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ORIGINAL RESEARCH

Assessment of Troponin Levels as a Biomarker of Myocardial Injury in Patients with Fatal Covid-19 for the Period 2020 to 2022: A Literature Review

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ABSTRACT

Background: COVID-19 initially described at the end of 2019. COVID-19 is caused by an uncommon coronavirus infection. Since then, it has been spreading rapidly and has caused a global pandemic, infecting more than 29 million people and causing more than 900,000 deaths as of September 15, 2020. In most cases this disease mainly affects the respiratory system and can cause a syndrome called acute respiratory distress, leading to acute respiratory failure. However, COVID-19 causes other systemic indications, such as myocardial injury, coagulopathy, and cytokine storm. Myocardial injury patients were determined by elevated troponin levels by large number of COVID-19 patients, ranging from "7.2% to 36%". COVID-19 patients may experience myocardial injury due to other complications such as arrhythmias, heart failure, or even sudden cardiac arrest, as well, COVID-19 is a complex disease that can cause severe respiratory failure. Understanding these complications is crucial for managing the disease and developing effective treatment.

Aim: This review research aims to assess the roles of troponin in COVID-19 patients at a higher risk of myocardial injury, as well as shed light on the most significant research articles conducted in this field of regard area between 2020 and 2022.

Methods and Materials: This review outlined the latest scientific research for the period from 2020 to 2022 associated with the involvement of cardiac injury in the population of COVID-19 patients by focusing on the use of troponin levels as a vital indication. Additionally, it is starting from encountered patients with COVID-19, as well as it is related to the increased risk of death data and it had a crucial role in the identification of COVID-19 with a high risk of hypoxia in the blood. At that point, it was going through the evidence regarding COVID-19 and cardiovascular biomarkers, such as troponin articles recognized using the electronic search, as performed via PubMed, Embase, and Google Scholar Database through a comprehensive search conducted by combining key terms for instance; “biomarkers”, ’’myocarditis”, “COVID-19”, “troponin”. English-language articles were screened for relevance and a full review of publications for the important studies was conducted, including additional publications which had been identified from individual article reference lists.

Conclusion: Cardiac troponin (cTn) is the most reliable test for detecting heart disease, particularly myocardial injury. Elevated levels of troponin (both cTnI and cTnT) are a critical risk factor for severe myocardial injury and hospitalizations, especially for COVID-19 patients who face a higher risk of adverse events. Therefore, measuring cTn levels is critical to monitor the progression of heart disease and effectively manage patients' care.

Keywords: COVID-19, Troponin levels, cardiac troponin, Myocardial injury.

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INTRODUCTION

Coronaviruses are a group of viruses with a single-stranded RNA enclosed in a protein envelope. They can be found in birds, humans, and other mammals like cattle, dogs, cats, and pigs. According to the World Health Organization, a new coronavirus called 2019- CoV emerged in the Chinese city of Wuhan at the end of 2019. This was a significant development (Shrikrushna etal., 2020 and Wiersinga etal., 2020). On 9 April, 1,436,198 cases were confirmed with a worldwide COVID-19 rate of almost 6% death (Wiersinga etal.,2020). This recent infection triggers respiratory disease normally mild or pneumonic in the upper respiratory tract, while most patients with COVID-19 have mild symptoms or are asymptomatic, a significant proportion of patients will experience multiple complications, potentially resulting in death (Lim etal., 2020). Biomarkers are crucial in decision-making to facilitate efficient resource allocation (Huang etal., 2020). Cardiac injury is frequently encountered in patients with COVID-19 and is associated with an increased risk of death (Nishiga etal., 2020; Shi etal., 2020 and Wang etal., 2020), as shown in Table (1). Acute Covid-19 patients associated with severe pneumonia may reveal some characteristics of so-called systemic hyper-inflammation under the overall term macrophage activation syndrome (MAS) or cytokine storm, as well as recognized secondary haemophagocytic lymphohistiocytosis (sHLH) (Shi etal., 2020; Shrikrushna etal.,2020).

Table (1): Show The Confirmed Coronavirus Disease 2019 (COVID-19) Cases, Deaths, and Deaths per 1000 Cases in the US by Age Group

Age	NO./Confirmed COVID-19 cases	NO./Deaths from COVID-19	NO./Deaths /1000
<18	116	17650	COVID-19 cases
18-29	339 125	385	0.4 b
30-39	328249	1137	1.1
40-49	325190	2804	3.5
50-64	482338	14316	8.6
65-74	185942	19520	29.7
75-84	116937	24621	105.0
≥85	98382	29999	210.5

Data are from the American Academy of Pediatrics for persons younger than 18 years and the Centers for Disease Control and Prevention for persons 18 years and older (as of June 23, 2020). in 42 states and New York City, children made up 0% to 0.6% of all COVID-19 deaths; 24 states reported no child deaths.

Coronavirus is a dangerous disease caused a severe acute respiratory syndrome (SARS), SARS-CoV-2 had specific features, as a diameter of 60 nm to 140 nm and distinct spikes ranging from 9 nm to 12 nm, giving an appearance of a solar corona (Figure 1) (Wiersinga etal., 2020).

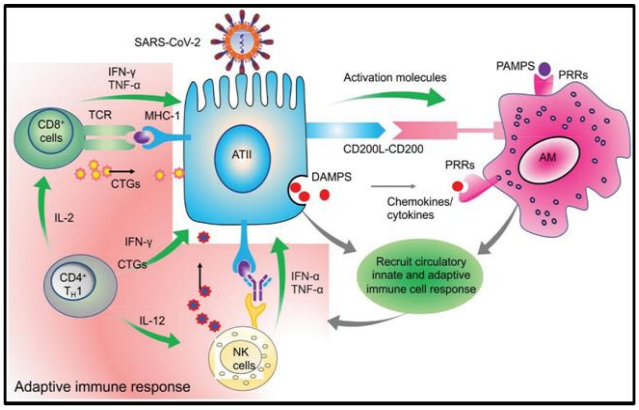

Figure 1: Immunopathogenesis of Covid-19
(Cited by: Janiuk etal., 2021)

Human Corona Viruses (HCoVs) constitute a very large group of corona viruses associated with many respiratory diseases of varying gravity, including the common cold, pneumonia and bronchiolitis (Hasan & Tuğba, 2020), moreover; the range genome of COVID-19 which from 26 to 32 kb base, and it is the largest known viral genome for viral RNA, and includes single coated, unfragmented, positive-sense RNA genomes (Geng etal., 2020; Hasan and Tuğba, 2020). Corona viruses can cause severe inflammation of the lungs and damage the digestive tract and nervous system (Xu etal., 2020). Next the first cases in China of serious coronavirus 2 respiratory syndrome, the increase of hyper inflammatory syndrome similar in patients with either a macrophage-activation or cytokine-release syndrome combined with chimeric antigen receptor T-cell therapy was demonstrated in patients with extreme signs of the COVID-19 disease (Mehta etal., 2020).

Direct Damage of SARS-CoV-2 in the Cardiovascular System

One possible mechanism for direct damage is the cytotoxic effect of SARS-CoV-2 on the endothelium which can cause diffuse microthrombosis (Chapman etal.,2020). At post-mortem evaluation, non-occlusive fibrin microthrombia (without ischemic injury) are common (12/15 patients with COVID-19) (Sandoval etal.,2020). Another potential mechanism is direct virus-induced myocardial injury and the potential for myocarditis. SARS-CoV-2 has been detected in the myocardium and, in a multicenter autopsy study, in which increased interstitial myocardial macrophages were identified in most of the cases but lymphocytic myocarditis in only a small fraction. Clinical studies of one thesis suggest that myocarditis caused by SARS-CoV-2 is uncommon (Inciardi etal.,2020). Other hypotheses for direct damage include the possibility of infection and replication of the virus within non-contractile cells in the heart such as endothelial cells, fibroblasts, and pericytes with matrix inflammation and fibrosis because coronavirus and its complications as well as the effects of this virus on all body systems (Mehta etal.,2020).

Frequency of Myocardial Injury in Patients with COVID-19

Numerous investigations in this field have employed specific criteria and thresholds to describe myocardial injury, while some have relied on non-high sensitivity cTn assays. The proportion of myocardial injury cases identified through cardiac troponin assay (hs-cTn levels surpassing the 99th percentile URL or designated thresholds) (Xiang etal., 2020). The incidence of myocardial injury varies greatly depending on the patients selected for the study. In studies of patients admitted to intensive care units (ICUs), myocardial injury occurs at a rate of 50% or more. However, studies conducted by Xiang etal., (2020) and Goyal etal., (2020), include a wider range of patients, indicate a frequency that ranges from 15% to 55%. This variation is likely due to the specific assay and/or threshold used, patient selection, and population baseline characteristics. Only a few studies have applied specific 99th percentiles, as recommended (Goyal etal.,2020).

Troponin

A troponin test is a type of blood test that measures the level of troponin, a protein found in both the skeletal and cardiac muscles, under normal circumstances, troponin is not present in the blood (Chapman etal.,2020). However, if there is any damage or impairment to the heart muscles, troponin is released into the bloodstream (Demir etal.,2021). The amount of troponin present in the blood is directly proportional to the extent of heart damage. As the level of damage increases, greater amounts of troponin are released into the blood. The troponin test is an effective way to determine the severity of heart damage (DeMichieli etal., 2022).

Biochemistry and Release Kinetics of Troponin

The troponin complex is located on the thin filament of the striated muscle contractile apparatus. It is made up of three components - troponin T (39 kD), troponin I (26 kD), and troponin C (18 kD). Each of these components is coded by a separate gene, and specific cardiac and skeletal muscle isoforms are expressed in adult cardiac and skeletal striated muscle (Demir etal.,2021). Troponins are mostly bound to the myofibrils, although 6-8% of cTnT and 2.8-4.1% of cTnI exist in the cytosol (DeMichieli etal., 2022). The release kinetics are influenced by an ischemic injury. Initially, there is a rapid release of cytosolic cTnT followed by a more prolonged release of myofibrillar troponin, resulting in a biphasic release pattern, as cTnI has a smaller cytosolic pool, the release is most likely to be monophasic. The concentrations of both markers start to increase within 4 to 8 hours following the injury and peak at 12 to 24 hours (Koerbin etal., 2010; Koerbin etal., 2012). Troponin is the most commonly used biomarker to diagnose acute myocardial injury (AMI). It consists of three subunits: Troponin T (TnT), Troponin I (TnI), and Troponin C (TnC). TnT is a tropomyosin-binding subunit, TnI is an inhibitory subunit, and TnC is the calcium-binding part of the complex (DeMichieli etal., 2022). Troponin is a protein that plays a vital role in the contraction and relaxation of striated muscles by regulating the interaction between actin and myosin, as this regulation is achieved through the effect of calcium (Demir etal.,2021). Troponin I (TnI) is a subunit of troponin that specifically inhibits the ATPase activity of actinomyosin. TnI is a polar protein with positively charged residues. The expression of TnI dependents on the developmental stage, as well both cardiac and slow skeletal types are present in the heart of human fetus's (Dong etal., 2020). Studies have shown that a nine-month-old baby has only cTnI and no slow skeletal muscle fibers (Giannitsis etal., 2020). In adults, cTnI can be detected in the bloodstream 4 to 6 hours after a heart attack, with peak levels occurring approximately 18 to 24 hours later. Increased levels may persist for up to 14 days. The automated assay for cTn-I is currently one of the most sensitive and specific methods for diagnosing a heart attack (Giannitsis etal., 2020; Yang etal., 2021). Additionally, measuring high-sensitivity CRP levels is considered one of the most reliable markers in laboratories for estimating cardiovascular risk, by way of CRP is made up of five identical and symmetrically organized promoters, each weighing 23-kDa, and is folded into two antiparallel sheets, similar to the structure of lectins (Khalid etal., 2022).

The Importance of Troponin

There is an increasing realization of the limitations of standard biochemical indicators for detecting heart damage in patients with acute coronary syndromes; therefore, there is a need to enhance the sensitivity and specificity of these indicators by searching for markers that are uniquely expressed by the myocardium (Koerbin etal., 2012). Cardiac troponins T and I (cTnT and cTnI) have been identified as superior indicators of myocardial injury, with excellent sensitivity and specificity compared to creatine kinase-MB (CK-MB) (Koerbin etal., 2010). Studies have shown that using cTnT or cTnI as a diagnostic marker, the positivity rate ranges from 20% to 48%. The incidence of death and acute myocardial infarction (MI) varies from 11% to 30% during a follow-up period of 28 months (Lala etal., 2020). These variations are mainly due to differences in the risk associated with the populations studied and the varying lengths of follow-up. Troponins are a helpful tool in diagnosing and assessing the risk of patients with acute chest pain. According to study by Lombardi and his colleagues (2020), the raised troponin concentrations can also indicate which patients may benefit from additional therapeutic measures (Demir etal.,2021).

Troponin levels as a biomarker for cardiac injury in Patients with Covid-19

Since the description of coronavirus in late 2019, COVID-19, a disease caused by severe acute respiratory syndrome-novel coronavirus 2 has become a pandemic that has infected over 29 million people and caused more than 900,000 deaths as of September 15, 2020 (Shi etal., 2020; Lala etal., 2020). Severe cases of COVID-19 are associated with acute respiratory distress syndrome, as well as systemic manifestations, such as myocardial injury, cytokine storm, and coagulopathy (Guo etal., 2020; Lala etal., 2020). COVID-19 a pandemic caused by the SARS-CoV-2 infection continues to have a severe global impact, which caused some huge lethal complications (Manocha etal., 2021). Since the earliest reports from China, it has been clear that cardiac involvement is frequent in patients with COVID-19, especially in those with concomitant cardiovascular diseases (Shi etal., 2020; Lala etal., 2020). Patients with known heart failure, myocardiopathy, or serious valvular diseases may experience serious compromise to their cardiac function as a consequence of a severe infectious state. Cardiac biomarkers, such as troponin, are essential in evaluating heart damage and diagnosing cardiac involvement early on. These biomarkers can guide a possible prognosis and provide useful follow-up information. Dong etal., (2020) emphasized that the significance of cardiac biomarkers in detecting heart damage, especially in patients with pre-existing heart conditions (Connor-Schuler etal., 2020). Cardiac troponin levels tend to be higher in patients with severe infections, those admitted to intensive care units, or those who have died, as in the case of COVID-19, an increased troponin level indicates myocardial injury, which can occur due to non-ischemic myocardial processes, these processes include severe respiratory infections with hypoxia, sepsis, systemic inflammation, pulmonary thrombosis, cardiac adrenergic hyperstimulation during cytokine storm syndrome, and myocarditis (Manocha etal., 2021). The elevation of troponin in myocardial injury has been observed in 7.2% to 36% of patients with COVID-19, as this has been associated with increased mortality and is associated with adverse events and short-term mortality (Dong etal.,2020). The majority of troponin elevations seem to be due to pre-existing cardiovascular conditions and acute non-ischemic myocardial injury (Inciardi etal., 2020). Many studies in this area have used random definitions to describe myocardial injury, and others have relied on less sensitive cTn assays. Table (2), presents a variety of references based on different levels of troponin concentrations, and the incidence of myocardial injury can vary widely depending on patient selection. In studies that focus on patients admitted to intensive care units (ICUs), the frequency of myocardial injury is as high as or greater than 50% (Stefanini etal., 2020). Research studies that include a broader spectrum of patients suggest a frequency that ranges from 10% to more than 45% (Stefanini etal., 2020; Demir etal., 2021). This variation is likely due to the specific assay and/or threshold used, patient and the population baseline characteristics of the population being studied (DeMichieli etal., 2022).

AIMS OF THE STUDY

This review research aims to assess the roles of troponin in COVID-19 patients at a higher risk of myocardial injury, as well as shed light on the most significant research articles conducted in this field of regard area between 2020 and 2022..

Table 2: Summary of references regarded this review (keywords used: "biomarkers", "Myocardial Injury", "COVID-19", "troponin").

Study	Location	Population Patients with Covid-19	Age	Cardiac Troponin Assay Threshold	Frequency of Cardiovascular Diseases
Cao et al., 2020	Wuhan, China	(244) Males & Females	**A**dults	11% of COVID-19 patients had increased Troponin level (> 40 ng/mL)	High levels of Troponin had performance for severe or critical conditions in-hospital fatality (adjusted hazard ratio [95%]: 4.79).
Fan et al, 2020	Wuhan china	(353) Vary	Vary	High sensitive levels of Troponin (>34.2 pg/mL for Men >15.6 pg/mL for Women)	22.4%
Chen et al., 2020	Wuhan china	(726) Vary	Vary	> 28 ng/mL	37.4% in critical patients 10.4% in severe patients
He et al, 2020	Wuhan china	(1031) Vary	Vary	Increased up to 99%	20.7%
Singh et al., 2020	Chicago USA	(276) Vary	Vary	17 ng/L (median in their population)	48%
Raad et al., 2020	Southeast Michigan, USA	(1020) Vary	Vary	> 18 ng/mL	38%
Manocha et al., 2020	USA	(1053) Males & Females	Median age (65) years	High level > 0.34 ng/mL	Hypoxia After 30-day mortality about 43.7%
Inciardi et al., 2020	Brescia, Italy	(99)	Vary	> 14 ng/mL	71% patients with cardiac disease 47% without cardiac disease
Arcari et al., 2020	Rome, Italy	(111) Vary	Vary	< 14 pg/mL < 35 pg/mL	38%
Zaninotto et al., 2020	Padova, Italy	(113) Vary	Vary	>16 ng/L for women >34 ng/L for men	45%
Cecconi et al., 2020	Milano, Italy	(239) Vary	Vary	>19.8 ng/L	27.7% overall
Ferrante et al., 2020	Milano. Italy	(332) Vary	Vary	>20 ng/L	37%
Ghio et al., 2020	Pavia, Italy	(405) Vary	Vary	Increased up to 99%	22%
Lombardi et al., 2020	Italy, Multicenter	(614) Vary	Vary	Increased up to 99%	45%

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Study	Location	Population Patients with Covid-19	Age	Cardiac Troponin Assay Threshold	Frequency of Cardiovascular Diseases
Karbalai Saleh et al., 2020	Tehran, Iran	(386) Vary	Vary	>11 ng/L for women >26 ng/mL for men	29.8%
Heberto et al., 2020	Mexico	(254) Vary	Vary	>17.5 ng/L	28.7%
Khalid et al., 2020	Iraq	(45) Included Males & Females	Adults 60 years' old Males & Females	Mean rank 51.66 ng/L	The elevated Troponin I had many more cardiac comorbidities and showed a higher risk of death, both during the time from symptoms onset and admission to the endpoint. (survival patients to be 2.55% (4.73)(mg/L), while for non-survivor was 40.75% (652.83) (mg/L) with P-value < 0.001).
Metkus et al., 2021	Baltimore, USA	(243) Vary	Vary	> 99 ng/L	51%
Chehab et al., 2021	Detroit, USA	(270) Vary	Vary	100 ng/L	32.6%
De Michieli etal,27 2021	USA, multicenter	(367) Vary	Vary	>10 ng/L for women ,>15 ng/L for men	46%
Poterucha et al., 2021	New York, USA	(887) Vary	Vary	>20 ng/L	43%
Demir et al., 2021	London, UK	(176) Vary	Vary	> 14 ng/mL	56%
Larcher et al., 2021	France	(111) Vary	Vary	> 14 ng/mL	55%
Myhre et al., 2021	Akershus University Hospital Norway	(123) Vary	Vary	>10 ng/L for women, >15 ng/L for men	42% with viremia 33% without
Perrone et al., 2021	Italy, multicentric	(543) Vary	Vary	>14 ng/L	46%
de Falco et al., 2021	Naples, Italy	(174) Vary	Vary	16 ng/L for women, 34 ng/L for men	**15**%
Cipriani et al., 2021	Padova, Italy	(109) Vary	Vary	16 ng/L for women 34 ng/L for men	38%

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Study	Location	Population Patients with Covid-19	Age	Cardiac Troponin Assay Threshold	Frequency of Cardiovascular Diseases
De Michieli et al., 2021	Padova, Italy	(426) Vary	Vary	16 ng/L for women 34 ng/L for men	27.2%
Peiro` et al., 2021	Tarragona, Spain	(196) Vary	Vary	>21 ng/L	39.3%
Guadianne-Romualo et al., 2021	Spain	(1,280) Males	Median age (67) years	Increased up to 99%	Myocardial Injury
Bieber et al., 2021	Munich, Germany	(32) Vary	Vary	>14 ng/L	**55**%
Ozer et al., 2021	Turkey	(73) Vary	Vary	>11.5 ng/L	39.7%
Barman et al., 2021	Turkey	(607) Vary	Vary	>14 pg/mL	24.7%
Salbach et al., 2021	Heildeberg, Germany	(104) Vary	Vary	>14 pg/mL	44.2%
Khalid et al., 2022	Iraq	(45) Included Males & Females	Adults (18–60) years old	0.4635 ng/mL	(Myocardial Injury) 13% mortality rate during hospitalization.
Ali et al., 2022	Iraq	(132) Included Males & Females	Adults (50-60) Males & Females	0.7782 ng/L	Troponin levels were significantly high caused myocardial injury and have been correlated positively with mortality

DISCUSSION:

A search was conducted on PubMed, Embase, and Google Scholar to identify relevant research on troponin levels in individuals with COVID-19 were done. The initial search resulted in a total of retrieved journal articles that focused on the outcomes of troponin levels in COVID-19 patients (Karin etal., 2020 and Sandoval etal., 2020). Overall, one of the causes of myocardial injury in COVID-19 patients is direct damage of SARS-CoV-2 in the cardiovascular system due to COVID-19 infection is linked to myocardial injury and other forms of cardiac involvement, such as heart failure with reduced ejection fraction and arrhythmias. One possible mechanism of this direct damage is the cytotoxic effect of SARS-CoV-2 on the endothelium, which can lead to diffuse microthrombosis Dong etal., (2020) and Zeng etal., (2020b). It has been found that nonexclusive fibrin microthrombi, without ischemic injury, are common in 12 out of 15 patients with COVID-19 at post-mortem evaluation (Lim etal., 2020). Additionally, direct virus-induced myocardial injury and potential myocarditis are other possible mechanisms (Han etal., 2020). SARS-CoV-2 has been detected in the myocardium and an autopsy study has found increased interstitial myocardial macrophages in most cases, but only a small fraction showed lymphocytic myocarditis. Several hypotheses suggest direct damage to the heart due to COVID-19 infection. One possibility is the virus infecting and replicating within non-contractile cells in the heart, including endothelial cells, fibroblasts, and pericytes, as this can lead to inflammation and fibrosis in the heart's matrix (Gong etal.,2020). These mechanisms

contribute to the damage caused by COVID-19 infection to the heart (Nishiga etal., 2020). There is a possibility that SARS-CoV-19 can directly damage the cardiovascular system by causing diffuse microthrombosis, at which may happen due to the cytotoxic effect of the virus on the endothelium (Nishiga etal.,2020; Shi etal.,2020).

In post-mortem evaluation, it has been found that non-occlusive fibrin microthrombia (without ischemic injury) is common in patients with COVID-19, with 12 out of 15 patients showing such symptoms (Lim etal.,2020). It has been suggested that SARS-CoV-2, the virus that causes COVID-19, may directly injure the heart and lead to myocarditis, which is inflammation of the heart muscle (Han etal.,2020). The virus has been found in the myocardium, which is the heart muscle tissue, and an autopsy study found increased levels of macrophages in the myocardium in most cases, but only a small number had lymphocytic myocarditis however; clinical studies suggest that myocarditis caused by SARS-CoV-2 is uncommon (Basso etal.,2020).

Several hypotheses suggest direct damage caused by COVID-19 to the heart. One possibility is that the virus may infect and replicate within non-contractile cells in the heart such as endothelial cells, fibroblasts, and pericytes, leading to matrix inflammation and fibrosis (Dong etal.,2020). SARS-CoV-2 may have non-direct effects on the cardiovascular system, which could be related to the downregulation or shedding of angiotensin-converting enzyme 2 (ACE2), resulting in subsequent hyperactivity (Basso etal.,2020 and Dong etal.,2020). Furthermore, SARS-CoV-2 can activate a cascade of thrombotic mechanisms through hyperactivated monocytes, platelets, and neutrophils generating neutrophil extracellular traps (NETs), as the hypercoagulation with diffuse microthrombia is considered the main cause of organ failure in severe cases (Calvo-Fernández etal., 2020).

Additionally, when there is a sudden injury to the heart muscle, a dynamic rise and/or fall pattern of cTn concentrations is observed, in which at least one cTn concentration is found to be above the 99th percentile, and there are signs and/or symptoms of acute myocardial ischemia, then a diagnosis of MI is made, as well as the increased sensitivity of hs-cTn assays, myocardial injury is detected far more frequently in various clinical situations not related to myocardial ischemia than in those with MI (Musher and Abers, 2019). Clinicians often face difficulties in identifying the specific reasons behind hs-cTn elevations, as it can occur in critical patients with COVID-19 infections can lead to changes in myocardial oxygen consumption, which can contribute to ischemia (Musher and Abers, 2019; Chapman etal.,2020).

Moreover, COVID-19 is also associated with other conditions such as pulmonary embolism (PE), myocarditis, critical illness, and direct effects of SARS-CoV-2 on the myocardium and possibly the microvasculature, as all these factors can make it challenging for clinicians to determine a discrete etiology of hs-cTn elevation (Chapman etal., 2020). Yet, the exact reason behind the rise of cTn levels in COVID-19 patients is not fully understood, thus the underlying cause of this phenomenon is believed to be an inflammatory response, as many critical COVID-19 patients show this symptom (Piccioni etal.,2020).

According to a recent review by Chapman etal., (2020), the levels of troponin in COVID-19 patients decreased to 220 ng/L after a week and 21 ng/L after three weeks, as the review also confirmed that the elevation of troponin in COVID-19 patients is probably due to multiple factors rather than a direct result of coronary atherosclerosis. Troponin has been used as a cardiac biomarker for diagnosis and risk stratification of patients with suspected acute coronary syndrome (ACS), as the blood levels of high sensitivity CRP (hs CRP) have been used to assess the risk of CVD, heart attack, and stroke (Bardají etal.,2021).

Currently, the biomarkers that have been discovered do not make a significant difference in distinguishing between the status of a person's health and disease, as there are still considerable challenges that scientists and clinicians face in finding new biomarkers that can help predict the risk of cardiovascular disease (CVD), track the progression of the disease, and potentially be used as targets for treatment before any clinical signs or symptoms appear (Chapman etal.,2020).

In previous research, high levels of hs-cTnI were linked to a poor prognosis (Piccioni etal.,2020). When heart muscle cells are damaged, troponin and creatine kinase leak out of the heart and into the bloodstream, causing elevated troponin levels and these high levels may indicate myocardial damage and predict mortality (Brigida etal., (2020). Though, it is still unknown how troponin performs as a prognostic marker and whether its value is affected by comorbidities that may be present in COVID-19 patients (Chapman etal., 2020; DeMichieli etal., 2021). Cardiac troponin (cTn) is the most reliable test for detecting heart disease, particularly myocardial injury. Elevated levels of troponin (both cTnI and cTnT) are a critical risk factor for severe myocardial injury and hospitalizations, especially for COVID-19 patients who face a higher risk of adverse events. Hence, measuring cTn levels is critical to monitor the progression of heart disease and effectively manage patients' care.

Essentially, in most studies involving COVID-19 patients, an elevated level of troponin I. It has been consistently linked with uncontrolled inflammation caused by cytokine storms and increased mortality rates, though increased troponin levels have been observed in most COVID-19 patients. Thus we have proposed further studies and continuous monitoring of troponin levels are required to confirm the essential role that play by high troponin levels in causing cardiovascular disease, which may lead to the death of patients.

CONCLUSIONS:

Cardiac troponin (cTn) is the most reliable test for detecting heart disease, particularly myocardial injury. Elevated levels of troponin (both cTnI and cTnT) are a critical risk factor for severe myocardial injury and hospitalizations, especially for COVID-19 patients who face a higher risk of adverse events. Therefore, measuring cTn levels is critical to monitor the progression of heart disease and effectively manage patients' care.

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REFERENCES:

Bardají A, Carrasquer A, Sánchez-Giménez R, et al. (2021): Prognostic implications of myocardial injury in patients with and without COVID-19 infection treated in a university hospital. Rev Esp Cardiol.; 74:24-32.

Basso C, Leone O, Rizzo S, De Gaspari M, Allard C and Stone JR. (2020): Pathological features of COVID-19-associated myocardial injury: a multicentre cardiovascular pathology study. European Heart Journal; (41): 3827-3835.

Brigida Loria V, Zanza C, Longhitano Y, and Candelli M. (2020): Role of troponin in COVID-19 pandemic: a review of literature. European Medical and Pharmacological Sciences; 24: 10293-10300.

Calvo-Fernández A, Izquierdo A, Subirana I, et al. (2020): Markers of myocardial injury in the prediction of short-term COVID-19 prognosis. Rev Esp Cardiol (Engl Ed).; 29:1885-5857.

Chapman AR, Bularga A, Mills NL. (2020): High-sensitivity cardiac troponin can be an ally in the fight against COVID-19. Circulation; 141:1733-1735.

Connor-Schuler R, Wong AI, Shah A, Fiza B, Lyle M, Ramonell R, etal. (2020): Experience with cardiology-oriented outcomes in critically ill patients

with coronavirus disease 2019. Crit Care Explor.; 2: e0288.

DeMichieli L, Jaffe AS, and Sandova Y, Clin MC. (2022): Use and prognostic implications of cardiac troponin in COVID-19. M Cardiol Clin.; 40: 287-300.

DeMichieli L, Ola O, Knott JD, Akula A and Mehta RA. (2021): High- Sensitivity Cardiac Troponin T for the Detection of Myocardial Injury and Risk Stratification in COVID-19. Clinical Chemistry; 67(8): 1080–1089.

Demir OM, Ryan C, and Ciril C. (2021): Impact and Determinants of High-Sensitivity Cardiac Troponin-T Concentration in Patients with COVID-19 Admitted to Critical Care. Am J Cardiol.; 147: 129−136.

Dong N, Cai J, Zhou Y, Liu J, Li F. (2020): End-stage heart failure with COVID-19: Strong evidence of myocardial injury by 2019-nCoV. JACC. Heart Fail.; 8: 515-517.

Gaze DC. (2020): Clinical utility of cardiac troponin measurement in COVID-19 infection. Ann Clin Biochem.; 57: 202-205.

Geng L, Yaohua F, Yanni L, Tiantian H, Zonghui L, Peiwen Z, Pan P, Wenbiao W, Dingwen H, Xiaohong L, Qiwei Z & Jianguo W. (2020): Coronavirus infections and immune responses. J Med Viral.; 92: 424-432.

Giannitsis E, Mueller-Hennessen M, Zeller T, etal. (2020): Gender specific reference values for high-sensitivity cardiac troponin T and I in well-phenotyped healthy individuals and validity of high sensitivity assay designation. Clin Biochem.; 78:18-24.

Goyal P, Choi JJ, Pinheiro LC, Schenck EJ, Chen R, Jabri A, Satlin MJ, Campion TR Jr, Nahid M, Ringel JB, et al. (2020): Clinical characteristics of Covid-19 in New York City. N Engl J Med.; 382: 2372–2374.

Guo T, Fan Y, Chen M, Wu X, Zhang L, He T, Wang H, Wan J, Wang X, Lu Z. (2020): Cardiovascular Implications of Fatal Outcomes of Patients with Coronavirus Disease 2019 (COVID-19). JAMA Cardiol.; 5:811-818.

Han H, Xie L, Liu R, Yang J, Liu F, Wu K, Chen L, Hou W, Feng Y, Zhu C. (2020): Analysis of heart injury laboratory parameters in 273 COVID-19 patients in one hospital in Wuhan, China. J Med Virol.; 92: 819-823.

Hasan T, & Tuğba B. (2020): Novel coronavirus disease (COVID-19) in children. Turk. J. Med Sci.; 50(3), p592–603.

Huang I, Lim MA, Pranata R. (2020): Diabetes mellitus is associated with increased mortality and severity of disease in COVID-19 pneumonia-a systematic review, meta-analysis, and meta-regression: diabetes and COVID-19. Diabetes Metab Syndr Clin Res Rev.; 14:395–403.

Imai Y, Kuba K, & Neely GG, etal. (2018): Identification of Oxidative Stress and Toll-Like Receptor 4 Signaling as a Key Pathway of Acute Lung Injury. Cell; 133, p235-249.

Inciardi RM, Lupi L, Zaccone G, Italia L, Raffo M, Tomasoni D, Cani DS, Cerini M, Farina D, Gavazzi E, etal. (2020): Cardiac involvement in a patient with coronavirus disease 2019 (COVID-19). JAMA Cardiol.; 5:819–824.

Janiuk K, Jabłonska E and Garley M. (2021): Review Significance of NETs Formation in COVID-19. Cells; 10(1): 151.

Karin KK, Kindermann I, Brucato A, De Rosa FG, Adler Y, and De Ferrar GM. (2020): COVID-19 pandemic and troponin: indirect myocardial injury, myocardial inflammation or myocarditis (Review). Heart.; 106(15):1127-1131.

Khalid SS, Ali ZM, and Raheem MF. (2022): Serum Levels of Homocysteine, Troponin-I, and High Sensitive C-Reactive Protein in Iraqi COVID-19 Patients. J Contemp Med Sci.; 8(3): 189–193.

Koerbin G, Tate JR, Hickman PE. (2010): Analytical characteristics of the Roche highly sensitive troponin T assay and its application to a cardio-healthy population. Ann Clin Biochem.; 47:524-528. 25.

Koerbin G, Tate J, Potter JM, Cavanaugh J, Glasgow N, Hickman PE. (2012): Characterisation of a highly sensitive troponin I assay and its application to a cardio-healthy population. Clin Chem Lab Med.; 50:871-878.

Lala A, Johnson KW, Januzzi JL, Russak AJ, Paranjpe I, Richter F, Zhao S, Somani S, Van Vleck T, Vaid A, et al. (2020): Prevalence and impact of myocardial injury in patients hospitalized with COVID-19 infection. J Am Coll Cardiol.; 76: 533-546.

Lim MA, Pranata R, Huang I, Yonas E, Soeroto AY, Supriyadi R. (2020): Multiorgan failure with emphasis on acute kidney injury and severity of COVID-19: systematic review and meta-analysis. Can J Kidney Health Dis.; 7:205-435.

Lombardi C.M., Carubelli V., Iorio A., Inciardi R.M., Bellasi A., Canale C. (2020): Association of troponin levels with mortality in Italian patients hospitalized with coronavirus disease 2010: results of a multicenter study. JAMA Cardiol.; 5: 1274–1280.

Lorente-Ros A, Monteagudo Ruiz JM, Rincón LM, et al. (2020): Myocardial injury determination improves risk stratification and predicts mortality in COVID-19 patients. Cardiol J.; 27: 489-496.

Manocha KK, Kirzner J, Ying X, Yeo I, Peltzer B, Ang B, Li HA, Lerman BB, Safford MM, Goyal P, Cheung JW. (2021): Troponin and other Biomarker Levels and outcomes among patients hospitalized with COVID-19: derivation and validation of the HA2T2 COVID-19 Mortality Risk Score. J Am Heart Assoc.; 16: 10(6): e018477.

Mehta P, McAuley DF, Brown M, Sanchez E, Tattersall RS, Manson JJ; Hlh (2020): Across Speciality Collaboration UK. COVID-19: consider cytokine storm syndromes and immunosuppression. Lancet.; 395:1033–1034.

Musher DM and Abers MS. (2019): Corrales-Medina VF. Acute infection and myocardial infarction. N Engl J Med.; 380(2):171–6.

Nahid M, Ringel JB, etal. (2020): Clinical characteristics of Covid-19 in New York City. N Engl J Med.; 382:2372–2374.

Nishiga M, Wang DW, Han Y, Lewis DB, Wu JC. (2020): COVID-19 and cardiovascular disease: from basic mechanisms to clinical perspectives. Nat Rev Cardiol.; 17:543–58.

Piccioni A, Brigida M, Loria V, Zanza C, Longhitano Y, et al., (2020): Role of troponin in COVID-19 pandemic: a review of literature. European Review for Medical and Pharmacological Sciences; 24: 10293-10300.

Sandoval Y, James L. Januzzi JR, and Jaff AS. (2020): Cardiac Troponin for Assessment of Myocardial Injury in COVID-19 JACC: Review Topic of the Week. Journal of The American College of Cardiology; 76(10): 1244-1258.

Shi S, Qin M, Shen B, Cai Y, Liu T, Yang F, Gong W, Liu X, Liang J, Zhao Q, et al. (2020): Association of cardiac injury with mortality in hospitalized patients with COVID-19 in Wuhan, China. JAMA Cardiol.; 41: 2070-2079.

Shrikrushna SU, Quazi BA, Shubham S, Suraj T, Shreya W, Rohit B, Suraj S & Biyani KR. (2020): A review on Corona Virus (COVID-19). World Journal of Pharmaceutical and Life Sciences; 6 (4): 109-115.

Stefanini GG, Chiarito M, Ferrante G, et al. (2020): Early detection of elevated cardiac biomarkers to optimise risk stratification in patients with COVID-19. Heart.; 106: 1512-1518.

Wang LX, Yan S, Yang F, Xiang L, Zhu J, Shen B, Gong Z. (2020): Clinical characteristics of 25 death cases with COVID-19: a retrospective review of medical records in a single medical center, Wuhan, China. Int J Infect Dis.; 94: 128-132.

Wiersinga WJ, Rhodes A, Cheng AC, Peacock SJ and Prescott HC. (2020): Pathophysiology, Transmission, Diagnosis, and Treatment of Coronavirus Disease 2019 (COVID-19). JAMA.; 324 (8): 782-79.

Wu AHB, Christenson RH, Greene DN, et al. (2018): Clinical Laboratory Practice Recommendations for the Use of Cardiac Troponin in Acute Coronary Syndrome: Expert Opinion from the Academy of the American Association for Clinical Chemistry and the Task Force on Clinical Applications of Cardiac Bio-Markers of the International Federation of Clinical Chemistry and Laboratory Medicine. Clin Chem.; 64:645-655.

Xiang H, Lei Z, Qin R, Junyi W, Anying X, Dehong W, Feng C, & Guoping L. (2020): Integrative Bioinformatics Analysis Provides Insight into the Molecular Mechanisms of 2019-nCoV. BMJ.; 26: 1-14.

Xu X, Chen P, & Wang J, et al. (2020): Evolution of the Novel Corona Virus from the Ongoing Wuhan Outbreak and Modeling of its Spike Protein for Risk of Human Transmission. Sci China Life Sci.; 63: 457-460.

Yang LS, Liu S, Liu J, Zhang Z, et al (2020): COVID-19: Immunopathogenesis and Immunotherapeutic. Signal Transduction & Targeted Therapy; 5(128):1-8.

Yang HS, Shemesh A, Li J, et al. (2021): No increase in the incidence of cardiac troponin I concentration above the 99th percentile by Siemens Centaur high-sensitivity compared to the contemporary assay. Clin Biochem.; 89 :77-80.

Zeng F, Huang Y, Guo Y, Yin M, Chen X, Xiao L, Deng G. (2020a): Association of inflammatory markers with the severity of COVID-19: a meta-analysis. Int J Infect Dis.; 96:467–474.

Zeng JH, Liu YX, Yuan J, Wang FX, Wu WB, Li JX, Wang LF, Gao H, Wang Y, Dong CF, Li YJ, Xie XJ, Feng C, Liu L. (2020b): First case of COVID-19 complicated with fulminant myocarditis: a case report and insights. Infection Apr 10: 1–5. doi:10.1007/ s15010-020-01424-5. Pub ahead of print.

Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, Xiang J, Wang Y, Song B, Gu X, Guan L, Wei Y, Li H, Wu X, Xu J, Tu S, Zhang Y, Chen H, & Cao B. (2020a): Clinical Course and Risk Factors for Mortality of Adult in Patients with COVID-19 in Wuhan, China: A Retrospective Cohort Study. Lancet.; 395, p1054– 1062.

Zhou P, Yang X-L, Wang X-G, et al. (2020b): A pneumonia outbreak associated with a new coronavirus of probable bat origin. Nature.; 579 :270-273.