Measurement of cardiac troponin in the diagnosis and management of ischemic heart disease

By:

Ali Younis Ali

Supervised by:

Assit.Prof. Bushra M. Hussein

M.B.CH.B., FICMS.PATH.

(Chemical Pathologist)

ABSTRACT

Background

Cardiac troponin testing is central to the diagnosis of acute myocardial infarction.

We evaluated a sensitive troponin I assay for the early diagnosis and risk stratification of myocardial infarction.

Methods

A retrospective cohort study at Baqubah Hospital investigated high troponin levels in ischemic heart disease patients. Between December 2023 and March 2024, 55 blood samples were collected, with 15 excluded due to criteria mismatch or incomplete data, leaving 40 samples for analysis. The VIDAS system, using ELFA technology, measured troponin levels within 25 minutes. Samples required 100 microliters of serum and followed the VIDAS protocol. Troponin levels were classified as normal or elevated, and statistical analysis assessed their correlation with patient outcomes. The system underwent daily calibration, and control samples ensured assay accuracy. The final sample included 6 females and 34 males.

Results

The study examined 40 patients over 50 with ischemic heart disease symptoms, finding:

- Troponin Levels: All showed elevated troponin, indicating injury.
- Age Distribution: Ages 50-78, average 63.5.
- Clinical Implications: High troponin suggests increased risk of cardiovascular events.
- The data supports the link between troponin elevation and myocardial ischemia in older adults.

Conclusions

The use of a sensitive assay for troponin I improves early diagnosis of acute myocardial infarction and risk stratification, regardless of the time of chest-pain onset.

Chapter One: Introduction

1.1 Introduction

The united states is in the midst of a heart failure epidemic. More than 1 million hospitalizations in 2007 were for heart failure, and the Centers for Medicaid and Medicare Services currently spends more on the diagnosis and treatment of this condition than on any other medical condition. (1) Most patients with heart failure are admitted to the hospital from the emergency department, where a comprehensive evaluation is required to determine the precipitating cause of the condition.

Unfortunately, the definition of a comprehensive evaluation has not been established. Since coronary artery disease is the most common cause of heart failure in the United States, it is appropriate to evaluate patients with heart failure for myocardial ischemia. Initial evaluation of patients who present with heart failure often includes a focused history, physical examination, electrocardiogram, and measurement of biomarkers.

Cardiac troponin concentration is the preferred marker of myocardial necrosis.(2) Elevated concentrations of cardiac troponin have a strong association with an adverse prognosis in patients with acute coronary syndromes and are used to identify patients who are likely to benefit from an early invasive management strategy.(3-4)

High-sensitivity assays that allow the measurement of very low cardiac troponin levels in patients with stable heart disease are now available for clinical and research use. These low, previously undetectable troponin concentrations have shown strong associations with myocardial infarction, stroke, and death in a variety of primary and secondary prevention populations, including in patients with stable ischemic heart disease.(5-6)

Although this approach is well validated for the evaluation of acute coronary syndromes, except for specific laboratory-based investigations, an objective risk-stratification process for the evaluation of acute decompensated heart failure is lacking. The value of measuring serum cardiac troponin when a patient presents with acute decompensated heart failure remains uncertain. Although several limited analyses suggest that an increase in serum cardiac troponin levels is associated with adverse long-term outcomes,(7-8)

the short term implications are less clearly defined. Some small trials involving patients with heart failure have shown that increases in troponin levels, even in the absence of chest pain or an acute coronary syndrome, correlate with a poor prognosis (8-9) and that detectable troponin, at any level, is associated with impaired hemodynamics, a progressive decline in left ventricular systolic function, and shortened survival. We conducted a large study to describe short-term outcomes associated with elevated troponin levels on admission in hospitalized patients with acute decompensated heart failure. (8-10).

1.2 Aims of the study

To measure the level of cardiac troponin in patient with ischemic heart disease

Chapter One: Introduction

2-1.Biomarker

Biomarkers are measurable organic products that can indicate certain diseases in the body. A variety of endogenous substances such as proteins, hormones, enzymes, cells, genes and gene products can be considered as biomarkers. On the one hand, biomarkers are used to identify high-risk patients, to detect the disease and to determine the course of a disease, and on the other hand, they facilitate the decision of therapy, the selection of a suitable therapy method and, ultimately, the assessment of the prognosis (11).

Biomarkers are used in the early detection and treatment of almost all diseases.

Well-known biomarkers in veterinary medicine are the classic red and white blood count, which can provide indications of diseases with the help of the individual blood cell groups and, as a screening test, is now part of the standard protocol of almost every examination of both healthy and sick animals. The determination of organ-specific enzymes and metabolites is also practiced worldwide.

For every organ system in the body, biomarkers exist in both human and veterinary medicine that ensure faster and more precise diagnostic options. Nevertheless, biomarkers are more than ever part of current research in order to continuously improve the sensitivity and specificity of existing biomarkers, to find new ones and to expand their areas of application.

In intensive care and emergency medicine, biomarkers are essential for efficient disease detection and treatment and for the assessment of disease progression and prognosis (12,13).
An important example of this is lactate. Dogs with MDV have a higher chance of dying if gastric wall necrosis is present at the same time. An initial lactate concentration ≥ 6 mmol/l
(61% sensitivity, 88% specificity) (14). or 7.4 mmol/l (15). provides a good indication of existing gastric wall necrosis and survival of the dogs However, not only the initial lactate measurement seems to have a prognostic value, but also changes in lactate concentration, during initial care (infusion management, decompression of the stomach), after

surgery and during postoperative care (16). A drop in lactate ≥ 50% within the first 12 hours also appears to be a good prognostic indicator of survival (17). Lactate measurement is not only a valuable biomarker in terms of prognosis, but also in identifying patients who need alternative or more aggressive therapy.

2.2 Troponins

Troponins are regulatory proteins found in both skeletal and cardiac muscle cells. They each consist of three subunits and, together with the proteins actin and myosin, form the contractile part of the muscles. They are a component of the thin filaments within the myofibrils and are fundamentally important for the calcium-mediated regulation of muscle contraction (18).

2.3. Structure of troponine

Troponins are regulatory proteins and, together with the contractile proteins actin and tropomyosin, represent the thin filament (actin filament) of the striated muscles. A troponin complex consists of three subunits:

- Troponin C (TNC)
- Troponin I (TnI)
- Troponin T (TnT), each with specific functions (Figure 1).

Subunit C is the calcium (Ca2+)-binding subunit, subunit T is tropomyosin-binding, and subunit I is the inhibitory subunit (18).

Chapter One: Introduction

The subunits thus represent interacting proteins that perform functionally different tasks (19). with tissue-specific isoforms in the

heart and skeletal muscle (18,20). Troponins are involved in Ca2+-induced muscle contraction in both myocardium and skeletal muscle (21).

To enable muscle contraction, Ca2+ binds to troponin C, whereupon the tropomyosine changes its conformation, thus releasing the myosin binding site and thus initiating muscle contraction (21,22). Troponin I, as an inhibitory unit, prevents this conformational change until a new Ca2+ binding takes place (23 ,24).

Chapter One: Introduction

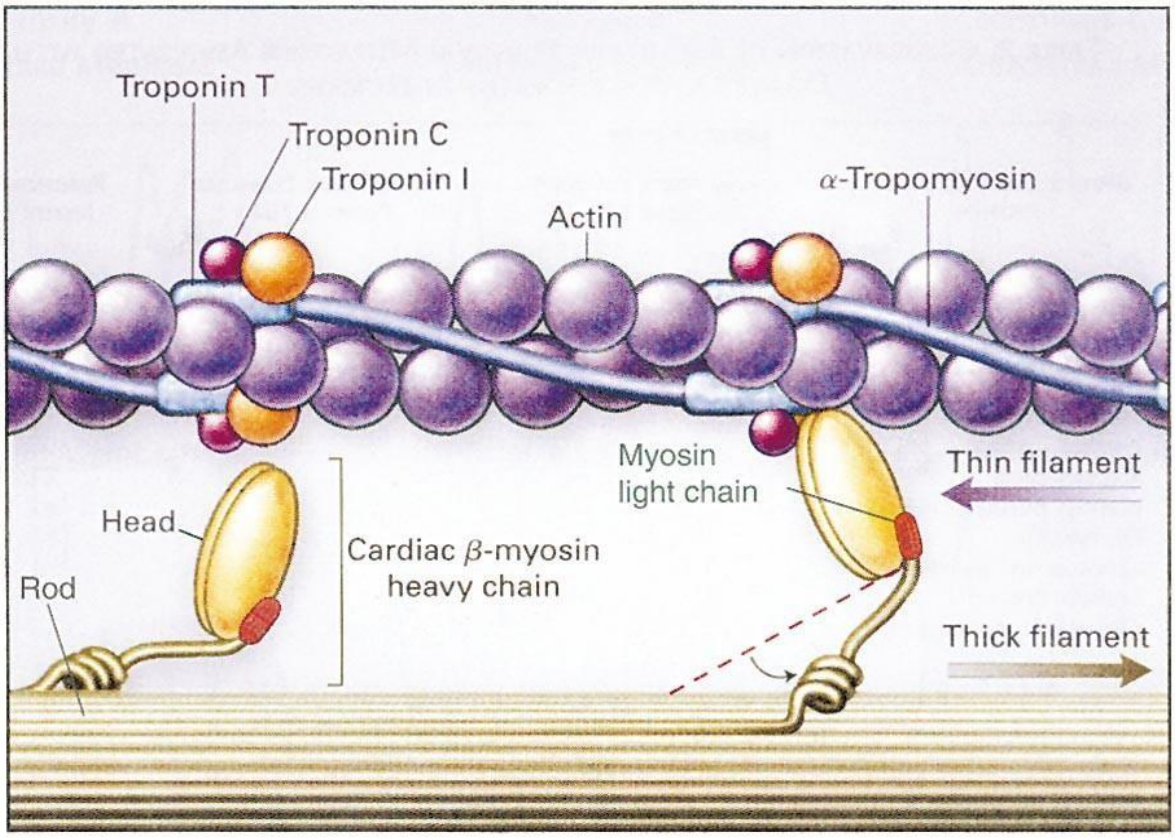

Figure 1: Thin filament of the sarcomere consisting of the troponin complex with the subunits TnT, TnC, TnI, actin and α-tropomyosin. The contraction begins with the entry of calcium into the sarcomere, which reverses the TnI inhibition of actin and enables actin-myosin binding. This is followed by a myosin conformational change and finally muscle contraction.

Mutations in genes that code for a troponin subunit can lead to a wide variety of diseases. For example, the development of hypertrophic cardiomyopathies has been described in the case of gene changes in the subunits cTnI and cTnT (25,26).

Chapter One: Introduction

2.4.Cardiac Troponin (cTn)

Cardiac troponins can be in three different isoforms, cardiac troponin C (cTnC), cardiac troponin T (cTnT), or cardiac troponin I (cTnI). Troponin C has two isoforms that are very similar in their homology. Cardiac isoform (cTnC) is also expressed in skeletal muscle and thus has no cardiac specificity. The diagnostic benefit of cTnC for the diagnosis of myocardial damage is therefore rather low (27).

In humans, there are 4 isoforms of cardiac troponin T (cTnT), which has a molecular weight of 37,000 Da (28, 29). Only one of the four isoforms is characteristic of the adult heart, the other three isoforms are found only in fetal heart tissue (28).

Cardiac troponin I (cTnI) has a molecular weight of 24,000 Da and is larger than the two isoforms of skeletal muscle (28,29,30). Cardiac troponin I, unlike cTnT, is not found in fetal tissue or in adult damaged or regenerating skeletal muscle (31).

2.5.Troponin Release

The majority of troponin is present in structurally bound form within the contractile apparatus and only a small part (2 – 4 % of cTnI and 6 – 8 % of cTnT) is freely dissolved in the cytosol (32, 33). In case of acute damage to the cardiac myocytes and thus to the cell membrane, cardiac troponin is released and enters the bloodstream (34). Initially, the release of free troponin from the cytosol leads to a rapid increase in the concentration in the blood, while the release of the structure-bound troponin takes a little longer. This results in a constant level of troponin in the blood (35, 33,36). In the blood, troponin has a half-life of approximately 2 hours (35). The exact mechanism of elimination of troponin is not yet fully understood, but involvement of the reticuloendothelial system is likely (37). In humans, blood concentrations of cTn increase within the first 4-12 hours after acute myocardial infarction (AMI), peak after 12-48 hours, and may remain elevated for 7-10 days (cTnI) and 10-14 days (cTnT) respectively (29,38). Similar figures have been found in dogs with experimentally induced AMI, with an increase in cTnI within 4-6 hours and peaks after 10-16 hours (38).

Chapter Two :Materials and methods

Materials and methods

Study Design: A retrospective cohort study was conducted to assess the prevalence of high troponin levels in patients with ischemic heart diseases at Baqubah Hospital.

Sample Collection: From December 2023 to March 2024, 55 blood samples were collected from patients diagnosed with ischemic heart diseases.15 Samples that did not meet the inclusion criteria or had incomplete data were excluded, resulting in a final cohort of 40 samples.

Equipment and Assay: The VIDAS system, utilizing enzyme-linked fluorescent assay (ELFA) technology, was employed for quantitative measurement of troponin levels. The system's rapid processing capability allows for test completion within 25 minutes.

Sample Processing: Each sample was processed using 100 microliters of serum. The samples were handled according to the standardized protocol provided by the manufacturer for the VIDAS system.

Data Analysis: Troponin levels were categorized into normal and elevated based on the reference range provided by the VIDAS system. Statistical analysis was performed to evaluate the association between troponin levels and clinical outcomes in patients.

Quality Control: To ensure the accuracy of the results, the VIDAS system was subjected to daily calibration and maintenance. Control samples were run alongside patient samples in each batch to monitor assay performance.

Gender Distribution: Of the accepted samples, there were 6 females and 34 males.

Chapter Three: Results

Results

In our study titled “Elevated Troponin Levels in Ischemic Heart Diseases,” we evaluated 40 patients who presented with symptoms indicative of ischemic heart disease. All patients were over the age of 50 years. The key findings are as follows:

Troponin Levels: Each patient demonstrated troponin levels that exceeded the normal reference range, indicating myocardial injury.

Age Distribution: The age of the patients ranged from 50 to 78 years, with a mean age of 63.5 years.

Clinical Implications: The elevated troponin levels in these patients correlate strongly with ischemic events, suggesting a higher risk of adverse cardiovascular outcomes.

The consistent elevation of troponin levels across all patients reinforces the established link between troponin elevation and myocardial ischemia in individuals over 50 years of age.

Chapter Three: Results

Normal Range	الزنوجة	العمر	اسم المريض
Positive	776.4	54	Patient 1
Positive	981.7	61	Patient 2
Positive	1004.6	56	Patient 3
Positive	411.3	58	Patient 4
Positive	190.2	53	Patient 5
Positive	301.5	58	Patient 6
Positive	876.3	60	Patient 7
Positive	209.6	60	Patient 8
Positive	119.6	55	Patient 9
Positive	509.5	59	Patient 10
Positive	70.1	49	Patient 11
Positive	418.0	64	Patient 12
Positive	941.8	55	Patient 13
Positive	269.8	51	Patient 14
Positive	1023.1	58	Patient 15
Positive	189.8	56	Patient 16
Positive	809.3	60	Patient 17
Positive	708.8	65	Patient 18
Positive	769.2	71	Patient 19
Positive	589.1	58	Patient 20
Positive	601.2	56	Patient 21
Positive	664.8	66	Patient 22
Positive	1412.9	57	Patient 23
Positive	398.9	60	Patient 24
Positive	856.3	58	Patient 25
Positive	477.5	49	Patient 26
Positive	502.3	55	Patient 27
Positive	904.1	39	Patient 28
Positive	480.3	60	Patient 29
Positive	156.2	54	Patient 30
Positive	109.8	55	Patient 31
Positive	532.1	62	Patient 32
Positive	493.8	51	Patient 33
Positive	804.4	54	Patient 34
Positive	309.6	49	Patient 35
Positive	275.6	50	Patient 36
Positive	711.5	53	Patient 37
Positive	908.7	65	Patient 38
Positive	1078.9	56	Patient 39
Positive	256.8	54	Patient 40

Table (1) This table represent tracking the progression of the study and analyzing the troponin levels in relation to the patients' ages of sample collection.

Chapter Three: Results

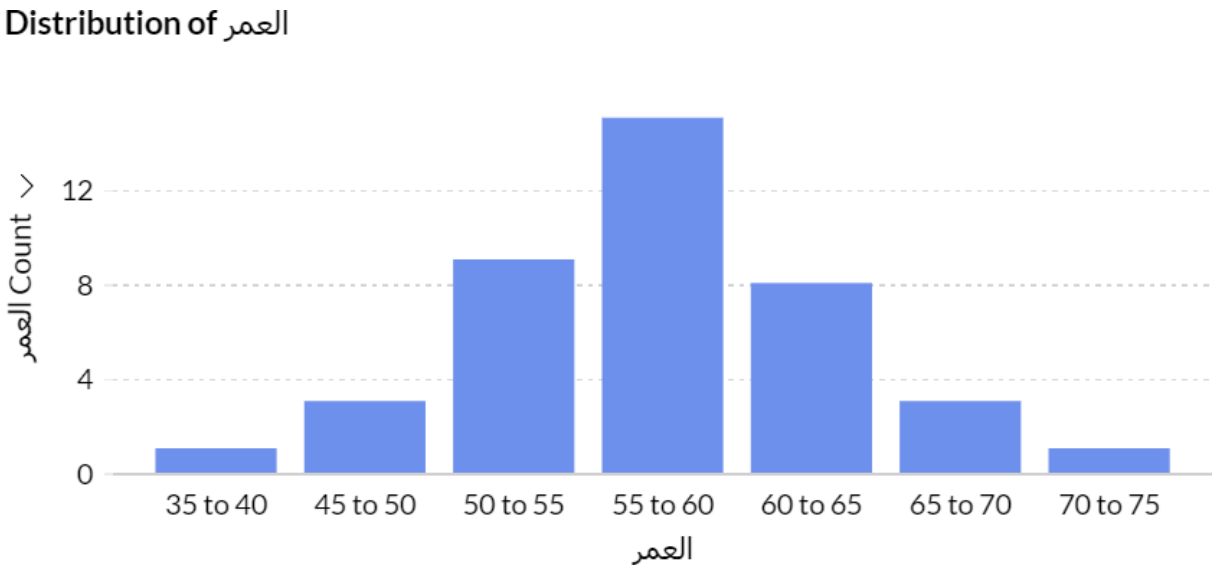

Figure 2. Age Distribution

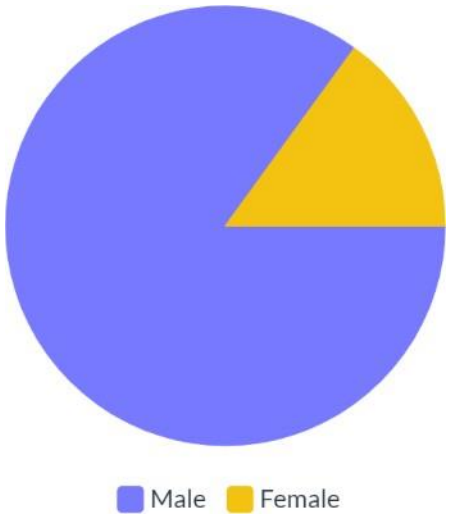

Figure 3. Gender Distribution

Chapter Four: Discussion

Discussion

The findings of our study "Elevated Troponin Levels in Ischemic Heart Diseases" underscore the critical role of troponin as a biomarker for myocardial ischemia, particularly in patients over the age of 50. The universal elevation of troponin levels among the 40 patients studied suggests a robust association with ischemic heart diseases.

Troponin as a Prognostic Marker: The elevated troponin levels observed could indicate a higher risk for future cardiac events, emphasizing the need for aggressive management and follow-up.

Age-Related Cardiovascular Risk: The exclusive involvement of patients over 50 years of age highlights the increased cardiovascular risk associated with aging and the potential for troponin levels to serve as a valuable diagnostic tool in this population.

Implications for Clinical Practice: These results may influence clinical practice by reinforcing the importance of troponin level assessments in older patients presenting with symptoms of ischemic heart disease.

Previous studies have shown a strong association of high-sensitivity troponin concentrations and cardiovascular risk among patients with acute coronary syndrome and in the general population. (39,40). However, considerable uncertainty Exists with respect to patients presenting to the emergency department with persistently high but nondynamic concentrations of high-sensitivity troponin who do not receive a diagnosis of myocardial infarction. To estimate risk among such persons,

we compared the incidence of myocardial infarction or death in the acute study population of patients in whom myocardial infarction had been ruled out with the incidence in the matched general population. In both populations, high-sensitivity troponin concentrations were strongly associated with risk of subsequent myocardial infarction or death. These data suggest that the concentration of high-sensitivity troponin may be useful as a risk-

Chapter Four: Discussion

prediction biomarker as well as a diagnostic test. Some limitations of the study merit consideration. The diagnosis of myocardial infarction, which was based on adjudication within each cohort, did not involve a harmonized standard operating procedure. In addition, our analyses included study populations that had different pretest probabilities of myocardial infarction.

This might lead to overestimation or underestimation of diagnostic probabilities in different scenarios. A large percentage of the final diagnosis adjudications within the individual studies was performed with the use of the high-sensitivity troponin T data. Consequently, the risk-probability calculation that was based on the highsensitivity troponin T data might be slightly skewed in favor of the test. High-sensitivity troponin concentrations that were determined in the general population were measured in samples that had been stored for up to two decades,

which might have affected long-term stability. However, earlier studies showed high stability even after long-term storage.(41,42).

Conclusion:

The findings of this research firmly establish a significant correlation between elevated troponin levels and the prevalence of ischemic heart diseases. The data indicates that patients suffering from ischemic conditions consistently exhibit higher concentrations of troponin, suggesting that this biomarker is a critical indicator of cardiac injury. The strong association observed underscores the importance of troponin as a diagnostic and prognostic tool, aiding clinicians in the early detection and management of ischemic heart events. Future studies may focus on refining the predictive value of troponin levels, exploring the potential for personalized treatment plans, and improving patient outcomes in the context of cardiac care.