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Current Concepts in Cardiac CT Angiography for Patients With Acute Chest Pain

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ABSTRACT

This article presents specific examples of delayed diagnosis of acute coronary syndrome, acute aortic dissection, and pulmonary embolism resulting from evaluating patients with nonspecific acute chest pain who did not undergo immediate dedicated coronary CT angiography (CTA) or triple rule-out protocol (TRO). These concrete examples of delayed diagnosis may advance the concept of using cardiac CTA (i.e., dedicated coronary CTA versus TRO) to triage patients with nonspecific acute chest pain. This article also provides an overall understanding of how to choose the most appropriate examination based on the specific clinical situation in the emergency department (i.e., dedicated coronary CTA versus TRO versus dedicated pulmonary or aortic CTA), how to interpret the CTA results, and the pros and cons of biphasic versus triphasic administration of intravenous contrast material during TRO examination. A precise understanding of various cardiac CTA protocols will improve the diagnostic performance of radiologists while minimizing hazards related to radiation exposure and contrast use. **(Korean Circ J 2010;40:543-549)**

KEY WORDS: Tomography, X-ray computed; Acute coronary syndrome; Acute aortic syndrome; Pulmonary embolism.

Introduction

The one-stop CT examination for chest pain, the so-called "triple rule-out (TRO) protocol" used to diagnose acute coronary syndrome (ACS), pulmonary embolism (PE), and acute aortic syndrome (AAS) is increasingly being performed in many institutions equipped with 64-slice multi-detector CT (MDCT) or newer generation MDCT scanners. Although there have been many articles dealing with TRO, these studies did not provide the specific examples of delayed diagnosis in assessing patients with nonspecific acute chest pain who do not undergo immediate cardiac CT angiography (CTA) (i.e., dedicated coronary CTA and TRO study).[1-10] In addition, there is limited information regarding overall concepts such as how to choose the optimal examination (i.e., dedicated coronary CTA versus TRO versus dedicated PE or aortic CTA) based on the specific presentation to the emergency department (ED), how to interpret the results of TRO, and the pros and cons of biphasic versus triphasic administration of intravenous contrast material during TRO examination. This article focuses on these issues.

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Cardiac CT Angiography in Patients With Acute Chest Pain

The cost to manage patients with nonspecific acute chest pain is 10 billion dollars in the United States annually.[1)2)] However, only 15-25% of hospitalized patients with nonspecific acute chest pain prove to have ACS.[11)] In addition, 2-5% of all ACS is missed with the conventional chest pain protocol, even though ED physicians have a low threshold for admitting the patients with unspecified acute chest pain (Fig. 1).[1)2)]

The diagnostic delay of AAS is also a serious problem worldwide. According to studies, the annual incidence of ACS, PE,

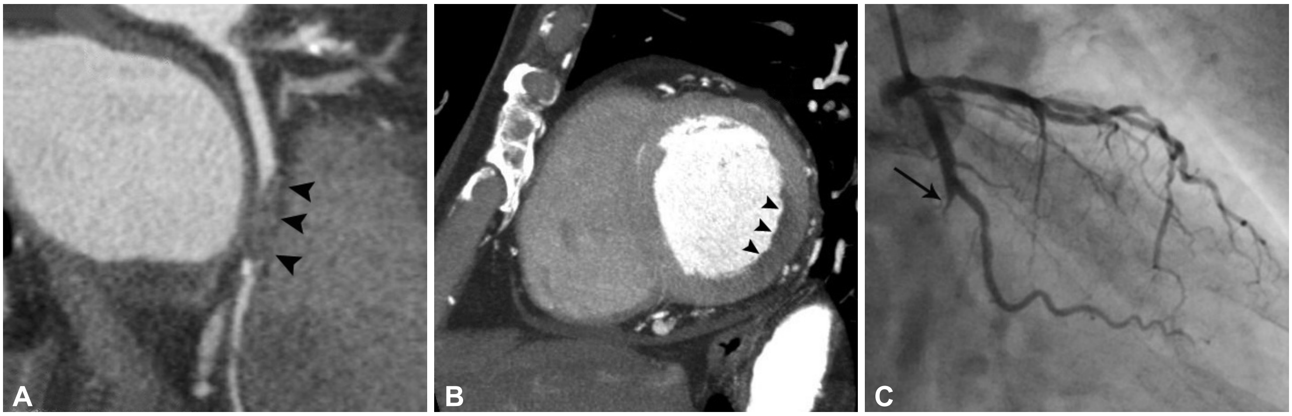

Fig. 1. Diagnostic delay in a 66-year-old male patient with acute coronary syndrome. The patient presented with acute chest pain. Dedicated coronary CT angiography was performed 7 days after symptomatic onset because the attending physician did not consider acute coronary syndrome as a primary diagnosis. A: curved multi-planar reformatted image shows total occlusion of distal left circumflex coronary artery (arrowheads). B: short axis curved multi-planar reformatted image at the basal level of the left ventricle demonstrates perfusion defect with low attenuation (arrowheads) in the territory of the left circumflex coronary artery. C: coronary angiogram shows complete obstruction (arrow) at the origin of distal left circumflex coronary artery.

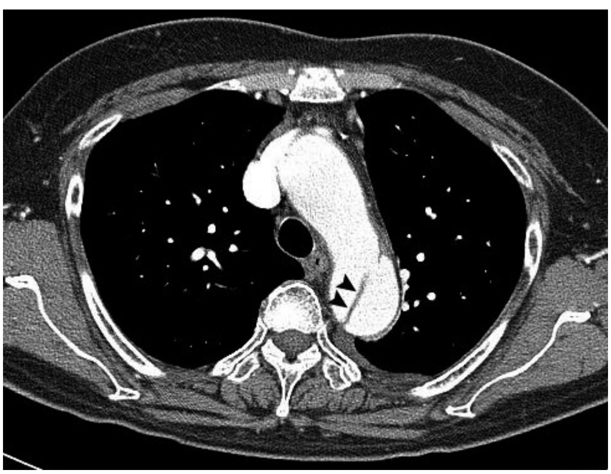

Fig. 2. Diagnostic delay in a 66-year-old female patient with Stanford type B dissection. This patient had a history of coronary stent insertion 2 years ago. The patient presented with acute chest pain to the emergency department. Emergent coronary angiography showed no significant stenosis in the coronary arteries. A Stanford type B aortic dissection (arrowheads) is noted on a trans-axial CT image at the level of aortic arch obtained 24 hours after coronary angiography.

and AAS is 440, 69, and 3 per 100,000 individuals, respectively.[12)13)] As AAS is much less frequent compared with ACS and there is substantial overlap in clinical symptoms and signs between ACS and AAS, ED physicians tend to mistake AAS for ACS, and the reverse also occurs. One study reported that up to 39% of aortic dissections have a diagnostic delay of at least 24 hours (Fig. 2).[14)] Because the highest mortality of AAS occurs within the first 48 hours after onset of symptoms,[15)] there has been great interest in developing new approaches to reduce diagnostic delay or missed diagnosis. PE also has a nonspecific clinical presentation, rendering its immediate diagnosis difficult (Fig. 3).

The diagnosis of ACS is straightforward if a patient has at least two of following findings: typical chest pain; elevated serum cardiac enzymes; or typical electrocardiography (ECG) changes. In these patients, coronary catheterization should be immediately performed without further non-invasive imaging studies. However, the diagnosis of ACS can be difficult because the nature of acute chest pain is often nonspecific, serum cardiac enzymes may remain normal within the first 6 hours after onset of symptoms, and ECG changes are frequently nonspecific.

Serial follow-up of ECG and serum cardiac enzymes over 12-24 hours with or without performing bicycle stress testing or radionuclide stress perfusion imaging is the mainstay of the conventional protocol to triage patients with nonspecific acute chest pain. However, the conventional protocol is not cost-effective for the diagnosis of ACS.[1)2)]

Furthermore, the diagnosis of unstable angina can be delayed with conventional protocols because serum cardiac enzymes are not elevated in patients with unstable angina.

When performing a diagnostic work up in patients with nonspecific acute chest pain, we have encountered occasions in which serial coronary angiography and chest CT are negative (Fig. 4). The final diagnosis in these cases may be esophageal, musculo-skeletal, or cryptogenic in origin. Such patients are the best candidates for TRO studies. Rogg et al.[16)] reported performing multiple diagnostic examinations (e.g., coronary angiography and dedicated PE CTA) to exclude at least two of ACS, PE, or AAS in 139 cases (22%) among 626 cases presenting with acute chest pain. The specific multiple examinations for combinations of ACS and PE, ACS and AAS, and ACS, PE, and AAS were performed in 121 (19%), 14 (2%), and 4 cases (0.6%), respectively.[16)]

Based on this investigation, patients with clinical concern for all three major acute chest pain diagnoses (i.e., ACS, PE, and AAS) are rare. In contrast, clinical scenarios where exclusion of either ACS and PE or ACS and AAS is necessary are fairly common.

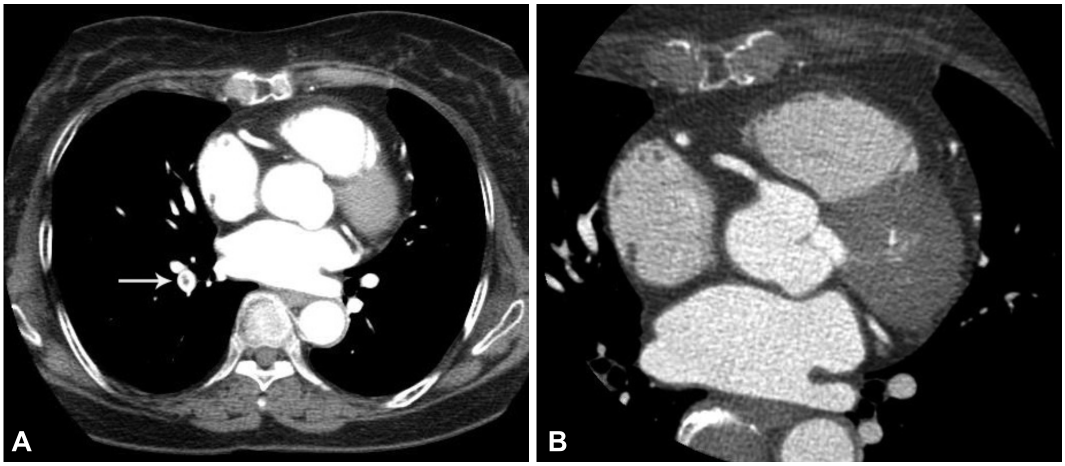

Fig. 3. Diagnostic delay in a 62-year-old female patient with acute pulmonary embolism. This patient presented with nonspecific acute chest pain. As atypical chest pain of non-urgent cause was the initial impression, dedicated coronary CT angiography was performed 3 days later. Coronary artery assessment was negative. A: segmental pulmonary embolism (arrow) is noted in posterior segmental pulmonary artery of the right lower lobe on a trans-axial CT image at the level of left atrium. B: note that this finding is not identified on a trans-axial CT image with small field of view. This case shows the importance of using a wide field of view image when interpreting dedicated coronary CT angiography.

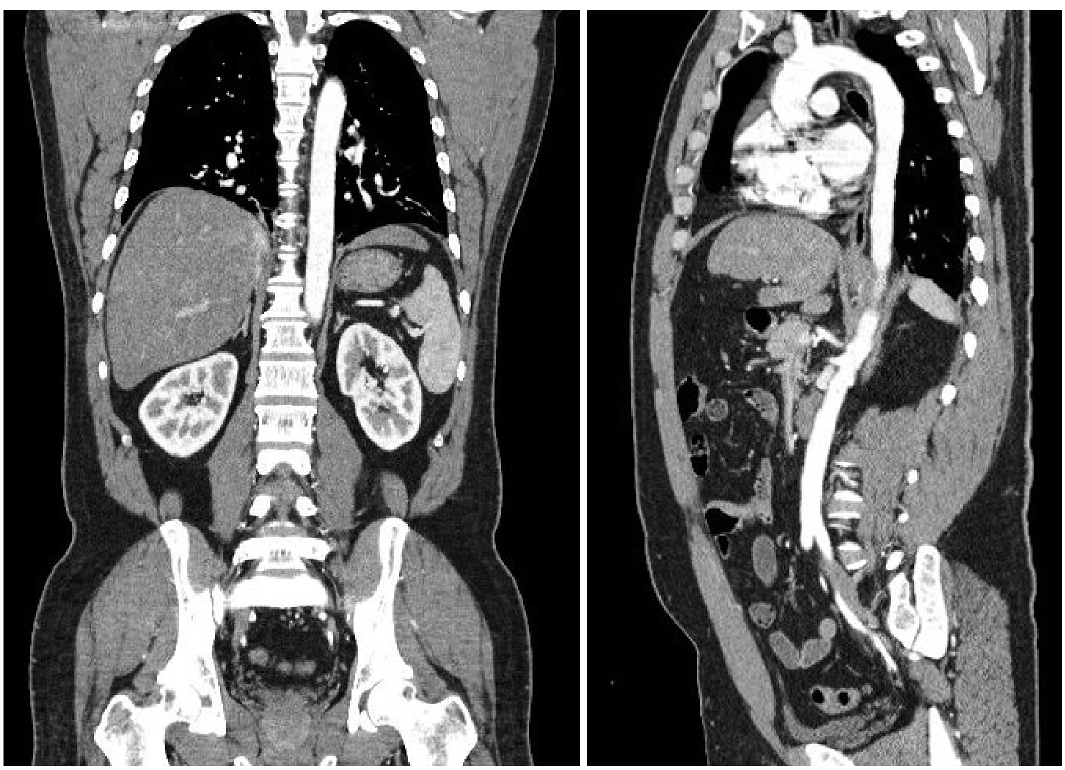

Fig. 4. A case of negative coronary angiography and dedicated aortic CT angiography in a 42-year-old male patient with nonspecific acute chest pain. The patient presented with severe acute chest pain in both the anterior chest and back. Emergent coronary angiography was negative. Dedicated aortic CT angiography performed on the next day was also negative. The cause of acute chest pain in the patient was determined to be esophageal spasm.

Multi-Detector CT Protocols for Acute Chest Pain and Indication for Triple Rule-Out

As suggested in the previous section, the choice of MDCT protocol depends greatly on the clinical presentation. Dedicated coronary CTA is generally indicated in patients with acute chest pain with normal or nonspecific ECG changes and normal initial cardiac enzyme levels.[2] TRO is associated with increased radiation exposure due to an extended z-axis compared with dedicated coronary CTA (Fig. 5). With respect to PE, one study reported that low clinical probability of PE (i.e., Well's criteria ≤4) supported by a negative D-dimer test was associated with a low 3-month incidence of a venous thrombo-embolic event (0.5%).[17] With respect to AAS, von Kodolitsch et al.[18] indicated that the probability of aortic dissec-

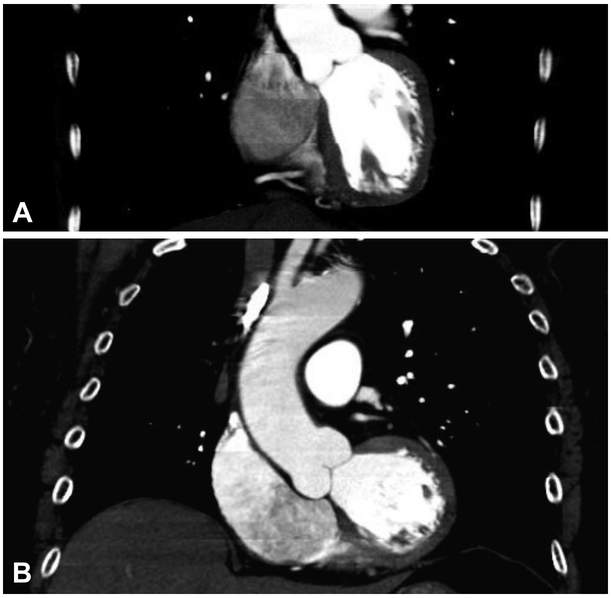

Fig. 5. Typical Z axis coverage in dedicated coronary CT angiography versus triple rule-out study. A: the field of view in a dedicated coronary CT angiography is demonstrated. B: note the increased Z axis length in the triple rule-out study compared with dedicated coronary CT angiography.

tion is low in patients lacking three variables (pulse or blood pressure differentials, mediastinal widening on chest radiography, and severe chest pain with sudden onset or ripping nature or both). Therefore, if the clinical pretest probability of PE and AAS is low and ACS is the only major concern, a dedicated coronary CTA is the most appropriate examination.

In contrast, if the clinical pretest probability of either PE or AAS is high, a dedicated PE or aortic CTA should be performed because these can be obtained without ECG-gating (i.e., lower radiation exposure compared with dedicated coronary CTA or TRO). Gallagher and Raff[19] have suggested that most central PE and aortic dissections can be diagnosed with dedicated coronary CTA because the field of view of dedicated coronary CTA includes much of the lower two-thirds of the thorax. Specifically, the entire thoracic aorta, except the arch and both main pulmonary arteries, is largely located within the field of view of dedicated coronary CTA. Therefore, TRO may be restricted to patients in whom the pretest probability of ACS and PE or AAS is intermediate. The TRO has some advantages in evaluating PE and AAS compared with an aortic CTA or dedicated PE study because of ECG-gating, namely more precise evaluation of aortic valve and coronary artery involvement by a dissection flap and better demonstration of PE in the paracardiac pulmonary arteries.[5]

There is concern that similar to the experience with PE CTA,[13] TRO with an even higher radiation dose will be overused in the ED setting. Contraindications to the TRO protocol include clinical instability, severe arrhythmia, renal failure, allergy to contrast material, use in young women, and a high thrombolysis in myocardial infarction score (score ≥5). Rapid heart rate (>65 beats/min) is a relative contraindication to TRO on 64-slice MDCT because coronary artery motion artifact often impairs precise evaluation at higher heart rates.[3] However, with the faster temporal resolution of newer scanners, such as the 128-slice dual source CT (75 msec), diagnostic imaging quality of the entire coronary arteries may be feasible, even with heart rates up to 75 beats/min and beyond. Finally, as severe coronary artery calcification may compromise evaluation of coronary artery stenosis, a high coronary artery calcium score (>1,000) can also be a relative contraindication of TRO.[19]

Prerequisites for Optimal Triple Rule-Out Evaluation

It is best to have the CT room located in or near the ED because patients with acute chest pain have the potential to be unstable. As noted above, it is important to keep the patient's heart rate low to enable TRO imaging of optimal quality. This is generally done with beta-blockers, using one of two methods. The first is to administer an oral beta-blocker in the ED, and then, if the patient's heart rate remains high (>65 beats/min) in the CT room, an intravenous beta-blocker is also administered. In the second approach, an intravenous beta-blocker is initially used to control heart rate.[20] The latter approach has the advantage of reducing the time for heart rate control but requires a physician to be present for the CT scan.

Once the examination is performed, rapid interpretation is mandatory to facilitate an immediate triage decision in patients with acute chest pain. Although advances in 3-dimensional software technology facilitate multi-planar reconstruction including volume rendering imaging, trans-axial CT images with or without curved multi-planar reformatted images are primarily used to establish the extent of coronary artery stenosis in patients with acute chest pain. When an experienced cardiac radiologist reads the TRO by this method, it can take approximately 30 minutes from the patient's arrival in the CT room to the final reading. For 24-hour coverage, remote reading may be a more cost-effective way to handle final interpretations, although on-site personnel with cardiac imaging training is the best option. For example, a remote reading capability is now provided by various venders and allows radiologists to interpret a TRO study from anywhere. Specific technical aspects of cardiac CTA protocols in patients with acute chest pain are not provided in this article because many previous articles have thoroughly discussed these points.[1-3)5-10)19]

Interpretation of Results of Dedicated Coronary CT Angiography or Triple Rule-Out

The recent ROMICAT trial reported that the negative predictive value for excluding ACS is 100% and showed no shortterm major cardiac events in patients with acute chest pain who had no plaque on dedicated coronary CTA.[21] Accordingly, it was possible to discharge these patients immediately. It should be stressed that there were seven cases of ACS (7/31, 23%) with non-obstructive coronary artery stenosis (<50%) on coronary CTA. This may have been caused by inaccuracies in the coronary CTAs to evaluate distal small coronary braches (i.e., <2 mm in diameter).[22] It may also have resulted from embolism into the coronary artery, sustained spasm of coronary artery, or spontaneous thrombolysis.[23)24] Therefore, patients with acute chest pain and non-obstructive coronary artery stenosis (<50%) on coronary CTA should not be discharged immediately and may require serial ECG and serum cardiac enzyme follow-up.

Immediate coronary angiography is mandatory in patients with acute chest pain and critical coronary artery stenosis (>70%) (Fig. 6). For patients with indeterminate coronary artery stenosis (50-70%) or non-diagnostic coronary CTA caused by coronary motion artifact, severe calcified plaque, or low contrast-noise ratio, radionuclide stress perfusion imaging is a possible option to further triage these patients.[25] However, if a patient has a positive result on radionuclide stress perfusion imaging, the total radiation exposure becomes quite high because coronary angiography is generally performed next. This is a drawback in using CT as part of the triage system to evaluate patients with acute chest pain. For this reason, alternative modalities that do not involve radiation exposure, such as stress echocardiography or stress MRI, may be considered to mitigate high radiation exposure in this subgroup of patients with acute chest pain, although there has not been a well-designed study addressing this scenario.

Principle of Contrast Media Use in Triple Rule-Out Study

In contrast to dedicated coronary CTA, the pulmonary arteries, as well as the aorta and coronary arteries, must be well opacified in the TRO protocol to simultaneously evaluate these arteries. Therefore, a different approach to performing the CTA examination is necessary for TRO.[2] In performing a TRO study with 64-slice MDCT, the intravenous administration of contrast material during the scanning time (approximately 10-15 seconds) plus a trigger delay (about 5 seconds) is used to opacify the aorta and coronary arteries. Because the pulmonary transit time (the time for contrast material to travel from pulmonary circulation to left circulation) is approximately 10 seconds, the total time necessary to administer the contrast material in TRO is approximately 25-30 seconds.[26] This time is shorter for newer scanners such as 256-slice MDCT or 128-dual source CT because of shorter scan times, which permits a decrease in the amount of contrast material used (State the advantage of this to the patient).

Because of the relatively high amount of contrast material (i.e., flow rate of 4-5 mL/s) with iodine concentration of 350-400 mg/mL used in many institutions, irrespective of patient's body mass index (BMI), special care should be taken to restrict the amount of contrast material for emergent cardiac CTA, especially in slim patients. Iodine concentrations of 0.5 g/kg are sufficient to opacify the target vessels in TRO.[4]

There are two methods to administer contrast material in a TRO protocol, the biphasic and triphasic method.[1)4-7] In the biphasic method, there are two phases during which 100% contrast material and saline flush are administered consecu-

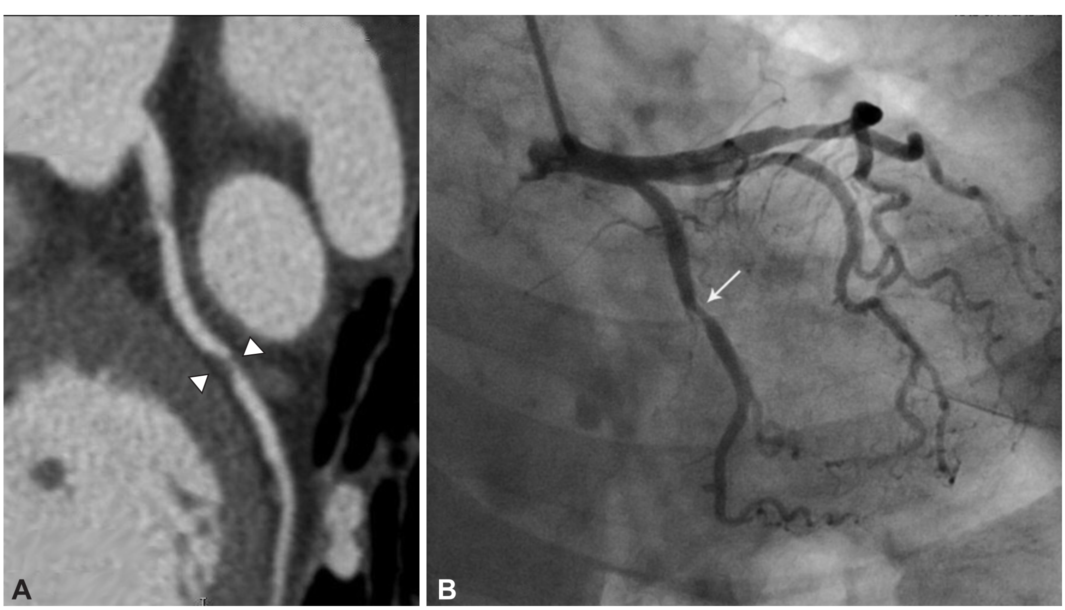

Fig. 6. A 67-year-old female patient with a critical coronary artery stenosis (>70%) in a triple rule-out study. A: critical coronary artery stenosis (>70%, arrowheads) with non-calcified plaque is identified at the proximal left circumflex coronary artery on a curved multi-planar reformatted image. B: critical coronary artery stenosis (arrow) is also identified in the same segment on coronary angiography.

Fig. 7. Mild streak artifact in a triple rule-out study using a biphasic administration of contrast material. There is no significant steak artifact in the right coronary artery (arrow), even with a high concentration of contrast material within the right ventricle.

tively. In the triphasic method, a third phase is added consisting of a mixture of contrast material and saline between the first and last phases. The triphasic method has the advantage that there is less streak artifact within the right coronary artery caused by a high concentration of contrast material in the right atrium or ventricle compared with biphasic method. However, the triphasic method may lead to poorer contrast enhancement within the pulmonary artery because the pulmonary circulation is opacified by dilute contrast material during the second phase, so that a PE may be missed. Although there may be cases which have streak artifact through the right coronary artery with a biphasic administration of contrast material, streak artifact severe enough to disturb the evaluation of the right coronary artery appears to be rare with TRO using the biphasic method (Fig. 7).

Radiation Dose in the Triple Rule-Out Protocol

Every possible strategy should be used to reduce radiation exposure associated with TRO. ECG-gated tube pulsing in which the radiation dose is automatically reduced in the systolic phase is one promising method which makes it possible to reduce the total radiation dose up to 50%.[1)2)27)28)] ECG-gated tube pulsing is the best option to reduce radiation dose in an MDCT scanner that does not offer a "step and shoot method" (i.e., coronary CTA performed by prospective gating).

BMI-based kV and tube current should be used to reduce radiation dose whenever possible. Lower kV and tube current (e.g., 100 kV and 450 mA) are often sufficient to obtain diagnostic image quality in slim patients (BMI less than 25 kg/m^2).[29)]

Recent MDCT scanners are equipped with prospective gating capabilities. With prospective gating, radiation is emitted only during a targeted time period, usually a mid-diastolic phase.[29-31)] One study reported that this method has better resolution compared with retrospectively gated image, because the CT table does not move while scanning is being performed (i.e., conventional versus spiral acquisition).[29)] However, prospective gating cannot be used in patients with an irregular or fast heart rate. In addition, no information about cardiac function is obtained with prospective gating because only a part of the cardiac cycle is imaged. Nevertheless, the radiation dose savings of prospective gating is considerable compared with retrospective gating with a higher radiation dose.[1)32)33)] According to one study using 64-slice MDCT, the average radiation dose of TRO using prospective gating was 9.2$\pm$2.2 mSv (BMI=28$\pm$5 kg/m^2).[7)] In another study, the radiation dose of dedicated coronary CTA using prospective gating was less than 3.0 mSv (1.1-3.0 mSv) with lower BMI patients (BMI=26.1$\pm$4.0 kg/m^2).[29)] Therefore, TRO can be performed with radiation exposures in the 6-8 mSv range in non-obese patients on 64-slice MDCT.

Future Directions

TRO is expected to be more widely used for patients with nonspecific acute chest pain because it can be performed with lower radiation exposure (<5 mSv) using the recently released 128-dual source MDCT if the patient's heart rate is regular and slow. The scanning time of TRO with this scanner is approximately one second. Further advances in temporal resolution of MDCT scanners may increase the number of patients who can undergo radiation-sparing prospectively gated TRO examinations and achieve a sufficient imaging quality. Because various MDCT scanners with different capabilities (64, 128, 256, and 320-slice MDCT) are used for TRO, the radiation dose and utilization of contrast material should be individualized according to the body configuration of the individual patient and the scanner type.

Conclusion

Various CT protocols exist for evaluating patients with nonspecific acute chest pain. Accordingly, the choice of an optimal CT examination should be individualized according to the specific clinical presentation. To avoid unnecessary radiation exposure and contrast use, it is advisable to restrict the TRO protocol to patients in whom the pretest probability of ACS and PE or AAS is intermediate.

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