CARDIAC BIOMARKERS IN PATIENTS WITH ACUTE PULMONARY EMBOLISM

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Abstract:
Objective: To determine the cardiac biomarkers in patients with acute pulmonary embolism.

Patients And Methods: The two year cross sectional multidisciplinary and multicenter study (2015-2017) was conducted at tertiary care hospital while the data was also recruited from few private hospitals as well. All the patients diagnosed as cases of pulmonary embolism were explored to have detail history, clinical examination and along with routine investigations had transthoracic echocardiography (TTE) to detect right ventricular dysfunction. Venous plasma and serum samples were obtained on admission and serum cTnT levels were determined with the use of a commercial kit while plasma concentrations of H-FABP and NT-proBNP were measured qualitatively using a commercial enzyme-linked immunosorbent assay (ELISA) whereas the frequency / percentages (%) and means ±SD computed for study variables.

Results: During two year study period total fifty patients were explored and study. The mean ± SD for age (yrs) of population was 49.21±7.54 while the mean ± SD for cardiac biomarkers detected as H-FABP (ng/mL) 1.9±0.7 NT-proBNP (pg/mL) 183.3±56.4, cTn-T (ng/mL) 0.10±0.8, myoglobin, (ng/mL) 69.6±87.9, CK-MB (ng/mL) 12.1±8.9 and CRP (mg/dL) 6.1±5.3 respectively.

Conclusion: The highest concentrations of HFABP, NT-proBNP, and cTn-T were observed in patients with PE.

Keywords: Cardiac biomarkers and pulmonary embolism

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INTRODUCTION:
Cardiac biomarkers, such as cardiac troponin T (cTn-T), myoglobin (Mb), brain natriuretic peptide (BNP), and the N-terminal fragment of its prohormone (NT-proBNP), as well as heart-type fatty acid-binding protein (HFABP), have been successfully used in the diagnosis of acute coronary syndromes and congestive heart failure for several years [1]. It was recently shown that they are also potential useful prognostic biomarkers in patients with pulmonary embolism (PE). It was demonstrated that the absence of cardiac troponin elevation can exclude an adverse in-hospital outcome with a high negative predictive value in patients with acute PE [2]. It was shown that HFABP, as a biomarker, provides earlier and superior prognostic information than troponin in the first hours of acute coronary syndromes. Recently, circulating HFABP levels have also been shown to be relevant for risk stratification in PE. Small cytoplasmic molecules, like myoglobin and HFABP, rise earlier (2-4 h) than bigger ones that are mainly associated with myofibrils, such as cardiac troponins. Right ventricular dysfunction is an independent predictor of early mortality in PE not only for patients presenting with arterial hypotension and cardiogenic shock but also for normotensive patients [3, 4]. Therefore, after having confirmed PE, echocardiography may play an important role for risk stratification of patients presenting with PE. In the present study, we evaluated RVD and cardiac biomarkers (HFABP, NT-proBNP, and cTn-T) for myocardial damage and short-term mortality in patients with acute PE.

PATIENTS AND METHODS:
The two year cross sectional multidisciplinary and multicenter study (2015-2017) was conducted at tertiary care hospital while the data was also recruited from few private hospitals as well. All the patients diagnosed as cases of pulmonary embolism were explored to have detail history, clinical examination and along with routine investigations had transthoracic echocardiography (TTE) to detect right ventricular dysfunction. After measuring all of these parameters, right ventricular systolic pressure, a visual estimate of RV function, and the modified Simpson’s method for the estimation of right and left ventricular ejection fraction (EF) were performed. Venous plasma and serum samples were obtained on admission, as well as 4, 8, and 24 h later, and were immediately stored and were later analyzed. Serum cTnT levels were determined with the use of a commercial kit while plasma concentrations of HFABP and NT-proBNP were measured qualitatively using a commercial enzyme-linked immunosorbent assay (ELISA). The data was collected on pre-designed proforma and analyzed in SPSS to manipulate the frequencies and percentages.

RESULTS:
During two year study period total fifty patients were explored and study. The mean ± SD for age (yrs) of population was 49.21±7.54. The demographical and clinical profile of study population is presented in Table 1.

| TABLE 1: THE DEMOGRAPHICAL AND CLINICAL PROFILE OF STUDY POPULATION |
| Parameter     | Frequency (N=50) | Percentage (%) |
|---------------|------------------|----------------|
| AGE (yrs)     |                  |                |
| 30-39         | 04               | 8.0            |
| 40-49         | 18               | 36             |
| 50-59         | 13               | 26             |
| 60-70         | 07               | 14             |
| 70+           | 08               | 16             |
| GENDER        |                  |                |
| Male          | 25               | 50             |
| Female        | 25               | 50             |
| RESIDENCE     |                  |                |
| Urban         | 18               | 36             |
| Rural         | 32               | 64             |
| CO-MORBIDITIES|                  |                |
| Hypertension  | 08               | 16             |
| Diabetes mellitus | 11    | 22             |
Obesity 12 24  
Cancer 06 12  
History of venous thrombosis 05 10  
COPD 03 6.0  
CAD 05 10  

| CARDIAC BIOMARKERS | MEAN ± SD |
|--------------------|-----------|
| HFABP, ng/mL       | 1.9±0.7   |
| NT-proBNP, pg/mL   | 183.3±56.4|
| cTn-T, ng/mL       | 0.10±0.8  |
| Myoglobin, ng/mL   | 69.6±87.9 |
| CK-MB, ng/mL       | 12.1±8.9  |
| CRP, mg/dL         | 6.1±5.3   |
| RVEF, %            | 43.8±4.3  |
| LVEF, %            | 58.3±5.0  |

DISCUSSION:
The highest levels of systolic and mean PAPs and concentrations of HFABP, NT-proBNP, and cTn-T were observed in patients with PE. The size of the embolus and the underlying cardiopulmonary function are the most determinants of morbidity and mortality in patients with acute PE. A sudden increase in pressure load on the right ventricle and the increased pulmonary artery pressure may not be tolerated due to the inability of its thin wall to develop and sustain high wall tension and stress. It is important to risk-stratify patients with PE at presentation for the management strategy. Although patients with hemodynamic instability at presentation have high mortality, hemodynamically stable patients with RVD have also high mortality; however, these patients are more difficult to recognize. Echocardiography may not always be available, and there is the potential for biomarkers to provide additive prognostic information. Myocardial wall stress is a potent stimulus for the increased synthesis and secretion of BNP and NT-proBNP. Tulevski et al [5] showed that 29% of normotensive patients had increased BNP and normal troponin T at presentation; in half of them, BNP remained increased after treatment, and they were diagnosed with chronic PE and RV pressure overload during the follow-up. Microinfarction in the right ventricle can be potentially detected by even small increases in troponin levels. Cardiac troponins are highly sensitive and specific indicators of myocardial cell damage, and elevated troponin levels were correlated with in-hospital mortality or complications in unselected patients with acute PE. However, intracellular HFABP tends to appear early in the circulation after myocardial injury [6, 7]. Puls M, et al [8] showed that HABP is superior to NT-proBNP and cTn-T for predicting 30-day mortality or a complicated outcome in 107 consecutive patients with acute PE. The present study results confirm that there may be a relationship between cardiac biomarkers, arterial hypoxemia, pulmonary hypertension, and RV dysfunction in patients with PE.

CONCLUSION:
The highest concentrations of HFABP, NT-proBNP, and cTn-T were observed in patients with PE. Therefore, a multi-cardiac biomarker approach in association with echocardiographic evaluation may provide more meaningful short-term risk stratification.

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