Original Article

Clinical Indications for Requesting High-sensitivity Troponin I in the Emergency Department

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Abstract

Objectives: The aim of this study is to evaluate the presenting symptoms, risk factors and cardiac origin of high-sensitivity troponin I (Hs-TnI), the tendency of emergency physicians to use Hs-TnI in a general emergency room (ER) and the validity of requesting an Hs-TnI routinely. **Methodology:** A retrospective cohort study with 904 patients presenting at a tertiary hospital ER with an Hs-TnI requested. The study was conducted for 15 months. **Results:** Of the sample, 20.4% (n = 184) presented with dyspnea, 18.03% (n = 163) with chest pain and a small proportion (12.94%, n = 117) with epigastric abdominal pain. Patients presenting with chest pain and a history of dyslipidemia were at a higher risk of developing acute coronary syndrome compared to the group without dyslipidemia (relative risk [RR] = 1.62 [1.01–2.58] P = 0.044). Diabetes and hypertension were the most prevalent chronic comorbidities in patients with dyspnea with a risk of (RR = 5.19 (0.68–39.27) P < 0.068). Patients who presented with epigastric pain and had a history of dyslipidemia had a risk of (RR = 5.23 (1.33–20.54) P = 0.009). **Conclusion:** The presenting symptoms should be taken into consideration by the emergency department physician to support the request for an Hs-TnI laboratory test. The yield and risk were both low in random screening.

Keywords: Chest pain, myocardial infarction, myocardial ischemia, troponin I

Introduction

Despite advances in the diagnosis of acute myocardial infarction (AMI), it remains the leading cause of mortality globally. Rapid medical intervention in this life-threatening disease is of the utmost importance. Patients with typical AMI present with chest pain and exertional dyspnea. However, many patients present with atypical symptoms, which might confuse clinicians and lead to a wrong diagnosis such as heartburn, acid reflux, and esophagitis. Literature reports that the proportion of AMI patients misdiagnosed ranges from 2% to 6%.[1-3] Approximately 26% of the misdiagnosed patients die within 3 days after hospital discharge compared to 12% after hospitalization.[4]

Clinicians could rule out acute coronary syndrome (ACS) after a detailed history, physical examination, and initial investigation. However, patients with atypical symptoms, fewer risk factors, and an atypical age at presentation are more likely

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to be misdiagnosed.[2,5] A bedside electrocardiogram (ECG) is an efficient tool to support the diagnosis of AMI, but the ECG may be normal initially. A study reported that 62% of patients with a missed AMI diagnosis had a completely normal ECG.[4] A reliable clinical indicator can assist the clinician to exclude AMI.[6]

Laboratory tests have long been used for the detection and diagnosis of AMI. The classical cardiac enzymes have been replaced by a more sensitive and specific test to diagnose AMI, high-sensitivity troponin I (Hs-TnI). Hs-TnI levels are used daily for the diagnosis and risk stratification of coronary arterial disease (CAD).[7] However, a high troponin level is not always due to CAD. Elevated levels are also found in conditions not associated with CAD, for example, pulmonary embolism, septic shock, acute heart failure, as well as iatrogenic causes such as cardiotoxic drugs.[8]

Nearly 6 million Emergency Department (ED) admissions in the United States present with chest discomfort or symptoms suggestive of CAD, but the majority have noncardiac causes for their symptoms, such as musculoskeletal pain.[9-11] It is challenging for physicians, especially in an ED setting, to know when to request an Hs-TnI. Requesting unnecessary Hs-TnI tests will increase the cost burden on the hospital as well as increasing the diagnostic and management dilemma. The objective of the study was to evaluate the tendency of emergency physicians using Hs-TnI in emergency room (ER).

Methodology

Study design

A retrospective cohort study was performed at the ED, King Abdulaziz Medical City, Jeddah, with patients referred to Cardiac Services. The study was approved by the Institutional Review Board of King Abdullah International Medical Research Center, Jeddah, Saudi Arabia, No 18/124/J.

The study was a retrospective cohort study. The patients were selected using a nonprobability sampling technique, convenience sampling. All patients who presented at the ED for any reason for whom the ED physician requested at least one Hs-TnI laboratory test from January 2017 to April 2018 and older than 18 years were included in the study. Any patients with a previous cardiac event or insufficient reported data were excluded from the study. There were 20,735 troponin requests in the sample. The standard sample size formula ($n = N \times X/[X + N - 1]$) was used to determine representative sample size for this population, and 1035 cases were randomly selected for data collection. Patients who met the inclusion and exclusion criteria were enrolled, and the sample size realized as 904 cases (CI 95% ±3.19) [Figure 1]. Data were collected from the electronic healthcare information system used in the hospital, Best Care 2.1, and entered in a Microsoft Office Excel sheet. Patient's demographic profile, risk factors including dyslipidemia, hypertension, and diabetes mellitus, Hs-TnI, chief complaint and final diagnosis were collected. There were little family-related history available in the medical record,

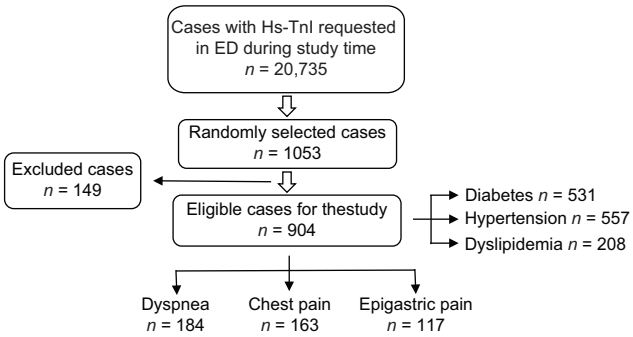

Figure 1: Study flow chart

and we omitted family history from our data collection sheet. An Hs-TnI result was considered positive if ≥120 mmol/L. We used the "ARCHITECT STAT Hs-TnI" kit to measure the troponin I level. A diagnosis of ACS was established based on the clinical features as well as the ECG finding. An ED physician interpreted both results. The diagnosis of MI was confirmed by a coronary angiogram.

Simple descriptive statistics were used to describe the demographic profile of the sample. Mean and standard deviation was used for quantitative variables, with frequency, percentage, and interquartile range for qualitative data.

Based on the presenting symptom, the participants were categorized into three groups. The first group included patients with acute chest pain, the second, patients presenting with dyspnea, and the third, patients with epigastric pain. The patient characteristics and diagnoses were analyzed for each group.

Inferential analysis was performed to compare the three groups to find any clinical or statistical significance. SPSS version 19 (SPSS version 19; IBM Corp., Armonk, New York, USA) was used for the analysis. Chi-square test was used for each variable and *t*-test for quantitative variables. A value of $P \leq 0.05$ was deemed statistically significant.

Results

Of 20,735 h-TnI request in the study period, a sample of 1035 was included in the study, of which 904 (87.34%) were eligible for the study. The reasons for exclusion were incomplete clinical data and the Hs-TnI requested after transfer from the ED. The male participants in our sample size were 619 (68.47%). The mean age was 60.86 ± 19.52, and the average body mass index 28.52 ± 8.44 kg. More than half of the cases were diabetic 531 (58.73%), 557 (61.61%) were hypertensive, and 208 (23.0%) were dyslipidemic [Table 1]. The main presenting symptoms associated with the Hs-TnI request in the ED were dyspnea ($n = 184$, 20.35%), chest pain ($n = 163$, 18.03%), and epigastric pain ($n = 117$, 12.94%) [Table 1].

A small proportion of the candidate had a positive Hs-TnI ($n = 125$, 13.82%) with the first request. The diagnosis of ACS accounted for 70 (7.72%) person of the study participants, followed by heart failure ($n = 38$, 4.20%) and a

Table 1: Patient demographics

Characteristic	Hs-TnI ≥120 (*n*=125), *n* (%)	Hs-TnI <120 (*n*=779), *n* (%)	Total (*n*=904), *n* (%)
Gender (male)	96 (10.61)	523 (57.85)	619 (68.47)
Age	64.12±19.47	60.34±19.49	60.86±19.52
BMI	28.71±7.91	28.49±8.53	28.52±8.44
Diabetes mellitus	86 (9.51)	445 (49.22)	531 (58.73)
Hypertension	87 (9.62)	470 (51.99)	557 (61.61)
Dyslipidemia	35 (3.87)	138 (19.13)	208 (23.00)
Chest pain	41 (4.53)	122 (13.49)	163 (18.03)
Typical cardiac	5 (0.55)	9 (0.99)	14 (1.54)
Atypical cardiac	1 (0.11)	4 (0.44)	5 (0.55)
Noncardiac	35 (3.87)	109 (12.05)	144 (15.92)
Dyspnea	31 (3.42)	153 (16.92)	184 (20.35)
Epigastric pain	12 (1.32)	105 (11.60)	117 (12.94)
Palpitation	1 (0.11)	19 (2.10)	20 (2.21)
Fever	13 (1.43)	87 (9.62)	100 (11.06)
ACS	42 (4.64)	28 (3.09)	70 (7.72)
STEMI	9 (0.99)	6 (0.66)	14 (20.00)
NSTEMI	22 (2.43)	6 (0.66)	28 (40.00)
Unstable angina	11 (1.21)	17 (6.87)	28 (39.99)
Stable angina	1 (0.11)	2 (0.22)	3 (0.33)
Heart failure	7 (0.77)	31 (3.42)	38 (4.20)
COPD	1 (0.11)	10 (1.10)	11 (1.21)
Motor vehicle accident	6 (0.66)	28 (3.09)	34 (3.76)
Septic shock	4 (0.44)	17 (1.88)	21 (2.32)
Cancer	4 (0.44)	21 (2.32)	25 (2.76)

Hs-TnI: High-sensitivity troponin I, BMI: Body mass index, ACS: Acute coronary syndrome, STEMI: ST-segment elevation myocardial infarction, NSTEMI: Non-STEMI, COPD: Chronic obstructive pulmonary disease

motor vehicle accident (MVA) (*n* = 34, 3.76%) [Table 1]. The proportion of 7.72% of all patients with an Hs-TnI request reflects a high tendency of ER physicians to overuse Hs-TnI even in a low-risk patient. Moreover, none of the patients presenting due to MVA were diagnosed with ACS with no chest pain or ECG changes.

In patient who had troponin requested for them, chest pain was a presenting symptom only in 163 (18.03%) patients. Forty-eight (29.44%) of them diagnosed later with ACS. 39 (17.48%) patients presented with chest pain combined with dyspnea. 11 (28.20%) of the presentation of the last subgroup were due ACS. Participants who had dyslipidemia and presented with chest pain were at a higher risk of developing ACS compared to the subgroup without dyslipidemia (relative risk [RR] = 1.62 [1.01–2.58]; *P* = 0.044) [Table 2].

In the second group who had troponin requested, 184 (20.35%) patients presented with dyspnea. 12 (6.52%) of them was secondary to ACS. Patients presenting with dyspnea as the primary symptom of symptom of ACS were older and more likely to have diabetes and hypertension with a risk of (RR = 5.19 [0.68–39.27]; *P* = 0.068) and dyslipidemia with a risk of (4.11 [1.40–12.00] *P* = 0.006) [Table 2].

In the third group who had troponin requested, epigastric pain was the presenting symptom in 117 (12.94%) persons. The epigastric pain of a small proportion of this group (*n* = 12, 10.25%) was justified by ACS. The age ranged from 49 to 82 years, which is relatively wider than the age range of other presentations. The risk of ACS in a patient who presented with epigastric pain associated with diabetes was (RR = 4.60 [0.58–36.15]; *P* = 0.104), epigastric pain associated with hypertension was (RR = 3.97; [0.50–31.19]; *P* = 0.148), and epigastric pain combined with dyslipidemia (RR = 5.23 [1.33–20.45]; *P* = 0.009) [Table 2].

We further studied the patients whose Hs-TnI results were ≥120 mmol/L and presented with unusual ACS presentation; however, they ended up with ACS. The group who presented with chest pain had a risk of (4.16 [2.65–6.54]; *P* < 0.001) to be diagnosed with ACS and dyspneic patients were at risk of (9.87 [3.16–30.75]; *P* < 0.001) of developing ACS. Finally, patients with epigastric pain were at a risk of (26.00 [5.89–114.73]; *P* < 0.001) developing ACS [Table 2].

The sample size of patients who presented with other clinical features such as palpitations, syncope, abdominal pain, back pain, and chest tightness was too small for the statistical analysis.

Discussion

In this retrospective cohort study investigated 904 patients who were admitted to a tertiary hospital ER with an Hs-TnI

Table 2: Data statistical analysis, the relative risk of developing acute coronary syndrome for the patient with these presenting symptoms and comorbidities compared to those who just presented in the emergency department with the presenting symptoms without associated comorbidities

	ACS	Non-ACS	*P*
Chest pain			
DM	1.50 (0.92-2.46)	0.84 (0.69-1.03)	0.095
HTN	1.59 (0.96-2.64)	0.82 (0.68-1.01)	0.064
DM and HTN	1.60 (0.98-2.60)	0.82 (0.66-1.00)	0.053
Dyslipidemia	1.62 (1.01-2.58)	0.80 (0.63-1.01)	0.044
Hs-TnI ≥120	4.16 (2.65-6.54)	0.37 (0.24-0.59)	<0.001
Dyspnea			
DM	4.45 (0.58-33.619)	0.93 (0.87-0.99)	0.105
HTN	3.66 (0.48-27.63)	0.94 (0.88-1.00)	0.168
DM and HTN	5.19 (0.68-39.27)	0.92 (0.87-0.98)	0.068
Dyslipidemia	4.11 (1.40-12.00)	0.86 (0.74-1.00)	0.006
Hs-TnI ≥120	9.87 (3.16-30.75)	0.76 (0.61-0.93)	<0.001
Epigastric pain			
DM	4.60 (0.58-36.15)	0.92 (0.84-1.00)	0.104
HTN	3.97 (0.50-31.19)	0.92 (0.85-1.01)	0.148
DM and HTN	5.88 (0.74-64.35)	0.90 (0.82-0.99)	0.051
Dyslipidemia	5.23 (1.33-20.54)	0.85 (0.71-1.01)	0.009
Hs-TnI ≥120	26.00 (5.89-114.73)	0.51 (0.28-0.89)	<0.001

Elderly: Male ≥65, Female ≥60. DM: Diabetes mellitus, HTN: Hypertension, Hs-TnI: High-sensitivity troponin I, ACS: Acute coronary syndrome

requested. Of the sample, 20.4% (n = 184) presented with dyspnea, 18.03% (n = 163) with chest pain and a small proportion (12.94%, n = 117) with epigastric abdominal pain. Patients presenting with chest pain and a history of dyslipidemia were at a higher risk of developing ACS compared to the group without dyslipidemia. Diabetes and hypertension were the most prevalent chronic co-morbidities.

It was noted in a previous article that one-third of AMI patients did not complain of chest pain.[12] Their second-most frequent presenting symptom was dyspnea followed by diaphoresis, nausea, and syncope.[13]

The atypical presentations were observed in patients older than 67 years and patients with comorbidities, similar to findings in the literature confirming that the elderly, women, DM, and patients with a history of heart failure usually presented with vague symptoms.[14,15] On average, they are 7-year-older than other patients, 80% is diagnosed with coronary artery disease and presented with an atypical and confusing picture due to the comorbidities and complaints related to this age group.[16,17]

As expected, chest pain and dyspnea were the two most frequent presenting symptoms, and these symptoms should be considered as baseline risk factors. Some risk factors can change the presentation of the patient, for example, diabetic patients are more likely to present without chest pain,[18] and an ECG is critical for a diagnosis.

A systematic review reported that requesting an Hs-TnI in a patient with chronic heart failure provides a prognostic stratification and is a reliable predictor of cardiovascular mortality.[19] An increase in the Hs-TnI level in sepsis has been investigated and linked to left ventricular dysfunction with a poor outcome. The release in troponin is due to the loss of membrane integrity with troponin leakage or microvascular thrombotic injury.[20]

The setting for the current study is also a trauma center, close to a highway, admitting a high proportion of MVA cases. A literature review reported no benefit in the routine request for Hs-TnI or troponin for all MVA victims. The recommendation was to limit requests to patients with polytrauma or chest trauma. Knowing the level of Hs-TnI in other MVA cases did not support a diagnosis or health-care management.[21-23] The multiple causes of elevated Hs-TnI caused reservations about its specificity for the cardiac-related disease. To differentiate between cardiac and noncardiac increased troponin levels, new terms describing Hs-TnI of noncardiac origin such as troponitis, troponin leak, and Type 2 AMI were developed.[24]

Two limitations should be considered for the study, the sample was obtained from the ED alone, and due to the proximity of the highway, there may have been a higher proportion of MVA-related ED admissions, possibly resulting in selection bias.

Conclusion

A request for troponin should depend on a combination of symptoms and risk factors. Atypical symptoms in the elderly, diabetic, or hypertensive patients, especially patients presenting with dyspnea, should be considered. Routine screening is not justified and does not improve patient outcome.

The data used to support the findings of this study are restricted by the King Abdullah International Medical Research Center Institution Review Board to protect PATIENT PRIVACY. Data are available from the Institutional Review Board irb@ngha.med.sa or via the corresponding author, for researchers who meet the criteria for access to confidential data.

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Conflicts of interest

There are no conflicts of interest.

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