The administration of a CD31 agonist peptide exerts a beneficial effect in experimental heart failure with both reduced and preserved ejection fraction

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Background: CD31 is a mechanosensory receptor and recent studies in CD31 knockout mice have suggested a protective role for CD31 in the prevention of heart failure.

Purpose: To directly assess the role of CD31 signaling in the development of heart failure (HF) with both reduced and preserved ejection fraction (HFrEF and HFP EF, respectively).

Methods: Permanent ligature of the proximal left coronary in C57Bl6 mice was used for modeling experimental HFrEF. Five days after surgery, mice displaying a myocardial infarction involving >30% of the left ventricle (LV) at echocardiography were randomized to receive either a CD31 agonist peptide (P8RI, 2.5mg/Kg) or placebo by subcutaneous continuous infusion (osmotic pumps).

Low dose angiotensin II infusion was applied to apolipoprotein E knockout (ApoE KO) mice as a model of HFP EF. The osmotic pumps delivered angiotensin II (200µg/Kg/day) alone or together with P8RI. The Ejection Fraction (EF%) and the E/E’ ratio were evaluated by echocardiography.

Results: In the HFrEF model, the daily treatment with the CD31 agonist peptide starting from the 5th day after the myocardial infarction, improved both the EF% (68 ±3 % vs 47±4%, p=0.05) evaluated 30 days later. Also the LV filling pressure was improved by the treatment, as reflected by the E/E’ ratio (24.6 ±2.4 % vs 49.7±7.5, p=0.05).

An even more striking beneficial effect was observed in the model of HFP EF, in which the CD31 agonist treatment prevented the development of the diastolic LV dysfunction induced by the low dose of angiotensin II infusion as determined by the variation of the E/E’ ratio at the end of the treatment period (6±7 in P8RI treated mice vs 37±8 in controls, p<0.02).

Conclusions: The administration of a CD31 agonist treatment may contribute to improve the heart function by favouring a physiologic endothelial-cardiomyocyte communication in response to the mechanic stress that is associated with heart failure. CD31 agonist drugs may represent a novel therapeutic strategy in heart failure with both reduced and preserved ejection fraction.