

# Exercise After Myocardial Infarction: a Controlled Trial

P. CARSON, BM, FRCP, FACC, *Consultant Cardiologist and Senior Research Fellow*, ROSALIND PHILLIPS, MB, M. LLOYD, MB, HELEN TUCKER, MB and M. NEOPHYTOU, DM, *Research Fellows*, N. J. BUCH, MD, MRCP(UK) and A. GELSON, MB, MRCP(UK), *Hon. Senior Registrars and Research Fellows*, A. LAWTON, BA, FRSS, *Statistician and Systems Analyst, Cardiology and Computer Departments, North Staffordshire Hospital Centre, Stoke-on-Trent*, and Department of Postgraduate Medicine, Keele University, Staffordshire, and T. SIMPSON, DIC, Dip Ed, *Lecturer in Physical Education, Cauldon College of Further Education, Stoke-on-Trent*

In the last twenty years it has become evident that strenuous exercise can be safely undertaken by many patients following recovery from acute myocardial infarction (MI). Hellerstein *et al.*[1] published in 1963 an account of an exercise training programme for patients with coronary disease, stressing the value for morale of this form of treatment. Since then there have been several trials reviewed by Haskell[2] and by Greenberg[3]. Problems have included small numbers, poor matching between exercise and control groups and high drop-out rates. Sanne[4] and Wilhelmsen *et al.*[5] reported a trial with a well-matched control group but did not establish a significant decrease in mortality. Kellerman[6] and a Finnish trial still in progress[7] have suggested a beneficial effect on mortality, but to date this is not proven. Two large current multi-centre trials in North America have not so far shown any significant reduction in mortality[8,9]. In 1973 we reported the feasibility of an exercise rehabilitation programme[10]. We now report a controlled trial on the effects of exercise in men following MI.

## Patients and Methods

During a 3½ year period, 1,311 men with MI were admitted to our coronary care unit. The diagnosis was based on ECG changes and/or elevation of serum glutamic oxaloacetic transaminase (SGOT) or lactic dehydrogenase (LDH) taken on three consecutive days. Twelve and a half per cent of the patients died in hospital, a further 4.2 per cent died between discharge and the first coronary follow-up clinic six weeks after admission, and 4.8 per cent failed to attend this clinic for other reasons. The remaining 1,029 (78 per cent of admissions) attended.

Patients were excluded from the study for the reasons

**Table 1.** Reasons for exclusion from the study.

---

Age over 70 years
Heart failure at follow-up clinic
Cardio-thoracic ratio exceeding 59%
Severe chronic obstructive lung disease
Hypertension requiring treatment
Diabetes requiring insulin
Disabling angina during convalescence
Orthopaedic or medical disorders likely to impede progress in the gym
Personality disorders likely to render patient unsuitable for the course

---

shown in Table 1 and 442 patients (34 per cent of admissions and 43 per cent of clinic attenders) were assessed as suitable. The course was described and then offered to these patients; 139 declined for apparently practical reasons. The 303 patients who accepted were then randomly allocated to an exercise group (151) and a control group (152).

There was no difference between these two groups, within 95 per cent confidence limits, in the site of MI (shown in Table 2), the number of non-transmural and transmural MIs, the means of the highest enzyme levels, smoking habits, known diabetes before MI, previous history of angina or MI, hypercholesterolaemia, family history of coronary heart disease, left ventricular failure during admission, or type of occupation at the time of MI. The mean age of the exercise group was 50.3 years ( $\pm 0.65$ , the standard error of the mean (SEM)) and of the control group 52.8 years ( $\pm 0.67$  SEM); these values lie outside the 95 per cent confidence limits for the population mean (50.7–52.5 years).

**Table 2.** Site of infarction. Definition of site of MI: anterior—changes in leads V1-V4; lateral— changes in leads V4-V6; inferior—changes in leads II, III and AVF; posterior—increase in height of R or T waves in V1-V2.

	Exercise 151	Control 152	Total 303
Anterior	19	13	32
Lateral	13	14	27
Antero-lateral	44	43	87
<b>Total</b>	<b>76</b>	<b>70</b>	<b>146</b>
Inferior	44	43	87
Infero-posterior	11	12	23
Infero-lateral	9	15	24
<b>Total</b>	<b>64</b>	<b>70</b>	<b>134</b>
Infero-antero-lateral	2	4	6
Posterior	5	4	9
Unknown	4	4	8

The patients were assessed at their first clinic visit by history, examination, chest radiograph and 12 lead ECG. They were similarly assessed at subsequent visits 5 months after MI and at one, two and three years after MI. The mean time of clinical follow-up with exercise testing in both groups was 1.6 years ( $\pm 0.24$  SEM). The mean follow-up time for survival and mortality at the end of the study was 2.1 years ( $\pm 0.18$  SEM).

Exercise testing was performed on a cycle ergometer after each clinic visit. The work-load was started at 50 watts and was increased every 4 minutes by 25 watts. A two-channel ECG was obtained from V1 and V6 positions, with the negative electrode on the right shoulder. The systolic blood pressure was obtained from the right arm by palpation. The test was terminated when the heart rate reached 85 per cent of the age-predicted maximum (maximum heart rate =  $210 - \text{age} \times 0.65$ [11,12]) or if angina, uncomfortable breathlessness, fatigue, or failure of the systolic blood pressure to rise with increase in work-load occurred. Fitness was expressed as the total cycling time.

Following the first exercise test, the exercise group attended the hospital gym twice weekly for 12 weeks. They were supervised by a doctor and a physical educationalist and full resuscitative equipment was available in an adjacent room. The exercises were arranged on a circuit basis and pure isometric exercise was avoided. (Details of the course are available from the authors on request.) On completion of the course patients were advised to maintain their fitness by continuing with similar types of exercises or with other methods of their choice but we did not attempt to assess what further exercise was taken.

*Drop-outs.* Twenty (13 per cent) in the exercise group failed to attend the gym after selection and testing. A further 25 (17 per cent) dropped out after starting the

course, 14 for non-medical reasons and 11 for medical reasons (two had further MI at home, two developed heart failure, two developed supraventricular tachycardia in the gym, one developed Dressler's syndrome, one developed glaucoma, one had backache, one developed thyrotoxicosis and one injured his hand at home). Two patients died during the course. The remaining 104 (69 per cent of those selected and 79 per cent of those who started in the gym) completed the course.

In the control group 9 (6 per cent) failed to attend for first and/or second testing. Another five patients were excluded from second testing for medical reasons (two developed heart failure, one developed Dressler's syndrome, one developed myxoedema and one developed paroxysmal ventricular tachycardia). Three patients died between the first and second test. In the control group 135 patients were tested twice.

*Symptoms during testing and the exercise course.* During testing there were no complications or arrhythmias requiring treatment.

No deaths or cardiac arrests occurred in the gym.

In the gym 73 patients (70 per cent of those who completed the course) reported no symptoms and required no treatment. Nineteen patients reported angina on one or more occasions. Other reported symptoms included occasional dyspnoea and fatigue.

*Patients receiving beta-blockers.* Of those who completed the exercise course eight were on beta-blockers at first testing and 16 at second testing. Seven of these were on beta-blockers at both tests and throughout the course. In the control group 20 were on beta-blockers at first testing and 25 at second testing. Eighteen of these were on beta-blockers at both tests. The difference in numbers of exercise and control patients on beta-blockers is not significant.

#### Statistical Methods

Chi-square, Fisher's exact probability and Student *t*-test were used to test for significance. Cumulative survival curves and cusum (cumulative sum) charts[13] were used to analyse mortality and comparisons between the groups were made with Peto's[14] logrank test.

The values given in the text are followed by the ( $\pm$ ) standard error of the mean.

#### Results

*Mortality.* Total mortality is shown in Table 3(a) and the mortality after completing the course, i.e. excluding the drop-outs and deaths from both exercise and control groups during the exercise period, is shown in Table 3(b). There does appear to be a reduction in mortality in the exercised patients with inferior MI, which is not explained by drop-outs from the exercise course who died later.

The mean age of death in the exercise group was 49.8 years ( $\pm 2.1$  SEM) and in the control group 57.2 ( $\pm 1.6$  SEM). This difference is significant ( $P < 0.05$ ). It can be

**Table 3(a).** Total mortality in exercise and control groups.

	Exercise Group		Control Group		P
	Total	Deaths	Total	Deaths	
Ant/Lat	76	10 (13%)	70	8 (11%)	NS
Inferior	64	1 (2%)	70	10 (14%)	<0.01
Others	11	1 (9%)	12	3 (25%)	NS
Total	151	12 (8%)	152	21 (14%)	NS

**Table 3(b).** Mortality of those who completed the exercise programme period.

	Exercise Group		Control Group		P
	Total	Deaths	Total	Deaths	
Ant/Lat	50	7 (14%)	59	4 (7%)	NS
Inferior	49	0	65	8 (12%)	<0.05
Others	5	0	11	3 (27%)	NS
Total	104	7 (8%)	135	15 (11%)	NS

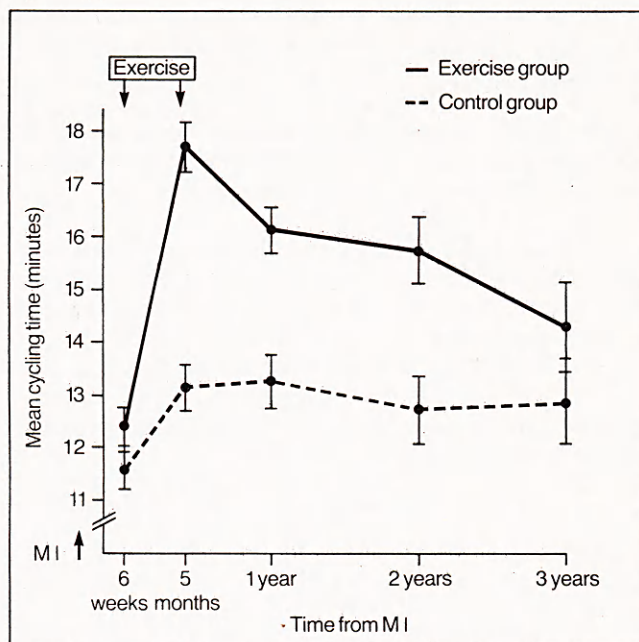
partially explained by the difference in the mean ages of the total groups. In those who died, and in the sub-groups with inferior MI, there was no difference between exercise and control groups in the incidence of previous MI, smoking habits before MI, previous hypertension, incidence of diabetes, angina before MI, whether the MI was transmural or non-transmural, mean highest levels of SGOT or LDH, or in physical fitness at first testing.

**Further Myocardial Infarction with Survival.** During the time of the exercise course, three patients in the exercise group and four control patients survived further MI. After completion of the course by the exercise group eight exercise patients and six control patients survived further MI. Neither these differences nor the site of the first MI was significant.

**Physical Fitness.** The results of the exercise testing in the two groups are shown in Fig. 1 and the statistical analysis of this data is given in Tables 4 and 5. There were no significant differences in the pattern of changes in physical fitness between those patients in either group with inferior or anterior MI.

The results shown in Fig. 1 and Tables 4 and 5 include patients who were on beta-blockers. When these patients were excluded there were no differences in the results.

**Angina of Effort.** After the course, angina of effort was reported in 23 per cent of the exercise group and 38 per cent of the control group. This difference is significant ( $P < 0.05$ ) and is due to less angina in those with inferior MI. After the course, nine of the exercise patients with inferior MI were having angina of effort compared with 25 of the control patients. This difference is significant ( $P < 0.05$ ). Of those with angina after the course, there was no significant difference between the exercise and control groups in history of previous MI or hypertension, angina before MI or in smoking habits. None of the patients who dropped out before or during the exercise programme admitted to angina as the reason for doing so.



**Fig. 1.** Fitness as assessed by mean cycling time. Vertical bars represent standard error of mean.

**Table 4.** Statistical analysis of exercise testing in those who completed the exercise course. Exercise versus control group at follow-up tests. (Unpaired *t*-tests).

At	<i>t</i> value	d.f.	Probability
1st Follow-up	1.25	237	>0.1 NS
2nd Follow-up	7.38	237	<0.001
3rd Follow-up	4.18	174	<0.001
4th Follow-up	3.58	104	<0.001
5th Follow-up	1.15	44	>0.1 NS

**Table 5.** Comparison of changes within the groups between the first and second follow-up (paired *t*-tests).

Group	<i>t</i> value	d.f.	Probability
Exercise	13.71	102	<0.001
Control	4.77	133	<0.001

**Return to Work.** Eighty-one per cent of both exercise and control groups who were working before MI returned to work after MI. There was no significant difference between the two groups in the mean time of return to work following MI (exercise 13 weeks, control 12 weeks).

**Heart Size.** Heart size assessed by cardiothoracic ratio was the same in the exercise and control groups before and after the course, with a mean value of 45 per cent. Heart size in those who died or who survived further MI in both groups was not significantly different from the total.

**Smoking Habits.** Seventy-five per cent of all patients were smokers at the time of MI. When in hospital all patients were advised to stop smoking and this advice was repeated at follow-up visits. At the first follow-up clinic 26 per cent in both groups were smoking and on completion of

the course 30 per cent of the exercise patients and 25 per cent of the control patients were smoking. This difference is not significant.

**Weight.** There was no difference in the mean weight of either group at first or second follow-up. There was no significant change in weight in either group.

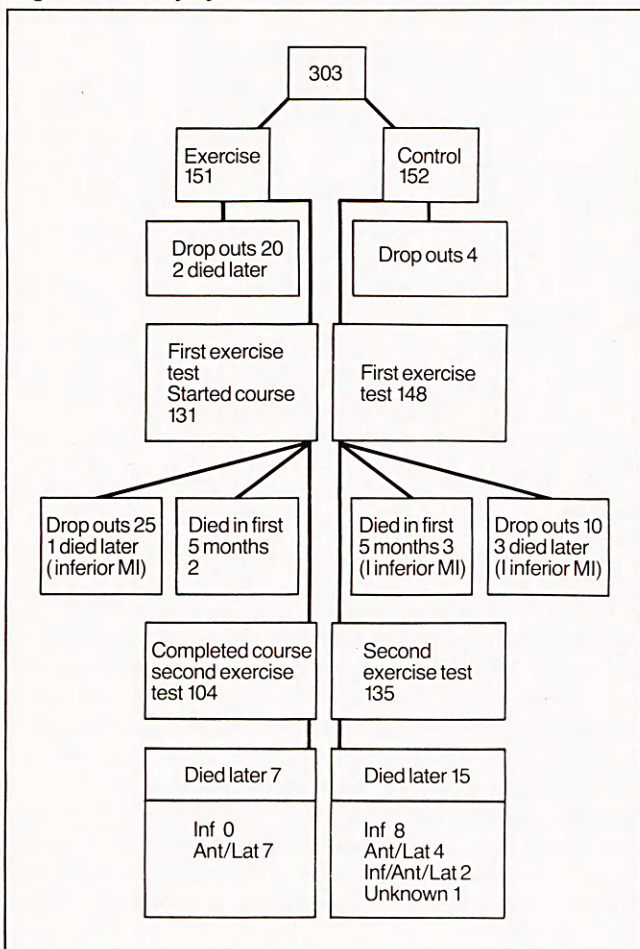
**Fasting Blood Lipids.** There was a significant reduction in fasting triglycerides in the exercise group after completion of the course (Table 6). There was no significant change in serum cholesterol.

A summary of the trial is shown in Fig. 2.

**Table 6.** Fasting blood triglycerides. (Mean values in mmol/litre and in mg/100 ml in brackets.)

	Exercise Group	Control Group
First Follow-up	2.07 (182) ± 0.16	1.96 (172) ± 0.13
Second Follow-up	1.64 (144) ± 0.11	1.77 (156) ± 0.14
	<i>P</i> < 0.05	NS

**Fig. 2.** Summary of trial.



## Discussion

This work confirms that supervised exercise training after MI is safe. No disasters occurred during the exercise

testing or subsequent exercise training in the gymnasium. The difference in fitness between the exercise and control patients after completion of the course was highly significant ( $P < 0.001$ ) and so was the increase in fitness in the exercise group ( $P < 0.001$ ).

Kallio[7] has indicated that the time of return to work after MI may not be affected by exercise rehabilitation. This was so in our study. The exercise patients returned to work no earlier than the control group. This disappointing result was probably due to a combination of factors, including the patients' reluctance to return to work before completing the course.

Both exercise and control groups showed a similar reduction in smoking after MI. Fasting blood triglycerides were reduced in the exercise group slightly but significantly. There was no change in serum cholesterol. These results are similar to those in other studies[15].

Sanne[4] emphasised the high drop-out rate that occurred during exercise rehabilitation and that the longer the course the higher this became. In our study 13 per cent failed to attend the gymnasium after they had been selected and exercise tested, and a further 17 per cent dropped out after starting the course.

Two current trials[8,9] have used methods of selection different from ours and their results are not, therefore, comparable with ours. Their results to date have not shown any significant reduction in mortality in the exercise group.

As in other studies, our work has shown no significant decrease in mortality for the exercise group. However, it does raise the possibility that exercise training reduces the mortality of those with inferior infarction. None of the exercise patients with inferior MI who completed the course died, compared with eight of the control group ( $P < 0.05$ ). This difference is not explained by patients with inferior MI dropping out from the course and subsequently dying. In spite of the random allocation of patients it is possible that the control group with inferior MI had more severe coronary disease than the exercise group who completed the course. The slight but significant difference in age in the control group would be compatible with this and the increased incidence of angina and the higher mortality might be due to the presence of more severe coronary disease. Nevertheless, the alternative possibility is that the exercise course was responsible for the apparent improvement in mortality and the lower incidence of angina. These results for inferior infarction patients are, however, open to question, as the site of MI was not one of the criteria for randomisation. Since the majority of inferior MI is due to right coronary disease it is possible that exercise induces a greater increase in collateral circulation in such patients. Thallium flow studies[16] suggest that this may be so. We are unaware of other exercise rehabilitation studies correlating the site of MI with mortality and further investigation of this interesting aspect would require a large randomised trial of patients with inferior MI.

One-third of all our male admissions with MI to the coronary care unit were considered suitable for an exercise course six weeks after MI. Since our contraindications to exercise were probably more rigid than was

necessary for safety, it is apparent that many patients are suitable for an exercise course. Heart failure and angina with slight exertion were the commonest contraindications. Improvement in morale was obvious and increase in fitness was impressive. For these reasons a course such as ours seems desirable for patients after MI and we continue to run our course as a service commitment.

### Summary

Six weeks after acute myocardial infarction, 303 men were randomly divided into exercise and control groups. The exercise group attended the hospital gymnasium twice weekly for a three-month supervised exercise course. Both groups were exercise tested before and after the course and at subsequent follow-up.

The exercise group increased their physical fitness greatly compared with the control group.

Eight per cent of the exercise group died during the period of follow-up, compared with 14 per cent of the control group; this difference is not significant. There was an apparent improvement in mortality in those with inferior MI who completed the exercise course, which was not seen in those with MI in other sites.

For many patients after MI progressive exercise is safe, improves physical fitness and may reduce mortality for those after inferior MI.

### Acknowledgements

We wish to thank the DHSS for a grant which made this work possible. We are indebted to Dr Malcolm Clarke who permitted us to include his patients. We thank the many residents who helped in the documentation of in-patient data, Miss Kath Heraty and the technicians of the cardiac department who performed the exercise tests, and Miss Lesley Knock for secretarial assistance.

### References

1. Hellerstein, H. K., Hirsch, E. Z., Cumler, W., Polster, S. and Zucker, N. (1963) In *Coronary Heart Disease*, p. 448. (ed W. Likoff and J. H. Moyer.) New York: Grune and Stratton.
2. Haskell, W. L. (1977) In *Exercise in Cardiovascular Health and Disease*, p. 344. (ed E. A. Amsterdam, J. H. Wilmore and A. N. DeMaria.) New York: Yorke Medical Books.
3. Greenberg, M. A., Arbeit, S. and Rubin, I. L. (1979) *American Heart Journal*, **97**, 527.
4. Sanne, H. (1973) *Acta Medica Scandinavica*, Suppl. 551.
5. Wilhelmsen, L., Sanne, H., Elmfeldt, D., Grimby, G., Tibblin, G. and Wedel, H. (1975) *Preventive Medicine*, **4**, 491.
6. Kellerman, J. J. (1973) *Schweizerische Medizinische Wochenschrift*, **103**, 79.
7. Kallio, V. (1978) *Advances in Cardiology*, **24**, 153.
8. Shaw, L. W. (1981) *American Journal of Cardiology*, **48**, 39.
9. Rechnitzer, P. A. (1979) *Medicine and Science in Sports*, **11**, 382.
10. Carson, P., Neophytou, M., Tucker, H. and Simpson, T. (1973) *British Medical Journal*, **4**, 213.
11. Åstrand, I. (1960) *Acta Medica Scandinavica*, Suppl. 169.
12. Spiro, S. G., Juniper, E., Bowman, P. and Edwards, R. H. T. (1974) *Clinical Science and Molecular Medicine*, **46**, 191.
13. Davies, O. L. and Goldsmith, P. L. (eds) (1976) *Statistical Methods in Research and Production* (4th edn.) Edinburgh: Oliver and Boyd.

14. Peto, R., Pike, M. C., Armitage, P., Breslow, N. E., Cox, D. R., Howard, S. V., Mantel, N., McPherson, K., Peto, J. and Smith, P. G. (1976) *British Journal of Cancer*, Part I, **34**, 585, Part II, **35**, 1.
15. Fletcher, G. F. and Cantwell, J. D. (1974) In *Exercise and Coronary Heart Disease*, p. 33. Illinois: Charles C. Thomas.
16. Wainwright, R. J., Maisey, M. N., Edwards, A. C. and Sowton, E. (1980) *British Heart Journal*, **43**, 47.

## Prints of The Royal College of Physicians

High quality, hand coloured facsimilies of the 19th Century engraving after Thos. H. Shepherd originally published in 1828.

These prints show an interesting view of the elegant building in Pall Mall occupied by the College from 1822 to 1964.

Each print is presented in a colour card mount. Overall size: 8½" × 10½".

Price: £8.00 + £1.50 to include VAT, postage, and packing.

Money back guarantee if not completely satisfied

Please send request and cheque made payable to FOULSHAM HOUSE PRINTS to:

H. G. Chapman, 86 Upper St. Giles Street, Norwich, Norfolk NR2 1LT.

Also available on request; free Catalogue of Hospital prints.