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Resumo	A key feature of heart failure is adverse extracellular matrix (ECM) remodeling, which is associated with increases in the collagen cross-linking enzyme, lysyl oxidase (LOX). In this study, we assess the progression of cardiovascular remodeling from the compensatory to decompensatory phase, with a focus on the change in LOX expression and activity as it relates to alterations in ECM composition and changes in cardiac function. Adult male Sprague-Dawley rats were studied after 4, 14, or 21 weeks of aortocaval fistula-induced volume overload (VO). Progressive increases in the left and right ventricular mass indicated biventricular hypertrophy. Echocardiography revealed significant increases in the posterior wall thickness and internal diameter of the left ventricle as early as 3 weeks, which persisted until the 21 week endpoint. There were also significant decreases in eccentric index and fractional shortening in VO animals. Hemodynamic measurements showed progressive decreases in contractility, indicative of systolic dysfunction. There were progressive VO-induced increases in LOX expression and activity, collagen, and collagen cross-linking during the course of these experiments. We observed a negative correlation between LOX activity and cardiac function. Additional rats were treated with an inhibitor of LOX activity starting at 2 weeks post-surgery and continued to 14 weeks. LOX inhibition prevented the cardiac dysfunction and collagen accumulation caused by VO. Overall these data suggest a detrimental role for the chronic increase of cardiac LOX expression and activity in the transition from compensated remodeling to decompensated failure.
Fomento	