GLP-1 is an independent predictor of long-term mortality in patients with myocardial infarction complicated by cardiogenic shock – a substudy of the IABP-SHOCK II trial

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Background: The incretin hormone Glucagon-like-peptide 1 (GLP-1) is a major stimulus for glucose dependent insulin secretion and holds cardioprotective efficacy. This has made the GLP-1 system a preferred target for diabetes therapy. Secretion of GLP-1 happens in response to nutritional but also inflammatory stimuli. Consequently, marked elevation of circulating GLP-1 levels were found in critically ill patients featuring marked association to markers of inflammation.

Purpose: Our study sought to investigate GLP-1 levels in patients with cardiogenic shock (CS) complicating myocardial infarction and a possible prognostic correlation to short- and long-term outcome.

Methods: We serially assessed circulating GLP-1 levels in a prospectively planned biomarker substudy in the IABP-SHOCK II trial. Blood samples were drawn during index PCI and at day 2. The blood was centrifuged immediately, and serum was frozen at –87°C. GLP-1 was measured with a standard ELISA-kit. All-cause mortality at short- (30 days), intermediate- (1 year) and long-term (6 years) follow-up was used for outcome assessment.

Results: In this study we found circulating GLP-1 to be markedly elevated in patients with myocardial infarction complicated by CS (n=172) at time of index PCI. Patients with fatal short-term outcome (n=70) exhibited higher GLP-1 levels (86 [45–130] pM) at ICU admission in comparison to patients with 30-day survival (48 [33–78] pM; $p<0.001$) (n=102). In repeated measures ANOVA the course of GLP-1 levels between baseline and day 2 showed a significant interaction between survivors and non-survivors ($p=0.04$). By univariate Cox-regression analysis GLP-1 levels >median were predictive of short- (hazard ratio [HR] 2.43; 95% confidence interval [CI] 1.50–3.94; $p<0.001$), intermediate- (HR 2.46; 95% CI 1.62–3.76; $p<0.001$) and long-term (HR 2.12; 95% CI 1.44–3.11; $p<0.001$) outcome. This association remained after multivariable correction (HR 2.01; 95% CI 1.37–3.07; $p<0.001$). In a landmark analysis we found a significant higher mortality in patients with GLP-1 levels >median from day 30 to 1 year (HR 2.56; 95% CI 1.08–6.09; $p=0.03$). In contrast, beyond 1 year up to 6 years no difference has been observed anymore (HR 1.02; 95% CI 0.41–2.58; $p=0.96$).

Conclusions: Elevated plasma levels of GLP-1 are an independent predictor for impaired prognosis in patients with myocardial infarction complicated by CS at short-, intermediate and long-term follow-up. In a landmark analysis this prognostic effect is sustained up to 1 year. The functional relevance of GLP-1 in this context is currently unknown and needs further investigations.