Regulation of caspase 3 and Fas in pressure overload-induced left ventricular dysfunction.

BACKGROUND: The presence of apoptotic cell death in cardiac myocytes is now well established and the contribution of apoptosis for the development of heart failure has been suggested. However, the mechanism responsible for the induction of apoptosis remains unclear. The present study was designed to investigate the involvement of Fas and caspase 3 in the transition from pressure overload-induced left ventricular hypertrophy (LVH) to left ventricular dysfunction (LVD).

METHODS: Pressure overload induced LVH (10 days) and LVD (30 days) were induced by thoracic aortic banding. Changes in apoptosis-related genes were studied in rats with thoracic aortic banding. After 10 and 30 days, cardiac Fas mRNA expression was measured by RT-PCR. The mRNA expression of caspase 3 was detected by RNase protection assay. The activity of caspase 3 was measured by fluorometric assay. Protein levels of caspase 3 were measured by Western blot. RESULTS: Rats with aortic banding had increased heart/body weight ratios after 10 and 30 days, compared to controls. Central venous pressure and lung weights were increased, left ventricular contractility was significantly impaired only in rats after 30 days of aortic banding, indicating LVD. Caspase 3 mRNA expression (7.1 +/- 0.1 vs. 2.8 +/- 0.4, P<0.05), caspase 3 activity (1418 +/- 181 vs. 849 +/- 154 AU,
P<0.05) as well as caspase 3 protein levels were increased in rats with LVD but not with LVH. Similarly, Fas mRNA was increased in rats with LVD. CONCLUSIONS: The activation of Fas and caspase 3 only after 30 days of aortic banding suggests that induction of these pathways may be involved in pressure overload-induced LVD.