

**Multi-slice CT Angiography “Triple Rule Out technique” in the Evaluation of
Emergency Department Patients with Acute Chest Pain Having Low to Intermediate
Risk for Acute Coronary Syndrome**

**Ashraf Mohammed Elaggan^{a*}, Reem Prince Mohamed Ibrahim^a, Mai Mohamed Abd
Elmonen Salama^b, Manal Ezzat Badawy^a**

^aRadiodiagnosis Department, Faculty of Medicine, Tanta University, Tanta, Egypt

^bCardiology Department, Faculty of Medicine, Tanta University, Tanta, Egypt

Abstract

Background: A large number of individuals visit an emergency department (ED) complaining of chest pain that cannot be diagnosed, which remains a formidable clinical challenge.

Objectives: In this study, we set out to determine how useful triple rule out (TRO) MSCT angiography is for diagnosing acute chest pain (ACP) in patients who are present to the emergency room.

Patients and Methods: This study was conducted on 50 patients, presented to ED and the cardiac care unit (CCU) complaining from ACP. 12-leads an electrocardiography (ECG) examination, cardiac enzymes (Troponin, CKMB) and TRO CT angiography were assessed to all patients.

Results: Thirty patients were diagnosed with ACS, four patients were diagnosed with aortic aneurysm, the diagnosis in another four patients was pulmonary embolism, six patients were normal, and another six patients have a non-vascular cause. There was highly statistically significant relation between diagnosis as regard coronary angiography and CTA TRO ($p < 0.05$). There was highly statistically significant relation between diagnosis as regard coronary angiography and TRO CT angiography ($p < 0.05$). CTA TRO can diagnose ACP with sensitivity 93.75%, specificity 50%, positive predictive value 93.75%, negative predictive value 50% and diagnostic accuracy 88.89%.

Conclusions: An appealing option is the TRO protocol, which can be used to avoid all three possibly deadly reasons for acute chest pain with a single scan. This is particularly true for older patients who have a relatively lower risk of radiation-induced cancer, and for emergency department patients with atypical chest pain who are not at high risk.

Keywords: Triple Rule out; Multi-slice CT; Acute Chest Pain; Angiography.

***Correspondence:** ashrafelagan@yahoo.com

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Introduction

Following abdominal pain, acute chest pain (ACP) is the most prevalent symptom that patients experience upon visiting an emergency department (ED) (Maroules et al., 2023). Due to its wide differential diagnosis, which can include everything from harmless to potentially fatal reasons, ACP poses a significant diagnostic problem in emergency care (Dedic et al., 2013). Pulmonary embolism (PE), acute aortic syndrome (AAS), and acute coronary syndrome (ACS) are the most important therapeutically significant causes of chest pain that need to be distinguished (Eltabbakh et al., 2019).

The first step in assessing ACP is to identify whether the patient requires a referral to a more advanced facility in order to exclude ACS (McConaghy et al., 2020).

Coronary CT angiography (CCTA) is now used in the emergency department to triage patients presenting with acute coronary syndrome (ACP) thanks to the rapid advancements in multi-slice computed tomographic (CT) technology. This modality can be beneficial to the practitioner because it allows for direct visualization of the coronary anatomy, can image the rest of the thorax simultaneously to rule out aortic dissection and pulmonary embolism, and can provide alternate causes of chest pain, such as pneumonia, pericardial fluid, and oesophageal inflammation (Kumar and O'Neil, 2022).

One noninvasive method of assessing coronary circulation and seeing the arteries of the lungs and thoracic aorta all in one scan is the triple rule out computed tomography (TRO-CT), which is based on electrocardiography (ECG) (Russo et al., 2021a). Thanks to this capabilities, TRO-CT became a standout diagnostic tool in some clinical contexts. It is particularly useful for patients with ACP who are at low to moderate risk for ACS and should also be considered for PE or AAS as part of their differential diagnosis (Monica et al., 2020).

In many individuals with ACP, TRO-CT can reliably exclude away ACS and identify those with severe coronary artery stenosis. It also has high negative predictive values. Further, TRO-CT anatomic imaging of the entire chest can identify non-coronary causes of ACP, allowing emergency room doctors to swiftly guide patients to the best in- or out-patient treatment (Stoevesandt and Buerke, 2011, Russo et al., 2021a).

Finding out how useful TRO MSCT angiography is for assessing patients who come in with ACP was the driving force for this study.

In this study, we set out to determine how useful TRO MSCT angiography is for diagnosing ACP in patients who are present in the emergency room.

Patients and methods

Fifty patients, half male and half female, meeting the clinical criteria for chest pain and low to intermediate risk for ACS were included in this study. The research took place from April 2023 to November 2023 at Tanta University Hospitals in Tanta, Egypt, with the permission of the Ethical Committee. (Approval code: 36264PR606/3/24). An informed written consent was obtained from all patients.

Pregnancy, renal impairment, known contrast media or cardiac enzyme allergies, and an electrocardiogram (ECG) indicative of acute myocardial infarction (AMI) were all grounds for exclusion.

A comprehensive history was obtained from each patient, followed by a clinical examination, an electrocardiogram (ECG) with 12 leads, testing for cardiac enzymes (Troponin and CKMB), and TRO CT angiography.

Triple Rule Out CT Angiography (TRO CT)

All CT examinations of patients suffering from ACP were examined using a MSCT system. Patients with normal or irregular heart rates are not given beta-receptor blockers prior CT. The cardiologist and the

radiologist were present at the time of the examination.

Setting Up the Scan

Scout: The heart and the whole thoracic aorta should be included in the TRO CT scan. Scans of the TRO are often set to begin 1 cm over the aortic arch, typically at the inferior margins of the clavicular heads, after reviewing the scout to program. The premonitoring phase involves positioning the ROI over the descending thoracic aorta. Bolus triggering technique is used for contrast administration, where the acquisition curve is triggered at 60 Hounsfield Unit (HU) level. CT acquisition is done in a cranio-caudal direction, with standard scan delay of 3 seconds and scan time of 2 seconds. Two protocols for contrast administration were used.

Single phase contrast administration protocol: where a large amount of nonionic contrast (about 90 to 120ml) is injected continuously. Images acquisition starts during contrast administration, resulting in simultaneous opacification of the aorta, coronaries, pulmonary arteries and veins. The drawback of this technique is the opacification of the SVC which may hinder image quality, as streak artifact may interfere with proper interpretation of the images of the RCA.

Double phase contrast administration protocol: where the entire volume of the contrast was divided into 2 parts, the 1st part is the un-diluted iodinated contrast, about 60 ml, followed immediately by another 50 ml of contrast/saline. Images acquisition starts during second phase diluted contrast administration, resulting in simultaneous opacification of the aorta, coronaries and pulmonary arteries, where the SVC is only semi-opacified, resulting in better images of the RCA as well as significant contrast media volume reduction. The drawback of this technique is the narrow time window and small amount of contrast media,

requiring experienced personnel and optimum timing.

Data Processing: Is done using a multi-modality advanced software visualization system. The raw data obtained ranges about 1000 image per examination. The axial images and multiplanner reformatted images are used primarily for provisional diagnosis and exclusion of major pulmonary and aortic disease. Maximum Intensity Projection (MIP), Virtual 3D (VRT) and curved reconstructed images for the coronary arteries and the heart were later obtained and examined thoroughly, as well as reexamination of the pulmonary and aortic vessels, for final diagnosis and reporting.

Statistical analysis

Data was analyzed using SPSS v26, which was developed by IBM Inc. and is based in Chicago, IL, USA. The mean and standard deviation (SD) were used to display the quantitative variables. Frequency and percentage (%) were used to display the qualitative factors. The diagnostic discrimination performance of each test was evaluated using receiver operating characteristics (ROC) curve analysis. When assessing the overall performance of a test, the area under the curve (AUC) is used; an AUC more than 50% is considered acceptable, while an AUC close to 100% is considered optimal.

Results

The amount of contrast administration for every patient included at the study

The maximum volume of contrast was 135 ml. The minimum volume was 90ml. The mean volume of contrast for every patient was about 102 ml. As one will notice, there was a steady decline in the volumes and amounts of contrast administration to patient through the time of the study. This was attributed to the more understanding of the technique, the more expertise both technician and radiologist gain with time and also, better understanding the different contrast administration techniques and methods used in TRO CT angiography.

The amount of radiation exposure for every patient included at the study

The maximum radiation dose was 19 mSv. The minimum radiation dose was 15 mSv. The mean radiation exposure dose was 16.3 mSv. In contrary to the contrast administration figures, there was no such a steady decline in the radiation exposure for patient included in the study with time. There could be attributed to the large heterogeneity of the factors related to the radiation exposure dose, including: The body built of the patient, i.e. length of the chest and weight of the patient. Technical considerations hindering full implementation of the radiation reduction measures. Presence of co-morbidities, so, technical modifications of the initial technique were mandatory to overcome such conditions. i.e., inability to long enough breath holds and border line renal functions.

The number of males was remarkably higher than the number of females, contributing to 84% of the study

population. The age group from 60 to 70 years had the highest percentage among the current patients. ACS was the most encountered diagnosis, contributing to 60% of the patients (30 out of 50). Four patients were diagnosed to have a pulmonary embolism. Also, there were four patients diagnosed to have aortic aneurysms. Six patients were diagnosed to have non-vascular causes of ACP. Six patients had a non-diagnostic examination, meaning there were no radiological clue to explain the clinical condition. Diabetes Mellitus (DM) was the commonest risk factor, found in 32 patients, contributing to 64% of the study population. Hypertension (HTN) was the second commonest risk factor, found in 22 patients, contributing to 44% of the study population. Many patients have more than just a single risk factor, most of them had DM and HTN, contributing to 32% of the study population. The mean volume of contrast for every patient was about 102 ml. (Table. 1).

Table 1. Patient characteristics of the studied patients

Variables		N = 25
Age (years)	30- 50 years	12(24%)
	51- 60 years	14 (28%)
	61-70 years	16 (32%)
	> 70 years	8 (16%)
Sex	Male	42 (84%)
	Female	8 (16%)
Risk Factors		
Diabetes Mellitus		32 (64%)
Hypertension		22 (44%)
Previous ACS		8 (16%)
Hyperlipidemia		12 (24%)
Recent Surgery		2 (4%)
DM and HTN		16 (32%)
DM and Hyperlipidemia		6 (12%)
HTN and Hyperlipidemia		8 (16%)
DM, HTN and Hyperlipidemia		4 (8%)

Data are presented as frequency (%). ACS: acute coronary syndrome, DM: diabetes mellitus, HTN: hypertension

The mean radiation exposure dose was 16.3 mSv. In contrary to the contrast administration figures, there was no such a steady decline in the radiation exposure for

patient included in the study with time. Out of the 30-patient, 28 patients diagnosed ACS underwent reperfusion therapy- Percutaneous Trans-luminal

coronary interventional was done according to the standard protocols, as follows: 10 patients underwent angioplasty. 18 patients underwent angioplasty and stenting. Two patient was free of any significant coronary artery disease, with the lesion detected in CTA TRO turned out to be due to technical

error (False positive). Another two patient, with radiological examination revealed no diagnostic (normal), turned out to have ACS (false negative). Among these 30 patients, the coronary artery lesions were found to affect the LAD, followed by the RCA, then LCX and finally the LMT. (Table. 2).

Table 2. Radiological, final diagnoses and ACS distribution according to cardiac catheterization of the patients of the study

Diagnosis	No.
Radiological diagnosis	
Coronary Artery Disease	30 (60%)
Pulmonary Embolism	4 (8%)
Dissecting Aortic Aneurysm	4 (8%)
Non-Vascular	6 (12%)
Non-Diagnostic	6 (12%)
Final diagnoses	
ACS	30 (60%)
A. Aneurysm	4 (13.3%)
PE	4 (13.3%)
Nonvascular	6 (20.0%)
Normal	6 (20.0%)
ACS distribution according to cardiac catheterization	
CAD	30 (60%)
LAD	18 (60.0%)
RCA	6 (20.0%)
LCX	4 (13.3%)
LMT	2 (6.7%)

Data are presented as frequency (%). CAD: Coronary artery disease, LAD: left anterior descending artery, RCA: right coronary artery. LCX: Left Circumflex artery, LMT: left main trifurcation. ACS: acute coronary syndrome

28 patients out of the 30-patient diagnosed ACS underwent reperfusion therapy-Percutaneous Trans-luminal coronary interventional was done according to the standard protocols, as follows: 10 patients underwent angioplasty. 18 patients underwent angioplasty and stenting. two patients were free of any significant coronary artery

disease, with the lesion detected in CTA TRO turned out to be due to technical error (False positive). Another two patient, with radiological examination revealed no diagnostic (normal), turned out to have ACS (false negative). There was highly statistically significant relation between diagnosis as regard coronary angiography and CTA TRO (p-value <0.05). (Table. 3).

Table 3. Relation between diagnosis according to coronary angiography and CTA TRO

Diagnosis	Cardiac catheter		p-value
	Positive	Negative	
Positive	30 (93.8%)	2 (50%)	0.047
Negative	2 (6.3%)	2 (50%)	

Data are presented as frequency (%).

CTA TRO can diagnose of ACP with sensitivity 93.75%, specificity 50%, positive predictive value 93.75%, negative

predictive value 50% and diagnostic accuracy 88.89%. (Fig.1).

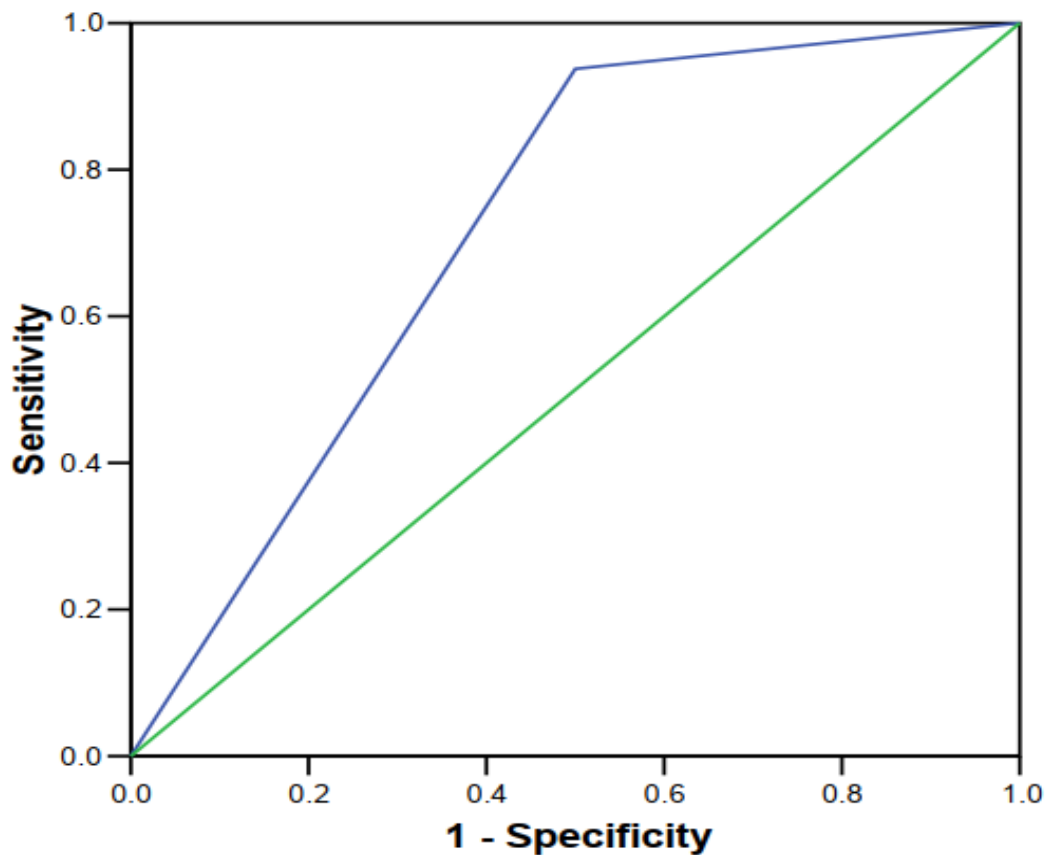


Fig.1. ROC curve for diagnosis of patients presenting with acute chest pain

Case 1

Female patient 59 years old. The patient was diabetic, not hypertensive, not smoker, not dyslipidemic with positive family history of ischemic heart disease. Recently started to experience recurrent attacks of atypical chest pain that was precipitated by effort and stress and relieved by rest. Presented complaining of chest pain, not relieved by rest or medication. She was referred from coronary care unit (CCU) to perform MSCT angiography. ECG showed no

significant abnormalities. Cardiac enzymes were pending at time of examination. TRO CTA was done.

CT angiographic findings: Normal CT angiography of the pulmonary and aortic arteries. Normal left main trunk (LMT), right coronary artery (RCA) and circumflex artery (LCX). LAD: Its middle segment showed focal concentric tight stenotic soft atheromatous lesion with tiny calcific focus. (Fig. 2)

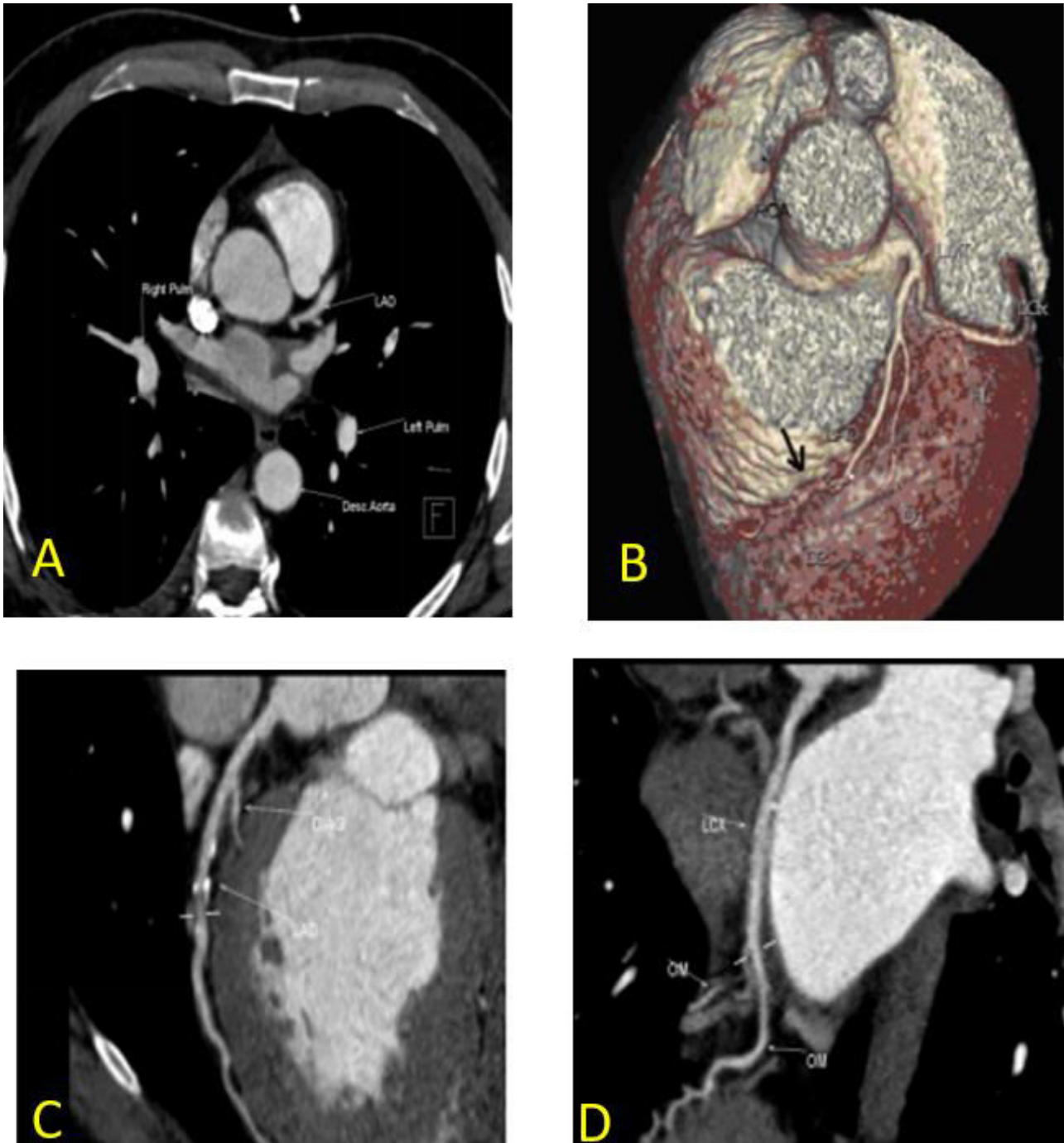


Fig. 2. A case of 59 years old female patient diabetic, not hypertensive showed (a) an axial cut at level of aorto-pulmonary window, (b) a VRT image of the heart, showing the LAD stenosis, (c) and (d) curved reconstructed images of LAD and LCX arteries, respectively, showing the LAD stenotic lesion

Case 2

Male patient 75 years old. He was hypertensive but not diabetic and chronic heavy smoker. He presented to CCU with ACP. He gave negative history of similar attacks of ACP with negative family history of ischemic heart disease. Cardiac

Enzymes were negative. ECG was negative. He was referred to perform MSCT angiography. TRO CTA was done. **CT angiographic findings:** Normal CT angiography of the coronary arteries and the pulmonary vessels. Aorta CT angiography revealed a very long and

sizable dissecting aortic aneurysm. Technical difficulty occurred. Unfortunately, the patient died 2 hours

after the examination before operation. (Fig. 3)

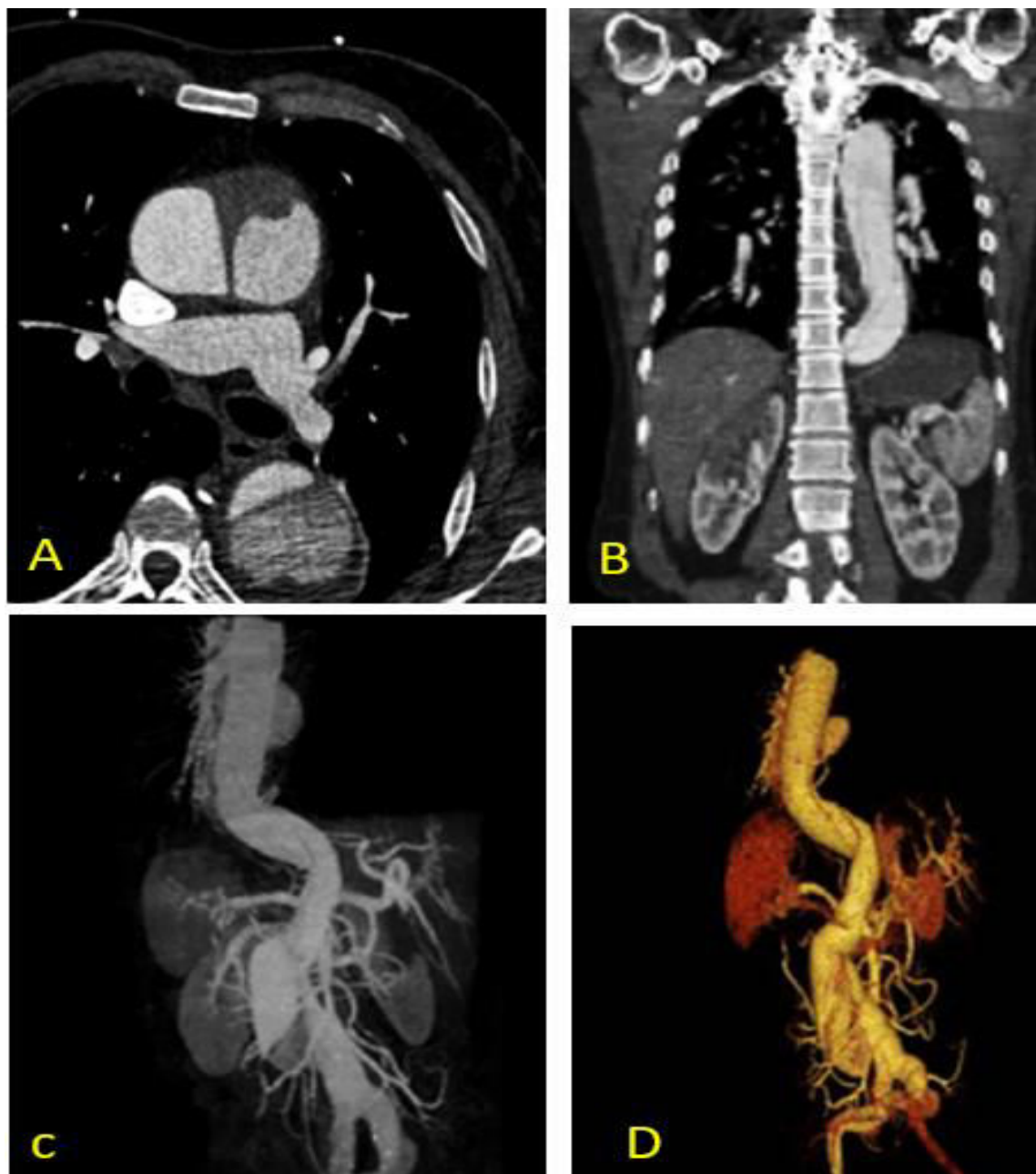


Fig. 3. A case of 75 years old male patient hypertensive but not diabetic showed: (a) an axial cut at level of main pulmonary trunk, (b) coronal MPR (c) coronal MPI of the aneurysm and (d) the 3D VRT reconstruction image

Case 3

Male patient 42 years old. The patient was not hypertensive nor Diabetic. He presented to the ER with ACP. The patient gave history of recurrent attacks of ACP, that was relieved by rest. He is not smoker

with negative family history of ischemic heart disease. Cardiac Enzymes were negative. ECG was negative. He was referred to perform MSCT angiography. TRO CTA was done. **CT angiographic findings:** Normal CT angiography of the aortic arteries and coronary arteries.

Pulmonary CT angiography revealed a thrombus within the common basal branch

of the right lower pulmonary artery of the right lung. (Fig.4)

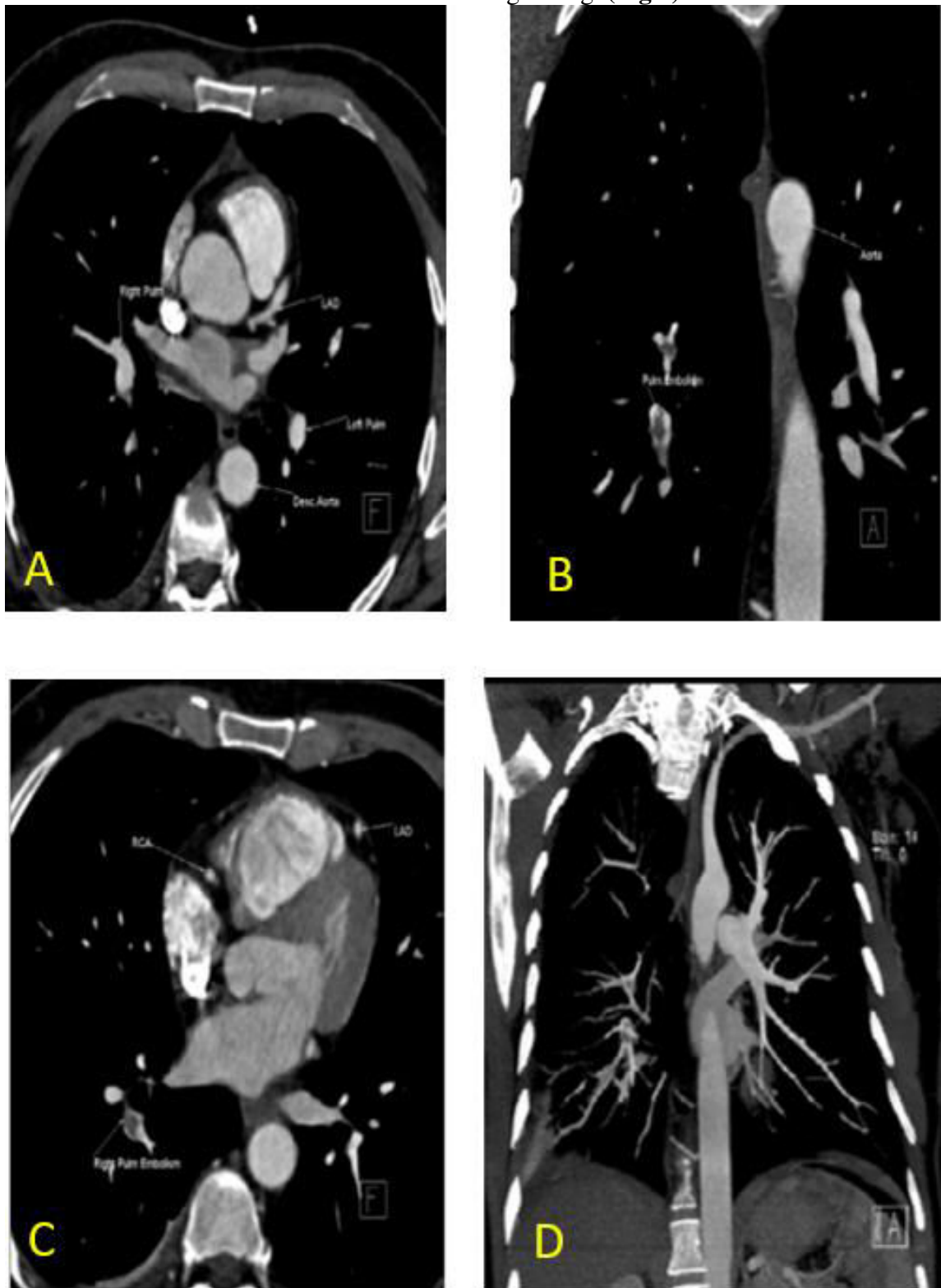


Fig. 4.A case of 42 years old male patient not hypertensive nor diabetic showed (a) an axial cut at level of aorto-pulmonary window, (b), (c) and (d) images showed pulmonary embolism of the right pulmonary artery in coronal, axial and coronal planes, respectively

Case 4

Male patient 60 years old. The patient was not diabetic or hypertensive. Came to the ER complaining of a crushing chest pain. There was history of previous similar attack the last week, that was relieved by rest. The patient was a chronic heavy smoker. ECG was negative. Cardiac enzymes were bending at time of the

examination. He was referred to perform MSCT angiography. TRO CTA was done. **CT angiographic findings:** Normal CT angiography of the pulmonary and aortic arteries. CT coronary angiography showed normal RCA, LCX and LMT. LAD: Its proximal segment showed focal severe tight stenotic soft plaque, causing almost total occlusion of the artery. (**Fig. 5**)

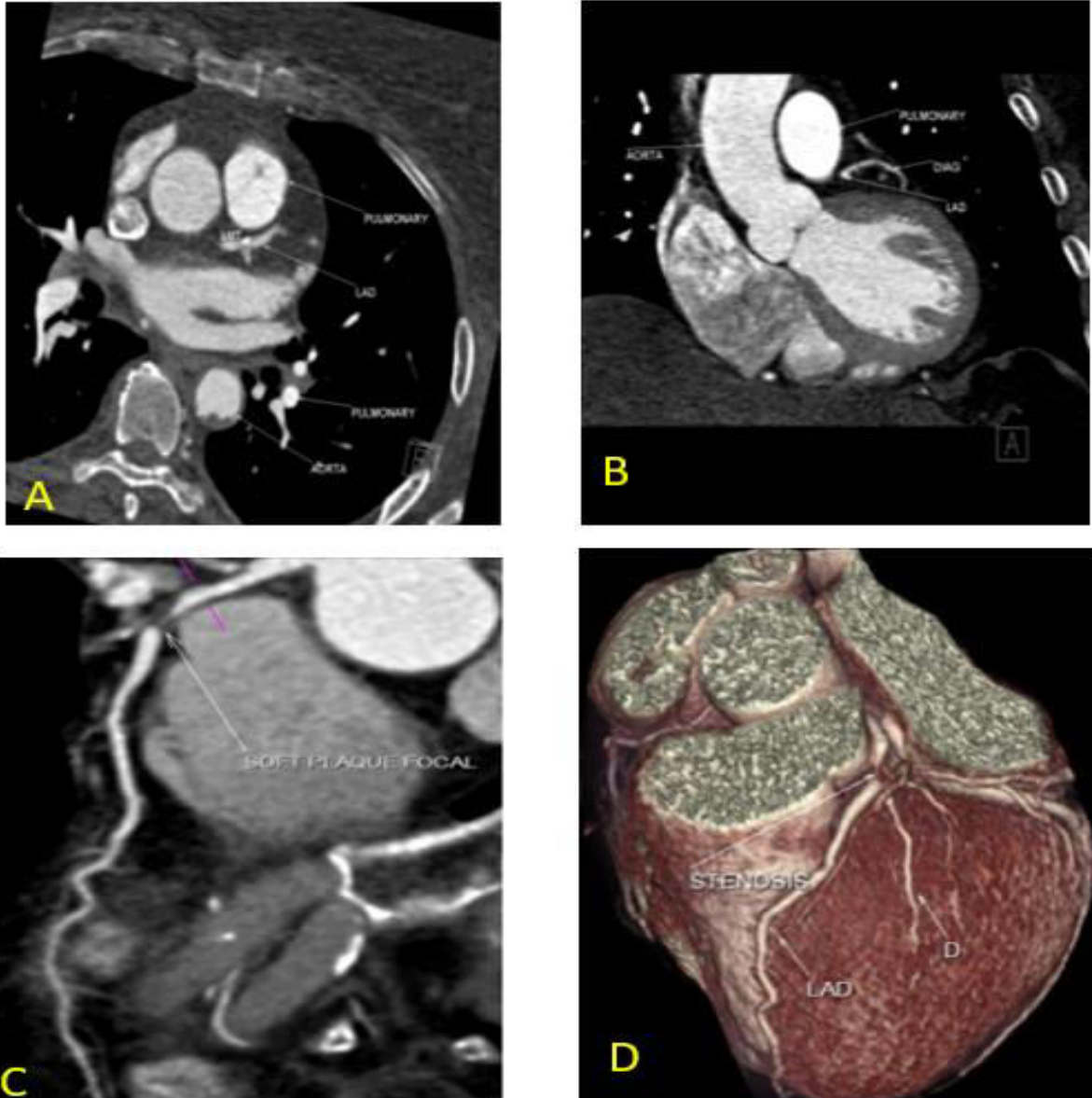


Fig. 5. A case of 60 years old male patient not diabetic or hypertensive showed: (a) an axial image at the aorto-pulmonary window, (b) a coronal image showing aorta, pulmonary and coronaries, (c) a curved image of the LAD showed the proximal segment stenotic lesion and (d) a VRT image of the heart

Discussion

In patients presenting with nonspecific chest pain, the TRO approach that makes use of specialized coronary CT scans can opacify the coronary arteries, aorta, and pulmonary arteries all at once (**Denewar et al., 2022**).

In most patients with ACP, TRO-CT can reliably exclude out ACS as well as detect individuals with severe coronary artery stenosis; it also has high negative predictive values (**Cetin et al., 2023**). Further, TRO-CT anatomic imaging of the entire chest can identify non-coronary causes of ACP, allowing emergency room doctors to swiftly guide patients to the best in- or out-patient treatment (**Russo et al., 2021b**).

In the current study, there was no control group to compare the amount of ionizing radiation between TRO technique and dedicated Coronary Angiography or Pulmonary Angiography. However, the main ionizing radiation exposure estimate for each patient in the study was 16.3mSv. it is near to that reported in Pattereth et al. (**Pattereth et al., 2023**) study as the mean effective radiation dose of the entire TRO was 19.024 ± 3.319 mSv (range = 13.89–25.95 mSv) according to their findings.

It is relatively higher than the main radiation exposure in other similar studies. This is basically due to the higher exposure rates for our early cases, where protocol modifications followed, we managed to reduce the rates of radiation exposure for the patients to come. Leschka et al. (**Leschka et al., 2008**) suggested It is possible to lower the radiation exposure using a variety of methods to a level that is as low as reasonably achievable (ALARA). Actually, Stolzmann et al. (**Stolzmann et al., 2008**) mentioned that An effective dosage of about 8-9 mSv is achieved during a cardiac DSCT examination when this ECG-pulsing technique is used.

By Gerber et al., An example of a standard dose of radiation to a diagnostic

catheter coronary angiography would be 2 to 23 mSv (**Gerber et al., 2005**).

In this investigation, we did not find any significant variations in image quality between the TRO CTA and dedicated coronary CTA. Following image processing, a blinded third-party cardiologist or radiologist reviewed the pictures retrospectively. Ayaram et al. (**Ayaram et al., 2013**) reviewed mentioned four studies evaluated the TRO CT's picture quality in comparison to that of specialized CT. There was no significant distinction in picture quality between the two sets. After excluding the two studies with the poorest methodologic quality scores, the combined effect estimate remained consistent.

As regard diagnostic accuracy, Ayaram et al. (**Ayaram et al., 2013**) mentioned thatThe diagnostic accuracy of TRO CT was examined in four trials that used coronary angiography as the gold standard technique for CAD identification.

Jonson et al. (**Johnson et al., 2008**) noticed that together, the estimations for diagnostic accuracy were as follows: sensitivity: 94.3%, specificity: 97.4%, LR+: 17.71, and LR-: 0.08. By Ayaram et al. (**Ayaram et al., 2013**) one study reported did not disclose estimates of diagnostic accuracy comparing coronary angiography and TRO CT, although there was no difference in the percentage of patients diagnosed with CAD using either modality.

Recently Shaimaa et al. (**SHAIMAA et al., 2022**) reported that TRO CTA is a trustworthy imaging method that can concurrently examine the lung parenchyma and the three thoracic vascular beds and hence offers precise results in COVID-19 patients presenting with acute chest discomfort.

In the current investigation, there was highly statistically significant correlation between both diagnosis as regard coronary angiography (p-value <0.05). Our results are supported by Elsherif et al. (**Elsherif et al., 2021**) who revealed that there was a

significant relation agreement between CTA and cardiac catheterization regarding the severity of CAD ($P < 0.001$). Also, Burris et al. (Burris et al., 2015) reported that Diagnostic yield was comparable between TRO and coronary CTA (17.4% vs. 18.3%; $p = 0.37$), with CAD being the primary driver (15.5% vs. 17.2%, $p = 0.093$). PE and AD yielded 1.1% and 0.4%, respectively ($p = 0.004$) and 1.7% and 1.1%, respectively ($p = 0.046$).

As regard practical and research implications, Foster & Shapiro, (Foster and Shapiro, 2012) explained that Radiation-based imaging examinations should only be conducted when absolutely necessary due to the fact that a person's lifetime radiation exposure can build up to dangerous levels. Although this review's findings show that TRO and dedicated CT produce equivalent images, there is currently not enough evidence to recommend TRO CT for the diagnosis of aortic dissection or PE. In sum, TRO CT should not be recommended for the diagnosis of PE or aortic dissection because to the elevated radiation and contrast exposure as well as the absence of data on diagnostic accuracy.

We found that a majority of the included studies involved patients with low to moderate risk for ACS who were experiencing chest pain in the present study. The number of cases diagnosed to be due to PE or aortic dissection was exceedingly low (Yoon and Wann, 2011). According to Ayaram et al. (Ayaram et al., 2013) in theory, It is challenging to rule out PE and/or AD in the perfect TRO-CT patient since they have a history that is alarming for ACS. Patients with negative biomarkers and normal or nonspecific ECG readings should be considered to have a low to intermediate risk for ACS.

Fast and/or irregular heart rate, existing coronary artery disease, and decreased glomerular filtration rate are all reasons TRO-CT cannot be performed. How effective TRO-CT is for this specific group of individuals is still up in the air

(Halpern, 2009). There is obviously not enough evidence to warrant its implementation at this time. Many people, especially young women and those with weak immune systems, could be exposed to dangerous levels of radiation and iodinated contrast if TRO-CT is used improperly. Additional downstream testing, expenses, and patient worry could result from an increase in the number of incidental results (Halpern, 2009).

Several factors hindered our study: first, the sample size was too small; second, there was no control study to compare our findings to; third, the time frame was too short; and lastly, our research team lacked sufficient expertise.

Conclusion

An appealing option is the TRO protocol, which can be used to neglect all three potentially fatal reasons for acute chest pain via a single scan. This is particularly true for older patients who have a relatively lower risk of radiation-induced cancer, and for emergency department patients with atypical chest pain who are at low to intermediate risk.

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Conflict of Interest: Nil

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