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CLINICAL STUDIES

Elderly Patients With Hypertrophic Cardiomyopathy: A Subset With Distinctive Left Ventricular Morphology and Progressive Clinical Course Late in Life

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This report describes a subgroup of 52 elderly patients with obstructive hypertrophic cardiomyopathy in whom certain clinical and morphologic features differed importantly from those of many other patients with this disease. Ages ranged from 60 to 84 years (mean 69) and 45 [87%] were women.

Echocardiographic examination showed a relatively small heart, having only modest ventricular septal hypertrophy associated with marked distortion of left ventricular outflow tract morphology. By virtue of selection, left ventricular outflow tract size at end-diastole was substantially reduced, and anterior displacement of the mitral valve within the left ventricular cavity was particularly marked. Sizable deposits of calcium in the region of the mitral anulus, posterior to the mitral valve, appeared to contribute to the outflow tract narrowing. Systolic anterior motion of the mitral valve was severe (with apposition of the mitral valve and ventricular septum) in 32 patients and more moderate in 20. The mechanism by which systolic contact between the mitral valve and septum occurred in most patients appeared to differ from that observed more typically in many other patients with hypertrophic cardiomyopathy; in most elderly study patients, anterior excursion of the mitral valve leaflets was relatively restricted, and systolic apposition between the mitral valve and septum resulted from a combination of anterior motion of the mitral valve and posterior excursion of the septum.

The vast majority (50 of 52) of the patients remained asymptomatic (or only mildly symptomatic) for most of their lives and often did not develop severe and intractable symptoms until the 6th or 7th decade (ages 56 to 81 years; mean 66). Of the 49 patients with at least 1 year follow-up study, only 12 had improvement with pharmacologic therapy; however, 14 of the 18 patients who underwent ventricular septal myotomy-myectomy or mitral valve replacement obtained symptomatic benefit from operation.

In conclusion, obstructive hypertrophic cardiomyopathy in many elderly (and predominantly female) patients may assume a distinctive morphologic appearance and a progressive clinical course. This subgroup of patients appears to constitute an important segment of the disease spectrum of hypertrophic cardiomyopathy of cardiac disease in the elderly that previously has not been precisely defined nor fully appreciated.

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Hypertrophic cardiomyopathy is a primary disease of cardiac muscle characterized by a broad pathophysiologic spectrum and a clinical course in which sudden death or severe symptoms most often occur within the first 5 decades of life (1–11). However, not uncommonly, we (12) and others (13–16) have evaluated elderly symptomatic patients who demonstrate many of the features of hypertrophic cardiomyopathy. It has been our experience that some of these patients show distinctive morphologic findings consisting of particularly severe left ventricular outflow tract narrowing in the presence of relatively mild ventricular septal hypertrophy as well as calcification in the mitral anulus region and systolic anterior motion of the mitral valve. It is the purpose of the present investigation to characterize in detail the clinical and morphologic profile of this subgroup of patients with respect to the overall disease spectrum of hypertrophic cardiomyopathy as well as the presentation of this cardiac disease in the elderly segment of the general population.

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Methods

Selection of patients. Case records of the echocardiography laboratory of the National Heart, Lung, and Blood Institute were reviewed for the period from January 1982 to June 1987. During that time, 223 nonoperated patients with hypertrophic cardiomyopathy ≥60 years of age had been evaluated with echocardiography. Four patients known to have coexistent and hemodynamically significant aortic valve stenosis and 10 patients with technically inadequate echocardiographic studies were excluded. Of the remaining 209 patients (110 women and 99 men), 52 (25%) were selected for the present study by virtue of showing each of the following echocardiographic features: 1) hypertrophied and nondilated left ventricle (17); 2) narrowed left ventricular outflow tract at end-diastole (transverse dimension ≤20 mm from mitral valve closure point to ventricular septum); 3) moderate to severe systolic anterior motion of the mitral valve (mitral valve to septal distance ≤10 mm in systole); and 4) evidence of calcification in the region of the mitral anulus.

Study patients ranged in age from 60 to 84 years (mean 69) at the most recent evaluation; 7 patients were ≥75 years of age. Forty-five patients (87%) were women, and 7 (13%) were men.

Fourteen patients had documented systemic hypertension (≥140/90 mm Hg) requiring antihypertensive medication. Eleven patients in the study group (three with hypertension and eight without) had associated extramural atherosclerotic coronary artery disease involving one artery in four patients, two arteries in six patients and three arteries in one patient.

Control group. Fifty younger patients (<40 years of age) with hypertrophic cardiomyopathy were selected only for the purpose of comparing certain echocardiographic features of the left ventricle with those in the 52 elderly study patients. These youthful patients with hypertrophic cardiomyopathy had moderate to severe systolic anterior motion of the mitral valve, but no calcification in the mitral annular region,* and were evaluated by echocardiography between January 1986 and June 1987. Ages ranged from 10 to 39 years (mean 27); 31 patients (62%) were men and 19 (38%) were women.

Echocardiography. Two-dimensional echocardiograms were performed with either an Advanced Technology Laboratory Mark 500 or a Diasonics CV-400 mechanical sector scanner with a 2.25 or 3.0 MHz transducer. The magnitude and distribution of left ventricular hypertrophy were assessed by viewing two-dimensional echocardiograms in real time and slow motion, as previously described (18). In the parasternal short-axis plane, the left ventricle was divided into four regions: the anterior and posterior ventricular septum and the anterolateral and posterior left ventricular free walls. Wall thickness of these four left ventricular regions was evaluated during diastole at both the mitral valve and the papillary muscle level; only those patients in whom hypertrophy could be assessed in each left ventricular segment were included in this particular analysis. Cross-sectional area of the left ventricular outflow tract was measured in the short-axis plane at mitral valve level, using previously reported techniques (19).

M-mode echocardiograms were derived under direct anatomic visualization from two-dimensional images or were recorded with a dedicated Irex System II ultrasound unit. Measurements of left ventricular wall thickness and chamber dimensions were made according to the recommendations of the American Society of Echocardiography (20). The position of the mitral valve in the left ventricular cavity at end-diastole was assessed with use of the mitral valve position index; this index was calculated by dividing the distance (at the time of leaflet closure) between the mitral valve and the posterior left ventricular free wall endocardium by the distance between the mitral valve and ventricular septal endocardium (21). In those patients with substantial deposits of calcium (behind the mitral valve, obscuring the posterior wall endocardium), free wall thickness was assessed just distal to the region of calcification, where the left ventricular endocardium could be more readily identified.

Using a modification of the classification of Gilbert et al. (22), systolic anterior motion of the mitral valve was defined as marked if there was either brief or prolonged (≥30% of echocardiographic systole) mitral-septal contact, and moderate if the distance between the mitral valve and septum was ≤10 mm, but there was no contact between the mitral valve and ventricular septum.

Statistical methods. Data are expressed as mean values ± SD. Differences between group means were analyzed using the unpaired Student's *t* test.

Results

Left ventricular morphology (Table 1). Ventricular septal thickness assessed by M-mode echocardiography ranged from 16 to 30 mm (mean 21.5), but was ≥22 mm in only 25 of the 52 patients (Fig. 1 to 4). Posterior free wall thickness ranged from 8 to 18 mm (mean 12); septal/free wall ratio ranged from 1.3 to 2.6 (mean 1.8).

Overall distribution of left ventricular hypertrophy could be assessed by two-dimensional echocardiography in 39 of the 52 study patients. In 29 of these 39 patients, left ventricular wall thickening was diffuse, involving substantial portions of both the ventricular septum and anterolateral

*For the most part, calcification identified by echocardiography in this study in the region of the mitral anulus is probably largely in the space between the posterior mitral valve leaflet and the posterior left ventricular wall endocardium and not in the true anatomic anulus (the site where left atrial mural endocardium, posterior left ventricular wall and posterior mitral valve leaflet meet).

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Table 1. Echocardiographic Assessment of Left Ventricular Morphology and Mitral Valve Dynamics*

	Elderly Study Patients With HCM	Youthful Patients With HCM†	p Value
No. of patients	52	50	—
Age (yr)	69 ± 6 (60 to 84)	27 ± 8 (10 to 39)	—
VS thickness (mm)	21.5 ± 2.7 (16 to 30)	25.3 ± 4.5 (18 to 34)	<0.001
LV posterior wall thickness (mm)	12.2 ± 1.7 (8 to 18)	12.0 ± 1.8 (8 to 14)	NS
Systolic posterior VS excursion (mm)	5.4 ± 3.3 (1 to 13)	5.4 ± 3.8 (1 to 14)	NS
Systolic anterior mitral valve excursion (mm)	12.0 ± 2.9 (7 to 22)	18.0 ± 4.3 (8 to 27)	<0.001
Mitral valve position index	1.4 ± 0.3 (0.82 to 2.0)	0.9 ± 0.3 (0.42 to 1.5)	<0.001

*Data given as mean values ± SD (with ranges in parentheses). †This comparison group of patients consisted of 19 women (38%) and 31 men (62%). Measures of outflow dynamics in this group did not differ significantly between men and women, for example, systolic septal excursion (4.6 ± 3.5 versus 6.1 ± 3.5 mm), systolic mitral valve excursion (17.1 ± 4.6 versus 18.6 ± 4.1 mm) and mitral valve position index (0.9 ± 0.2 versus 0.9 ± 0.2). HCM = hypertrophic cardiomyopathy; LV = left ventricular; NS = nonsignificant; VS = ventricular septal.

free wall; posterior free wall was usually normal or only mildly increased in thickness (Fig. 3A). In six patients, hypertrophy involved only the anterior and posterior portions of the ventricular septum, and in four others was confined to the anterior septum. In each of the 39 patients, maximal left ventricular wall thickness was present in the anterior portion of the septum.

By selection, in the 52 study patients the left ventricular outflow tract was markedly narrowed (Fig. 1 to 4), as evidenced by substantially reduced mitral valve to ventricular septum transverse distance at end-diastole (17.7 ± 2.1 mm) (Table 1); in 9 of the 52 patients, the outflow tract was particularly small with an end-diastolic dimension ≤15 mm (Fig. 3 and 4).

This outflow tract narrowing was associated with marked anterior displacement of the mitral valve within the left ventricular cavity (mitral valve position index 1.4 ± 0.3; normal <0.4) (21). In the short-axis plane, the left ventricular outflow tract was elliptical or slit-like in shape, with greatly reduced cross-sectional area (1.5 to 4.1 cm^2; mean 2.8) (Fig. 3A) (19).

Mechanism of mitral valve-septal contact. Because of the distorted outflow tract geometry, only a relatively mild degree of systolic anterior excursion was usually necessary for the mitral valve to closely approach (in 20 patients) or make brief (13 patients) or prolonged (19 patients) contact with the ventricular septum during mid-systole (Fig. 1, 2, 4 and 5); systolic valve excursion was only 12.0 ± 2.9 mm (Table 1). Usually both mitral leaflets participated in the systolic anterior motion of the valve. The leaflets appeared to be relatively short (in the apex to base plane) and of approximately equal length; the anterior leaflet actually contacted or closely approached the ventricular septum in systole because of its anterior anatomic position (Fig. 2, 4 and 5). In most (45 of 52) patients, systolic mitral leaflet motion and flexibility appeared to be restricted; the leaflets maintained a flattened configuration (with little or no anterior bend) throughout systole, and the body as well as distal portions of the anterior mitral leaflet (and attached chordae tendineae) approached the septum (Fig. 2, 4 and 5). Posterior excursion of the ventricular septum toward the mitral valve during systole contributed substantially to overall systolic outflow tract narrowing (Table 1). In fact, in 15 of the 52 elderly study patients, posterior septal motion and anterior leaflet motion made virtually equal contributions to facilitating mid-systolic apposition of the mitral valve and septum.

This mechanism by which mitral-septal contact occurred in our elderly patients appeared to differ from that observed in the more youthful group of patients with obstructive hypertrophic cardiomyopathy who were analyzed for comparison. In these latter patients, the mitral leaflets showed substantial anterior excursion from their position at end-diastole to the point where the anterior leaflet made contact with the ventricular septum during mid-systole (Table 1). Posterior excursion of the septum (although similar in absolute magnitude to that observed in the elderly group) contributed relatively little, proportionately, to creating systolic apposition between the mitral valve and septum (Table 1).

Mitral annular calcifications. In each study patient, by selection, bright dense echoes were identified in the region of the mitral anulus; these echo densities were judged to represent deposits of calcium. The most substantial accumulations of calcium were usually located in the space between the posterior mitral leaflet and the posterior left ventricular

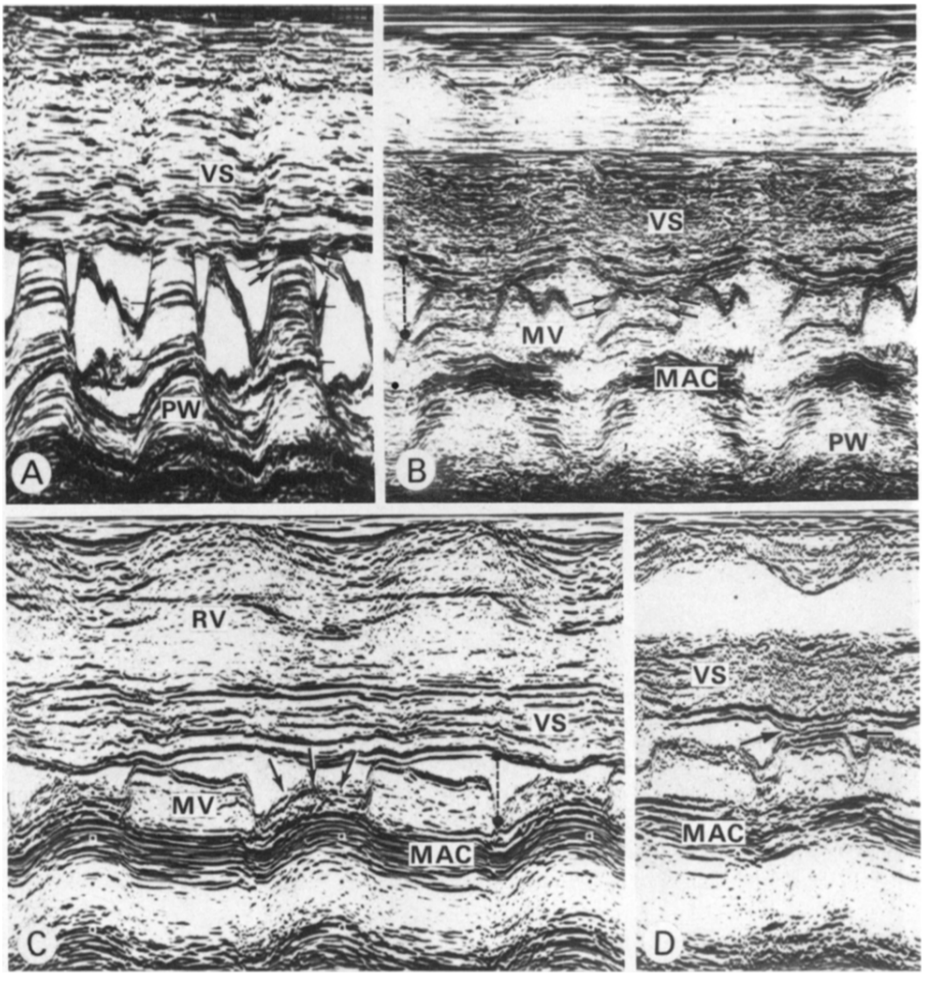

Figure 1. M-mode echocardiograms at the mitral valve level in four patients with obstructive hypertrophic cardiomyopathy: a 21 year old man (**A**) and three women, aged 74, 65 and 75 years (**B, C, D**). **A**, Marked systolic anterior motion and prolonged contact (**arrows**) between the mitral valve and ventricular septum (VS) are produced almost entirely by abrupt, marked anterior excursion of the mitral valve in early systole; the septum shows little posterior excursion toward the mitral valve. **B**, During systole, anterior excursion of the mitral valve (MV) toward the septum is much less than shown for the young patient in **A**, and posterior septal excursion (toward the mitral valve) contributes substantially more to creating contact between the mitral valve and septum (**arrows**). The left ventricular outflow tract dimension at end-diastole is greatly reduced (**vertical broken line**) and considerable mitral anulus calcium (MAC) is located posterior to the mitral valve between the posterior leaflet and posterobasal free wall (PW) endocardium. **C**, Morphologic features of the left ventricle are similar to those shown in **B**, although mitral systolic anterior motion (**arrows**) does not result in actual mitral-septal contact; left ventricular outflow tract dimension at end-diastole is greatly reduced (vertical broken line). **D**, Systolic contact between the mitral valve and septum (**arrows**) begins earlier and is more prolonged than in **B**. RV = right ventricle. Calibration dots are 1 cm apart.

wall endocardium (Fig. 1 to 5). These submitral deposits appeared to contribute to the anterior position of the mitral valve within the left ventricular cavity and, therefore, to narrowing of the outflow tract. Of the 52 patients, 32 also showed evidence of calcium in the anterior annular region at or near the junction of the anterior mitral leaflet and the posterior aortic wall. Calcification was judged to be severe in 39 patients and mild to moderate in the other 13. Most (43 of 52) patients also had bright echoes, which probably represented calcium, at other sites (that is, aortic valve [24 patients], aortic root [19 patients] and papillary muscle or chordal apparatus [22 patients]).

Hemodynamics. Thirty-nine of the 52 patients had complete cardiac catheterization studies performed within 5 years of the echocardiographic study (24 studies were performed within 1 year). Thirty-two of these 39 patients had a left ventricular outflow tract gradient ≥30 mm Hg under basal conditions (range 30 to 180, average 92). The other seven patients had no or a small gradient (<30 mm Hg) under basal conditions, but a larger gradient (60 to 120 mm Hg, average 93) was elicited by provocative maneuvers (that is, Valsalva maneuver, amyl nitrite inhalation or isoproterenol infusion). Thirteen patients either did not undergo cardiac catheterization or had incomplete catheterization studies in which no provocative maneuvers were performed. In these patients, the outflow tract gradient under basal conditions was either assessed at catheterization or was estimated by echocardiography (23); the gradient was ≥30 mm Hg in seven patients and 0 or <30 mm Hg in the other six.

Therefore, on the basis of available hemodynamic and echocardiographic data, 46 study patients showed basal or provocable obstruction to left ventricular outflow. The remaining six patients did not demonstrate evidence of basal outflow obstruction at cardiac catheterization or by echocardiography, but did not undergo provocative maneuvers. However, the moderate degree of systolic anterior motion of the mitral valve present under basal conditions in these patients was consistent with the propensity to develop a left ventricular outflow tract gradient with provocation (21,22). Of the 45 patients with left ventriculography performed at

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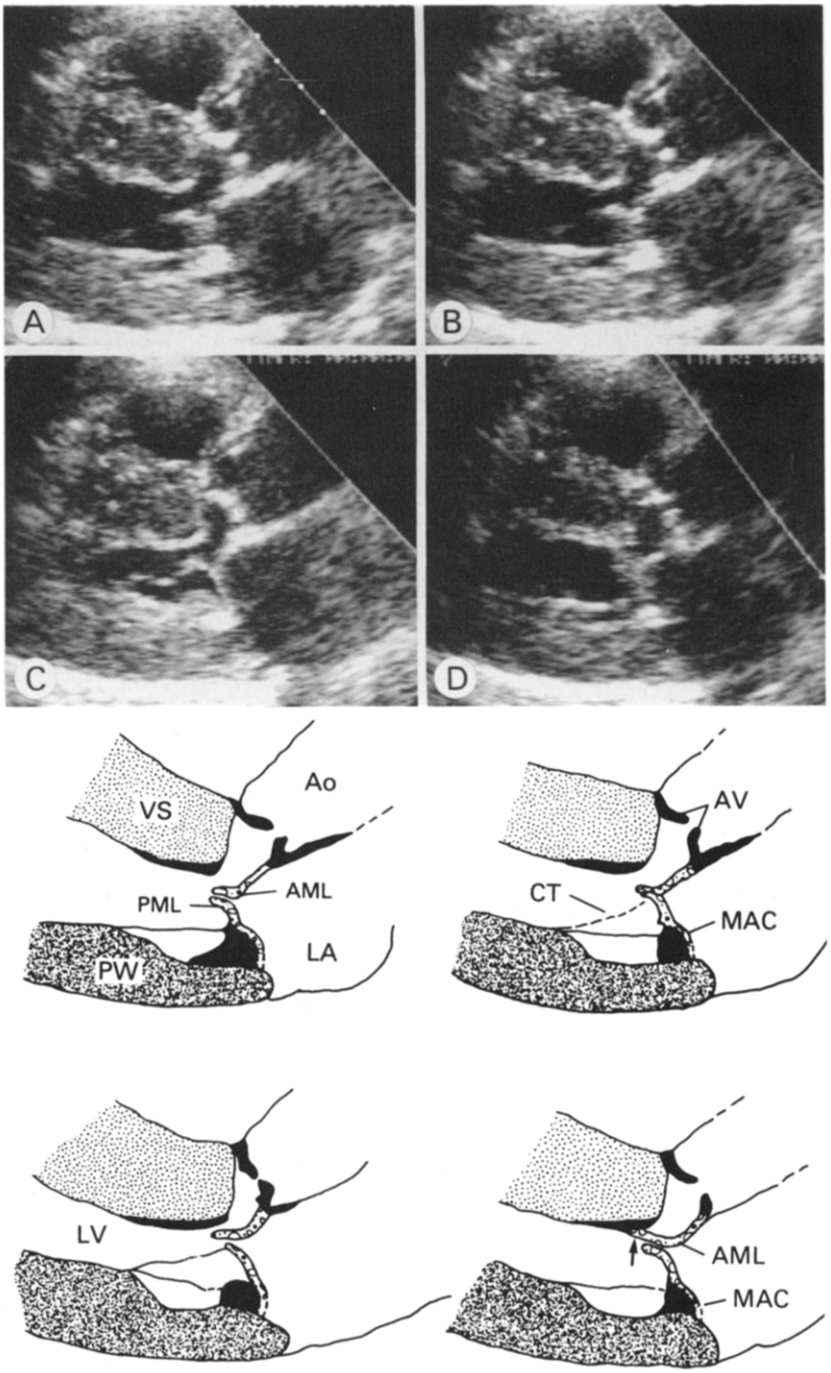

Figure 2. Top, Sequential two-dimensional echocardiographic stop-frame images obtained during the same cardiac cycle in the parasternal long-axis view from an 83 year old woman with obstructive hypertrophic cardiomyopathy. Each stop-frame is accompanied by a schematic illustration (**bottom**). **A**, Image at end-diastole. **B, C** and **D**, Images in systole. **A**, Anterior and posterior mitral leaflets (AML and PML) coapt at their distal margins. Mitral annular calcification (MAC) located behind the posterior leaflet appears to contribute to the anterior position of the mitral valve within the left ventricular (LV) cavity. The aortic valve (AV) is also calcified, but there was no clinical evidence of hemodynamically significant stenosis. **B** and **C**, Anterior and posterior leaflets remain relatively flat during early systole as they approach the ventricular septum (VS). **D**, Posterior motion of the septum facilitates contact with the distal portion of the mitral leaflet during midsystole. Ao = aorta; CT = chordae tendineae; LA = left atrium; PW = posterior wall. Calibration dots are 1 cm apart.

cardiac catheterization, mitral regurgitation was judged to be absent in 23, mild to moderate in 20 and marked in 2; no patient had a transmitral gradient.

Electrocardiographic findings. A variety of electrocardiographic (ECG) abnormalities were present in the study patients, but no particular pattern was characteristic of the group. The most common abnormalities were left ventricular hypertrophy (Romhilt-Estes score ≥5 points [24], 38 patients), ST segment and T wave alterations (42 patients) and left atrial enlargement (22 patients). In addition, a variety of conduction abnormalities were evident in 19 (37%) of the 52 patients. These included first degree atrioventricular block in eight patients, left bundle branch block in six, right bundle branch block in four, nonspecific intraventricular conduction delay in two, left anterior fascicular block in three and left posterior fascicular block in one.

Clinical findings and natural history. Fifty of the 52 patients had experienced marked symptoms and functional limitation (New York Heart Association functional class III or IV) at some time during their clinical course; the remain-

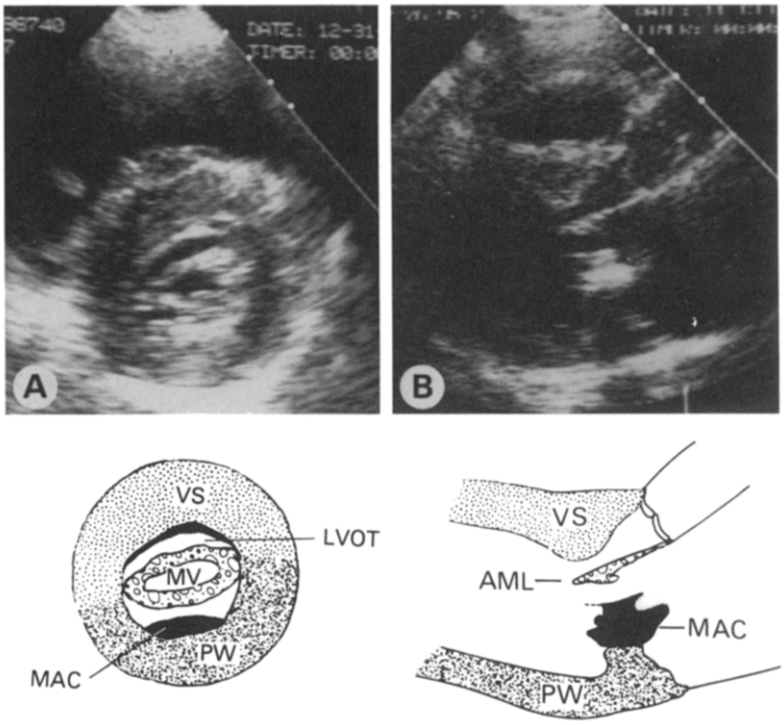

Figure 3. A. Two-dimensional stop-frame image (with schematic diagram below) obtained in the short-axis view at the mitral valve level in late diastole from the same patient shown in Figure 2. The left ventricular outflow tract (LVOT) is markedly narrowed and has a slit-like shape. In subsequent systolic frames (not shown here), the outflow tract appeared to be completely obliterated. **B.** Stop-frame image (with schematic diagram below) obtained in diastole in the parasternal long-axis view from a 74 year old woman with obstructive hypertrophic cardiomyopathy. Ventricular septal (VS) thickness is only modestly increased (21 mm), but a large accumulation of calcium evident in the region of the mitral anulus (MAC) appears to contribute to the anterior position of the mitral valve (MV) within the left ventricular cavity and the reduced size of the outflow tract. In this particular stop-frame image, the posterior mitral leaflet is not visualized. Abbreviations and calibration dots as in Figure 2.

ing 2 patients had only mild symptoms (class II). In each of these 50 patients, severe symptoms were not present earlier in life, but became evident only relatively late in life (that is, after age 55 years [range 56 to 81, mean 66]; 32 developed substantial symptoms relatively rapidly (over a period of several months) after having been asymptomatic or only minimally symptomatic for their entire life. In the other 18 patients, functional limitation developed more gradually over a period of 2 to 15 years.

The most common symptoms were exertional dyspnea and fatigue (48 patients), chest pain (33 patients), orthopnea or paroxysmal nocturnal dyspnea (22 patients) and syncope or near syncope (12 patients). Atrial fibrillation occurred in 22 patients (paroxysmal in 16 and chronic in 6) and was associated with the onset of severe symptoms and a marked change in clinical course in 8, the progression of pre-existing symptoms in 5 and no change in the other nine patients.

The clinical course could be evaluated for at least 1 year after the initial visit to the National Institutes of Health in 49 of the 52 patients; the follow-up period ranged up to 14 years (mean 3.4). Of these 49 patients, 47 were initially treated with drugs. Only 12 of these patients showed clinical improvement by at least one functional class; their therapy included verapamil (8 patients), propranolol (1 patient), the combination of calcium channel and beta-adrenergic blocking drugs (2 patients) and disopyramide in combination with verapamil (1 patient). The other 35 patients experienced no sustained improvement from drug therapy consisting primarily of a beta-adrenergic blocker or verapamil; 2 of these patients died of intractable congestive heart failure 2 and 7 years, respectively, after their initial evaluation.

Surgery. Eighteen of the severely symptomatic patients who did not improve with medical therapy and had obstruction to left ventricular outflow (≥50 mm Hg subaortic gradient at rest or with provocation, or both) underwent operation: 12 of these patients had ventricular septal myotomy-myectomy (4 in combination with coronary artery bypass surgery) and 6 had mitral valve replacement. The basal outflow gradient was measured postoperatively at catheterization in 11 of the 18 patients and was substantially reduced or obliterated (to 0 to 28 mm Hg) in 10.

Two patients died as a consequence of operation, one because of a ventricular septal defect created by myotomy-myectomy, and one from mediastinitis. Of the 16 patients who survived operation, 2 did not show symptomatic improvement. The other 14 showed improvement by at least one functional class during the follow-up period, but 2 of these 14 patients subsequently died 8 and 16 months after operation (suddenly and of congestive heart failure, respectively).

Discussion

Hypertrophic cardiomyopathy is a primary cardiac disease with a diverse morphologic and clinical spectrum and has been reported (1–16,25) in patients in all periods of life from infancy to old age. Typically, patients referred to centers for evaluation (usually because of symptoms) have

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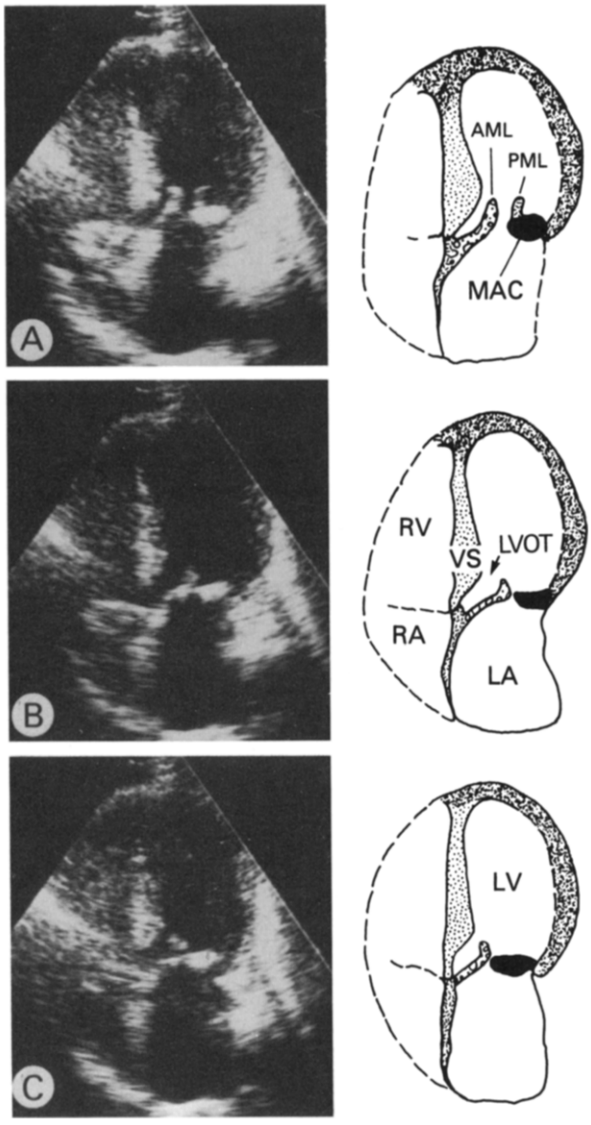

Figure 4. Sequential stop-frame images (with schematic diagrams) obtained from a 69 year old woman with obstructive hypertrophic cardiomyopathy in a rotated apical four chamber view to permit visualization of the markedly narrowed left ventricular outflow tract (LVOT). **A**, During diastole. **B** and **C**, During the subsequent systole. **A**, Relatively short anterior and posterior mitral valve leaflets (AML and PML) approach each other. **B**, Leaflets coapt near their distal margins; the posterior leaflet is obscured by the marked accumulation of calcium in the region of the mitral anulus (MAC). **C**, The ventricular septum has moved toward the mitral valve, the anterior leaflet bends slightly and the septum and valve closely approach each other. In subsequent systolic frames (not shown here), the anterior leaflet made contact with the septum. RA = right atrium; RV = right ventricle; other abbreviations and calibration dots as in Figure 2.

been young or middle-aged (2–6,9,11). However, over the past few years, an increasing number of elderly patients (>60 years) with many of the morphologic and clinical features of hypertrophic cardiomyopathy have been identified (12–16). The echocardiographic features and clinical course demonstrated by many of these patients appeared to us to differ in certain important respects from those of many other patients with more "typical" expressions of hypertrophic cardiomyopathy.

Left ventricular morphology and outflow dynamics in elderly patients. Our elderly study patients with hypertrophic cardiomyopathy had relatively small hearts with only a modest increase in left ventricular wall thickness; most had a septal thickness <22 mm. Although wall thickening was not particularly marked, left ventricular morphology was severely distorted, as evidenced by the greatly reduced end-diastolic cross-sectional and transverse dimensions of the outflow tract and exaggerated anterior displacement of the mitral valve within the left ventricular cavity; indeed, in some patients, the mitral valve was situated <15 mm from the ventricular septum at end-diastole. Deposits of calcium in the mitral annular region (26–31), often sizable and usually posterior to the valve (between the posterior mitral leaflet and free wall endocardium), seemed to contribute to the severe anterior displacement of the mitral valve. As a consequence of the high velocity of blood flow through this narrowed outflow tract, the mitral valve leaflets are pulled forward toward the ventricular septum during systole (that is, Venturi phenomenon) (9,32,33). This mitral systolic anterior motion and contact between the mitral valve and septum were apparently responsible for the dynamic left ventricular outflow gradient recorded either under basal conditions or with provocative maneuvers in the catheterization laboratory (9,11,21–23,33–37).

The mechanism by which systolic contact between the mitral valve and septum and dynamic subaortic obstruction occurred in the majority of our study patients appeared to differ from that more typically observed in many other patients with obstructive hypertrophic cardiomyopathy (Fig. 5) (9,21–23,34,38–40). For example, in many younger patients with this disease, systolic outflow tract narrowing occurs predominantly as a consequence of mitral valve motion toward the ventricular septum (9,21–23,34,38–40). The mitral valve exhibits abrupt and substantial excursion anteriorly from its end-diastolic position as it approaches the septum; contact with the septum is usually made by the distal portion of the mitral valve apparatus (most commonly by the anterior leaflet), which bends sharply near its tip during systole. This bend is often so acute that the leaflet assumes an "L" configuration, with as much as a 90° angle forming between the proximal and distal portions of the leaflets. In these patients, posterior excursion of the ventricular septum usually contributes little to the overall narrowing of the left ventricular outflow tract during systole. In contrast, in most of our elderly study patients, systolic contact between the mitral valve and the ventricular septum resulted from more equal relative contributions of anterior mitral valve excursion toward the septum and posterior

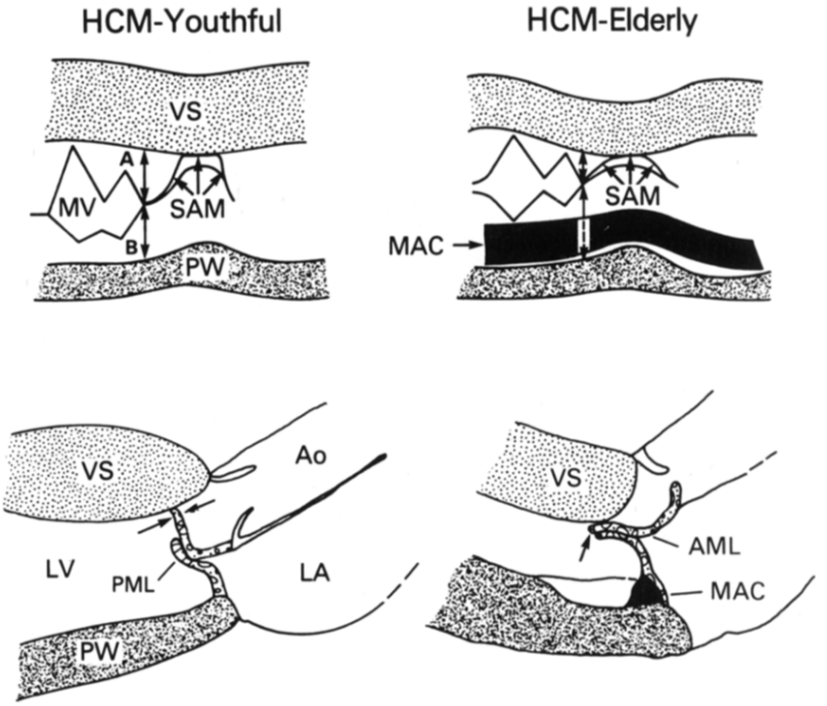

Figure 5. Schematic diagrams comparing the mechanisms by which systolic anterior motion (SAM) of the mitral valve (and subaortic obstruction) occur in youthful (**left**) and elderly (**right**) study patients with hypertrophic cardiomyopathy (HCM). Diagrammatic representations are of M-mode echocardiograms at the mitral valve level (**above**) and two-dimensional echocardiograms in the parasternal long-axis view (**below**). **Upper left**, *Youthful patient with hypertrophic cardiomyopathy*. Typically, at end-diastole, the distance (A) between the mitral valve (MV) and the ventricular septum (VS) and the distance (B) between the valve and posterior wall (PW) are approximately equal; during systole, the mitral valve shows abrupt substantial excursion from its end-diastolic position and makes contact with the ventricular septum. Posterior septal motion usually contributes minimally to this contact. **Lower left**, Same patient as in **upper left**. In mid-systole, both anterior and posterior mitral leaflets (AML and PML) have moved anteriorly toward the ventricular septum (VS); the anterior leaflet bends acutely as its distal margin makes contact with the septum (**arrows**). **Upper right**, *Elderly patient with hypertrophic cardiomyopathy*. At end-diastole, the distance between the mitral valve and septum is appreciably less than the distance between the mitral valve and posterior wall, indicating greater anterior displacement of the valve within the left ventricular cavity than that shown for the youthful patient with hypertrophic cardiomyopathy. Mitral anulus calcification (MAC) is present behind the posterior leaflet. During mid-systole, contact between the mitral valve and septum is facilitated by both anterior mitral valve motion and posterior excursion of the septum. **Lower right**, Same patient as in **upper right**. During systole, both anterior and posterior mitral leaflets have moved toward the septum (VS). The anterior leaflet maintains a flattened configuration with little bend, and the body as well as the distal margins of the leaflet make contact with the septum (**arrow**); posterior motion of the septum toward the mitral valve in systole usually contributes substantially to creating this contact. Abbreviations as in Figure 2.

excursion of the ventricular septum toward the mitral valve. In mid-systole, the mitral valve leaflets usually showed little or no bend and assumed a flattened appearance as they approached the septum with limited systolic excursion; consequently, contact between the mitral valve and septum appeared to be greatly facilitated by posterior motion of the septum toward the valve.

Clinical course in elderly patients. In addition, the clinical course of the elderly study patients with hypertrophic cardiomyopathy was notable. In these patients, severe symptoms were not present early in life, but developed after age 55 years (average 66), at which time marked and progressive functional limitation usually ensued. This prolonged period of symptomatic latency is perhaps surprising in a disease that is generally expressed morphologically by 20 years of age (10,41) and in which symptoms usually occur by age 40 to 50 years (2–5,9,11,25). Although the reason for this particular clinical evolution is not entirely clear, it is reasonable to speculate that certain dynamic alterations in left ventricular morphology may play an important role in the changing clinical picture. For example, the submitral calcification (between posterior mitral leaflet and posterobasal free wall endocardium) evident in our elderly study patients undoubtedly developed late in life (26,27,30,31). With time, this accumulation of calcium posterior to the mitral valve may have caused further anterior displacement of the valve apparatus within the left ventricular cavity (29), more marked narrowing of an already developmentally small left ventricular outflow tract and positioning of the mitral valve leaflets closer to the septum in both diastole and systole.

Such an alteration in left ventricular anatomy is likely to create the circumstances in which systolic mitral-septal contact and subaortic obstruction occur (9,11,21–23,32,33,35–37). In this way, it is possible that some patients with pre-existing left ventricular wall thickening, but without outflow tract obstruction early in life, might develop obstruction later and consequently first incur important symptoms at an advanced age. However, longitudinal clinical and echocardiographic studies will be necessary to substantiate this hypothesis. Furthermore, we do not wish to imply that the prevalence of severe symptoms demonstrated in our study patients is unique among elderly patients with hypertrophic cardiomyopathy. Indeed, because most patients >60 years of age referred to our institution are symptomatic, the clinical course demonstrated may have been importantly influenced by patterns of patient referral and selection (13,14,16,42).

Relation of age and other factors to disease spectrum of hypertrophic cardiomyopathy in our study group. We cannot be absolutely certain whether all of our patients, who demonstrate many morphologic features of hypertrophic cardiomyopathy, truly constitute part of the clinical spectrum of this disease or, alternatively, whether some represent a similar but etiologically distinct clinical entity. For example, we were not able to perform systematic echocardiographic studies in the parents and other relatives of these patients to assess genetic transmission (43). Also, previous investigators (44–46) have proposed that systemic hypertension might serve as a stimulus for the development of hypertrophic cardiomyopathy. However, there appears to be little evidence to support a consistent etiologic role for hypertension in the present study group. First, only about one-third of the patients had evidence of hypertension, and blood pressure elevations were generally mild. Second, the left ventricular wall thickening that occurs in patients with systemic hypertension is usually symmetrically distributed (47,48), whereas all of our study patients demonstrated an asymmetric pattern of hypertrophy, characteristic of patients with hypertrophic cardiomyopathy (18). Finally, left ventricular outflow tract obstruction due to systolic anterior motion of the mitral valve, which was present in our study patients, is exceedingly uncommon in systemic hypertension (49,50).

It should be emphasized that our patients represent a selected subgroup of elderly patients with hypertrophic cardiomyopathy and are not representative of all patients >60 years of age with this disease. Indeed, the 52 patients who met the selection criteria for the present study constitute only 25% of all patients in this age group who had been evaluated at our institution over a 5 year period. In addition, the marked predominance of women in our study group appears, in large measure, to be the consequence of the morphologic selection criteria used in this investigation (that is, all patients were required to have a greatly reduced left ventricular outflow tract dimension and mitral anulus calcification). Because annular calcium is more common in women (27,28,30,31) and left ventricular dimensions are related to body surface area (51) (and, therefore, are generally smaller in women), women would more likely have been selected for the present study group. It is also possible that women with hypertrophic cardiomyopathy survive to an advanced age more frequently than do men with this disease, and consequently would have been more likely to become part of our study.

Conclusions. We have described a group of elderly patients with obstructive hypertrophic cardiomyopathy who constitute an important part of the broad clinicopathologic spectrum of this disease. Their left ventricular morphology is characterized by a particularly small left ventricular outflow tract, marked anterior displacement of the mitral valve and submitral (annular) calcification; dynamic subaortic obstruction was due to systolic contact between the mitral valve and septum, which was effected by both anterior motion of the mitral valve and posterior motion of the septum. The clinical course was characterized in the majority of patients by the onset of severe and progressive symptoms late in life and poor response to medical therapy. However, many of the patients (despite their advanced age) improved symptomatically after operation.

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