

P21. TGF-beta Pathway Activation In Surgically Resected Leaflets Of Non Syndromic Mitral Valve Prolapse

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OBJECTIVES: Mitral valve prolapse (MVP) is the leading cause of mitral valve incompetence in western countries. Although its etiopathogenesis remains uncertain, a genetic defect has been identified in syndromic (ie, Marfan syndrome) and non syndromic cases. The finding that TGF-beta dysregulation may play an important role in the development of syndromic MVP prompted us to evaluate whether the Smad receptor-mediated intracellular TGF-beta pathway is activated also in isolated MVP.

METHODS: Myxomatous mitral valve specimens were obtained from patients (12 cases, 10 males, mean age 55.5±12.7 years) who underwent surgical repair of MVP. Age and sex-matched control mitral valves were obtained from homograft Tissue Bank (5 cases, mean age 49±9 years). Valve morphology and thickness were assessed on routinely stained histology sections. Primary antibodies recognizing active phosphorylated form of Smad2 (P-Smad2, Dako) in valvular myofibroblasts were used. To evaluate some target genes of TGFbeta PCR and RT-PCR were performed.

RESULTS: MVP leaflets exhibited alterations in architecture with fourfold increase in thickness (2,5±0,8 vs 0,6±0,3 mm, p<0.0001) and increased cell density in the spongiosa and in the ventricularis (110,9±64,6 vs 51,8±27,5 cells per high power field, p=0.04) compared to the normal valves. A higher density of nuclear staining for p-Smad-2 (38% vs 12%, p<0.0001) and altered expression of TGF-beta-related genes were observed, indicating an increased activation and signalling of TGF-beta.

CONCLUSIONS: Our data support the hypothesis that an increased activation of the intracellular TGF-beta response pathway contributes to the pathogenesis of non syndromic MVP.