Muscle dynamics in hypertrophic cardiomyopathy

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Summary: Previous reports have demonstrated that patients with hypertrophic cardiomyopathy (HCM) have prolonged isovolumic relaxation period (IRP) reflecting reduced rate of fall of left ventricular pressure. Eighty four patients with proven hypertrophic cardiomyopathy and 31 normal subjects were studied by simultaneous recordings of echocardiogram, apexcardiogram, phonocardiogram and ECG.

In normal subjects the IRP value was 61 ± 11 ms (mean ± s.d.). In the 84 patients there was enormous variability of the IRP value from 0 to 160 ms reflecting abnormal and incoordinate (but not necessarily impaired) relaxation and it was possible to identify three subgroups among the patients: 60 patients in sinus rhythm who had prolonged IRP and significantly above the normal values, 9 patients in atrial fibrillation in whom the IRP was within the normal range and 15 patients with IRP values between 0–45 ms, with the mean (26 ms) below the normal range (mean ± 2 s.d.). This group of patients with short IRP also had signs of outflow tract systolic pressure gradient, with partial mid-systolic closure of the aortic valve, systolic anterior motion of the anterior mitral valve leaflet and paradoxical splitting of the second heart sound. It is suggested that the short IRP is due to extremely delayed aortic valve closure and careful scrutiny of this subset with haemodynamic evaluation has shown that this non-invasive interval (A₂-M₀) may not always be a valid measure of left ventricular relaxation.

Introduction

Hypertrophic cardiomyopathy is a disease characterized by massive hypertrophy and impaired distensibility of the left ventricle (Goodwin, 1980). We believe that this abnormal diastolic relaxation and filling is the most important factor in determining symptoms and prognosis regardless of whether or not a gradient in the outflow of the left ventricle is present (Alvares, 1980; Alvares & Goodwin, 1982). We have studied the diastolic period using the following non-invasive techniques simultaneously: phonocardiogram, electrocardiogram (ECG), left ventricular echocardiogram and apexcardiogram reflecting the left ventricular pressure (Manolas & Rutishauser, 1980; Weisfeldt et al., 1974) in a qualitative fashion especially during the diastolic period (Figure 1). Once the aortic valve is closed, the starting point of diastole, there is a rapid fall of left ventricular pressure until the O point of the apexcardiogram and during this period when there is a gradient crossover between left atrium and left ventricle the mitral valve opens. This interval from A₂ to Mo is the isovolumic relaxation period (IRP) and its duration depends not only on the rate of fall of the left ventricular pressure but also on the pressure at the time of aortic valve closure and at the time of mitral valve opening. From the opening of mitral valve onwards, when the filling starts, the left ventricular pressure is a result of two major interdependent factors: the rate of relaxation and the rate of filling. The interval from Mo to O is the active suction period when the pressure drops at the moment when most of the filling occurs, and the O point is an equilibrium point between filling and relaxation.

The purpose of this presentation is to demonstrate the diastolic abnormalities in a large group of patients with proven hypertrophic cardiomyopathy and to identify for the first time a group of patients with extremely short IRP and to suggest a possible mechanism for this short IRP. All previous reports demonstrated that these patients had a prolonged IRP as a delay in mitral valve opening, reflecting a reduced rate of fall of left ventricular pressure (Sanderson et al., 1978; St. John Sutton et al., 1978; Hanrath et al., 1980, Traill et al., 1979).

Materials and methods

Thirty-one subjects and 84 patients with proven hypertrophic cardiomyopathy were studied with these
Figure 1 Simultaneous recording of the phonocardiogram, apexcardiogram, and echocardiogram with the electrocardiogram. The isovolumic relaxation period (IRP) is measured from the first high frequency vibration of the aortic component of the second heart sound (A₂) to the initial separation of the two leaflets of the mitral valve (mitral valve opening: Mo).

non-invasive techniques. Of the 84 patients 31 were female and 53 male, and their ages ranged from 11 to 75 years with a mean of 43.

The following parameters were measured in milliseconds in the group of normal subjects and in patients with hypertrophic cardiomyopathy: the interval from A₂ to Mo the interval from A₂ to O, the interval from Mo to O, and the intervals from the minimum left ventricular cavity dimension to the aortic valve closure and to the mitral valve opening. These last two measurements were obtained by digitizing these non-invasive techniques (which were done at Brompton Hospital, courtesy of Dr Derek Gibson), by moving a crosswire cursor along the left side of the septum, the posterior wall, both the leaflets of the mitral valve, and the apexcardiogram (Gibson et al., 1978).

From these digitized data, plots were made of the left ventricular cavity dimension and the rate of change of dimension. Then single points of physiological interest were identified, such as the aortic valve closure and mitral valve opening. In normal subjects the aortic valve closure always precedes the minimum left ventricular cavity dimension, and thus there was further reduction of left ventricular dimension after the aortic valve closure and mitral valve opening followed the minimum left ventricular cavity dimension (Figure 2).

Results and discussion

The diastolic time intervals were measured in milliseconds and the normal values are represented by the stippled area (Figure 3). The mean value of the isovolumic relaxation period in normal subjects was $63 \pm 11$ ms, but in patients with hypertrophic cardiomyopathy this period had an enormous variability from 0 to 160 ms with the mean of 76 ms when the whole group was considered.

The rapid relaxation period also had a wide variability from 105 to 275 ms and in normal subjects the mean was $140 \pm 9$ ms. The range of values for active suction period in patients varied from 35 to 190 ms with a mean of $99 \pm 32$ ms and in the group of
Figure 2 Computer printout showing (a) the left side of the septum (Sept), posterior endocardium of the left ventricle (Endo), anterior (MV. Ant.) and posterior (MV. Post.) mitral valve leaflet and the apexcardiogram (Apex). (b) Instantaneous left ventricular (LV) dimension. The small crosses on the tracing mark aortic valve closure, mitral valve opening, O point of the apexcardiogram, location of a physiological S2 and the F point of the apexcardiogram. Minimal left ventricular dimension occurs just before mitral valve opening and no significant dimension change occurs during the brief interval. (c) Rate of change of LV dimension. (d) Mitral valve velocity.

normal volunteers was 80 ± 7 ms.

Based on these results it was possible to identify three subgroups among the patients (Figure 4, the horizontal bars representing the normal values): 9 patients in atrial fibrillation, who probably have very advanced disease and had diastolic time intervals within the normal range; 60 patients in sinus rhythm with prolonged diastolic time intervals significantly above the normal mean based on previous reports; and a third group of 15 patients with extremely short isovolumic relaxation period two standard deviations below the normal mean (Figure 5).

This group of 15 patients had a mean value of 26 ms, which was significantly below the normal mean value and below the mean value when the whole group was considered. But when they were removed from statistical analysis of the whole group of 84 patients, the A2–Mo interval of the remaining 69 patients was significantly longer than that of the normal volunteers.

The interval from A2 to O was also measured in milliseconds, and in the normal subjects the mean value was 140 ms. In patients with hypertrophic cardiomyopathy the mean value was 169 ms, and when the 15 patients were removed there was a further increase to 178 ms. The shortening of this period in 15 patients was due to an extremely short IRP, since the interval from Mo to O was prolonged when compared with the rest of the patients.

Figure 6 represents two patients with short IRPs, and, as shown in these simultaneous recordings, the A2 is almost coincident with the mitral valve opening.

All the patients with short IRPs had paradoxical splitting of the second heart sound. This can be seen in Figure 7, which was obtained by simultaneous recording of the phonocardiogram, carotid pulse, and echocardiogram of the aortic valve where the A2 precedes the dicrotic notch and is coincident with the aortic valve closure.
**Figure 4** Histograms showing the mean values of IRP ($A_2-\text{Mo}$), RRP ($A_2-O$), and ASP ($\text{Mo}-O$) in patients in atrial fibrillation, with 'short IRP' and in sinus rhythm. Dotted lines = normal mean ± s.d. □ patients in atrial fibrillation; ◇ patients with 'short IRP'; ☐ patients in sinus rhythm.

**Figure 5** The IRP ($A_2-\text{Mo}$) in 84 patients with hypertrophic cardiomyopathy (HCM). Fifteen patients (open circles) have $A_2-\text{Mo}$ intervals 2 s.d. below the 31 normal volunteers ($63 \pm 22$ ms). ● patients with HCM and normal or prolonged $A_2-\text{Mo}$; ○ patients with short $A_2-\text{Mo}$ □ normal mean ± 2 s.d.
The interval from aortic valve closure to minimum left ventricular dimension was also measured in milliseconds, and zero means that these two events were coincident. In normal subjects the aortic valve closure always preceded the minimum left ventricular cavity dimension by a mean of -39 ms. By contrast, in patients with hypertrophic cardiomyopathy the values showed a wider scatter (-100 to +85 ms). Though the scatter was large, aortic valve closure followed the minimum left ventricular dimension by a mean of 9 ms when the whole group was considered. But in patients with short IRPs there was a more marked delay of the aortic valve closure in relation to the minimum left ventricular dimension with a mean of 33 ms.

The onset of the mitral valve followed the minimum left ventricular dimension in normal subjects by a mean of 25 ms, and there was an appreciable delay, when the whole group of patients was considered, by a mean of 79 ms. In patients with short IRPs this delay had a mean value of 59 ms, which was below the mean of remaining patients but above the mean value of normal volunteers.

This group of 15 patients were all in sinus rhythm and not only had a short IRP but also signs of outflow tract gradient such as systolic anterior motion of the anterior mitral valve leaflet and paradoxical splitting of the second heart sound.

Thus this short IRP was due to an extremely delayed aortic valve closure as shown on the digitized data, where there is a marked delay of the aortic valve closure in relation to the minimum left ventricular dimension and almost coincident with the mitral valve opening.

Figure 8 shows a simultaneous recording of left ventricular and central aorta pressures by a Millard catheter tip micromanometer during diagnostic catheterization. The first panel shows a marked prolongation of the left ventricular ejection time secondary to severe gradient producing a paradoxical splitting of the second heart sound. A3 occurs near the nadir of the left ventricular pressure curve resulting in a very short IRP. On the second panel, recorded later during the same catheterization, physiological splitting is now present with minimum gradient and a prolongation of the IRP.

During this study 6 patients died from the whole group of 84 patients and of these patients 5 had a short IRP.
Figure 7  Simultaneous phonocardiogram (phono), carotid pulse, echocardiogram (echo) and ECG in a patient with 'short IRP'. Note paradoxical splitting of second heart sound with partial mid-systolic closure of the aortic valve.

Figure 8  Simultaneous left ventricular, aortic, and left atrial pressure is recorded from high fidelity catheter-tip micromanometers (Millard) together with the external phonocardiogram (EXT PHONO) and the left ventricular phonocardiogram and the electrocardiogram. In the left two panels, equisensitive left ventricular and aortic pressures are recorded on a 0 to 100 mmHg scale. In the right two panels, equisensitive left ventricular and left atrial pressure are recorded on a 0 to 20 mmHg scale. In the right two panels, isovolumic relaxation period is the interval between A2 and mitral opening (Mo) at left ventricular and left atrial pressure crossover. See text for details.

Conclusion

In hypertrophic cardiomyopathy the highly organized sequential processes of normal diastolic function are completely disrupted and events are out of phase. The most striking feature in this study is an enormous variability of diastolic parameters reflecting abnormal and incoordinate (but not necessarily impaired) relaxation of the left ventricle in hypertrophic cardiomyopathy.

The muscle dynamics in hypertrophic cardiomyopathy are independent of the left ventricular haemodynamics. The diastolic time intervals in patients with atrial fibrillation were within the normal range.

A group of patients with a very short IRP was identified in this study and this was due to an extremely delayed aortic valve closure. A2 is not always an appropriate marker for the onset of left ventricular pressure decline, as a result the isovolumic relaxation period (A2–Mo) is not always an appropriate index of left ventricular relaxation.
References


