Corin as novel biomarker for myocardial infarction

Hans-Josef Feistritzer, Bernhard Metzler

University Clinic of Internal Medicine III, Cardiology and Angiology, Medical University of Innsbruck, A-6020 Innsbruck, Austria

Correspondence to: Bernhard Metzler. University Clinic of Internal Medicine III, Cardiology and Angiology, Medical University of Innsbruck, A-6020 Innsbruck, Austria. Email: Bernhard.Metzler@tirol-kliniken.at.

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The study by Zhou *et al.* recently published in the *J Am Coll Cardiol* provides new insights into the prognostic utility of the novel biomarker corin for risk stratification of patients with acute myocardial infarction (AMI) (1). In this prospective cohort study comprising more than 1,300 patients with ST-elevation myocardial infarction (STEMI) and non-STEMI (NSTEMI), low plasma corin concentrations were an independent predictor of major adverse cardiac events (MACE) defined as a composite endpoint of all-cause mortality, hospitalization for heart failure or recurrent AMI at a median follow-up duration of 634 days. This study impressively pointed out the incremental prognostic value of plasma corin concentrations in AMI patients beyond clinical characteristics and traditional cardiac biomarkers.

AMI is among the most frequent causes of morbidity and mortality in industrialized countries. Optimization of secondary prevention strategies is sought to be a cornerstone to improve outcome after AMI. Effective secondary prevention, again, is based on a comprehensive risk stratification of AMI patients, which preferably should be performed early after the index event. Multiple biomarkers, routinely available in clinical practice, have been linked to myocardial injury, left ventricular dysfunction and clinical outcome after AMI (2,3). However, during the last decade a number of novel biomarkers have been described, whose prognostic utility in AMI patients is either unknown or controversially discussed (4-6). As recently shown by O'Donoghue *et al.*, a multimarker model including novel biomarkers could more precisely predict the occurrence of cardiovascular death or heart failure at 30 days after STEMI (7).

Corin, a transmembrane serine protease, is highly expressed in cardiomyocytes (8). Biologically, corin contributes to activation of natriuretic peptide precursor molecules and therefore plays a key role in the regulation of blood volume and blood pressure. Shedding of corin from the cardiomyocyte cell surface has been described and might reflect corin activity and cellular homeostasis (9). In patients after STEMI, plasma corin concentrations have been linked to cardiac troponin T levels and infarct size derived from cardiac magnetic resonance imaging (10). Although the impact of this study is limited due to the small sample size, these data suggest high plasma corin concentrations as an indicator of myocardial injury which is among the strongest predictors of poor outcome in AMI patients.

Now, in this imposing prospective study by Zhou *et al.* low plasma corin concentrations were related with poor clinical outcome at a median follow-up of approximately 600 days. These findings disagree with the hypothesis stated above, that intensified corin release might reflect myocardial injury (10). To a certain extent, the time point of corin measurement after AMI might explain these conflicting data. In the study performed by Zhou *et al.*, corin concentrations were measured out of plasma samples collected on 'admission', which represents a rather broad time frame. On the other hand, in the study showing an association between high plasma corin concentrations and infarct size, plasma samples were collected at a median of 2 days after symptom onset. Possibly, data of the latter study reflect corin release in the setting of AMI and therefore the extent of myocardial damage. The data shown by Zhou *et al.*, however, might reflect the widely accepted long-term deleterious effect of corin deficiency on the cardiovascular system (11). For instance, low corin expression was related with myocardial fibrosis and contractile dysfunction in a murine model of dilated cardiomyopathy (12). Contrary, overexpression of corin could improve cardiac morphology

and function. In terms of these data, the study by Zhou *et al*. reflects chronic adverse effects of corin deficiency on the cardiovascular system rather than an association between corin and the extent of myocardial injury. Respectively, in this study no significant association between corin and cardiac troponin levels was observed.

In sum, the association between corin and outcome following AMI appears controversial. On the one hand, myocardial injury results in increased plasma corin concentrations suggesting intensified corin release (10). The extent of myocardial necrosis, preferably assessed using cardiac magnetic resonance imaging, is among the strongest surrogate endpoints for poor outcome after AMI (13,14). On the other hand, corin overexpression goes ahead with favourable effects on the myocardium. Hence, both mechanisms, myocardial injury and cellular overexpression, might result in increased plasma corin levels. In both cases, however, the pathophysiological agent causing corin release is completely different. The study by Zhou *et al*. suggests a predominant adverse effect of corin deficiency on prognosis after AMI. However, this study might underestimate the prognostic role of myocardial injury, particularly as cardiac troponin levels were not related with poor outcome in this study. Necessarily, larger studies are needed to further elucidate the relation of myocardial injury and corin release in the setting of AMI.

Finally, although an independent prognostic role of plasma soluble corin concentrations for poor outcome has been demonstrated in the study by Zhou *et al*., different pathophysiological mechanisms might determine plasma corin concentrations after AMI. Studies comprising corin concentrations together with established cardiac biomarkers and imaging parameters for myocardial injury, structure and function are needed to answer this open question.

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Footnote

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