Evaluation of left ventricular function by cardiac catheterization, echocardiography, and systolic time intervals

Ernesto E. Salcedo, M.D.

Augusto Pichard, M.D.*

Wayne Siegel, M.D.

Department of Cardiology

Assessment of left ventricular function is of primary importance in the evaluation of various forms of organic heart disease. Direct hemodynamic and angiographic measurements at cardiac catheterization have previously been the only standard method for obtaining this information.[1]

In the past decade systolic time intervals and echocardiography have been developed as alternative noninvasive techniques for deriving this information.[2-8] Both systolic time intervals and echocardiography, because of their noninvasive nature, may be performed serially at no patient risk or discomfort, and thus provide a convenient method of evaluating and following left ventricular performance.

In patients with left ventricular dysfunction, a good correlation has been found between systolic time intervals and ejection fraction derived at cardiac catheterization.[9] Several studies have demonstrated a good correlation of different parameters of left ventricular function between echocardiography and direct measurements obtained at cardiac catheterization.[3-6] The limitations of echocardiography in assessing overall ventricular function by studying only a small area of the ventricle have recently been emphasized.[10]

Present address: The Mount Sinai Hospital, Fifth Avenue and 100th Street, New York, New York 10029

The aim of this project was to define quantitatively a set of noninvasive measurements that have the greatest correlation with directly obtained information on left ventricular performance in normal subjects and in patients with segmental or diffuse left ventricular dysfunction. We have also determined the discriminative power of these techniques in differentiating the normal population from patients with coronary artery disease and normal and abnormal ventricles, and patients with primary myocardial disease. Theoretically, several indirect measurements in combination should yield a more sensitive indicator of ventricular function than a single measurement obtained with one noninvasive technique. A variety of echocardiographic and systolic time interval combinations of measurements have been subjected to multivariate statistical analysis for this purpose.

Materials and methods

Patient population. One hundred fifty patients, referred for evaluation of chest pain or congestive heart failure, were evaluated by cardiac catheterization, echocardiography, and systolic time interval measurements in the Cardiac Laboratory and Cardiac Function Laboratory at the Cleveland Clinic. Of this group, 122 patients were selected on the basis of technically good echocardiograms and systolic time interval measurements, and a ventriculogram of adequate quality for calculation of ejection fraction. The three procedures were done the same day; the cardiac catheterization was usually done 3 to 4 hours before the echocardiogram and systolic time interval measurements.

Fifty patients had normal coronary arteries, normal left ventricles and no other evidence of organic heart disease; they serve as the normal control group (group I normals). Fifty patients had coronary artery disease with at least one of the three major coronary arteries obstructed 75% or more. Of these, 21 had normal ventriculograms (group II) and 29 had abnormalities of ventricular motion (group III). These abnormalities included an inferior scar in ten patients; six patients had an anteroapical aneurysm, one had an anterior scar, and 12 had diffuse left ventricular dysfunction. Twenty-two patients had primary myocardial disease with normal coronary arteriograms (group IV). Of these, four had mild left ventricular dysfunction, nine had moderate, and nine had severe left ventricular dysfunction.

A. Cardiac catheterization. Cardiac catheterization was performed in the postabsorptive state after premedication with benzathine penicillin G, 1,200,000 U intramuscularly, and diazepam (Valium), 10 mg intramuscularly. Coronary angiography was performed according to the Sones technique.[11] A left ventricular angiogram was performed in the 30° right anterior oblique projection, using 40 ml meglumine diatrizoate (Renografin 76%) with a pressure injector using 250 to 300 pounds per square inch. In some cases, the ventriculogram was repeated in the 60° left anterior oblique projection.

The ejection fraction was calculated by subtracting the end systolic projected area from the end diastolic projected area, and dividing the result by the latter. The area-length method of Sandler and Dodge[12] was used for calculating end systolic and

end diastolic areas. Ectopic or postextrasystolic contractions were not selected for these calculations.

B. Echocardiogram. All echocardiograms were done with the patient in the left lateral decubitus position, (approximately 30°) and were recorded with a commercially available ultrasonoscope (Unirad Corporation, series 100, Denver, Colorado) attached to a photographic recorder (Model VR6, Electronics for Medicine). A bipolar lead electrocardiogram was used as reference and all tracings were recorded at a paper speed of 50 mm/sec. The transducer was placed on the third, fourth, or fifth intercostal space just to the left of the sternum, and the ultrasonic beam was directed posteriorly for identification of the interventricular septum, mitral valve, and posterior wall of the left ventricle. The echocardiograms for left ventricular measurements were recorded at the level of the chordae tendineae just under the mitral valve (*Fig. 1*). By angulating the transducer medially and superiorly, both mitral valve leaflets were identified and recorded; the A-C interval was visualized in all cases (*Fig. 2*).

The following measurements were made:

(a) End diastolic diameter (EDD) measured in centimeters at the peak of the QRS as the distance from the left endocardial surface of the interventricular septum to the endocardial surface of the posterior ventricular wall.

(b) End systolic diameter (ESD) as the distance from the left endocardial surface of the septum to the endocardial surface of the posterior left ventricular wall measured in centimeters at the time of the maximum approximation between the two surfaces.

(c) Percent of shortening of internal diameter (%Δ) calculated from the following formula:

$$\%\Delta = 100 - \frac{ESD \times 100}{EDD}$$

(d) End diastolic volume (EDV) and end systolic volume (ESV) calculated in milliliters from the equation:[3]
Volume = diameter^3

(e) Ejection fraction (EF) calculated from the following formula:

$$EF = \frac{EDV - ESV}{EDV}$$

(f) Septal motion (SM) measured in centimeters as the distance from the left endocardial surface of the interventricular septum at the peak of the QRS to the point of maximal posterior displacement (*Fig. 1*).

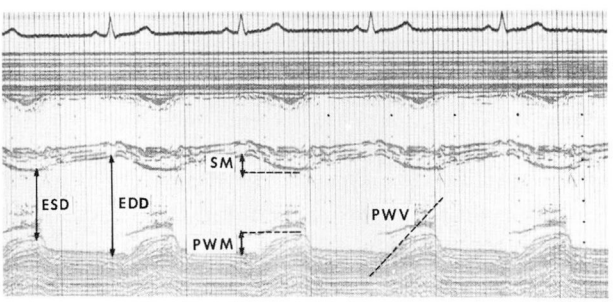

Fig. 1. Left ventricular echocardiogram. ESD = end systolic diameter, EDD = end diastolic diameter, SM = septal motion, PWM = posterior wall motion, PWV = posterior wall velocity.

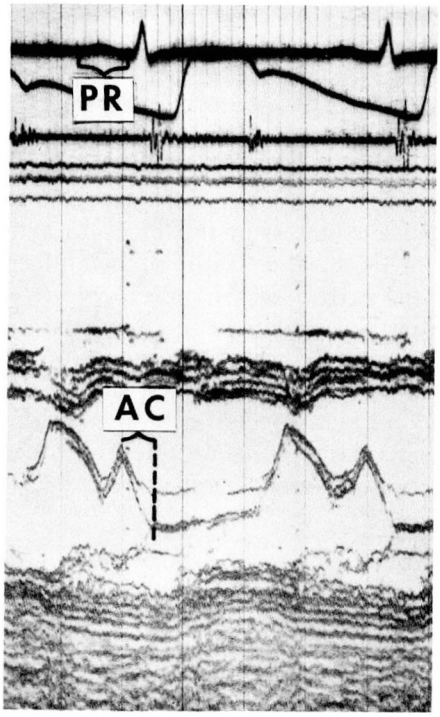

Fig. 2. Mitral valve echocardiogram. The PR-AC interval is obtained by subtracting the AC interval of the echocardiogram from the PR interval of the electrocardiogram.

(g) Posterior wall motion (PWM) measured in centimeters as the distance from the endocardial surface of the posterior wall of the left ventricle at the peak of the QRS to the point of maximal anterior motion (*Fig. 1*).

(h) Septal plus posterior wall motion (S+PWM) as the sum of the two prior values.

(i) Posterior wall velocity (PWV) measured in millimeters per second and calculated as the slope of the tangent to the endocardium of the posterior wall during systole (*Fig. 1*).

(j) PR-AC interval (PR-AC) measured in milliseconds by subtracting the AC interval of the mitral echocardiogram from the PR interval of the electrocardiogram (*Fig. 2*).

(k) Mean velocity of circumferential fiber shortening (Vcf) measured in circumferences per second (circ/sec) from the formula:[6]

$$Vcf = \frac{EDD - ESD/LVET}{EDD}$$

where LVET is the left ventricular ejection time measured from a carotid pulse tracing taken simultaneously or immediately before the echocardiographic recording.

C. Systolic time intervals. We used a six-channel recorder (Electronics for Medicine VR-6, White Plains, New York) in which the following determinations were obtained:

(a) A bipolar chest lead was used for determining the onset of ventricular depolarization.

(b) Carotid pulse tracing was obtained with an inductance displacement transducer (Hewlett-Packard APT-16) recorded with a 5-second time constant amplifier (Elema Schonander, Solna, Sweden).

(c) One microphone was placed in the second left intercostal space to record the initial high-frequency components of the second heart sound and another at the cardiac apex for recording the initial low-frequency components of the first heart sound.

(d) An apexcardiogram was recorded with an inductance displacement transducer (Hewlett-Packard APT-16) and a 5-second time constant amplifier (Elema Schonander, Solna, Sweden).

Measurement techniques

(a) Total electromechanical systole. The QS_2 was measured from the onset of ventricular depolarization to the initial high-frequency vibrations of the aortic component of the second heart sound.

(b) Left ventricular ejection time (LVET) was measured from the beginning of the upstroke to the dicrotic notch of the carotid pulse.

(c) Pre-ejection period (PEP) was obtained indirectly by subtracting LVET from the QS_2 interval.

(d) Isovolumic contraction time (IVCT) begins with ventricular contraction and ends with the beginning of ejection. This is measured from the U point of the apexcardiogram to the beginning of the upstroke of the carotid pulse corrected for the pulse transmission time.

The LVET and the PEP were corrected for heart rate according to the regression formula of Garrard[9] with the LVET index (LVETI) and PEP index (PEPI) obtained. The PEP/LVET ratio was determined in all cases.

Results

Table 1 shows the number of patients and mean ages of each group, and summarizes the catheterization data. The mean values of LVEDP and EF are compared between normals and patient groups. There was significant difference between the LVEDP and the EF of the normals when compared with the patients with coronary artery disease and abnormal left ventricles and patients with primary myocardial disease. There was no significant difference of these parameters between the normals and the patients with coronary artery disease and normal left ventricles.

Table 2 is a summary of the mean values of all the echocardiographic measurements obtained in the four groups and shows the statistical difference between group 1 and other groups. There was a significant difference in all the echocardiographic measurements between the normals and the patients with primary myocardial disease, and in all the echocardiographic measurements, except for the septal and posterior wall motion and posterior wall velocity between the normals and the patients with coronary artery disease and abnormal left ventricles. There was no significant difference between the normals and the patients with coronary artery disease and normal left

Table 1. Cardiac catheterization data*

Patient group†	No.	Age (yr)	LVEDP (mm Hg)	EF
I. Normals	50	44	9	.78
SD			±2.5	±.10
II. Coronary artery disease; normal LV	21	44	10	.79
SD			±3.4	±.07
p			NS	NS
III. Coronary artery disease; abnormal LV	29	45	16	.51
SD			±8.6	±.18
p			<.001	<.001
IV. Primary myocardial disease	22	47	18	.46
SD			±7.1	±.18
p			<.001	<.001

* Mean values.

† p values refer to differences between group I and other groups.

NS = Not significant.

SD = Standard deviation.

Table 2. Echocardiographic measurements*

Patient group†	EDD (cm)	ESD (cm)	% Δ	EDV (ml)	ESV (ml)	EF	SM (cm)	PWM (cm)	S+PWM (cm)	PWV (mm/sec)	PR-AC (sec)	Vcf (circ/sec)
I. Normals	4.6	2.9	36.5	103	28	.73	.67	1.1	1.8	58.5	.08	1.32
SD	±.54	±.5	±7.2	±37	±14	±.08	±.23	±.23	±.37	±12.0	±.01	±.27
II. Coronary artery disease;												
Normal LV	4.9	3.1	37.6	122	34	.74	.78	1.2	2.0	61.6	.08	1.31
SD	±.70	±.75	±8.99	±49	±22	±.11	±.23	±.25	±.27	±16.3	±.01	±.31
p	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
III. Coronary artery disease;												
Abnormal LV	5.5	4.1	25.7	182	89	.57	.58	1.0	1.6	51.5	.07	.94
SD	±1.0	±1.17	±9.30	±102	±83	±.17	±.27	±.27	±.44	±13.6	±.01	±.33
p	<.001	<.001	<.001	<.001	<.001	<.001	NS	NS	NS	NS	<.005	<.001
IV. Primary myocardial disease	6.2	5.0	19.2	254	141	.46	.48	.85	1.3	38.5	.05	.80
SD	±1.0	±1.03	±6.09	±112	±76	±.11	±.25	±.25	±.42	±13.3	±.01	±.21
p	<.001	<.001	<.001	<.001	<.001	<.001	<.001	<.001	<.001	<.001	<.001	<.001

* Mean values.

† p values refer to differences between group I and other groups.

NS = Not significant.

SD = Standard deviation.

ventricles in any of the echocardiographic measurements.

Figure 3 shows the correlation between the ejection fraction obtained by cardiac catheterization with that obtained by echocardiograms in the four groups. The correlation as can be seen was rather poor (R = .64). The analysis of the correlation coefficient in each of the four groups if analyzed individually was similarly poor.

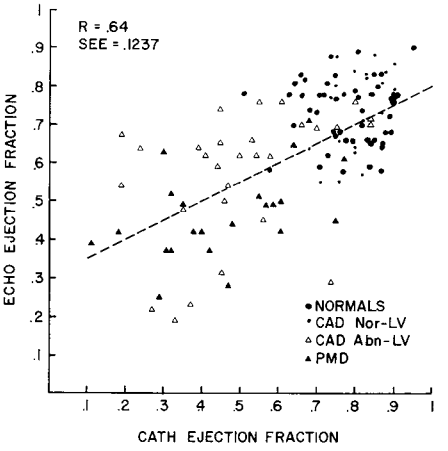

Fig. 3. Correlation between echocardiogram and catheterization ejection fraction. R = correlation coefficient, SEE = standard error of estimate.

Figure 4 shows that despite the poor correlation coefficient between the catheterization and echocardiographic ejection fraction, both methods have a similar distribution and discriminative power between the four groups. As a matter of fact, the T ratio was very similar by both methods in comparing the four groups, and was higher on the echocardiographic method in differentiating normals from primary myocardial disease.

Table 3 summarizes the mean values of the systolic time intervals and shows the statistical difference on systolic time intervals between group I and other groups. It shows that there was significant difference between all systolic time intervals, except for QS_2 between the normals and the primary myocardial disease groups. There was no significant difference between normals and the group of patients with coronary artery disease.

Tables 4, 5, and *6* summarize the statistical relationship between catheterization, echocardiographic, and systolic time interval measurements in the four groups. The differentiation of groups was made by angiogra-

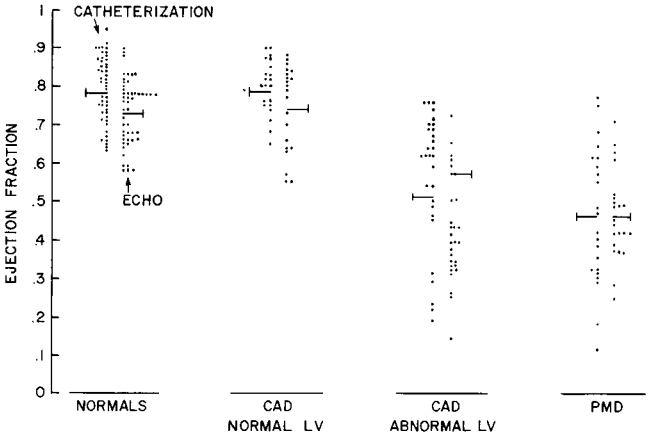

Fig. 4. Ejection fraction by echocardiogram and catheterization in the four groups of patients. Horizontal bands represent mean values.

Table 3. Systolic time intervals (msec)*

Patient group†	HR	QS_2	LVET	LVETI	PEP	PEPI	PEP/LVET	IVCT
I. Normals	76	374	277	396	97	126	.35	57
SD	±16	±33	±29	±17	±21	±21	±.09	±16
II. Coronary artery disease; normal LV	68	392	287	394	104	130	.37	68
SD	±11	±24	±31	±26	±32	±32	±.13	±21
p	NS	NS	NS	NS	NS	NS	NS	NS
III. Coronary artery disease; abnormal LV	72	383	272	388	111	139	.41	65
SD	±13	±37	±32	±22	±29	±30	±.12	±20
p	NS	NS	NS	NS	NS	NS	NS	NS
IV. Primary myocardial disease	83	365	236	371	129	162	.55	86
SD	±11	±38	±23	±23	±35	±34	±.16	±17
p	<.005	NS	<.001	<.001	<.001	<.001	<.001	<.001

* Mean values.
† P values refer to differences between Group I and the other groups.
NS = Not significant.
SD = Standard deviation.

Table 4. Statistical relationship between measurements in the four groups; catheterization

	Angiography	LVEDP	EF
I vs II	p < .001	NS	NS
I vs III	p < .001	p < .001	p < .001
I vs IV	p < .001	p < .001	p < .001
II vs III	p < .001	p < .005	p < .001
II vs IV	p < .001	p < .001	p < .001
III vs IV	p < .001	NS	NS

NS = no significant statistical difference.

phy; thus all groups show statistical difference by this method. The measurement of LVEDP and EF at catheterization differentiates normals from patients with coronary artery disease and an abnormal left ventricle or patients with primary myocardial disease. Normal subjects were not separated from patients with coronary artery disease and a normal left ventricle by LVEDP and EF determinations. These measurements also differentiated patients with coronary artery disease and normal left ventricles from those with abnormal left ventricles due to coronary artery disease or primary myocardial disease. Measurements of LVEDP or ejection fraction by catheterization did not allow differentiation of patients with coronary artery disease with abnormal left ventricles from patients with primary myocardial disease.

All echocardiographic measurements showed significant differences between the primary myocardial disease group and the normals or between the primary myocardial disease group and patients with coronary artery disease and normal left ventricles (*Table 5*). There were significant differences between the primary myocardial disease group and patients with coronary artery disease and abnormal left ventricles in the measurement of ESD, %Δ, PWV and PR-AC interval. In comparing patients with coronary artery disease and normal and abnormal left ventricles, there were significant differences in all echocardiographic measurements except PWM, PWV, and PR-AC interval. There was no significant difference in any of the echocardiographic measurements when comparing the normal group with the coronary artery disease normal left ventricle group. The correlation between LVEDP obtained at catheteri-

Table 5. Statistical relationship between measurements in the four groups; echocardiography

Groups	EDD	ESD	% Δ	EDV	ESV	EF	SM	PWM	S and PWM	PWV	PR-AC	Vcf
I vs II	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
I vs III	$p < .001$	$p < .001$	$p < .001$	$p < .001$	$p < .001$	$p < .001$	NS	NS	NS	NS	$p < .005$	$p < .001$
I vs IV	$p < .001$	$p < .001$	$p < .001$	$p < .001$	$p < .001$	$p < .001$	$p < .005$	$p < .001$	$p < .001$	$p < .001$	$p < .001$	$p < .001$
II vs III	$p < .005$	$p < .001$	$p < .001$	$p < .005$	$p < .001$	$p < .001$	$p < .005$	NS	$p < .001$	NS	NS	$p < .001$
II vs IV	$p < .001$	$p < .001$	$p < .001$	$p < .001$	$p < .001$	$p < .001$	$p < .001$	$p < .001$	$p < .001$	$p < .001$	$p < .001$	$p < .001$
III vs IV	NS	$p < .005$	$p < .005$	NS	NS	NS	NS	NS	NS	$p < .001$	$p < .001$	NS

NS = no significant statistical difference.

zation and the PR-AC interval by echocardiogram was poor, with the R value for the four groups combined of $R = -.46$. Despite this, there was a tendency for the patients with normal LVEDP to have the longer PR-AC intervals. There were only three patients with a normal LVEDP with a PR-AC interval of less than .06, and there were only four patients with LVEDP of 20 or more with PR-AC interval of more than .06 sec.

The systolic time intervals were of no help in differentiating the normals from the groups with coronary artery disease, nor in differentiating the group with coronary artery disease and normal left ventricle from the group with coronary artery disease and abnormal left ventricles (*Table 6*). All the intervals except the QS_2 showed significant differences between the normal and primary myocardial disease groups. There was significant difference in the LVET, PEPI, PEP/LVET, and IVCT between the group with coronary artery disease and normal left ventricles and primary myocardial disease. There was significant difference in LVET, PEP/LVET, and IVCT between the group with coronary artery disease and abnormal left ventricles and the primary myocardial disease group. The correlation coefficient between the PEP/LVET for all the groups with the ejection fraction obtained at catheterization was only $-.34$.

Discussion

The present study shows that despite a rather poor correlation between the ejection fraction obtained by cardiac catheterization and the echocardiogram, several of the echo-

Table 6. Statistical relationship between measurements in the four groups; systolic time intervals

Groups	QS_2	LVET	LVETI	PEP	PEPI	PEP/LVET	IVCT
I vs II	NS	NS	NS	NS	NS	NS	NS
I vs III	NS	NS	NS	NS	NS	NS	NS
I vs IV	NS	$p < .001$	$p < .001$	$p < .001$	$p < .001$	$p < .001$	$p < .001$
II vs III	NS	NS	NS	NS	NS	NS	NS
II vs IV	NS	$p < .001$	$p < .005$	NS	$p < .005$	$p < .001$	$p < .005$
III vs IV	NS	$p < .001$	$p < .005$	NS	NS	$p < .005$	$p < .001$

NS = no significant statistical difference.

cardiographic parameters were very useful in distinguishing patients with normal from patients with abnormal left ventricles. There was an especially high statistical difference between the normal and the primary myocardial disease groups. It is also of interest that some of the echocardiographic parameters differentiated between patients with abnormal left ventricles due to either coronary artery disease or primary myocardial disease. An end systolic diameter of 5 cm or more by echocardiography was seen almost exclusively in patients with primary myocardial disease. A posterior wall velocity of 40 mm/sec or less was also seen almost exclusively in patients with primary myocardial disease. A change of the minor axis during systole of less than 15% was again seen only in patients with primary myocardial disease. No echocardiographic measurements allowed differentiation of the normal group from patients with coronary artery disease and normal left ventricles. In general, the differentiation of groups by echocardiographic measurements was similar to that obtained by the analysis of ejection fraction or left ventricular end diastolic pressure by catheterization. This was observed despite a poor correlation between the two methods, probably because the value of ejection fraction by the two techniques is computed differently. Despite this, we feel this study validates the use of echocardiography for the analysis of left ventricular function, especially when trying to differentiate between patients with normal or abnormal left ventricles. We have observed patients with the diagnosis of primary myocardial disease made by echocardiography and then confirmed by catheterization even though the physical examination, chest x-ray, and electrocardiogram were normal. The present study confirms the high sensitivity of this technique in the diagnosis of primary myocardial disease.

The diagnosis of coronary artery disease without abnormality of the left ventricle does not appear possible with the present echocardiographic technology. Analysis of these parameters under stress may prove to be more useful. Motion of the interventricular septum and posterior wall did not differentiate the primary myocardial disease group from the coronary artery disease abnormal left ventricle group as has been reported by Corya et al.[13] We believe this will depend on which areas of the ventricle have segmental impairment. Results of a recent study by Dillon et al[14] indicate the diagnosis of segmental dysfunction of the left ventricle by echocardiography may be possible.

Systolic time intervals have been

advocated as useful indirect parameters of left ventricular function. Unfortunately, they are influenced significantly by several factors such as preload and afterload of the heart which cannot be adequately assessed or controlled clinically.[15] Although the theoretical basis for their use is attractive, in clinical practice one may anticipate significant limitations. This was the case in our series. Systolic time intervals were of no help in differentiating the normal group from the coronary artery disease group. Systolic time intervals did differentiate the group of primary myocardial disease from the normal group, despite the fact that left ventricular dysfunction in patients with primary myocardial disease ranged from mild to severe. Recent studies suggest that the sensitivity of this technique may improve by obtaining recordings at rest and after exercise.[16]

Summary

One hundred twenty-two patients were studied on the same day by cardiac catheterization, echocardiography, and systolic time intervals for analysis of left ventricular function. Fifty patients had normal coronary arteries, normal left ventricles, and no other evidence of organic heart disease (normals). Fifty patients had coronary artery disease with at least one major coronary artery obstructed 75% or more; of these 50 patients, 21 had normal ventriculograms and 29 had abnormal ventriculograms.

Despite poor correlation between the catheterization and echocardiogram ejection fraction (R = .64), the echocardiographic parameters of left ventricular function differentiated the normal group from the group with abnormal left ventricles due to coronary artery disease or to primary myocardial disease. Systolic time intervals did not differentiate the normal group from the coronary artery disease groups; it did differentiate the primary myocardial disease group.

We conclude that the echocardiogram is a sensitive technique in the detection of left ventricular dysfunction, and that the value of the systolic time intervals is limited in this respect.

Acknowledgment

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