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Full Length Article

Prognostic significance of electrocardiogram at presentation in patients with pulmonary embolism of different severity

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ABSTRACT

Background: Several electrocardiographic (ECG) abnormalities have been described in patients with acute pulmonary embolism (PE), with discordant reportings about their prognostic value.

Methods: Consecutive patients with echocardiography performed within 48 h from admission and ECG at presentation, were included in this analysis. The primary study outcome was in-hospital death for high-risk patients and in-hospital death or clinical deterioration for intermediate-risk patients. As secondary outcomes, the associations among ECG abnormalities and both right ventricular dysfunction at echocardiography and baseline troponin elevation were considered.

Results: 1194 patients were included in this analysis: 13.8% of patients were at high risk of early death, 61.7% were at intermediate risk and 24.5% were at low risk. ECG signs of RV strain showed a continuously decreasing prevalence from high-risk to intermediate-risk and low-risk patients. Differently, the prevalence of T- wave inversion was similar in high and intermediate-risk patients. In high-risk-patients, Qr pattern in lead V_1 was the only ECG abnormality associated with in-hospital mortality, but this sign was detected in only 15.9% of this risk category; the presence of at least one ECG abnormality was not associated with the risk of in-hospital death. In not high-risk patients, the presence of at least one ECG abnormality was significantly associated with RVD and this association was confirmed for each individual ECG abnormality. Similar results were obtained as regards the baseline troponin elevation in 816 patients.

Conclusions: Among the electrocardiographic signs of RV strain/ischemia, Qr pattern in lead V1 was the only ECG abnormality associated with in-hospital mortality in high-risk patients. In not high-risk patients the demonstrated association among baseline ECG signs of RV strain/ischemia and RV dysfunction at echocardiography or troponin elevation highlights the need for early further investigations in patients with such ECG abnormalities.

1. Introduction

The electrocardiogram (ECG) is one of the first test to be performed in the emergency department to patients with cardiac or respiratory symptoms because -it is rapidly and everywhere available, with very low cost and no adverse effects. Several different abnormalities have been described in patients with pulmonary embolism (PE) either in the past decades or recently [1–4], with discordant reportings about the prognostic significance of each of them [5–10]. As a result of such uncertainty, the last Guidelines of the European Society of Cardiology [11] did not include ECG among the variables to be considered in the initial prognostic stratification of PE.

The aim of this analysis was: 1) to describe the baseline ECG abnormalities in a wide population of patients with confirmed PE, included in the Italian Pulmonary Embolism Registry [12]; 2) to assess whether the presence of at least one ECG abnormality of right ventricular strain/ischemia affects the short-term mortality and the composite outcome of mortality and clinical deterioration in patients with acute PE of different severity and 3) to assess whether such ECG abnormalities are associated with right ventricular dysfunction (RVD) at

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echocardiography or with a baseline troponin elevation.

2. Patients and methods

2.1. Study design and population

The Italian Pulmonary Embolism Registry (IPER) is a prospective, multicenter, web-based registry. Patients were enrolled by 49 departments in 47 Italian hospitals. Study centres were cardiology, (37), emergency [6] and internal medicine departments [6]. Data regarding clinical status, imaging and laboratory examinations were collected at presentation, during the hospital stay, at discharge and during an extended follow-up period. Enrolment started on September 1, 2006 and was completed on August 31, 2010. The follow-up period ended on August 31, 2014.

The study was conducted in accordance with the Guidelines for Good Clinical Practice and the Italian regulation on observational studies. The protocol was approved by the institutional review board at the coordinating centre (San Carlo Borromeo Hospital Ethical Committee; approval number 364, April 12, 2006). The study protocol did not dictate any interference with patient management. The attending physician was in charge of diagnostic and treatment strategies.

The registry was endorsed by the Italian Association of Hospital Cardiologists (ANMCO) and was designed by the Working Group on Pulmonary Circulation. The principal investigator (FC) was responsible for the study design and protocol. The local investigator entered all the data into an on-line database. The principal investigator of the study (F.C.) checked all the data and phoned to the local investigator in case of doubts or discrepancies. All items included in the data collection form (DCF) were reviewed for consistency.

Patients aged 18 years or older with confirmed PE and able to give informed consent were eligible for inclusion in the study. Protocols for diagnostic studies and laboratory tests were reported according to local standards. Data fields on DCFs regarded the hospital phase and the follow-up visits. Data were achieved directly from the patients or from the medical records. PE was considered the cause of death if it was autopsy-confirmed or in case of sudden death that could not be explained by a more compelling alternative diagnosis. Patients with clinical suspicion of PE were included in the registry, provided that one of the following was met: 1 Computerized tomographic pulmonary angiogram (CTPA) positive for PE; 2. Positive perfusion lung scan according to PISA-PED criteria; 3. Pulmonary angiogram interpreted as positive for PE; 4. Combination of deep venous thrombosis at ultrasound of the lower or upper extremities in association with right ventricular dysfunction (RVD) on an echocardiogram; 5. Detection of free floating thrombi in the right atrium at echocardiography; 6 Autopsy.

2.2. Assessments

Right ventricular dysfunction (RVD) on echocardiography was defined by the presence of at least one of the following: 1) right-to-left ventricular end diastolic diameter ratio > 1 in apical four-chamber view, 2) right-to-left ventricular end diastolic diameter ratio > 0.6 in parasternal long-axis or subcostal four-chamber view, and 3) right ventricular-to-right atrial pressure gradient > 30 mm Hg. RVD was not considered to be of acute onset in the presence of RV wall thickness > 7 mm or documentation of RV overload at previous examinations. Electrocardiograms (ECG) were scheduled at presentation, at day 3 and at discharge. ECG abnormalities were adjudicated according to local evaluation. For the purpose of the present study, the ECGs at admission, usually before a confirmed diagnosis of PE, were considered. The emergency physician or the cardiologist on duty interpreted each ECG, usually in the emergency department. The following baseline ECG abnormalities were considered: 1) complete or incomplete right bundle branch block (RBBB), 2) S_1Q_3 pattern, 3) T-wave inversion in leads V_1-V_3 (V_4), 4) ST-segment elevation in inferior leads and 5) Qr pattern in lead V_1.

2.3. Patients' classification

Early clinical assessment and risk stratification to identify high-risk and not high-risk patients were performed according to 2008 European Society of Cardiology (ESC) recommendations [13]. High-risk patients were defined as those haemodynamically unstable, with a systolic arterial blood pressure (BP) at presentation ≤ 90 mm Hg, persisting before the starting of therapy, (we believe that BP measured later could have been affected by therapy) or a pressure drop of ≥ 40 mm Hg for > 15 min (if not caused by new-onset arrhythmias, ipovolaemia or sepsis).

All those patients who were haemodynamically stable at presentation were classified as not-high-risk patients. The only criterion used to categorize not-high-risk patients into intermediate or low-risk groups was the presence or absence of RVD at echocardiography, performed within 48 h from the presentation. Haemodynamically stable patients with RVD (Intermediate-risk patients) were further stratified into two subgroups a) those with a systolic BP higher than 90 mm Hg and lower or equal than 100 mm Hg and b) those with a blood pressure higher than 100 mm Hg.

2.4. Outcomes

The primary study outcome was in-hospital death for high-risk patients and in-hospital death or clinical deterioration in intermediate-risk patients. Clinical deterioration was defined as clinical worsening from a stable to an unstable haemodynamic condition that required at least one of the followings: 1) IV catecholamine infusion to maintain adequate tissue perfusion and prevent or treat cardiogenic shock, 2) endotracheal intubation, or 3) cardiopulmonary resuscitation. As secondary outcomes, RVD on echocardiography and baseline troponin elevation were considered.

2.5. Statistical methods

The characteristics of patients analyzed were summarized using frequency and percentage for categorical variables, and mean and standard deviation (SD) for continuous variables. Chi-square test (or Fisher's exact test, where necessary) for categorical variables, and Wilcoxon test for continuous variables were used to compare baseline clinical and demographic characteristics between patients with and without echocardiography and ECG at presentation.

At least one ECG abnormality and each ECG abnormality were compared among subgroups of patients defined by different levels of PE severity by means of Chi-square test for trend.

Univariate and multivariate logistic regression models were used to assess the effect of at least one ECG abnormality and of each ECG abnormality on in-hospital death or on death/clinical deterioration in the different risk categories.

Moreover, in the subgroups classified as not high-risk patients, the association among either at least one ECG abnormality or each ECG abnormality and both RVD and baseline troponin elevation was evaluated by univariate and multivariate logistic regression models.

All analyses were adjusted by age. Results were expressed as Odds Ratios (ORs) and their 95% confidence interval (95% CIs) and a p-value < 0.05 was considered to be statistically significant. Analyses were carried out using SAS statistical software (version 9.2).

3. Results

Over a 48-month period, 1787 patients diagnosed with PE were included in the study. Seventy-one patients were excluded due to incomplete data reporting. Thus, 1716 patients were included in this analysis: 1622 out-patients presenting to emergency department and 94