resting gradients across the LV outflow space generally are absent. The pseudoejection sounds in the present study were associated with patients who had consistently full SAM of the mitral leaflet obliterating the LV outflow space in all but two patients at rest and in all patients (with technically satisfactory echocardiograms) after provocative maneuvers. In contrast, only four of 13 patients without pseudoejection sounds demonstrated full SAM of the mitral leaflet reaching the septum even after provocative maneuvers. The remaining nine patients either lacked or had small and fragmentary SAM of the mitral leaflet at rest. These findings also support the view that patients with pseudoejection sounds are more likely to have higher LV outflow gradients.

It is not certain why some patients with clinical and echocardiographic evidence of outflow obstruction failed to demonstrate a pseudoejection sound. In some instances a prominent murmur may have masked sound transients, and in others the flow dynamics may have failed to provide sufficient energy to produce a discrete sound. The latter hypothesis can be investigated further by obtaining intracardiac phonocardiograms in the left ventricular outflow tract in patients with IHSS.

Acknowledgment

The authors are grateful to Dr. Paul N. Yu for reviewing this manuscript. The authors also express their appreciation to Mrs. Linda Sylvester for her expert technical assistance in performing the phonocardiograms, and to Mrs. Kaye Cherry for her secretarial help.

Echocardiographic Assessment of the Level of Cardiac Compensation in Valvular Heart Disease

ANDREW ROSENBLETT, M.D., RALPH CLARK, M.D., JUDITH BURGESS, B.A., AND KEITH COHN, M.D.

SUMMARY  The level of cardiac compensation in valvular disease was studied by relating echocardiographic and cardiac catheterization measurements. Three groups — compensated, intermittently compensated, and decompensated — were defined according to the left ventricular angiographic pattern and cardiac output. The echocardiographic ejection indices, percent left ventricular minor diameter shortening, ejection fraction, and fiber shortening rate were significantly higher than normal in compensated mitral regurgitation, lower then normal in compensated aortic stenosis, and within normal limits in compensated aortic insufficiency. In the decompensated state these indices were depressed. Intermediate compensation was best recognized by combining several echocardiographic variables into an echocardiographic score based on multivariate discriminant function analysis.

Thus, the compensated volume overload states (aortic and mitral regurgitation) and pressure overload state (aortic stenosis) have separate sets of “normal” echocardiographic values; low ejection indices characterize the decompensated group, while recognition of intermediate compensation requires analysis of multiple echocardiographic variables.

OVER THE LAST SEVERAL YEARS, echocardiography has facilitated the differential diagnosis of various types of valvular and congenital heart disease. Difficulties in assessing the degree of cardiac compensation in valvular dis-

References

which separate patients with valvular disease into different levels of cardiac compensation or decompensation. We have characterized myocardial function in individuals with stenotic or regurgitant lesions according to established hemodynamic and angiographic criteria, grouped these individuals by their level of performance, and then related these groups to a variety of standard echocardiographic measurements. In addition, we have attempted to introduce computer-based multivariate analysis to refine the echocardiographic separation of the levels of ventricular compensation.

Methods

Patient Selection

The study was comprised of patients admitted for evaluation of valvular heart disease, and included 47 with valvular aortic stenosis, 31 with aortic insufficiency, and 41 with mitral regurgitation. Each patient had combined hemodynamic study with cardiac catheterization, left ventricular cineangiography, and echocardiography. Patients with multiple valve abnormalities, combined stenosis and insufficiency, individuals with clinical or angiographic evidence of coronary disease with segmental disorders of left ventricular contraction, patients with valve prostheses, paradoxical interventricular septal motion, and technically unacceptable echocardiograms were excluded. All the subjects were adults, ranging in age from 19 to 84 years, except for one youth of 12. Echocardiographic data were also collected in our laboratory on 53 normal subjects without clinical evidence of heart disease.

In the initial phase of the investigation, 74 patients were studied retrospectively, correlating the echocardiographic and hemodynamic variables, with the purpose of establishing echocardiographic criteria which best characterized different levels of hemodynamic function. Once these criteria were established, a blind, prospective study was carried out in an additional 45 consecutive patients to validate the newly defined echocardiographic criteria of ventricular compensation.

Of 47 patients with pure valvular aortic stenosis (28 in the initial phase, 19 studied prospectively), the aortic valve area estimated by the Gorlin formula averaged 0.6 cm² (range 0.2 to 0.9 cm²).

Twenty-one patients studied retrospectively had isolated aortic insufficiency, this being acute or subacute and related to infectious endocarditis in seven. The remaining 14 were judged on historical, clinical, surgical, and/or pathologic grounds to have chronic regurgitation, related to rheumatic disease in six, lues in one, Marfan's syndrome in three, bicuspid aortic valve in two, a sinus of Valvula aeurism in one, and no definable etiology in one. In the prospective phase, aortic regurgitation was related to infectious endocarditis in two, to rheumatic disease in three, to aortic root dissection in one, and to no determined etiology in four. The degree of aortic regurgitation was judged to be severe (3–4+) on angiogram in all patients.

The etiologic basis determined by echocardiographic, surgical, or pathologic analysis in the 25 initial phase patients with mitral regurgitation included ten with mitral valve prolapse and intact chordae (i.e., myxomatous degeneration of the chordae and leaflets), eight with prolapse due to ruptured chordae tendineae, three with rheumatic mitral regurgitation, three with papillary muscle dysfunction (these patients having coronary disease but with symmetrically contracting left ventricular patterns), and one with infectious endocarditis. In the prospective study, two patients had mitral prolapse with intact chordae, ten had prolapse with ruptured chordae, one patient had rheumatic mitral regurgitation, and three had no determined etiology.

Hemodynamic Grouping

The forward, effective cardiac output was determined by direct Fick method, and the left ventricular end-diastolic pressure was utilized as a measure of LV "filling pressure.” The 9% potential error of the Fick method in our laboratory was minimized by corroborative dye-dilution estimates of output in most cases. Biplane LV cineangiograms were performed in the 30° right and 60° left anterior oblique position, using 76% Renografin recorded at 50 frames/second.

Indices of left ventricular contraction were obtained by tracing end-systolic and end-diastolic ventricular contours, excluding extra- and postextrasystolic beats. The long axis of the ventricle in the RAO position was determined by drawing a line from the mid-point of the aortic valve plane to the left ventricular apex, and the minor diameter (D) was constructed as a perpendicular to this long axis at its midpoint. Three to four beats were averaged in these 14 patients with atrial fibrillation. The earliest beats following injection which showed good opacification were chosen for analysis to minimize the initial effects of the dye. Measures of ventricular performance included: 1) angiographic ejection fraction (EFangio), derived using the single plane method of Greene; 2) percent minor diameter shortening (%Dangio), derived from the RAO view as the percent change in minor axis length; and 3) mean velocity of circumferential fiber shortening (Vefangio). The LV ejection time used in this measurement was estimated from the number of cineangiographic frames between end-diastole and systole. An arbitrary time period was not subtracted to correct for isovolumic systole, since the presence and duration of this time interval varies considerably among individuals, the different disease states (and is absent in mitral regurgitation), and in left ventricular dysfunction.

Patient Grouping

Three patient groups were defined on the basis of hemodynamic and angiographic performance:

1) Compensated. These were patients found to have normal cardiac performance in the face of valvular disease. Hence, all had a cardiac index above 2.5 L/min/m², and normal angiographic ejection indices: an angiographic ejection fraction (EFangio) exceeding 55%, and angiographic percent minor diameter shortening (%Dangio) in excess of 25%.

2) Intermediate Compensation. These patients had partial hemodynamic dysfunction, with a cardiac index below 2.5 L/min/m² (range 1.6–2.4 L/min/m²), but continued to have normal LV contractile patterns, with EFangio and %Dangio remaining above the aforementioned values. The AVO₂ differences were appropriately increased (≥ 5 Vol. %) in all patients.

3) Decompensated. This group encompassed those patients with impaired LV contractile function, apparent in
the form of subnormal EF$_{\text{angio}}$ and %D$_{\text{angio}}$. All had a cardiac index under 2.5 L/min/m$^2$, with the exception of three patients with aortic insufficiency and markedly enlarged LV dimensions. Heart rates did not differ significantly among the three groups. Several patients were taking digoxin, an agent capable of modifying the level of compensation; no patient was on propranolol.

Echocardiographic Analysis

Tracings were obtained in the standard manner, within three days of angiographic study, using a Smith-Kline Ekoline instrument interfaced with an Electronics-for-Medicine VR-6 strip chart recorder. Paper speeds of both 50 and 100 mm/sec were used to facilitate measurement of LV ejection time. Left ventricular internal dimensions were recorded just below the tip of the anterior mitral leaflet, from areas where only fragments of the leaflet echoes were visible. Specific measurements were made as follows, averaging multiple cardiac cycles (ten when atrial fibrillation was present).

1) **Left ventricular dimensions** (fig. 1). Internal LV end-diastolic minor diameter (EDD) was measured at the onset of the electrocardiographic QRS complex. Left ventricular end-systolic diameter (ESD) was measured between the LV posterior wall endocardium at its most anterior position during systole and the interventricular septal endocardium. Left ventricular end-systolic and end-diastolic volumes and ejection fraction were calculated by the method of Teichholz.\(^6\)

2) **Measurements of mitral valve motion.** These included total anterior mitral leaflet excursion (CE amplitude), initial diastolic closing EF slope, and the PR-AC interval, a previously reported index of ventricular “compliance.”

3) **The amplitude of aortic root excursion (AO),** determined as the degree of mobility of the ascending aorta between systole and diastole.

Derived echocardiographic indices of LV performance included:

1) **Left ventricular minor diameter percent shortening** (%D$_{\text{echo}}$), where

\[
%D_{\text{echo}} = \frac{\text{EDD} - \text{ESD}}{\text{EDD}} \times 100.
\]

2) **Echocardiographic ejection fraction,** where

\[
\text{EF}_{\text{echo}} = \frac{\text{EDV} - \text{ESV}}{\text{EDV}} \times 100.
\]

3) **Mean velocity of circumferential fiber shortening,** where Vc$_{\text{echo}} = \%D_{\text{echo}}/\text{LV ejection time} \ (\text{circ/sec}).$ The echocardiographic LV ejection time (fig. 1) was measured from the initial anterior motion of the LV posterior wall endocardium at end-diastole to its earliest point of maximal anterior excursion. This method of measurement was chosen for the sake of uniformity, since carotid arterial tracings, which provide a more accurate LV ejection time determination, were not routinely added to earlier echocardiographic tracings in our laboratory. Blind remeasurement in 50 patients by the same observers yielded a reproducibility of ± 6% in LVET measurement; greater reproducibility was noted in those patients with greater LV posterior wall amplitudes, as seen in the volume overloaded states. No correction for isovolumic systole was made (see above).\(^3\) %D$_{\text{echo}},$ EF$_{\text{echo}},$ and Vc$_{\text{echo}}$ are collectively referred to as “echocardiographic ejection indices.”

4) **Normalized velocity of posterior wall** ($V_p$) and interventricular septal ($V_{ivs}$) contraction were calculated by the method of Quinones et al.,\(^8\) where $V_p = \text{PWA}/\text{EDD} \times \text{LVET}$ and $V_{ivs} = \text{IVSA}/\text{EDD} \times \text{LVET} \ (\text{sec}^{-1}).$

Methods of Analysis

After evaluating the linear correlation of echocardiographic and hemodynamic parameters, the data were entered into a computer program for multivariate separation of groups using stepwise linear discriminant function analysis.\(^9\) Upon preliminary inspection of the data, nine echocardiographic variables were chosen which provided the best potential separation of patients: %D, Vc, EF, CE, AO, PWA, PWT, EDD, and EF slope. From among these, the computer program then selected, in stepwise fashion, the five variables which maximally separated the groups of patients being considered (see Appendix for details).

To validate the method, patients studied prospectively were classified blindly according to the criteria established in the initial 74 patients, without knowledge of their hemodynamic or angiographic findings.
Simple and multiple linear regression analyses were also applied to the determination of the echocardiographic correlates of left ventricular filling pressure, cardiac index, and angiographically determined ejection phase indices. The significance of differences of echocardiographic measurements and group means (table 1) was tested by a nonpaired t-test.

Results

Development of Echocardiographic Criteria for Estimating Hemodynamic Groups

Left Ventricular Ejection Phase Indices

The echocardiographic variables which most effectively separated patient groups were the LV ejection phase indices. A high correlation was found among these three indices, '%Decho and EFecho (r = 0.96), %Decho and Vcfecho (r = 0.94), and Vcfecho and EFecho (r = 0.91) (fig. 2). Hence, utilizing any one of the ejection indices provides a reasonable estimate of myocardial function, and combining two or three of these variables added little to group separation. Vpaw correlated less well with the other echocardiographic ejection indices: Vcfecho (r = 0.61) and %Decho (r = 0.52). Normalized mean rate of circumferential fiber shortening (Vcf) was not found superior to those measures of simple extent of shortening (%Decho and EFecho) in distinguishing compensated and decompensated levels of left ventricular function (see below), although it remains possible that utilization of an alternative means of measuring LV ejection time such as carotid pulse tracing would have modified the results. %Decho is the simplest and most reliably measured of the echocardiographic indices, and greatest emphasis is placed on this variable in the present study.

Table 2. Inter-Disease Differences

<table>
<thead>
<tr>
<th>Echo variable</th>
<th>Comp AI</th>
<th>Comp MR</th>
<th>Comp AS</th>
<th>AI vs AS</th>
<th>AS vs MR</th>
<th>AI vs MR</th>
</tr>
</thead>
<tbody>
<tr>
<td>%D (%)</td>
<td>36 ± 2</td>
<td>42 ± 3</td>
<td>29 ± 2</td>
<td>&lt;0.007</td>
<td>&lt;0.002</td>
<td>NS</td>
</tr>
<tr>
<td>EF (%)</td>
<td>65 ± 2</td>
<td>70 ± 3</td>
<td>54 ± 2</td>
<td>&lt;0.004</td>
<td>&lt;0.001</td>
<td>NS</td>
</tr>
<tr>
<td>Vcf (circ/sec)</td>
<td>1.34 ± 0.05</td>
<td>1.58 ± 0.14</td>
<td>0.87 ± 0.05</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>NS</td>
</tr>
<tr>
<td>CE (mm)</td>
<td>27 ± 2</td>
<td>33 ± 2</td>
<td>21 ± 1</td>
<td>&lt;0.01</td>
<td>&lt;0.001</td>
<td>&lt;0.03</td>
</tr>
<tr>
<td>PWA (mm)</td>
<td>15 ± 1</td>
<td>14 ± 1</td>
<td>10 ± 1</td>
<td>&lt;0.001</td>
<td>&lt;0.002</td>
<td>NS</td>
</tr>
<tr>
<td>IVSA (mm)</td>
<td>13 ± 1</td>
<td>12 ± 1</td>
<td>7 ± 1</td>
<td>&lt;0.002</td>
<td>&lt;0.006</td>
<td>NS</td>
</tr>
<tr>
<td>PWT (mm)</td>
<td>13 ± 1</td>
<td>10 ± 1</td>
<td>13 ± 1</td>
<td>NS</td>
<td>&lt;0.05</td>
<td>NS</td>
</tr>
<tr>
<td>EF slope (mm/sec)</td>
<td>114 ± 20</td>
<td>110 ± 17</td>
<td>61 ± 12</td>
<td>&lt;0.03</td>
<td>&lt;0.02</td>
<td>NS</td>
</tr>
<tr>
<td>EDD (cm)</td>
<td>6.4 ± 0.2</td>
<td>6.0 ± 0.3</td>
<td>5.5 ± 0.3</td>
<td>&lt;0.02</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>AO (mm)</td>
<td>9 ± 1</td>
<td>9 ± 1</td>
<td>8 ± 1</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
</tbody>
</table>

Abbreviations: Comp = compensated; AI = aortic insufficiency; MR = mitral regurgitation; AS = aortic stenosis. Echocardiographic variables as defined in text. ± 1 standard error of the mean.
Compensated Left Ventricular Function.

Interdisease Differences (table 2, fig. 3)

Echocardiographic ejection indices in normal subjects were similar to those obtained by other workers.\(^5\) Interdisease Differences were compensated however, the percentage of mean velocity of circumferential fiber shortening (\(V_{\text{cfecho}}\)) and ejection fraction (\(\text{EF}_{\text{echo}}\)) was significantly lower in the decompensated condition compared with the compensated group (table 3 and fig. 4). Patients with compensated valvular aortic stenosis had \(\%\text{Decho} = 16 \pm 1\%\) (range 13–18%), \(\text{EF}_{\text{echo}} = 33 \pm 1\%\) (28–37%), and \(V_{\text{cfecho}} = 0.51 \pm 0.02\) circ/sec (0.40–0.60 circ/sec). Patients with compensated mitral regurgitation had \(\%\text{Decho} = 23 \pm 4\%\) (range 9–31%), \(\text{EF}_{\text{echo}} = 45 \pm 6\%\) (25–57%), and \(V_{\text{cfecho}} = 0.86 \pm 0.16\) circ/sec (0.29–1.16 circ/sec). Patients with compensated aortic regurgitation had \(\%\text{Decho} = 23 \pm 2\%\) (range 21–29%), \(\text{EF}_{\text{echo}} = 46 \pm 3\%\) (40–55%) and \(V_{\text{cfecho}} = 0.85 \pm 0.05\) circ/sec (0.75–1.00 circ/sec). Certain other echocardiographic variables differed significantly between compensated and decompensated states (table 3); however, considered individually, none improved the differentiation of levels of function achieved by the echocardiographic ejection indices. Of particular note was the lack of significant difference in diastolic left ventricular chamber size between compensated and decompensated patients.

2) Intermediate compensation. In contrast to compensated and decompensated groups, identification of the intermediate ranges of ventricular function is not so reliably

Intradisease Differences.

Distinguishing Levels of Compensation

1). Comparison of compensated and decompensated states. When each type of valvular disease is looked at separately, it was evident that the ejection indices were significantly lower in the decompensated condition compared with the compensated group (table 3 and fig. 4). Patients with compensated valvular aortic stenosis had \(\%\text{Decho} = 16 \pm 1\%\) (range 13–18%), \(\text{EF}_{\text{echo}} = 33 \pm 1\%\) (28–37%), and \(V_{\text{cfecho}} = 0.51 \pm 0.02\) circ/sec (0.40–0.60 circ/sec). Patients with compensated mitral regurgitation had \(\%\text{Decho} = 23 \pm 4\%\) (range 9–31%), \(\text{EF}_{\text{echo}} = 45 \pm 6\%\) (25–57%), and \(V_{\text{cfecho}} = 0.86 \pm 0.16\) circ/sec (0.29–1.16 circ/sec). Patients with compensated aortic regurgitation had \(\%\text{Decho} = 23 \pm 2\%\) (range 21–29%), \(\text{EF}_{\text{echo}} = 46 \pm 3\%\) (40–55%) and \(V_{\text{cfecho}} = 0.85 \pm 0.05\) circ/sec (0.75–1.00 circ/sec). Certain other echocardiographic variables differed significantly between compensated and decompensated states (table 3); however, considered individually, none improved the differentiation of levels of function achieved by the echocardiographic ejection indices. Of particular note was the lack of significant difference in diastolic left ventricular chamber size between compensated and decompensated patients.

2) Intermediate compensation. In contrast to compensated and decompensated groups, identification of the intermediate ranges of ventricular function is not so reliably
Table 3. Intra-Disease Differences

<table>
<thead>
<tr>
<th>Disease</th>
<th>Echo variable</th>
<th>Compensated</th>
<th>Decompensated</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>AS</td>
<td>%ΔD (%)</td>
<td>29 ± 2</td>
<td>16 ± 1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>EF</td>
<td>54 ± 2</td>
<td>33 ± 1</td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Vcf (circ/sec)</td>
<td>0.87 ± 0.05</td>
<td>0.51 ± 0.02</td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>AO (mm)</td>
<td>8 ± 1</td>
<td>5 ± 1</td>
<td>&lt;0.05</td>
<td></td>
</tr>
<tr>
<td>PWT (mm)</td>
<td>13 ± 1</td>
<td>17 ± 1</td>
<td>&lt;0.02</td>
<td></td>
</tr>
<tr>
<td>AI</td>
<td>%ΔD (%)</td>
<td>36 ± 2</td>
<td>23 ± 1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>EF</td>
<td>65 ± 2</td>
<td>46 ± 3</td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Vcf (circ/sec)</td>
<td>1.34 ± 0.05</td>
<td>0.85 ± 0.05</td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>AO (mm)</td>
<td>10 ± 1</td>
<td>6 ± 1</td>
<td>&lt;0.02</td>
<td></td>
</tr>
<tr>
<td>PWT (mm)</td>
<td>27 ± 2</td>
<td>22 ± 3</td>
<td>&lt;0.04</td>
<td></td>
</tr>
<tr>
<td>MR</td>
<td>%ΔD (%)</td>
<td>42 ± 3</td>
<td>23 ± 4</td>
<td>&lt;0.004</td>
</tr>
<tr>
<td>EF</td>
<td>70 ± 3</td>
<td>45 ± 6</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Vcf (circ/sec)</td>
<td>1.58 ± 0.14</td>
<td>0.86 ± 0.16</td>
<td></td>
<td>&lt;0.008</td>
</tr>
<tr>
<td>AO (mm)</td>
<td>9 ± &lt;1</td>
<td>6 ± 1</td>
<td>&lt;0.01</td>
<td></td>
</tr>
<tr>
<td>CE (mm)</td>
<td>33 ± 2</td>
<td>25 ± 2</td>
<td>&lt;0.02</td>
<td></td>
</tr>
<tr>
<td>PWA (mm)</td>
<td>14 ± 1</td>
<td>9 ± 1</td>
<td>&lt;0.002</td>
<td></td>
</tr>
<tr>
<td>IVSA</td>
<td>12 ± 1</td>
<td>7 ± 1</td>
<td>&lt;0.03</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: AS = aortic stenosis; AI = aortic insufficiency; MR = mitral regurgitation; echocardiographic variables as defined in text.

made; analysis of multiple echocardiographic variables facilitates this distinction. Several points are noteworthy: first, the ejection phase indices of intermediate patients were similar to those of compensated patients in both aortic stenosis and aortic insufficiency, but were depressed in intermediate compared to compensated mitral regurgitation patients. Secondly, stepwise linear discriminant function analysis further enhanced distinction of the various levels of compensation. Of the echocardiographic ejection indices, %ΔΔecho alone was employed in this analysis, since it is the simplest to measure and EFecho and Vcfecho used alone or in combination with %ΔΔecho added little discriminating power. The intermediate level of compensation was least reliably distinguished in aortic stenosis, whereas the discriminant function analysis successfully classified over 90% of the intermediate mitral and aortic insufficiency patients (see Appendix).

- Compensated
- Decompensated

3) Echocardiographic prediction of left ventricular filling pressure and cardiac output. Echocardiographic left ventricular end-diastolic dimensions, posterior wall thickness, mitral valve closing, EF slope, mitral valve CE excursion, posterior wall amplitude of motion, aortic root amplitude of motion, and the echocardiographic ejection indices, considered individually or in multiples of from two to seven variables, failed to correlate with left ventricular filling pressure (multiple r for seven variables = 0.44). In addition, the derived PR-AC interval failed to correlate with left ventricular filling pressure (r = 0.03).

Certain echocardiographic measurements often considered to be influenced by cardiac index were evaluated. Neither the ejection indices (%ΔΔecho, EFecho, Vcfecho), nor measurements such as the aortic root amplitude of motion or mitral valve excursion (CE), correlated with cardiac index in linear fashion. In addition, the correlation coefficients between CE or aortic motion and stroke volume (based on the Fick method) were < 0.5. This was the case whether all patients, patients within each valvular disease state, or patients within a given level of ventricular function were considered. Similarly, the correlation of angiographic ejection indices with echocardiographic ejection indices was substantially poorer than has been reported in the literature4, 11, 13 (fig. 5), perhaps partially related to differences of heart rate and arterial pressure during the two procedures. Nonetheless, decompensated patients, those with low cardiac indices and poor contractile patterns, had depressed echocardiographic ejection indices, while compensated patients, with normal cardiac indices and contractile patterns, had normal echocardiographic ejection indices.

Prospective Study

On the basis of the echocardiographic criteria derived from the initial retrospective study, the “optimal” means of differentiating levels of myocardial compensation were tested. As shown in figure 6, a two-step procedure was employed, using %ΔΔecho as the first criterion, and then, whenever necessary, the multivariate echocardiographic score (see Appendix). All cases with left ventricular decompensation (17/17, 100%) were accurately predicted, while 10/12 (83%) intermediate compensation patients and 14/16 (87%) compensated patients were correctly classified. Thus, 41/45 (91%) of all prospective cases were accurately grouped by echocardiogram.

Discussion

Assessing left ventricular function in patients with valvular heart disease has critical importance with both prognostic and therapeutic implications. Although no unequivocally valid index of left ventricular performance is available, most such assessments rely on invasive hemodynamic and angiographic measurements. A sensitive, yet simple, noninvasive means of estimating left ventricular function would clearly constitute a valuable asset to the clinician, and echocardiography appears at present to be the technique with the greatest likelihood of achieving this goal. Although several previous attempts have been made at evaluating functional impairment using echocardiographic measurements, this field of investigation remains far from completely developed5, 6, 8, 11-13, 16-18.
Classification of Left Ventricular Performance

In the present study we approach the problem of echocardiographic assessment of left ventricular function in patients with pressure or volume overloaded valvular disease states. Three levels of left ventricular compensation were defined by hemodynamic and angiographic means. This grouping, although somewhat arbitrary, is physiologically and clinically relevant, has been used previously,\(^6\) and does not impose the prior restraint of demanding linear correlation between echocardiographic and angiographic or hemodynamic measurements.

Hence, the compensated state is defined by a normal effective forward flow and normal left ventricular contractile pattern. In this state, the stress placed upon the heart by the stenotic or regurgitant valve lesions is overcome by several compensatory adjustments, among which are ventricular hypertrophy and dilatation, sarcomere replication, tachycardia, and the utilization of sympathetic reserves.\(^9\) These protective mechanisms are, by their very nature, inherently limited, and when their capacity is exceeded, the resting cardiac output may fall. This we have considered to be the intermediate level of compensation, in which myocardial contraction patterns remain normal, but the forward cardiac output is depressed. The more advanced degrees of cardiac failure occur when intrinsic myocardial cell contractility is disturbed. Thus, the decompensated state is defined primarily by a subnormal left ventricular contractile pattern, with an associated depression of cardiac output.

It is readily appreciated that any characterization of ventricular function is imperfect. Other means of estimating left ventricular function might have been based on the clinical level of disability, left ventricular filling pressure, various other measures of cardiac "performance," such as isovolumic phase indices, as well as the performance of the heart during the stress of exercise. Each of these, unfortunately, is influenced by a myriad of factors, including the degree of cardiac hypertrophy, diastolic compliance of the left ventricle, vascular volume, utilization of diuretics, and subjective interpretation of symptoms. The isovolumic phase indices of contractile function, moreover, are generally considered unreliable in detecting depressed contractile function,\(^20\) and may be inapplicable in volume overloaded regurgitant states. Thus, in view of the complexity potentially brought about by using these alternative estimates of myocardial performance, and because the cardiac output and ejection phase contractile indices have previously been shown to provide a practical and physiologically reasonable means of assessing the level of cardiac compensation in the basal state,\(^5\) these were utilized in the current investigation.

Echocardiographic Ejection Phase Indices

It was of interest, and in variance with other reports in the literature,\(^6\) that, in the present study, the linear correlation of echocardiographic ejection phase indices, \(\%D_{\text{echo}}\), \(\text{EF}_{\text{echo}}\), and \(\text{Vcf}_{\text{echo}}\) with similar angiographic measurements was poor. Such a finding is not altogether unexpected, since only a limited "ice pick" view of the heart is "seen" by echocardiography, and the interventricular septal and posterior left ventricular walls recorded using ultrasound differ from those regions of the left ventricle visualized in the

\[
\text{AORTIC STENOSIS}
\]
\[
\% D \geq 20 \% \quad \overbrace{\text{Int. or Comp.}}^\text{Echo Score} \quad \overline{\text{Compensated}} \quad \text{Hi} \quad \text{Intermediate}
\]
\[
\% D < 20 \% \quad \overbrace{\text{Decomp.}}^\text{Echo Score} \quad \overline{\text{Decompensated}}
\]

\[
\text{AORTIC INSUFFICIENCY}
\]
\[
\% D \geq 30 \% \quad \overbrace{\text{Int. or Comp.}}^\text{Echo Score} \quad \overline{\text{Compensated}} \quad \text{Hi} \quad \text{Intermediate}
\]
\[
\% D < 30 \% \quad \overbrace{\text{Decomp.}}^\text{Echo Score} \quad \overline{\text{Decompensated}}
\]

\[
\text{MITRAL REGURGITATION}
\]
\[
\% D \geq 35 \% \quad \overbrace{\text{Compensated}}^\text{Echo Score}
\]
\[
\% D < 35 \% \quad \overbrace{\text{Decomp.}}^\text{Echo Score} \quad \overline{\text{Decompensated}}
\]

\[
\text{FIGURE 6. Flow chart for prospective classification of LV function using the echocardiographic ejection index, } \%D_{\text{echo}}, \text{ and the echocardiographic score. Int = intermediate, Comp = compensated, Decomp = decompensated.}
\]
right and the left anterior oblique angiographic projections.

Of particular note, in addition, was the observation that each of these echocardiographic indices of left ventricular "function" correlated highly with the other, and none was found superior to the others in detecting functional impairment (fig. 2). Thus, although it has been reported that the mean rate of circumferential fiber shortening may detect left ventricular dysfunction in certain clinical situations when it is not evident from the other ejection indices,3, 5, 14 this circumstance did not pertain in our series. The three indices of contractile function tended, with few exceptions, to be concordantly normal or depressed in a given patient. It should be emphasized in this regard that left ventricular ejection time, necessary for the calculation of Vcfecho, is difficult to define or measure accurately in practical echocardiography. The range of ejection time varies widely in normal subjects and may be further altered by left ventricular disease.3, 4 Thus, assuming an arbitrary period for isovolumic systole, as has been previously done, may not be satisfactory.3 The linear correlation of normalized posterior wall velocity of contraction (Vw) with %Decho and Vcfecho was poorer than that found among Vcfecho, %Decho, and EFecho. Posterior wall velocity may not, in fact, reliably reflect the other echocardiographic ejection indices or left ventricular function, a point debated in recent investigations.6, 9, 13, 16, 21 Moreover, the problems and fallacies of echocardiographic estimation of ventricular volumes and ejection fraction have been extensively reviewed previously.6, 17, 22, 23 Thus, since the extent of minor diameter shortening expressed as a percentage (%Decho) is the simplest and quickest measurement and does not rely on a cubed function as does ejection fraction nor on measurement of the duration of LV ejection as does Vcfecho, %Decho is considered the ejection phase index most optimally suited for general use.11

Ejection Phase Indices in Valve Disease

Heretofore, it has been a general practice to define normality and abnormality of hemodynamic function in terms of a single range of values. Such an approach is potentially faulty, especially when dealing with different valvular disease categories. The extent and velocity of myocardial shortening are heavily influenced by wall stresses, loading conditions, and heart rate, so that change in pre- and afterload may affect the basal ejection indices of contractility. Hence, the systolic burden placed on the left ventricle in mitral regurgitation is markedly reduced, since the regurgitant volume is expelled into a low impedance, low pressure left atrial chamber, while systolic unloading is slight in aortic insufficiency where the left ventricle initiates ejection against the lowered aortic diastolic pressure.19, 25, 26 Aortic stenosis represents the other end of the spectrum, whereby a substantially elevated left ventricular pressure, especially in the absence of marked left ventricular hypertrophy, may raise afterload and thereby depress velocity and extent of myocardial shortening. Recent studies have investigated the effects of acutely altered loading conditions on the echocardiographic ejection indices.26, 27

In our study, then, the compensated level of myocardial function was manifested by ejection indices with separate sets of limits in each of the disease states under consideration: aortic stenosis, mitral and aortic regurgitation. We found that %Decho, EFecho, and Vcfecho fell below the currently accepted normal limits in compensated aortic stenosis, were augmented in compensated mitral regurgitation, and fell between the two, within the accepted range of normal, in compensated aortic insufficiency.

Decompensated and Intermediate States

Utilizing the above-mentioned levels of compensation for each of the diseases, we were then able to recognize "compensated" left ventricular function echocardiographically with a high degree of reliability. An important positive yield from the study was the recognition that, in spite of an imperfect point-for-point correlation between angiographic and echocardiographic measurements, the extremes of compensation and decompensation remain definable.

This apparent disparity is accounted for by two factors: 1) the level of compensation was defined in this study not only by the angiographic ejection fraction and percent minor diameter shortening, but also by the cardiac output. Echocardiographic estimates of %D and EF, therefore, appear to relate reasonably well to the combination of these measures of left ventricular performance; 2) as discussed above, the echocardiographic ejection indices have different limits in each of the valvular lesions. In the compensated state of mitral regurgitation, the echocardiographic %D ranges from 31–66%, while in aortic stenosis it ranges from 21–41%. Thus, of two patients with anapatic %D = 32%, one with mitral regurgitation might have an echocardiographic %D = 41% and one with aortic stenosis might manifest a 25% echocardiographic %D. In each instance, the patients were categorized as "compensated" within their respective disease states by the echocardiographic technique. The angiographic and echocardiographic ejection indices, therefore, tend to be concordant in appropriate compensated or decompensated groups (fig. 5), even though, as exemplified in the extreme cases cited, the angiographic and echocardiographic values may be dissimilar on a point-for-point basis.

Intermediate compensation patients with, by definition, normal angiographic contractile patterns had normal echocardiographic ejection indices in aortic stenosis and aortic insufficiency. Patients with mitral incompetence having intermediate levels of compensation, however, were found to have subnormal ejection phase indices measured echocardiographically, perhaps explicable on the basis of the compensatory mechanism called into play in mitral regurgitation. A hyperdynamic left ventricular wall motion represents one of the more important physiologic adjustments occurring in mitral insufficiency,29 and one commonly sees augmented septal and posterior LV wall amplitudes of motion on the echocardiographic tracing.1, 15 These indices tend to decrease from compensated to intermediate and intermediate to decompensated levels, although only the compensated vs decompensated values reach statistical significance (table 1). It seems reasonable to propose, therefore, that the echocardiogram provides a sensitive means of detecting subtle degrees of diminished cardiac function, in the form of a slight diminution in interventricular septal and posterior left ventricular wall contractions.

Evaluation of Other Echocardiographic Variables

In attempting to distinguish different levels of cardiac compensation, other echocardiographic variables were
analyzed, including amplitudes of aortic root motion and mitral CE excursion, the degree of left ventricular dilatation as evidenced by the end-diastolic dimension, posterior wall thickness and motion, the mitral anterior leaflet diastolic closing (EF) slope, and the PR-AC interval. These variables would logically be expected to reflect the basal level of cardiac compensation since 1) the degree of swing of the aortic root and the amplitude of opening of the mitral valve have previously been related to cardiac output and stroke volume, and markedly low amplitudes are oftentimes seen in low output states; 2) cardiac decompensation generally leads to extreme left ventricular dilatation (a late phenomenon in isolated aortic stenosis); and 3) the EF slope is often reduced when the left ventricle becomes less distensible or "noncompliant." In view of these theoretical considerations, as well as the observations of many groups that these generalities may hold in the individual case, it was disappointing to note that the relationship between each of these echocardiographic measurements and cardiac index, forward stroke volume, angiographic ejection fraction, or left ventricular end-diastolic pressure was weak, the correlation coefficients falling below 0.5. It becomes evident, of course, that any single echocardiographic measurement has multiple determinants. For example, decreased ventricular filling rate, mitral valve fibrosis, and decreased left ventricular compliance all may produce an abnormally depressed EF slope. One must conclude on the basis of such findings that, while contractility, left ventricular filling pressure, and ventricular compliance each may influence the echocardiographic parameters under consideration, lack of a reasonable linear correlation prevents the use of any one of these echocardiographic measurements in reliably predicting the level of cardiac compensation.

Stepwise Multivariate Linear Discriminant Function Analysis

A stepwise, multivariate linear discriminant function analysis permits selection of those variables which best separate groups of patients with differing ventricular function and uses multiple echocardiographic measurements to assess performance, even though the independent linear correlation of any one measurement with standard hemodynamic and angiographic parameters of ventricular function may be imperfect. Employing such an approach, then, enhances the recognition of each of the levels of myocardial function. This is of particular import, since the intermediate state is not always distinguished by means of the echocardiographic ejection indices used alone.

Prospective Study

The initial phase of the investigation, using hemodynamic and echocardiographic measurements obtained retrospectively, was designed to develop those echocardiographic criteria which would best discriminate levels of compensation. The prospective phase of the study served as an independent validation of the established criteria and identification of the level of compensation was accomplished with reasonable accuracy (see Appendix).

Left Ventricular Filling Pressure

Finally, consideration should be given to the attempt at estimating left ventricular end-diastolic pressure. A variety of echocardiographic measurements, taken singly or combined in multiple linear regression analyses, were considered, each having a theoretical likelihood of being influenced by left ventricular filling pressure. Thus, increased end-diastolic dimension or posterior wall thickness, depressed ejection indices, or lowered ventricular compliance as reflected in the PR-AC interval might aid in recognizing the presence of an elevated left ventricular end-diastolic pressure. These considerations notwithstanding, correlations with left ventricular end-diastolic pressure were poor (r < 0.5).

This result was neither unanticipated nor disappointing. Although an elevated ventricular end-diastolic pressure was previously considered to signify the presence of "heart failure," many recent studies have attested to the insensitivity, nonspecificity, and limitations of this hemodynamic measurement. Left ventricular end-diastolic pressure may be profoundly altered by a number of factors other than the functional status of the myocardium, including the shape of the left ventricular pressure-volume curve, diastolic compliance, the level of left ventricular contractility, and the degree of vascular congestion. Such observations imply that failure to estimate left ventricular end-diastolic pressure by echocardiography should not be considered a serious shortcoming of this noninvasive tool. Rather left ventricular end-diastolic dimensions, posterior wall thickness, contractility (as reflected by ejection phase indices), and the overall assessment of levels of myocardial compensation described in this paper represent variables of greater import than left ventricular end-diastolic pressure in the evaluation of the patient with valvular heart disease. Their determination by echocardiography allows frequent, noninvasive follow-up of individual patients' progress, and facilitates the timing of critical decisions involving catheterization and surgery.

Acknowledgment

We are indebted to Ms. Barbara Kamm for her assistance in the statistical analysis and interpretation of our data.

Appendix

Discriminant analysis is employed to distinguish between two or more groups or cases statistically. The mathematical objective is to weight and linearly combine the discriminating variables so that the groups are forced to be statistically as distinct as possible. This is done by forming one or more linear combinations of discriminating variables such that E = C1V1 + C2V2 + ... + CNVN where E is the score of the discriminant function, C the weighting coefficient, and V the variables.*

The determination of the level of cardiac compensation using an echocardiographic score based on step-wise linear discriminant function analysis can be performed in one of two ways. 1) The five "best variables" and their coefficients are selected according to disease, as shown in Table 4, and the products of these variables and their corresponding coefficients are then added for determination of the "echo score." This test is so designed that three computations, using different coefficients, are made for any given patient, testing consecutively whether that individual falls into the uncompensated, compensated, or decompensated groups. Table 4 also lists the echocardiographic score limit, values greater than this figure placing the patient in the more normal of the two levels of hemodynamic function being compared. The Mahalanobis distance provides an estimate of the degree of separation achieved between the groups being compared. 2) Determination of the level of ventricular compensation may be more simply attained using the flow diagram in Figure 5. Here, patient is seen to fall into one or two of the levels of hemodynamic function depending on the most minor diameter shortening, %ΔDmin and further discrimination of level of cardiac function is made employing the echocardiographic score. Hence, using this modification, one need perform only two computations of the echocardiographic score in order to classify a patient. Echocardiographic score calculations were simplified in our study by using a programmed Hewlett-Packard HP-65 calculator, although the scores can be easily computed manually.
**TABLE 4. Stepwise Linear Discriminant Function Analysis: Separation of Levels of Compensation Employing Five “Best Variables”**

<table>
<thead>
<tr>
<th>Disease</th>
<th>Levels of function compared</th>
<th>%D</th>
<th>Coefficients</th>
<th>Echo score limit*</th>
<th>MD²</th>
</tr>
</thead>
<tbody>
<tr>
<td>AI</td>
<td>Decomp vs Comp</td>
<td>+8.701</td>
<td>-0.023</td>
<td>+0.035</td>
<td>-0.018</td>
</tr>
<tr>
<td></td>
<td>Decomp vs Inter</td>
<td>+62.070</td>
<td>-0.002</td>
<td>+0.035</td>
<td>-0.028</td>
</tr>
<tr>
<td></td>
<td>Inter vs Comp</td>
<td>-0.019</td>
<td>+0.049</td>
<td>+0.066</td>
<td>-0.010</td>
</tr>
<tr>
<td>MR</td>
<td>Decomp vs Comp</td>
<td>-0.044</td>
<td>+0.190</td>
<td>+0.041</td>
<td>-0.367</td>
</tr>
<tr>
<td></td>
<td>Decomp vs Inter</td>
<td>-2.285</td>
<td>+0.046</td>
<td>+0.098</td>
<td>+0.074</td>
</tr>
<tr>
<td></td>
<td>Inter vs Comp</td>
<td>+2.225</td>
<td>-0.022</td>
<td>-0.028</td>
<td>+0.055</td>
</tr>
<tr>
<td>AS</td>
<td>Decomp vs Comp</td>
<td>3.337</td>
<td>-0.028</td>
<td>-0.051</td>
<td>-0.058</td>
</tr>
<tr>
<td></td>
<td>Decomp vs Inter</td>
<td>13.666</td>
<td>-0.128</td>
<td>-0.100</td>
<td>-0.187</td>
</tr>
<tr>
<td></td>
<td>Inter vs Comp</td>
<td>-0.475</td>
<td>-0.004</td>
<td>-0.005</td>
<td>+0.009</td>
</tr>
</tbody>
</table>

*Echo score values less than this limit place the patient in the first of the groups compared; values greater than this limit place the patient in the second hemodynamic level.*

**References**

Echocardiographic assessment of the level of cardiac compensation in valvular heart disease.
A Rosenblatt, R Clark, J Burgess and K Cohn

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