

# Troponin estimation identifies myocardial infarction patients with different characteristics

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## ABSTRACT

**Objective:** To investigate the impact of new myocardial infarction definition based on troponin, the rate of myocardial infarction diagnosis, patients' characteristics, and short-term prognosis.

**Methods:** We enrolled 1,255 consecutive myocardial infarction patients from the Kuwait Registry of Acute Coronary Syndromes from December 2003 to May 2004. Two patient groups were identified, those diagnosed with elevated creatine kinase-MB (CK group) and those diagnosed with elevated troponin with normal CK-MB (Troponin group).

**Results:** The use of troponin have increased the number of myocardial infarctions by 49%. Compared with the CK group, the Troponin group were older [age  $60.3 \pm 12.5$

years versus  $53.7 \pm 12.2$  years,  $p < 0.001$ ], more likely to have diabetes (59% versus 41%,  $p < 0.001$ ), hypertension (59% versus 36%,  $p < 0.001$ ), and hypercholesterolemia (37% versus 24%,  $p < 0.001$ ). The Troponin group were more likely to suffer heart failure at presentation than the CK group (32% versus 14%,  $p < 0.001$ ) and, subsequently, increase incidence of heart failure during their hospital stay (17% versus 8%,  $p < 0.001$ ).

**Conclusions:** A substantial increase in the rate of myocardial infarction occurred with the adoption of the new diagnostic criteria. The clinical outcome for the additional patients diagnosed was not better than that of patients diagnosed by the old criteria.

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The introduction of measures of cardiac troponin, a very sensitive and specific marker for cardiac necrosis, has redefined the diagnosis of myocardial infarction (MI). The "old" definition according to World Health Organization criteria has largely been replaced by the consensus definition of the European Society of Cardiology and the American College of Cardiology (ESC/ACC) introduced in 2000.<sup>1,2</sup> This

has led to an increased rate of diagnosis of MI.<sup>3-8</sup> The impact of the changing definition on patients' characteristics and prognosis is unclear. Due to the higher sensitivity of troponin compared with other cardiac biomarkers, the added patients diagnosed by the inclusion of cardiac troponin may have lower levels of myocardial damage, leading to an apparent improvement of overall prognosis.<sup>2</sup> However, the

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powerful prognostic value of troponin as an indicator of future adverse cardiac events could result in a worse overall prognosis for these patients.<sup>9-11</sup>

In this study, we aimed to investigate the impact of adopting the new MI definition on the rate of MI diagnosis and on patients' characteristics and short-term prognosis.

**Methods.** This study used the data from a nationwide, 6 month, prospective Registry of Acute Coronary Syndromes (ACS) in Kuwait. Kuwait is a relatively small Arab Middle-Eastern country with a population of 2.5 million. All cases of MI get admitted to one of the 7 general hospitals distributed in the different governorates of Kuwait. All 7 general hospitals participated in this Registry. At each hospital, designated physicians identified consecutive patients admitted with ACS over a period of 6 months, from December 2003 through May 2004. They prospectively filled a standardized case report form during the patient's hospital stay. Several variables were collected including patients' demographics, past medical history, diagnosis on admission, vital signs at presentation, diagnostic electrocardiogram (ECG), peak creatine kinase (CK), peak CK-MB, peak cardiac troponin I, blood sugar, fasting cholesterol, diagnosis on discharge, in-hospital, and discharge medications, in-hospital outcomes including recurrent ischemia, reinfarction, heart failure (HF), cardiogenic shock, and in-hospital mortality. Data forms were checked for completeness in a national coordinating center and were returned for corrections to the participating hospitals when necessary.

The diagnosis of MI was based on the definition of the Joint Committee of the ESC/ACC published in September 2000. Patients were considered to have MI if they had a typical rise and fall of troponin, CK or CK-MB with at least one of the following: ischemic symptoms, development of pathological Q waves on the ECG or ECG changes indicative of ischemia (ST segment elevation or depression). Cardiac biomarkers were measured locally at each hospital's laboratory using its own assays and reference ranges. Patient care at each hospital was performed according to usual practice, independent of the Registry.

**Statistical analysis.** Baseline and clinical characteristics of patients were presented as frequencies and means. Continuous variables were compared, between the troponin and the CK groups, using Mann-Whitney U test and categorical variables were compared using the Z-test of proportion. The  $p < 0.05$  was considered statistically significant. Logistic regression was used to calculate the odds ratios and 95% confidence intervals for in-hospital

mortality and in-hospital HF, before and after adjustment for factors that were thought to be potential confounders. Potential confounders that were assessed included age, gender, history of diabetes, and history of hypertension. All data analyses were carried out using SPSS program version 10.

**Results.** The Kuwait ACS Registry included a total of 2130 patients. For the purpose of this study, 1255 consecutive patients with the discharge diagnosis of MI were included. Of the 1255 MI patients included in this study, 841 had the diagnosis of MI based on elevated CK or CK-MB (CK group). The remaining 414 patients had the diagnosis of MI based on an elevated cardiac troponin I level in the absence of raised CK or CK-MB (Troponin group). The use of troponin in the diagnosis of MI increased the number of MIs by 49%.

Demographics and risk factors of both groups are shown in **Table 1**. Compared with the CK group, patients in the Troponin group were older (mean age  $60.3 \pm 12.5$  years versus  $53.7 \pm 12.2$  years,  $p < 0.001$ ) and more often females (31% versus 12%;  $p < 0.001$ ). They were significantly more likely to have diabetes (59% versus 41%;  $p < 0.001$ ), hypertension (59% versus 36%;  $p < 0.001$ ), and hypercholesterolemia (37% versus 24%;  $p < 0.001$ ). In addition, they were significantly more likely to have suffered from a previous MI (35% versus 22%;  $p < 0.001$ ).

**Table 2** summarizes the differences in presentation and administration of thrombolytic therapy between the 2 groups. Compared with patients in the CK group, patients in the Troponin group were more likely to present with non-ST elevation MI (NSTEMI) (79% versus 33%;  $p < 0.001$ ). They also had a significantly higher heart rate and blood pressure on admission. In addition, they had a significantly higher incidence of HF at presentation (32% versus 14%;  $p < 0.001$ ). As expected, patients in the Troponin group, who mostly had NSTEMI, received thrombolytic therapy less often than patients in the CK group (17% versus 56%;  $p < 0.001$ ).

As shown in **Table 3**, patients in both groups had similar rates of in-hospital recurrent ischemia, reinfarction, cardiogenic shock, and death following MI. However, we found an increased incidence of HF during the hospital stay in the Troponin group compared with the CK group (17% versus 8%;  $p < 0.001$ ). Even after adjusting for age, gender and diabetes, the in-hospital mortality rates did not differ significantly between the 2 groups (**Table 4**). Further, the increase in HF during hospital stay was found to be independent of age, gender, diabetes, hypertension or previous MI (**Table 4**).

**Table 1** - Demographics and risk factors.

Characteristics	Troponin group N = 414 n (%)	Creatine kinase group N = 841 n (%)	P-value
<b>Gender</b>			
Male	287 (69)	737 (88)	<0.001
Female	127 (31)	104 (12)	<0.001
Age (mean ± SD)	60.3 ± 12.5	53.7 ± 12.2	<0.001
Past history of myocardial infarction	143 (35)	181 (22)	<0.001
<b>Risk factors</b>			
Current smoker	143 (35)	413 (49)	<0.001
Diabetes	244 (59)	348 (41)	<0.001
Hypertension	243 (59)	301 (36)	<0.001
Hypercholesterolemia	155 (37)	200 (24)	<0.001

**Table 2** - Presentation and thrombolytic therapy use.

Variables	Troponin group N = 414 n (%)	Creatine kinase group N = 841 n (%)	P-value
<b>Discharge diagnosis</b>			
STEMI	89 (22)	563 (68)	<0.001
NSTEMI	325 (79)	278 (33)	<0.001
<b>Examination on presentation</b>			
Heart rate (beats/minute)	91 ± 23	84 ± 24	<0.001
Systolic blood pressure (mm Hg)	144 ± 31	138 ± 31	<0.001
Heart failure at presentation	131 (32)	118 (14)	<0.001
Thrombolytic therapy	71 (17)	474 (56)	<0.001
STEMI - ST elevation myocardial infarction, NSTEMI - non-ST elevation myocardial infarction Values are presented as mean ± standard deviation			

**Table 3** - In-hospital outcomes.

Variables	Troponin group N = 414 n (%)	Creatine kinase group N = 841 n (%)	P-value
Recurrent ischemia	93 (23)	160 (19)	Not significant
Infarction	9 (2)	30 (4)	Not significant
Heart failure	71 (17)	66 (8)	<0.001
Cardiogenic shock	14 (3)	29 (3)	Not significant
Mortality	19 (5)	24 (3)	Not significant

**Table 4** - Crude and adjusted risk estimates (Odds ratio and 95% CI) of the effect of diagnosis based on troponin compared with CK for in-hospital mortality and heart failure, (N=1255).

Variables	Odds Ratio (95% CI)	
	In-hospital mortality	Heart failure
Unadjusted estimate	1.64 (0.89-3.02)	2.43 (1.69-3.48)
Age adjusted	1.54 (0.83-2.84)	2.29 (1.60-3.29)
Gender adjusted	1.41 (0.75-2.66)	2.01 (1.39-2.91)
Age and gender	1.34 (0.71-2.53)	1.92 (1.32-2.78)
Age, gender and diabetes	1.18 (0.62-2.25)	1.79 (1.23-2.61)
Age, gender and hypertension	1.22 (0.64-2.32)	1.77 (1.22-2.59)
Age, gender and previous MI	1.18 (0.62-2.24)	1.78 (1.22-2.24)

CI - confidence interval, CK - Creatine kinase, MI - myocardial infarction

**Discussion.** The data used in this study was from a nationwide Registry reflecting the standard clinical practice in Kuwait. The use of troponin as a diagnostic marker has resulted in a substantial increase in the number of patients diagnosed with MI. In our study, the diagnosis of MI increased by 49%. The proportion of the increase in MI reported by different studies varied from approximately 10-80%.<sup>3-9</sup> This variation can reflect the use of different assays for troponin, as well as different cut off points for both CK-MB and troponin in different studies.<sup>12,13</sup>

The additional patients diagnosed as having MI, based on elevated troponin, had different characteristics and presentations compared with the patients diagnosed according to old criteria using only CK or CK-MB as cardiac biomarker. These patients were older and had higher prevalence of coronary risk factors. Many more patients were diagnosed with NSTEMI when troponins were used in MI definition. Furthermore, we have found a higher rate of HF at presentation in the Troponin group. Recently, cardiac troponins were shown to be elevated in a percentage of patients who suffered acute HF without MI; and this finding was associated with a worse prognosis in such patients.<sup>14</sup> It has also been noted that patients admitted with HF are more likely to be diagnosed with MI under the new diagnostic criteria.<sup>3</sup> It is difficult to ascertain whether some of these patients had acute HF with leakage of troponin due to secondary myocardial necrosis, rather than an MI complicated by HF. However, our patients who were recruited in the Registry were those with suspected ACS. Therefore, we believe that our finding of an increased rate of HF at presentation in the Troponin group is a genuine finding that indicates a high risk presentation

in this group of patients. Different results have been reported on the effect of utilizing troponin estimation on the prognosis of MI, and specifically mortality. It was postulated that owing to the higher sensitivity of troponin compared with other cardiac biomarkers, the additional patients diagnosed due to the inclusion of cardiac troponin may have lower levels of myocardial damage, leading to a better prognosis and decreased mortality.<sup>2</sup> In our study, the additional patients diagnosed with troponin had similar rates of in-hospital mortality. Some published studies have reported higher 30 days, 6 months, and 1 year mortality.<sup>5-7,10</sup> Other studies found that the addition of troponin did not affect 30 days mortality.<sup>3,4</sup> Interestingly, Meier et al<sup>6</sup> found that the 6 month mortality, not in-hospital mortality, was affected by the addition of troponin. Furthermore, we found that the additional patients diagnosed by troponin had similar rates of in-hospital recurrent ischemia, infarction, and cardiogenic shock, and a higher rate of HF as compared with the patients diagnosed by elevated CK.

Despite some differences between studies regarding the prognosis of patients diagnosed with MI, based on elevated troponin and a normal CK, it is important to note that all the studies, including this one, show that such patients do not represent a group with a more favorable outcome.

In conclusion, the changing diagnostic criteria with reliance on troponin measurement resulted in a substantial increase in the diagnosis of MI. This increase represents a true increase in the MI burden, as those additional patients diagnosed, although different in demographics and characteristics, have a similar morbidity and mortality to the patients diagnosed according to the old criteria.

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