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The 50-Year History, Controversy, and Clinical Implications of Left Ventricular Outflow Tract Obstruction in Hypertrophic Cardiomyopathy

From Idiopathic Hypertrophic Subaortic Stenosis to Hypertrophic Cardiomyopathy

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Dynamic obstruction to left ventricular (LV) outflow was recognized from the earliest (50 years ago) clinical descriptions of hypertrophic cardiomyopathy (HCM) and has proved to be a complex phenomenon unique in many respects, as well as arguably the most visible and well-known pathophysiologic component of this heterogeneous disease. Over the past 5 decades, the clinical significance attributable to dynamic LV outflow tract gradients in HCM has triggered a periodic and instructive debate. Nevertheless, only recently has evidence emerged from observational analyses in large patient cohorts that unequivocally supports subaortic pressure gradients (and obstruction) both as true impedance to LV outflow and independent determinants of disabling exertional symptoms and cardiovascular mortality. Furthermore, abolition of subaortic gradients by surgical myectomy (or percutaneous alcohol septal ablation) results in profound and consistent symptomatic benefit and restoration of quality of life, with myectomy providing a long-term survival similar to that observed in the general population. These findings resolve the long-festering controversy over the existence of obstruction in HCM and whether outflow gradients are clinically important elements of this complex disease. These data also underscore the important principle, particularly relevant to clinical practice, that heart failure due to LV outflow obstruction in HCM is mechanically reversible and amenable to invasive septal reduction therapy. Finally, the recent observation that the vast majority of patients with HCM have the propensity to develop outflow obstruction (either at rest or with exercise) underscores a return to the characterization of HCM in 1960 as a predominantly obstructive disease. (J Am Coll Cardiol 2009;54:191–200) © 2009 by the American College of Cardiology Foundation

It has now been more than 50 years since the first modern descriptions of hypertrophic cardiomyopathy (HCM) by Brock (1), in 1957, based on hemodynamics at cardiac catheterization or operation, and by Teare (2), in 1958, from the autopsy laboratory. Over that considerable period of time, literally thousands of reports have been published describing various elements of HCM (3–16). Consequently, we now recognize HCM to be the most common familial heart disease characterized by substantial heterogeneity with respect to presentation, phenotypic expression, clinical course, and genetic substrate, as well as the management strategies applicable to this broad clinical spectrum.

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Following initial reports from Brock (1) and others (3,17–19) describing intraventricular systolic pressure gradients regarded as examples of "functional stenosis of the left ventricle," dynamic obstruction to left ventricular (LV) outflow rapidly achieved distinction as the most visible feature of HCM, dominating the initial comprehensive description of the disease (4) and other early reports. However, outflow pressure gradients have also been the source of periodic and often intense controversy regarding their clinical and pathophysiologic significance (20–23). Indeed, this uncertainty surrounding obstruction is typical of the considerable confusion that in many other ways has also influenced the understanding of this complex disease within the cardiovascular community (5). Therefore, having recently celebrated the 50th (golden) anniversary of HCM, it seems particularly appropriate to revisit and focus attention on the evolution in our understanding of LV outflow obstruction, which has profoundly affected clinical practice.

Abbreviations and Acronyms

HCM = hypertrophic cardiomyopathy

LV = left ventricular

SAM = systolic anterior motion

Historical Context

Virtually from initial recognition in the late 1950s, dynamic obstruction to LV outflow has been regarded as an integral component of HCM (Fig. 1). In fact, in the early pre-echocardiographic era (1960 to 1969), an outflow gradient was a virtual prerequisite for the diagnosis of HCM, either by physical examination (e.g., auscultation of the characteristic systolic murmur) or by invasive measurement of a peak systolic pressure gradient between LV cavity and proximal outflow tract (4) (Fig. 2). Indeed, the nonobstructive form of HCM, although recognized in the early 1960s (24,25), received little attention until the emergence of M-mode echocardiography in the early 1970s (26–31).

Adding to the mystique surrounding obstruction in HCM has been its dynamic nature (first described in 1962) (32), in which pressure gradients can vary considerably with a variety of pharmacologic and physiologic provocations that reduce peripheral arterial pressure or ventricular volume, or enhance myocardial contractility, and may change even after heavy meals or alcohol intake or spontaneously on a day-to-day or hour-to-hour basis (4,32–34). Almost from the inception, it was recognized that dynamic outflow gradients could be provoked by physiologic exercise (4,35) or a variety of nonphysiologic maneuvers including sympathomimetic agents, such as infused isoproterenol or dobutamine, or by introducing premature ventricular beats, amyl nitrite inhalation or nitroglycerin, as well as the Valsalva maneuver (4,36).

With the possible exception of disopyramide (37), drug therapy does not reliably mitigate intraventricular pressure gradients (5) under basal (resting) conditions although beta-blockade is known to blunt gradients provoked with exercise (4). Spontaneous and permanent loss of outflow obstruction appears to be largely confined to those circumstances in which substantial LV remodeling occurs, such as with progression to the end-stage phase when systolic dysfunction appears (38,39). Conversion from the nonobstructive to obstructive state may be evident during adolescence, with the development of the HCM phenotype, at the time of accelerated growth and maturation (40).

Initially, several names were promoted to describe this disease entity, each of which is dependent on the presence of obstruction: idiopathic hypertrophic subaortic stenosis in the U.S., muscular subaortic stenosis in Canada, and hypertrophic obstructive cardiomyopathy in the United Kingdom (41). These terms persist occasionally, but rarely appear in the current literature. Indeed, hypertrophic cardiomyopathy predominates as the formal name for this disease (41), because this terminology is inclusive allowing for both the obstructive and nonobstructive forms of the disease.

Controversy and Dilemma

Although dynamic LV outflow gradients have been widely recognized as clinical markers of HCM since the early 1960s, considerable controversy rapidly developed (20,23,42–46) concerning the clinical implications of intraventricular pressure differences that were identified with increasing frequency in the catheterization laboratory and believed to result from excessive muscular constriction of the proximal outflow tract (18). Indeed, in an early description of surgical myotomy and myectomy in the treatment of HCM, Morrow et al. (47) stated that "when the finger is introduced into the left ventricle, the muscle mass is usually felt to be hemispherical. . .forceful contraction of the outflow tract upon the examining finger is evident during systole." Therefore, even though recognition of outflow gradients was ultimately the impetus for the septal myectomy operation, paradoxically, the surgical strategy of muscular resection was originally devised to interrupt the outflow tract "contraction ring" before the recognition 7 to 10 years later that systolic

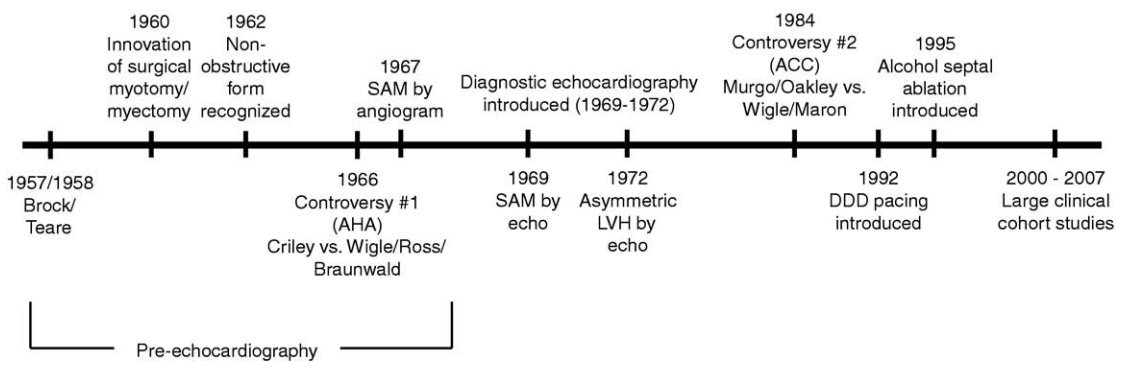

Figure 1 Timeline

Timeline summarizes major events that comprise the history of left ventricular outflow tract obstruction in hypertrophic cardiomyopathy. ACC = American College of Cardiology; AHA = American Heart Association; DDD = dual-chamber; echo = echocardiography; LVH = left ventricular hypertrophy; SAM = systolic anterior motion.

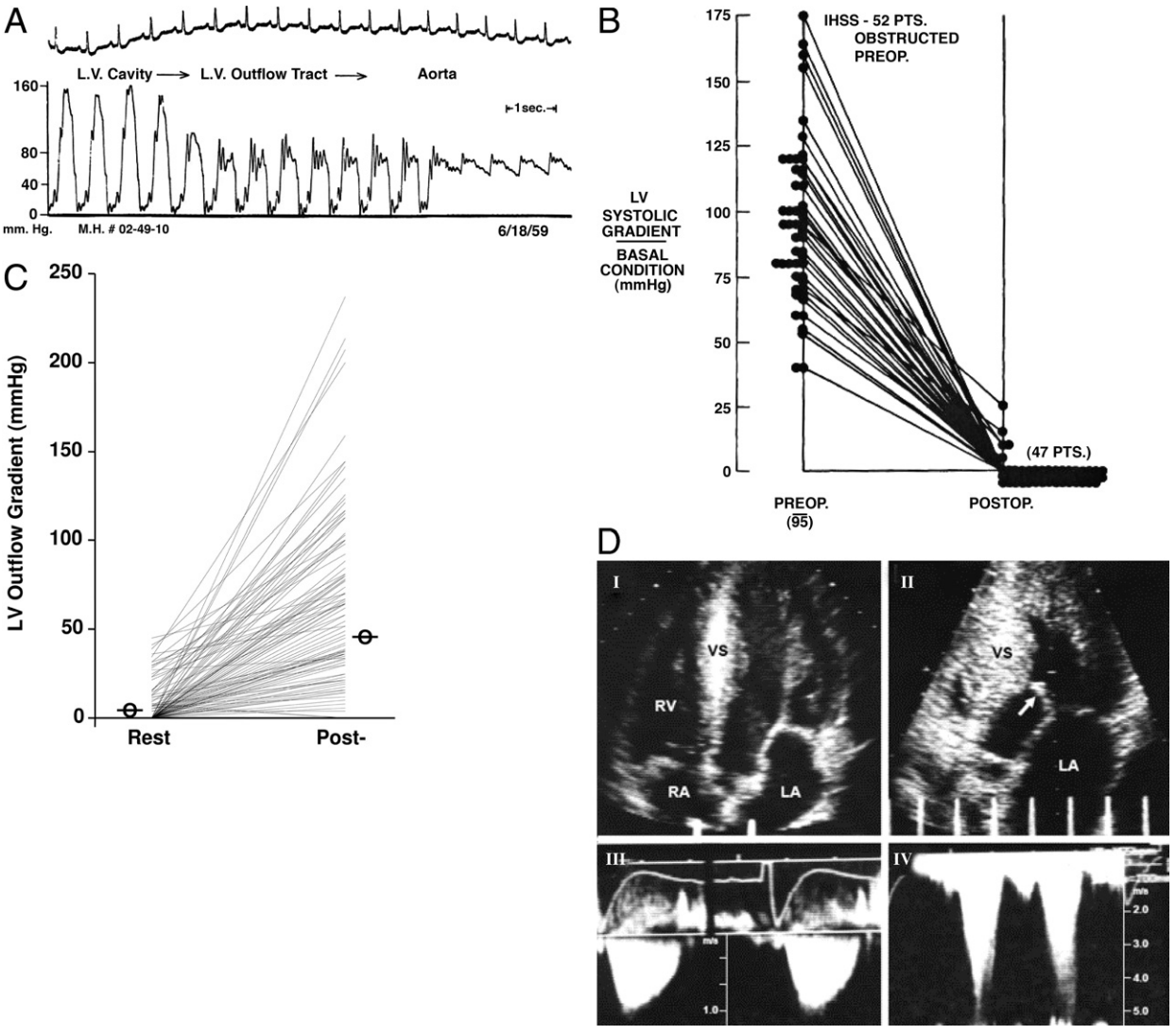

Figure 2 **Identification of LV Outflow Tract Gradients in HCM**

(A) Cardiac catheterization pull-back tracing from left ventricular (LV) cavity to outflow tract to aorta, recording intraventricular pressure gradient. Reprinted, with permission, from Braunwald et al. (4). **(B)** Data from early National Institutes of Health experience with surgical myectomy showing virtual obliteration of resting LV outflow tract gradients post-operatively. **(C)** Provocation of outflow gradients following physiologic exercise in a consecutive group of 201 hypertrophic cardiomyopathy (HCM) patients without marked obstruction at rest. Each patient is depicted by a line connecting two gradient measurements. ⊖ = mean. Reprinted, with permission, from Maron et al. (35). **(D)** Development of marked obstruction provoked by exercise, and at rest. Apical 5-chamber view showing mitral valve at end-diastole (SAM was absent in systole) **(I)** with normal Doppler velocity in the outflow tract **(III)**. After exercise, demonstrating typical SAM-septal contact **(II; arrow)** with corresponding velocity of 5 m/s (gradient: 100 mm Hg) **(IV)**. Reprinted, with permission, from Maron et al. (35). IHSS = idiopathic hypertrophic subaortic stenosis; LA = left atrium; POSTOP = after operation; PREOP = before operation; PTS = patients; RA = right atrium; RV = right ventricle; VS = ventricular septum; other abbreviations as in Figure 1.

anterior motion of the mitral valve was actually the mechanism of obstruction (29–31,48).

Even the very existence of LV obstruction in this new disease was seriously questioned (20,21) and became a major and contentious controversy in cardiovascular medicine at the 1966 American Heart Association meeting in New York that devoted a full 90-min session to this topic as the *only* scheduled program event at that time, attracting virtually all meeting attendees (Fig. 1). Michael Criley (20) of Johns Hopkins Hospital, the first skeptic to question the legitimacy of obstruction, argued that the outflow gradient in HCM did not represent true mechanical impedance, but rather was the consequence of premature, excessively rapid ejection from a vigorously contracting LV ("pressure gradients without obstruction"). This position was summarized as follows: excessively rapid ejection with systolic obliteration of portions of the LV cavity itself provides a sufficient explanation for pressure gradients and is compatible with all available hemodynamic and angiographic observations, while belief in obstruction would ultimately impede a full understanding of HCM (21).

Alternatively, others asserted that the pressure gradients measured in the laboratory could also represent artifacts produced when the catheter becomes physically enfolded and entrapped within recesses of hypertrophied LV trabeculations during vigorous isometric contraction (in the presence of distal cavity obliteration), recording intramural rather than intracavity systolic pressure.

Challenges to the presence of obstruction in HCM cast doubt on the prudence associated with early surgical attempts at relieving obstruction (49–51). However, Ross and Braunwald (then of National Institutes of Health) (42) and Wigle (43,45), strongly opposed this view, defending the legitimacy of the outflow gradient with several avenues of evidence: the characteristically prolonged LV ejection time in the presence of gradients (45), and demonstration that a transseptal catheter passed through the mitral orifice into the nonobliterated LV inflow area recorded systolic pressures identical to those in the distal chamber. The latter observation was critical because it demonstrated that elevated systolic pressures were not limited to empty regions of the LV and, in the process, refuted the Criley hypothesis that gradients were only a consequence of cavity obliteration (20,21).

Although a general consensus began to emerge that true obstruction occurred in patients with HCM and operative intervention (with ventricular septal myectomy or myotomy) was a valid strategy by which severe heart failure-related symptoms could be relieved by abolition of the outflow gradient (4,46,47,49–51), investigators at Hammersmith Hospital (London) continued to be highly vocal opponents of obstruction and critics of myectomy surgery until only very recently, persisting in the view that outflow gradients were simply incidental to the clinical disease process (9,31,33).

Contributions of Echocardiography

Noninvasive echocardiographic imaging was introduced to HCM from 1969 to 1973 demonstrating the characteristic asymmetric pattern of LV hypertrophy (26–28), systolic anterior motion (SAM) of the mitral valve as the mechanism by which obstruction occurs (29–31,52,53) (although first identified with angiography [42,48,54]), as well as underscoring that the nonobstructive form is a substantial part of the HCM disease spectrum. Systolic anterior motion and mitral-septal contact, usually produced by the leading edge of anterior mitral leaflet (29–31,52,53,55) (but in some patients by the posterior leaflet) (56), is responsible for obstruction to LV outflow in 95% of cases (55). Midcavity obstruction may also occur in the absence of SAM (57,58) due to muscular apposition or anomalous insertion of the anterolateral papillary muscle directly into anterior mitral leaflet (59). In virtually all patients, SAM redirects a fraction of LV stroke volume into the left atrium, producing secondary (and posteriorly directed) mitral regurgitation, the magnitude of which is usually related to the severity of obstruction (46,54,60). Determinants of SAM and outflow obstruction include the vigorous LV ejection, as well as the unusual chamber geometry and morphology (40,61,62): 1) reduced outflow tract cross-sectional area (to which the hypertrophied septum contributes); 2) exaggerated anterior displacement of the mitral valve apparatus and papillary muscles; and 3) primary enlargement and elongation of mitral leaflets.

Such insights from echocardiographic imaging raised clinical awareness and increased the number of patients diagnosed with obstructive HCM, resulting in greater numbers of candidates for surgical septal myectomy. Prosthetic mitral valve replacement has been promoted as a primary surgical strategy to relieve obstruction and symptoms (63). However, enthusiasm for this strategy was short-lived and ultimately abandoned due to the potential long-term post-operative complications of prosthetic valves (64). Mitral valve replacement has a role only in those exceedingly rare patients in whom the anterior basal septum is not sufficiently thickened to permit an effective and safe muscular resection (65).

Skepticism and Controversy Returns

Based on the 1980 study of Murgo et al. (22), controversy regarding the significance of LV outflow gradients re-emerged after almost 20 years, predicated largely on the Criley premise that early LV ejection and cavity emptying and powerful contraction were responsible for outflow gradients, in the process triggering old doubts about the legitimacy of surgical intervention in this disease. This hemodynamic investigation, performed in a small number of HCM patients, used novel catheter-mounted electromagnetic flow meters, as well as high-fidelity catheters to record LV and aortic pressures. Reporting mid-systolic deceleration of forward flow in both patients *with* and *without* subaortic gradients (but not in normal controls), Murgo et al. (22) concluded that LV outflow gradients in HCM (and presumably mitral valve SAM) were incidental to the disease process. However, these data were soon contradicted by studies assessing ascending aorta Doppler instantaneous flow velocity (66).

Reignited by these findings, the old obstruction debate was publicly resurrected in a panel discussion at the 1984 American College of Cardiology meeting in Dallas dedicated to the question: Is there obstruction in HCM? The debate pitted Murgo and Oakley against Wigle and Maron (Fig. 1). Although much of the session was dominated by a detailed discussion of flow dynamics and ventricular mechanics, the Murgo hypothesis ultimately failed to answer the fundamental *clinical* question implicit in the debate: if subaortic gradients are pathophysiologically irrelevant features of HCM, how can that assertion be consistent with the extensive and favorable operative experience from surgical centers throughout the world reporting marked symptomatic benefit following relief of the intraventricular pres-

sure gradient (by myectomy)? Furthermore, in view of compelling surgical data, would it not be unethical to deny an operation known to be efficacious to severely symptomatic drug-refractory patients, based solely on the argument of whether it is proper to equate "gradient" with "obstruction"? It was concluded that increased intraventricular systolic pressure is the most important pathophysiologic component of the complex ejection dynamics that occur in HCM.

Another popular (but flawed) anti-obstruction position, which also suppressed the myectomy option and may have deprived some patients of potentially beneficial treatment, noted that patients with the obstructive or nonobstructive forms could both experience progressive heart failure symptoms and concluded from this observation that the gradient was not a clinically important feature of the disease (9,67). However, this critique ignored the important pathophysiologic principle that outflow obstruction is just 1 of the possible determinants of heart failure symptoms in HCM, and *other* mechanisms such as impaired diastolic filling and myocardial ischemia can be responsible for exertional limitation in the absence of obstruction (5,68,69).

The Dual-Chamber Pacing Controversy

Debate over outflow obstruction in HCM continued in the early 1990s in the context of dual-chamber (DDD) pacing to relieve subaortic gradients and severe heart failure-related symptoms refractory to maximal medical management (70–76). Observational, uncontrolled studies heavily promoted pacing as a strategy to alter the natural course of the disease (72). Several reports described dramatic reduction in both gradient (often to 0) and functional disability, and it was suggested that the mechanism by which pacing reduced subaortic obstruction was likely asynchronous ventricular septal activation.

However, several randomized double-blind cross-over studies showed that the perceived symptomatic benefit from pacing largely represented a placebo effect (74–76), and reduction in gradient was both inconsistent and generally only modest. In 1 study (75), elderly patients appeared to derive true short-term benefit from dual-chamber pacing, which remains a therapeutic option for some patients in this subgroup on a case-by-case basis, or selectively in severely symptomatic patients who are not candidates for surgical septal myectomy. The pacing era and the controversy it generated, nevertheless, once again focused substantial attention on the clinical significance of obstruction in HCM, its pathophysiologic role in the genesis of symptoms, and the importance of reducing outflow gradients in severely symptomatic patients.

Clinical Evidence Resolves the Controversy

Residual ambivalence concerning the clinical and hemodynamic significance of obstruction and the importance of surgical myectomy (or more recently, selective alcohol septal ablation) as treatment strategies (77,78) has been resolved by a series of clinical investigations in the last several years.

Echocardiography Doppler studies. Several noninvasive imaging studies (79–88) have presented overwhelming evidence for true obstruction and significant LV pressure overload in HCM (Fig. 3). 1) The LV is not devoid of blood in mid-to-late systole after an early rapid systolic ejection phase, but conversely a large (but highly variable) proportion of stroke volume (about 50%) remains to be ejected when the gradient is present and is mechanically impeded in its egress by SAM-septal contact; the earlier and more prolonged the septal contact, the greater is the obstructed flow. 2) Systolic anterior motion is a primary event, timed to the onset of the pressure gradient, and not secondary to cavity obliteration. 3) Forward flow persists throughout systole (to aortic valve closure), with ejection time prolonged and related to the magnitude of the gradient. 4) Ejection dynamics in nonobstructive HCM and normal subjects are virtually identical. 5) Biphasic aortic flow patterns and mid-systolic drop in LV ejection velocity are consistent with the "spike and dome" arterial pulse and mid-systolic aortic valve closure. 6) Increased LV outflow tract cross-sectional area created by muscular (myectomy) resection abolishes SAM, the pressure gradient (and mitral regurgitation). 7) A quantitative relationship is evident between time of onset and duration of SAM-septal contact and the magnitude of the gradient. 8) Doppler echocardiography reliably estimates gradient using the Bernoulli equation, virtually eliminating need for routine cardiac catheterization. Finally, SAM (and obstruction) is caused by hydrodynamic forces on the mitral valve, with drag (i.e., pushing force of flow) (81,83) predominant over the Venturi effect (i.e., mitral leaflets sucked toward the septum by a high velocity outflow jet) (85,89).

Multicenter cohort studies. Most importantly, over the last several years, clinical studies performed in large HCM patient populations (not previously available in the HCM literature) (90–95) have identified a consistent relationship between LV outflow tract gradients at rest and heart failure symptoms and cardiovascular events. For example, a 2003 long-term follow-up of a large HCM cohort of >1,100 patients established highly significant linkage between peak instantaneous LV outflow obstruction (gradient ≥30 mm Hg at rest) and unfavorable outcome (90) (Fig. 4). Overall probability of death due to HCM was significantly greater among patients with outflow obstruction than in those without obstruction (relative risk [RR]: 2.0), as was progression to severe New York Heart Association functional class III or IV symptoms or death from heart failure or stroke (RR: 4.4). These disease complications were most common in patients ≥40 years old, suggesting that longer duration of obstruction promotes more adverse disease consequences. However, increasingly higher resting gradients ≥30 mm Hg did not increase the likelihood of

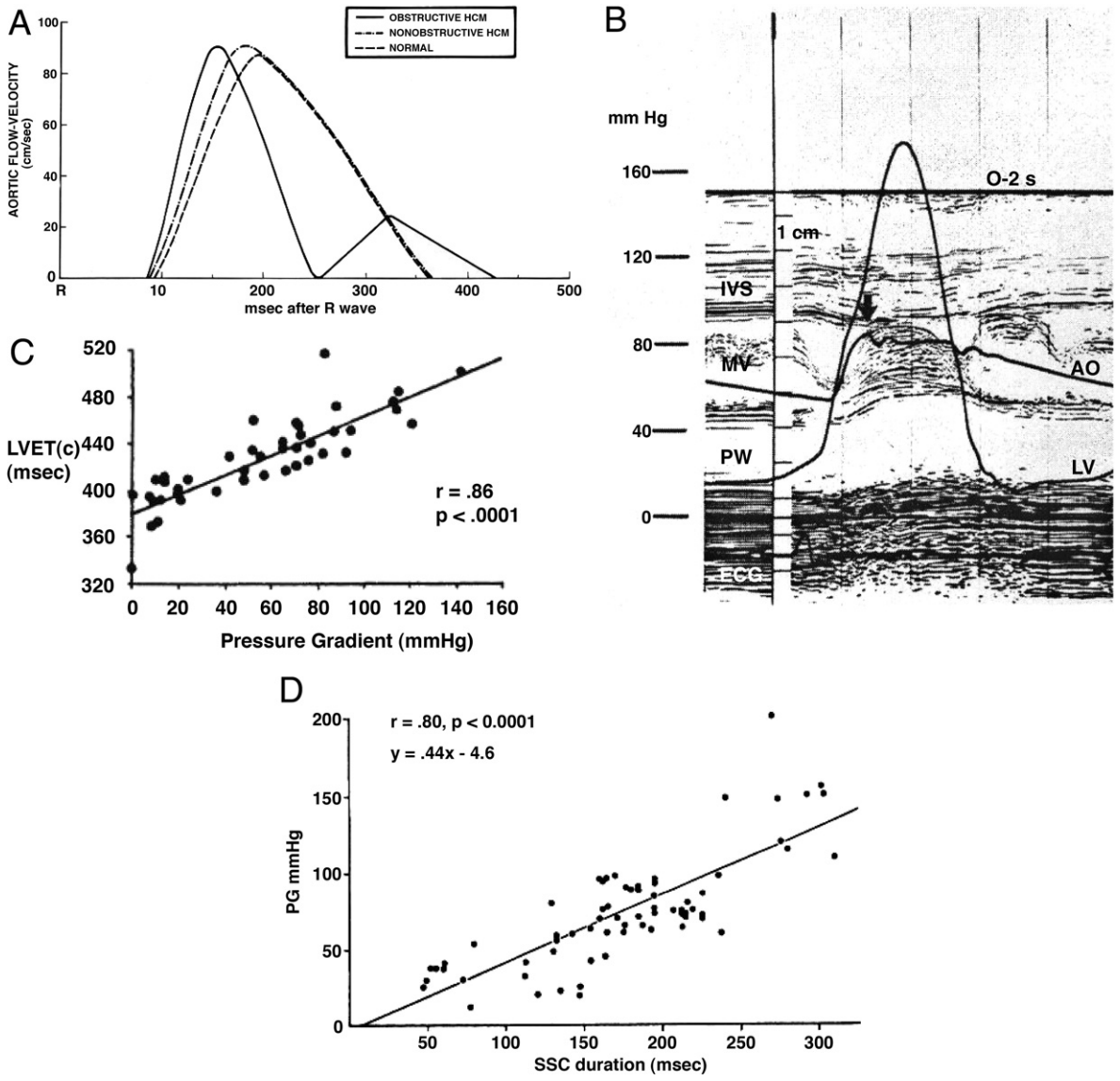

Figure 3 Evidence That Subaortic Gradients Represent Impedance to LV Outflow

(A) Composite flow-velocity waveforms in the ascending aorta from patients with obstructive or nonobstructive HCM and normal subjects. Obstructive curve differs from the curves for normal subjects and nonobstructive HCM with characteristic early rapid emptying, mid-systolic deceleration (due to systolic anterior motion [SAM]), and the late lower flow phase. Reprinted, with permission, from Maron et al. (88). **(B)** Simultaneous hemodynamic and echocardiographic recordings in a patient with obstruction (gradient: 85 mm Hg). **Arrow** indicates onset of SAM-septal contact, simultaneous with onset of pressure gradient. Reprinted, with permission, from Pollick et al. (85). **(C)** Direct relation between corrected left ventricular ejection time (LVETc) and peak systolic pressure gradient. Reprinted, with permission, from Sasson et al. (84). **(D)** Direct relation between magnitude of pressure gradient (PG) and duration of SAM-septal contact (SSC). Reprinted, with permission, from Pollock et al. (85). AO = (central) aortic pressure; IVS = interventricular septum; LV = left ventricular pressure; MV = mitral valve; PW = posterior wall; other abbreviations as in Figure 2.

unfavorable outcome. In addition, a weaker association has been identified between outflow gradients and specifically sudden and unexpected death (usually in patients with no or only mild limiting symptoms) (90,91). Subsequent analysis in a smaller Italian HCM cohort offered confirmation that outflow obstruction was a strong and independent predictor of cardiovascular mortality, particularly in those patients without significant symptoms at study entry (92) (Fig. 4).

Another multicenter study used stress echocardiography to assess physiologically provocable outflow gradients and identified 70% of HCM patients with the propensity to develop outflow obstruction either at rest or with exercise (35) (Fig. 2). These data represent a paradigm shift in our understanding of the frequency with which outflow gradients occur in HCM, supporting the contemporary view that this disease should be regarded as one in which outflow obstruction predominates (35).

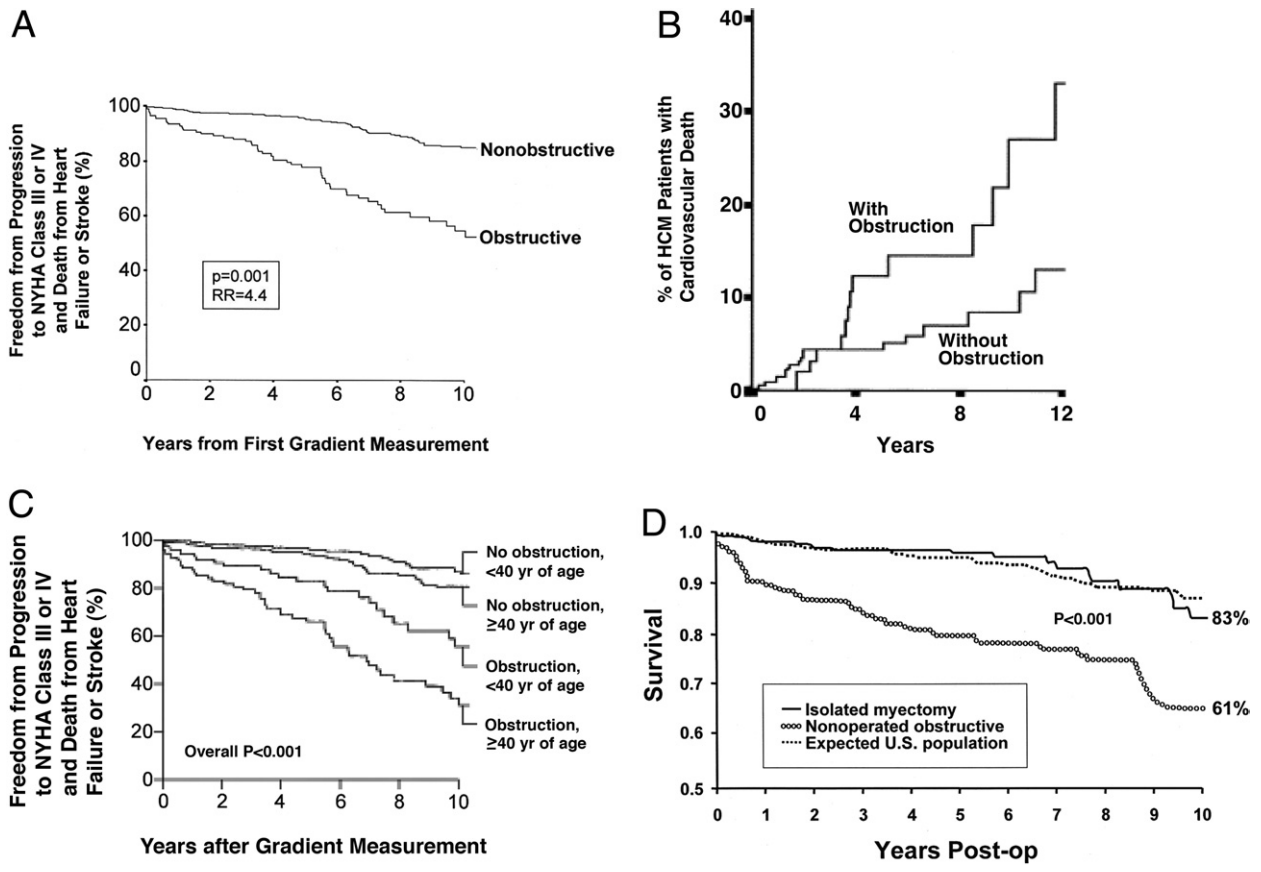

Figure 4 **Data From HCM Cohort Studies Supporting the Clinical Significance of LV Outflow Gradient**

(A) Kaplan-Meier estimates showing greater probability of progression to severe heart failure (New York Heart Association [NYHA] functional class III or IV) or death from heart failure or stroke among patients with outflow obstruction (gradient ≥30 mm Hg at rest) compared with patients without obstruction. From an international multicenter study comprising 1,101 patients (90). Reprinted, with permission, from Maron et al. (90). **(B)** Italian study showing that the proportion of patients with LV obstruction at rest who died of cardiovascular causes exceeds that of patients without obstruction. Reprinted, with permission, from Autore et al. (91). **(C)** From the multicenter study depicted in **A**, showing effect of age and LV outflow tract obstruction on probability of progression to severe heart failure or death from heart failure or stroke. Reprinted, with permission, from Maron et al. (90). **(D)** Abolition of LV outflow gradient in severely symptomatic patients undergoing surgical septal myectomy results in survival (depicted with respect to all-cause mortality) similar to that expected in a matched general U.S. population, and exceeding HCM patients with outflow obstruction who were not operated on. Reprinted, with permission, from Ommen et al. (93). Abbreviations as in Figure 2.

Based on substantial post-operative surgical data assembled for septal myectomy (and with shorter follow-up for alcohol septal ablation [77,78]), the relief of outflow obstruction and normalization of LV systolic pressure (Fig. 2) is accompanied by long-lasting reduction in disabling symptoms of heart failure (77). This is associated with objective improvement in myocardial metabolism, oxygen consumption, and exercise capacity (96,97). Furthermore, and of particular importance, myectomy conveys a long-term survival benefit, as demonstrated most recently by retrospective, nonrandomized, post-operative studies from Mayo Clinic (93,98) and Toronto General Hospital (94) in >1,600 patients. In the larger Mayo Clinic series, 10-year overall survival after myectomy was 83% (freedom from all-cause mortality), which was equivalent to that expected in the general U.S. population (Fig. 4) and also superior to that of patients with obstructive HCM who were not operated on (10-year survival only 61%) (93); freedom from HCM mortality following myectomy was 95%. Therefore, surgical abolition of obstruction was strongly and independently associated with survival, and myectomy reduced the mortality risk in severely symptomatic patients with obstruction; also, progression to the end-stage with systolic dysfunction and remodeling is no more common following myectomy than in the general HCM population (40). Taken together, these data substantiate that myectomy with relief of mechanical obstruction favorably alters the basic disease course, definitively refuting any consideration that obstructive HCM represents a progressive heart muscle disorder with continued LV remodeling, despite the best available treatment interventions (5).

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Current Management Strategies for LV Outflow Obstruction

The numerous clinical studies assembled over the past 50 or more years have ultimately led to the contemporary diagnostic and management strategies for LV outflow tract obstruction, which are now part of standard clinical practice (5). In particular, the data that have recently emerged in large patient cohorts confirmed that LV outflow obstruction (at rest) is an important determinant of cardiovascular morbidity and mortality in HCM patients (90–98), thereby underscoring the importance of properly identifying and aggressively treating (and abolishing) subaortic gradients in severely symptomatic and drug refractory patients by surgical septal myectomy or, alternatively and selectively, by alcohol septal ablation.

In addition, those LV outflow gradients commonly induced with physiologic exercise by stress echocardiography are often of clinical importance (35). Though many such patients are asymptomatic (35), others may develop progressive heart failure symptoms with exertion due to physiologically provoked outflow obstruction and may benefit from septal reduction intervention in a fashion similar to that of patients with more typical obstruction under resting conditions (5,35,77,99). Taken together, these principles surrounding outflow obstruction in HCM are also supported by current American College of Cardiology/European Society of Cardiology expert consensus recommendations (5) stating that invasive septal reduction therapy should be reserved for those patients with advanced heart failure symptoms refractory to maximum pharmacologic therapy (principally with beta-blockers, verapamil, or disopyramide): New York Heart Association functional class III or IV associated with a peak instantaneous outflow gradient ≥50 mm Hg at rest or with physiologic (exercise) provocation.

The more modest (but statistically significant) relationship between LV outflow gradient (at rest) and the risk for sudden cardiac death (90,92) is not sufficiently strong to establish LV outflow obstruction as an independent risk factor or justify decisions for primary prevention implantable-defibrillators based either solely or predominantly on the presence of a subaortic gradient (100). Marked outflow gradients can, however, be a supplemental factor and arbitrator in such decisions for patients with other risk factors and ambiguous risk stratification on a case-by-case basis.

Over the last 10 years, with the emergence of percutaneous alcohol septal ablation, a controversy has ensued concerning the most effective strategy for reducing or abolishing LV outflow tract gradients and severe heart failure symptoms unresponsive to maximum medical management (77,78). Surgical myectomy, which has been used for almost 50 years, and alcohol ablation both reduce outflow obstruction, and interventions that substantially mitigate gradient can also be expected to reduce symptoms. The risk for procedural death and complications is comparable for both techniques, if not higher for ablation. Most importantly, ablation (in contrast to myectomy) creates a sizeable transmural myocardial infarction comprising about 10% of the LV, which could serve as a substrate for potentially life-threatening ventricular tachyarrhythmias and sudden death. Consequently, an expert consensus panel has retained surgical myectomy as the primary treatment for patients with obstructive HCM and unrelenting symptoms, with alcohol ablation reserved as an alternative option for those patients who are judged not to be appropriate surgical candidates (5).

Conclusions

Understanding the significance and frequency of LV outflow obstruction in patients with HCM has indeed been a "winding road," but one that has eventually provided clinically relevant answers directly related to patient management. Indeed, we have come full circle to the positions held in the early 1960s that HCM can be characterized as a predominantly obstructive disease, and that outflow gradients are of pathophysiologic significance and often represent a therapeutically reversible form of mechanical obstruction to LV outflow and heart failure.

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