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Not all left ventricular hypertrophy is created equal

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Epidemiology of left ventricular hypertrophy

Left ventricular (LV) hypertrophy is a frequent finding in a population with established systemic hypertension with an echocardiographically determined prevalance of up to 48% depending on the definition of the upper normal limit of LV mass. LV hypertrophy is primarily a compensatory mechanism in response to the increased workload imposed on the heart in hypertensive subjects. However, LV hypertrophy represents a major risk factor with respect to cardiovascular morbidity and mortality in primary and secondary arterial hypertension and in end-stage renal disease (ESRD) [1–3]. The increased risk is attributable to several sequelae of LV hypertrophy such as an impaired diastolic filling of the LV cavity, one of the earliest negative consequences of hypertensive heart disease, or an impaired systolic function which both ultimately lead to clinical signs of congestive heart failure. The increased risk is also related to vascular changes in coronary arteries leading to a decreased coronary blood flow (in addition to the increased risk for coronary atherosclerosis). Last but not least, increased ectopic ventricular activity found in patients with LV hypertrophy increases the risk of sudden cardiac death.

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Pathophysiology of LV hypertrophy

Arterial blood pressure is clearly one important determinant of LV hypertrophy, with ambulatory blood pressure correlating better with parameters of LV hypertrophy than office blood pressure. Data have now been accumulated that non-haemodynamic factors such as gender, age, increased body mass index, angiotensin II, aldosterone and parathyroid hormone play a modulating role in the extent of LV hypertrophy. It has been documented beyond any doubt that LV hypertrophy does regress after starting antihypertensive therapy. Several studies now provide indirect evidence for an improved prognosis after regression of LV hypertrophy. Data from the Framingham study at first showed that cardiovascular mortality was reduced when LV hypertrophy was reduced [4].

Geometry of LV hypertrophy

LV hypertrophy is defined by arbitrary criteria, such as posterior wall thickness exceeding 1.1 cm, or better LV mass index exceeding 131 g/m^2 in men (110 g/m^2 in women). LV hypertrophy represents a remodelling process of the heart architecture to normalize wall stress. The particular pattern of hypertrophy is dependent on the type of load that is imposed on the LV. Increased afterload leads to an increase in end-systolic and peak wall stress and the addition of sarcomers in parallel to an increase in LV wall thickness at the expense of chamber volume thus increasing relative wall thickness [5]. This pattern has been termed 'concentric remodelling' and if LV mass is above the upper normal limit 'concentric hypertrophy'. However, some hypertensive patients, especially those with concomittant volume overload states such as obesity or patent

arterio-venous fistula, develop 'eccentric hypertrophy', characterized by an increased left ventricular mass but normal relative wall thickness [6]. In contrast to 'physiologic hypertrophy' as encountered in athletes, pathologic forms of LV hypertrophy are accompanied by interstitial fibrosis. Due to decreased relaxation in early diastole, an impaired LV filling is the diagnostic criteria that favours the diagnosis 'pathologic' LV hypertrophy (decreased E:A ratio, i.e. the ratio of early to late diastolic filling), in contrast to a normal or even supranormal LV diastolic filling in 'physiologic' LV hypertrophy.

LV hypertrophy in ESRD

Among ESRD patients, the prevalance of LV hypertrophy with up to 70% and the degree of LV hypertrophy in relation to a similar afterload is even higher than among patients with essential hypertension. LV hypertrophy in ESRD patients is predictive of cardiovascular mortality independently of other well-known risk factors [2,3] with a 5-year survival rate more than two times higher in patients with normal LV mass as opposed to patients with increased LV mass [7]. In addition to the above mentioned risk factors, further risk factors for the development of LV hypertrophy, such as anaemia, a patent arterio-venous fistula, a disturbed elasticity of central arteries with elevated impedance, hypervolaemia, and hyperreninaemia are encountered in ESRD patients. With duration of dialysis treatment LV mass increases progressively—even in normotensive patients—and usually ESRD patients present with LV hypertrophy of mostly eccentric pattern. Compared with controls LV mass is higher in normotensive ESRD patients, but LV mass:volume ratio remains similar since LV volume is also elevated. However, in hypertensive ESRD patients, the LV mass:volume ratio is usually decreased compared to hypertensive non-uraemic patients, i.e. the increase in LV mass:volume ratio is less than expected for a given systolic pressure. Thus, the LV hypertrophy is inadequate. This abnormal adaptation of the LV is related with at least two factors. The first is arterial hypertension itself; in ESRD patients the deviation of the LV mass:volume ratio from predicted values for normal controls is greater, the higher the blood pressure. Second is hyperparathyroidism; among the many substances that have been incriminated to be responsible for the 'cardiopressor' effect in uraemia, parathormone plays the most intriguing role [8].

LV geometry in ESRD

The clinical importance of LV hypertrophy in ESRD patients seems predominantly determined by the corresponding LV geometry. With the exception of some studies most authors report an increase in the internal dimensions of LV cavities in parallel to an increase in LV wall thickness, i.e. eccentric LV hypertrophy, as being characteristic and frequent in haemodialysis. This pattern of LV hypertrophy is related to chronic volume and flow overload, that is associated with three factors: presence of an arterio-venous shunt, sodium and water retention, and anaemia. Since a dilated LV is a poor prognostic marker in dialysis patients, Foley *et al.* investigated 433 patients on ESRD therapy [9]. They found in patients with normal LV diameter that high LV mass and mass:volume ratios were associated with an adverse prognosis, similar to observations in the general population and in patients with essential hypertension. In contrast, in patients with increased LV volume an elevated LV mass had no independent effect on cardiovascular prognosis. Of the echocardiographic variables tested, LV cavity volume (especially in excess of 120 ml/m^2) had the worst prognosis. These patients that have an inadequate low compensatory LV hypertrophy for yet unknown reasons are at very high risk to develop congestive heart failure with high mortality rate for ESRD patients.

Based on these findings Foley *et al.* developed a geometric classification for patients with ESRD. (i) Normal LV volume and normal LV mass (<120 g/m^2); (ii) LV volume 90–120 ml/m^2 irrespective of LV mass; (iii) Normal LV volumen with LV mass >120 g/m^2; (iv) LV volume >120 ml/m^2 irrespective of LV mass. Compared with Group I patients, the adjusted relative risk of death after 2 years on dialysis rose stepwise from 2.5 in Group II to 3.29 in Group III and 17.4 in Group IV. The proposed classification appears to be superior to one based merely on LV mass index alone, since patients with LV hypertrophy and a dilated left ventricle, i.e. low LV mass:volume ratio would be classified corresponding to their clinical status, namely incipient or overt congestive heart failure. Clearly in patients with a dilated LV and most likely depressed cardiac pump function impaired LV function is more predictive for cardiovascular morbidity and mortality than LV mass per se.

Therapy of LV hypertrophy in ESRD

The therapeutic options in patients with secondary hypertension and in ESRD patients should be chosen according to the prevailing values of theses parameters. In ESRD patients with elevated LV volume the main therapeutic option should be to reduce hypervolaemia, to counteract LV remodelling by blocking the action of angiotensin II and sympathetic nervous system, to correct anaemia and to treat hyperparathyroidism [8]. In ESRD patients with increased LV mass index in face of a normal or reduced LV volume, antihypertensive therapy including ACE inhibitors or AT_1-receptor antagonists should be favoured, since first according to a metaanalysis of only randomized double-blind trials the greatest benefit with regard to reducing LV mass was seen with angiotensin II blocking drugs [10] and second blocking the effects of angiotensin II in patients with dilated LV has clearly positive effects

according to several prospective studies in congestive heart failure.

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