# Left Ventricular Performance in Normal Subjects: A Comparison of the Responses to Exercise in the Upright and Supine Positions

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SUMMARY **Left ventricular (LV) performance at rest and during multilevel exercise in the supine and upright positions was studied in seven normal subjects with equilibrium radionuclide ventriculography. The mean left ventricular end-diastolic volume (LVEDV) during supine rest was 107 ± 10 ml (± SEM) and 85 ± 6 ml ($p < 0.02$) in the upright position; the mean resting left ventricular end-systolic volumes (LVESV) were not different in the upright and supine positions. The LV ejection fraction (LVEF) tended to be slightly higher in the supine (76 ± 2%) than in the upright position (72 ± 4%). The resting heart rate was 89 ± 5 beats/min upright, compared with 71 ± 6 beats/min supine ($p < 0.05$). Multilevel exercise testing was carried out at a low work load of 300 kpm/min, an intermediate work load of 600–750 kpm/min and a peak work load of 1092 ± 66 kpm/min supine and 946 ± 146 kpm/min upright ($p < 0.05$). With peak exercise, supine LVEDV increased significantly, to 135 ± 13 ml (27%), but LVESV did not change. LVEF increased from 76 ± 2% to 84 ± 2% ($p < 0.05$). With upright exercise, LVEDV increased 39% above the resting level, to 116 ± 8 ml ($p < 0.02$), but remained lower than the supine LVEDVs at intermediate ($p < 0.05$) and peak work loads. LVESV decreased significantly by 41%, to 19 ± 3 ml, and was significantly smaller than the corresponding supine volume at intermediate and peak exercise ($p < 0.05$). LVEF increased from 72 ± 4% to 91 ± 2% ($p < 0.05$), which was significantly higher than peak supine LVEF ($p < 0.05$). Heart rates at rest and during exercise were higher in the upright position ($p < 0.05$), but arterial pressures and double products did not differ significantly.**

**Measurements of LV volumes at rest and during exercise in both the supine and upright positions by dynamic radionuclide scintigraphy suggest that stroke volume during exercise is maintained by a combination of the Frank-Starling mechanism and an enhanced contractile state.**

THE EFFECTS OF EXERCISE on left ventricular (LV) function in man have been investigated extensively by various techniques. Hemodynamic studies have been supplemented by data on dynamic changes in LV dimensions. Measurements have been obtained by several different methods, but there is disagreement regarding the interactive effects of posture and exercise on LV volumes and performance.

Changes in posture at rest are associated with significant changes in LV filling and stroke volume. A transition from the supine to the upright position produces a decrease in LV end-diastolic pressure[1-3] and volume[4-6] and in stroke volume.[1-4, 6-10] The results of previous studies of the alterations in LV end-diastolic volume during exercise in the supine position have varied.[5, 6, 11-15] There is general agreement that end-systolic volume is smaller during exercise than at rest;[6, 11, 12, 14, 15] most investigators[3, 6, 12, 13] have reported an exercise-induced increase in stroke volume, although others have not.[1, 4] These data are generally consistent with an enhanced contractile state during supine exercise, but the role of the Frank-Starling mechanism remains uncertain.[11-15]

Left ventricular stroke volume increases markedly during the transition from rest to exercise in the upright position and is almost as great as during supine exercise.[1, 8, 9, 16] Limited dimensional data suggest that changes in stroke volume are associated with a marked increase in end-diastolic volume.[5, 17]

The conflicting results of previous studies may be attributed in part to technical limitations. Radiographic techniques based on implanted metallic markers or angiography encounter potential difficulty due to alterations in cardiac position or geometry. M-mode echocardiography allows the measurement of ventricular dimensions, but the extrapolation of these determinations to actual volumes is unclear. In addition, angiographic contrast agents have significant effects on ventricular function[18-20] and peripheral vascular regulation.[21, 22] Measurement of LV volumes and ejection fraction (EF) by radionuclide angiography are less affected by complex or changing geometric cardiac characteristics,[17, 23-29] and the imaging agents have no cardiovascular pharmacologic effects. A newly developed, nongeometric radionuclide technique[27-29] that provides absolute ventricular volume data was therefore used to reexamine left ventricular performance at rest and during exercise in the upright and supine positions in subjects without demonstrable cardiac disease.

## Methods

Seven normal subjects (six men and one woman) with a mean age of 26 years and a mean body surface

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area of 1.83 $m^2$ underwent graded, multilevel exercise testing. Supine exercise was performed on an exercise table with a bicycle ergometer (Engineering Dynamics Corporation). Upright exercise was performed on a bicycle ergometer (Monark) with special support to stabilize the torso. Heart rate (ECG) and blood pressure (Electrosphygmomanometer, Narco Systems, Inc.) were recorded at each work load. Rate-pressure products (heart rate times systolic blood pressure) and estimated oxygen consumptions were calculated for the peak work load.

Exercise was performed at a low level (300 kpm/min), an intermediate level (600–750 kpm/min), and at peak work loads. The same low and intermediate work loads for each subject were used in the supine and upright positions. Maximal exercise levels were determined separately for each position. The subjects exercised continuously for 4 minutes at each level of work. Supine and upright studies were performed on sequential days for six of the subjects and on the same day for the remaining subject, who was allowed sufficient time to recuperate from the first study.

Radionuclide angiography was performed after in vivo labeling of red blood cells with technetium-99 sodium pertechnetate (30 mCi) according to the technique previously described.[30, 31] Data were collected with a standard scintillation camera (Ohio Nuclear Series 100) equipped with an all-purpose, parallel-hole collimator and interfaced with a dedicated on-line computer system (Ohio Nuclear VIP 450). Resting and exercise equilibrium gated blood pool scintigrams were obtained with the collimator positioned in an approximately 35° left anterior oblique view (LAO), with a 15° caudad tilt to separate the ventricles optimally and minimize septal thickness. Resting studies were acquired for: (1) a preselected time interval (5–8 minutes), (2) 28 frames per cardiac cycle, and (3) 90–100% of the cardiac cycle. This resulted in a minimum of 50,000 counts per frame of the study. Resting LV volume and EF were measured before supine exercise with the subject's legs flat and again after elevation into the ergometer pedals. The upright resting study was performed with the subject sitting quietly on the bicycle. Exercise scintigrams were obtained for: (1) a preselected interval of 3 minutes, (2) 24 frames per cardiac cycle and (3) 90–100% of the cardiac cycle. At each of the three exercise stages, data acquisition began after 1 minute of equilibration at the onset of each new work level.

LVEF was determined by constructing a region of interest (ROI) over the left ventricle at end-diastole and end-systole. Counts within the ROI were corrected for background and used to calculate EF using the formula: (end-diastolic counts − end-systolic counts)/end-diastolic counts. LVEF measured by this method correlates well with results obtained by contrast ventriculography.[24]

LV volumes were estimated by a totally nongeometric technique recently developed and validated in our laboratory.[28, 29] Further support for this technique comes from the independent work of Slutsky et al.[27] In brief, the end-diastolic and end-systolic frames were isolated and used for further processing. Correction for background activity was performed using a single directional interpolated background subtraction technique that provided a reproducible and objective assessment of background activity.[28] ROIs were constructed over the left ventricle at end-diastole and end-systole; left atrial activity was carefully excluded and strict criteria were used to define the LV borders. The 35° LAO–15° caudad view used in this study frequently allows visualization of the mitral valve plane and, hence, separation of left atrial and LV activity. If no clear delineation of the mitral valve plane was apparent, the valve plane was assumed to be perpendicular to the plane of the interventricular septum originating at the uppermost definable point of the septum. Scintigraphic estimates of left ventricular volumes were calculated using the following formula:

$$\text{LV volume} = \frac{\text{LV activity (counts/sec)} - \text{background}}{\text{peripheral blood counts/sec/ml}}.$$

Because these count data were not acquired simultaneously, the peripheral blood activity was corrected for isotope decay using the general expression $e^{-\lambda t}$, where $\lambda = 0.693/\text{isotope half-life}$ and t = time difference. LV activity was derived from the ratio of the total number of LV counts acquired during the imaging period (ROI counts) and the actual duration of data acquisition for each end-systolic or end-diastolic frame (total duration of the imaging period times the fraction of the cardiac cycle used for sampling divided by the number of frames per cycle). Using this method, we and others have found excellent correlations ($r = 0.95$) between scintigraphic and angiographic volume measurements.[27-29] Because of chest wall attenuation, the scintigraphic estimates of volumes are consistently smaller than the angiographic estimates. A regression equation was defined (angiographic volume = 4.98 × scintigraphic volume estimate + 6.91 ml) and used to estimate actual volumes. Because the Y intercept of the regression equation is not zero, LVEFs determined from the regressed volumes will differ slightly from the reported LVEFs that were based on count ratios.

LV end-diastolic volume, LV end-systolic volume, LVEF, stroke volume and cardiac output were measured at rest and at each work load in the supine and upright positions. Statistical analysis was performed using the paired *t* test and a two-way analysis of variance with Newman-Keuls multiple comparison test.[32] The results of the statistical analysis were similar with each method ($p < 0.05$ considered significant).

## Results

### LV Performance at Rest

LV end-diastolic volume was 107 ± 10 ml (mean ± SEM) at rest in the supine position and 21% (22 ml) lower in the sitting position ($p < 0.02$) (fig. 1 and table

TABLE 1. *Cardiovascular Response to Supine and Upright Exercise*

| | | Rest | | Stage I | | Stage II | | Peak exercise |
|---|---|---|---|---|---|---|---|---|
| | Supine | 107 ± 10 | $p < 0.01$ | 123 ± 11 | $p < 0.02$ | 137 ± 12 | NS | 135 ± 13 |
| LVEDV (ml) | | $p < 0.02$ | | NS | | $p < 0.05$ | | NS |
| | Upright | 85 ± 6 | $p < 0.001$ | 113 ± 12 | $p < 0.05$ | 117 ± 12 | NS | 116 ± 8 |
| | Supine | 34 ± 4 | NS | 31 ± 4 | NS | 32 ± 4 | NS | 29 ± 4 |
| LVESV (ml) | | NS | | NS | | $p < 0.02$ | | $p < 0.05$ |
| | Upright | 32 ± 5 | NS | 28 ± 3 | NS | 24 ± 3 | NS | 19 ± 3 |
| | Supine | 76 ± 8 | $p < 0.01$ | 92 ± 9 | $p < 0.05$ | 105 ± 8 | NS | 106 ± 9 |
| SV (ml) | | $p < 0.05$ | | NS | | NS | | NS |
| | Upright | 55 ± 5 | $p < 0.001$ | 85 ± 7 | NS | 92 ± 10 | NS | 99 ± 7 |
| | Supine | 5.4 ± 0.4 | $p < 0.001$ | 9.1 ± 0.9 | $p < 0.01$ | 13.8 ± 1.1 | $p < 0.01$ | 18.3 ± 1.6 |
| CO (l/min) | | NS | | NS | | NS | | NS |
| | Upright | 4.8 ± 0.3 | $p < 0.001$ | 10.4 ± 1.4 | $p < 0.02$ | 15.1 ± 1.5 | NS | 18.0 ± 1.2 |
| | Supine | 76 ± 2 | NS | 80 ± 2 | NS | 82 ± 2 | NS | 84 ± 2 |
| LVEF (%) | | NS | | NS | | NS | | $p < 0.05$ |
| | Upright | 72 ± 4 | $p < 0.05$ | 80 ± 2 | $p < 0.05$ | 84 ± 2 | $p < 0.05$ | 91 ± 2 |
| | Supine | 71 ± 6 | $p < 0.01$ | 100 ± 4 | $p < 0.01$ | 133 ± 2 | $p < 0.01$ | 172 ± 4 |
| HR (beats/min) | | $p < 0.05$ | | $p < 0.001$ | | $p < 0.01$ | | $p < 0.05$ |
| | Upright | 89 ± 5 | $p < 0.01$ | 124 ± 4 | $p < 0.01$ | 165 ± 4 | $p < 0.01$ | 182 ± 2 |
| | Supine | 125 ± 8 / 76 ± 4 | | 152 ± 6 / 81 ± 5 | | 169 ± 8 / 91 ± 6 | | 206 ± 7 / 96 ± 6 |
| BP (mm Hg) | | | | | | | | |
| | Upright | 125 ± 5 / 84 ± 4 | | 161 ± 7 / 86 ± 4 | | 190 ± 8 / 89 ± 6 | | 204 ± 8 / 91 ± 6 |

Values for ventricular volumes are mean ± SEM (n = 7).

Abbreviations: LVEDV = left ventricular end-diastolic volume; LVESV = left ventricular end-systolic volume; SV = left ventricular stroke volume; CO = cardiac output; LVEF = left ventricular ejection fraction; HR = heart rate; BP = blood pressure.

1). The LV end-systolic volume was not affected by posture. The LVEF (fig. 2) was slightly but not significantly larger in the supine position (76 ± 2% vs 72 ± 4%) (fig. 2). Cardiac output (fig. 3) was similar in both positions, but the heart rate was higher (89 ± 5 vs 71 ± 6 beats/min, $p < 0.05$) and stroke volume lower (55 ± 7 vs 76 ± 8 ml, $p < 0.05$) in the upright position. Systolic arterial pressure (table 1) was the same in both positions, but pulse pressure was lower and diastolic pressure higher in the upright position (84 ± 4 vs 76 ± 4 mm Hg, $p < 0.05$). There were no significant differences between supine measurements obtained with the legs flat and those obtained with the legs elevated onto the ergometer pedals.

### Stage I: Low-level Exercise

Exercise at stage I was carried out at 300 kpm/min. There were no changes in LV end-systolic volumes compared with mean values at rest, but LV end-diastolic volume increased by 33% during upright exercise ($p < 0.001$) and by 15% ($p < 0.01$) during supine exercise (fig. 1 and table 1). The mean LVEF was 80% in both positions, which represented a significant increase of 9% ($p < 0.05$) above resting values in the upright position (fig. 2). Cardiac output increased significantly ($p < 0.01$) to similar levels during supine and upright exercise (fig. 3), but the heart rate was higher (124 ± 4 vs 100 ± 4 beats/min, $p < 0.001$) and stroke volume slightly lower (85 ± 7 vs 92 ± 9 ml) in the upright position. The increase in stroke volume with the transition from rest to exercise was much larger in the sitting position (54% vs 21%).

### Stage II: Intermediate Exercise

LV end-diastolic volume (fig. 1 and table 1) showed a further increase compared with stage I at the intermediate exercise level (work load 600–750 kpm/min) in both the supine ($p < 0.02$) and sitting ($p < 0.05$) positions. Absolute LV end-diastolic volumes remained smaller in the upright position ($p < 0.05$). End-systolic volume showed a further significant decrease only in the upright position. The increase in cardiac output compared with stage I paralleled the increase in work load without any significant postural

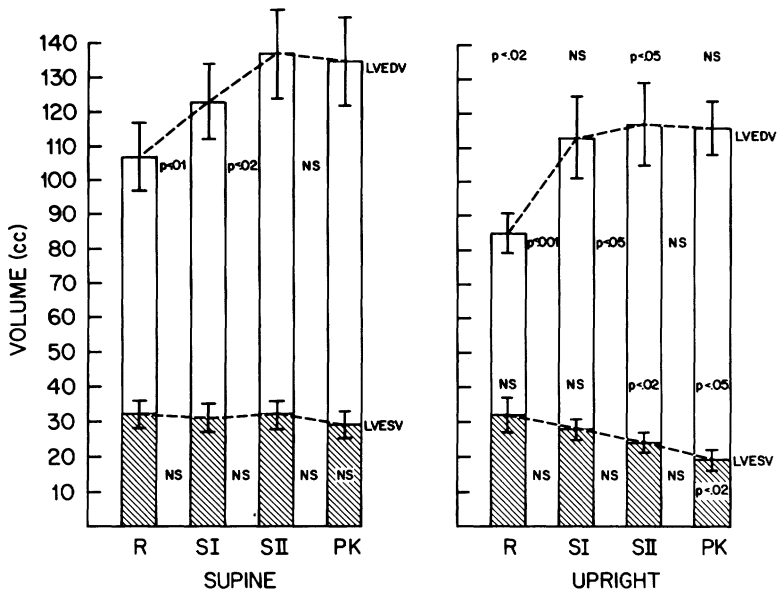


FIGURE 1. *Left ventricular end-diastolic volume (LVEDV), left ventricular end-systolic volume (LVESV), and stroke volume at rest (R) and during three levels of exercise. The top value of each bar represents LVEDV (mean ± SEM), the shaded portion represents LVESV, and the clear portion between the values of LVEDV and LVESV represents LV stroke volume. Above the upright data bars of the right-hand panel, the* p *values compare the significance between the corresponding upright and supine measurements of LVEDV at each work load; in the upright data panel, the* p *values above the LVESV data compare the significance of the corresponding supine measurements of LVESV;* p *values between adjacent bars indicate the significance of the change between progressive work loads; and* p *values enclosed within the small boxes of the peak exercise (PK) bars indicate the significance of change from rest to peak exercise for LVESV in each position. LVEDV also increased significantly between rest and peak exercise in both positions (*p < *0.001 supine,* p < *0.02 upright). SI = low level work (300 kpm/min); SII = intermediate level work (600–750 kpm/min).*

effect (fig. 3). Differences between positions with respect to heart rate and absolute stroke volume were similar to those at stage I.

**Peak Exercise**

There was no further increase in LV end-diastolic volume or stroke volume between stage II and peak exercise (1092 ± 174 kpm/min supine and 946 ± 146 kpm/min upright). End-diastolic and end-systolic volumes and stroke volume remained slightly smaller in the upright than in the supine position, but the differences were not significant (figs. 1–3 and table 1). LVEF continued to show a slight increase between stage II and peak exercise in the upright position ($p < 0.05$). During peak effort, LVEF was significantly higher ($p < 0.05$) in the upright than in the supine

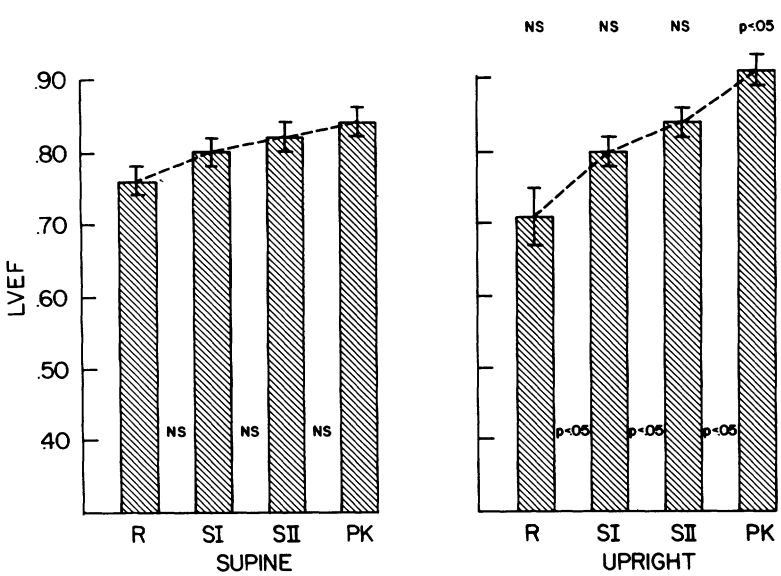


FIGURE 2. *Left ventricular ejection fraction (LVEF) at rest (R) and during three levels of exercise. The format and the abbreviations are the same as in figure 1. The difference between rest and peak exercise was significant in both positions (*p < *0.05 supine,* p < *0.01 upright).*

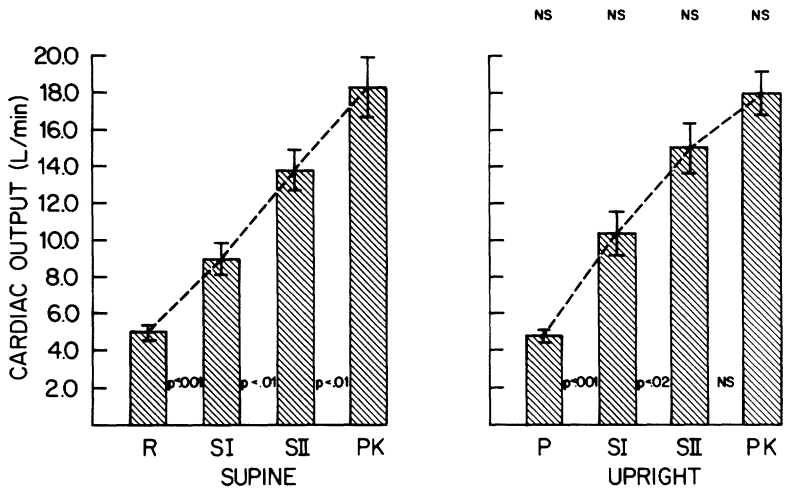


FIGURE 3. *Cardiac output at rest (R) and during three levels of exercise. The format and abbreviations are the same as in figure 1.*

position (fig. 2). Cardiac output (fig. 3), arterial pressures and the rate-pressure product (table 1) were similar in both positions, but peak heart rate was slightly lower in the supine position (172 ± 4 vs 182 ± 2 beats/min, $p < 0.05$).

## Discussion

The interactive effects of posture and exercise on LV dimensions and performance in man remain controversial despite extensive study. Methodologic limitations may account for the lack of consistency in the results from previous studies. Equilibrium radionuclide ventriculography offers important advantages over other methods because the technique is not dependent on geometric assumptions and the imaging agent has no intrinsic effect on the cardiovascular system. A newly developed scintigraphic method[29] that generates measurements of absolute LV end-diastolic and end-systolic volumes was therefore used to compare the effects of upright and supine exercise on the left ventricle.

Early studies in animals suggested that the Frank-Starling mechanism was inoperative during exercise. Rushmer et al. found nearly maximal LV size in resting, supine, unanesthetized animals and reported that LV diastolic diameter decreased during exercise with a concomitant increase in stroke volume.[4, 33] However, Chapman et al.[16, 34] showed a progressive increase in stroke volume with increasing exercise levels and concluded that the response is produced by a combination of increased contractility and the Frank-Starling mechanism. More recently, several investigators[35-39] have shown in exercising dogs that LV end-diastolic dimensions increase, LV end-systolic dimensions decrease and stroke volume increases, thus verifying, at least in the dog, that both the Frank-Starling mechanism and increased contractility are involved.

The data on left ventricular performance during exercise in man are inconclusive. Hemodynamic studies have generally, but not unanimously, shown that stroke volume increases with transition from rest to exercise in both the upright and supine positions.[1, 4, 8-10, 40-42] LV end-diastolic volume during supine exercise has been shown to decrease in studies in which metallic epicardial markers[11] and angiography were used.[14] Using angiography, Gorlin et al.[12] found no substantial change in LV end-diastolic volume. Crawford et al.[6] demonstrated echocardiographically that diastolic diameter does not change during moderate supine and upright bicycle exercise. In Crawford's study, diastolic diameter was larger in the supine position at rest and during exercise. In half the subjects, LV diastolic diameter increased with exercise in the upright but not in the supine position. Systolic dimensions decreased significantly in both positions. Stein et al.[43] reported no change in echocardiographic end-diastolic diameter during supine exercise, but a marked increase during early recovery. Weiss et al.,[13] also using echocardiographic techniques, found an increase in diastolic diameter during exercise at moderately high work loads in the semisupine position, but no change in systolic dimensions. An increase in angiographic LV end-diastolic volume in the supine position was described by Sharma et al.[14]

Our measurements during supine exercise showed a significant increase in stroke volume with the transition from rest to exercise and from light to moderately heavy exercise, but no further change at peak exercise. These changes in stroke volume were paralleled by changes in end-diastolic volume. End-systolic volume did not change, but ejection fraction showed a small progressive increase, and the difference between rest and peak exercise was significant. Systolic blood pressure and heart rate increased progressively during exercise. The measurements of end-systolic and end-diastolic volumes, combined with the stroke volume measurements, strongly imply large increases in stroke work and ejection rate. These changes are consistent with the increase in LVEF and may also be viewed as manifestations of an increased contractile state.

Our data on LV volumes at rest and during exercise in the upright position reveal a slightly different pattern. LV end-diastolic volume remained smaller

than in the supine position, but the response to increasing levels of exercise paralleled the supine results. Stroke volume and LVEF were lower at rest in the sitting than in the supine position, and showed larger increases from rest to mild exercise. LVEF continued to increase progressively during exercise, and the end-systolic volume decreased progressively through the three levels of exercise. LVEFs were higher and end-systolic volumes were lower in the upright than in the supine position during heavy exercise. Heart rates during exercise were higher in the upright position, but systolic blood pressures were similar in both positions. These data indicate that the LV response to exercise, irrespective of position, includes a combination of a Frank-Starling mechanism and an increased contractile state; however, changes in contractility are of greater relative importance in the upright than in the supine position.

Peak work loads were slightly higher in the supine than in the upright position in our study, which is in agreement with the findings of Holmgren and Ovenfors[5] in well-trained subjects; Åstrand and Saltin,[44] however, reported a higher work capacity and Bevegård et al.[9] reported an equal work capacity in the upright position. A slight mechanical disadvantage caused by a change from optimal work position to accommodate the imaging equipment may be the primary reason for the lower work capacity in the upright position in the subjects we studied.

In conclusion, this study shows the utility of dynamic myocardial scintigraphy for serial evaluation of LV function. With this technique, measurements of LV volumes and LVEF at rest and during exercise in both the supine and upright positions can be obtained. Our data indicate that during supine and upright exercise in man, both the Frank-Starling mechanism and increased contractility play a role in augmenting cardiac output.

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