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ORIGINAL ARTICLE

Association of Serum Cholesterol Levels with Short-term Mortality in Patients with Acute Pulmonary Embolism

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Background Serum cholesterols play an important role in pathophysiology and prognosis of acute thrombotic diseases. The aim of the present study was to investigate the prognostic value of serum lipid parameters in acute pulmonary embolism (APE).

Methods From January 2008 to January 2014 a total of 275 patients who were hospitalised with a diagnosis of APE were retrospectively screened. Clinical data, laboratory parameters, serum cholesterol levels were recorded and pulmonary embolism severity index (PESI) scores were calculated. Mortality rate at 30 days was investigated as the clinical outcome.

Results In our study population, 24 patients (8.7%) died within 30 days. Serum total cholesterol, LDL-C, HDL-C and triglyceride levels were significantly lower in deceased patients when compared to the survived patients (3.1 ± 0.6 vs. 4.7 ± 1.2 mmol/L, $p < 0.01$; 1.8 ± 0.9 vs. 2.9 ± 0.9 mmol/L, $p < 0.01$; 0.9 ± 0.3 vs. 1.2 ± 0.3 mmol/L, $p < 0.01$; 1.4 ± 0.7 vs. 1.7 ± 0.6 mmol/L, $p = 0.04$, respectively). In multivariate regression analysis; PESI scores (OR: 1.06 95% CI: 1.01-1.11, $p < 0.01$), right ventricular diameter (OR: 11.31 95% CI: 3.25-52.64, $p < 0.01$), total cholesterol (OR: 1.09 95% CI: 1.02-1.17, $p < 0.01$), LDL-C (OR: 1.06 95% CI: 1.01-1.12, $p = 0.02$), HDL-C (OR: 1.21 95% CI: 1.04-1.41, $p < 0.01$) and triglyceride (OR: 1.03 95% CI: 1.01-1.05, $p < 0.01$) levels were independently correlated with mortality.

Conclusions Serum total cholesterol, LDL-C, HDL-C and triglyceride levels, obtained within the first 24 hours of hospital admission, may have prognostic value in patients with APE.

Keywords Acute pulmonary embolism • Lipoproteins • Mortality

Introduction

Acute pulmonary embolism (APE) is a common vascular disease with high mortality and morbidity rates. To date, the prognostic importance of several clinical and laboratory parameters such as advanced age, congestive heart failure, chronic obstructive pulmonary disease, acute right ventricular dysfunction, troponin, brain natriuretic peptide (BNP), H-FABP (Heart type fatty acid binding protein), myoglobin, creatinine, neutrophil gelatinase-associated lipocalin,

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cystatin C levels, white blood cell (WBC) count have been established in APE patients [1]. In addition, patients with lower low density lipoprotein cholesterol (LDL-C) levels and higher high density lipoprotein cholesterol (HDL-C) levels have been shown to have lower recurrence rates after APE [2,3].

Large-scale studies have repeatedly shown the strong association of plasma lipoprotein levels with atherosclerotic process and risk of cardiovascular events [4,5]. Early initiation of statins decreases the risk of adverse events after myocardial infarction (MI) [4]. Whereas, in critically ill patients, in patients with infective endocarditis, acute exacerbation of chronic obstructive pulmonary disease (COPD) and rheumatoid arthritis, lower levels of lipoproteins were associated with worse prognosis [6–10]. In a recent study, lower levels of LDL-C and HDL-C have emerged as predictors of short-term mortality after MI [11]. However, prognostic significance of serum lipoproteins in APE patients has not been studied yet. The aim of this study was to investigate the association between plasma lipoprotein levels and short-term mortality in patients with APE.

Material and Methods

Study Population

Medical records of all consecutive patients with confirmed APE admitted to our institution between January 2008 and January 2014 were retrospectively screened and a total number of 322 subjects were initially recruited. Thirty-two patients who were on statin therapy and 15 patients without a recorded measurement of lipoprotein levels during the index hospitalisation were excluded from the study. Finally, a total number of 275 patients were included in the study.

Data regarding clinical and demographic properties and laboratory parameters were collected from medical records. Short-term mortality was defined as all cause mortality within 30 days of the index event and was determined from medical records. The study protocol was approved by the local ethics committee.

Definitions

According to the current guidelines, definite diagnosis of APE was ascertained with a combination of the following criteria: (1) transthoracic echocardiographic findings confirming APE, (2) lower limb venous ultrasonography findings interpreted as positive for deep venous thrombosis, (3) presence of radiological criteria of APE on computerised tomography (CT) angiography within 30 days after the beginning of shortness of breath or chest pain [1]. The duration of symptoms was defined as the time between beginning of shortness of breath or chest pain and admission to emergency service.

Hypertension (HT) was defined as use of antihypertensive drugs or systolic blood pressure (SBP) $\geq$ 140 mmHg and/or a diastolic blood pressure (DBP) $\geq$ 90 mmHg, diabetes mellitus (DM) was defined as use of antidiabetic drugs or fasting plasma glucose levels of > 7 mmol/L. Smoking status was defined as current tobacco use. Hypotension was defined as a systolic blood pressure < 90 mmHg or a pressure drop of more than 40 mmHg from emergency admission value for longer than 15 minutes if not caused by a new-onset arrhythmia, hypovolaemia or sepsis [1]. All patients' original PESI scores (which includes age, sex, pulse rate, systolic blood pressure, respiratory rate, temperature, arterial oxyhaemoglobin saturation, presence of cancer, chronic heart failure, chronic pulmonary disease and altered mental status as parameters) were calculated for clinical risk stratification [1].

Echocardiography and Computed Tomography Imaging

A complete echocardiographic study was performed with Vivid 3 system (General Electric, made in Norway) during the initial evaluation of the patients. Right ventricular (RV) dimensions were measured from apical four-chamber view in diastole at mid-ventricular level. Right ventricular dilation was defined by RV dimension > 3.3 cm [12]. Systolic pulmonary arterial pressure (sPAP) was calculated by adding transtricuspid pressure gradient to mean right atrial pressure estimated from inferior vena cava diameter and motion during respiration as follows: mean right atrial pressure was estimated to be 5 mm Hg if there was complete collapse of a normal diameter inferior vena cava during inspiration; 10 mm Hg if a normal diameter inferior vena cava collapse was >50%; 15 mm Hg if a dilated inferior vena cava collapsed by >50% with inspiration; and 20 mm Hg if there was no visible collapse of a dilated inferior vena cava with inspiration [12].

Multislice spiral CT was performed in the radiology clinic, using pulmonary embolism protocol (field of view: 35 cm, section thickness: 3 mm, contrast material volume: 135 mL, contrast material injection rate: 4 mL/sec). Diagnosis of APE was established in case of a complete or partial luminal filling defect in the main pulmonary artery or its branches.

Laboratory Analysis

According to the hospital protocol, venous blood samples were taken from antecubital vein and collected in calcium EDTA tubes daily. Complete blood counts were studied by an auto-analyser (Cell-dyn 3700 Abbott, USA) within 30 minutes after blood sampling. Fasting blood samples for measurement of total cholesterol, HDL-C and triglyceride levels were collected within the first 24 hours of hospitalisation and were measured enzymatically (Architect c-Systems, Abbott, USA). Low density lipoprotein cholesterol was calculated using the Friedewald equation. The results of other routine biochemical laboratory parameters and maximum Troponin-I, BNP, D-dimer levels were collected by using the electronic database of the hospital. According to the protocol of our biochemistry clinic, Biosite Triage BNP kits (Biosite Diagnostics, San Diego, ABD) were used for analysis of plasma BNP levels, Alere Triage Cardiac Panel (Alere, Galway, Ireland) for Troponin-I analysis and mLabs D-Dimer kits (Micropoint, Brussels, Belgium) for D-dimer analysis.