

## CLINICAL USE OF ULTRA-SENSITIVE TROPONINS IN THE DIFFERENTIAL DIAGNOSIS OF ACUTE MYOCARDIAL INFARCTION

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**Abstract:** Acute Myocardial Infarction (AMI) is when myocardial necrosis occurs through acute obstruction of a coronary artery. Its main symptom is chest pain, which is a sudden constant and constricting pain that can radiate to different parts of the body. It is usually intense and prolonged accompanied by a feeling of heaviness or tightness over the chest. However, other symptoms may occur, such as: dyspnea, nausea and/or diaphoresis. AMI can have major mechanical complications, for example, mitral valve regurgitation with or without papillary muscle rupture; ventricular septal rupture; rupture of the free wall of the ventricle; and left ventricular aneurysm. In order to have the diagnosis of AMI, there is a need to perform an ECG and verify the existence or absence of biomarkers. These biomarkers have the role of reducing the time between the onset of the heart attack and the restoration of myocardial perfusion, thus, they help in the diagnosis of AMI, risk stratification, choice of adequate treatment and prediction of events after Acute Coronary Syndrome (SCA). Among these biomarkers, we can mention the ultrasensitive troponin, which can significantly increase the diagnostic sensitivity when there is a very early phase of myocardial ischemic injury. It is also effective for detecting the risk of mortality and cardiac events in patients with unstable angina, for knowing the size of the infarction after reperfusion and because it is a specific biomarker of cardiac injury when coronary artery bypass grafting is performed.

**Keywords:** Myocardial necrosis biomarkers. AMI differential diagnosis. ACS diagnosis. ultrasensitive troponins.

## INTRODUCTION

Cardiac troponin levels are important biomarkers in the diagnosis, risk stratification and prognosis of patients with myocardial infarction (MI). As laboratory tests become

more sensitive and accurate, they are useful tools in the differential diagnosis of anginal patients. Ultrasensitive troponin measurement has been widely introduced into clinical practice.

This laboratory test can detect minimally elevated levels of troponin a few hours earlier compared to detection methodologies from previous generations (Giuseppe Lippi; Fabiano Sanchis-Gomar, 2018).

The Universal Definition of MI brought about a shift in the diagnosis of MI from an approach primarily based on electrocardiography (ECG) to one based primarily on biomarkers. Currently, the detection of an increase and/or decrease in the concentration or activity of biomarkers of myocardial necrosis, preferably cTns, with at least one value above the upper reference limit (URL) of the 99th percentile, is the essential component for the diagnosis of MI. High-sensitivity cardiac troponin (hs-cTn) assays with their superior analytical performance are designed to make clinical decision-making even easier. The ability of hs-cTn assays to detect measurable cTn concentrations in at least 50% of healthy subjects, along with their improved accuracy (expressed as a coefficient of variation  $\leq 10\%$  at the 99th percentile RLU) associated with increased recognition of variable values, leads to increased risk stratification of patients with suspected myocardial infarction and also allows them to be used as potentially useful prognostic tools in other subsets of patients (Marek kozinski; Madalena Krintus; Jacek Kubica; Grazyna Sypniewska, 2017).

## METHODOLOGY

Bibliographical research in scientific journals available on the Pubmed and Scielo bases, is characterized by being an analytical, prospective study, with a qualitative approach, of a descriptive nature. We searched for articles from 2015 to 2023 that had in the title or abstract the terms “differential diagnosis

AMI”, “ACS diagnosis” and “ultrasensitive troponins” available in the aforementioned database. In total, 10 articles were found. Results without complete publication and unrelated to the topic were excluded.

Key analytical cornerstones of cardiac troponin immunoassays include the limit of blank (LoB), limit of detection (LoD), functional sensitivity, the 99th percentile of a healthy reference population, along with the percentage of “ostensibly healthy” individuals exhibiting values measurable  $< 99$ th percentile. The latest generation of cardiac troponin immunoassays, conventionally defined as “high sensitivity” (HS), are characterized by more than 100-fold lower LoD compared to early commercialized techniques and a percentage of consistently measurable values  $> 50\%$  overall healthy population. The very recent commercialization of methods with even improved analytical sensitivity (i.e., “ultra-sensitive” assays), which allow measuring cardiac troponin values in the vast majority of healthy individuals, is now challenging the diagnostic paradigm based on the early exclusion of individuals with cardiac troponin values between 99 percentile and LoD (Giuseppe Lippi; Fabiano Sanchis-Gomar, 2018).

## RESULTS

Acute coronary syndromes are characterized by obstructions in the coronary arteries. Its consequences depend on the site and degree of obstruction and range clinically from unstable angina to non-ST-segment elevation myocardial infarction (NSTEMI), ST-segment elevation myocardial infarction (STEMI) and sudden cardiac death. Symptoms are similar in each of these syndromes (with the exception of sudden death), involving chest discomfort with or without dyspnoea. The diagnosis is made by ECG and by the existence or absence of serological markers.

In AMI, a vulnerable plaque ruptures, caused by an increase in shear force in the

lumen of the vessel or by an inflammatory process within the plaque. The vulnerable plaque consists of a thin fibrous cap and a large content of macrophages and lipids in the center. With rupture of the fibrous cap, exposure of lipids leads to platelet aggregation and, consequently, thrombosis at the site, with partial or total reduction of the vessel lumen, triggering ischemia and myocardial infarction.

Troponin serum levels are elevated around two to three hours after myocardial injury with the use of Ultrasensitive Troponin (cTn-US), the degree of sensitivity with a single dosage reaches 95%. Therefore, high-sensitivity troponin and ECG form an excellent strategy, with a very high negative predictive value, to rule out AMI in patients with chest pain in the emergency room, regardless of risk factors for cardiovascular disease and time of onset of symptoms. According to their clinical significance, such markers may reflect tissue injury, as revealed by the measurement of lactate dehydrogenase (LDH) and aspartate aminotransferase (AST) and the myocardial injury itself, as evidenced

by creatine phosphokinase (total CPK) and its myocardial fraction (CKMB ), troponins (TROs) and myoglobin (MIO).

Cardiac troponins T and I are markers considered highly sensitive and specific for the diagnosis of acute myocardial infarction. Currently, with the advent of ultrasensitive assays, a series of non-primarily cardiac abnormalities can be manifested through the elevation of these assays. The reduction of its detection threshold promoted earlier diagnosis and the use of evidence-based therapeutic measures, however, this characteristic increases the spectrum of detectable non-coronary heart diseases, bringing challenges to the characterization of acute coronary syndromes and a new role for these tests in known disorders in the intensive care unit setting, in particular sepsis. The approach to patients through a greater understanding of the behavior of these markers must be resized for their correct interpretation (Humberto Andres Vaz; Raphael Boesche Guimarães; Oscar Dutra, 2019).

For a better scientific understanding, the action time curve of certain biomarkers is used as a basis. Figure 1 represents the level of cardiac troponin x percentile value of cardiac troponin:

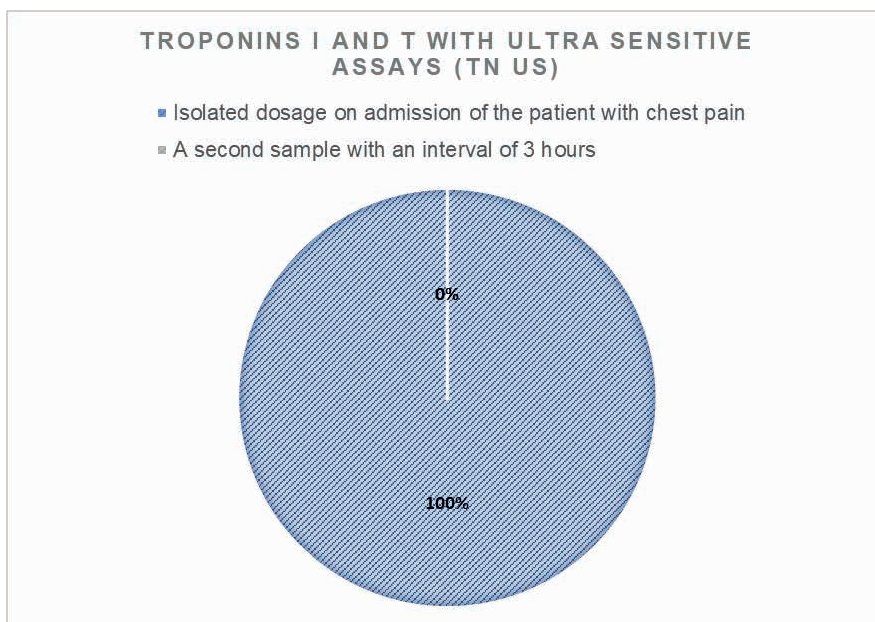
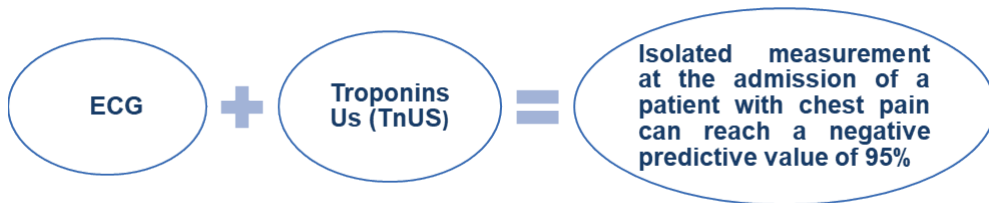


Figure 1: Troponins I and T with Ultra Sensitive (TnUs)

Source: own authorship



## CONCLUSION

In summary, the clinical use of ultrasensitive troponins plays a very important role with regard to the set of other complementary tests that help in the differential diagnosis of the syndromic entities that make up the ACS. patient length of stay in the emergency department and the rate of unnecessary hospitalizations, thereby reducing emergency room overcrowding and the cost of care for healthcare systems around the world.

One of the great advantages of measuring troponin instead of CK-MB is that the former reaches peak values of up to more than 40 times the detection limit, while the latter is restricted to six to nine times. It is also known that both troponin I and troponin T have equivalent sensitivity for the diagnosis of myocardial cell injury (Luiz Carlos Mendes Bonoto; Luiz Gustavo de Oliveira, 2020).

With the advent of ultrasensitive assays, it has also been possible to detect several series of non-primarily cardiac abnormalities that can be manifested through the elevation of these assays. Which, from a clinical point of view, promoted earlier diagnosis and the use of evidence-based therapeutic measures.

Biochemical markers are essential to aid both in the diagnosis and prognosis of patients with Acute Coronary Syndrome (ACS). Several studies demonstrate the importance of the test, not only in its specificity and sensitivity in the detection of Acute Myocardial Infarction compared to first-generation tests, but also in the prognosis and risk classification of patients affected by cardiovascular diseases, making it easier for the clinical staff to choose the best conduct for each patient (Luiz Carlos Mendes Bonoto; Luiz Gustavo de Oliveira, 2020).

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