Troponin I Blood Level Value and its Utility in Differentiating Myocardial Infarction from Pulmonary Embolism

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Abstract: **Troponin I (Trop-I) is considered the most sensitive cardiac biomarker for diagnosis of acute MI. However, it lacks specificity since it can be elevated with other conditions such as pulmonary embolism and non-coronary cardiac disorders. Our primary objective is to determine the cut-off blood level values of Trop-I that has the best sensitivity and specificity for differentiating MI from PE.**

Methods: We performed a retrospective chart review of 122 patients admitted to King Abdulaziz Medical City-Western Region with diagnosis of MI or PE between October 2012 and March 2014. We included patients with measured Trop-I blood level and excluded patients with end stage renal disease or chronic elevation of Trop-I. The primary outcome was to estimate the sensitivity and specificity of Trop-I at different level in comparison to the clinical diagnosis. Diagnosis of MI was based on the third universal consensus definition of MI, and the diagnosis of PE was based on CT pulmonary angiogram or ventilation perfusion scan. The secondary objectives were to determine any association between Trop-I elevation with left ventricular (LV) dysfunction among MI patients and with right ventricular (RV) dysfunction among PE patients. Data was analyzed using chi-square, *t* test, or regression analysis as appropriate. Statistical significance was determined using two-tailed p-value of 0.05.

Results: Among 122 patients included, 64 were diagnosed to have MI and 58 were diagnosed to have PE. 58% were males with mean age of 61 years.

Figure 1 shows the ROC curve, which describes the diagnostic performance of Trop-I for differentiating MI from PE. At Trop-I blood level of 0.05, the sensitivity is 98.4% (95% CI: 91.6 – 100%) and specificity is 84.5% (95% CI: 72.6 – 92.7%). At the level of 0.1, the sensitivity is reduced to 76.6% (95% CI: 64.3 – 86.2%) but with almost perfect specificity of 98.3% (95% CI: 90.8 – 100%).

No association was identified between post-MI Trop-I level and echocardiographic finding of ventricular wall motion abnormality (OR, 1.02; 95% CI: 0.98 – 1.05) or LV dysfunction (OR, 1.02; 95% CI: 0.99 – 1.04). There was a strong association between post-PE elevation of Trop-I and RV dysfunction (p-value = 0.002).

Conclusion: The blood level of Trop-I may have clinical implication in differentiating MI from PE at the initial presentation. Trop-I level is not associated with LV dysfunction among MI patients, but has strong association with RV dysfunction among PE patients.

Keywords: **Troponin I (Trop-I), RV dysfunction, myocardial infarction.**

1. INTRODUCTION

Myocardial infarction is a major health problem worldwide that is associated with high morbidity and mortality rate. It has been estimated that 15 to 20 thousand patients per million individuals every year present to the emergency department with symptoms suggestive of acute myocardial infarction (MI) in Europe and United States (1). Acute MI is diagnosed based on typical clinical presentation, typical electrocardiac (ECG) changes, and elevation of cardiac specific biomarkers. However, not every patient with acute MI present with typical clinical presentation or ECG changes. Among different cardiac biomarkers Troponin I (Trop-I) is considered the most sensitive for diagnosis of acute MI (2). Trop-I, however, lack specificity since it can be elevated with other non-coronary cardiac disorders such as pulmonary embolism (PE), severe sepsis and septic shock, stroke, acute perimyocarditis, Takotsubo, acute heart failure and tachycardia. In addition, end stage renal disease can cause chronic elevation of Trop-I (3). Early diagnosis of acute MI is even crucial for the prompt treatment that is required to improve the outcome (4).

Troponins are proteins that regulate the muscle contraction and are present in cardiac and skeletal muscles but not in smooth muscles. However, their different amino acids sequence allow detecting specific cardiac troponins related to any cardiac injury. Most cardiac troponins are bound to myofilaments and the rest is free in the cytosol. This explains the double peak with the free troponin being released first in response to injury followed by the bound troponin (5).

Although Trop-I can be elevated through different mechanisms that cause myocardial injury, higher blood level values of Trop-I have been identified with acute MI as compared to non-coronary cardiac disorders (6).

We hypothesize that a certain level of Trop-I can accurately discriminate acute MI from other disorders that also cause elevated Trop-I, but with lower blood level value.

2. METHODS

Participants:

We evaluated 122 patients diagnosed with MI or PE between October 2012 and March 2014 whose Trop-I blood level was measured at King Abdulaziz Medical City-Western Region. They were 71 male (85.2%) and 51 female (41.8%) and their age ranged from 18 to 102 years (M=62, SD=17.8).

The diagnosis of MI was based on the third universal consensus definition of MI, The diagnosis of PE was based on CT pulmonary angiogram or ventilation perfusion scan confirmation. We excluded patients with end stage renal disease or chronic elevation of Trop-I.

Materials and study design:

This is a retrospective chart review study. The data was collected from the medical records and laboratory database (QuadraMed) at King Abdulaziz Medical City-Western Region. The sensitivity and specificity of Trop-I at different blood level values were measured to determine the cut-off values that differentiate MI from PE with high accuracy.

Endpoints:

Our primary objective is to determine the cut-off blood level values of Trop-I that has the best sensitivity and specificity for differentiating MI from PE, using the ROC curve. The secondary objectives were to determine any association of Trop-I elevation with left ventricular (LV) dysfunction among MI patients and with right ventricular (RV) dysfunction among PE patients.

Statistical Analysis:

Association between variables was analyzed using chi-square, t test, or regression analysis as appropriate using the SPSS and the STATA programs. Statistical significance was determined using two-tailed p-value of 0.05.

3. RESULTS

181 patients were found to have a final diagnosis of MI and 136 with PE at the time period from October 2012 till March 2014 at King Abdulaziz Medical City-Western Region. Of the MI patients 64 were eligible, 7 were excluded due to end stage renal disease and the rest had no sufficient date. As for the PE patients 58 were eligible, 2 were excluded due to end stage renal disease and the rest had no sufficient date.
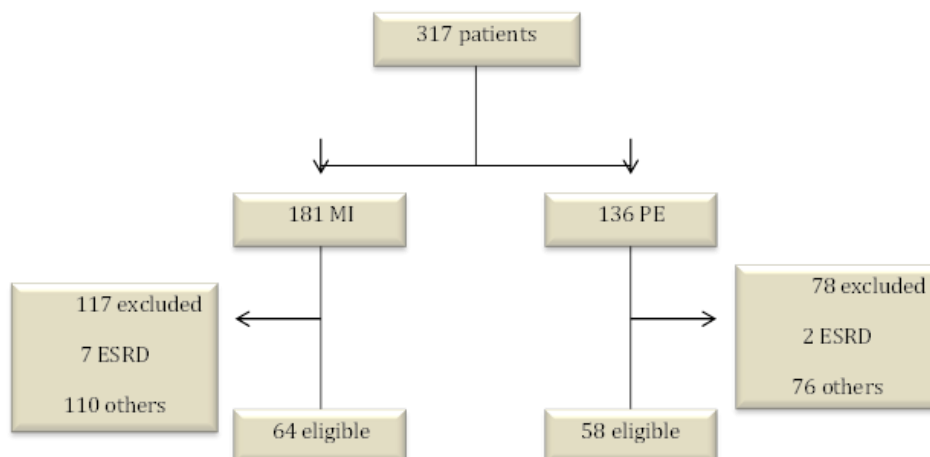
The whole study included 122 patients with 58% of them being males and their mean age was 61 years. Table 1 shows the baseline characteristics of the population included.

The first Trop-I blood level value at presentation was higher with MI (median, 1.49 ng/ml; Interquartile range, 7.14 ng/ml) than with PE (median, 0.01ng/ml; Interquartile range, 0 ng/ml), (p-value <0.001). The maximum blood level value of Trop-I was also significantly higher in patients presenting with MI (median, 8.12 ng/ml; Interquartile range, 24.53 ng/ml) than PE (median, 0.01 ng/ml; Interquartile range, 0.01 ng/ml), (p-value <0.001) (Figure 2)

At Trop-I blood level of 0.05, the sensitivity is 98.4% (95% CI: 91.6 – 100%) and specificity is 84.5% (95% CI: 72.6 – 92.7%). At the level of 0.1, the sensitivity is reduced to 76.6% (95% CI: 64.3 – 86.2%) but with almost perfect specificity of 98.3% (95% CI: 90.8 – 100%).

No association was identified between post-MI Trop-I level and echocardiographic finding of ventricular wall motion abnormality (OR, 1.02; 95% CI: 0.98 – 1.05) (Figure 2) or LV dysfunction (OR, 1.02; 95% CI: 0.99 – 1.04) (Figure 3).

There was, however, a strong association between post-PE elevation of Trop-I and RV dysfunction (Figure 4), since it was elevated in all patients with RV dysfunction and in only 10% of patients without RV dysfunction (p-value = 0.002).

4. DISCUSSION

In this retrospective chart review of 64 patients with MI and 58 patients with PE, we evaluated the utility of Trop-I blood level value in the accurate diagnosis of MI and PE and we determined the cut off points at which the level of Trop-I presented the highest sensitivity and specificity. Patients were diagnosed with MI based on the third universal consensus definition of MI, which is an elevation of cardiac biomarker values with at least one of the following:

• Symptoms of ischemia.

• Development of pathologic Q waves in the ECG.

• New or presumed new significant ST-segment-T wave (ST-T) changes or new left bundle branch block (LBBB).

• Identification of an intracoronary thrombus by angiography or autopsy.

• Imaging evidence of new loss of viable myocardium or a new regional wall motion abnormality (7)

While the diagnosis of PE was based on CT pulmonary angiogram or ventilation perfusion scan confirmation.

We also investigated the association between Trop-I level and LV dysfunction in patients with MI by comparing the level of Trop-I with the Echo findings mainly the LV ejection fraction and the regional wall motion abnormality and RV dysfunction or dilatation in patients with PE.

5. LIMITATIONS

First not all patients diagnosed with PE had Trop-I level measurement, also not all PE patients had Echo to view the RV dysfunction. Second, we couldn't evaluate the level of Trop-I in patients with ESRD because they were excluded from the study due to chronic elevation of Trop-I. Third, we were only given a week by the Research Summer School to collect the data which limited the number of cases that can be reviewed. 4th, there's no previous studies to compare it with our results.

6. CONCLUSION

The blood level value of Trop-I may have important clinical implication for differentiating MI from PE at the initial presentation of patients with atypical clinical, electrocardiographic, or radiologic features. We've reached 2 cut off points: 0.05 ng/ml where the sensitivity is 98.4% (95% CI: 91.6 – 100%) and specificity is 84.5% (95% CI: 72.6 – 92.7%) and the other point: 0.1 ng/ml where the sensitivity is reduced to 76.6% (95% CI: 64.3 – 86.2%) but with almost perfect specificity of 98.3% (95% CI: 90.8 – 100%).

Trop-I level is not associated with LV dysfunction among MI patients, but has strong association with RV dysfunction among PE patients.

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APPENDIX - A

Table 1. Demographics and disease characteristics of the study subjects

| Characteristics	All patients (n=122)	MI patients (n=64)	PE patients (n=58)	P value
Age	62	69.03	54.24	0.02
Gender	71 male (58.2%) 51 female (41.8%)	46 male (71.9%) 18 female (28.1%)	25 male (43.1%) 33 female (56.9%)	0.140
History of: DM[1]	61 (50%)	43 (67.2%)	18 (31%)	<0.001
HTN[2]	59 (48.4%)	44 (68.8%)	15 (25.9%)	<0.001
Smoking	11 (9%)	10 (15.6%)	1 (1.7%)	0.070
Malignancy	39 (32%)	7 (10.9%)	32 (55.2%)	<0.001
Renal Impairment	16 (13.1%)	14 (21.9%)	2 (3.4%)	0.003
Cardiac disorder	39 (32%)	30 (46.9%)	9 (15.5%)	<0.001
Recent surgery	12 (9.8%)	0	12 (20.7%)	<0.001
Dyslipidemia	26 (21.3%)	23 (35.9%)	3 (5.2%)	<0.001
Deceased	26 (21.3%)	9 (14.1%)	17 (29.3%)	0.040

APPENDIX - B
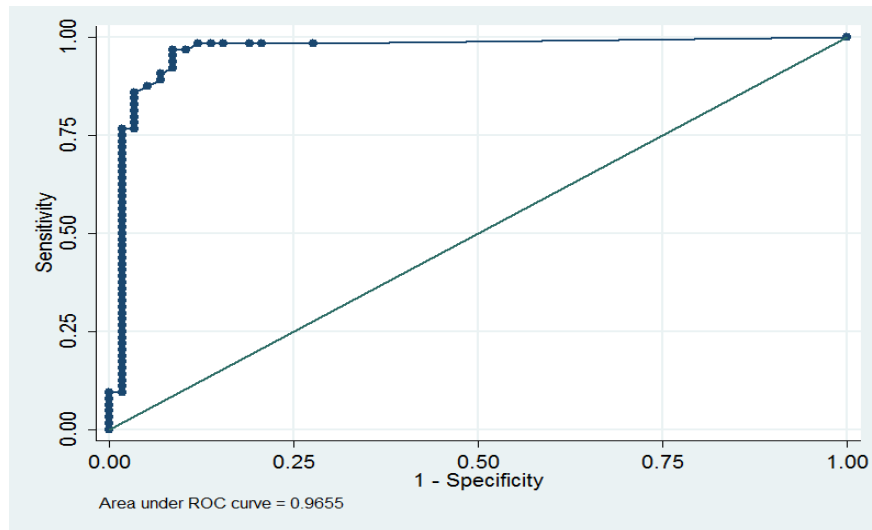
Figure 1: ROC curve describing the diagnostic performance of troponin I blood level in differentiating myocardial infarction from pulmonary embolism.
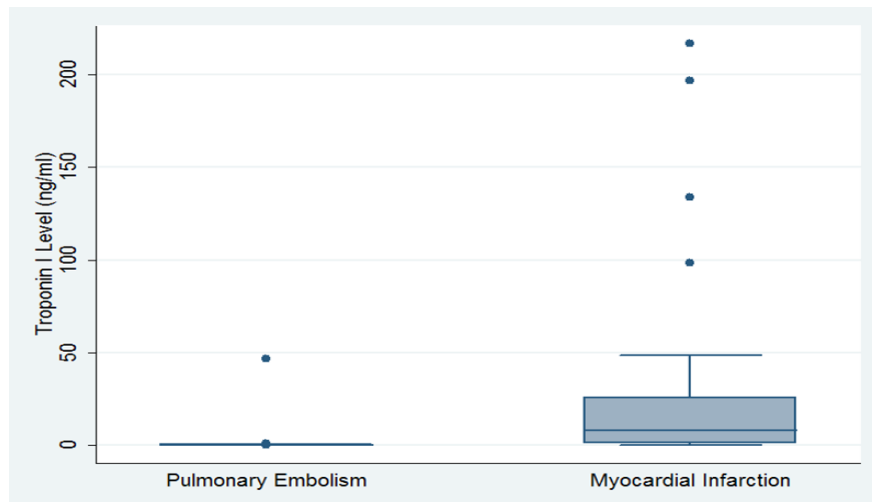

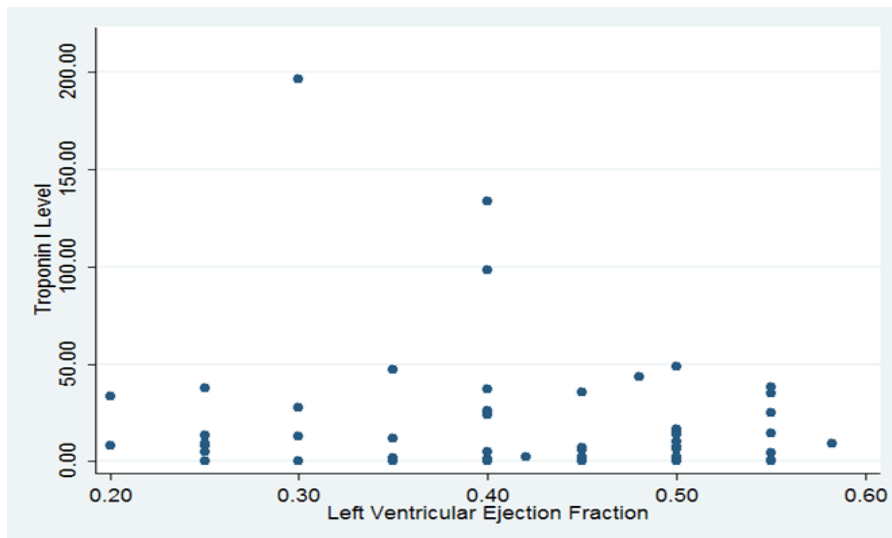**Figure 2: Boxplot showing the higher elevation in troponin I blood level in myocardial infarction than pulmonary embolism**.

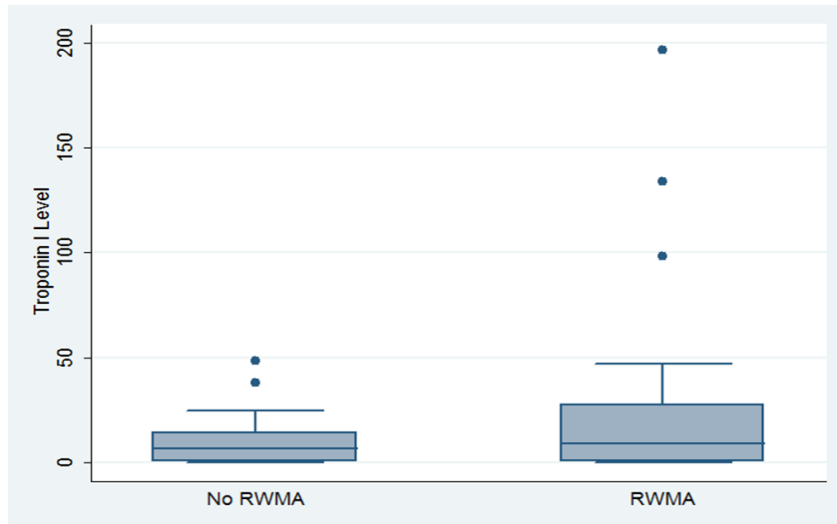**Figure 3: Poor association between Trop-I level and LV ejection fraction in MI patients.**

Page | 1975

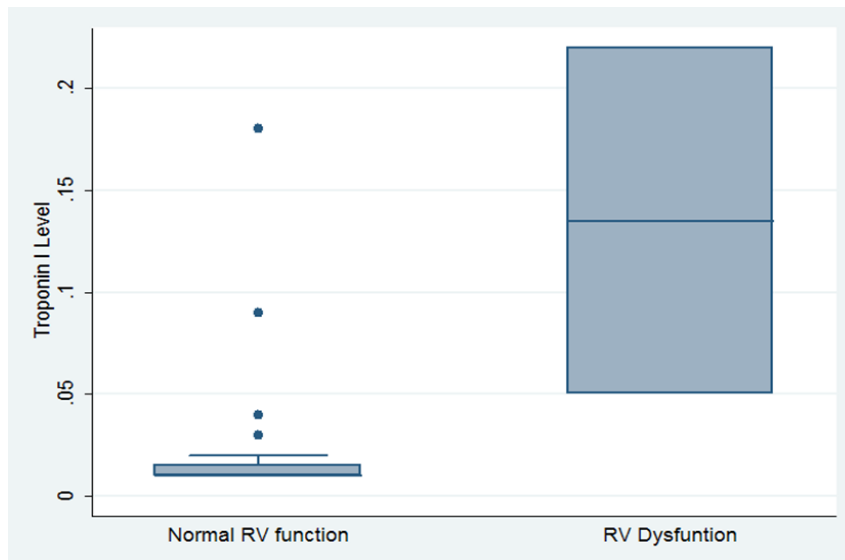**Figure 4: Poor association between Trop-I level and RMWA in MI patients.**

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Figure 5: Boxplot showing the strong association between Trop-I level and RV dysfunction in PE patients