Plasma bio-adrenomedullin is a marker of acute heart failure severity in patients with acute coronary syndrome

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Abstract: Background: The assessment of acute heart failure (AHF) in patients with acute coronary syndrome (ACS) is challenging. This study tested whether measuring plasma adrenomedullin in patients admitted for ACS provides valuable information regarding the presence of AHF at admission or its occurrence during hospitalization. Methods and results: The study population consisted of 927 prospectively enrolled patients with ACS. Blood samples for the measurement of plasma bio-adrenomedullin (bio-ADM) were collected at admission. Patients with alveolar pulmonary edema and interstitial pulmonary edema on chest radiography at admission had stepwise higher plasma concentrations of bio-ADM compared to patients with no or mild pulmonary congestion: 54.3 ± 10.6 vs. 27.6 ± 2.1 vs. 22.5 ± 0.7 ng/L, overall P < 0.001. Patients with ACS complicated by AHF during the index hospitalization displayed higher plasma bio-ADM concentrations at admission compared to patients without AHF (33.8 ± 2.7 vs. 21.8 ± 0.7, P < 0.001): the higher the severity of AHF, the higher plasma bio-ADM concentrations at admission. Patients with cardiogenic shock displayed the highest values. Accordingly, bio-ADM concentrations at admission were associated with a higher risk of occurrence of AHF during index hospitalization (odds ratio 1.018, 95% confidence interval 1.011-1.026, P < 0.001). Conclusions: Plasma adrenomedullin is a marker associated with AHF severity in patients with ACS.

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Plasma bio-adrenomedullin is a marker of acute heart failure severity in patients with acute coronary syndrome

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1. Introduction

Acute coronary syndrome (ACS) and acute heart failure (AHF) often coexist and have reciprocal detrimental effects on prognosis [1–3]. The assessment of AHF in patients with ACS remains challenging because imaging techniques might be time-consuming and cause unacceptable delays in coronary revascularization, and the performance of natriuretic peptides in this context is modest [4]. Adrenomedullin is a vasoactive hormone reflecting excessive volume overload and plays an essential role in the development of acute circulatory failure. The aim of this study was to test whether the measurement of circulating adrenomedullin in patients admitted for ACS might provide valuable information regarding the presence of AHF at admission or its occurrence during hospitalization.

2. Materials and methods

Consecutive patients with acute coronary syndrome (ACS) admitted to University Hospital of Brno, (Czech Republic), from 2009 to 2012 were enrolled [5]. The diagnosis of ACS was based on the criteria of the European Society of Cardiology and the Third universal definition of myocardial infarction [6,7]. Exclusion criteria were age > 85 years, known malignancy or inflammatory disease, and absence of culprit lesion on coronary angiography. Venous EDTA-blood samples were immediately drawn upon admission, refrigerated, centrifuged within 10 min, and plasma was stored at −80 °C. Measurement of biologically active adrenomedullin (bio-ADM) in the plasma samples was performed, blinded to clinical data, by Sphingotec GmbH (Henningsdorf, Germany) using a chemiluminescence immunoassay (sphingotest® bio-ADM®). As previously reported, the bio-ADM analytical assay sensitivity is 2 pg/mL, the median concentration in healthy adults equals 21 pg/mL [8]. Pulmonary congestion at admission was graded by certified radiologists blinded to laboratory values in 3 categories using conventional chest radiographs taken upon cardiac care unit admission: no or mild pulmonary congestion, interstitial pulmonary edema, alveolar
pulmonary edema. The severity of acute heart failure (AHF) at admis-

sion and/or during the index hospitalization was graded according to
the Killip classification [9]: cardiogenic shock (Killip IV), pulmonary
edema (Killip III), mild heart failure (Killip II), no clinical signs of
congestion (Killip I). The study was performed in accordance with
the ethical standards of the Declaration of Helsinki and was approved by
the local Ethics Committee. Written informed consent was obtained
from all subjects before inclusion in the study. Values are expressed as
mean (±standard error) or as number (percentage), as appropriate.
Groups were compared with the Kruskal-Wallis H-test with pairwise
comparisons and correction of the p-value for multiple comparisons.

The association between biomarker concentration and outcome was
assessed by logistic regression and is expressed as odds ratio with 95%
confidence interval. The null hypothesis was rejected with an adjusted
two-sided P < 0.05. All analyses were performed with the use of IBM
SPSS Statistics, Version 25 (IBM Corp, Armonk NY, USA).

3. Results

From a total of 1021 prospectively enrolled ACS patients, 94 (9%)
were excluded because of lack of chest radiography at admission.
The study population (n = 927) consisted prevalently of middle-aged
men (median age 61 years), with a high burden of cardiovascular risk
factors. Two-thirds of patients presented with ST-elevation myocardial
infarction. The baseline characteristics of the study population have
been published previously [5].

For the overall population, plasma concentration of bio-ADM was
23.5 ± 0.71 ng/L. Patients with alveolar pulmonary edema (n = 20)
and interstitial pulmonary edema (n = 72) on chest radiography at ad-
mission had stepwise higher plasma concentrations of bio-ADM com-
pared to patients with no or mild pulmonary congestion (n = 835):
54.3 ± 10.6 vs. 27.6 ± 21 vs. 22.5 ± 0.7 ng/L, overall P < 0.001 (Fig. 1A).

Patients with ACS complicated by AHF during the index hospitaliza-
tion (n = 136, 17%) displayed higher plasma bio-ADM concentrations at
admission compared to patients without AHF (21.8 ± 0.7 vs. 33.8 ± 2.7,
P < 0.001).

As shown in Fig. 1B, the higher the severity of AHF during the index
hospitalization, the higher plasma bio-ADM concentrations at admis-
sion (P < 0.001). The highest values were displayed by patients with
cardiogenic shock (41.1 ± 7.4 ng/L), followed by patients with pulmonary
edema (35.1 ± 3.1 ng/L), and those with mild congestion (26.9 ±
2.9 ng/L). Patients with no evidence of AHF displayed the lowest bio-
ADM concentrations at admission (21.8 ± 0.7 ng/L). Consistent results
were found after removal of patients with evidence of insufficient revas-
cularization (post-procedural TIMI flow 0–1, n = 16). Accordingly, bio-
ADM concentrations at admission were associated with a higher risk of
occurrence of AHF during index hospitalization (odds ratio 1.018, 95%
confidence interval 1.011–1.026, P < 0.001).

4. Discussion

This study firstly describes adrenomedullin, a vasoactive peptide
hormone reflecting excessive volume overload, as a marker associated
with pulmonary congestion and the risk of occurrence of AHF during
hospitalization in patients admitted for ACS. Very recent data described
bio-ADM as potential marker of AHF with greater discriminatory value
for congestion compared to natriuretic peptides [10]. Bio-ADM showed
consistently strong diagnostic properties for AHF both at admission and
during hospitalization. Our analysis confirms the strength of bio-ADM
for diagnosing pulmonary congestion at admission and AHF during the
index hospitalization in patients admitted with ACS.

5. Limitations

Our study has some limitations. First, the results of this single-center
prospective cohort study should be confirmed in multi-centric cohorts.
Moreover, despite a considerable number of included patients, the pro-
portion of patients with radiological evidence of pulmonary congestion
was relatively small. Second, pulmonary congestion was assessed by
conventional chest radiography at admission by one experienced, certi-
fied radiologist. Although this method reflects clinical practice, this
might not always be reproducible. Third, the group of patients with
alveolar edema displayed some relevant differences in baseline charac-
teristics, which may have contributed to the observed differences in bio-
ADM concentrations. Forth, no data about pre-existing chronic heart
failure was recorded.

6. Conclusions

Plasma adrenomedullin is a marker associated with acute heart
failure severity and congestion in patients with acute coronary syndrome.

Disclosures

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