

A 30-Year Follow-Up of the Dallas Bed Rest and Training Study

I. Effect of Age on the Cardiovascular Response to Exercise

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Background—Cardiovascular capacity declines with aging, as evidenced by declining maximal oxygen uptake ($\dot{V}O_{2\max}$), with little known about the specific mechanisms of this decline. Our study objective was to assess the effect of a 30-year interval on body composition and cardiovascular response to acute exercise in 5 healthy subjects originally evaluated in 1966.

Methods and Results—Anthropometric parameters and the cardiovascular response to acute maximal exercise were assessed with noninvasive techniques. On average, body weight increased 25% (77 versus 100 kg) and percent body fat increased 100% (14% versus 28%), with little change in fat-free mass (66 versus 72 kg). On average, $\dot{V}O_{2\max}$ decreased 11% (3.30 versus 2.90 L/min). Likewise, $\dot{V}O_{2\max}$ decreased when indexed to total body mass (43 versus 31 mL · kg⁻¹ · min⁻¹) or fat-free mass (50 versus 43 mL/kg fat-free mass per minute). Maximal heart rate declined 6% (193 versus 181 bpm) and maximal stroke volume increased 16% (104 versus 121 mL), with no difference observed in maximal cardiac output (20.0 versus 21.4 L/min). Maximal AV oxygen difference declined 15% (16.2 versus 13.8 vol%) and accounted for the entire decrease in cardiovascular capacity.

Conclusions—Cardiovascular capacity declined over the 30-year study interval in these 5 middle-aged men primarily because of an impaired efficiency of maximal peripheral oxygen extraction. Maximal cardiac output was maintained with a decline in maximal heart rate compensated for by an increased maximal stroke volume. Most notably, 3 weeks of bedrest in these same men at 20 years of age (1966) had a more profound impact on physical work capacity than did 3 decades of aging. (*Circulation*. 2001;104:1350-1357.)

Key Words aging ■ oxygen ■ exercise ■ body composition

In 1966, 5 healthy 20-year-old men were studied extensively at baseline, after 3 weeks of bedrest, and after 8 weeks of intensive dynamic exercise training. The results of this investigation were published in 1968 as a supplement to *Circulation* in the now widely cited Dallas Bedrest and Training Study.¹ Capitalizing on the extensive nature of the former evaluations, the present study was designed to investigate the age-associated changes in cardiovascular capacity, evaluated by determining the maximal oxygen uptake ($\dot{V}O_{2\max}$),²⁻⁴ and to provide insight into the specific mechanisms contributing to these changes.

Cardiovascular capacity declines with aging and has been consistently documented as a decline in $\dot{V}O_{2\max}$. This deterioration in aerobic power has been suggested by numerous cross-sectional evaluations,⁵⁻¹³ demonstrated by several longitudinal studies,^{6,7,14-23} and recently subjected to a meta-analysis.²⁴ Despite the extensive literature, there remain a number of deficiencies with the accumulated data. Most

notable among these include the inherent limitations of cross-sectional studies that provide most of the data and the small number of longitudinal evaluations over extended intervals.

In the present study, a 30-year follow-up has been carried out on the 5 subjects previously studied in 1966. The study design included a health evaluation, activity quantification, anthropometric measurements, and cardiovascular response to maximal exercise.

Methods

The subjects were 5 healthy men 50 to 51 years of age who were originally studied by 3 of the present investigators (B.S., C.G.B., and J.H.M.) in 1966. All subjects were screened by a medical history, physical examination, routine laboratory tests, and resting ECG, and they provided informed consent to a study protocol approved by the University of Texas–Southwestern Medical Center Institutional Review Board.

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Tables A through E can be found Online at www.circulationaha.org

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TABLE 1. Baseline Characteristics

	1966		1996
	Baseline	After Bedrest	Baseline
Height, cm	184	184	185
Weight, kg	77 (15)	76 (14)	100 (37)
Body fat, %	13.9 (4.1)	15.7 (4.5)	28.0 (3.0)*
Systolic blood pressure, mm Hg	131 (23)	134 (10)	140 (4)
Diastolic blood pressure, mm Hg	75 (14)	74 (10)	88 (7)
Mean arterial pressure, mm Hg	94 (17)	94 (9)	104 (8)
HR, bpm	76 (27)	83 (15)	90 (17)
$\dot{V}O_2$, L/min	0.3 (0.04)	0.3 (0.09)	0.4 (0.13)
$\dot{V}O_2$, mL · kg ⁻¹ · min ⁻¹	4.3 (0.69)	4.4 (0.98)	3.7 (0.23)
$\dot{V}O_2$, mL/kg fat-free mass per min	5.0 (0.77)	5.3 (1.3)	5.1 (0.2)
CO, L/min	5.7 (1.3)	4.9 (0.7)	5.9 (1.1)
SV, mL/min	79 (23)	60 (13)	68 (18)
AVDO ₂ , mL O ₂ /100 mL blood	5.8 (1.2)	7.0 (2.3)	6.1 (1.2)
X-ray heart volume, mL	860 (181)	770 (130)	1127 (130)

Values are averages (SD).

**P*<0.05 for 1996 data vs 1996 baseline.

Screening Exercise Test

Each subject underwent a screening exercise treadmill test with gas exchange analysis to exclude prohibitive coronary artery disease using a modified Åstrand-Rhyming protocol.²⁵ Graded maximal testing was performed at constant speed individually determined on a level treadmill to produce a heart rate ≈70% of the age-predicted maximum, with the incline raised 2% every 2 minutes to exhaustion. Ventilatory flow was evaluated using an in-line pre-vent pneumotach (MedGraphics), and in-line gas exchange was evaluated using a metabolic cart (MedGraphics CPX/D).

Exercise Testing

Maximal exercise treadmill testing was performed within 2 weeks of the screening evaluation, with the results of the screening exercise tests used to determine treadmill speed for each subject. Heart rate was monitored continuously by ECG, and blood pressure was monitored every 2 to 3 minutes by recording brachial artery cuff pressure (Suntech Biosystems). Gas exchange analysis was performed by the technique of Douglas,²⁶ with [CO₂], [N₂], and [O₂]determined by mass spectrometry (Marquette MGA 1100); ventilatory volume was measured from a ≥45-second bag with a calibrated dry gas meter (Rayfield). In-line breath-by-breath evaluation by mass spectrometry served as backup to the Douglas bag collections, and ventilatory flow was determined by a turbine flowmeter in a Ventilatory Measurement Module (Interface Associates, Inc). Cardiac output (CO) was determined with a standard inert gas rebreathing technique, with acetylene as the soluble gas and helium as the insoluble gas.^{27,28} This technique has previously been validated at rest and exercise in subjects with and without cardiopulmonary disease.²⁷⁻³⁰ Our laboratory has compared this method

TABLE 2. Baseline Fasting Laboratory Values

	1966		1996
	Baseline	After Bedrest	
Cholesterol, mg/dL	166	178	209
Triglycerides, mg/dL	83	65	158
Hematocrit, %	44	45	47
Hemoglobin, g/dL	15.5	14.8	16.2

against standard invasive techniques, including thermodilution and direct Fick, over a range of CO from 2.8 to 27.0 L/min and found an excellent correlation (*r*=0.95).²⁹ This technique was also used in these same subjects in the 1966 evaluations, along with the dye dilution method, with a high degree of correlation at maximal exercise (*r*=0.92).¹ Adequate mixing of the rebreathing gas in the lung was confirmed by a constant level of helium in all cases. Arterialized lactate was determined via fingerstick samples at the end of exercise (Yellowspring International 2300 Stat Plus).

Oxygen uptake and CO were determined at rest and at maximal effort. At rest, Douglas bags were collected for 3 minutes, and CO was measured in triplicate and averaged. During maximal treadmill exercise testing, Douglas bags were collected in the second minute of each of the final 3 stages (as predicted from screening test data), with consecutive 45-second collections when the subject was nearing maximal effort. CO was determined during the final 10 seconds of maximal exercise, followed within 2 minutes by fingerstick sample collection for lactate determination. Maximal exercise was defined as an inability to continue exercise despite vigorous encouragement and confirmed by respiratory exchange ratio ≥1.1, $\dot{V}E/\dot{V}O_2 > 35$, arterialized lactate >6.0 mmol/L, heart rate ≥100% predicted maximum, and respiratory rate ≥30.

Mean arterial pressure obtained during each CO determination was divided by the respective CO to estimate total peripheral resistance.³¹ CO was divided by heart rate during rebreathing to calculate stroke volume. Oxygen uptake ($\dot{V}O_2$) was divided by CO to calculate AV oxygen difference (AVDO₂) according to the Fick³² equation.

Body Composition

Underwater weighing was performed, with residual volume corrections made by rebreathing an inert mixture of helium.³⁴ Measurements were made in triplicate and averaged, with body density calculated with the formula of Goldman and Buskirk³⁵ and percent body fat calculated according to the Siri³⁶ equation.

Roentgenological Heart Volume Determination

End-diastolic heart volumes were estimated by the same techniques as in the 1966 study, using a modification of the technique of Larsson and Kjelberg.³⁷ Posterior-anterior chest x-rays were taken with a source-to-image distance of 72 in. with the subjects in the prone position. Exposures were gated to an ECG and timed to end expiration. Cardiac outlines were traced on plane films, with the long axis of the ellipsoid defined by a line connecting the superomedial and inferolateral margins and the perpendicular bisector of this line defining the radius. Volume calculations were performed with the equation for a prolate ellipse. For comparison, end-diastolic total cardiac volume was determined by gated cardiac MRI on 4 of the 5 subjects through techniques standard at our institution.³⁸ One subject was unable to tolerate the confines of the closed magnet.

Physical Activity Quantitation

Physical activity was estimated with an interviewer-administered 7-day physical activity recall instrument (PAR).³⁸ This technique uses an intensity-weighted calculation to estimate daily energy and includes time spent sleeping.

Statistical Analysis

Nonparametric statistical analyses were performed on paired data from the 1966 baseline and 1996 data, and Pearson's correlational analysis was used for select dependent variables (SAS System for Windows, SAS Institute). We acknowledge the limitations of statistical analyses resulting from the small sample size, with the focus on individual data and group trends.

Results

Baseline clinical evaluations revealed no prohibitive medical conditions. None of the subjects were taking medications

TABLE 3. Confirmation of Maximal Exercise Testing

	Subject A	Subject B	Subject C	Subject D	Subject E
Respiratory exchange ratio	1.21	1.17	1.18	1.14	1.10
\dot{V}_E/\dot{V}_{O_2}	45.0	34.9	46.7	36.5	41.2
Arterialized lactate, mmol/L	10.6	7.0	10.0	8.6	8.2
% Predicted HR _{max}	115	99	112	111	94
Maximum respiratory rate	34	42	34	31	56

regularly, and none were smokers. All subjects completed the study protocol without complications.

Group Average Results

Average baseline characteristics are presented in Table 1 and selected blood data in Table 2, with comparative values from 1966 included. There was a 30% increase in total body weight for the group compared with 1966 (77 versus 100 kg). The weight increase was primarily due to a large, statistically significant increase in body fat (13.9% versus 28.0%; $P=0.012$). Fat-free mass was largely unchanged over the interval (65.7 versus 71.0 kg). Resting end-diastolic cardiac volume increased by 31% (860 versus 1127 mL); there was a close correlation between the values obtained by roentgenography and those obtained by MRI ($r=0.83$).

All subjects achieved maximal exertion on cardiopulmonary exercise testing as defined by the protocol (Table 3). Group average results from exercise testing are presented in Table 4. A moderate correlation was observed between the energy expenditure estimated by PAR and the maximal oxygen uptake indexed to total body weight ($r=0.63$; Figure 1).

Compared with 1966 baseline data, a number of trends are interesting despite the lack of statistical significance. Absolute $\dot{V}_{O_2\max}$ decreased 11% (3.3 versus 2.9 L/min; Figure 2). Likewise, decreases were observed in maximal oxygen uptake indexed to total body mass (43 versus 31 mL · kg⁻¹ · min⁻¹) and to fat-free mass (49.7 versus 42.9 mL/kg fat-free mass per minute; Figure 3). A 6% decline in maximal heart rate (HR_{max}; 193 versus 181 bpm) was balanced by a 16% increase in maximal stroke volume (SV_{max}; 104 versus 121 mL). Remark-

ably, there was no decrement in maximal CO over the 30-year interval (20.0 versus 21.4 L/min; Figures 4 through 6). Maximal AVDO₂ declined 17% (16.2 versus 13.8 vol%; Figure 7).

Individual Observations

The data from individual subjects are published in *Circulation* online as Tables A through E, including data from the 1966 baseline and post bedrest assessments for comparison.

Subject A was sedentary before the 1966 study, had maintained a moderate level of exercise for 4 years after the initial evaluation, but had not performed regular exercise for >20 years. His estimated average daily energy expenditure was 32.3 kcal · kg⁻¹ · d⁻¹. Over the 30-year interval, weight (75 versus 84 kg) and percent body fat (16% versus 28%) increased; $\dot{V}_{O_2\max}$ declined by 16% (2.5 versus 2.1 L/min; Figure 2); HR_{max} was unchanged (196 versus 197 bpm) (Figure 5); and declines were observed in SV_{max} (93 versus 80 mL; Figure 6), CO_{max} (18.2 versus 15.8 L/min; Figure 4), and AVDO_{2\max} (13.8 versus 12.9 vol%; Figure 7).

Subject B ran up to 75 miles weekly before the 1966 study and had continued a regular training program throughout the interval period. Distance covered had declined to an average of 12 to 15 miles weekly over the 2 years before the present study. His estimated average daily energy expenditure was 34.7 kcal · kg⁻¹ · d⁻¹. Over the 30-year interval, weight (70 versus 95 kg) and percent body fat (10% versus 27%) had dramatically increased; $\dot{V}_{O_2\max}$ declined by 12% (4.2 versus 3.7 L/min; Figure 2); and HR_{max} declined (201 versus 168 bpm; Figure 5), with increases in SV_{max} (113 versus 149 mL;

TABLE 4. Results of Maximal Treadmill Exercise Test: Group Averages

	1966		
	Baseline	After Bedrest	1996
$\dot{V}_{O_2\max}$, L/min	3.3 (1.1)	2.4 (1.0)	2.9 (0.7)
$\dot{V}_{O_2\max}$, mL/kg lean body mass per min	49.7 (10.9)	37.4 (11.4)	42.9 (9.5)
$\dot{V}_{O_2\max}$, mL · kg ⁻¹ · min ⁻¹	43.0 (10.9)	31.8 (11.1)	31.0 (7.6)
CO, L/min	20.0 (4.1)	14.8 (4.8)	21.4 (5.1)
HR, bpm	193 (8)	197 (7)	181 (16)
SV, mL	104 (22)	75 (22)	121 (39)
AVDO _{2\max} , mL O ₂ /100 mL blood	16.2 (2.3)	16.4 (3.2)	13.8 (2.0)
Systolic blood pressure, mm Hg	204 (49)	153 (42)	206 (23)
Diastolic blood pressure, mm Hg	81 (9)	63 (16)	96 (22)
Mean arterial pressure, mm Hg	122 (21)	93 (24)	133 (15)
Total peripheral resistance, dyne · sec ⁻¹ · cm ⁻⁵	484 (72)	525 (148)	519 (138)

Values are averages (SD).

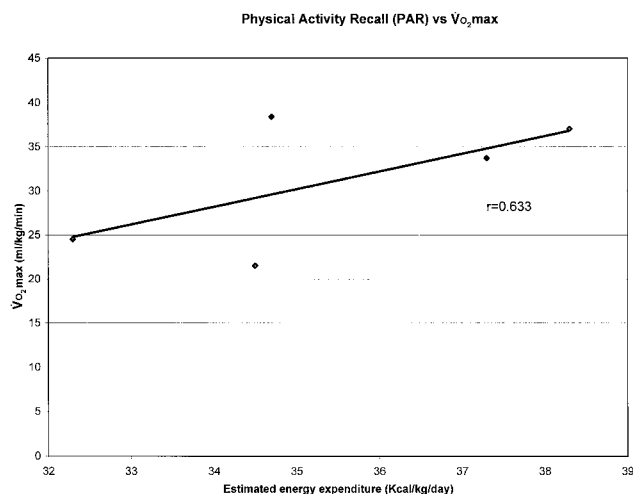


Figure 1. Correlation of estimated daily energy expenditure based on results of PAR interview with measured maximum oxygen uptake.

Figure 6) and CO_{max} (22.8 versus 25.0 L/min; Figure 4) and a decline in $\text{AVDO}_{2\text{max}}$ (18.2 versus 14.6 vol%; Figure 7).

Subject C had participated in high school athletics but was active only in bowling and golf before the 1966 study. During the 30-year interval, he had intermittently jogged and pedaled a stationary bicycle, and he did vigorous yard work 1 to 2 hours weekly throughout the interval. He was last active on a regular basis ≈ 6 months before the present study, averaging the equivalent of 20 miles weekly on a stationary bicycle. His estimated average daily energy expenditure was $37.3 \text{ kcal} \cdot \text{kg}^{-1} \cdot \text{d}^{-1}$. Over the 30 years, weight (73 versus 83 kg) and percent body fat (19% versus 29%) had increased; $\dot{V}\text{O}_{2\text{max}}$ increased by 16% (2.4 versus 2.8 L/min; Figure 2); HR_{max} declined (198 versus 190 bpm; Figure 5); SV_{max} was unchanged (88 versus 86 mL; Figure 6); CO_{max} declined (17.4 versus 16.4 L/min; Figure 4); and $\text{AVDO}_{2\text{max}}$ increased 23% (13.7 versus 16.8 vol%; Figure 7).

Subject D had only occasionally participated in recreational sports before the 1966 study. In the years since, he played soccer in a semiprofessional city league 6 to 7 months yearly but stopped 3 years before the current evaluation and

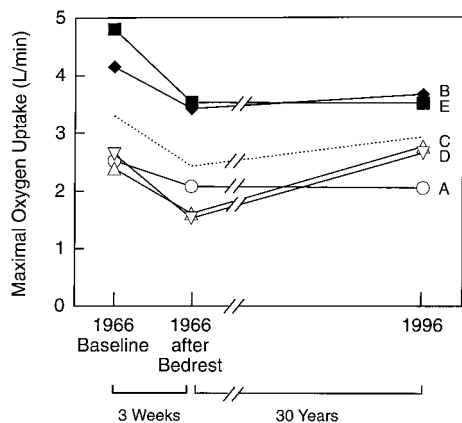


Figure 2. Absolute $\dot{V}\text{O}_{2\text{max}}$ before and after bedrest in 1966 and current values.

has had no regular activity since. He was diagnosed with hypertension 2 years before the present evaluation, but he achieved blood pressure control with weight loss and dietary modification and had been off medication for 2 months before the present evaluation. His estimated average daily energy expenditure was $38.3 \text{ kcal} \cdot \text{kg}^{-1} \cdot \text{d}^{-1}$. Over the 30-year interval, weight increased modestly (62 versus 73 kg) with a 139% increase in body fat (10% versus 24%); $\dot{V}\text{O}_{2\text{max}}$ was unchanged (2.6 versus 2.7 L/min; Figure 2); increases were observed in HR_{max} (182 versus 189 bpm; Figure 5) and SV_{max} (88 versus 120 mL; Figure 6); there was a remarkable 49% increase in CO_{max} (16.0 versus 22.6 L/min; Figure 4); and $\text{AVDO}_{2\text{max}}$ declined 29% (16.5 versus 11.7 vol%; Figure 7).

Subject E had played football at the college and semiprofessional level in 1966. Since then, his only notable activity has been fairly regular weight training, averaging 2 hours weekly with free weights and, for the 3 months before this evaluation, Nautilus circuit training. His estimated average daily energy expenditure was $34.5 \text{ kcal} \cdot \text{kg}^{-1} \cdot \text{d}^{-1}$. Over the 30-year interval, his weight dramatically increased (102 versus 163 kg) with a 113% increase in percent body fat (15% versus 32%); $\dot{V}\text{O}_{2\text{max}}$ declined by 27% (4.8 versus 3.5 L/min; Figure 2). HR_{max} declined (187 versus 160 bpm; Figure 5); SV_{max} increased 23% (138 versus 169 mL; Figure 6); CO_{max} increased (25.8 versus 27.0 L/min; Figure 4); and $\text{AVDO}_{2\text{max}}$ declined 30% (18.6 versus 13.0 vol%; Figure 7).

Despite the long study interval, none of the subjects had a $\dot{V}\text{O}_{2\text{max}}$ below the 1966 post bedrest levels when they were 20 years old. Amazingly, 3 weeks of bedrest when these 5 subjects were healthy young men resulted in a more profound deterioration of cardiovascular capacity than did 30 years of aging (Figure 2).

Discussion

The present study, spanning 3 decades, represents 1 of the longest longitudinal studies that evaluates the effect of age on cardiovascular capacity and anthropometric measures. The study of nonathletic subjects broadens the generalizability of the findings compared with most prior longitudinal studies limited to athletes, and the quantitative estimation of activity levels provides new insight into the relationship between physical activity and the impact of aging on aerobic power.

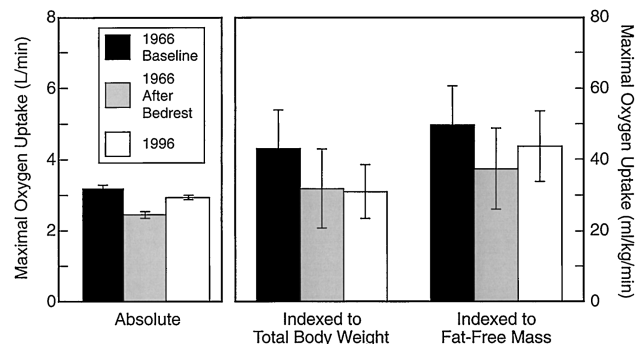


Figure 3. $\dot{V}\text{O}_{2\text{max}}$ during interval of study reported as absolute values and indexed to body weight and fat-free body mass.

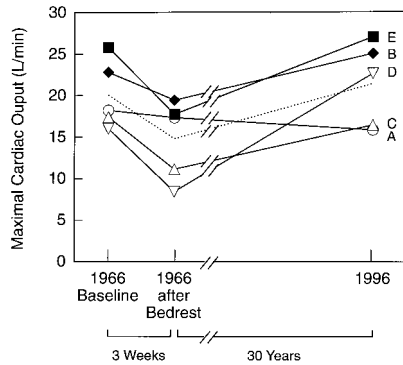


Figure 4. Maximal CO before and after bedrest in 1966 and current values.

The most remarkable finding of the study is the observation that 3 weeks of bedrest in 1966 caused a greater deterioration in cardiovascular and physical work capacity than did 30 years of aging in these 5 men. Another novel finding is that maximal oxygen uptake declined as expected but unexpectedly did so primarily via a decrement in the peripheral oxygen extraction. There was no decline in maximal cardiac function despite the 3 decades of aging, with a decline in HR_{max} balanced by an increase in SV_{max}. Fat-free mass was unchanged, but a doubling of percent body fat resulted in large increases in total body weight. Finally, with the use of a validated physical activity instrument, an association was observed between physical activity and cardiovascular capacity, suggesting that physical inactivity accounts for as much as 40% of the age-related decline in maximal oxygen uptake.

Aging and Cardiovascular Capacity

Cross-sectional data suggest that aerobic power declines linearly throughout adulthood,^{3-13,39,40} with an average annual decrement of weight-adjusted $\dot{V}O_{2max}$ of $0.45 \text{ mL} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$.⁴⁰ However, there is substantial interstudy variation, ranging from 0.20 to $0.52 \text{ mL} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$.^{12,13} Longitudinal studies have demonstrated similar declines with aging, but with even more interstudy variability, ranging from annual decrements of 0.2 to $1.04 \text{ mL} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ (Table 5).^{14,16} The present data, suggesting a relatively modest decrement of maximal oxygen uptake scaled to total body weight ($0.4 \text{ mL} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ per year), are

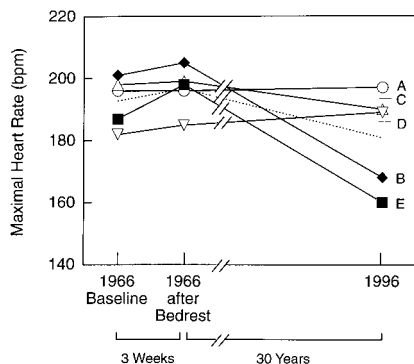


Figure 5. HR_{max} (bpm) before and after bedrest in 1966 and current values.

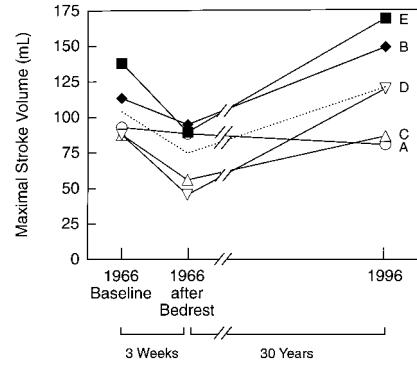


Figure 6. SV_{max} before and after bedrest in 1966 and current values.

consistent with the 2 prior studies most similar in design.^{18,20} The variability in these data most likely derives from the nearly exclusive study of athletes with relatively high initial $\dot{V}O_{2max}$ who subsequently become less active, with deconditioning adding to the effect of senescence.⁶ Moreover, the variability with regard to intervals of study, age ranges, and activity levels included in prior studies further limits interstudy comparisons.

Maximal oxygen uptake declined over the 30-year interval with both absolute $\dot{V}O_{2max}$ (ie, reported as liters per minute) and $\dot{V}O_{2max}$ indexed to fat-free mass, with substantial interindividual variability. Two of the individuals had declined to their 1966 bedrest levels (subjects A and E); 1 was intermediate between former baseline and bedrest (subject B); 1 was at his former baseline (subject D); and 1 (subject C) was above his baseline state 30 years ago. On average, current $\dot{V}O_{2max}$ was midway between the 1966 bedrest and baseline levels.

Mechanistic Considerations

The relative contributions of central (ie, cardiac) and peripheral (ie, circulation and O₂ extraction) factors in the aerobic decline with aging have long been debated, and the specific mechanisms remain unclear. Several have been proposed, and include the aging process itself (senescence); the decline of cardiac function via blunted inotropic and chronotropic responsiveness; an impaired efficiency of peripheral oxygen extraction and utilization; a decreased muscle mass simultaneous with increasing body fat; a decreased volume and efficiency of physical activity; superimposed pathological

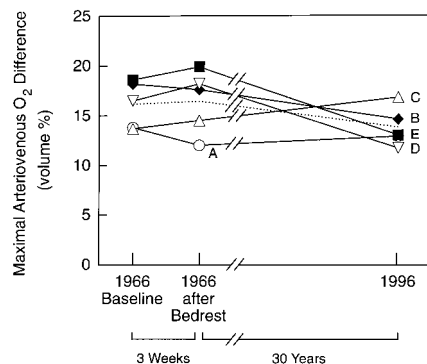


Figure 7. Maximal AVDO₂ (vol%) before and after bedrest in 1966 and current values.

TABLE 5. Summary of Longitudinal Studies

Author	Year	n	Sex	Population	Age at Follow-Up (mean), y	Duration (mean), y	$\dot{V}O_{2\max}$ Decline	
							$L \cdot \text{min}^{-1} \cdot \text{y}^{-1}$	$\text{mL} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ per y
Dill et al ¹⁴	1967	16	M	Athletes	49	24	0.06	1.1
Dehn et al ²¹	1972	40	M	Controls	52	2	NA	0.9
Pollock et al ¹⁵	1987	24	M	Athletes	62	10	0.03	0.4
Rogers et al ²⁰	1990	14	M	Controls	61	8	0.04	0.4
		15	M	Athletes	62	8	0.02	0.3
Marti et al ¹⁸	1990	23	M	Controls	35	15	0.003	0.6
		27	M	Runners	42	15	0.03	0.6
Kasch et al ^{16,17}	1995	12	M	Controls	69	21	0.05	0.7
		11	M	Athletes	76	33	0.02	0.3
Hagerman et al ²²	1996	9	M	Athletes	44	20	0.07	0.9
Åstrand et al ²³	1997	27	F	Nonathletes	55	33	0.02	0.3
		26	M	Nonathletes	59	33	0.03	0.5

processes (evident and occult); and hereditary factors, among others. A better understanding of these mechanisms is necessary to guide efforts at intervening in the seemingly inevitable cardiovascular deterioration.

An age-related decline in HR_{\max} has been proposed as the predominant contributor to the senescent decline in aerobic power after controlling for activity level and body composition.^{9,11} In the present study, changes in HR_{\max} played little role in the loss of cardiovascular capacity, an observation that is consistent with prior longitudinal data.¹⁸ Only 2 of the 5 subjects in the present study had a decline in HR_{\max} , and on average, that decline was much less than expected.^{9,15,16,41,42} The small decline in HR_{\max} was balanced by an increase in SV_{\max} , and remarkably, CO_{\max} was maintained at the 1966 baseline levels. Therefore, deterioration of cardiac function from youth to middle age played no role in the decrement of aerobic power in the present study.

The maintenance of SV_{\max} and CO_{\max} is in contradiction to several cross-sectional studies^{43–48} but is supported by others.^{10,39,49} There have been no prior longitudinal evaluations addressing this question. Similar to the present findings, Rodeheffer et al¹⁰ demonstrated an increased stroke volume compensating for the age-related decline in HR_{\max} to maintain CO at high workloads in a cross-sectional evaluation of 61 participants 25 to 79 years of age in the Baltimore Longitudinal Study on Aging. Fleg et al⁴⁹ demonstrated that stroke volume is maintained and even enhanced with advancing age via end-diastolic dilatation in a cross-sectional evaluation of 145 men and women. It is possible that a shift in mechanisms to maintain CO occurs with aging, from catecholamine enhancement of inotropy and chronotropy in the young to a relative dependence on the Frank-Starling mechanism with advancing age.³⁹ The 30% increase in resting end-diastolic cardiac volume over the 30-year interval observed in the present study supports but does not prove this hypothesis. The increased end-diastolic volume, as determined by the x-ray method, may represent an increase in left ventricular end-diastolic volume, an increase in left ventricular wall thickness, or both; therefore, more detailed interpretation of these data is limited.

In the present study, a decrement in $AVDO_{2\max}$ was the dominant mechanism of cardiovascular decline, which is supported by prior data.^{43,50} Whether the decline is due to deconditioning, a manifestation of subclinical pathology of the circulation and skeletal musculature, heredity, or an effect of aging per se is unclear from the present data and is likely a combination of these effects. Alterations in skeletal muscle associated with aging may negatively influence cardiovascular capacity by decreasing $AVDO_{2\max}$ via a number of proposed mechanisms. These include loss of capillary density; replacement of viable muscle with fibrotic material; changes in microvascular regulation and recruitment; and loss of myocyte mitochondrial volume, among others. These changes in skeletal muscle, along with an impaired distribution of blood flow during peak exercise and aberrations of the autonomic system associated with aging, likely contributed to the observed age-related decline of $AVDO_{2\max}$.

The relative contributions of central versus peripheral circulatory changes and the specific mechanism(s) of those changes in the age-associated decline in aerobic power warrant continued investigation.

Role of Physical Activity

Physical activity is important for the maintenance of cardiovascular capacity. The short-term physical inactivity of 3 weeks of bedrest in the 1966 study of these 5 subjects when they were healthy young men caused a more profound reduction in $\dot{V}O_{2\max}$ than did 30 years of aging, reemphasizing the detrimental effects of inactivity so clearly demonstrated in the 1966 study. The observation that none of the subjects achieved an aerobic power lower than the postbedrest values suggests that aerobic power after bedrest may have approached a physiological nadir for these individuals. The correlation of the PAR interview activity estimates, derived from the 2 weeks before the current evaluations, with $\dot{V}O_{2\max}$ provides additional support for the importance of short-term physical activity. Likewise, the PAR data qualitatively paralleled the self-reported level of activity throughout the 30-year interval, supporting the importance of long-term

physical activity on the maintenance of aerobic power. These observed relationships suggest that much of the age-associated decline may be avoidable or reversible with regular exercise.

Anthropometric Changes

Age-associated changes in body composition have been demonstrated in a number of studies.^{18,51–53} In the present study, remarkable increases in percent body fat were observed and fat-free mass remained unchanged, consistent with prior observations.¹⁸ However, this is in contradiction to other studies that have demonstrated a rectilinear loss of muscle mass across a population of 22- to 87-year-old subjects.^{51,53} It is likely that age-associated loss of muscle mass has yet to become measurable by our techniques in middle age. In addition, increasing total body weight from increasing fat mass may have necessitated maintenance of muscle mass for the given level of activity of these individuals.

Scaling $\dot{V}O_2\text{max}$

Because of the inherent intersubject variability in height and weight among any population, especially across sexes, the scaling of $\dot{V}O_2\text{max}$ to total body mass has become standard practice. This convention originated in 1927 with Herbst⁵⁴ and was advanced in 1938 by Robinson.⁵⁵ Åstrand,⁵ evaluating 2 cohorts matched by age and sex but not height and weight, applied the same weight correction of $\dot{V}O_2\text{max}$ with the important stated assumption of a constant percent of body fat between the comparison groups. However, in the same report, she discouraged such indexing over ranges of age because of the age-associated variation in fat content.

Because fat has little impact on oxygen utilization, especially during exercise, a more rational index is that of oxygen uptake scaled to fat-free mass, as has been suggested by several investigators.^{6,7,9,19,49} If $\dot{V}O_2\text{max}$ is adjusted for total body mass in the present study, the average decline over the 30-year interval in aerobic power is 28%, or 0.4 mL · kg⁻¹ · min⁻¹ per year. However, the likely overestimation of the true decrement is demonstrated by scaling $\dot{V}O_2\text{max}$ to fat-free body mass, yielding a modest 12% decrement, or 0.2 mL/kg fat-free mass per minute per year. This decline parallels that of absolute $\dot{V}O_2\text{max}$ and is at the lower limit of previously reported observations. Given the discrepancies observed in body composition over the study interval, especially the potential error introduced by the dramatic absolute and relative increases in body fat, scaling to fat-free mass appears to provide the more accurate estimate of the age-associated decline in cardiovascular capacity.

Study Limitations

The present study has several limitations. The study was uncontrolled with regard to many confounding variables, including activity level, lifestyle, diet and nutrition, coexistent pathology, biology, and other factors potentially contributing to the observed changes. Therefore, as with prior studies, the present study is limited by the inability to differentiate the influence of each of these confounders on cardiovascular decline. This study examines changes from youth to middle age in men only, and the results may not be

generalizable to women or to individuals of more advanced age. Different techniques used between the studies could introduce some variability. However, all current techniques have been validated directly against those used in 1966. The small number of subjects precludes meaningful statistical evaluation. Finally, these subjects are relatively young compared with the subjects of most prior aging studies, affording little opportunity for interstudy comparisons.

Conclusions

In summary, the age-related decline in cardiovascular capacity among these 5 middle-aged men occurred at a rate consistent with previous longitudinal studies of nonathletes. However, 3 weeks of bedrest in 1966 had a more profound impact on cardiovascular capacity than that observed in the present evaluations despite 30 years of aging. The mechanism of the observed deterioration was primarily an impaired efficiency of maximal peripheral oxygen extraction, with CO_{max} sustained over the 3 decades. Physical inactivity accounted for some but not all of the observed decline in aerobic power and was confounded by a remarkable doubling of percent body fat. Finally, it is recommended that weight-based scaling of oxygen consumption be indexed to fat-free mass for longitudinal evaluations to minimize errors associated with the variability of body composition associated with aging.

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