Arterial attenuation in individualized computed tomography pulmonary angiography injection protocol adjusted based on the patient's body mass index

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Background: The aim of this study was to optimize computed tomography pulmonary angiography (CTPA) protocols with regard to improve vascular attenuation without increasing contrast media (CM) volumes. Therefore, we compared the standard CTPA protocol to an individualized contrast media injection protocols adjusted for the patient's body mass index (BMI). **Materials and Methods:** Two groups of 295 patients with suspected pulmonary embolism (PE) have been receiving CTPA. Group 1 received a standard protocol without taking patient's BMI into account. Group 2 received a CTPA scan, where dose and flow rate of CM injections were adjusted for the patient's BMI. Images were retrospectively analyzed by drawing regions of interests in defined positions in the superior vena cava, descending aorta, the pulmonary main trunk as well as the left and right lower lobe arteries. Intravascular attenuation, contrast volumes, and flow rates were compared using unpaired t-tests. Furthermore, a qualitative image analysis was performed by two experienced readers blinded for the protocol used for image acquisition to evaluate the image quality and arterial attenuation. **Results:** Patient's BMI was similar in both the groups (27.5 ± 1.5 kg/m^2 vs. 28.4 ± 2.1 kg/m^2; $P = 0.67$). Contrast volumes were lower (54.2 ± 4.8 ml vs. 55 ml; $P < 0.05$), and flow rates (4.1 ± 0.3 ml/s vs. 3.5 ml/s; $P < 0.05$) were significantly higher in the individualized protocol. The qualitative image analysis yielded an agreement on diagnostic interpretability in the individualized and standard group of 49% and 51% (95% Wilson confidence interval for mean), respectively. **Conclusion:** An individualized CTPA protocol based on the patient's BMI reduced the contrast media volume and led to an increased pulmonary artery enhancement improving image quality, particularly in the evaluation of the peripheral pulmonary arteries. Thus, contrast media volumes in CTPA should be adjusted for the patient's BMI.

Key words: Body mass index, computed tomography pulmonary angiography, contrast media, pulmonary embolism

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INTRODUCTION

Pulmonary embolism (PE) is still one of the most common causes of early mortality in acute cardiovascular disease in patients with long hospitalization despite developments in diagnosis and treatment.[1] PE is a complication of underlying venous thrombosis.[2] Epidemiological data indicate that of the more than 1.1 million cases of venous thromboembolism that occur in the European Union each year, approximately one-third are PE cases.[3] With the improved and increased accuracy of diagnosing PE, 25% of those who currently die from PE could be saved.[4] However, the diagnosis of PE may be missed because of its nonspecific clinical symptoms,[2] including chest pain, dyspnea, and syncope. Clinical risk stratification and D-dimer assay can be useful in suspected PE, but D-dimer tests can also be positive in many other conditions that are associated with a procoagulant state.[5] If the clinical

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suspicion of PE is high, computed tomography pulmonary angiography (CTPA) is required.[6] CTPA is the method of choice for emboli detection.[7-10]

To ensure reliable diagnostic accuracy, vascular enhancement in the territory of suspected emboli needs to be optimized with a substantial difference between vascular attenuation and thrombus. However, very strong vascular attenuation can lead to blurring artifacts and result in impaired diagnostic reliability. Thus, optimal bolus geometry and timing considering individual patient parameters and other factors, for example, scan parameters, are necessary to obtain the best results.[9-11]

Contrast media enhancement in first-pass vascular territories such as pulmonary arteries strongly correlates with the patient's BMI since large patients have larger blood distribution volumes than small patients which leads to increased contrast dilution. Therefore, patients with high BMI often require higher flow rates and/or increased contrast media volumes.

The purpose of our retrospective study was to analyze vascular attenuation in the pulmonary arteries, superior vena cava, and thoracic aorta, to assess diagnostic reliability, and to compare a standardized injection protocol for CTPA using the same amount of contrast media (CM) and an identical flow rate in each patient with an individualized injection protocol taking into account the individual patient's body mass index (BMI).

MATERIALS AND METHODS

Study design and participants

Institutional review board approval was waived due to the retrospective approach of the study, and written informed consent including anonymized data use for research was obtained from every patient. The goal of this retrospective study was to evaluate CM attenuation in the pulmonary arteries in patients with suspicion of pulmonary embolism comparing two different approaches in contrast administration. Patients were assigned to the standard protocol (Group 1) or the individualized protocol (Group 2). All patients with known allergic reactions to contrast media as well as patients with known renal failure (eGFR <30 ml/min/1.73 m^2), pregnant women, and patients <18 years of age were excluded from the study. In Group 1, one patient had undergone right lobectomy, and in Group 2, one patient had undergone left upper lobe resection and one patient had undergone right pneumonectomy. In an attempt to minimize bias, these patients were excluded from the study.

Before May 2015, all patients were scanned routinely with a standard contrast administration protocol of 55 ml iomeprol 400 (Imeron 400, Bracco Imaging, Konstanz, Germany) at a flow rate of 3.5 ml/s.

From May 2015 to December 2015, a software integrated into the injection pump (Certegra®, Bayer Healthcare, Berlin, Germany) allowing for individualization of CM application was used to optimize vascular attenuation in the territory of interest based on patient weight and height.

A total of 295 patients were included in the study and were divided into two groups including 147 and 148 patients. Group 1 received a standard protocol for CTPA and Group 2 an individualized CM protocol. Height and weight of all patients were recorded at the time of the scan.

Computed tomography pulmonary angiogram protocol

Group 1 consisted of 147 patients routinely scanned with a standard contrast injection protocol of 55 ml iomeprol 400 at a flow rate of 3.5 ml/s without consideration of BMI.

Group 2 consisted of 148 patients scanned with an individualized contrast injection protocol which was made possible by the implementation of a software in the power injector used for contrast media application. To avoid painful injections and to reduce the risk for contrast extravasation, the maximum flow rate was limited to 5.5 ml/s.

Computed tomography imaging protocol

All patients were examined in the supine position. Patients of both the groups underwent computed tomography (CT) examinations with the same imaging protocol (X-ray tube voltage of 100 kVp, dose modulation of X-ray tube current of 30–120 mAs, and noise index of 22) by the use of a clinical 64-slice-CT scanner (GE Lightspeed VCT, GE Healthcare, Waukesha, Wisconsin). The main pulmonary artery was identified and chosen as the level of bolus tracking for the scan. Image acquisition was started when the relative attenuation threshold of 200 HU was exceeded.

Image analysis

Quantitative and qualitative image analysis was performed on high-definition LCD monitors routinely used for reporting CT images (Display: 1.Rx 240, Resolution: 1600 × 1200, Orientation: Landscape). Contrast attenuation was measured on the original 1.2-mm thin transverse images by placing circular regions of interest in the center of the pulmonary trunk, the right and left lower lobe arteries, as well as in the superior vena cava and descending aorta at the level of the main pulmonary trunk.

Qualitative image analysis

Two radiologists with CT experience of more than 10 years blinded for the chosen CTPA protocol independently evaluated CTPA scans in terms of visual qualitative comparisons. For this evaluation, the contrast attenuation was rated on a 2-grade scale (1 diagnosable and 0 not diagnosable) in all segmental arteries.

Statistical analysis

Statistical analysis was performed using Software (IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp).

The independent sample *t*-test was used to compare attenuation values between both the protocols and for the comparison of BMI.

Normal distribution was tested using Kolmogorov–Smirnov test. Since the parameters contrast media volume and flow rate did not pass this test, both the groups were analyzed using the nonparametric Mann–Whitney U-test. $P < 0.05$ was considered statistically significant.

Subjective image parameters were compared with the Wilson confidence interval for a risk difference between two groups to the confidence level $1-\alpha = 95\%$ using GraphPad Prism software (GraphPad 8 Software, Inc., CA, USA). The kappa score for the interreader agreement was used to measure the percentage of agreement.

RESULTS

Patients data

The patients in Group 1 ($n = 147$, age 59 ± 17, height 173 ± 10 cm, weight 79 ± 20 kg) consisted of 75 men and 72 women (male-to-female ratio = 1.04). Group 2 ($n = 148$, age 62 ± 17, height 170 ± 15 cm, weight 78 ± 21 kg) consisted of 81 men and 68 women (male-to-female ratio = 1.19).

There was no statistically significant difference in the distribution of BMI between the two study groups (Group 1: 28.4 ± 2.1 kg/m^2 [range 17.5–39.8], Group 2: 27.5 ± 1.5 kg/m^2 [range 18.6–50.0 kg/m^2]; $P = 0.67$). The demographic characteristics are summarized in Table 1.

Contrast media volumes and enhancement parameters

Significant differences in contrast media volume and administration rate were found between the two groups. While Group 1 had been administered a volume of 55 ml at a constant rate of 3.5 ml/s, the corresponding values in Group 2 were a volume of 54.2 ± 4.8 ml at a flow rate of 4.1 ± 0.3 ml/s, respectively. The results are outlined in Figure 1 and Table 2.

Our results showed that at the same BMI-range, contrast enhancement was slightly higher in all anatomic sites of interest when the individualized injection protocol was used. The obtained results are summarized in Table 3.

Subjective grading of image quality

On the basis of a subjective scoring system, no difference between the two protocols with regard to diagnostic reliability has been observed. The results also indicate, that the differences between both groups evaluated by two readers are not significant.

The kappa score for the interreader agreement was κ = 0.91 for group 1 and κ = 0.86 for group 2. Both the scores indicated "excellent agreement."

The confidence interval of all segmental arteries that were considered to have sufficient quality for assessment of PE did not significantly differ between Group 1 (mean: 0.49; lower limit: 0.43 and upper limit: 0.55) and Group 2 (mean 0.51; lower limit: 0.45 and upper limit: 0.57).

Table 1: Demographic characteristics

Characteristic	Group 1 standard protocol	Group 2 individualized protocol	*P***
Number of patients	147	148	
Male-to-female ratio	1.04	1.19	
Age*	59±17	62±17	0.13
BMI (kg/m^2)*,§	28.4±2.1 (17.5-39.8)	27.5±1.5 (18.6-50.0)	0.67

*The data are presented as mean±SD, ***P* values calculated using Independentsamples *t*-test, §Data in square brackets are ranges. SD=Standard deviation; BMI=Body mass index

Table 2: Contrast media volumes and injection rates

Characteristic	Standard group	Individualized group	P
CM-volume (ml)*	55.0±0.0	54.2±4.8	<0.05**
Injection rate (ml/s)*	3.5±0.0	4.1±0.3	<0.05**
Number of patients with PE	23	39	<0.05‡

*The data are presented as mean±SD, ***P* values calculated using nonparametric Mann-Whitney U-test, ‡*P* values calculated using independentsamples *t*-test. PE=Pulmonary embolism; SD=Standard deviation; CM=Contrast media

Table 3: Attenuation values in main pulmonary trunk, right lower lobe and left lower lobe arteries, descending aorta, and superior vena cava

Location	Standard group*	Individualized group*	*P***
Main pul. trunk	422.1±147.4	442.9±147.7	0.61
RLL	397.6±143.4	410.2±143.2	0.26
LLL	404.1±142.2	419.6±137.5	0.99
Aorta	275.5±119.7	261.6±98.7	0.17
SVC	672.5±442.8	697.8±413.5	0.79

*The data are presented as mean±SD, ***P* values calculated using independentsamples *t*-test. RLL=Right lower lobe; LLL=Left lower lobe; SVC=Superior vena cava; SD=Standard deviation

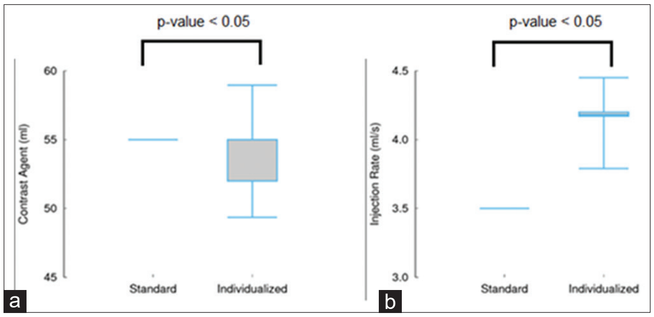

Figure 1: Comparison of standard and individualized computed tomography pulmonary angiograph injection protocols. CM volume (a) and flow rate (b) in computed tomography pulmonary angiography protocols using a standard and individualized injection protocol. The results are shown as box plots including the average ± standard deviation, median, 25th to 75th percentile; *P* values are calculated using nonparametric Mann–Whitney U-test (a $P = 0.05$ was considered statistically significant)

Representative CTPA images acquired by the standard and individualized protocol at the level of the pulmonary trunk are shown in Figure 2.

DISCUSSION

Currently, CTPA is accepted as the gold standard for the detection of PE.[7,8] This method requires the optimal enhancement of pulmonary arteries to be diagnostically accurate and reliable. The quick, easy, and correct identification of patients with PE helps to reduce morbidity and costs of hospitalization.[12]

Arterial enhancement depends on the iodine administration rate (or iodine flux), the amount of contrast media used as well on other patient-related aspects, for example, cardiac output and BMI.[13,14] Iodine flux can be controlled by the injection flow rate (ml/s) and/or the iodine concentration of the contrast medium (mg iodine/ml). An increased delivery rate leads to greater arterial enhancement. Many studies confirmed that a flow rate of 4 ml/s is sufficient for diagnostic CTPA.[9,15,16] For vascular imaging, the increase of injection rate does affect peak enhancement and results in substantially higher intraluminal enhancement, therefore achieving optimal visualization of pulmonary vessels throughout the peripheral pulmonary branches.[17]

One of the most important patient-related factors affecting vascular enhancement is BMI. Numerous studies have examined the effect of BMI on vascular enhancement.[18-22] The CM administered to a patient with higher BMI is more diluted than that administered to a patient with lower BMI due to the larger blood distribution volumes than in smaller patients.[23,24] Thus, when an appropriate contrast enhancement is needed, theoretically, the amount of iodine should be adjusted for the body weight.

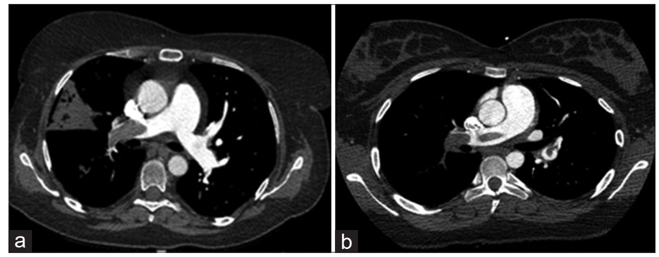

Figure 2: Transverse computed tomography images (a) and (b); multidetector computed tomography scans of chest obtained with the standard protocol of CM-injection (a) and individualized protocol of CM-injection (b)

Our analysis showed that adjusting contrast media volume and flow rate to patient's BMI allowed us to reduce the amount of contrast media for CTPA even in patients with high BMI. Even though we observed an increase of vascular attenuation by 4.8%, 7.4%, and 3.7% in the main pulmonary trunk, the right lobe artery, and left lower lobe artery, respectively, this difference was not significant. More obviously and in agreement with previously published data, the adjustment of flow rate (or iodine flux in other words) can help to increase vascular attenuation in the pulmonary territory. A qualitative analysis performed by two experienced readers yielded comparable results with regard to diagnostic reliability.

Some studies, such as Behrendt *et al*. reported, that the use of 300 mg I/ml CM results in better contrast enhancement than the use of 370 mg I/ml CM in CT of the chest.[18,25,26] This, at the first sight, contradictory phenomenon is explained by higher viscosity with increasing iodine concentration. In our institution, a contrast agent with an iodine concentration of 400 mg l/ml is used for all contrast-enhanced CT protocols. The flow rates ranged from 3.3 mL/s to 5.5 ml/s and were at least in part substantially higher than recommended in the literature. Accordingly, the iodine flux (up to 2.2 g iodine/s) exceeded the current recommendation (<1.5 g iodine/s).

Contrast media volume and flow rate were automatically chosen by the power injector based on individual BMI. While the reasons for the automatic selection of high iodine delivery rates by the software remain unknown, we did not observe any significant disadvantages. The slightly higher contrast in the superior vena cava (SVC) did not impair the image quality substantially; however, the contrast agent remaining in the SVC did not contribute to the attenuation of the pulmonary arteries. Based on this observation, we hypothesize that the amount of contrast agent can be further reduced without impairing diagnostic reliability.

Isolated thromboembolism of the subsegmental pulmonary arteries occurs in 6%–30% of patients with PE.[27] Since the diagnostic reliability of CTPA is mainly influenced by intravascular contrast enhancement, the use of individualized contrast administration protocols may improve visualization of small emboli, thereby improving diagnostic accuracy, particularly in the evaluation of peripheral pulmonary arteries. Our study showed a significantly higher PE detection rate in the individualized protocol's group ($P < 0.001$). However, due to a lack of gold standard, the interpretation of this observation is difficult. In an attempt to minimize bias, we included all patients with suspicion of pulmonary embolism in our study. However, we cannot exclude a selection bias that may have resulted in a higher detection rate of PE in Group 2. The software-based technique used in our study is not widely available. Moreover, the detailed underlying equations that are used by the software have not been disclosed by the manufacturer. Thus, our results cannot be translated easily into other institutions or other, especially faster CT technology which may potentially lead to a further reduction of contrast volume further decreasing the risk of contrast related risks, for example, renal failure. Tube voltage, another important CT parameter, that substantially effects attenuation should also be considered when individualizing injection protocols. Thus, further prospective multicenter studies are necessary, where patients are randomly assigned to either the standard or individualized protocol to warrant the reproducibility of our result in a larger cohort of patients of different age and BMI and between different CT machines. Furthermore, an individualization of contrast media application is recommended not only in CTPA imaging but also in CT angiographies of other vascular territories and should be evaluated in additional studies.

CONCLUSION

An individualized CTPA protocol based on a patient's BMI reduced the contrast media volume and led to an increased pulmonary artery enhancement improving image quality, particularly in the evaluation of peripheral pulmonary arteries. Thus, contrast media volumes in CTPA should be adjusted for the patient's BMI.

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Conflicts of interest

There are no conflicts of interest.

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