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Left ventricular systolic function in aortic stenosis

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In aortic valve stenosis, concentric hypertrophy develops which is characterized by a reduced end-diastolic radius-to-wall thickness ratio (r/h) with an essentially normal cavity shape. As long as the product of (r/h) and LV systolic pressure remains constant, hypertrophy is appropriate. An increase in the product, which represents an increase in wall stress signals inadequate LV hypertrophy. Although at first glance, massive LV hypertrophy appears favourable for the maintenance of a normal LV ejection fraction in aortic stenosis, data from 23 studies of the literature have shown an inverse relationship between ejection fraction and LV angiographic mass m^{-2} ($r = -0{\cdot}59$). *Both a degree of hypertrophy inadequate to keep systolic wall stress within normal limits and a reduction of LV contractility may explain the depression of ejection fraction when LV angiographic mass is sizeably increased. Conversely, a normal ejection fraction in aortic stenosis may not be indicative of normal systolic myocardial function under all circumstances. In the presence of mildly reduced contractility, a normal ejection fraction may be maintained by the use of preload reserve. Assessment of myocardial structure from LV endomyocardial biopsies revealed no differences in muscle fibre diameter, interstitial fibrosis and volume fraction of myofibrils between patients with aortic stenosis having a normal and those with a depressed ejection fraction. Preoperative ejection fraction is a poor predictor of postoperative survival, whereas markedly increased preoperative angiographic mass and end-systolic volume have been reported to predict an unsatisfactory postoperative outcome characterized by either death or poor LV function.*

Ventricular geometry and its implications for systolic function

Left ventricular (LV) chronic pressure overload in response to aortic valve stenosis leads to marked hypertrophy of the myocardium characterized by a decrease of end-diastolic radius-to-wall thickness ratio (r/h) with the cavity shape remaining essentially normal. The decrease of (r/h) is the typical feature of concentric hypertrophy. As long as the product of (r/h) and LV systolic pressure remains constant, hypertrophy is appropriate[1]. An increase of the product which represents an increase in wall stress signals inadequate LV hypertrophy. The increase of wall thickness at essentially normal cavity dimensions is of importance for the ejection dynamics of the left ventricle. To achieve a normal LV ejection fraction in concentric hypertrophy, a lower percentage of midwall fibre shortening than in a non-hypertrophied ventricle is required because the contribution of wall thickening to inward wall displacement and hence reduction of cavity size is increased[2–4].

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Systolic function, left ventricular muscle mass and myocardial contractility

Left ventricular systolic function as assessed from ejection fraction is within normal limits in about two-thirds of the patients who are referred for catheterization with a view to aortic valve replacement. In one-third ejection fraction is depressed despite a massive increase of LV angiographic muscle mass which at first glance should be favourable for maintaining ejection fraction within normal limits. In 64 patients with pure aortic stenosis (aortic reflux absent in 22 and aortic regurgitant fraction $<0{\cdot}20$ in 42) but without coronary artery disease, we found an inverse relationship between biplane ejection fraction and left ventricular angiographic muscle mass index (LMMI), ($r = -0{\cdot}47$, $P < 0{\cdot}001$). Similarly, 30 mean values of ejection fraction and LMMI taken from 23 studies of the literature[5–12,14–18,20–27,29–31] (Table 1), yielded a significant inverse correlation, as depicted in Fig. 1. Ejection fraction was also inversely correlated with LV end-diastolic pressure (Table 1).

The reason why ejection fraction is depressed in aortic stenosis despite massive increase of angiographic mass has been a matter of debate. Gunther

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Table 1 Regression analyses in aortic stenosis based on data (mean values) taken from the literature

	n	*P*	*r*	References
EF *vs.* LMMI	30	0·001	−0·589	6–12, 14–18, 20–27, 29–31
EDVI *vs.* LMMI	30	0·001	0·608	6–12, 14–18, 20–27, 29–31
ESVI *vs* LMMI	30	0·001	0·657	6–12, 14–18, 20–27, 29–31
LVEDP *vs.* LMMI	25	0·02	0·487	6, 9–12, 14–18, 20, 22–27, 29, 31
EF *vs.* LVEDP	30	0·001	−0·719	5, 6, 9–20, 22–29, 31

EF, left ventricular ejection fraction (%); LMMI, left ventricular angiographic mass index ($g\,m^{-2}$); EDVI, left ventricular end-diastolic volume index ($ml\,m^{-2}$); ESVI, left ventricular end-systolic volume index ($ml\,m^{-2}$); LVEDP, left ventricular end-diastolic pressure (mmHg); *n*, number of observations; *P*, probability (least-square regression analysis); *r*, correlation coefficient.

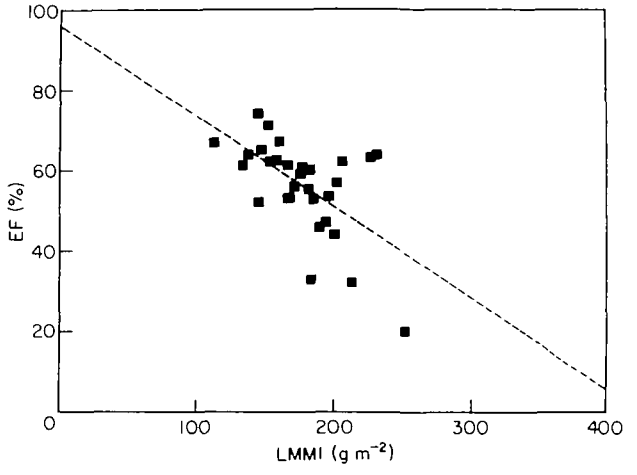

Figure 1 Relationship between left ventricular ejection fraction (EF) and left ventricular angiographic muscle mass index (LMMI) derived from published mean values. There is a significant inverse correlation. The dashed line is the calculated regression line. $r = -0{\cdot}59$, $n = 30$, $P < 0{\cdot}001$

and Grossman[17] have considered excess afterload due to inadequate hypertrophy of normally functioning cardiac muscle to be at the origin of impaired left ventricular shortening. They described an excellent ($r = -0{\cdot}96$) inverse relationship between ejection fraction and mean systolic wall stress in 14 patients with aortic stenosis. However, more recent studies have shown that in aortic stenosis at similar peak systolic circumferential wall stress, either normal or increased, patients with depressed isovolumic contractile indexes have a significantly lower ejection fraction than do those with normal isovolumic contractility[25] and that in the diagram correlating ejection fraction to peak systolic or end-systolic wall stress the values of many patients fall down and to the left of the normal range[28,31,32]. Thus, although afterload mismatch may adversely affect LV ejection fraction, depression of contractility associated with advanced LV hypertrophy appears to be the major determinant of LV pump dysfunction in aortic stenosis. Another argument that afterload mismatch is not the main reason for depressed ejection fraction comes from observations early after reduction or removal of LV

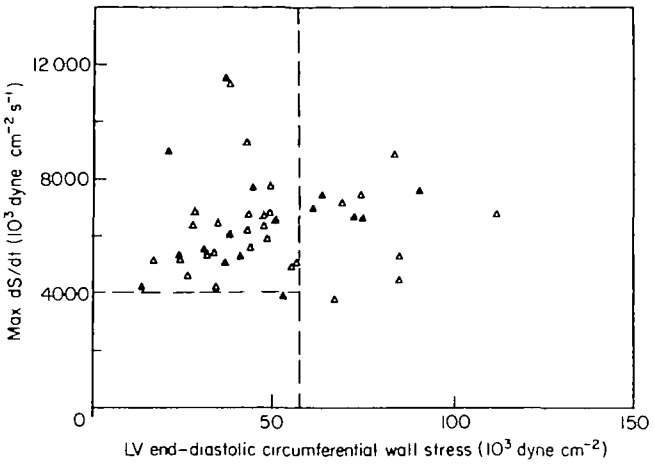

Figure 2 Relationship between maximal rate of rise of left ventricular circumferential wall stress (max dS/dt) and left ventricular end-diastolic circumferential wall stress in 44 patients with aortic stenosis (AS) and an ejection fraction (EF) $\geqslant 57\%$. The shaded area encompasses the values found in 23 controls. Thus the upper left quadrant defines the normal relationship between max dS/dt and end-diastolic stress In 12 patients the relationship was shifted to the right. Hence left ventricular myocardial contractility appeared to be mildly depressed in these patients. Mobilization of preload reserve allowed maintenance of ejection fraction within normal limits

pressure burden. After aortic balloon valvuloplasty in patients with ejection fraction $\leqslant 55\%$ McKay *et al.*[33] reported only a modest immediate increase of ejection fraction from 40 to 46% and in patients with aortic stenosis and depressed ejection fraction (mean preoperative ejection fraction 33%) Schwarz *et al.*[34] have found an increase to 43% 17 days after valve replacement, whereas nine months after surgery ejection fraction had finally increased to 71%.

A LV ejection fraction within the limits of ejection fractions obtained in control subjects is generally considered to be indicative of a normal LV contractility in patients with aortic stenosis except in situations where afterload is below normal as in patients with congenital aortic stenosis who show supranormal LV shortening[35]. Moreover, in evaluating the meaning of a normal ejection fraction in aortic stenosis it has to be taken into account that the magnitude of ejection fraction is also influenced by preload.

To analyse further LV contractility in our 44 patients with a normal ejection fraction, we have assessed the relationship between maximal rate of rise of circumferential wall stress (max dS/dt) and end-diastolic stress (S_{ed})[36]. Thirteen patients had an abnormal relationship in this isovolumic function diagram (Fig. 2) whereby in 12 preload, as assessed by S_{ed}, was increased. Thus in the presence of mildly reduced contractility, a normal ejection fraction may be maintained by the use of preload reserve.

Systolic function and myocardial structure

Myocardial structure was assessed from LV endomyocardial biopsies in the same 64 patients with aortic stenosis mentioned above. Muscle fibre diameter and interstitial fibrosis (IF) in 44 patients with normal ejection fraction did not differ from the corresponding values in 20 patients with depressed ejection fraction. LV fibrous content (FC) was 29·6 g m^{-2} in those with normal and 37·9 g m^{-2} ($P < 0{\cdot}025$) in those with depressed ejection fraction. This difference was mainly due to the fact that LMMI which enters the formula for calculation of FC (IF × LMMI/100) was higher ($P < 0{\cdot}001$) in those with depressed (199 g m^{-2}) than in those with preserved ejection fraction (158 g m^{-2}). The volume

fraction of myofibrils (VFM) did not differ in patients with depressed and normal ejection fraction. This observation is at variance with the results of Schwarz *et al.*[24] who found VFM to be significantly reduced in patients with aortic stenosis and an ejection fraction $<55\%$.

Systolic function and prognosis after aortic valve replacement

In patients with aortic stenosis or combined aortic valve lesions and an ejection fraction $<50\%$, more early deaths in the first month after aortic valve replacement have been reported than in patients with an ejection fraction $\geqslant 50\%$[37]. However, the difference was not significant. Subsequent long-term survival was not affected by the preoperative ejection fraction. Other studies[19,30,32,38–40] have also found no relationship between preoperative ejection fraction and long-term survival. This lack of relationship appears to stem from the fact that postoperative death due to myocardial dysfunction is uncommon and most deaths are related to prosthetic valve complications or co-existent coronary artery disease[38]. When surgical outcome was assessed by both postoperative death and inadequate restoration of LV function, preoperative angiographic muscle mass index[30] and end-systolic volume index[32] were found to be preoperative predictors of an unsatisfactory postoperative outcome.

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