Troponin is elevated in 43% of patients hospitalized in intensive care units, with diagnoses of sepsis, septic shock or systemic inflammatory response syndrome. In stroke, the prevalence was estimated at 18%. Additionally, no precipitous decisions should be reached - after the next marathon in your city - you see a runner in poor physical condition with elevated cTn levels and no AMI. The prevalence of cTn elevation during heavy physical exercise may reach 47% when measured by traditional kits and up to 87% when checked through high sensitivity cTn. End-stage kidney disease is another important constraint, as almost 100% of these patients present positive for high sensitivity cTn. This non-specific characteristic of cTn is reminiscent of lactic dehydrogenase (LDH) and glutamic oxaloacetic transaminase (GOT) precursors.

The difficulties begin with a diversity of nomenclature and concepts, as cTn consists of three sub-units: C, I and T. The latter two are more specific for diagnosing myocardial lesions. There is still no consensus on the criteria for defining high sensitivity troponin. Korley and Jaffe claim that high sensitivity cTn has powers of detection above 50% in the reference population. High sensitivity cTn may be classified as first, second and third generation, depending on its relative capacity to detect 50% and 75%; 75% and 95%; and greater than 95% respectively, in a reference population. There are questions about how these reference populations are selected. The more rigorous the selection, excluding patients with structural cardiac alterations, the lower the values found. Using the 99 percentile criterion, it is possible to find altered cTn in up to 1% of the population.
Another technical issue is the existence of three reference values: a) the 99 percentile, used as a positive cut-off point; b) the lowest detectable value; and c) a <10% coefficient of variation. Traditional kits use ng/mL. The more sensitive traditional kits detect low values, but with coefficient of variations exceeding 10%, meaning that they are clinically less reliable. High sensitivity kits detect values as low as 0.003 ng/mL. To make it easier, the unit is changed through multiplying it by 1 000. Thus, these kits detect values at 3 pg/mL with 12 pg/mL as a <10% coefficient of variation.

Initially, the cTn kits were designed to diagnose AMI and were qualitative, with positive or negative dichotomic findings. Once the cTn became a continuous variable, with minute detectable values, possibilities opened up of exploring its prognostic value for the population in general. Studies show a positive relationship between cTn values and prognoses. The presence of cTn was detected in between 25% and 66% of younger and older people respectively in the general population. There was a correlation with the incidence of events such as death, HF and coronary artery disease. Eggers et al. measured cTn in 1,004 individuals over seventy years old in Sweden, and found detectable values in 96% and 99% of them five years after the initial measurement. There was a positive correlation with cardiovascular events. Sensitivity rises as specificity drops. This study confirmed that cTn is higher among men and has a linear relationship to age.

There are surely other interferences that must be explained, and very probably the clinical interpretations will have to be adjusted to variables such as age, gender, body mass index, kidney dysfunction, ventricular mass and others. Imagine seeing a male patient, 75 years old, with a known diagnosis of heart failure and cardio-renal syndrome, admitted to the emergency room with chest pain. Elevated troponin might reflect AMI or a ‘false-positive’ for CMP and kidney failure. And does ‘false-positive’ exist?

‘False-positive’ troponin is found frequently when, in a context of chest pain, the cTn is elevated with normal coronaryography. In these cases, consideration must be given to the possibility of other underlying myocardial diseases: ‘false-positive’ for AMI, but really positive for a series of other conditions, and even with poor prognosis value. Patients with acute HF and elevated cTn in the ADHERE records presented lower blood pressure, more lower left ventricle ejection fractions and more hospital admissions during follow-up.

What is the real value of high sensitivity cTn measurements for diagnosing ACS? And how safe is it to disregard this syndrome? Dr. Lori B. Daniels has warned about the need to improve the interpretation of the examination. Initially, it is necessary to ask what is the clinical purpose of requesting the cTn in an emergency room setting, and for the patient in question. Confirming a diagnosis of ACS or dismissing it and letting the patient go home, or to be admitted to a hospital ward with peace of mind? Considering the high number of patients seen with precordial pain in emergency rooms and the relatively low level of ACS diagnoses with ST segment elevation, when interventionist conduct is urgent and top priority, it seems more useful and pragmatic to have a biomarker that safely dismisses the possibility of ACS.

The same line of thinking is shared with Dr. W.F. Peacock, an emergency physician at the Baylor College of Medicine, Houston, TX, USA. There are six million people a year in the USA who seek emergency care for precordial pain, with 85% of them discharged. Consequently, a negative result will have greater clinical and economic impacts than a positive result. Dr. Peacock gifted us with the participation of this editorial in a recent meeting with Humberto Villacorta, during the IV Italian GREAT Network Congress in Rome. According to him, cTn kits detecting lower concentrations offer an opportunity for emergency physicians. This may be exemplified in studies comparing the rapid discharge of ACS patients, safe discharge from hospital and the use of lower level detection cTn kits.

The ASPECT study assessed the strategy of releasing ACS patients with admission tests using this rapid option, although unable to detect low values, compared to the best laboratory methods. The ASPECT study used as its inclusion criteria patients with suspected ACS, although with a non-diagnostic ECG, TIMI score of zero and negative cTn measurements on admission and two hours later. In this study, 9.8% of patients were discharged safely. Although discharging 9.8% of them is useful, this represents a minority of patients with chest pain.

The significant consequences of improving the low level detection was demonstrated subsequently in the ADAPT/APACE studies. Using the same inclusion strategy and what are known as ‘high sensitivity’ kits, they managed to discharge 41.5% of patients safely. Representing an increase of more than 400% in the discharge rate, this demonstrates the obvious and valuable clinical impact of lowering detection levels in the emergency room.
However, there are questions about whether these kits exclude patients with unstable angina and no significant necrosis, but with known risks of complications, meaning that the exclusion of necrosis does not eliminate the risk of events over the long term. It is necessary to check for myocardial ischemia or other underlying diseases subsequently, at the outpatient level.

There are doubts about the kinetics of cTn and the real value of serial measurements. It seems that this strategy improves specificity, although the exact progressive variation percentage still prompts discussions. Seeking a reply to this question, Haaf et al. studied 887 patients admitted with chest pain starting less than twelve hours previously, measuring the baseline high sensitivity cTn and an hour after admission, deciding on a variation of more than 30% between the cTn measurements. They compared patients with elevated cTn caused by AMI with others suffering from non-coronary cardiac causes. The high sensitivity cTn was more elevated at the baseline levels, with a greater variation in an hour in patients with AMI, compared to those with non-coronary cardiac causes. According to this study, it was possible to distinguish between these two conditions. The European Society of Cardiology reviewed this issue and proposed the following: if the initial cTn is detectable but at a value below the 99 percentile, a 50% elevation in three hours is indicative of ischemia. If the initial cTn is higher than the benchmark, a 20% elevation already indicates ischemia.

Undetectable high sensitivity troponin seems to eliminate the possibility of AMI. Elevated troponin may indicate AMI, but requires attention, as this is frequently a sign of some other cardiopathy, clinical condition or underlying systemic disease. Sovereign clinical practice must be put in its proper place. First of all is clinical suspicion, then supplemented by diagnostic tests, thus enhancing the accuracy of these diagnoses.

In conclusion, reproducing the message of Professor Alan Maisel – a leading name in biomarker studies - in his magnificent lecture in Lisbon given at the European Congress on Heart Failure in May 2013: “Biomarkers make bad physicians worse and good physicians better!”

**Keywords:** Troponin; Myocardial infarction, diagnosis; Coronary disease

**Potential Conflicts of Interest**
I hereby declare that there are no material conflicts of interest.

**References**