学位論文（博士）

Longitudinal changes in renal volumes evaluated by automated three-dimensional volumetric computed tomography of the whole kidney: The association with the renal function and disease progression.

（CTによる自動3次元容積測定により評価された腎容積の長期的変化の評価と腎機能･腎臓病の増悪との関連の検討）

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令和5年12月

学位論文の関連論文の研究背景及び要旨

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〔題名〕

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（CT による自動 3 次元容積測定を利用した腎容積の長期的変化の評価と腎機能・腎臓病の増悪との関連の検討）

European Journal of Radiology 2023　doi: 10.1016/j.ejrad.2023.111245

〔研究背景〕

腎実質容積の変化は、腎疾患の病因と密接に関連しており、重要な指標と考えられている。腎容積の減少は、慢性腎臓病や腎動脈狭窄のある患者で起こりうる。早期の糖尿病患者では、腎腫大は腎不全の危険因子であり、進行とともに腎容積は減少し、最終的には糖尿病性腎不全に至る。したがって、正確で再現性の高い腎容積の画像評価法は、疾患の早期診断、疾患の増悪のモニタリング、治療効果判定など、腎疾患の評価において臨床的に重要である。

これまでの研究で、超音波検査（US）が腎臓容積測定に有効なモダリティであることが示されている。しかし、腎臓の形状のばらつきが考慮されておらず、以前の研究では腎容積の過小評価が報告されている。一方で、コンピュータ断層撮影（CT）による腎臓全体の容積測定の有用性を示した研究もあり、腎臓の輪郭を手作業でトレースし、各スライスの面積の合計に再構成間隔を乗じて容積を算出する方法が報告されている。しかし、この方法では腎臓をトレースするのに時間がかかり、オペレータ間のばらつきが生じるとされる。また、この手法で計測された腎容積と腎機能の関係についても検討されており、腎容積の減少は腎機能の低下と関連していることが示唆されている。

最近、腎臓全体の容積測定を含む腹部臓器の CT 容積測定のための自動セグメンテーション法が開発され、検証されている。これらの研究では生体腎摘出術を受けた患者について検討し、3 次元 CT ボリュームメトリーによる腎臓の計測が術後のドナー腎機能の予測に有効であることが示された。しかし、自動 3 次元 CT 容積計測法を用いて評価された腎容積の経時的変化と腎機能との関係については十分に検討されていない。

本研究では、両腎の自動 3 次元容積計測を用いて、腎機能の変化に伴う両腎容積の経時的変化を評価し、慢性腎臓病（CKD）のグレード増悪予測に対する CT による腎容積計測の有用性を検討した。

〔要旨〕

方法 当院において2017年1月1日から2021年12月31日の間に腹部CTを受けた患者を検索した。最終的に、この期間に2回以上の腹部CT検査を受け初回CTと最終CTの間隔が4年以上あった患者のうち、961人の患者を評価した。それぞれの症例について、初回、最終CT撮影日から直近の血液検査データを調査し、血清クレアチニン、eGFR、尿素窒素、グルコース、コレステロールのデータを収集した。

CT 画像はすべてマルチスライス CT 装置(Somatom Force, or Somatom Sensation, Siemens, Erlangen, Germany; Optima CT660, GE Healthcare, Milwaukee, WI, USA; Aquilion Precision; Canon Medical Systems, Otawara, Japan)を使用し、通常の腹骨盤部撮影のプロトコルで撮影された。腎臓の自動容積測定は、Volume Analyzer SYNAPSE VINCENT image analysis system (Fujifilm Medical, Tokyo, Japan)を用いて、初回腎容積と最終腎容積について評価された。

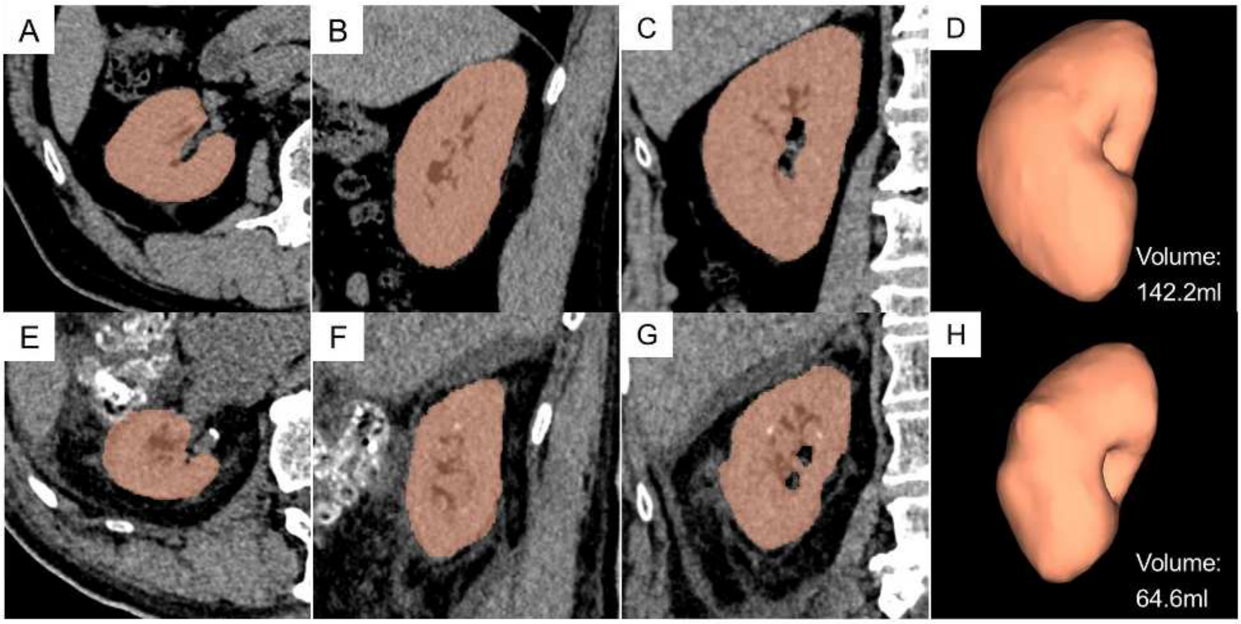

図1 Volume Analyzer SYNAPSE VINCENT image analysis systemによる右腎容積測定の一例
初回CT（A; 体軸断, B; 矢状断, C; 冠状断, D; 3D像, 右腎容積142.2ml）
最終CT（E; 体軸断, F; 矢状断, G; 冠状断, H; 3D像, 右腎容積64.6ml）

結果 全腎の自動3次元容積計測が961例すべてで実施された。初回CTにおいて、両腎容積（267.3±58.6ml）はeGFR（70.9±17.0ml/min/1.73m2、r＝0.490、p＜0.001）と正の相関を示した（表1）。一方、初回CT時の両腎容積は、血中尿素窒素値（15.3±7.1mg/dL、r＝-0.188）、クレアチニン値（0.80±0.52mg/dL、r＝-0.111）、グルコース値（108.6±27.8mg/dL、r＝0.137）、コレステロール値（200.9±39.4mg/dL、r＝-0.128）とは相関を示さなかった。

Parameter	Value	Spearman correlation coefficient (*r*)	*p* value
Blood urea nitrogen (mg/dL)	15.3 ± 7.1	-0.188	< 0.001
Creatinine (mg/dL)	0.80 ± 0.52	-0.111	< 0.001
eGFR (ml/min/1.73 ㎡)	70.9 ± 17.0	0.490	< 0.001
Glucose (mg/dL)	108.6 ± 27.8	0.137	< 0.001
Cholesterol (mg/dL)	200.9 ± 39.4	-0.128	< 0.001

Values are means ± standard deviations.

表 1. 初回両腎容積と血液検査結果の相関

初回 CT における腎容積の左右差については、左腎容積が右腎容積よりも有意に大きかった（136.7±31.2ml vs. 130.6±28.8ml、p＜0.001）。
CKD グレード間の腎容積の比較では、初回両腎容積は CKD グレード分類間で有意に異なっていた（G1 318.7 ± 60.5 ml、G2 275.5 ± 53.5 ml、G3 233.7 ± 46.9 ml、G4 183.2 ± 22.5 ml、G5 157.7 ± 77.4 ml、p < 0.001）（表 2）。

CKD grade category	No. of Patients	Initial total renal volume (ml)
G1	100	318.7 ± 60.5
G2	637	275.5 ± 53.5
G3	215	233.7 ± 46.9
G4	6	183.2 ± 22.5
G5	3	157.7 ± 77.4

Data are means ± standard deviations.

表 2 CKD グレード間での両腎体積の比較

初回 CT 時の CKD グレード G2 群（n＝637）では、追跡期間中に 142 例が G3-G5 に増悪し（増悪群）、495 例は増悪しなかった（非増悪群）。CKD G2 の増悪群と非増悪群を比較すると、初回 CT 検査時の両腎容積は、非増悪群よりも増悪群で有意に小さかった（252.4±50.6ml vs. 278.9±53.7ml、p＜0.001）（表 3）。また、右腎、左腎ともに年間減少量は増悪群で非増悪群より有意に大きかった（右腎：2.21±3.39ml vs. 0.66±2.49ml、p＜0.001、左腎：2.59±3.67 vs. 0.99±2.86ml、p＜0.001）（表 3）。

Parameter	**Progression group (n = 142)**	**Non-progression group (n = 495)**	***p* value**
Initial total renal volume (ml)	252.4 ± 50.6	278.9 ± 53.7	< 0.001
Annual reduction volume in both kidneys (ml)	4.8 ± 6.77	1.65 ± 4.92	< 0.001
Initial right renal volume (ml)	123.7 ± 25.8	136.2 ± 26.6	< 0.001
Annual reduction volume in the right kidney (ml)	2.21 ± 3.39	0.66 ± 2.49	< 0.001
Initial left renal volume (ml)	128.7 ± 27.5	142.7 ± 29.1	< 0.001
Annual reduction volume in the left kidney (ml)	2.59 ± 3.67	0.99 ± 2.86	< 0.001

Data are means ± standard deviations.

表 3 CKD G2 内での増悪群と非増悪群の比較

CKD G2 の増悪・非増悪群ともに、左腎の年間減少量は右腎より有意に大きかった（増悪群 : 2.59±3.67ml vs. 2.21±3.39ml、p＜0.001、非増悪群 : 0.99±2.86ml vs. 0.99±2.86ml）： 0 .99 ± 2.86 vs 0.66 ± 2.49 ml、p < 0.001）。
CKD G2 群における臨床的予後の予測に関しては、初回 CT における両腎容積のカットオフ値 227.5ml は、腎機能低下を予測する感度 35.9%、特異度 80.0%であった。

考察 本研究により、初回 CT 検査時に自動 3 次元容積計測で測定した両腎容積は、eGFR と正の相関があり、CKD グレードに応じて有意に減少することが示された。これらの所見は、自動 3D 容積測定 CT で測定された両腎容積が腎障害の程度を反映し、腎機能の指標として使用できる可能性を示唆している。
本研究では、CKD G2 患者の初回 CT 検査において、増悪群の両腎容積は非増悪群よりも有意に小さかった。本研究で示された G2 患者の初回腎容積の臨床予後を判定するためのカットオフ値は高い感度を有するものではなかったものの、腎機能低下が軽度な G2 患者においても腎サイズが小さいことは臨床経過観察中の腎機能悪化を示唆する重要な早期所見である可能性が示唆された。また、両腎の年間減少量は増悪群で非増悪群より有意に大きかったことから、経時的な腎量の減少は CKD の増悪を予測する指標として利用でき、臨床経過観察中は年間減少量に注目することが重要であることが示唆された。初期腎容積と年間腎容積減少量の複合評価が予後予測の

改善に寄与する可能性がある。

本研究の結果は、自動 3D 容積測定 CT によって測定された腎容積の経時的変化と CKD の増悪との関係について新たな知見を提供するものであり、これらの関係性を理解するのに重要な所見と思われる。

結論 全腎容積の CT による自動容積測定は、腎機能の変化に伴う経時的な腎容積の変化を反映している可能性があり、長期的にみて CKD のグレードが増悪するリスクの高い患者を予測するのに役立つ可能性がある。

European Journal of Radiology 170 (2024) 111245

Contents lists available at ScienceDirect

European Journal of Radiology

journal homepage: www.elsevier.com/locate/ejrad

Longitudinal changes in renal volumes evaluated by automated three-dimensional volumetric computed tomography of the whole kidney: The association with the renal function and disease progression

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ARTICLE INFO

Keywords:
Kidney
Multidetector computed tomography
Imaging
Three-dimensional
Renal insufficiency
Chronic

ABSTRACT

Purpose: To clarify the changes in the total renal volume over time with changes of the renal function using automated 3D volumetric CT of the whole kidney and to evaluate the usefulness of the total renal volume CT measurement in predicting chronic kidney disease (CKD) grade progression.

Methods: A total of 961 patients who underwent abdominal CT at least twice (an interval of more than 4 years) were included. The automated 3D volumetric CT measurement of the whole kidney was performed at the initial and latest CT examination. Patients with CKD grade G2 at the time of the initial CT were divided into two groups: a progression group (CKD grade progressed to G3-G5) and a non-progression group. Changes in the renal volume over time were compared between the two groups.

Results: The volume of both kidneys measured on initial CT was positively correlated with eGFR ($\rho = 0.490$, $p < 0.001$). There was a significant difference in the initial volume of both kidneys among CKD grades ($p < 0.001$, G1:318.7 ± 60.5 ml, G2:275.5 ± 53.5 ml, G3:233.7 ± 46.9 ml, G4:183.2 ± 22.5 ml, G5:157.7 ± 77.4 ml). When comparing the progression and non-progression groups, the initial volume of both kidneys was significantly smaller in the progression group, compared with the non-progression group (252.0 ± 50.6 ml vs. 278.9 ± 53.7 ml). In addition, the annual reduction volume in both the right and left kidneys was significantly greater in the progression group than in the non-progression group ($p < 0.001$).

Conclusion: The automated 3D volumetric CT measurement of the whole kidney has the potential to monitor changes in renal volume over time with changes of the renal function.

1. Introduction

Alterations in the renal parenchymal volume are closely related to the pathogenesis of renal disease and are considered important clinical indicators [1]. A reduction in renal volume can occur in patients with chronic kidney disease or renal artery stenosis. In patients with early-stage diabetes, renal enlargement is a risk factor for nephropathy, with the volume declining during the course of the disease and eventually leading to diabetic renal insufficiency [2]. Therefore, accurate and reproducible imaging methods for assessing the renal volume are clinically important for evaluating renal diseases, including an early-stage diagnosis of the disease, monitoring of disease progression, and effectiveness of therapies.

Previous studies have shown that ultrasonography (US) is the modality of choice for measuring renal size [3]. Kidney length has traditionally been measured because of its convenience, although it cannot appropriately represent the renal volume. Volume measurement of the kidney calculated by applying the dimensions of the three orthogonal axes to the ellipsoid formula is an alternative method [4,5]. However, this method does not consider the variability in the shape of kidneys, and a previous study reported a substantial systematic underestimation (25%) of the renal volume [6]. In contrast, some studies have demonstrated the utility of computed tomography (CT) volumetry of the whole kidney, in which the renal contours were manually traced in contiguous axial CT images with 1- to 2.5-mm slice thickness, and the volume was calculated by multiplying the sum of areas from each slice by the reconstruction interval [7,8]. The relationship between the renal volume and function has been investigated in a limited number of

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https://doi.org/10.1016/j.ejrad.2023.111245
Received 3 October 2023; Received in revised form 20 November 2023; Accepted 27 November 2023

patients [7], suggesting that a reduced renal volume is associated with an impaired renal function. However, this method requires time to trace the kidney, leading to interoperator variability.

Recently, an automated segmentation method was developed and validated for CT volumetry of abdominal organs, including volume measurements of the whole kidney [9,10]. These studies investigated patients who underwent living donor nephrectomy and demonstrated that measuring the kidney using CT volumetry is effective in predicting the postoperative donor renal function. However, the relationship between longitudinal changes in the renal volume evaluated using automated three-dimensional (3D) CT volumetry and the renal function has not been fully investigated.

In the present study, we assessed the changes in the total renal volume over time with the change of the renal function using automated 3D volumetric CT measurements of the whole kidney and evaluated the usefulness of the total renal volume CT measurement for predicting chronic kidney disease (CKD) grade progression.

2. Materials and methods

2.1. Study population

This retrospective study was approved by our Institutional Review Board, and the requirement for written informed consent was waived.

Using our radiology database system, patients undergoing abdominal CT between January 1, 2017, and December 31, 2021, were retrieved. Ultimately, 1611 patients had undergone at least 2 abdominal CT scans during this period, with an interval of at least 4 years between the initial and latest CT. We excluded the following patients: post-renal surgery (n = 106), post-renal transplantation (n = 4), post-radiotherapy (n = 2), renal tumor (n = 6), ureteral tumor (n = 8), renal cyst that protruded beyond the outer edge of the kidney (n = 206), polycystic kidney disease (n = 4), horseshoe kidney (n = 2), hydronephrosis (n = 29), ureterolithiasis (n = 7), renal infarction (n = 1), insufficient scan coverage of the kidney (n = 1), and severe metallic artifacts (n = 1). We also excluded patients who did not undergo blood tests, including the estimated glomerular filtration rate (eGFR) measurement, within 1 month before or after the date of the initial and latest CT scans (n = 273). After these exclusions, the remaining 961 patients were evaluated (Fig. 1).

The study patients consisted of 487 men and 474 women (mean age, 65.0 ± 11.2 [range, 32–84] years old). The interval between the initial and latest CT for these patients was 4.39 ± 0.27 (range 4.00–4.98) years. For each case, the blood laboratory data closest to the date of the initial and latest CT scans were examined, and data on the serum creatinine, eGFR, and blood urea nitrogen (BUN), glucose, and cholesterol values were collected because they are considered parameters related to changes in renal function and renal volume.

2.2. *CT technique*

Multidetector CT scans were performed at a single center using scanners from multiple vendors (Somatom Force or Somatom Sensation; Siemens, Erlangen, Germany; Optima CT660, GE Healthcare, Milwaukee, WI, USA; Aquilion Precision; Canon Medical Systems, Otawara, Japan). The imaging parameters were as follows: tube voltage of 100–110 kVp for the Somatom Force and 120 kVp for the others with modulated tube current, matrix size of 512 × 512, and reconstruction interval of 1.0–1.25 mm. Unenhanced CT scans were obtained for all patients and used for data analyses.

2.3. Imaging analyses

Automated 3D volumetric CT measurements of the kidney were performed on unenhanced CT using a volume analyzer software program (SYNAPSE VINCENT; Fujifilm Corporation, Tokyo, Japan) on the workstation by one radiologist (M.T., twenty years of experience in body imaging) without access to any clinical information. Using this automated segmentation program, the contours of both the right and left kidneys were automatically outlined in all 1-mm slices of unenhanced CT images, and the segmented renal area was automatically summed to calculate the right and left renal volumes (Fig. 2). The segmentation error of the kidney was manually modified if correction was necessary. Renal volumes were evaluated for the initial and latest CT scans. The total renal volumes on the initial CT findings correlated with the blood laboratory data, and then they were compared among the various CKD grade categories. Additionally, the annual reduction volume of the kidney was calculated using the renal volumes of the initial CT and the latest CT findings.

2.4. Statistical **analyses**

All statistical analyses were performed using the IBM SPSS software program (v. 27; Armonk, NY, USA). The relationships between the initial and latest kidney volumes and the age, height, weight, body mass index (BMI), serum creatinine, eGFR, BUN, glucose, and cholesterol values were evaluated using Spearman's rank correlation coefficient. The Kruskal-Wallis test was used to compare the initial and latest renal

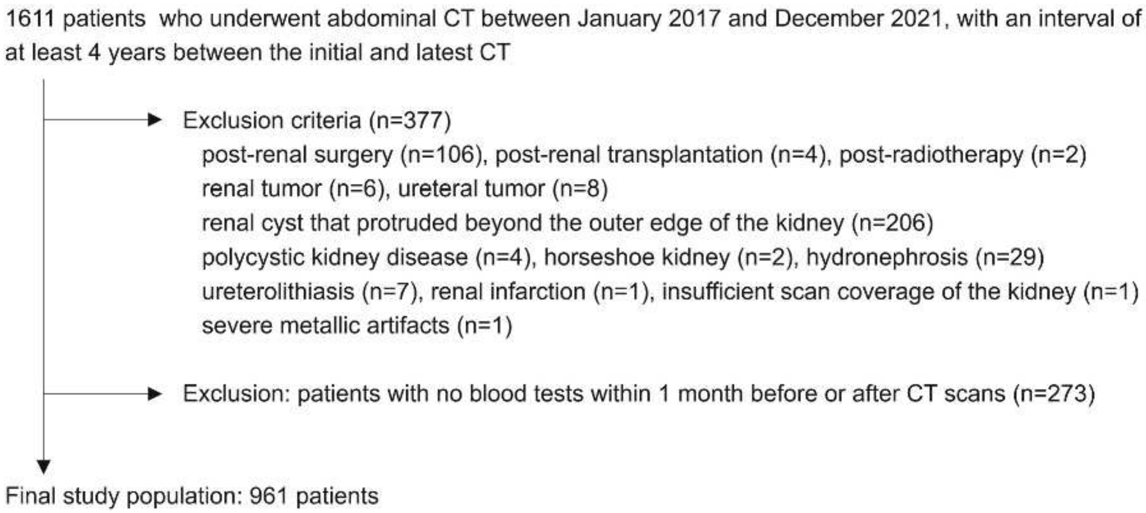

Fig. 1. Flowchart of patient selection.

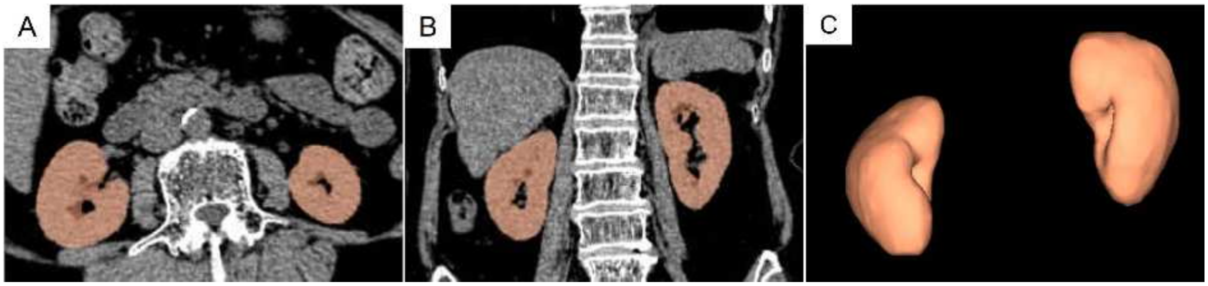

Fig. 2. Automated 3D volumetric CT measurement of the whole kidney (A; axial image, B; coronal image, C; 3D image).

volumes among the CKD grades. For patients with CKD grade G2 at the time of initial CT, comparisons were made using the Mann-Whitney *U* test for initial total renal volumes and the annual reduction volume in both the right and left kidneys between the progression and non-progression groups. In addition, receiver operating characteristic (ROC) curves were created and examined to determine the cutoff value for predicting the progression group.

3. Results

Automated 3D volumetric CT measurements of the whole kidney were successfully performed in all 961 patients. On initial CT, the total renal volumes (267.3 ± 58.6 ml) were positively correlated with the eGFR (70.9 ± 17.0 ml/min/1.73 m^2, $r = 0.490$, $p < 0.001$) (Table 1). In contrast, the total renal volumes at initial CT showed no correlation with the blood urea nitrogen (15.3 ± 7.1 mg/dL, $r =$ -0.188), creatinine (0.80 ± 0.52 mg/dL, $r =$ -0.111), glucose (108.6 ± 27.8 mg/dL, $r = 0.137$) or cholesterol (200.9 ± 39.4 mg/dL, $r =$ -0.128) levels.

Regarding the left–right difference in the renal volume on initial CT, the left renal volume was predominantly larger than the right renal volume (136.7 ± 31.2 ml vs. 130.6 ± 28.8 ml, $p < 0.001$).

In the comparison of renal volumes among CKD grade categories, initial total renal volumes were significantly different among CKD grade categories (G1 318.7 ± 60.5 ml, G2 275.5 ± 53.5 ml, G3 233.7 ± 46.9 ml, G4 183.2 ± 22.5 ml, G5 157.7 ± 77.4 ml, $p < 0.001$) (Table 2). In the CKD grade G2 group (n = 637) at the initial CT, 142 patients progressed to G3-G5 during follow-up (progression group), and 495 patients did not progress (non-progression group). Comparing the progression and non-progression groups for CKD G2, the total renal volumes were significantly smaller in the progression group than in the non-progression group at the initial CT examination (252.4 ± 50.6 vs. 278.9 ± 53.7 ml, $p < 0.001$) (Table 3). In addition, the annual reduction volume in both the right and left kidneys was significantly greater in the progression group than in the non-progression group (right kidney: 2.21 ± 3.39 ml vs. 0.66 ± 2.49 ml, $p < 0.001$, left kidney: 2.59 ± 3.67 vs. 0.99 ± 2.86 ml, $p < 0.001$) (Table 3) (Fig. 3).

In both the progression and non-progression groups with CKD G2, the annual reduction volume of the left kidney was significantly greater than that of the right kidney (progression group: 2.59 ± 3.67 vs. 2.21 ± 3.39 ml, $p < 0.001$, non-progression group: 0 0.99 ± 2.86 vs 0.66 ± 2.49 ml, $p < 0.001$).

Regarding the prediction of the clinical prognosis in the CKD G2 group, a cutoff value of 227.5 ml for the total renal volume on initial CT had a sensitivity of 35.9% and specificity of 80.0% for predicting the reduction in the renal function.

Table 1
Correlation between initial total renal volumes and blood tests.

Parameter	Value	Spearman correlation coefficient (*r*)	*p* value
Blood urea nitrogen (mg/dL)	15.3 ± 7.1	−0.188	<0.001
Creatinine (mg/dL)	0.80 ± 0.52	−0.111	<0.001
eGFR (ml/min/1.73m^2)	70.9 ± 17.0	0.490	<0.001
Glucose (mg/dL)	108.6 ± 27.8	0.137	<0.001
Cholesterol (mg/dL)	200.9 ± 39.4	−0.128	<0.001

Values are means ± standard deviations.

Table 2
Comparison of initial total renal volumes among CKD grade categories.

CKD grade category	No. of Patients	Initial total renal volume (ml)
G1	100	318.7 ± 60.5
G2	637	275.5 ± 53.5
G3	215	233.7 ± 46.9
G4	6	183.2 ± 22.5
G5	3	157.7 ± 77.4

Data are means ± standard deviations.

Table 3
Comparison between the progression and non-progression groups for CKD G2.

Parameter	Progression group (n = 142)	Non-progression group (n = 495)	*p* value
Initial total renal volume (ml)	252.4 ± 50.6	278.9 ± 53.7	<0.001
Annual reduction volume in both kidneys (ml)	4.8 ± 6.77	1.65 ± 4.92	<0.001
Initial right renal volume (ml)	123.7 ± 25.8	136.2 ± 26.6	<0.001
Annual reduction volume in the right kidney (ml)	2.21 ± 3.39	0.66 ± 2.49	<0.001
Initial left renal volume (ml)	128.7 ± 27.5	142.7 ± 29.1	<0.001
Annual reduction volume in the left kidney (ml)	2.59 ± 3.67	0.99 ± 2.86	<0.001

Data are means ± standard deviations.

4. Discussion

This study showed that total renal volumes measured by automated 3D volumetric CT at the initial CT examination were positively correlated with the eGFR and significantly decreased according to CKD grade. These findings suggest that the total renal volume measured by automated 3D volumetric CT may reflect the degree of renal damage and can be used as an indicator of the renal function.

US has been used to estimate the renal volume [3–6] by measuring the three orthogonal axes of the kidney and applying these measurements to the ellipsoid formula. However, this formula does not accurately reproduce the variation in the shape of the kidney; as a result, a substantial systematic underestimation of the renal volume has been reported when calculating the volume using US with the ellipsoid formula [6]. Recently, several 3D CT methods for measuring the renal volume have been reported, including the voxel count method, semi-automated method, and automated methods [7,10–12]. Some groups

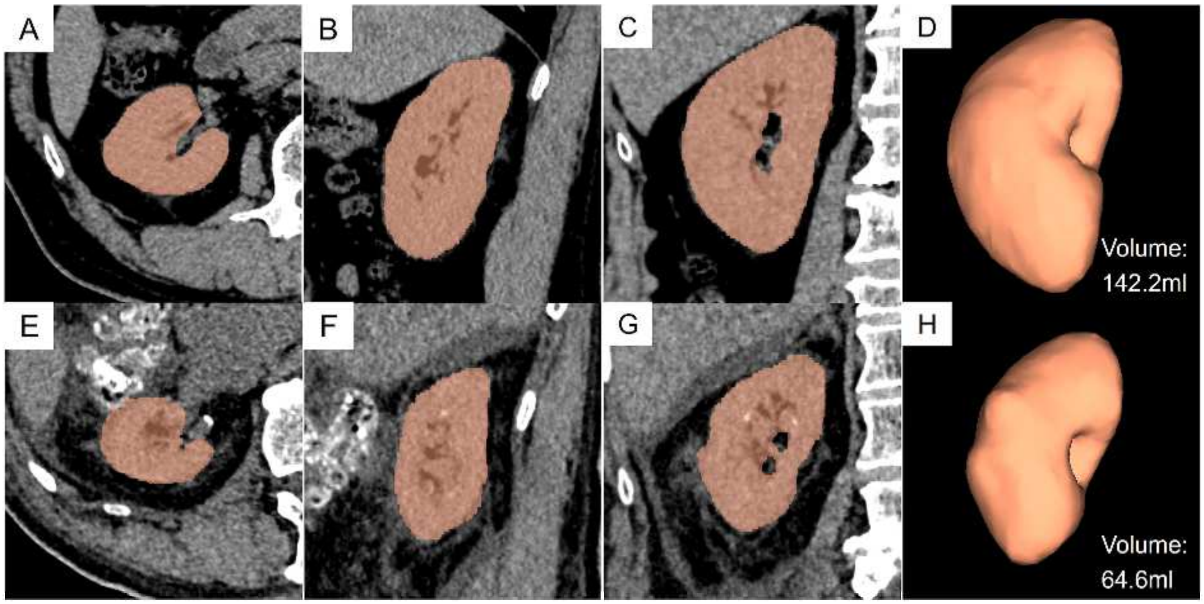

Fig. 3. Representative images of the right kidney obtained from volume analyzer SYNAPSE VINCENT in a patient of the progression group. Initial CT (A; axial image, B; sagittal image, C; coronal image, D; 3D image, right renal volume = 142.2 ml) and latest CT obtained 4.86 year after (E; axial image, F; sagittal image, G; coronal image, H; 3D image, right renal volume = 64.6 ml) showed the decreased volume of the right kidney with the annual reduction volume of 16.0 ml during the follow-up periods.

have reported a correlation between the GFR and kidney volume measured by semi-automated 3D CT volumetry using 1- or 5-mm slice thickness with manual segmentation of the kidney [7,11]. Mitsui et al. reported that automated 3D volumetric CT with a slice thickness of 1 mm, similar to our study, was able to measure the total volume of the kidney more accurately than previous studies using the ellipsoid method or using 2-mm-slice CT [9]. In addition, they showed that a dedicated 3D CT volumetric software program similar to that used in this study provides reproducible results for measuring the renal volume without the influence of observers because of its fully automated function [9].

Few previous reports have assessed the differences in the volumes between the right and left kidneys. In the present study, the left renal volume was predominantly larger than the right volume on initial CT. The definitive reason for these findings is unclear but may be related to the anatomic differences between the right and left kidneys. Anatomically, the left renal vein (LRV) is longer than the right renal vein (RRV) and flows across the abdominal aorta into the inferior vena cava. The LRV is then usually compressed and narrowed between the superior mesenteric artery and the abdominal aorta. These anatomical features of the LRV might result in physiological congestion of the left renal venous blood flow as well as the left renal parenchyma, ultimately causing a relatively increased volume of the left kidney [13].

In the present study, the total renal volumes in the patients with CKD G2 in the progression group were significantly smaller than in the non-progression group at the initial CT examination. This result indicated that, even in G2 patients with a mildly impaired renal function, a small renal size may be an important early finding that suggests worsening of the renal function during clinical follow-up, although the cutoff values for initial renal volumes in G2 patients presented in this study did not have high sensitivity for predicting the clinical prognosis. In addition, the annual reduction volume in both kidneys was significantly greater in the progression group than in the non-progression group, suggesting that a decrease in the renal volume over time can be used as an indicator to predict the progression of CKD and that it is important to focus on the annual reduction volume during clinical follow-up. A combined assessment of the initial renal volume and annual reduction volume may contribute to an improved prognostic prediction.

Furthermore, the annual reduction in the volume of the left kidney was significantly greater than that of the right kidney. This finding suggests that the left kidney is potentially more prone to congestion due to anatomic factors and is therefore affected by continuous congestion, resulting in a decrease in the renal volume with renal damage over time. A previous study reported that increased renal venous pressure due to venous congestion and increased renal interstitial pressure are associated with a worsening renal function in patients with heart failure [14,15], supporting our findings. The results of this study provide new insights into the relationship between longitudinal changes in the renal volume measured by automated 3D volumetric CT and CKD progression, and it would be valuable to understand these relationships with clinical relevance.

Several limitations of the present study warrant mention. First, the data were collected retrospectively, so some selection bias which was an inevitable limitation may have occurred. Further prospective studies are needed to validate our results. Second, all measurements of the renal volume were performed by one observer; therefore, the reproducibility of automated 3D CT volumetry was not evaluated. However, we believe that variations in automated 3D volumetric CT measurements would not be caused by automatically indicating the boundaries of the kidneys. Finally, the measurement of the renal volume by CT over a long follow-up period raises the issue of radiation exposure. It is essential to reduce radiation exposure as much as possible using dual-energy CT and Sn filters.

In conclusion, the automated 3D volumetric CT measurement of the whole kidney has the potential to monitor changes in the renal volume over time with changes of the renal function, and it may be helpful for predicting patients with an increased risk of progressing CKD grades during the longitudinal follow-up.

CRediT authorship contribution statement

Koji Narikiyo: Writing – original draft, Formal analysis. **Masahiro Tanabe:** Data curation. **Mayumi Higashi:** Methodology. **Yosuke Kawano:** Investigation. **Atsuo Inoue:** Investigation. **Haruka Kiyoyama:** Investigation. **Naohiko Kamamura:** Investigation. **Taiga Kobayashi:** Writing – review & editing. **Takaaki Ueda:** Writing – review & editing. **Katsuyoshi Ito:** Supervision, Data curation, Conceptualization.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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