SUMMARY

Introduction

Pulmonary embolism (PE) is a major cause of mortality, morbidity and hospitalization in Europe. In 30-40% cases of the PE, the cause (idiopathic or unprovoked PE) cannot be determined. Nowadays, metabolomics becomes important part of clinical studies. It can help to understand the disease process and propose diagnostic and prognostic biomarkers. Until now there was no study using traditional methods and untargeted metabolomics in population of acute PE patients.

Aim

Application of traditional methods and metabolomics to evaluate and identify novel diagnostic and prognostic markers for acute PE, what can also bring new insight into disease pathophysiology. Indication of plasma metabolites differentiating patients hospitalized due to PE from control group, with particular focus on patients with idiopathic and non-idiopathic PE; and with and without deep vein thrombosis, in order to identify new potential diagnostic and prognostic markers for PE.

Methods

Prospective analysis of plasma samples collected from 36 patients hospitalized in Cardiology Department (with proven acute PE, treated with low molecular weight heparin (LMWH, enoxaparin)) and 13 healthy controls (matched with age, sex, BMI, treated with adequate dose of LMWH) was performed. Samples were fingerprinted with LC-QTOF-MS and GC-MS. Differences between PE patients with healthy control after drug (CAD), subgroups of idiopathic and non-idiopathic PE patients, patients with and without deep vein thrombosis (DVT) and controls were evaluated.

Results

Significantly higher concentration of d-dimers, and reduced TAPSE values in patients with idiopathic PE in comparison to patients with non-idiopathic PE was showed in traditional analysis. Patients with PE and DVT characterized with lower total cholesterol and LDL level, larger right ventricle and IVC dimension in the echocardiographic evaluation regarding non-DVT patients.

Performed metabolomics analysis resulted in detection of 105 significantly altered metabolites. Multivariate statistics confirmed clear separation between the examined groups. Venn diagrams allow to select common and differentiating compounds for particular comparison. Significant changes were observed in level of acylcarnitines, phospholipids, fatty acid and their amides sphingolipids. Complementary analysis of metabolic profile of patients with PE in comparison to healthy control showed changes in glycero- and lysoglycerophosphocholines, lysoglycerophosphoethanolamines, carnitines, fatty acids, amino acids and sphingosins level. Metabolism of glycerophospholipids played a major role in PE patients in contrast to CAD. Metabolism of sphingolipids significantly differ patients with idiopathic PE from non-idiopathic PE. Reduction of concentration of lysophosphatidylcholines and lysophosphatidylethanolamines was associated with a greater impairment of RV function and higher risk of early death in patients with PE with regard to CAD.

Conclusions

1. This publication is the first in the literature attempt to comprehensively characterize patients with PE using traditional and metabolomic methods.
2. Complementary analysis using the "metabolomic fingerprint" showed significant differences in the metabolic profile of patients with PE relative to healthy control.
3. The above-mentioned changes find their explanation in the pathophysiological processes taking place in PE. The metabolites significantly different in acute PE patients were associated with hypoxia, lipid-related energy imbalance, alterations in mitochondrial function, signal transduction and genetic information pathways.
4. No changes in the concentration of individual metabolites, but the entire set of them included in the metabolic pathways differentiated groups of patients with PE and CAD, patients with idiopathic PE in relation to non-idiopathic patients and patients with and without DVT.
5. Metabolic fingerprinting could be helpful to improve diagnosis and to understand pathophysiological mechanisms related to acute PE.