Multi-omics approach to post-CABG renal impairment

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Background: Renal impairment is a common complication after CABG (coronary artery bypass graft) surgery associated with an adverse outcome.
Purpose: To further characterize the molecular framework of the disease through omics analyses.
Methods: In N=165 CABG patients we performed multi-omics-analyses in preoperatively collected blood and tissue samples as well as 991 creatinine measurements. We used multivariable mixed-model regression analyses to analyse post-operative creatinine increase and to find common genetic polymorphisms, transcripts, metabolites and/or proteins associated with changes in postoperative creatinine increase. Multiple testing was accounted for by setting a 5%-limit on the false discovery rate (FDR) using the Benjamini-Hochberg procedure.
Results: Post-operative increase of log transformed creatinine was 0.035 (8%); 95% confidence interval (CI) 0.025, 0.045; P<0.001. We identified 55 gene expressions and two proteins associated with post-CABG renal impairment. On the metabolomic and single nucleotide point mutation (SNP) level, no relevant targets were found. The three most important identified gene expressions were MIR3202.1 (beta of log transformed creatinine increase per standard deviation gene expression increase –0.034; 95% CI: –0.048, 0.020; P<0.001), LOC105374386 (–0.032; 95% CI: –0.046, 0.019; P<0.001) and maternal embryonic leucine zipper kinase (MELK) (–0.022; 95% CI: –0.032, 0.013; P<0.001). Expression of all three was associated with a lower risk of post-CABG renal impairment. The same applies to the identified protein CAPRIN2 (–0.042; 95% CI: –0.062, 0.022; P<0.001), while expression of the protein TUBB6 was associated with a higher risk (0.033; 95% CI: 0.017, 0.048; P<0.001).
Conclusions: In an integrated approach we identified omics-biomarkers for the prediction of renal impairment after CABG surgery. The underlying pathophysiological associations of these genes and proteins are not fully understood. MELK might be an interesting target for further investigations, as it plays a prominent role in cell cycle control, cell proliferation, apoptosis, cell migration and cell renewal. Our results may help to better identify individuals at risk and lay the methodological groundwork for further omics analyses.