Exercise Capacity in Patients with Severe Left Ventricular Dysfunction

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SUMMARY Normal or near-normal exercise capacity has been thought to reflect normal left ventricular function. Many compensatory mechanisms could preserve exercise capacity in patients with severe left ventricular dysfunction. We evaluated exercise capacity using a treadmill exercise test in 26 patients with severe left ventricular dysfunction defined by a left ventricular ejection fraction of 30% or less by isotope ventriculography. One half of the patients had normal exercise capacity and a normal cardiothoracic ratio on chest x-ray. This study indicates that traditional predictors of left ventricular function that have been widely used in clinical evaluation of the patients with cardiac disease (cardiothoracic ratio and exercise capacity) can be normal in a significant number of patients with severe left ventricular dysfunction. Thus, left ventricular function cannot be accurately estimated using these traditional predictors and should be assessed quantitatively. The isotope ventriculogram appears to be ideal for this purpose.

IN PATIENTS with suspected or established cardiac disease, normal or near-normal exercise capacity has generally been thought to reflect normal left ventricular function. The rationale for this assumption is based on studies that have shown a close linear correlation between maximal oxygen consumption and cardiac output.1,4 Furthermore, the assumption that exercise capacity relates to the severity of heart disease has formed the basis of the most commonly used clinical classification of patients with heart disease (New York Heart Association).

Although left ventricular dysfunction may alter exercise capacity, many compensatory mechanisms could preserve exercise tolerance despite severe left ventricular dysfunction, including preservation of absolute stroke volume, chronotropic competence, increased oxygen extraction, altered left ventricular compliance or augmented pulmonary lymphatic flow. Therefore, we reevaluated exercise capacity in patients with severe left ventricular dysfunction. If a substantial number of patients with severe left ventricular dysfunction and near-normal exercise tolerance could be identified, the concept that exercise capacity is a predictor of left ventricular performance would be challenged.

Methods

Patient Selection

This study was a retrospective analysis of patients referred to the University of Iowa Hospitals and Iowa City Veterans Administration Hospital who had an ejection fraction of 30% or less and who also had a graded treadmill exercise test during the 24-month period from February 1977 through February 1979. Patients were excluded from the study if a major change in therapy (medical or surgical) was instituted between the two tests. The interval between the tests was 0.9 ± 1.5 weeks (mean ± sd).

The study included 26 patients, 20 men and six women, ranging in age from 30–76 years (56 ± 15 years, mean ± sd). In 23 patients the cardiac diagnosis was coronary artery disease as defined by: 1) the presence of abnormal Q waves (≥ 0.04 second duration) and a history of myocardial infarction; 2) coronary arteriography with greater than 70% stenosis in at least one major coronary vessel; or 3) a left ventricular aneurysm on isotope ventriculogram or left ventricular contrast angiography. The remaining three patients had cardiomyopathy with diffuse left ventricular dysfunction. Coronary arteries were normal in one patient and not studied in the last two patients.

Among the 26 study patients, nine had cardiac catheterization within 3 months of the treadmill or isotope ventriculogram with no intervening changes in medical or surgical management. To further assess the accuracy of the isotope ventriculogram in evaluating left ventricular ejection fraction, 29 patients with a variety of heart diseases were also reviewed retrospectively. These 29 were consecutive patients in whom both contrast left ventricular angiography and isotope ventriculogram determination of ejection fraction had been performed. Patients were excluded if either study was technically inadequate or if atrial fibrillation was present.

Eighteen normal, healthy male subjects ranging in age from 17–22 years had an isotope ventriculogram. The evaluation of these normal subjects was approved by the Human Use Committee of the University of Iowa Hospitals, and informed consent was obtained from each subject.

Cardiac Imaging Procedures

Gated isotope ventriculograms were obtained in all patients. Technetium-99m-labeled human red cells or
human serum albumin (20 mCi) was used as the imaging agent. Images were obtained with a Picker 1680 Dyna camera with an all-purpose collimator. The energy window was centered at 140 keV with a width of 20%. The images were constructed from about 300 cardiac cycles recorded over 3-5-minute periods with the patient at supine rest. Data were collected with a Medical Data Systems computer and a left ventricular ejection fraction was calculated from the left anterior oblique projection using a method described by Burow et al. None of the patients had significant ventricular ectopy during isotope ventriculography.

**Contrast Left Ventricular Angiography**

All cardiac catheterizations were performed for diagnostic purposes. Single-plane left ventricular angiograms were obtained in a 30° right anterior oblique position. Angiograms were obtained with a power injection of 40-60 ml of Renographin-76 (meglumine diatrizoate) and recorded on 35-mm film at 60 frames/sec. Ejection fraction was calculated using the area-length method of Kennedy.

**Treadmill Exercise Testing**

All patients performed graded treadmill exercise tests according to the Sheffield protocol, that is, to include stage 0 and stage ½, both 3 minutes long. All exercise tests were monitored by a physician and a 12-lead ECG was recorded before, during and after exercise. End points for exercise included dyspnea, fatigue or attainment of 85% of the predicted maximum heart rate. Thus, we did not determine maximum exercise capacity in all patients. Exercise duration longer than 11 minutes was considered normal.

**Cardiac Medications**

There were no major alterations in clinical status or in therapy (medical or surgical) between the isotope ventriculogram and treadmill exercise testing. Medications at the time of the studies included: 1) digoxin (n = 19); 2) diuretics (n = 15); 3) propranolol (n = 3); 4) long-acting nitroglycerin preparations (n = 8); 5) quinidine (n = 3); and 6) procainamide (n = 1).

**Cardiothoracic Ratio**

Twenty-five of 26 patients had chest x-rays available for evaluation. The cardiothoracic ratio was obtained using a standard 6-foot posteroanterior roentgenogram at full inspiration. Cardiac size was measured as the distance between vertical lines parallel to the right and left heart borders and was divided by the widest horizontal distance from the right to left inner rib margins. A cardiothoracic ratio greater than 0.50 was considered evidence of cardiomegaly. The chest x-rays were also evaluated for evidence of pleural effusion or pulmonary congestion, defined as redistribution of blood flow to the upper lobes, presence of Kerly B lines or perihilar infiltrates.

**Results**

**Accuracy of Ejection Fractions Determined by Isotope Ventriculogram**

Figure 1 depicts anterior and left anterior oblique isotope ventriculogram images at end-systole and end-diastole from a normal subject and in two patients. The ejection fractions of these patients represent the extremes of ejection observed in the study group (6-30%), and the isotope ventriculogram from a normal subject (70%).

To assess the accuracy of isotope ventriculogram determination of ejection fraction, the isotope-determined ejection fraction was compared with the contrast angiogram-determined ejection fraction among nine study patients and 29 other patients with a variety of heart diseases (fig. 2). A close correlation (r = 0.88) between ejection fractions determined by these two methods was observed over a wide range (6-80%) and among the study patients as a subgroup (r = 0.74). The mean interval between the isotope and angiographic measurement of ejection fraction was 4.8 ± 4.2 weeks.

The left ventricular ejection fractions in the study patients and normal subjects were compared. The highest ejection fraction in the study group was nearly 5 standard deviations below the mean ejection fraction of the normal subjects. Thus, the study patients had severely decreased left ventricular ejection fractions.

**Figure 1.** Anterior (Ant.) and left anterior oblique (LAO) isotope ventriculogram images at end-systole and end-diastole from a normal subject with an ejection fraction (EF) of 70% (left panel), a subject with an EF of 30% (center panel) and a subject with an EF of 6% (right panel). White arrows point to the left ventricle (LV) and the dark arrows to the interventricular septum in the LAO projection.
Comparison of Treadmill Performance
and Isotope Ventriculogram Ejection Fractions

Resting heart rate and blood pressure, obtained during the treadmill test and the isotope ventriculogram, were similar. Figure 3 compares left ventricular ejection fraction to treadmill exercise duration. About half of these patients exercised into a normal range. Thus, in some patients with poor left ventricular function, exercise capacity can be well preserved.

Comparison of Ejection Fraction and Cardiothoracic Ratio

Figure 4 is a comparison of the cardiothoracic ratio and ejection fraction. The ejection fraction was not closely correlated to cardiothoracic ratio ($r = 0.30$). Thirty-eight percent had other roentgenographic signs suggesting left ventricular failure (venous congestion and pleural effusion). The data point marked by the arrow in figure 4 is from a patient whose cardiothoracic ratio was 0.46 and whose duration of exercise on graded treadmill was 15.5 minutes. His ejection fraction was 14%. Thus, a patient with suspected or established cardiac disease with normal heart size and normal exercise capacity can have severely decreased left ventricular function.

Discussion

We conclude from this study that exercise capacity and the chest x-ray are normal in many patients with severe left ventricular dysfunction. We will focus on three aspects of this investigation: validity of the isotope ventriculogram, limitations of the study and possible explanations for our findings.

Isotope Ventriculogram

Over a wide range, left ventricular ejection fraction measured with the isotope ventriculogram correlates closely ($r = 0.88$) with values obtained with contrast angiography, although in patients with ejection fractions less than 30% the correlation coefficient was only 0.74. There is no reason to suspect that these patients don't have left ventricular dysfunction. Also, the isotope measurements of ejection fraction have been shown to be highly reproducible. Thus, the isotope ventriculogram accurately measures the left ventricular ejection fraction.

An important assumption critical to the interpretation of the data is that left ventricular ejection fraction is a valid index of left ventricular performance. Two major lines of evidence support this assumption. First, the left ventricular ejection fraction compares favorably with the combination of other indexes of left ventricular performance such as $V_{\text{max}}$, end-diastolic...
pressure, contraction pattern, and velocity of contractile element shortening. Second, various studies have emphasized the prognostic significance of the left ventricular ejection fraction in patients with coronary artery disease, valvular heart disease and cardiomyopathy.14-19

Limitations of the Study

Our conclusions are based on data obtained from referred patients with coronary artery disease optimally treated with digitalis, diuretics and vasodilators. Therefore, extrapolating our findings to patients with various untreated cardiac ailments would be inappropriate even if the severity of left ventricular dysfunction were similar.

Also, our study group had a narrow range of ejection fractions, which could obscure a positive relationship between exercise duration and left ventricular ejection fraction. When exercise duration in patients with a wide range of ejection fractions was examined, Paine and co-workers90 observed a significant direct relationship. However, in the 14 patients in Paine's study with low ejection fractions (≤30%), exercise capacity was variable.

Normal exercise in sedentary individuals as established by Bruce24 is at a relatively low level of oxygen consumption compared with the maximal oxygen consumption reached among trained athletes29 (41 ml/kg • mm of O2 vs 61 ml/kg • mm of O2, respectively). Thus, although our patients could exercise into the normal range as defined by Bruce, their maximal exercise capacity after training would probably be less than that of a normal trained subject.

Possible Mechanisms for Preservation of Exercise Capacity

Several mechanisms can preserve exercise capacity despite severe left ventricular dysfunction. These include preservation of absolute stroke volume, maintenance of chronotropic responsiveness, increased oxygen extraction, augmented pulmonary lymphatic flow and altered left ventricular compliance.

Preservation of stroke volume via an increase in left ventricular end-diastolic volume as seen in patients with coronary artery disease23, 24 may be important in maintaining volume exercise capacity in some of the study patients. Furthermore, left ventricular volume has also been shown to increase with upright exercise.25

Tachycardia can also maintain cardiac output in a failing ventricle. Although some patients with coronary disease have chronotropic incompetence,26 at peak exercise, heart rate responses in our patients averaged 134 ± 37 beats/min and one-third achieved 85% of their predicted maximum rate.

Increased oxygen extraction27, 28 during exercise is common in patients with coronary disease.29 Elevated 2, 3 DPG levels or local tissue acidosis30 may facilitate oxygen extraction in these patients.

Enhanced pulmonary lymphatic flow could increase exercise capacity by limiting the pulmonary conges-

tion associated with pulmonary venous hypertension. This has been demonstrated in an animal model.31 Finally, chronic alterations in diastolic compliance of the left ventricle can limit increases in filling pressure during exercise. This would prevent pulmonary congestion and increase exercise capacity.

Prospective hemodynamic studies in patients similar to those in our study group are ongoing.32 Preliminary results in a subgroup with low ejection fraction (mean 17 ± 3%) and normal exercise capacity (exercise duration 13.6 ± 7 minutes [Sheffield protocol]) have shown an impressive tolerance of high pulmonary capillary wedge pressures (mean 33 mm Hg) during supine exercise without limiting dyspnea. With upright exercise stroke volume increased (40%), heart rate increased (70%), cardiac output increased threefold, and peripheral vascular resistance decreased substantially (60%). Thus, several compensatory mechanisms contributed to the preservation of exercise capacity in these patients.

In conclusion, among patients with severely decreased left ventricular function, exercise capacity can be variable and is a poor predictor of left ventricular performance. While exercise testing provides valuable information about the integrated response to exercise, one should seek a more reliable and direct assessment of left ventricular performance than can be provided by exercise testing or the chest x-ray. Noninvasive evaluation of left ventricular function with the isotope ventriculogram appears to be ideal for this purpose.

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