

C109. Reduced Circulating Endothelial Progenitor Cells In Patients With Aortic Valve Stenosis: A Novel Concept For Valve Repair

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OBJECTIVES: Endothelial destruction and calcification primarily occurs at the aortic side of the calcified aortic valves (AVs). Recent studies suggest that endothelial cell (EC) layer is kept intact after injury either by division of mature ECs or by circulating endothelial progenitor cells (EPCs). This study investigated whether degenerative aortic valve stenosis (AS) is associated with the presence of valvular endothelial senescence and a reduction in the levels of EPCs.

METHODS: 15 patients with severe AS and 18 age-matched control subjects were included into this study. Explanted calcified AVs were examined for senescence-associated β -gal staining. The amount and functional capacity of EPCs were assessed by FACS analysis or migration assay. The expression of telomere repeating factor-2 (TRF-2) was quantified by western blot and the caspase-3 activity was also measured biochemically.

RESULTS: Senescence-associated β -gal activity was mostly localized on the valve endothelium and highly coincided with the calcified lesion at the aortic side. The number (9.3 ± 1.5 vs. 20.5 ± 1.7 cells per 106 mononuclear cells; $p < 0.01$) and the migratory capacity (107.8 ± 14.1 vs. 185.0 ± 16.2 cells per 1000 cells; $p < 0.01$) of EPCs were significantly reduced in AS when compared to control. Caspase-3 activity was significantly increased, whereas the TRF-2 expression was significantly reduced in EPCs isolated from AS when compared to control.

CONCLUSIONS: This study reports the reduced regenerative capacity of valvular ECs due to senescence and decreased levels of EPCs related to “biological” aging in patients with AS. These data may offer a novel pathophysiological concept for impaired endogenous valve repair, leading to progression of age-associated AV disease.