

C110. Apelin And Its Receptor APJ In Human Aortic Valve Stenosis

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OBJECTIVES: Aims: Aortic valve stenosis (AS) is an actively regulated pathobiological process showing some hallmarks of atherosclerosis. Apelin and its receptor APJ are highly expressed in the heart and the proposed effects of apelin-APJ -system are opposite to the effects of the Ang II-AT1 -pathway. The role of apelin-APJ signalling pathway in the calcified aortic valve diseases is unknown. Here we have characterized and compared expression of apelin and APJ as well as Ang II (AT1 and AT2) receptors in aortic valves of patients with normal valves (n=6), aortic regurgitation (n=9), regurgitation and fibrosis/mild sclerosis (n=14) and AS (n=25).

METHODS: Gene-expressions of apelin-APJ was measured by reverse-transcriptase polymerase chain reaction (RT-PCR). Localization of protein levels of apelin and AT2 was determined by immunohistochemistry.

RESULTS: Gene expression of apelin (3.63-fold, P=0.001) as well as APJ receptor (2.70-fold, P=0.01) were significantly up regulated in stenotic valves when compared to controls. In patients with AS, apelin was localized by immunohistochemistry to valvular endothelial cells in neovessels as well as macrophages and fibroblasts adjacent to vessels. AT2-receptor mRNA levels were 90% (P<0.001) lower in stenotic valves and AT2-receptor positive staining was not detected in stenotic valves. In contrast, the gene expression of AT1-receptors did not differ significantly between the groups.

CONCLUSIONS: Aortic valve stenosis is characterized by up regulation of apelin-APJ signalling pathway revealing a possible novel target for drug discovery in calcified aortic valve disease in terms of suppressing chemotaxis, angiogenesis and osteoblast activity.

Patient Characteristics

	Control	AI	AI+fibrosis	AS
Patients, n (male %)	6 [5(83%)]	9 [9(100%)]	14 [11(79%)]	26 [17(65%)]
Bicuspid valve, n (%)	2 (33%)	3 (33%)	11 (79%)	17 (65%)
LDL level (mmol)	2.97±1.21	2.84±0.49	3.12±1.89	2.99±0.81
statins, n (%)	0	1 (9%)	3 (21%)	10 (38%)
age	48.0±20.8	43.2±13.5	56.7±12.8	66.8±12.0
LVEF (%)	63.0±13.6	56.0±7.2	53.4±9.9	60.2±11.7