Mechanisms for increasing stroke volume during static exercise with fixed heart rate in humans

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Nóbrega, Antonio C. L., J on W. Williamson, J orge A. Garcia, and J ere H. Mitchell. Mechanisms for increasing stroke volume during static exercise with fixed heart rate in humans. J. Appl. Physiol. 83(3): 712–717, 1997.—Ten patients with preserved inotropic function having a dual-chamber (right atrium and right ventricle) pacemaker placed for complete heart block were studied. They performed static one-legged knee extension at 20% of their maximal voluntary contraction for 5 min during three conditions: 1) atrioventricular sensing and pacing mode (normal increase in heart rate [HR; DDD]), 2) HR fixed at the resting value (DOO-Rest; 73 ± 3 beats/min), and 3) HR fixed at peak exercise rate (DOO-Ex; 107 ± 4 beats/min). During control exercise (DDD mode), mean arterial pressure (MAP) increased by 25 mmHg with no change in stroke volume (SV) or systemic vascular resistance. During DOO-Rest and DOO-Ex, MAP increased (+25 and +29 mmHg, respectively) because of a SV-dependent increase in cardiac output (+1.3 and +1.8 l/min, respectively). The increase in SV during DOO-Rest utilized a combination of increased contractility and the Frank-Starling mechanism (end-diastolic volume 118–136 ml). However, during DOO-Ex, a greater left ventricular contractility (end-systolic volume 55–38 ml) mediated the increase in SV.

echocardiography; pacemaker; left ventricular volume; Frank-Starling mechanism; myocardial contractility

During static exercise in healthy subjects, cardiac output (CO) and arterial blood pressure increase while systemic vascular resistance does not change (11, 12, 14, 17). The increase in CO depends primarily on the acceleration in heart rate (HR) because stroke volume (SV) remains constant (8, 13, 14, 17). Although this is the pattern of the hemodynamic response to mild static exercise (<50% of maximal voluntary contraction [MVC]) in healthy subjects, there is considerable plasticity of these responses. Several studies have demonstrated that the increase in blood pressure is preserved even when there is little change in HR, such as in patients with heart transplant (10, 22) or Chagas’ disease (13) or in healthy subjects submitted to pharmacological autonomic blockade (11, 14). In these studies, HR and SV did not change, and the blood pressure response was caused by an increase in systemic vascular resistance. However, the positive inotropic effect of exercise, and therefore a potential increase in SV, may not be expressed during autonomic blockade or in patients with Chagas’ disease or cardiac transplant, introducing a confounding factor on the interpretation of the role of HR in producing the pressor response during static exercise.

The cardiovascular responses to sustained static contraction in patients with complete atrioventricular block and otherwise functionally normal hearts who have dual-chamber (right atrium and right ventricle) pacing and sensing pacemakers have been studied previously (1). When the patients exercised with the sensing feature of the pacemakers turned off and static exercise was performed with the HR fixed, SV increased and compensated for the lack of a chronotropic response, allowing for CO to rise and to produce the pressor response, whereas systemic vascular resistance remained constant. However, in that study the changes in left ventricular volumes were not assessed.

The increase in SV that produces the CO and blood pressure responses to static exercise with fixed HR could be mediated by an increase in end-diastolic volume by utilizing the Frank-Starling mechanism, by an increase in myocardial contractility (inotropic state), reducing or keeping end-systolic volume constant, or by both mechanisms. Therefore, the purpose of the present study was to determine the mechanism by which SV increases during static exercise with fixed HR in patients with complete heart block and dual-chamber pacemakers by using measurements of left ventricular dimensions by echocardiography. We hypothesized that, because of the relatively longer ventricular filling time, the increase in SV during pacing at the resting rate would be caused by an increase in end-diastolic volume (Frank-Starling mechanism). On the other hand, during exercise with fast pacing rate, the increase in SV would be caused by a decrease in end-systolic volume (increased contractility).

METHODS

Subjects

Five male and five female patients with permanent programmable dual-chamber (right atrium and right ventricle) pacing and sensing pacemakers were selected for the study. The mean age was 22 ± 8 (SD) yr, height was 164 ± 22 cm, and weight was 72 ± 18 kg. The pacemakers were placed for complete atrioventricular conduction block of the following etiology: congenital (n = 4), secondary to atrioventricular nodal ablation for atrial tachyarrhythmias (n = 4), and idiopathic (n = 2). On the basis of a full history, medical examination, and revision of past medical records, all patients were considered healthy aside from the atrioventricular block, without any evidence of inotropic dysfunction. All presented with sinus rhythm, and no one was taking any medication with cardiovascular or autonomic effects. The patients were instructed to abstain from smoking and drinking caffeine-containing beverages on the day of the experiment and to avoid strenuous physical activity in the preceding 24 h. The research protocol was approved by the Institutional Review Board of the University of Texas Southwestern Medical Center, and all subjects, or the legal guard-
ian in the case of a 17-year-old girl, gave written informed consent before participating in the study.

Echocardiographic and Hemodynamic Measurements

Ventricular dimensions were assessed by two-dimensional echocardiography (ATL-UM9) from an apical four-chamber view by using a handheld 3.0-MHz probe. Care was taken to maintain the transducer at the same position and to keep the same images on the screen for each trial. The cardiac images were stored on a videotape by a VHS recorder (AG-7350, Sony) for off-line analysis.

Left ventricular volumes were determined by one investigator, who was blind as to the pacing mode of the trial being analyzed. The images were reviewed, and several cardiac cycles before and during exercise were frozen on the screen for analysis. The ventricular volumes were derived automatically by a software incorporated in the echocardiogram equipment employing the area-length calculation (7): left ventricular volume $= \frac{A}{2} \times \frac{L}{3}$, where $A$ is the left ventricular area, and $L$ is the left ventricular longest length. The ventricular area was determined from tracing along the inner edge of the endocardial targets, and the length was obtained from measuring the distance from the left ventricular apex to the midpoint of the mitral annulus (5). The end-diastolic measurements were obtained at the onset of the electrocardiographic QRS complex recorded simultaneously on the videotape, and the end-systolic measurements were determined from the frame showing the minimum left ventricular dimensions just before mitral valve opening. Individual values were calculated as the mean of the three trials with the clearest images. SV, presented in milliliters, was obtained by subtracting the end-diastolic from the end-systolic volume.

HR was monitored continuously by electrocardiography (Mingograph 7, Siemens-Elema) and arterial blood pressure by infrared finger photoplethysmography (Finapres 2300TM, Ohmeda, Madison, WI). CO (SV x HR) and systemic vascular resistance (MAP/CO, where MAP is mean arterial pressure) were calculated and reported in liters per minute and millimeters mercury per liter per minute, respectively.

CO was also determined by the acetylene rebreathing method modified for use with a mass spectrometer (25) for comparison with echocardiography. Briefly, subjects breathed for 20 s from a bag containing 0.61% C2H2-9.0% He-45.0% O2-balance N2. The disappearance rate of C2H2 sampled by a mass spectrometer (MGA 100, Perkin Elmer, Pomona, CA) was computed over the rebreathing period to calculate pulmonary blood flow, i.e., CO, by using customized software and a minicomputer (MINC RT11, Digital, Maynard, MA). The values for HR and MAP during rebreathing were also digitized and stored in the computer. SV was also calculated (CO/HR) for comparison.

Procedures

The patients sat on a straight-back chair and performed static knee extension of the dominant leg with the knee flexed at 90° while the generated force was measured by a strain gauge fixed to a strap placed around the ankle. MVC was defined as the peak force generated during three separate attempts sustained for 2 s. After a rest period, the patients performed 5 min of static knee extension at 20% of MVC. This was accomplished on a dual-beam oscilloscope by matching (Tektronic 536, Portland, OR) a line representing the generated force with another one equivalent to the calculated 20% MVC.

Pacing Modes

They performed three separate bouts of static knee extension with different pacing modalities. All patients exercised first in the rate-responsive dual-chamber sensing and pacing mode (DDD), which tracked the intrinsic atrial rate and, after an appropriate atrioventricular delay (150–200 ms), paced the ventricle. Therefore, the observed HR increase simulates the normal physiological chronotropic response to static exercise. Then, the sensing feature of the pacemakers was turned off (DOO mode) and, in randomized order, the HR was fixed either at resting rate (DOO-Rest) or at the peak exercise rate (DOO-Ex) obtained during DDD mode. The exercise during the DDD pacing mode had to be performed first to determine the peak exercise HR, which was set on the pacemaker for the DOO-Ex mode. No other pacemaker parameters were altered. In these modes of pacing, the pacemaker does not sense any intrinsic sinus electrical activity and paces the atria according to the programmed rate and, after a delay, paces the ventricle. In the presence of a faster competing intrinsic sinus activity, successful atrial pacing may not occur because of failure to capture. Ventricular pacing would still occur at the programmed fixed rate because the presence of complete heart block would prevent conduction of any atrial activity. Therefore, during the DOO-Rest mode, the pacemaker is firing to both atria and ventricles at a slower rate than the sinus node, and intermittent loss of atrioventricular synchrony may occur.

Once the sensing mode of the pacemaker was turned off and HR was fixed, at least 10 min were allowed for stabilization of hemodynamic variables before the exercise was performed again. Hemodynamic measurements and echocardiographic images were obtained in all patients before exercise and repeated at 1 and 5 min during one-legged static knee extension.

Statistical Analysis

The results are expressed as means ± SE, unless stated otherwise. Two-way analysis of variance with repeated measures (main factors: pacing mode and time) was used to compare the hemodynamic variables (CO, HR, SV, MAP, and systemic vascular resistance) and left ventricular volumes (end-diastolic and end-systolic). Because end-systolic volume and systemic vascular resistance presented a non-Gaussian distribution and heteroscedasticity, these data were transformed logarithmically to allow the use of parametric statistical procedures. When the analysis of variance yielded an F-value with $P < 0.05$, a multiple-range test, the Student-Newman-Keuls procedure, was used for post hoc analysis to localize the pairwise differences (27). A $P < 0.05$ was chosen as the level of probability required to reject the null hypothesis.

RESULTS

Rest

The resting CO values obtained by echocardiography for all three modes and those obtained by acetylene rebreathing did not differ statistically (Table 1). The resting SV values, using the two methods, were also similar.

During the DOO-Ex mode, resting HR was higher and resting SV was lower than during the DDD mode. On the other hand, during DOO-Rest there were no statistical differences for the hemodynamic variables compared with DDD mode at rest (Table 1; Figs. 1–3).
Static Exercise

DDD mode. When HR was allowed to increase from rest to exercise (34 beats/min), MAP rose by 25 mmHg from rest to 5 min of mild static exercise (Table 1; Fig. 1). This resulted from an HR-dependent increase in CO of 1.7 l/min (Table 1; Figs. 1 and 2), whereas SV and systemic vascular resistance did not change (Table 1; Fig. 2). Neither left ventricular end-diastolic nor

![Fig. 1. Mean arterial pressure (top) and heart rate (bottom) responses to 5 min of 1-legged sustained static extension at 20% of maximal voluntary contraction. Values are means ± SE; n = 10 subjects. DDD, dual-chamber sensing and pacing mode; DOO-Rest, heart rate fixed at resting value; DOO-Ex, heart rate fixed at peak exercise value; Ex-1, after 1 min; Ex-5, after 5 min; echo, values determined by two-dimensional echocardiography; rebreath, values determined by acetylene rebreathing method. *P < 0.05 compared with rest at same pacing mode. †P < 0.05 compared with DDD pacing mode at same time point. See Table 1 for specific comparisons.]

![Fig. 2. Cardiac output (top), stroke volume (middle), and systemic vascular resistance (bottom) responses to 5 min of 1-legged sustained static extension at 20% of maximal voluntary contraction. Values are means ± SE; n = 10 subjects. Symbols and P values are defined as in Fig. 1. See Table 1 for specific comparisons.]

Table 1. Hemodynamic data for subjects at rest and during static exercise in different pacing modes

<table>
<thead>
<tr>
<th></th>
<th>DDD Rest</th>
<th>Ex-1</th>
<th>Ex-5</th>
<th>DOO-Rest</th>
<th>Ex-1</th>
<th>Ex-5</th>
<th>DOO-Ex</th>
<th>Ex-1</th>
<th>Ex-5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean arterial pressure, mmHg</td>
<td>95 ± 7</td>
<td>106 ± 4*</td>
<td>120 ± 3*</td>
<td>93 ± 3</td>
<td>108 ± 4*</td>
<td>118 ± 5*</td>
<td>98 ± 3</td>
<td>115 ± 5†</td>
<td>127 ± 5*</td>
</tr>
<tr>
<td>Heart rate, beats/min</td>
<td>74 ± 3</td>
<td>84 ± 3*</td>
<td>108 ± 4*</td>
<td>73 ± 3</td>
<td>73 ± 3†</td>
<td>73 ± 3†</td>
<td>107 ± 4†</td>
<td>107 ± 4†</td>
<td>107 ± 4</td>
</tr>
<tr>
<td>Cardiac output, l/min</td>
<td>4.6 ± 0.3</td>
<td>5.3 ± 0.4*</td>
<td>6.3 ± 0.4*</td>
<td>4.5 ± 0.3</td>
<td>5.2 ± 0.3*</td>
<td>5.8 ± 0.4*</td>
<td>4.9 ± 0.4</td>
<td>5.7 ± 0.4*†</td>
<td>6.7 ± 0.5*</td>
</tr>
<tr>
<td>Stroke volume, ml</td>
<td>62 ± 5</td>
<td>64 ± 7</td>
<td>58 ± 9</td>
<td>63 ± 5</td>
<td>71 ± 5</td>
<td>78 ± 7†</td>
<td>46 ± 5†</td>
<td>53 ± 6</td>
<td>62 ± 7*</td>
</tr>
<tr>
<td>Echo</td>
<td>64 ± 5</td>
<td>66 ± 5</td>
<td>62 ± 4</td>
<td>62 ± 4</td>
<td>74 ± 5</td>
<td>76 ± 5†</td>
<td>47 ± 5†</td>
<td>49 ± 4†</td>
<td>60 ± 7*</td>
</tr>
<tr>
<td>Rebreath</td>
<td>20.7 ± 0.6</td>
<td>20.1 ± 0.4</td>
<td>19.0 ± 0.5</td>
<td>20.7 ± 0.5</td>
<td>20.8 ± 0.5</td>
<td>20.7 ± 0.5</td>
<td>20.1 ± 0.5</td>
<td>20.3 ± 0.6</td>
<td>19.1 ± 0.6</td>
</tr>
<tr>
<td>End-diastolic volume, ml</td>
<td>113 ± 8</td>
<td>116 ± 12</td>
<td>111 ± 13</td>
<td>118 ± 7</td>
<td>128 ± 11</td>
<td>136 ± 14†</td>
<td>101 ± 7</td>
<td>102 ± 10</td>
<td>100 ± 11</td>
</tr>
<tr>
<td>End-systolic volume, ml</td>
<td>51 ± 6</td>
<td>53 ± 8</td>
<td>51 ± 7</td>
<td>55 ± 4</td>
<td>57 ± 5</td>
<td>58 ± 6</td>
<td>55 ± 6</td>
<td>49 ± 7</td>
<td>38 ± 6†</td>
</tr>
<tr>
<td>Systemic vascular resistance, mmHg·l⁻¹·min⁻¹</td>
<td>20.7 ± 0.6</td>
<td>20.1 ± 0.4</td>
<td>19.0 ± 0.5</td>
<td>20.7 ± 0.5</td>
<td>20.8 ± 0.5</td>
<td>20.7 ± 0.5</td>
<td>20.1 ± 0.5</td>
<td>20.3 ± 0.6</td>
<td>19.1 ± 0.6</td>
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</table>

Values are means ± SE; n = 10 subjects. DDD, dual-chamber sensing and pacing mode; DOO-Rest, heart rate fixed at resting value; DOO-Ex, heart rate fixed at peak exercise value; Ex-1, after 1 min; Ex-5, after 5 min; echo, values determined by two-dimensional echocardiography; rebreath, values determined by acetylene rebreathing method. *P < 0.05 compared with rest at same pacing mode. †P < 0.05 compared with DDD pacing mode at same time point.
end-systolic volumes changed during the sustained static contraction (Table 1; Fig. 3).

DOO-Rest mode. MAP increased from rest at 1 and 5 min and was similar to that in the DDD mode (Table 1; Fig. 1). This pressor response was brought about by an increase in CO of 1.3 l/min, which was because of an elevation in SV of 15 ml because HR was fixed and systemic vascular resistance remained unchanged (Table 1; Fig. 2). The elevation in SV was because of an increase in end-diastolic volume (118–136 ml) at 5 min of static exercise and became greater than in the DDD mode, whereas the end-systolic volume did not differ statistically from rest (Table 1; Fig. 3). During exercise in this mode of pacing, when loss of atrioventricular synchrony may have occurred, SV and CO increased to a similar extent observed during exercise with fast pacing and control exercise. Therefore, if loss of atrioventricular synchrony occurred, it had no apparent effect on SV and CO.

DOO-Ex mode. MAP increased from rest to 5 min of contraction with DOO-Ex similar to the DDD and DOO-Rest pacing modes (Table 1; Fig. 1). Similar to DOO-Rest, CO was also increased by an elevation in SV of 16 ml (Table 1; Fig. 2). However, during the DOO-Ex mode, the mechanism that caused the increase in SV was a smaller end-systolic volume (55–38 ml) because end-diastolic volume did not change from rest (Table 1; Fig. 3). Systemic vascular resistance during exercise was similar to rest and to the values obtained during exercise in the DDD and DOO-Rest pacing modes (Table 1; Fig. 2).

DISCUSSION

The hemodynamic data obtained in the present study demonstrated that an increase in SV compensated for the lack of HR response in the patients to produce the normal increase in blood pressure during mild static exercise. Although this finding is consistent with previous studies (1, 9, 21), it disagrees with other investigations using autonomic blockade (11, 14) or patients with Chagas' disease (13) or orthotopic heart transplant (10, 22), in which HR and CO could not increase properly and a normal blood pressure response still occurred as a result of an increase in systemic vascular resistance. However, in these studies, a potential increase in SV could occur neither through increased myocardial contractility, because of the pharmacological blockade or compromised ventricular function, nor through the Frank-Starling mechanism, because of the rapid resting HR found in most of the subjects. Individuals with dual-chamber (right atrium and right ventricle) sensing and pacing mode but normal contractile function provide a more adequate model for study of the physiology of these circulatory mechanisms because HR can be controlled and left ventricular function is not compromised.

The main purpose of the present study was to determine the mechanism by which SV increases during static exercise when the HR response is abolished in patients with normal ventricular function. Previously, Alexander et al. (1) speculated that the compensatory increase in SV during exercise with fixed HR could be explained by the Frank-Starling mechanism, by increased myocardial contractility, or by both mechanisms. This issue was addressed in the present study by using two-dimensional echocardiography to assess ventricular dimensions. The left ventricular volumes were estimated by using an ellipsoid model from measurements of the chamber area obtained on a single plane. Although such a technique might be expected to underestimate the absolute values for ventricular volumes (5), this seemed not to be the case because the CO and SV values obtained by echocardiography and acetylene rebreathing were similar in the present study. Even if there were an underestimation of the actual ventricular volumes, this would not change the interpretation or conclusions because the purpose of the study was to describe the relative changes in ventricular dimensions during exercise across the different pacing modes, in which each subject served as his/her own control. In addition, the results showed different directional changes in ventricular volumes during exercise in the pacing modes. For these reasons, we believe that the technique utilized proved to be adequate to test the central hypothesis of the study. The results showed that, when HR was fixed at a rate found at peak exercise, SV increased by means of a lower end-systolic volume, i.e., increased myocardial contractility. On the other hand, when HR was fixed at the resting level, SV increased because of a larger end-diastolic volume (Frank-Starling mechanism). However, myocardial con-
tractility was also increased in this condition because end-systolic volume was kept constant in face of the increased blood pressure.

A similar experimental model was employed by Bergenwald et al. (2), who reported a rise in systemic vascular resistance during sustained static handgrip in healthy subjects with their hearts paced at 109 beats/min. Although this observation is in disagreement with the present report, a direct comparison between the studies is difficult because of important methodological differences such as contractions of a muscle group of smaller mass (handgrip) and the use of subjects with normal atrioventricular conduction, precluding the observation of the responses to a fixed low HR. More importantly, Bergenwald et al. used a pacing rate that was at least 10 beats/min beyond the peak value obtained during the control exercise bout, causing an increase in CO and MAP and a reflex decrease in resting systemic vascular resistance. This reduced vascular resistance at rest could have facilitated the expression of an increase in this variable during static contraction.

In the DOO-Rest pacing mode, the increase in SV during static exercise occurred with a larger left ventricular end-diastolic volume. This rise in end-diastolic volume denotes an increase in effective ventricular filling pressure, considering that there was no sudden increase in ventricular compliance. According to the ventricular length-tension relationship (Frank-Starling mechanism), pump performance, i.e., SV, is determined by ventricular filling pressure (preload) (3). Therefore, the higher end-diastolic volume and thus myocardial fiber length during the DOO-Rest mode allowed for the increase in SV. This increase in end-diastolic volume probably reflects the longer ventricular filling time in the DOO-Rest mode than during the DDD and DOO-Ex modes. An increase in aortic pressure (afterload) reduces ejection and thus increases end-systolic volume if contractility and preload are not changed (3, 24). On the other hand, a constant or decreased end-systolic volume when afterload is increased denotes an enhanced myocardial contractility. Therefore, during DOO-Rest, a combination of increased contractility and the Frank-Starling mechanism elicited the increase in SV, which ultimately caused the rise in CO and blood pressure. During exercise in the DOO-Ex mode, end-diastolic volume did not change and the increased SV was mediated solely through an increase in myocardial contractility. Other studies have shown that myocardial contractility increases during static exercise with fixed HR by atrial pacing (9, 21), but their focus was on left ventricular performance. SV and CO data during pacing were not reported in the studies.

Myocardial contractility is influenced by cardiac cycle length (interval-force relationship) and autonomic activity (3, 24). With regard to the positive effect of increased HR on contractility (HR was fixed at a value ~45% higher during DOO-Ex than in DOO-Rest), this difference was already present at rest and therefore could not explain the reduced end-systolic volume during DOO-Ex. Thus the increased contractility was most likely mediated by autonomic adjustments, i.e., increased sympathetic stimulation and inhibited vagal activity. The neural mechanisms responsible for inducing these autonomic adjustments are the subject of intense investigation. It is believed that the autonomic responses to exercise are driven by two main mechanisms: central command (parallel activation of motor and autonomic activity) and exercise pressor reflex (activation induced by mechanoreceptors and metaboreceptors in skeletal muscle) (16, 23). These neural mechanisms seem to modify the characteristics of reflexes modulating the cardiovascular function, such as the arterial baroreflex (6). The augmented myocardial contractility during exercise, especially during DOO-Ex, was probably mediated by increased adrenergic outflow that can be induced by activation of muscle receptors during static exercise (15, 23). Although the arterial baroreflex keeps blood pressure fairly constant at rest through modifications of HR and vascular resistance, the contraction-induced neural input interacts with the arterial baroreflex and allows for the increase in blood pressure and myocardial contractility in the face of an increased HR and unchanged systemic vascular resistance. Further studies should be conducted in these groups of patients, including the use of selective sympathetic and parasympathetic blockade and different protocols to determine the reflex mechanisms and autonomic adjustments involved with the observed responses.

In a combination of the results from previous studies (10, 11, 13, 14, 22) with those from the present one, it appears that the mechanisms of cardiovascular control operate with sufficient plasticity to modify the hemodynamic components of the response to static exercise to increase blood pressure under various circumstances. In the case of patients with isolated chronotropic insufficiency but preserved myocardial function, SV, instead of HR, produces the increase in CO and blood pressure. In this case, SV rises through an increase in myocardial contractility and involvement of the Frank-Starling mechanism if cardiac filling time is long enough. However, when the HR is fixed at a fast rate, end-diastolic volume does not change and SV increases because of a smaller end-systolic volume. In the situations in which myocardial function is affected along with the HR response, thus blunting the increase in CO during static exercise, an adequate blood pressure response can still be elicited by an increase in systemic vascular resistance (13, 14).

Although the cardiovascular responses to dynamic exercise differ substantially from those observed during static contractions (11, 12, 14, 17, 23), a similar pattern of compensatory mechanisms may be present in both types of exercise. During dynamic exercise with subjects in the upright posture, CO increases through increases in SV and HR. SV typically increases by a combination of larger end-diastolic volume and decreased end-systolic volume (20, 26). When dynamic exercise is performed with fixed HR, end-diastolic volume increases further, allowing for an increase in
SV that can partially compensate for the lack of HR response to elevate CO (4, 11). In addition, during dynamic exercise with reduced CO produced by venous occlusion (18) or by administration of metoprolol (19), the decrease in peripheral vascular resistance is blunted and blood pressure increases.

In summary, when HR is fixed at resting level during static exercise in patients with normal inotropic function, SV increases by means of a larger end-diastolic volume (Frank-Starling mechanism) and increased contractility. On the other hand, when the heart is paced at a faster rate corresponding to that during peak exercise, SV increases because of a lower end-systolic volume, i.e., increased myocardial contractility.

We appreciate the technical assistance of David Maass. We also thank Dr. Daniel Friedman for help and suggestions.

This project was supported by the Lawson and Rogers Lacy Research Fund in Cardiovascular Disease and the Frank M. Ryburn, Jr., Chair in Heart Research. J. W. Williamson was supported by an Individual National Research Science Award-National Institutes of Health Grant 1F–32-HL-08976. A. C. L. Nóbrega was supported by a fellowship from Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES)-Brazil (no. 213292–3).

A preliminary report of this study has been presented in abstract form (FASEB J. 8: A304, 1994).

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Received 11 November 1996; accepted in final form 28 April 1997.

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