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Letter to the Editor

Circulating corin concentrations are related to infarct size in patients after ST-segment elevation myocardial infarction☆

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Corin, a type II transmembrane serine protease, is expressed almost exclusively by cardiomyocytes [1,2]. It converts the precursor molecules of A- and B-type natriuretic peptides into active proteins [3]. Thus, corin plays a key role in the regulation of blood volume, blood pressure and cardiac function. Corin is shed from the myocyte cell surface and enters circulation, a process that might reflect homeostasis within the heart [4]. Recently, plasma corin concentrations were shown to be lower in patients with heart failure compared to healthy controls [5]. Chronic loss of cardiomyocytes as well as reduced corin synthesis and shedding might be responsible for this finding.

To the best of our knowledge, plasma corin concentrations have not yet been linked to infarct size (IS) after acute myocardial infarction (AMI). Cardiac magnetic resonance (CMR) imaging provides the current gold standard for the quantification of IS as well as left ventricular (LV) function and structure [6]. We hypothesize that plasma corin concentrations, assessed 2 days after reperfused ST-segment elevation myocardial infarction (STEMI), are related to IS as assessed by CMR.

Fifty consecutive STEMI patients treated with primary percutaneous coronary intervention (p-PCI) were included as described previously [7]. Circulating corin concentrations were measured out of EDTA blood samples drawn at a median of 1.9 days (IQR 1.1–3.3 days) after symptom onset using a commercially available immunofluorescent assay (DCRN00, R&D Systems Europe, Ltd., Abingdon, UK). Maximum cardiac troponin T (cTnT) and N-terminal pro-B-type natriuretic peptide concentrations were measured as described previously [6]. All patients underwent CMR imaging 4 months (median: 123 days, IQR 120–131 days) after the index event. We used a standardized protocol described in detail previously [6,7]. IS was evaluated on late gadolinium enhanced images. LV function and structure were assessed by cine trueFISP sequences. SPSS Statistics 22.0.0 (IBM, Armonk, NY, USA) was used for statistical analysis. Spearman's rank correlation coefficients were calculated for continuous variables. Group differences were assessed by χ^2-test (categorical data) or Mann–Whitney U test (continuous variables). To test for the predictive value of corin concentrations for large IS (IS > second tertile) receiver operator characteristic (ROC) analyses were performed. Variables, significantly different between patients with baseline IS above and below the second tertile, were included into ROC models (Table 1). Two-tailed p-values <0.05 were defined as statistically significant. The study protocol is in conformity with the ethical guidelines of the 1975 Declaration of Helsinki. The local ethics committee approved the study and written informed consent was obtained from all patients.

Median age of the study cohort was 59 years (IQR 51–66 years, 14% female). Median IS was 20 g (IQR 13–30 g) and median LV ejection fraction (LVEF) was 57% (IQR 52–64%). Plasma corin concentrations (median: 1084 pg/ml, IQR 841–1341 pg/ml, range 135–2297 pg/ml) were significantly associated with 4-month IS ($r = 0.366$, $p = 0.009$) (Fig. 1). Furthermore, corin was significantly correlated with maximum cTnT ($r = 0.346$, $p = 0.014$) concentrations. No association was detected between corin and the estimated glomerular filtration rate ($r = -0.022$, $p = 0.881$). According to ROC analysis, a model including maximum cTnT concentrations showed an area under the curve (AUC) of 0.95 (95% CI 0.89–1) for the prediction of large 4-month IS. Including corin instead of cTnT resulted in an AUC of 0.90 (95% CI 0.81–0.98). Inclusion of corin in addition to cTnT resulted in an AUC of 0.94 (95% CI 0.88–1).

This is the first study showing that 2-day plasma corin concentrations are associated with cTnT peak concentrations as well as CMR-derived IS measured 4 months after acute STEMI. Furthermore, we demonstrated that a ROC model including corin instead of cTnT resulted in similar prognostic value for the prediction of large 4-month IS. No

☆ These authors take responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

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Table 1
Differences in baseline characteristics between patients with 4-month infarct size below and above the second tertile.

	Infarct size at 4 months, g		
	<Second tertile	>Second tertile	p
Baseline characteristics			
Age, years	61 [52–67]	54 [49–68]	0.332
Female, n (%)	6 (18)	1 (6)	0.402
Body mass index, kg/m^2	26 [24–28]	27 [26–31]	0.115
Anterior STEMI, n (%)	11 (33)	7 (44)	0.537
cTnT max, ng/l	4451 [2362–6311]	8381 [7013–11745]	<**0.001**
NT-proBNP max, ng/l	779 [463–1362]	1319 [398–2434]	0.138
Corin, pg/ml	1004 [796–1254]	1333 [1085–1465]	**0.004**
CMR characteristics			
LVEF, %	60 [55–67]	53 [46–58]	**0.006**
EDVI, ml/m^2	71 [58–79]	79 [62–82]	0.136
ESVI, ml/m^2	28 [21–34]	35 [30–45]	**0.006**
LVMM, g	118 [108–133]	136 [128–142]	**0.013**
Infarct size, g	18 [9–21]	30 [25–36]	<**0.001**

STEMI = ST-segment elevation myocardial infarction; CK = creatine kinase; cTnT = cardiac troponin T; NT-proBNP = N-terminal pro-B-type natriuretic peptide; CMR = cardiac magnetic resonance; LVEF = left ventricular ejection fraction; EDVI = end-diastolic volume index; ESVI = end-systolic volume index; LVMM = left ventricular myocardial mass at end diastole.
Bold type indicates statistical significance.

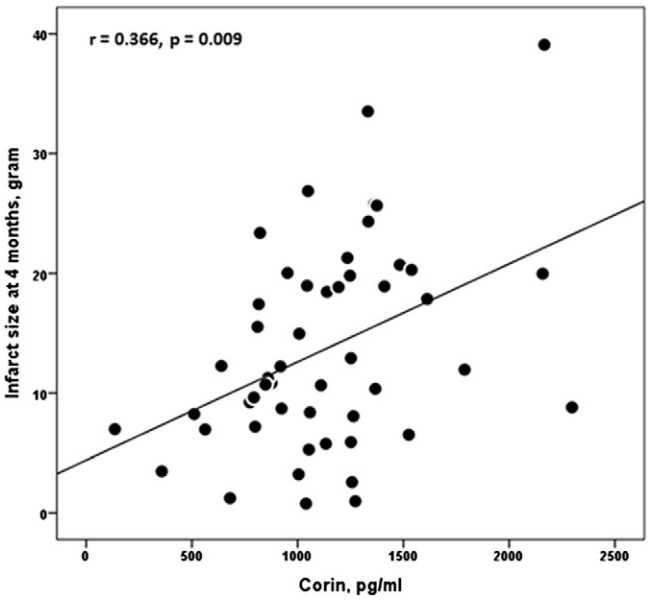

Fig. 1. Linear correlation of corin concentrations and 4-month infarct size (r = 0.366, p = 0.009).

specific secretion mechanism for corin has been reported as yet, strengthening the hypothesis that corin is shed from the cell surface and enters circulation [4]. This process is likely to reflect cellular turnover within the myocardium. Potentially, corin release might be extensively increased in the setting of myocardial ischemia. In the present study, we showed a significant correlation of corin and 4-month IS. Notably, CMR-derived IS measured in the chronic stage after infarction more accurately reflects definite myocardial scar compared to CMR imaging in the acute phase [8]. Increased wall thickness due to myocardial edema might be one reason for IS overestimation in the acute setting. For the prediction of large 4-month IS, including corin in addition to cTnT did not further improve the predictive value, presumably due to the already excellent accuracy of cTnT in the prediction of IS [9]. The potential rise and fall in plasma corin concentrations in the acute setting after STEMI should be addressed in future studies. Furthermore, the impact of high plasma corin concentrations on the occurrence of adverse clinical events after STEMI should be subject of future investigations.

In conclusion, plasma corin concentrations, assessed 2 days after acute STEMI, are associated with biomarkers of myocardial necrosis as well as IS as assessed by CMR.

The authors of this manuscript have certified that they comply with the Principles of Ethical Publishing in the International Journal of Cardiology.

Conflict of interest

The authors declare that there is no conflict of interest.

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