Improved Exercise Capacity in Patients after Minor Ischemic Stroke Undergoing a Supervised Exercise Training Program

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Key words: stroke, exercise training, treadmill, exercise capacity

Abstract

Background: Regular physical activity is known to have a beneficial impact on multiple cardiovascular risk factors, but there is no routine provision of exercise training programs for patients after ischemic stroke.

Objectives: To assess the tolerability, safety and effect of an outpatient supervised exercise training program in patients after a non-disabling ischemic stroke.

Methods: Patients discharged home following a minor ischemic stroke (modified Rankin scale; mRS ≤ 2) were referred to a 3 month outpatient supervised exercise training program, performed twice weekly as prescribed by a physiologist and supervised by physical therapy. Exercise capacity was evaluated by the 6 minute walk test and the modified Bruce exercise test.

Results: Of the 52 patients who met the selection criteria, 43 underwent supervised exercise training within 2 months of stroke onset and 9 did not (control group). The baseline characteristics were comparable between the two groups. Following the exercise training program, an improvement in exercise capacity was observed manifested by improvement in the 6 minute walk test (444 ± 90 to 557 ± 99 meters in the exercise group vs. 438 ± 101 to 418 ± 126 in the control group; $P = 0.002$ for the score changes) and in the exercise duration achieved in the modified Bruce test and the metabolic equivalents achieved [9.6 ± 3.7 to 12.4 ± 3.2 minutes and 6.2 ± 2.8 to 8.5 ± 3.4 respectively in the exercise group (n=41) vs. 9.2 ± 3.5 to 8.0 ± 3.4 min and 5.8 ± 1.8 to 5.8 ± 2.8 in the control group (n=7); $P = 0.0009$ and 0.01 for score changes, respectively].

Conclusions: An outpatient supervised exercise training program after a minor ischemic stroke is feasible, well tolerated and is associated with improvement in exercise capacity. We strongly recommend that an aerobic exercise program be offered to suitable patients after an ischemic stroke.

IMAJ 2008;10:113–116

Stroke is the leading cause of major neurological disability in the adult population and the third leading cause of mortality in Israel [1,2]. According to a national survey the annual incidence of acute cerebrovascular events in Israel is about 15,000 [3]. Stroke survivors are often deconditioned and predisposed to a sedentary lifestyle [4]. Several studies demonstrate functional aerobic impairment across all phases of stroke recovery. Furthermore, exercise training and physical activity among stroke survivors have a beneficial impact on multiple cardiovascular disease risk factors, suggesting that such benefits are likely to translate into reducing the high risk for recurrent cardiovascular events [5-9]. Indeed, physical activity has been shown in multiple observational studies to reduce the risk of stroke [10] and is recommended for secondary prevention by authoritative guidelines [6,11].

At present, conventional rehabilitation treatment after stroke focuses on the sub-acute phase and its main purpose is to improve functional activity and basic mobility [12]. In Israel, almost 60% of stroke patients surviving the acute phase are discharged home [13], and those with no or mild disability may not receive any conventional rehabilitation or any structured exercise training program. The aims of the present study were to assess the safety and tolerability of a supervised exercise training program among ambulatory patients after a minor stroke with or without preexisting cardiovascular disease, and to test for any associated improvement in exercise capacity.

Patients and Methods

Eligible patients were identified and recruited to the study either at the time of discharge from hospital or on follow-up evaluation at the stroke center. The level of functional disability was assessed by the modified Rankin Scale (0–5 scale, minimal to severe disability), a widely used scale with proven validity and reliability [14]. Functional status was further assessed by the Functional Independence Measure, assessing activities of daily life, mobility, communication and cognition [15], and by the Stroke Impact Scale [16], a subjective assessment of recovery following stroke. Patients were evaluated by both a neurologist and a rehabilitation cardiologist.

Inclusion criteria included a minor ischemic stroke (mRS ≤ 2) within 6 months after the stroke, and independence in the activities of daily living prior to the stroke. Exclusion criteria included sensory or global aphasia, dementia with a mini-mental state examination score ≤ 21, major depression, systolic blood pressure ≥ 200 mmHg, diastolic blood pressure ≥ 110 mmHg, unstable angina pectoris, severe valvular stenosis, arrhythmia, congestive heart failure, ST depression ≥ 2 mm on electrocardiogram at rest, third-degree atrioventricular block with no pacemaker, severe peripheral vascular disease, severe lung disease, and orthopedic or neurological disability incompatible with a cardiovascular rehabilitation program.

mRS = modified Rankin Scale

Intervention program

Patients were educated on vascular risk factors and the importance of physical exercise and a healthy lifestyle. After the baseline evaluation, the patients in the exercise group were enrolled in a supervised exercise-training program performed twice a week for 3 months. The exercise training included a 15 minute warm-up period followed by 45 minutes of exercise on a treadmill, a stair machine, and a bicycle at 60–70% of maximal heart rate, as prescribed by a physiologist and supervised by the physical therapy and cardiac rehabilitation staff. Compliance was monitored, and the exercise prescription was adjusted if maximal exercise capacity improved.

Evaluation of physical fitness

The following tests were used to evaluate physical fitness at baseline and following the training period:

- Treadmill exercise testing following the modified Bruce protocol that includes eight phases of walking on the treadmill with changing velocity and progressive graded treadmill. Throughout the test there was continuous ECG and vital signs monitoring. The test was terminated on the patient's request, upon reaching target pulse or if there were cardiac symptoms or ECG ischemic changes. The physical fitness was calculated using METS equation
- Six minute walk test, measuring the maximal distance the subject walks within 6 minutes [17], a measure of functional exercise capacity
- Additional tests assessing physical parameters: 10 meter walk test assessing the time to complete a 10 meter walk; timed up-and-go test assessing the time required to get up off a chair, walk 3 meters and sit down again; and the functional reach test assessing flexibility and balance.

Table 1. Baseline characteristics of study stroke population

	Exercise group (N=41)	Control group (N=7)	*P*
Age (yrs)	61 ± 10 Range 40–83	58 ± 5 Range 52–64	0.25
Men (%)	93%	71%	0.15
Time following stroke (days)	65 ± 37	93 ± 60	0.27
Hypertension	63%	43%	0.42
Diabetes mellitus	39%	29%	0.70
Smoker	7%	14%	0.47
Past smoker	54%	48%	0.7
Dyslipidemia	88%	86%	1
Previous stroke	27%	29%	1
Coronary heart disease	22%	14%	0.40
Myocardial infarction	24%	0%	0.32
Previous coronary bypass	32%	14%	0.66
Medications			
Anti-platelets	90%	86%	0.56
Statins	76%	57%	0.37
ACE inhibitors	44%	29%	0.68
Beta blockers	30%	43%	0.66
Total cholesterol (mg/dl)	187 ± 31	214 ± 45	0.08
Triglycerides (mg/dl)	151 ± 64	174 ± 47	0.25
Fibrinogen (mg/dl)	367 ± 59	377± 77	0.79
Functional independence measure	123 ± 5	122 ± 5	0.99
Stroke impact scale	89 ± 11	89 ± 9	0.72
6 minute walk (m)	444 ± 90	438 ± 101	0.88
Exercise duration achieved in the modified Bruce test (min)	9.6 ± 3.7	9.2 ± 3.5	0.64
Metabolic equivalents achieved	6.2 ±2.8	5.8 ±1.8	0.76

Values are expressed as mean ± SD or percent

Statistical analysis

Comparisons of baseline characteristics between the two groups were performed with non-parametric Mann-Whitney tests for continuous variables and chi-square tests for categorical variables. We used a matched pair, before and after design, to evaluate the exercise training in each group. The paired Wilcoxon signed ranks test was used to compare the scores of the different rating scales. The score changes after the 3 months training period were ranked. One-way ANOVA on the ranks was used to estimate the effect of the training period. Statistical analyses were performed with SAS software.

Results

Of the 52 patients who met the selection criteria 43 underwent exercise training (exercise group) within a mean of 2 months after stroke onset, while 9 patients did not participate in any physical activity program. Of the 43 patients undergoing exercise training (38 at the Cardiac Rehabilitation Institute and 5 without any significant cardiac disease at their home setting), 2 withdrew due to an orthopedic problem and 41 were reevaluated at the end of the program. Of the control patients, two were not reevaluated (one due to pancreatitis and one due to non-medical reasons). Baseline characteristics [Table 1] and use of medications were overall comparable between the exercise and control groups. The age of the patients in the study ranged between 40 and 83 years; 90% were men; about a third had evidence of preexisting coronary heart disease and a third a prior stroke or transient ischemic attack. The total distance walked during 6 minutes and the metabolic equivalents achieved in the modified Bruce test were significantly lower than those expected by prediction equations for healthy adults [18,19].

None of the study patients experienced a cardiovascular event or stroke while training and there was a single transient ischemic attack during the study period in a patient in the exercise group. One patient also had a minor bruise from a fall during the treadmill exercise. Changes in physical parameters in the exercise group and in the control group are summarized in Table 2. Following the exercise training program, an improvement in exercise capacity was observed, manifested by improvement in the 6 minute walk test (444 ± 90 to 557 ± 99 m in the exercise group vs. 438 ± 101 to 418 ± 126 in the control group; $P = 0.002$ for the score changes) and in the exercise duration achieved in

METS = metabolic equivalents

Table 2. Change in exercise capacity and physical parameters in exercise and control groups

	Exercise group			Control group		
	Baseline	Program end	*P*	Baseline	Program end	*P*
6 minute walk (m)	444 ± 90	557 ± 99	< 0.0001	438 ± 101	418 ± 126	0.25
Modified Bruce test						
Exercise duration achieved (min)	9.6 ± 3.7	12.4 ± 3.2	< 0.0001	9.2 ± 3.5	8 ± 3.4	0.44
METS achieved	6.2 ± 2.8	8.5 ± 2.8	< 0.0001	5.8 ± 1.8	5. 8 ± 2.8	1
Resting pulse	75.3 ± 14	75.7 ± 13.3	0.85	72.5 ± 17.2	74.5 ± 14.7	0.53
Peak pulse	116.5 ± 23.3	125.2 ± 20.9	< 0.0001	111.5 ± 15.6	111.7± 12.5	1
Systolic BP rest (mmHg)	130 ± 17.9	126.3 ± 16.4	0.15	126.7± 25	125 ± 24.3	0.91
Systolic BP peak exercise (mmHg)	162.9 ± 27.3	164.4 ± 22.9	0.74	163 3 ± 36.1	163.3 ± 36.7	1
10 m walk test (m/sec)	1.2 ± 0.3	1.3 ± 0.4	0.27	1 ± 0.2	1.1 ± 0.2	0.38
Functional reach (cm)	33.5 ± 6.6	30.3 ± 9.8	0.32	32.5 ± 8.9	27.3 ± 12.4	0.13
Timed up and go (sec)	10.2 ± 2.7	9.1 ± 2.8	< 0.05	10.5 ± 1.9	9.3 ± 2.3	0.13

the modified Bruce test and the metabolic equivalents achieved [9.6 ± 3.7 to 12.4 ± 3.2 min and 6.2 ± 2.8 to 8.5 ± 3.4 respectively in the exercise group (n = 41) vs. 9.2 ± 3.5 to 8.0 ± 3.4 min and 5.8 ± 1.8 to 5.8 ± 2.8 in the control group (n = 7), *P* = 0.012 and 0.0009 for score changes, respectively]. As may be expected in patients after a minor stroke with no or minimal residual neurological deficits, there was no change in standard physical parameters.

Discussion

Our findings demonstrate that a supervised exercise training program after a minor ischemic stroke is feasible, safe, and significantly improves exercise capacity. Patients, even after a non-disabling stroke, were significantly deconditioned with indices substantially lower than expected in healthy adults. These findings add further support to a growing body of evidence that treadmill exercise training with aerobic training achieves significant gains in fitness and ambulatory function in patients with cerebrovascular disease [5-9].

Both ischemic stroke and coronary artery disease share underlying pathogenic processes and the same predisposing risk factors. Hypertension, impaired glucose metabolism, low high density lipoprotein-cholesterol, high triglycerides and central obesity were found to be important stroke risk factors in the Israeli population [20, 21]. Modification of these risk factors through a combination of comprehensive lifestyle interventions and appropriate pharmacological therapy is the key to the prevention of recurrent cardiovascular events among stroke survivors. Exercise tends to lower blood pressure and weight, improve glucose tolerance and promote cardiovascular health [6,11]. Furthermore, through lifestyle modification, exercise can minimize the need for more intensive medical and pharmacological interventions and enhance treatment endpoints in stroke patients. Indeed, exercise training is currently recommended for patients after an ischemic stroke [6]. Increasing evidence also suggests that regular physical activity may reduce the brain damage from a subsequent stroke [22,23].

A large proportion of patients after an ischemic stroke, as seen in our study population, have concomitant coronary artery disease or prior stroke. Our findings support the safety of a supervised exercise training program in these patients. There were no cardiovascular events or strokes during exercise training and the single transient ischemic attack during the study period is well within the expected, given the well-known high risk of recurrent stroke with the first few months after a cerebrovascular event [24]. Following the initial supervised program, patients were prescribed a non-supervised training program. A major barrier to providing this service is that, in contrast to patients after an acute myocardial infarction, patients after a non-disabling ischemic stroke in Israel are currently not entitled to a supervised exercise training program as a medical service.

Study limitations

This was a pilot non-randomized trial, in which the control group included patients who did not participate in the exercise training program because of reimbursement or travel issues, and therefore

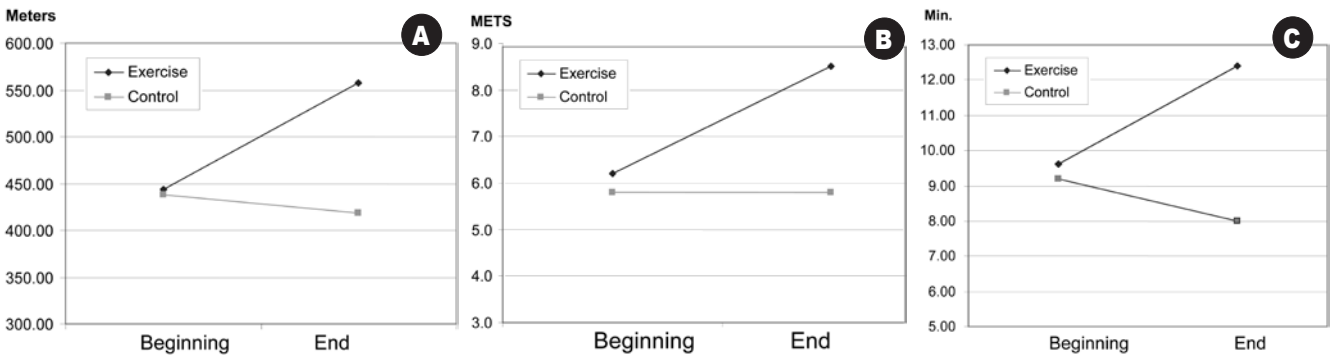

Figure 1. Changes in **[A]** the 6 minute walk test, **[B]** the metabolic equivalents (METs), and **[C]** exercise duration achieved in the modified Bruce test during the study period for the exercise and control groups. *P* values for the score changes were 0.002 for the 6 minute walk distance, 0.012 for METS, and 0.0009 for exercise duration.

a potential for referral and enrolment bias exists. Accordingly, although patients from both study groups had similar baseline characteristics, caution should be used in interpreting these findings. The results should be interpreted, however, in the context of the increasing body of evidence and current authoritative guidelines advocating exercise training for secondary prevention after stroke. Treadmill training after a disabling stroke requires a different setting with body weight support [25] not evaluated in the context of the current study.

Conclusions

A supervised exercise training program after a minor ischemic stroke is feasible, safe and significantly improves exercise capacity. Based on these findings, we are conducting a randomized clinical trial assessing the safety of early initiation of supervised treadmill training after a minor ischemic stroke. The current status in Israel is that patients are entitled to an exercise training program as a medical service after an acute myocardial infarction, but not after a non-disabling stroke. Patients after an ischemic stroke, even if non-disabling, should receive exercise training tailored to their medical needs. Further research is required to determine the best approaches for integrating exercise training into a comprehensive risk-reduction program for stroke survivors in general, and how to tailor exercise training for specific subgroups of patients.

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