A Heart Rate-Dependent Protocol of “One-Stop” Computed Tomography Angiography of Coronary Combined with Pulmonary Arteries Reduces the Dosages of Contrast Agent

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Abstract

Background: The personalized, heart rate-dependent computed tomography angiography (CTA) protocol can reduce the use of contrast medium (CM) and the radiation dose. This is especially beneficial for patients with CTA of coronary combined with pulmonary arteries.

Purpose: To evaluate the feasibility of low CM in one-stop coronary and pulmonary arterial CTA tailored by patients’ heart rate.

Material and Methods: 94 patients set to undergo CTA of coronary combined with pulmonary arteries with one-stop scans. Patients were prospectively randomized into two groups: For group A (n = 47), the timing of the scans was determined according to the patient’s HR using 30 mL CM; For group B (n = 47), in which the routine bolus tracking was applied by setting the ascending aortic threshold of 80 HU with 70 mL CM, scans were performed simultaneously.

Results: Compared with group B, group A had slightly higher computed tomography (CT) value and image quality of pulmonary artery (CT value: group A 484.7HU; group B 457.9HU; t = 2.446, P = .016; image quality: χ² = 8.292, P = .016), but in coronary artery wasn’t statistically different between two groups(image quality: χ² = 2.516, P = .642).

Conclusion: The heart rate-dependent CM injection protocol can greatly reduce the use of CM, simplify the work-flow, and may obtain comparable or even better image quality compared with the routine bolus tracking.

Keywords
low volume contrast agent administration, heart rate, coronary computed tomography angiography, pulmonary artery computed tomography angiography, image quality

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Introduction

Chest pain, shortness of breath, and syncope are common symptoms related to coronary heart disease. Other life-threatening diseases such as aortic dissection (AD) and pulmonary embolism (PE) may also cause chest pain and require immediate medical intervention. Indeed, PE is a potentially fatal disorder, and is the third most common acute cardiovascular disease worldwide after myocardial infarction and stroke. Moreover, a missed diagnosis of PE can be fatal. Unfortunately, PE-related clinical symptoms are often nonspecific, and a timely correct diagnosis mainly relies on clinical imaging, including computed tomography angiography (CTA). Indeed, multislice computed tomography (CT) has been shown to reduce the time spent in the diagnosis of PE and it diminishes patient costs. However, CTA also has important shortcomings, including contrast agents and radiation exposure—contrast agents reportedly can be toxic to the kidneys. Therefore, reducing the contrast agent dosages has become an interesting and important study topic in the clinic.

By combining a low voltage setting and the iterative algorithm, it may be possible that a low volume of the contrast agent could be used for cardiovascular and the other vascular high-pitch scanning. Revolution CT scanners with high speed and high maneuverability have a 16-cm wide detector for one-stop CTA of the coronary and pulmonary artery. Compared with the traditional triple rule-out protocol, the one-stop protocol is triggered manually tailored by patients’ heart rates, which greatly reduces the volume of contrast agent. At the same time, the images obtained are pure pulmonary artery and pure coronary artery in a single injection, avoiding the interference of venous imaging and obtaining higher quality image. The aim of this study was to further evaluate the feasibility of administering a small volume (30 mL) of contrast agent (iopamidol-370) in one-stop coronary and pulmonary arterial computed tomography angiography (CTA) tailored by patients’ heart rates.

Methods

Demographic and Clinical Characteristics of the Patients

This study protocol was approved by the Ethics Committee of Liaocheng People’s Hospital. Written informed consent were obtained from all participants. A total of 94 patients with chest pain, or/and shortness of breath, or/and syncope or/and patients with suspected pulmonary embolism or/and coronary artery disease were enrolled. All patients with a body mass index (BMI) between 18 and 26 underwent CTA of coronary and pulmonary arteries with one-stop contrast agent injection. These patients were randomly divided into two groups (A and B) with different CT scanning protocols being performed in the patients of these two groups (see below). Group A included 18 males and 29 females, with a mean age of 59.06 ± 11.44 years (range: 23–83 years). Group B consisted of 25 males and 22 females, with a mean age of 58.69 ± 10.63 years (range: 31–81 years). The heart rate, heart rate during the scan, GFR, and BSA in Group A were 68.60 ± 7.24 bpm, 67.51 ± 10.89 bpm, 94.53 ± 6.32, and 1.72 ± 0.16 m², respectively. The heart rate, heart rate during the scan, GFR, and BSA in Group B were 70.34 ± 11.18 bpm, 68.43 ± 11.22 bpm, 94.28 ± 6.13, and 1.73 ± 0.15 m², respectively. Risk factors include hypertension, diabetes, and smoking history, and the amount of Group A is 29, 9, and 11 and the amount of Group B is 32, 12, and 15, respectively.

Protocol for group A and B ECG-gating methods: For patients with a HR > 80 beats per minute (bpm), HR = 60–80 bpm, underwent retrospective ECG-triggered spiral scan. HR < 60 bpm, underwent prospective ECG-triggered axial scan. No drugs are used to interfere with heart rate changes before the CT scan.

Computed Tomography Examination

An American GE256 row, 512-slice spiral CT scanner was used for the patients’ examination. Scan parameters were X-ray tube rotation speed of .28s/r, tube voltage kV assist of 80–140 kV, baseline of 100kV, tube current SmartmA of 150–650 mA, and NI of 20. The detector covered 12–14 cm, 50% ASIR-V, with a conventional scanning thickness of .625 mm. The helical pitch is 1, Cardiac blood vessels related scanning parameters were: window width 800 HU and window location 180 HU. All images were transmitted to the workstation (AW461) through the PACS system.

Computed Tomography Scanning Protocols

Protocol for group A (one-stop protocol). For patients in group A (n = 47), scanning was performed with an injection of 30 mL contrast agent and the scan timings were set according to the patients’ heart rates (HR) to determine the delay between the initiation of pulmonary artery CTA and the initiation of coronary CTA (ΔT). For patients with a HR > 80 beats per minute (bpm), the pulmonary artery CTA scan started 5s after the injection of contrast material and the delay between the initiation of pulmonary artery CTA and initiation of coronary CTA were 6–8s. For patients with a HR = 60–80 bpm, the pulmonary artery CTA scan started 7s after the injection of contrast material and the delay between the initiation of pulmonary artery CTA and the initiation of coronary CTA was 9–11s. For patients with a HR < 60 bpm, the pulmonary artery CTA scan started 9s after the injection of contrast material and the delay between the initiation of pulmonary artery CTA and the initiation of coronary CTA was 12–15s. A total of 30 mL contrast medium was used for each patient in group A. The whole scan was divided into two steps of
scanning, that is, helical scans for the pulmonary artery CTA and axial scans for the coronary artery CTA. The contrast agent flow rate was 5 mL per second. Scan start timing is 17.48±3.14 s. Protocol for group A undergoing prospective ECG-triggered axial scan.

Protocol for group A underwent prospective ECG-triggered axial scan: For patients with a HR>80 beats per minute (bpm), we only acquire the systolic phase, HR = 60–80 bpm, acquire the both systolic and diastolic phase, HR <60 bpm, only acquire the diastolic phase. This scanning protocol can obtain pure pulmonary artery and pure coronary artery images in a single injection, avoiding the interference of venous imaging and obtaining higher quality image.

Protocol for Group B (Traditional CT Scan Protocol)

For patients in group B (n = 47), the routine bolus tracking technique was applied by setting the ascending aortic threshold of 80 HU with an injection of 70 mL contrast agents. Scanning of coronary and pulmonary arteries was performed simultaneously. The contrast agent flow rate was 5 mL per second. Scan start timing is 17.42±3.28 s. Protocol for group B undergoing retrospective ECG-triggered spiral scan.

Image Evaluation

The CT values of left anterior descending artery (LAD), left circumflex artery (LCX), right coronary artery (RCA) were measured. The image quality was evaluated by two experienced radiologists based on a 5-point Likert scale (1–un-assessable to 5–excellent): 1, failure in meeting the diagnosis; 2, poor image quality; 3, basically meeting the diagnosis; 4, good image quality; and 5, high image quality. The radiation dose and contrast agent volume were also recorded.

Statistical Analysis

All statistical analyses were performed using the SPSS v15.0 statistical software package (SPSS Inc., Chicago, IL.) Univariate analysis of variance was used to determine the differences in the CT values of LAD, LCX, and RCA between group A and B. Rank sum test was used to determine the difference of image quality between these two groups. A P-value less than .05 was considered statistically significant.

Results

Comparison of CT Values of Pulmonary Artery and Three Major Coronary Arteries between Group A and B

Figures 1A-1D and Figures 2A-2D show the representative images of CTA of coronary and pulmonary arteries. As shown in Table 1, the CT value of pulmonary artery in group A (484.7HU) was slightly but significantly higher than in group B (457.9HU) (t = 2.446, P = .016), while no significant differences in the CT values of LAD, LCX, or RCA were found between these two groups (P > .05). Thus, based on the CT scan timings defined according to patients’ HRs, a smaller amount of contrast agent (i.e., 30 mL) obtained a better CT

Figure 1. Coronary and pulmonary artery CTA images of a patient receiving 30 mL of contrast medium. (A–D) The axial CT images of pulmonary artery, RCA, LAD, LCX, and associated CT values. (E–G) Three-dimensional volume-rendered reconstruction of coronary CTA. (H–J) Curved multiplanar reformatted view of RCA, LAD, and LCX. RCA: right coronary artery; LAD: left anterior descending artery; LCX: left circumflex artery.
The quality of images obtained from scanning of pulmonary artery and coronary arteries of two group patients based on the 5-point Likert scale system mentioned above were compared. Table 2 shows the analysis of the quality of images of pulmonary artery; 27.7% of images of pulmonary artery from group A scored 5 compared with only 12.8% of pulmonary arterial images from group B ($\chi^2 = 8.292$, $P = .016$), indicating that the image quality of pulmonary artery was significantly better in group A than in group B.

The quality of images of coronary arteries was not statistically different between these two groups ($\chi^2 = 2.516$,
This suggests that the CTA protocol using less contrast agent in group A obtained better image quality for the pulmonary artery than the traditional tracking technique used in group B.

**Radiation Dose in DLP and ED**

The DLP and ED of group A are $217.05 \pm 37.31$ and $3.15 \pm .54$, respectively. The DLP and ED of group B are $230.31 \pm 36.98$ and $3.34 \pm .54$, respectively.

**Discussion and Conclusion**

In conclusion, in the present study, we have found that a smaller volume of contrast medium (30 mL of iopamidol 370) could still qualitatively enhance the CTA images of the pulmonary artery. With regard to the diagnostic performance and image quality of the HR-dependent contrast agent administration protocol, we reduced the amount of contrast agent used in the routine bolus tracking technique protocol (30 mL vs 70 mL) by more than 50% with no significant differences in the quality of images of three major coronary arteries obtained between these two protocols. Compared with traditional scanning protocol, HR-dependent contrast agent administration protocol has more advantages including obtaining pure pulmonary and coronary artery images.

The personalized, HR-dependent contrast agent administration protocol was set according to the patient’s HRs to determine the initiation time of scanning. Depending on the patient’s HRs, the timing of scanning the pulmonary artery varied. When the HR was $>80$ bpm, the pulmonary artery CTA scan started 5s after the injection of contrast material; after 7 s for 60–80 bpm; and after 9 s for HR <60 bpm. Our analysis of the pulmonary artery CT values showed that there was a small but significant difference between the personalized protocol and the traditional protocol, that is, the protocol dependent on the patient’s HR produced the CT values of the pulmonary artery higher than the traditional automatic trigger scanning. The use of the smaller diagnostically appropriate amount of contrast material (30 mL) was beneficial because it minimized the possibility of contrast induced nephropathy.

| Group   | Cases | Image quality of coronary artery |       |       |       |       |
|---------|-------|---------------------------------|-------|-------|-------|-------|
|         |       | 1 (cases, %)                    | 2 (cases, %) | 3 (cases, %) | 4 (cases, %) | 5 (cases, %) |
| Group A (30 mL) | 47   | 1 (2.1)                         | 3 (6.4) | 25 (63.2) | 15 (31.9) | 3 (6.4) |
| Group B (70 mL) | 47   | 0 (0)                           | 2 (4.2) | 22 (46.8) | 17 (36.2) | 6 (12.8) |
| $\chi^2$ | 2.516 |                                 |        |        |        |        |
| $P$     | .642  |                                 |        |        |        |        |

Table 4. Comparison of CT Values of Pulmonary Artery and Three Major Coronary Arteries between Group A and B.

|                | Group A | Group B | $P$   |
|----------------|---------|---------|-------|
| Age (years)    | 59.06 ± 11.44 | 58.68 ± 10.75 | .868  |
| Male, n (%)    | 18 (38.3)   | 25 (53.2)   | .147  |
| Heart rate (bpm) | 68.60 ± 7.24 | 70.34 ± 11.18 | .371  |
| Heart rate during the scan (bpm) | 67.51 ± 10.89 | 68.43 ± 11.22 | .689  |
| Scan start timing(s) | 17.48 ± 3.14 | 17.42 ± 3.28 | .929  |
| Hypertension, n (%) | 29 (61.7)   | 32 (68.1)   | .517  |
| Diabetes, n (%) | 9 (19.1)     | 12 (25.5)    | .458  |
| Smoking history, n (%) | 11 (23.4)   | 15 (31.9)    | .356  |
| GFR            | 94.53 ± 6.32 | 94.28 ± 6.13 | .843  |
| BSA (m2)       | 1.72 ± .16   | 1.73 ± .15   | .742  |
| DLP            | 217.05 ± 37.31 | 230.31 ± 36.98 | .087  |
| ED             | 3.15 ± .54   | 3.34 ± .54   | .087  |

Abbreviations: LAD, Left anterior descending; LCX, left circumflex artery; RCA, Right coronary artery.
indicated that it was possible to reduce the amount of contrast material to <1.0 mL/kg (30 mL of the total amount of contrast material). Clinical parameters for both groups and relative statistics have been presented in Table 4. The minimum CT values of the main branches of coronary arteries (LAD, LCX, and RCA) were 336 HU, and no differences were found between these two groups in the CT values of LAD, LCX, or RCA; this was in accordance with previous reports.\(^{26-28}\)

Collectively, per results indicated that the adequate attenuation of the coronary artery was approximately 300-350 HU. Our findings were better than those reported by Yamamuro et al.,\(^{25}\) who showed that in some patients a total contrast material injection volume of <.9 mL/kg yielded contrast enhancement of <250 HU, a value insufficient for coronary CTA. Additionally, the present study demonstrated that (at the contrast material injection time) revolution CT has very high speed scanning, only taking 5s with contrast agent injection. Unlike a previous report showing that protocols that carried contrast material injection time (CT), left anterior descending artery (LAD), left circumflex artery (LCX) and right coronary artery (RCA), body mass index (BMI), heart rates (HR), Hounsfield unit (HU).

There are some limitations in our study. First, traditional pulmonary and coronary artery scanning takes place simultaneously, while our HR-dependent contrast medium injection protocol was axial scanning and included two scanning steps: pulmonary artery implemented spiral scanning, and coronary artery implemented axial scanning. Second, the HR-dependent protocol used a slightly higher radiation dosage than the traditional scanning. Third, we are failure to reduce the volume of contrast medium according to different body habitus.

The HR-dependent contrast medium injection protocol can greatly reduce the use of contrast medium without compromising of the image quality of major coronary arteries. Furthermore, it can simplify the work-flow and may obtain better CTA image quality of pulmonary artery compared with the traditional bolus tracking technique.

**Authors’ contributions**

PJS contributed to the study conception and design. XML SHY, and HRY performed the Material preparation, data collection and analysis. XML was a major contributor in writing the manuscript. HW, ZG, GYC, and HS performed reconstruction images. All authors read and approved the final manuscript.

**Declaration of Conflicting Interests**

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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**Abbreviations**

Computed tomography angiography (CTA), computed tomography (CT), left anterior descending artery (LAD), left circumflex artery (LCX) and right coronary artery (RCA), body mass index (BMI), heart rates (HR), Hounsfield unit (HU).

**Ethics approval and consent to participate**

This study was approved by the Ethic Committee of Jinan Central Hospital. Written informed consent was obtained from all patients.

**Availability of data and materials**

The datasets used and/or analyzed during the current study are available from the corresponding author (Peiji Song: 1597292215@qq.com), without undue reservation.

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**References**

1. Bean DB, Roshon M, Garvey JL. Chest pain: diagnostic strategies to save lives, time, and money in the ed. Emerg Med Pract. 2003;5(6):1-32.
2. Haro LH, Decker WW, Boie ET, Wright RS. Initial approach to the patient who has chest pain. Cardiol Clin. 2006;24(1):1-17.
3. Boie ET. Initial evaluation of chest pain. Emerg Med Clin North Am. 2005;23(4):937-957.
4. Tapson VF. Acute pulmonary embolism. N Engl J Med. 2008;358(10):1037-1052.
5. Swap CJ, Nagurney JT. Value and limitations of chest pain history in the evaluation of patients with suspected acute coronary syndromes. JAMA. 2005;294(20):2623-2629.
6. Zipes DP. Braunwald’s heart Disease. W.B. Saunders; 2006.
7. Horlander KT, Mannino DM, Leeper KV. Pulmonary embolism mortality in the united states, 1979-1998: an analysis using multiple-cause mortality data. Arch Intern Med. 2003;163(14):1711-1717.
8. Lilienfeld DE, Chan E, Ehland J, Godbold JH, Landrigan PJ, Marsh G. Mortality from pulmonary embolism in the united states: 1962 to 1984. Chest. 1990;98(5):1067-1072.
9. van Belle A, Buller HR, Huisman MV, et al. Effectiveness of managing suspected pulmonary embolism using an algorithm combining clinical probability, d-dimer testing, and computed tomography. JAMA. 2006;295(2):172-179.
10. Stein PD, Woodard PK, Weg JG, et al. Diagnostic pathways in acute pulmonary embolism: recommendations of the pioped ii investigators. Radiology. 2007;242(1):15-21.
11. Ladapo JA, Jaffer FA, Hoffmann U, et al. Clinical outcomes and cost-effectiveness of coronary computed tomography angiography in the evaluation of patients with chest pain. J Am Coll Cardiol. 2009;54(25):2409-2422.
12. May JM, Shuman WP, Strote JN, et al. Low-risk patients with chest pain in the emergency department: negative 64-mdct coronary angiography may reduce length of stay and hospital charges. AJR Am J Roentgenol. 2009;193(1):150-154.
13. Branch KR, Bresnahan BW, Veenstra DL, et al. Economic outcome of cardiac ct-based evaluation and standard of care for suspected acute coronary syndrome in the emergency department: a decision analytic model. Acad Radiol. 2012;19(3):265-273.
14. Barrett BJ, Parfrey PS. Clinical practice. Preventing nephropathy induced by contrast medium. N Engl J Med. 2006;354(4):379-386.
15. Stacul F, van der Molen AJ, Reimer P, et al. Contrast induced nephropathy: updated esur contrast media safety committee guidelines. Eur Radiol. 2011;21(12):2527-2541.
16. Kurtkoti J, Snow T, Hiremagalur B. Gadolinium and nephrogenic systemic fibrosis: association or causation. Nephrology (Carlton). 2008;13(3):235-241.
17. Zhao L, Bao J, Guo Y, et al. Ultra-low dose one-step CT angiography for coronary, carotid and cerebral arteries using 128-slice dual-source CT: a feasibility study. Exp Ther Med. 2019;17(5):4167-4175.
18. Lee HY, Yoo SM, White CS. Coronary CT angiography in emergency department patients with acute chest pain: triple rule-out protocol versus dedicated coronary CT angiography. Int J Cardiovasc Imaging. 2009;25(3):319-326.
19. Cao LX, Zhang H, Liu B, et al. Evaluation of high-pitch flash scan for pulmonary venous cta on a 128-slice dual source ct: compared with prospective ecg-triggered sequence scan. Int J Cardiovasc Imaging. 2013;29(7):1557-1564.
20. Josephson SA, Dillon WP, Smith WS. Incidence of contrast nephropathy from cerebral ct angiography and ct perfusion imaging. Neurology. 2005;64(10):1805-1806.
21. Bredahl KK, Taudorf M, Lonn L, Vogt K, Sillese H, Eiberg J. Contrast enhanced ultrasound can replace computed tomography angiography for surveillance after endovascular aortic aneurysm repair. Eur J Vasc Endovasc Surg. 2016;52(6):729-734.
22. Gurtler VM, Sommer WH, Meimarakis G, et al. A comparison between contrast-enhanced ultrasound imaging and multislice computed tomography in detecting and classifying endoleaks in the follow-up after endovascular aneurysm repair. J Vasc Surg. 2013;58(2):340-345.
23. Nakamura T, Awai K, Yauaga Y, et al. Contrast injection protocols for coronary computed tomography angiography using a 64-detector scanner: comparison between patient weight-adjusted- and fixed iodine-dose protocols. Invest Radiol. 2008;43(7):512-519.
24. Bae KT, Seeck BA, Hildebolt CF, et al. Contrast enhancement in cardiovascular mdct: effect of body weight, height, body surface area, body mass index, and obesity. AJR Am J Roentgenol. 2008;190(3):777-784.
25. Yamamuro M, Tadamura E, Kanao S, et al. Coronary angiography by 64-detector row computed tomography using low dose of contrast material with saline chaser: influence of total injection volume on vessel attenuation. J Comput Assist Tomogr. 2007;31(2):272-280.
26. Becker CR, Hong C, Knez A, et al. Optimal contrast application for cardiac 4-detector-row computed tomography. Invest Radiol. 2003;38(11):690-694.
27. Cademartiri F, Mollet NR, van der Lugt A, et al. Intravenous contrast material administration at helical 16-detector row ct coronary angiography: effect of iodine concentration on vascular attenuation. Radiology. 2005;236(2):661-665.
28. Fei X, Du X, Yang Q, et al. 64-mdct coronary angiography: phantom study of effects of vascular attenuation on detection of coronary stenosis. AJR Am J Roentgenol. 2008;191(1):43-49.