Rev Port Cardiol. 2014;33(3):127–136

Revista Portuguesa de Cardiologia
Portuguese Journal of Cardiology
www.revportcardiol.org

ORIGINAL ARTICLE

Multimarker approach with cystatin C, N-terminal pro-brain natriuretic peptide, C-reactive protein and red blood cell distribution width in risk stratification of patients with acute coronary syndromes

Catarina Vieira*, **Sérgio Nabais, Vítor Ramos, Carlos Braga, António Gaspar, Pedro Azevedo, Miguel Álvares Pereira, Nuno Salomé, Adelino Correia**

Department of Cardiology of Hospital de Braga, Braga, Portugal

Received 14 January 2013; accepted 10 September 2013
Available online 24 March 2014

KEYWORDS
Cystatin C;
C-reactive protein;
N-terminal pro-brain natriuretic peptide;
Multimarker stratification;
Acute coronary syndromes

Abstract
Introduction and aim: Biomarkers have emerged as interesting predictors of risk in patients with acute coronary syndromes (ACS). The aim of this study was to determine the utility of the combined measurement of cystatin C (CysC), C-reactive protein (CRP), N-terminal pro-brain natriuretic peptide (NT-proBNP) and red blood cell distribution width (RDW) in the risk stratification of patients with ACS.
Methods: In this prospective study including 682 patients consecutively admitted to a coronary care unit for ACS, baseline measurements of CysC, CRP, NT-proBNP and RDW were performed. Patients were categorized on the basis of the number of elevated biomarkers at presentation. The primary outcome was 6-month mortality.
Results: The number of biomarkers elevated on admission (study score) was an independent predictor of 6-month mortality; patients with four biomarkers elevated on admission had a significantly higher risk of 6-month mortality compared with patients with none or one. In addition, in patients with high risk defined by the GRACE score, our multimarker score was able to further categorize their risk of 6-month mortality.
Conclusions: A multimarker approach using CysC, NT-proBNP, CRP and RDW was an independent predictor of 6-month mortality and added prognostic information to the GRACE risk score in patients with ACS and high risk defined by GRACE, with increasing mortality in patients with a higher number of elevated biomarkers on admission.

* Corresponding author.
E-mail address: katarinafvieira@gmail.com (C. Vieira).

PALAVRAS-CHAVE
Cistatina C;
Proteína C reativa;
Pro-peptídeo natriurético tipo B;
Estratificação multimarcadores;
Síndromes coronárias agudas

Abordagem multimarcadores com a cistatina C, pro-peptídeo natriurético tipo B cerebral, proteína C reativa e índice de anisocitose na estratificação de risco dos doentes com síndrome coronária aguda

Resumo
Introdução e objetivo: Os biomarcadores têm surgido como interessantes preditores de risco em doentes com síndrome coronária aguda (SCA). O objetivo deste estudo foi definir a utilidade da combinação da cistatina C (CysC), da proteína C reativa (CRP), a porção N-terminal do peptídeo natriurético tipo B (NT-proBNP) e do índice de anisocitose (RDW) na estratificação de risco dos doentes com SCA.
Métodos: Estudo prospetivo, incluindo 682 doentes admitidos consecutivamente na nossa unidade coronária por SCA. À admissão foi feito o doseamento plasmático da CysC, CRP, NT-proBNP e RDW. Os doentes foram categorizados de acordo com o número de biomarcadores elevados à admissão. O evento primário estudado foi a mortalidade aos seis meses.
Resultados: O número de biomarcadores elevados à admissão (*score* estudado) foi preditor independente de mortalidade aos seis meses; os doentes com quatro biomarcadores elevados à admissão tiveram um risco de morte aos seis meses significativamente superior aos doentes sem nenhum ou com apenas um biomarcador elevado. Adicionalmente, nos doentes com alto risco definido pelo *score* GRACE, o nosso *score* multimarcadores teve a capacidade de os categorizar adicionalmente quanto ao risco de morte aos seis meses.
Conclusão: A abordagem multimarcadores baseada na CysC, NT-proBNP, CRP e RDW foi preditor independente de mortalidade aos seis meses e proporcionou informação prognóstica adicional nos doentes de alto risco definido pelo *score* GRACE, com maior da mortalidade nos doentes com maior número de biomarcadores elevados à admissão.

Abbreviations

ACS	acute coronary syndrome
AUC	area under the receiver operating characteristic curve
BNP	brain natriuretic peptide
CG	Cockcroft-Gault equation
CI	confidence interval
CRP	C-reactive protein
cTnI	cardiac troponin I
CysC	cystatin C
GFR	glomerular filtration rate
hsCRP	high sensitivity C-reactive protein
MI	myocardial infarction
NT-proBNP	N-terminal pro-brain natriuretic peptide
LV	left ventricular
NSTE-ACS	non-ST-segment elevation acute coronary syndrome
OR	odds ratio
PCI	percutaneous coronary intervention
RDW	red blood cell distribution width
STE-ACS	ST-segment elevation acute coronary syndrome

Introduction

Various risk factors have been identified in patients with acute coronary syndrome (ACS) and incorporated into scoring systems that enable the clinician to stratify risk and guide treatment.[1] In recent years, a deeper understanding of the pathobiology of atherothrombosis as the underlying mechanism of ACS has directed studies towards the evaluation of novel serum biomarkers as potential diagnostic tools for the clinical setting.[2,3] Recognition of the importance of including all the major mechanisms of ACS in risk stratification has increased the appeal of the multimarker approach. However, the ideal biomarkers and the ideal combination to improve risk stratification have not been defined.

The aim of this study was to assess the value of a multimarker approach with cystatin C (CysC), C-reactive protein (CRP), N-terminal pro-brain natriuretic peptide (NT-proBNP) and red blood cell distribution width (RDW) in the risk stratification of patients with ACS.

Another objective of the study was to determine the hierarchy of these biomarkers in terms of predictive power for 6-month mortality.

Methods

Study design and population

Of a total of 902 consecutive patients admitted to our department's coronary care unit between July 1, 2009 and June 30, 2011 with a diagnosis of ACS, we prospectively studied 682 patients. The time between the onset of ACS symptoms and the time of blood sampling to assess biomarkers was <24 hours. The remaining 220 patients were excluded for two main reasons: more than 24 hours between