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Original Article

Clinical value and feasibility of CT pulmonary angiography with personalized injection of contrast agent in pulmonary embolism

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Abstract: Objective: To determine the clinical value and feasibility of CT pulmonary angiography (CTPA) with personalized injection of contrast agent in pulmonary embolism (PE). Methods: In the present retrospective study, 130 patients who underwent CTPA examination in our hospital from June 2019 to May 2020 were evaluated. Among them, 67 cases were detected by CTPA with personalized injection of contrast agent as the observation group (Obs group), and 63 cases were detected by CTPA with bolus-tracking (BT) as the control group (Con group). The specificity, sensitivity and accuracy of the detection in the two groups were compared. The image quality score and superior vena cava artifact score of the two diagnostic methods were compared. Additionally, the volumetric CT dose index (CTDIvol) and dose length product (DLP) of the two groups were compared. Results: The Obs group yielded a significantly higher specificity in diagnosing PE than the Con group ($P<0.05$), but there were no significant differences between the two groups in the sensitivity and accuracy ($P>0.05$). The image quality score and superior vena cava artifact score of the two groups were not significantly different ($P>0.05$), and the Obs group showed significantly lower CTDIvol and DLP than the Con group ($P<0.05$). Conclusion: CTPA with personalized injection of contrast agent has good diagnostic value for PE, with good imaging effect and safe profile, and has a lower radiation dose requirement.

Keywords: Personalized injection of contrast agent, CTPA, pulmonary artery embolism, diagnose

Introduction

Pulmonary embolism (PE) is a common life-threatening cardiovascular disease, with terribly high morbidity and mortality. It is the third most common cause of cardiovascular death after myocardial infarction and stroke, with an overall mortality over 10% [1, 2]. Reportedly, PE is triggered by thrombosis originating from deep veins of lower limbs, which gives rise to pulmonary artery embolism. Cancer patients, cardiovascular patients and patients with hereditary hypercoagulable diseases face a high risk of PE [3, 4]. The clinical manifestations of PE vary to a great extend without recognizable clinical symptoms. Its common symptoms include dyspnea, chest pain, and syncope [5, 6]. Therefore, early diagnosis of PE is of great importance.

Many diagnostic methods are available for PE, and pulmonary angiography is a frequently-adopted diagnostic method in clinical practice [7]. Multi-slice spiral CT has advantages of fast, thin layer and large-scale volume scanning, and the post-processing of image is relatively simple and fast [8]. At the current stage, CT pulmonary angiography (CTPA) has become the first selection for PE diagnosis because of its high sensitivity and specificity [9, 10]. Despite above-mentioned advantages, multi-slice spiral CT still gives rise to a risk of contrast agent nephropathy (CIN) due to the application of a large number of iodine contrast agents [11]. For

some patients, if iodine contrast agent is used in a large dose or several times in a short time, it may cause contrast agent-induced acute renal injury, and patients with hypertension, chronic kidney disease or diabetes are the high-risk population [12]. Therefore, how to keep the dose of contrast agent at a low safety limit without affecting the overall quality of the image is of critical importance.

In terms of CTPA with personalized injection of contrast agent adopted in the present study, a small amount of contrast agent is first injected to observe the enhancement during the examination, and a personalized scanning scheme is then designed according to the patient's blood vessel and physical condition. The lowest standard contrast agent is given under the premise of maintaining good imaging effect.

The present study explored the clinical value of CTPA with personalized injection of contrast agent in PE diagnosis to improve the safety to patients and reduce the overall scanning cost.

Materials and methods

Data about patients

In the present retrospective study, 130 patients who underwent CTPA examination in our hospital from June 2019 to May 2020 were enrolled and evaluated. Among them, 67 cases (40 males and 27 females, with an average age of 53.4±7.2 years) were detected by CTPA with personalized injection of contrast agent as the observation group (Obs group), and 63 cases (39 males and 24 females, with an average age of 54.1±6.7 years) were detected by CTPA with automatic bolus-tracking (BT) as the control group (Con group). The study was conducted with approval from the Medical Ethics Committee (Ethnical approval number: 2022II0-41302) and each patient signed an informed consent form after being informed of the study.

Inclusion and exclusion criteria

The inclusion criteria: Patients suspected with PE due to clinical manifestations (meeting one or more symptoms of PE); patients who had not received PE treatment; patients who were willing to accept imaging diagnosis; and patients with detailed clinical data and imaging data [13].

The exclusion criteria: Patients with severe cardiac or renal dysfunction; patients allergic to contrast agent; patients with coagulation dysfunction; pregnant women; or lactating women.

Determination methods

Each patient was scanned using Philips 256-slice spiral CT from the thoracic apex to the basis pulmonis, with the scanning direction from foot side to head side. A 20G tubing needle was preset in the median cubital vein of the patient's right hand, and contrast agent (iodixanol, 320 mg/ml) and normal saline were injected with an Ulrich high-pressure syringe. Patients in the Obs group were given the low-dose bolus test technique. The pulmonary trunk was selected as the detection layer below the tracheal bifurcation layer. The low-dose bolus test scanning was performed first, and 10-15 mL contrast agent and 20 mL normal saline were injected successively by a high-pressure injector. The low-dose monitoring scanning (120 kV, 20 mA) was performed in the region of interest 5 seconds after injection, and the time-density curve of pulmonary artery and pulmonary vein was obtained. The values obtained from the time-density curve were substituted into the mathematical model, and the personalized dose of contrast agent and saline was obtained. The dose of normal saline = the peak time of pulmonary artery × injection speed, and the dose of contrast agent = (scanning time + delay time of scanning - the peak time of pulmonary artery) × injection speed.

The parameters were as follows: The collimation width of the X-ray tube: 128×0.625 mm; rotation time: 0.28 s/r; pitch: 0.992; FOV: 350 MM; reconstruction layer thickness: 0.9 mm; reconstruction interval: 0.45 mm; tube voltage: 100 KV, automatic mAs. The raw data acquired by scanning were transmitted to the nebula workstation, and MPR, VR, and MIP were adopted as post-processing technologies. Patients in the Con group were given CTPA with bolus-tracking. The mixed injection (20 ml), a mixture of contrast agent (iodixanol, 320 mg/ml) and 0.9% normal saline at a ratio of 1:4, was injected into each patient at 5.0 ml/s through the patient's anterior cubital vein with a high-pressure syringe. Then, 4 ml contrast agent was injected through the syringe A of a double syringe, and 16 ml 0.9% normal saline was injected through the syringe B. With pulmo-

Table 1. Baseline data

	The control group (n=63)	The observation group (n=67)	X^2/t	*P*-value
Age (year)	54.1±6.7	53.4±7.2	0.573	0.568
Gender			0.362	0.547
Male	39 (61.90)	38 (56.72)		
Female	24 (38.10)	29 (43.28)		
BMI (kg/m^2)	22.5±2.6	23.1±2.9	1.239	0.218
Clinical symptoms				
No obvious symptoms	4 (6.35)	3 (4.48)	0.223	0.637
Dyspnea	40 (63.49)	42 (54.55)	1.143	0.285
Faint	2 (3.17)	4 (5.97)	0.576	0.448
Cough	10 (15.87)	15 (22.39)	0.887	0.346
Chest pain	31 (49.21)	36 (53.73)	0.266	0.606
Clinical signs				
Tachypnea	12 (19.05)	17 (25.37)	0.750	0.387
Tachycardia	31 (49.21)	30 (44.78)	0.256	0.613
Lung wheezing sound	6 (9.52)	10 (14.93)	0.878	0.349
Unconsciousness	3 (4.76)	5 (7.46)	0.410	0.522
D-dimer detection result			0.200	0.655
Positive	39 (61.90)	44 (65.67)		
Negative	24 (38.10)	23 (34.33)		
With DVT			1.943	0.163
Yes	42 (66.67)	52 (77.61)		
No	21 (33.33)	15 (22.39)		
Smoke			0.666	0.414
Yes	37 (58.73)	44 (65.67)		
No	26 (41.27)	23 (34.33)		
History of pulmonary infection			1.028	0.311
Yes	33 (52.38)	41 (61.19)		
No	30 (47.62)	26 (38.81)		

nary trunk as the detection region of interest (ROI) and 120 HU as the threshold value, CT scanning was performed when the ROI of pulmonary trunk reached 120 HU after the injection by the double syringe. At the same time of scanning, 20 ml contrast agent was continuously injected via the syringe A and 30 ml normal saline was continuously injected via the syringe B. The injection operation and sequence were automatically carried out by an automatic high-pressure syringe without interval.

Outcome measures

(1) After image processing, two experienced imaging doctors were arranged to evaluate the images of pulmonary artery and its branches by the double-blind method.

The image quality was evaluated subjectively and objectively. Objective evaluation involved pulmonary arteriovenous enhancement degree and contrast agent residue in the superior vena cava. Subjective evaluation involved image quality and image artifacts. Image quality scoring criteria: 5 points: perfectly enhanced marginal pulmonary artery branches, fully enhanced pulmonary veins, and full diagnostic confidence; 4 points: good pulmonary arteriovenous enhancement that can help fully diagnose the sub-segment level; 3 points: pulmonary arteriovenous enhancement that can help diagnose the segment level; 2 points: mild enhancement of pulmonary arteries and veins that can help only diagnose the trunk; 1 point: hardly strengthened pulmonary artery and vein. A score of 3 or above indicates qualified result. Superior vena cava artifact score: 0 point: no artifact; 1: with artifact that does not disrupt diagnosis; 2 points: with artifact that disrupts diagnosis (radiating to the right upper lobe pulmonary artery). The CT values of the main pulmonary artery, left/right pulmonary artery,

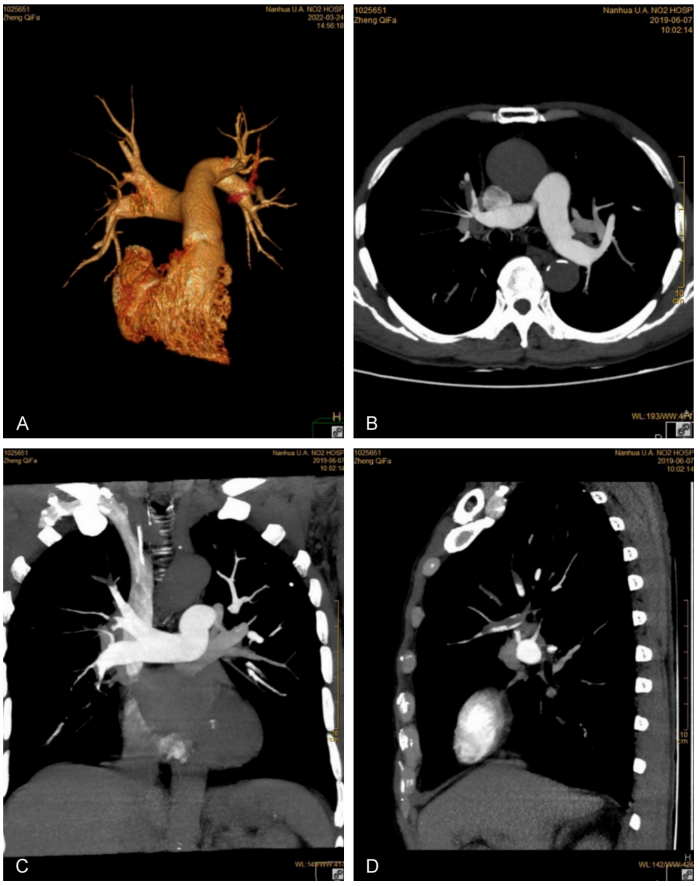

Figure 1. Image of a 67-year-old male patient. (A) The volume rendering (VR) of pulmonary artery. (B-D) The maximum density projection (MIP) of transverse, coronal and sagittal positions respectively. (A-D) shows that the branches of pulmonary artery at all levels were well displayed, the pulmonary vein was lightly developed, there was no hardening artifact of superior vena cava contrast agent, the image quality was good, and multiple thrombi in the upper lobe of the right lung were found.

lobar pulmonary artery and segmental pulmonary artery were measured objectively and quantitatively three times, and the average CT values were calculated. If PE occurred during measurement, the contralateral side was adopted [14].

(2) The radiation dose received by patients was measured by volumetric CT dose index (CTDIvol), and dose length product (DLP) was automatically recorded by CT.

Statistical analyses

SPSS 20.0 (SPSS Inc., Chicago, IL, USA) was adopted for statistical analyses of all obtained data. Rates were compared via the chi-square test and expressed by X^2. All measurement data were in normal distribution and analyzed by the independent sample t test, and expressed by t. The ranked data were analyzed using the rank sum test, and expressed by Z. Graphpad prism 7 (GraphPad Software, Inc., San Diego CA, USA) was used for drawing figures. $P<0.05$ was considered significantly different.

Results

Baseline data of the patients

According to comparison of baseline data between the two groups, there were no significant differences between the two groups in age, gender, body mass index (BMI), clinical symptoms, clinical signs, D-dimer detection results, DVT, smoking history and pulmonary infection ($P>0.05$, **Table 1**).

Comparison of subjective evaluation of image quality

The image quality was subjectively evaluated by image quality score and superior vena cava artifact score. In the Con group, 96.83% of the images had quality score ≥3, while in the Obs group, 94.03% of images had quality score ≥3, so the two groups were similar in image quality score ($P>0.05$). The comparison shown in **Figures 1** and **2** showed no significant difference in vein artifact score between the two groups ($P>0.05$, **Table 2**).

Comparison of CT value of vascular enhancement between the two groups

According to the comparison of the two groups in the contrast-enhanced CT values of pulmonary artery trunk, left pulmonary artery, right pulmonary artery and segmental artery, the Obs group showed slightly and insignificantly lower values than the Con group ($P>0.05$, **Figure 3**).

Comparison of radiation dose between the two groups

In order to compare the radiation doses received by the two groups, we counted their

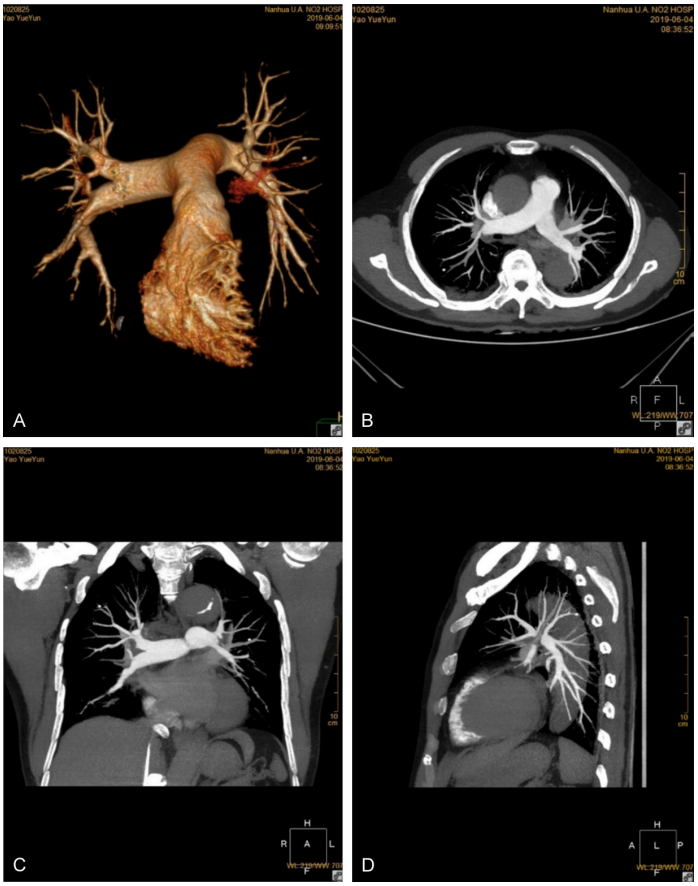

Figure 2. The patient, a 73-year-old male, was re-examined after pulmonary embolism treatment. (A) the pulmonary artery volume reconstruction (VR) diagram, and (B-D) the maximum density projection (MIP) diagrams of transverse, coronal and sagittal positions respectively. (A-D) All branches of the pulmonary artery were fully developed, the contrast agent was filled evenly, and the pulmonary vein was lightly developed. There was no hardening artifact of the superior vena cava contrast agent, and the image quality was good.

CTDIvol and DLP, and found that there was a significantly lower CTDIvol and DLP in the Obs group than those in the Con group ($P<0.05$, **Figure 4**).

Discussion

PE is a common clinical cardiovascular disease. PE patients are prone to other secondary systemic diseases after PE, so their manifestations are diverse. Patients with different degrees of cough, dyspnea, pulmonary hypertension, chest tightness and chest pain can be suspected as PE [15, 16]. However, it is difficult to make an accurate judgment only based on nonspecific manifestations, which may lead to misdiagnosis and missed diagnosis, so early and accurate diagnosis of PE is particularly important to alleviate PE [17, 18].

The present study first compared the diagnostic efficiency of personalized contrast agent injection method and the traditional BT method in PE. The results revealed that personalized injection of contrast agent required less contrast agent while maintaining good diagnostic efficiency. In addition, two experienced imaging doctors were arranged to compare the image quality by subjective evaluation and objective evaluation. The two groups were similar in the subjective evaluation results of image quality score and superior vena cava artifact score. Moreover, the contrast-enhanced CT values of pulmonary artery trunk, left pulmonary artery, right pulmonary artery and segmental artery had no statistical difference between the two groups. According to the evaluation results of image quality, the subjective and objective evaluation results of CTPA with personalized injection of contrast agent were good, which can meet the needs of diagnosis.

Patients with PF may suffer accidental death if they are not identified in time, so many tests have to be carried out under the low threshold [19-21]. Alshumrani et al. [22] mentioned that only 33% of clinically suspected PE cases were diagnosed as positive by CTPA, and most of patients were diagnosed as PE-negative after repeated CTPA scans, resulting in excessive use of CTPA scans. It not only brought high detection costs to patients, but also brought risks of radiation exposure and intravenous injection of contrast agents, which greatly increased the incidence of CIN. Mitchell et al. [23] found that at least 10% of patients would suffer CIN after CTPA, which substantially increase the PE-irrelevant death after CTPA but strongly related to the development of CIN. Nowadays, in order to prevent CIN, contrast agent is generally chosen [24]. With it, the frequency of adverse reactions is reduced, but a large dose of bolus injection of contrast agent can still increase the burden on the heart and kidney of patients, so the patients also have the possibility of getting allergy and CIN. Therefore, a more reasonable and optimized personalized scheme

Table 2. Subjective evaluation of image quality

	The control group (n=63)	The observation group (n=67)	X^2	*P*-value
Image quality score			0.576	0.448
5 points	37 (58.73)	34 (50.75)		
4 points	16 (25.40)	20 (29.85)		
3 points	8 (12.70)	9 (13.43)		
2 points	2 (3.17)	4 (5.97)		
1 point	0 (0.00)	0 (0.00)		
≥ 3 points	61 (96.83)	63 (94.03)		
Superior vena cava artifact score			0.611	0.541
0 points	40 (63.49)	39 (58.21)		
1 point	19 (30.16)	23 (34.33)		
2 points	4 (6.35)	5 (7.46)		

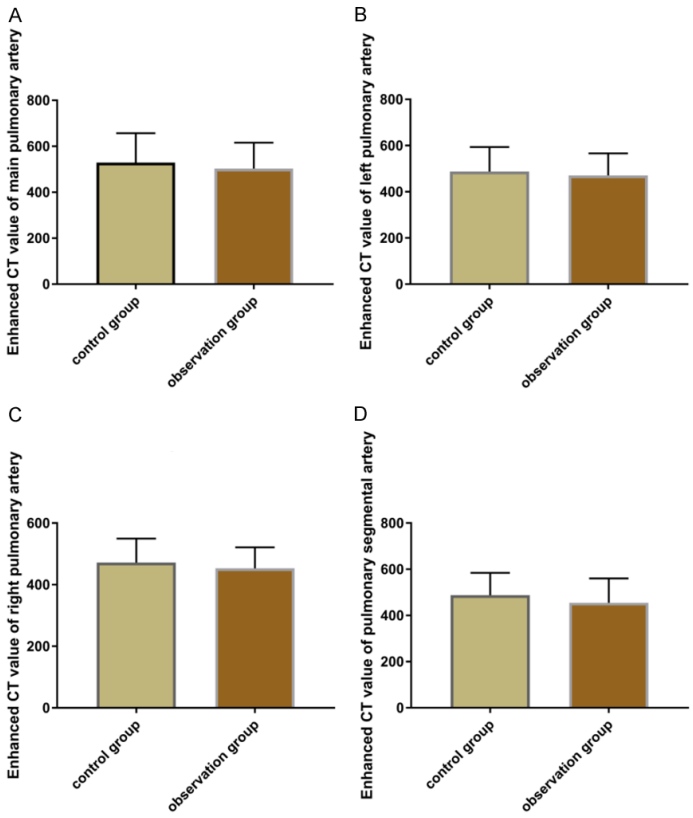

Figure 3. Comparison of CT values of vascular enhancement between the two groups. A. The two groups had no notable difference in the enhanced CT value of pulmonary artery trunk (t=1.218, P=0.225). B. The two groups had no notable difference in the enhanced CT value of left pulmonary artery (t=0.959, P=0.340). C. The two groups had no notable difference in the enhanced CT value of right pulmonary artery (t=1.429, P=0.155). D. The two groups had no notable difference in the enhanced CT value of pulmonary artery (t=1.816, P=0.072).

is adopted to achieve the purpose of definite diagnosis with the lowest radiation dose, thus reducing the burden on the kidney of patients.

The present study compared the radiation dose received by patients based on CTDIvol and DLP, and found that the CTDIvol and DLP in the group given personalized injection of contrast agent were significantly lower than those in the group given the traditional BT method. Personalized injection of contrast agent greatly reduced the required dosage of contrast agent to only less than 50 ML, which reduced the waste of contrast agent and the examination cost of patients. The previous results showed that CTPA with personalized injection of contrast agent can significantly reduce the adopted contrast agent dose and radiation dose without affecting the image quality, especially the CT value. In the study by Brendlin et al. [25], ultra-low dose CTPA achieved good image quality and diagnostic confidence in pulmonary embolism, and the image noise was reduced with advanced modeling iterative reconstruction, which also provided us with research ideas.

The innovation of this study lies in the establishment of a new mathematical model to achieve CTPA with personalized injection of contrast agent, which can not only improve the work efficiency and image quality, but also ensure the image quality of CTPA, with a smaller dose of contrast agent, and reduce the incidence of corresponding adverse

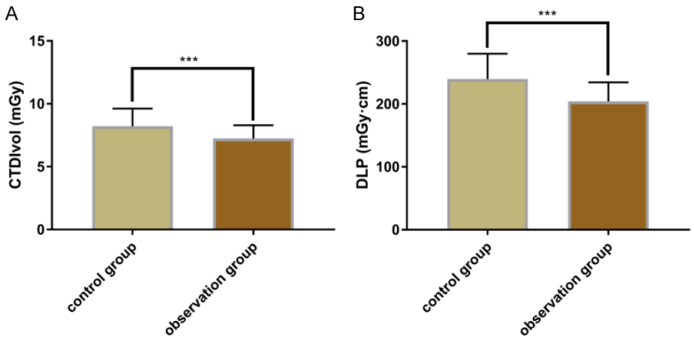

Figure 4. Comparison of radiation dose between the two groups. A. The Obs group showed significantly lower CTDIvol than the Con group (t=4.533, P<0.001). B. The Obs group showed significantly lower DLP than the Con group (t=5.679, P<0.001). Note: ***means P<0.001.

reactions. However, this study has some limitations. First, there may be potential selection bias and subjective bias in evaluation, although we tried our best to avoid them. Second, it is not clear whether this examination method can be extended to the examination of other parts, and the diagnosis results are probably strongly related to the equipment used, hospital conditions and patient conditions, so we need to do more research later to further support our conclusions. Finally, many studies are investigating effective non-invasive diagnosis methods that reduce the risk of radiation to patients for PE, and some serological indicators have thus captured attention, but most of them have their limitations. We hope to carry out research with some effective serological indicators [26] in subsequent studies.

To sum up, CTPA with personalized injection of contrast agent has good diagnostic efficacy, with ability to provide qualified image that can meet the needs of PE diagnosis, and it contributes to the use of a small dose of contrast agent, which can lower the risk of radiation to patients.

Disclosure of conflict of interest

None.

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