Subvalvular Gradients in Patients With Valvular Aortic Stenosis
Prevalence, Magnitude, and Physiological Importance

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Background—Although subvalvular gradients in patients with aortic stenosis have been described, their behavior and response to exercise have not been well characterized.

Methods and Results—Left ventricular and aortic pressures and linear flow velocity were measured with a catheter-tip manometer at rest and during supine exercise in 27 patients with valvular aortic stenosis. A subvalvular gradient was measured in each patient that represented, on average, 48% of the total resting transvalvular gradient. With exercise, both total (rest: 80±26 mm Hg; exercise: 90±25 mm Hg) and subvalvular gradients (rest: 37±13 mm Hg; exercise: 60±22 mm Hg) increased significantly. There was a significant inverse relationship between change in exercise cardiac output and total and subvalvular gradients. However, only the exercise subvalvular gradient predicted cardiac output response.

Conclusions—Subvalvular pressure gradients are universally present in patients with severe aortic stenosis and comprise approximately half of the total transvalvular gradient. The extent of exercise cardiac output increase is inversely related to the subvalvular gradient magnitude. (Circulation. 2001;104:1019-1022.)

Key Words: valves ■ aorta ■ hemodynamics

Subvalvular pressure gradients in the absence of anatomic obstruction have been described in patients with aortic stenosis. However, their clinical and physiological relevance remains unexplored.

Methods

Patient Population
Twenty-seven patients (mean age 58±7 years; range 41 to 71 years) with clinical evidence of aortic stenosis were referred for cardiac catheterization and angiography. All patients had normal left ventricular size and function, no more than trivial aortic regurgitation, no significant obstructive coronary artery disease, and no evidence of anatomic or dynamic subvalvular obstruction.

Study Protocol
Micromanometric left ventricular and aortic pressures were obtained with a custom-designed multisensor catheter (Millar Instruments, Inc) with a distal (tip) pressure sensor, a more proximal (5 cm from the tip) laterally mounted pressure sensor, and an electromagnetic velocity probe at the site of the proximal pressure sensor, inserted via the right brachial artery. The catheter was advanced to the deep left ventricular cavity. An appropriate gain setting for recording the velocity waveform was obtained and not adjusted thereafter. The catheter was then slowly withdrawn, and continuous recordings were obtained. After resting data collection was completed, patients underwent 5 minutes of supine bicycle exercise.

Data Analysis
At least 5 consecutive beats were analyzed; reported data represent their mean (±SD). Peak transvalvular gradient was defined as the largest difference between deep left ventricular pressure and the “true” ascending aortic pressure (vide infra). Peak subvalvular gradient was defined as the largest difference between deep left ventricular systolic pressure and the systolic pressure recorded from the proximal sensor just before the appearance of the true aortic pressure. The true aortic pressure recording was defined as a stable, unchanging waveform (at least 3 consecutive beats) with characteristic “parvus et tardus” pattern, displaying a distinct dicrotic notch and unchanging end-diastolic and peak systolic pressures. The amplitude of the simultaneous flow velocity signal had to be organized and ever-increasing on catheter pullback, providing assurance that the proximal sensor was upstream from either the valve orifice or vena contracta (the region of maximal velocity).

Results

Resting Valvular and Subvalvular Hemodynamics
Mean aortic valve area was 0.73±0.2 cm² (range 0.4 to 1.0 cm²), and mean peak transvalvular gradient was 80±26 mm Hg (range 37 to 154 mm Hg). A subvalvular pressure gradient could be recorded in every patient, with a group mean of 37±13 mm Hg (range 18 to 65 mm Hg). The mean fraction of the total transvalvular gradient represented by the subvalvular gradient was 0.48±0.18 (range 0.14 to 0.78).
Figures 1 to 4 illustrate pertinent findings in 4 representative patients. In each, a characteristic decrease in peak systolic pressure recorded from the proximal sensor (LVP-2) during pullback can be seen. Corresponding to this systolic pressure decrease was an increase in flow velocity amplitude. In all cases, a systolic pressure gradient was recorded before inscription of the classic slow-rising aortic pressure waveform. A hybrid waveform was often recorded from the

**Figure 1.** Two sensors deep within left ventricular cavity record identical pressures (A). Middle tracing represents instantaneous linear velocity at proximal pressure sensor (LVP-2). With catheter withdrawal, systolic pressure decrease is recorded from proximal sensor, accompanied by increased magnitude of linear velocity (B). With further catheter withdrawal, "true" valve orifice is engaged (C). Note characteristic delay in ascending aortic pressure recording. Further catheter withdrawal places proximal sensor within zone of pressure recovery (D).
proximal sensor, with 2 distinctive features: (1) a virtually identical rate of pressure rise recorded from the proximal and distal sensors and (2) an inflection that corresponded in time to peak velocity on the proximal sensor recording as it was withdrawn into the subvalvular region. The typical appearance of slow-rising pressure at the proximal sensor did not occur until further withdrawal (Figure 3), at which time, in this case, peak recorded pressure was higher and velocity amplitude lower than the preceding beats (pressure recovery).

**Exercise Hemodynamics**

Cardiac output increased significantly (rest: 6.3±1.1 L/min; exercise: 8.4±1.8 L/min; \( P<0.001 \)), chiefly as a result of increased heart rate (stroke volume at rest: 76±19 mL; on exercise: 80±21 mL). Peak transvalvular gradient (rest: 80±26 mm Hg; exercise: 90±25 mm Hg; \( P<0.001 \)) and subvalvular gradient (rest: 37±13 mm Hg; exercise: 60±22 mm Hg; \( P<0.001 \)) increased significantly. The subvalvular fraction of the total transvalvular gradient also increased significantly with exercise (rest: 0.48±0.16; exercise: 0.66±0.08; \( P<0.001 \)).

There were statistically significant inverse (univariate) relationships between the magnitude of cardiac output increase and the total \((r=-0.51)\) and subvalvular \((r=-0.57)\) exercise gradients. Multiple stepwise regression with measures of stenosis severity (aortic valve area, rest and exercise transvalvular gradient, rest and exercise subvalvular gradient) as independent variables and cardiac output increase as the dependent variable revealed that only exercise subvalvular gradient predicted cardiac output response (coefficient \(-0.024; P=0.002\)).

**Discussion**

The first report of the presence of resting subvalvular pressure gradients in patients with aortic stenosis and no anatomic basis for obstruction suggested a mechanism based on principles of fluid dynamics. These authors subsequently developed an elegant mathematical model that fully explained the presence of these resting gradients as a manifestation of significant inertial effects within a rapidly tapering flow field. In the present study, careful exploration revealed no evidence of a resting pressure gradient within the deep left ventricular cavity, a small gradient accompanied by an increase in local linear flow velocity with slight catheter withdrawal, and a larger and continuously increasing gradient (accompanied by progressive local velocity increase) up to the subvalvular...
At this point, proximal sensor recordings exhibited morphologies consistent with both aortic and ventricular origins (hybrid). However, in every instance, 2 distinctive features of the proximal sensor waveform suggested a predominantly ventricular (therefore subvalvular) origin: (1) virtual identity in the rate of pressure development (dP/dt) to that of the distal sensor recording and (2) appearance of a distinctive inscription on the pressure tracing corresponding in time to the peak velocity. The former consideration, of necessity, supports a ventricular source. The latter pertains when convective acceleration forces are solely responsible for the pressure loss. Because local acceleration at the point of peak velocity (dV/dt) is zero, these findings are most likely to be detected within the rapidly tapering subvalvular region.

With light supine exercise, the transvalvular gradient and the subvalvular component increased significantly. Importantly, the fraction of the total transvalvular gradient represented by the subvalvular component increased from 48% to 66%. The only independent (negative) correlate of the cardiac output response was the exercise subvalvular gradient.

The examples illustrate the difficulty of obtaining “stationary” recordings in the beating heart. Translational motion of the catheter will result in pressure and velocity recordings over a finite segment of the axial stream. Sensor motion across the true valve orifice will give rise to hybrid waveforms. Therefore, we defined the true aortic pressure in a manner that was conditional on both pressure and velocimetric criteria. That the sequence of appearance of the subvalvular gradient was reproducible between patients supports the validity of our data. Given the linear dimension of the proximal sensing element (0.5 mm), we can only claim spatial precision to this degree. Because pressure in the short, tapering subvalvular zone is rapidly diminishing, even this small sensing element may not have the requisite spatial resolution to provide what is, admittedly, a point-by-point pressure determination.

In summary, we report the universal presence of invasively determined subvalvular pressure gradients in patients with severe aortic stenosis and no anatomic basis for subvalvular obstruction. These subvalvular gradients constitute approximately half of the total measured transvalvular pressure gradient and increase further with exercise. The extent of cardiac output increase on exercise is inversely related to this subvalvular gradient.

References
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