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COMPUTED TOMOGRAPHY

Dual adrenal venous phase contrast-enhanced MDCT for visualization of right adrenal veins in patients with primary aldosteronism

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Abstract
Purpose To evaluate the frequency of visualization of the right adrenal vein (RAV) on dual adrenal venous phase multi-detector computed tomography (MDCT) in patients with primary aldosteronism.
Materials and methods Images of contrast-enhanced dual adrenal venous phase MDCT (45- and 55-second delays) in 90 patients with primary aldosteronism who underwent adrenal venous sampling were retrospectively evaluated. The degree of RAV visualization on each phase image was evaluated by two radiologists using a five-point scale and RAV visualization rates were estimated.
Results The RAV visualization rates on the first- and second-phase images were 89 % and 91 % by radiologist A, and 93 % and 90 % by radiologist B, respectively. No significant differences in the score of RAV visualization were observed between the first- and second-phase images by the two readers (P=0.164 and P=0.06). The kappa values for inter-observer agreement of RAV visualization on the first- and second-phase images were 0.57 and 0.46, respectively. The consensual RAV visualization rates on the first- and second-phase images were 91 % and 92 %, respectively. The overall RAV visualization rate by using both phase images was 98 %.
Conclusion Dual adrenal venous phase MDCT can visualize the RAV in almost all patients with primary aldosteronism.

Key Points
- *Dual adrenal venous phase MDCT images can visualize the right adrenal veins.*
- *The adrenal venous phase lies between the arterial and portal phases.*
- *Anatomical information will contribute to the technical success of adrenal venous sampling.*

Keywords Adrenal venous sampling · Adrenal vein · CT · MDCT · Venography

Introduction

Adrenal venous sampling (AVS) has been increasingly performed because of acknowledgement of the screening methods for primary aldosteronism [1, 2] and the limitations of cross-sectional imaging in diagnosing hormonal laterality for deciding surgical indications [3–5]. However, selective AVS of the right adrenal vein (RAV) remains difficult because of its small size and variable anatomy: it is a vein that usually drains directly into the inferior vena cava (IVC) at a variable height and angle [6, 7]. Therefore, prior information on the location and anatomy of the RAV is key to the technical success of AVS.

Contrast-enhanced multi-detector computed tomography (MDCT) is often used for visualizing the adrenal veins. Until recently, however, published RAV visualization rates have been less than 80 % (76–78 %) even when using MDCT [6, 8]. A more recently published report indicates an RAV visualization rate of 93 % using 64-row MDCT [9], which is still unsatisfactory as a pre-procedural mapping for AVS. When adrenal tumours are suspected, double- or triple-phase dynamic contrast-enhanced images (arterial phase: 30- – 40-second delays; portal phase: 70- – 90-second delays; and delayed

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phase: 120- – 600-second delays) are usually obtained to evaluate enhancement patterns of the tumours for differential diagnosis [10, 11]. In terms of the adrenal veins, acquisition timing of the arterial phase will be too early and the portal phase will be too late to enhance these veins strongly. However, the visualization rate of the adrenal veins on the timing between arterial and portal phases, termed the adrenal venous phase, remains uncertain.

The purpose of this study, therefore, is to evaluate the frequency of visualizing the RAV on dual adrenal venous phase MDCT in patients with primary aldosteronism.

Materials and methods

Subjects

This retrospective, single-institution study was approved by the institutional review board of our facility. Reapplication of informed written consent was not required because of the retrospective nature of the investigation. Between June 2012 and May 2014, AVS was performed in 105 patients with primary aldosteronism to investigate surgical indications. Diagnosis of primary aldosteronism was made according to the published guidelines [1]: plasma aldosterone concentration/plasma renin activity ratio was more than 200, and 2 or 3 of the loading tests (captopril challenge test, upright furosemide loading test, and saline loading test) were positive. Fifteen of the 105 patients were excluded because dual adrenal venous phase MDCT was not performed: computed tomography (CT) with different protocols had been obtained at other hospitals (n=7) and at our hospital in the past (n=8). Thus, the final study group consisted of 90 patients (35 men and 55 women; median age, 52 years; range, 23–79 years).

CT examinations

Contrast-enhanced dual adrenal venous phase MDCT was performed prior to AVS. The median interval between CT and AVS was 36 days (range, 1–434 days). Images were obtained using a 64-row detector scanner (Aquilion 64; Toshiba Medical Systems, Otawara, Japan) or a 320-row detector scanner (Aquilion One; Toshiba Medical Systems) at the following settings: a 1:1 table pitch; collimation, 0.5–1 mm; reconstruction thickness/interval, 1.0 mm/1.0 mm; and 100–120 kVp with "Real EC". Dual adrenal venous phase images were obtained at 45 and 55 seconds after injecting contrast materials for 30 seconds. The total iodine dose was 600 mg/kg body weight (maximum dose: 45 g). These images were obtained during the same breath-holding at the shallow expiratory phase. With regard to radiation exposure, in a patient with a body weight of 70 kg, for example, the volume CT dose index was about 12 mGy with adaptive iterative dose reduction (AIDR) and about 28 mGy without AIDR in each phase. The dose–length product was about 240 mGy with AIDR and 560 mGy without AIDR in each phase as the scan range covered the upper abdomen.

Image analysis

Image interpretation was retrospectively performed by two radiologists (A and B), each with experience of more than 50 cases of AVS. One of the first- or second-phase images in each patient was displayed at random to conceal information about which phase was displayed. At first, the readers independently evaluated transaxial images with 1-mm slice thickness using a viewer (ShadeQuest/ViewR; Yokogawa Medical Solutions, Tokyo, Japan). An enhanced tubular or linear structure that arose from the right adrenal gland and eventually entered the IVC either directly or indirectly was recognized as the RAV, in accord with previous reports [6, 8]. The quality and reliability of imaging for visualization of the RAV was scored using a five-point semi-quantitative confidence scale (5, excellent; 4, good; 3, moderate; 2, poor; 1, not visible) according to the previous report [8]. Scores of 3–5 represented adequate visualization. If there were discrepancies in visualization scores of 3–5 versus 1–2 between the readers, the images were evaluated together to achieve a consensual visualization rate on each phase image. Finally, if the RAV was visualized on the first- or second-phase images, it was regarded as visualized for the purposes of the study. Thus, the overall RAV visualization rate was estimated by using both phase images. If the RAV formed a common trunk with an accessory hepatic vein, it was recorded. If multiple RAVs were detected, the dominant vein was used for the evaluation. All findings were evaluated by agreement between the observers.

Radiologist A measured the CT value of the RAV and the right adrenal gland of each phase image using an operator-defined region of interest (ROI) in cases where the RAV was visualized. The size of the ROI was chosen to include a large representative portion of the structure. The contrast ratio of the RAV to the right adrenal gland was calculated using the following formula: CT value of the RAV/CT value of the right adrenal gland.

Although a similar evaluation was performed for the left adrenal vein, the results are not included in this paper for two reasons. First, in all patients, the common trunk of the left adrenal vein and subphrenic vein was visualized in both phases. Second, the information regarding the orifice of the left adrenal vein was not essential to the AVS procedure, while that of the RAV was essential.

Statistical analysis

Statistical analyses were performed using JMP 10 software (SAS Institute, Cary, NC, USA). A p value of less than 0.05

was considered statistically significant. Inter-observer variability was assessed with weighted kappa analysis, measuring the degree of agreement between the two observers. The Wilcoxon test was used to compare the score of RAV visualization between the first- and second-phase images in each reader. The student's t-test was used to compare the CT value of the RAV, the CT value of the right adrenal gland, and the contrast ratio between the first- and second-phase images.

Results

The degree of RAV visualization on the first- and second-phase images, respectively, was rated by radiologist A as excellent in 45 and 31 patients, good in 16 and 27 patients, moderate in 19 and 24 patients, poor in 9 and 5 patients, and not visible in 1 and 3 patients. Visualization by radiologist B was rated as excellent in 53 and 38 patients, good in 17 and 29 patients, moderate in 14 and 14 patients, poor in 5 and 6 patients, and not visible in 1 and 3 patients. No significant differences in these scores between the first- and second-phase images were observed (p=0.164 by radiologist A, and p=0.06 by radiologist B), although the number of patients with an excellent rating was larger on the first-phase images. The kappa values for inter-observer agreement of the RAV visualization score on the first- and second-phase images were 0.57 and 0.46, respectively. Example cases of visualization of the RAV on the first- and second-phase images are shown in Figs. 1, 2, and 3.

The RAV visualization rates on the first- and second-phase images by radiologist A were 89 % (80 of 90 patients) and 91 % (82 of 90 patients), respectively, and those by radiologist B were 93 % (84 of 90 patients) and 90 % (81 of 90 patients), respectively. The consensual RAV visualization rates on the first- and second-phase images were 91 % (82 of 90 patients) and 92 % (83 of 90 patients), respectively. In six of eight patients whose RAV was not visualized on the first-phase images, the RAV was visualized on the second-phase images. In five of seven patients whose RAV was not visualized on the second-phase images, the RAV was visualized on the first-phase images. In two patients, the RAV was not visualized on both phase images. Thus, the overall RAV visualization rate using both phase images was 98 % (88 of 90 patients).

In total, 22 patients (24 %) had a common trunk of the RAV with an accessory hepatic vein. This was detected in 8 patients (9 %) on the first-phase images and 22 patients (24 %) on the second-phase images. In total, multiple RAV was suspected in three patients (3 %).

No significant difference in the CT value of the RAV between the first- and second-phase images was observed [186±51 Hounsfield units (HU) vs. 175±44 HU, p=0.138]. The CT value of the right adrenal gland of the first-phase images was higher than that of the second-phase images (150±34 HU vs. 129±28 HU, p<0.001). The contrast ratio of the RAV to the right adrenal gland of the second-phase images was higher than that of the first-phase images (1.37±0.32 vs. 1.27±0.34, p=0.045).

Fig. 1 A 56-year-old man with primary aldosteronism with typical visualization of the right adrenal vein on adrenal venous phase MDCT images. **a** The right adrenal vein is clearly visualized with strong enhancement (score of 5) on the first-phase image (*arrow*). **b** It is also well-visualized (score of 4–5) on the second-phase image (*arrow*)

Discussion

Although MDCT has been commonly performed for mapping of the RAV during AVS, the reported RAV visualization rates have been not satisfactory until recently [6, 8]. The previous study reporting a 76 % RVA visualization rate using the arterial phase describes that unequivocal identification of the RAV may be caused by inappropriate acquisition timing, and that RAV visualization would likely be further improved if more optimal scan timing for the RAV is established [6]. The other study using late portal phase images (90-second delay) reported a RAV visualization rate of 77–78 % [8]. The RAV visualization rate in our study (91 % on the first-phase images and

Fig. 2 A 56-year-old woman with primary aldosteronism with different visualization of the right adrenal vein on dual adrenal venous phase MDCT images. **a** Identification of the right adrenal vein (*arrow*) is slightly difficult (score of 3) on the first-phase image, as there is little contrast between the right adrenal vein and the right adrenal gland because of strong enhancement of the right adrenal gland. **b** The right adrenal vein (*arrow*) is well-visualized (score of 5) on the second-phase image because of good contrast with the right adrenal gland

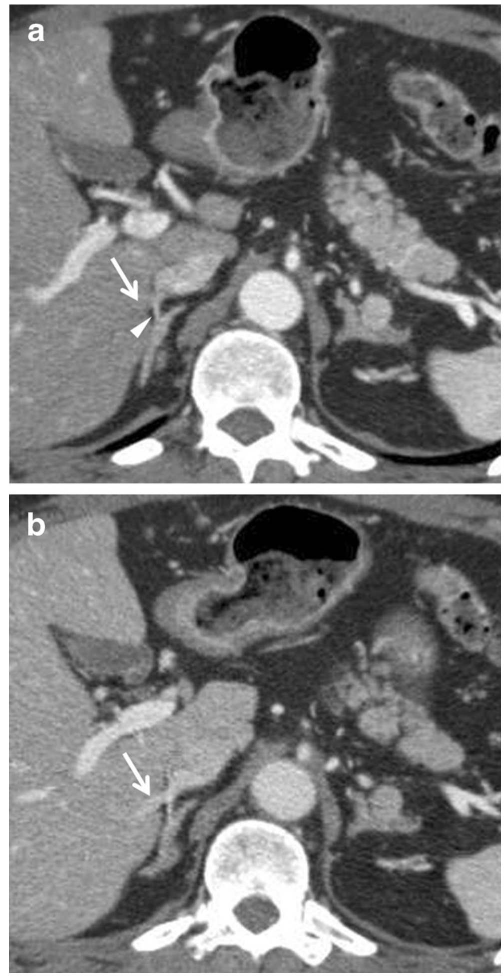

Fig. 3 A 61-year-old man with primary aldosteronism with a common trunk of the right adrenal vein and with an accessory hepatic vein. **a** A common trunk of the right adrenal vein (*arrow head*) with an accessory hepatic vein is difficult to recognize on the first-phase adrenal venous phase MDCT image because of poor enhancement of the accessory hepatic vein (*arrow*). **b** The common trunk can be recognized on the second-phase image because of strong enhancement of the accessory hepatic vein (*arrow*)

92 % in the second-phase images) is considerably higher than those of the previous reports, the difference being due to the difference in acquisition timing. Our results are similar to those of the recently published report of a 93 % RAV visualization rate using 64-row MDCT mainly in the second arterial phase [9]. As the RAV is a tiny structure, adequate contrast enhancement is required for both visualization and thin sectional reconstruction. We conclude that acquisition during the adrenal venous phase, which lies between the arterial and portal phases, is adequate for visualizing the RAV. However, in some cases, the RAV could not be visualized on single adrenal venous phase images. If complete visualization of the RAV in every patient is required, the dual adrenal venous phase is feasible, as shown in this study.

During the adrenal venous phase, no significant difference in the RAV visualization rate was observed between the first- and second-phase images (91 % vs. 92 %). Strictly speaking, the number of excellent ratings on the first-phase images was greater than that on the second-phase images. Considering the results of the quantitative analyses, this may be because, in many cases, contrast enhancement of the RAV on the first-phase images is generally higher than that on the second-phase images, although, in some cases, it becomes poor because the acquisition timing is too early. However, in some cases, contrast enhancement of the RAV to the right adrenal gland will become poor on first-phase images, as contrast enhancement of the right adrenal gland is too strong.

For a common trunk of the RAV with an accessory hepatic vein, the detection rate on the second-phase images (24 %) is higher than that on the first-phase images (9 %), and the detection rate on the second-phase images is equivalent to that of previous reports [6, 12, 13]. This is simply because recognition of the accessory hepatic vein is difficult on the first-phase images, as the hepatic veins are not yet enhanced at the earlier phase. In cases involving such variation, a common trunk can act as a landmark for catheterization of the RAV [6]. In addition, the location of the tip of the catheter should be cautiously decided upon to avoid blood contamination from the accessory hepatic vein. Special catheters, such as the three-dimensional type, are occasionally required for selecting the RAV. Thus, information regarding the presence or absence of this variation prior to AVS is important for the technical success of AVS. From this point of view, the second-phase images have an advantage over the first-phase images. If only a single phase is obtained for reducing radiation exposure, the second phase is better for visualizing the RAV, leaving other factors such as the tumour enhancement pattern out of consideration.

A limitation of this study is that we did not set a gold standard for visualization of the RAV. Although a previous study compared the anatomy of the RAV on MDCT with that on venograms [8], venograms were not used for estimating the RAV visualization rate in our study. Using venograms as a gold standard has problems; namely, the location of the RAV changes due to the respiratory phase during MDCT, and AVS and venograms cannot be used in cases of failure of laboratory testing of cortisol in blood samples selectively taken from the RAV. Further study is required to confirm how adrenal venous phase MDCT contributes to the technical success of AVS. Another limitation was that we could not know the most appropriate acquisition timing for visualizing the RAV. We only evaluated images with 45- and 55-second delays, which were selected because the images could be obtained during the same breath-hold among the adrenal venous phases. In addition, we did not evaluate possible negative effects, such as the effect on the diagnostic capability of the tumour enhancement pattern, by changing the acquisition timing. Reducing radiation exposure is an additional issue in the future, for example, with virtual non-contrast enhanced images using dual-energy CT [14].

In conclusion, visualization of the RAV using MDCT is improved by obtaining images at the adrenal venous phase, which lies between the arterial and portal phases. In addition, dual adrenal venous phase images, with 45- – 55-second delays, can visualize the RAV in almost all patients with primary aldosteronism. The later adrenal venous phase images have the advantage of visualizing a common trunk of the RAV with an accessory hepatic vein. The information on the location and variation of the RAV supplied by this accurate visualization will contribute to the technical success of AVS.

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Methodology: retrospective, observational, performed at one institution.

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