RELATIONSHIPS BETWEEN BIOMARKERS OF HYPOXIA AND INFLAMMATION IN ELDERLY PATIENTS WITH CHRONIC CARDIORENAL SYNDROME

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Background:

Multibiomarker models are promising for assessing the prognosis in chronic heart failure (CHF). Inflammation and hypoxia are important prognostic factors in chronic cardiorenal syndrome.

Objective:

The aim of this study was to investigate relationships between biomarkers of hypoxia and inflammation in elderly patients with chronic cardiorenal syndrome.

Methods:

80 elderly patients with CHF (32 males and 48 females, mean age 70.7±8.7 years) were examined. CHF was defined according to Acute and Chronic Heart Failure ESC Guidelines, 2016. Chronic kidney disease (CKD) was diagnosed and classified according to the KDIGO guidelines (2012). Serum levels of N-terminal propeptide of type B natriuretic hormone (NT-proBNP), cystatin C, hypoxia-inducible factor 1-alpha (HIF-1α), endogenous erythropoietin (eEPO), interleukin-6 (IL-6), interleukin-8 (IL-8), interleukin-18 (IL-18) were assessed. The follow-up period was 12 months; the primary endpoint was total mortality.

Results:

CKD with estimated glomerular filtration rate (eGFR) < 60 ml/min/1.73m2 was diagnosed in 49 (61.3%) elderly patients with CHF. Patients with chronic cardiorenal syndrome had higher levels of eEPO (8.2 (IQR2.4; 16.5) and 4.9 (IQR1.9; 7.9) mIU/ml resp., p=0.02), NT-proBNP (734.3 (IQR 163.2; 1420.5) and 134.3 (IQR 134; 232.5) pg/ml, resp., p=0.002),cystatin C(1.26 (IQR 0.93; 1.62) 0.86 (IQR 0.7; 1.2) mg/l , resp., p=0.003) and IL-6 level (14.1 (IQR 8.4;32.9) and 8,1 (IQR 4.7;11.3) pg/ml, resp., p=0.0005) compared to patients without CKD. There was a significant relationship between eGFR and NT-proBNP (r=-0.43, p<0.001). There was positive relationship between hypoxia biomarkers and NT-proBNP: HIF-1α (r=0.25, p=0.024) and eEPO(r=0.36, p=0.001); between IL-6 and NT-proBNP (r=0.53, p<0.0001). There was positive relationship between hypoxia biomarkers and cystatin C: HIF-1α (r=0.25, p=0.027), eEPO (r=0.71, p<0.001). When

assessing relationships between biomarkers of hypoxia and inflammation, we defined significant relationships between IL-6 and eEPO (r=0.47, p<0.0001) and between IL-8 and HIF-1α (r=0.37, p=0.0006). At the same time, there was no relationship between HIF-1α and eEPO (p=0.15). However, there was significant correlation between composite index (the ratio of NT-proBNP to eEPO) and HIF-1α (r=0.37, p=0.0006). The composite index (eEPO> 16.19 mIU/mL and NT-proBN> 232.5 pg/mL) predicted annual mortality in elderly patients with CHF (RR 15; 95% CI 3.6–62.7; p=0.0008) (sensitivity 50%, specificity 93.7% (AUC=0.72); p=0.001).

Conclusion:

There were complex relationships between biomarkers of myocardial, renal dysfunction, hypoxia, and inflammation in elderly patients with chronic cardioprenal syndrome. The use of biomarkers combination (myocardial stress and hypoxia) to assess the prognosis in chronic cardiorenal syndrome is promising.