Monoamine oxidase contributes to the valvular oxidative stress in patients with mitral valve regurgitation

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Background: Oxidative stress plays a central role in the pathogenesis of cardiovascular diseases but the role of enzymatic sources of reactive oxygen species (ROS) remains elusive. There is scarce information in the literature regarding valvular oxidative stress. Monoamine oxidases (MAOs), with 2 isoforms, A and B, have emerged as important sources of oxidative stress in the cardiovascular system.

Purpose: To assess whether MAOs-related oxidative stress occurs in the pathological valves in patients with severe mitral regurgitation (due to valve degeneration and chordae rupture) and surgical indication and its interference with the activation of the renin-angiotensin aldosterone (RAAS) system.

Material and methods: Samples of mitral valve (n=17) were harvested during the valvular replacement procedure and used for reactive oxygen species (ROS) assessment (immune-fluorescence, spectrophotometry) and MAO mRNA and protein expression (qPCR and immune-fluorescence) measurement. Inflammatory markers, biochemical parameters and echocardiography (GE, Vivid 9, Vivid E95) data were also collected.

Results: Both MAO isoforms are expressed in the diseased mitral valves, with a predominance of MAO-A isoform. Ex vivo incubation with angiotensin 2 (12 h, 100 nM) of samples obtained from patients without RAAS medication lead to MAO upregulation and high ROS production. MAO-related oxidative stress was mitigated by MAO inhibition with clorgyline (MAO-A inhibitor, 10 microM) and selegyline (MAO-B inhibitor, 10 microM) and also by the angiotensin II receptor type 1 (AT1) antagonist, irbersartan (10 microM).

Conclusions: Monoamine oxidase is expressed in the pathological mitral valves, regardless the etiology. Its expression and the related-oxidative stress are modulated by angiotensin 2, irbesartan. Whether the latter effect is present in valvular patients treated with RAAS inhibitors is currently under investigation.