Radionuclide assessment of left ventricular function in hypertrophic cardiomyopathy

D.D. Sugrue and W.J. McKenna¹

Division of Cardiovascular Disease, Mayo Clinic, Rochester, Minnesota 55905, U.S.A. and ¹Division of Cardiovascular Disease, Royal Postgraduate Medical School, DuCane Road, London W12 0HS, UK.

Summary: To determine the relationship of left ventricular function and ventricular tachycardia, 48 hour ECG monitoring and technetium-99m gated equilibrium radionuclide angiography were performed in 84 consecutive patients with hypertrophic cardiomyopathy and sinus rhythm. Measurements of ejection fraction (EF), peak ejection rate (PER, edv/s), peak filling rate (PFR, edv/s) and time to peak filling rate (PFR, ms) were derived from radionuclide activity time curves generated from data acquired in list-mode. Left ventricular function was compared in patients with and without ventricular tachycardia. Left ventricular ejection fraction was significantly lower in 16 patients with ventricular tachycardia compared to 68 patients without (67 ± 17 vs 78 ± 10 , $P < 0.05$) and time to peak filling rate was significantly prolonged (152 ± 32 vs 120 ± 36 , $P < 0.05$). Thus patients with hypertrophic cardiomyopathy at greatest risk of sudden death had significant impairment of systolic and diastolic left ventricular function.

Introduction

Abnormalities of systolic and diastolic function are common in hypertrophic cardiomyopathy. Standard methods for assessing these abnormalities by invasive techniques or using echocardiography have several potential limitations; the technology is either complex and not widely available or measurements are not very reproducible. For example, construction of pressure volume loops requires cardiac catheterization and data interpretation may be difficult; digitized echocardiography is not widely available and measurements made using this technique are critically dependent on ventricular geometry.

High temporal resolution gated radionuclide cine angiography offers the potential for serial non-invasive assessment of left ventricular ejection and filling; the technical success rate of the technique is high, error margins for measurements obtained using the technique are acceptably low (Sugrue *et al.*, 1985) and radionuclide measurements correlate reasonably with similar measurements obtained using contrast angiography (Sugrue *et al.*, 1984a). We have used this technique in patients with hypertrophic cardiomyopathy in order to assess the relationship between left ventricular gradients and stroke volume ejected during early and late systole (Sugrue *et al.*, 1984b), and to study the effect of an antiarrhythmic drug (amiodarone) on left ventricular ejection and

filling (Sugrue *et al.*, 1984c). Recently we have used a radionuclide technique to study the relationship of clinical and prognostic features to left ventricular function in hypertrophic cardiomyopathy.

Materials and methods

Radionuclide studies were performed at rest in the supine position using a large field of view rotating gamma camera. Red blood cells were labelled *in vivo* using 15 mCi of technetium-99m and images were acquired in list-mode. Data were acquired from 600 to 900 consecutive cycles and stored on computer for subsequent analysis. An R-R interval histogram was constructed and cycles more than 20% from the mean cycle length were rejected. A background corrected composite left ventricular activity time curve was generated at a frame rate of 10–25 ms per frame by combined forward and reverse gating from the R-wave. A standard count-based method was used for calculation of left ventricular ejection fraction (LVEF) (Sugrue *et al.*, 1985). Peak rates of ejection and filling were computed automatically in left ventricular counts per second, were normalized to end-diastolic counts and expressed as change from end-diastolic volume per second (edv/s). This approach does not assume knowledge of absolute left ventricular volume. Time to end systole (TES), in milliseconds, was

Correspondence: W.J. McKenna, M.D.

defined as the interval from the R-wave to the minimum of the curve; time to peak ejection rate (TPER) was defined as the interval from the R-wave to the point of peak ejection and time to peak filling rate (TPFR) was defined as the interval from the minimum of the curve to the point of peak filling (Figure 1).

Ambulatory electrocardiographic monitoring was performed for at least 48 hours in each patient off all antiarrhythmic medications.

Eighty-four consecutive patients with hypertrophic cardiomyopathy were studied. They were aged 7–72 years, mean 44; 46 were male and 38 female. Values for radionuclide indices of left ventricular ejection and filling were determined in 28 normal volunteers. (The values given are mean $\pm$ s.d.)

Results

Forty-five of 84 patients (54%) had an ejection fraction above the upper limit of normal ($> 75\%$), 27 of 84 (32%) had above normal peak ejection rates (> 4.09 edv/s) and 24 of 84 (29%) had a shortened (< 144 ms) time to peak ejection rate. Five of 84 patients (6%) had an ejection fraction below the lower limits of normal ($< 53\%$), 7 of 84 (8%) had decreased peak ejection rate (> 2.64 edv/s) and 3 of 84 (4%) had a prolonged time to peak ejection rate (> 264 ms).

Twenty-one patients (25%) had supranormal (> 3.89 edv/s) peak filling rates and 4 (5%) had shortened time to peak filling rates (< 61 ms). Fifteen of 84 (18%) patients had below normal peak filling rates (< 2.40 edv/s) while 25 (30%) had prolonged (> 191 ms) time to peak filling rate.

Sixteen patients (19%) had one or more episodes of ventricular tachycardia (> 3 consecutive beats) documented during 48 hour ambulatory monitoring. In those patients with ventricular tachycardia, mean

Figure 1 A schematic representation of a radionuclide activity-time curve. Ejection and filling rates were normalized to end-diastolic counts and expressed as change from end-diastolic volume per second (edv/s). Time to peak ejection rate (TPER) was defined as the interval from the beginning of the curve to the point of peak ejection and time to peak filling rate (TPFR) as the interval from end-systole (minimum of the curve) to the point of peak filling. PER = peak ejection rate; PFR = peak filling rate; TES = time to end-systole.

left ventricular ejection fraction was decreased (66 ± 17 vs $78 \pm 10\%$, $P < 0.05$) and time to peak filling rate was prolonged (152 ± 37 vs 120 ± 36 ms, $P < 0.05$) (Table I).

Discussion

These results emphasize the heterogeneity of left ventricular dysfunction in patients with hypertrophic cardiomyopathy. This spectrum of abnormalities in diastolic function has been previously noted using a

Table I Relationship of radionuclide measurements of left ventricular ejection and filling to previously documented ventricular tachycardia in 84 patients with hypertrophic cardiomyopathy

	Ventricular tachycardia n = 16 (19%)	No ventricular tachycardia n = 68 (81%)	
Ejection fraction (%)	67 $\pm$ 17	78 $\pm$ 10	$P < 0.05$
Peak ejection rate (edv/s)	3.3 $\pm$ 1.0	3.9 $\pm$ 1.0	NS
Time to peak ejection rate (ms)	174 $\pm$ 35	174 $\pm$ 34	NS
Time to end-systole (ms)	375 $\pm$ 49	358 $\pm$ 53	NS
Peak filling rate (edv/s)	2.8 $\pm$ 1.2	3.3 $\pm$ 1.2	NS
Time to peak filling rate (ms)	152 $\pm$ 37	120 $\pm$ 36	$P < 0.05$
Heart rate (beats/min)	64 $\pm$ 9	65 $\pm$ 8	NS
Systolic blood pressure (mm Hg)	127 $\pm$ 11	131 $\pm$ 12	NS
Diastolic blood pressure (mm Hg)	78 $\pm$ 9	75 $\pm$ 11	NS

NS = not significant.

variety of techniques for assessing LV filling, including echocardiography (St. John Sutton *et al.*, 1978), contrast angiography (Sanderson *et al.*, 1977) and radionuclide angiography (Bonow *et al.*, 1981). Impairment of systolic function in hypertrophic cardiomyopathy has been less well documented although Bonow *et al.* (1981) noted a subnormal left ventricular ejection fraction in one of 40 patients studied, using a radionuclide technique similar to ours. It has been suggested that, as the disease progresses, the left ventricle becomes dilated with loss of outflow tract gradient and by implication, a decline of systolic pump function (Goodwin & Oakley, 1972).

The relationship between impairment of systolic and diastolic function and previously documented ventricular tachycardia is of some interest. Because of the cross-sectional nature of the study, the results do not provide direct evidence that impairment of filling *per se* is an independent predictor of subsequent sudden death. However, we have previously performed a prospective comparison of contrast angiographic measurements of ejection and filling in 88 patients with hypertrophic cardiomyopathy of whom 11 subsequently died during a mean follow-up period of 8 years, to similar measurements in survivors (Newman

et al., 1985). Patients who died suddenly had a significantly lower normalized peak rate of left ventricular ejection and filling at diagnosis compared to survivors. The results of these two studies are concordant and it therefore seems likely that in adult patients, impairment of left ventricular function predicts poor prognosis. The relative power and independence of these individual predictors of sudden death remains to be determined. Although ventricular tachycardia is the presumed antecedent of sudden death in most, though perhaps not all patients with this disease, it has been suggested that a primary haemodynamic mechanism, i.e. rapid heart rates, coupled with impairment of left ventricular filling may lead to an acute decrease in stroke output with a concomitant decline in diastolic coronary flow and cardiovascular collapse (Goodwin & Krikler, 1976). The results of our studies support this hypothesis and suggest that impairment of left ventricular filling may be an essential substrate which determines whether or not ventricular tachycardia is well tolerated or precipitates ventricular fibrillation. It remains to be seen if drugs such as calcium antagonists, which improve diastolic filling, also improve prognosis.

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