ORIGINAL ARTICLE

Neutrophil gelatinase-associated lipocalin, cystatin C and eGFR indicate acute kidney injury and predict prognosis of patients with acute pulmonary embolism

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See Editorial, p 1185

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ABSTRACT

Objective Risk stratification in acute pulmonary embolism (APE) includes the assessment of clinical status, right ventricular dysfunction and troponin concentrations. Since acute renal impairment is one of the important predictors of mortality in cardiovascular diseases, the authors hypothesised that it is an independent mortality marker in APE.

Material and methods The authors observed 142 consecutive patients (52 M/90 F, 64±18 years) with APE diagnosed with contrast enhanced multislice CT. On admission, blood samples were collected for neutrophil gelatinase-associated lipocalin (N-GAL), cystatin C and creatinine assays. Estimated glomerular filtration rate (eGFR) was calculated using MDRD formula.

Results Fourteen (10%) of 142 patients died by the 30th day of observation. eGFR≤60 ml/min was noted in 68 (48%) patients and eGFR≤30 ml/min in 11 (8%) patients. eGFR was higher in survivors than in non-survivors (66 (17—169) vs 46 (10—119) ml/min, respectively, p=0.02). In 80 (56%) patients, N-GAL was >50 ng/ml indicating acute kidney injury. N-GAL was higher in non-survivors than in survivors (88.8 (28.4—200.0) vs 53.0 (7.1—200.0) ng/ml, p<0.01). N-GAL level >50 ng/ml was found in 11 (79%) patients with fatal outcome. Area under the curve of N-GAL for all-cause mortality in ROC analysis was 0.715. N-GAL>75 ng/ml was present in 44 (31%) patients, while cystatin C >1900 ng/ml in 14 (10%) subjects. They showed sensitivity, specificity, positive predictive value and negative predictive value for prediction of all-cause death ((64%, 73%, 21%, 95%) and (36%, 91%, 30% 93%), respectively). N-GAL>75 ng/ml and cystatin C>1900 ng/ml increased the risk of death (HR 4.4 (95% CI 1.48 to 13.2, p<0.01) and 4.7 (95% CI 1.56 to 13.9, p=0.01), respectively).

Conclusions Acute kidney injury assessed by N-GAL occurs in 30% of APE and may contribute to the impairment of renal function present in half of them. Moreover, N-GAL, cystatin C elevation and low eGFR are associated with a poor 30-day prognosis in APE.

INTRODUCTION

Current guidelines for the management of acute pulmonary embolism (APE) recommend to include in the risk stratification the assessment of haemodynamic stability, evaluation of right ventricular (RV) function and myocardial injury biomarkers.[1 2] However, haemodynamic compromise in APE affects the pulmonary circulation and other organs including the kidneys. Decreased cardiac output, hypoxaemia and elevated central venous pressure can result in acute renal dysfunction. Glomerular filtration rate is one of the generally accepted indicators of an increased mortality in various cardiovascular diseases. In acute coronary syndromes, renal dysfunction on presentation is associated with an increased early mortality, independently of other conventional risk factors,[3] and has been included in the GRACE risk scale.[4] Moreover, the impairment of the renal function also predicts mortality and hospitalisation rate in patients with heart failure.[5]

Neutrophil gelatinase-associated lipocalin (N-GAL) was identified to activate nephron formation in the embryonic kidney and is rapidly and massively induced in renal failure and possesses kidney protective activity. N-GAL was rapidly detected in the urine in animal models of acute kidney injury (AKI).[6] Plasma and urine N-GAL are reported to be excellent biomarkers for the early prediction of AKI following a cardiopulmonary bypass,[7] contrast administration[8] and kidney transplantation.[9] Plasma and urine N-GAL are proven biomarkers for AKI early prediction, even in heterogeneous clinical situations, where the timing of kidney injury is unknown, such as in the critical care or emergency settings.[10 11]

Cystatin C is an endogenous marker of kidney dysfunction, detected earlier than plasma creatinine. It is used to both help diagnose renal dysfunction and to identify progress of AKI. Cystatin C is an endogenous inhibitor of cysteine proteinases, produced by all nucleated cells of the body and released into the bloodstream at a constant rate. And therefore, the assessment of serum cystatin C concentrations may be a marker of glomerular filtration.[12] Serum concentrations of cystatin C may be used to detect renal dysfunction in critically ill patients with AKI even 24—48 h earlier than creatinine measurements.[13]

Our previous study showed that approximately 47% of patients with APE have at least moderately impaired kidney function, and patients with an estimated glomerular filtration rate (eGFR) ≤35 ml/min are at a fatal outcome.[14] However, eGFR