Redistribution of Visceral Blood Volume in Upright Exercise in Healthy Volunteers

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Exercise induced changes in the blood volume of visceral organs (cardiopulmonary and liver, spleen, and kidneys) were determined by scintillation camera imaging of the distribution of technetium-99m-labeled red blood cells in the thorax and abdomen of ten healthy adult volunteers. Graded upright bicycle exercise was performed to the point of exhaustion with the volunteer positioned with his/her back to the scintillation camera and data recording was synchronized to the pedal cycle to minimize patient motion artifacts within the data. The first image from each level of exercise was analyzed by placing regions of interest over the spleen, liver, kidneys, and right lung. The counts in each organ were expressed as a percent of activity at zero workload. Analysis of data using Hotelling's t-squared analysis to see if overall differences existed between the last four measurements (up to the time of exhaustion) regarding percent change from baseline for spleen, kidney, liver, and right lung were made. The splanchnic bed had a significant decrease in blood volume. The spleen decreased 39%, while the liver decreased 14%. For the kidney and liver, no significant differences were achieved ($p > 0.24$, $p < 0.15$, respectively). The lung increased its blood volume to 128% of control, significant with $p < 0.02$. This data demonstrates that in healthy volunteers there is normal redistribution of blood volume during maximal exercise with a significant reduction in blood volume of the spleen as well as a significant rise in blood volume within the lungs.

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Previous measurements of changes in the distribution of cardiopulmonary volume in man from rest to exercise have led to a spectrum of results: Braunwald et al. (*1*) found an increase in blood volume, Kattus et al. (*2*) found a decrease in blood volume, while others found the volume to remain unchanged during exercise (*3,4*). Other investigators have stated that a rise in pulmonary blood volume, over rest levels, during exercise indicates coronary artery disease (*5,6*). These disparate conclusions may result from the use of volume estimates based on different techniques and concepts (*7–13*). In some studies (*5,6*) normal individuals were not examined as control subjects, which raises a question about the specificity of an increase in pulmonary blood volume as an indicator of coronary artery disease. To address this controversy, we studied the distribution of both cardiopulmonary and gastrointestinal visceral blood volume during upright bicycle exercise, in a series of healthy volunteers using a large field scintillation camera and blood pool imaging.

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MATERIALS AND METHODS

Patient Selection

Following approval of the Subcommittee on Human Studies, volunteers between the ages of 21 and 34 yr of age, in good physical condition with no history of serious illness were solicited. All volunteers were prescreened for medical problems which would interfere with maximal exercise (i.e., heart or lung disease, overweight, previous deep venous thrombophlebitis, current medications, etc.) and all were examined by a board certified cardiologist screening for heart disease or murmurs. Pregnant females were excluded from the study. Those individuals who passed the prescreening examination underwent a 12-lead EKG. Ten volunteers qualified for the study (seven females, three males, mean age = 28 yr, s.d. = 4.88).

Exercise Testing

Subjects were studied in the late afternoon or evening, after fasting for a minimum of 3 hr. Graded, continuous exercise was performed on a constant load bicycle ergometer, calibrated in kiloponds. Workload was increased 150 kilopond-

meters/minute (kpm/min) every 200 bicycle pedal revolutions (approximately every 3 min) until the volunteer could exercise no more (collapse).

Data Acquisition

Following the modified in vivo labeling of the volunteer's own red blood cells with 10 mCi (370 MBq) of technetium-99m (*14*), the volunteers were positioned in front of a large field-of-view gamma camera (Technicare 410) with their backs to the gamma camera (Fig. 1). The camera was fitted with a general all purpose collimator, pulse height analyzer (PHA) centered at 140 keV with 25% window and attached to a Technicare 560 computer. The camera was positioned with the apex of the lungs at the top of the field of view and the lower abdomen at the bottom of the field. In all volunteers, this encompassed the lungs, spleen, liver, and kidneys (gastrointestinal visceral organs).

The bicycle ergometer was fitted with an apparatus to identify a specific point in the pedal rotation. The image data was recorded as a "multigated" collection, using the pedal in place of the R wave as the physiological trigger. The data was acquired as a multigated acquisition since motion during bicycling would degrade the images and would not allow precise identification of boundaries of the visceral organs. The acquisition program was gated to the position of the bicycle pedals and each revolution of the pedal was divided into eight 128 × 128 pixel image frames, and the program was set up to terminate acquisition at 200 beats (200 pedal cycles). Utilizing this technique, there are ~50,000 counts per image for analysis.

Quantitative Treatment of Data

The first frame from each stage of exercise was selected for analysis. Regions of interest (ROI) were placed over the spleen, kidneys, right lung, and liver. The right lung was chosen over the left lung or total thorax because of the difficulty in separating cardiac activity from left lung activity. This also provided for a larger region of interest to analyze.

The regions of interest were the same for each stage of exercise, thus counts per ROI were used for computation. Counts at rest (no workload) were used as baseline and all subsequent measurements were expressed as a percent of counts at rest (Table 1).

Statistical Analysis

Data analysis was carried out by the Henry Ford Hospital, Detroit, MI, Department of Biostatistics. Data was analyzed using Hotelling's t-squared analysis (Appendix 1) to see if an overall difference existed between the last four measurements

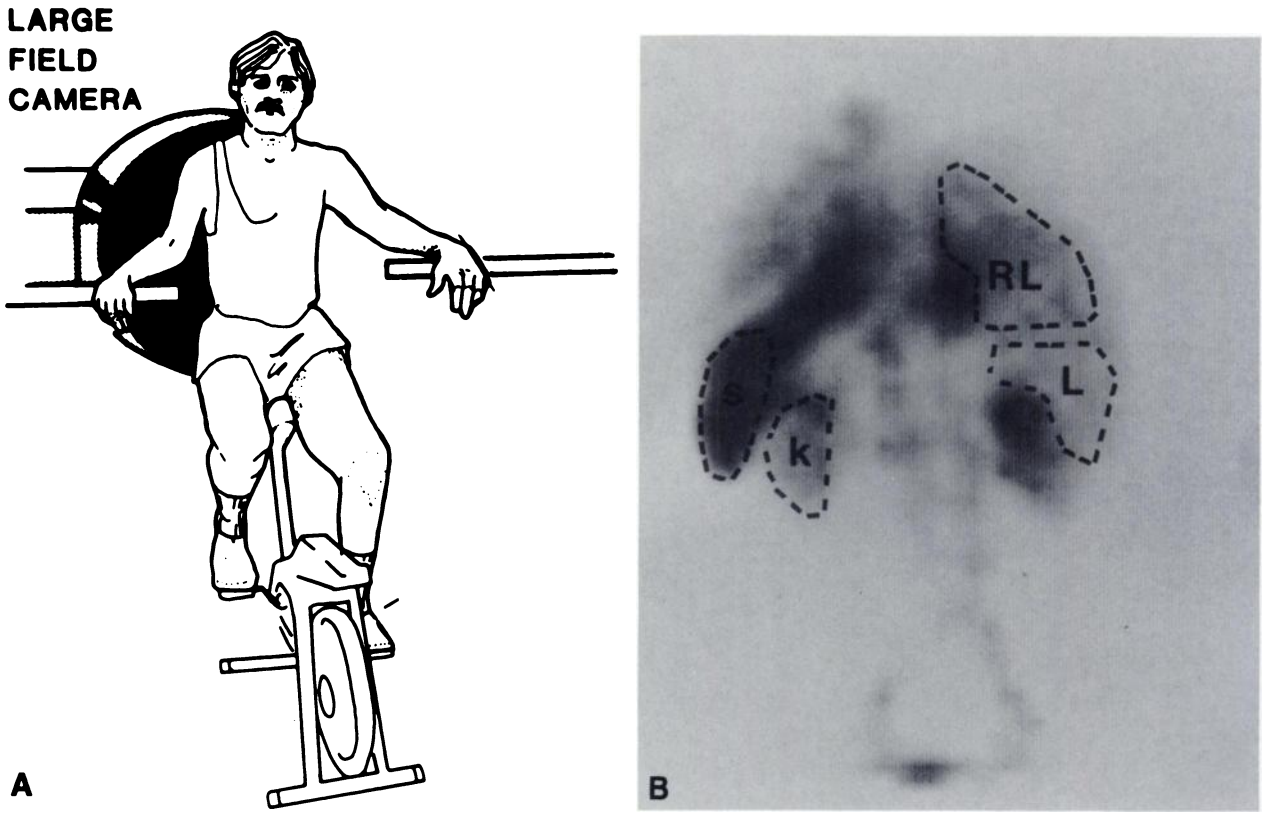

FIGURE 1
A: The volunteer was positioned upright on the bicycle ergometer with a large field-of-view gamma camera behind the thorax-abdomen. B: This figure demonstrates the regions of interest used for measuring blood volume changes. (K = Kidney, S = Spleen, RL = Right Lung, L = Liver)

(up to the time of exhaustion) regarding percent change from the baseline for spleen, kidney, liver, and right lung (*15*). For those variables which show an overall difference, paired t-tests were used to make all possible pairwise comparisons of the four measurements. The results are summarized, where the cutoff p-value is reduced from 0.05 to 0.008 for all pairwise comparisons (the Bonferroni multiple comparison adjustment), in Table 2.

RESULTS

The maximal heart rate for the group was 188 beats per minute. All volunteers exercised through at least five stages of exercise (620 kpm/min) with a mean of 5.8 stages (885 kpm/min), and one volunteer exercised to eight stages. All studies were terminated due to fatigue and EKGs were normal throughout exercise.

Since the number of stages required to reach exhaustion in each volunteer was variable, data analysis had to be performed as a comparison of "exhaustion" to the three stages preceding that. Table 1 contains the number of stages that each volunteer was able to perform before reaching exhaustion (collapse). The maximal exercise percent of baseline volume is presented for the four organs of interest. The spleen demonstrated the largest change in blood volume, with a reduction of 39% from baseline. The right lung demonstrated an average increase of 28% over rest values, while the kidney and liver decreased 9% and 14%, respectively.

The Hotelling's t-squared analysis to measure overall difference between the last four measurements (the three stages preceding exhaustion and the exhaustion phase) regarding percent change from baseline demonstrated a p-value for the spleen of <0.0001, p-value for the kidneys of greater than 0.24 (not significant), for the liver a p-value <0.15 (not significant), and for the right lung a p-value <0.02 (significant). For the spleen and right lung, which did demonstrate significant differences, further paired t-test analysis was performed as illustrated in Table 2. For the spleen, the t-test analysis between the exhaustion (collapse) phase and the preceding three phases, there is significance ($p < 0.0001$). For the right lung, comparing exhaustion (collapse) with the preceding three phases, there is significance ($p < 0.002$).

DISCUSSION

Most of the data previously reported on changes in pulmonary blood volume during exercise is based on indicator dilution techniques which measure blood volume between the site of injection (i.e., superior vena cava) and the site of withdrawal (i.e., brachial artery) (*16–18*). Wade et al. demonstrated a reduction in splenic volume during exercise (*19*) and our results are in line with theirs. No significant reduction in kidney volume would be expected, since renal perfusion is preserved during exercise. The rise in lung volume may be explained by capillary recruitment and increased lung perfusion associated with high level exercise.

During the follow-up imaging, splenic blood volume increased and pulmonary blood volume decreased as the subjects recovered. The increase in pulmonary blood volume observed in healthy subjects conflicts with previous published data (*5,6*) stating that a rise in

TABLE 1
Exercise Redistribution Data

Volunteer	Age	Sex	# Stages	Spleen*	Rt. Lung*	Kidney*	Liver*	Max. Heart Rate
KK	23	F	6	43.8	120.5	96.1	84.5	200
LR	26	F	5	68.9	139.6	98.1	89.7	160
DG	34	F	5	63.9	155.0	83.3	90.4	185
JD	31	F	5	62.9	157.6	81.6	74	200
WY	33	M	7	56.0	125.6	83.0	84.8	175
WN	34	M	6	63.2	108.0	96.2	80.0	170
BT	29	F	6	61.4	120.8	96.7	82.8	198
AM	21	F	5	68.7	108.3	101.7	87.5	185
WS	26	M	8	63.3	145.8	83.3	87.8	180
CH	23	F	5	58.9	102.6	93.6	95.7	200
Mean	28.0		5.8	61.1	128.4	91.4	85.7	185.3
s.d. =	4.88		1.03	7.2	20.0	7.7	6.2	14.2
n = 10				$p < 0.0001$	$p < 0.02$	$p > 0.24$(N.S.)	$p < 0.15$(N.S.)	

* Values expressed as % of rest volume.

TABLE 2
Hotelling's T-Squared Analysis

For spleen	p Value
Overall Hotelling's t-squared analysis	<0.0001*
Paired t-test analyses	
collapse vs. collapse-1	<0.0001*
collapse vs. collapse-2	<0.0001*
collapse vs. collapse-3	<0.0001*
collapse-1 vs. collapse-3	<0.0001*
collapse-1 vs. collapse-3	<0.0001*
collapse-2 vs. collapse-3	<0.0001*
For kidney	**p Value**
Overall Hotelling's t-squared analysis	<0.24
Paired t-test analyses are not applicable	
For liver	**p Value**
Overall Hotelling's t-squared analysis	>0.15
Paired t-test analyses are not applicable	
For right lung	**p Value**
Overall Hotelling's t-squared analysis	<0.02*
Paired t-test analyses	
collapse vs. collapse-1	<0.002*
collapse vs. collapse-2	<0.002*
collapse vs. collapse-3	<0.002*
collapse-1 vs. collapse-2	>0.01
collapse-1 vs. collapse-3	>0.01
collapse-2 vs. collapse-3	>0.13
n = 10	

* Denotes statistical significance.

pulmonary blood volume correlates with coronary artery disease. In the Okada study, subjects were exercised in the supine position; in the Nichols study, subjects were not exercised to exhaustion. The present study suggests that a rise in pulmonary blood volume during upright exercise is a normal response and cannot serve as an indicator of left ventricular failure.

This data clearly indicates that at peak exercise in normal subjects there is a significant rise in pulmonary blood volume, a significant decrease in splenic blood volume, without significant changes in the renal or liver blood volumes.

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APPENDIX 1

Hotelling's t^2 test

Consider a common situation in multivariate analysis. You have several different measurements taken on each of several subjects, and you want to know if the means of the different variables are all the same. For example, you may have used different recording devices to measure the same phenomenon, or you may have observed subjects under a variety of conditions and administered a test under each of the conditions. If you had only two means to compare, you could use the familiar *t* test, but it is important to use an analysis that takes into account the correlations among the dependent variables, just as in the previous examples, even though there are no independent factors in the model, that is, no terms on the right side of the MODEL statement. In this situation you could use Hotelling's t^2 test.

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