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Sensitivity and Specificity of Troponins in AMI

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Article History	*Abstract*
	A review was carried out to relate the presence of Acute Myocardial Infarction (AMI) by determining biomarkers, detailing their sensitivity and specificity, with the aim of determining the specificity and sensitivity of biomarkers in AMI. Different studies were evaluated, taking into consideration that they included clinical, electrocardiographic and enzymatic diagnosis, where the sensitivity and specificity of the different cardiac enzymes will be specified. The sex most affected with IMA was the female, after 60 years. Troponin T, of great importance in the prediction of events in patients with ACS. High values of brain natriuretic peptide have been associated with ventricular remodeling. The enzyme with the highest sensitivity and specificity for diagnosis is TnI. The CPK MB enzyme behaved with a higher sensitivity and specificity than TnT, in diabetic patients at Hospital General Ambato.
	Keywords: *Sensitivity, Specificity, Infarction, Acute Coronary Syndrome, Troponins.*

1. Introduction

Within the cardiac pathologies, those originated in the coronary vasculature are in a top place because of their high incidence, complications and high costs, in management and rehabilitation. According to Braunwald within the main causes of these pathologies, we find atherosclerotic disease, coronary vasospasm, thrombosis or sudden increase in myocardial needs (Ryan, 2019; Mann et al., 1997). The clinical manifestations are due to the imbalance between coronary supply and myocardial oxygen demand. Supply is determined by vascular lumen, vascular tone and perfusion pressure. Demand is driven by preload, afterload, systemic arterial resistance, heart rate, and heart muscle contractibility. (Mann et al., 1997; Guyton & Hj, 1996) As a result, acute ischemic disease appears, where the heart muscle undergoes a wide range of injury ranging from ischemia to necrosis (Ruiz, 2009).

The diagnosis of acute myocardial infarction should be made under the correlation between clinical findings, electrocardiogram (ECG) and laboratory tests such as enzyme determination (biomarkers).

(Beard, 2007) Acute coronary syndromes (ACS) go through five main stages, the severe degree of disease involving the myocardium. Injuries occur due to erosion or rupture of an atherosclerotic plaque, causing the formation of an intracoronary thrombus, thus causing the appearance of unstable angina (IA), acute myocardial infarction (AMI) or sudden death, all of them included in the ACS. Thus, IA and AMI have a common pathophysiological link, with clinical manifestations that may be difficult to differentiate at the beginning until the performance of an electrocardiogram (ECG).

Cardiovascular diseases are considered, at the present time, the most significant pandemic of the twenty-first century. The WHO offers some statistics, where numerous assessments are established on, heart disease, stroke and other cardiovascular diseases, as evidenced below (Association, 2017). Every 40 seconds or so, a person in the United States will have a heart attack. Ischemic heart disease is the leading cause of death in the United States, followed by deaths from stroke, heart failure, high blood pressure, arterial disease and other cardiovascular diseases. Cardiovascular disease is the leading cause of mortality worldwide. Coronary heart disease develops slowly and progressively over many years, it is one of the leading causes of instant death (sudden death) in a third of cases.

In 2016, according to the statistical records of Ecuador in figures by INEC reports, in relation to the first 10 causes of death, ischemic heart diseases occupy the first place with a rate of 39.40, the main cause of female mortality were ischemic heart diseases with 2,766 reaching a percentage of 9.04%. According to many researchers, it is precisely in the female sex, after 50 years that this type of event prevails. In the male sex the main cause coincides with ischemic heart diseases with a total of 3,747 deaths, reaching 10.15%, a fact that exceeds the female sex, contrary to what was raised by many authors. (Ecuadorenfigures, 2016) Mortality from cerebrovascular diseases ranked fourth in this period, which is higher in advanced ages, reaching a rate of 26.19 to 5.81%. (Ecuadorenfigures, 2016) The overall mortality rate in 2020 is 28,397 deaths with a difference of 8,763, compared to the previous year, according to INEC reports. According to the classification of the main causes of death, the indicator was completely modified, occupying the first; place diseases related to the respiratory system (INEC, 2021).

To establish the definitive diagnosis of acute ischemic coronary heart disease, we must meet different requirements. The electrocardiographic diagnosis should include the right leads, V4R to V6R, in addition to the dorsal leads from V7 to V9, to rule out the participation of the right ventricle in this process (Lorenzo, 2013).This facilitates the clinical classification of patients with ACS into: ACS with ST-segment elevation (also called supra ST) and another group of ACS without ST elevation (infra ST). Patients with supra ST may be carriers of different causes of this electrical manifestation, some benign, not serious. It is necessary to take into account the voltage of the ST segment elevation, to be considered pathological, expressed by numerous authors in more than 1mm in the standard leads and more than 2mm in the precordial leads from V1 to V4. On the other hand, we must consider that usually these patients present with complete and acute occlusion of a coronary artery, developing a myocardial infarction, with the electrocardiographic expression of necrosis, which is the Q wave, as Lorenzo raises in his research (Lorenzo, 2013).

There is another smaller group of patients who present supra ST and who do not necessarily have a heart attack, such as pericarditis, left ventricular overload, electrolyte disorders such as hypercalcemia, hyperkalemia, variant or Prinzmetal angina, thromboembolism, among others. It is worth remembering, that, in electrocardiograms, the appearance of new blockages or presumably, should be considered as acute myocardial ischemia. Patients with infra ST respond to partial occlusion of a coronary artery, with high probability an AI or an IMA without Q wave (non-Q AMI) (Lorenzo, 2013). The high incidence of AMI in our environment, and the complexity of the diagnosis, leads us to have to use biomarkers as a key link to clarify the clinical situation, which is why we conducted this research, with the general objective of determining the specificity and sensitivity of biomarkers in AMI.

2. Materials And Methods

A descriptive research was carried out with a qualitative approach, through a documentary review, with a systematic review of different scientific documents on the subject in question, which were available on the Internet in any language and in full text. These articles had to be framed in the last five years and books of the last 10 years, fundamentally.

3. Results and Discussion

Coronary heart disease, characterized by its silent behavior, has driven the investigation of molecules that allow its early diagnosis and serve as prognostic predictors in both the chronic and acute phases, such as biomarkers. According to Mann et al. (1997) the identification of new biomarkers of cardiovascular disease depends on the complementary potential of genetics, transcriptional profiling, proteomics and metabolomics. Cardiac enzyme studies measure enzyme and protein levels, the elevated results of which may be related to heart muscle injury. Troponin proteins, described by Braunwuald, are of two types, troponin I (TnI) and troponin T (TnT). Other previously used and less specific enzymes may also be found elevated in blood during an IMA, in relation to the time of ischemia. The enzyme called creatine kinase (CPK) being CPK MB the most specific isoenzyme for cardiac muscle, reported with lower specificity than troponins.

Braunwald, refers to the clinical utility of the new biomarkers, pointing out the importance of a personalized clinical evaluation, to establish the treatment and prognosis of each patient. It is necessary to evaluate risk biomarkers and diagnoses, which help us to discern in the differential diagnosis of pathologies such as; reversible myocardial ischemia, pulmonary embolism and aortic dissection, infarction with left bundle branch block, among others. Biomarkers require mapping, with serial and frequent determinations, which allow us to draw the evolutionary behavior of the curve, detailing the sensitivity and specificity, thus determining the importance of these in clinical practice (Mann et al., 1997). Ultrasensitive troponins (TnTus) are used in the early diagnosis of AMI. The determinations of albumin modified by ischemia, has a high negative predictive value for the detection of myocardial ischemia. The soluble CD40 ligand for the classification and individualization of treatment, the usefulness of C-reactive protein as a marker of coronary heart disease risk (Guyton & Hj, 1996).

Conducted a study on the determination of ultrasensitive troponin T (TnTus) simplifying the diagnosis of AMI, significantly increasing the number of cases (Nacke et al., 2014). Cardiac troponins allow differentiating between acute myocardial infarction (AMI) and unstable angina, chest pain encompasses numerous causes, this should be evaluated considering "history-electrocardiogram-age-risk factors-troponin" (HEART). We analyzed 428 patients with precordialgia, in the IESS Quito Sur hospital, 81 developed AMI (18.93%), with 72.8% male and 69.1% older than 65 years. The sensitivity of troponins was 96% and specificity was 78%. Sánchez Fernández et al. (2015), studied the three leading causes of death in Guanajay, Cuba. The IMA was secondly female. The most affected age group was 67 to 83 years in both sexes TORRES (2019). The study by Till Keller et al. (2011) evaluated a total of 1818 patients who presented to the emergency department with symptoms suggestive of acute coronary syndrome who were sampled to measure levels of ultrasensitive troponins, detecting IMA in 22.7%, reporting the use of Troponin I (TnI) on admission (with the diagnostic cut-off value at the 99th percentile of 30 pg/mL) which obtained a sensitivity of 82.3% and a negative predictive value (to rule out AMI) of 94.7% (specificity). At 3 hours of admission, the sensitivity was 98.2% and the negative predictive value was 99.4%. Combining both results, the value increased in sensitivity from 82.3% on admission to 98.2%, 3 hours later, and for cTnI increased from 80.9% on admission to 96.1% after 3 hours (Keller et al., 2011).

Based on the above, new troponin detection techniques using ultrasensitive assays increase diagnostic effectiveness in the early detection of acute coronary syndrome; However, more studies are still required to standardize the methodology and evaluate its cost-effectiveness when used, based on the sensitivity and specificity of each of the cardiac enzymes. Nacke's study included 148 patients, with a mean age of 64+12 years. 68% were male, diagnosed IMA by 59.5%. The TnTus for the diagnosis of IMA on admission was 0.84, and a cut-off point of 38ng/L, with a sensitivity of 80% and specificity of 72%. (10) Laguapillo conducted a study at the Ambato Teaching General Hospital, where he

concluded that the sensitivity for the TN T troponin test was 48.5% with a specificity of 48.2% for diabetic patients diagnosed with IMA, while the sensitivity for the CK isoenzyme MB test was 51.4% with a specificity of 51.7% for diabetic patients diagnosed with IMA (Laguapillo et al., 2017). According to Macin et al (2020) in their study evaluates the behavior of high-sensitivity cardiac troponin T, which had the best cut-off point in the COR curve of hs-cTnT. A cut-off point of hs-cTnT >2,310 ng/L identified events, being an independent predictor, together with the left ventricular ejection fraction (LVEF), a very powerful indicator after IMA and, together with an NT-ProBNP value ≥900 pg/ml, associated with ventricular remodeling. The highly sensitive troponin T has great importance in predicting events in patients with ACS. (Macin et al., 2020) The extent of myocardial injury was evaluated by Macin et al, using CK-MB isoenzyme release curves. Numerous researchers have used the CK-MB peak to obtain a qualitative estimate of the size of the IMA, and it is currently proposed that when its value increases 10 times, so does the increase in the risk of events. However, well-known limitations of CK-MB measurements, such as the short duration of the increase after IMA, frequent sampling for evaluation of maximum concentrations and lack of specificity for cardiac damage, have stimulated the search for a more suitable biomarker to size heart attacks. Cardiac troponins have recently been proposed as a biochemical standard for the diagnosis of IMA (INEC, 2021; Labrada et al., 2021).

4. Conclusion

The sex most affected with AMI was female, after 60 years. Troponin T, of great importance in the prediction of events in patients with ACS. High values of brain natriuretic peptide have been associated with ventricular remodeling. The enzyme with the highest sensitivity and specificity for diagnosis is TnI. The CPK MB enzyme behaved with a sensitivity and specificity superior to TnT, in diabetic patients of the Ambato General Hospital.

Conflict of interest:
The authors declare no conflict of interest.

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