Effect of Contrast Timing, Volume, and Flow Rate on Image Quality of Pulmonary Arteries in CTA

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Purpose To evaluate the effect of contrast timing, contrast volume, and contrast flow rate on the image quality of pulmonary arteries in computed tomography angiography (CTA) and to assess if bolus-tracking region of interest (ROI) positioning in the left atrium, which is used for triple-rule-out CTA, allows for sufficient depiction of the pulmonary arteries.

Methods In this retrospective single-center study, data were collected for patients who underwent thoracic CTA during a specific period. Two groups of 121 patients each were created based on bolus-tracking ROI positioning in the main pulmonary artery or left atrium using propensity score matching. Image quality of the pulmonary arteries was evaluated using quantitative and qualitative scores. Subgroups were formed to examine the influence of contrast volume and flow rate. Two radiologists determined if pulmonary embolism was present, if pulmonary embolism could be excluded with certainty, and from which level pulmonary embolism could be excluded with certainty. Interrater reliability also was evaluated.

Results ROI positioning in the main pulmonary artery scored significantly higher compared with the left atrium. There was no significant difference in subgroups of patients who were examined with 60 mL or more contrast volume and less than 4 mL/s flow rate; scores were similar or better than in the overall study population. Pulmonary embolism was not able to be excluded with certainty for each 1 patient in these subgroups compared with a high percentage in the overall study population.

Discussion ROI positioning in the left atrium in combination with the 60 mL or more contrast volume and less than 4 mL/s flow rate does not adversely affect depiction of the pulmonary arteries compared with conventional ROI positioning in the main pulmonary artery.

Conclusion When using 60 mL or more contrast volume and less than 4 mL/s flow rate, ROI positioning in the left atrium, which is used in triple-rule-out CTA, is sufficient for the assessment of pulmonary arteries.

Keywords | *computed tomography angiography, pulmonary artery, pulmonary embolism, signal:noise ratio, propensity score*

Multiple factors contribute to the quality of computed tomography angiography (CTA) imaging. Contrast volume, contrast flow rate, and the timing of contrast injection are important variables that need to be adapted to achieve optimal contrast filling based on patients' heart rate and cardiac output. Several studies evaluated contrast timing for computed tomography pulmonary angiography,[1] and a level of 210 HU was determined an acceptable enhancement of the central pulmonary arteries.[2] After motion artifacts, poor contrast enhancement was found to be the major cause of indeterminate computed tomography pulmonary angiography.[3]

Test-bolus and bolus-tracking techniques are commonly used methods in CTA. For bolus tracking in computed tomography pulmonary angiography, the region of interest (ROI) typically is placed in the main pulmonary artery. In triple-rule-out CTA, which is performed to evaluate coronary arteries, the aorta, and pulmonary arteries, the ROI usually is placed in the left atrium.[4]

A recent study showed that in regard to coronary arteries, excellent, comparable image quality can be achieved with ROI positioning in the left atrium or the ascending aorta. Furthermore, image quality of the pulmonary arteries has been shown to improve substantially when the ROI is positioned in the left atrium compared with the ascending aorta.[5] No study was found that compares image quality of the pulmonary arteries using ROI positioning in the left atrium vs the main pulmonary artery, and evidence is insufficient to support the routine use of triple-rule-out CTA to diagnose pulmonary embolism.[6]

The aim of this study was to evaluate the effect of contrast timing, contrast volume, and contrast flow rate on image quality of pulmonary arteries in CTA and to assess if bolus-tracking ROI positioning in the left atrium, which is used for triple-rule-out CTA, allows for sufficient depiction of pulmonary arteries.

Methods

This single-center study was approved by the local ethics committee at Technical University Dresden, which is registered as an institutional review board at the Office for Human Research Protections (registration number IRB00001473 and IORG0001076). Because of the retrospective design of this study, written informed consent was waived. This study was conducted from 2021 through 2022.

Study Population and Data Collection

Two groups were created based on the bolus-tracking ROI positioning. For group A, data were collected from patients who underwent CTA at the University Hospital Dresden with bolus-tracking ROI positioning in the main pulmonary artery between January 2015 and August 2020 on a third-generation dual-source computed tomography (CT) scanner (Somatom Force, Siemens Healthineers). For group B, data were collected from patients who underwent CTA with bolus-tracking ROI positioning in the left atrium in the same period on the same dual-source CT scanner.

Patients were examined in supine position. First, a scout view was performed to determine the relevant position to acquire a single axial slice, which allows for bolus-tracking ROI positioning in the respective vessel (see **Figure 1**). The ROI was then placed in the main pulmonary artery or in the left atrium. Iopromide (Ultravist 370, Bayer HealthCare) was applied intravenously followed by saline, using a dual-head injector. Five seconds (ROI placement in the main pulmonary artery) or 10 seconds (ROI placement in the left atrium) after the start of contrast injection, repetitive low-dose scans of the same axial slice were initiated and performed every 1.13 seconds. After the threshold of 100 or 120 HU, respectively, was reached in the determined ROI, data acquisition was started after a further

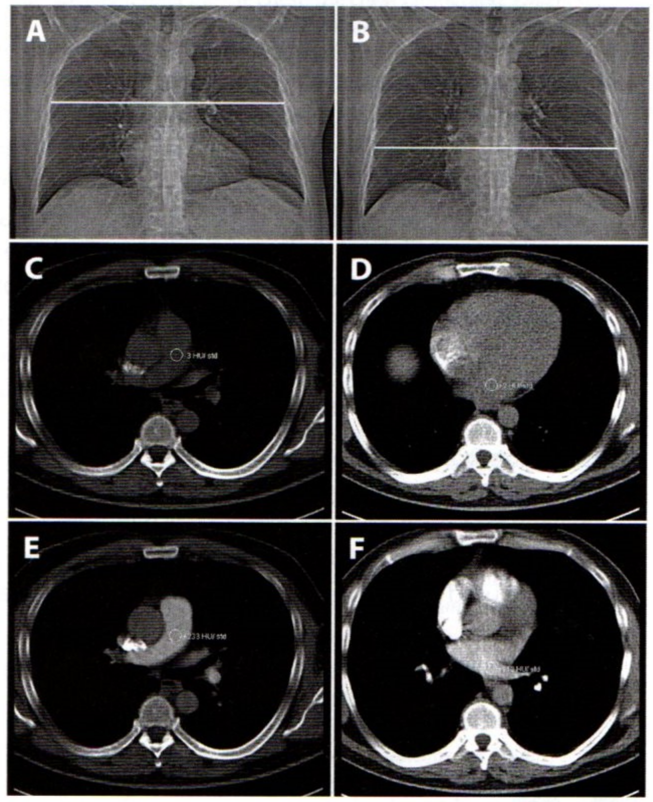

Figure 1. *Bolus-tracking technique with region of interest (ROI) in the main pulmonary artery (left column) and left atrium (right column). A. Selection of the slice for placement in the main pulmonary artery. B. Selection of the slice for placement in the left atrium. C. Placement of the ROI in the main pulmonary artery. D. Placement of the ROI in the left atrium E. Reaching of the threshold in the main pulmonary artery. F. Reaching of the threshold in the left atrium. Images courtesy of the Institute and Polyclinic for Diagnostic and Interventional Radiology, University Hospital Carl Gustav Carus, Technische Universität Dresden.*

delay of 5 seconds. In these 5 seconds, the patient table automatically moved into the starting position, and the patient was instructed to inhale and hold the breath. The required bolus-tracking software, CARE Bolus, was provided by the CT manufacturer (Siemens Healthineers). CARE Dose 4D (Siemens Healthineers) was used to adjust tube voltage, depending on physical characteristics of the patient.

A total of 321 patients fulfilled the inclusion criteria, including 189 patients with bolus-tracking ROI positioning in the main pulmonary artery and 132 patients with ROI positioning in the left atrium. In most of the examinations, ROI threshold was 100 or 120 HU. However, 11 patients with bolus-tracking ROI positioning in the left atrium were examined with an ROI threshold of 150 or 170 HU; they were excluded before matching was performed. To select pairs with similar characteristics to minimize the influence of covariates, propensity score matching[7] was performed using R software Version 4.0.3 and the matching package for R (R Foundation).[8,9] Pairs were matched according to sex, contrast volume, and contrast flow rate. The nearest-neighbor method was applied for contrast volume and contrast flow rate, whereas sex was matched exactly.[10] After propensity score matching, 121 pairs of patients (121 patients with bolus-tracking ROI positioning in the main pulmonary artery and 121 patients with bolus-tracking ROI positioning in the left atrium), composed of 156 males and 86 females with a median age of 65 years, were included in this study (see **Figure 2**).

Image Quality Analysis

Image quality of pulmonary arteries was assessed quantitatively, using signal intensity and signal:noise ratio (SNR), and qualitatively, based on a scoring system. SNR is defined as the quotient of the mean signal intensity and the standard deviation of signal intensity. SNR was evaluated by placing circular ROIs with a diameter of 10 mm in the right pulmonary artery and left pulmonary artery (see **Figure 3**). The mean value was calculated and set as the quantitative score.

To generate qualitative scores, 2 radiologists independently assessed the overall image quality of pulmonary arteries. One reader had 15 years of experience with CTA, and the other had 3 years of experience with CTA. Readers were blinded to the position of the ROI and used a 5-point Likert scale:

- 5 – perfect
- 4 – very good
- 3 – good
- 2 – poor
- 1 – insufficient

Image noise and vessel wall definition were evaluated to determine image quality (see **Figure 4**). If the scores differed between the readers, the final qualitative score was decided by consensus.

Pulmonary Embolism Analysis

For all CT examinations, each radiologist independently decided if pulmonary embolism was present and on which level (central, lobar, segmental, or

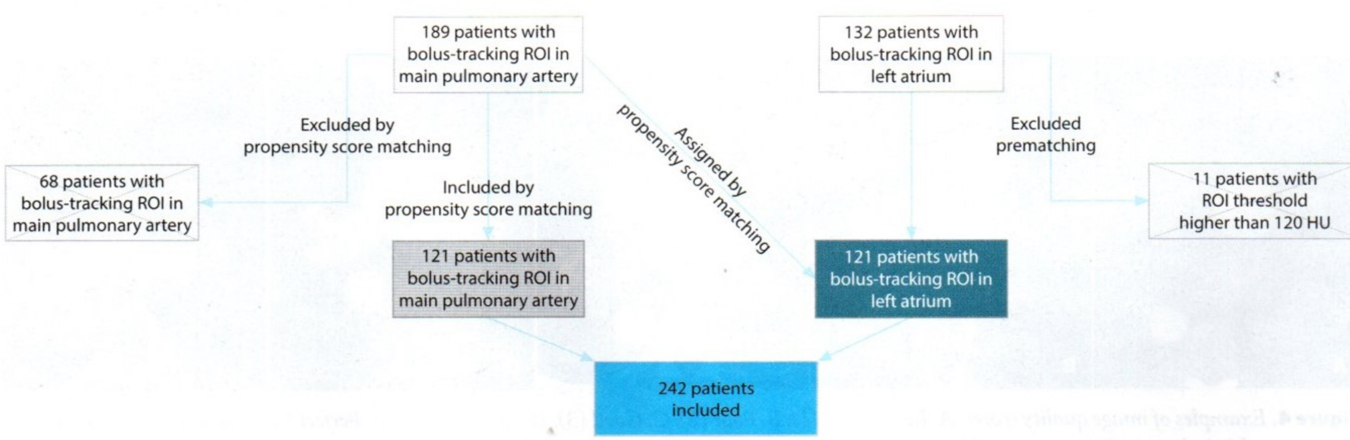

Figure 2. *Flowchart illustrating study design. Figure courtesy of the authors.*

subsegmental). They also indicated whether the pulmonary embolism could be excluded with certainty and specified from which level they could not exclude with certainty.

Statistical Analysis

All variables were examined for normal distribution using the Shapiro-Wilk test.[11] For most, there was no normal distribution, thus nonparametric tests were used for all comparisons.[12] To determine the success of propensity score matching, the standardized differences for sex, contrast volume, contrast flow rate, and ROI threshold were compared before and after matching. Based on the recommendation of Austin, the assumption is that no significant difference concerning a variable is present when the standardized difference is less than 0.1.[13] Tests for paired samples were used to compare the matched groups of patients as recommended by Austin, Ho et al, and Rubin.[14-16] To compare the unpaired subgroups, tests for unpaired samples were used. Thus, signal intensity, SNR, and qualitative scores were compared using the Wilcoxon signed rank test (significance level set at $\alpha = .05$). Interrater reliability for qualitative scores and assessment of pulmonary embolisms were evaluated using Cohens weighted kappa (κ)[17-19]:

- ≤ 0 – poor
- 0.01-0.20 – slight
- 0.21-0.40 – fair
- 0.41-0.60 – moderate
- 0.61-0.80 – substantial
- 0.81-1.00 – almost perfect agreement

To examine influencing factors in more depth, subgroups of patients were created for those who were examined with at least 60 mL contrast volume; less than 4 mL/s contrast flow; between 4 and less than 5 mL/s contrast flow; and 5 mL/s contrast flow. Another subgroup of patients, who were examined with at least 60 mL contrast volume and contrast flow rate less than 4 mL/s, was created. Because subgroups were not matched, signal intensity, SNR, and qualitative scores of the subgroups were compared using the Mann-Whitney test (significance level set at $\alpha = .05$).

The Shapiro-Wilk test, Wilcoxon signed rank test, Mann-Whitney test, and the calculation of Cohens

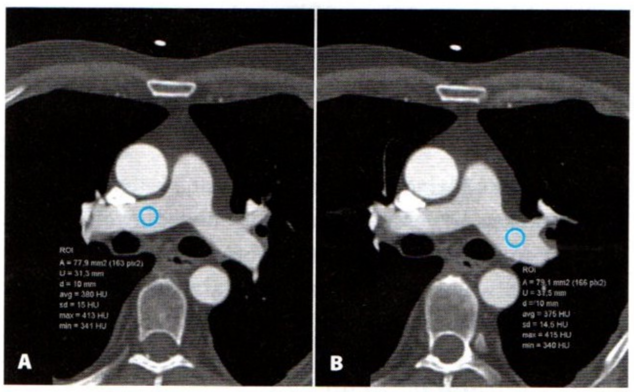

Figure 3. *Positions of ROIs for quantitative analysis of pulmonary arteries. A. ROI (blue circle) in right pulmonary artery. B. ROI (blue circle) in left pulmonary artery. Images courtesy of the Institute and Polyclinic for Diagnostic and Interventional Radiology, University Hospital Carl Gustav Carus, Technische Universität Dresden.*

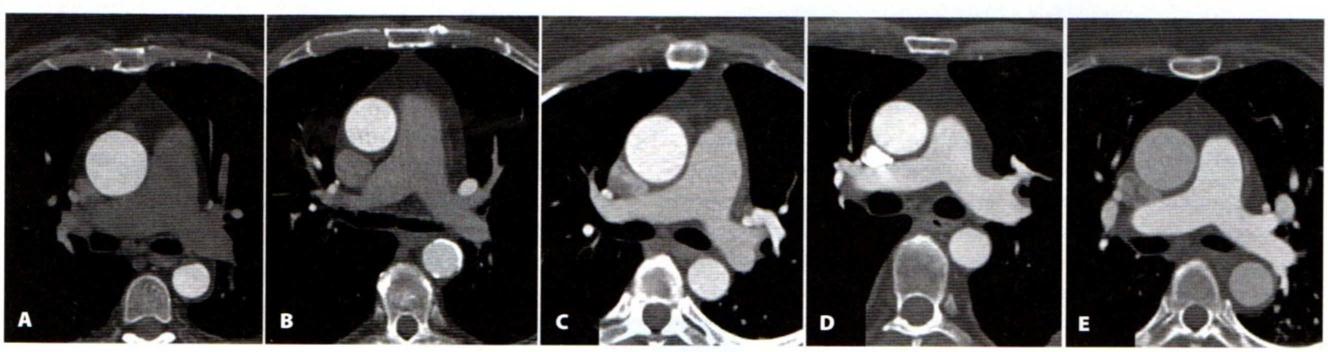

Figure 4. *Examples of image quality scores. A. Insufficient (1). B. Poor (2). C. Good (3). D. Very good (4). E. Perfect (5). Images courtesy of the Institute and Polyclinic for Diagnostic and Interventional Radiology, University Hospital Carl Gustav Carus, Technische Universität Dresden.*

weighted kappa were performed using MedCalc 18.10.02 (MedCalc Software Bv). Diagrams and tables were created using Excel 2019 (Microsoft).

Results

When comparing both groups, the standardized differences before matching were higher than after matching with regard to sex, contrast volume, and contrast flow rate, as well as ROI threshold. After matching, standardized differences were lower than 0.1 for sex (matched exactly) and contrast flow rate; therefore, the assumption was that there was no significant difference concerning these variables in the matched samples.[13] For contrast volume and ROI threshold, standardized differences were higher than 0.1, indicating that a significant difference remained after matching for both groups of patients regarding these variables (see **Table 1**).

Quantitative Analysis

Mean signal intensity for group A (bolus-tracking ROI positioning in the mean pulmonary artery) was 428.87 HU (SD = 163.78), and for group B (bolus-tracking ROI positioning in the left atrium) it was 324.79 HU (SD = 166.06) (see **Figures 5** and **6**). Signal intensity was significantly higher in group A than in group B ($P < .001$) (see **Table 2**).

The mean SNR for group A was 22.18 (SD = 7.04), and for group B it was 19.31 (SD = 8.26), so the SNR was significantly higher for bolus-tracking ROI positioning in the main pulmonary artery compared with bolus-tracking ROI positioning in the left atrium ($P = .002$).

Qualitative Analysis

Among the 121 patients in group A, image quality was rated 5 in 82 cases (67.8%), 4 in 30 cases (24.8%), 3 in 8 cases (6.6%), 2 in 0 cases (0.0%) and 1 in 1 case (0.8%), and the mean qualitative score was 4.59 (SD = 0.69). Among the 121 patients in group B, the image quality was rated 5 in 22 cases (18.2%), 4 in 26 cases (21.5%), 3 in 57 cases (47.1%), 2 in 15 cases (12.4%) and 1 in 1 case (0.8%), and the mean qualitative score was 3.44 (SD = 0.96). Image quality scores for bolus-tracking ROI positioning in the main pulmonary artery were significantly higher than the image quality scores for bolus-tracking ROI positioning in the left atrium ($P < .001$) (see Table 2).

Quantitative Analysis of Subgroups

In the subgroups of patients who were examined with 60 mL or more contrast volume and less than 5 mL/s contrast flow rate, SNRs were higher for ROI positioning in the left atrium than in the main

Table 1

Comparison of Variable Data Before and After Propensity Score Matching of Groups

	Before matching			After matching		
Variable	Group A (n = 189)[a]	Group B (n = 132)[b]	Standardized difference	Group A (n = 121)	Group B (n = 121)	Standardized difference
Sex						
Male	92	82	0.257	78	78	0
Female	97	50		43	43	
Contrast volume, M (SD), mL	40.19 (9.14)	55.13 (10.85)	0.805	41.86 (10.33)	53.07 (8.48)	0.604
Contrast flow rate, M (SD), mL/s	3.38 (0.45)	4.31 (0.75)	0.050	3.58 (0.36)	4.40 (0.70)	0.044
ROI threshold, M (SD), HU	100.0 (0.0)	120.23 (15.60)	1.090	100.0 (0.0)	116.20 (7.88)	0.826

[a] *Group A had bolus-tracking ROI positioning in the main pulmonary artery.*
[b] *Group B had bolus-tracking ROI positioning in the left atrium.*
Abbreviation: ROI, region of interest.

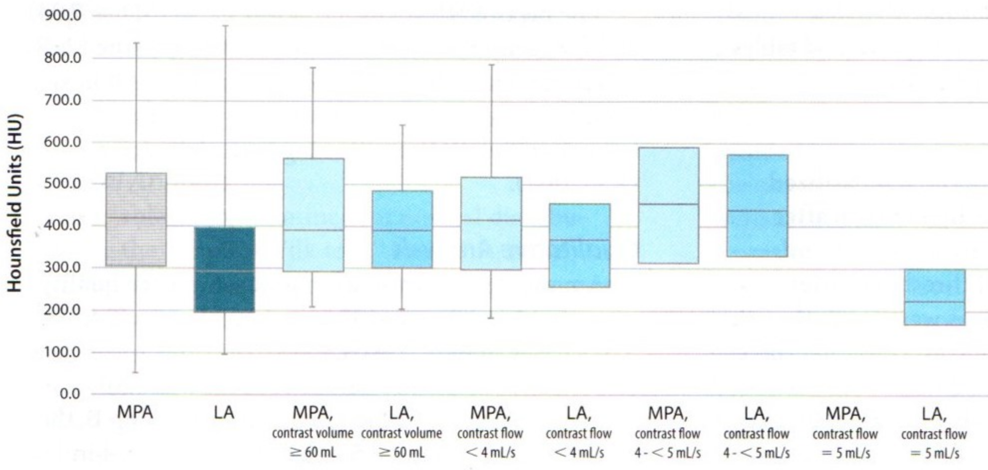

Figure 5. *Signal intensities in the pulmonary arteries categorized by bolus-tracking ROI positioning (main pulmonary artery [MPA] or left atrium [LA]) and by subgroup: 60 mL or more contrast volume; contrast flow rate less than 4 mL/s; contrast flow rate of 4 to less than 5 mL/s; and contrast flow rate of 5 mL/s. Figure courtesy of the authors.*

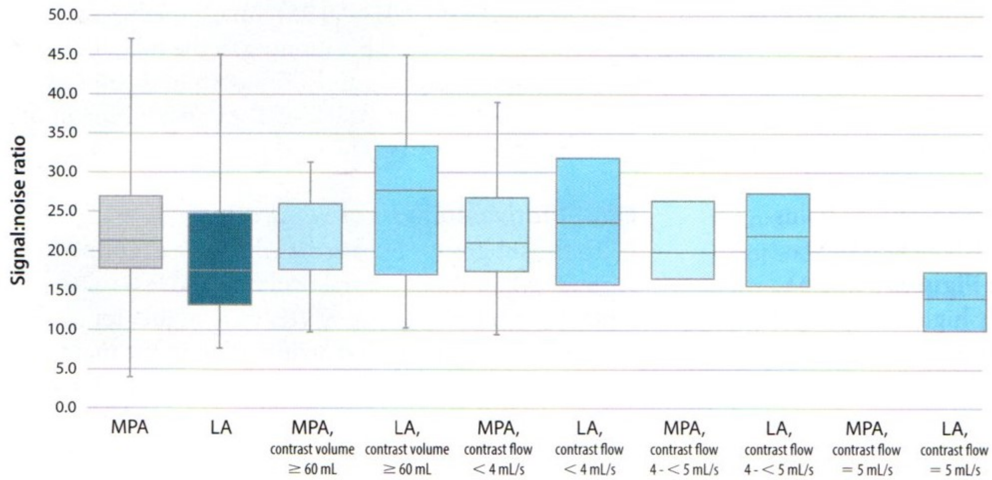

Figure 6. *Signal:noise ratios in the pulmonary arteries categorized by bolus-tracking ROI positioning (MPA or LA) and by subgroup: 60 mL or more contrast volume; contrast flow rate less than 4 mL/s; contrast flow rate of 4 to less than 5 mL/s; and contrast flow rate of 5 mL/s. Figure courtesy of the authors.*

pulmonary artery, but the difference in all quantitative scores (signal intensity and SNR) of these subgroups was not significant (see Table 2). There were no patients with bolus-tracking ROI positioning in the main pulmonary artery who were examined with a contrast flow rate of 5 mL/s. In this subgroup of patients with bolus-tracking ROI positioning in the left atrium, mean signal intensity was 236.76 HU and mean SNR was 15.45, which are very low when compared with all other subgroups in which mean signal intensities ranged from 358.50 to 454.10 HU and mean SNRs ranged from 21.10 to 26.33 (see Figures 5 and 6).

Qualitative Analysis of Subgroups

Qualitative scores were nearly equal in the subgroups of patients who were examined with 60 mL or more of contrast volume and with a contrast flow rate less than 4 mL/s. A contrast flow rate of 4 to less than 5 mL/s resulted in a significantly higher qualitative score for ROI positioning in the main pulmonary artery compared with the left atrium. There were no patients with bolus-tracking ROI positioning in the main pulmonary artery who were examined with a contrast flow rate of 5 mL/s. In this subgroup of patients with bolus-tracking ROI positioning in the left atrium, the

Table 2

Results from Quantitative and Qualitative Analyses of Total Group and Subgroups

Total group and subgroups[a]	Signal intensity, M (SD), HU	*P*	Signal:noise ratio, M (SD)	*P*	Qualitative score, M (SD)[b]	*P*
Total						
A (n = 121)	428.87 (163.78)	< .001	22.18 (7.04)	.002	4.59 (0.69)	< .001
B (n = 121)	324.79 (166.06)		19.31 (8.26)		3.44 (0.96)	
Contrast volume ≥ 60 mL						
A (n = 15)	433.30 (179.22)	.560	21.35 (6.19)	.137	4.73 (0.46)	> .999
B (n = 19)	395.24 (135.96)		26.33 (10.01)		4.74 (0.45)	
Contrast flow rate < 4 mL/s						
A (n = 79)	416.52 (152.78)	.253	22.04 (6.50)	.268	4.54 (0.66)	.922
B (n = 23)	378.59 (153.36)		24.25 (9.08)		4.52 (0.73)	
Contrast flow rate 4-< 5 mL/s						
A (n = 42)	452.09 (182.36)	.998	22.43 (8.03)	.840	4.67 (0.75)	< .001
B (n = 34)	454.10 (189.28)		23.24 (8.96)		3.62 (0.99)	
Contrast flow rate = 5 mL/s						
A (n = 0)		-	-	-		-
B (n = 64)	236.76 (87.15)		15.45 (5.17)		2.95 (0.60)	
Contrast volume ≥ 60 mL; contrast flow rate < 4 mL/s						
A (n = 12)	421.58 (173.23)	.406	21.10 (6.69)	.347	4.75 (0.45)	> .999
B (n = 13)	358.50 (127.86)		24.51 (10.05)		4.69 (0.48)	

[a] *Group A had bolus-tracking ROI positioning in the main pulmonary artery. Group B had bolus-tracking ROI positioning in the left atrium.*

[b] *Image quality was scored from 1 (insufficient) to 5 (perfect).*

mean qualitative score was 2.95, which is very low when compared with all other subgroups in which mean qualitative scores ranged from 3.62 to 4.75.

Pulmonary Embolisms

Among the 121 patients in group A, 26 patients (21.5%) were assessed as having pulmonary embolisms: 7 central, 9 lobar, 9 segmental, and 1 subsegmental. Among 15 patients (12.4%), a pulmonary embolism could not be excluded with certainty: from the central level in 1 case; from the lobar level in 0 cases; from the segmental level in 4 cases; and on the subsegmental level in 10 cases.

Among the 121 patients in group B, 3 patients (2.5%) were assessed as having pulmonary embolisms (1 central, 2 lobar, 0 segmental, 0 subsegmental). In 94 patients (77.7%), pulmonary embolism could not be excluded with certainty: from the central level in 1 case; from the lobar level in 10 cases; from the segmental level in 55 cases; and on the subsegmental level in 28 cases. Of those 94 patients, 63 were examined with a contrast flow rate of 5 mL/s.

Among the 12 patients in the subgroup with 60 mL or more contrast volume, less than 4 mL/s contrast flow rate, and with bolus-tracking ROI positioning in the main pulmonary artery, 3 patients (25.0%) were assessed as having pulmonary embolisms (1 central, 2 lobar). Pulmonary embolism could not be excluded with certainty in 1 patient (8.3%) (subsegmental level).

Among the 13 patients in the subgroup with 60 mL or more contrast volume, less than 4 mL/s contrast flow rate, and with bolus-tracking ROI positioning in the left atrium, 1 patient (7.7%) was assessed as having pulmonary embolism (lobar level). In another patient (7.7%), pulmonary embolism could not be excluded with certainty (subsegmental level).

Interrater Reliability

Identical qualitative scores were assigned by both readers in 193 of 242 cases (79.8%). Readers disagreed by more than 1 grade in 1 case. The resulting weighted kappa was 0.706, indicating substantial interrater agreement.[19]

Both radiologists assessed the same 29 patients as having pulmonary embolisms ($\kappa = 1.000$; perfect interrater agreement), and in all 29 cases, the embolisms were diagnosed on the same artery level ($\kappa = 1.000$; perfect interrater agreement).[19]

They decided in the same 108 cases, and in 1 other case each, that pulmonary embolisms could not be excluded with certainty ($\kappa = 0.983$; almost perfect interrater agreement). In 97 of those 108 cases (89.8%), they chose the same level from which pulmonary embolisms could not be excluded with certainty, and they differed by more than 1 level in 1 case. The resulting weighted kappa was 0.801, indicating almost perfect interrater agreement.[19]

Discussion

This study shows that significantly better image quality of the pulmonary arteries is achieved with bolus tracking in the main pulmonary artery versus the left atrium. Further analysis of the subgroups showed that bolus-tracking ROI positioning in the main pulmonary artery or the left atrium leads to comparable image quality of pulmonary arteries when using 60 mL or more contrast volume and less than 4 mL/s flow rate with scores similar to or better than in the overall study population. This result indicates that ROI positioning in the left atrium in combination with 60 mL or more contrast volume and less than 4 mL/s flow rate does not adversely affect depiction of pulmonary arteries compared with conventional ROI positioning in the main pulmonary artery.

When using 4 to less than 5 mL/s contrast flow rate, quantitative scores also were comparable, whereas qualitative scores were significantly higher in patients with ROI in the main pulmonary artery compared with the left atrium. A possible explanation is that the quantitative scores were measured in the central pulmonary arteries, and qualitative analysis scored all pulmonary arteries from the central to subsegmental level.

However, a contrast flow rate of 5 mL/s was not used in any patient with bolus-tracking ROI positioning in the main pulmonary artery but was used in many patients with bolus-tracking ROI positioning in the left atrium. In these patients, image quality of pulmonary arteries was very low when compared with all other subgroups. A possible explanation is that the contrast agent had already passed through the pulmonary arteries at the time of image data acquisition due to the high flow rate.

In a recent study published in 2021, image quality of pulmonary arteries was shown to improve when the bolus-tracking ROI positioning is placed in the left atrium rather than in the ascending aorta, while good image quality of the coronary arteries is achieved at the same time.[5] These results support ROI positioning in the left atrium, when triple-rule-out CTA is performed. A systematic review and meta-analysis by Ayaram et al showed that triple-rule-out CTA and coronary CTA lead to similar sensitivity and specificity for coronary stenoses, but they could not examine the accuracy in diagnosing pulmonary embolism because of the low prevalence in the included studies.[20]

In this study, pulmonary embolism could not be excluded with certainty in many cases with bolus-tracking ROI positioning in the left atrium, mostly on the segmental or subsegmental levels. Most of those patients were examined with a contrast flow rate of 5 mL/s, which supports the use of lower contrast flow rate. Accordingly, in the subgroup with 60 mL or more contrast volume, less than 4 mL/s contrast flow rate, and bolus-tracking ROI positioning in the left atrium, pulmonary embolism could not be excluded with certainty in only 1 patient (subsegmental level).

The evaluation of interrater reliability shows substantial agreement between both radiologists on the qualitative analysis of pulmonary arteries. For assessing patients as having pulmonary embolisms and at which artery level, interrater agreement was perfect. Regarding the decisions about whether and from which level pulmonary embolisms could not be excluded with certainty, interrater agreement was almost perfect. These results indicate that the qualitative measurement methods used in this study are very reliable, especially considering the difference in CTA experience of both raters.

The 2021 study[5] and this study collectively show that ROI positioning in the left atrium can lead to comparable image quality of the pulmonary arteries compared with ROI positioning in the pulmonary artery and of the coronary arteries compared with ROI positioning in the ascending aorta. These results indicate that triple-rule-out CTA with ROI positioning in the left atrium does not adversely affect depiction of coronary and pulmonary arteries compared with conventional ROI positioning. To examine the effect of bolus-tracking ROI positioning in the left atrium on image quality of the aorta to rule out acute aortic syndrome, further studies are necessary.

Limitations

A limitation of this study is the retrospective study design and the remaining difference in contrast volume after matching. By building subgroups to examine influencing factors in more depth, this limitation could be resolved at the cost of relatively low case numbers. The remaining difference in ROI threshold probably is not a limitation because the threshold was 100 or 120 HU for all patients in this study. Considering that signal intensity for bolus tracking was measured in intervals of approximately 1 second, the start of image data acquisition likely would have been the same if the threshold was 100 HU or 120 HU. Another limitation is that propensity score matching can only eliminate known influencing factors.

There are other options to increase image quality of pulmonary CTA. Recent studies showed that pulmonary CTA should be performed in the resting expiratory position[21] and that the image quality of the pulmonary artery depiction in CTA can be further improved by using a weight-adapted contrast bolus.[22]

Conclusion

ROI positioning in the left atrium and the main pulmonary artery leads to good image quality of pulmonary arteries when using 60 mL or more contrast volume and less than 4 mL/s flow rate. Therefore, ROI positioning in the left atrium, which is used in triple-rule-out CTA, is sufficient for the assessment of pulmonary arteries with CTA.

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