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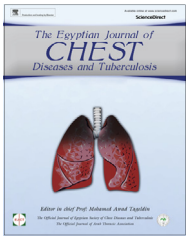

ORIGINAL ARTICLE

Value of cardiac biomarkers in patients with acute pulmonary embolism

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KEYWORDS

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Abstract *Background:* Prognostic stratification of patients with PE is important in management and potentially improve clinical outcome. Cardiac biomarkers are used as an adjunct to clinical and echocardiographic risk stratification in a variety of circumstances, (Creatine-kinase-MB "CK-MB") and cardiac troponin I (cTnI) are most widely used because of their high sensitivities, and very high specificity of troponin for heart muscle injury. Evidence is mounting that myoglobin's sensitivity for myocardial necrosis combined with its unique release and clearance properties may render it particularly attractive as a risk marker either alone or in combination with other markers.

Objectives: The aim of the current study is to assess the levels of cardiac specific biomarkers in relation to different clinical, ECG and echocardiogrphic findings in patients with acute PE, as well as evaluating the prognostic value of these biomarkers for inhospital mortality and adverse clinical events.

Patients and methods: This study comprised 40 patients with proved PE (22 males and 18 females), their mean age was 50.05 ± 13.09 years (range 22–70 years). The following investigations were performed for all patients; 12-leads ECG, Full echo Doppler study, spiral CT of the chest, and laboratory testing: arterial blood gas, serum myoglobin, serum troponin, total CK and CK-MB, kidney and liver function tests.

Result: Significant elevation of CK-MB (>10 μ/L) was noted only in 7.5% of patients, while cardiac cTnI was elevated ($\geqslant 0.07$ ng/ml) in 45% of patients and elevated serum myoglobin was found very early after symptoms (<4 h) in 55% of patients. Elevated serum cTnI and myoglobin were significantly associated with ECG signs of right ventricular strain and echocardiographic evidence of right ventricular dysfunction.

Conclusion: The results of the present study demonstrate the prognostic value of cardiac specific biomarkers, cardiac troponin I & myoglobin in acute pulmonary embolism. Thus, the current data combined with the results of previous studies strongly support the integration of troponin and myoglobin testing into the risk stratification and management of patients with established acute PE.

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Introduction

Acute pulmonary embolism (PE) has a wide spectrum of clinical presentations. The short-term clinical outcome of patients with PE varies from early recovery of symptoms to hemodynamic deterioration and death [1]. Echocardiography has emerged as the principal tool for risk stratification in acute PE. From a prognostic point of view, echocardiography helps to classify patients with PE, right ventricular dysfunction on the echocardiogram is an independent and powerful predictor of early death in patients with acute PE [2].

Among patients with normal blood pressure on admission, right ventricular (RV) dysfunction at echocardiography (Echo) identifies those at high risk for in- hospital mortality. In those patients, elevated levels of cardiac biomarkers have been associated with RV dysfunction at Echo [3].

Severe dyspnea, cyanosis, and syncope indicate life-threatening PE. The clinical examination may reveal signs of acute right ventricular dysfunction, including tachycardia, a low arterial blood pressure, distended neck veins, an accentuated P 2, or a tricuspid regurgitation murmur. On the ECG, T-wave inversion or a pseudoinfarction pattern (Qr) in the anterior precordial leads indicates right ventricular dilation and dysfunction [4].

Myoglobin is a heme protein found in all striated muscles. Although the sensitivity of myoglobin for cardiac necrosis is similar to that of cardiac troponin (Tn) and creatine-kinase myocardial band (CK-MB), its diagnostic use is limited by concerns about its lack of specificity [5]. However, evidence is mounting that myoglobin sensitivity for myocardial necrosis combined with its unique release and clearance properties may render it particularly attractive as a risk marker either alone or in combination with other markers. Myoglobin may be detectable above the upper limits of normal in the serum within 1–3 h of the onset of myocardial injury, but becomes no longer detectable within 12–18 h. This unique profile offers special opportunities for using myoglobin in diagnostic and risk stratification purposes [6]. The relationship between serum levels of myoglobin and clinical outcomes in patients with PE has been assessed in a limited number of studies, but – however – remains unclear [2].

Cardiac troponins are the most sensitive and specific biomarkers of myocardial cell damage, reflecting microscopic myocardial necrosis [7]. Elevated Tn levels predict adverse outcomes in patients with acute myocardial infarction (MI) and in critically ill patients without acute coronary syndromes [8]. Troponin is a regulatory protein of the thin filament of striated muscle and consists of 3 subunits: TnC at 18 kDa, cTnI at 21 kDa, and TnT at 37 kDa. The serum levels of TnT and cTnI are increased for many days after MI, but less elevation occurs with PE; being of short duration [9].

The current study aimed at assessing the levels of these cardiac biomarkers in relation to the different clinical, ECG, and Echo findings in patients with acute PE; as well as evaluating the prognostic value of these biomarkers for in-hospital mortality and adverse clinical events in this category of patients.

Patients and methods

This study comprised 40 consecutive patients (22 male and 18 female) aged 50.1 ± 13.1 years. These patients were proved to have acute PE by spiral contrast-enhanced computed tomography (CT) of the chest. Only the patients referred within 12 h of the onset of symptoms were included in this study.

Exclusion criteria included delayed presentation after the onset of symptoms, patients with ischemic, valvular, or congenital heart diseases, renal or hepatic failure, connective tissue disorders, endocrine disorders, and recent trauma or surgery.

All patients were subjected to thorough history taking (with stress on the analysis of chest pain, dyspnea, hemoptysis, and cardiovascular collapse) and complete general and local examination. All patients underwent the following investigations: standard transthoracic 12-leads ECG, full Echo-Doppler study (to evaluate left ventricular size and function, cardiac valves, pericardium, RV size and function, pulmonary artery diameter and pressure), spiral chest CT, and laboratory tests (arterial blood gases, serum myoglobin, serum troponin, total CK and CK-MB, kidney and liver function tests).

Clinical end points of the study included overall mortality and complicated in-hospital course; which is defined as one or more of the following: need for thrombolytic therapy, catecholamine support of blood pressure, endotracheal intubation or cardiopulmonary resuscitation. Other in-hospital adverse clinical events include: ischemic stroke (confirmed by CT brain) and major bleeding (defined according to standardized criteria). Recurrent PE was confirmed by spiral chest CT. The mean duration of in-hospital stay was 25.2 ± 9.6 days. The cutoff levels of both cTnI and myoglobin in cases of acute pulmonary embolism (> 0.07 ng/ml, > 70 ng/ml), respectively, were applied in the current study as mentioned according to European guidelines on the diagnosis and management of pulmonary embolism [10].

Laboratory methods

Venous blood sample (5 ml) was drawn from each patient through antecubital vein and the separated sera were aliquoted and preserved at −70 °C till the time of Tn, CK-MB, and myoglobin assay.

cTnI assay: this was estimated using chemiluminscence autoanalyzer (Imnulite 1000, USA).

Myoglobin assay: this was done through the immunoturbidimetry method using automated Cobas Integra instrument (Roche, Germany).

CK-MB assay: this was done through the immunoinhibition method.

Statistical methods

Data were analyzed using SPSS program version 16. Qualitative data were presented as number of patients (percentage). Quantitative data were tested for normality by Kolmogrov–Smirnov test. Normally distributed data were presented as mean ± SD. Independent-samples *t*-test was used to compare between two groups. Pearson correlation co-efficient was used to correlate between variables. A two-tailed p-value < 0.05 was regarded as significant.

Results

The clinical and other characteristics of the study population are shown in Table 1. As shown in the table, almost all patients