

Coronary vasodilator reserve in left ventricular hypertrophy

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Cardiac hypertrophy is a morphological adaptive increase in myocardial mass in response to chronic work overload and is a common clinical finding affecting 23% of men and 33% of women over the age of 59 years¹. Pressure or volume overload on the myocardium results in an increase in myocardial wall stress and hypertrophy may be seen as an attempt to normalise wall stress and oxygen demand^{2,3}. The increased myocardial mass requires an increase in coronary blood flow to maintain function. Indeed, ventricular hypertrophy may be associated with myocardial ischaemia even with angiographically normal coronary arteries⁴⁻⁶. Left ventricular hypertrophy (LVH) significantly increases the risk of myocardial infarction, congestive heart failure and sudden cardiac death⁷⁻⁹. It is also associated with a greater prevalence of cardiac arrhythmias¹⁰ and is an important risk factor for cardiac morbidity and mortality^{11,12}.

Coronary vasodilator reserve in left ventricular hypertrophy

The coronary vasodilator reserve (CVR), defined as the ratio of myocardial blood flow (MBF) during near maximal hyperaemia to baseline MBF, is reduced in LVH due to hypertension¹³, aortic stenosis¹⁴, aortic regurgitation¹⁵, supraaortic stenosis and hypertrophic cardiomyopathy¹⁶ and in experimental models of LVH¹⁷⁻²⁰ (Fig. 1). The reduced CVR limits the ability of hypertrophied hearts to meet the metabolic requirements when demand is increased. Despite normal myocardial oxygen consumption²⁰ and myocardial perfusion per unit mass^{21,22} at rest, the hypertrophied heart is more vulnerable to ischaemia²³⁻²⁶.

Experiments in animals^{3,23} have demonstrated that the impairment of CVR is more marked in the subendocardial layers of the left ventricle, with some evidence of an alteration in the normal subendocardial-subepicardial distribution of perfusion during near maximal vasodilatation in patients with hypertrophic cardiomyopathy²⁷. More recently¹⁴ we have demonstrated that CVR is impaired in patients with LVH secondary to aortic stenosis and that the impairment correlates with the severity of the transvalvular gradient. In addition, as the gradient increases, subendocardial CVR becomes progressively more impaired than subepicardial CVR (Fig. 2).

Effect of left ventricular hypertrophy regression on the impairment of coronary vasodilator reserve

Experimental studies have reported that antihypertensive treatment of spontaneously hypertensive rats reduces LVH²⁸⁻³¹ with improvements in left ventricular compliance and reduced vulnerability to ischaemia although CVR remained impaired³². In contrast, other studies have demonstrated some recovery in coronary vascular morphology^{33,34} and CVR³⁵ with regression of experimental hypertrophy. Reduction in echocardiographically measured left ventricular mass has been observed clinically after treatment³⁶⁻⁴³ in patients with hypertension. Regression of LVH does occur following aortic valve replacement⁴⁴ but may remain incomplete in 50% of such patients⁴⁵. In contrast to the intense interest in regression of left ventricular mass, few studies have examined whether this is accompanied by reversal of the pathophysiological effects of LVH. Pre-

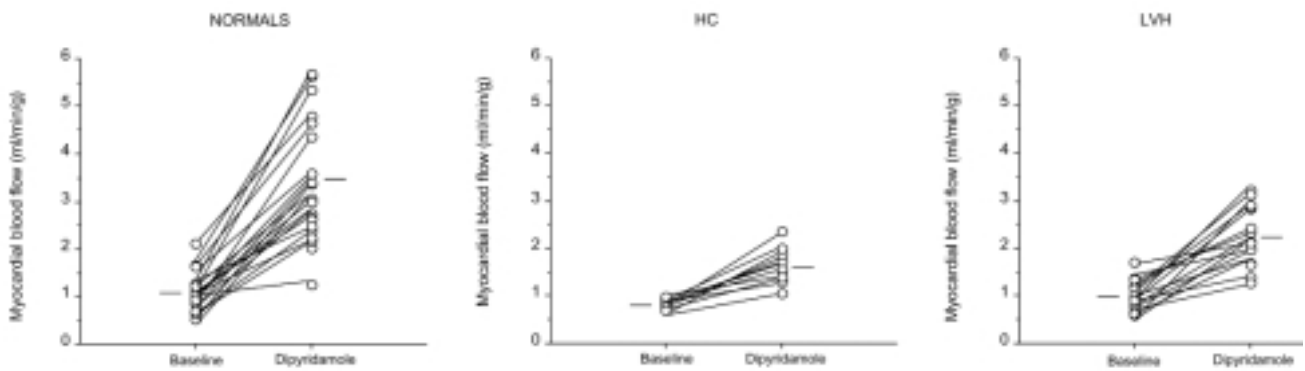


Figure 1. Myocardial blood flow measured by position emission tomography with oxygen-15 labelled water at rest and during near-maximal coronary vasodilatation (dipyridamole 0.56 mg/kg) in normal subjects (left panel), in patients with hypertrophic cardiomyopathy (HC, middle panel), and in patients with left ventricular hypertrophy (LVH) secondary to hypertension or aortic stenosis (right panel). Note the significant reduction in hyperaemic blood flow both in HC and LVH compared to normals.

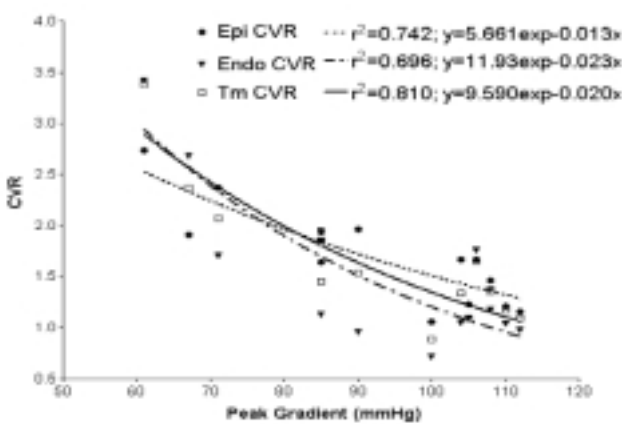


Figure 2. Correlation of coronary vasodilator reserve (CVR) with aortic valve gradient. Relationship between full thickness (transmural-Tm), subendocardial (Endo) and subepicardial (Epi) CVR (measured by positron emission tomography with oxygen-15 labelled water at rest and during near-maximal coronary vasodilatation with dipyridamole 0.56 mg/kg) and severity of aortic valve gradient in patients with aortic stenosis. Note the progressive decline of CVR with the increase of the gradient severity particularly in the subendocardial layers.

liminary results from our study in patients with aortic stenosis and LVH show that reduction in left ventricular mass following aortic valve replacement is associated with a marked improvement of overall CVR¹⁴. It is unclear whether similar changes occur with regression of LVH in hypertension. One study has demonstrated an improvement in CVR with antihypertensive treatment⁴⁶, although it remains to be established whether regression of LVH correlates with improvement in CVR.

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