# Exercise training increases arterial compliance in patients with congestive heart failure

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A B S T R A C T

Systemic arterial compliance (SAC) makes an important contribution to cardiac afterload, and thus is a significant determinant of left ventricular work. Previous studies have suggested that arterial compliance may be reduced in patients with congestive heart failure (CHF), and that SAC is increased after a 4-week exercise training programme in healthy, sedentary individuals. The present study aimed to investigate the effects of an 8-week exercise training programme on arterial mechanical properties, left ventricular performance and quality of life in CHF patients. A total of 21 patients with NYHA class II or III CHF (mean $\pm$ S.D. age 55 $\pm$ 13 years) were randomly allocated to either an 8-week exercise training group or a 'usual lifestyle' control group. SAC, as determined non-invasively using applanation tonometry and Doppler aortic velocimetry, increased from 0.57 $\pm$ 0.11 to 0.77 $\pm$ 0.14 arbitrary compliance units (mean $\pm$ S.E.M.; $P = 0.01$) in the exercise group, while no change occurred in the control group. Left ventricular structure and function was assessed by echocardiography, and these parameters were unchanged over the 8-week study period. Exercise training significantly increased exercise capacity, measured by a 6-min walking test (474 $\pm$ 27 to 547 $\pm$ 34 m; $P = 0.008$). Quality of life, as assessed using the Minnesota Living with Heart Failure Evaluation, demonstrated a decrease in heart failure symptoms from 46 $\pm$ 7 to 24 $\pm$ 5 units ($P = 0.01$) following the exercise training programme. These data show that exercise training improves SAC in patients with CHF. The accompanying improvement in exercise capacity may be due, in part, to an improvement in arterial function.

## INTRODUCTION

Congestive heart failure (CHF) is characterized by reduced ventricular performance in conjunction with neurohormonal activation and fluid retention. As a component of this syndrome, elevated peripheral vascular resistance is classically observed, representing the consequence of the vasoconstrictor action of neurohormones on resistance vessels. In this context, the clinical utility of vasodilator drugs that reduce peripheral vascular resistance, and thereby cardiac afterload, is well recognized. Recently it has become increasingly appreciated that the mechanical properties of the large arteries also contribute significantly to afterload. Systemic arterial compliance (SAC) has been shown to decrease with age [1] and in some cardiovascular disorders, such as hypertension [1,2]. It is thought that arterial compliance is reduced in CHF patients [3,4], although the implications of this observation remain uncertain.

In addition to pharmacological therapy, participation in a moderate exercise programme has been shown to reduce fatigue and dyspnoea [5,6], symptoms commonly

**Key words:** arteries, exercise, heart failure, mechanical properties.

**Abbreviations:** a.c.u., arbitrary compliance units; CHF, congestive heart failure; E/A ratio, E-wave velocity/A-wave velocity; PWV, pulse wave velocity; SAC, systemic arterial compliance.

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associated with the daily lifestyle of patients with heart failure. However, the mechanism(s) by which exercise improves these parameters is uncertain. In healthy subjects, it is now well established that aerobic training improves arterial compliance [7–11]. To date, the effect of an exercise training programme on arterial compliance in CHF has not been investigated.

Reduced SAC is potentially disadvantageous in patients with CHF, due to an adverse impact on ventricular performance; effects include increased cardiac afterload and arterial impedance, as well as reduced diastolic pressure and thus coronary blood flow. It has been shown that regional arterial compliance is decreased in heart failure patients [3,4,12,13]; however, SAC has not been determined in CHF patients to date. It also remains unclear whether heart failure patients can exercise sufficiently to improve arterial compliance. In order to address these issues, the aim of the present study was to investigate the effects of an 8-week exercise training programme on SAC and quality of life in CHF patients.

## METHODS

### Subjects

A total of 21 patients (mean ± S.D. age 55 ± 13 years) with stable CHF (mean ± S.E.M. left ventricular ejection fraction 25 ± 2%) were recruited from the Heart Failure Clinic at the Alfred Hospital. NYHA class II and III patients on stable anti-failure therapy aged between 17 and 70 years, who were able to participate in an exercise programme, were selected for the study. Prior to experimentation, subjects gave written informed consent; in addition, the research was carried out in accordance with the Declaration of Helsinki (1989) of the World Medical Association, and the study was approved by The Alfred Healthcare Group Ethics Committee.

### Protocol

Patients recruited from the Alfred Heart Failure Clinic were allocated randomly either to an 8-week exercise programme or to continue with their usual lifestyle. The patients allocated to the 'usual living' group were instructed not to change their regular daily activities for the 8-week study duration. The exercise programme was conducted over 8 weeks; patients were required to exercise at 50–60% of maximum heart rate, and to progressively increase their exercise duration from three 30 min sessions per week to approx. 60 min per day on 5–7 days per week. An individualized programme of walking, light hand weights and stationary cycling was tailored according to an individual's capacities, and was increased progressively over the 8-week period according to individual responses. Measurements of arterial compliance, pulse wave velocity (PWV), blood pressure, quality of life, left ventricular function and exercise capacity were performed at baseline and after the 8-week intervention.

### Assessment of arterial mechanics

SAC, broadly defined as the change in volume of a vessel associated with a given change in pressure within that vessel [8], was determined by the area method described by Liu et al. [14] and validated in our laboratory [7]. The technique involves the simultaneous non-invasive measurement of ascending aortic blood flow velocity and right carotid arterial pressure, as described previously [7,15]. Ascending aortic blood flow velocity was measured by continuous-wave Doppler flow velocimetry with a 3.5 MHz transducer (Multi-doplex; Huntleigh Technology, Cardiff, U.K.) placed at the suprasternal notch. The product of aortic flow velocity and left ventricular outflow tract area was used to calculate aortic volumetric flow. An estimate of central systolic pressure was derived from applanation of the proximal right carotid artery using a pressure transducer (Miller Mikro-Tip SPT-301; Miller Instruments, Houston, TX, U.S.A.). Pressures were calibrated by simultaneous measurement of brachial arterial pressure, using a Dinamap vital signs monitor (18465X; Dinamap, Critikon, FL, U.S.A.). Arterial compliance was reported in arbitrary compliance units (a.c.u.), dimensionally equal to ml/mmHg. [7] PWV, which is inversely related to arterial compliance, was measured centrally (between the right carotid artery and the right femoral artery) and peripherally (between the right femoral artery and the right dorsalis pedis artery) by simultaneous applanation tonometry [15].

### Augmentation index

Carotid pressure waveforms obtained for the determination of SAC were used to calculate the augmentation index, defined as the difference between the first and second systolic peaks of the central arterial waveform, expressed as a percentage of pulse pressure [16]. Pressure data for each cardiac cycle selected were linearly detrended assuming equality of pressure at the start and end of each cardiac cycle, and then scaled to brachial artery mean and diastolic pressure. The features of the carotid arterial waveform were characterized, including pressure at inflection, peak systolic pressure and augmented pressure [16]. The values of augmentation index and augmented pressure were defined as positive or negative depending on whether pressure at inflection occurred before or after peak systolic pressure.

### Assessment of cardiac function

A trained operator who was blinded to the training status of each subject performed and interpreted all measure-

ments with the use of two-dimensional echocardiography (Hewlett–Packard 77020A). M-mode images of the left ventricle using the parasternal short axis view at the level of the mitral chordae were used to obtain left ventricular dimensions. Flow through the mitral valve was measured via pulsed-wave Doppler echocardiography.

### Assessment of quality of life and functional performance

Quality of life was assessed by the completion by the patient of a questionnaire, the Minnesota Living with Heart Failure Evaluation [17]. Functional performance was determined by a 6-min walking test, as described previously [18]. Distance walked, heart rate and perceived exertion were the primary measurements taken during the walking test.

### Statistical analysis

Statistical analysis was performed using SPSS Version 10.0 (SPSS Inc., Chicago, IL, U.S.A.). The significance level employed was $P < 0.05$. Repeated-measures ANOVA was performed for blood pressure, weight, SAC, PWV, left ventricular dimensions, mitral flow, quality of life and the exercise test. All results, including those in Figures, are presented as means $\pm$ S.E.M., excluding age, which is given as mean $\pm$ S.D.

## RESULTS

A total of 21 patients with moderate to severe CHF were included in the study, of which 11 participated in the exercise programme and 10 acted as control subjects. The two groups were similar in age (controls, $53 \pm 11$ years; exercise group, $57 \pm 15$ years; Table 1) and body mass index (controls, $26.0 \pm 0.7$ kg·m$^{-2}$; exercise group, $27.4 \pm 1.7$ kg·m$^{-2}$), and there were no significant differences in resting heart rate or blood pressure between the groups at baseline (see Table 3). All patients were taking the typical range of anti-failure medications (Table 2); these regimes had been stable for at least 2 weeks before beginning the study, and remained stable throughout the study. There were significantly more ($P = 0.03$) patients taking digoxin in the control group than in exercise group. All patients were previous or non-smokers.

**Table 1 Baseline characteristics of the study groups**

LVEF, left ventricular ejection function.

| Characteristic | Exercise group | Control group |
|---|---|---|
| NHYA class (II/III) | 7/4 | 7/3 |
| Gender (male/female) | 10/1 | 9/1 |
| Age (years) | $57 \pm 15$ | $53 \pm 11$ |
| LVEF (%) | $25 \pm 2$ | $24 \pm 3$ |
| Diagnosis (ischaemic/non-ischaemic) | 2/9 | 4/6 |

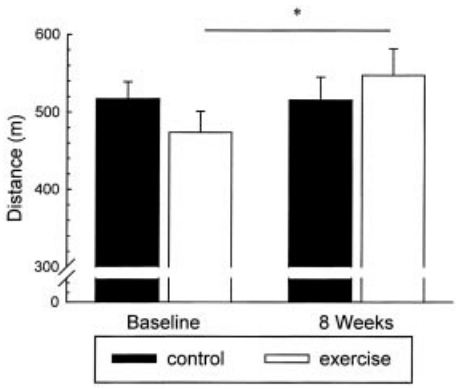


**Figure 1 Exercise capacity in the two groups of CHF patients, as assessed by distance walked during a 6-min walking test**

The control group is represented by closed bars, and the exercise group by open bars. Significance of differences: $^*P = 0.008$.

### Effects of exercise training in CHF

Following the 8-week exercise training programme, patients walked significantly further during the 6-min walking test (before, $474 \pm 27$ m; after, $547 \pm 34$ m; $P = 0.008$), while the control group showed no change in exercise capacity (before, $517 \pm 21$ m; after, $515 \pm 29$ m) (Figure 1). Moreover, there was a decrease in heart rate following participation in the exercise programme (from $66 \pm 3$ to $62 \pm 2$ beats/min; $P = 0.037$), whereas there was no significant change in 'usual living' group (from $76 \pm 5$ to $70 \pm 2$ beats/min). There was no significant difference

**Table 2 Drug regimes of the subjects**

ACEi, angiotensin-converting enzyme inhibitors. Significance of difference: $^*P = 0.03$ compared with exercise group.

| | Subjects taking drug (%) | | | | | |
|---|---|---|---|---|---|---|
| Subjects | ACEi | Diuretics | Aspirin | Digoxin | $\beta$-Blockers | Warfarin |
| Total | 100 | 100 | 57 | 67 | 76 | 52 |
| Exercise group | 100 | 100 | 45 | 45 | 72 | 36 |
| Control group | 100 | 100 | 70 | 90* | 80 | 70 |

**Table 3 Cardiovascular parameters**

PP, pulse pressure; SBP, systolic blood pressure; DBP, diastolic blood pressure; MAP, mean arterial pressure; AI, augmentation index; LVIDd, end-diastolic left ventricular internal diameter; LVIDs, end-systolic left ventricular internal diameter; IVST, interventricular septum thickness; PWT, posterior wall thickness; FS, fractional shortening; EWV, E-wave velocity; AWV, A-wave velocity.

| | Exercise group | | Control group | |
|---|---|---|---|---|
| Parameter | Baseline | 8 weeks | Baseline | 8 weeks |
| Heart rate (beats/min) | 66 ± 3 | 62 ± 2 | 75 ± 7 | 76 ± 6 |
| Central PP (mmHg) | 46 ± 6 | 48 ± 5 | 42 ± 5 | 38 ± 4 |
| SBP (mmHg) | 106 ± 7 | 108 ± 8 | 110 ± 6 | 104 ± 5 |
| DBP (mmHg) | 62 ± 2 | 60 ± 3 | 67 ± 2 | 66 ± 2 |
| MAP (mmHg) | 79 ± 5 | 79 ± 6 | 83 ± 3 | 81 ± 4 |
| AI (%) | 5.73 ± 3.33 | 7.27 ± 2.63 | 2.10 ± 2.63 | 3.20 ± 1.47 |
| LVIDd (cm) | 6.79 ± 0.36 | 6.89 ± 0.24 | 6.93 ± 0.41 | 6.92 ± 0.35 |
| LVIDs (cm) | 5.66 ± 0.42 | 5.67 ± 0.3 | 5.83 ± 0.36 | 5.89 ± 0.37 |
| IVST (cm) | 1.04 ± 0.09 | 1.07 ± 0.12 | 0.91 ± 0.07 | 0.92 ± 0.11 |
| PWT (cm) | 1.00 ± 0.05 | 0.98 ± 0.07 | 0.96 ± 0.06 | 1.10 ± 0.16 |
| FS (%) | 17.61 ± 2.22 | 18.10 ± 2.07 | 15.74 ± 1.35 | 15.14 ± 2.31 |
| EWV ($cm \cdot s^{-1}$) | 81.7 ± 8.7 | 83.5 ± 5.6 | 77.5 ± 7.7 | 74.8 ± 9.8 |
| Deceleration time (ms) | 219.4 ± 21.8 | 225.8 ± 18.6 | 189.4 ± 21.7 | 185.7 ± 17.5 |
| AWV ($cm \cdot s^{-1}$) | 52.8 ± 7.6 | 56.3 ± 7.4 | 58.1 ± 10.9 | 53.2 ± 10.8 |
| E/A | 1.96 ± 0.38 | 1.77 ± 0.36 | 1.74 ± 0.42 | 1.62 ± 0.38 |

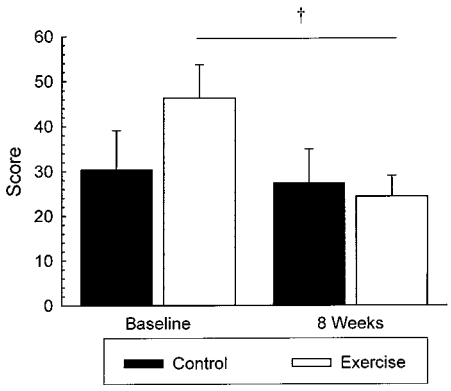


**Figure 2 Quality of life in the two groups of CHF patients**

Quality of life was assessed using the Minnesota Living with Heart Failure Evaluation, both at baseline and after the 8-week study period, in the control (closed bars) and exercise (open bars) groups. Significance of differences: †$P = 0.01$.

in resting heart rate between the two groups at baseline; however, after 8 weeks, the exercise group had a significantly lower heart rate when compared with the control group ($P = 0.03$). There were no changes in resting blood pressure in either the exercise or the control group following the 8-week study period (Table 3).

Quality of life did not differ between the two groups at baseline. However, following involvement in the exercise programme, the symptoms associated with heart failure, determined using the Minnesota Living with Heart Failure Evaluation, decreased from 46 ± 7 to 24 ± 5 units ($P = 0.01$) in the exercise training group (Figure 2).

## Arterial mechanics

There were no differences in arterial mechanics between the exercise and control groups at baseline (Figure 3). While the control group showed no change in SAC after 8 weeks of usual living [before, 0.59 ± 0.10 a.c.u. (95% confidence intervals 0.34–0.83 a.c.u.); after, 0.55 ± 0.08 a.c.u. (0.30–0.81 a.c.u.)], the exercise training group demonstrated a significant increase in SAC following the training programme [before, 0.57 ± 0.11 a.c.u. (0.34–0.80 a.c.u.); after, 0.77 ± 0.14 a.c.u. (0.53–1.02 a.c.u.); $P = 0.01$] (Figure 3, upper panel). However, neither central nor peripheral PWV had changed in either the exercise group or the control group after the 8-week study period (Figure 3, lower panel). These improvements in SAC are not explained by changes in mean arterial pressure, pulse pressure or wave reflection (augmentation index), the values of which remained similar throughout the study (Table 3).

## Cardiac function

At baseline, there was no difference in left ventricular ejection fraction between the control and exercise groups (Table 1). Furthermore, left ventricular dimensions and function were unchanged following the 8-week intervention period in both the control and exercise groups (Table 3).

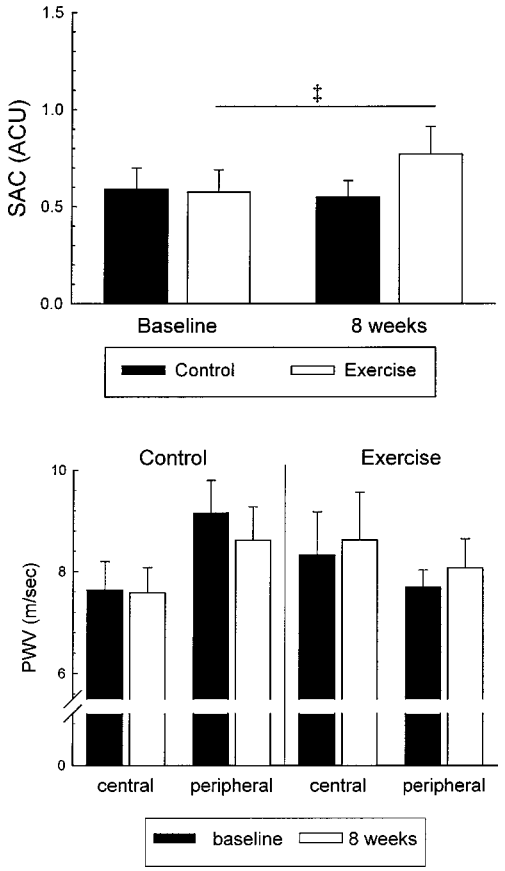


**Figure 3 Measures of arterial mechanics in the two groups of patients**

Upper panel: SAC at baseline and after the 8-week study period in the control (closed bars) and exercise (open bars) groups. Significance of differences: ‡$P = 0.01$. Lower panel: central and peripheral PWV in the control (left panels) and exercise (right panels) groups before (closed bars) and after (open bars) the 8-week study period.

## DISCUSSION

CHF is a common cardiovascular disorder characterized by poor cardiac performance, fluid retention and vasoconstriction. Vasodilator drug therapy alleviates heart failure symptoms by reducing peripheral vascular resistance and thereby afterload. Recently it has also become apparent that the mechanical properties of large arteries (arterial compliance) may also contribute significantly to afterload. It is recognized that the symptomatic improvements in CHF patients following an exercise programme are due, in part, to an attenuation of the peripheral vascular abnormalities, rather than to central haemodynamic changes [19]; however, the mechanisms responsible for the exercise-induced improvements in heart failure symptoms have not been entirely identified. Previous studies have shown that SAC increases following an exercise training programme in healthy subjects [7]; therefore the aims of the present study were to determine the effects of an exercise training programme on arterial compliance in CHF patients. The effects of this exercise programme on left ventricular structure and function and on the patients' quality of life were also investigated.

### Exercise capacity and quality of life

CHF patients were able to walk significantly further during the 6-min walking test following the 8-week training programme, whereas for the control group the distance walked remained unchanged. To our knowledge, the present study is the first report in which the effects of this type of training regime (a combination of light weights and aerobic exercise using both cycling and walking) has been examined in heart failure patients. It is well documented that aerobic training alone results in an improvement in exercise capacity in CHF patients [5,6,20,21], and a recent study demonstrated an improvement in muscular strength and peak oxygen consumption in CHF patients enrolled in an 8-week circuit weight training programme [22]; however, results from combined training programmes have not been documented. Not only did the training programme in the present study produce an improvement in the exercise capacity of CHF patients, an improvement was also evident in their quality of life, which supports previous studies on exercise training in CHF [6,20]. By improving fitness and strength with involvement in the present exercise programme, quality of life may have improved due to a combination of increases in patient confidence and in physical capacity.

### Arterial mechanics

In the present study we demonstrated that an exercise training programme caused an increase in SAC in patients with CHF, independent of any change in mean arterial blood pressure and central pulse pressure. Reduced arterial compliance has been shown to increase left ventricular end-systolic stress [12] and afterload [8], and to decrease coronary perfusion [23]. As a corollary, an improvement in SAC would reduce the afterload placed on the left ventricle, decreasing left ventricular end-systolic stress and increasing coronary perfusion. Kelly et al. [24] demonstrated that an acute decrease in arterial compliance was accompanied by a 32% increase in myocardial oxygen demand. Therefore the 35% increase in arterial compliance demonstrated in the present study may have resulted in a significant decrease in myocardial oxygen demand.

Although improvements were evident in SAC following exercise training, no improvements were evident in PWV or the augmentation index. Central PWV did show a slight, but non-significant, improvement following exercise training (from $8.32 \pm 0.86$ to $8.62 \pm 0.94$ m·s$^{-1}$), raising the possibility that a longer exercise programme or greater patient numbers may produce a

significant change. The augmentation index, derived from carotid tonometry, also demonstrated no change following exercise, indicating no change in pulse wave reflection. This supports the PWV data, further suggesting that a longer exercise programme will be necessary to establish an improvement. As SAC is determined using flow through the ascending aorta as a determinant of whole-body arterial compliance, it is perhaps concentrating on the changes in the ascending aorta, a section eliminated from the PWV calculations [10], and this may account for the discrepancy between the two results.

It is well understood that endothelium-dependent vasodilation is impaired in CHF [25–28]. Hambrecht and colleagues [28] showed that an improvement in endothelial function in heart failure patients may be associated with an increase in exercise capacity. Further, it has been suggested that regular physical exercise improves endothelial nitric oxide formation and consequent vasodilation of the skeletal muscle vasculature. In the context of the present study, it has been suggested that repetitive increases in flow caused by physical training result in an up-regulation of nitric oxide production, thereby reducing peripheral vascular tone [25]. As endothelial dysfunction has been proposed to reduce arterial distensibility [27], an improvement in the function of the endothelium following exercise training may have contributed to the increased arterial compliance demonstrated in the present study.

It is also well understood that sympathetic activity is increased in CHF [29,30]. Grassi et al. [31] suggested that the reduction in radial arterial compliance observed in their study could have been a consequence of sympathetic activation. There is mounting evidence that the beneficial effect of endurance exercise training in heart failure patients occurs via neurohumoral modulation, particularly through a reduction in sympathetic activity [32]. A study of an exercise training programme involving 20 min sessions on 5 days per week for 8 weeks showed a shift from sympathetic activity towards enhanced vagal activity after training [6]. As exercise capacity increased in the present study, sympathetic activation may have decreased, lowering vasoconstrictor concentrations, thus allowing greater relaxation of the vessels and consequently increasing arterial compliance.

As an alternative to functional changes as an explanation for the effects of exercise training on arterial compliance, intrinsic alterations in the vessel wall have also been proposed. Kingwell et al. [9] demonstrated that an elevation in arterial compliance following spontaneous running in Wistar–Kyoto rats may have a structural basis, whereby the loading of collagen and elastin may be altered, and not be the result of reduced blood pressure or vasodilation. Other possible causes of the improvement in arterial compliance could be decreased wall thickness or intrinsic changes in wall composition and/or smooth muscle activation.

### Cardiac structure and function

No changes were demonstrated in left ventricular structure in the present study. Previous work has largely shown that training has no direct influence, either beneficial or detrimental, on the myocardium in CHF [33]. However, in healthy subjects, increases in left ventricular diameters are apparent after 4 weeks of exercise training [34]. It is thought that the reduced stress and afterload induced following an exercise programme may induce structural changes, but a longer follow-up period may be required to illustrate these changes in CHF patients. Although the E/A ratio (E-wave velocity/A-wave velocity) has been demonstrated to improve following an exercise programme in healthy subjects [34], the present study showed no variation in either E/A ratio or deceleration time, demonstrating no change in diastolic dysfunction. The lack of a change in ventricular function parameters suggests that training has no direct effect upon the heart, and that the observed beneficial effect may occur in the peripheral vascular system. It has been suggested that the exercise-induced increase in sympathetic activation could contribute to an acute decrease in diastolic function in CHF patients, which may persist for at least 24 h following an exercise bout [35]. This information raises the question of exercise frequency in CHF patients, as adequate periods between exercise episodes may be essential to reduce the risk of the progression of heart failure during long-term training.

### Conclusion

This study demonstrates for the first time that a tailored exercise programme increases SAC in CHF patients. A restoration of endothelial function through an exercise training programme may play a major role in the improvement in SAC. While there were no changes in either the structure or the function of the left ventricle following the exercise training programme, indices of improvement in the patients' quality of life was evident. The maintenance and improvement of arterial compliance, as occurred in the present study in response to an exercise training programme, may be of great benefit to CHF patients, by reducing left ventricular afterload and improving coronary perfusion.

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## REFERENCES


1 Laogun, A. and Gosling, R. (1982) *In vivo* arterial compliance in man. Clin. Phys. Physiol. Meas. **3**, 201–212
2 Stella, M. L., Failla, M., Mangoni, A. A., Carugo, S., Giannattasio, C. and Mancia, G. (1998) Effects of isolated systolic hypertension and essential hypertension on large and middle-sized artery compliance. Blood Pressure **7**, 96–102
3 Lage, S., Kopel, L., Monachini, M. et al. (1994) Carotid arterial compliance in patients with congestive heart failure secondary to idiopathic dilated cardiomyopathy. Am. J. Cardiol. **74**, 691–695
4 Giannattasio, C., Failla, M., Stella, M. et al. (1995) Alterations of radial artery compliance in patients with congestive heart failure. Am. J. Cardiol. **76**, 381–385
5 Jette, M., Heller, R., Landry, F. and Blumchen, G. (1991) Randomized 4-week exercise program in patients with impaired left ventricular function. Circulation **84**, 1561–1567
6 Coats, A., Adamopoulos, S., Radaelli, A. et al. (1992) Controlled trial of physical training in chronic heart failure. Circulation **85**, 2119–2131
7 Cameron, J. and Dart, A. (1994) Exercise training increases total systemic arterial compliance in humans. Am. J. Physiol. **266**, H693–H701
8 Belz, G. (1995) Elastic properties and Windkessel function of the human aorta. Cardiovasc. Drugs Ther. **9**, 73–83
9 Kingwell, B. A., Arnold, P. J., Jennings, G. L. and Dart, A. M. (1997) Spontaneous running increases aortic compliance in Wistar-Kyoto rats. Cardiovasc. Res. **35**, 132–137
10 Vaitkevicius, P., Fleg, J., Engel, J. et al. (1993) Effects of age and aerobic capacity on arterial stiffness in healthy adults. Circulation **88**, 1456–1462
11 Tanaka, H., Dinenno, F. A., Monahan, K. D., Clevenger, C. M., DeSouza, C. A. and Seals, D. R. (2000) Aging, habitual exercise, and dynamic arterial compliance. Circulation **102**, 1270–1275
12 Arnold, M., Marchiori, G., Imrie, J., Burton, G., Pflugfelder, P. and Kostuk, W. (1991) Large artery function in patients with chronic heart failure. Circulation **84**, 2418–2425
13 Finkelstein, S., Cohn, J., Collins, R., Carlyle, P. and Shelley, W. (1985) Vascular hemodynamic impedance in congestive heart failure. Am. J. Cardiol. **55**, 423–427
14 Liu, Z., Brin, K. and Yin, F. (1986) Estimation of total arterial compliance: an improved method and evaluation of current methods. Am. J. Physiol. **251**, H588–H600
15 Kingwell, B., Berry, K., Cameron, J., Jennings, G. and Dart, A. (1997) Arterial compliance increases after moderate-intensity cycling. Am. J. Physiol. **273**, H2186–H2191
16 Murgo, J., Westerhof, N., Giolma, J. and Altobelli, S. (1980) Aortic input impedance in normal man: Relationship to pressure wave forms. Circulation **62**, 105–116
17 Rector, T. and Cohn, J. (1992) Assessment of patient outcome with the Minnesota Living with Heart Failure questionnaire: Reliability and validity during a randomized, double-blind, placebo-controlled trial of pimobendan. Am. Heart J. **124**, 1017–1025
18 Lipkin, O., Scriven, A., Crake, T. and Poole-Wilson, P. (1986) Six min walking test for assessing exercise capacity in chronic heart failure. Br. Med. J. **292**, 653–655
19 McKelvie, R. S., Teo, K. K., McCartney, N., Humen, D., Montague, T. and Yusuf, S. (1995) Effects of exercise training in patients with congestive heart failure: a critical review. J. Am. Coll. Cardiol. **25**, 789–796
20 Coats, A., Adamopolous, S., Meyer, T., Conway, J. and Sleight, P. (1990) Effects of physical training in chronic heart failure. Lancet **335**, 63–66
21 Adamopoulos, S., Coats, A., Brunotte, F. et al. (1993) Physical training improves skeletal muscle metabolism in patients with chronic heart failure. J. Am. Coll. Cardiol. **21**, 1101–1106
22 Maiorana, A., O'Driscoll, G., Cheetham, C. et al. (2000) Combined aerobic and resistance exercise training improves functional capacity and strength in CHF. J. Appl. Physiol. **88**, 1565–1570
23 Nichols, W. and O'Rourke, M. (1990) McDonald's Blood Flow in Arteries – Theoretical, Experimental and Clinical Principles, Edward Arnold, London
24 Kelly, R., Tunin, R. and Kass, D. (1992) Effect of reduced aortic compliance on cardiac efficiency and contractile function of in situ canine left ventricle. Circ. Res. **71**, 490–502
25 Hornig, B., Maier, V. and Drexler, H. (1996) Physical training improves endothelial function in patients with chronic heart failure. Circulation **93**, 210–214
26 Kaye, D., Jennings, G. and Angus, J. (1994) Evidence for impaired endothelium dependent vasodilation in experimental left ventricular dysfunction. Clin. Exp. Pharmacol. Physiol. **21**, 709–719
27 Ramsey, M., Goodfellow, J., Jones, C., Luddington, L., Lewis, M. and Henderson, A. (1995) Endothelial control of arterial distensibility is impaired in chronic heart failure. Circulation **92**, 3212–3219
28 Hambrecht, R., Fiehn, E., Weigl, C. et al. (1998) Regular physical exercise corrects endothelial dysfunction and improves exercise capacity in patients with chronic heart failure. Circulation **98**, 2709–2715
29 Kaye, D., Lambert, G., Lefkovits, J., Jennings, G., Morris, M. and Esler, M. (1994) Neurochemical evidence of cardiac sympathetic activation and increased central nervous system catecholamine turnover in severe congestive heart failure. J. Am. Coll. Cardiol. **23**, 570–578
30 Hasking, G., Esler, M., Jennings, G., Burton, D. and Korner, P. (1986) Norepinephrine spillover to plasma in patients with congestive heart failure: evidence of increased overall and cardiorenal sympathetic nervous activity. Circulation **73**, 615–621
31 Grassi, G., Giannattasio, C., Failla, M. et al. (1995) Sympathetic modulation of radial artery compliance in congestive heart failure. Hypertension **26**, 348–354
32 Middlekauff, H. and Mark, A. (1998) The treatment of heart failure: the role of neurohumoral activation. Intern. Med. **37**, 112–122
33 Letac, B., Cribier, A. and Desplanches, J. (1977) A study of left ventricular function in coronary patients before and after physical training. Circulation **56**, 375–378
34 Dart, A. M., Meredith, I. T. and Jennings, G. L. (1992) Effects of 4 weeks endurance training on cardiac left ventricular structure and function. Clin. Exp. Pharmacol. Physiol. **19**, 777–783
35 Morikawa, M., Sato, H., Koretsune, Y. et al. (1998) Sustained left ventricular diastolic dysfunction after exercise in patients with dilated cardiomyopathy. Heart **80**, 263–269


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