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Serial measurements of troponin and echocardiography in patients with moderate-to-severe acute respiratory distress syndrome☆

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ABSTRACT

Purpose: To assess the clinical significance of serial troponin I levels (measured in the first 72 hours from admission) in 42 consecutive patients with moderate-to-severe acute respiratory distress syndrome (ARDS). Echocardiography and electrocardiogram testings were serially performed in the time window.
Materials and methods: Troponin I was measured every 12 hours in the first 72 hours from intensive care unit (ICU) admission. Echocardiography and electrocardiogram testings were serially performed in the same time window to clinically interpret Tn I levels.
Results: Patients with admission positive Tn I (38.1%) showed higher values of systolic pulmonary hypertension ($P = .013$) associated with significantly lower values of tricuspid annular plane excursion ($P = .011$). Twenty-five patients (25/42, 59.5%) exhibited positive peak Tn I and at second echocardiographic assessment exhibited significant lower tricuspid annular plane excursion values ($P = .005$). At stepwise regression analysis the following variables were an independent predictor for in-ICU mortality: Pco_2 (OR 1.08, 95% CI 1.011-1.161, $P = .023$), systolic pulmonary arterial hypertension (OR 0.83, 95% CI 0.701-0.977, $P = .002$), log peak Tn I (OR 3.56, 95% CI 1.045-12.132, $P = .042$).
Conclusions: In moderate-to-severe ARDS, serial troponin I assessment together with echocardiography evaluation helped to identify a subgroup at higher risk for in-ICU death. Moreover, troponin release can be related to right ventricular dysfunction, thus highlighting the clinical role of echocardiography in ARDS patients.

1. Introduction

Acute respiratory distress syndrome (ARDS) has been associated to considerable cardiovascular strain, which may be related to severe respiratory compromise and hypoxemia [1].

Elevated levels of cardiac biomarkers are associated with increased mortality and length of stay in critically ill patients, though the mechanism(s) responsible for biomarker elevations are still to be completely elucidated [2]. Data on the clinical significance of elevated levels of blood biochemical markers of myocardial necrosis in ARDS patients are so far scarce [3–5] and discrepancies exist among investigations [3–5] especially because of different timing of troponin measurements and the incorporation of electrocardiogram (ECG) testings and echocardiograms in the analysis.

The aim of the present investigation was to assess the clinical significance of serial troponin I levels (measured in the first 72 hours from intensive care unit [ICU] admission) in 42 consecutive patients with moderate-to-severe ARDS. Echocardiography and electrocardiogram testings were serially performed in the time window to clinically interpret Tn I levels.

2. Methods

From 1 January 2013 to 31 December 2014, 42 patients with moderate-to-severe ARDS [6] were consecutively admitted to our ICU.

Baseline characteristics were collected for all patients and the simplified acute physiology score (SAPS II) score was calculated [7].

On ICU admission, the following parameters were measured: glucose (mg/dL), troponin I (Tn I, ng/mL, normal values <0.10 ng/mL), creatinine (mg/dl) and NT-proBNP (pg/mL). Tn I and creatinine were also measured every 12 hours for the first 72 hours after admission and peak values were considered.

Abbreviations: ARDS, acute respiratory distress syndrome; ECG, electrocardiogram; LV, left ventricle; RV, right ventricle; sPAP, systolic pulmonary arterial hypertension; TAPSE, tricuspid annular plane excursion; Tn I, troponin I; TTE, transthoracic echocardiography; TEE, transesophageal echocardiography.

☆ No conflict of interest.

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Data on cardiovascular risk factors were obtained from the history upon admission and coronary artery disease was considered to be present if documented in the medical record, reported by the patients or their kins or if there were confirmatory testing data available.

2.1. Echocardiographic assessment

According to the protocol of our Center, echocardiography is performed routinely within the first 12 hours after ICU admission and repeated within the first 72 hours after admission and, afterward, throughout ICU course when clinical needed. In patients who showed a positive Tn I levels in the first 72 hours from ICU admission, echocardiography was performed on the same day of positive Tn I measurement.

According to our protocol [8–12] the echocardiographic examination is transthoracic (TTE), transesophageal (TEE) or both, according to the best acoustic window (Esaote MyLab30Gold Cardiovascular, Esaote S.p.A, Genoa, Italy) [12]. The left ventricular (LV) ejection fraction (LVEF) was estimated by "visual" examination on short-axis views [13]. LV systolic dysfunction was defined as LV ejection fraction less than 45% [14,15].

The right ventricle size was assessed by the right ventricular (RV) end-diastolic area and the ratio between end-diastolic areas of the right and left ventricles was calculated. This ratio classifies RV function as normal (<0.6), moderately altered (0.6-0.8), severely altered (>0.8) [16].

Systolic pulmonary artery pressure (sPAP) was obtained using the simplified Bernouilli's equation: 4 • (Vmax tricuspid regurgitation)2 + central venous pressure (CVP). To reduce the lack of precision of CVP estimation based on the size of the inferior vena cava, CVP was invasively measured through central venous catheters [17].

Tricuspid annular plane excursion (TAPSE) [17] was also measured, as the difference of displacement during diastole and systole [12,16,17]. A TAPSE <16 mm is known to indicate RV dysfunction [12,17,18].

The echocardiographic examination was blinded to the troponin results.

2.2. Electrocardiogram testing

Electrocardiogram testings were performed simultaneously to the echocardiograms and was examined for the presence or absence of myocardial ischemia [19]. The ECG interpretation was carried out by a cardiologist (CL), unaware of the clinical condition and of the results of blood examinations of the single patient.

2.3. Outcome

The outcome was mortality during ICU.

All participants (or their kins) signed a written informed consent for storing their clinical data. The study design was approved by our institutional committee, since it is a retrospective analysis of data and it does not need an ethical approval.

2.4. Statistical analysis

Statistical analysis has been conducted with SPSS 13.0 for Windows software (SPSS Inc, Chicago, IL) A 2-tailed $P < .05$ was considered statistically significant. Categorical variables are reported as frequencies and percentages; continuous variables are reported as mean ± SD. For continuous variables, between-group comparisons have been performed with Student t test or analysis of variance (followed by Bonferroni post-tests if overall P was significant) or by means of Kruskal-Wallis H test. Categorical variables have been compared with χ^2. Log transformation was performed on peak Tn levels to achieve normality. Pearson's correlation analysis was performed to assess the relation between log peak Tn I and systolic pulmonary hypertension, TAPSE, pH, and P_{CO_2}. Multivariate correlation with in-ICU mortality was investigated with logistic regression analysis (backward stepwise selection algorithm): candidate variables were carefully chosen among those known to be clinically related or those with significant differences in baseline characteristics to outcome in order to avoid model overfitting; Hosmer-Lemeshow goodness-of-fit test, and Nagelkerke pseudo-R^2 are reported.

3. Results

Our population comprises 42 consecutive patients with ARDS and it was constituted mainly by males (31/42, 73.8%). The main cause of ARDS was pneumonia (78.6%). Hypertension was the most frequent risk factor, being detectable in the 35.7% of patients (Table 1). Sixteen patients (38.1%) showed positive admission Tn I levels and, when compared to patients with normal admission Tn I, they showed significantly higher values of admission glycemia ($P = .016$) and NT-proBNP ($P = .019$), together with lower values of pH, higher P_{CO_2} and higher values of plateau pressure ($P = .004$, $P = .018$ and $P = .02$, respectively). No difference in ICU mortality was observed between the two subgroups (Table 1).

Table 2 shows the echocardiographic findings at first assessment. In our series, echocardiography was transthoracic in 15 patients (35.7%) and trans esophageal in 20 patients (47.6%) and both in the remaining 7 patients (16.7%). Patients with positive admission Tn I showed higher values of systolic pulmonary hypertension ($P= .013$) associated with significantly lower values of TAPSE ($P = .011$). No new onset segmental wall abnormalities were detected in the two subgroups at first echocardiography.

In our series, one patient was submitted to elective coronary angiography since she showed a significant increase of Tn I values (peak values 16 ng/mL) associated with reduced LVEF (50%, though in the lack of segmental wall abnormalities and ECG findings indicative of acute coronary ischemia). No coronary lesion was documented at coronary angiography. Patients with positive admission Tn I showed a higher incidence of T-wave flattening ($P = .03$, statistical power 82%).

As shown in Table 3, 25 patients (25/42, 59.5%) exhibited positive peak Tn I. In particular, among the 16 patients with admission positive Tn I, two patients normalized Tn I levels, while 11 patients with normal admission Tn I showed positive peak Tn I. In-ICU mortality was significantly higher in patients with positive peak Tn I in respect to patients with normal Tn I ($P = .011$, statistical power 85%). At the second echocardiographic examination (transthoracic in 18 patients, trans esophageal in 19 and both in the remaining 5), patients with positive peak Tn I showed significant lower TAPSE values ($P = .005$, statistical power 88%). no differences were observed in ECG findings between the two subgroups (Table 3).

At Pearson's correlation analysis, log Tn I showed a significant direct relation with sPAP ($r = 0.37$, $P = .016$) and P_{CO_2} ($r = 0.41$, $P = .001$) and an inverse relationship with TAPSE ($r = -0.51$, $P = .001$) and pH ($r = -0.32$, $P = .038$).

At stepwise regression analysis the following variables were independent predictor for in-ICU mortality: P_{CO_2} (OR 1.08, 95% CI 1.011-1.161, $P = .023$), sPAP (OR 0.83, 95% CI 0.701-0.977, $P = .002$), log peak Tn I (OR 3.56, 95% CI 1.045-12.132, $p = 0.042$). Hosmer-Lemeshow χ^2 18.2, $P = .20$; Nagelkerke pseudo-R^2 0.45.

4. Discussion

The main findings of investigation are as follows: a) positive admission Tn I is associated with RV dysfunction (as indicated by lower values of TAPSE), pulmonary arterial hypertension, and hypercapnic acidosis; c) positive peak Tn I is quite common (being detectable in the 59.5%), and it is a predictor for in-ICU mortality.

To date, data on the clinical and prognostic significance of troponin levels in ARDS patients are scarce and not univocal since investigations differed mainly in timing of Tn measurements and whether other evaluations such as ECG testings and echocardiographic exams were incorporated in the analysis.

Bajwa et al [3] documented that the presence of an elevated cardiac marker was an independent predictor of 60-day mortality in 305 ARDS