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LETTERS TO THE EDITOR

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Prognostic value of circulating chromogranin A levels in acute coronary syndrome

We refer to the orginal paper by Jansson *et al.*[1] to which we would like to address some comments.

Chromogranin A (CgA) has been accepted as a marker for the neuroendocrine tumours (NET), with some limits concerning its value for diagnostic purposes, and greater strength for monitoring their treatment.

Chromogranin A levels in patients with NET, however, often are markedly increased. In the group of patients with acute coronary syndromes (ACS) studied by Jansson *et al.*, CgA levels were only slightly or moderately increased, reaching the levels observed in numerous other pathological conditions of which some most important and frequently occurring are: occult gastric inflammation caused by Helicobacter pylori, atrophic gastritis, some chronic bowel inflammatory diseases, renal or hepatic insufficiency, benign prostatic hypertrophy, hypertension with increased sympathetic tone, rheumatoid arthritis.[2,3]

Raised CgA levels can be induced by various drugs: not only proton-pump inhibitors but also H-2 antagonists, glucocorticoids and various other drugs acting on sympathetic tone activity or stimulating release of endogenic catecholamines. Finally, an increase of CgA level may appear after consumption of a meal.[4]

Apart from that, another important issue is the method of blood collection, as CgA level appears to be 30–50% higher when measured in EDTA plasma than in serum.[5,6]

All these matters mean that it seems hard to accept the author's conclusion that CgA plasma levels obtained within the first 24 h of admission can be independently associated with the incidence of death in patients with ACS, and therefore may have prognostic value.

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Wojciech Jeske
Department of Endocrinology
Centre of Postgraduate Medical Education
Warsaw, Poland
Tel: +48 22 5690 168
Fax: +48 22 8343 131
Email: jeske.wojciech@gmail.com

Piotr Glinicki
Department of Endocrinology
Centre of Postgraduate Medical Education
Warsaw, Poland

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Prognostic value of circulating chromogranin A levels in acute coronary syndrome: reply

In their letter to the editor, Jeske *et al.* make some comments relevant to our article entitled: 'Prognostic value of circulating chromogranin A level in acute coronary syndromes' recently published in the European Heart Journal.[1] First, the observation that chromogranin A (CgA) levels in our patients were only moderately elevated compared with levels in the normal population is consistent with prior findings in other cohorts of patients with acute coronary syndromes (ACS).[2,3] Despite of this, even only mildly to moderately elevated CgA levels discriminate well between patients with a favourable and poor prognosis in various types of heart disease,[2–4] suggesting that CgA elevation reflects detrimental processes specific to the subgroup of patients with acute myocardial ischaemia and a poor prognosis, and not processes found in ACS patients in general. Of note, fourth quartile CgA levels (>33.7 U/L) in our patients were clearly increased compared with reference values (<18 U/L), demonstrating that a proportion of ACS patients has clearly elevated CgA levels. As these patients also had the highest number of events during follow-up, CgA seems to identify the subgroup of ACS patients with an unfavourable prognosis.

Jeske *et al.* also raise an important question regarding the impact of comorbidities on CgA levels in patients with heart disease. We clearly show that CgA levels in our patients are influenced by a number of factors, including reduced renal function. However, by multivariate Cox proportional hazard regression analysis used in our study, we adjusted for these confounders and found that CgA levels provided independent prognostic information to conventional risk markers. We acknowledge that we lack information on some of the conditions mentioned by Jeske *et al.*, including gastric inflammation by H. pylori, atrophic gastritis, and benign hypertrophy of the prostate, but we believe it is unlikely that these conditions had a major impact on mortality or the secondary endpoints in our study. In fact, we believe that the presence of these factors would have tended to obscure the association between CgA levels and events in our study. Similarly, the influence on CgA levels by medications generally not considered harmful to patients with heart disease would also be expected to attenuate the association between CgA levels and outcome in our patients. Thus, the major novel finding of our study is that CgA levels, although being influenced by comorbidities and medications, still provided independent prognostic information in patients with ACS. More importantly, CgA also provided incremental information to the information obtained by

estimating left ventricular ejection fraction, and measuring the contemporary cardiac biomarkers, troponin T, and pro-BNP.

Finally, as is the case for all biochemical markers, analytical issues must be taken into account when evaluating CgA measurements.[5] However, as all our measurements were performed in serum and with the same method, this should not be a problem in our study.

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Helge Røsjø
Torbjørn Omland
Department of Internal Medicine
Akershus University Hospital
Norway

Anna M. Jansson
Karolinska Institutet
Molecular Medicine and Surgery
Stockholm, Sweden

Kenneth Caidahl
Karolinska Institutet
Molecular Medicine and Surgery
Clinical Physiology N2:01
Karolinska University Hospital, SE 17176
Stockholm, Sweden
E-mail: kenneth.caidahl@ki.se

Allan Flyvbjerg
Medical Department
Aarhus University Hospital
Aarhus, Denmark