Fine-tuning of risk prediction in PE: GFR and sPESi combined– powerful predictor of survival in patients with Pulmonary Embolism

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Abstract:

Background: The PESI score is an established prognostic score of the severity of the acute -pulmonary embolism (PE). A recent randomized trial established the identification of low-risk PE (PESI classes I and II), as possible criteria for outpatient treatment of acute PE. Simplified PESI (sPESI), that can be calculated using six equally weighted variabales (age, history of cancer, history of chronic lung disease - COPD or chronic heart failure - CHF, heart rate - HR, systolic blood pressure - BP, arterial oxyhaemoglobin saturation < 90%) can also provide reliable prognostic information. In the already published investigation, the simplified PESI was non-inferior for identification of low risk patients versus imaging and biomarker criteria proposed by the ESC. Patients with sPESI class 0 represented a low-risk PE. Unfortunately, sPESI based therapeutic regimen is still questionable.

However, several laboratory and echocardiographic parameters not included in sPESI score may represent the features of worse outcome in PE. Onset and prognostic implication of acute kidney injury, or acute kidney dysfunction on admission or during hospitalization, were underestimated in patients with acute pulmonary embolism (APE). In acute settings, changes in pulmonary circulation may induce hemodynamic disorder of systemic circulation, causing decreased cardiac output, hypoxemia and elevated central venous pressure leading to reduction of glomerular filtration and appearance of kidney injury.

Purpose: To investigate whether adding biomarkers such as brain natriuretic peptide (BNP) and cardiac troponin (cTn) blood concentrations, echocardiographic parameters or glomerular filtration rate to sPESI can improve the prognostic value of acute PE.

Methods: The source of data was the Serbian multicenter PE registry which successively included 8 hospitals (7 university hospitals and one general hospital) during the period from 2014 to 2020. The study included 1201 consecutive patients with PE which was confirmed using MDCT. All patients underwent echocardiography examination on admission and blood samples were collected for troponin I (TnI), B-type natriuretic peptide (BNP), creatinine and other routine laboratory analyses. Renal function, or the glomerular filtration rate (GFR), was estimated using the Cockroft Gault formula : {(140 - Age) x wt (kg) x F} / Serum Creatinine (μmol), where F = 1.23 if male, and 1.04 if female. According to the presence of severe hypotension and right ventricle dysfunction during the entire hospitalization, patients were stratified into three risk groups according to 2019 ESC PE guidelines as high-, intermediate- and low-risk patients. All-cause mortality was recorded during the period of 30 days starting from the first hospitalization day. All discharged patients had scheduled visits at 30+7 days from the hospitalization.

Results: Intra-hospital mortality rate was 11.5%. Comorbidities such as chronic lung disease, prior stroke, diabetes, coronary artery disease, history of cancer in the last six months ($p<0.05$), chronic heart failure, abnormal liver function and kidney injury ($p<0.001$), were significantly more associated with lethal outcome. In the group of patients with in-hospital death, sPESI ≥2 was more prevalent ($p<0.001$), as expected. In the group of patients who survived, sPESI 0, sPESI 1 and sPESI ≥2 are almost equally present. Using three levels sPESI model: sPESI 0, sPESI 1 and sPESI ≥2, patients were divided into three groups. All-cause mortality and mortality rate due to pulmonary embolism only, were statistically significant different between three groups based on sPESI score ($p<0.0001$). Patients with sPESI≥2 were treated with systemic thrombolytics more frequently than patients with sPESI 1 and sPESI 0, as expected ($p<0.0001$) Analysis of the values of routine laboratory markers such as BNP, TnI, estimated GFR and right ventricular dysfunction across the groups based on sPESI score, revealed statistically significant differences of all mentioned parameters between groups of patients with sPESI0, sPESI 1 I sPESI ≥2 ($p<0.001$). The most important fact was that the statistically significant difference of all-cause mortality rate between the groups of patients with sPESI 0, sPESI 1 and sPESI ≥2 was ((HR 0.127 (CI 0.071-0.226); p <0.0001; (HR 0.330 (CI 0.219-0.498); p <0.0001), respectively. There was also a statistically significant difference in mortality rate due to pulmonary embolism between groups of patients with sPESI 0, sPESI 1 and sPESI ≥2 ((HR 0.113 (CI 0.052-0.247); p <0.0001; (HR 0.362 (CI 0.218-0.601); p <0.0001), respectively.

In order to find another parameter that could be added to sPESI, we performed Cox regression analysis of BNP, GFR, TnI, and right ventricular dysfunction in all three groups, based on sPESi score. The best predictor of 30-day mortality rate was GFR ((HR 2.24 (CI 1.264-3.969); p =0.006). Neither TnI level ((HR 0.608 (CI 0.296-1.251); p=0.177), BNP level ((HR 0.733 (CI 0.288-1.866); p=0.514), nor right ventricular dysfunction ((HR 1.608 (CI 0.977-4.203); p =0.262), BNP level ((HR 0.733 (CI 0.288-1.866); p=0.514) and TnI level ((HR 0.608 (CI 0.296-1.251); p=0.177) improved risk assessment in combination with a different stratification tool based on three levels sPESI model and were not predictors of 30-day mortality rate independently of sPESI score.

Conclusion: Troponin, BNP, right ventricular dysfuncton are widely used for risk stratification and for guiding therapy regimen. Another marker that is still underused is estimated GFR. In our study, estimated GFR was, among biomarkes such as TnI, BNp and RVD, the only prognostic marker for 30-days all-cause mortality. Insight into complex multimodal risk estimation guide, offers an opportunity for using eGFR in risk stratification: due to its availability, simplicity and reproducibility. Rise in serum creatinine sometimes may be a sign for worsening of renal function. Nevertheless, eGFR is a precise marker for declining renal function in acute and/or chronic kidney injury and also in cardiovascular diseases. Hemodynamic disturbances in acute PE may be the cause of acute kidney injury Renal dysfunction on admission, in patients with acute PE, is strongly associated with high intrahospital mortality risk. Three levels model of sPESI score, can be used as a more accurate prognostic stratification tool in patients with acute pulmonary embolism. Established sPESI score may have greater discriminative power by using a simple calculation of GFR in prediction of survival of patients with PE and possible outpatient treatment. In spite of that, GFR calculation has still not become the clinical routine in PE.

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