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Adaptation of human left ventricular volumes to the onset of supine exercise

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Summary. The purpose of this study was to measure the changes and rates of adaptation of left ventricular volumes at the onset of exercise. Eight asymptomatic subjects, in whom intramyocardial markers had been implanted 3—6 years previously during aortocoronary bypass surgery, exercised in the supine position at a constant workload of 73.6 W for 5 min. Six also exercised first at 16.4 W, and then against a workload which progressively increased by 8.2 W every 15 s. Cardiac volumes were measured by computer assisted analysis of the motion of the implanted markers. In the constant workload test, cardiac output increased rapidly from $5.7 \pm 1\,\mathrm{l\,min^{-1}}$ to $10.3 \pm 1.9\,\mathrm{l\,min^{-1}}$ by 2 min and then increased more slowly to $10.8 \pm 2.0\,\mathrm{l\,min^{-1}}$ by 5 min. The cardiac output increase was mainly due to an increase in heart rate from 68 ± 12 beats $\mathrm{min^{-1}}$ to 120 ± 16 beats $\mathrm{min^{-1}}$ with minimal changes in stroke volume. The time constant for the early increase in cardiac output was 45 s and for heart rate, 35 s. With progressively increasing workloads, there was an almost linear increase of heart rate and cardiac output, but these increased at a slower rate than during the early phase of the constant load exercise test. In conclusion: (i) rapid changes in cardiac output during supine exercise were produced by changes in heart rate; (ii) changes in stroke volume provided minor adjustments to cardiac output; (iii) the end-diastolic volume was almost constant.

Key words: Cardiac output — Cardiac volumes — Kinetics

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Introduction

Because of the technical difficulties in measuring cardiac volumes, there is little information on how cardiac volumes adapt with the increased cardiac output at the start of exercise (Cerretelli et al. 1966; Jones et al. 1970; Raynaud et al. 1973; Rochester et al. 1960; Stein et al. 1978). This information is, however, of importance for our understanding of the kinetics of the adaptation to exercise. Furthermore, it is of practical importance for planning exercise protocols and for interpreting the volumes obtained by such steady state techniques as radionuclide equilibration, blood-pool imaging. At Stanford University Medical Center a group of patients have had intramyocardial markers implanted at the time of aortocoronary bypass surgery which allows the subsequent analysis of left ventricular volumes noninvasively by computer assisted fluoroscopy (Ingles et al. 1975). These measurements can be done beat by beat and thus allow an assessment of dynamic adaptations of volume. The purpose of this study was therefore to measure changes in cardiac output and some of its determinants — end-diastolic volume, end-systolic volume, heart rate, and velocity of circumferential fiber shortening during the first few moments of constant load supine exercise. Subjects also exercised against a progressively increasing workload to determine whether the changes in volume and rate of adaptation are affected by the pattern of workload increases. These subject had no symptoms of ischemic heart disease at the time of study, nor did they have wall motion abnormalities on ventriculography, but by virtue of their previous aortocoronary bypass procedure, they cannot be considered to be completely normal. However they provide a unique opportunity to obtain repeated, accurate,

noninvasive measurements of ventricular volumes.

Methods

Patients. The study population consisted of 8 males, aged 44 to 61 years, in whom myocardial tantalum markers had been implanted 3—6 years previously during aortocoronary bypass surgery as has been previously reported (Daughters et al. 1977; Ingles et al. 1975). Subjects were asymptomatic and were not taking any cardiac medication. No subjects had significant left ventricular wall motion or valvular abnormalities and the mean ejection fraction in the supine position was 48±4% (range 43—53) (Table 1). They had sedentary lifestyles; none were actively engaged in any fitness program.

Exercise protocol

Constant workload. Subjects lay supine at rest for at least 10 min with their feet on the pedals of an electrically braked cycle ergometer. At a signal, they pedalled against a workload of 73.6 W. This workload was chosen so that it would be a moderate stress for our subjects. Fluoroscopic recordings of three consecutive cardiac cycles were obtained at 15 s, 30 s, one minute, and thereafter at one minute intervals for 5 min. Recordings were obtained with held normal inspiration. Care was taken to ensure that the subject's diaphragm and abdomen were relaxed, so as to avoid the Valsalva maneuver.

Progressively increasing workload. Subjects first lay supine for 10 min with their feet up and then pedalled for 4 min at 16.4 W. Thereafter the workload was increased every 15 s by 8.2 W until the subject stopped from fatigue. Left ventricular volumes were recorded (again, using three-beat samples) at rest, 3 min, 4 min and 15 s, 4 min and 30 s, 5 min, and then at one minute intervals until the end of exercise. A final recording was obtained just before the subject stopped exercising. Six of the 8 subjects who had completed 5 min of constant load exercise completed this protocol.

Data reduction and analysis. Left ventricular volumes were assessed by computer assisted analysis of fluoroscopic motion of surgically implanted midwall markers as previously described (Ingles et al. 1975). Each patient had seven intramyocardial markers implanted 5 mm from the epicardial surface; one at the apex, and six at equidistant points from the apex to the base along the anterolateral and inferior margins of the left ventricle to outline the left ventricle in the 30° right anterior oblique projection. Two markers were attached to aortic adventitia to delineate the position of the valve. Left ventricular volumes were measured throughout the cardiac cycle using a computer-assisted analysis of the motion of the left ventricular markers displayed by cinefluoroscopy at 30 frames s^{-1} and recorded on a video disc recorder.

For each measurement, three beats were analyzed. For each beat, end-diastolic volume and end-systolic volume were taken as the largest and smallest ventricular volumes respectively. Left ventricular volumes were calculated by the single plane area-length method after correction of the marker coordinates for magnification of the radiographic system. A regression equation relating angiographically determined ventricular volume (V) to simultaneously measured volume using the marker technique (V_m) is: $V = 0.99\ V_m - 29.4$, $r = 0.97$. The intercept (29.4 ml) represents the average volume of myocardium within bounds delineated by the markers in the endocardium. 6,7 Stroke volume for each beat was calculated as the end-diastolic volume minus the end systolic volume. The average stroke volume for the 3 beat sequence was then multiplied by the heart rate to obtain cardiac output. The normalized mean circumferential shortening (Vcf) in circumferences per second ($c\,s^{-1}$) during ejection was calculated as the mean shortening rate of the average normalized diameter from end-diastole to 167 ms after the occurrence of the maximum end-diastolic diameter (Daughters et al. 1977).

Calculations. For each subject, the time dependence of the responses of cardiac output, heart rate and Vcf during the constant load workload were characterized by fitting an exponential of the form

$$y = a(1 - e^{-t/\tau}) + y_0$$

(using the least squares method) to the five data points obtained during the first two minutes of exercise (Linnarsson 1974) where a is the amplitude of the final change in y, t is the time, τ is the time constant and y_0 is the initial value of the variable. We then calculated the average τ of the 8 subjects.

Repeated measures were analyzed by a non-parametric analysis of variance. Data are presented as mean ±SD.

Table 1. Patient data

Patients	Age (years)	Time Post-surgery (years)	EF (% EDV)
N	51	5	47
H	48	3	47
M	60	6	53
W	44	3	48
L	54	3	46
C	61	6	43
R	54	6	43
K	43	4	52

Results

Constant workload

Table 2 gives the mean and standard deviation for each variable at rest and at 15 s, 30 s, 1, 2, 3, 4, and 5 min of constant load exercise. Mean cardiac output increased from the control value of 5.7 ± 1.7 l min^{-1} to 10.8 ± 2.0 l min^{-1} at 5 min. Of the total increase, 33% occurred by 15 s, 69% by one min and 90% by 2 min. Between 2 and 5 min there was a small further rise from 10.3 ± 2.0 l min^{-1} to 10.8 ± 2.0 l min^{-1} ($p < 0.05$). The increase in cardiac output was mainly due to the increase in heart rate which rose from 68 ± 12 to 120 ± 16 beats min^{-1} ($p < 0.001$); 38% of the total increase occurred by 15 s, 67% by 1 min and

Table 2. Mean data during 5 min of constant load exercise ($n=8$)

	Rest	15 s	30 s	1 min	2 min	3 min	4 min	5 min
Cardiac output ($l \times min^{-1}$)	5.7 ± 1.7	7.4 ± 1.7*	8.6 ± 1.9*	9.2 ± 2.0*	10.3 ± 1.9*	10.3 ± 2.0*	10.5 ± 2.1*	10.8 ± 2.0*
Heart rate (beats min^{-1})	68 ±12	88 ±10*	96 ±10*	103 ±14*	112 ±13*	114 ±15*	117 ±15*	120 ±16*
Stroke volume ($ml \times b^{-1}$)	85 ±20	84 ±20	90 ±21	91 ±20	83 ±20	92 ±20	92 ±22	92 ±23
Ejection fraction (%)	48 ± 4	47 ± 4	50 ± 4	51 ± 6	51 ± 8	52 ± 7	51 ± 8	53 ± 8*
End diastolic volume (ml)	176 ±38	175 ±36	179 ±35	177 ±33	181 ±32	179 ±30	180 ±33	175 ±32
End systolic volume (ml)	91 ±20	90 ±18	89 ±15	88 ±21	86 ±21	86 ±21	90 ±21	83 ±19*
Vcf (circumferences $\times s^{-1}$)	0.62 ± 0.20	0.74 ± 20*	0.80 ± 18*	0.89 ± 22*	0.91 ± 0.29*	0.98 ± 25*	1.01 ± 0.30*	1.07 ± 0.30*

[a] ($n=7$); * ($p<0.05$) compared to control

87% by 3 min. A 13% increase in heart rate occurred between 3 and 5 min.

The time constant of adaptation of cardiac output was 45 ± 10 s and for heart rate 35 ± 5 s.

At 15 s the change in stroke volume was variable, but by one min, 7 of the 8 subjects showed small increases in stroke volume. At the end of exercise, the mean increase in stroke volume of 8% was not significant.

There was no change in the mean end diastolic volume during the 5 min of exercise, and only one subject had a substantial increase in end-diastolic volume and he started with the smallest end diastolic volume. The mean end systolic volume decreased from 91 ± 20 ml to 86 ± 21 ml at 2 min (p = NS) and to 83 ± 19 ml at 5 min ($p<0.02$).

The ejection fraction increased from 48 ± 4 to 51 ± 8% at 3 min (p = NS) and to 53 ± 8% at 5 min ($p<0.05$). The Vcf increased in a manner similar to cardiac output and heart rate from 0.62 ± 0.20 to 1.07 ± 0.30 c s^{-1} ($p<0.01$). Twenty-seven percent of this change occurred by 15 s, 60% one min, 80% by 3 min and another 20% between 3 and 5 min. The time constant for rise of Vcf was 33 s.

The rapid frame speed of the video allowed us to obtain filling curves of the left ventricle by plotting the frame by frame volume against time. In all 8 subjects the maximal rate of filling increased; the mean rose from 503 ± 275 ml s^{-1} at rest to 881 ± 244 ml s^{-1} at the end of exercise ($p<0.02$). Besides the faster maximum rate of diastolic filling, in some subjects a more prolonged period of rapid filling as well as earlier start to rapid filling also contributed to the increase in ventricular filling and produced it in a shorter time. Three examples are shown in Fig. 1.

Progressively increasing workload

The mean cardiac output, heart rate, stroke volume, end-diastolic volume, end-systolic volume, and ejection fraction during the ramp test are shown in Table 3. The Vcf was excluded because of insufficient data. There were no significant differences between the resting heart rate, cardiac output and ejection fraction in the constant load and progressively increasing load exercise test for the 6 subjects who did both tests. However, the average stroke volume of 73 ± 19 ml was significantly lower ($p<0.05$) than the value before the constant load exercise test (85 ± 20 ml) because the end diastolic volume was lower at rest before

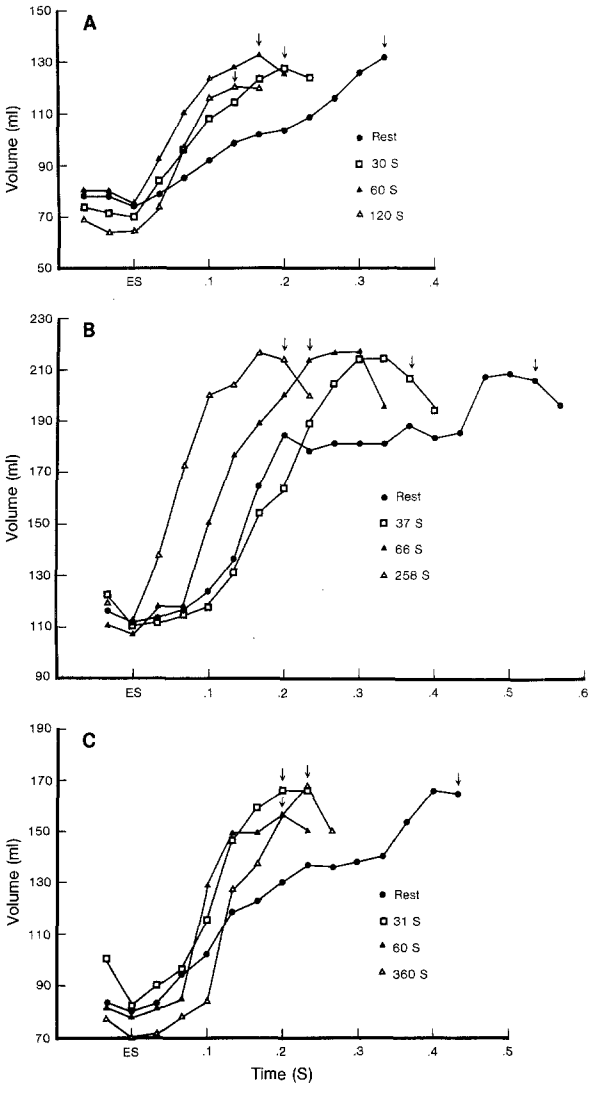

Fig. 1 A—C. Three examples of frame by frame analysis (30 frames s^{-1}) of left ventricular volumes during diastole from 3 subjects. ES signifies end systolic volume. The ordinate is the instantaneous left ventricular volume and the abscissa is time in diastole; timing began with ES. The individual curves represent single diastoles at rest or various times during exercise; the time of each curve is given with the symbols. The arrow marks the beginning of systole as determined by the R-wave on the ECG. **A** Control 30 s, 60 s, 120 s. This example shows how the filling is more rapid during exercise. **B** Rest, 30 s, 60 s, 300 s of exercise. In this example, the filling was more rapid during exercise and contributed to a larger end diastolic volume. In the resting curve the atrial contraction gave a final augmentation of volume. **C** Rest, 30 s, 60 s, 300 s of exercise. The rate of filling was again increased in this subject during exercise and continued to the end of diastole. As in **B**, in the resting state the volume plateaued before a final augmentation by atrial contraction

the progressively increasing work test in 4 of 6 subjects.

After 3 min of exercise against the minimal load 16.4 W, the cardiac output increased from the resting value of 5.2 ± 1.4 l min^{-1} to 6.8 ± 1.4 l min^{-1} with a mean increase in heart rate of 15 beats min^{-1}, ($p < 0.01$) and stroke volume of 4 ml ($p =$ NS). Ejection fraction increased in 5 of 6 subjects. In 4 this was due to a decrease in end systolic volume. During the progressively increasing phase, the mean cardiac output rose to 9.6 ± 2.0 l min^{-1} at 8 min which was not different from the value the same subjects reached after 5 min in the constant test, although the latter was not designed as a maximal test. No significant increases in stroke volume occurred during the progressively increasing phase of exercise and by the end of exercise, the final stroke volume was lower in the progressively increasing test than in the constant load test in 5 of the 6 although the mean difference was not significant.

The heart rate and cardiac output kinetics were studied during the progressively increasing work, test by measuring the interval between the time when a workload of 74 W was reached (5.75 min) to the time when the same heart rate or cardiac output as in the constant laod test was reached. This value is called the "time lag" and should be approximately equal to the time constant in a simple control system (Whipp et al. 1981). The mean time lag for heart rate was 49 ± 38 s ($n = 6$). In 5 out of 6 it was longer than the time constant for heart rate in the constant load exercise test ($p =$ NS).

The lag times for cardiac output during the progressively increasing work test were also different from the time constant for cardiac output measured in the constant load test. Two subjects did not even achieve the same cardiac output in the progressively increasing work test as they did during the constant load test and therefore the lag time could not be calculated (or could be considered infinite). In the other 4, the time lag was 74 ± 22 s which was larger ($p < 0.01$) than the time constant for adaptation of cardiac output in the constant load test of the same subjects.

Discussion

The subjects in this study all had previous aorto-coronary bypass procedures but at the time of the study they had no angina, no evidence of ischemia electrocardiographically either at rest or with exercise and no wall motion abnormalities at rest or with exercise. However latent coronary disease or myocardial scarring cannot be ruled out and caution should applied when extrapolating the data to all normal men.

Table 3. Mean data during ramp exercise test ($n=6$)

	Rest	(3 min) 16.4 W	Ramp				
			4.25 min 24.5 W	4.5 min 32.7 W	5 min 49.1 W	6 min 81.8 W	7 min[a] 114.5 W
Cardiac output (l/min)	5.2± 1.4	6.8± 1.4*	7.3± 1.6*	7.5± 1.4*	8.0± 1.4*	8.4± 1.5*	9.6± 2.0*
Heart rate (beats min^{-1})	71 ±13	86 ± 9*	91 ±10*	93 ± 6*	100 ±10	105 ±10	113 ± 8*
Stroke volume (ml × b^{-1})	73 ±19	77 ±15	81 ±18	79 ±15	80 ±15	79 ±15	82 ±19
Ejection fraction (%)	47.1± 5.1	47.6± 5.8	52.3± 5.4*	51.7± 5.3*	52.3± 5.6*	54.2± 6.7*	54.7± 8.1*
End-diastolic volume (ml)	138 ±55	155 ±26	155 ±28	154 ±27	154 ±23	147 ±26	150 ±25
End-systolic volume (ml)	81 ±24	77 ±15	72 ±16	72 ±15	68 ±19*	68 ±19	62 ±19*

* $p<0.05$ compared to control; [a] min was last workload that all subjects reached

With the onset of constant load exercise in the supine position, cardiac output increased rapidly. This implies that venous return increased rapidly which in turn implies that peripheral vascular resistance fell rapidly (Smith et al. 1976). Indeed, Donald and Shepherd (1980) found that peripheral vascular resistance begins to decrease by 0.5 s after the onset of exercise. Cadiac output can increase by an increase in heart rate or stroke volume. We found that the adaptation was mainly due to an increase in heart rate. Whereas the stroke volume was increased in 7 of 8 subjects, the mean change was not significant, possibly because of our small sample size. In previous studies with normal young males (Bevegard et al. 1966), as well as healthy old males exercising at workloads comparable to those in our study (Granath and Strandell 1964), the stroke volumes also only increased by 8—15%.

In those subjects in whom stroke volume increased, the increase occured only 15—30 s after the onset of exercise and it actually fell in 4 of 8 in the first 15 s. Similarly, Rochester et al. (1960) using a Krypton-85 dilution technique and Jones et al. (1970) using blood flow velocity analysis also found that the heart rate often increased faster than cardiac output and therefore stroke volume could fall initially.

The time constant for the adaptation of heart rate determined in this study is slower than that found in young subjects at comparable workloads (Linnarsson 1974). This may have been because of a lower level of fitness in our subjects. A surprising observation was the slower adaptation of heart rate in 5 of 6 subjects during the progressively increasing work test than in their constant load test. If heart rate adapts as in a simple control system with little delay in the response, the time constant during a constant load test should equal the time lag in the progressively increasing work test (Whipp et al. 1981). Since the time lag was longer than the time constant it appears that the simple control model of heart rate is not adequate.

The slower adaptation of cardiac output during the progressively increasing work test as compared to the constant work test demonstrates that this variable, too, does not follow a simple control model. Indeed, the cardiac output adaptation in the ramp test was more affected than heart rate. A delay in the increase of cardiac output could occur because of delayed cardiac muscular adaptation or delayed peripheral adaptation, that is, a delayed increase in venous return. If left ventricular adaptation was delayed, the end diastolic volume should have increased, but it did not. Thus delayed venous return to the left heart appears to be the primary factor. This, in turn, could have been due to increased right heart pressures obstructing the venous return or decreased peripheral adaptation and we cannot differentiate these two possibilities.

The mean end diastolic volume did not change during exercise and in subjects in whom stroke volume increased, the increase was usually due to a decrease in end-systolic volume. In the only other study in which transients of ventricular volumes were examined, echocardiography was used to assess ventricular volumes (Stein et al. 1978). These investigators found that 4 of 10 subjects had an initial fall in end-diastolic volume with no further change in end-diastolic volume during the

subsequent exercise. Since end-diastolic volume decreases when heart rate is artificially increased by pacing (McLaughlin et al. 1978) or when contractility is increased, the maintenance of end-diastolic volume in our subjects suggests that the Frank-Starling mechanism was also contributing to the augmented output of our patients.

An increase in cardiac output without a change in end diastolic volume and a fall in end-systolic volume implies that myocardial contractility increased for a change in heart rate alone results in a fall in end-diastolic volume (McLaughlin et al. 1978). A rise in contractility is supported by the rise in Vcf although a decrease in peripheral vascular resistance which probably occurred would also be associated with an increased Vcf. The rise in Vcf had approximately the same time constant as heart rate which suggests that the Bowditch phenomena, that is an increase in myocardial contractility with increasing frequency may have been a factor (Sonnenblick 1965).

We found that after the initial rapid adaptation there was a further increase in cardiac output, heart rate and Vcf. This could have been due to adjustments to steady state needs; alternatively, the cardiac output demand may have continued to increase since adaptations of $\dot{V}_{O_2}$ and heart rate are slower when subjects approach their maximal capacities (Hagberg et al. 1978). Although we chose a low workload, the cardiac output at the end of the steady state study was close to the same level that our subjects reached with the progressively increasing test suggesting that this low workload may have been near their maximal effort.

There is controversy in the literature as to what happens to end diastolic volume during steady state exercise in the supine position. Our results support those studies which have found that end diastolic volume measured by radionuclide techniques (Manyari et al. 1981; Slutsky et al. 1979; Sorensen et al. 1980), myocardial markers (Braunwald et al. 1963; Caldwell et al. 1978; McLaughlin et al. 1978; Sonnenblick et al. 1965), and echocardiography (Crawford et al. 1979; Sugishita et al. 1979) does not increase during supine exercise. However, there are studies which have found that end diastolic volume does increase during exercise and contributes to the increase of stroke volume (Poliner et al. 1980). Experiments with dogs (Erikson et al. 1971; Horwitz et al. 1972; Vatner et al. 1972) have also shown that end-diastolic volume increases at higher workloads but in these experiments the dogs' legs were dependent and humans also show an increase in end diastolic volume during exercise when the legs are dependant (Poliner et al. 1980; Rerych et al. 1978; Sonnenblick et al. 1965). Weiss et al. (1979), using echocardiography, found that end-diastolic diameter increased at near maximum exercise, but their subjects were semisupine and therefore should have had less venous return at rest than subjects whose legs are raised to the pedals before exercise. In contrast to results from normal subjects, end diastolic volume has been shown to increase during exercise in patients with coronary artery disease (Manyari et al. 1981; Sharma et al. 1976), although one study found no change (Slutsky et al. 1979).

In summary, we found that during supine exercise against a constant load, an immediate increase in heart rate occurred, accompanied by a rapid increase in cardiac output which plateaued between 3 and 4 min and then continued to rise slowly. Small increases in stroke volume tended to occur after the first 30 s, due to a decrease end-systolic volume with little change in end-diastolic volume. Similar adaptive patterns were observed with progressively increasing workloads except that the adaptation of cardiac output was slower.

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References

Bevegård S, Freyschuss U, Strandell T (1966) Circulatory adaptation to arm and leg exercise in supine and sitting position. J Appl Physiol 21:37—46

Braunwald E, Goldblatt A, Harrison DC, Mason DT (1963) Studies on cardiac dimension in intact unanesthetized man. Circ Res 13:448—467

Caldwell JH, Stewart DK, Dodge HT, Frimer M, Kennedy JW (1978) Left ventricular volume during maximal supine exercise: a study using metallic epicardial markers. Circulation 58:732—738

Cerretelli P, Sikand R, Farhi LE (1966) Readjustments in cardiac output and gas exchange during onset of exercise and recovery. J Appl Physiol 21:1345—1350

Crawford MH, White DT, Amon KW (1979) Echocardiographic evaluation of left ventricular size and performance during handgrip and supine and upright bicycle exercise. Circulation 59:1188—1196

Daughters GT, Ingels NB, Stinson EB, Alderman EL, Mean CW (1977) Computation of left ventricular dynamics from surgically implanted markers. Proc San Diego Biomed Symp 16:97—103

Donald KW, Bishop JM, Cumming G, Wade OL (1958) The effect of exercise on the cardiac output and circulatory dynamics of normal subjects. Clin Sci 14:37—73

Donald DE, Shepherd JT (1980) Autonomic regulation of peripheral circulation. Ann Rev Physiol 42:429—439

Erickson HH, Bishop VS, Kardon MB, Horwitz LD (1971) Left ventricular internal diameter and cardiac function during exercise. J Appl Physiol 30:473—478

Granath A, Strandell T (1964) Relationships between cardiac output, stroked volume and intracardiac pressures at rest and during exercise in supine position and some anthropometric data in healthy old men. Acta Med Scand 176:447—466

Gunnar G, Nilsson NJ, Sanne H (1966) Repeated serial determination of cardiac output during 30 minute exercise. J Appl Physiol 21:1750—1756

Hagberg JM, Mullin JP, Nagle FJ (1978) Oxygen consumption during constant load exercise. J Appl Physiol 45:381—384

Horwitz LD, Atkins JM, Leshin SJ (1972) Role of the Frank-Starling mechanism in exercise. Circ Res 31:868—875

Ingels NB, Daughters GT, Stinson EB (1975) Measurement of midwall myocardial dynamics in intact man by radiography of surgically implanted markers. Circulation 52:859—867

Ingels NB, Ricci DR, Daughters GT, Alderman EL, Stinson EB (1977) Effects of heart rate augmentation on left ventricular volumes and cardiac output of the transplanted human heart. Circulation 56:32—37

Jones WB, Finchum RN, Russel RO Jr, Reeves TJ (1970) Transient cardiac output response to multiple levels of supine exercise. J Appl Physiol 25:183—189

Linnarsson D (1974) Dynamics of pulmonary gas exchange and heart rate changes at start and end of exercise. Acta Physiol Scand [Suppl] 415:1—68

Manyari DE, Melendex LJ, Driedger AA, Cradduck TD, MacDonald AC, Kostuk WJ (1981) Left ventricular function and volume during supine exercise in subjects with coronary artery disease. J Appl Physiol 50:636—642

McLaughlin PR, Kleiman JH, Martin RP, Doherty PW, Reitz B, Stinson EB, Daughters GT, Ingels NB, Alderman EL (1978) The effect of exercise and atrial pacing on left ventricular volume and contractility in patients with innervated and denervated hearts. Circulation 58:476—483

Poliner LR, Dehmer GJ, Lewis SE, Parkey RW, Blomqvist CG, Willerson JT (1980) Left ventricular performance in normal subjects: a comparison of the responses to exercise in the upright and supine position. Circulation 62:528—534

Raynaud J, Bernal H, Bourdarias JP, David P, Durand J (1973) Oxygen delivery and oxygen return to the lungs at onset of exercise in man. J Appl Physiol 35:259—262

Rerych SK, Scholz PM, Newman GE, Sabiston DC, Jones RH (1978) Cardiac function at rest and during exercise in normals and in patients with coronary heart disease. Am Surg 187:449—464

Rochester DF, Durand J, Parker JO, Fritts HW, Jr, Harvey RM (1960) Estimation of right ventricular output in man using radioactive krypton (Kr^{85}). J Clin Invest 40:643—648

Sharma B, Goodwin JF, Raphael MJ, Steiner RE, Rainbow RG, Taylor SH (1976) Left ventricular angiography on exercise. A new method of assessing left ventricular function in ischemic heart disease. Br Heart J 38:59—70

Slutsky R, Karliner J, Ricci D, Schuler G, Pfisterer M, Peterson K, Ashburn W (1979) Response of left ventricular volume to exercise in man assessed by radionuclide equilibrium angiography. Circulation 60:565—571

Smith EE, Guyton AC, Manning RD, White RJ (1976) Integrated mechanisms of cariovascular response and control during exercise in the normal human. Prog Cardiovasc Dis 18:421—443

Sonnenblick EH, Braunwald E, Williams JF, Jr, Glick G (1965) Effects of exercise on myocardial force-velocity relations in intact unanesthesized man: relative roles of changes in heart rate, sympathetic activity, and ventricular dimensions. J Clin Invest 44:2051—2062

Sorensen SG, Ritchie JL, Caldwell JH, Hamilton GW, Kennedy JW (1980) Serial exercise radiocluide angiography. Circulation 61:600—609

Stein RA, Michielli D, Fox EL, Krasnow N (1978) Continuous ventricular dimensions in man during supine exercise and recovery. Am J Cardiol 41:655—660

Sugishita Y, Kosfki S (1979) Dynamic exercise echocardiography. Circulation 60:743—752

Vatner SF, Franklin D, Higgins CB, Patrick T, Braunwald E (1972) Left ventricular response to severe exertion in untethered dogs. J Clin Invest 51:3052—3060

Weiss JL, Weisfeldt ML, Mason SJ, Garrison JB, Livengood V, Fortuin NJ (1979) Evidence of Frank-Starling effect in man during severe semisupine exercise. Circulation 59:655—661

Whipp BJ, Davis JA, Tones T, Wasserman K (1981) A test to determine parameters of aerobic function during exercise. J Appl Physiol 50:217—221

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