

Does left ventricular outflow tract obstruction increase the risk of sudden death in cardiomyopathy?

Original article Elliott PM *et al.* (2006) Left ventricular outflow tract obstruction and sudden death risk in patients with hypertrophic cardiomyopathy. *Eur Heart J* 27: 1933–1941

SYNOPSIS

KEYWORDS hypertrophic cardiomyopathy, left ventricular outflow tract obstruction, sudden cardiac death

BACKGROUND

Approximately a quarter of patients with hypertrophic cardiomyopathy (HCM) have left ventricular outflow tract obstruction (LVOTO) and this has been associated with poor outcome. The association between LVOTO and survival in relation to other risk factors for sudden cardiac death (SCD) has not, however, previously been studied.

OBJECTIVE

To determine whether the relationship between LVOTO and SCD is influenced by the presence of other risk factors.

DESIGN AND INTERVENTION

This observational study took place at St George's Hospital, London, UK between January 1988 and March 2002 and enrolled patients aged 16 years or older with a diagnosis of HCM. Patients were excluded if they had other conditions known to cause ventricular hypertrophy. Patient assessment included physical examination, 48h ambulatory electrocardiography, and exercise on either a bicycle or treadmill with concurrent analysis of systolic blood pressure and respiratory gases. Patients also underwent echocardiography for the measurement of left ventricular (LV) outflow gradient.

OUTCOME MEASURES

The outcomes were SCD, internal cardioverter-defibrillator (ICD) discharge, heart transplantation, death from congestive heart failure, other cardiovascular death (e.g. stroke, thromboembolism, or myocardial infarction), or noncardiac death.

RESULTS

A total of 917 eligible patients were enrolled in the study; 60.4% were male and the mean age was 43 years (range 16–88 years). Patients were divided into five groups on the basis of increasing LV outflow gradient. LVOTO was defined as an LV outflow gradient of 30mmHg or higher and was present in 31.4% of patients. After a median follow-up of 61 months, 122 patients had died, undergone a heart transplant, or experienced an ICD discharge; 40.2% of these individuals had LVOTO. The 5-year survival rate for all-cause death or transplantation was significantly lower in patients with an obstruction than in those without (86.5% versus 90.1%; $P=0.006$) and there was an incremental increase in mortality and incidence of transplantation with increasing severity of LVOTO (relative risk [RR] per 20 mmHg increase = 1.24; $P=0.003$). Similarly, the 5-year survival rate for SCD or ICD discharge was lower in patients with LVOTO than in those without obstruction (91.4% versus 95.7%; $P=0.004$). There was also a trend towards worse survival with increasing LV outflow gradient (RR per 20 mmHg increase = 1.36; $P=0.001$). In patients with LVOTO, there was a significant correlation between 5-year all-cause survival and NYHA status (91.0% for NYHA class I versus 82.6% for NYHA class III/IV; $P=0.002$). Five-year survival was not significantly affected by a history of chest pain or syncope. Multivariate analysis indicated that LVOTO was an independent predictor of SCD and ICD discharge; the RR for an LV outflow gradient of 90mmHg or higher, when compared with patients with less severe or no LVOTO, was 3.8 ($P=0.005$).

CONCLUSION

The risk of SCD or ICD discharge is higher in patients with LVOTO, and the risk increases incrementally with severity of obstruction.

COMMENTARY

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LVOTO in HCM has been a matter of debate for decades. The presence of true intraventricular obstruction to blood flow was fully recognized 20 years ago,¹ but its negative impact on patient outcome, in terms of disease progression and increased cardiovascular mortality, has been demonstrated only recently.² In 2003, Maron *et al.* reported that the annual rate of SCD was slightly higher in patients with LVOTO than in those without obstruction (1.5% versus 0.9%). Although the absolute difference was small, there was a twofold increase in the RR of SCD in patients with LVOTO.²

The relationship between the presence of LVOTO and poor prognosis has now been confirmed by Elliott *et al.*, who recently reported that the presence of obstruction was associated with a 2.4-fold increased risk of SCD or ICD discharge, and had low positive and high negative predictive values (9% and 95%, respectively) for SCD. Furthermore, the risk of SCD increased with additional risk factors, namely nonsustained episodes of ventricular tachycardia, abnormal blood pressure in response to exercise, severe LV hypertrophy, syncope, and family history of SCD, but SCD was rare in asymptomatic patients without risk factors.

Elliott *et al.* also reported an association between varying degrees of LV outflow gradient and risk of SCD or ICD discharge. Systolic gradients are, however, dynamic and are influenced by several factors, including volemia and adrenergic tone. Exercise can easily elicit high systolic gradients in a substantial proportion of patients who do not appear to have obstructive disease at rest.³ Thus, risk stratification of patients with HCM using values that are largely volatile, such as systolic gradients, must be interpreted with great caution. Very high systolic gradients (>90 mmHg) could constitute a possible exception, as these are less likely to change at follow-up examination, once they are clearly distinguished from the often associated mitral regurgitant flow by continuous wave Doppler

echocardiography. Notably, SCD also occurred in patients receiving adequate doses of amiodarone, confirming the poor protection provided by this drug.

The clinical management of HCM poses several challenging and unresolved questions, such as how to select patients for ICD implantation or relief of LVOTO.⁴ Decision-making should consider the patient's age, the presence of additional risk factors, and left atrial diameter as a marker of disease progression. Our poor ability to predict individual risk for SCD should be also considered, as well as the potential negative psychological consequences of ICD implantation, particularly in the young. Patients should be carefully evaluated, preferably in centers with experience in treating HCM.

The recent demonstration that patients with HCM who underwent a septal myectomy had an excellent outcome confirms the importance of LVOTO and the potential long-term benefit of its relief by myectomy.⁵ Relief of obstruction clearly matters in patients with HCM. Perhaps it is time to reconsider myectomy, not only for the improvement of symptoms and quality of life, but also to lower the risk of disease progression and SCD.

References

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Competing interests

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PRACTICE POINT

SCD is rare, and aggressive intervention is not indicated in asymptomatic patients with obstructive HCM but no additional risk factors, but septal myectomy should be considered in those with additional risk factors