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Role of Triple Rule-Out Computed Tomography Angiography in the Management of Covid-19 Patients Presenting with Acute Chest Pain in Emergency Department

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Abstract

Background: Acute chest pain is one of the most common presentations in the emergency department (ED). It could be difficult to reach the specific cause of the acute chest pain,yet rapid diagnosis could be lifesaving. After the COVID-19 pandemic, it has been more complex to reach a specific diagnosis, meanwhile there was increased need for rapid non-invasive testing. Coronary artery disease (CAD), pulmonary thromboembolism (PTE), and acute aortic syndromes (AAS) are the most serious causes of acute chest pain. Triple rule-out computed tomography angiography (TRO CTA) can examine the three vascular beds as well as lung parenchyma in a single study, so TRO CTA may play a crucial role in managing patients in this emergency condition.

Aim of Study: To assess the clinical role of TRO CTA as a practical imaging tool in COVID-19 patients presented to the emergency department with acute chest pain.

Patients and Methods: Retrospective study reviewed images of sixty-nine (69) patients who presented to ED with acute chest pain and diagnosed as COVID-19 positive patients, underwent TRO CTA, and were evaluated for the presence of any parenchymal or vascular cause of acute chest pain.

Results: In the current study, the most detected cause of acute chest pain was parenchymal lung disease without significant vascular disease (50.7%), followed by pulmonary embolism (21.7%). The coronary causes of chest pain represent only 8.7%. We also found pericarditis in two cases (2.9%), hiatus hernia in two cases (2.9%), and aortic dissection in one case (1.4%).

Conclusion: This study has shown that TRO CTA is a reliable imaging tool that can simultaneously evaluate the lung parenchyma and the three thoracic vascular beds and thus gives accurate results in COVID-19 patients presenting with acute chest pain.

Key Words: *Triple rule out (TRO) – Computed tomography angiography – Chest pain – Covid-19.*

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Introduction

AFTER abdominal pain, acute chest pain is the second-most common cause of admission to the emergency room (ED) **[1]**. Due to its wide range of differential diagnoses, which can range from benign causes to life-threatening illnesses, acute chest pain poses a significant diagnostic problem in emergency treatment **[2,3]**. A definitive clinical diagnosis of ED chest pain is not always attainable based only on clinical presentations and laboratory results **[4]**.

Acute coronary syndrome (ACS), pulmonary embolism (PE) and acute aortic syndrome (AAS) are the three most clinically significant diseases that need to be distinguished while treating patients with chest pain **[5-7]**.

Coronary artery disease is one of the major factors contributing to morbidity and mortality in developed countries **[8]**. Acute coronary syndrome (ACS) diagnosis includes unstable angina, non-ST-elevation myocardial infarction and ST-elevation myocardial infarction **[9,10]**. The "gold standard" test for diagnosing obstructive coronary artery disease is invasive coronary angiography; however, it has a small risk of major complications **[11,12]**. On the other hand, dedicated Coronary CT angiography (CCTA) offers an excellent noninvasive alternative imaging tool for the coronary vessels **[13,14]**.

PE is the third most common cause of cardiovascular death and is a potentially lethal condition associated with high morbidity and mortality **[15]**. Therefore, pulmonary CTA has become the standard imaging technique in diagnosing pulmonary embolisms **[16]**.

The term "acute aorta syndrome" (AAS) refers to a group of life-threatening conditions that include penetrating aortic ulcer (PAU), intramural hematoma (IMH), and thoracic aortic dissection (TAD) [17].

Making a differential diagnostic list for acute chest pain in the ED has become increasingly challenging in the era of the new COVID-19 pandemic. According to muchresearch, COVID-19 induces hypercoagulability, which raises the risk of PE [18,19], increasing the need for CTA study. Additionally, during the pandemic, coronary CTA was helpful for COVID-19 patients with increased cardiac troponin levels and non-specific ECG abnormalities in whom the etiology was unknown and, in certain cases, to avoid invasive coronary angiography. In the COVID-19 era, coronary CTA gained more acceptance as a diagnostic modality in such cases due to its ability to guide important management decisions, enhance patient outcomes, reduce hospital admissions, shorten the time of stay in the emergency department, and eliminate the necessity for invasive tests [20].

Triple rule-out computed tomography angiography can examine the lung parenchyma and the three thoracic and vascular structures in a single study [21].

This study aims to assess the clinical role of TRO CTA as a practical imaging tool in COVID-19 patients presented to the emergency department with acute chest pain.

Patients and Methods

Study population:

Our Institutional Review Board approved this investigation, and as it was a retrospective study, written informed consent was not needed. Patients who sought treatment in the emergency department (ED) for acute chest pain and had TRO CTA between June 2020 and April 2021 were collected from our radiology picture archiving system. According to hospital policy, patients with the possibility of pulmonary embolism or low risk of ACS should be sent to the radiology department for TRO CTA protocol.

Inclusion criteria:

This research included patients older than 18 years with proven COVID-19 infection who presented to the ED with acute chest pain and underwent TRO CTA.

Exclusion criteria:

Patients with inaccessible clinical or laboratory data and insufficient documentation of their final clinical diagnosis and follow-up were excluded. Patients with inadequate imaging quality were also excluded. The study finally included sixty-nine patients (40 female and 29 male).

Pre-exam patient preparation:

All our patients were initially assessed for heart rate, blood pressure, and detailed medical history by reviewing serum creatinine before intra-venous contrast administration and measuring the patient's weight to determine the proper dose of contrast media. Fasting for 6 hours was needed. An adequate breath hold, and a regular heartbeat were necessary to obtain a good-quality study. This was carried out by reassuring the patients in the radiology department, explaining the entire process to the patients, and giving sublingual diazepam (5mg) to severely anxious patients. The ability of the patient to hold their breath long enough throughout the examination was routinely tested. The administration of oxygen through a nasal cannula is sometimes needed in cases with significant heart rate variability or with frequent premature contractions. Patients with average heart rates of more than 70 beats per minute and no contraindications received oral beta blockers 1 hour before the exam to achieve a heart rate of fewer than 70 beats per minute. When the patient's heart rate was appropriate, a 16-18 G intravenous catheter was inserted into the right antecubital fossa vein to achieve IV access. Patients received 0.4mg of nitroglycerin sublingually 2 minutes before the assessment if there was no contraindication (hypertension, current nitrate drug use, or migraine sensitivity to nitrates). The patient was positioned supine in the center of the CT gantry. ECG leads were fitted on the patient's chest and the arms above the head.

TRO-CTA protocol:

The study was performed utilizing a 320-multislice CT scanwith a 0.5mm Detector-row dimension, beam width of 160mm, 0.35s gantry rotation, and 175s temporal resolution. The routine scanning parameters were set to 120kVp and 600 mAs per section. For heavier patients, tube current was increased to 800-1000mAs per section for patients weighing 90.7-113.4kg, and voltage was increased to 140kVp.

First, a conventional prospective ECG-triggered non-enhanced CT was performed to assess any aortic, lung, and severe coronary calcification abnormalities.

The biphasic injection method was employed to opacify the coronary and pulmonary arteries; 80ml of undiluted contrast material (Ultravist

370ml) was injected at 5 ml/s followed by injection of 25ml of the same contrast, diluted with 25ml of saline, at a rate of 5ml/s. The first phase of injection opacifies coronary arteries, while the second phase opacifies pulmonary arteries. Bolus-tracking approach was used to get the diagnostic vascular opacification level. ECG-gated acquisition automatically started 5 s after a threshold of 200 HU was reached in the left atrium, scanning from the level of the lung apex to the diaphragm. Prospective ECG triggering (30-80% of the cardiac cycle) was used depending on regular heart rate intervals.

Image reconstruction and post-processing:

The raw data were processed using dedicated advanced software programs to allow accurate assessment of the different vascular structures in different orientations and formats. Maximum intensity projection (MIP), multi-planar reformation (MPR), curved planar reformation (CPR) and Volume-rendered (VR) reconstructions were used.

Assessment of any extra-vascular abnormality was also made, including parenchymal, pleural, and pericardial abnormalities that could contribute to the presentation of chest pain.

Data evaluation:

One experienced radiologist (with more than 10 years of experience) revised the TRO CTA scans, looking for any PE, obstructive coronary artery disease (CAD) or AAS, as well as any other lung parenchymal abnormalities or any significant findings. For evaluation of CAD, each major coronary artery (left main, left anterior descending, left circumflex, and right coronary artery) and all significant obtuse marginal and diagonal branches were evaluated for stenosis more than or equal to 50% to be considered as obstructive.

Patient follow-up:

The final assessment was made based on discharge reports, reviewing of hospitalization records and telephone contact with the patients. Any major adverse cardiac events within the following 60 days after the CT examination were recorded. In addition, patients were asked about any further hospitalization and other cardiac and non-cardiac tests, or procedures performed, including cardiac echocardiography, stress test and invasive cardiac catheterization.

Statistical analysis:

Data were gathered, revised, coded, and put into the statistical analysis of social science (SPSS) version 26. The qualitative data were presented as numbers and percentages.

Results

A retrospective search found a total of 69 patients with laboratory-proven COVID-19 infection who underwent TRO CTA due to acute chest pain between June 2020-April 2021.

Our study included forty (58%) females and 29 (42%) males. Their ages ranged from 23 to 72 years; the mean was 52±13.6 years. ECG-Gated MDCT angiography for all these cases was done and eventually correlated with a 60-day follow-up final diagnosis.

In 8 patients (11. 6%), no abnormality was detected (negative examination). In 35 patients (50.7%), only parenchymal findings of COVID-19 pneumonia were found. Pulmonary embolism was diagnosed in 15 patients (21.7%). Significant coronary artery stenosis was found in 4 patients (5.8%). Two cases (2.9%) with malignant anomalous right coronary artery were found. Two cases (2.9%) were diagnosed as pericarditis, and two others (2.9%) showed sliding hiatus hernia. Aortic dissection was diagnosed in 1 case (1.4%).

Non-vascular causes of acute chest pain were found in 39/69 cases (56.5%). Vascular causes were detected in 22/69 cases (31.9%). The overall non-coronary causes of acute chest pain represent 79.7% (55 of 69 cases). The coronary causes of chest pain represent only 8.7% of cases in our study (compromised of four cases of significant LAD stenosis and two cases of significant coronary anomaly that could explain chest pain).

The most common parenchymal findings of COVID- 19 pneumonia were ground glass opacities (GGO) (Fig. 1), seen in 30/35 cases and lung consolidations, seen in 15/35 cases, with predominant peripheral and basal distribution.

Among the fifteen patients with pulmonary artery embolism, five showed pulmonary embolism in the main pulmonary vessels, while ten showed embolization in pulmonary segmental and subsegmental branches. In addition, the right pulmonary artery and its branches were affected in 6 patients, the left pulmonary artery and its branches were affected in 4 cases, bilateral involvement in 4 cases and one case with saddle-shaped with the affection of both right and left pulmonary arteries (Fig. 2). All pulmonary embolisms were acute.

Four of our patients had coronary artery disease; all showed moderate lesions causing 50-70% stenosis. All significant coronary artery stenoses were found in the LAD artery and its branches (Fig. 3).

In addition, two cases show a malignant anomalous right coronary artery (Fig. 4), which was considered the cause of the chest pain after excluding other causes.

Two cases were diagnosed as pericarditis by CT imaging (Fig. 5) and confirmed clinically and supported by ECG findings. Two other causes of hiatus hernia (Fig. 6) showed no other causes of chest pain.

One patient in our study had an aortic dissection in the ascending Aorta, aortic arch, and descending Aorta (Stanford type A) (Fig. 7).

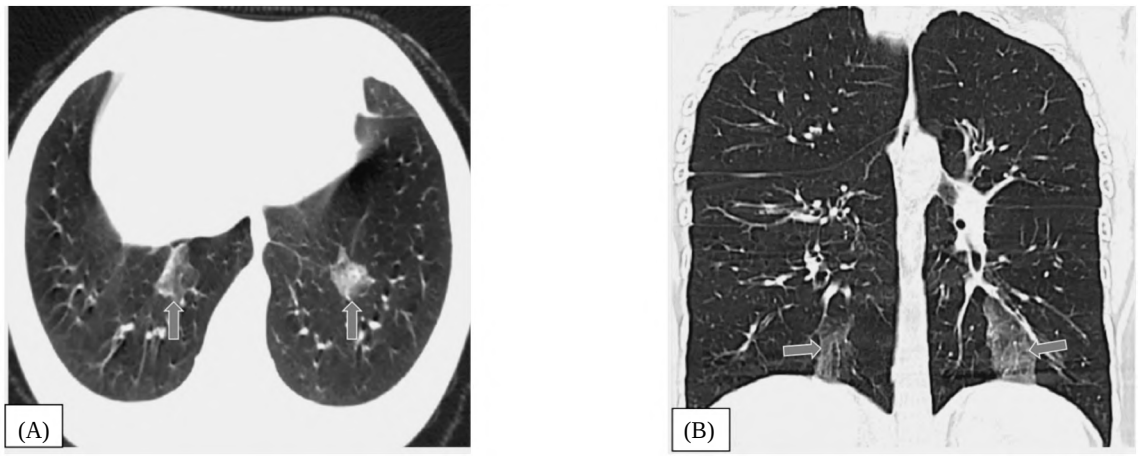

Fig. (1): A 45-year-old female patients presented with acute chest pain, with positive PCR for Covid-19 infection. (A) Axial and (B) Coronal reformatted images (lung window) show ground glass opacities at both lower lung lobes (red arrows).

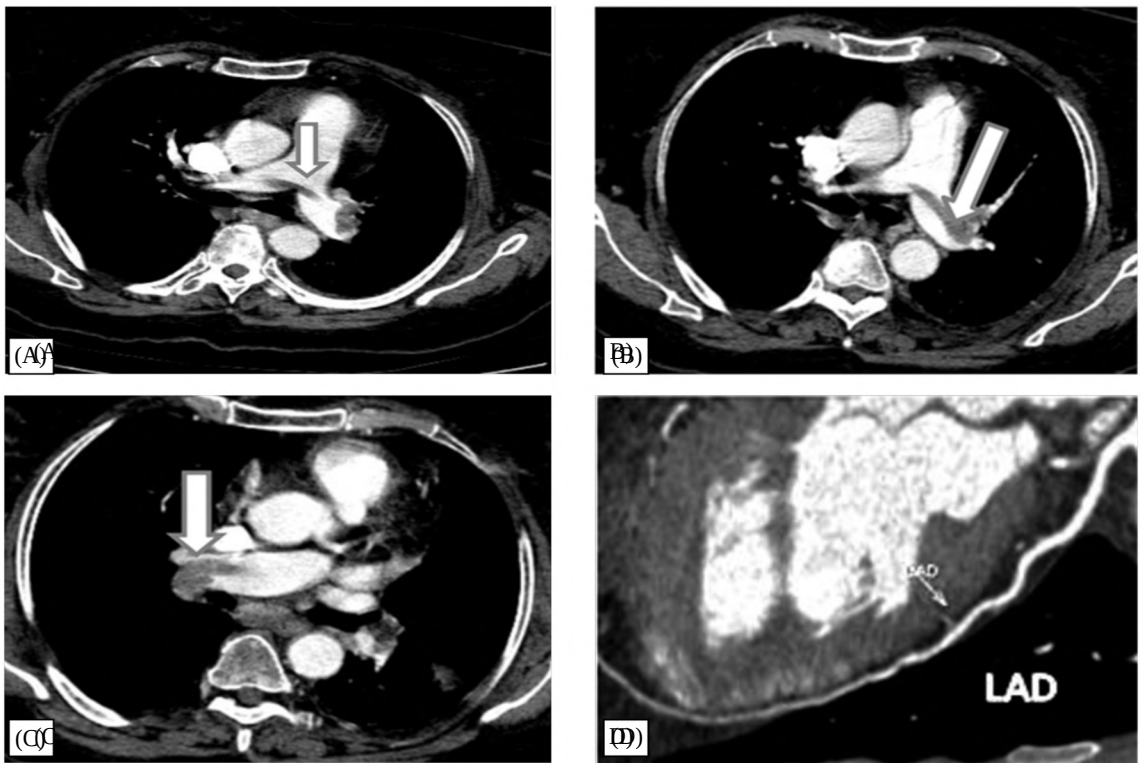

Fig. (2): A 65-year-old female patients presented with acute chest pain. CTA (A), (B) and (C) Axial cuts (mediastinal window) show the filling defect within the main pulmonary trunk, extending to the right and left pulmonary arteries (Saddle thrombus pulmonary embolism) (open arrow). (D) CPR image shows normal course and caliber of LAD.

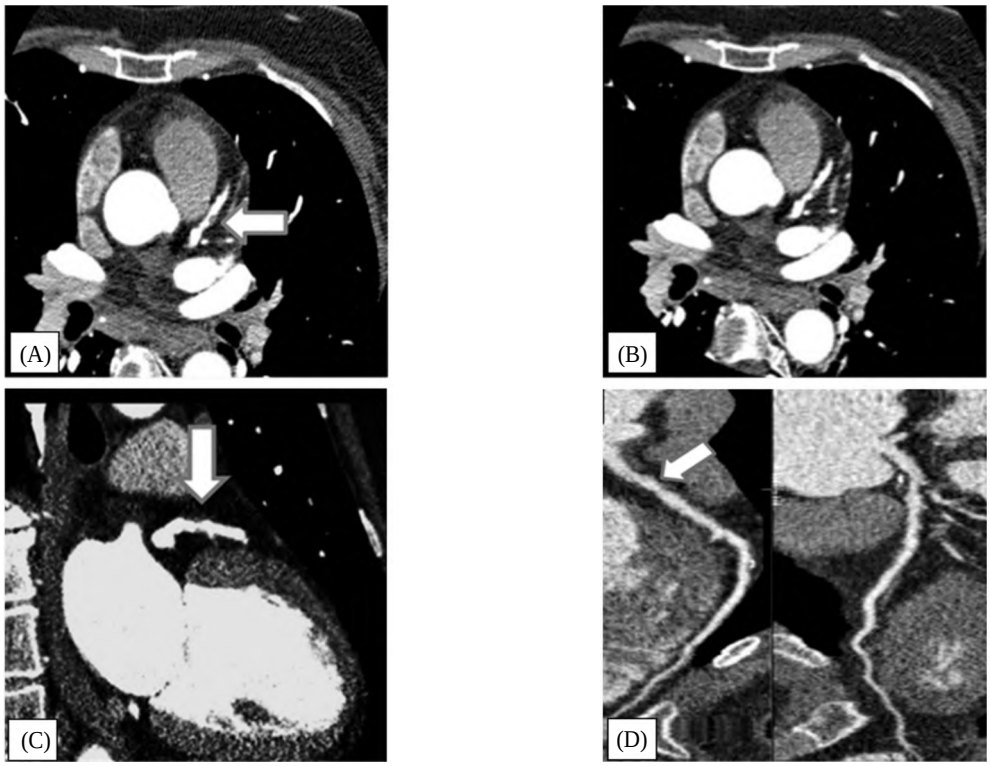

Fig. (3): A 51-year-old male patients presented with acute chest pain. ECG-Gated CTA (A) and (B) Axial and (C) Sagittal MPR images (mediastinal window) show decrease in diameter of proximal LAD by soft plaque (D) CPR image shows decrease in diameter of proximal LAD with soft plaque (open arrow).

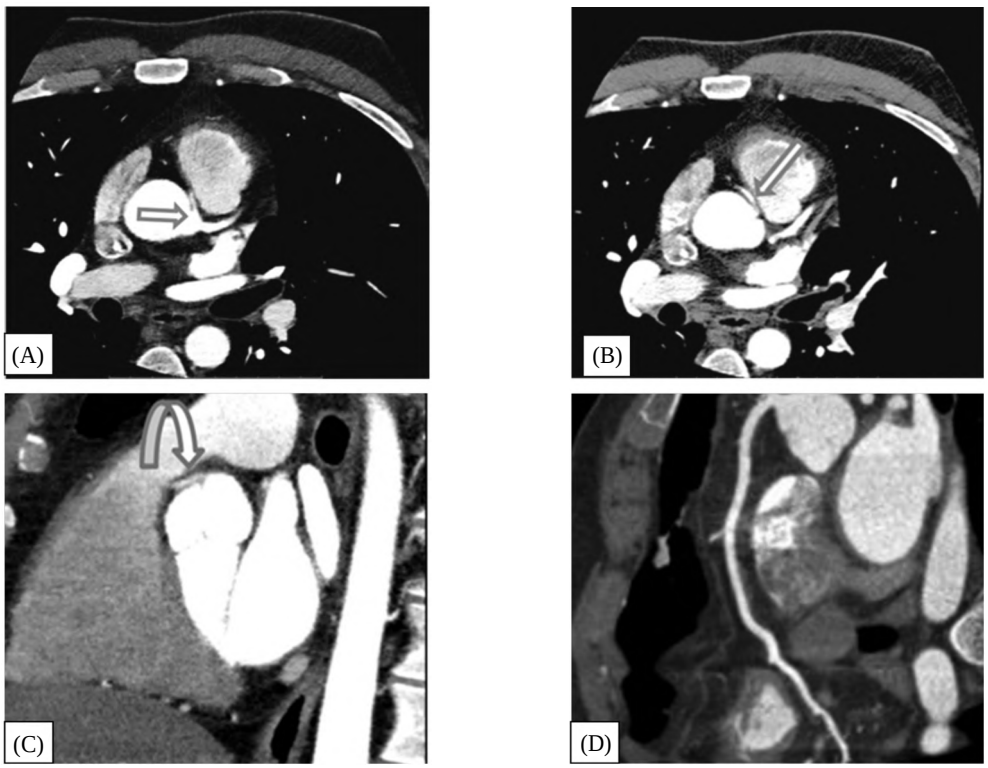

Fig. (4): A 45-year-old female patients presented with acute chest pain and shortness of breath. CTA (A) Axial image shows common origin of RCA and left main coronary artery from left aortic sinus (arrow). (B) Axial image shows anomalous intra-arterial course of the RCA between the Aorta and Pulmonary trunk (arrow). (C) Sagittal MPR shows anomalous intra-arterial course of the RCA between the Aorta and pulmonary trunk (curved arrow). (D) CPR image shows normal course and caliber of RCA.

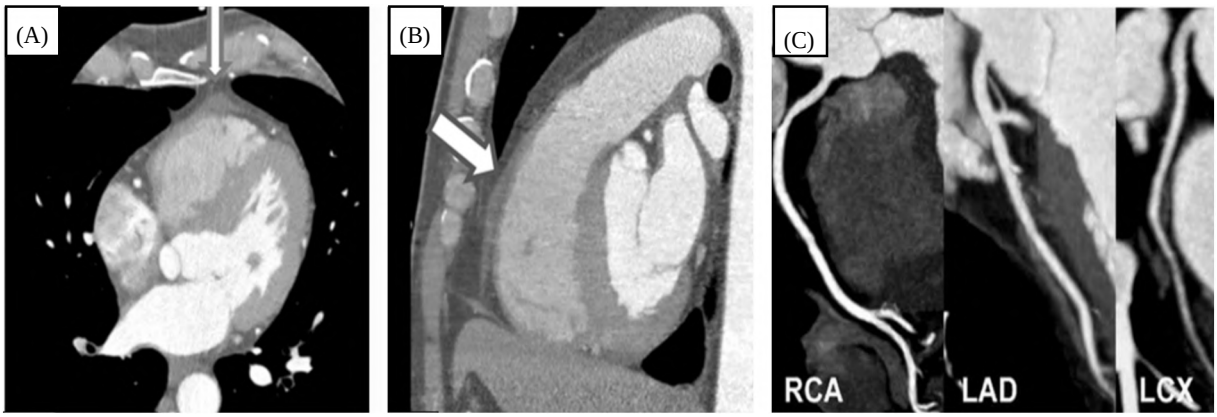

Fig. (5): A 30-year-old male patients presented with chest pain. CTA (A) axial and (B) Sagittal reformatted images show mild pericardial thickening, minimal fluid, and mild pericardial fat stranding. (C) CPR images show normal coronary vessels.

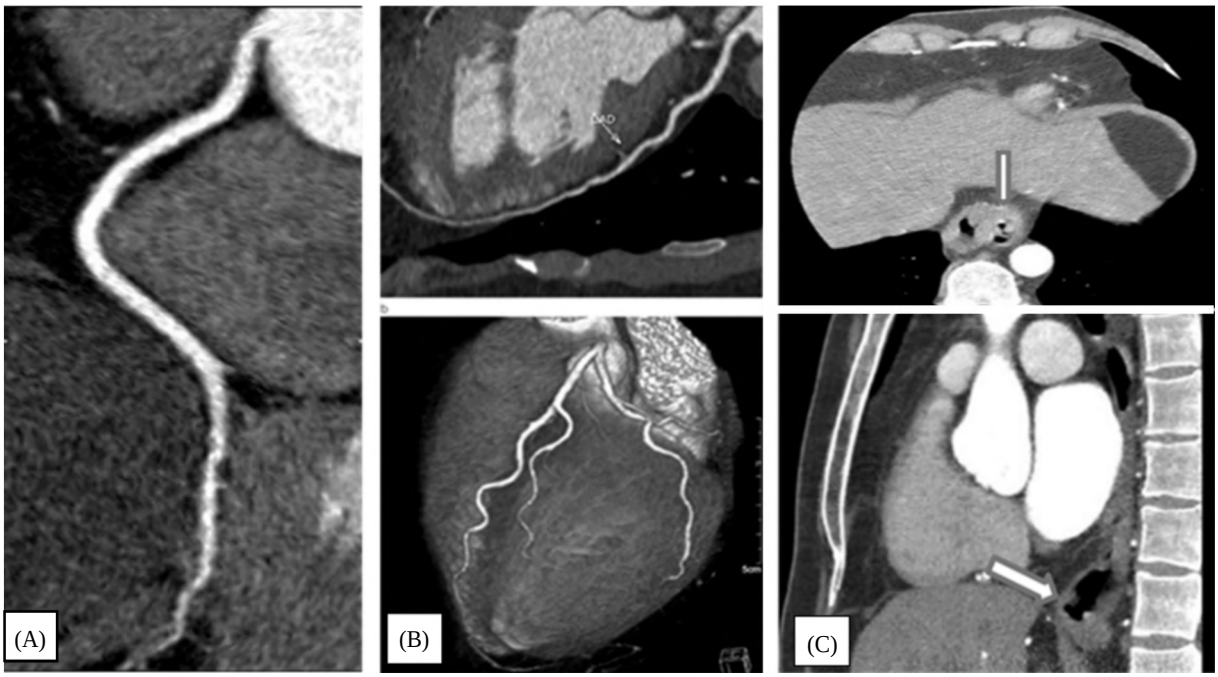

Fig. (6): A 51-year-old female patients presented with chest pain. CTA (A) and (B) CPR and 3D reformatted images show normal coronary vessels. (C) axial (above) and Sagittal (below) MPR (mediastinal window) sections show hiatus hernia with oesophageal mucosal thickening (arrow). The accepted clinical cause of chest pain was hiatus hernia and lower oesophagitis.

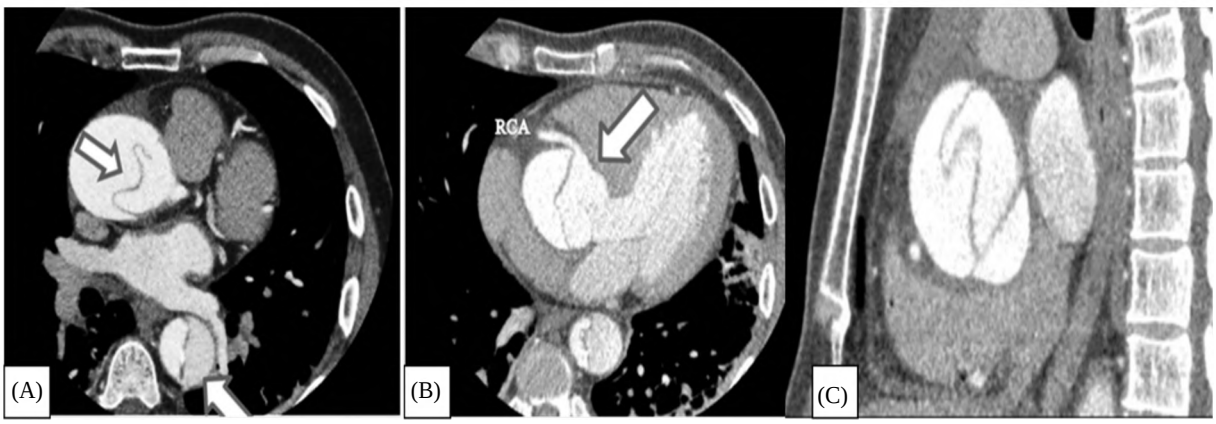

Fig. (7): A 73-year-old male patients presented with acute chest pain. ECG-Gated CTA (A) and (B) Axial cuts (mediastinal window) show an intimal flap within the ascending and descending aorta (open arrow). Normal origin of the right coronary artery with no evidence of dissection extension (RCA) (C) Sagittal MPR (mediastinal window) shows an intimal flap within the ascending aorta with true and false lumens noted. Stanford type (A) Aortic dissection.

From Table (1), we can note that the pulmonary parenchymal lesions were the most common findings among our studied patients, detected in 35 patients with an incidence of 50.7%.

Table (1): Illustrating the incidence of different CT findings among our studied population.

CT Findings	No. (%)
Normal	8 (11.6%)
Parenchymal lung abnormality	35 (50.7%)
Pulmonary Embolism	15 (21.7%)
Coronary artery disease	4 (5.8%)
Coronary anomaly	2 (2.9%)
Aortic dissection	1 (1.4%)
Pericarditis	2 (2.9%)
Hiatus hernia	2 (2.9%)
Total	69 (100%)

Discussion

Acute chest pain is one of the most common presentations in the ED. Acute chest pain in COVID-19 patients could result from pneumonia or concomitant vascular events that raise the risk of thrombosis [22,23]. As previously stated, the risk of pulmonary thromboembolic events is increased by COVID-19 [24]. The coronary arterial disease can be a differential diagnosis and significantly increase the mortality rate of COVID-19 cases [25]. Therefore, easy, accurate, and rapid diagnosis of accompanying pathologies can help guide treatment and reduce mortality/morbidity rates. To our knowledge, Bahadir et al. [19] study is the only research about TRO CTA results in COVID-19 patients.

Our study was performed using 320-multislice CT. Previous studies have demonstrated the application of TRO protocol with 16-multislice CT in the emergency department. With the introduction of 64-, 256-, and 320-multislice CT scanners, coronary artery imaging has improved [26-28]. However, With the most recent 320-multislice CT technology, the Aorta, pulmonary arteries, and coronary arteries can be easily and quickly acquired in a single breath hold [29,30].

In the current study, negative cases stand for 11.6% of cases. The most detected cause of acute chest pain was parenchymal lung disease without the significant vascular disease (50.7%), followed by pulmonary embolism (21.7%). Coronary causes of chest pain represent only 8.7% of cases. The overall non-coronary causes of acute chest pain represent 79.7% (55 of 69 cases).

Henzler et al. [31], using 320 multislice CT, found that 20% of patients showed non-coronary abnormalities that explain chest pain, including pulmonary embolism (PE), pleural effusion, left ventricular hypertrophy and pneumonia. A study done by White et al. [32] estimated that significant non-coronary findings accounted for chest pain were 4.3% of the patients. Kevin and Ethan concluded that the non-coronary diagnosis that explained the chest pain was about 11% [33]. Furthermore, a study on 201 patients evaluated with TRO CTA identified a non-coronary cause of acute chest pain in 11 % of patients [34]. These results were much smaller than our study estimated 79.7% because of the considerable number of parenchymal abnormalities in patients with COVID-19 infection.

In our study, 8/69 patients (11.6 %) showed no imaging abnormality detected, and 35/69 patients (50.7%) showed only parenchymal lung abnormality. This is similar to the Bahadir et al. [19] studies, whichevaluated TRO CTA in COVID-19 patients in ED and found that in 65.9% of cases, there was no pathology apart from COVID-19 pneumonia parenchymal findings.

We identified pulmonary embolism in 21.7% of our patients, similar to the Bahadir et al. [19] study results (in 23.4% of their cases). This contrasts with the study done by Savino et al. [35], who found that pulmonary embolism accounted for chest pain in 8.7% of the patients. This could be explained by the fact that COVID-19 patients have a higher risk of pulmonary embolism.

In contrast to the study by Wnorowski and Halpern, which showed that pulmonary embolism was the most noted non-coronary diagnosis [36], in our study, parenchymal lung abnormality was the most noted diagnosis by the incidence of 50.7%, obviously because our study was done in only COVID-19 positive patients.

In the current study, 5.8% (4 of 69) of our population had significant coronary stenosis, all showed moderate lesions causing 50-70% stenosis, and all were seen in the left anterior descending artery or its branches. Three of our cases underwent subsequent invasive coronary angiography, and two showed significant stenosis in keeping with CT findings. However, the third case showed mild non-obstructive CAD. These results are like Bahadir et al. [19], who found significant CAD in 8.5% of their study population.

Many studies were done to evaluate TRO CTA in non-COVID-19 patients with acute chest pain. Thomas et al. [31] used 320-multislice CT with a

larger study population. They selected cases with intermediate risk for ACS. They found that 19% of their patients had significant coronary stenosis. This is similar to a study by White et al. [32], who evaluated 69 patients with acute chest pain by TRO CTA and found coronary findings that explained the chest pain in 19% of the patients. Another study by Savino et al. [35] found the coronary disease in 34.8% of patients. A study by Takakuwa and Halpern on low-to-intermediate risk patients suggested the presence of moderate-to-severe coronary stenosis in about 11% [34]. A large study by Wnorowski and Halpern reported that CAD was the most common diagnosis that explained acute chest pain, found in 11.7% of the patients [36]. In our study, we included only COVID-19 patients and patients with low risk for ACS, which could explain our study's low incidence of significant CAD.

In our study, all patients who showed no obstructive CAD showed no major acute cardiovascular event (MACE) during the 60-day follow-up. This is comparable to the findings of a previous study by Takakuwa and Halpern [34], in which 76% of their patients didn't need any more tests, giving an NPV of 99.4%. In addition, studies by Rubinshtein et al. [37] and Pundziute et al. [38] also found that CCTA has a high NPV for ACS at 30-day follow-up. This may enable patients' safe and rapid discharge directly from ED after negative CT results in properly selected patients [39-42].

Few studies compared TRO CTA with invasive coronary angiography for assessment of CAD and showed high agreement [43], with a sensitivity of 100% and a negative predictive value of 100% [11].

Soliman (2015) estimated that 10 cases (25%) with only aortic lesions accounted for acute chest pain in his study population [44]. The study by Wnorowski and Halpern [36] also estimated the incidence of different aortic pathologies in their study population (27.5%). These incidences were higher than that estimated by our study. In our study, only one case had aortic dissection with an incidence of 1.4%, similar to Bahadir et al. [19] studies, which found only 2.1% of cases had aortic disease explaining the acute chest pain. The small population size could explain this in our study.

Although TRO CTA may not be readily available in all centers and requires a greater volume of contrast material and higher radiation dose [45], however, it is still reasonable to use TRO CTA instead of separate examinations, not only for acute thoracic and vascular emergencies but also for parenchymal pathologies in COVID-19 patients [29], especially after new CT technologies become increasingly available that allowed for rapid scanning, contrast and radiation dose reduction [36].

Our study estimated the diagnostic accuracy by comparing our final report with the final diagnoses obtained after 60 days of follow-up. The result came up to be a sensitivity of 91.4%, specificity of 100%, a positive predictive value of 100% and negative predictive value of 90%;a positive likelihood ratio couldn't be estimated as specificity is 100% and negative likelihood ratio of 0.086 with an overall diagnostic accuracy of 97.8%.

The present study has a few limitations, including small sample size and the fact that our hospital's criteria for ordering TRO CTA chest pain protocol are not standardized. As a result, full study indications were not accessible for review. In addition, there was no comprehensive list of the pre-test probability for ACS and different non-coronary diagnoses in our population.

However, our study found that the appropriate use of TRO CTA protocol and proper patient selection in ED can help accurate and rapid patient triage and reduce the number of required diagnostic tests and ED costs. Further studies with larger sample volumes are recommended to support our study results.

Conclusion:

We concluded that TRO CTA could play a crucial role in COVID-19 patients presented to the emergency department with acute chest pain.

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دور التصوير المقطعى للأوعية بتقنية الاستبعاد الثلاثى فى إدارة مرضى كوفيد-١٩ الذين يعانون من آلام حادة فى الصدر فى قسم الطوارئ

خلفية الدراسة : يعد ألم الصدر الحاد أحد أكثر الأعراض شيوعاً فى قسم الطوارئ. قد يكون من الصعب الوصول إلى السبب المحدد لألم الصدر الحاد لكن التشخيص السريع قد ينقذ حياة المريض. بعد جائحة كورونا، أصبح الوصول إلى تشخيص محدد أكثر تعقيداً، وفى الوقت نفسه أصبحت هناك حاجة متزايدة للاختبارات السريعة غير التداخلية. يعد مرض الشريان التاجى والسدة الشريانية الرئوية ومتلازمات الأبهر الحادة من أخطر أسباب آلام الصدر الحادة. يتميز التصوير المقطعى للأوعية بتقنية الاستبعاد الثلاثى بقدرته على دراسة الوعائية الثلاثة بالإضافة إلى نسيج الرئة فى دراسة واحدة، لذلك قد يلعب دوراً مهماً فى إدارة المرضى فى مثل هذه الحالات الطارئة.

الهدف من البحث : لتقييم الدور الإكلينيكى للأشعة المقطعية الشريانية بتقنية الاستبعاد الثلاثى كأداة تصوير عملية لمرضى كورونا المتقدمين إلى قسم الطوارئ والذين يعانون من آلام حادة فى الصدر.

المرضى وطرق البحث : استعرضت الدراسة بأثر رجعى صور تسعة وستين مريضاً تقدموا إلى قسم الطوارئ بآلام حادة فى الصدر، وتم تشخيصهم بمرض كورونا، وخضعوا للأشعة المقطعية الشريانية بتقنية الاستبعاد الثلاثى وتم تقييمهم للبحث عن أى سبب فى نسيج الرئة أو فى الأوعية الدموية يكون سبباً لآلام الصدر الحادة.

نتائج البحث : فى الدراسة الحالية كان السبب الأكثر اكتشافاً لألم الصدر الحاد هو أمراض نسيج الرئة بدون أمراض الأوعية الدموية (٥٠.٧٪)، يليه الانسداد الشريانى الرئوى (٢١.٧٪). تمثل الأسباب التاجية لألم الصدر ٨.٧٪ فقط. وجدنا أيضاً التهاب غشاء القلب فى حالتين (٢.٩٪)، وفتق المرئ فى حالتين (٢.٩٪)، وتمزق الشريان الأورطى فى حالة واحدة (١.٤٪).

الخلاصة : أظهرت دراستنا أن الأشعة المقطعية الشريانية بتقنية الاستبعاد الثلاثى تعتبر أداة تصوير موثوقة يمكنها فى وقت واحد تقييم نسيج الرئة والأسرة الوعائية الصدرية الثلاثة، وبالتالى تعطى نتائج دقيقة فى مرضى كورونا الذين يعانون من ألام حادة فى الصدر.