The Prognostic Potential of Growth Differentiation Factor-15 on Bleeding Events and Patient Outcome after Cardiac Surgery – A prospective cohort study


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Background

GDF-15 (growth/differentiation factor 15) is induced by myocardial stretch, volume overload, inflammation and oxidative stress. Its expression is tightly linked with cardiovascular events as well as the risk for major bleeding and all-cause mortality. The study aimed to elucidate the prognostic potential of GDF-15 in patients after cardiac surgery.

Patients and Methods

504 patients undergoing elective cardiac valve and/or coronary artery bypass graft surgery were prospectively enrolled. GDF-15 levels were measured prior surgery to evaluate the impact on bleeding events, thromboembolic events and mortality.

Results

Preoperative GDF-15 was associated with the primary endpoint of intra- and postoperative red blood cell transfusion (for bleeding risk factors adjusted [adj] OR [odds ratio] per 1-SD [standard deviation] of 1.62 [95%CI:1.31-2.00]; p<0.001). Higher concentrations of GDF-15 were observed in patients waiting for the secondary endpoint of major or clinically relevant minor bleeding (for bleeding risk factors adj. OR per 1-SD of 1.70 [95%CI:1.05-2.75]; p=0.030) during the 1st postoperative year, but not for thromboembolic events. GDF-15 was a predictor for cardiovascular mortality (for comorbidities adj. HR [hazard ratio] per 1-SD of 1.67 [95%CI:1.23-2.27]; p=0.001) and all-cause mortality (for comorbidities adj. HR per 1-SD of 1.55 [95%CI:1.19-2.01]; p=0.001). A combined risk model of GDF-15 and EuroSCORE II outperformed the EuroSCORE II alone for long-term survival (c-index: 0.75 [95%CI: 0.70-0.80], p=0.046; net reclassification improvement: 33.6%, p<0.001).

Conflict of Interest: Nothing to declare.
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Conclusion

Preoperative GDF-15 concentration is an independent predictor for intra- and postoperative major bleeding, major bleeding during the first year and for long-term cardiovascular or all-cause mortality after cardiac surgery.

Table 1: Baseline characteristics stratified by GDF-15 tertiles. Categorical data are presented as counts and percentages and analyzed using Chi-square test. Continuous data are presented as median and the respective interquartile range and analyzed using Kruskal Wallis Test. Correlations between continuous variables and GDF-15 tertiles were calculated using Spearman correlation coefficient.

Figure 1: Boxplots for frequencies of intra- and postoperative red blood cell transfusions with preoperative GDF-15 levels.

Figure 2: Kaplan-Meier curve for the cumulative probability of all-cause mortality. Hazard ratio per 1-SD for all-cause mortality comparing low preoperative GDF-15 to high preoperative GDF-15 is p-value for log-rank test: <0.001