AN APPROACH TO ELEVATED TROPONIN LEVELS DUE TO CAUSES OTHER THAN OCCLUSION MYOCARDIAL INFARCTION IN EMERGENCY SITUATIONS

Abstract

Introduction:

Troponin plays a crucial role in evaluating acute coronary syndrome (ACS) and occlusion myocardial infarction (OMI). However, it is important to note that troponin levels can also be elevated in conditions other than OMI.

Objective:

This narrative review aims to provide emergency clinicians with a comprehensive understanding of troponin elevation in patients who have a myocardial injury caused by conditions other than OMI.

Discussion:

ACS involves the diagnosis of myocardial infarction (MI), which includes assessing troponin levels. Troponin I and T are commonly used biomarkers to evaluate the myocardial injury, and their elevation can occur due to myocyte injury and necrosis, myocyte apoptosis and cell turnover, as well as oxygen supply-demand mismatch. Troponin elevation indicates myocardial injury and can be observed in various critical illnesses, both cardiac and non-cardiac. Cardiac conditions such as heart failure, dysrhythmia, and dissection, as well as non-cardiac causes like pulmonary embolism, sepsis, and stroke, among others, can lead to troponin elevation. When evaluating patients with elevated troponin, clinicians should consider the clinical context, patient symptoms, electrocardiogram, and ultrasound findings. In most cases, elevated troponin levels are associated with poor outcomes, including higher mortality rates.

Conclusions:

Troponin elevation can occur in numerous critical situations, stemming from both cardiac and non-cardiac conditions. It is crucial for clinicians to carefully consider the clinical context and other relevant factors to avoid an inappropriate diagnosis of OMI, which could potentially harm the patient and result in the misdiagnosis of another condition.

INTRODUCTION

Troponin plays a vital role in emergency medicine evaluations, particularly in assessing various conditions, with acute coronary syndrome (ACS) being the most common. ACS encompasses myocardial infarction (MI), and the diagnosis of MI relies on elevated levels of cardiac troponin, which is generally considered the standard biomarker for diagnosing acute MI [1-3]. However, it is important to note that troponin is a marker of myocardial injury and is not specific to coronary ischemia caused by acute MI [1,4-12]. Incorrectly diagnosing another condition associated with troponin elevation can increase the risk of bleeding due to unnecessary anticoagulation, expose patients to potential risks from cardiac catheterization and stenting, and interfere with other important procedures [4,9,10].

With the increased utilization of troponin and improved assay sensitivity, elevated troponin levels are frequently observed in diseases other than acute MI [11,12]. One study even found an alternative condition in up to 45% of patients with elevated troponin [13]. Therefore, troponin is more accurately described as organ-specific rather than disease-specific. This review focuses on the evaluation of elevated troponin in emergency medicine, discussing both cardiac and non-cardiac causes, followed by an approach to the diagnostic workup for patients with troponin elevation.

1.1. Cardiac Troponins

Troponins are essential proteins involved in the regulation of both cardiac and skeletal muscle contraction [1,5-9]. The cardiac troponin complex, consisting of troponin C, troponin I (TnI), and troponin T (TnT), differs in structure from the skeletal troponin isoforms. Troponin C binds to calcium ions, TnI binds to actin and inhibits the interaction between actin and myosin, and TnT binds to tropomyosin and aids in contraction [1,5-9,14,15]. These proteins are organized within sarcomeres. In addition to their presence in sarcomeres, cardiac troponins can also be found in the cytosol of myocytes, where they can freely exchange with sarcomere troponins [1,4-8]. TnI and TnT are the primary biomarkers used in current clinical practice [1-3]. Although there are slight differences between TnI and TnT, their interpretation in clinical use is similar [1]. Conventional troponin assays can detect troponin elevation within 2-3 hours of injury, but high-sensitivity assays may detect elevation at an earlier stage [1]

1.2. Current Troponin Testing Methods

The fourth universal definition of myocardial infarction, published in August 2018, provides a clear framework for assessing troponin levels. It defines myocardial injury as an elevation of troponin above the 99th percentile upper reference limit, with acute injury indicated by a rise and/or fall in troponin values [1]. This updated definition encompasses both conventional and high-sensitivity troponin assays [1]. However, diagnosing acute myocardial infarction (MI) requires additional criteria beyond troponin changes.

Type I MI is characterized by intraluminal coronary plaque disruption and thrombus formation. It is diagnosed when there is a rise and/or fall in troponin levels, with at least one value exceeding the 99th percentile, accompanied by symptoms of acute MI, new electrocardiogram (ECG) changes, development of pathological Q waves on ECG, imaging evidence of new

myocardial loss or regional wall motion abnormality, or identification of a coronary thrombus through angiography [1]. Occlusion MI (OMI), including ST-segment elevation myocardial infarction (STEMI), is a subset of Type I MI and requires emergent coronary reperfusion therapy.

Type 2 MI shares similar criteria to Type 1 MI, involving troponin changes and evidence of ischemia. However, it differs in that it is caused by an imbalance between oxygen supply and demand rather than acute coronary thrombosis [1-4,12]. Type 2 MI is part of the broader category known as non-occlusion MI (NOMI). When there are no findings of myocardial ischemia despite troponin rise and/or fall, a diagnosis of myocardial injury can be made [1].

While cardiac troponins remain the standard biomarkers for assessing acute coronary syndrome (ACS) and myocardial injury, there are some differences and potential limitations in current troponin testing. Firstly, multiple generations of troponin assays exist, with each subsequent generation demonstrating increased sensitivity but potentially reduced specificity for diagnosing OMI. Contemporary assays can detect even minor levels of myocardial necrosis [1,5-8,15,16]. Additionally, different assays employ distinct calibration methods, reagents, and exhibit variations in clinical performance. Cut-off levels may also differ among assays [1-3]. Lastly, troponin autoantibodies can interfere with troponin testing, posing a potential challenge [1,17,18].

2. Materials And Methods

In this focused evaluation, the authors conducted a comprehensive literature search to explore troponin elevation in patients with myocardial injury excluding occlusion myocardial infarction (OMI). The search was performed on PubMed and Google Scholar, using relevant keywords such as "troponin," "elevation," and "increase." The search covered articles published from the inception of the databases up until September 1, 2019. Over 600 articles were found on PubMed, and the first 200 articles on Google Scholar were also reviewed.

The authors considered various types of studies, including case reports, case series, retrospective and prospective studies, systematic reviews, meta-analyses, and other narrative reviews. Additionally, they examined guidelines and supporting references cited in the included articles. The search was limited to English-language publications, with a focus on emergency medicine and critical care literature. The consensus among the authors determined the selection of studies for inclusion in this review.

Systematic reviews and meta-analyses were given priority, followed by randomized controlled trials, prospective studies, retrospective studies, case reports, and other narrative reviews in the absence of alternative data. In total, 208 articles were chosen to be included in this narrative review, providing a comprehensive analysis of the topic.

3. Results and Discussion

3.1. Mechanisms of troponin elevation

Troponin elevation is commonly caused by myocyte injury and cell death, which involves the destruction of cell membranes, increased intracellular calcium, degradation of cardiac troponin complexes, and subsequent release of these complexes into the bloodstream. However, there are other mechanisms of troponin elevation that do not involve cell death [1,4-9,11]. For instance, increased myocyte membrane permeability and the normal breakdown of troponin into smaller fragments can allow troponin to enter the systemic circulation, even in the absence of myocyte necrosis [15,19]. This mechanism of troponin elevation can occur in inflammatory conditions such as sepsis [4-9]. Additionally, normal turnover of myocardial cells, including apoptosis and the release of membranous blebs, can lead to troponin release [5-7,11].

Demand ischemia refers to an imbalance between myocardial oxygen demand and supply, typically seen in the context of critical illness without significant obstruction in the coronary vasculature [1-3,12,14]. Various factors contribute to this imbalance, including reduced myocardial perfusion, microvascular dysfunction, myocardial depression, dysrhythmias, and increased systemic oxygen requirements related to an underlying condition [1,5-12]. Ultimately, increased myocardial oxygen demand and decreased oxygen delivery to the myocardium result in myocardial injury and troponin release.

The term "false-positive" is occasionally used to describe elevated troponin levels in patients without significant coronary disease, which can rarely be attributed to laboratory errors [20-23]. Several laboratory-related factors can cause false-positive troponin results, such as heterophilic antibodies, fibrin clot formation, microparticles, or analyzer malfunctions [21-23]. However, it is important to note that laboratory errors are uncommon causes of elevated troponin, and clinicians should consider potentially life-threatening conditions before assuming a laboratory error. In the setting of critical illness, troponin elevation most likely reflects myocardial injury [1,4]. This elevation serves as a prognostic factor for increased mortality, morbidity, and hospital stay duration in various clinical scenarios [1,4,9,10]. Table 1 illustrates some of the etiologies associated with troponin elevation [4-12,24].

3.2. Causes of Troponin Elevation in Non-occlusion MI and Myocardial Injury

This narrative review will explore several common causes of troponin elevation in patients presenting to the emergency department (ED), many of which can lead to significant morbidity and mortality. However, chronic conditions associated with troponin elevation, such as left ventricular hypertrophy, chronic kidney disease, or pulmonary hypertension, will not be discussed in this review [1,4-12,24].

Occlusion MI	**Non-Occlusion MI or Myocardial Injury**
● Acute Coronary Vessel Thrombus Formation	● Acute and Chronic Heart Failure ● Acute Inflammatory Myocarditis ● Acute Noncardiac Critical Illness ● Acute Pulmonary Edema ● Acute Pulmonary Embolism ● Aortic Dissection ● Aortic Valve Disease ● Apical Ballooning Syndrome/Takotsubo cardiomyopathy, Bradyarrhythmia, ● Heart Block Cardiac contusion from trauma Cardiac surgery, ● Post-percutaneous Coronary ● Cardiotoxic Drugs ● Cardioversion ● Chronic renal failure ● Chronic Obstructive Pulmonary Disease ● Direct Myocardial Trauma ● Endocarditis/Pericarditis ● Extensive Burns

	• Hypertrophic Cardiomyopathy • Infiltrative Disease (Amyloidosis) Intervention, • Endomyocardial biopsy • Rhabdomyolysis • Sepsis • Severe Pulmonary Hypertension • Strenuous Exercise/Extreme Exertion • Stroke, • Subarachnoid hemorrhage • Tachycardia/Tachyarrhythmia

Table 1 : Causes of Troponin Elevation in Non-occlusion MI and Myocardial Injury

3.2.1. Cardiac Etiologies

3.2.1.1. Heart failure:

Both acute and chronic heart failure (HF) with left ventricular dysfunction can lead to troponin elevation, with up to 50% of patients experiencing elevated troponin levels during acute HF exacerbation [27-31]. The elevation of troponin in this context is believed to result from increased preload and myocardial strain, leading to myocardial injury [1,9,11,30]. Myocyte loss through necrosis and apoptosis occurs due to the aggravation of heart failure, regardless of the underlying cause of exacerbation [4-10,31]. The degree of troponin elevation is associated with the severity and prognosis of HF, as patients with troponin elevation during acute HF exacerbation demonstrate higher mortality rates (odds ratio [OR] 2.55), greater degrees of hypotension, reduced ejection fraction, and worse functional HF class [32].

3.2.1.2. Takotsubo cardiomyopathy:

Takotsubo cardiomyopathy, also known as stress-induced cardiomyopathy or broken heart syndrome, accounts for 0.7-2.5% of patients with the acute coronary syndrome (ACS) [1,33]. This condition primarily affects older women experiencing emotional or physiological stress, although it can rarely occur in men and younger patients as well [33-35]. The underlying pathophysiology is not fully understood but is believed to involve catecholamine-induced myocardial injury, multivessel epicardial or multivessel spasms, and focal myocardial inflammation [33,34]. Patients typically present with chest pain and/or dyspnea, and their electrocardiograms (ECGs) may show ST elevation accompanied by troponin elevation [33,36]. Acute-phase echocardiography often reveals a dyskinetic or akinetic apical and midventricular wall motion abnormality [33,36]. Troponin levels usually peak within the first 24 hours but are lower compared to patients with ST-elevation myocardial infarction (MI) [1,33].

3.2.1.3. Pericarditis and myocarditis:

Although cardiac troponin is not present in the pericardium, troponin elevation occurs in 32-49% of patients with acute pericarditis, most likely due to epicardial inflammation [1,37-39]. When pericarditis is accompanied by evidence of myocardial dysfunction on imaging or elevated troponin levels, it is referred to as myopericarditis [37,38]. Patients with myopericarditis are often male, younger, more likely to exhibit ST-segment elevation, and present with gastrointestinal symptoms and recent febrile syndrome compared to those with pericarditis alone [40]. They also have a higher incidence of dysrhythmias and reduced ejection fraction [40]. The clinical course of myopericarditis is typically self-limited, with most patients recovering without significant complications [37-40].

Myocarditis, characterized by myocardial inflammation, can result in variable troponin elevation, ranging from none to significantly elevated levels [1,41-44]. Myocarditis can lead to coronary vasomotility and vasospasm, coronary artery thrombus, cardiac ischemia, cardiomyopathy, dysrhythmias, and sudden cardiac death [41-44]. The magnitude of troponin elevation provides valuable information about the extent of myocardial injury and damage [1,41,44].

3.2.1.4. Tachycardias:

Tachycardia is a common cause of troponin elevation [1,5-9,24]. Studies have shown that up to 28% of cases with elevated troponin and normal coronary angiogram can be attributed to tachycardia [24]. Troponin elevation can occur after supraventricular tachyarrhythmias, including supraventricular tachycardia (SVT) and atrial fibrillation (AF), due to shortened diastole and increased oxygen demand leading to subendocardial ischemia [4,5,45-48]. Troponin elevation is seen in 12-48% of patients with SVT, but it is typically not associated with coronary artery disease (CAD) [24,45-49]. However, the available literature on troponin elevation in SVT is limited to case reports, series, or small cohort studies, and most recommendations advise against routine troponin assessment in SVT [49-57]. Some retrospective studies suggest that troponin elevation in SVT, particularly in patients with significant cardiac comorbidities like prior myocardial infarction (MI), heart failure (HF), AF, and CAD, may be associated with a poor outcome [57]. However, further evaluation of the data does not support this association [45-56]. Overall, troponin elevation in SVT does not demonstrate worse outcomes or an increased risk of CAD [45-56].

In patients with AF, troponin elevation is associated with an increased risk of major cardiac events such as acute coronary syndrome (ACS) and MI, as well as a greater risk of other conditions like stroke, systemic embolism, and recurrent AF [24,58-63]. A study of hospitalized AF patients found that troponin elevation was associated with an increased risk of death (hazard ratio [HR] 2.35-3.77), depending on the degree of elevation [61]. Another study including over 6,000 AF patients demonstrated that troponin elevation was associated with stroke and systemic embolism [62], while a study of stable anticoagulated AF patients found that elevated troponin was associated with an increased risk of cardiovascular events and mortality [63].

3.2.1.5. Aortic dissection:

Acute aortic dissection (AAD) involves the disruption and separation of the layers of the aortic wall, and although rare, it carries significant mortality [1,64,65]. Distinguishing AAD from occlusive myocardial infarction (OMI) is crucial, as AAD can present similarly to OMI and cause elevated troponin levels [1,4-11]. Misdiagnosis of AAD as OMI with subsequent inappropriate anticoagulation increases mortality to around 70%, often due to hemorrhagic pericardial tamponade [66-68]. Troponin may be elevated in a significant number of patients with AAD, ranging from 6% to 33% [68,69]. The elevation of troponin in AAD can occur due to OMI (in approximately 7% of AAD cases), oxygen supply-demand mismatch, systolic dysfunction, microvascular derangement, endothelial dysfunction, and concomitant stroke [1,4-11,67]. Elevated troponin in AAD is associated with up to a four-fold increase in mortality and indicates a poor prognosis [68,69].

3.2.1.6. Cardiac trauma:

Thoracic trauma accounts for 5-12% of trauma center admissions, and direct myocardial injury can occur as a significant cause of death [70-76]. Blunt cardiac injury is associated with up to 20% of deaths from motor vehicle accidents [70-74]. It can occur in 3-71% of patients with blunt chest trauma, and troponin plays a key role in its diagnosis [70-77]. The sensitivity and specificity of troponin in diagnosing blunt cardiac injury vary depending on the study and assay

used [70,72,78,79]. A negative electrocardiogram (ECG) and troponin can safely exclude blunt cardiac injury, while a positive troponin is associated with increased rates of dysrhythmias, cardiac dysfunction, and mortality [70-79].

3.2.1.7. Procedures:

Cardioversion, cardiac ablation, and defibrillation for cardiac arrest may cause troponin elevation due to direct myocardial injury and supply-demand mismatch. However, most patients undergoing cardioversion or ablation do not demonstrate troponin elevation [1,5-12,80-86]. Studies have shown conflicting results regarding troponin elevation after cardioversion, with some reporting no increase, while others found an elevation in a significant percentage of patients, particularly those with atrial fibrillation (AF) [82-84,87]. Troponin elevations, if they occur, are typically mild and resolve within 6 hours [1,85,86]. In the case of cardiac arrest and a shockable rhythm, defibrillation is more likely to cause troponin elevation, although the underlying etiology of the cardiac arrest may also contribute [1,5-11,88,89].

3.2.2. Non-cardiac Causes

Troponin elevation is observed in 12–85% of critically ill patients admitted to the intensive care unit (ICU), and it is associated with poorer outcomes and a 2.5-fold increased risk of in-hospital mortality [24,90-102]. Various conditions requiring ICU care are commonly associated with elevated troponin levels, including acute pulmonary embolism (PE), stroke, hypotension from significant hemorrhage or hypovolemia, gastrointestinal (GI) bleeding, sepsis, acute respiratory distress syndrome (ARDS), and others [1,24,90-102].

3.2.2.1. Acute pulmonary embolism:

Troponin is a crucial component for risk assessment in acute PE. Approximately 10–50% of patients with acute PE may experience elevated troponin levels, which is one of the most common causes of myocardial injury leading to troponin elevation [103-108]. Submassive PE is characterized by evidence of right ventricular dysfunction, either through imaging or biomarkers, while massive PE is defined by evidence of hemodynamic instability resulting in shock [109]. Troponin elevation in acute PE occurs due to several factors, including right ventricular strain caused by pulmonary artery resistance, hypoxemia from ventilation-perfusion mismatch, and reduced coronary blood flow leading to hypoperfusion [109-113]. Compared to troponin elevation in acute myocardial infarction (OMI), troponin elevation in PE is lower and persists for a shorter duration [1,5-11,109-113]. However, patients with acute PE and troponin levels above 0.04 ng/mL demonstrate a tenfold higher risk of adverse clinical outcomes [103-106,109-115]. One meta-analysis suggests an increased risk of short-term mortality in PE patients with elevated troponin [114], while another meta-analysis found a fourfold increased risk of death in normotensive patients with acute PE and elevated troponin levels [115].

3.2.2.2. Stroke:

Both ischemic and hemorrhagic acute stroke are associated with myocardial injury and troponin elevation [116-121]. A meta-analysis of 15 studies (n = 2901 patients) found that 18% of patients with acute ischemic or hemorrhagic stroke had elevated troponin levels, although the reported prevalence of troponin elevation varied between 0% and 35% in the included patients [117]. Other studies suggest even higher rates of elevation, ranging from 20% to 55% when using high-sensitivity troponin assays [116,118-121]. Stroke is also linked to acute cardiac dysfunction and ECG findings such as ST-segment depression and T-wave inversion [122]. Troponin elevation in the context of stroke is associated with worse patient outcomes, including stroke severity, longer hospital stays, and increased mortality [116-128]. The major causes of long-term mortality in patients with acute stroke are the extent of ischemic penumbra and concomitant coronary disease

[127,128]. Troponin elevation in acute stroke can be attributed to various factors, including excess sympathetic activity leading to an imbalance in the autonomic nervous system, intracellular calcium release, myocyte dysfunction, acute cytokine-mediated injury, endothelial dysfunction, microvascular spasm, and left ventricular systolic dysfunction [122-133]. One study found that troponin elevation is associated with a cardioembolic source of ischemic stroke [133]. However, a significant proportion of patients with ischemic stroke may have elevated troponin due to concomitant OMI, with one study reporting that 24% of patients had coronary culprit lesions resulting in troponin elevation [134]. While not all patients require revascularization, it is important for patients with ischemic stroke to receive appropriate platelet inhibition and anticoagulation, along with serial troponin assessments [5-10].

3.2.2.3. Sepsis:

Sepsis and systemic inflammatory response syndrome (SIRS) can lead to troponin elevation in a wide range of patients [90-92,100,101]. Troponin elevation is most commonly observed in patients with severe sepsis and septic shock [24,90-94,120,135,136]. Studies suggest that troponin may be elevated in over 85% of sepsis patients admitted to an ICU, and a meta-analysis of sepsis patients showed troponin elevation in over 40% of the included patients [91,94,137-140]. The variation in reported rates of elevated troponin is likely due to the different troponin assays and cut-off values used in the studies [91]. The exact pathophysiology of elevated troponin in sepsis is not fully understood. Global myocardial ischemia is believed to be the primary cause of troponin elevation, resulting from an imbalance between oxygen supply and demand, leading to reduced myocardial function and injury [4-9,24,110,136-141]. Increased oxygen demand in sepsis and SIRS occurs due to elevated metabolism, fever, and tachycardia, while oxygen supply is reduced through hypotension, microcirculatory dysfunction, respiratory failure, and anemia [5-10,136]. Other causes of myocardial injury in sepsis include cytokines, endotoxins, and reactive oxygen radicals [142,143]. Patients with elevated troponin in the setting of sepsis experience significantly worse outcomes, including higher mortality rates [90,91,137-141].

3.2.2.4. Acute respiratory distress syndrome:

ARDS is characterized by systemic and pulmonary inflammation, resulting in epithelial injury, respiratory distress, and failure [144-146]. Right ventricular strain and myocardial injury can occur due to pulmonary hypertension, and oxygen supply-demand mismatch can also lead to injury [146-153]. Mechanical ventilation can further exacerbate cardiac strain and injury by increasing intrathoracic pressures [146]. Over 50% of ARDS patients exhibit elevated troponin levels, with some studies reporting rates exceeding 90% [145-148,154]. This troponin elevation is associated with a higher risk of mortality, increased organ failure rates, and prolonged stays in the ICU and hospital [146-148,154].

3.2.2.5. End-stage renal disease:

Renal failure is associated with adverse cardiac outcomes, and the primary cause of death in patients with end-stage renal disease (ESRD) is coronary artery disease (CAD) [1,155-161]. Patients with ESRD often present in atypical ways with acute myocardial infarction (MI) [156]. Furthermore, patients with ESRD have higher rates of baseline troponin elevation, ranging from 50% to 73% [156-161]. It is a misconception that troponin elevation in ESRD is solely due to poor renal excretion. Intact troponin molecules are typically not excreted by the kidneys, and patients with renal disease have higher rates of adverse outcomes, including mortality, in the context of an acute coronary syndrome (ACS) [1,156-161]. These patients are typically evaluated with repeated troponin assessments [1,5-10]. However, patients with ESRD and elevated

troponin levels experience higher peak levels and detectable troponin for longer durations, as well as worse outcomes [1,5-10].

3.2.2.6. Chronic obstructive pulmonary disease (COPD):

COPD is a common respiratory condition that often coexists with coronary artery disease (CAD). In patients with acute exacerbations of COPD, approximately 18-38% exhibit elevated troponin levels. This elevation is attributed to factors such as increased intrathoracic pressure, worsened pulmonary hypertension, hypercapnia, and hypoxemia, leading to myocardial injury. The severity of troponin elevation in COPD exacerbations is associated with lower pulse oximetry readings, older age, greater hypercapnia, and lower serum pH. Elevated troponin in COPD exacerbations is linked to more severe exacerbation, the need for intensive care unit (ICU) care, and higher short- and long-term mortality rates.

3.2.2.7. Extreme exercise:

After strenuous exercise, such as prolonged aerobic activities like running, cardiac troponin levels can be significantly elevated. Studies indicate that troponin elevation is most commonly observed in individuals who have less training and experience in prolonged endurance events. Even 30 minutes of high-intensity exercise can result in troponin elevation. The underlying mechanism involves muscle fatigue and cardiac myocyte involvement, leading to troponin release. However, the elevation is typically mild and short-lived compared to an acute myocardial infarction (AMI), and there is little evidence of adverse patient outcomes associated with exercise-induced troponin elevation.

3.2.2.8. Toxicologic:

Ingestion or exposure to certain toxic substances can cause troponin elevation due to increased supply-demand mismatch and myocardial strain. Examples include cyanide, sympathomimetics, carbon monoxide (CO), chemotherapeutic agents, and others. Troponin elevation associated with toxic ingestion is linked to increased mortality. Cocaine intoxication, even in the absence of acute myocardial infarction, can result in troponin elevation in up to 11% of users. Carbon monoxide poisoning leads to morphological, functional, and electrical abnormalities, with a significant proportion of patients demonstrating evidence of myocardial injury. Troponin elevation and acute myocardial injury in CO toxicity are associated with higher mortality rates.

3.2.2.9. Upper gastrointestinal hemorrhage:

Approximately 20% of patients with upper gastrointestinal bleeding exhibit elevated troponin levels, primarily due to supply-demand mismatch. In patients with upper GI bleeding, troponin elevation is associated with prolonged stays in the ICU and increased mortality rates.

3.2.2.10. Burns:

Both thermal and electrical burns can result in troponin elevation due to global cardiac dysfunction and direct myocardial injury. Burns involving more than 15% of the total body surface area (TBSA) and burns in older patients are particularly associated with troponin elevation and poor patient outcomes.

3.2.2.11. Rhabdomyolysis:

Rhabdomyolysis, characterized by the breakdown of striated muscle, can lead to troponin elevation. The underlying causes of rhabdomyolysis, such as crush injury, infection, heat injury, and stress-induced injury, contribute to the elevation. While a significant number of rhabdomyolysis cases may exhibit troponin elevation (ranging from 10% to 50% of patients), troponin levels commonly normalize with appropriate treatment, including hydration.

3.2.2.12. Heat stroke:

Heat stroke, characterized by hyperthermia and neurologic dysfunction or confusion, is associated with troponin elevation and an increased risk of sudden cardiac death. A considerable proportion of patients with heat stroke demonstrate elevated troponin levels, likely due to factors such as ventricular strain, endothelial dysfunction, neural excitation, increased catecholamine activity, and supply-demand mismatch. Troponin elevation in heat stroke is associated with multiorgan failure and higher mortality rates.

3.3. Approach to NOMI and Myocardial Injury Troponin Elevation in Emergency Medicine

Given the numerous conditions that can cause troponin elevation, it is essential to have a systematic approach to further evaluation and management [1,4]. In critically ill patients, such as those with pulmonary embolism (PE), heart failure (HF), stroke, trauma, and other severe conditions, troponin elevation often indicates a more severe and fulminant disease course, leading to adverse outcomes including increased hospital stay and higher mortality rates [4-11,90-92]. The diagnostic challenge lies in differentiating acute myocardial infarction (OMI) from non-occlusive myocardial infarction (NOMI) and other myocardial injury conditions, as OMI requires emergent revascularization [1,208]. Although troponin is highly sensitive for diagnosing myocardial injury, its specificity for identifying OMI varies significantly [1,4,208]. Therefore, the clinician's pretest probability of OMI plays a crucial role in patient assessment. Ordering a troponin test in a clinically ill patient with a low suspicion of OMI may yield a positive result that does not confirm OMI but rather indicates myocardial injury.

The evaluation and management approach should consider the clinician's pretest probability and the likelihood of the diagnosis being OMI versus NOMI/myocardial injury, as well as the potential outcomes of diagnosis and available therapies, along with the risks of adverse events or complications associated with further diagnostic and therapeutic measures (Table 2) [208]. The assessment of potential troponin elevation should be conducted concurrently with or after evaluating cardiac risk factors, ischemic symptoms, and electrocardiogram (ECG) findings [4-9,208]. Patients who meet the criteria for type 1 myocardial infarction according to the 4th universal definition or those with suspicion of OMI should be treated with antiplatelet medications and undergo catheterization [1]. However, if troponin levels are elevated without other clinical findings suggestive of OMI, and another potentially dangerous condition is suspected based on the patient's history, examination, and additional studies, the focus should be on managing the underlying disease (e.g., sepsis, PE, COPD) rather than solely anchoring on the diagnosis of OMI [1-9,208]. A thorough history and examination are likely to lead to the identification of the underlying cause of troponin elevation, which may indicate a myocardial injury condition or NOMI, rather than OMI. This differentiation is critical because inappropriate coronary angiography and invasive revascularization in the context of myocardial injury or NOMI can harm the patient and lead to delays in treating the underlying condition responsible for troponin elevation.

Table 2

Differentiating Type 1 MI and Other Etiology Resulting in Troponin Elevation

Consideration	OMI	Myocardial Injury Condition or NOMI
Situation	Presentation suggestive of OMI	Presentation suggestive of non-cardiac pathology or NOMI

Presence of acute, clinical stressor	Usually none or low, other than acute OMI	Severe physiologic stress from underlying etiology and patient hemodynamics (ie, septic shock, PE, toxic ingestion, etc.)
ECG	Suggests acute OMI	Nonspecific or minimal ECG changes, which usually resolve with treatment of the underlying disease
Echocardiogram	Suggests acute OMI with focal wall motion abnormality	Demonstrates hyperkinetic cardiac function, but may demonstrate findings of another etiology (RV dilation in PE)
Troponin elevation	Typically more significant troponin elevation (ie, Troponin I N 10 ng/mL)	Typically more moderate troponin elevation (b 10 ng/mL); however, a severe fixed lesion can result in significant troponin elevation

There is limited available data on the management of patients with demand ischemia associated with a critical illness. The primary focus should be on treating the underlying disease process. Administering aspirin, if there are no contraindications, is a reasonable approach. Other forms of anticoagulation, such as heparin, should be avoided. Hemodynamic optimization is crucial, including ensuring the appropriate intravascular fluid status and attempting to reduce beta-agonist stimulation if possible.

Patients presenting with ischemic symptoms but with findings indicating another condition can be challenging to diagnose. The symptoms may be due to myocardial infarction (OMI) complicated by another dangerous condition or a supply-demand mismatch. Patients with preexisting coronary artery disease (CAD) are more susceptible to oxygen supply-demand mismatch with a lower threshold for myocardial ischemia. It is recommended to reassess patients with a detailed history, physical examination, and serial electrocardiograms (ECGs) while treating the suspected myocardial injury condition. For example, a patient experiencing severe gastrointestinal bleeding may also have chest pain and ECG findings of ischemia. If resuscitation leads to the resolution of symptoms and ECG changes, it is likely that the gastrointestinal bleeding was the cause of myocardial injury. However, if the patient is resuscitated, the GI hemorrhage is treated, but ischemic symptoms and ECG changes persist, further evaluation for OMI is recommended.

Point-of-care ultrasound (POCUS) can be helpful in differentiating OMI from other myocardial injury conditions. The degree of troponin elevation is associated with an increased likelihood of abnormalities on POCUS. An echocardiogram showing a focal wall motion abnormality with a significant increase in troponin is diagnostic of OMI. POCUS with no focal myocardial wall motion abnormality suggests a diagnosis other than OMI, and POCUS demonstrating

hyperkinesis indicates physiologic compensation. POCUS can also reveal findings suggestive of other conditions such as pulmonary embolism (PE) or aortic dissection.

Regarding patient disposition, considering admission to a monitored setting is recommended for those with troponin elevation, as they have higher morbidity and mortality rates. Patients with troponin elevation due to supraventricular tachycardia (SVT) or extreme exercise may be suitable for discharge. However, troponin elevation in the presence of other conditions such as heart failure (HF), PE, chronic obstructive pulmonary disease (COPD), and sepsis is associated with a higher risk of adverse outcomes, and these patients should be admitted to a monitored setting. Critically ill patients may require intensive care unit (ICU) care.

Conclusion:

In conclusion, troponin is a cardiac biomarker used in the evaluation of acute coronary syndrome (ACS) and the diagnosis of OMI. Troponin I and T may be released in various cardiac and non-cardiac conditions, including myocyte injury, necrosis, apoptosis, cell turnover, and oxygen supply-demand mismatch. Therefore, troponin is indicative of myocardial injury rather than exclusively OMI. Many critically ill patients exhibit troponin elevation, which is generally associated with increased mortality and hospital stay. Clinicians should rely on their clinical assessment and ECG findings to evaluate the patient and focus on treating the underlying cause of troponin elevation, rather than solely focusing on the diagnosis of OMI.

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