. For the precise evaluation, the renal function should have been based on the inulin clearance measurement, which is a more accurate index than the Cre, BUN, and eGFR levels. However, it is not practical to measure the inulin levels in critically ill patients before and after CT. Therefore, in most cases, the renal function was estimated based on the serum creatinine level assessed when medical intervention was performed. The CIN evaluation criteria also depended on the serum creatinine level. However, it is important to keep in mind the fact that many patients undergoing daily contrast-enhanced CT have a serious general condition associated with increased creatinine levels even without the administration of contrast agents [9].

In conclusion, the renal parenchymal retention of iodinated contrast agent the day after contrast-enhanced CT was a frequently recognized finding and shown to be associated with renal dysfunction. This finding, especially the diffuse parenchymal and cortical patterns, may be a useful biomarker of CIN development.

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Shoko Ariyoshi: Conceptualization, Methodology, Investigation, Software, Writing - original draft. **Masahiro Tanabe:** Project administration, Software. **Katsuyoshi Ito:** Investigation, Writing - review & editing, Supervision.

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