Implication of anti-angiogenic VEGF-A165b in angiogenesis and systolic function after reperfused myocardial infarction

V. Marcos Garces[1], C. Rios-Navarro[2], L. Hueso[2], A. Diaz[3], C. Bonanad[1], A. Ruiz-Sauri[4], M.J. Sanz[5], F.J. Chorro[1], L. Piqueras[5], V. Bodi[1]

[1]University Hospital Clinic of Valencia, Department of Cardiology, Valencia, Spain; [2]Instituto de Investigacion Sanitaria INCLIVA, Valencia, Spain; [3]University of Valencia, Central Unit for Research in Medicine (UCIM), Valencia, Spain; [4]University of Valencia, Department of Pathology, Valencia, Spain; [5]University of Valencia, Department of Pharmacology, Valencia, Spain

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Background: Angiogenesis participates in re-establishing microcirculation after myocardial infarction (MI).

Purpose: In this study, we aim to further understand the role of the anti-angiogenic isoform vascular endothelial growth factor (VEGF)-A165b after MI and explore its potential as a co-adjuvant therapy to coronary reperfusion.

Methods: Two mice MI models were formed: 1) permanent coronary ligation (non-reperfused MI), 2) transient 45-min coronary occlusion followed by reperfusion (reperfused MI); in both models, animals underwent echocardiography before euthanasia at day 21 after MI induction. Serum and myocardial VEGF-A165b levels were determined. In both experimental MI models, functional and structural implication of VEGF-A165b blockade was assessed. In a cohort of 104 ST-segment elevation MI patients, circulating VEGF-A165b levels were correlated with cardiovascular magnetic resonance-derived left ventricular ejection fraction at 6-months and with the occurrence of adverse events (death, heart failure and/or re-infarction).

Results: In both models, circulating and myocardial VEGF-A165b presence was increased 21 days after MI induction. Serum VEGF-A165b levels inversely correlated with systolic function evaluated by echocardiography. VEGF-A165b blockage increased capillary density, reduced infarct size, and enhanced left ventricular function in reperfused, but not in non-reperfused MI experiments. In patients, higher VEGF-A165b levels correlated with depressed ejection fraction and worse outcomes.

Conclusions: In experimental and clinical studies, higher serum VEGF-A165b levels associates with a worse systolic function. Its blockage enhances neoangiogenesis, reduces infarct size, and increases ejection fraction in reperfused, but not in non-reperfused MI experiments. Therefore, VEGF-A165b neutralization represents a potential co-adjuvant therapy to coronary reperfusion.