CONSENSUS

Consensus Statement for the Management of Patients with Chest Pain

Argentine Society of Cardiology Consensus Statement

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INDEX

Abbreviations

LBBB	Left bundle branch block
CK-MB	Creatine kinase MB
CPK	Creatine phosphokinase
CV	Coefficient of variation
CHD	Coronary heart disease
ECG	Electrocardiogram
MPI	Myocardial perfusion imaging
RMPI	Rest myocardial perfusion imaging
AMI	Acute myocardial infarction
HF	Heart failure
LR	Likelihood ratio
GXT	Graded exercise test
CMR	Cardiac magnetic resonance
ACS	Acute coronary syndrome
MSCT	Multislice computed tomography
Tn	Troponin
hs-Tn	High-sensitivity troponin
CPU	Chest pain unit

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According to mortality statistics, cardiovascular disease continues to be the major cause of death in Argentina, followed by tumors and infections.

The analysis of cardiovascular mortality, shows that coronary heart disease (CHD), together with heart failure (HF) are the most frequent causes of death in our country.

Chest pain is the most common form of presentation of patients with CHD and its proper assessment depends on the diagnosis of acute coronary syndrome (ACS) that without hospitalization and appropriate treatment is associated with high mortality. On the other hand, the unnecessary hospitalization of a patient with noncardiac chest pain is risky for the patient and generates high costs to the health system.

We consider a Consensus statement is necessary because:

- Chest pain is the second most common cause of care in emergency departments.
- The prompt classification of patients with chest pain aims mainly to differentiate an ACS from other causes.
- Although 50% of these patients present with a clinical condition suggestive of ACS, this diagnosis is reached only in half of the cases.
- It represents a medical challenge and an important issue for health systems from an economic point of view.

INTRODUCTION

Consultation for chest pain at the emergency department is very common. Between 60% and 90% of these consultations are not associated with cardiovascular disease, (1-4) albeit a large number of diseases can present with this symptom (Table 1). Around 1% of the consultations to general practitioners' offices correspond to chest pain (5) and only 1.5% of these is caused by an ACS. (6)

Table 1. Causes of chest pain

Cardiac
- *Coronary:* angina on exertion and at rest
- *Non-coronary:* pericarditis, cardiomyopathies, valve diseases, mitral valve prolapse
Noncardiac:
- *Esophageal:* spasm, reflux, etc.
- *Gastroduodenal:* gastritis, duodenitis, peptic ulcer, hiatal hernia, biliopancreatic diseases.
- *Pulmonary:* thromboembolism, pneumothorax.
- *Pleural:* pleuritis.
- *Vascular:* acute aortic syndromes.
- *Chest wall:* pectoral muscles, chondritis, neuropathies.
- *Soft tissues:* mammary gland pathology.
- *Psychogenic:* hyperventilation, etc.

Due to the risk involved, the first step is to determine if the pain is of coronary origin. The prevalence of angina increases with age in both sexes reaching 10-12% in women aged 65-84 years, and 12-14% in men aged 65-84 years. (7) Angina is more common in middle-aged women than in men, probably due to the higher prevalence of functional CHD as microvascular angina, (8, 9) and conversely, in people over 65 years of age. The annual incidence of angina in Western populations between 45-65 years is estimated in 1%, reaching 4% in men and women aged 75-84 years. (10)

Pain characterization of coronary etiology has a strictly clinical component, based on the clinical history and physical examination, electrocardiogram (ECG), detection of biomarkers and imaging methods.

CLINICAL ASSESSMENT

Physical facility

The care unit for these patients requires the possibility to perform an ECG and clinical assessment. The number of beds that should be available to handle this type of emergency is calculated according to the size of the hospital and the number of annual emergencies. Thus, a referral hospital in a health area (250,000 inhabitants) assists about 9,000 monthly emergencies; among these, about 200-250 per month will be patients with chest pain, half of which will require on average 17 hours of observation. Therefore, to manage about 108,000 emergencies annually, two to four beds would be necessary for this referral hospital.

For patients who remain under observation for intermediate or high CHD probability, noninvasive blood

pressure monitoring and continuous electrocardiographic monitoring with automatic detection of arrhythmias, as well as defibrillator and cardiopulmonary resuscitation equipment should be available for each patient, although a central monitoring station is not an essential condition. (11)

Staff required

The emergency department must be organized to simplify the flow of patients and adopt a system of categorization or triage for the patient's prompt care, based on the severity of his condition. Patients presenting with chest pain should be promptly evaluated to confirm or rule out the presence of myocardial ischemia. The staff in charge of performing the triage (usually nurses) should be trained in the assessment of symptoms and signs of patients and their categorization on admission.

The final assessment of patients with chest pain should ideally be performed by cardiologists, or eventually by general practitioners, intensivists or emergentologists qualified to handle this conditions and ECG reading.

Clinical parameters to identify pain of coronary origin

While a history of cardiovascular risk factors (diabetes, hypertension, dyslipidemia) helps to predict the risk of CHD, pain characteristics are more useful to define if it is of cardiovascular origin. (12) Chest pain of myocardial origin (angina) has special characteristics: location, duration and precipitating factors. It is generally located in the chest near the sternum but can be felt anywhere from the epigastrium to the base of the neck or teeth, arms, wrists and fingers. (Figure 1) The discomfort is referred to as tightness or heaviness, sometimes as constrictive or burning, with or without fatigue, dyspnea, nausea or vomiting. The duration of pain in ACS is generally greater than 10 minutes; pain lasting a few seconds is often noncardiac. Although its manifestation associated with physical exertion or a situation of emotional stress and its disappearance with rest or nitrate therapy are very characteristic of chronic coronary pain, (13) ACS typically presents as pain starting at rest or with minimal efforts, or with an in crescendo pattern in patients with chronic stable angina.

Atypical angina is defined as pain that has the same characteristics, location and response to nitrates, but with differences in precipitating factors: it starts at rest with low intensity that increases progressively and per-

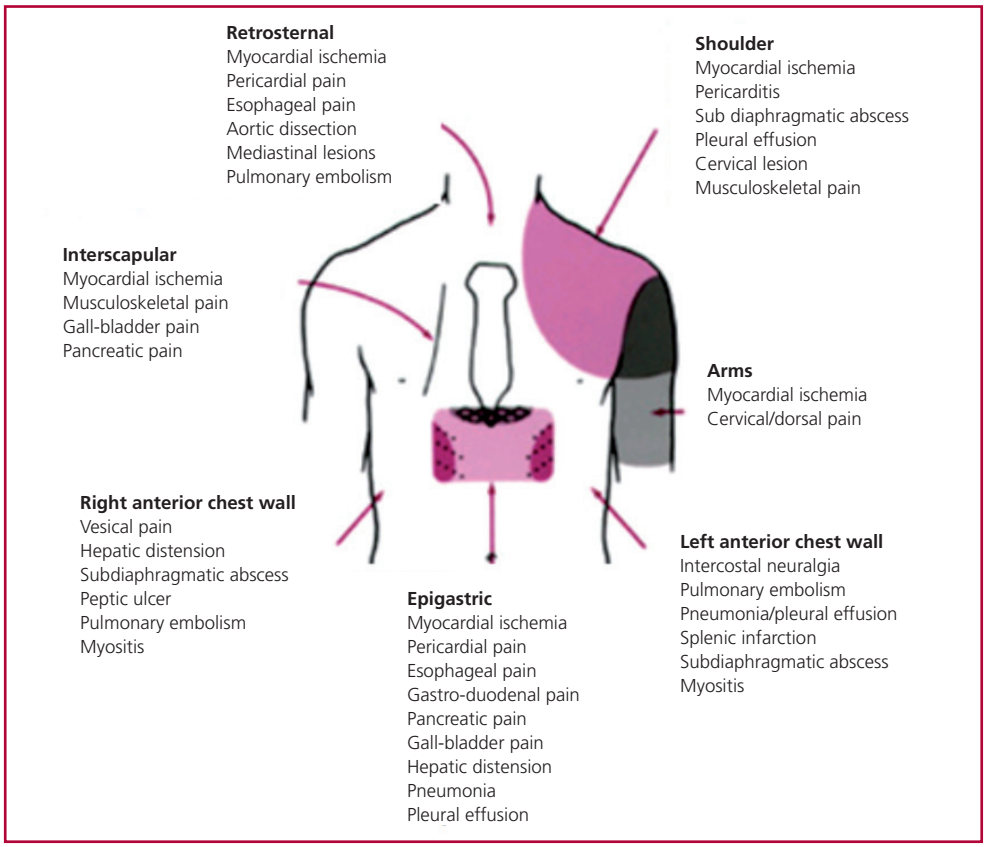

Fig. 1. Pain characterization according to location

sists for about 15 minutes and then slowly decreases. This description should alert on the possibility of coronary vasospasm. (14). Another atypical form is observed in patients with microvascular angina, with similar location and quality of typical angina but with low response to nitrates. (15)

Nonanginal pain has none of these characteristics and can only engage a small portion of the right or left hemithorax and may last for hours or days. It is generally unresponsive to treatment with nitroglycerin (except esophageal spasm) and can be reproduced by palpation. Table 2 describes the possible characteristics of chest pain and its relation with the probability of being of coronary origin.

Physical examination is important to establish differential diagnoses such as aortic dissection, pericarditis, rib pain, etc., precipitating or associated factors with pain of cardiac origin (anemia, hypertension, murmurs, arrhythmias) and to detect prognostic signs (rales, crackles, third sound, etc.) in angina.

Although individual characteristics may not be useful to detect ACS, (16) a combination of signs and symptoms can increase diagnostic safety. (17)

At this point it is very important to understand that in order to securely define whether a coronary pain is of coronary origin we must follow a "Bayesian analysis". Bayes's theorem states that the predictive value of a clinical trial depends on the prevalence of the disease being investigated within the epidemiological group to which the studied patient belongs. (18) In other words, post-test should be conditioned to pre-test probability. In the case of chest pain, patient's age, gender, risk factors and pain characteristics, can constitute the pre-test probability that the pain is of coronary origin.

Patients with defined angina have nearly 90% prevalence of CHD, (19) those with possible anginal pain 50% prevalence and when pain is nonanginal it does not exceed 10%, if they belong to an epidemiological group that

Table 2. Clinical assessment of chest pain

	Increases angina probability	Indifferent or variable: depending on the clinical condition it may increase, decrease or not modify the probability of angina	Dispels the probability of angina
Location	Retrosternal, central, all over the chest, neck, jaw, upper limbs.	Epigastrium, dorsal, precordial.	Infraumbilical, upper jaw, lateral chest area, in a dermatome distribution.
Characteristics	Oppressive, heaviness, tightness, burning.	Just pain: the patient does not identify any characteristic	Defined, sharp, piercing, tearing pain, dull ache. Sudden pain onset with maximum intensity from the beginning.
Surface extension	Painful area of the size of the hand palm or larger		Punctiform, the patient points with his finger
Duration	2 to 20 minutes	More than 20 minutes	Seconds, fleeting instantaneous. Many hours, more than a day..
Precipitating factors	Physical exertion, especially after eating or with cold.	Emotional, mental stress. Supine. Night onset.	Inspiration, cough, movement of the affected part of the body, palpation, swallowing food or alcohol intake, fasting.
Relieving factors	Rest, nitrites.	Belching, Valsalva maneuver.	Inspiration, cough, movement of the affected part of the body, palpation, swallowing, vomiting, antacids, common analgesics
Associated symptoms	Cold sweats. Syncope.	Nausea, watery or food vomiting. Dyspnea, restlessness, palpitations.	Dizziness, cough, dysphagia, heartburn, regurgitation, salivation. Hematic, bilious or green vomiting. Diarrhea, melena, enterorrhagia, fever, dark urine, jaundice

matches this suspicion (high pre-test probability), but it is significantly lower in groups with very low CHD probability (e.g. women under 45 years without risk factors) (Table 3).

The group with white squares has pre-test probability <15%

Table 3. Pre-test probability of coronary heart disease according to gender, age, and type of pain (20, 21)

	Asymptomatic		Nonanginal pain		Atypical angina		Atypical angina	
Age (years)	Male	Female	Male	Female	Male	Female	Male	Female
30-39	1.9	0.3	5.2	0.8	21.8	4.2	69.7	25.8
40-49	5.5	1.0	14.1	2.8	46.1	13.3	87.3	55.4
50-59	9.7	3.2	21.5	8.4	58.9	32.4	92.0	79.4
60-69	12.3	7.5	28.1	18.6	67.1	54.4	94.3	90.6

The group with gray boxes has 15-45% pre-test probability. They require ischemia evocative testing to complete the assessment.

The group with light blue boxes has pre-test probability of 45-85%. They require ischemia evocative testing to complete the assessment.

The group with red boxes has pre-test probability >85%. It is assumed that they most probably have coronary heart disease and ischemia evocative testing is indicated to stratify risk.

This reinforces the need to "stagger" a diagnostic algorithm, in which the post-test probability of an analysis is considered the pre-test probability of the next, as long as the study or test to be applied is considered to have adequate predictive value , i.e. with a chance to identify the really ill patients among those who seem to be ill (positive predictive value) or those who are really healthy among those with a negative test or study (negative predictive value) (Figure 2).

The definition of chest pain of cardiac origin is directly associated with prognostic differences and therefore, with the need to evaluate admission and specific treatments, with the ensuing patient discomfort and concern and increased health costs.

To minimize the risk of sub-diagnosing cases that require closer control and also to avoid unnecessary hospital admissions, diagnostic algorithms stratified in steps of growing complexity are recommended:

- First step: clinical assessment of previous history and symptom characteristics.
- Second step: ECG and biochemical marker analysis.
- Third step: diagnostic imaging methods and functional tests.

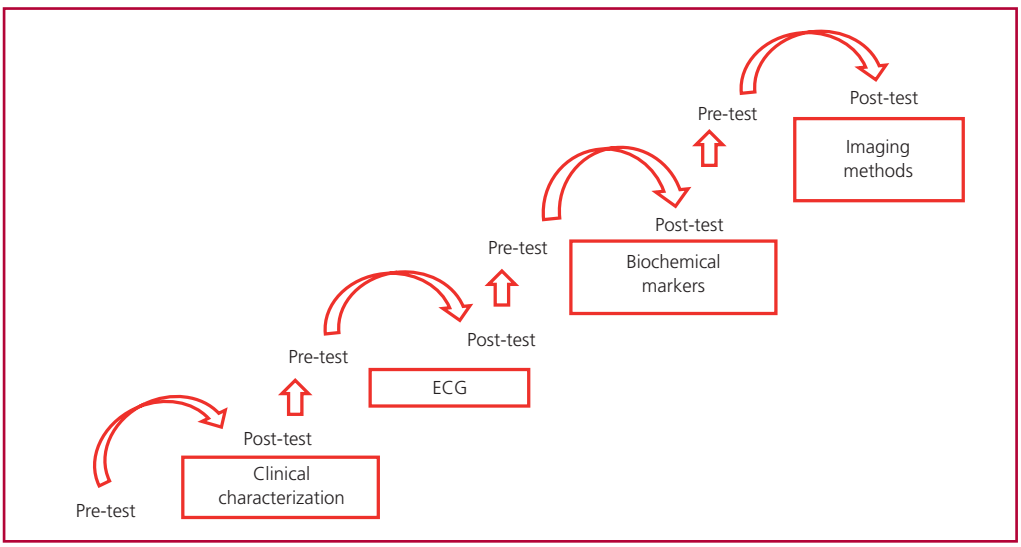

Fig. 2. Stratified chest pain analysis steps according to Bayes' theorem. ECG: Electrocardiogram.

This evaluation map should never be strict and will mainly depend on the availability of methods at each institution. For example, it is not necessary to wait for the result of a biomarker to perform an echocardiogram when this method can provide useful information. Likewise, it will not be necessary to continue with imaging studies or functional tests when a diagnosis may be reached with less complex studies or may be completed on an outpatient basis when it is considered that the patient has no high complication risks.

Recommendation	Class	Level of evidence
Recommendations on physical facilities for the assessment of patients with chest pain	I	B
The number of beds that should be available to handle this type of emergency is calculated according to the size of the hospital and the number of annual emergencies (1 or 2 beds per 50,000 emergencies per year).		
Noninvasive monitoring of blood pressure for each patient and continuous electrocardiographic monitoring with automatic detection of arrhythmias, as well as a defibrillator and cardiopulmonary resuscitation equipment must be available without the essential requirement of a central monitoring station.	I	C
Recommendations on the staff required for the triage of patients with chest pain		
It must be performed by trained personnel (generally nurses) during early detection and categorization of patients with chest pain or symptoms suggestive of myocardial ischemia.	I	A
Recommendations on the staff required for the assessment of chest pain		
Cardiologists.	I	C
Emergentologist and intensivist physicians, advanced medical residents in cardiology and emergentology, clinicians trained in the management of chest pain and ECG reading.	IIa	C
Untrained doctors in the management of chest pain and ECG reading.	III	C
Recommendations on the clinical assessment of chest pain		
The Diammond & Forrester classification of chest pain evaluation is recommended to define coronary etiology (angina).	I	B
No score can be considered superior to clinical criteria.	I	C

ECG: Electrocardiogram.

ELECTROCARDIOGRAM

The ECG is one of the main diagnostic tools in patients with suspected ACS, and should be performed and interpreted by a qualified physician within 10 minutes of patient admission. (22)

Prompt and proper ECG interpretation is essential for diagnosis and therapeutic decision-making, in patients with suspected ACS. Among ACS patients inappropriately sent home, the most frequent predictor which motivated inadequate discharge was an initial ECG interpreted as normal, affecting more women than men. (3, 16) In addition, only half of patients with acute myocardial infarction (AMI) underwent an initial ECG diagnosis in a timely and orderly manner. (23-25)

In patients with ischemic ECG abnormalities (about 20% to 30%) (Table 4), the conduct to follow is defined from the emergency room: reperfusion strategies (lytics or angioplasty) in the presence of ST-segment elevation or acute left bundle branch block (LBBB), and invasive or conservative strategies according to the level of clinical risk when ST-segment depression or changes in the T wave are observed.

Table 4. Electrocardiographic changes in patients with acute ischemia.

ST segment elevation
New ST-segment elevation at the J point in two contiguous leads with cutoff point >0.1 mV in all leads except V2-V3, where the cutoff points are >0.2 mV in men ≥40 years, or >0.25 mV in men <40 years or >0.15 mV in women.
ST-segment depression and T wave changes
ST horizontal or downward sloping ≥0.05 mV in two contiguous leads and/or T-wave inversion >0.1 mV in two contiguous leads with high R or R/S ratio >1.

Conversely, faced with an ECG without ischemic changes, conduct is more controversial, especially considering that up to one third of ACS may initially present with an ECG without abnormalities. (23, 25) We could add to the latter group unspecific ECG changes (ST/T <0.1 mV changes, ST sloping, ST segment <0.5 mm depression, peaked T waves but <25% of QRS voltage), diffuse abnormalities (supra-ST or infra-ST, suggestive of pericarditis), or QRS axis deviation to the right with SI, QIII, TIII pattern, acute right bundle branch block and/or negative T waves in V1 to V3 suggesting pulmonary thromboembolism. Table 5 shows differential diagnosis with other pathologies that can alter ECG repolarization.

Table 5. Confounding electrocardiographic findings in the diagnosis of acute myocardial infarction

False positives
• Early repolarization
• Pericarditis
• Pre-excitation (Wolf-Parkinson-White)
• J-point elevation syndrome; e.g: Brugada syndrome
• Takotsubo
• Pulmonary embolism
• Subarachnoid hemorrhage
• Metabolic disorders, e.g. hyperkalemia
• Hypertrophic cardiomyopathy
• Persistent juvenile pattern
• Tricyclic antidepressants or phenothiazines
False negatives
• Prior infarction with Q waves and persistent ST-segment elevation
• Right ventricular stimulation (pacemaker)
• Acute left bundle branch block

Atypical ECG presentations in ACS are summarized in Table 6. The diagnosis of infarction is more difficult in the presence of LBBB and with history of CHD. In those cases, the possibility of analyzing a previous ECG would allow the comparison with the new changes. (Table 7)

Electrocardiogram sensitivity is variable depending on factors such as history of infarction or prior revascularization, time from onset of symptoms, territory of the affected artery (the circumflex artery may be poorly represented) and dynamic ST-segment changes (the ECG normalizes quickly after the end of the ischemic episode). (23, 25) This leads to multiple ECG studies and the incorporation of additional information from the clinical assessment in order to adopt the adequate conduct.

Table 6. Atypical electrocardiographic presentations in patients with suspected acute myocardial infarction.

• Left bundle branch block
• Patients without ECG changes but with persistence of ischemic symptoms
• Posterior wall myocardial infarction (circumflex artery occlusion)
• ST-segment elevation in aVR lead

Table 7. Electrocardiographic changes associated with prior myocardial infarction

Any Q-wave in leads V2 and V3 >20 ms or QS complex.
Q-wave >30 ms and >0.1 mV or QS complex in leads LI, LII, aVL, aVF or V4-V6; or grouped into two contiguous leads (LI, aVL, V1 to V6, or LII, LIII, aVF);
R wave >40 ms in V1-V2 and R/S ratio >1 with concordant positive T.

Electrocardiographic findings: diagnostic value

Normal ECG or nonspecific ST changes: In the context of precordial pain, taking multiple populations, ECG sensitivity ranges from 1% to 13% and specificity between 48% and 77%, and the likelihood ratio (LR) is 0.2. This means that a normal ECG decreases but does not rule out the probability of acute myocardial infarction.

ECG with ST-segment elevation: It progresses to AMI in about 80%-90% of cases; however, initially it is only present in about a third of patients with chest pain who develop AMI. (16, 23, 26) It has sensitivity of 31% to 56%, specificity of 97% to 100% and LR of 22.3.

E***CG with ST segment depression:*** It generally indicates myocardial ischemia, but its power to identify an ongoing AMI is limited: only 30%-50% develop AMI. The sensitivity ranges from 20% to 62%, specificity between 79% and 96% and the LR is 3.9.

T wave inversion: It provides poor specific information because it may present in many diseases, some acute and severe (pulmonary embolism, myocarditis, myocardial ischemia), and others with better prognosis (pericarditis, "labile" T, left ventricular overload, or metabolic disorders). The sensitivity ranges from 9% to 39%, specificity from 84% to 94% and LR is 2.9. (16)

New Q waves: The presence of new pathological Q waves, even if no repolarization disorders are verified, should be considered as high AMI suspicion (see Table 7).

Conduction disorders (acute LBBB): It is a poor prognosis marker associated with extensive AMI with proximal left anterior descending artery territory involvement, with a prevalence of 8% to 10% in different series. (16, 26) In the analysis of patients with LBBB, concordant ST-segment elevation in positive QRS leads appears as one of the best AMI indicators (16, 23, 26)

Recommendations on electrocardiogram in chest pain assessment

Recommendation	Class	Level of evidence
ECG should be performed and promptly analyzed in any patient consulting for chest pain (<10 minutes after admission).	I	C
In symptomatic patients and initial non-diagnostic ECG, it should be repeated every 15 to 30 minutes for the first hour until detection of ischemic changes.	I	C
In patients with non-diagnostic ECG it is reasonable to make right and posterior leads to detect ischemic changes	IIa	B
In asymptomatic patients with high risk of ACS, electrocardiographic monitoring is reasonable during the observation period.	IIa	B

ECG: Electrocardiogram. ACS: Acute coronary syndrome

BIOMARKERS

Although both clinical assessment and ECG are essential tools for diagnosis, risk stratification and management of patients with suspected ACS, they lack sufficient accuracy to perform this task in isolation. Biomarkers that reflect and quantify the degree of myocardial injury are therefore a mandatory supplement in all patients presenting with a condition compatible with ACS.

Troponins (Tn) T and I, structural proteins which are expressed exclusively in the heart, are the biomarkers of choice. When myocardial necrosis occurs, there is a gradual release of Tn contained in the myofibrils, which may be quantified in a prompt and reproducible manner. Advances in technology have led to a refinement of the assays measuring Tn, improving detection capacity and dosage of the degree of myocardial injury, and in the case of high sensitivity tests, they allow the detection of troponin (Tn) in up to 90% of healthy subjects. (27)

The 2012 Third Universal Definition of Myocardial Infarction, (26) states that AMI diagnosis requires the increase or decrease of Tn values, with at least one value above the 99th percentile of the normal reference population, combined with a clinical condition compatible with myocardial ischemia. This 99th percentile value must be determined for each specific test with adequate quality control in each laboratory. Optimal precision to use these tests, or coefficient of variation (CV) corresponding to the 99th percentile of the upper reference limit for each test should be ≤10%.

The increase and decrease pattern of Tn concentrations is critical to differentiate acute from chronic elevations associated with structural cardiomyopathy. (28) Table 8 shows Tn elevation causes.

Table 8. Elevation of cardiac troponin levels due to myocardial injury

Lesions related with primary myocardial ischemia
- Plaque rupture
- Intraluminal thrombus formation in the coronary artery
Myocardial ischemia lesions related to the imbalance between supply and demand
- Tachyarrhythmias or bradyarrhythmias
- Aortic dissection or severe aortic valve disease
- Hypertrophic cardiomyopathy
- Cardiogenic, hypovolemic or septic shock
- Severe respiratory failure
- Severe anemia
- Hypertension with or without left ventricular hypertrophy
- Coronary spasm
- Coronary vasculitis or embolism
- Coronary endothelial dysfunction without significant coronary artery disease
- Strenuous physical exertion
Lesions not related with myocardial ischemia
- Cardiac contusion, surgery, ablation, pacemaker or defibrillator shocks
- Rhabdomyolysis with cardiac impairment
- Myocarditis
- Cardiotoxic agents such as anthracycline or herceptin
Multifactorial or undetermined myocardial lesion
- Heart failure
- Stress cardiomyopathy (Takotsubo)
- Severe pulmonary embolism or pulmonary hypertension
- Sepsis and critically ill patients
- Renal failure
- Severe and acute neurological conditions such as stroke or subarachnoid hemorrhage
- Infiltrative diseases such as amyloidosis or sarcoidosis

High sensitivity troponins

High-sensitivity troponins (hs-Tn) are currently considered the biological marker par excellence and should be available in chest pain units. (CPU)

It is important to emphasize that Tn levels of traditional assays are performed in μg/L, while those of high sensitivity are performed in ng/L. Thus, while a dosage of 5 μg/L corresponds almost invariably to a large infarction, one of 5 ng/L (or 0.005 μg/L) is compatible with normality. This change seeks to avoid associated errors with the addition of decimals, but may initially become confusing for professionals accustomed to using fourth-generation Tn.

The main characteristic that differentiates hs-Tn from fourth-generation Tn is precisely its higher sensitivity, which is apparent in values close to the 99th percentile (upper reference limit). Assays using fourth generation Tn have a detection limit of around 10-50 ng/L, a 99th percentile value of 50 to 100 ng/L and a coefficient of variation (CV) of 10% above the 99th percentile. Conversely, hs-Tn may have detection limits below 1 ng/L, are able to detect and quantify the Tn level in most of the healthy population and thus they allow a more accurate calculation of the 99th percentile. Compared with previous methods, hs-Tn assays have a CV of 10% below the 99th percentile value (29, 30) and adjust to the recommendations established in the universal definition of AMI. Table 9 shows the comparison between different commercially available hs-Tn assays.

Table 9. Analytical comparison between different available high sensitivity troponin assays

hs-Tn	Detection limit (ng/L)	99th percentile (ng/L)	99th percentile (ng/L)
hs-cTn T			
Roche Elecsys	5.0	14	14
hs-cTn I			
Abbot ARCHITECT	1.2	16	16
Beckman ACCES	2 a 3	8.6	8.6
Mitsubishi Pathfast	8.0	29	29
Nanosphere	0.2	2.8	2.8
Radiometer AQT90	9.5	23	23
Singulex Erenna	0.09	10.1	10.1
Siemens Vista	0.5	9	9
Siemens Centaur	6.0	40	40

CV: Coefficient of variation. hs-cTn T: High-sensitivity cardiac troponin T. hs-cTn I: High-sensitivity cardiac troponin I.

The enhanced sensitivity of the new Tn increases the area under the ROC curve and, hence, a proportion of patients who were not identified as having an ACS with conventional Tn are now classified as such (31) (Figure 3).

Another important advantage lies in the kinetics of hs-Tn. The hs-Tn release curve is faster than that of prior methods. With these assays, the proportion of patients with necrosis that can be recognized in the early hours is significantly higher than that achieved with previous generation Tn assays. (31) (Figure 3). This is a great advantage as it reduces the window period for decision-making in the emergency room.

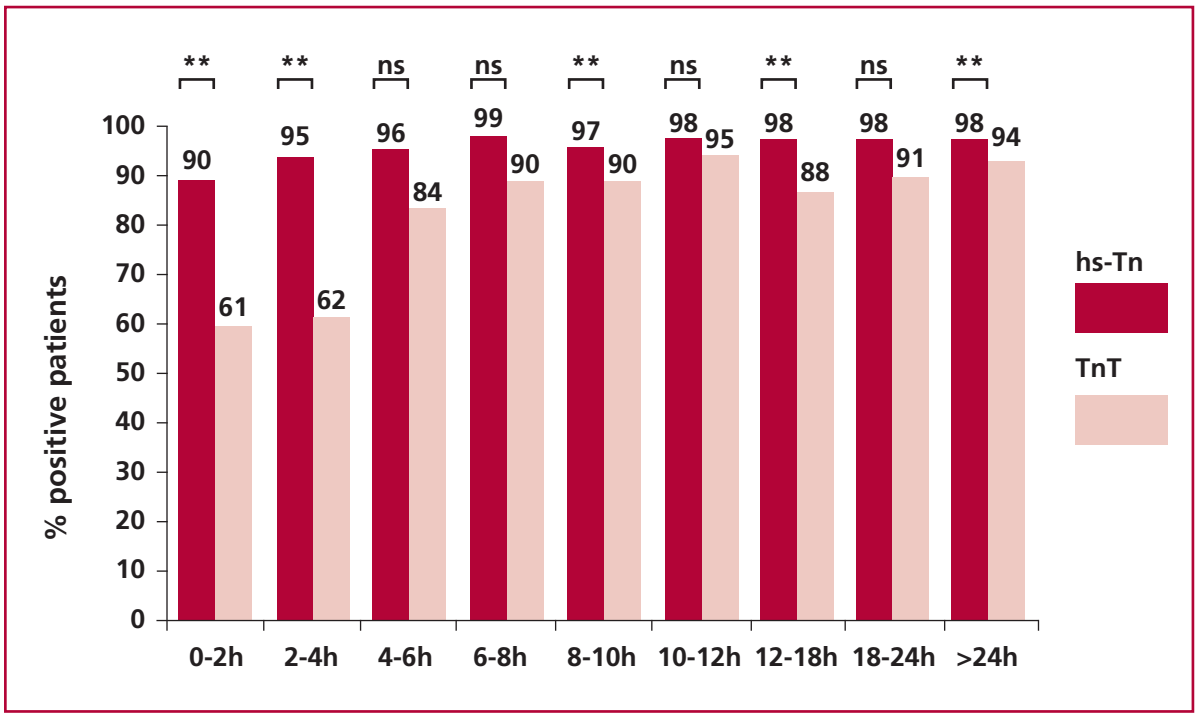

Fig. 3. Relationship between Tn assay and time window. Modified from Weber et al. (31). ns: Not significant. * p <0.05. ** p <0.01. hs-Tn: High sensitivity troponin. TnT: Troponin T

Algorithms for the use of high sensitivity troponin in the emergency unit

Using hs-Tn, 0.9% of patients without risk factors in the general population, 3.4% with risk factors, 9% aged >65 years and 50% presenting with HF have chronically abnormal Tn levels. (32) When these patients consult for chest pain, a complex situation is generated for physicians in emergency areas, who must discern whether these Tn elevations are chronic or acute. This is not a minor problem, since these chronically elevated levels can induce ischemia misdiagnosis in patients presenting with chest pain due to other causes.

Serial dosage is used to increase Tn specificity for the diagnosis of acute injury. (33-37) A change, whether increase or decrease in Tn serum levels in samples separated for a few hours is interpreted as an indicator of acute injury, while stable values suggest that these elevations are chronic.

Recently, a "two step" strategy has been developed. (38) In the first step, the ischemic etiology is discarded (rule out) using the most negative predictive value, considering that baseline values below the 99th percentile, without variations in the second dosage, minimizes immediate and remote ischemic risk.

The second step (rule in) is dedicated to confirm ischemic etiology. In this case, the scenario is the coronary care unit, and for the reasons mentioned above a more specific approach is preferred. If percent variations are used, the larger the percentage of variation, the greater the specificity, but the possibility of not detecting an infarction also increases.

Rule in and rule out algorithms vary in the time interval for the collection of a second Tn sample and in the cutoff points used to consider the change as significant.

0 hours/3 hour algorithm

This algorithm is not solely based on hs-Tn dosage, but also on the clinical probability (GRACE score <140). (39) Additionally, the initial time of chest pain comes into consideration. Thus, patients with pain onset of more than 6 hours prior to presentation at the emergency center and with dosage below the upper reference limit may be safely discharged without a second sample.

Therefore, the second sample obtained three hours after the first, is restricted to those patients with pain that has started less than 6 hours earlier or to all initial dosages above the 99th percentile value (Figure 4).

An abnormal variation suggestive of a recent event is considered if there is a relative variation between baseline and the next value of over 20% or, in the case of hs-cTn T, an absolute dosage variation over 9 ng/L separated by 2-3 hours. (40, 41)

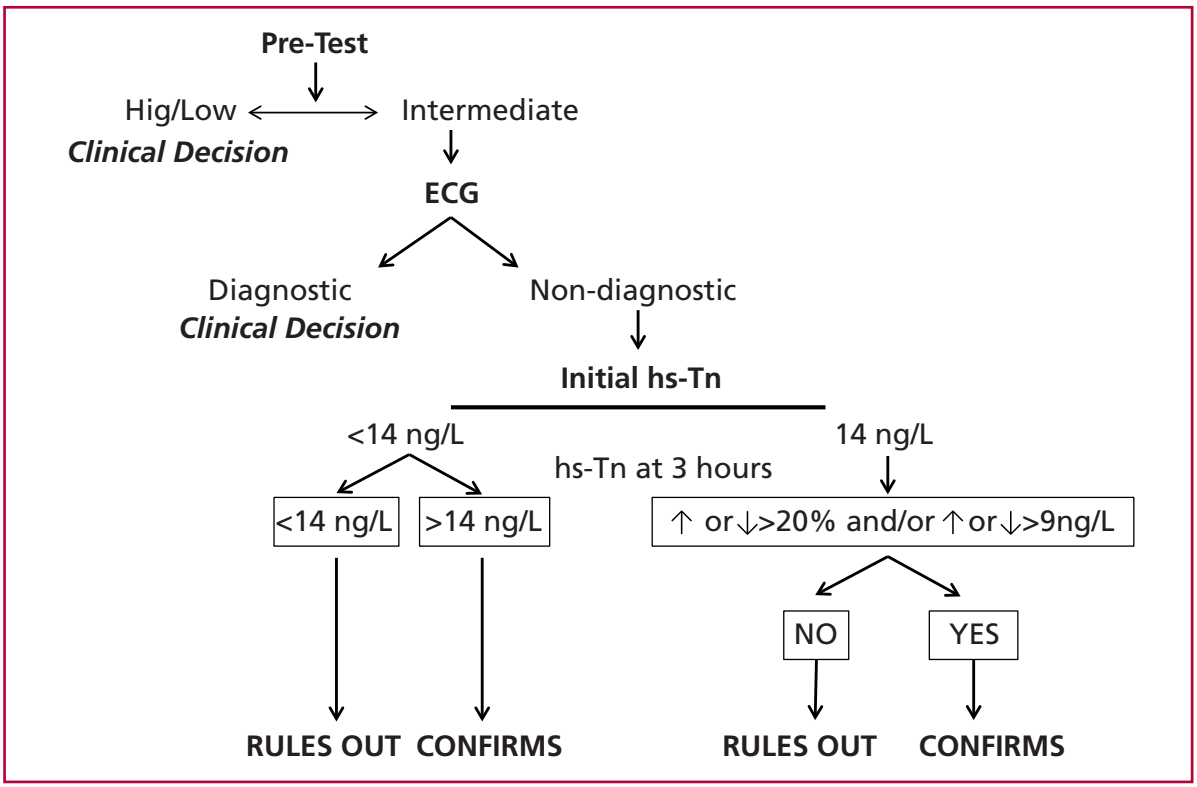

Fig. 4. Diagnosis algorithm of chest pain using high sensitivity troponin T (hs Tn T).(42)

If hs-Tn I is available, the 99th percentile cut off value corresponding to each assay should be used. The variation of absolute values >9 ng/L was only validated with hs-Tn T.

0 hour/1 hour algorithm

As an alternative to the previous algorithm, Tn measurements at 0 hour/1 hour can be performed safely, provided a validated hs-Tn assay is used. (43-45) This algorithm is based on two concepts: first, hs-Tn is a continuous variable and the probability of infarction increases with increasing Tn values, and second, absolute changes in Tn values can be used as surrogate of absolute changes at 3 or 6 hours, providing additional diagnostic value to the initial Tn value.

Non-ST-segment elevation myocardial infarction can be ruled out with a high negative predictive value by adding a low Tn level at the time of presentation, to little variation in the second sample obtained at one hour. On the contrary, the presence of very high initial values of hs-Tn T (>52 ng/L), or a significant rise in the second sample, confirms with a positive predictive value of 75% to 84% the presence of non-ST segment elevation AMI. The cutoff points for hs-Tn levels at 0 hour/1 hour algorithm are specific for each assay (Figure 5). Table 10 summarizes the characteristics of both algorithms.

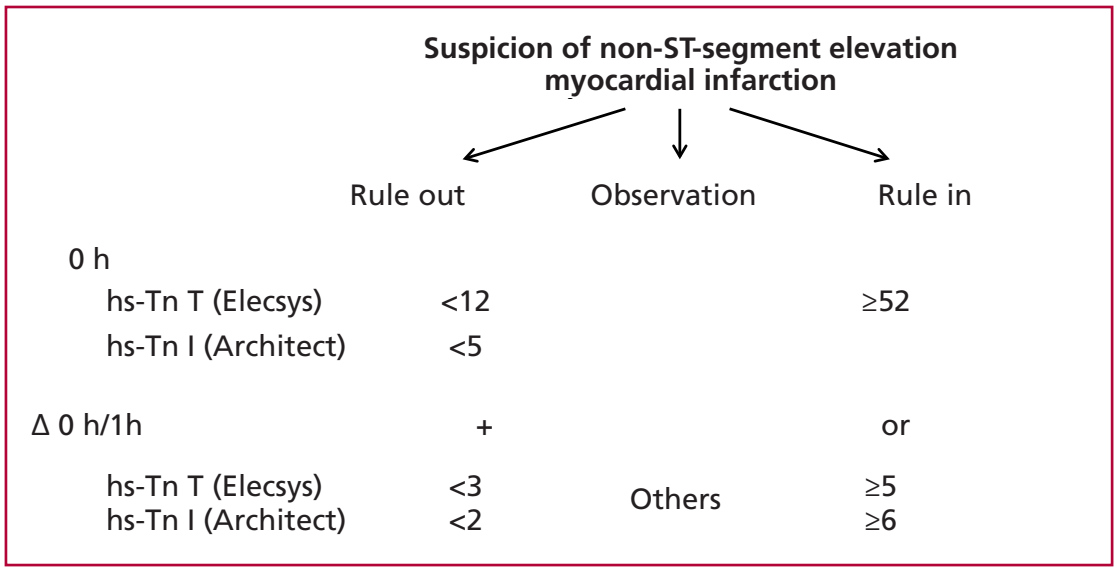

Fig. 5. 0 hour/1 hour algorithm with high sensitivity troponin T and I (hs-cTn T; hs-cTn I).

Table 10. Characteristics of the 0 hour/3 hour and 0 hour/1 hour algorithms*

	0 hour/3 hour	0 hour/1 hour
Negative predictive value for non-ST-segment elevation myocardial infarction	98-100%	98-100%
Positive predictive value for non-ST-segment elevation myocardial infarction	Unknown, depends on the assay and Δ magnitude	75-84%
Effectiveness**	++	+++
Applicability	++, requires GRACE score	+++
Challenges	The onset of pain cannot always be specified	Cutoff points are specific for each assay and different from the 99th percentile
Validation in large multicenter studies	+	+++
Additional benefits	Already used in clinical care	Less time to decision

GRACE: Global Registry of Acute Coronary Events.
* Adapted from Roffi et al. (46)
** Effectiveness is measured as the percentage of consecutive patients with chest pain clearly classified as rule in and rule out acute myocardial infarction (approximately 60% for the 0 hour/3hour algorithm and 75% for 0 hour/1 hour)

Other algorithms

A 2 hour rule out protocol combining Thrombolysis in Myocardial Infarction (TIMI) risk score with ECG and hs-Tn dosage at the time of presentation allowed a safe early discharge in up to 40% of patients. (47-49)

Finally, safety of a single Tn measurement below the detection limit of the method at the time of consultation in conjunction with the ECG, has been recently evaluated for both hs-cTn T and cTn I. (43, 50-53) The results are promising, with a negative predictive value over 99%.

Algorithm with troponins different from high sensitivity ones

As previously detailed, conventional troponin assays are less sensitive and have slower release kinetics; therefore, a larger time window is necessary to safely rule out ACS. Two dosages separated by 6-9 hours are required. When pain-consultation time is more than 24 hours a single dosage below the 99th percentile value would be sufficient.

High-sensitivity troponins in patients with generalized involvement and complex diagnosis

As previously described, clinical trials using hs-Tn have greatly improved AMI diagnosis sensitivity, though at the expense of reduced specificity.

The aforementioned algorithms are useful only when applied in patients with clinical suspicion of ACS, as there is no algorithm that will per se allow clear identification of AMI from other causes capable of elevating Tn levels (Table 8). Therefore, the pre-test probability of CHD as well as those conditions increasing Tn levels should be considered when interpreting the results of these markers. The combination of clinical judgment, other laboratory tests and imaging diagnostic methods are on occasions necessary to reach the correct diagnosis.

Critical patients constitute an especially complex group, as 32% to 53% present elevated Tn (54) levels and frequently refer precordial pain and/or dyspnea. Use and interpretation of hs-Tn in these patients must be prudent as it may overestimate the presence of ischemia and erroneously lead the clinical decision.

The magnitude of hs-Tn elevation is a criterion to distinguish between ischemic and non-ischemic Tn elevations. In general, non-ischemic elevations are of low magnitude (<100 ng/L). Values above this level correspond more frequently to AMI, and large transmural infarctions present with Tn >500 ng/L to several thousands (Figure 6).

However, the diagnosis of ACS in these patients is still a challenge, and use of invasive diagnostic methods as coronary angiography should be reserved for selected cases.

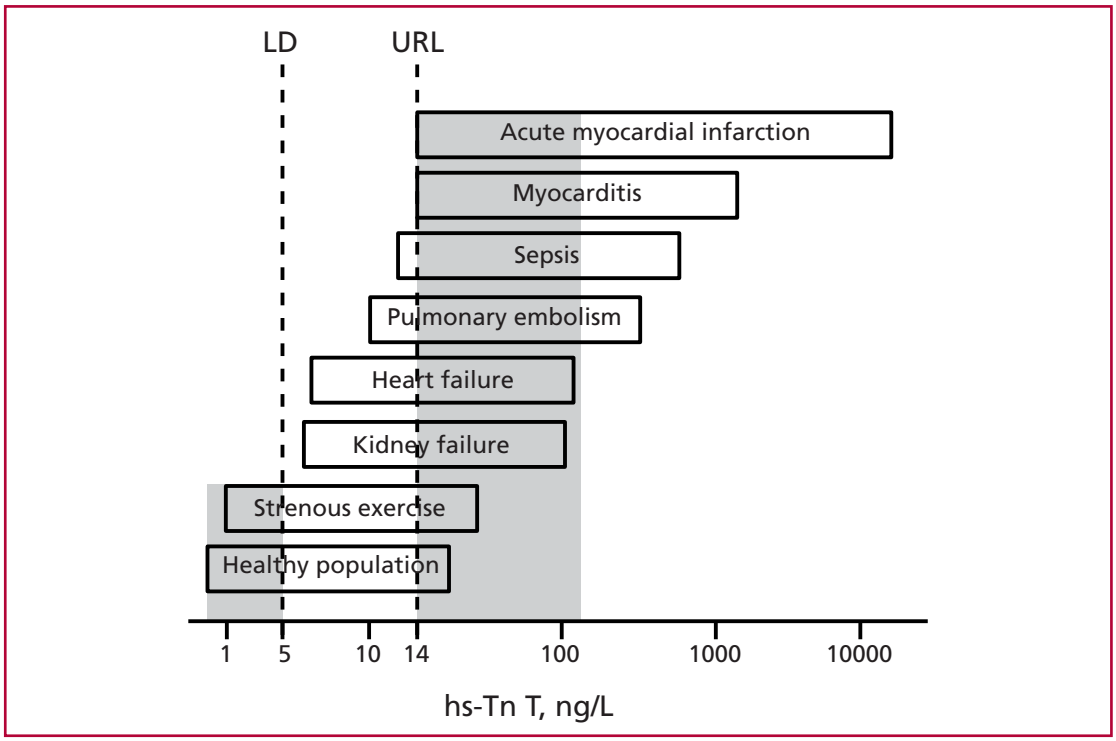

Fig. 6. Typical high-sensitivity troponin T (hs-Tn T) concentrations in cardiac and non-cardiac diseases. [Adapted from Jarolim et al. (55)]
LD: Limit of detection. URL: Upper reference limit

CPK and CK-MB

The sensitivity of these markers is lower than that of Tn, especially compared with hs-Tn, for the detection of myocardial injury, and a substantially higher amount of involved tissue is necessary to identify them. Due to their greater precision, Tn are the biomarkers of choice to rule out an ACS, and use of creatine phosphokinase (CPK) and creatine kinase-MB (CK-MB) is not recommended to evaluate patients with chest pain.

Other markers

There is not enough evidence to recommend the use of other serological markers studied for the management of chest pain, as copeptin, fatty acid transport protein or myeloperoxidase, among others.

Recommendations on the use of serological markers in patients presenting with chest pain

Recommendation	Class	Level of evidence
Centers evaluating chest pain should have dosage of necrosis markers.	I	A
hs-Tn are the markers of choice. Their use is recommended within the first hours after qualifying pain onset.	I	C
hs-Tn dosage should be repeated 3 hours after the first measurement to rule out AMI.	IIa	C
When hs-Tn is not available, standard Tn is preferable. Its use is recommended in patients consulting 8 hours after qualifying pain onset and within 15 days of its presentation.	IIa	B
CPK and CK-MB are not recommended as biomarkers to assess patients with chest pain.	III	B

hs-Tn: High-sensitivity troponin. AMI: Acute myocardial infarction. CPK: Creatine phosphokinase. CK-MB: Creatine kinase-MB.

RISK STRATIFICATION IN PATIENTS WITH SUSPICION OF ACUTE CORONARY SYNDROME

Stratification of patients consulting for chest pain in which ACS cannot be clearly ruled out, poses a challenge in daily practice. The prediction of adverse events (death, AMI, infarction recurrence, HF, potentially lethal severe arrhythmias, and symptom recurrence) in patients presenting with chest pain aims to identify low risk groups who can be directly discharged from the emergency department, avoiding unnecessary hospitalizations. (56, 57)

Directed anamnesis is a cornerstone in the evaluation of patients with chest pain, together with serial ECG and biomarker assessment.

History taking should provide information including: sex, age, cardiovascular risk factors, documented coronary heart disease, history of revascularization procedures (percutaneous and surgical), vascular disease in other arterial territories and characteristics of chest pain at presentation (site, irradiation, duration, associated symptoms, etc), as they are indicators of events and allow identifying a population at higher risk at 30 days. The addition of variables increases the risk of adverse events (58, 59)

It is important to consider the characteristics of chest pain in case the possibility of ACS is discarded, as differential diagnoses can be also associated to high risk (e.g. aortic dissection, pulmonary thromboembolism, etc).

A 12-lead ECG provides prognostic information as a function of the magnitude and intensity of the changes found. It should be obtained within the first 10 minutes of contact with the patient, and its interpretation should be in charge of adequately trained staff. Presence of ST-segment dynamic alterations is an indicator of bad prognosis, as shown in all the risk scores based on population studies or clinical trials [GRACE, (60) FRISC, (61) PURSUIT, (62) TIMI (63)] or as evidenced by CPU in the HEART score. (30, 64)

Currently, hs-Tn is considered the biological marker of choice as values below the 99th percentile identify a population at very low risk with highly negative predictive value.

Use of risk scores to stratify patients in chest pain units

Use of risk scores aim to identify patients especially at the score limits: high risk patients requiring hospitalization and immediate interventions and low risk patients, not requiring hospitalization, who can be discharged with very low probability of adverse events.

In patients admitted to CPU with probability of presenting an ACS, use of scores obtained from clinical trials as PURSUIT, (62) TIMI, (63) and FRISC (61), as well as the GRACE score (60) from a population study, are very useful, but the HEART score (65), designed for unselected populations, presents better probability of identifying groups at the risk limits (Table 11). It considers patients with 0 to 3 score as low risk (MACE <5% with probability >98%), 4 to 6 scores as intermediate risk and >7 as high risk.

The comparison of different risk scores shows increased area under the curve for the HEART score (Table 12).

Use of algorithms based on clinical history, ECG, biomarkers and pre-test probability enable protocols for a fast diagnosis (in 2 to 3 hours), identifying patients at very low risk with 99.7% sensitivity and 99,7% negative

Table 11. HEART score (65)

Clinical history	
Highly suspicious	2
Moderately suspicious	1
Slightly suspicious	0
Electrocardiogram	
Significant ST-segment depression	2
Inspecific repolarization abnormalities	1
Normal	0
Age	
>65 years	2
45 to 65 years	1
<45 years	0
Risk factors	
>3 risk factors or atherosclerotic disease	2
1 or 2 risk factors	1
No risk factors	0
Troponin	
>2 times the normal limit	2
1 or 2 times the normal limit	1
<normal limit	0

Table 12. Comparative analysis of the different risk scores

Population Consequence	PURSUIT UA/NSTEACS 9,461 Death Death/MI	TIMI UA/NSTEACS 1,957	GRACE All ACS 11,389	FRISC UA/NSTEACS 1,235 Death Death/MI	HEART All chest pains 1,002
Key elements	5	7	8	7	5
Age	X	X	X	X	X
Sex	X			X	
History of:	X	X		X	X
CHD orMI		X		X	X
CVRF, DM Symptoms/history		X			X
Use of aspirin		X			
Weight			X		
HR			X		
SBP			X		
CHF / Killip class	X		X		
ECG	X	X	X	X	X
CK-MB/Tn		X	X	X	X
Serum creatinine			X		
Serum Interleukin 6 / PCR				X	
Cardiac arrest			X		
Máximum score	18	7	372	7	10
Area under the curve	0.84 0.67	0.65	0.83	0.77 0.7	0.9

Recommendations on risk stratification in patients presenting with chest pain

Recommendation	Class	Level of evidence
Any patient presenting with symptoms and/or signs suggestive of ACS should be stratified on the possibility of coronary events (death, AMI, etc) through anamnesis, physical exam, ECG and biomarkers.	I	A
Use of scores to predict risk of events is recommended in patients with suspected ACS (HEART).	I	C

ACS: Acute coronary syndrome. AMI: Acute myocardial infarction. ECG: Electrocardiogram.

Recommendations on the use of CPU

Recommendation	Class	Level of evidence
The use of a Chest pain Unit is recommended	I	A

ACS: Acute coronary syndrome. AMI: Acute myocardial infarction. ECG: Electrocardiogram.

predictive value, with 23.4% specificity and 19% positive predictive value, as validated in the ASPECT study (47) or the ADAPT trial. (48)

CHEST PAIN UNIT

Chest pain units emerged in the last decades with the aim of standardizing the care of patients with suspected ACS, reduce the stay in the emergency department and avoid the discharge of patients with ACS. Most of the evidence originates from observational cohorts. (66-68) CPU is a functional area, not a physical space, whose purpose is the observation of these patients.

Traditionally, the CPU protocol consists in 8 hours of observation under continuous monitoring, serial ECG performance (at admission, at 4 and 8 hours) and serum markers of myocardial injury (CPK, CK-MB and Tn) according to the hours elapsed since pain onset. The emergence of new hs-Tn assays will probably modify the CPU structure, since they have demonstrated the ability to rule out the presence of ACS with better sensitivity and less time. If an abnormality is found during this period, the patient is definitively hospitalized. If all results are negative, a functional test is indicated according to medical criteria and patient characteristics.

USEFULNESS OF REST CARDIAC IMAGING STUDIES AND ROLE OF FUNCTIONAL TESTING

Non-invasive rest cardiac imaging studies and functional tests have been incorporated to protocols evaluating chest pain for the early identification of undetected ACS at the initial clinical evaluation.

According to the initial presentation of the patient with chest pain, one of the following strategies is usually considered at the emergency department:

1. Patients with significant tests of ACS will be admitted for their immediate corresponding treatment;
2. Patients without real evidence of ischemia at presentation (normal ECG or with unspecific changes and baseline negative and/or indefinite myocardial injury markers) will be admitted in an observation unit for evaluation through serial ECG, serial assessment of myocardial injury markers and, in selected patients with persistent suspicion of ACS, a non-invasive cardiac imaging study to rule out the presence of myocardial ischemia. (13, 69-71)

Taking into account the sequence of events occurring in myocardial ischemia, the usefulness of each diagnostic test will be based on the evaluation of the different moments of the ischemic cascade.

The first abnormality is the decrease of regional flow in the involved artery and hence the relative flow heterogeneity can be evaluated with a highly sensitive myocardial perfusion study at rest. (72, 73) The following stage will be altered diastolic function; its usefulness is not currently well established due to its lack of specificity. Then, wall motion abnormalities occur, which are highly specific and can be evaluated by means of echocardiography. Finally, electrocardiographic changes and clinical manifestations will appear.

Rest imaging studies

They include the study of myocardial perfusion with radionuclides, echocardiography, non-invasive coronary angiotomography and cardiac magnetic resonance (CMR) imaging.

This study modality is less useful for the diagnosis of ACS in patients with previous AMI, and is more suitable when a previous study is available to compare results.

Rest myocardial perfusion imaging (RMPI): It provides useful diagnostic and prognostic information for the triage of patients with chest pain. The ACC/AHA/ASNC guidelines recommend the performance of RMPI in patients with possible ACS without changes in ECG or LBBB, initial negative Tn and recent or ongoing chest pain (less than 2 hours since symptom onset). (73, 74)

Taking into consideration the ischemic cascade, RMPI presents high sensitivity for the diagnosis of CHD. Currently, Tc-99m sestamibi is used and the injection of the radioisotope is recommended during the presence of symptoms or within 2 hours of their resolution, as perfusion alterations may persist longer after symptom disappearance secondary to myocardial ischemia. (75-78) It is also possible to evaluate left ventricular wall motion and ejection fraction. (79)

Rest myocardial perfusion imaging has a highly negative predictive value. Several studies have demonstrated a low rate of cardiac events (cardiovascular death or nonfatal AMI) at 30 days (<1%) in patients with chest pain and normal RMPI, allowing safe discharge with shorter hospital stay and lower hospital costs. (75, 79)

Rest echocardiography: The purpose of this study is the evaluation of wall motion abnormalities, which present high specificity for the diagnosis of AMI (93%) and ACS (88%), and moderate sensitivity for AMI (78%) and ACS (53%). (80, 81) Current guidelines of the European Society of Cardiology emphasize early echocardiography indication in patients with acute chest pain, as it is a quickly accessible and widely available technique which in expert operators is able to detect transient segment motion abnormalities present during ischemia.

It also provides information on left ventricular systolic function, a highly important prognostic variable in patients with CHD, and is able to detect AMI complications as well as evaluating other possible causes of acute chest pain, as proximal aortic dissection, stress cardiomyopathy and pulmonary thromboembolism. (39)

Ischemia evocative tests

Studies at rest may provide normal results, even when CHD and intermittent ischemia may be present; for this reason, ischemia evocative tests (functional tests) are useful to differentiate cardiac chest pain from other etiologies. (82, 83) Functional tests require a careful analysis to ensure that the patient is free from symptoms at rest and does not present evidence of rest myocardial necrosis or ischemia through serial ECG and assessment of biochemical markers.

The main purpose of functional tests as part of a CPU evaluation is to minimize the probability of ACS to a level low enough for hospital discharge to be a safe strategy.

Test selection

Functional tests in patients with suspected ACS is recommended after at least 6 to 8 hours of observation without ischemic recurrence, with normal 12-lead ECG or without acute ischemic changes compared with previous ECG and at least two negative myocardial injury biomarker assessments. (83) (Figure 7)

The choice of stress testing modality (exercise of pharmacologic) will depend on the patient's physical capacity. If the patient is able to perform exercise, this will be the stress chosen, as it will also provide information

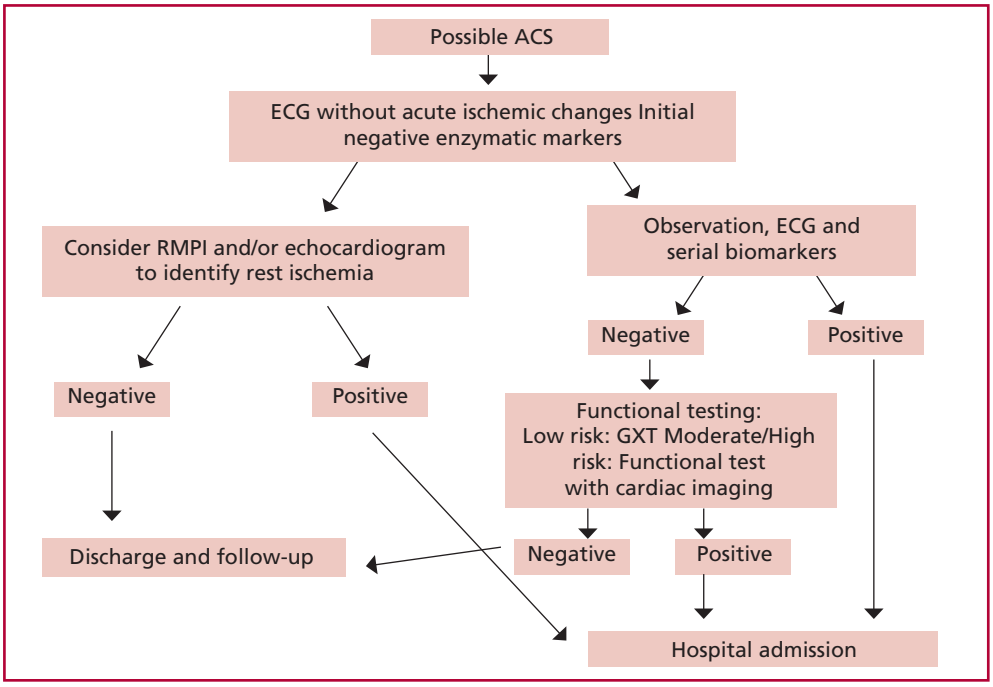

Fig. 7. Suggested algorithm for the indication of functional tests. ACS: Acute coronary syndrome. ECG: Electrocardiogram. RMPI: Rest myocardial perfusion imaging. GXT: Graded exercise testing.

on functional capacity. In cases where the choice is a pharmacologic stress test, the options include vasodilators (adenosine, dipiridamol and regadenoson) or dobutamine-atropine stress.

The choice of the type of evocative test will depend on the availability and experience of each center on these techniques and on patient characteristics (presence of chronic obstructive pulmonary disease, baseline conduction abnormalities such as LBBB, quality of the ultrasound window, and patient age considering radiation exposure). (84, 85)

The decision regarding on whether the functional test should include a cardiac imaging study should be based on two conditions. One condition is the presence of baseline ECG abnormalities, as in case this is not interpretable to assess changes suggestive of myocardial ischemia, an ischemia evocative test should be performed associated with a cardiac imaging study. The other condition is the pre-test probability of CHD in the patient, as myocardial perfusion imaging (MPI) studies and stress echocardiography present significantly greater sensitivity for the detection of CHD than conventional graded exercise testing (GXT). (86-87)

In patients with very low pre-test probability of CHD a functional test is little useful. (88)

Regarding the moment to perform functional tests, it is better to conduct them during the observation period in the CPU, prior to discharge, However, its early ambulatory performance (within 72 hours) is an option in patients with low or intermediate pre-test probability of low risk ACS, who will respond to alarm patterns, and with close follow-up. (89)

12-lead graded exercise testing

Graded exercise testing without cardiac imaging is preferred in patients who can perform exercise and baseline ECG does not present changes that can impair its interpretation (pre-excitation syndrome, ventricular pacemaker, LBBB, patients under digoxin treatment or with electrocardiographic criteria of left ventricular hypertrophy). (83)

Limited GXT due to symptoms after 6 to 8 hours of evaluation in the observation unit has been shown to be safe and useful in patients with low to intermediate risk for CHD. In these cases, submaximal heart rates should be reached and also consider that the sensitivity of this method is limited (60% sensitivity). (90) An abnormal exercise test would justify hospital admission.

Ischemia evocative test associated with cardiac imaging: myocardial perfusion scan and stress echocardiography

In patients with intermediate-high risk for CHD, without ischemic recurrence after 6 to 8 hours, negative biomarkers and no electrocardiographic changes, it is useful to perform a functional test associated with cardiac imaging studies, as the sensitivity of this method is significantly greater than GXT.

The main advantage of MPI is that it affords higher sensitivity to detect CHD than GXT, (95% sensitivity and 83% specificity); (91, 92) moreover, the imaging quality is not affected by the physical condition of the patient.

Stress echocardiography presents 85% sensitivity and 87% specificity for obstructive CHD and, similarly to MPI, it is a useful tool to identify low risk patients who can be safely discharged after evaluation in a CPU from those presenting some degree of coronary stenosis with flow limitation, where it is necessary to continue their evaluation and treatment. (93-95)

Recommendation	Class	Level of evidence
Recommendations on the use of rest imaging studies in patients presenting with chest pain		
A rest myocardial perfusion imaging study is recommended in patients presenting with chest pain or within 2 hours of presentation and suspected acute coronary syndrome, with negative first enzymatic assessment and ECG without acute ischemic changes, in centers with available technique.	I	A
Rest echocardiography is recommended in centers with available technique, performed by an expert operator.	I	C
Recommendations on the use of ischemia evocative tests in patients presenting with chest pain		
A functional test with cardiac imaging is recommended in patients with suspected acute coronary syndrome, with ECG without acute ischemic changes and negative or indefinite biomarkers, without pain recurrence, prior to discharge from the chest pain unit or within 72 hours of hospital presentation.	I	B
In the patient referred for ambulatory and differed functional test, indication of daily aspirin is recommended until its performance.	IIa	C
A 12-lead GXT is recommended in patients stratified as low risk, without pain recurrence after at least 6 to 8 hours of observation, with normal and interpretable serial ECG and two negative biomarker assessments, to evaluate the presence of inducible ischemia, with the condition of reaching submaximal heart rates.	IIb	B

ACS: Acute coronary syndrome. AMI: Acute myocardial infarction. ECG: Electrocardiogram.

In addition to published evidence, local availability and center experience in each technique influence the selection of the adequate imaging method for clinical decision-making, as well as the evaluation of exposure to radiation and quality of the acoustic window. (79, 96, 97)

Patients with functional testing revealing the presence of inducible ischemia or indefinite result will require hospitalization and evaluation with possible invasive angiography, whereas a low risk patient with negative functional test can be discharged with appropriate indications concerning the activity he can perform, eventual treatment and subsequent follow-up.

USEFULNESS OF MULTISLICE COMPUTED TOMOGRAPHY AND CARDIAC MAGNETIC RESONANCE IMAGING

Multislice computed tomography

Multislice computed tomography (MSCT) is a very sensitive technique and with elevated negative predictive value, which allows ruling out CHD in patients with chest pain and suspected ACS. Several multicenter studies and meta-analyses have demonstrated that MSCT has sensitivity and specificity above 90% to evaluate significant coronary stenosis. (1-4) As MSCT can be quickly performed, it is particularly useful for use at the emergency department to promptly rule out CHD in a few minutes.

All studies evaluating the usefulness of MSCT in patients presenting with chest pain are performed with ≥64 slice systems. (91, 92) Selected patients were those with low to intermediate risk of CHD, ECG without ischemic abnormalities and non-conclusive enzymatic markers. When compared with the usual evaluation routine in patients with chest pain without ECG abnormalities or Tn elevation, MSCT did not present differences in clinical events, it reduced the time of in-hospital evaluation (which was associated to cost reductions) and was accompanied by the performance of invasive coronary angiography and revascularization procedures.

On the other hand, MSCT was associated with greater exposure to radiation with long-term consequences. (11) However, new generation systems with 256, 320 or more slices have reduced radiation to very low values, ranging between 3 to <1 mSv. (12)

It is important to emphasize that none of the studies mentioned used hs-Tn, which could have also reduced hospital stay; neither did they evaluate the usefulness of the method in previously revascularized patients in the context of an acute event, so that it is not validated in these populations. Additionally, there are factors limiting the use of MSCT, as severe coronary artery calcification (high calcium score) and elevated or irregular heart rate.

Recommendation	Class	Level of evidence
Recommendations on the use of multislice computed tomography in patients presenting with chest pain		
MSCT may be considered as alternative to a stress test in patients with chest pain without ECG ST-segment abnormalities and negative biomarkers, and low or intermediate probability of CHD.	IIa	A
Recommendations on the use of stress cardiac magnetic resonance in patients presenting with chest pain		
Stress CMR may be considered as alternative to other stress tests in patients with chest pain, negative biomarkers, intermediate probability of CHD and inability to perform exercise or with non-interpretable ECG.	IIa	C

Stress cardiac magnetic resonance imaging

Stress CMR is a technique to evaluate myocardial perfusion with gadolinium injection. Gadolinium is quickly distributed in the myocardium accelerating proton relaxation and increasing the intensity of the myocardial signal, detecting hypoperfused areas through the first-pass CMR technique. Pharmacologic stress is performed with vasodilators such as adenosine or dipyridamole or inotropic drugs as dobutamine to stimulate the contractile reserve. In a meta-analysis, dobutamine CMR sensitivity and specificity were 83% and 86%, respectively, and 91% and 81% for pharmacologic stress with vasodilator drugs. (15)

In a study evaluating 103 patients presenting with chest pain at the emergency room without evidence of ischemia in the ECG or cardiac biomarker elevation, use of stress CMR was safe and allowed the detection of low risk patients at follow-up, becoming an alternative to nuclear medicine and stress echocardiography studies. (23)

Additionally, CMR is a technique that allows full patient evaluation, analyzing ventricular function, regional motility, presence of edema, perfusion defects, and areas of infarction. However, the systematic implementation of CMR in the emergency context is difficult, and hence its application is reserved for selected patients.

SUMMARY AND CONCLUSIONS

Acute chest pain is a highly prevalent clinical situation and one of the most frequent reasons of consultation in any emergency department.

It is a challenging condition because a balance between diagnosis and prognostic stratification must be established in order to reduce to a minimum the number of patients with acute ischemic syndromes who are erroneously discharged to their homes, since it is well known that this situation doubles mortality compared with their hospitalization (false negatives), and the number of hospitalized low risk cases (false positives) with the concomitant excessive use of resources.

The above lines have analyzed a number of clinical, electrocardiographic, biochemical and imaging techniques allowing a refined discrimination of exclusion (rule-out) and inclusion (rule in) cases, reducing to a minimum diagnostic and treatment errors.

The same pattern already established in the previous Consensus on the Management of Patients with non-ST-segment Acute Ischemic Syndrome was followed to recommend methodologies: the proposals assume high technology availability to follow the Consensus recommendations.

The Editorial Committee acknowledges the high heterogeneity of resources distributed throughout the country. It is also conscious that it is sometimes necessary to adapt as best as possible to available resources.

However, this is no obstacle for making the best quality proposal trying to establish it as the standard to which all centers should rightfully aspire and dedicate the best possible efforts to achieve it.

Conflicts of interest

None declared. (See author's conflicts of interest forms in the website/Supplementary materiall).

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