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Review article

Biomarkers of renal function in prognostic stratification of patients with acute coronary syndrome

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ARTICLE INFO

Article history:
Received 21 March 2017
Received in revised form
30 May 2017
Accepted 31 May 2017
Available online xxx

Keywords:
Acute coronary syndrome
NSTEMI
STEMI
Unstable angina
Prognostic stratification
Biomarkers
Renal function
Creatinine
Urea
Glomerular filtration
Cystatin C
NGAL
Interleukin-18

ABSTRACT

There is close pathophysiological interaction between the kidneys and the heart, affecting, among others, the risk for development and prognosis of many cardiovascular disease. Early risk stratification of patients with acute coronary syndrome (ACS) is important for optimizing their therapy. Presented is an overview of prognostic stratification of ACS patients according to baseline levels of renal function biomarkers. Apart from classic biomarkers (creatinine, urea) having a dominant role in advanced chronic kidney disease, some novel biomarkers are listed (cystatin C, neutrophil gelatinase-associated lipocalin, interleukin-18) that bring an added value as they are directly associated with the pathological mechanisms of the course of ACS.

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http://dx.doi.org/10.1016/j.crvasa.2017.05.018

Please cite this article in press as: J. Přeček et al., Biomarkers of renal function in prognostic stratification of patients with acute coronary syndrome, Cor et Vasa (2017), http://dx.doi.org/10.1016/j.crvasa.2017.05.018

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Introduction

Cardiovascular diseases, in particular acute coronary syndrome (ACS), continue to be responsible for a considerable proportion of deaths in developed countries, representing a major socio-economic problem. According to the CZECH-2 registry that analyzed an unselected population sample in four regions of the Czech Republic in October and November 2012, the estimated annual incidence of ACS in the country was 2149 cases per 1,000,000 population. Most of them were patients with non-ST-segment elevation myocardial infarction (NSTEMI; 47.6%), followed by those with ST-segment elevation myocardial infarction (STEMI; 30.8%) and unstable angina (UA; 21.6%) [1].

The prognosis of patients with ACS varies depending on a range of factors. In the CZECH-2 registry study, the in-hospital and 30-day mortality rates were 4.2% and 5.7%, respectively. The highest mortality rates were noted in patients with a discharge diagnosis of Q-wave myocardial infarction (MI), namely 10% in-hospital mortality and 12% 30-day mortality. The lowest rates were observed in the UA subgroup (0.5% and 1.6%, respectively). Patients with non-Q-wave MI had 3.8% in-hospital mortality and 4.8% 30-day mortality [1]. In addition to providing information on prognosis as such, early risk stratification of ACS patients is mainly useful for identification of high-risk patients who may benefit, for example, from earlier invasive therapy or more intensive monitoring and prolonged observation to prevent serious complications, as well as of low-risk patients who may be referred to outpatient care soon.

The prognostic factors in ACS patients include the baseline level of renal function and the presence of some degree of chronic kidney disease. The association between cardiovascular diseases and chronic kidney disease is well established. Patients with chronic kidney disease are exposed to a higher risk of developing cardiovascular events as well as to higher rates of subsequent complications [2]. Between the heart and the kidneys, similar to other organs, there is a complex exchange of information and a system of feedback provided by numerous soluble and cell mediators. Under normal conditions, this mechanism is responsible for the normal function of the organism; during pathological events, however, dysfunction of an organ may potentiate dysfunction of other organs. These complicated interactions are a part of *cardiorenal syndrome*, defined as a complex pathophysiological disorder of the heart and the kidneys in which acute or chronic dysfunction in one organ may induce acute or chronic dysfunction in the other organ [3]. Based on the time course of the interaction and primary/secondary organ dysfunction, cardiorenal syndrome may be classified into several subtypes as shown in Table 1 [4].

Patient prognosis is influenced by not only the baseline level of renal function but also potentially impaired renal function following ACS [5]. As seen from the overview of cardiorenal syndrome subtypes, an important clinical entity that may complicate the course of ACS and may be closely associated with both short-term and long-term prognosis of ACS patients is *acute kidney injury* (AKI). The condition is characterized by rapid (within hours to days) decline in renal function. It is a dynamic process with varied clinical manifestations ranging from a small, clinically asymptomatic, increase in serum creatinine (for stage 1 AKI, the thresholds are a 50% increase in serum creatinine or a 25% decrease in glomerular filtration rate over baseline) to anuric renal failure requiring the use of renal replacement therapy [6].

When treating cardiovascular patients, it is always necessary to respect this cardiorenal relationship, assess the current level of renal function and to select therapy with respect to possible problems leading to kidney damage (e.g. the use of potentially nephrotoxic drugs and contrast agents or dosage adjustments). There are numerous laboratory markers of renal function, which differ in their source, function, distribution and in the time of their release (Fig. 1). Presented is an overview of individual laboratory markers that may be used for initial stratification of ACS patients.

Serum creatinine

Serum creatinine (SCr) is the most frequently used marker for renal function assessment. Despite its wide and long use, it is not an ideal laboratory marker and may produce a lot of inaccuracies. Creatinine arises in muscle tissue as the end product of metabolism of creatine and creatine phosphate, a source of energy for the muscle. It is excreted by glomerular filtration; with normal SCr levels, its amount in primary urine flowing down the tubules remains unchanged. With increased

Please cite this article in press as: J. Přeček et al., Biomarkers of renal function in prognostic stratification of patients with acute coronary syndrome, Cor et Vasa (2017), http://dx.doi.org/10.1016/j.crvasa.2017.05.018