Dynamic Subaortic Obstruction in Hypertrophic Cardiomyopathy: Criteria and Controversy*

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Concept of subaortic obstruction in hypertrophic cardiomyopathy. This concept had its origin in two observations: 1) the anatomic restriction of the left ventricular outflow tract related to hypertrophy of the interventricular septum (1-4), and 2) the pressure gradient measurable across the outflow tract and varying in response to physiologic interventions (5,6). In particular, the presence of this gradient has been generally considered the criterion for obstruction in hypertrophic cardiomyopathy. Early concerns (7) that the gradient reflected catheter entrapment between hypertrophied trabeculations were addressed by demonstrating that a pressure difference could be measured with a catheter located in the left ventricular inflow tract and freely mobile in a blood-filled portion of the chamber (8,9).

The hypothesis that the gradient was not a primary phenomenon, but rather secondary to the rapid and unimpeded ejection of blood from the ventricle early in systole, was proposed in 1964 by Hernandez et al. (10). In this formulation, the gradient would relate to cavity obliteration, with contraction of the ventricular walls around a virtually empty chamber after the bulk of ejection had occurred. This concept was based on the observation that aortic blood flow abruptly decreased in mid-systole in patients with hypertrophic cardiomyopathy and a pressure gradient, and that 80% of ejection was accomplished during the first half of systole in that group.

Muro et al. (11), using an intraaortic electromagnetic flow probe, later demonstrated a similarly abnormal pattern of ejection in patients with hypertrophic cardiomyopathy with or without a subaortic gradient. They concluded that the presence of a gradient is not an impediment to left ventricular outflow because it did not affect the time course of ejection in their patients.

The current study. The article by Maron et al. (12) in this issue of the Journal represents a major contribution to this field. It introduces two methodologic innovations. First, Doppler ultrasound and imaging echocardiography are combined as an effective means of timing and quantitating flow events in the heart and aorta. Second, a simple and physiologic criterion for subaortic obstruction is enunciated, namely, the presence of a pressure gradient during the period of systolic ejection. The magnitude of obstruction is then proportional to the fraction of forward flow ejected in the presence of a subaortic gradient. Although this concept appears to be intuitively reasonable and obvious, and although it is implicit in the analysis of intraoperative pressures and flows by Pierce et al. (6), it had not been applied in a quantitative manner to the other pressure-flow investigations cited (10,11).

The patient group studied by Maron and his coworkers included 20 patients with a measured gradient (n = 16) and mitral-septal contact, which is generally recognized as correlating with the presence of a gradient (13-17). Thirty patients without evidence of a gradient were also studied, along with 20 normal control subjects. In the group with a gradient or septal contact with the mitral valve it was found that: 1) an average of 58% of forward aortic flow was ejected while a gradient or mitral-septal contact was present; 2) a late systolic second peak of aortic flow was seen in 80% of these patients despite the persistence of a gradient and mitral-septal contact; 3) the left ventricle continued to shorten and empty after the onset of a gradient; and 4) left ventricular ejection time was longer in this group than in patients without a gradient. Although the catheterization and Doppler flow studies were generally performed at different times, similar results were obtained in a smaller group of patients who underwent simultaneous catheterization and echocardiographic studies. In comparison with the group with obstruction, aortic flow profiles in patients with hypertrophic cardiomyopathy without a gradient or close approach of the mitral valve and septum were similar to those seen in the normal control subjects. Maron et al. conclude, therefore, that patients with a gradient or its echocardiographic correlate have physiologic subaortic obstruction to left ventricular outflow by the criterion of flow in the presence of a gradient.

This study also confirms the relation between systolic anterior motion of the mitral valve and obstruction (13-18). In the patients with obstruction, a rapid deceleration of aortic flow occurs at approximately the same time that the mitral valve contacts the interventricular septum. Patients without a gradient, however, demonstrate neither the flow abnormality nor close approach of the mitral valve to the septum.

*Editorials published in Journal of the American College of Cardiology reflect the views of the authors and do not necessarily represent the views of JACC or the American College of Cardiology.

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Consonance and divergence. We can now review the data presented by Murgo et al. (11) and analyze their simultaneous pressure and flow data using the criterion for obstruction just described. From their representative tracings obtained from a patient with a gradient, it is evident that the vast majority of forward flow occurs in the presence of a subaortic gradient (Fig. 4 of reference 11). In addition, a late systolic aortic flow peak, similar to that reported by other groups (12,19,20), can be demonstrated. In other words, physiologic obstruction to flow occurs in the presence of a subaortic gradient. In this regard, the data are consistent with those of Maron et al. (12).

We cannot, however, easily reconcile the discrepancy between the two studies regarding aortic outflow in patients without a significant pressure gradient in the baseline state. Maron et al. found that these patients have a normal systolic flow profile, whereas Murgo et al. observed rapid mid-systolic deceleration of flow. On closer examination, we find that these two groups without obstruction may not be strictly comparable, with the group studied by Murgo et al. manifesting a more hyperdynamic state. At the time of the flow studies, half of the patients in this category studied by Maron et al. were receiving medications having negative inotropic effects, whereas those studied by Murgo et al. had not been taking medications for at least 72 hours. It is not surprising, therefore, that peak aortic blood flow velocity was normal in the former group but significantly increased in the latter group. Furthermore, the patients without obstruction studied by Maron et al. had no or only mild systolic anterior motion of the mitral valve and a mitral-septal separation of at least 5 mm. Of the patients studied by Murgo et al., 6 (28%) of 21 had a moderate to severe degree of mitral systolic anterior motion, while the presence and degree of mitral systolic anterior motion were undefined in two others.

In summary, therefore, the data in both studies show that in patients with hypertrophic cardiomyopathy and a sub-aortic pressure gradient, the majority of forward flow is ejected in the presence of a gradient. The patient groups without obstruction in the two studies are not strictly comparable, and differ in ways that could explain the discrepancies in the flow profiles. Indeed, it is perhaps unreasonable to expect a uniform physiology in a condition as pleomorphic as hypertrophic cardiomyopathy (21,22).

Unresolved questions. Although the current study of Maron et al. establishes the physiologic significance of obstruction related to systolic anterior motion of the mitral valve, fundamental questions remain regarding the causes and mechanism of this motion:

1. What are the flow events in the outflow tract, and how do they relate to the onset of systolic anterior motion of the mitral valve? The current study demonstrates only that the magnitude and time course of flow velocity in the left ventricle proximal to the outflow tract are normal in the majority of patients with a gradient. Application of the continuous wave Doppler technique should clarify this issue (23,24).

2. If mitral systolic anterior motion is flow-related, how is it maintained in late systole when aortic flow velocity is low or negligible? This question is further complicated by our expectation that a reverse Venturi effect related to the high velocity jet of mitral regurgitation would act during that period of the cardiac cycle and draw the leaflet posteriorly. The problem demands a more complete understanding of outflow tract velocity in late systole (23,24) and of the forces promoting and opposing systolic anterior motion of the mitral valve. The answer to this question may relate in part to the fact that once anterior motion has begun, the distal leaflet faces directly into the path of flow, so that the drag forces of ejection continue to move the leaflet anteriorly. (Drag forces are defined as forces acting parallel to the direction of flow, whereas lift or Venturi forces act perpendicular to the direction of flow [25].) In addition, as long as a gradient is being generated by left ventricular contraction, the pressure differential across the leaflet portions involved in systolic anterior motion will act to maintain their anterior position even in the absence of measurable forward flow.

3. How can a second peak of aortic flow occur while mitral-septal contact persists? The observed reflow could be explained if mitral-septal contact is not uniformly maintained around the circumference of the outflow tract, but rather resolves along the lateral margins of the valve not scanned by the centrally positioned M-mode ultrasound beam.

Maron et al. (12) observed a normal flow profile in the left ventricular cavity in 13 of 17 patients with physiologic obstruction in whom such tracings were recorded and in 23 patients in the group without obstruction. These findings raise questions about the concept of the hyperdynamic ventricle of hypertrophic cardiomyopathy. Perhaps the complete emptying observed and the high ejection fractions measured relate primarily to small end-diastolic volumes and the presence of mitral regurgitation.

It is unclear why the current study failed to demonstrate the virtually uniform association between obstruction and mitral regurgitation reported by other groups (26–28). The discrepancy between the normal-appearing left ventricular flow profiles and the truncated aortic flow patterns in the majority of the group with obstruction, however, suggests a decrement in anterograde flow in mid- to late systole that most likely represents mitral regurgitation.

Finally, Maron et al. noted a lack of uniform correlation between clinical activity status and obstructive physiology, although other reports do suggest some association (29).
This observation does not detract from the physiologic significance of obstruction, but rather it reminds us that a complex combination of systolic, diastolic, electrical, and coronary flow abnormalities contribute to the clinical presentation of hypertrophic cardiomyopathy.

References