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Optimisation of contrast medium volume and injection-related factors in CT pulmonary angiography: 64-slice CT study

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Abstract

Objective To compare the image quality of computed tomography pulmonary angiography (CTPA) obtained with the injection of various low doses of contrast medium (CM) with different injection-related factors. **Methods** A total of 90 patients (42 females, 48 males; 54.3 ± 18.6 years) undergoing CTPA were included. Three CM protocols, each containing 30 patients, were created. Protocols 1, 2 and 3 consisted of a CM of 60 ml, 55 ml and 50 ml, and a bolus trigger level of 120 HU, 90 HU and 75 HU, respectively. Injection was uniphasic for protocols 1 and 2 (flow rate 5 ml/s), and biphasic for protocol 3 (flow rates 5 and 4 ml/s); with saline flushing afterwards. Enhancement was measured in three central and six peripheral pulmonary

arteries. **Results** The mean attenuation value for pulmonary arteries was over 250 HU for all protocols. There was no difference between the attenuation levels with the protocols ($p > 0.05$). The percentage of pulmonary arteries exceeding optimal attenuation (≥ 250 HU) showed that protocols 2 and 3 were 90–100% successful ($p < 0.05$). **Conclusion** The use of proper injection-related factors during CTPA, such as a low trigger level and a high flow rate with saline injection following a decreased CM volume (55 ml or 50 ml), will enable adequate pulmonary artery contrast enhancement.

Keywords Computed tomography · Pulmonary embolism · Pulmonary artery · Computed tomography angiography · MSCT

Introduction

Computed tomography pulmonary angiography (CTPA) is a routine technique used safely for the diagnosis of patients suspected of having pulmonary embolism [1–3]. The purpose of this technique is to determine an attenuation difference between the pulmonary artery and the thrombus to ensure that the thrombus is directly visible by increasing the enhancement in the pulmonary arteries by means of contrast medium (CM). An adequate amount of contrast enhancement in the pulmonary arteries is therefore essential for the success of CTPA and is affected by many factors such as the CT device, CM injection-related factors and volume [1, 4–13]. One of the goals during CTPA is to achieve

maximum enhancement using minimum CM, as this can help reduce CM-induced side effects as well as prevent the economic burden of this increasingly popular method [14].

Our hypothesis in this prospective study was that optimal enhancement of the pulmonary arteries can be achieved by decreasing the CM volume used in CTPA acquired with 64-slice CT scanner. Therefore, we created three different CM protocols, each containing different injection-related factors suitable for decreased CM volumes in the CTPA performed with 64-slice CT. We then investigated the effects on enhancement and optimal enhancement both in the central and peripheral pulmonary arteries, and the effects on the global image quality.

Materials and methods

Patient populations

A total of 90 patients (22 female, 48 male; mean age, 54.3 ± 18.6 years) who applied to our CT unit with suspected pulmonary embolism and underwent CTPA between January 2009 and July 2009 were included. Known allergy to contrast medium, renal insufficiency, pregnancy and age under 18 years were considered contraindications for participating in the study. Before the examination, informed consent was obtained from the participants of this prospective study that had the approval of the Institutional Review Board.

CTPA

All imaging was performed by 64-slice CT (Aquilion 64, Toshiba Medical Systems, Otowara, Japan) with the automatic dose modulation technique (Real Exposure Control, Toshiba Medical System). Patients were examined in a supine position with both arms extended above the head. The CTPA was obtained in the caudocranial direction and imaging length ranged from the level of the diaphragm to the lung apices. A standard collimation of 0.5 mm was used with a gantry rotation speed of 0.5 s, and a pitch factor of 0.8. For post-processing, thin-slice reconstruction was performed with a slice thickness of 0.5 mm, and an increment of 0.3 mm.

CM administration

Following the CM with a concentration of 300 mg iodine per millilitre administration, 20-ml saline injection was performed by a dual-head power injector. The type (peripheral or central venous line) and side (left or right arm) of the peripheral venous access site were noted. The imaging delay for the individual contrast optimisation was based on a bolus tracking technique (Sure Start, Toshiba Medical System) in the main pulmonary artery (MPA) using different trigger levels for each protocol. For this purpose, a single unenhanced low-dose CT was first obtained at the MPA level for use as the reference image. A region of interest (ROI) was then set in the lumen of the MPA (by a CT technologist) on the basis of this image. A series of

dynamic low-dose monitoring images were obtained to measure early enhancement 2 s after initiation of the CM injection. The patient was instructed to hold his/her breath as soon as the signal density in this ROI reached exact threshold values (bolus trigger time) and the patient was prepared for the CT data acquisition while the CT table moved. This transit time took 2–4 s depending on the distance needed for the CT table to move from the level used for bolus tracking. Finally, the delay before initiating the CT data acquisition (which is from the start of the CM injection to the start of the diagnostic investigation) was calculated as the sum of the bolus trigger time plus the transit time, and the total imaging time to cover the entire thorax was calculated using the delay period plus the duration of the CT data acquisition.

The patients were allocated into three groups and a different CM protocol (1, 2 or 3) was implemented in each group of 30 patients (Table 1).

Image interpretation

Quantitative CT image analysis

All CT were loaded on a clinical workstation (Vitrea 2 version 4.0 Workstation, Toshiba Medical Systems, Japan) for the post-processing of the volumetric MSCT data sets. Measurements were performed by a radiologist (S.U.R. with 10 years' experience in interpreting CT images of the chest), who was blinded to the patient groups.

Imaging length was determined by the distance between the table positions of the first and the last slices. Quantitative analysis was performed with ROI measurements in the axial MIP images at 0.5-mm slice thickness after investigating thrombus presence in the central and segmentary pulmonary arteries. Attenuation measured along the following vessels: central pulmonary arteries [MPA, right pulmonary artery (RPA), left pulmonary artery (LPA)], peripheral pulmonary arteries [right upper lobe artery (RULA), right middle lobe artery (RMLA), right lower lobe artery (RLLA), left upper lobe artery (LULA), left lingular artery (LLA), left lower lobe artery (LLLA)], ascending aorta and subclavian vein.

An ROI cursor covering nearly the whole vessel diameter in the axial images (Fig. 1) was placed by a radiologist (S.U.R.). The mean attenuation was recorded for each measurement. Measurement was limited to

Table 1 CM protocols applied to the patients included in the study

CTPA protocol	CM amount ^a	Total iodine dose	CM flow rate	Iodine flow rate	Total (CM + saline) injection time	Bolus tracking trigger level
Protocol 1	60 ml	18 g	5 ml/s	1.5 g I/s	16 s (12 + 4 s)	120 HU
Protocol 2	55 ml	16.5 g	5 ml/s	1.5 g I/s	15 s (11 + 4 s)	90 HU
Protocol 3	50 ml	15 g	First 25 ml at 5 ml/s the remaining 25 ml at 4 ml/s	1.5 g I/s and 1.2 g I/s	16.3 s (11.3 + 5 s)	75 HU

^aCM with 300 mg I/ml iodine concentration was administered in all three protocols and 20-ml saline flushing was performed following the CM injection

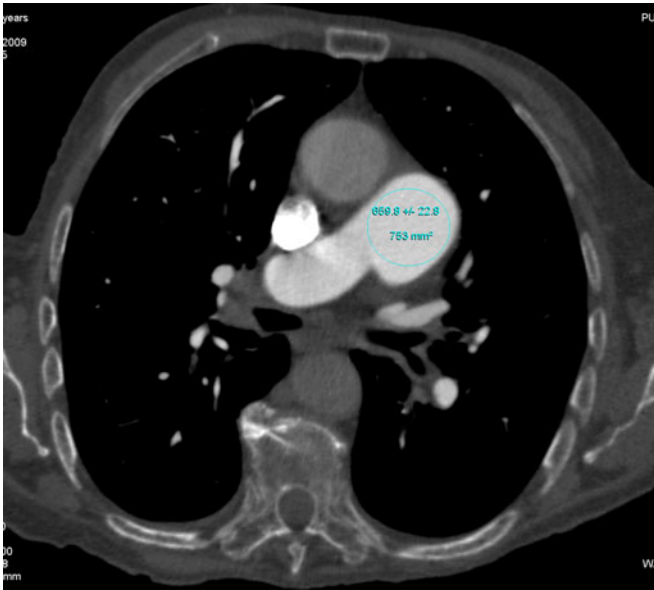


Fig. 1 Density measurement from MPA in the axial MIP image at 0.5-mm slice thickness

unaffected vessels if pulmonary embolism was present. It has been reported that the optimal attenuation value should exceed 250 HU in the MPA to achieve diagnostic adequacy in a CTPA [4]. The success of the attenuation values of three central and six segmentary pulmonary arteries in exceeding 250 HU was, therefore, investigated in order to objectively analyse the adequacy of each protocol. While performing this comparison, individual analyses were performed for each of the three central pulmonary arteries and a total comparison was made by adding those with attenuation values exceeding 250HU and those with attenuation values lower than 250 HU for each protocol in six segmentary pulmonary artery branches.

Qualitative CT image analysis

A subjective evaluation was performed by two radiologists (P.N.K. with 15 years' experience in chest CT and S. U.R.). The radiologists had no previous knowledge of the injection protocol used and they independently graded the studies for perivenous artefacts and subjective image quality.

Evaluation of the perivenous artefacts associated with dense CM was performed in the superior vena cava (SVC) on axial MIP images with 0.5-mm slice thickness. For evaluation, perivenous artefacts adjacent to the SVC were graded using a four-point scale: grade 0 (no artefact), grade 1 (negligible artefacts), grade 2 (moderate artefacts but all vessel portions diagnostic), and grade 3 (severe or extensive artefacts that might lead to misinterpretation in some vessel portions).

Final subjective global image quality with regard to pulmonary vessel contrast was based on axial and coronal

MIP images with a slice thickness of 10 mm. A three-point scale (1 non-diagnostic, 2 diagnostic and 3 excellent) was applied for evaluation of subjective image quality (Fig. 2).

Statistical analysis

Statistical analysis was performed using the SPSS for Windows, version 15.0, statistical package. Relations between the categorical variables were analysed with the chi-square test. Age, weight, and difference in the imaging lengths between the protocols were detected with one-way analysis of variance following Tukey's HSD test. Pearson's correlation coefficient was used to determine the association between the continuous variables. The relationship between the attenuation values and the protocols (adjusted by weight) was

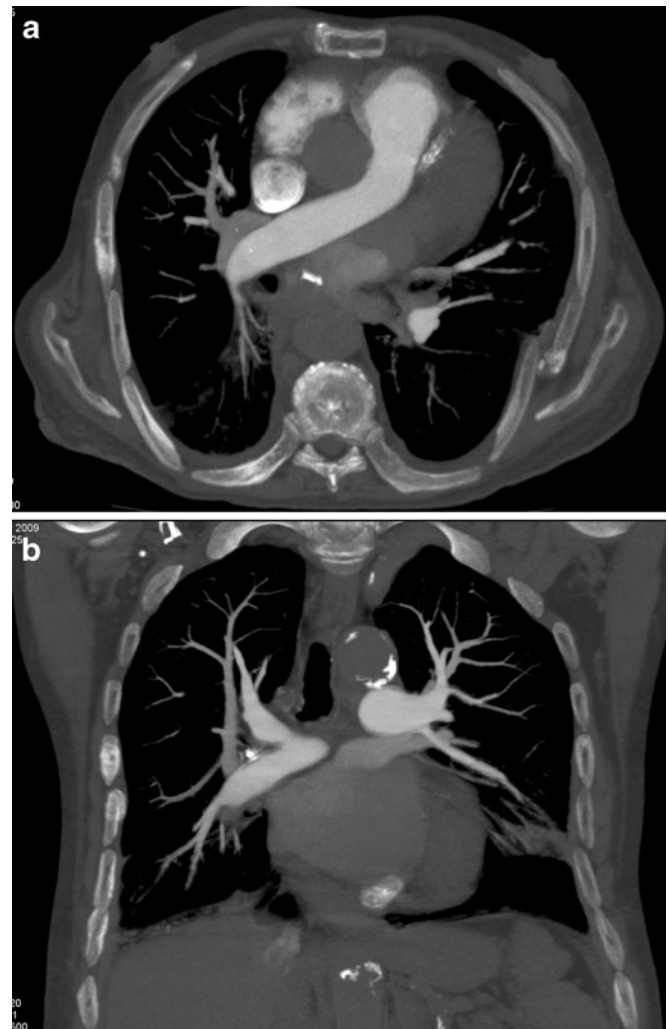


Fig. 2 An example of a subject (male patient at the age of 67 referred by the emergency unit) interpreted as "excellent" in the global image scoring in axial (a) and coronal (b) MIP images at 10-mm slice thickness

Table 2 Investigation of the demographic characteristics of the patients, imaging length, thrombus presence, type of venous access through which the CM was administered for each group and the statistical differences in these definitive parameters among the groups (*SD* standard deviation, *n.s.* not significant)

Characteristic	Protocol 1	Protocol 2	Protocol 3	<i>p</i> value
Total number of the patients (females/males)	30 (15/15)	30 (11/19)	30 (16/14)	n.s.
Mean age (\pm SD) year	57.7 \pm 15.5	54.2 \pm 20.0	50.9 \pm 19.8	n.s.
Mean body weight (\pm SD) kg	77.9 \pm 12.5	69.2 \pm 13.0	63.9 \pm 14.8	0.001 ^a
Imaging length (cm)	251.3 \pm 45.6	268.1 \pm 38.6	263.2 \pm 44.0	n.s.
Thrombus occurrence				
Present	7	2	3	n.s.
Absent	23	28	27	
Venous access				
Peripheral (right/left arm)	25/5	25/5	27/1	n.s.
Central	0	0	2	

^aStatistically significant

investigated with multivariate analysis of covariance. Interobserver agreement was verified with Spearman's correlation coefficient. A *p* value less than 0.05 was considered significant.

Results

CTPA was performed without complications in all patients, and none of the studies had to be repeated.

Patient characteristics

Demographic characteristics of the patients are listed in Table 2. Mean imaging delay time, mean imaging duration, and mean total imaging time of the protocols are shown in Table 3. CM venous access was obtained from the peripheral venous line [from the right arm in 77 patients and left arm in 11 patients] in 88 (97.8%) patients while it was achieved from the central catheter in two (2.2%) patients. Pulmonary embolism was present in 12 patients (13.3%), while it was not detected in 78 patients (86.7%).

No difference was detected between the patients in the three protocols in terms of age, sex, venous CM access, the side the access was achieved if it was performed via the peripheral venous route, imaging length, and thrombus presence (Table 2). However, the mean weight of the patients in the third group was lower than that of the other two groups ($p=0.001$). Therefore, we compared the differences in attenuation values in the measured vessels among the protocols taking weight into account.

Table 3 Mean imaging delay time, mean imaging duration and mean total imaging time for three protocols (the imaging delay time was calculated as the sum of the bolus trigger time plus the transit

	Protocol 1 mean (min–max)	Protocol 2 mean (min–max)	Protocol 3 mean (min–max)
Imaging delay time (s)	8.5 (7.0–10.2)	8.0 (6.4–9.7)	7.2 (5.8–7.7)
Imaging duration (s)	5.0 (4.6–5.6)	5.1 (4.4–5.7)	4.9 (4.7–5.4)
Total imaging time (s)	13.5 (11.6–15.8)	13.1 (10.8–15.4)	12.1 (10.5–13.1)

Image interpretation

Quantitative CT image analysis

Mean attenuation values of the measured pulmonary arteries, ascending aorta and subclavian vein are summarised in Table 4. Mean pulmonary artery attenuation values were well over 250 HU in all three protocols. No difference was detected among the three groups when mean attenuation values in each protocols were compared taking weight into consideration ($p>0.05$).

The weight of the patient was found to be an effective parameter for enhancement in all pulmonary arteries ($p<0.007$) and it was inversely proportional to the enhancement levels ($r=-0.36$, $p<0.001$). However, other characteristics of the patients, such as age, sex, location of venous access, imaging length and thrombus presence, did not have any effect on enhancement in the pulmonary arteries ($p>0.05$). CM protocol type, or the other demographic characteristics of the patients did not have any effect on the enhancement of the ascending aorta and the subclavian vein ($p>0.05$).

The success rates when the criterion to get an adequate CTPA was accepted as achieving an attenuation level of 250 HU or over for the pulmonary arteries are summarised in Table 5. The higher number of patients displaying optimal enhancements in MPA, RPA and LPA in protocols 2 and 3 was statistically significant ($p=0.024$, $p=0.006$ and $p=0.010$, respectively). When peripheral pulmonary arteries were examined, a total of 180 segmentary pulmonary artery attenuation values were measured in each protocol. Areas of optimal enhancement in the segmentary arteries were found in 148 (82%), 169 (94%) and 173 (96%) patients in protocols 1, 2 and 3, respectively. The higher optimal enhancement rates in protocols 2 and 3 were statistically significant ($p<0.001$) (Table 5).

time, and the total imaging time was calculated using the imaging delay time plus imaging duration)

Table 4 Mean, minimum (*min*) and maximum (*max*) enhancements in nine pulmonary arteries, an ascending aorta and a subclavian vein, and the *p* values indicating the statistical relation between these attenuation values in the protocols (MPA main pulmonary

artery, RPA right pulmonary artery, LPA left pulmonary artery, RULA right upper lobe artery, RMLA right middle lobe artery, RLLA right lower lobe artery, LULA left upper lobe artery, LLLA left lingular artery, LLLA left lower lobe artery)

Measured vessels	Vessel enhancement (HU)			<i>p</i> value
	Protocol 1 mean ± SD (min–max)	Protocol 2 mean ± SD (min–max)	Protocol 3 mean ± SD (min–max)	
MPA	390±144 (222–689)	401±102 (242–604)	386±97 (270–660)	n.s.
RPA	380±137 (218–652)	393±89 (238–562)	376±94 (253–662)	n.s.
LPA	382±145 (209–720)	395±101 (242–594)	367±98 (259–648)	n.s.
RULA	368±138 (210–712)	385±93 (210–579)	370±95 (250–678)	n.s.
RMLA	369±122 (210–646)	370±79 (202–538)	367±109 (209–652)	n.s.
RLLA	375±130 (202–714)	371±103 (208–601)	369±109 (251–665)	n.s.
LULA	374±133 (202–686)	385±97 (214–593)	360±117 (245–650)	n.s.
LLA	368±122 (223–646)	377±88 (220–557)	370±97 (233–648)	n.s.
LLLA	371±128 (202–647)	382±85 (254–569)	370±102 (242–693)	n.s.
Subclavian vein	946±748 (92–2,700)	7,376±521 (180–2300)	848±392 (287–1529)	n.s.
Ascending aorta	240±81 (75–407)	232±69 (60–345)	252±97 (40–422)	n.s.

Qualitative CT image analysis

No interobserver difference was detected between the two investigators in terms of SVC perivenous artefact and subjective image quality ($r=0.72$ and $r=0.63$, respectively; $p<0.001$).

Perivenous artefact of SVC could not be evaluated in two subjects in protocol 3 because of central venous catheter usage. A perivenous artefact was observed in 24 (80%), 24 (80%) and 26 (90%) patients in protocols 1, 2 and 3, respectively (Table 6). However, none of these artefacts affected the evaluation of the pulmonary artery. No statistical difference was detected among the three groups in the comparison performed for perivenous artefact ($p=0.090$).

None of the examinations was evaluated as non-diagnostic in the subjective global image quality evaluation (Table 7). Image quality was evaluated as diagnostic in 21 (23%) patients and excellent in 69 (77%) subjects. Subjective image quality was better in protocols 2 and 3 than in protocol 1 ($p=0.009$).

Discussion

CTPA has now become an examination with high sensitivity and specificity that is widely used in patients with suspected pulmonary embolism [1, 2, 15–17]. The conspicuity of the thrombus during evaluation of CTPA depends on the density difference between the thrombus

and the contrast-enhanced pulmonary artery. The significance of the enhancement level in the pulmonary arteries has, therefore, led to the requirement for creating various CTPA protocols according to CT technology [5, 7–9, 16]. The CTPA protocols in the literature generally belong to the 16-slice and older CT scanners and these protocols cannot be transferred directly to examinations performed with 64-slice CT. The short imaging duration of CTPA with 64-slice CT (4.4–5.7 s in our study) indicates the requirement for arranging the CM protocols accordingly. Additionally, the common view of the authors is that 64-slice CT examination can be performed using less CM without compromising arterial enhancement, although there are limited experiments with 64-slice CT [4, 6].

Various patient-related factors, such as weight, age, sex and imaging length, were investigated by different authors [4, 6, 15, 16, 18–20]. Similar to our study, enhancement in the pulmonary arteries was found to be negatively affected by the patient's weight in most of these studies [4, 6, 16, 18, 21]. The effect of patient age on the pulmonary arterial enhancement is controversial and this effect has not been demonstrated in many studies including ours [4, 6]. Similar to our study, an affect of sex and imaging length on the pulmonary arterial enhancement is not found in most studies [4, 6, 18, 19].

CM injection-related factors are another group that may affect pulmonary arterial enhancement [5, 19]. The level of enhancement is determined by the number of iodine molecules given to the patient in a second, indicated by the flow rate rather than the iodine concentration of CM

Table 5 Success of the examination in the three protocols according to the central (MPA, RPA, and LPA) and peripheral (segmentary) pulmonary artery attenuation values

Protocols	Attenuation values							
	MPA (<i>n</i> =90)		RPA (<i>n</i> =90)		LPA (<i>n</i> =90)		Segmentary arteries	
	≥250 HU	<250 HU	≥250 HU	<250 HU	≥250 HU	<250 HU	≥250 HU	<250 HU
Protocol 1	25 (83%)	5 (17%)	24 (80%)	6 (20%)	24 (80%)	6 (20%)	148 (82%)	32 (18%)
Protocol 2	27(90%)	3 (10%)	29 (97%)	1 (3%)	28 (93%)	2 (7%)	169 (94%)	11 (6%)
Protocol 3	30 (100%)	0 (0%)	30 (100%)	0 (0%)	30 (100%)	0 (0%)	173 (96%)	7 (4%)

Table 6 Distribution of the perivenous artefact observed in the SVC according to the 3 protocols

PROTOCOLS	SVC perivenous artefact				Total
	No artefact	Negligible artefact	Moderate artefact	Severe artefact	
Protocol 1	6 (20%)	9 (30%)	11 (37%)	4 (13%)	30 (34.1%)
Protocol 2	6 (20%)	14 (47%)	10 (33%)	0	30 (34.1%)
Protocol 3	2 (7%)	11 (39%)	11 (39%)	4 (15%)	28 (31.8%) ^a

^a Subclavian artefact scoring was not performed in the two subjects included in protocol 3 as CM was administered via the central catheter route in them

[16, 18, 19]. In general, researchers found that a flow rate of 4 ml/s (3–5 ml/s) was sufficient for CTPA [4, 6, 14, 18, 22–24]. Increasing the flow rate shortens the time required to reach optimal enhancement in the pulmonary arteries [5, 16]. This requires the CTPA to be performed faster. Kim et al. [25] demonstrated that higher peak contrast enhancements in pulmonary arteries are achieved but the contrast enhancement plateau does not last long when using higher flow rates of CM, and capturing this period with the CT is more difficult [16]. However, capturing this short period has become easier with the use of the bolus tracking method in 64-slice CT. Consequently, adequate pulmonary arterial enhancements for CTPA were achieved in each protocol with high flow rate as a result of the imaging in our study.

Multiphasic injection protocols help uniform aortic contrast enhancement in CT angiography [5, 26, 27]. The aim of using the biphasic injection in protocol 3 was to provide homogeneous enhancement in the pulmonary arteries and prolong the injection time, because of the risk of the short injection time of 50 ml compared with the imaging duration. The fact that enhancement of the pulmonary arteries was greatest in protocol 3 can be related to achieving homogeneous enhancement in both central and peripheral pulmonary arteries with biphasic injection.

If the imaging delay time is not suitable, no matter at what flow rate CM was administered, it will either cause the CT to start before or after adequate CM reaches the pulmonary arteries. As a result, it is concluded that determining this time individually would be more suitable, as the time differs according to the CT technology, CM flow rate, and from person to person [5, 16, 18, 28]. The bolus-tracking technique is one of the methods developed to determine this time [16, 17, 29]. The bolus trigger level varies, depending on the CT used for CTPA, such as 100 HU in four-slice CT [19], 100–150 HU in 16-slice CT, and 150 HU in 64-slice CT [4]. The reason for raising the trigger level as CT technology advances is to allow the imaging to start later in order to achieve maximal enhancement time because of the reduction in the imaging duration of the CT [4, 28]. However, pulmonary arterial

attenuation levels well over 250 HU were achieved with lower trigger levels (120, 90, and 75 HU) in our study. We believe these areas of high enhancement were achieved by using a combination of low trigger levels and high flow rates in the CTAPs performed with 64-slice CT. Therefore, the CT data acquisition is often complete before most of the administered CM has left the pulmonary system and passes into the systemic circulation with this technique in our study. The fact that the mean ascending aorta attenuation was lower than the pulmonary artery attenuation in each of the three protocols supports this theory.

The CM volume used for CTPA has been reported to be 80–150 ml [4, 6, 14]. When we consider that the imaging duration drops below 5 s in examinations performed with 64-slice CT, reducing the CM volume is essential in CTPA. Therefore, a decrease of 50–60% was achieved in the iodine dose in our study. Performing a saline flush following the CM pushes the CM located in the upper arm and SVC towards the heart and a more effective use of the CM is, therefore, achieved with this method [5, 14, 30–32]. In our study, saline flush was performed following the CM injection in all protocols. Moreover, high density levels in the subclavian vein in all three groups indicate that CM passage continues in the subclavian vein during the CTPA. The CM volume can be reduced even more, therefore, when using 64-slice CT for CTPA.

Various authors have assumed different values, such as 200 HU, 250 HU and 300 HU, for optimal enhancement levels for CTPA to be an adequate examination [4–6, 18]. All three protocols produced adequate results when the optimal pulmonary artery enhancement limit was 250 HU. Protocols 2 and 3 were more successful in achieving optimal enhancements in pulmonary arteries compared with protocol 1. This result indicates that preferring protocols 2 or 3 in CTPA performed with 64-slice CT will increase the success of the imaging regarding pulmonary artery enhancement. In parallel to this finding, the subjective image qualities of protocols 2 and 3 were better than that of protocol 1.

Saline injection helps not only in reducing the CM volume but also decreases the perivenous artefact around

Table 7 Results of the subjective image quality evaluation in the three protocols

PROTOCOLS	Subjective image quality			Total
	Non-diagnostic	Diagnostic	Excellent	
Protocol 1	–	12 (41%)	18 (60%)	30 (33.3%)
Protocol 2	–	2 (7%)	28 (93%)	30 (33.3%)
Protocol 3	–	7 (23%)	23 (77%)	30 (33.4%)
Total	–	21 (23%)	69 (77%)	90 (100%)

the SVC. We detected no difference among the three protocols in terms of the artefacts observed around the SVC. This finding, which is slightly higher than in other similar studies, may be related to the short imaging delay time [5, 30–33].

Conclusion

In conclusion, in our experience the use of proper injection-related factors during CTPA with 64-slice CT,

such as a low trigger level (90 HU or 75 HU) and a high flow rate (5 ml/s, or 5 ml/s and 4 ml/s) with 20-ml saline injection following a decreased CM volume (55 ml or 50 ml) will enable adequate pulmonary artery contrast enhancement in the central and peripheral arteries. Using these two protocols for CTPA examination helps reduce CM side effects, such as allergic reactions and renal toxicity, and the costs of the examination.

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