Comparison of different volumes of saline flush in the assessment of perivenous artefacts in the subclavian vein during cervical CT angiography

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Objectives: The aim of this study was to examine attenuation values in the central vein and perivenous artefacts at the subclavian vein in cervical CT angiography (CTA) when using 40 ml contrast material (CM) followed by different volumes (25 ml vs 40 ml) of saline flush (SF).

Methods: 61 patients underwent CTA between the aortic arch (AA) and distal to the circle of Willis (cW). After calculating test-bolus time to peak enhancement at the cW (Tc), scanning delay was represented as [(Tc+4) – scan duration between AA and cW] s. 28 patients (Group A) received 40 ml of 370 mg iodine (I) ml⁻¹ CM followed by 25 ml of SF, and 33 patients (Group B) received the same CM followed by 40 ml of SF, both administered through the right antecubital vein. Arterial attenuation was measured at seven points in the aorto-carotid artery and at three points in the vertebrobasilar artery. Venous attenuation in the central vein was measured at four points. Mean attenuation values were analysed quantitatively. Axial and post-processing three-dimensional images were assessed qualitatively.

Results: When Groups A and B were compared, there were no differences in the mean attenuation values in either the aorto-carotid artery ($p=0.78$) or the vertebrobasilar artery ($p=0.82$). Mean venous attenuation values were lower ($p=0.002$) in Group B than in Group A. Although the qualitative assessment of arterial images showed no differences between the two groups overall, perivenous artefacts at the subclavian vein were assessed as less prominent ($p<0.01$) in Group B.

Conclusions: When compared with CTA followed by 25 ml of SF, CTA followed by 40 ml of SF can reduce venous attenuation values and perivenous artefacts at the subclavian vein.

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Cervical CT angiography (CTA) has high sensitivity and specificity for the detection of carotid artery stenosis, suggesting that it is suitable for screening symptomatic patients with atherosclerotic disease in anterior and posterior circulation [1]. In modern 32- or 64-multidetector row CT (MDCT) systems, small volumes of contrast material (CM) can provide sufficient early arterial enhancement in the cervical CTA [1–3].

Several reports on thoracic CT and CTA have stated that saline flush (SF) after injection of the main CM bolus into the central veins can help to reduce perivenous streak artefacts at the brachiocephalic vein and superior vena cava [4–7]. In general, the suggested flush volumes range from 15 to 50 ml, but most authors report using 15–20 ml of SF [4–9].

To reduce perivenous artefacts in cervical CT on a 16-MDCT system, Yoon et al [9] used 80 ml CM followed by 40 ml of SF [9], and de Monyé et al [2] suggested the craniocaudal scan direction. We recently reported that CTA on a 32-MDCT in the caudocranial direction can

provide adequate arterial enhancement using 40 ml of highly concentrated CM followed by 25 ml of SF [3]; however, perivenous artefacts were often present in the subclavian vein. To improve images of the subclavian artery and upper extremity vasculature, pushing an extra flush volume of 30–40 ml injected at a rate equal to that of CM injection has been recommended [10]. Therefore, we anticipated that a combination of 40 ml of SF would reduce perivenous artefacts at the subclavian vein. Thus, the purpose of this study was to compare the CTA images obtained using 40 ml of 370 mg iodine (I) ml⁻¹ CM followed by either 40 ml or 25 ml of SF qualitatively (in terms of prevalence of artefacts) and quantitatively (in terms of arterial and venous enhancement).

Methods and materials

Patients

This study aimed to evaluate retrospectively cervical CTA carried out from July 2007 to April 2009 in 63 consecutive patients for routine checks of their cervical vasculature. 30 patients undergoing CTA examination

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between July 2007 and July 2008 (hereafter referred to as Group A) received 40 ml of CM with a high concentration of 370 mg of I ml⁻¹ (Iopamiron 370 (Iopamidol); Bayer Pharmacy, Osaka, Japan) followed by a 25 ml of SF. A further 33 patients, examined by CTA between August 2008 and April 2009 (hereafter referred to as Group B), received 40 ml of the same CM followed by 40 ml of SF.

The inclusion criteria for this study were (a) patients with a history of known or suspected atherosclerotic disease in the carotid or vertebral vascular system, including amaurosis fugax, transient ischaemic attacks, ischaemic stroke and dizziness [1]; (b) patients with venous access through the right antecubital vein to mitigate the venous reflex of CM into the cervical veins [4]; (c) patients without severe heart failure; and (d) patients with no previous allergic reaction to iodinated CM, renal insufficiency (serum creatinine level of >1.5 mg dl⁻¹), respiratory failure or a previous history of asthma. We did not include patients with suspected dissection of the cervical artery.

2 of the 63 patients were excluded because of technical problems. The remaining 61 (48 male and 13 female; age range, 43–87 years; mean age $\pm$ SD, 69.9 $\pm$ 8.3 years) were included in the study.

Approval for this study was obtained from the institution's review board for human studies, and therefore, informed consent was waived for this retrospective clinical study.

CT protocol

All participants underwent CTA examinations using a 32-detector row scanner (Light speed VCT select; GE Healthcare, Milwaukee, WI). First, the test bolus technique was performed at the circle of Willis (cW) to obtain accurate information about CM arrival time in the individual circulation. After a 20-gauge catheter was placed into the right antecubital vein, 20 ml of CM followed by 15 ml of SF was administered at a flow rate of 4.0 ml s⁻¹ using a double injector (Dual-shot DX injector; Nemoto-kyorindo, Tokyo, Japan). Patients were placed in the supine position with their arms along the body and their heads tilted slightly forward. On the basis of our earlier findings, single-level dynamic CT scans were performed with the tilted gantry parallel to the anterior skull base. This range could scan the internal carotid arteries (ICAs), basilar artery (BA) and sigmoid sinus (SS) in reference to intracranial anatomy at the skull base. After scanning anterior and lateral localiser images, low-dose (automatic tube current modulation using a noise index of 20, 120 kVp) dynamic CT scans (5 mm section thickness) were acquired every 2 s, starting 8 s after intravenous administration of the test bolus. Scans were continued until CM appeared as hyperattenuating spots in these vessels (Figure 1a).

A time-attenuation curve for each vessel was then generated by placing small circular regions of interest (ROI) without calcification of the arterial wall and temporal bone (0.5–1.0 mm²). Time to peak enhancement at the cW (Tc) was selected as the largest among three arteries (Figure 1b). In addition, the time interval between peak enhancement at the ICA and that at the SS was measured (TI_{ICA-SS}) (Figure 1c). Any difference between time to peak enhancement at the ICA and that at

the BA (TI_{ICA-BA}) was also determined. When an artery showed no show time to peak enhancement because there was no increase or only a slight increase in attenuation in that artery, arterial occlusion on the affected side was considered. In such cases, the Tc selected was the largest among the measurable values.

Scanning coverage ranged between the aortic arch and area distal to the cW. The fastest table feed was selected as 96.9 mm s⁻¹ for head and neck (collimation 32 $\times$ 1.25 mm; rotation time 0.4 s per rotation; pitch 0.969 in a caudocranial scan direction). The other acquisition parameters were applied as follows: tube voltage 120 kVp, current time 650 mA, matrix of 512 $\times$ 512, field of view 20 cm, section thickness 1.25 mm and reconstruction interval 0.625 mm (50% overlapping). Patients were instructed to breathe quietly without swallowing.

According to our previous experience, we designed protocols with an additional delay of 4 s at the cW and decided that the actual scanning delay was the time left after subtracting the duration of the scan between the aortic arch and cW (sd). Consequently, each scanning delay was represented as [(Tc+4)–sd] s.

We recorded age (years), sex, body weight (kg), height (cm), sd (s), Tc (s), TI_{ICA-SS} (s), TI_{ICA-BA} (s) as characteristic parameters for each patient.

Image analysis

Source axial images were loaded on a separate workstation (Advantage workstation 4.3; GE Healthcare) and were displayed with a window/level setting of 700/200 HU [1]. To analyse the entire cervical vascular system between the epiaortic arteries and cW, axial source images (slice thickness 0.625 mm) made in cine mode were utilised to evaluate vascular anatomy and pathology. For qualitative evaluation of post-processing three-dimensional images, coronal maximum intensity projection (MIP) with a sliding thin slab (6–7 mm) was utilised for analysis of the aortocarotid and vertebrobasilar arteries and the subclavian vein.

Quantitative analysis

Axial source images were used to evaluate arterial and venous enhancement. One radiologist (YK) measured arterial attenuation values at seven points in the aortocarotid artery between the aortic arch and ICA. The regions of interest (ROIs) were placed at the following points: (1) aortic arch; (2) proximal common carotid artery; (3) distal common carotid artery; (4) proximal ICA; (5) distal ICA; (6) ICA at the cavernous segment; and (7) ICA at the communicating segment. In the same fashion, arterial attenuation values were measured in the vertebrobasilar artery at ROIs placed in three positions as follows: (1) proximal vertebral artery; (2) distal vertebral artery; and (3) distal BA. The ROI was not placed near the edge of a vessel. In cases in which a vessel of interest had severe narrowing and was obscured by severe dental-filling artefacts, the attenuation values of the affected vessel segments were not measured.

In addition, venous attenuation values in the central vein were measured at four points as follows: (1) subclavian vein from the junction of the cephalic vein and axillary vein to the lateral border of the first rib; (2) subclavian vein at the costoclavicular space between the

(a)

(b)

(c)

Figure 1. Test bolus technique at the circle of Willis (cW) in an 84-year-old woman. (a) Single level dynamic CT scan with tilted gantry parallel to the anterior skull base at the level of cW scanned the right internal carotid arteries (rtICA), left internal carotid artery (ltICA), basilar artery (BA) and sigmoid sinus (SS). Scans were continued until the contrast material appeared as hyperattenuating spots in the bilateral ICAs, BA and SS, respectively. (b) Time-attenuation curves in the bilateral ICA (1), SS (2) and BA (3) were generated by placing small circular regions of interest (ROI). Time to peak enhancement at the cW (T_c) was selected as the largest from among the three arteries. (c) Time interval (TI_{ICA-SS}) can be measured as the time between peak enhancement at the ICA (1) and that at SS (2).

first rib and the clavicle; (3) brachiocephalic vein between the junction of the right internal jugular vein and the junction of the bilateral brachiocephalic veins; and (4) superior vena cava between the junction of the bilateral brachiocephalic veins and the right atrium. An attempt was made to place ROIs near the edge to trace the venous lumen fully, including any deposited CM. Each ROI varied from 100 to 200 mm².

To compare arterial enhancement in the two groups, we calculated the mean attenuation values in the aortocarotid artery, the vertebrobasilar artery and the central vein.

Qualitative analysis

Two experienced radiologists (YO and TH) evaluated image quality, reaching a consensus for each image. First, they assessed the perivenous artefacts for the right

subclavian artery in source axial images, the two readers were then asked to rate quality of images of the subclavian vein using a four-point scale:

- (1) no dense CM within the venous lumen and perivenous artefacts not recognised;
- (2) dense CM in less than one-half of the venous lumen and minimum perivenous artefacts recognised;
- (3) dense CM in greater than one-half of the venous lumen and moderate perivenous artefacts recognised; and
- (4) dense CM fills the venous lumen and severe perivenous artefacts recognised (Figure 2).

Next, the overlap between the subclavian artery and the subclavian vein was also assessed by evaluating coronal MIP images with sliding thin slabs (6–7 mm) in the right subclavian vein. Again, a four-point scale was used:

- (1) dense CM did not persist, there was only slight attenuation (less than in the subclavian artery) and there was minimum overlap of venous structures;

- (2) a small volume of dense CM remained with mild attenuation (close to that in the subclavian artery), and there was mild overlap of venous structures;
- (3) a moderate volume of dense CM remained with high attenuation (greater than that in the subclavian artery), and there was moderate overlap of venous structures; and
- (4) a massive volume of CM remained with markedly high attenuation (much greater than in the subclavian artery), and there was severe overlap of venous structures (Figure 3).

Finally, arterial enhancement in the aortocarotid and vertebrobasilar arteries was assessed qualitatively using coronal MIP and a four-point scale: (1) poor, (2) acceptable, (3) good and (4) excellent.

Statistical analysis

Statistical analysis was performed using SPSS 14.0 (Chicago, IL). Patient and scan characteristics were compared using the unpaired Student's *t*-test. Mean

(a)

(b)

(c)

(d)

Figure 2. Assessment of source axial images for perivenous artefacts in the subclavian vein using a four-point scale: (a) score 1, there is dense contrast material (CM) within the venous lumen and no perivenous artefacts are visualised; (b) score 2, dense CM fills less than one-half of the venous lumen and minimum perivenous artefacts were recognised; (c) score 3, dense CM fills more than one-half of the venous lumen and moderate perivenous artefacts are recognised; and (d) score 4, dense CM fully fills the venous lumen and severe perivenous artefacts are recognised.

Figure 3. Evaluation of coronal maximum intensity projection (MIP) images for perivenous artefacts in the subclavian vein. A four-point scale was used: (a) score 1, dense contrast material (CM) does not persist, there is slight attenuation (less than in the subclavian artery) and there is minimum overlap of venous structures; (b) score 2, a small volume of dense CM remains with mild attenuation (close to that in the subclavian artery), and there is a mild overlap of venous structures; (c) score 3, a moderate volume of dense CM remains with high attenuation (more than that in the subclavian artery), and there is a moderate overlap of venous structures; and (d) score 4, a massive volume of CM remains with markedly high attenuation (much more than in the subclavian artery), and there is severe overlap of venous structures.

arterial and venous attenuation was also investigated using the unpaired Student's *t*-test. Values for each patient were expressed as the mean $\pm$ SD. Sex distribution for the two protocols was analysed with the χ^2 test. The Mann-Whitney *U* test was used for qualitative assessment. Probability values of less than 0.05 were considered significant.

Results

Patient characteristics and scan parameters were not significantly different between Groups A and B (Table 1).

When images of the carotid artery were assessed, Group A contained three patients with ICA occlusion and one with near occlusion, whereas Group B contained two patients with ICA occlusion and two with near occlusion. Consequently, measurements of arterial enhancement were hampered in 10 segments in images from Group A and in 11 segments in images from Group B because of the occlusion or severe narrowing of the arterial lumen. Dental-filling artefacts hampered analysis in 2.7% (10/364) of all measurements in Group A and in 2.8% (12/429) of all measurements in Group B.

When images of the vertebrobasilar artery were assessed, no patient had BA occlusion. Severe narrowing of the arterial lumen in vertebrobasilar artery hampered analysis in 4.3% (6/140) of all segments in Group A and in 6.7% (11/165) of all segments in Group B.

Quantitative and qualitative measurements of arterial enhancement

Table 2 demonstrates that the mean arterial attenuation value in the aortocarotid artery did not show a significant difference ($p=0.78$) between Group A (431 ± 72 HU) and Group B (436 ± 57 HU). Furthermore, the mean arterial attenuation value in the vertebrobasilar artery showed

no significant difference ($p=0.84$) between Group A (390 ± 61 HU) and Group B (393 ± 54 HU). Likewise, qualitative assessment of arterial enhancement in the aortocarotid ($p=0.84$) and vertebrobasilar arteries ($p=0.36$) showed no differences between groups (Table 3).

Quantitative assessment at the central vein and qualitative assessment at the subclavian vein

Table 2 demonstrates a significant difference between Groups A and B in venous attenuation at four points. In addition, the mean venous attenuation value in the central vein was significantly lower in Group B (289 ± 154 HU) than in Group A (462 ± 244 HU; $p=0.002$). Table 3 shows that perivenous artefacts at the subclavian vein were significantly less severe in Group B than in Group A when assessed using either source axial images or MIP images.

Discussion

The removal of under-used CM in the cardiovascular system by SF allows the reduction of perivenous artefacts from the brachiocephalic vein and superior vena cava, but the necessary CM volume for cerebrovascular CTA remains controversial [11]. In the study by Awai et al [12], approximately 20–30 ml of CM was unused after termination of CM injection in humans, with about 10–20 ml in the dead space between the brachial vein and the superior vena cava and 10 ml between the power injector and catheter inserted into the antecubital vein. On the basis of these data, the optimal volume of SF was assumed to be approximately 25 ml. However, the present study shows that 40 ml of SF after injection of CM can reduce the high attenuation of the subclavian vein, resulting in better visualisation of the right subclavian artery on post-processed MIP images. When perivenous artefacts in the subclavian vein hamper the

Table 1. Patients' characteristics and scan parameters

	Group A	Group B	p-value
No. of patients	28	33	
Sex (male/female)	24/4	24/9	0.35
Age (years)			0.78
Mean	70.3 ± 9.3	69.7 ± 7.5	
Range	4–87	60–84	
Body weight (kg)			0.72
Mean	61.7 ± 8.5	60.9 ± 7.4	
Range	47–86	50–75	
Height (cm)			0.74
Mean	162.0 ± 6.5	161.4 ± 6.6	
Range	152–170	145–170	
Tc (s)			0.55
Mean	19.9 ± 4.2	19.3 ± 2.8	
Range	14–28	16–24	
Sd (s)			0.17
Mean	3.0 ± 0.2	2.9 ± 0.3	
Range	2.6–3.5	2.5–3.3	
TI _{ICA-SS} (s)			0.63
Mean	6.8 ± 1.3	7.3 ± 1.3	
Range	4–10	6–10	
TI _{ICA-BA} (s)			0.92
Mean	1.0 ± 1.2	1.0 ± 1.3	
Range	0–4	0–6	

Tc, time to peak enhancement at the circle of Willis; Sd, scan duration; TI_{ICA-SS}, time interval between peak enhancement at the internal carotid arteries and that at the sigmoid sinus; BA, basilar artery.

evaluation of the subclavian artery on MIP images, additional evaluation using thin-slice source images and multiplanar reformation images may be needed. If the subclavian artery is clearly recognised with small venous attenuation of the subclavian vein, additional evaluation using thin-slice source images is unnecessary. We believe that additional viewing of source images can be omitted for arterial images with minimal venous overlap (Figure 3), and this was effective for post-processing volume rendering images and segmentation.

In both the group injected with 25 ml of SF and that injected with 40 ml of SF, residual CM remained mainly in the thoracic outlet area between the costoclavicular

space and lateral border of the first rib at the right subclavian vein. To our knowledge, no reports in the English language literature explain this phenomenon. We considered several reasons from the anatomy and characteristics of CM relative to blood.

First, the influence of the venous valve and curved shape of the subclavian vein are noted. There are several reports of central venous stenosis or occlusion in the thoracic outlet area, without a history of previous central venous catheter placement, in patients with haemodialysis [13, 14]. Stenoses through the central veins cause fibrosis and thickening of the venous valves under long-term pressure due to arterial flow.

Table 2. Mean attenuation value at each position in the arterial and venous systems

	Group A	Group B	p-value
Arterial system			
Aorto-carotid artery			
Aortic arch	433 ± 63	440 ± 52	0.63
Proximal common carotid artery	413 ± 65	412 ± 66	0.97
Distal common carotid artery	469 ± 76	471 ± 71	0.92
Proximal ICA	447 ± 76	460 ± 70	0.47
Distal ICA	436 ± 75	447 ± 67	0.60
ICA at the cavernous sinus	417 ± 84	424 ± 68	0.74
ICA at the communicating segment	380 ± 82	372 ± 65	0.70
Vertebrobasilar artery			
Proximal vertebral artery	383 ± 64	372 ± 56	0.51
Distal vertebral artery	416 ± 63	427 ± 59	0.46
Distal basilar artery	360 ± 71	360 ± 69	0.97
Venous system			
Superior vena cava	150 ± 118	99 ± 31	0.03
Right brachiocephalic vein	185 ± 123	130 ± 48	0.03
Right subclavian vein	600 ± 314	361 ± 190	0.001
at the costoclavicular space			
Right subclavian vein	912 ± 637	552 ± 465	0.02
lateral the first rib			

ICA, internal carotid artery.

Table 3. Qualitative assessment of the arterial and venous images

	Group A	Group B	p value
MIP images			
Arterial images			
Carotid artery	3.9 ± 0.4	3.9 ± 0.4	0.84
Vertebrobasilar artery	3.7 ± 0.6	3.8 ± 0.5	0.36
Venous images			
Overlap between subclavian vein and subclavian artery	3.1 ± 1.1	2.4 ± 0.9	0.005
Axial images			
Perivenous artefact at subclavian vein	3.2 ± 1.0	2.3 ± 0.9	0.001

MIP, maximum intensity projection.

Second, we considered the muscular and skeletal anatomy of the costoclavicular space. The costoclavicular space is an anatomically tight passageway between the clavicle on the upper side, the first limb on the lower side and the costoclavicular ligament at the inner boundary. The subclavian vein descends into the thoracic inlet through this narrow costoclavicular space [15]. Venous thoracic outlet syndrome, which includes both thrombotic and non-thrombotic subclavian vein compression, is thought to result mainly from severe compression within the narrow costoclavicular space [16].

Third, the different characteristics of highly concentrated CM and saline are noted: there are substantial differences in gravity, viscosity and osmolarity. In one angio-model phantom study, flushing saline flowed through CM on the upper side while pushing SF into the CM in the connecting tube, and a small amount of CM was retained on the lower side [17]. The author concluded that this was because the gravity and viscosity of CM are higher than those of saline. We agree with this hypothesis, and this phenomenon was confirmed by clinical images at the subclavian vein. In addition, differences in the gravity, viscosity and osmolarity of moderately and highly concentrated CM might have an effect [18]. If moderately concentrated CM (300 mg I ml⁻¹) is used with the same iodine flux, the perivenous artefacts may be smaller than those in this study.

Despite being a retrospective study, Groups A and B showed no difference in patient characteristics: sex, age, body weight and height. When individual circulation and cerebral haemodynamics were considered, Tc, TI_{ICA-SS} and TI_{ICA-BA} also showed no differences between the groups. The mean Tc was approximately 20 s and mean sd was approximately 3 s; therefore, the mean scanning delay [(Tc+4)-sd] was 21 s. In Group A, the injection durations for CM and SF were 10 s and 6 s, respectively. In Group B, the injection durations for CM and SF were 10 s each. Consequently, Group A had 5 s and Group B had 1 s of waiting time before CT acquisition began. We considered that this difference of 4 s could induce the differences in venous attenuation in the central vein and perivenous artefacts at the subclavian vein. Mean TI_{ICA-SS} was approximately 7 s, and intracranial circulation did not differ between the groups as is consistent with the literature [11]. Mean TI_{ICA-BA} was approximately 1 s. TI_{ICA-BA} ranged from 0 to 2 s in most patients, but in a patient with near occlusion caused by slow arterial flow on the affected ICA, TI_{ICA-BA} was 6 s. Even for a small volume of CM administered at a high injection rate and a fast acquisition scan using the new 256- or 320-MDCT system, this result might

demonstrate that an injection duration of at least 6 s is required for adequate arterial attenuation in cervical CTA.

The present study has several limitations. First, the two groups were not randomly allocated and this was a retrospective study. Further studies are required to validate the present results prospectively. Second, we decided to use 40 ml of SF in Group B, mainly because the package was labelled as containing 50 ml. Because the maximum volume of this package was 60 ml, we decided to use 40 ml of SF in the CTA and 15 ml of SF in the test injection.

Conclusion

CTA followed by 40 ml of SF enables better visualisation of the subclavian artery and minimal venous overlap in comparison with CTA followed by 25 ml of SF.

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