Left Ventricular Volume During Maximal Supine Exercise: A Study Using Metallic Epicardial Markers

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SUMMARY Changes in left ventricular (LV) volumes and ejection fraction between rest and maximal supine exercise were evaluated in 11 patients who had had four epicardial markers placed during coronary artery surgery. After calibrating marker distances with respect to volume \( r = 0.92-0.99 \) over one cardiac cycle for each patient, regression equations were used to compute LV volume from marker measurements for beats before and during exercise.

The response of the left ventricle to exercise and the extent of revascularization could not be predicted from resting LV volume or ejection fraction. Ten patients had normal resting end-diastolic volumes and eight had normal resting ejection fractions. With exercise, three had a rise in end-diastolic volume and four had a fall in ejection fraction. Graft patency was greater in the group with an unchanged or increased ejection fraction (86 vs 50%, \( P < 0.05 \)).

Epicardial clip motion can be used to determine LV volumes and ejection fraction during supine maximal exercise in man. The revascularized ventricle with normal or nearly normal performance in studies done at rest responds by decreasing end-diastolic and end-systolic volume and by increasing the ejection fraction. Increases in volumes or decreases in ejection fraction reflect old myocardial damage from infarction, fibrosis or ischemia from incomplete revascularization.

STUDIES OF HEART PERFORMANCE in man during exercise have primarily been focused on measurements of aortic pressure, heart rate, stroke volume, arteriovenous oxygen difference and cardiac output. Because of the lack of suitable methods, studies of ventricular volumes and volume changes in man during exercise during near-maximal exertion have been few, particularly those using serial measurements of chamber volumes. Braunwald and associates demonstrated a reduction of end-diastolic and end-systolic dimensions of the right and left ventricles as assessed by epicardial markers with low levels of exercise in subjects with near-normal cardiovascular systems. Using thermodilution techniques, Gorlin et al. found that mean end-diastolic volume was unchanged and end-systolic volume decreased in a group of 20 subjects. Using left ventricular (LV) angiography immediately after supine exercise for 6 minutes, or until angina developed, Sharma and coworkers reported that end-diastolic and end-systolic volumes decreased or were unchanged in normal subjects and in subjects with coronary artery disease who did not develop angina. In subjects with coronary artery disease who developed angina pectoris during the exercise stress, both end-diastolic and end-systolic volumes increased. Recently, Borer and coworkers, using radionuclide cineangiography, have demonstrated an increased ventricular ejection fraction in normal subjects and a fall of ejection fraction associated with regional dysfunction with exercise in patients with coronary artery disease.

The purpose of this paper is to describe changes in LV chamber volumes during supine exercise to symptom-limited maximum levels in a group of patients who have undergone aortocoronary (saphenous vein) bypass surgery. Chamber volumes were determined serially from biplane cine films of epicardial radioopaque markers by a technique previously reported from this laboratory. Changes in LV volumes during exercise were compared with resting LV performance and with the extent of revascularization achieved by the saphenous vein bypass grafting.

Methods

Eleven patients, all men, with an average age of 51 years (41–66 years) who had had four or more radioopaque markers attached to the epicardium at the time of aortocoronary bypass surgery, were selected for study after informed consent was obtained. This selection was based on the patients’ willingness to participate in the study rather than on any characteristic of their clinical course. All had arteriosclerotic heart disease and, postoperatively, were clinically assessed as being in functional class I or II at the time of the studies, which were performed 6–27 months after surgery. They had an average of 2.2 saphenous vein bypass grafts.

The radioopaque markers were silver vascular clips which were attached to the epicardial surface of the left ventricle at four or more sites: at or near the apex and approximately two-thirds of the distance from the apex to base, adjacent to the anterior and posterior interventricular grooves and on the lateral free wall.

To further evaluate the patients’ functional
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capacity, symptom-limited maximal exercise capacity was determined in each subject, in the upright position on a motor-driven treadmill by the Bruce multistage test protocol, on the day before the postoperative cardiac catheterization study. Fatigue and dyspnea were the limiting symptoms at maximal exercise capacity. None of the patients experienced angina pectoris. Oxygen consumption was measured at rest, during the third minute of each stage of the exercise, and during each minute of the last stage to define whether oxygen uptake plateaued or fell at the last minute of exertion, as objective evidence of maximal uptake.

As a procedure temporally separate from the upright exercise studies by several hours to one day, LV volumes and volume changes during the course of graded supine exercise carried to symptom-limited maximum levels were determined from biplane cine films of the epicardial markers as follows: Each patient was allowed to familiarize himself with pedaling a bicycle ergometer above heart level while supine on a cardiac catheterization table. With the subject's feet on the pedals, oxygen consumption was determined for 3 minutes from collected air samples which were measured for minute volume of ventilation, using a Beckman paramagnetic analyzer to determine oxygen tensions and to compute oxygen concentration with and without CO₂ absorption. Oxygen consumption was then computed by the equation described elsewhere. At the end of the air collection, biplane 35 mm cine films of the epicardial markers were made at 60 frames/sec during held inspiration, and the film exposure was timed in relation to the electrocardiogram. The patient then pedaled at work levels of 200–300 kilopond meters (kpm) for 3 minutes, with a progressive increase of work levels at 200 or 300 kpm increments at 3-minute intervals until he reached his symptom-limited capacity. Symptoms were fatigue or dyspnea, the same symptoms which limited each subject during upright exercise. No subject developed angina. Patients with more limited exercise capacities were exercised, using the 200-kpm increments. Oxygen consumption was measured during the last minute of each stage, and filming of the epicardial markers was done during suspended inspiration at the last 10 seconds of each exercise level and at the maximum level.

The following day, biplane cine ventriculograms of the left ventricle were taken at 60 frames/sec in the antero-posterior and left lateral projections for calibration of the epicardial markers, as previously described. For these studies, a catheter was passed retrograde into the left ventricle and the left ventriculogram was performed, using 30–50 ml of Renografin-76. In three patients ventriculograms were also performed during submaximal exercise (300 kpm in two subjects, and 200 kpm in one subject) approximately 20 minutes after filming the initial resting ventriculogram. This was done so that epicardial marker calibrations relative to the LV chamber volume at rest and exercise could be compared. In two patients a catheter was positioned in the pulmonary artery and cardiac output and stroke volumes were determined by the Fick method at the maximum level of exercise and compared with those determined by the epicardial marker method. Blood oxygen content was determined using the Lex-O₂-Con system.

Next, each subject had coronary arteriography with selective injection of the coronary arteries and grafts by the Sones angiographic technique.

LV chamber volumes for at least one heart beat were determined from each set of frames of the biplane cine ventriculograms by the area length method with correction for magnification. For the same heart beat, the spatial distances between the epicardial markers were also determined from biplane films, and the areas of spatial triangles determined by the markers were related to the angiographically measured chamber volumes to calibrate, by a regression equation, the marker measurements that related chamber volume and triangular areas, as previously described, and as illustrated in figure 1. The correlation coefficients relating these triangles and chamber volumes with the markers used for calibrations were 0.92–0.99 (mean 0.97 ± 0.02).

![Figure 1](image-url)  
**Figure 1.** Plot of LV volumes determined from the ventriculogram over one cardiac cycle against the spatial area of the triangle formed by three epicardial markers. There is a close correlation with \( r = 0.99 \) and \( \text{SEE} = 4.4 \text{ ml} \). LV = left ventricular.
See for volume estimation by the defined regression equations was 4–13 ml (mean 7 ± 2).

LV chamber volumes and volume curves for an average of three heart beats at rest, during each stage of exercise, and at maximal supine exercise were determined from the biplane films of the epicardial markers. The spatial distances between the markers and the areas enclosed by the spatial triangle formed by three markers were measured and computed as described. The regression equations which were defined as described from the angiographic studies were applied to convert marker measurements to chamber volumes. Figure 2 illustrates computed LV volumes as a function of time. As is shown, these curves were generally quite smooth, with little scatter of the points. LV end-diastolic and end-systolic

![Figure 2](http://circ.ahajournals.org/)

**Figure 2.** Beat-by-beat LV volume curve derived from epicardial marker measurements at rest and following two levels of exercise (300 and 600 kilopond meters (kpm)) demonstrating a fall in end-diastolic and end-systolic volumes. The horizontal axis is the cine frame number.

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**Abbreviations:** FAI = functional aerobic impairment; VO₂ = oxygen consumption in ml/min/m²; EDV = end-diastolic volume in ml/m²; ESV = end-systolic volume in ml/m²; SV = stroke volume in ml/m²; EF = ejection fraction in %; CI = cardiac index in l/min/m²; Max Ex = maximum exercise.
volumes and stroke volume were determined from these curves, and normalized for body surface area. Cardiac index was calculated from the product of normalized stroke volume and heart rate.

**Results**

These untrained postoperative patients who were exercised in the supine position reached maximal workload levels with heart rate and oxygen consumption values as is shown in table 1. Their mean supine resting heart rate was 81 ± 14 beats/min (mean ± 1 sd). This increased linearly with the increasing workloads to a maximum of 141 ± 27 beats/min (range of 86–176) (table 1). Subject 10 reached a peak heart rate of only 86 during moderate exercise which seemed related to an orthopedic problem with his knees that interfered with exercise. Maximal heart rate reached during maximal upright testing on a treadmill (156 ± 17) was significantly greater than that achieved with supine exercise.

Supine resting oxygen consumption was 150 ± 14 ml/min/m² (mean ± 1 sd). Maximal supine oxygen consumption was 377–861 (mean 695 ± 157), 2.4–5.9 (mean 4.7) times the basal level of oxygen consumption. This was 67% of the mean maximum level of oxygen consumption obtained with maximal upright treadmill exercise (997 ± 178 ml/min/m²) (table 1).

Left ventricular end-diastolic volume (LVEDV) in the resting control state was normal in all patients except #3 (table 1). Three patients (3, 7 and 8) had ejection fractions below 0.55 at rest. For eight of the 11 patients there was either no change or only a slight increase or decrease in end-diastolic volume during supine exercise (fig. 3, table 1). However, three of the patients had a substantial increase of LVEDV: 51% (#3), 35% (#5), and 45% (#7). In each case, the increased LVEDV was observed at initial workloads and little change occurred with additional workloads, as shown in figure 3.

End-systolic volume (ESV) during exercise also was unchanged, or decreased slightly during the progressive exercise loads in seven of the 11 patients (table 1 and fig. 4). However, in the same three patients (3, 5 and 7) in whom LVEDV increased, ESV also increased and by the same pattern as LVEDV; namely, it increased at the first level of workload and changed relatively little after that. ESV also increased in patient 4, but only at the highest workload (900 kpm).

The mean stroke volume for the entire group did not change significantly from rest to supine exercise (table 1 and fig. 5). Three patients had a decrease of stroke volume: in #3 this was 13 ml, or 19%; in #4, was 12 ml, or 24%; and in #6, it was 7 ml, or 14%. In three patients, the stroke volume increased with exercise: 11 ml (26%) in patient 1, 7 ml (16%) in patient 7, and 7 ml (19%) in patient 11. Of the three patients who had an increase of LVEDV and ESV with exercise (3, 5 and 7), stroke volume decreased in one and increased in two from the resting levels.

The mean value for the ejection fraction for the group of all 11 was 61% at rest, and 60%, or unchanged, during exercise (table 1, fig. 6). In five, it increased; in two, it was unchanged; and in four, it decreased with exercise. The decrease was observed in the three patients (3, 5 and 7), who had an increase of LVEDV and ESV, and in patient 4, who had an isolated increase of ESV during exercise stress. Stroke volume in these four subjects decreased during exercise stress in two and increased in two from the resting levels.
To test the validity of applying the resting regression equation to calculate exercise LV volumes, angiographic and marker-determined volumes were compared at the same submaximal levels of exercise (200–300 kpm) in three patients. The results of these studies are shown in figure 7 for end-diastolic and end-systolic volumes. There is a close correlation (0.99) with a standard error of 6.1 ml. In two of the patients, stroke volume as determined by the Fick and epicardial marker methods were compared at maximal supine exercise. These were 37 and 30 ml/m², respectively, for patient 7, and 44 and 42 ml/m², respectively, for patient 11.

Postoperative coronary arteriography demonstrated that 71% of all the aortocoronary grafts were patent. In the seven patients (1, 2, 6, 8, 9, 10 and 11) in whom ejection fraction remained the same or increased, five had all grafts patent while two had one of two grafts occluded (6 and 10). In this group, one patient (9) had a 50% narrowing of the left anterior descending which was not grafted. Of the remainder, no significantly diseased left anterior descending or dominant right or circumflex artery was not grafted. In the four patients with a fall of ejection fraction during exercise (3, 4, 5 and 7), three of four (3, 4 and 7) had occluded grafts (table 1). The fourth (5) had an estimated 50% narrowing of a large ungrafted left anterior descending coronary artery. Patient 4 also had a dominant ungrafted circumflex with a 60% narrowing. No patient with a fall in ejection fraction with exercise had total coronary revascularization.

**Discussion**

This is the first study in which serial LV volume and volume changes in man have been quantified during progressively increasing exercise workloads carried to symptom-limited maximal levels. The patients were exercised in the supine position. Maximum heart rates and oxygen consumption were less than those achieved
with maximal upright exercise on a treadmill. This is consistent with findings reported by others.11, 12

Patients (1, 2, 9 and 10) with normal resting ventricular function and all aortocoronary grafts patent responded to maximal exercise with an increase in ejection fraction. The increase in ejection fraction was achieved by a fall in end-systolic volume and by an unchanged or smaller end-diastolic volume.

Sharma and coworkers, using angiographic methods to determine LV volumes at rest and during submaximal exercise, found that LVEDV and ESV decreased and ejection fraction increased from resting values in normal subjects.8 In patients with ischemic heart disease and without induced angina, they found volumes and ejection fractions to be essentially unchanged. Borer and coworkers, using radionuclide cineangiography, demonstrated an increase of LV ejection fractions with maximal exercise in 14 normal subjects.4 In 11 patients with significant coronary artery narrowing and normal resting LV function, ejection fraction decreased and regional contraction abnormalities of the ventricular wall occurred during maximal supine exercise. Braunwald and coworkers found that both end-diastolic and end-systolic LV volumes decreased during low levels of supine exercise using epicardial radiopaque markers in patients with relatively normal ventricular function following surgical repair of atrial septal defects or mitral valve disease.1 Rushmer demonstrated a decrease of LV end-diastolic and end-systolic dimensions13 and Chapman and coworkers demonstrated a decrease of end-diastolic and systolic volumes during submaximal exercise in dogs.14 Using instrumented free-running dogs and high levels of exercise, Vatner and coworkers found greater LV end-diastolic dimensions than those of resting, standing animals.18 However, with exercise, these dimensions did not exceed the end-diastolic dimensions in the same animals lying at rest. End-systolic dimensions decreased and stroke volume increased during exercise.

The finding in this study that end-diastolic and end-systolic volumes decrease with symptom-limited maximal supine exercise in patients with patent grafts and normal ventricular function at rest is similar to findings reported with submaximal exercise in normal man and with strenuous exercise in dogs. The finding of increased ejection fractions with submaximal and maximal exercise is also similar to results previously reported by others in normal man and in experimental animals. It also appears that in men with normal ventricular performance, and in dogs,18 the Frank-Starling mechanism is not used to increase stroke volume, even with maximal exercise. The findings are consistent with the concept of increased contractility of the left ventricle during exercise.

Two of the eleven patients (6 and 8) had no, or insignificant, changes of ejection fraction with maximal exercise. Both had normal end-diastolic volumes at rest but a low normal or depressed ejection fraction at rest. The finding that ejection fraction was unchanged with exercise is similar to that of Sharma and co-workers, using submaximal exercise, in a group of patients with ischemic heart disease but no angina during testing.3 Failure of the ejection fraction to increase may be due to consequences of moderate ischemia during exercise or of depressed ventricular performance from old myocardial infarction or myocardial fibrosis.

In four patients with a fall of ejection fraction during exercise, three had occluded aortocoronary grafts and two had significantly narrowed vessels which were not grafted. The abnormal responses during exercise in two of the subjects might have been the result of previous myocardial damage. One had a depressed ejection fraction and one a marginal ejection fraction at rest. However, patient 8, who had all grafts patent, had the lowest ejection fraction at rest and showed no fall of ejection fraction or stroke volume with exercise. Therefore, a low ejection fraction per se does not necessarily become further depressed with exercise. Sharma and coworkers have reported similar changes of ejection fraction during submaximal supine exercise in patients with angina during exercise testing.8 Our findings suggest that exercise caused significant depression of ventricular performance due to ischemia even in the absence of chest pain.

In our study, ventricular performance at rest, as evaluated by end-diastolic volume and ejection fraction, was normal in three (4, 5 and 7) of four patients who had a fall of ejection fractions during exercise. In three of these four patients, end-diastolic volume increased during exercise, indicating that these hearts utilized the Frank-Starling mechanism to maintain stroke volume. In spite of an increased end-diastolic volume, stroke volume decreased in one subject in this study. It is of interest that in the patients who had an increase of end-diastolic and end-systolic volumes with exercise, the increases were observed at the first stage of exercise, as shown in figures 2 and 3. Only in one patient was the end-systolic volume increased and the ejection fraction depressed at maximal but not at submaximal levels of exercise.

The method used for determining volume changes during exercise in this study requires precise measurement of marker locations from biplane films and computations to correct for image distortion and to determine the spatial distances between markers. In using the method, one assumes a constant relationship between marker distances and chamber volumes at rest during exercise. The relationships might vary if there were ventricular contraction patterns altered with exercise-induced ischemia, or with marked changes of volume. These relationships were tested in patients by comparing chamber volumes computed by the epicardial marker method with those determined from biplane angiograms at rest and at submaximal exercise levels. Volumes determined by these independent methods were close, as shown in figure 7. In addition, stroke volumes determined by the Fick and the angiographic methods at maximum exercise were shown to have reasonable agreement in two additional subjects, one of whom demonstrated regional
hypokinesia in the ventriculogram performed at rest. In previous studies of this method, volume changes with and following premature contractions were accurately determined.\(^\text{5, 10}\)

The results of this study demonstrate that patients with coronary artery disease and adequate revascularization may have essentially normal LV volume and ejection fraction changes with maximum supine exercise. On the other hand, patients with occluded grafts or inadequate grafting may have abnormal responses with increases in volume and depression of ejection fraction during exercise, in spite of having normal resting chamber volumes and ejection fractions. Furthermore, the results of this study indicate that abnormal changes in end-diastolic and end-systolic volumes may occur that are not detected by measurement of maximal exercise capacity, oxygen consumption or stroke volume.

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