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Case Report

The Role of Troponin I in the Evaluation of Chest Pain in Children and Adolescents

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Abstract

Although cardiac chest pain is rare in children and adolescents, it is a frequent cause of emergency visits in this population. They are often managed similar to adults. This commonly leads to unnecessary investigations and hospital admissions. Troponin I is one of the commonly ordered biomarkers of myocardial injury. However, its diagnostic value is debatable in the younger population. This article reviews the different causes of chest pain in pediatric and adolescents and the role of troponin I in different conditions.

Keywords: *Troponin I; Chest Pain; Children and Adolescents*

Introduction

Chest pain is a frequent symptom in children and adolescents and is one of the most common causes of emergency room (ER) visits in this population with about 650,000 physician visits each year. Musculoskeletal causes and asthma account for the majority of cases while cardiac causes are actually extremely rare, accounting for < 1 % [1,2]. However, these patients are commonly evaluated by ER physicians who may not be familiar with pediatric patients and accordingly manage them like adult patients with chest pain. This often results in unnecessary testing and subsequent hospital admissions. We frequently encounter children and adolescents presenting with chest pain in our ER as expected. The following case is an example.

Case: A previously healthy 16-year-old male presents to the ER with a 1-day history of chest pain. The pain is described as a pressing, precordial, non-radiating pain with an intensity of 6/10 on the pain scale. He was afebrile and with stable vital signs on presentation. Physical examination was unremarkable except for chest wall tenderness. Despite having a normal EKG and chest X-ray, troponin I level was obtained with a result of 0.30 ng/ml (NL: < 0.030 ng/ml). The patient received IV fluids and oral aspirin (325 mg) and because of the elevated troponin level, he was admitted to the hospital for observation and further work up. An echocardiogram showed normal cardiac anatomy and function and normal appearing coronary arteries. Serial troponin I levels are shown in the table below:

Time	0 Hr	4 Hr	8 Hr
Troponin-I ng/ml	0.30	0.47	0.002

The chest pain resolved with ibuprofen and the patient was discharged after 2 days. This is a classic example of over-diagnosis and wasting of resources. The history and physical examinations were not suggestive of a cardiac origin of the chest pain. Obtaining biochemical markers in this case was not indicated and could potentially create anxiety for the patient and his family and lead to further unnecessary investigations and hospital admissions.

In the following article, we review the common causes of chest pain in children and the role of troponin I in the diagnosis and management.

Non-Cardiac causes of chest pain

Musculoskeletal chest pain caused by muscle strains/sprains, costochondritis and even rib fractures is the most frequent. History and physical examination as well as a normal EKG usually confirm this diagnosis. Pulmonary infections such as pneumonia and empyema may also lead to chest pain. However, this type of chest pain is pleuritic in nature and the patient usually has associated signs and symptoms of the underlying respiratory disease. Other causes of non-cardiac chest pain include gastro-esophageal reflux disease and esophageal dysmotility. The pain in these cases is commonly epigastric, with radiation to the chest and usually resolves with antacids. Anxiety, panic attacks and depression are non-organic causes of chest pain which may be discovered with a detailed history. Checking troponin I level has a limited role in the cases described above and again may create anxiety for the family and unnecessary further investigations and hospital admissions.

Cardiac causes of chest pain

Myocarditis

Myocarditis is an inflammatory disease of the myocardium and is pathologically identified as an infiltration of mononuclear cells. Myocarditis can be acute, sub-acute, or chronic and may either involve focal or diffuse areas of the myocardium. Its presentation is extremely variable and may mimic ischemic heart disease. However, the majority of patients with acute myocarditis have mild disease that usually resolves within a few days.

EKG may show nonspecific T waves and ST-segment changes but has low sensitivity. Echocardiography may show decreased systolic function. Endomyocardial biopsy (EMB) shows lymphocytic infiltration in association with myocyte necrosis/death (Dallas Criteria) and is the gold standard for diagnosis.

Role of Troponin I: Patients with myocarditis represent the largest group of pediatric patients in whom troponin I has been extensively studied. Troponin I is usually elevated in all patients with myocarditis and indicates myocardial strain. It has been found to have some utility in the diagnosis of this illness. However, some studies suggested that elevated troponin I levels in patients suspected to have myocarditis led to unnecessary cardiac catheterization to rule out myocardial infarction [2]. A study by Kobayashi., *et al*. evaluated the role of troponin I in predicting outcomes in 12 pediatric patients with myopericarditis. All patients in their study had elevated troponin I levels though none of them had evidence of myocardial dysfunction on echocardiograms. None of these patients had any short term cardiac sequelae which suggested that the clinical evolution of myocarditis was benign even in the presence of significantly elevated troponin I levels. Thus, the utility of routinely checking troponin I levels in patients who are clinically improving and have normal cardiac function on an echocardiogram is still undetermined [3].

Pericarditis

Inflammation of the pericardial lining by infections, drugs or neoplastic causes may lead to pericarditis and pericardial effusions [4]. Pericarditis typically presents with precordial or sub-sternal chest pain that is described as sharp, squeezing and is exacerbated by lying down. Sitting upright and leaning forward usually alleviates the pain [5]. Characteristic physical examination findings include a frictional rub best heard at the cardiac apex or left sternal border with the patient leaning forward. Absence of the rub, however, does not rule out pericarditis as it may not be present in patients with large effusions. These patients may actually have muffled heart sounds instead [5].

Chest X-ray may show an enlarged cardiac silhouette with a triangular shape in patients with pericardial effusion. EKG may demonstrate ST segment elevation in leads I, II, aVF, aVL, V4-V6 in the early course of illness. Echocardiogram is helpful in the visualization of a pericardial effusion [6]. Cardiac catheterization and MRI are helpful but not necessary for the diagnosis of pericarditis.

Role of Troponin I: The typical history, presentation and EKG findings seen in pericarditis sometimes overlap with those seen in myocarditis. Troponin I and other biomarkers are routinely elevated in patients with pericarditis similar to patients with myocarditis. However, the degree of elevation of troponin I does not help to distinguish between pericarditis and myocarditis. Also, similar to studies on myocarditis, elevated troponin I levels have not been demonstrated to determine prognosis in patients with pericarditis.

Cocaine/drug abuse/coronary vasospasm

Children without pre-existing cardiac disease may develop transient myocardial ischemia and infarction with cocaine or other substance abuse. A history of recent drug abuse is helpful but often unreliable and hence other diagnostic tests are often necessary [7]. Patients usually present with precordial chest pain, anxiety, diaphoresis, dizziness, nausea and dyspnea. Since the physical examination is usually benign, the clinical suspicion is crucial in these cases. Therefore, urine drug screen is recommended in adolescents presenting with chest pain where suspicious history of drug. EKG may demonstrate ST segment elevation or myocardial strain pattern. However, a vast majority of patients have a normal EKG [8]. Echocardiography may be useful to assess the myocardial function and wall motion [9].

Role of Troponin I: Coronary vasospasm can be a challenging diagnosis in adolescents. Chest pain and EKG changes in this group of patients may raise concerns about coronary artery anomalies or even myocardial infarction. However, troponin I levels in this setting are unreliable and may trigger extensive workup and hasten the administration of thrombolytic/anticoagulant therapy. Desai., *et al.* studied 9 patients aged 16 - 18 years who presented with chest pain over a period of 8 years [10]. Mean troponin I values were 14 ng/ml and all of those patients underwent coronary angiography. However, all of them had patent coronaries without vasospasm even after provocative testing. In spite of the absence of evident coronary artery vasospasm, 5 out of the 9 patients were treated with aspirin with or without calcium channel blockers. They concluded that even though elevated troponin I levels may indicate a cardiac etiology of the chest pain, adolescents are unlikely to have atherosclerotic heart disease in the absence of risk factors. Schwartz., *et al.* studied 16 adolescent patients presenting with chest pain in the absence of other cardiac risk factors and troponin I was elevated in all the patients [11]. Fifteen patients underwent cardiac catheterization which showed patent coronaries with no evidence of vasospasm. This study further re-enforced the findings of Desai., *et al.* that the probability of thrombotic coronary disease in an adolescent presenting with chest pain (no cardiac risk factors) is remarkably low.

Hypertrophic obstructive cardiomyopathy

Hypertrophic obstructive cardiomyopathy (HOCM) is asymmetrical thickening of the inter-ventricular septum. It is the most common genetic condition affecting the heart with 1:500 prevalence in the general population [12]. It is also the most common cause of sudden cardiac death in athletes with syncope/pre-syncope being other common presenting symptoms [12]. Family history of sudden death with exercise is present in about one third of cases. On physical examination, patients with HOCM usually have a systolic ejection murmur which becomes louder with valsalva maneuvers or with standing.

An EKG is abnormal in up to 90% patients with HOCM. However, it is neither diagnostic nor prognostic (does not indicate the presence or the degree of outflow tract obstruction) [13]. In the presence of a typical history, an echocardiogram must be obtained which measures the left ventricular wall thickness as well as the degree of outflow tract obstruction. Cardiac MRI may also be helpful in the diagnosis as it can localize focal areas of hypertrophy which may be missed on echocardiography [14].

Role of Troponin I: Studies evaluating the role of troponin I as a screening test in the ER have demonstrated that a normal troponin I level does not rule out HOCM. A large study looked at the serum troponin I levels in 116 patients with HOCM over a 17-year period. Only 62 patients (53.4 %) had an elevated troponin I level demonstrating the low sensitivity and specificity of troponin I in diagnosing HOCM [15]. On the other hand, studies have demonstrated the significance of troponin T as a marker for the prediction of adverse effects in HOCM. It has been shown that patients with HOCM and abnormal troponin T values had more adverse events, and an abnormal troponin T level was an independent predictor of cardiac events. Thus, measurement of serum troponin T level may have some diagnostic and prognostic significance in patients with HOCM [16].

Anomalous coronary arteries

Anomalous origin of the coronary arteries is extremely rare and its incidence varies from 0.17% in autopsy studies to 1.2% in patients evaluated with angiography [17].

Anomalous origin of right coronary artery from the left sinus of Valsalva is seen in 30% of cases of coronary artery anomalies. In this case, the right coronary artery passes between the aorta and the pulmonary artery and may get squeezed during exercise causing chest pain, syncope and even sudden cardiac death [17].

Physical examination in these patients is almost always normal. EKG is not specific but may be helpful to delineate ventricular hypertrophy, myocardial strain patterns, evidence of previous infarction or the presence of arrhythmias. Echocardiogram, MRI or CT angiograms may be needed for diagnosis [18].

Anomalous origin of left coronary artery from the pulmonary artery (ALCAPA)

Anomalous origin of left coronary artery from pulmonary artery (ALCAPA) has been associated with early cardiac death. The left coronary artery usually arises from the pulmonary artery posterior to the left posterior facing sinus [19].

In infants/children presenting with myocardial infarction, abnormal Q waves in leads I, aVL, V4-V6 on an EKG are usually seen. Although an EKG is not diagnostic, such a pattern may be suggestive of ALCAPA. Echocardiogram with color Doppler, CT scan and cardiac MRI are helpful in the diagnosis [20]. Cardiac catheterization is rarely needed.

Role of Troponin I: Thankavel., *et al*. described two patients with ALCAPA in whom the troponin I levels were found to be elevated [3]. The median troponin I levels were elevated at presentation to 84.6 ng/ml, peaked to 209.0 ng/ml and dropped to 8.7 ng/ml at discharge/death. However, both patients presented with exertional symptoms and ST segment changes on an initial EKG and diagnosis was made by routine echocardiography. Schwartz., *et al.* described a patient with a coronary artery anomaly who presented with exercise induced chest pain and elevated troponin I levels. The coronary anomaly was clearly demonstrated on a routine echocardiography [11]. Thus, in patients with exercise induced symptoms and EKG changes, elevated troponin I levels usually trigger a physician to obtain an echocardiogram and may indirectly aid in the diagnosis of coronary artery anomalies.

Kawasaki disease

Kawasaki disease (KD) is a type of vasculitis disease that occurs primarily in children with a peak incidence between ages 1 and 2 years. Up to 9% of children with KD have acute cardiac complications, while 3% develop cardiac sequelae [21]. Chest pain from coronary artery involvement is usually a late presentation, however chest pain early in the course of the disease may result from myopericarditis. In addition, these children may present with signs of congestive heart failure [21].

EKG may demonstrate arrhythmias, prolonged PR intervals and non-specific ST-T wave changes [21].

Echocardiogram is helpful in diagnosing coronary artery aneurysms and thrombi. It can define the size of dilations (ectasia). However coronary artery changes may not be visible for upto 10 days after symptom onset [21]. Cardiac MRI is also helpful in diagnosing coronary artery dilation/aneurysms as well as for regional wall motion and perfusion [22].

Role of Troponin I: KD is a clinical diagnosis and cardiac biomarkers are not required for the diagnosis of the disease. However, there has been a lot of debate regarding the ability of biomarkers to predict early development of myocarditis and myocardial injury in patients with KD. A study performed by Kim., *et al.* demonstrated that troponin I levels were elevated in 40% of patients with KD [23]. They showed that a significant rise of troponin I in the acute stage of KD was associated with early development of myocarditis/myocardial cell injury and they suggested that such early elevation should prompt treatment with IVIG to reduce associated complications. However, a study by Checchia., *et al*. demonstrated that there was no significant elevation of troponin I in patients with KD and there was no demonstrable cor-

relation between troponin I measurements and the development of myocarditis or coronary artery abnormalities [24]. This finding was corroborated in a study by Sato., *et al* [25]. Their study failed to demonstrate any correlation between troponin I level elevation and other markers of systemic inflammation, oxidative stress or echocardiographic parameters of myocardial injury [21]. Hence troponin I levels are currently not considered to be useful in predicting the risk of myocardial injury in patients with KD. Treatment should not be withheld in the absence of elevated biomarkers and should be guided by clinical criteria and suspicion for the disease.

Supraventricular Tachycardia

Supraventricular tachycardia (SVT) is the most common arrhythmia in children and its prevalence has been reported to be as high as 1 in 250 children [26]. The incidence of SVT peaks in infancy, early childhood and during adolescence. SVT is a narrow complex tachycardia that predominantly originates at the level of atria or AV nodal tissue. In majority of patients, clinically significant SVT is caused by the presence of accessory pathways between the atria and the ventricles.

A rhythm strip at the time of symptoms is usually sufficient to make the diagnosis of SVT. However, alternative methods such as holter monitoring, event recorders or a 12 lead EKG may also be used. EKG findings include a heart rate > 220 beats per minute in infants and > 180 beats per minute in older children with a narrow QRS complex and the absence of P waves before each QRS complex.

Role of Troponin I: Limited data is available on the role of troponin I levels in the diagnosis of pediatric ventricular or supraventricular tachycardia. In a large study of pediatric patients, 7 patients with cardiac chest pain were found to have SVT and 1 patient was diagnosed with ventricular tachycardia. History, physical examination and EKG were found to be diagnostic in all patients. No role of troponin I levels was mentioned [2]. In a study by Moore., *et al.* 29% of patients with SVT were found to have elevated troponin I levels [27]. However, all of these patients had a benign course without any increase in risk for coronary artery disease.

Ventricular Tachycardia

The incidence of ventricular tachycardia (VT) is about 1/100,000 without any age predilection [28]. VT is defined as three or more premature ventricular contractions (PVCs) in a row at a rate faster than 120 beats per minute. The QRS morphology is usually wide, bizarre and not proceeded by P waves.

An EKG or a rhythm strip is usually diagnostic. Echocardiography, cardiac MRI or cardiac catheterization may be needed for diagnosis of the underlying pathological condition. Similar to SVT, troponin I levels have a limited role in VT and no pediatric studies evaluating their role are currently available.

Discussion

Troponin I level is a measure of myocardial strain and could be a valid indicator of myocardial injury even in the pediatric population [29]. Troponin I level ≥ 2 ng/ml increases the likelihood of a cardiac etiology [29]. Although troponin I levels are helpful in the adult population to rule out myocardial infarction, its utility in the pediatric population is yet established.

There are several limitations to the routine use of troponin I levels in pediatrics. The incidence of cardiac pathology of pediatric chest pain is extremely low and the incidence of coronary artery disease is even lower. The most common cause of pediatric chest pain with elevated troponin I levels is myopericarditis. In these patients, the elevated troponin I values are suggestive of myocardial strain, but they are neither diagnostic nor prognostic. Elevated troponin I levels have been associated with an increased number of invasive procedures in the pediatric and adolescent population with myopericarditis however. They are not useful in differentiating between patients with preserved versus depressed left ventricular systolic function [3]. Thus, troponin I levels have a very limited role in this patient population.

Adolescents presenting with coronary vasospasm also have elevated troponin I levels. In the absence of risk factors, myocardial infarction is extremely rare in this population. In 2 different studies, cohorts of these patients underwent coronary angiography to rule out

coronary artery disease and were treated like adults with myocardial infarction; however, none of these patients had evidence of coronary artery disease on angiography. Serial trending of levels in otherwise asymptomatic patients prolongs hospital stay and was not prognostic in the studies performed. Drug screens should be routinely performed in the adolescent population presenting with chest pain and clinical suspicion for drug use. In patients with a negative drug screen, elevated troponin I levels may indicate myocardial strain; however, the results need to be carefully interpreted.

Troponin I has been demonstrated to have a low sensitivity for the diagnosis of HOCM even in those presenting with symptoms of chest pain and EKG changes. Relying on troponin I alone as a screening test for HOCM may lead to a high number of false negative results. The diagnosis is best made by an echocardiogram and/or MRI.

In patients with coronary artery anomalies, elevated troponin I levels indicate a non-specific myocardial strain pattern, but are not diagnostic. Cardiac arrhythmias such as SVT and VT are diagnosed by EKG, and troponin I levels have limited role in these conditions. Kawasaki disease is a clinical diagnosis and troponin I levels should not be used to establish the diagnosis.

Conclusion

While troponin I levels have are excellent diagnostic and prognostic tools in adults presenting with, their role in pediatric and adolescent patient remains to be established. A pediatric patient presenting to the ER with chest pain should receive a complete evaluation, which includes a thorough history and physical exam, EKG and an echocardiogram if indicated.

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