CRITICAL REVIEW

Idiopathic Hypertrophic Subaortic Stenosis
(Hypertrophic Obstructive Cardiomyopathy)*
Changing Concepts—1975

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Idiopathic hypertrophic subaortic stenosis (IHSS), or hypertrophic obstructive cardiomyopathy (HOCM), is one of the few common diseases virtually unknown 20 years ago. Since the early case report in 1957† and the pathologic description in 1958,‡ numerous articles have appeared, and yet the disorder (or more accurately the spectrum of disorders) continues to be an enigma and a source of controversy. This review will attempt to summarize some of the currently known facts and fancies. No attempt will be made to suppress the opinions and bias of this reviewer, who has been especially fascinated by this disorder since the early 1960s while working in the laboratory of Professor John F. Goodwin at the Postgraduate Medical School of London. Goodwin and his associates§,‖ have made and continue to make important contributions to our understanding. In North America, most prominent early work originated from Braunwald and his colleagues¶,¶¶ at the National Heart Institute (since called the National Heart and Lung Institute) and from Wigle and his associates¶¶¶ at the University of Toronto in Canada.

Although IHSS is the more widely used term in the United States, HOCM is probably a more accurate description. The disorder is a form of primary myocardial disease (cardiomyopathy); asymmetric hypertrophy is a prominent and necessary feature, and ventricular outflow obstruction is a common accompaniment. The term, IHSS, strongly emphasizes a common clinical syndrome of subaortic stenosis, although we must not lose sight of the frequent lack of outflow obstruction or the rare occurrence of subpulmonic stenosis. Despite its imperfections, it seems that the name is indelibly stuck, at least for the present. We shall continue to use the term, IHSS, for the disorder in this review.

CHARACTERISTICS OF IHSS

It is now common knowledge that the patients (of all ages and both sexes) have the symptoms of left ventricular (LV) outflow obstruction (ie, dyspnea, angina, dizziness, and syncope) and the objective signs of mitral regurgitation. The arterial pulse is characteristically brisk and may be bimodal much like the bisferious pulse of aortic regurgitation but without the wide pulse pressure. Clinical and electrocardiographic evidence of left ventricular hypertrophy is commonly but not uniformly present. The apical impulse has some of the most prominently visible palpable, and demonstrable presystolic outward motion (or “A” wave) and often has a double systolic outward impulse. A murmur of subaortic stenosis has its onset during early ejection with the characteristic medium frequencies of an ejection murmur along the left sternal border intermixed with the characteristic high frequencies of a regurgitant murmur over the apex. Typically the murmur is accentuated during the straining phase of Valsalva’s maneuver and following amyl nitrite inhalation. In general, the murmur correlates with the presence and severity of outflow obstruction and is as dynamic and variable as the obstruction itself.

Hemodynamic characteristics of this disorder have been well defined. Obstruction to LV outflow is variable and dynamic, in contrast to the fixed obstruction of aortic valve stenosis. Numerous physiologic and pharmacologic interventions associated with decrease in preload, afterload, and augmentation of cardiac contractility result in accentuation of this dynamic obstruction. It has been suggested that the common underlying determinant is LV

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Although actual obstruction between LV inflow and outflow is clearly demonstrable, spurious pressure gradients may also be recorded due to catheter entrapment and to cavity obliteration. In addition to outflow obstruction, cardiac hypertrophy decreases ventricular distensibility and produces impairment of diastolic filling. Atrial systole is especially conspicuous and significantly contributes to ventricular filling. Thus, although cardiac output is generally well maintained, it may drop precipitously in the presence of atrial fibrillation or marked tachycardia. Rarely, muscular obstruction to right ventricular (RV) outflow alone may be observed. The systolic ejection murmur then has the characteristics of infundibular pulmonic stenosis. However, other signs of LV involvement may be apparent.

Selective angiographic studies reveal distorted, hypertrophied LV and RV chambers with reduced end-diastolic and end-systolic dimensions. Systolic emptying may be supernormal, despite outflow obstruction with sharp reduction in end-systolic volume. Mitral regurgitation, generally of mild degree, is present in a large proportion of cases. Wigle and his co-workers have shown this to be a constant accompaniment of outflow obstruction. Cineangiograms in the steep left anterior oblique projection may demonstrate systolic reopening of the anterior mitral valve into the LV outflow. Marked geometric distortion of the left ventricle with its apex displaced anteriorly has been reported, although the specificity of this finding remains to be established.

Echocardiography has proved to be a useful non-invasive technique in the study of this disorder. Various anatomic and physiologic features are easily recognized. The LV outflow space is narrowed, the mitral valve is anteriorly displaced, the interventricular septum is massively thickened, and the anterior mitral leaflet shows classic functional abnormalities which are probably causally related to LV outflow obstruction. It can be readily demonstrated on M-mode echocardiography that the mitral leaflets close early in systole in a normal fashion. Sometime after early ejection, the anterior mitral valve opens into the LV outflow space and may be opposed to the interventricular septum. In the latter part of systole, the leaflet returns to its closed position; subsequently, in early diastole, it opens in a normal fashion. This abnormal systolic anterior (opening) movement (SAM) is commonly associated with outflow obstruction (Fig 1). Different maneuvers that accentuate LV outflow obstruction also help to bring out SAM more prominently. Earlier studies from our laboratory demonstrated three types of mitral valve motion in systole in the resting state:

1. complete and constant SAM seen in the vast majority of the beats, with the mitral leaflet reaching up to the septum;
2. partial and inconstant SAM noted only in infrequent beats; and
3. no resting SAM. In the latter two varieties, provocative maneuvers, such as Valsalva's maneuver and amyl nitrite inhalation, will promote or accentuate the abnormal SAM. It was observed that type 1 was associated with higher resting outflow gradients and type 2 with lower and labile resting outflow gradients, while non-gradients were generally observed in type 3. In all three situations, appropriate provocative maneuvers will accentuate LV outflow obstruction.

Important contributions to the echocardiographic diagnosis were made by Abbasi et al and by Henry and associates with the development of criteria for the diagnosis of asymmetric septal hypertrophy (ASH). Although ASH is noted to be present in the vast majority of patients with IHSS, its specificity has not yet been established. The presence of ASH on the echocardiogram should point to a need to look for other features of the disease; it should not

![Figure 1. Schematic diagram representing, from top to bottom, aortic root echocardiogram, mitral valve echo, phonocardiogram, electrocardiogram, and pressure pulses of LV outflow obstruction in IHSS. Mitral valve closes at onset of LV systole coincident with first heart sound. (Initial systolic ejection is unobstructed when aortic valve opens normally toward margins of aortic root concomitant with LV and aortic pressure rise.) Sometime after onset of ejection, mitral valve moves anteriorly to abut against interventricular (IV) septum. Left ventricular outflow obstruction is manifest in pressure pulses with drop in aortic pressure and rise in intracavity LV pressure. This coincides with onset of systolic murmur. Aortic cusp closes in mid-systole. In latter part of systole, mitral valve returns to its closed position away from IV septum. This is associated with second systolic wave in aortic pressure, and aortic cusp reopening. At end of systole, diastolic notch coincides with second heart sound and aortic valve closure with cusp in middle of aortic root.](http://journal.publications.chestnet.org/pdfaccess.ashx?url=/data/journals/chest/20974/ on 06/26/2017)
be accepted as a sole evidence for the disease. Additional features include systolic flutter or mid-systolic closure of the aortic valve cusps.

**Etiology and Natural History of IHSS**

Despite refinements in clinical, hemodynamic, and echocardiographic criteria for the diagnosis of this disorder, our understanding of its etiologic mechanisms and of its natural history remains meager. While it is clear that the disease represents a diffuse myocardial disorder and that most familial studies suggest a strong genetic predilection, it is not certain if sporadic cases can and do occur. Since association with hypertension, aortic valve disease, and aortic coarctation has been observed, it may be postulated that work overload in some subjects with appropriate genetic predisposition could result in asymmetric rather than concentric hypertrophy.

Outflow obstruction is not a constant feature, and patients with obstruction may have siblings having this disorder without any evidence of resting or provokable obstruction. It is possible that the nature and degree of distortion in ventricular geometry may determine the presence and severity of outflow obstruction.

Several studies on the natural history of this condition have been reported, although these can only be looked upon as preliminary, since the mean length of follow-up has been generally less than five years per patient. A recent multicenter study of 190 patients with an average follow-up of 5.2 years provided the following interesting observations: (1) Generally a decade elapses between the detection of a murmur and the onset of symptoms. (2) Older patients are more severely symptomatic, suggesting progressive deterioration with age. (3) The severity of outflow obstruction and the intensity of the murmur are unrelated to the clinical class, although all patients with a resting outflow gradient in excess of 100 mm Hg were symptomatic. (4) Eighty-three percent of survivors were clinically stable or improved. (5) Sudden death was the most common mode of demise, accounting for 26 of 30 deaths unrelated to surgery. (6) There were no recognizable clinical predictors of sudden death. (7) Excluding surgical deaths, the average mortality was 3.4 percent per year. Despite several stable patients over a long follow-up period, this disorder can by no means be considered benign. Insight into the mechanisms of sudden death may provide avenues for appropriate therapy. It is suspected, although not proved, that ventricular arrhythmias may be the underlying cause. The report by Ingham et al (see page 759) represents a systematic attempt to categorize and quantitate the arrhythmic events using treadmill testing in patients with IHSS. Previously unsuspected arrhythmias were detected in 50 percent of the patients tested. This approach can be extended to document the effectiveness of antiarrhythmic agents. In this regard a recent pathologic study by James et al is also of interest. They were able to show extensive fibrosis of pacemaking and conducting tissues in patients with IHSS who died suddenly. These anatomic changes may form a basis for electrical instability.

Despite a lack of correlation between the severity of outflow obstruction and the clinical symptoms or prognosis, several studies have observed clinical improvement following surgical amelioration of outflow obstruction. It is not clear if ventriculomyotomy does offer a partial protection against sudden death. A preferred surgical approach at most centers is transaortic ventriculomyotomy or myectomy, or both. This operation results in the relief of obstruction and of mitral regurgitation, as well as the echocardiographic abnormalities in mitral valve motion (SAM). However, surgery is reserved for severely symptomatic patients, since the primary fault is in the heart muscle and since operative mortality is high at most centers. Alternate surgical approaches have been proposed, but in the opinion of this reviewer, mitral valve replacement is only indicated in a rare patient with severe independent mitral regurgitation.

Medical management at the present time is unsatisfactory. Beta-adrenergic blocking agents are the mainstay of drug therapy, based on earlier observations that sympathetic and catecholamine stimulation results in the accentuation of outflow obstruction. Amelioration of a rather uncommon symptom of cough syncope with propranolol administration, as reported by White et al, is of interest. Similarly, the accentuation of outflow obstruction with Wolff-Parkinson-White syndrome is also thought provoking, and the amelioration of the obstruction following intravenous administration of ajmaline with the disappearance of Wolff-Parkinson-White syndrome represents a new approach to therapy.

Finally, it is being increasingly recognized that IHSS is a ubiquitous disorder, and with the many useful echocardiographic signs, it is often detected in association with other conditions. Thus, it may be associated with valvular heart disease, coronary artery disease, mitral valve prolapse, or forms of congenital heart disease. These associations often result in a difficult bedside diagnostic dilemma and should provide enough justification for pursuing noninvasive echocardiographic studies as part of a complete cardiac evaluation.
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