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Identification of Reduced Circulating Haptoglobin Concentration as a Biomarker of the Severity of Pulmonary Embolism: A Nontargeted Proteomic Study

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Name: insenser-2014-ide ...
Size: 667.8Kb
Format: PDF

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Abstract:

Risk stratification of patients with pulmonary embolism (PE) may identify patients at high risk of early death who may benefit from more intensive surveillance or aggressive therapy. Nontargeted proteomics may identify biomarkers useful for the risk stratification of patients with acute symptomatic pulmonary embolism (PE). We studied 6 patients presenting with low-risk PE and 6 patients presenting with intermediate (n = 3) or high-risk (n = 3) PE. Two-dimensional difference gel electrophoresis was used to compare their plasma protein abundances. Candidate protein markers were identified by matrix assisted laser desorption ionization time-of-flight mass spectrometry. A panel of four biomarkers (haptoglobin,

hemopexin, α2-macroglobulin, and Ig α1-chain C region) showed differences in plasma abundance among patients with acute symptomatic PE of different severity. Haptoglobin and hemopexin were decreased, whereas α2-macroglobulin and Ig α1-chain C region were increased, in patients with high or intermediate-risk PE compared with low-risk PE patient. In a separate clinical population consisting of 104 adults with acute PE, serum haptoglobin concentrations had an 85% chance of correctly identifying patients with high-risk PE according to receiving operating characteristics curve analysis. Moreover, serum haptoglobin concentrations ≤1 g/l showed an 80% sensitivity and a 96% specificity for the diagnosis of high-risk PE. Nontargeted proteomics identified protein biomarkers for the severity of PE that are involved in iron metabolism pathways and acute-phase response. Among them, reduced serum haptoglobin concentrations show a high accuracy for the biochemical detection of high-risk PE.

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