Left Ventricular Ejection Time in Valvular Aortic Stenosis

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SUMMARY

Hemodynamic data obtained at cardiac catheterization from 40 patients with valvular aortic stenosis demonstrated that, although left ventricular ejection time was prolonged, the usual linear inverse relationship between heart rate and ejection time was preserved at a longer than normal mean ejection time. In contrast to this, the direct linear relationship between ejection time and stroke volume which exists in normal human subjects was totally obliterated in patients with aortic stenosis so that ejection time appeared to be totally unrelated to stroke volume. However, the degree of prolongation of left ventricular ejection time above that predicted from stroke volume (ΔLVET) was closely correlated with aortic valve area (AVA), so that aortic valve area could be predicted as AVA = 0.91 – 3.6 ΔLVET within 95% confidence limits of ±0.16 cm². Alternatively, if ejection time was not abnormally prolonged, it was possible to predict with 95% confidence that the aortic valve area was greater than 0.75 cm² in cross-sectional area and thus not within the range generally requiring surgical therapy.

Additional Indexing Words:
Duration of ejection  Systolic ejection period  Heart rate  Stroke volume
Aortic valve area

Valvular aortic stenosis results in characteristic distortion of the arterial systolic pulse with prolongation of the upstroke of the pulse and introduction of vibrations and a prominent anacrotic notch.1-4 In addition, the total duration of the arterial systolic pulse (which corresponds to left ventricular ejection time) is prolonged.5-6 Although previous studies have shown some degree of correlation between the systolic pressure gradient across the stenotic aortic valve and the left ventricular ejection time in patients with aortic stenosis, this relationship was not close enough to be of practical use in predicting the severity of aortic stenosis.5

The present study was designed to examine the characteristics of the prolongation of left ventricular ejection time in patients with valvular aortic stenosis, and to determine whether this prolongation of ejection time could be correlated with the severity of the aortic stenosis. Studies were performed using data obtained during cardiac catheterization where the left ventricular ejection time could be precisely defined, and so that simultaneously obtained hemodynamic measurements would be available for study.

Methods

Data were obtained from 40 patients with isolated valvular aortic stenosis during diagnostic cardiac catheterization. Patients ranged in age from 16 to 72 years. All patients had clinical evidence of valvular aortic stenosis which was confirmed by cardiac catheterization. Twenty-three patients had no aortic insufficiency by clinical examination and aortography, while 17 patients had 1+ aortic insufficiency (defined as a barely discernible blush of contrast material in the left ventricular outflow tract during diastole which cleared with the first subsequent ventricular contraction). Patients with greater degrees of aortic insufficiency were eliminated from the study because of the previously documented prolongation of ejection time produced by aortic insufficiency.5-7 Patients with detectable mitral valvular disease were excluded from this study. All patients were in sinus rhythm.

Right heart catheterization was performed using a median basilic or cephalic vein. For pressure measurements the ascending aorta was catheterized either with a no. 5 French thin-wall Teflon catheter introduced percutaneously through a brachial artery by the Seldinger technic or with a no. 8 French Lehman catheter introduced percutaneously through a femoral...
artery. Left ventricular pressure measurements were obtained either by retrograde passage across the aortic valve of a similar Teflon catheter introduced through the brachial artery of the opposite arm or by means of the Brockenbrough transseptal technic. Pressures were measured simultaneously using Statham P23Db pressure transducers. Data were recorded on an Electronics for Medicine model DR-12 optical recorder at a paper speed of 100 mm/sec. Cardiac output was determined by the Fick method, using the Van Slyke manometric apparatus for determination of oxygen content of pulmonary artery and aortic blood specimens. Prior to termination of study, left ventriculography was performed using either a Brockenbrough transseptal catheter or a no. 8 French polyethylene catheter advanced from a femoral artery in a retrograde manner across the aortic valve. Ascending aortography was performed in each patient using either a no. 8 French Lehman catheter or a no. 8 French polyethylene catheter introduced via a femoral artery. Injections of 45–55 ml of 75% sodium diatrizoate were delivered within 1.2 sec while 35-mm cineangiography was performed at 60 frames/sec in the left posterior oblique position.

Since no significant difference was found between data from patients with no detectable aortic insufficiency and those with 1+ aortic insufficiency, data from all patients were considered together. Heart rate and left ventricular and ascending aortic pressures were measured directly from the recordings. Left ventricular ejection time per beat was measured as the interval from the beginning of the upstroke of the aortic pressure pulse to the dicrotic notch. Although the incisura of the dicrotic notch is sometimes obscured in the external carotid pulse tracing of patients with aortic stenosis making determination of the end of ejection difficult, the central aortic pressure recordings obtained in the present study invariably showed an identifiable dicrotic notch so that ejection times could be measured in all patients. The mean systolic pressure gradient across the aortic valve was determined by planimetric integration of the area between the left ventricular and aortic pressure tracings during systole divided by the left ventricular ejection time. Individual measurements were performed on four consecutive heart beats.

Aortic valve area was calculated according to the formula of Gorlin and Gorlin: AAVA = \( \frac{Q}{44.5 \cdot \text{VMSG}} \), where Q = systolic aortic blood flow rate (ml/sec) determined as cardiac output (ml/min) divided by systolic ejection time (sec/min), and MSG = mean pressure gradient measured across the aortic valve during systole.

Left ventricular ejection time (LVET) predicted from heart rate (HR) was calculated using the formula of Weissler et al.: LVET = 0.413 – 0.0017 HR for males, and LVET = 0.418 – 0.0016 HR for females. Left ventricular ejection times predicted from stroke volume (SV) were calculated according to the formula of Harley, Starmer, and Greenfield: LVET = 0.106 + 0.0020 SV. Paired data analysis using Student’s t test and linear regression analysis were carried out using standard statistical methods.

Results

Clinical and hemodynamic data are shown in table 1. Heart rates ranged from 51 to 107 beats/min while cardiac outputs ranged from 2950 to 7300 ml/min. Left ventricular ejection times ranged from 0.280 to 0.395 sec (mean ± sd = 0.330 ± 0.030 sec) while the mean systolic gradient across the aortic valve ranged from 29 to 97 mm Hg (mean = 63 ± 16 mm Hg). Aortic valve area ranged from 0.24 to 0.93 cm² (mean = 0.57 ± 0.18 cm²).

Left ventricular ejection time was plotted against heart rate to determine whether the regular relationship between ejection time and heart rate previously described by Weissler et al. in normal individuals also existed in patients with aortic stenosis. As shown in figure 1, all but one of the patients with aortic stenosis had ejection times significantly longer than predicted from heart rate. However, it is apparent that an inverse relationship between ejection time and heart rate was preserved in these patients with aortic stenosis, although the mean ejection time was prolonged. No difference was observed in this relationship between patients with normal or with abnormally elevated left ventricular end-diastolic pressures (fig. 1). There was no significant correlation between the degree of prolongation of left ventricular ejection time and either cardiac output or mean aortic valve systolic pressure gradient.

When left ventricular ejection time was plotted against stroke volume, it was found that the progressive increase in ejection time which normally occurs with increasing stroke volume (described by Weissler et al. and Harley et al.) was absent in

![Figure 1](https://example.com/figure1.png)
these patients with aortic stenosis (fig. 2). Unlike the plot of ejection time against heart rate where a regular relationship was preserved at a longer than normal mean ejection time, the relationship between ejection time and stroke volume was totally obliterated. Mean ejection time for patients with stroke volumes above 50 ml/beat was 0.330 ± 0.020 sec while mean ejection time for patients with stroke volumes below 50 ml/beat was 0.320 ± 0.030 sec, not significantly different (P > 0.5).

To determine whether the degree of systolic pressure gradient across the stenotic aortic valve resulted in a predictable prolongation of ejection time, mean aortic valve systolic pressure gradient was plotted against ejection time (fig. 3). Ejection time generally increased with increasing aortic valve pressure gradients. This relationship, although statistically significant, was of no predictive value with a correlation coefficient of only r = 0.55.

An attempt was made to determine whether the degree of prolongation of ejection time could be related to computed aortic valve area. For each patient a predicted ejection time was computed from heart rate according to the equation of
Weissler et al. This value was subtracted from the actual ejection time measured for that patient, and the resulting deviation of the ejection time from the predicted value was plotted against aortic valve area (fig. 4). A relatively poor inverse relationship was found between aortic valve area and the deviation of the measured ejection time from that predicted from heart rate (correlation coefficient \( r = -0.52 \)). It may be seen in figure 4 that one reason for the wide scatter of these variables was that the relationship demonstrated considerable sensitivity to aortic blood flow. Thus, if patients were divided into two groups with cardiac indexes above and below 2500 ml/min/m\(^2\), each individual group demonstrated a considerably improved correlation between aortic valve area and deviation of ejection time from that predicted from heart rate.

In order to exploit this dependency on aortic blood flow, aortic valve area was plotted against the prolongation of ejection time above that predicted by stroke volume (fig. 5). The prolongation of ejection time was determined by computing a predicted ejection time from stroke volume for each patient according to the formula of Harley et al.\(^9\) and subtracting this predicted value from the actual measured ejection time. This plot shows that aortic valve area was closely correlated with the degree of prolongation of ejection time above that predicted from stroke volume with a correlation coefficient of \( r = -0.91 \). The prolongation of ejection time predicted aortic valve area within 95% confidence limits of 0.16 cm\(^2\). When a graph was constructed encompassing these 95% confidence limits for aortic valve area, it was noted that if ejection time was not prolonged above that appropriate for the observed stroke volume the stroke valve area would be greater than 0.75 cm\(^2\) 95% of the time (fig. 6).

In order to test the validity of this relationship between prolongation of ejection time and aortic valve area, cardiac catheterization data were obtained from 25 additional patients with isolated valvular aortic stenosis and fitted to the graph (fig. 6). All but one of these patients fell within the previously defined 95% confidence limits, thus validating the ability of prolongation of ejection time to predict aortic valve area within the proposed confidence limits.

**Discussion**

Previous studies of Weissler et al.\(^5,11\) and Harley et al.\(^9\) have shown that in normal subjects left
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Figure 5

Relationships observed between computed aortic valve area and the difference between measured left ventricular ejection time and ejection time predicted from stroke volume by the formula of Harley and associates.6 9

Ventricular ejection time is a closely regulated physiologic variable which bears a predictable relationship to stroke volume and heart rate. Weissler et al.6 9 have shown that even in patients with congestive heart failure or mitral valve disease (when stroke volume tends to be abnormally depressed) the left ventricular ejection time is depressed to a commensurate degree so that the normal stroke volume-ejection time relationship is preserved. Thus, stroke volume appears to be a fundamental determinant of left ventricular ejection time.

It was thus of considerable interest that ejection time was prolonged out of proportion to both stroke volume and heart rate in patients with valvular aortic stenosis. The inverse relationship between heart rate and ejection time was still apparent in these patients, but at a considerably longer than normal mean ejection time. However, the close direct relationship which normally exists between ejection time and stroke volume was totally obliterated in patients with aortic stenosis. Of interest was the fact that the observed left ventricular ejection times were appropriate for stroke volumes greater than 100 ml, but as stroke volumes were depressed below this level there was no significant decrease in left ventricular ejection time. This suggests that the perturbation of the normal stroke volume-ejection time relationship in patients with aortic stenosis does not result from a uniform prolongation of ejection time, but rather from retention of an ejection time appropriate for a normal or large stroke volume even after the stroke volume becomes abnormally depressed. Previous studies have documented that cardiac index (and thus stroke volume) frequently is depressed in patients with moderate-to-severe aortic stenosis.12 13

In an attempt to determine whether congestive failure superimposed upon aortic stenosis would further alter left ventricular ejection time, ejection times were compared in patients having normal left ventricular end-diastolic pressures ( \( \leq 13 \) mm Hg) with those in patients having abnormally elevated end-diastolic pressures ( \( > 13 \) mm Hg). Although left ventricular end-diastolic pressure is not a precise indicator of left ventricular function, it might be expected to provide a rough separation of patients on the basis of ventricular function. No difference was found in the relationship of ejection time to either heart rate or stroke volume between patients with normal and those with elevated left ventricular end-diastolic pressures. Thus, the presence of elevated left ventricular filling pressures did not influence left ventricular ejection time in these patients. Similarly, in patients without aortic valve disease, Weissler et al.6 9 found that the

Figure 6

The shaded area indicates the 95% confidence limits within which the deviation of measured left ventricular ejection time from ejection time predicted from stroke volume (\( \Delta \text{LVET} \)) predicted aortic valve area (AVA). Individual data points represent measurements from 25 additional patients which were used to test the validity of this relationship.
normal relationship between stroke volume and ejection time was not altered by the presence of congestive failure.

Patients with coronary artery disease and angina pectoris have been reported to have a slightly longer left ventricular ejection time at rest than normal subjects. Six of the present patients underwent coronary arteriography after hemodynamic data had been obtained. Three (patients 30, 31, and 36) had no significant coronary artery disease demonstrated, while three (patients 28, 32, and 33) had at least 75% obstruction of one or more major coronary arteries. Heart rate, stroke volume, mean aortic systolic pressure gradient, left ventricular ejection time, and aortic valve area were similar in these two groups. There was no significant difference between patients with normal coronary arteries and those with coronary artery disease in the degree of prolongation of left ventricular ejection time above that predicted from either heart rate or stroke volume. Although these findings suggest that coronary artery disease does not alter the relationships between left ventricular ejection time and other hemodynamic variables in patients with aortic stenosis, larger numbers of patients must be studied to substantiate this conclusion.

Parisi et al. reported finding a close relationship between cardiac index and "rate-corrected duration of ejection" (computed as observed LV ejection time/LV ejection time predicted from heart rate according to Weissler et al. with a correlation coefficient r = 0.90 for 11 patients with aortic stenosis. In contrast to this, a similar regression analysis performed on the present 40 patients with aortic stenosis showed no significant relationship between these two variables with a correlation coefficient of r = 0.03. Part of this disparity may be explained by the fact that Parisi and associates selected patients on the basis of the surgical condition of their stenotic aortic valve. Thus, their regression analysis included preoperative data only from patients who subsequently underwent replacement of their aortic valve with a Starr-Edwards prosthesis, while the present study included all patients with isolated aortic stenosis. Nevertheless, we have been unable to confirm any significant relationship between left ventricular ejection time or "rate-corrected duration of ejection" and cardiac index in patients with valvular aortic stenosis.

Previous studies of patients with aortic stenosis have demonstrated a marked reduction of left ventricular ejection time, often to within the predicted normal range, following surgical replacement or repair of the stenotic valve. Thus, the prolongation of left ventricular ejection time appears to result directly from mechanical obstruction to left ventricular outflow, rather than from any predictable myocardial dysfunction. This prolongation of ejection time secondary to the increased left ventricular afterload imposed by the stenotic aortic valve is in agreement with the behavior of isolated myocardial papillary muscle where an inverse relationship between the rate of muscle shortening and afterload has been demonstrated. Similarly, Braunwald et al. demonstrated that in the stable isolated heart preparation of the dog marked elevation of left ventricular ejection pressure resulted in a lengthening of the duration of ejection.

The close relationship between the prolongation of left ventricular ejection time above that predicted from stroke volume makes it possible to predict with 95% confidence aortic valve area within ± 0.16 cm² by the simple measurement of cardiac output and duration of ejection or, if duration of ejection is not prolonged above the normal value for the measured stroke volume, to predict that the aortic valve area is greater than 0.75 cm² in cross-sectional area and not within the range generally considered to require surgical therapy. This relationship may thus be employed to estimate the severity of aortic stenosis without requiring left ventricular catheterization.

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