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# Thoracic non-traumatic cardiovascular diseases: current perspective and multi-detectors Computed Tomography protocols optimization in the emergency setting

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**Abstract. Cardiovascular diseases (CVDs) are among the most common causes of access to the Emergency Department and among the leading causes of death worldwide.**

**Accurate diagnostic algorithms are mandatory to ensure a rapid life-saving treatment. However, non-specific clinical presentation and unnecessary referrals to other subspecialties may lead to misinterpretation of the diagnosis and delays.**

**In recent years, the development of imaging technologies has allowed Computed Tomography (CT) to play a prominent role in the concepts of CVD rule-in and rule-out. An optimization strategy for CT protocols is needed to reduce variability and improve image quality.**

**A correct diagnostic suspicion is crucial, as different districts (i.e., heart, aorta and pulmonary circulation) may require different investigation techniques.**

**Additionally, the CVD pre-test probability assessment is highly correlated with CT accuracy.**
**The purpose of this narrative review is to analyze the current role of CT in the approach to the CVDs in the ED, and to analyze the main strategies of CT optimization.**

*Key Words:*
Thoracic emergency, Non-traumatic, Cardiovascular disease, CT, CCTA, CTPA, Acute coronary syndrome, Acute aortic syndrome, Pulmonary embolism, Triple-rule-out.

## Introduction

Cardiovascular diseases (CVD) are a common presentation to the Emergency Department (ED) and represent the most common cause and leading cause of death worldwide[1,2].

Acute coronary syndrome or aortic syndromes (ACS and AAS, respectively) and pulmonary embolism (PE) are the major entities of the acute non-traumatic chest CVDs.

Appropriate risk stratification is required in a patient suspected of acute CVD in the ED, although some considerations are necessary[3]:

a. The clinical presentation of acute CVD can be non-specific.

The most commonly occurring symptom is chest pain. However, chest pain is the second most common reason for emergency room access after abdominal pain[4,5]. Chest pain may be common to benign and life-threatening conditions, and presen-

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tation, severity and irradiation of chest pain may be nonspecific for a defined clinical interpretation[6-9].

A less severe clinical presentation is indeed common, particularly in the early stages of the disease, with good CV compensation and good hemodynamic stability.

As a result, a non-specific clinical presentation associated with unnecessary referrals to other sub-specialties can lead to misinterpretation of the diagnosis and delays.

b. Clinical algorithms for managing chest pain in the emergency room are complex, and the limitations of each step should be considered in clinical practice.

Different CVD require specific treatments, and the genesis of cardiogenic and noncardiogenic pain should be properly differentiated.

Management algorithms should include time-saving steps specifically designed to identify the disease or its clinical mimics[10-12].

In addition to clinical interpretation, the clinical steps include: i./ identification of laboratory and instrumental biomarkers of disease; ii./ Integration with advanced imaging for diagnostic confirmation as a first- or second-line test[13].

## Laboratory/Instrumental Biomarkers

Troponin and D-Dimer are well-established biomarkers for rule-in and rule-out CVDs[14].

Troponins are critical to the suspicion of cardiac pain. Dynamic changes in serum troponin may be indicative of acute rather than chronic injury[15,16].

Recently, highly sensitive isoforms (hs) have been used in clinical practice to avoid diagnostic delays, however resulting in an unnecessary increase in invasive procedures and a decrease in functional testing.

Furthermore, the abbreviated 0-1 hour protocol has shown no benefit over the standard 0-3 hours in reducing cardiac event in a 30-day observation. An additional increase of all-cause death and myocardial infarction (MI) was observed in a long-term 12-month follow-up when the 0-1 hour protocol was used as a rapid discharge protocol, as highlighted by the recent RAPID-TnT trial[17-20].

D-Dimer is a well-established biomarker for ruling-out PE, also providing high sensitivity for AAS. However, D-Dimer is generally insufficient as a single test to rule-out AAS, although Aortic Dissection Detection Risk Score as a pre-test risk assessment plus D-Dimer could be effective for ruling-out AAS as highlighted by the recent ADvISED trial[21-25].

Finally, BNP can be used to assess ventricular injury or strain[26].

Among instrumental biomarkers, the use of a 12-lead ECG is recommended, however not as a single conclusive test, as also stated in the recent position paper by the Acute Cardiovascular Care Association for diagnosis and risk stratification of patients with pain in the ED[27].

Acute CVDs may not show typical ECG patterns, thus reducing its clinical utility.

These uncertainties are paralleling the increasing effectiveness of advanced imaging in rule-in and rule-out CVDs also in an emergency context, with a particular focus on computed tomography (CT)[28-32].

## Multi-Detector Computed Tomography (MDCT)

MDCT has become the preferred imaging technique for CVD and chest emergencies[33-35].

Benefits of CT include i./ Accessibility of CT scanners. While computed tomography is not a bedside technique, CT scanners are often present at the ED, making it easier to use in emergency management. Moreover, less attention needs to be paid to the potential interaction with magnetic objects than magnetic resonance imaging (MRI)[36].

ii./ Fast scanning. In contrast to other techniques, CT allows for immediate image availability. MR, in fact, can be considered as an optimum imaging option in the subacute phase due to the long scan times.

iii./ Excellent diagnostic accuracy. CT indicates a precision of about 100% for major vessel disease and has a negative predictive value of about 100% for coronary artery disease (CAD)[37-40].

MDCT thus becomes the preferred imaging technique for acute chest pain assessment with suspected CVDs excluding ACS with persistent ST elevation[41-44].

CT angiography (CTA) should be performed according to the ALARA principle (as low as reasonably achievable) to obtain a diagnostic test and reduce the risk to the patient from radiation exposure. In this regard, scanner technology is crucial.

### Basics of CTA

The spatial (a) and temporal (b) resolution for MDCT depends on the acquisition technology:

a. the latest scanners are characterized by a sub-millimetric collimation (i.e., 0.5 mm)

which allows high spatial definition MIP and 3D reconstructions with non-stair step artifacts (useful also in preoperative planning).

b. Wide detectors (up to 320 rows) can acquire 16 cm volumes in a single heartbeat. Temporal resolution in 320-row scanners is one half the gantry rotation time (i.e., 135 ms in second generation scanner using a prospective acquisition) and is increased to 63 ms by the latest dual-source technology[45,46].

- ECG-gated arterial acquisition is mandatory for cardiac analysis, and it is advisable also for the analysis of the aortic root and the ascending aorta (to avoid motion artifacts related to cardiac pulsatility)[47,48]. Conversely, the acquisition of the remaining aortic segment and pulmonary artery is less affected by the cardiac pulse.
- ECG-gating could be performed with prospective or retrospective acquisition (i.e., limited to the diastolic phase or extended to the entire cardiac cycle, respectively). Dosimetric considerations should also be considered given that retrospective scans require higher radiation exposure than prospective scans.
- Diagnostic accuracy has recently increased also through the introduction of high-pitch scanners[23,49,50]. Although the standard-of-care for the assessment of the aortic root and ascending aorta is ECG-gated acquisition, the use of high-pitch scanners has allowed to reduce artifacts related to both cardiac pulsatility and breathing[49,51-55] (Figure 1).

This may be critical, particularly in an emergency setting, where: i./ CVDs can be a collateral finding on a non-targeted examination for a non-vascular clinical suspicion (as demonstrated in the CaPaCT trial or in the study by Verdini et al[56], that highlights the need for an adequate training on cardiovascular disease)[54-56] (Figure 2); ii./

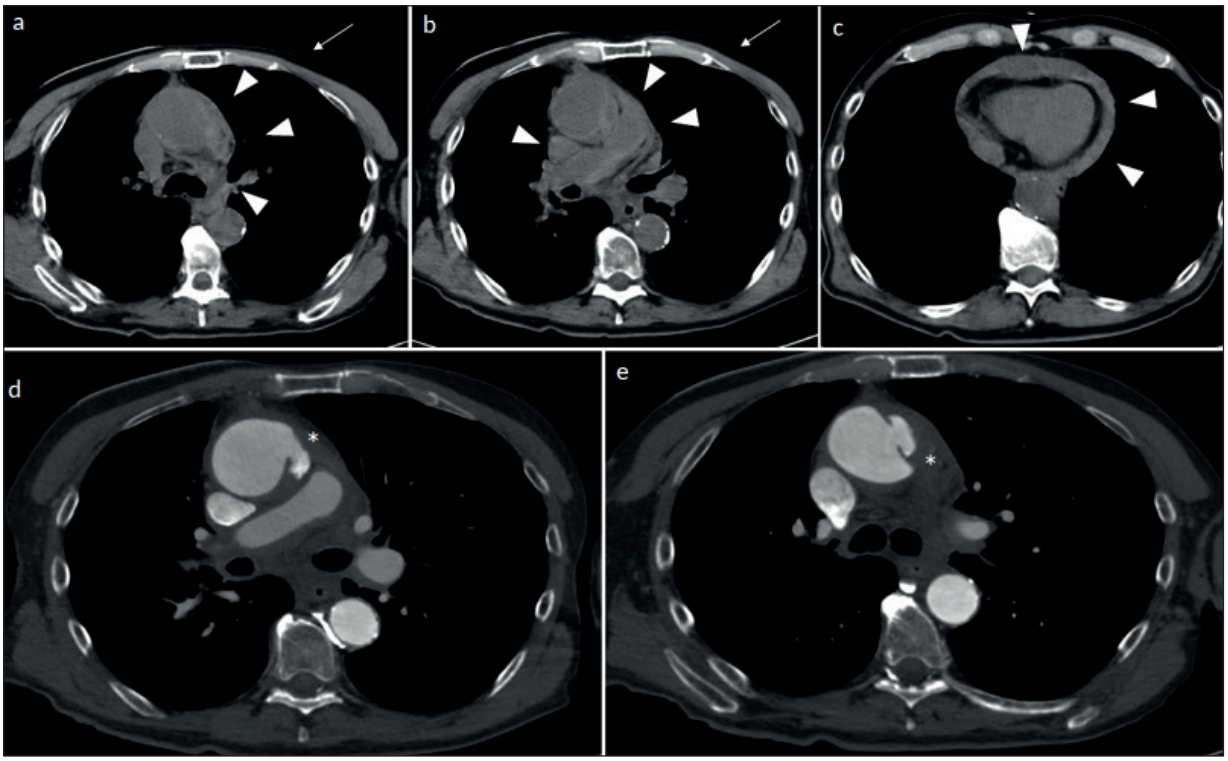


**Figure 1.** P atient with chest pain and hypotension. Basal CT scans (images **a**, **b** and **c**) show diffuse high-attenuated fluid among mediastinal structures and pericardial layers. CTA was acquired with a non-synchronized (thin white arrows) high-pitch technique (images **d** and **e**). CTA shows a complicated PAU with aortic rupture and pseudoaneurysms of the ascending aorta. High-pitch technique allows for good image quality.
Abbreviations: CT: computed tomography; CTA: computed tomography angiography; PAU: penetrating aortic ulcer.

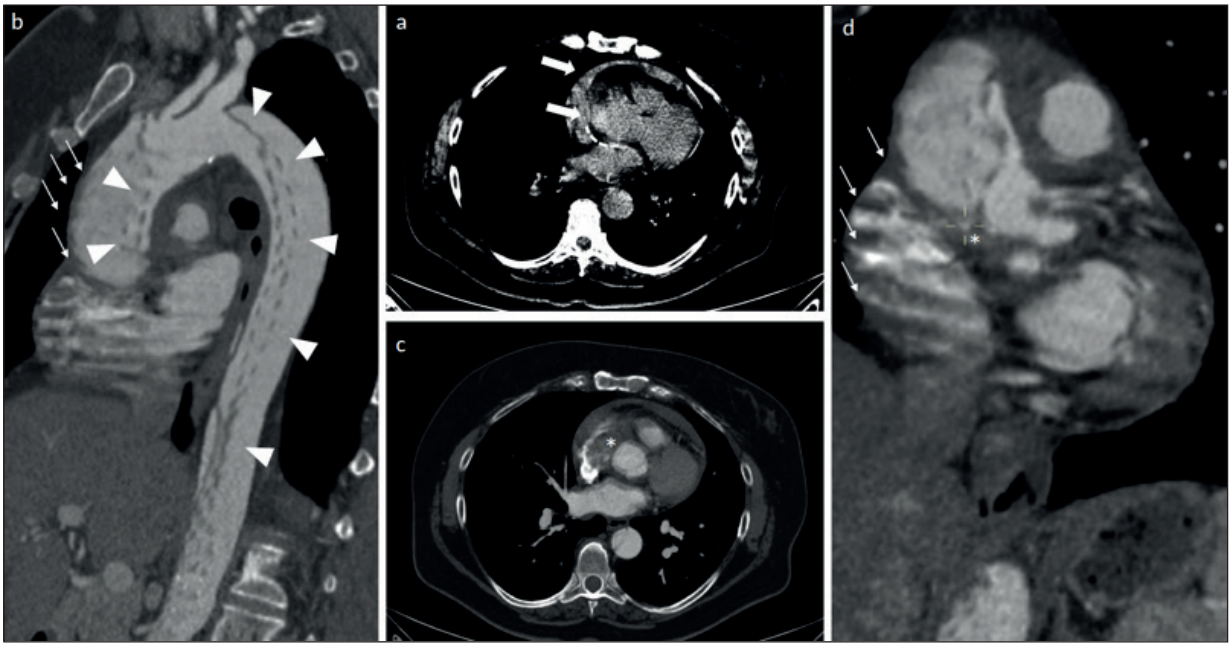


**Figure 2.** Patient underwent CT for epigastric pain and abdominal tenderness. Cranial scans (image **a**) reveal high-attenuated area of the aortic profile, and high-attenuated pericardial fluid (thick white arrows and dashed curved line). The exam was urgently completed with a non-optimized CTA of the aorta (image **b**), which shows a type A AD (white arrowheads). CTA shows severe pulsatility artifacts (thin white arrows). In images **c**) and **d**), a focal arterial blush-like image seems appreciable under the aortic root (white asterisks). The blush-like image was interpreted as a suspected aortic rupture, however poorly characterized given the non-optimized technique. The patient urgently underwent aortic surgery, which confirmed all the CT findings.
Abbreviations: CT: computed tomography; CTA: computed tomography angiography; AD: aortic dissection.

Cardiac gating may not be optimal as a result of patient clinical conditions.

- Optimal contrast opacification remains a challenging task. Main determinants of optimal opacification are a./ acquisition time; b./ Tube voltage, adjusted according to patient morphometrics. Contrast volume administration is determined by scan timing and examination dose since X-ray absorption with iodine contrast is maximized for 70-80 kV. Therefore, in non-obese patients, optimal arterial opacification may be obtained with a low dose and contrast media administration.
- The automatic dose exposure algorithm for the mAs setting should be used where available.
- Recently, the use of artificial intelligence technologies in the acquisition and interpretation of chest imaging has produced considerable benefits[57-63].
- An adequate angiographic acquisition is mandatory to properly assess acute CVD. A correct diagnostic suspicion is crucial, as different districts (i.e., heart, aorta and pulmonary circulation) may require different study techniques for a patient-focused approach based on imaging[64,65].

## Acute Coronary Syndrome (ACS) and Myopericarditis

CCTA shows high diagnostic accuracy in identifying coronary artery anatomy and disease (CAD), with a sensitivity and negative predictive value close to 100% in different studies[29,66-71] (Figure 3).

Different clinical trials[72-82] have highlighted the prognostic impact of these data.

From the PROMISE study, CCTA identified CAD better than conventional stress tests, with a better prediction of cardiac events, especially in non-obstructive CAD. In particular, the analysis by Hoffmann et al[73,74] shows that the ability of CCTA to identify a low-risk group corresponds to an event rate of 0.9% over a two-year period *vs.* 2.1% observed in patients managed with normal stress test.

The results of the PROMISE trial parallel the ones of the SCOT-HEART trial. Again, in patients

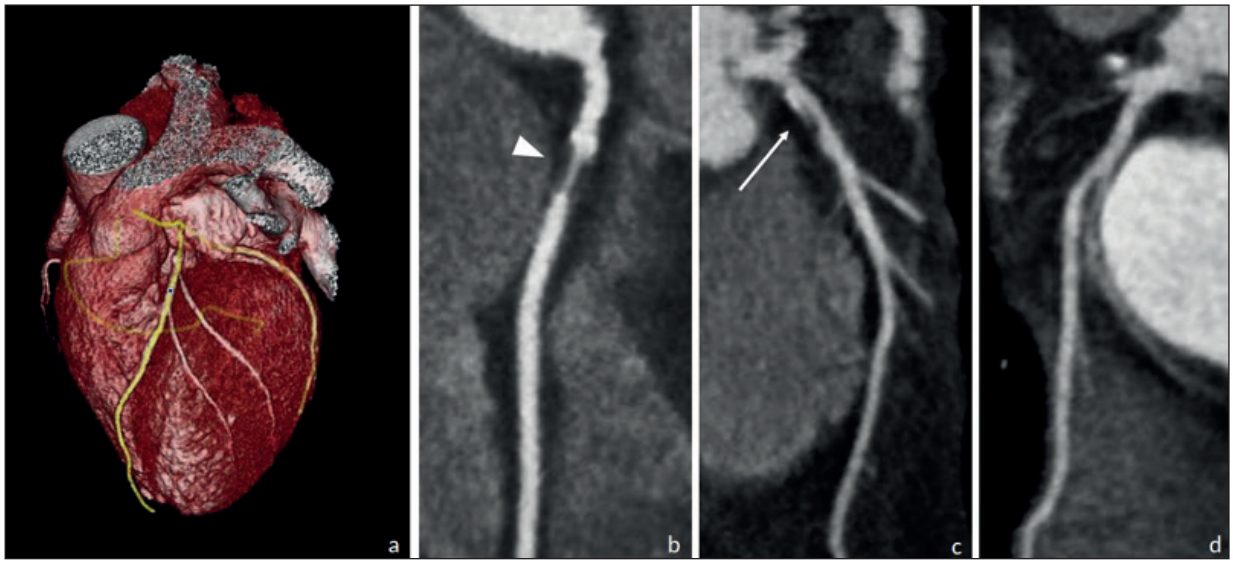


**Figure 3.** In image **a**), the volume rendering reconstruction of a CCTA performed in a patient referred for angina and lower limb edema, with no other cardiovascular risk factors. Dynamic troponins changes were not specific for ACS. CCTA reveals a severe low-attenuated lesion of RCA (image **b**, white arrowhead). Other non-obstructive lesions were detected at the proximal tract of the LADA (image **c**, thin white arrow). No CAD was detected on LCA (image **d**).
Abbreviations: CCTA: coronary computed tomography artery; ACS: acute coronary syndrome; RCA: right coronary artery; LADA: left anterior descending artery; LCA: left circumflex artery.

with chest pain, there was a lower risk of death from CAD or non-fatal myocardial infarction (MI) in patients managed with CCTA compared to SOC alone (2.3% *vs.* 3.9% / HR: 0.59, 95% CI: 0.41-0.84; *p*-value 0.004)[75-82].

As mentioned above, the use of the CCTA in an emergency can also offer significant benefits.

While no advantage has been shown in the use of non-invasive strategy in patients with suspected ACS and persistent ST-segment elevation, 2020 ESC guidelines on ACS management and non-persistent ST-segment elevation recommend CCTA as IA class study in patients with low-to-intermediate probability of CAD and non-specific/conclusive troponin elevation or ECG alterations[27,83-87].

Different randomized trials[88-90] have highlighted the advantages of CCTA in patients with acute chest pain and low risk of CAD over other strategies (i.e., SOC, functional or invasive tests).

The CCTA enables a fast and effective diagnosis that results in a drastic reduction in the length of stay at the ED.

From the ACRIN-PA 4005 trial, 50% of patients were safely discharged in the CCTA harm with a 30% shorter length of stay than SOC management (17 *vs.* 24.7 hours)[91]. Similarly, from the ROMICAT II trial, the CCTA helps to reduce the length of stay of patients by approximately 8 hours compared to only 10% of patients assigned to the SOC harm, thus determining a significant reduction in costs of management for patients whose ACS has been ruled-out[92-95].

From the CONSERVE trial, the incidence of 1-year MACE was similar in patients managed with CCTA or invasive angiography, although an initial strategy based on CCTA was associated with lower costs[96].

Finally, an increase in troponins and cardiogenic chest pain may also be observed with myopericarditis which is included in the differential diagnosis with ACS. The role of CT in ED for myopericarditis exclusion is restricted to a second-line assessment[97].

MDCT enables differentiation between pericardial exudate and transudate, and assessment of the vascularization of pericardial layers after intravenous injection of contrast agent[98,99].

Currently, the CCTA in the management of myopericarditis is limited to excluding ACS in patients with a low risk of CAD. Conversely, cardiac MRI plays an essential role in tissue characterization and structural heart disease, allowing an accurate assessment of myocardial inflammation in stable patients without complication[100-112]. However, recent results suggest improved diagnostic

performance of the CTA protocol implemented with late iodine enhancement scans in the identification also of non-ischemic patients in ED[113,114].

### Optimized CCTA Protocol

Extensive literature was reserved to the optimization of CCTA protocols[115].

CCTA is based on ECG-gated acquisition for which a minimum of 64-slice scan and fast gantry rotation is required.

### Heart Rate Control

According to the ALARA principle, a prospective scan is preferable to reduce the dose given during the study. The target frequency required for a prospective scan depends on the time resolution of the scanner.

The first-generation wide detector scanners had a temporal resolution of 175 ms (350 ms rotation time). A 175 ms temporal resolution, associated with a volume of acquisition up to 16 cm, allows a "one beat" acquisition technique with a target heart rate not exceeding 64 beats per minute. Second-generation scanners have a temporal resolution of 135 ms, further enhanced by dual-source technology (about 73 ms), which enables scanning at higher frequencies. Though the possibility of acquiring at higher cardiac frequencies, heart rate control is currently recommended to increase pre-test probability of an excellent image quality and effective reduction of the delivered dose[116-118].

As a first line treatment for heart rate control, the use of beta blockers is recommended, among which metoprolol is a valid e.v. choice (5 mg as initial dose)[119].

### Vasodilatation

For an adequate evaluation of the coronary arteries, the administration of nitrates or calcium antagonists to vasodilate the coronary arteries is also recommended, with acquisition obtained no earlier than 5 minutes. However, beta-blockers and vasodilators may not be compatible with certain urgent conditions associated with hypotension[119].

### Contrast Medium

The amount of contrast medium delivered depends on the duration of the scan and the injection rate. Although the prospective acquisition with large detectors allows for short-term scans, it is not always possible to adjust the patient's heart rate. Furthermore, the width of the detectors is variable, and "shoot-and-step" techniques are available over the "one-beat" acquisition. Therefore, the scan duration can be variable, and the injection duration should be as long as the estimated scan duration. Conversely, for short duration scans, the injection duration should be at least 10 seconds.

The contrast can be administered with a biphasic protocol (at least 50 mL of undiluted contrast at 4-7 cc/sec, followed by 50 mL of saline solution at the same rate) or with a three-phasic protocol in case it is necessary to have a good representation of the septum as well (at least 50 mL of undiluted contrast followed by 50-to-70 mL diluted 50:50 contrast: saline solution with the same injection rate or undiluted contrast with slower rate – 2-3 mL – and final saline solution).

Finally, the contrast medium should be administered *via* the right antecubital vein since the possibility of streak artifact increases from the left.

### Scan Protocol

To reduce the scan dose, low-tube voltage (100 kVp) is recommended in patients with low BMI (<27 g/m$^2$), which enables a good image quality and significant dose reduction. From the PROTECTION VI, tube potential reduction is a feasible strategy that lowers radiation exposure and contrast volumes, also through the implementation of artificial intelligence technologies[59,120-123].

In addition, many scanners are equipped with modulation systems for the correction of the tube current by means of automatic exposure control.

In patients with higher BMI, it is recommended to increase the tube voltage up to 120-140 kVp.

Scan range should include the heart alone (i.e., from below the carina to the lower edge of the heart) to avoid an overexposure of the patient.

Prospective acquisition with an end-diastolic evaluation should be preferred to obtain excellent image quality and reduce patient exposure.

Both bolus tracking and bolus test technique show high validity. Despite bolus test allows a patient-oriented approach, bolus tracking is also preferred to reduce the variability among acquisition and the amount of contrast medium[124].

Recommended coronary Hounsfield Unit (HU) values after contrast injection should be ≥250 HU.

No delay should be applied from the target HU in tracking ROI to the final acquisition.

The coronary analysis must be done on a slice thickness not exceeding 0.6 mm, preferably by integrating curved multiplanar reconstructions and 3D volume rendering.

Finally, it is unclear whether the calcium score may or may not be useful in an emergency setting.

Some studies[125-128] show that patients with acute chest pain in the absence of acute CVDs were often associated with CAC 0. However, the ability of Calcium Score to be a good method for ruling-out CVDs remains uncertain.

## Acute Aortic Syndromes (AASs)

AASs include aortic dissection (AD; accounting for approx. 80% of AASs), intramural hematoma (IMH) and penetrating aortic ulcer (PAU)[129-134]. Mortality associated with AASs is high, particularly when the ascending aorta and the aortic root are involved, with the risk of death increasing by 1 to 1.4% per hour of diagnostic delay. Mortality decreases when the descending aorta is involved, and non-invasive treatments show good efficacy (risk of death 11% lower with conservative treatment in uncomplicated type B dissections)[135,136].

From the meta-analysis by Shiga et al[137], advanced imaging techniques (i.e., transesophageal ultrasound, MDCT and MRI) are characterized by a similar high diagnostic accuracy. MDCT shows the highest pooled sensitivity (100%, 95% CI: 96-100) and lowest negative likelihood ratio. MRI, on the other hand, shows the highest positive likelihood ratio, with high advantage for the confirmation of AASs and flow analysis, even though MRI is not available in the ED and is not applicable in unstable patients[111,137-140].

Two important considerations derive from the same analysis:

a) MDCT is the preferred technique in ED given its high sensitivity;
b) The pre-test probability of AAS is highly correlated with the post-test probability of disease.

A pre-test probability of AAS of 5% (low-risk population) is associated with a post-test probability of AAS ranging from 0.1% to 0.3%.

In this regard, AAS are statistically infrequent (5-15 cases/100,000 individuals/year) and unfortunately often misdiagnosed (14% to 39%). According to some case series, only 2.4% of MDCT performed in suspected AAS were positive[23].

Interesting results derive from the ADVISED trial. The predictive model based on a low ADD-score (≤1) plus a negative D-Dimer (<500 ng/mL) achieves a failure rate of 0.3 % (95% CI, 0.1-1) and an efficiency of 49.9% (95% CI, 47.7-52.2), thus proposing an efficient strategy to adequately skim the population at the greatest risk, worthy of MDCT investigation[21,23,141].

### Optimized Aortic Protocol

Aortic root and ascending aorta are prone to pulsation artifacts; therefore, ECG-gated CTA strategy should be included in the evaluation of aorta. Motion-free images are mandatory for the evaluation of intimal flap in a supravalvular plane; moreover, adequate risk assessment includes evaluation of coronary sinus considering the potentially fatal consequences of an involvement of coronary arteries in a type A AD case[142].

#### Contrast medium

Adequate opacification values should not be less than 250 HU.

Bolus test or bolus tracking technique could be applied for an optimal aortic opacification[124,143,144].

Similarly to CCTA, injection duration should be as long as the estimated scan duration.

High injection rate should be preferred (i.e., 4-7 cc/sec).

Biphasic injection protocol is usually adequate to ensure homogeneous opacification of the aorta.

Contrast medium should be administered *via* a right antecubital vein.

#### Scan protocol

CTA of the aorta should be performed according to the ALARA principle.

Scan range should include the thoracic aorta alone, up to the diaphragmatic sulcus, except for high-risk patients or known disease. Moreover, IMH and PAU rarely affect the abdominal aorta.

The scan protocol should start with an unenhanced acquisition to exclude high attenuation areas of the aortic wall or the pericardium, indicative of IMH or hemopericardium, respectively (Figure 4).

ECG gated acquisition is the recommended strategy to reduce motion artifacts and radiation dose (Figure 5). This strategy is preferable also considering that prevalence of motion artifacts in unsynchronized CT is estimated to be ranging from 57 to 93%. If a non-target heart rate is present other strategies could be applied to reduce motion artifacts. High pitch in high-temporal-resolution scanner, in fact, allows acquisition of the aorta also without gating. Moreover, high pitch is useful to reduce the radiation dose.

Reduced tube voltages allow optimization of the contrast acquisition in patients with low BMI (<27 Kg/m$^2$), reduction of the radiation dose and optimization of the amount of contrast medium.

Acquisition protocols may vary based on heart rate, and prospective ECG gating acquisition should be preferred. In patients in whom a target

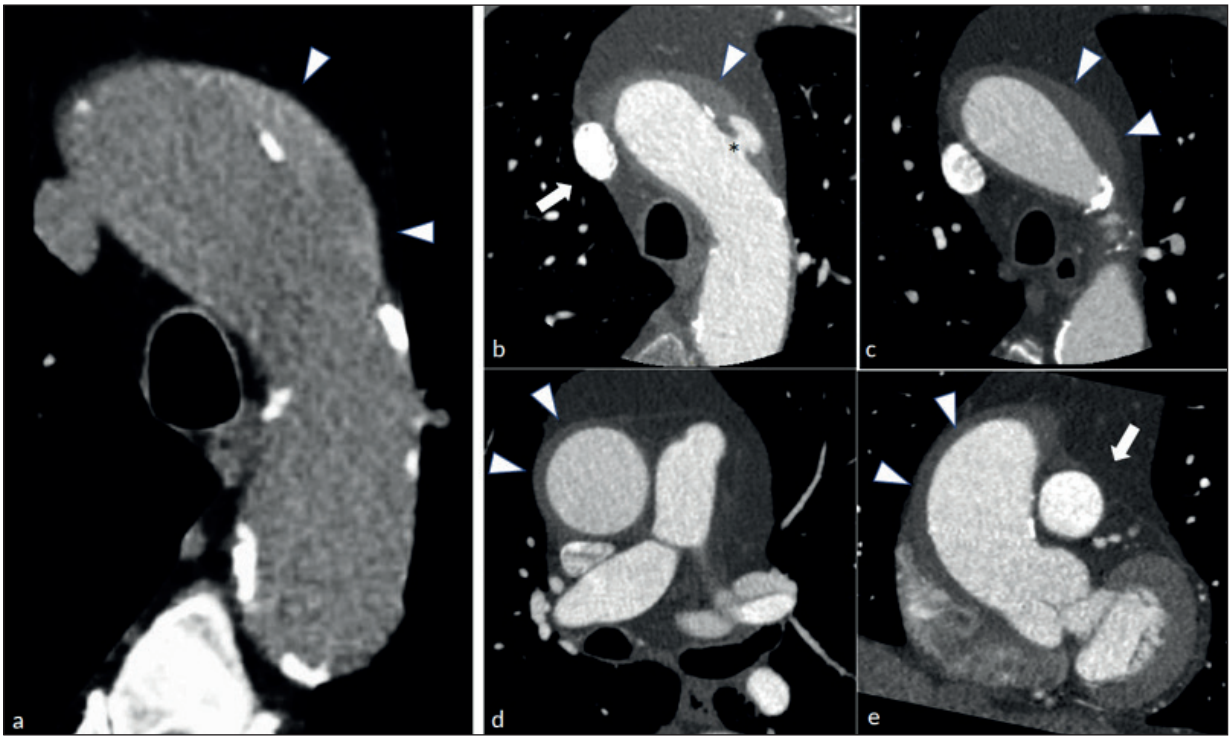


**Figure 4**. A complicated PAU (black asterisk) with IMH of the ascending aorta and aortic arch (type A) (white arrowheads in images **b**, **c** and **d**). Basal scan (image **a**) shows the high-attenuated area within the aortic wall. CTA was optimized with an ECG-synchronized technique which allows a correct analysis of the ascending aortic wall (images **d** and **e**). Identification of ascending aorta involvement allows a proper definition of the diseases with a different risk stratification[196]. Contrast medium amount was higher than necessary as pulmonary artery and superior vena cava resulted highly opacified (thick white arrows) (image **b** and **e**).
Abbreviations: PAU: penetrating aortic ulcer; IMH: intramural hematoma; CTA: computed tomography angiography; ECG: electrocardiography.

heart rate is not obtainable, retrospective helical acquisition of the whole chest is also feasible, significantly increasing the radiation dose.

The acquisition protocol depends on the scanner technology. Some scanners can combine synchronized acquisition for the study of the heart-aortic root-ascending aorta volume with the unsynchronized helical acquisition of the remaining aortic segments. Another acquisition technique is the "shoot-and-step", applicable to all scanners including wide-detectors up to 16 cm, which allows to cover the whole thoracic volume with two acquisitions.

## Pulmonary Embolism (PE)

PE is the third most common cause of CVD after MI and stroke, and it is also associated with high mortality ranging from 5% to 30%. PE has emerged as one the main complication of the new coronavirus and is also one of the major causes of death in pregnant women, raising the question of what the management algorithm should include considering the potential exposure to both non-useful and potentially harmful tests[145-148].

Risk stratification of acute PE, therefore, remains critical and includes the presence of hypotension, right ventricle dilation with/without signs of dysfunction/injury[149]. From the ICOPER study, patients with unstable PE reported a 3-month mortality rate of 58.3%[150]. For these reasons, different scores (e.g., the Pulmonary Embolism Severity Index [PESI] or simplified PESI [sPESI]) have been developed to stratify the risk of patients with acute PE[151-158].

An early diagnosis is therefore critical, and CT has recently assumed a key role in the management of patients with suspected acute PE, despite the increasing availability of CT has led to a strong, unjustified, overuse of this technique[159-161].

Clinical scores and laboratory biomarkers have proven to be useful in defining the pretest risk of acute PE.

From the PROPER randomized clinical trial, PERC score proved useful in identifying very-low

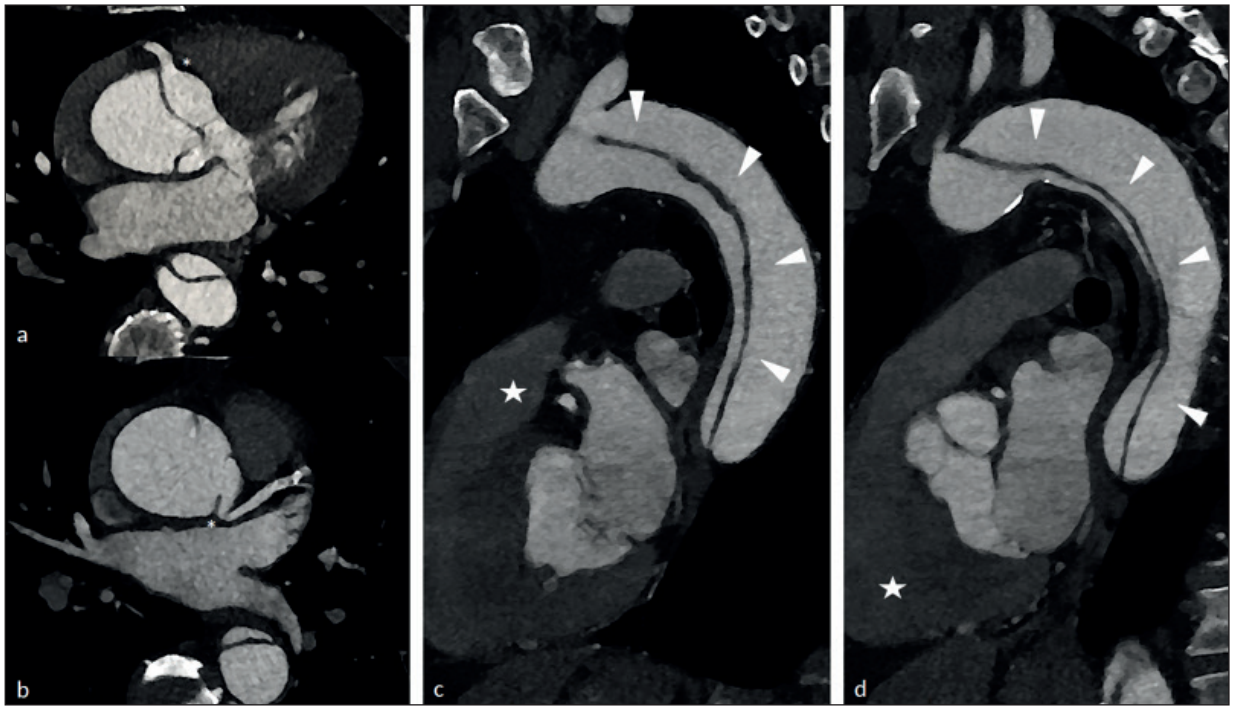


**Figure 5**. A type A AD (images **c**, and **d**; white arrowheads). CTA was optimized with an ECG-synchronized technique which allows a correct visualization of the intimal tear and coronary ostia (images ***a***, and **b**; white asterisks). White stars indicate the non-opacification of right chamber, enhancing an optimal arterial acquisition.
Abbreviations: AD: aortic dissection; CTA: computed tomography angiography; ECG: electrocardiography.

risk patients, both in the diagnostic definition (diagnosis rate of PE was 1.5% in PERC harm *vs.* 2.7 % conventional strategy) and in the indication of a CT strategy (CT rate 13% in the PERC harm *vs.* 23% of conventional strategy), with a failure rate of 0.1%[162].

Among the laboratory biomarkers, D-Dimer is a well-known biomarker largely used for the exclusion of acute PE, in consideration of its high NPV. However, the specificity of D-Dimer tends to decrease as age increases by about 10% over 80 years. Therefore, an age-adjusted cutoff has been proposed[163]. From the ADJUST-PE trial, an adjusted cutoff demonstrated a failure rate of 0.3%, allowing to increase the exclusion of the disease from 6.4% to 29.7%, without an increase of false negative cases[164-166].

To define indication to CT, the pre-test probability of disease is critical[167].

From the PIOPED II trial, the overall sensitivity of CT was 83%, with a specificity of 96 %. However, in patients with low-to-intermediate pre-test probability of PE, high NPV (ranging from 92 to 98%), and low PPV (58%) were observed. Conversely, in patients with intermediate-to-high pre-test probability, a high PPV (92-96%) and low NPV (60%) were observed[168-171].

With these premises, recent ESC guidelines for the management of suspected acute PE recommend CT as a class IA study for the exclusion of PE in patients with low-to-intermediate risk; otherwise, CT is class IIA in patients with high risk of PA to confirm the disease[172-175].

Due to the low NPV in patients with high risk of the disease, indeed, a negative test should not be considered conclusive if clinical doubt remains high, and further tests should be done for diagnostic confirmation[176].

### *Optimized PE Protocol*

CT of Pulmonary Artery (CTPA) generally does not require an ECG gated strategy, thus allowing for fast and low radiation dose acquisition.

### *Contrast Medium*

The amount of contrast medium, as for other angiographic studies, should be determined by the injection rate and the duration of the scan.

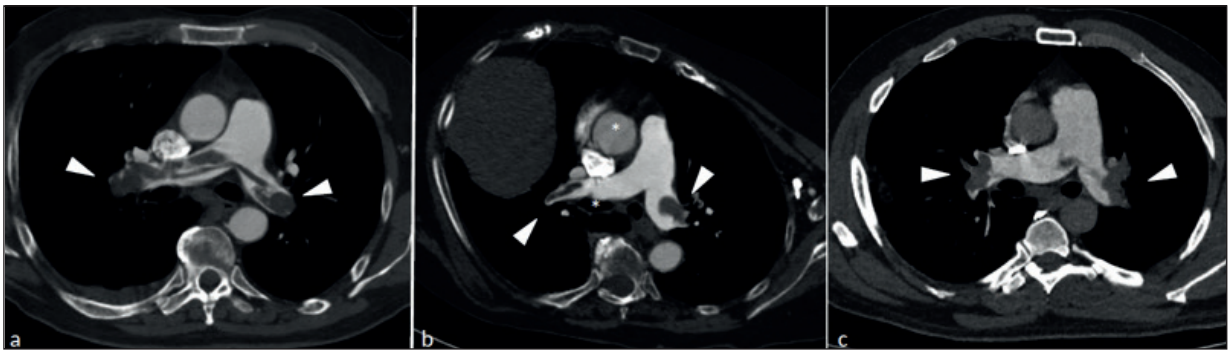


**Figure 6**. Three cases of PE (white arrowheads). Image **a**) and **c**), show a saddle pulmonary embolism. Adequate opacification was obtained in all CTPA (i.e., HU ≥ 90). However, different technical errors were observed. Image **a**) shows a delayed acquisition with higher contrast medium amount, opacifying also the aorta. Image **b**) shows more evident striking artifacts (white asterisk) than image **c**), due to the higher amount of contrast medium in superior vena cava.
PE: pulmonary embolism; CTPA: computed tomography of pulmonary artery; HU: Hounsfield unit.

A density of at least 93 HU in PA should be reached for an adequate evaluation of acute thrombus (Figure 6).

The most used technique for scanning is bolus tracking with a ROI positioning at the level of the pulmonary artery trunk. Threshold for the start of the scan should be set at 100 HU with a scan delay to ensure a maximum opacification, or with a higher threshold (i.e., 150 HU) without delay.

### *Scan Protocol*

The scan range should cover the entire chest.

CTPA should be followed by a venous acquisition. From the PIOPED II, a venous scan in addition to CTPA improved the sensitivity of CT for PE up to 95%[169].

Low-voltage protocols can be used for further reduction of the radiation dose. This makes of CTPA a safe technique even in pregnant women. During pregnancy, current guidelines primarily recommend scintigraphy for diagnosing suspected PE, being scintigraphy a lower-radiation and contrast medium sparing procedure. However, ongoing trials such as OPTICA (The Optimized Computed Tomography Pulmonary Angiography in Pregnancy, Quality and Safety Study) are attempting to demonstrate the safety of the CTPA protocol also during pregnancy.

Cranio-caudal scanning direction should be used to ensure opacification even in the lower vessels and to minimize streak artifacts.

Scans during prolonged inspiration should be avoided due to the risk of increased intrathoracic pressures which would not allow adequate filling (i.e., opacification) of the pulmonary vessels. In these cases, a second expiratory scan could facilitate vessel opacification, impairing image quality of the lung.

## Triple Rule-Out CTA (TRO-CTA)

TRO-CTA refers to an arterial CT acquisition which allows a simultaneous evaluation of coronary, aorta, and pulmonary arteries[177]. Actually, this acquisition protocol allows analysis of the whole chest, thus including non-vascular structures also, i.e., chest involvement in inflammatory or rheumatic disease[61,178-182]. Therefore, the term "triple" would seem inadequate to fully express all the potential of this acquisition protocol[183].

The interest on TRO-CTA derives from the theoretical ability of this technique to overcome the lack of specificity that often characterizes CVDs symptoms[184,185].

Moreover, TRO-CTA showed to be independent from the experience of the reader. From the study of Russo et al[185], a 100% of concordance between readers with different fields of interest and years of training was found for PE and AD; conversely, an agreement from 90 to 97% was found in non-obstructive CAD, resulting even lower for the evaluation of obstructive CAD.

As for other MDCT protocols, the high validity of MDCT resulted especially in the exclusion of the disease, with a TRO-CTA NPV close to 100% (99.4%; 95% CI: 96.9-100%) as from the study by Takakuwa et al[186,187].

On the other hand, from the study of Martin et al[188], the implementation of TRO-CTA with FFR-

CT processing proved to be a better predictor of revascularization and MACE also reducing unnecessary tests. FFR-CT analysis, therefore, showed advantageous also in the emergency setting, as also highlighted by the recent AHA guidelines for the assessment and diagnosis of chest pain[29].

In the study by Takx et al[189], in a very similar way to the dedicated protocols, TRO-CTA would allow a reduction in the ED and hospital length of stay, with fewer visit returns in a 30-day follow-up, and reduced costs of management when compared to an initial strategy including SOC.

However, uncertainties result from large meta-analyses.

In the meta-analysis by Ayaram et al[190] including 11 studies and 3,539 patients, despite the diagnostic accuracy comparable to dedicated CT protocols, a low prevalence of PE and AD was found, that did not allow a diagnostic accuracy analysis; these data, added to a mean higher radiation dose generally linked to TRO-CTA, are not sufficient to recommend TRO-CTA for routine use in ED[190,191].

### TRO-CTA Protocol Optimization

The protocol offers an ECG-gated acquisition of the whole chest, up to the lower edge of the heart. The prospective acquisition and the use of high pitch are effective strategies for dose reduction[192]. However, many studies[193,194] carried out with radiation exposure linked to TRO-CTA are limited by the use of older generation scanners; conversely, wide-detector scanners and dual source scanners resulted capable of a significant reduction in the delivered dose[193]. For example, in the study by Chen et al, the use of two wide-detector axial scans was useful to reduce the radiation dose[194].

Another dose modulation technique is the use of low voltages for patients with a <27 $Kg/m^2$ BMI, reserving 120 kVp for higher BMIs.

Reduced FOV proved efficient in dose reduction[195].

To allow adequate opacification of all vascular structures, a double injection protocol is usually employed. This involves the use of a first dose of contrast medium of about 70 ml at 5 ml/s, followed by a diluted dose of 25 ml of contrast plus 25 ml of saline solution, also at 5 ml/s.

Bolus tracking, acquired at 5 s after injection of the contrast medium, is usually preferred to the bolus test technique, not for a proven technical superiority, but to avoid the additional contrast dose. Furthermore, localizing the ROI for tracking in the atrium proved to be an improvement factor for a correct opacification of all structures.

## Conclusions

CVDs represent a leading cause of death worldwide. The main clinical sign is chest pain, although nonspecific and common to both benign and malignant conditions. Clinical algorithms for management of acute chest pain for the suspicion of CVDs should consider laboratory and imaging biomarkers over clinical presentation, for a rapid diagnosis and risk assessment.

During the latest years, CT has played a pivotal role in the management of CVDs, also in an emergency setting, although a clinical pre-test probability should be assessed to predict post-test CT accuracy.

Different trials have shown that validity of CT remains high in different settings, despite strategies of CT optimization should be adopted to reach an optimal diagnostic yield.

### Conflicts of Interest

The authors declare that they have no conflicts of interest.

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