Left ventricular hypertrophy and aortic stenosis: a commentary

Routledge *et al*. have addressed an increasingly topical issue. They demonstrate in a small cohort of patients with aortic stenosis (AS) that the use of angiotensin-converting enzyme (ACE) inhibitors may be safe, particularly with some degree of systemic hypertension.[1] This adds to the evidence that the use of ACE inhibitors in this patient population should not be strictly contraindicated. However, the more searching question of whether they *should* be used remains unanswered.

As the authors point out, the hypertrophic response of the left ventricle to pressure overload in AS may be initially beneficial in normalising myocardial wall stress. But, as with hypertensive left ventricular hypertrophy (LVH), it is associated with unfavourable alterations in myocardial pathophysiology i.e. long ventricular (LV) systolic dysfunction, ischaemia, and arrhythmias, as well as adverse prognosis.[2] After aortic valve replacement, the persistence of LVH is associated with a worse outcome,[3] with patient-related factors, particularly systemic blood pressure, being significant causes of late residual LVH.[4] It may be justifiable to extrapolate that the use of ACE inhibitors in this phase is beneficial, as in hypertensive LVH, although no studies have specifically explored this. Whether prevention of the development of LVH or regression of existing hypertrophy in these patients before aortic valve replacement is of benefit remains unclear.

The evidence for an inextricable link between the renin-angiotensin-aldosterone system (RAAS) and LVH in AS is widely available in experimental models and the RAAS is an obvious focus as it has an independent direct role in modulating cardiac growth.[5,6] Local renin-angiotensin systems within the LV tissue itself may also regulate myocardial growth in hypertensive LVH through the local generation of angiotensin II.[7] Despite some conflict in reports, evidence increases for a relationship between LVH and genotypic determinants affecting the RAAS in patients with AS.[8,9] Recently, deposition of components of the RAAS including ACE and angiotensin II has been demonstrated on calcific aortic cusps;[10] ACE inhibitors may reduce progressive aortic valve calcification.[11]

The findings of Routledge *et al*. need to be tempered with a note of caution. Their conclusions have to be interpreted in the light of all the usual limitations of a retrospective observational study. In severe AS, valve replacement is the only truly therapeutic strategy. The use of ACE inhibitors is unlikely to have any significant positive impact on this stage of the disease and may in fact be detrimental. However, on available evidence, prospective studies of safety and tolerability in patients with mild and moderate AS should be fully supported, followed by investigation of the effect of ACE inhibitors on prevention/regression of LVH and prevention of disease progression.

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