Impaired platelet function reduces myocardial infarct size in Galphaq knock-out mice in vivo.

Abstract:
Platelet aggregation and secretion play a crucial role in acute coronary syndromes. In Galpha(q) knock-out mice (Galpha(q)(-/-)) platelet function is eliminated in terms of aggregation and secretion of cytokines. We investigated whether restricted platelet aggregation and secretion reduces myocardial infarct size in vivo. Thirty minute regional myocardial ischemia was followed by 24 h reperfusion (I/R) in vivo. Infarct size was determined by counterstaining. Left ventricular function was measured by ultrasound. Infarct size to area at risk ratio was significantly smaller in Galpha(q)(-/-) mice (5.6+/-1.6%) compared to wild-type (WT) mice (27.2+/-3.0%, p<0.01). Fractional shortening was improved in Galpha(q)(-/-) mice compared to WT (42.2+/-1.4% versus 30.5+/-1.4%, respectively, p<0.01). WT mice, transplanted with Galpha(q)(-/-) bone marrow showed a significant reduction in infarct size compared to control (7.8+/-2.2% versus 18.4+/-2.7%, respectively, p<0.01). Platelets of Galpha(q)(-/-) mice had an impaired aggregation and secretion phenotype. In the in vivo model of ischemia and reperfusion, beyond impaired platelet aggregation, platelet secretion plays an additional role in myocardial infarct extension. Blocking platelet aggregation in combination with secretion might be a promising supplementary therapeutic strategy in acute myocardial infarction.