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REVIEW

Optimal triage of patients with acute chest pain

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ABSTRACT

Acute chest pain (ACP) is one of the most common symptoms in patients admitted to emergency departments (ED). It can be related to several life-threatening cardiovascular conditions such as acute coronary syndrome (ACS), aortic dissection, and pulmonary embolism. The optimal triage of patients with ACP is a clinical and healthcare necessity given the large number of patients daily admitted to ED with this symptom. The first contact with the patient in ED includes the clinical appraisal of the characteristics of ACP and coexisting symptoms, and the assessment of the patient's medical history. Risk scores may help stratify a patient's likelihood of having cardiac chest pain. The ECG examination allows the identification of patients with ST-segment elevation, depression, or T-wave changes, but may be normal in patients with non-ST-segment elevation ACS. Rapid protocols based on serial high-sensitivity cardiac troponin assays within one or two hours are recommended for identifying candidates for early discharge. Due to the bedside feasibility, non-invasiveness, and wide availability, transthoracic echocardiography represents the first-line imaging modality for evaluating patients with ACP. In selected cases, computed tomography angiography may also be performed. A practical approach to ACP in ED should improve patient outcomes and reduce healthcare system costs. This review aimed to provide an overview of the characteristics of patients with ACP of cardiac origin and to describe the state of the art about their management in the ED.

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KEY WORDS: Acute coronary syndromes; Echocardiography; Troponin.

Acute chest pain (ACP) is one of the most common symptoms in patients admitted to emergency departments (ED). It can be related to several life-threatening cardiovascular conditions such as acute coronary syndrome (ACS), aortic dissection (AD), and pulmonary embolism (PE).[1] Chest pain is an unpleasant and discomforting sensation, often reported as constriction or burning, in the anterior or posterior chest region with possible radiation to the neck or arms.

Optimal triage of patients with ACP is a healthcare necessity given the large number of patients admitted to the ED daily with this symptom. The aim is to reduce the diagnostic delay and early discharge patients without evidence of ongoing acute diseases. A practical approach

to this condition may improve patient prognosis and reduce costs for the healthcare system at the same time.

Distinguishing life-threatening cardiovascular and non-cardiovascular diseases from benign conditions may be difficult and represents a current clinical challenge. Many have to be considered in the differential diagnosis of ACP, and the pretest risk evaluation is influenced by patients' age, sex, comorbidities, and the individual medical history. In younger subjects, conditions such as arrhythmias, myocarditis, gastro-esophageal disorders, pneumothorax, and anxiety prevail. ACS, PE, congestive heart failure, exacerbations of chronic obstructive pulmonary disease, or pneumonia are more frequent in elderly subjects.[2]

Almost half of the patients are discharged with a diagnosis of non-specific pain, and this phenomenon may contribute to their readmission for the same symptom within a short time. A small percentage of subjects (about 3%) recur for adverse cardiovascular events, including ACS, within six months.[1]

The development of new risk scores and early rule-in/rule-out protocols based on serum cardiac biomarkers has significantly reduced the number of undiagnosed cases. The current availability of sophisticated non-invasive imaging modalities may also help to discriminate critical patients ("rule in") from those who can be early discharged directly from the ED ("rule out").

Sharing diagnostic protocols promotes good clinical practice in ED and chest pain units.[3] This review summarizes the main cardiovascular causes of ACP and provides a practical perspective on the diagnosis and triage of these patients in the ED.

Current standards in the evaluation of patients with ACP and suspected ACS

In patients admitted to the ED for ACP, the first step of the clinical management includes the clinical appraisal of the symptoms and of patient's medical history, and the assessment of the hemodynamic status.

The characteristics of chest pain, including onset, location, duration, and the presence of precipitating and relieving factors, are essential to guide the clinician toward the most appropriate management.[4]

ACP suspicious for ACS is generally reported as either tightness, tension, pressure, heaviness, discomfort, or burning in the precordial region of the chest with possible radiation to the arm, neck, shoulder, back, upper abdomen, or jaw.[4] In some cases, like elderly or diabetic patients, the presence of equivalent symptoms, like shortness of breath, fatigue, syncope or presyncope, diaphoresis, nausea, or vomiting, can be considered suggestive of ACS. Chest pain described as sharp, very localized to a specific point, influenced by inspiration and position is poorly suggestive for ACS.

This heterogeneity of the clinical presentation of ACP has discouraged the use of the previous classification in "typical" and "atypical" forms and supports the adoption of the following terms: cardiac, possible cardiac, and non-cardiac pain.[2] When the onset of symptoms is chronic or associated with precipitating conditions such as exertion, chest pain is described as "stable".[2] The second step is the investigation of traditional risk factors for coronary artery disease (*e.g.*, tobacco use, hypertension, diabetes, family history, and hypercholesterolemia) or personal medical history of cardiovascular diseases.

The ECG examination allows to identify patients with ST-segment elevation (STE) myocardial infarction (MI). Non- ST-segment elevation (NSTE)-ACS may present with ST-segment depression or T-wave changes, but sometimes with normal or quite-normal ECG.

Thus, the characterization of ACP and ECG may guide toward further non-invasive examinations (*e.g.*, cardiac biomarkers of myocardial damage dosage, computed tomography, etc.), urgent coronary angiography, or, in a few cases, early discharge.

Use of risk scores in patients with suspected acute coronary syndrome

After clinical and ECG evaluation, the use of risk score may be helpful in stratifying the patient's likelihood of having cardiac chest pain. Overall, the currently available risk scores have shown

to be good in identifying subjects with very low risk of ACS, who can be early discharged from the ED.

Table I provides an overview of the principal risk scores that can be used in ED to evaluate patients with ACP. One of the most used and validated is the HEART score, which includes clinical, ECG, and laboratory variables, and classifies patients as having a low, moderate, and high risk for major adverse cardiovascular event (MACE) within six weeks.[5] An external validation study including 604 subjects admitted in ED for ACP and evaluating the 30-day risk of MACE showed that ruling-out patients with HEART score of ≤3 had a sensitivity of 99% and a negative predictive value of 98%.[6, 7] Therefore, the HEART score may help identify patients who can be early discharged. The disadvantages of the HEART score are the need for information about the patient's medical history and symptoms, the interpretation of symptoms on a subjective basis, and ECG and laboratory results.

The EDACS-ADP (Emergency Department Assessment of Chest Pain Score) score also showed a good performance (99% sensibility) in identifying subjects with ACP at very low risk of MACE at 30 days.[8, 9] However, this score was validated only in Australasian patients and may be affected by inter-observer variability.[10]

The combined use of both HEART and EDACS-ADP scores with a 0-hour/1-hour hs-cTnT protocol emerged as a valuable and safe approach for the early ruling-out of subjects with ACP and an estimated low risk for MACE.[11, 12]

The Chest Pain Score is another validated score for stratifying the likelihood of ACS. This score includes only clinical variables and can be easily calculated in a few minutes, already at the first medical contact.[13]

Many risk scores have been developed to evaluate the likelihood of alternative cardiovascular causes of ACP in the individual patient. Among these, the ADD (Aortic Dissection Detection Risk Score) and the Wells score are extensively used in cases of clinical suspicion of acute aortic syndrome and of PE, respectively.[14, 15]

TABLE I.—*Risk scores in patients presenting with acute chest pain.*

Score	Variables	Strengths	Limitations
HEART	History, ECG, age, risk factors, troponin	High sensitivity and NPV in low-risk patients	Subjective interpretation of the symptoms Need of ECG and laboratory tests
EDACS	Age, sex, symptoms and signs	High sensitivity and NPV in low-risk patients More specific symptoms	Lack of data about inter-operator variability Not validated for European population
CPS	Pain localization and specific features, associated symptoms/signs	Fast and easy to perform at bedside No need for instrumental tests	Subjective interpretation of the symptoms
T-MACS	Symptoms and signs, troponin, H-FABP	Safe ruling-out in low-risk patients	Based on a single troponin sample H-FABP assay is not widespread
North American Chest Pain Rule	Age, ECG, medical history, symptoms, troponin	Safe ruling-out in low-risk patients	Not validated for European population
Vancouver Chest Pain rule	Symptoms, ECG, medical history	Safe ruling-out in low-risk patients	Poorly validated in external cohorts Designed with troponin T
ADD	Risk factors, symptoms, clinical findings	High sensitivity, easy to perform at bedside	Low sensitivity in low-risk patients Need for imaging
Wells Score	Risk factors, symptoms	High sensitivity and NPV in low-risk patients Fast and easy to perform	Low specificity Need for D-dimer testing

EDACS: Emergency Department Assessment of Chest Pain Score; CPS: Chest Pain Score; T-MACS: Troponin – Manchester Acute Coronary Syndromes; ADD: Aortic Dissection Detection Risk Score; NPV: negative predictive value; H-FABP, heart-type fatty acid binding protein.

High-sensitivity cardiac troponin assays

Cardiac troponin (cTn) I and cTn T are the gold-standard biomarkers of myocardial injury, and their assessment is critical for the evaluation of patients admitted to the ED for ACP.[2]

High-sensitivity cardiac troponin (hs-cTn) assays measure the same analytes of conventional tests and currently represent the gold standard for assessing patients with ACP.[16] hs-cTn assays have to respect the standards of the International Federation of Clinical Chemistry and Laboratory Medicine Task Force on Clinical Applications of Cardiac Biomarkers: 1) the assay imprecision at the 99th percentile value should be ≤10% and 2) at least 50% of apparently healthy men and women should have hs-cTn concentrations above the assay's limit of detection (LoD).[17]

In clinical practice, the widespread use of high-sensitivity tests for cTn in ACP patients brought significant advantages in terms of time for patients' ruling-in/ruling-out and costs (MI).[18]

Diagnostic performance for myocardial infarction

The main clinical application of hs-cTn assays is the diagnosis of MI.[19] According to the Fourth universal definition of MI, this diagnosis requires the detection of a rise and/or fall of cTn with at least one measurement above the 99th percentile upper reference limit (URL) associated with a clinical context of myocardial ischemia.[19]

In recent years, evidence from large multicentre studies has consistently shown that hs-cTn assays, compared to conventional cTn assays, improve the diagnostic accuracy for the detection of acute MI and allow for early diagnosis and treatment.[20] In absence of the MI clinical framework, elevated hs-cTn assays may be determined by cardiac and non-cardiac conditions, including heart failure, renal dysfunction, PE and sepsis; therefore, they need to be contextualized clinically.[21]

Recent evidence has showed the association between hs-cTn and the outcome of patients admitted to the ED for ACP. In a prospective multicenter study including 1117 patients admitted to the ED for symptoms suggestive of acute MI, hs-cTn assay at admission showed a higher accuracy in predicting two-year mortality compared to conventional assay.[22]

Moreover, a recent meta-analysis including 24 studies and 203,202 individuals from the general population showed an association between hs-cTn serum levels and the risk of cardiovascular adverse events, including mortality.[23]

Coelho-Lima *et al.* investigated the prognostic value of hs-cTnT serum levels at admission and at twelve hours after myocardial reperfusion in patients with STEMI undergoing primary percutaneous coronary intervention. The assessment of hs-cTnT at admission, but not at twelve hours after reperfusion, was significantly associated with higher in-hospital and long-term mortality.[24]

Therefore, hs-cTn assay has replaced the conventional assay in ED owing to a higher accuracy for the diagnosis of MI and for better prognostic stratification. Clinicians should be familiar with these assays as they, together with the patient's clinical presentation, may improve differential diagnosis, early recognition of ACS, and avoid treatment delay.

Rule-out protocols

A key advance in the management of ACP patients has been the ability of hs-cTn assays to detect small serum cTn elevations in the first few hours after MI onset, thus reducing the initial "troponin-blind" time interval.[25] This characteristic allowed the development of early rule-in/rule-out protocols that represent the current standard of care in patients admitted to ED for ACP.

Current guidelines recommend the adoption of the 0/1 and 0/2-hour algorithms, which are based on early serial hs-cTn testing and have been validated in large multicenter patient cohorts.[25-27]

These rapid protocols are based on two concepts: 1) hs-cTn is a continuous variable, and the probability of MI increases with higher hs-cTn values; and 2) early absolute changes of hs-cTn serum levels within 1 or 2 hours provide additional information compared to the basal level.[18] The 0/1- and 0/2-hour algorithms have been demonstrated to be valuable and safe approaches, with a negative predictive value and sensitivity of over 99%.[28, 29] Moreover, three recent large studies demonstrated that the 0/1-hour algorithm

has even a more favorable balance between effectiveness and safety compared to the conventional 0/3-hour algorithm.[30, 31]

A disadvantage of the 0/1-0/2-hour algorithms is their susceptibility to not detect MI in patients with late presentations to the ED, in whom minimal or no increase of hs-cTn serum levels may be observed within 1 or 2 hours. The evaluation should be based on the correlation with clinical and cardiac imaging findings in these cases.[32]

Therefore, when contextualized with clinical information, the 0/1- and 0/2-hour algorithms allow the identification of patients who are candidates for early discharge and outpatient management.

Differential diagnosis in the Emergency Department

In patients admitted to ED for ACP, the differential diagnosis between ACS and other cardiovascular and non-cardiovascular conditions may be challenging.[33] Indeed, more than 50% of those patients are subsequently discharged with diagnosis of ACP of non-ischemic origin.[34] In ED, transthoracic echocardiography (TTE), due to the bedside feasibility, non-invasiveness, and the wide availability also in peripheral centers, represents the first-line imaging modality for identifying ACS or alternative cardiac causes of ACP.[35] Table II summarizes the main cardiovascular and non-cardiovascular causes of ACP with related clinical and echocardiographic findings. AD is clinically characterized by the sudden onset of severe chest or back pain often associated with systolic blood pressure difference >20 mmHg between patient's limbs.[36] TTE allows to suspect AD diagnosis by detecting the intimal flap into a dilated aortic lumen, and by showing mechanical complications related to proximal extension of the dissection, such as cardiac tamponade, severe acute aortic regurgitation and ACS.[37, 38] As TTE does not allow the visualization of the entire aorta, computed tomography angiography (CTA) is often necessary to evaluate the extension of AD. Furthermore, CTA allows to differentiate AD from intramural hematoma and penetrating aortic ulcer, which may have important treatment and prognostic implications.[36]

PE is a clinical condition presenting with no specific symptoms such as dyspnea, syncope, and chest pain of pleural origin.[39] CTA is the gold standard for the definitive diagnosis in hemodynamically stable patients; sometimes, in hemodynamically unstable patients, a bedside TTE may be sufficient for the diagnosis and for starting therapy. The echocardiographic signs of PE are the consequence of an acute right ventricular (RV) pressure overload: RV dilation and dysfunction, systo-diastolic septal shift with D-shaped left ventricle, akinesia of RV free wall with sparing of the apical segment (McConnell's sign), pulmonary hypertension, and inferior vena cava dilation without respiratory collapsibility; in some cases, right heart thrombi may be detected.[40]

Acute pericarditis occurs with typical chest pain, increased by breathing and stand-up position, in addition to PR interval depression and diffuse ST elevation without specularity on ECG.[41] TTE is the first imaging modality for the diagnosis of acute pericarditis since it allows for the detection of pericardial effusion and signs of cardiac tamponade. However, it is possible that some patients with diagnosis of acute pericarditis show normal TTE.[42, 43]

Myocarditis is an inflammatory disease of the myocardium that frequently involves the pericardium. Clinical manifestations of myocarditis are multiple and not specific, including ACP and signs and symptoms of heart failure. TTE can detect regional left ventricular (LV) wall motion abnormalities without epicardial coronary artery distribution, global LV systolic dysfunction, increased wall thickness due to myocardial edema, LV diastolic dysfunction, and the potential coexistence of pericardial involvement.[44] Cardiac magnetic resonance (CMR) with late gadolinium enhancement represents the imaging modality of choice for the diagnosis of myocarditis.[45]

ACP is also reported by patients with valvular heart diseases such as severe aortic stenosis because of concomitant obstructive coronary artery disease or microvascular dysfunction with severe LV hypertrophy. ACP may also be reported by patients with TTE evidence of acute severe aortic regurgitation secondary to AD or in patients with acute severe mitral regurgitation secondary

TABLE II.—*Main cardiovascular and non-cardiovascular causes of acute chest pain and related findings.*

Clinical syndrome	Clinical findings	Echocardiographic findings
Cardiovascular causes		
Acute aortic syndrome (dissection/ intramural hematoma/penetrating aortic ulcer	Sudden onset of chest or back pain, often migrating along aortic dissection direction Asymmetric blood pressure (>20 mmHg) between limbs Malperfusion syndrome Dysphagia/dyspnea/hemoptysis Syncope	Intimal flap Dilated aortic lumen Aortic insufficiency/wall motion abnormalities/ pericardial effusion (proximal extension) Pleural effusion Ulcerated plaque Crescentic or circumferential thickening of aortic wall– Intramural hematoma (better visualized by TEE) Wall ulceration with hematoma within the media – penetrating aortic ulcer (better visualized by TEE)
Pulmonary embolism	Dyspnea and pleural origin chest pain	RV dilation and dysfunction LV D-shaped McConnell's sign Pulmonary hypertension Right heart thrombi Dilated and not collapsing inferior vena cava
Acute pericarditis	Pleural origin chest pain, increased by breathing and sitting up position	Pericardial effusion Need to evaluate for signs of hemodynamic impact/cardiac tamponade
Myocarditis	Chest pain Signs and symptoms of heart failure	LV systolic/diastolic dysfunction Regional LV wall motion abnormalities without coronary distribution
Valvular heart diseases	AS: rude systolic ejection murmur, often irradiated to carotid arteries; parvus and tardus pulse AR: diastolic murmur at right of sternum MR: systolic murmur at mitral focus	Specific echocardiographic diagnostic criteria
Hypertrofic cardiomiopathy	Dyspnea, acute chest pain or syncope	Asymmetric septal hypertrophy Apical hypertrophy Preserved ejection fraction (in the initial phase)
Takotsubo syndrome	Acute chest pain	LV systolic/diastolic dysfunction Apical ballooning pattern
Non-cardiovascular causes		
Gastrointestinal		
Esofagitis	Epigastric and/or precordial burning and pain; variable duration between minutes and hours, often occurs after meals or at night	
Respiratory		
Pneumonia	Fever, dyspnea and pleural origin chest pain	
Pneumothorax	Dyspnea and chest pain during inspiration	
Chest wall		
Costochondritis	Pain with digitopression at costochondral joints	
Chest wall trauma	Pain with digitopression	
Herpes zoster	Herpetiform vesicles developing on erythematous base with dermatomal distribution, pain	
Other		
Sickle cell crisis	May be associated to shortness of breath, fever, arm and leg pain	Need to evaluate for new wall motion abnormalities as MI as it may occur at early age without traditional risk factors
Panic/anxiety disorder		

AR: aortic regurgitation; AS: aortic stenosis; LV: left ventricular; MI: myocardial infarction; MR: mitral regurgitation; RV: right ventricular.

to ischemic papillary muscle rupture.[46] TTE and transesophageal echocardiogram (TEE), if TTE is not diagnostic, represent the first-line imaging exams to reveal the presence and to assess the severity of acute valvular heart diseases.[4]

ACP, along with dyspnea and syncope, is frequently reported by patients with hypertrophic cardiomyopathy (HCM).[47] HCM is clinically characterized by dyspnea and chest pain with variable electrocardiographic abnormalities that may mimic ischemic heart diseases.[48] The differential diagnosis can be challenging in case of apical HCM, since TTE may not adequately visualize LV apex; in these cases, CMR may clarify the diagnosis of HCM.[49]

Takotsubo syndrome (TTS) typically occurs with signs and symptoms suggestive for ACS, including ACP and ECG abnormalities.[50-52] TTE shows typical LV involvement with apical and midventricular segments wall motion abnormalities ("apical ballooning") associated with hyperkinesia of the basal segments.[53] Sometimes, atypical "midventricular" and "basal" forms can be detected. TTE may also allow the identification of typical TTS mechanical complications: acute mitral regurgitation, RV involvement, LV outflow tract obstruction, ventricular thrombi, and pericardial effusion.[50, 54-56]

Is there a role for coronary computed tomography angiography in the acute setting?

Computed tomography angiography (CTA) has gained prominence for the evaluation of coronary artery disease (Figure 1). The European Society of Cardiology guidelines recommend CTA for those with chronic coronary syndrome or stable chest pain and a lower likelihood of obstructive coronary artery disease.[57] CTA provides valuable information for risk stratification and management of a patient with chest pain due to the possibility for a non-invasive and accurate anatomical characterization of coronary arteries.[58] Much effort, therefore, has been put into understanding the potential role of CTA in the assessment of ACP in the ED, with the possibility to identify or exclude ACS.

One of the key advantages of coronary CTA in the emergency setting is its ability to rapidly and definitively rule out obstructive coronary artery disease. By obtaining high-resolution images of the coronary arteries, clinicians can visualize the presence of stenosis, characterize the features of coronary plaques, and identify the presence of other cardio-thoracic conditions potentially associated with ACP (*e.g.*, PE and AD).

This rapid assessment aids in making timely and informed decisions, particularly in cases where the patient's symptoms cannot be undoubtedly attributable to a cardiac cause. The negative predictive value of coronary CT is high, allowing emergency physicians to confidently exclude significant coronary artery disease and consider alternative diagnoses, thereby avoiding unnecessary hospitalizations and invasive procedures.[59]

In patients with elevated cTn levels, CTA shows high sensitivity in detecting atherosclerotic plaques and identifying the infarct-related artery.[60] Moreover, CTA showed that approximately three-quarters of patients with elevated cTn serum levels and a low clinical suspicion for ACS have few to no atherosclerotic plaques. This highlights the potential role of CTA not only in detecting pathology but also in providing information on normal coronary arteries that affects the long-term management of these patients, especially by avoiding unnecessary invasive procedures.

Identifying high-risk features, such as the presence of vulnerable plaques, coronary dissection, or significant stenosis, enables a more targeted and individualized approach to patient care, optimizing resource utilization and improving outcomes. CTA provides information allowing timely initiation of appropriate interventions, whether medical therapy, percutaneous coronary intervention, or coronary artery bypass grafting.

Furthermore, coronary CTA contributes to a more comprehensive evaluation of patients with ACP by assessing not only the coronary arteries but also the myocardium by use of late contrast enhancement[61] and other structures, including the aorta and pulmonary arteries. This broader assessment is particularly relevant in the ED, where the differential diagnosis of chest pain includes non-cardiac causes such as AD and PE.

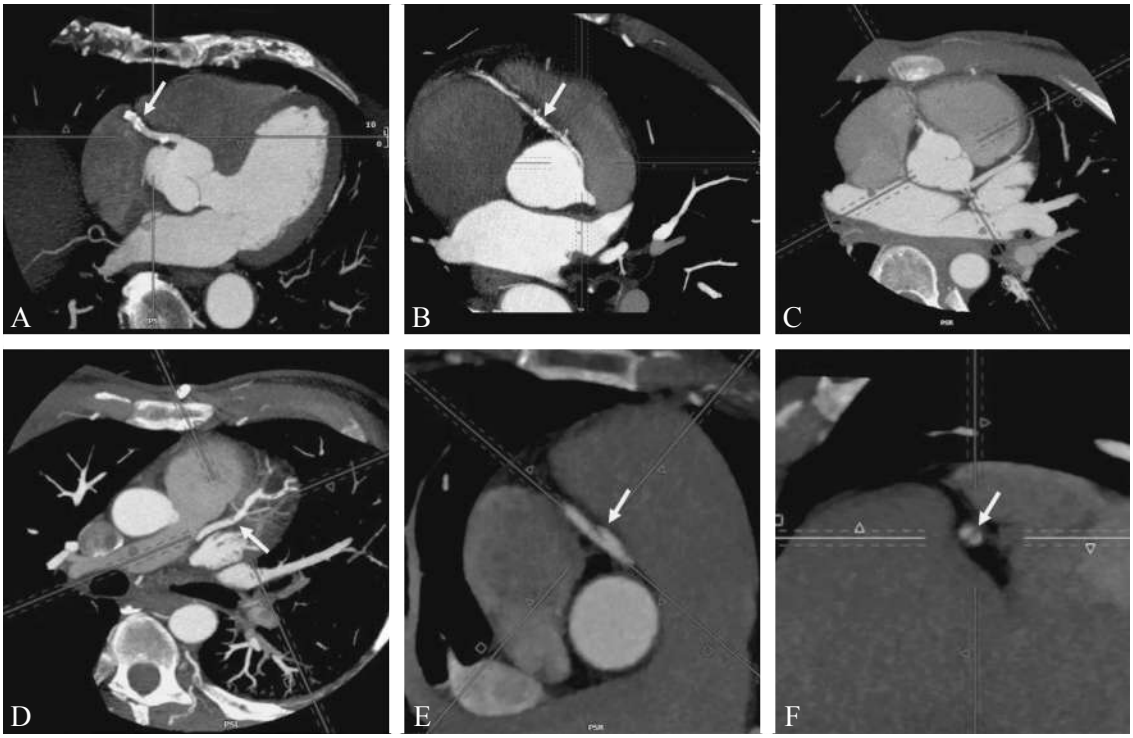

Figure 1.—Possible CTA findings in patients admitted in emergency department for acute chest pain: A) multiples calcified plaques in the proximal RCA causing 50% stenosis; B) abnormal origin of RCA from the left coronary sinus with proximal sub-occlusive mixed plaque; C) normal coronary arteries; D) small lipid plaque in the mid-segment of the left anterior descending coronary artery; E) and F) proximal right coronary artery dissection.

There are several ongoing studies evaluating CTA and its associated technologies that will define and potentially expand its application in patients with non-ST-segment elevation myocardial infarction. The Better Evaluation of Acute Chest Pain with Computed Tomography Angiography (BEACON) trial recruited 500 patients with suspected ACS,[62] and the Rapid Assessment of Potential Ischemic Heart Disease with coronary TCA (RAPID-CTCA)[63] trial enrolled 1749 patients with suspected ACS with half of them ultimately being diagnosed with unstable angina or myocardial infarction. Both BEACON and RAPID-CTCA trials compared CTA with standard of care. They showed that CTA allows a better individualization of patients deserving invasive coronary angiography, lowering the rate, the risks, and consequently the cost of this invasive procedure.

In conclusion, coronary CTA has emerged as a valuable tool in the assessment of ACP in the ED. Its non-invasive nature, rapid acquisition of high-quality images, and ability to exclude or identify significant coronary artery disease make it an indispensable component of the physician's diagnostic armamentarium in this clinical setting.

Future directions

ACP is one of the most frequent and dangerous symptoms that leads subjects to seek medical attention in the ED. The causes may be different and range from potential life-threatening emergencies, such as ACS, to almost harmless conditions. In the ED, often overcrowded with patients with heterogeneous diseases and severity, doctors must quickly recognize which patients deserve greater attention and further tests and which ones can be safely discharged early. Figure 2 provides a practical overview of the current management of patients with ACP in ED. The ideal decision-making algorithm for patients admitted for ACP should be easy to use, rapid,

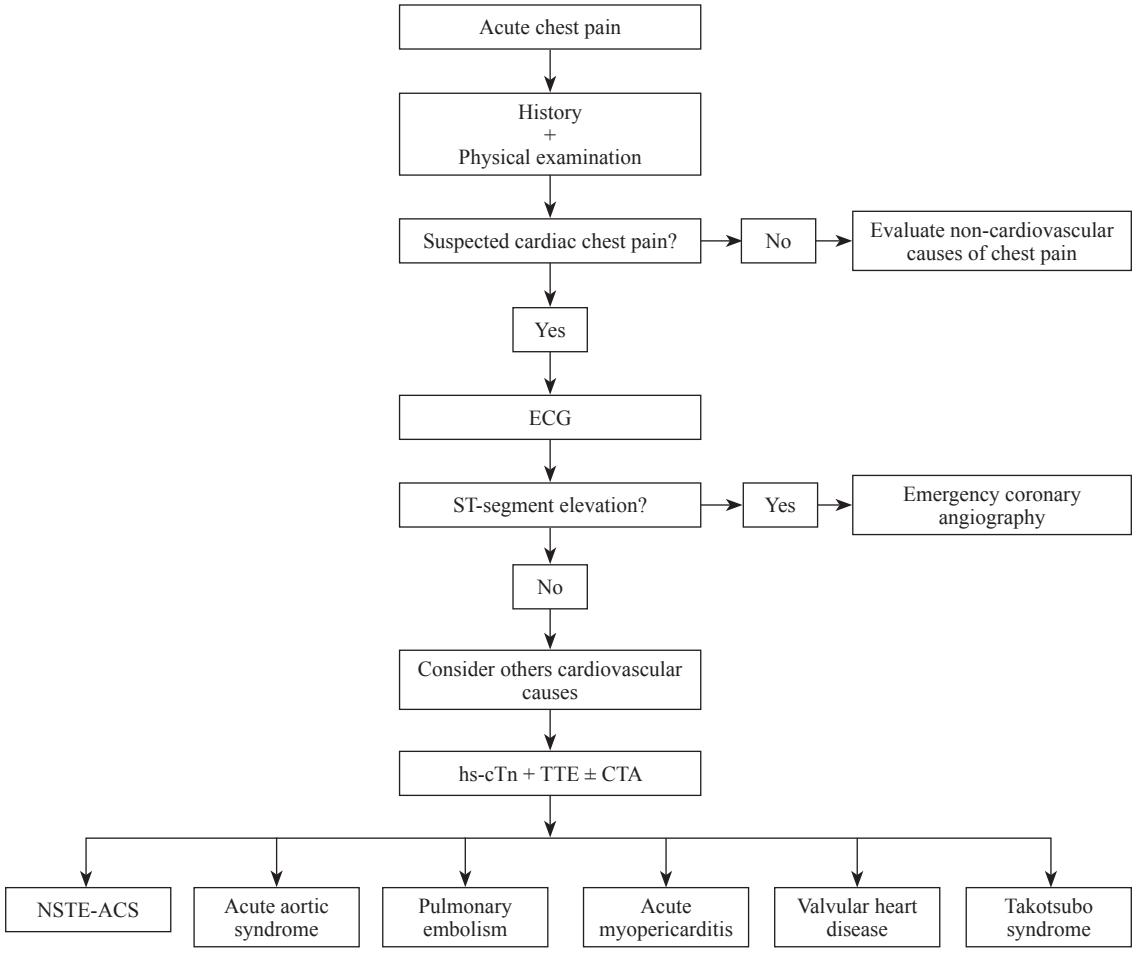

Figure 2.—Current management of patients with acute chest pain in the Emergency Department.
CTA: computed tomography angiography; ED: Emergency Department; hs-cTn: high-sensitivity cardiac troponin; NSTE-ACS: non-ST-elevation acute coronary syndromes; TTE: transthoracic echocardiography.

and safe. In this view, a comprehensive evaluation of medical history and physical examination combined with risk scores should be the first-line approach. After admission, patients should undergo ECG in a few minutes and, when needed, TTE or other second-level imaging modalities (*e.g.*, CTA). These findings, combined with 0/1- or 0/2-hour hs-cTn assay information, provide a valuable and standardized approach for most patients.

Unfortunately, concerns may persist for patients falling into a "grey area", such as those with uncertain pain characteristics, non-specific ECG findings, and with positive but not rising serial hs-cTn values. The risk of not recognizing ACS is very high in these patients.

Conclusions

In this view, the future perspectives include: 1) validation and development of point-of-care for rapid hs-cTn measurements, in less than 20 minutes; 2) widespread application of second-level imaging modalities, like coronary CTA, that may help to reduce the amount of unnecessary invasive coronary angiographies and may identify patients with non-obstructive coronary artery diseases, who can be early discharged; 3) development and validation of artificial intelligence-based protocols for estimating the individual risk of ACS and adverse cardiac events, combining different clinical and instrumental findings;[64, 65] and 4) development of work-up al-

gorithms addressing gender differences (not just sex) in the management of patients with ACP.

Key messages

• The optimal triage of patients with acute chest pain (ACP) is a healthcare necessity.

• After clinical appraisal of ACP characteristics and coexisting symptoms, risk stratification and ECG should be performed in every patient. Rapid protocols based on serial high-sensitivity cardiac troponin assays are recommended for identifying candidates for early discharge.

• Computed tomography angiography provides valuable information for risk stratification and management of a patient with ACP due to the possibility for a non-invasive characterization of coronary anatomy.

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Conflicts of interest
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Authors' contributions
Angelo Silverio has given substantial contributions to study conception, Francesco Caiazza, Pasquale Guarini, Pasquale Campana, Santo Dellegrottaglie, Francesco De Stefano, Dario Fabiani, Germano Junior Ferruzzi, Francesco Melillo, Alberto Morello, Roberto Franco Enrico Pedretti, Alessandra Scatteia, Angelo Silverio and Laura Adelaide Dalla Vecchia to manuscript writing. All authors read and approved the final version of the manuscript.

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