ORIGINAL RESEARCH

High prevalence of intracranial aneurysms in patients with aortic dissection or aneurysm: feasibility of extended aorta CT angiography with involvement of intracranial arteries

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ABSTRACT
Introduction Previous studies have suggested a higher prevalence of intracranial aneurysms (IAs) in patients with aortic aneurysms (AAs).
Objective To carry out a preliminary study to evaluate the prevalence of IAs in these patients and the diagnostic feasibility of extended aorta CT angiography (CTA), including intracranial arteries as well as the aorta.
Materials and methods We retrospectively reviewed all patients with a clinical diagnosis of AA or aortic dissection (AD) who had undergone aorta CTA as well as MR angiography, CTA, and/or DSA of the brain between 2009 and 2014. Since 2012, the extended aorta CTA protocol has been applied in these patients. Characteristics of IAs were classified with baseline clinical data. For quantitative and qualitative assessment by two independent raters, brain images obtained by extended aorta CTA and brain CTA were compared. The radiation dose of the two aorta protocols was compared.
Results The prevalence of IA was 22.2% (35/158). All IAs were detected by extended aorta CTA, except one small aneurysm (<3 mm). The mean vascular attenuation value between brain images showed no difference (p=0.83), but the contrast-to-noise ratio was significantly lower in extended aorta CTA (p<0.001). In qualitative assessment, the interobserver agreement was substantial (k=0.79). For the radiation dose, the dose–length product of the extended aorta CTA increased with increment of the scan range (p=0.048).
Conclusions With a high prevalence of IAs in patients with ADs or AAs, extended aorta CTA could be used to evaluate aorta disease and IA in a single session. However, further prospective studies are needed to prove efficacy and safety of the extended aorta CTA protocol in patients with AAs or ADs.

INTRODUCTION
The association between intracranial aneurysm (IA) and aortic diseases, such as aortic aneurysm (AA) or aortic dissection (AD), has been discussed in previous publications, which found that patients with AAs had a higher prevalence of IA than the general population.1–3 Although some authors1–6–3 proposed a genetic association between the two different pathologies, the cause of their concurrence is under debate. Despite a high prevalence of IA, it is still controversial whether or not routine brain imaging for these patients is needed.

In diagnosis and follow-up imaging of aortic disease, aorta CT angiography (CTA) is widely applied and its advantages include rapid image acquisition, simple postprocessing with three-dimensional (3D) reconstruction, and its easy availability.6 Since 2012, our institute has applied an extended aorta CTA protocol with involvement of intracranial vessels as a substitute for the standard aorta CTA protocol. By expanding coverage of the brain, this new aorta CTA protocol allows visualization of the intracranial vessels and the entire aorta in a single session.

Therefore, we aimed to examine the prevalence and characteristics of IAs in patients with AAs or ADs and evaluate diagnostic feasibility of extended aorta CTA.

MATERIALS AND METHODS
Patients
After approval of the institutional review board for this retrospective study, informed consent was waived. Between January 2009 and December 2014, consecutive patients in this institute were retrospectively reviewed. Inclusion criteria for this study were as follows: (1) patients who had undergone aorta CTA for their diagnostic or follow-up investigation as well as additional brain imaging, such as brain CTA, MR angiography (MRA), or DSA; (2) a confirmed aortic disease, including AD or AA, as the indication of the aorta imaging; (3) an absence of contraindications. Exclusion criteria were patients with renal failure (creatinine clearance <30 mL/min) and/or any contraindications to iodinated contrast material injections, traumatic aortic disease, and known connective tissue diseases.

Image acquisition
All aorta CTA was performed by using a 64-channel multi-detector CT scanner (Sensation 64, Siemens Healthcare, Forchheim, Germany) with ioversol (Optiray 350 mg iodine/mL; Mallinckrodt Medical Imaging, Dublin, Ireland). The patient was placed in the supine, head-first position with both arms up. The following parameters were used: tube voltage 100 kV, tube current 160 mA with automatic tube current modulation (CARE Dose 4D), 64×0.6 collimation, 0.5 s rotation time, pitch of 1, cranial-caudal scan direction.
In the scanning range, the standard protocol started from 2 cm above the aortic arch level to the lesser trochanter of the femur (figure 1A). Until December 2011, standard aorta CTA was performed in this institute with the scan range between the aortic arch and the inguinal level. Since 2012, the scan range of aorta CTA has been extended to the upper margin of the frontal sinus, 1–2 cm above the circle of Willis (figure 1B) and the extended aorta CTA protocol was implemented, and was applied in 99 patients. The aorta CTA protocol generally consisted of non-contrast, arterial and delayed phase, and extension of the scan range was applied only to the arterial phase, not other series.

The arterial phase was achieved by injecting iodinated contrast material according to the weight of the patients (2 mL/kg, maximum volume 150 mL in both protocols) followed by a 40 mL saline chaser. The saline chaser was administered with a dual-head power injector (Dual Shot, Nemoto Kyorindo) at 4.5 mL/s through an 18-gauge cannula placed in the antecubital vein of the right arm. Image acquisition was triggered by automatic bolus tracking technique (CARE Bolus, Siemens, Forchheim, Germany). A region of interest was placed into the ascending thoracic aorta and image acquisition started 7 s after a trigger threshold of 150 HU was reached. The delayed phase was acquired after 3 min of contrast injection. Axial images were reconstructed, and used for image reconstructions, including multiplanar reformation and the volume-rendered technique.

Brain CTA was performed using a 128-channel multi-detector CT scanner (SOMATOM Definition AS+; Siemens, Forchheim, Germany) with iopromide (Ultravist 370 mg iodine/mL; Schering Korea, Seoul, Korea). The imaging parameters included an exposure setting of 120 kV and 140 mA with automatic tube current modulation (CARE Dose 4D), a collimation of 64×0.6 mm, slice acquisition of 128×0.6 mm using a z-flying focal spot technique, a gantry rotation time of 0.5 s, and a pitch of 0.45. The imaging volume ranged from the

Figure 1 Standard aorta CT angiography (CTA) shows the scan range from mid-neck level to the lesser trochanter of the femur (A). Since 2012, extended aorta CTA with involvement of the intracranial arteries has been performed and the scan range was extended 1–2 cm above the circle of Willis (B). The right distal internal carotid artery aneurysm is clearly seen on the axial image of the extended aorta CT angiogram (C), which is confirmed by brain CTA (white arrow, D).
vertex of the skull to the posterior arch of the C1 vertebra. Axial scans were reconstructed for quantitative and qualitative image analysis.

Brain MRA was performed using a 3 T scanner (Discovery MR750; GE Healthcare, Milwaukee, Wisconsin, USA). Scan parameters were as follows: repetition time/echo time 23/2.5 ms; field of view 21×19 cm; layer thickness 1.4 mm; flip angle 20°; number of excitations 1; and matrix size 416×224. Axial source data were reviewed with reference to maximum intensity projection images.

Cerebral angiography was performed using a biplane angiography suite (Artis ze, Siemens Healthcare, Forchheim, Germany) to acquire images of an IA.

Image analysis
Two experienced neuroradiologists (SHS and SJA) reviewed brain axial images independently on the PACS (Centricity PACS; GE Healthcare, Milwaukee, Wisconsin, USA), together with the maximum intensity projections (axial, sagittal, and coronal) and volume-rendered images of the cerebral arteries. The presence of an IA was determined in a consensus reading and any clinical information or knowledge about this study was not provided to the readers.

In quantitative assessment of the brain axial image, a dataset of all patients, who had undergone the extended aorta CTA as well as the brain CTA, were compared. On the axial images, the vascular attenuation (in Hounsfield units) of the internal carotid artery at the level of distal bifurcation and the image noise were measured by a board-certified radiologist (E-SC) with the same method as in the previous study.10 The contrast-to-noise ratio (CNR) was then calculated using the following formula:11 CNR=(mean arterial attenuation value−mean brain parenchyma attenuation value)/image noise.

In qualitative image analysis, two neuroradiologists (SJA and WSJ) also compared the brain axial images and rated them on a three-point scale (1 = non-diagnostic; 2 = good; 3 = excellent image quality).

Measurement of the radiation dose
For measurement of the radiation dose, the CT dose index and dose-length product were used, which were automatically calculated by the scanner and provided together with other CT images. To minimize dose variation by patients’ body mass index,12 34 patients who underwent standard and extended aorta CTA as the initial and follow-up imaging, were selected and both parameters were compared between the arterial series of both aorta CTA protocols.

Statistical analysis
Continuous variables are described as mean±SD, and categorical variables, as frequency in percentages. Univariate analysis was performed with a χ² test or Fischer exact test for categorical variables. Binary logistic regression analysis was performed to determine independent variables associated with the presence of an IA. A value of p<0.05 was considered statistically significant. The κ statistic was used to evaluate interobserver agreement and was interpreted as follows:13 slight, <0.20; fair, 0.21−0.40; moderate, 0.41−0.60; substantial, 0.61−0.80; and perfect agreement, >0.81. All statistical analyses were performed using SPSS software (V23.0 for Windows, SPSS Inc, Chicago, Illinois, USA).

RESULTS

Demographic characteristics
One hundred and fifty-eight consecutive patients (male: female=103:55, mean age 68.6±12.2 years, range 30–91 years) were enrolled in this study (table 1). Twenty-five patients (15.8%) had AD and 133 (84.2%) had AA; 96 (60.8%) were located in the thoracic area and 62 (39.2%) in the abdominal aorta (table 1). In the 25 patients with AD, coarctation of the aorta was not found. In the brain imaging, CTA was performed in 67 patients, MRA in 91 and DSA in 14. Ninety-two patients (58.2%) underwent brain imaging for evaluation of non-specific neurologic symptoms as well as known IAs, 61 (38.6%) for screening, and 5 (3.2%) for the follow-up imaging, who were treated with surgical clipping. These five patients underwent brain imaging before the aorta imaging.

IA prevalence and characteristics
Of 158 patients, IA was found in 35 (22.2%), of which 8 IAs were seen in patients with AD and 27 in those with AA (32%, 8/25 vs 20.3%, 27/133, respectively, p=0.198). In all patients, female sex (OR=2.77, 95% CI 1.24 to 6.17, p=0.0128) and abdominal lesion location (OR=3.31, 95% CI 1.49 to 7.36, p=0.0034) were significantly associated with the presence of IA. Comorbidities, including hypertension, diabetes, hyperlipidemia, and polycystic kidney disease, were not associated with IA formation. While no variable was associated with formation of IAs in patients with only ADs, age (OR=1.07, 95% CI 1.01 to 1.13, p=0.025), female sex (OR=2.81, 95% CI 1.08 to 7.32, p=0.0345), and abdominal AA (OR=3.39, 95% CI 1.34 to 9.61, p=0.0109) were independently associated with IA prevalence in patients with only AAs. On multivariate logistic regression analysis, no independent variable was found. Table 2 summarizes the characteristics of the 35 patients with IAs. In the AA group, IAs were predominantly located in the anterior

| Table 1 Demographics of 158 patients with AD or AA who underwent brain imaging |
|--------------------------|--------------------------|--------------------------|--------------------------|
| Characteristics          | AD (N=25)                | No IA (N=17)             | AA (N=133)               |
| Age (years), mean (SD)   | 62.0 (14.9)              | 61.7 (15.7)              | 75.6 (8.16)              |
| Sex                      |                         |                         |                         |
| Female                   | 4 (50)                  | 8 (47.1)                | 14 (51.9)                |
| Reason for brain imaging |                         |                         |                         |
| Screening                | 3 (37.5)                | 4 (23.5)                | 7 (25.9)                 |
| Symptomatic              | 4 (50)                  | 13 (76.5)               | 16 (59.3)                |
| Follow-up*               | 1 (12.5)                | 0                       | 4 (14.8)                 |
| Medical history           |                         |                         |                         |
| Hypertension             | 6 (75)                  | 12 (70.6)               | 21 (77.8)                |
| DM                       | 0                       | 3 (17.6)                | 5 (18.5)                 |
| Hyperlipidemia           | 1 (12.5)                | 0                       | 2 (7.4)                  |
| Previous stroke          | 1 (12.5)                | 7 (41.2)                | 7 (25.9)                 |
| Smoking                  | 2 (25)                  | 2 (11.8)                | 7 (25.9)                 |
| PKC                      | 0                       | 0                       | 1 (3.7)                  |
| Aorta location           |                         |                         |                         |
| Abdominal                | 2 (25)                  | 0                       | 19 (70.4)                |
| Thoracic                 | 6 (75)                  | 17 (100)                | 8 (29.6)                 |

Results are shown as number (%) unless stated otherwise.

*Brain imaging was performed for follow-up after clipping in five aneurysms.

AA, aortic aneurysm; AD, aortic dissection; DM, diabetes mellitus; IA, intracranial aneurysm; PKC, polycystic kidney disease.
circulation (24/27, 88.9% in AA vs 4/8, 50% in AD, p=0.033). The mean diameter of the IAs was 5.09±3.57 mm and more than 50% of IAs were >5 mm in size (16/30, 53%). The shape of most of IAs was saccular (28/30, 93.3%) and eight IAs (8/35, 22.9%) had ruptured.

**IA detectability of the extended aorta CTA**

Of the 99 patients who underwent extended aorta CTA, IAs were found in 10, which was confirmed by the additional brain imaging (table 3). Seven saccular aneurysms were clearly detected on the axial image of the extended aorta CT angiogram and two IAs with previous surgical clipping were found. One aneurysm with a diameter of 2 mm was depicted not on the extended aorta CT angiogram, but by MRA.

**Quantitative and qualitative assessment of the extended aorta CTA**

The mean vascular attenuation value at the bifurcation of the distal internal carotid artery showed no difference between brain axial images (414.7±85.3 in the extended vs 433.3±78.2 in the brain CTA, p=0.83), while the image noise was significantly different for the extended aorta CTA and standard CTA (19.8±3.5 vs 11.6±3.0, respectively, p<0.001). Therefore, the CNR was lower in the extended aorta CTA than brain CTA (19.8±5.9 vs 35.5±11.6, respectively, p<0.001). In the qualitative assessment of brain images, the interobserver agreement between two readers was substantial, with a κ value of 0.79 and all image quality ratings were good to excellent.

**Comparison of radiation dose between aorta CTA protocols**

In this study, we reported a 22.2% net prevalence of IA, which was at least sevenfold higher than that in the general population and about twice as high as that in similar diseased groups. Vlak et al estimated the overall prevalence of IAs in the general population as 3.2%. Kuzmik et al reported a 9% prevalence of IAs in 212 patients with thoracic AA, but some authors reported that the prevalence of IA was more than 11% in patients with AA and AD. Interestingly, our study showed that the prevalence of IA was quite different according to the aortic disease. Thus it was 32% (8/25) in AD compared with 20.3% (27/133) in the AA group, and these patients had no comorbidity. In contrast to the AA group, there were few case reports of concurrent IAs in patients with ADs, all of which were associated with Marfan syndrome.

**DISCUSSION**

This preliminary result demonstrated that the extended aorta CTA could detect IAs, compared with other brain imaging. Although it had a low CNR due to increment of the image noise, the mean vascular attenuation value of the brain image was not significantly different for the extended aorta CTA and the standard brain CTA. Furthermore, IA prevalence in this study was much higher than that described in previous publications in the general population.

In this study, we reported a 22.2% net prevalence of IA, which was at least sevenfold higher than that in the general population and about twice as high as that in similar diseased groups. Vlak et al estimated the overall prevalence of IAs in the general population as 3.2%. Kuzmik et al showed a 9% prevalence of IAs in 212 patients with thoracic AA, but some authors reported that the prevalence of IA was more than 11% in patients with AA and AD. Interestingly, our study showed that the prevalence of IA was quite different according to the aortic disease. Thus it was 32% (8/25) in AD compared with 20.3% (27/133) in the AA group, and these patients had no comorbidity. In contrast to the AA group, there were few case reports of concurrent IAs in patients with ADs, all of which were associated with Marfan’s syndrome.

Some authors reported that the prevalence of IAs in patients with coarctation of the aorta was >10%. The discrepancy in the results for IA prevalence may be explained by the following assumptions: (1) the limitation inherent in a retrospective study; (2) relatively fewer patients enrolled in this study; (3) ethnic difference; and (4) a lack of knowledge of the true IA prevalence in patients with AA or AD. To elucidate the true IA prevalence in patients with AA or AD, a prospective cohort study is mandatory. Whatever the cause of the differences in IA prevalence, it is important for clinicians to consider...
the possible presence of IAs in the management of patients with AAs or ADs because by clamping the aorta during aortic surgery, cerebral perfusion pressure may increase temporarily, which might cause IA rupture.\(^1^8\)

In detection of IAs, extended aorta CTA was comparable to other brain imaging methods, and the interobserver agreement for image quality was good. In the mean vascular attenuation of brain images, extended aorta CTA was similar to brain CTA (>400 HU), and proved by Kim et al\(^2\) to be of diagnostic value. In this study, seven saccular IAs and two IAs with clipping were found using extended aorta CTA. One aneurysm was sac- cular and <3 mm in size and might have been missed owing to the diagnostic limitation of aneurysm size inherent to brain imaging. Wang et al\(^9\) reported that the overall sensitivity, specificity, and accuracy of brain CTA were 96.3%, 100%, and 94.6%, respectively, but 81.8%, 100%, and 93.3%, respectively, for small aneurysms (<3 mm). Sailer et al\(^1^2\) found that brain MRA had high sensitivity of 74–98%, but a large variation in specificity, ranging from 50% to 100%, due to higher rates of false-positive results, mainly in aneurysms of <3 mm. In addi- tion, the clinical impact on management of small IAs (<3 mm) is still under debate in recent randomized clinical trials.\(^2^3\),\(^2^4\)

Compared with the standard protocol, extended aorta CTA has some drawbacks, such as the radiation dose and low CNR. Increment of the radiation dose in extended aorta CTA was closely associated with the scan range. To decrease the radiation, Kok et al\(^2^5\) proposed the new aorta CTA protocol with a 23–57% reduction of the radiation dose compared with standard CTA protocol. As an alternative to CTA, brain MRA may be a good choice for evaluating concurrent IAs in these patients, but MRA is likely to be limited under special circumstances, such as patients with claustrophobia, anxiety disorder, or economic hardship. A low CNR in this CTA protocol was also associated with high image noise, which may be affected by various para- meters, such as X-ray energy of the source, field of view, thickness of the body part and the beam-hardening artifact by the raised arms. Higashigaito et al\(^2^6\) recently introduced a low-volume con- trast CTA protocol without increment of image noise.

**Limitations**

This study had several limitations. First, it was a retrospective design with a limited number of cases. Owing to the retrospective nature and a potential selection bias of this study, we could not exclude the possibility that the prevalence of IAs was overes- timated or underestimated. Second, we attempted to evaluate the diagnostic feasibility of extended aorta CTA and could not collect enough evidence to recommend it for screening. Rarely, some authors used MRA or CTA as for brain screening; Curtis et al\(^2^8\) performed MRA as screening to detect IAs in 117 patients with coarctation of the aorta, and Furtado et al\(^2^7\) proposed a comprehensive CTA protocol with a wide range from the vertex of the head to the diaphragm in patients with acute stroke. Although coarctation of the aorta is included in the screening indications for unruptured IAs, there is still a lack of evidence for screening patients with AAs or ADs.\(^2^9\) A prospective study will be needed to prove the true IA prevalence, disease morbidity and mortality, cost-effectiveness of the screening test, accessibility of a low-risk and effective treatment, and patients’ psychological condition. Third, various imaging modalities, including MRA, CTA, or DSA, were used for reference, which could influence accuracy or specificity in detection of IAs. Moreover, IA was confirmed in only 14 patients using DSA because most patients were unable to undergo DSA owing to the morbidity of prior aortic disease and follow-up loss. Finally, the brain coverage on the ‘extended aorta’ CT angiogram, which was from 1–2 cm above the circle of Willis to neck vessels, is not complete, and did not include the whole brain. Thus some kinds of aneurysms might have been missed, such as those in particular pericallosal region lesions. This might leave people with the impression that they have been screened, when they have not.

**CONCLUSION**

This preliminary study showed that patients with AAs or ADs have a high prevalence of IA, and extended aorta CTA provides a feasible diagnostic option for evaluation of aortic disease and brain aneurysm in a single scanning. However, further prospect- ive studies will be needed to demonstrate a substantial prevale- nce of IAs and prove the efficacy and safety of the extended aorta CTA protocol in patients with AAs or ADs.

**Correction notice** This article has been corrected since it published Online First. The ‘material and methods – patients’ section has been amended.

**Contributors** All authors met the requirements for authorship. The corresponding author takes full responsibilities for the data, analyses, and interpretation, and the conduct of the research. The corresponding author had full access to all the corresponding author had full access to all of the data and has the right to publish any and all data separate and apart from any sponsor. DL and SHS: substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; drafting the work or revising it critically for important intellectual content; final approval of the version to be published. YBK and S-WS: contributions to the conception or design of the work; acquisition of data for the work: the work or revising it critically for important intellectual content; final approval of the version to be published. WSI, SJA and E-SC: contributions to the analysis of data for the work.

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