Cardiovascular Responses to Exercise in Middle-aged Men After 10 Days of Bedrest

VICTOR CONVERTINO, PH.D., JOSEPH HUNG, M.B., DANIELLE GOLDWATER, M.D., AND ROBERT F. DEBUSK, M.D.

SUMMARY The cardiorespiratory response to 10 days of continuous recumbency was assessed in 12 healthy men, age 50 ± 4 years, who underwent supine and upright graded maximal exercise testing before and after bedrest. The decrease in peak oxygen uptake after bedrest was greater during upright exercise (15.1%, p < 0.05) than during supine exercise (6.1%, NS); from 25.8 ± 5.2 to 21.9 ± 4.5 ml/kg/min and from 24.6 ± 5.2 to 23.1 ± 4.8 ml/kg/min. The decrease in submaximal work was also greater in the upright than in the supine position (p < 0.05). Ventilation volume was significantly elevated (p < 0.05) after bedrest during maximal and submaximal effort in both the supine and upright positions. After bedrest, peak heart rate increased 5.7% and 5.9% during supine and upright testing, respectively (p < 0.05). The increases in rate-pressure product after bedrest were significantly larger (p < 0.05) during upright than during supine exercise. These results indicate that orthostatic stress is the most important factor limiting exercise tolerance after bedrest in normal middle-aged men. This mechanism also increases the myocardial oxygen demands during submaximal effort after bedrest. Intermittent exposure to gravitational stress during the bedrest stage of hospital convalescence may obviate much of the deterioration in cardiovascular performance that follows myocardial infarction.

BEDREST adversely affects the cardiorespiratory response to exercise of normal persons and contributes to the reduced cardiorespiratory capacity after myocardial infarction. The diminished exercise tolerance after prolonged recumbency in healthy subjects results from a lack of physical activity and from a lack of exposure to orthostatic stress. In evaluating the reduced effort tolerance of patients recovering from myocardial infarction, it is difficult to distinguish the role of cardiac damage from that of bedrest deconditioning. One method for making this distinction is to examine the effects of prolonged bedrest on healthy subjects. However, previous investigations of this question, including the classic work of Saltin et al., involved young, healthy subjects ages 18–25 years. It is therefore important to determine the extent to which bedrest affects the cardiorespiratory response of normal persons of an age at which myocardial infarction is common.

The major purposes in this study were to evaluate the magnitude of cardiorespiratory conditioning due to bedrest in middle-aged men and to differentiate two effects of prolonged recumbency: physical inactivity and lack of exposure to orthostatic stress. One method of distinguishing these effects is to compare cardiovascular responses to upright and to supine exercise before and after bedrest.

Methods

Subjects were recruited through an employment service. Those with a history of any major medical illness and those requiring daily medications were excluded. Disqualifying illnesses included cardiovascular, pulmonary, musculoskeletal and neurologic disorders, severe allergies, diabetes mellitus, renal disease, hepatic disease, thrombophlebitis or a history of pulmonary embolism or proteinuria. Twenty-one men were selected to undergo a screening evaluation that consisted of a detailed history, physical examination, complete blood count, urinalysis, chest x-ray, resting ECG, bicycle exercise test and a chemistry panel of fasting glucose, blood urea nitrogen, creatinine, sodium, potassium, chloride, bicarbonate, uric acid, cholesterol, calcium, phosphate, alkaline phosphatase, bilirubin, serum transaminase and lactate dehydrogenase. Subjects also underwent echocardiographic imaging of the heart at rest and during administration of lower body negative pressure.

Nine of the 21 subjects were excluded after the screening evaluation: one because of a lung mass on chest x-ray; one because of hypertension, interstitial lung disease by chest x-ray and abnormal liver function test; one because of elevated blood urea nitrogen and proteinuria; one because of hematuria and crystalluria; one because of chronic obstructive pulmonary disease; one because of hypertension; one because of a history of renal stones; and three subjects because of poor echocardiographic definition of the left ventricle. The remaining 12 subjects, mean age 50 ± 4 years, gave written informed consent to participate as paid volunteers for this 15-day study. No subject was taking medication at the time of the study. Subjects were not allowed to smoke during the study or within 2 weeks before the start of the study.

Screening exercise testing was performed in the upright position on a Monark bicycle ergometer, the initial work load of 30 W increasing in 30-W increments.
every 3 minutes until exhaustion. A bipolar electrocardiographic lead was continuously monitored and was recorded at the end of each minute of exercise and each 5 minutes of recovery. Systolic pressure was recorded by sphygmomanometer at the end of each 3 minutes of exercise and at peak effort. Resting ECGs were normal in all 12 subjects and no chest discomfort, ischemic ST-segment depression or significant ventricular arrhythmias were noted during or after the screening exercise test.

The study group of 12 subjects was admitted to the Clinical Research Center of the Stanford University Hospital. During a 4-day ambulatory control period, subjects underwent baseline studies of endocrine and metabolic function, which will be reported separately. On the morning of the second day before bedrest, subjects performed one supine and one upright test on a bicycle ergometer carried to the point of maximal effort, i.e., to exhaustion. The two tests were separated by a 60-minute rest period. Six subjects were randomly assigned to perform supine exercise initially and six performed upright exercise initially. The same sequence was retained during testing after bedrest (fig. 1).

Supine and upright exercise testing consisted of four uninterrupted stages (I, II, III, IV [max]) of exercise approximating 20%, 45%, 70% and 100% of the work loads used during the prehospital screening evaluation. Absolute work loads for these four stages were 250 ± 73, 525 ± 121, 835 ± 135, and 1165 ± 194 kg-m/min, respectively. These work loads, which were performed before and after bedrest, were designed to produce exhaustion during the 12 minutes available for imaging of left ventricular function during exercise.

Upright testing was performed on a Schwinn electrically-braked bicycle ergometer calibrated in kg-m/min. Supine exercise testing was performed on a padded table with a Collins electrically braked bicycle ergometer calibrated in watts. Schwinn ergometer work loads of 150 kg-m/min were compared to Collins ergometer work loads of 25 W by the relationship 1 W = 6.1 kg-m/min. As a check on the physiologic comparability of work loads provided by these two ergometers, measurements of oxygen uptake (VO2) before bedrest were compared in these same 12 patients. At work loads of 300 kg-m and 600 kg-m, values of VO2 were nearly identical for the Collins and Schwinn ergometers: 1.03 ± 0.23 and 1.37 ± 0.17 l/min for the former and 1.01 ± 0.26 and 1.41 ± 0.26 l/min for the latter.

VO2 was measured during the last 30 seconds of each work load. Subjects used a Daniels respiratory valve and the volume of expired gas was measured with a Parkinson-Cowan high-velocity, low-resistance meter. A potentiometer at the gas meter dial transmitted an electrical output to a two-channel recorder (MFE Model M22) to record ventilatory volume continuously. Expired air was drawn from a 5-l mixing chamber (R-Pel) into a 2-l anesthesia bag (Ohio Medical) by means of a Dynapump (Scientific Products). The composition of the expired air was determined by a Beckman E2 oxygen analyzer and a Godart capnometer CO2 oxygen analyzer. VO2, carbon dioxide production (VCO2) and the respiratory exchange ratio were calculated using standard equations.

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<th>SUBJECTS</th>
<th>EXERCISE TEST</th>
<th>RECOVERY</th>
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**FIGURE 1.** Exercise test design.
To maintain a constant mechanical efficiency before and after bedrest, the position of the ergometer during supine testing and of the bicycle seat height during upright testing was maintained constant for each subject. During upright exercise testing, subjects underwent gated cardiac blood pool scanning with a gamma camera positioned to record left ventricular function in the left anterior oblique (LAO) position. The results of this evaluation will be reported separately. A specially constructed Lucite brace was used to minimize movement of the torso (fig. 2). The gamma camera was positioned to image left ventricular function in the LAO position during supine exercise (fig. 3).

During the 10 days of bedrest, subjects remained in the horizontal position continuously. On the morning of the tenth day of bedrest, subjects repeated the same sequence of upright and supine exercise testing that they had undergone before bedrest. Before performing upright exercise, subjects sat on the exercise table with their legs dangling while blood pressure and heart rate stabilized. The interval between assumption of the sitting posture and the beginning of upright exercise averaged 17 ± 10 minutes. No subject experienced syncope before upright exercise. After upright exercise, four subjects experienced dizziness or presyncope during the 4 minutes of quiet sitting required for measurement of left ventricular function during recovery. This was accompanied by a mean fall in systolic pressure of 35 ± 13 mm Hg. No significant complications were noted during or after exercise testing.

Data were analyzed by means of paired and unpaired t tests for two-group comparisons and by analysis of variance for comparisons involving more than two groups. Differences were considered significant for p values less than 0.05.

Results

Mean body weight decreased 2% during bedrest, from a baseline value of 83.5 ± 3 kg to 82.0 ± 3 kg (p < 0.05). Left ventricular end-diastolic volume measured echographically in the supine position immediately before exercise testing fell 16% from a baseline mean value of 121 ± 7 cm³ to 100 ± 9 cm³ after bedrest (p < 0.05). Mean values of VO₂ max were 21% lower on the upright exercise test before bedrest, in which the torso was immobilized, than on the screening exercise test, in which there was no such restraint: 25.8 ± 5.2 ml/kg/min vs 31.3 ± 5.9 ml/kg/min (p < 0.05). Despite the lower values of peak VO₂ noted on the test before bedrest, peak heart rate values were similar to those during screening, 170 ± 3 vs 173 ± 4 beats/min.

The order in which subjects performed supine or upright exercise had no significant influence on maximal or submaximal values for VO₂, ventilatory volume, respiratory exchange ratio, heart rate, systolic pressure or rate-pressure product.

Cardiorespiratory Responses Before vs After Bedrest Measurements at Maximal Exercise (table 1)

After bedrest, VO₂ max fell from 25.8 ± 1.5 to 21.9 ± 1.3 ml/kg/min during upright exercise and from 24.6 ± 1.5 to 23.1 ± 1.4 ml/kg/min during supine exercise. The decrease in VO₂ max after bedrest was greater during upright testing (15.1%, p < 0.05) than during supine testing (6.1%, NS). Similarly, the reduction in exercise duration during supine effort (3.2%, NS) was significantly less (p < 0.05) than that measured during upright effort (7.1%, NS).

Maximal ventilation volume increased 12% (NS) during supine exercise and 10.6% (p < 0.05) during upright exercise. Peak ventilatory volume was higher during upright than during supine exercise before and after bedrest (p < 0.05). After bedrest, the respiratory exchange ratio was significantly increased (p < 0.05) during upright exercise but not during supine exercise.

The increase in maximal heart rate after bedrest was similar for upright and for supine exercise: 5.9% and 5.7% respectively (both p < 0.05). Maximal systolic pressures were similar during supine and upright exercise before bedrest and were slightly lower during upright exercise after bedrest (NS). The rate-pressure product measured during peak exercise was similar
TABLE 1. Mean Maximal Oxygen Uptake, Test Duration, Ventilation Volume, Respiratory Exchange Ratio, Heart Rate, Systolic Blood Pressure, and Rate-Pressure Product Before and After 10 Days of Bedrest

<table>
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<th>Supine</th>
<th>Upright</th>
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<tr>
<td></td>
<td>Pre-BR</td>
<td>Post-BR</td>
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<tr>
<td>VO₂ max (ml/kg/min)</td>
<td>24.6 ± 5.2</td>
<td>23.1 ± 4.8</td>
</tr>
<tr>
<td>Test duration (sec)</td>
<td>680 ± 45</td>
<td>658 ± 69</td>
</tr>
<tr>
<td>VE BTPS (l/min)</td>
<td>83.1 ± 14.5</td>
<td>93.1 ± 24.2</td>
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<tr>
<td>RER</td>
<td>1.05 ± 0.02</td>
<td>1.10 ± 0.03</td>
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<tr>
<td>HR (beats/min)</td>
<td>159 ± 14</td>
<td>168 ± 17*</td>
</tr>
<tr>
<td>SBP (mm Hg)</td>
<td>214 ± 17</td>
<td>211 ± 24</td>
</tr>
<tr>
<td>RPP</td>
<td>342 ± 46</td>
<td>358 ± 67</td>
</tr>
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*p < 0.05 vs corresponding pre-BR value.
†p < 0.05 vs corresponding supine value.

Abbreviations: BR = bedrest; VO₂ = oxygen uptake; VE BTPS = ventilation volume; RER = respiratory exchange ratio; HR = heart rate; SBP = systolic blood pressure; RPP = rate-pressure product.

during supine and upright exercise before and after bedrest.

Measurements During Submaximal Exercise (fig. 4)

After bedrest, VO₂ at all three submaximal levels of upright effort was significantly lower than before bedrest (p < 0.05). In contrast, VO₂ during supine submaximal exercise was significantly diminished only at stage III. After bedrest, oxygen uptake at all three submaximal work loads was lower during upright than during supine effort (p < 0.05).

After bedrest, increases in heart rate and decreases in VO₂ during submaximal exercise and at peak work loads were greater in the upright than in the supine position (fig. 5).

Resting and submaximal heart rates after bedrest were increased (p < 0.05) at all three levels of submaximal effort in the upright position, whereas heart rate at rest and during the two lower stages of submaximal supine effort were not significantly different from values before bedrest. After bedrest, greater increases in heart rate were noted during upright submaximal exercise than during supine submaximal exercise (p < 0.05).

The systolic pressure at rest and during all three levels of submaximal effort was not significantly changed after bedrest. However, as a result of the higher heart rate after bedrest, the rate-pressure product during all three levels of submaximal upright effort and during supine effort at stage III was significantly increased (p < 0.05). At all submaximal work loads, the rate-pressure product was higher (p < 0.05) after bedrest during upright effort than during supine effort.

Pulmonary ventilation was significantly higher after bedrest at all three submaximal work loads during upright effort and at the two highest submaximal work loads during supine effort. After bedrest, the respiratory exchange ratio during submaximal effort was significantly elevated during all three levels of supine and upright exercise.

Discussion

The principal finding of the present study was a significantly greater decline in peak VO₂ during upright than during supine exercise after bedrest, i.e., 15% vs 6%. In fact, the decrease in VO₂ max during supine exercise was not statistically significant. Thus, the decrease in physical working capacity in middle-aged men after bedrest is largely a reflection of orthostatic factors.

The duration of bedrest for this study is similar to that of middle-aged patients recovering from acute myocardial infarction. A major objective of the present study was to document the magnitude of cardiovascular changes attributable to bedrest alone. In young subjects, 13 and 14 days of bedrest have been associated with a decrease in VO₂ max during supine exercise of 8.6% and 9.1% respectively. The largest fraction of the decrease in VO₂ max after more prolonged bedrest appears to occur in younger subjects during the initial 15–20 days of confinement. Other investigators have noted decreases of 12.9% and 12.6% in VO₂ max during supine exercise after 20 and 30 days of bedrest, respectively; these values are only 25% higher than those observed in similar subjects during 13–14 days of bedrest. These data suggest that the deconditioning effects noted with 10 days bedrest in our subjects were similar to those to be expected after a longer period of bedrest.

When our subjects were allowed to grasp the handbars during the screening bicycle exercise test, we found VO₂ max was 21% higher (31.3 ± 5.9 vs 25.8 ± 5.2 ml/kg/min) than that recorded during testing performed immediately before bedrest, in which subjects could not use the handbars. In contrast, VO₂ max during upright exercise immediately before bedrest, when arm and trunk muscles were immobilized by the radionuclide imaging device, was almost identical to that measured during supine exercise, 25.8 ± 5.2 vs 24.6 ± 5.2 ml/kg/min. This close similarity of values reflects the inability of the immobilized arm and trunk muscles to contribute to VO₂ max. Poliner et al. reported the mechanical disadvantage imposed by radionuclide imaging equipment to explain a lower work capacity in the upright than in the supine position. Although not a primary objective of our protocol, arm restriction during upright bicycle ergometry before and after bedrest helped to standardize the muscle mass involved and facilitated the comparison
between the cardiovascular response to upright and supine exercise.

Saltin et al.\(^1\) demonstrated postural effects after bedrest that were similar to those found in our subjects. They\(^1\) noted a 10% decline in fluoroscopically measured cardiac volume after bedrest. Stroke volume measured during supine rest fell 17%, compared with a 24% decrease in stroke volume during upright rest.\(^2\) Similarly, stroke volume during supine submaximal exercise (600 kg-m) fell 23%, compared with a 35% decrease during upright submaximal exercise (\(\dot{V}O_2\) 1.8 l/min). Direct comparison of the response to upright and supine exercise in the study of Saltin et al. was not possible, for supine exercise was performed on a bicycle ergometer and was submaximal, while upright exercise was performed on a treadmill and was maximal. Our protocol permitted direct comparison of the cardiovascular response to supine and to upright exercise at the same maximal and submaximal work loads before and after bedrest.

With slight increases in their submaximal and peak heart rates, our middle-aged subjects could maintain their \(\dot{V}O_2\) during supine exercise at values close to those measured before bedrest. In contrast, they could not sustain \(\dot{V}O_2\) during submaximal and peak upright exercise, despite even greater increases in exercise heart rates. The increase in peak heart rate noted in our subjects is well documented by other investigators.\(^10-18\) Orthostatic factors therefore appear to account for the largest portion of the decrease in \(\dot{V}O_2\) in our patients after bedrest.

The significantly greater decrease in submaximal
and in peak VO₂ during upright exercise in our subjects indicates that orthostatic stress is the major cause of the decrease in oxygen transport capacity after bedrest. Venous pooling after assumption of the upright posture reduces left ventricular volume and filling pressure.¹⁰,¹²,¹⁴-¹⁶ Thus, upright exercise in normal subjects is much more dependent than supine exercise upon venous return from the legs and on the Frank-Starling mechanism to augment stroke volume during exercise.¹⁰,¹²,¹⁴-¹⁶ Cardiac output and oxygen transport capacity during exercise in the erect posture are therefore highly sensitive to venous pooling and to underfilling of the heart during upright exercise. Deterioration in the control of venous capacitance vessels associated with bedrest may magnify the effects of orthostatic stress during upright exercise.¹

The reduction in stroke volume even during supine submaximal exercise noted by Saltin et al. suggested that poor postural adaptation and impaired venous return could not completely account for the deterioration in upright exercise capacity after bedrest. They suggested that a nonspecific deterioration in myocardial function occurs after bedrest deconditioning. This does not appear to be a major factor in our middle-aged subjects, considering the relatively well-main-
tained VO₂ max in the supine position after bedrest. Differences in age and physical conditioning may well explain why supine VO₂ max was better maintained after bedrest in our subjects than in those of Saltin et al.¹ Younger, physically conditioned normal persons have a higher resting stroke volume, exercise cardiac output and VO₂ max than older, relatively sedentary persons.¹⁷ In the study of Saltin et al.,¹ the two subjects who were best conditioned before bedrest had the highest values of heart volume and VO₂ max. These subjects had the greatest absolute decrease in heart volume and VO₂ max after bedrest. Since our older subjects had initial values of VO₂ max of only 2.5 l/min, it is expected that they would show smaller decreases in oxygen consumption and stroke volumes during maximal supine exercise after bedrest than younger subjects whose initial values of VO₂ max were 3–4 l/min.

Peak ergometer work load did not change after bedrest in our subjects despite a decrease in VO₂ max. This finding, which corroborates studies in younger subjects,⁶,⁷ reflects a shift from aerobic to anaerobic metabolism during peak exercise. Because of a limit on stroke volume and cardiac output after bedrest,¹ anaerobic mechanisms are recruited to maintain working capacity.¹⁸ This shift to anaerobic metabolism is manifested by an increased arterial carbon dioxide concentration and hydrogen ion concentration, which result in increased values of respiratory exchange ratio and minute ventilation. A shift from aerobic to anaerobic metabolism appears to be a major mechanism by which physical working capacity, especially during upright exercise, is maintained after bedrest.

Strategies to limit the decrease in functional capacity after myocardial infarction have emphasized low-level exercise training,¹⁹,²⁰ but our data indicate that simple exposure to gravitational stress substantially accomplishes this purpose. Convertino et al.²¹ found a 14% reduction in VO₂ max during upright bicycle ergometry in subjects who underwent 14 days of continuous bedrest, but only a 5% decrease in subjects who for 3 hours daily had undergone exposure to a reverse gradient garment that simulated the effects of standing. The 5% decrease in VO₂ max was attributed to the effects of physical inactivity and the 14% decrease in VO₂ max was thought to reflect the additional effects of orthostatic intolerance resulting from a lack of exposure to gravitational stress. In the study of Convertino et al.²¹ orthostatic factors appear to account for almost two-thirds of the observed decrease in VO₂ max after bedrest. Similarly, Birkhead et al.²² noted a smaller decrease in VO₂ max during chair rest than during bedrest. Even vigorous exercise training in the supine posture fails to prevent the deteriorative effects of bedrest on VO₂ max.²³,²⁴ This underscores the importance of exposure to gravitational stress in the maintenance of physical working capacity. It appears that deterioration of oxygen transport capacity resulting from bedrest may be largely obviated by gravitational stress such as intermittent sitting or standing.

The results of the present study are relevant to the
management of patients after acute myocardial infarction, many of whom undergo a similar duration of bedrest. The heart rate during quiet sitting and during all three submaximal levels of upright exercise was higher after bedrest. Similarly, the rate-pressure product during all three levels of submaximal upright effort was higher after bedrest. Because heart rate and rate-pressure product are important determinants of VO$_2$ in normal subjects$^{24}$ and in patients with chronic ischemic heart disease,$^{26}$ the increased heart rate and rate-pressure product during submaximal effort following bedrest may increase the risk of angina pectoris and of clinical coronary events in patients with significantly restricted coronary flow. However, the decreased left ventricular size after bedrest, especially in the upright posture, tends to diminish left ventricular wall stress, another major determinant of VO$_2$.$^{24,27}$ Further study of the cardiovascular effects of bedrest is needed in patients with chronic ischemic heart disease.

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