
Ambulatory Monitoring of Left Ventricular Function during Cardiopulmonary Exercise Tests in Normal Sedentary Subjects

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Ambulatory monitoring (VEST) of left ventricular (LV) function is a useful and accurate method to measure cardiac function during exercise and rest. The aim of this study was to evaluate LV response to exercise in normal sedentary subjects. **Methods:** Ten normal sedentary subjects underwent continuous ambulatory monitoring of LV function by VEST during upright bicycle exercise associated with combined analysis of pulmonary gas exchange. All parameters of LV function were measured in control conditions at rest, at the anaerobic threshold (point of non-linear increase in ventilation relative to oxygen uptake) and at peak oxygen uptake (peak VO_2). **Results:** Heart rate and cardiac output significantly increased from control conditions to anaerobic threshold ($p < 0.001$) and from anaerobic threshold to peak VO_2 ($p < 0.001$). Ejection fraction, end diastolic volume and stroke volume significantly increased from control conditions to anaerobic threshold ($p < 0.001$), showing no significant change from anaerobic threshold to peak VO_2 . Finally, end-systolic volume significantly decreased from control conditions to anaerobic threshold ($p < 0.001$), showing no significant change from anaerobic threshold to peak VO_2 . **Conclusion:** VEST is particularly useful in the evaluation of cardiac response to exercise in normal sedentary subjects, providing a better understanding of the spectrum of the normal LVEF response to exercise. Our data demonstrate that ejection fraction response to exercise is variable after anaerobic threshold, and a uniform increase is not necessarily expected in normal sedentary subjects.

Key Words: vest; left ventricular function; anaerobic threshold; cardiopulmonary exercise test

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The exercise test is important in evaluating patients with cardiac and pulmonary diseases because abnormalities not evident at rest may be unmasked during stress (1). In recent years, different techniques, such as echocardiography, contrast angiography and radionuclide ventriculography, have been used to evaluate left ventricular (LV) func-

tion response to exercise in humans. Each of these methods has distinct disadvantages and limitations, and the results have been often conflicting (2–5). The recent development of a new radionuclide system (VEST, Capintec Inc., Ramsey, NJ) capable of continuous ambulatory monitoring of LV function has expanded the diagnostic potential of exercise testing (6,7). This technique may be performed simultaneously with noninvasive measurement of respiratory gas exchange during exercise in various cardiac diseases (8). Previous papers suggested a different change of ejection fraction after anaerobic threshold during exercise in normal subjects. In particular, Boucher et al. (9) showed that the anaerobic threshold ejection fraction response may be variable and an uniform increase is not necessarily expected, even in normal subjects. On the other hand, Rodrigues et al. (10) demonstrated that ventricular performance increases steadily during exercise and is not limited by the conversion of aerobic to anaerobic metabolism.

The aim of this study was to evaluate cardiac responses to exercise in normal sedentary subjects using continuous ambulatory monitoring of LV function associated with combined analysis of pulmonary gas exchange. In particular, we studied the change in systolic performance during the aerobic and anaerobic phases of bicycle exercise in order to assess whether the development of anaerobic metabolism during exercise is associated with altered LV function response to exercise.

MATERIAL AND METHODS

Patient Population

Ten normal sedentary subjects (7 male and 3 female, age range 23–60 yr, mean age 42 ± 11 yr) were studied. No patient had a history of chest pain, systemic hypertension or other cardiac disorders. Each subject was considered free of cardiac disease on the basis of history, physical examination and normal rest and stress electrocardiographic findings. They were all nonsmokers with good exercise tolerance and normal resting left and right ventricular function evaluated on equilibrium radionuclide ventriculography. Subjects were not receiving any cardioactive medication at the time of the study. The protocol was approved by the

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Institutional Clinical Research Subpanel of our university and all subjects gave informed consent.

Study Protocol

Equilibrium radionuclide ventriculography was performed immediately before the VEST study. All subjects underwent continuous ambulatory monitoring of LV function by VEST during upright bicycle exercise with combined analysis of pulmonary gas exchange. In each study, LV function was continuously monitored for at least 2 hr. All parameters of LV function were measured in control conditions at rest, at the anaerobic threshold (point of nonlinear increase in ventilation relative to oxygen uptake), at peak oxygen uptake (peak VO_2) and after 3 min of recovery.

Equilibrium Radionuclide Ventriculography

In vivo labeling of red blood cells was performed with 555 MBq of ^{99m}Tc . Equilibrium radionuclide ventriculography was performed in the 45° left anterior projection with a 15° cranio-caudal tilt with the patient in the supine position under control conditions, as previously described (11,12). A small field of view gamma camera equipped with a low-energy, all-purpose collimator was used. Data were recorded at a frame rate of 30 frames/cardiac cycle on a dedicated computer system. For each study, at least 200,000 counts/frame were acquired.

Cardiopulmonary Exercise Testing

All subjects underwent upright bicycle exercise in the morning. Patients were connected with a 2001 instrument (Medical Graphics, St. Paul, MN) to analyze breathing patterns and to measure oxygen uptake (VO_2), carbon dioxide release and ventilation. Reproducibility of this system in our laboratory was documented by the techniques described by Jones (13). The variability was less than 10% of the gas exchange with a variable obtained in four subjects over 6 mo. The electrocardiogram was continuously monitored and blood pressure serially measured by the auscultatory method. All subjects exercised at constant speed (60 rpm) for 3 min; the workload was then increased by 1 watt every 3 sec (ramp protocol) according to the previously established exercise tolerance until exhaustion. No test was interrupted for angina, ST depression, arrhythmias or hypotension. Maximal VO_2 was considered as the 30-sec averaged peak exercise value at the point when oxygen uptake did not increase despite increase in workload (peak VO_2). Peak VO_2 was considered as an index of functional capacity. The anaerobic threshold was determined by the gas-exchange criteria as the point of nonlinear increase in the ventilatory equivalent for oxygen, which has been previously associated with elevations in simultaneously obtained arterial lactate samples without a simultaneous increase in ventilatory equivalent for CO_2 (13). Heart rate, blood pressure, workload, VO_2 at rest, anaerobic threshold, and peak exercise were noted.

VEST

The ambulatory ventricular function monitor has been previously described in detail (11,12). At the conclusion of equilibrium radionuclide ventriculography, all subjects wore the VEST and the radionuclide detector was positioned over the left ventricle. The position of the detector was confirmed by acquiring 30-sec static image with the gamma camera (11,12). At the conclusion of the VEST study, a second 30-sec static image was obtained to confirm that the detector did not move during recording. Each patient wore the VEST during cardiopulmonary exercise testing.

Data Analysis

Equilibrium radionuclide ventriculography was analyzed using standard commercial software, as previously described (11,12). Briefly, left ventricle regions of interest (ROIs) were automatically drawn for each frame. A background ROI was also computer-delineated on the end-systolic frame. After background correction, a LV time-activity curve was generated. Ejection fraction was computed on the raw time-activity curve.

VEST studies were analyzed as previously described (11,12). Briefly, at the end of the VEST study, data were reviewed for technical adequacy. The decay-corrected average count rate of the entire recording was displayed. The VEST study was considered technically adequate if the decay-corrected curve had less than 10% deviation from a straight line. Sudden shifts in the slope of the line were indicative of detector movement or instrument malfunction. The radionuclide and ECG data were summed for 30-sec intervals (14). Ejection fraction was computed as the stroke counts divided by the background-corrected end-diastolic counts. Background was determined by matching the initial resting VEST ejection fraction value to that obtained by the gamma camera. These background values ranged from 70% to 82%. Relative end-diastolic volume was expressed as 100% at the beginning of the study, end-systolic volume was expressed relative to end-diastolic volume and cardiac output was calculated as relative stroke volume multiplied by heart rate.

Statistical Analysis

All values are expressed as mean \pm one standard deviation. Comparisons of left ventricular function obtained at rest and during exercise were made by analysis of variance for repeated measures. When the F-test was significant, individual comparisons of resting values and those of each work level were made by Duncan's multiple-range test. The comparison between anaerobic threshold and peak exercise was made by paired t-test. A p value less than 0.05 was considered statistically significant.

RESULTS

Mean exercise duration was 12 ± 2 min and mean exercise workload was 123 ± 18 watts. Figure 1 shows the hemodynamic parameters recorded in control conditions, at anaerobic threshold and at peak VO_2 . Figure 2 shows the individual values of the hemodynamic parameters recorded in control conditions at anaerobic threshold and at peak VO_2 . Heart rate significantly increased from control conditions (85 ± 13 bpm) to the anaerobic threshold (123 ± 13 bpm) ($p < 0.001$), and from anaerobic threshold to peak VO_2 (150 ± 13 bpm) ($p < 0.001$). Ejection fraction significantly increased from control conditions ($62\% \pm 8\%$) to anaerobic threshold ($68\% \pm 12\%$) ($p < 0.001$), showing no significant change from anaerobic threshold to peak VO_2 ($66\% \pm 14\%$). End-diastolic volume significantly increased from control conditions ($96\% \pm 7\%$) to anaerobic threshold ($102\% \pm 8\%$) ($p < 0.001$), with no significant change from anaerobic threshold to peak VO_2 ($104\% \pm 10\%$). End-systolic volume significantly decreased from control conditions ($37\% \pm 12\%$) to the anaerobic threshold ($31\% \pm 15\%$) ($p < 0.001$), showing no significant change from anaerobic threshold to peak VO_2 ($34\% \pm 16\%$). Stroke volume significantly increased from control conditions ($60\% \pm 8\%$) to the anaerobic threshold ($69\% \pm 14\%$) ($p <$

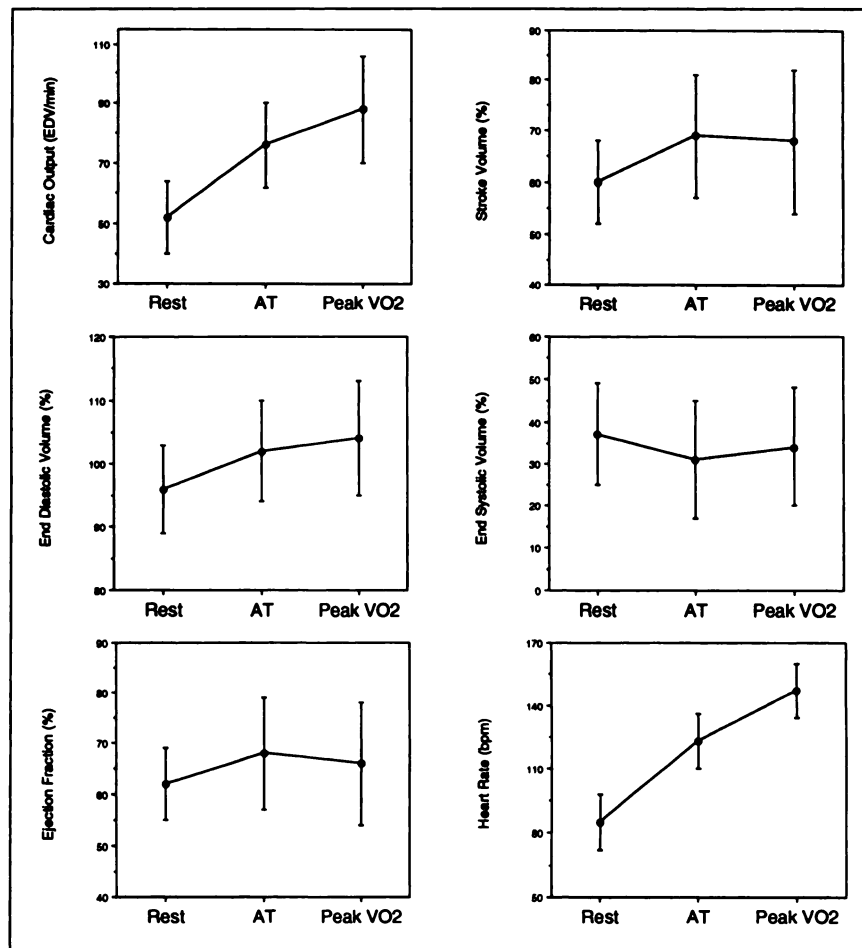


FIGURE 1. Mean values of hemodynamic parameters recorded in control conditions (Rest), at anaerobic threshold (AT) and at peak oxygen uptake (Peak VO₂).

0.001), with no significant change from anaerobic threshold to peak VO₂ (68% ± 18%). Finally, cardiac output significantly increased from control conditions (52% ± 12% end-diastolic volume/min) to anaerobic threshold (76% ± 16% end-diastolic volume/min) ($p < 0.001$) and from anaerobic threshold to peak VO₂ (88% ± 21% end-diastolic volume/min) ($p < 0.001$).

DISCUSSION

Several techniques have been used to evaluate LV function response during exercise in normal subjects (2,5,16). However, the results obtained from these measurements have been often conflicting (2–5). The introduction of a portable scintillation probe (VEST) similar to a miniaturized nuclear stethoscope has proven useful for measuring LV function both at rest and during exercise (11,12,17). This study was undertaken to assess LV response during exercise in a group of normal sedentary subjects using VEST. In particular, we evaluated changes in LV function before and after reaching the anaerobic threshold to determine whether the development of anaerobic metabolism during exercise is associated with impairment of LV response to exercise. The anaerobic threshold was considered as the work level at which lactic acid accumulates in the blood due to a shift to anaerobic metabolism in the

working muscles (15). This shift is the result of inadequate peripheral oxygen delivery, and therefore reflects overall cardiovascular capacity (9). We measured the anaerobic threshold by pulmonary gas-exchange analysis as the point of nonlinear increase in the ventilatory equivalent for oxygen (9). The anaerobic threshold measurement has been used to estimate the degree of cardiovascular impairment, with the magnitude of the anaerobic threshold reduction correlating well with the degree of hemodynamic abnormalities (18,19).

Furthermore, whereas previous studies demonstrated that in normal subjects ejection fraction increases from resting conditions to peak effort during exercise testing, only a few investigators evaluated the change in ejection fraction below and above the anaerobic threshold (9,10). In particular, Boucher et al. measured ejection fraction during exercise in normal subjects by radionuclide ventriculography and concluded that above the anaerobic threshold, LVEF response may be highly variable and a uniform increase is not necessarily expected (9). In the present study, ejection fraction significantly increased from resting conditions to the anaerobic threshold, showing no change from anaerobic threshold to peak VO₂. There are many factors that may explain this difference in ejection fraction change before and after reaching the anaerobic threshold.

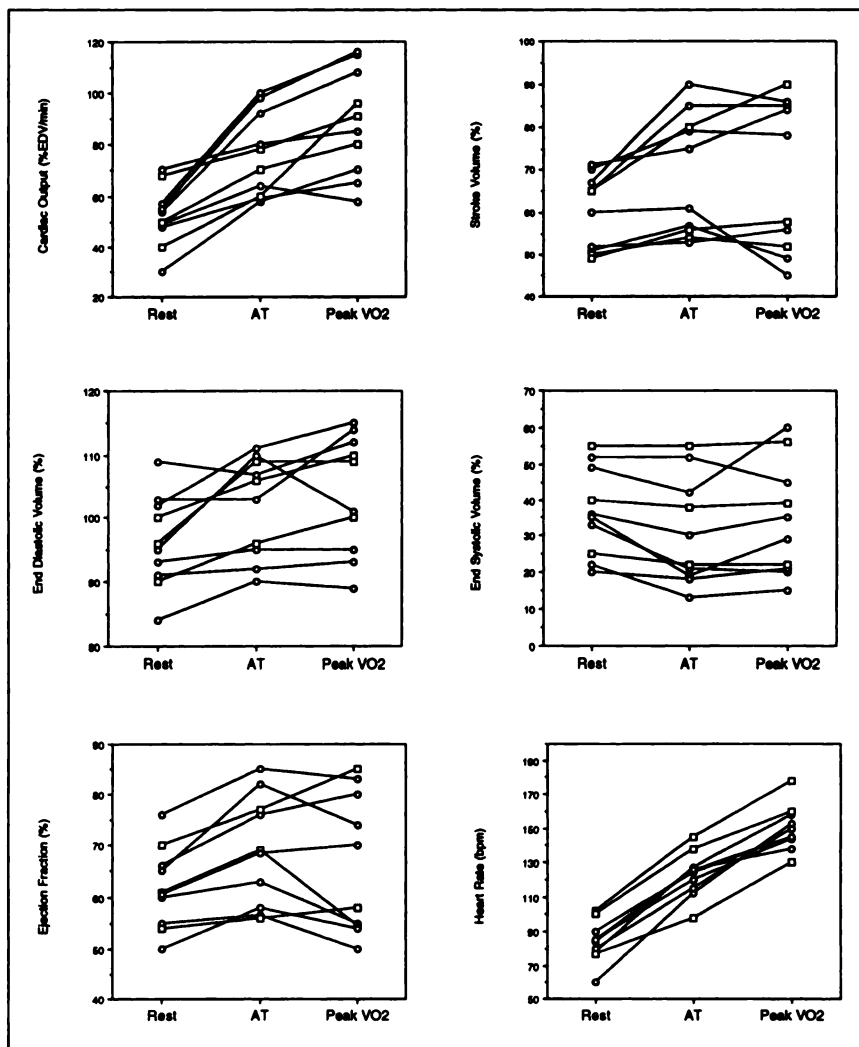


FIGURE 2. Individual values of hemodynamic parameters recorded in control conditions (Rest), at anaerobic threshold (AT) and at peak oxygen uptake (Peak VO₂). Open circles indicate males and open squares indicate females.

It is possible that lactic acid accumulation has an adverse impact on the myocardium, so that no further augmentation is possible. In addition, LV response to exercise probably utilizes most of the compensatory mechanisms such as preload and contractility during lower early work with only little further increase at higher levels (9).

In contrast to the results of previous studies and our findings, Rodrigues et al. recently suggested that LVEF during exercise in normal subjects continued to rise beyond the anaerobic threshold (10). In the present study, the anaerobic threshold occurred at a significantly higher heart rate during exercise testing than that reported by Rodrigues et al. (10). Thus, it is possible that there is dynamic shortening of diastole associated with no corresponding increase of end-diastolic volume at a higher heart rate which could limit or decrease any further preload compensation and thereby ejection fraction response of the left ventricle. Boucher et al. evaluated true peak exercise using the first-pass technique (9), whereas Rodrigues et al. studied ventricular function during maximal exercise over a 2-min period using equilibrium radionuclide ventriculography (10). Thus, it is conceivable that a fall in ejection

fraction occurring abruptly during the last few seconds of peak exercise could have been missed by Rodrigues et al. (10). Finally, possible differences in patient population such as sex, age or subclinical cardiac diseases could account for the different results.

In conclusion, this study demonstrates that VEST is particularly useful in the evaluation of cardiac response to exercise in normal sedentary subjects and provides a better understanding of the spectrum of normal LVEF response to exercise. Our data suggest that anaerobic threshold reasonably represents LV function at maximal or near maximal stress. In addition, the results of our study demonstrate that LV performance during exercise testing is limited by the conversion of aerobic to anaerobic metabolism. Therefore, VEST may be helpful in defining appropriate exercise limits for patients with cardiac diseases and may provide prognostic information for future coronary events.

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ERRATUM

Due to a production error, in the December 1994 issue of *JNM*, the radiotracer on page 1922 in the article "Dopamine D2 Receptor Imaging with Iodine-123-Iodobenzamide SPECT in Idiopathic Rotational Torticollis" by Hierholzer et al., was misprinted. The correct radiotracer is Iodine-123-IBZM.