Comparison of Bicycle and Treadmill Radionuclide Angiocardiography

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The purpose of this study was to test motion-correction algorithms for initial-transit radionuclide angiocardiograms acquired at rest and during bicycle and treadmill exercise. Treadmill data was spatially reoriented by computer software designed to eliminate motion of a ^{125}I point source simultaneously recorded at a lower energy window. A second algorithm based on left ventricular centroid counts further corrected for motion on all studies. Exercise left ventricular ejection fraction was higher on the treadmill (0.68 ± 0.07) compared to the bicycle (0.64 ± 0.08) ($p < 0.0001$, $r = 0.88$). Treadmill exercise also resulted in larger end-diastolic volumes (180 ± 30 versus 157 ± 36, $p < 0.0001$), stroke volumes (124 ± 28 versus 101 ± 29, $p < 0.0001$) and cardiac outputs (19.9 ± 4.6 versus 15.9 ± 5.0, $p < 0.0001$). Similar variances for these hemodynamic measurements suggest that the mean differences observed were physiologic and that error from body motion was effectively corrected by this approach. We conclude that the measurement of left ventricular function during treadmill exercise, when combined with these techniques for correcting motion, is a reasonable alternative to conventional bicycle exercise.

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The diagnostic and prognostic value of exercise initial-transit radionuclide angiocardiography (RNA) is well documented (*1–6*). Bicycle exercise remains the accepted standard for stress-radionuclide imaging. Though alternative methods have been investigated, bicycle exercise allows for high workloads with little chest motion and image degradation.

The treadmill is commonly used for exercise electrocardiography and myocardial perfusion imaging. During treadmill exercise, subjects achieve a higher oxygen uptake compared to bicycle exercise and are more likely to reach aerobic capacity or their peak predicted heart rate (*7*). Treadmill exercise has not been routinely applied to the radionuclide evaluation of ventricular function because of logistic constraints imposed by excessive patient motion and ponderous imaging hardware.

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Portable camera design and the development of motion-correcting techniques now make feasible treadmill testing in conjunction with RNA. The purpose of this study was to evaluate new computer based motion-correcting algorithms for RNA and compare motion-corrected left ventricular (LV) performance during peak treadmill exercise with that of bicycle exercise in a normal population.

METHODS

Population

This investigation was approved by the Duke University Medical Center Institutional Review Board. Twenty subjects were entered into the study after written informed consent was obtained. The study group consisted of eleven men and nine women, mean age 42 yr (range 22–63 yr). Absence of cardiac symptoms and a normal resting 12-lead ECG characterized the population as having a less than 5% likelihood of coronary artery disease.

Study Design

Studies were obtained on two separate days, with subjects randomly allocated to perform either bicycle or treadmill exercise at their first session. Forced balancing of groups was employed to ensure equivalent exercise sequencing. The mean interval between the two exercise studies was 5 days (range 1–16 days). All radionuclide angiocardiograms were performed using a portable multicrystal gamma camera. A 20-gauge Teflon catheter was placed into an external jugular vein and baseline blood pressure and heart rate recorded. Rest studies on the bicycle were obtained with the subject seated and upright and those on the treadmill with the subject standing. A 10-mCi dose of ^{99m}Tc diethylenetriaminepentaacetic acid (DTPA) in a volume less than 1 ml was then rapidly administered with a brisk flush of 20 ml of normal saline. Bicycle exercise was performed upright on an isokinetic ergometer. Exercise was begun at a 200 kpm/min workload and increased by 100 kpm/min every minute until 85% of the age-predicted maximum heart rate was reached. Heart rate, blood pressure and ECG were recorded every 2 min throughout the study. At the specified endpoint, a 30-mCi dose of ^{99m}Tc DTPA was injected and the exercise RNA obtained. Treadmill exercise was performed using the standard Bruce protocol. An external point source of 8 mCi of ^{125}I, contained within a 1-cm diameter lead shielded cup weighing 58 g, was applied to the lower right border of the sternum on the patient's chest. The gamma camera was set for dual-energy acquisition with windows centered at 140 keV for the ^{99m}Tc and 28 keV for the ^{125}I. Imaging during treadmill exercise was performed while the subject was walking and when 85% of maximum-age-predicted heart rate was at-

tained. If at their target heart rate, a subject was running, the treadmill was manually programmed to return to the stage at which they were last observed walking. Target heart rate was maintained despite this slight decrease in workload. At the time of imaging, a lab member stood behind the subject to assist positioning of the chest near the detector head. All subjects completed both exercise periods without chest pain, ECG evidence of ischemia or significant arrhythmias.

Data Processing

The RNA was acquired from the anterior projection, at 25 msec intervals, for 24 sec. Raw data were temporally smoothed and corrected for detector nonuniformity and deadtime. Exercise studies were additionally corrected for pre-existing background activity. Motion-correcting software was integrated within the processing format and employed left ventricular and point source centroids to amend motion. Rest and bicycle exercise studies were processed using only the LV centroid patient motion-correcting algorithm (PMC). Treadmill exercise studies, however, were initially processed with point source motion correction and then with PMC correction.

Point source motion correction required dual-isotope acquisition. In this mode, two simultaneous sets of data were collected. Data recorded within the ^{99m}Tc window represented tracer transit through the central circulation. Data within the ^{125}I window indicated point source and chest motion during the treadmill study. Each 25 msec frame of point source data was subject to a predefined threshold level and the center of mass (COM) of the remaining counts within each frame determined. This data defined the relative location of the point source in all frames and was used to spatially realign data within the ^{99m}Tc window and eliminate point source motion.

Point source corrected treadmill data and rest and bicycle exercise studies were all processed with the PMC algorithm. PMC generated a representative cardiac cycle from all beats identified after clearance of tracer from the lung up to the point where the descending aorta became apparent. A generous LV region of interest (ROI) was then manually determined from the end-diastolic image of the representative cycle. The COM of counts contained within this ROI defined a relative position for each frame of the representative cycle. Using the same ROI, the COM of counts was ascertained for each frame of data from the selected beats. Individual frames from selected beats were then realigned by repositioning their centers of mass to the respective centers of mass of individual frames from the representative cycle. An end-diastolic image acquired during Stage III of the Bruce protocol in a normal subject with and without point source and PMC correction is shown in Figure 1.

After motion correction, all studies were worked up in a customary manner. Only beats with an end-diastolic count of at least 70% of the recorded peak end-diastolic activity were selected. Summation of these beats generated a final background-corrected representative cardiac cycle from which left ventricular ejection fraction (LVEF) and cardiac volumes were determined. LVEF and volume determination were based on software previously developed and validated at this institution (4).

Statistical Analysis

Comparison of bicycle and treadmill performance was based on a randomized crossover design with stratification and blocking to ensure balance of each stratum. The subject represented the block and the exercise modality the "treatment" while the various

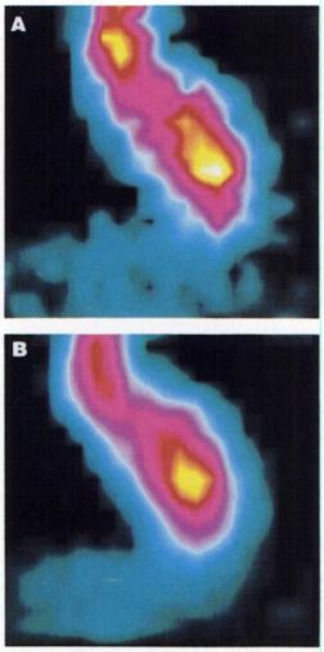

FIGURE 1. End-diastolic image obtained during treadmill exercise (A) without motion correction and (B) with point source and PMC correction. Note improved image quality, particularly in regard definition of the left ventricular cavity.

cardiac parameters were the response variables. As the "treatments" were not completely balanced between Day 1 and Day 2, the effect of sequence and patient assignment was also estimated. Carry-over and period effects were not considered applicable. Variability of performance on the bicycle and treadmill was estimated by the variance and compared by using an F-test. Rest studies were analyzed to compare performance on Day 1 with Day 2, while exercise studies compared Day 1 with Day 2 and bicycle versus treadmill. Analysis of variance was used to test for differences between the rest studies and between the bicycle and treadmill exercise studies. Linear regression analysis was applied using the principle of least squares. A p value of 0.05 or less was considered significant.

RESULTS

Variability of Rest Studies

The F statistic confirmed equal variances for all rest response variables. Rest mean arterial pressure was 100 ± 12 on Day 1 compared to 95 ± 8 on Day 2 ($p < 0.05$). No significant difference was observed at rest in heart rate, ejection fraction, end-diastolic volume or other derived cardiac values. Variation in resting measurements of mean arterial pressure, heart rate, ejection fraction and end-diastolic volume from Day 1 to Day 2 are depicted graphically as scatterplots (Figs. 2–5). Lines of identity are drawn and correlation coefficients derived from regression analyses are given.

Variability of Exercise Studies

The F-test was again used to confirm equal variances of measured variables for the two exercise modalities. Mean values for hemodynamic parameters measured with bicy-

cle and treadmill exercise are summarized (Table 1). No significant difference was observed in exercise heart rate or end-systolic volume on the treadmill and bicycle studies. Significant differences occurred in LVEF and most cardiac volumes between the two exercise tests. There was no confounding sequence or patient assignment effect. Regression analysis gave an excellent correlation in ejection fraction (r = 0.88), end-diastolic volume (r = 0.87), stroke volume (r = 0.91) and cardiac output (r = 0.89) when exercise measurements from the treadmill and bicycle were compared. Using the randomized repeated-measures design, variability owing to individual differences was eliminated from the error term, increasing the likelihood of observing significant differences between levels of "treatment." Similar variances from these comparisons suggested that treadmill derived measurements were not intrinsically subject to greater variation than those obtained by bicycle exercise.

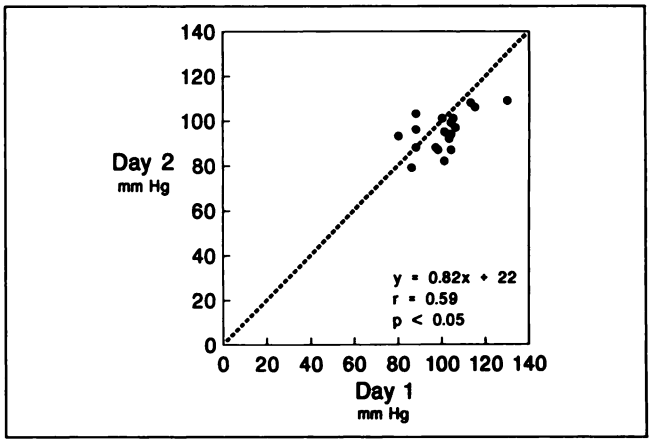

FIGURE 2. Variability of mean arterial pressure at rest. The regression equation (y), correlation coefficient (r), and probability of significant difference (p) from Day 1 to Day 2 are given. Lines of identity are drawn.

Comparison of Bicycle and Treadmill Exercise

Exercise mean arterial pressure was 126 ± 14 mm Hg on the bicycle compared to 110 ± 12 mm Hg on the treadmill ($p < 0.0001$). Exercise LVEF was 0.68 ± 0.07 on the treadmill compared to 0.64 ± 0.08 on the bicycle ($p < 0.0001$). Treadmill exercise also resulted in larger end-diastolic volumes (180 ± 30 versus 157 ± 36, $p < 0.0001$), stroke volumes (124 ± 28 versus 101 ± 29, $p < 0.0001$), and cardiac outputs (19.9 ± 4.6 and 15.9 ± 5.0, $p < 0.0001$). Rate-pressure product, on the other hand, proved to be significantly higher with bicycle exercise, 30,400 ± 5200, than the treadmill, 27,100 ± 3700 ($p < 0.0001$). Mean exercise end-systolic volume was the same for both the bicycle (56 ± 15 ml) and the treadmill (56 ± 13 ml) (p = ns).

DISCUSSION

The treadmill offers several important advantages over the bicycle for exercise stress testing. The wide range of treadmill speed and slope affords greater flexibility in test design and administration. Maximal exertion on the treadmill is less often limited by fatigue, weakness or discomfort of the quadriceps muscles than with bicycle exercise. In population studies, treadmill exercise results in a more uniform stress than bicycle exercise as reflected by comparable O_2 requirements per unit body weight at similar workloads for all subjects, regardless of their state of health or physical fitness (*8–9*). Individuals are therefore more likely to reach aerobic capacity and peak-predicted heart rate with treadmill exercise.

During dynamic cardiac scintigraphy, motion artifact may be introduced by motion of the entire body or by structures within the thorax. Immediate post-treadmill exercise RNA has been used to assess LV performance but rapid normalization of hemodynamics toward resting baseline after cessation of exercise limits the usefulness of these measurements (14). We began performing RNA during peak treadmill exercise in 1988. The influence of body motion on the image was blunted by having subjects, without assistance, firmly embrace the detector head to their chest during imaging, so that detector motion mirrored body motion. This often worked with the cooperation of motivated and compliant patients, however, the approach was not applicable to a broad patient population.

Previously described methods for correcting motion during dynamic scintigraphy have focused on tracking target organ or point source centroids (*15–21*). Oppenheim and Hoffer et al. corrected translational organ and subject motion during liver scintigraphy by determining the center of hepatic radionuclide activity and repositioning this and subsequent centroids to a fixed reference point (*15–16*). Fleming detailed a successful technique to correct translational and rotational subject motion using two ^{57}Co point sources in patients undergoing renography (*19*). Similar approaches for correcting motion have been reported with bicycle exercise and equilibrium RNA and tomographic cardiac perfusion imaging (*20–21*).

In our study, body motion was corrected using the ^{125}I point source and cardiac motion within the thorax addressed by tracking the center of mass of the LV blood pool. Body movement during bicycle exercise was largely rotational with lack of point source movement suggesting limited translational motion. Therefore, correction for point source motion during bicycle exercise did not alter the RNA results. Intrinsic cardiac motion resulting from rotation and the motion of breathing during bicycle exercise was addressed by the LV centroid algorithm. This algorithm appeared equally applicable for correction of studies performed at rest which were influenced primarily by respiratory movements.

The 8-mCi ^{125}I point source used in this study was developed in conjunction with the radiopharmacy. Constructed by impregnating resin beads with liquid ^{125}I, the source emitted more than 100,000 cps of activity when

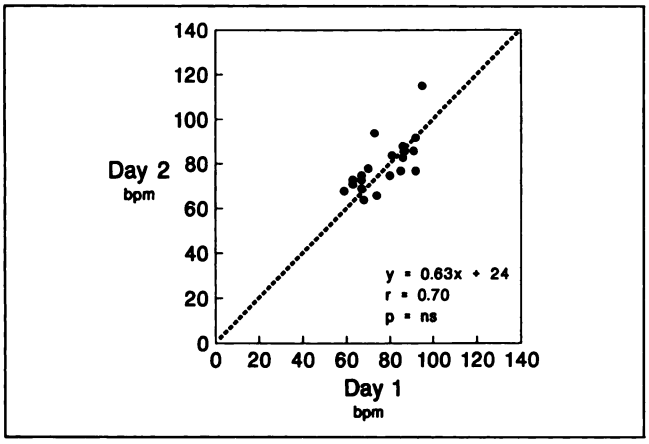

FIGURE 3. Variability of heart rate at rest. The regression equation (y), correlation coefficient (r), and probability of significant difference (p) from Day 1 to Day 2 are given. Lines of identity are drawn.

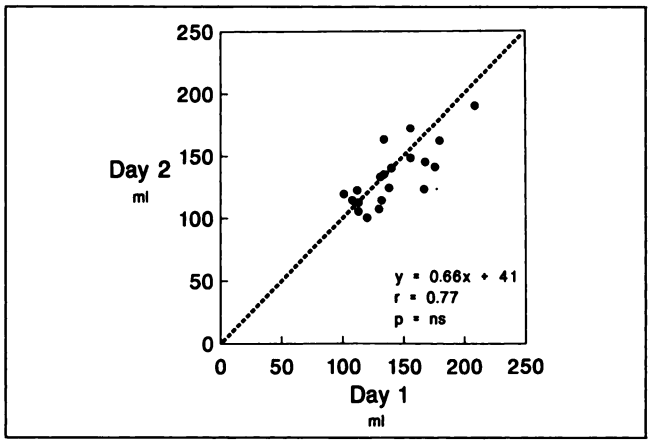

FIGURE 5. Variability of end-diastolic volume at rest. The regression equation (y), correlation coefficient (r), and probability of significant difference (p) from Day 1 to Day 2 are given. Lines of identity are drawn.

new and possessed an effective life of 2–3 mo. A snap fastener fitted to the base of the lead case allowed the point source to be attached to a standard ECG electrode pad. When monitor pads were applied for the stress study, an additional pad for the source was placed to the right of the lower border of the sternum. Imaging was performed in Stage I for one subject, Stage II for six subjects and Stage III for thirteen subjects. By Stage IV, most people were running and motion so excessive that the point source risked moving from the field of view of the detector. We exercised subjects to the highest stage attained but, just prior to injection of tracer, returned the treadmill to the stage at which the individual could walk when imaging. This maneuver was necessary for five subjects, all male. It required 10–15 additional seconds before imaging and resulted in no significant reduction in the exercise heart rate. During the time of study acquisition, gentle stabilization of the subject's chest ensured correct positioning of the heart for imaging, reduced rotational motion and confined translational motion within a plane parallel to the detector surface.

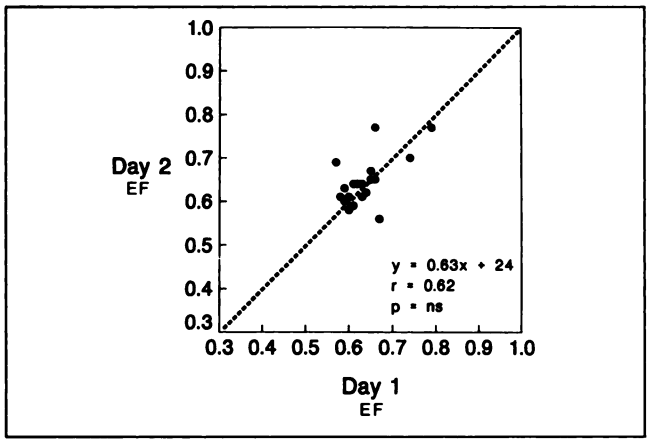

FIGURE 4. Variability of ejection fraction at rest. The regression equation (y), correlation coefficient (r), and probability of significant difference (p) from Day 1 to Day 2 are given. Lines of identity are drawn.

Invasive and noninvasive techniques have been used to assess the various hemodynamic and ventilatory responses to multistage bicycle and treadmill exercise (*11–13,22–26*). Comparisons at equivalent submaximal and maximal exercise workloads generally note higher heart rates, rate-pressure products, peripheral vascular resistances and pulmonary ventilations with bicycle exercise. Stroke volume and cardiac output, however, have been reported to be 5%–10% higher with treadmill exercise. We observed a 23% and 25% increase in stroke volume and cardiac output, respectively, with treadmill exercise compared to the bicycle. While larger than that reported in the literature, our measurements reflect comparison with a different exercise end-point (85% MPHR) and a more diverse study population with regard to age, sex and training. Mean arterial pressure (MAP) is 10%–20% higher with the bicycle at maximal exercise, compared to the treadmill, but similar at submaximal levels in athletic young males, while in fit middle-aged men a higher MAP is noted at all levels of exercise (*11,22*). We noted a 15% increase in cuff-

TABLE 1
Hemodynamic Measurements at Exercise

	Bicycle	Treadmill	p
Heart rate (bpm)	156 ± 9	158 ± 8	ns
Mean arterial pressure (mm Hg)	126 ± 14	110 ± 12	<0.0001
Ejection fraction	0.64 ± 0.08	0.68 ± 0.07	<0.0001
End-diastolic volume (ml)	157 ± 36	180 ± 30	<0.0001
End-systolic volume (ml)	56 ± 15	56 ± 13	ns
Stroke volume (ml)	101 ± 29	124 ± 28	<0.0001
Cardiac output (liter/min)	15.9 ± 5.0	19.9 ± 4.6	<0.0001
Rate-pressure product (10^3 mm Hg bpm)	30.4 ± 5.2	27.1 ± 3.7	<0.0001

All measures mean ± standard deviation.

derived mean arterial pressure with bicycle exercise compared to the treadmill. Lower maximum oxygen uptake observed in most subjects during bicycle exercise has been associated with a lower cardiac output, lower arteriovenous oxygen difference and reduced lower limb blood flow compared to treadmill exercise (*11–13,25,26*). Greater impairment to muscle blood flow ultimately contributes to a reduced venous return with bicycle exercise. Discrepancies in the working muscle mass of bicycle and treadmill exercise additionally enhance these differences in venous return (*12*).

With centroid, count-based motion-correcting algorithms, spatial resolution can be degraded by errors in determining centroid positions and by statistical noise. Characteristics of dual-isotope motion correction with americium 241 have been described with phantom experiments and quantitative assessment of spatial resolution (*20*). We evaluated the clinical reliability of our motion correcting algorithms by comparing measured responses to treadmill exercise with the exercise standard, the bicycle. The use of a randomized block design using factorial analysis of variance provided a technique to ascertain the magnitude of contribution of identified sources of variation to the total variation and give statistical control for between-subject and within-subject variability. Estimates of the population variance were then used to draw conclusions regarding the sample means. This is a powerful experimental design to detect differences between the effects of treatment within individual subjects. Prior to testing, homogeneity of variances between measured variables was confirmed using the F-test. With this analysis we observed highly significant mean differences in exercise LVEF, EDV, SV and MAP. Through the elimination of sequencing and patient assignment effect, these differences can be attributed either to differing exercise physiology or error introduced by our methodology. While definitive conclusions cannot be made, we feel that given the similar variances observed with each exercise modality, they indeed reflect true differences ascribed to the differing hemodynamics and physiology of bicycle and treadmill exercise. Our data, moreover, indicate motion-corrected, treadmill-acquired RNA to be a reasonable alternative to bicycle stress testing.

New radiopharmaceuticals that allow for the simultaneous assessment of myocardial perfusion and function provide an ideal setting for the application of treadmill stress testing (*28,29*). Treadmill exercise is already a well-established standard for stress testing in this country. The capacity to evaluate patients during a single study period, simultaneously measuring the electrocardiograph and myocardial perfusion and function has broad clinical appeal and application.

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