Hepatocyte growth factor concentration during the first day of acute coronary syndrome

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Hepatocyte growth factor (HGF) can be produced by various cells and elicits multiple biological responses such as motility, proliferation, morphogenesis and survival in a cell type-dependent fashion. Apart from its physiological importance, HGF may contribute to many organ diseases [1-3]. We have already shown that conversely to routinely measured biomarkers of myocardial injury, human HGF (hHGF) increases to high levels in the very early phase of acute coronary syndrome (ACS) and then decreases rapidly during the first 24 h of ACS [4]. As described in our previous article, we measured hHGF concentration only twice, namely at admission and 24 h later [4]. We decided to establish the dynamicity of hHGF level changes on the first day of myocardial injury and to determine the usefulness of its measurement in the case of untimely complications.

In 4 patients with ST-segment elevation myocardial infarction (STEMI) and in 2 patients with non ST-segment elevation myocardial infarction (NSTEMI), who were eligible for coronary angiography and, possibly, primary percutaneous coronary intervention (PPCI), hHGF measurements were repeated 10 times during the first day of ACS and once at discharge from hospital (Figure 1). Each subject expressed their informed consent to participate in the study. Patients' informed consent and the protocol of the study were approved by the Institutional Local Ethics Committee. Patients' detailed particulars are presented in the Table I.

Human HGF was determined in plasma using the Quantikine Elisa kit from R&D Systems, Minneapolis, MN, USA. The mean value of hHGF evaluated in EDTA plasma using the Quantikine Elisa kit and presented in the manufacturer's brochure as a reference value was 787 pg/ml (range: 469-1113 pg/ml).

In the first measurement, as illustrated in the Figure 1, a marked increase in hHGF levels was observed in STEMI patients. Very high values (maximally about 20 000 pg/ml) were reduced to almost normal values within 5 h from the first measurement. In NSTEMI patients, even in the first assessment we did not observe very high levels of hHGF, and during the first 24 h of ACS, hHGF levels were stable. Contrary to patients with an uncomplicated acute course of STEMI, 2 patients with serious cardiovascular events in the acute stage of myocardial infarction, namely cardiac arrest and early reocclusion of the coronary artery, revealed a second increase of hHGF levels during the first 24 h of ACS (Figure 1).

We have already revealed that during the first 24 h of ACS HGF showed properties comparable with troponin I and N-terminal prohormone B-type natriuretic peptide (NT-proBNP), which are routinely used as markers of ischemic myocardial damage and risk stratification in patients with

Table I. Detailed description of six patients with ACS

Patient	1	2	3	4	5	6
Age [years]	70	56	66	61	72	39
Gender	Male	Male	Male	Male	Female	Male
Duration of chest pain [min]	370	570	900	160	125	120
Type of ACS and localization of MI (wall)	STEMI inferior and posterior MI	NSTEMI	STEMI anterior MI	NSTEMI	STEMI posterior MI	STEMI posterior and lateral MI
cTnI [ng/ml] – first day of ACS	0.23	6.54	4.78	0.11	0.01	0.03
cTnI [ng/ml] – second day of ACS	14.99	11.55	18.98	9.25	1.18	24.24
PPCI	Yes	No	Yes	No	Yes	Yes
Infarct-related artery	CRX		LAD		CRX	CRX
Stent implantation	Yes	No	Yes	No	Yes	No
Clopidogrel in loading dose 600 mg before PPCI	Yes	Yes	Yes	Yes	Yes	Yes
Aspirin [mg]	300	150	300	300	300	300
Abciximab during PPCI	Yes	No	Yes	No	No	No
Complications during acute stage of ACS	CA (VF)	No	No	No	No	CRX reocclusion during PCI
EF – second day of ACS [%]	46	55	60	60	70	50

ACS – acute coronary syndrome, MI – myocardial infarction, STEMI – ST-segment elevation myocardial infarction, NSTEMI – non-ST-segment elevation myocardial infarction, cTnI – cardiac troponin I with diagnostic cut-point 0.1 ng/ml, PPCI – primary percutaneous coronary intervention, CRX – circumflex coronary artery, LAD – left descending coronary artery, CA – cardiac arrest, VF – ventricular fibrillation, EF – ejection fraction measured by echocardiography

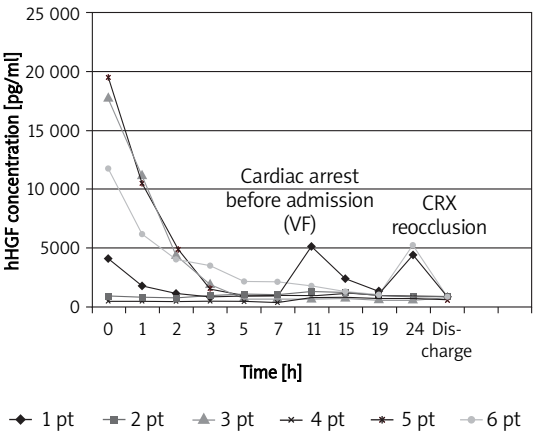

Figure 1. Human HGF concentrations in six patients with ACS
VF – ventricular fibrillation, CRX – circumflex coronary artery, pt – patient

impaired left ventricular function [4-7]. Troponin I reached peak values and confirmed myocardial necrosis when hHGF levels were already at a normal level [4]. Now, the very high hHGF values were observed in patients admitted within the first 2 h of STEMI presentation (patients 5 and 6) (Figure 1, Table I). In this aspect, the observed changes in hHGF concentrations in the early stage of myocardial infarction are a great advantage of this diagnostic method.

The time from the onset of ACS symptoms to treatment, effectiveness of reperfusion therapy measured as grade of flow in the infarct-related artery, and medical therapy applied during PPCI influence the levels of biomarkers [5, 8]. We supposed that in our study hHGF re-elevation was connected with acute complications of ACS. Due to the small number of patients we cannot definitely prove this relationship. We hope that subsequent research will confirm our preliminary observations. In conclusion, we found that: (1) in all our patients the highest hHGF values were observed at admission due to symptoms of acute coronary syndrome, (2) hHGF concentrations were reduced to normal values very quickly (within 5 h from the first measurement), (3) severe complications in the acute stage of STEMI most likely resulted in an additional increase in hHGF levels.

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References

1. Boros P, Miller CM. Hepatocyte growth factor: a multifunctional cytokine. Lancet 1995; 345: 293-5.
2. Toi M, Taniguchi T, Ueno T, et al. Significance of circulating hepatocyte growth factor level as a prognostic indicator in primary breast cancer. Clin Cancer Res 1998; 4: 659-64.
3. Funakoshi H, Nakamura T. Hepatocyte growth factor: from diagnosis to clinical applications. Clin Chim Acta 2003; 327: 1-23.
4. Konopka A, Janas J, Piotrowski W, Stępińska J. Hepatocyte growth factor – a new marker for prognosis in acute coronary syndrome. Growth Factors 2010; 28: 75-81.
5. Hamm CW, Bassand JP, Agewall S, et al.; ESC Committee for Practice Guidelines and Document Reviewers. ESC guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation. Eur Heart J 2011; 32: 2999-3054.
6. Irzmański R, Piechota M, Barylski M, et al. NT-proBNP in patients after acute coronary syndrome with ST segment elevation subjected to early posthospitalization cardiologic rehabilitation. Arch Med Sci 2006; 2: 262-7.
7. Waliszek M, Waliszek-Iwanicka A, Grycewicz T, et al. Prognostic value of plasma N-terminal pro-B-type natriuretic peptide concentration in patients with normal and impaired left ventricular systolic function undergoing surgery for abdominal aortic aneurysm. Arch Med Sci 2011; 7: 642-7.
8. Van de Werf F, Bax J, Betriu A, et al.; ESC Committee for Practice Guidelines and Document Reviewers. Management of acute myocardial infarction in patients presenting with persistent ST-segment elevation. Eur Heart J 2008; 29: 2909-45.