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CASE SERIES
Cardiac Imaging

Clinical utility of two-phase computed tomography angiography for the detection of myocardial perfusion defects related to acute coronary syndrome in patients with acute chest pain: a case series

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Background Evaluation of acute chest pain (ACP) in the emergency department is a major health issue and differential diagnosis remains challenging for the physician, particularly in patients with atypical symptoms and inconclusive changes in electrocardiogram (ECG) or biomarkers levels.

Case summary We present the potential value of the two-phase computed tomography angiography (TP-CTA) imaging protocol done in six different patients evaluated with ACP and underwent non-gated or gated computed tomography angiography (CTA) to exclude pulmonary embolism (PE), acute aortic syndrome (AAS), or acute coronary syndrome (ACS). All patients had new-onset chest pain and atypical clinical presentation with non-diagnostic ECG and initially negative or near-normal cardiac biomarkers.

Discussion The evaluation of myocardial computed tomography perfusion (MCTP) using TP-CTA imaging protocol might open a new diagnostic approach to evaluate MCTP in patients with ACP related to PE, AAS, or ACS.

Keywords Acute chest pain • Acute coronary syndrome • Myocardial CT perfusion • Computed tomography angiography • Emergency department • Case series

Learning points

- Early-phase imaging of computed tomography angiography is an effective tool to evaluate the anatomic data in patients with acute chest pain (ACP) related to pulmonary embolism, acute aortic syndrome, or acute coronary syndrome.
- Evaluating myocardial computed tomography perfusion with a late-phase contrast imaging might offer a novel approach in appropriately selected patients with ACP.
- Acute myocardial perfusion abnormalities are better observed at late-phase imaging than at early-phase imaging.

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Introduction

Evaluation of acute chest pain (ACP) in the emergency department (ED) is a major health issue and differential diagnosis remains challenging for the ED physician, particularly in patients with atypical symptoms and inconclusive changes in electrocardiogram (ECG) or biomarkers levels. Computed tomography angiography (CTA) is considered an effective tool in the ED to evaluate patients with ACP related to pulmonary embolism (PE), acute aortic syndrome (AAS), or acute coronary syndrome (ACS). A non-gated or gated CTA can be requested as it would be considered clinically appropriate to evaluate pulmonary arteries, aorta, and coronary arteries.

Using a two-phase CTA (TP-CTA) imaging protocol in this scenario is not a new concept. In patients with ACP related to PE or AAS, a late-phase non-gated CTA imaging obtained 60–120 s after bolus injection has been used to provide information about pseudo-filling defects on early-phase computed tomography (CT) images related to circulatory stasis, late filling of the false lumen, contrast extravasation from rupture, and slow endografts leaks. On the other hand, it has been shown that the evaluation of myocardial CT perfusion (MCTP) on resting gated CTA in patients with ACP is feasible and a late CT scan performed 7 min after first-pass acquisition for MCTP correlates closely with the presence of myocardial necrosis.[1,2] Furthermore, Koyama *et al.*[3] showed that an early perfusion defect seen on two-phase contrast-enhanced CTA might reflect a decrease in the volume of the vascular bed, i.e. a decrease in the myocardial blood flow. After the contrast medium reaches the microvascular bed, it gradually flows into the interstitium, and is washed out slowly. Therefore, myocardial enhancement in the late-phase mainly reflects the characteristics of the interstitium, i.e. the volume of the interstitial space.

With the following images, we show the potential value of the TP-CTA imaging protocol done in six different patients who were evaluated with ACP and underwent non-gated or gated CTA protocol according to the decision made by the physician involved in the standard clinical care of the patient in order to exclude AAS, PE, or ACS. All patients had new-onset chest pain and atypical clinical presentation with non-diagnostic ECG or non-ST-segment elevation and initially negative or near-normal cardiac biomarkers. No patients had previous history of coronary artery disease, myocardial infarction (MI), or ED visits.

All CTA scans were performed with a 64-multidetector row Lightspeed VCT scanner (GE Heathcare). All patients were in normal sinus rhythm at the time of the CTA. For coronary CTA patients, intravenous administration of metoprolol was indicated to achieve a resting heart rate <65 beats/min and isosorbide dinitrate was administered 5 min before contrast injection. Depending on the body mass index, 50–80 mL of non-ionic iodinated contrast media was injected with a flow rate of 3.5–5 mL/s by using an 18-G intravenous line followed by the same volume with 30% contrast media and 70% saline solution (only for coronary CTA) and followed by a saline chaser. Bolus-tracking technique was used to trigger the start of image acquisition. The delay time between reaching the threshold and the start of the early CTA acquisition was 6 s. Delay scan for late-phase imaging was obtained 60 s after the start of contrast medium administration and acquired with the same early-phase scanning parameters. Mean radiation dose exposure was 10.4 + 7.1 mSv per scan.

CT raw data were transferred to a dedicated workstation and reconstructed for CTA analysis for AAS or PE or ACS allowing independent window and level settings performed at the discretion of the observers. For generating reports, all studies at our institution are analysed independently by two readers with over 10 years' experience of interpreting CTA. Whenever they disagreed, a consensus had to be reached. All invasive coronary angiograms were correlated with CTA findings and analysed between imaging physicians and the interventional cardiologist who was involved in the standard clinical care of the patient.

Timeline

Case number	Age (years)	Presenting symptoms	Suspected diagnosis	CT protocol indicated	Final diagnosis using two-phase computed tomography angiography protocol and anatomical correlation
1	51	Progressive tearing chest pain	Aortic dissection	Non-electrocardiogram (ECG)-gated computed tomography angiography (CTA) of thoracic aorta	Non-transmural inferolateral myocardial computed tomography (CT) perfusion (MCTP) defect related to an ostial occlusion of the marginal obtuse showed by invasive coronary angiography (ICA)
2	61	Atypical angina	Unstable angina	Coronary ECG-gated CTA	Transmural mid anteroseptal MCTP defect associated with a total occlusion of mid left anterior descending artery (LAD)

Continued

Continued

Case number	Age (years)	Presenting symptoms	Suspected diagnosis	CT protocol indicated	Final diagnosis using two-phase computed tomography angiography protocol and anatomical correlation
3	34	Acute tearing chest pain after exercise	Aortic dissection	Non-ECG-gated CTA of thoracic aorta	Transmural apical and anteroseptal MCTP defect related to a total occlusion of the mid LAD showed by ICA
4	63	Nausea and acute epigastric pain radiated to the back	Aortic acute syndrome	Non-ECG-gated of the thoraco-abdominal aorta	Non-transmural mid-to-apical anterolateral MCTP defect. ICA showed a thrombus in the proximal segment of the ramus intermedius
5	61	Ongoing chest pressure radiating to the back	Non-ST-segment elevation myocardial infarction	Coronary ECG-gated CTA	Transmural mid-to-basal anterolateral myocardial perfusion defect associated with a total occlusion of ramus intermedius
6	49	Haemodynamic compromise after aortic valve replacement	Pulmonary embolism	Non-ECG-gated CT pulmonary angiogram	Pulmonary embolism was rule-out but a non-transmural apical and anteroseptal MCTP defect was shown associated to a coronary embolism

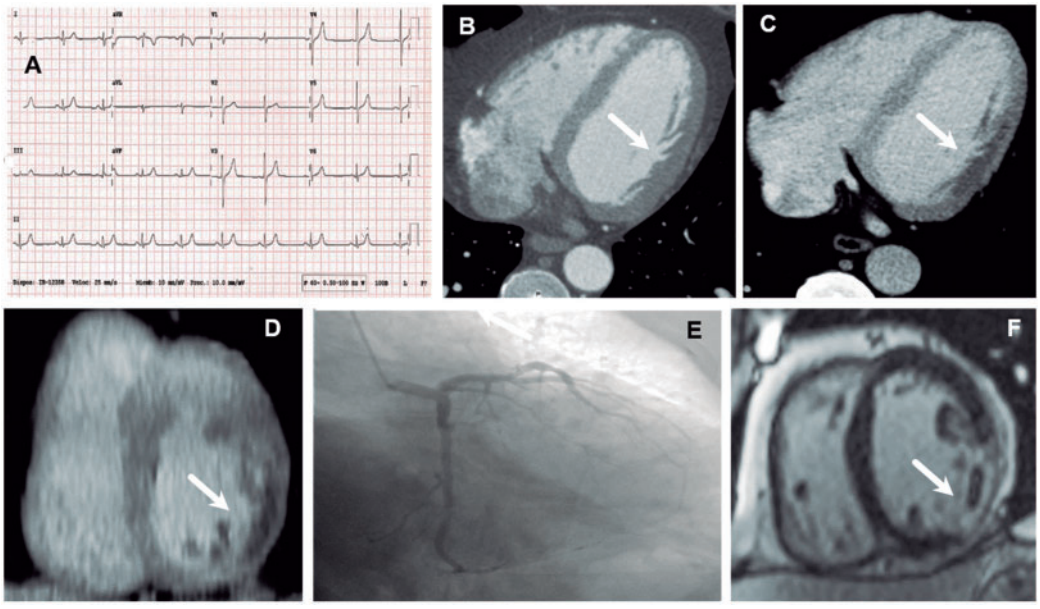

Figure 1 Two-phase computed tomography angiography non-gated imaging protocol in a patient with obtuse marginal occlusion. Electrocardiogram was obtained in a 51-year-old male with clinical suspicion of aortic dissection. The electrocardiogram shows sinus rhythm at 52 beats/min and non-specific electrocardiogram abnormalities (*A*). Patient was referred for a non-electrocardiogram-gated contrast-enhanced computed tomography angiography of the thoracic aortic. Early-phase axial image of computed tomography angiography of the aorta shows no perfusion defect in the territory of the left circumflex (arrow; *B*); however, late-phase contrast imaging, started 60 s after the end of the early-phase, shows a subendocardial to midmyocardial inferolateral perfusion defect (arrow; *C* and *D*). Right anterior oblique projection from the invasive coronary angiography shows a total occlusion at the origin of the obtuse marginal branch (arrow; *E*). Cardiovascular magnetic resonance shows a non-transmural inferolateral infarct that correlates with myocardial computed tomography perfusion using two-phase computed tomography angiography imaging protocol (arrow; *F*).

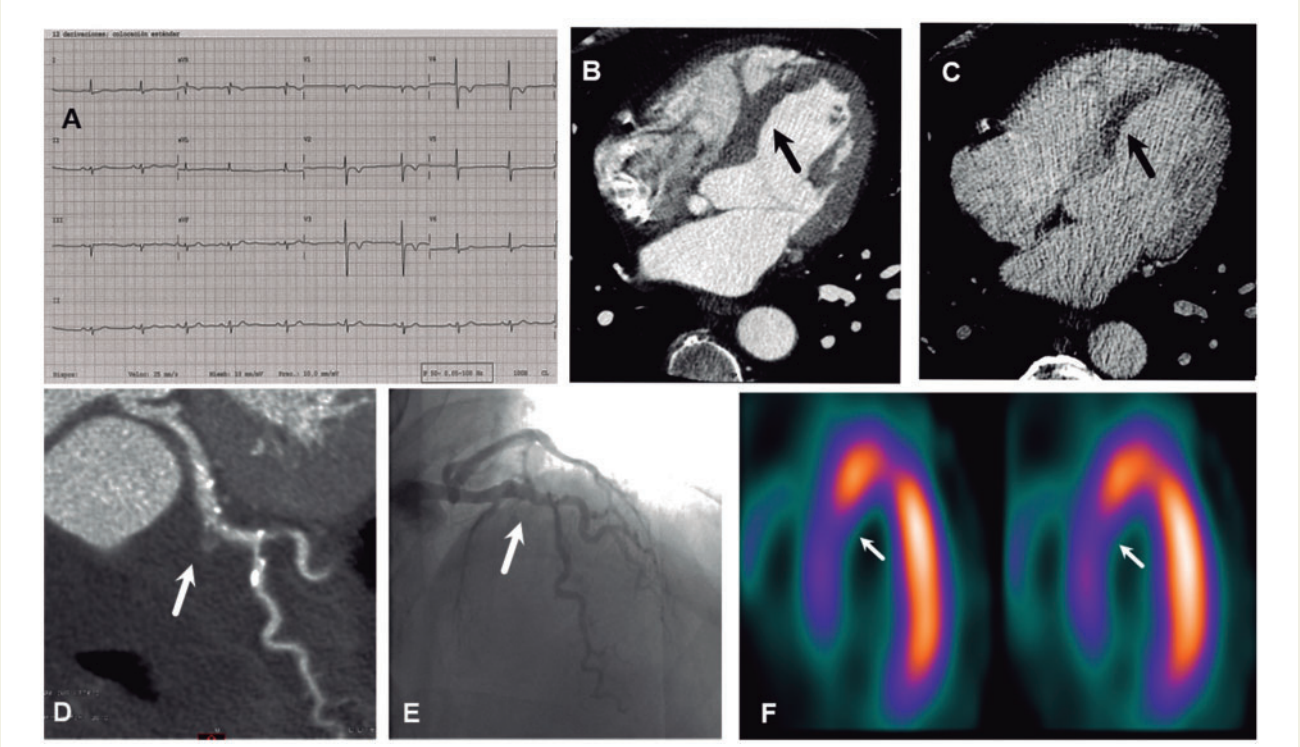

Figure 2 Two-phase computed tomography angiography-gated imaging protocol in a patient with left anterior descending artery occlusion. A 61-year-old male patient with clinical suspicion of unstable angina was referred for a coronary computed tomography angiography. The electrocardiogram shows sinus rhythm at a rate of 50 beats/min with left axis deviation associated to left anterior fascicular block. There is subtle ST-segment depression in V2–V5 with negative T waves in leads V1 through V4 (*A*). Early-phase axial image of coronary computed tomography angiography (arrow; *B*) showed no perfusion defect in the mid septum; however, late-phase contrast imaging, started 60 s after the end of the early-phase, revealed a transmural septal perfusion defect (arrow; *C*). Curved multiplanar reconstruction of coronary computed tomography angiography shows total occlusion of the mid-left anterior descending artery (arrow; *D*). Right anterior oblique projection from the invasive coronary angiogram confirms occlusion of the mid- left anterior descending artery in a patient with an anatomic variant of dual left anterior descending artery (arrow; *E*). An anteroseptal perfusion defect in the horizontal long-axis using rest single-photon emission computed tomography imaging suggests a non-transmural myocardial infarction which correlates with myocardial computed tomography perfusion using Two-phase computed tomography angiography imaging protocol (arrow; *F*).

Case presentation

Case 1

A 51-year-old male patient with active tobacco smoking presented at the ED with progressive tearing chest pain over 14 h radiating to the back. There were non-specific ECG abnormalities, high-sensitivity cardiac troponin I was lower than 3 ng/L (3–14 ng/L normal value) and no regional wall-motion abnormalities were shown by resting echocardiogram. A diagnosis of aortic dissection was suspected, and patient was referred for non-ECG-gated contrast-enhanced CTA of the thoracic aortic. While the thoracic aorta was normal a non-transmural inferolateral MCTP defect was demonstrated using the late-phase contrast imaging started 60 s after the end of the arterial phase. In consequence, invasive coronary angiogram was indicated showing an ostial occlusion of the marginal obtuse which was stented. Resting cardiac magnetic resonance imaging (cMRI), obtained before hospital discharge, demonstrated a non-transmural inferolateral infarct that correlates with MCTP imaging (*Figure 1*).

Case 2

A 61-year-old male patient with history of hypertension, diabetes, and active tobacco smoking presented with atypical chest pain at the emergency department. Patient ECG showed mild ST-segment depression and negative T waves in leads V1 through V4 and hs-cTn I was lower than 3 ng/L (3–14 ng/L normal value). Clinical suspicion was unstable angina and invasive coronary angiography (ICA) was recommended; however, patient declined doctor's recommendation. Then, he was referred for coronary CTA which revealed a total occlusion of mid left anterior descending artery (LAD) and also a transmural mid anteroseptal MCTP defect was demonstrated using the late-phase contrast imaging started 60 s after the end of the arterial phase. After knowing the results of cardiac computed tomography angiography (CCTA), patient agreed to proceed to ICA that showed dual LAD coronary artery with first diagonal mimicking the LAD. Mid-LAD was totally occluded after the first septal branch. According to the decision made by the physician involved in the clinical care of the patient no coronary intervention was indicated. Resting single-

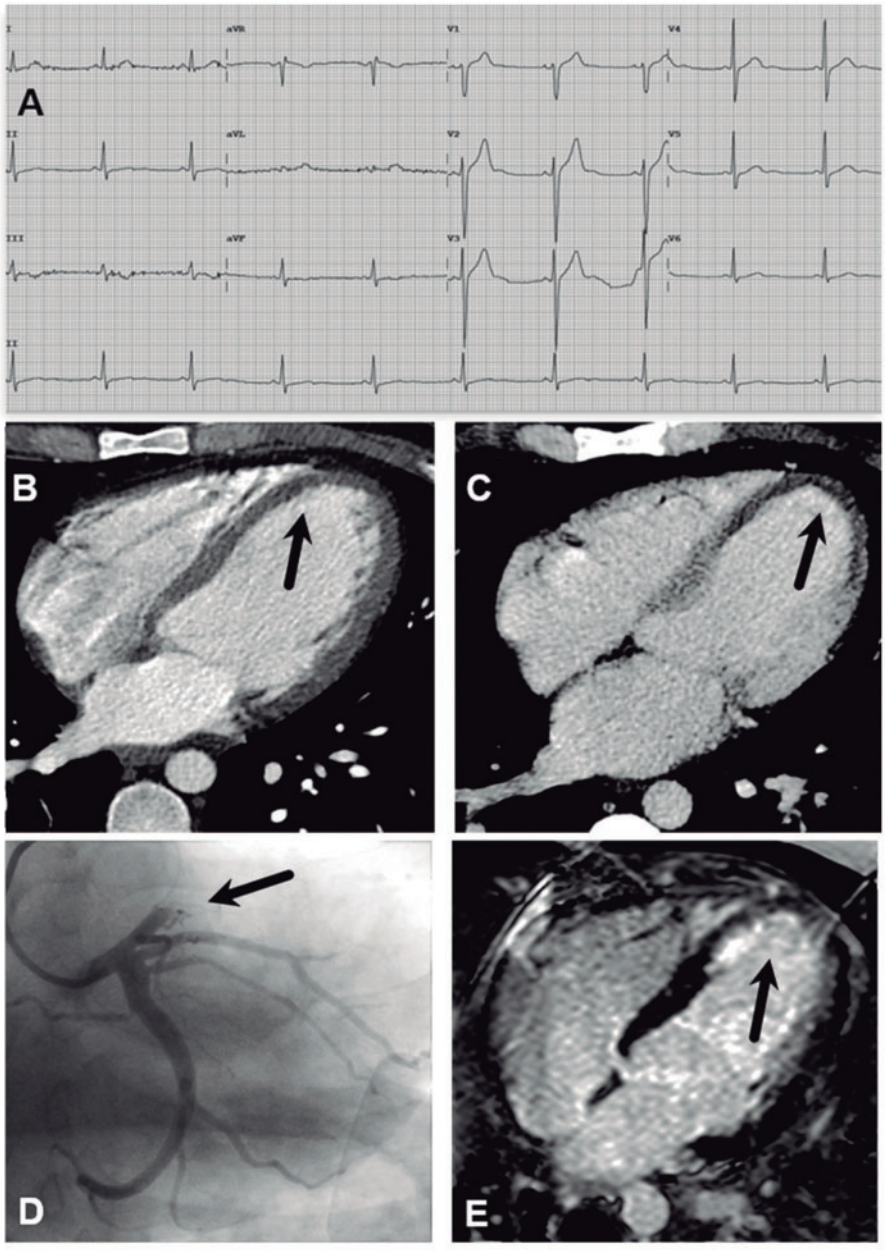

Figure 3 Two-phase computed tomography perfusion non-gated imaging protocol in a patient with left anterior descending occlusion. A 34-year-old male patient with clinical suspicion of aortic dissection was referred for a non-electrocardiogram-gated contrast-enhanced computed tomography perfusion of the thoracic aortic. The electrocardiogram shows sinus rhythm at a rate of 58 beats/min with symmetric T waves in leads V1 through V4 and slightly inverted T waves in lead III and aVF (*A*). Early-phase axial image of computed tomography perfusion of the aorta (arrow; *B*) showed no perfusion defects; however, late-phase contrast imaging, started 60 s after the end of the early-phase, revealed a transmural mid to apical septal perfusion defect and also at the apex (arrow; *C*). Cranial right anterior oblique projection from the invasive coronary angiogram shows a total occlusion of the mid-left anterior descending artery (arrow; *D*). Cardiovascular magnetic resonance confirms a non-transmural infarct at apex and anteroseptal region which correlates with myocardial computed tomography perfusion using two-phase-computed tomography perfusion imaging protocol (arrow; *E*).

photon emission computed tomography (SPECT) was performed during the patient's admission and demonstrated a non-transmural mid-anteroseptal infarct that correlates with MCTP imaging (*Figure 2*).

Case 3

A 34-year-old male patient without cardiovascular risk factors presented at the ED with acute tearing chest pain after exercise radiating to the interscapular region. Patient ECG showed sinus rhythm with

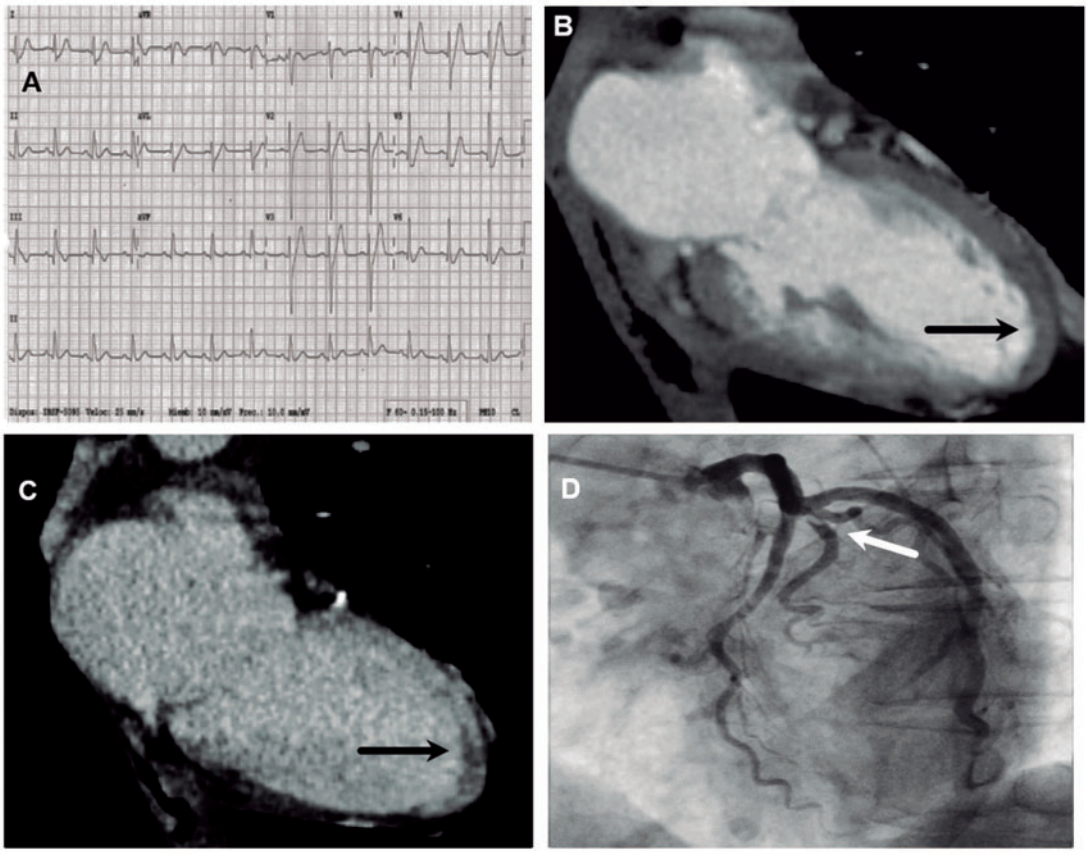

Figure 4 Two-phase computed tomography perfusion non-gated imaging protocol in a patient with a thrombus in ramus intermedius. A 63-year-old woman with clinical suspicion of aortic acute syndrome was referred for a non-electrocardiogram-gated-computed tomography perfusion of thoraco-abdominal aorta was indicated. The electrocardiogram shows sinus rhythm at a rate of 80 beats/min, mean QRS axis at 90°, qR complex in leads II, III and aVF with rS in leads I and aVL that might be related with left posterior fascicular block. There are non-specific intraventricular conduction abnormalities of leads II, III and aVF with QRS duration 0.12 s and QTc 416 ms. Electrocardiogram also shows J-point depression in leads I, aVL and V3 through V6, upsloping ST-segment depression with upright and symmetric T waves in leads V2 through V4 (*A*). Early-phase cardiac long vertical axis computed tomography perfusion showed no perfusion defects (arrow; *B*); however, late-phase contrast imaging, started 60 s after the end of the early-phase, revealed a non-transmural mid-to-apical anterolateral perfusion defect (arrow; *C*). Cranial left anterior oblique projection of invasive coronary angiogram shows a thrombus in the proximal portion of ramus intermedius having TIMI flow 2 (arrow; *D*) that explains the perfusion defect showed with myocardial computed tomography perfusion using two-phase-computed tomography perfusion imaging protocol.

symmetric T waves in leads V1 through V4 and hs-cTn T was 30.5 ng/L (3–14 ng/L normal value). Clinical suspicion was aortic dissection and patient was referred for non-ECG-gated contrast-enhanced CTA of the thoracic aortic. Normal aorta was shown and a transmural apical and anteroseptal MCTP defect was demonstrated using the late-phase contrast imaging started 60 s after the end of the arterial phase. In consequence, invasive coronary angiogram was indicated showing a total occlusion of the mid LAD which was stented. Resting cMRI, obtained before hospital discharge, demonstrated a non-transmural apical and anteroseptal infarct that correlates with MCTP imaging (*Figure 3*).

Case 4

A 63-year-old woman with a history of hypertension, chronic obstructive pulmonary disease, and percutaneous transluminal coronary angioplasty with LAD and right coronary artery (RCA) stenting 1 year ago was admitted to the ED for evaluation of nausea and acute epigastric pain radiating to the back. Pain began suddenly at home 2 h before admission and patient ECG showed sinus rhythm with symmetric T waves in leads V2 through V4 and hs-cTn T was 27 ng/L (3–14 ng/L normal value). In addition, 3 months before she had a normal cardiac stress SPECT imaging. Based on this cardiac SPECT result, clinical suspicion was an AAS and patient was referred for non-ECG-gated contrast-enhanced CTA of the thoraco-abdominal aorta. AAS was ruled out but the late-phase contrast imaging started 60 s after the end of the arterial phase revealed a non-transmural mid-to-apical anterolateral MCTP defect. Patient was transferred to catheterization laboratory for urgent cardiac catheterization. ICA showed LAD and RCA stent patency and a thrombus in the proximal portion of the ramus intermedius having

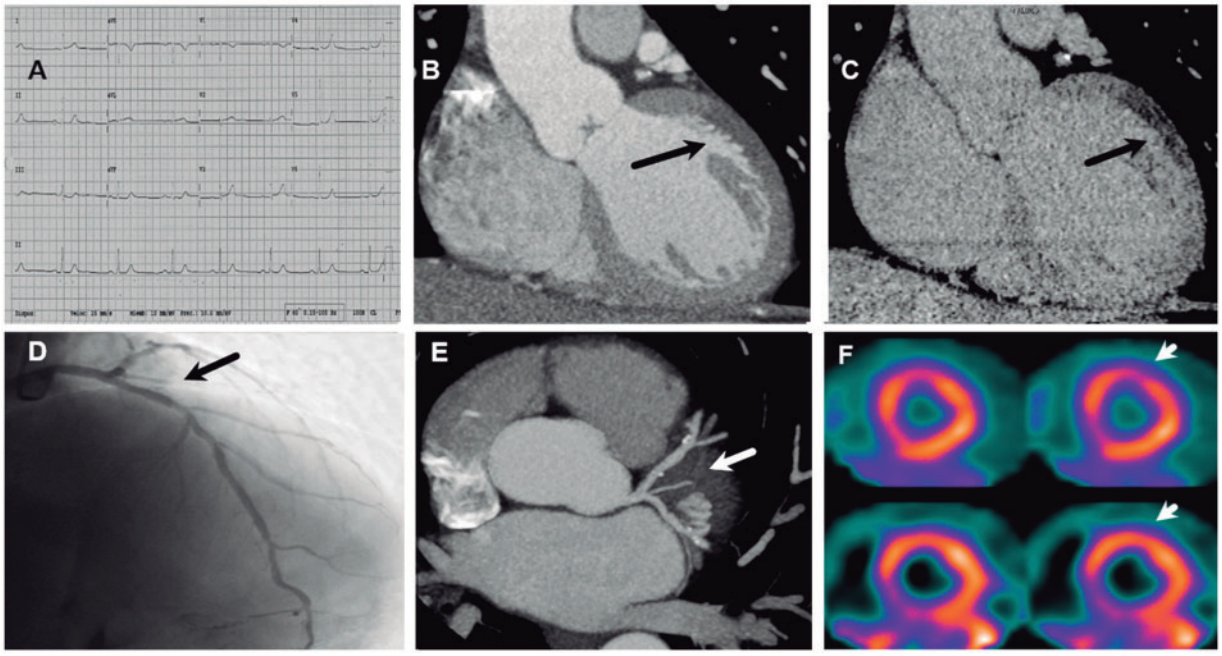

Figure 5 Two-phase computed tomography perfusion gated imaging protocol in a patient with ramus intermedius occlusion. A 61-year-old male patient with clinical suspicion of a non-ST-segment elevation myocardial infarction was referred for a coronary computed tomography perfusion. The electrocardiogram shows showed sinus bradycardia of 44 beats/min with slight horizontal ST-segment depression in leads III and aVF (*A*). Early-phase coronal image of coronary computed tomography perfusion shows no perfusion defects (arrow; *B*); however, late-phase contrast imaging, started 60 s after the end of the early-phase, shows a transmural anterolateral defect (arrow; *C*). Coronary computed tomography perfusion using maximum intensity projection shows a proximal and complete occlusion of the ramus intermedius (arrow; *D*). Invasive coronary angiogram confirms the occlusion of a less than 2 mm-diameter ramus intermedius (arrow; *E*). Stress single-photon emission computed tomography imaging shows a non-transmural basal anterolateral infarct with mild ischaemia that correlates with myocardial computed tomography perfusion using two-phase-computed tomography perfusion imaging protocol (arrow; *F*).

TIMI grade 2 flow. A bolus of intracoronary unfractionated heparin (1000 IU) was injected and continued intravenously for 72 h along with oral aspirin and clopidogrel. Patient was symptom-free after 24 h of treatment (*Figure 4*).

Case 5

A 61-year-old male patient with active tobacco smoking presented at the ED with ongoing chest pressure over 2 h radiating to the neck. Patient ECG showed sinus bradycardia with 0.5 mm horizontal ST-segment depression in leads III and aVF and hs-cTn T was 40.3 ng/L (3–14 ng/L normal value). Clinical suspicion was a non-ST-segment elevation MI and ICA was indicated; however, patient declined the recommendation of an invasive diagnostic procedure and he was referred for coronary CTA, which revealed a total occlusion of ramus intermedius and also a transmural mid-to-basal anterolateral MCTP defect was demonstrated using the late-phase contrast imaging started 60 s after the end of the arterial phase. The patient agreed to have an invasive angiography after being informed about the abnormal CT results. This showed a small occluded vessel which was medically managed. Cardiac stress SPECT imaging done 6 weeks later showed a non-transmural mid-to-basal anterolateral infarct with mild ischaemia (*Figure 5*).

Case 6

A 49-year-old man who had aortic valve replacement due to endocarditis became haemodynamically unstable after cardiac surgery. A preoperative CCTA did not reveal any significant coronary artery stenosis. ECG showed ST depression on anterior leads and right ventricular dysfunction, septal flattening and pulmonary dilatation with normal left ventricular (LV) function were shown by echocardiogram. Clinical suspicion was PE and patient was referred for a non-ECG-gated contrast-enhanced CT pulmonary angiography. There were no filling defects indicative of a PE, but late-phase contrast imaging showed a non-transmural apical and anteroseptal perfusion defect that was not present in the initial CCTA. Coronary emboli from aortic vegetations was suspected and patient was discharged from hospital 2 weeks later after conservative management and cardiac rehabilitation (*Figure 6*).

Discussion

Our data suggest that a TP-CTA imaging protocol is useful in the evaluation of patients presenting with chest pain and provides additional useful information beyond standard CT angiography.

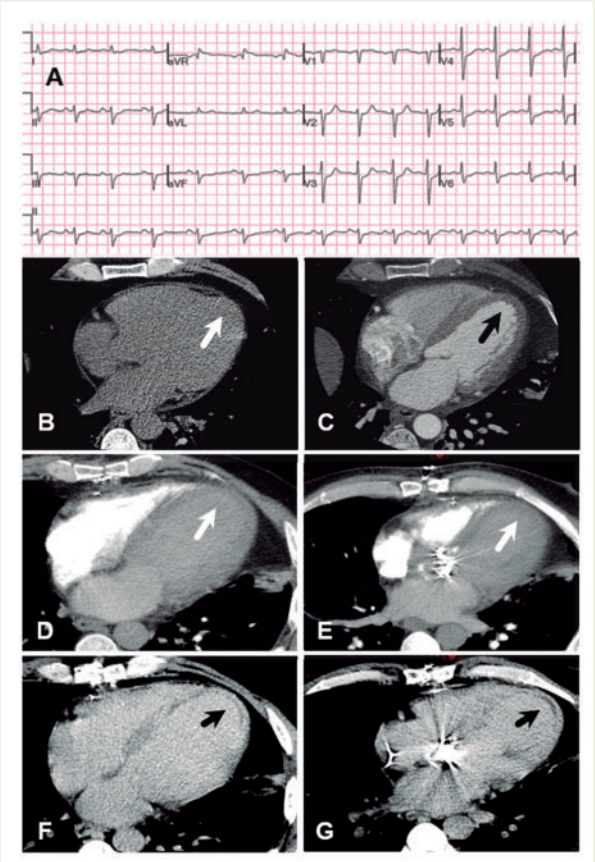

Figure 6 Two-phase computed tomography perfusion gated imaging protocol in a patient with anterior myocardial infarction after aortic valve replacement. A 49-year-old man with a clinical suspicion of pulmonary embolism after aortic valve replacement was referred for a non-electrocardiogram-gated contrast-enhanced computed tomography pulmonary angiography. The electrocardiogram shows sinus rhythm at a rate of 90 beats/min, left atrial abnormality and left axis deviation associated to left anterior fascicular block. Electrocardiogram also shows upsloping ST-segment depression in leads II, aVF and V2 through V6 (*A*). A preoperative cardiac computed tomography angiography did not reveal any significant coronary artery stenosis and no myocardial computed tomography perfusion defects were shown on non-contrast (arrow; *B*) and neither on contrast axial images (arrow; *C*). Early-phase axial image showed no filling defects at the pulmonary arteries and neither myocardial computed tomography perfusion defects (arrow; *D*, *E*); however, late-phase contrast imaging, started 60 s after the end of the early-phase, shows a non-transmural apical and anteroseptal perfusion defect that was not present at the first cardiac computed tomography angiography (arrow; *F*, *G*).

Interestingly, MCTP abnormalities were more evident during late-phase imaging compared to early-phase imaging. The pathophysiological basis of this observation might be based on the kinetics of the iodinated contrast agent that has a different inflow time through the myocardium in the setting of a normal or non-significant coronary artery stenosis vs. a high-grade coronary artery stenosis and also that the late-phase imaging may have a more favourable image noise and contrast-to-noise ratio with less highly attenuating cardiac structures related to the contrast-enhanced left ventricle in the early-phase imaging.[4]

It is important to note that hypoperfused myocardial regions at MCTP imaging might also represent a previous MI or artefacts associated with cardiac motion and beam hardening. However, an old MI has lower CT attenuation values than those with acute MI due to fatty infiltration of the myocardium and chronic MI showed LV wall thinning, whereas acute MI was not.[5] In addition, a true perfusion defect should be congruent with the coronary anatomy and distribution.

A limitation of the TP-CTA imaging protocol is that the mean effective radiation dose among our scans using a conventional 64-multidetector computed tomography scanner is higher than the estimated for triple rule out studies and for a dedicated CTA scan as well. Significant radiation dose reduction along with uncompromised TP-CTA imaging protocol efficiency might be explored using low tube voltage, prospective protocols, new generation scanners, and new reconstruction algorithms.

In conclusion, systematic TP-CTA imaging protocol might open a new diagnostic approach to evaluate MCTP in patients with ACP related to PE, AAS or ACS using a single non-gated or ECG-gated CTA examination and improving patient management. The reproducibility of our data and the diagnostic accuracy of these observations need to be addressed in further studies performed in larger numbers of patients and also with novel CT scanners that keep the radiation dose as low as 1 mSv per scan.

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Supplementary material

Supplementary material is available at *European Heart Journal - Case Reports* online.

Slide sets: A fully edited slide set detailing this case and suitable for local presentation is available online as Supplementary data.

Consent: The authors confirm that written consent for submission and publication of this case report including images and associated text has been obtained from the patients in line with COPE guidance.

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