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Quantification of systemic cardiac troponin overestimates infarct size in presence of left ventricular hypertrophy: insights into the underlying mechanisms

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Introduction and Purpose: Myocardial infarct size estimation using biomarkers - creatine kinase (CK) and troponin (cTn) - is commonly used as the primary endpoint in many experimental studies and clinical trials. We recently described for the first time in a retrospective study that peak of cTnI could overestimate infarct size in presence of left ventricular hypertrophy (LVH). Here we sought to decipher the mechanism underlying this clinical observation.

Methods: Pigs (n=10) with previously induced LVH by aortic banding and sham (non-LVH) control pigs (n=8) underwent myocardial infarction. Cardiac magnetic resonance (CMR) was performed 7 days after infarction, and CK and cTnI systemic values were serially measured. Histological sections from LVH and sham pigs were analyzed to detect cTnI expression by immunofluorescence confocal microscopy. Fluorescence intensity and size in cardiomyocytes were quantified, and the comparison of data was performed using the two-tailed Student’s t-test. The clinical prospective validation was done by evaluating CMR from 140 patients with anterior STEMI to quantify LVH and infarct size correlating these parameters with release of damage biomarkers by multiple linear regression analyses.

Results: Both in the experimental and clinical studies, LVH was associated with a significant increase in peak and area under the curve (AUC) of cTnI. These results were observed either when LVH was categorized or when indexed LV mass was evaluated as a continuous variable (p<0.05 for all analyses). No significant differences were found in peak/AUC of total CK between LVH vs. no-LVH neither in the experimental nor the clinical study.

Analysis of the fluorescence intensity revealed a significant increase in the content of cTnI in hypertrophic cardiomyocytes compared to regular cardiomyocytes derived from LVH and non-LVH pigs, respectively (p<0.05).

Conclusions: Quantification of released cardiac troponin-I overestimates infarct size in presence of LVH due to an increase in its content in the hypertrophic cardiomyocyte. Left ventricular hypertrophy should be taken into consideration when infarct size is estimated by troponin release.