Stroke: A Randomized Trial of Exercise or Relaxation

Gillian E. Mead, MD, Carolyn A. Greig, PhD,* Irene Cunningham,* Susan J. Lewis, PhD,* Susie Dinan, PGDip,‡ David H. Saunders, M Phil,† Claire Fitzsimons, PhD,* and Archie Young, MD**

OBJECTIVES: To determine the feasibility and effect of exercise training after stroke.

DESIGN: Randomized exploratory trial comparing exercise training (including progressive endurance and resistance training) with relaxation (attention control).

SETTING: Interventions were performed in a rehabilitation hospital.

PARTICIPANTS: Sixty-six independently ambulatory patients (mean age 72, 36 men) without significant dysphasia, confusion, or medical contraindications to exercise training who had completed their usual rehabilitation and had been discharged from hospital.

INTERVENTION: Both interventions were held three times a week for 12 weeks. Up to seven patients attended each session.

MEASUREMENTS: The Functional Independence Measure; Nottingham Extended Activities of Daily Living; Rivermead Mobility Index; functional reach; sit-to-stand; elderly mobility score; timed up-and-go; Medical Outcomes Study 36-Item Short Form Questionnaire, version 2 (SF-36); Hospital Anxiety and Depression Score; aspects of physical fitness (comfortable walking speed, walking economy, and explosive leg extensor power) were measured at baseline, immediately after interventions (3 months), and 7 months after baseline.

RESULTS: The median number of intervention sessions attended was 36 (interquartile range (IQR) 30.00–36.75) for exercise and 36 (IQR 30.50–37.00) for relaxation. Adherence to the individual exercises ranged from 94% to 99%. At 3 months, role-physical (an item in SF-36), timed up-and-go, and walking economy were significantly better in the exercise group (analysis of covariance). At 7 months, role-physical was the only significant difference between groups.

CONCLUSION: Exercise training for ambulatory stroke patients was feasible and led to significantly greater benefits in aspects of physical function and perceived effect of physical health on daily life. **J Am Geriatr Soc 55:892–899, 2007.**

Key words: stroke; exercise training; relaxation; randomized trial

Stroke patients have impaired aerobic fitness (endurance) and muscle strength, which almost certainly contributes to impaired physical function and disability. Physical fitness (exercise) training is "planned, structured and regular physical activity performed to improve one or more components of physical fitness."[1] Mixed (a combination of endurance and resistance) training might, via improvements in physical fitness, improve physical function and reduce disability. A recent Cochrane review[2] found only four trials of mixed training, of which only two (33 patients) were of sufficient duration to improve physical fitness.[3,4] There was little information about feasibility (e.g., whether patients could tolerate training) or about long-term retention of benefits.[2]

A recent home-based trial of mixed training reported significantly greater improvements in balance, endurance, peak aerobic capacity, and aspects of quality of life than with fortnightly visits from a therapist,[5] but the training was resource intensive, with each patient receiving more than 50 hours of one-to-one therapy. Another study suggested benefits of a community-based fitness intervention, but the control group received upper limb strength training, not a nonexercise control intervention.[6] Other small, recent trials did not provide mixed training and did not investigate long-term retention of benefits.

Because of the paucity of data about the feasibility and effect of exercise training,[2] an exploratory randomized, controlled trial of exercise training after stroke was designed, using a well-recognized framework for evaluating complex interventions.[7] Group exercise sessions that were less resource intensive than one-to-one instruction were provided. The control group attended relaxation sessions (attention control) to control for the effects of social inter-

From the *Department of Geriatric Medicine, and †Department of Physical Education, Sport and Leisure Studies, University of Edinburgh, Edinburgh, United Kingdom; and ‡Royal Free and University College, London Medical School, London, United Kingdom.

Address correspondence to Dr. Gillian E. Mead, Geriatric Medicine, School of Clinical Sciences and Community Health, Room F1424, Royal Infirmary, Little France Crescent, Edinburgh EH16 4SA, United Kingdom. E-mail: Gillian.E.Mead@ed.ac.uk

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action and activity associated with travel. Long-term retention of benefits was investigated.

The aims were to determine the feasibility of key parts of the trial (including acceptability of the interventions and outcome measurements) and to assess the effect of exercise training on important outcomes.[7] Because this was an exploratory trial, power calculations were not performed; rather, the goal was to obtain reliable data to inform power calculations for a definitive trial.[7] It was estimated that 90 patients could be recruited.

METHODS

Design

This was a randomized exploratory trial comparing "mixed" (endurance and resistance) training with relaxation (attention control) in stroke patients who had completed their usual rehabilitation (including physiotherapy, occupational therapy, and speech and language therapy) and who had been discharged from the hospital. Between October 2002 and July 2004, the exercise instructor (IC), one of the trial coordinators, or the principal investigator, (GM) screened inpatients at three hospitals in Edinburgh, Scotland, for eligibility. From August 2003, eligible patients who had been inpatients or who had attended the stroke clinic at a fourth hospital (Western General Hospital) were referred. All hospitals were part of the same clinical network, so stroke management was similar in all four hospitals.

Eligibility criteria were independently ambulatory, living within central or south Edinburgh, absence of dysphasia or confusion severe enough to prevent informed consent or impair safety in exercise classes, and absence of medical contraindications to exercise training (uncontrolled angina pectoris, resting systolic blood pressure >180 mmHg or resting diastolic blood pressure >100 mmHg, resting heart rate >100 beats per minute, unstable or acute heart failure, uncontrolled systemic illness, uncontrolled visual or vestibular disturbance, recent injurious fall without medical examination, and proven inability to adhere to the exercise program).[8]

Baseline Assessment

Eligible consenting patients attended the Human Performance Laboratory at the Royal Infirmary, Edinburgh, after hospital discharge and shortly before randomization. One of four physicians (including GM and AY) checked fulfillment of eligibility criteria and performed a limited neurological examination. One of four exercise physiologists (including CG, DH and CF) assessed Functional Independence Measure (FIM);[9] Nottingham Extended Activities of Daily Living (NEADLs);[10] Rivermead Mobility Index (RMI);[11] functional reach;[12] timed up-and-go;[13] sit-to-stand time; Elderly Mobility Scale (EMS);[14] functional ambulation category;[15] Medical Outcomes Study 36-item Short Form Questionnaire, version 2 (SF-36), which measures domains of quality of life,[16] and Hospital Anxiety and Depression Score (HADS).[17] Comfortable walking velocity (m/s) was measured during three sessions (separated by 5 minutes) of self-paced comfortable walking around a marked 17-m circuit, completing sufficient laps to achieve at least 3 minutes of walking per session.[18] During each walk, walking economy (oxygen consumption (VO_2) mL/kg per m), derived from walking speed and VO_2 toward the end of the walk minus VO_2 while standing, was calculated using data from a portable breath-by-breath metabolic measurement system (Metamax 3B, Cortex Biophysik, Leipzig, Germany). Leg extensor explosive power (W/kg) was measured using a Nottingham Power Rig (Medical Engineering Unit, University of Nottingham, Nottingham, UK).[19] Power was measured rather than muscle strength, because it is functionally more relevant.

Randomization was by the trial coordinator or principal investigator (not by the outcome assessors) via a secure Internet randomization service that stratified by sex, age, and FIM score (dichotomized at age 70 and FIM score of 120).

Interventions

An advanced exercise instructor delivered both interventions in a rehabilitation hospital three times a week (Monday, Wednesday, Friday) for 12 weeks to groups of up to seven patients. During Week 1, the instructor familiarized patients with techniques and equipment. At the start of the sessions, the instructor measured blood pressure (as an additional safety check) and inquired whether the patients had fallen since the last session. Each session lasted 1 hour 15 minutes (including "tea and chat" after the interventions). Transport (minibus or taxi) was provided. Patients unable to attend every session of the 12-week program were offered up to three additional make-up sessions.

There was insufficient information from the Cochrane review about the optimum training regime for stroke patients.[2] Therefore, the mode of exercise, initial exercise level, and rate of progression were based on the Falls and Exercise Management Study to reduce falls in older frailer participants (many of whom had had a previous stroke)[20] and community exercise sessions designed for the UK charity "Different Strokes" (further details available on request). Further adaptations (e.g., inclusion of the stair climbing and descending exercise) were by the study physiotherapist (see Acknowledgments). Patients unable to perform or complete a particular exercise were given a shortened, modified, or alternative task. Although progression every 2 to 4 weeks was aimed for, individuals not ready to progress (e.g., insufficient strength, endurance, or technique) remained at their current prescription and only progressed when assessed by the instructor to be ready. The length of the exercise program (12 weeks) was similar to those of previous studies in stroke patients.[3,4]

Each session started with a warm-up to enhance circulation and mobility (15–20 minutes). The total duration of the exercise training increased from 15 minutes at Week 1 to 40 minutes by Week 12. The endurance component began in Week 1 as a circuit of cycle ergometry, raising and lowering a 1.4-kg, 55-cm exercise ball, shuttle walking, and standing chest press performed consecutively. Between each circuit station, patients walked or marched in place to ensure continuous movement. A stair climbing and descending exercise was added in Week 4. The circuit duration increased from 9 minutes to 21 minutes by Week 12. Cycling intensity was increased weekly by small increments in pedaling resistance, cadence or both while maintaining per-

ceived rate of exertion in the range of 13 to 16.[21] Brisker efforts were encouraged during all endurance exercises as patients became more familiar with the session. The endurance training ended with a graded cool-down and standing stretches.

The resistance training included upper back strengthening and triceps extension exercise, both performed seated using elastic resistance training bands and progressing from four repetitions using the lowest-resistance band to 10 repetitions using the highest-resistance band by Week 12; a pole-lifting exercise performed standing, progressing from four repetitions with a 0.22-kg pole to 15 repetitions with a 3.6-kg pole by Week 12; and a sit-to-stand exercise, resisted by body mass, progressing from four to 10 repetitions by Week 12 and becoming more difficult by introducing pauses during lowering into the chair and then increasing the frequency and duration of the pauses and increasing the angle of the knee bend and the upper body levers (i.e., the arms). The resistance training ended with a gentle cool-down and flexibility exercises lasting 10 to 15 minutes.

The relaxation intervention was seated and included deep breathing and progressive muscular relaxation. Techniques involving muscular contraction were omitted to avoid unintentional fitness training. Duration increased from 20 minutes (Week 1) to 49 minutes (Week 12).

Patients were blinded to the underlying hypothesis by reiterating the possible benefits of both interventions. Outcome assessors were blinded by asking patients not to discuss their allocated intervention.

The exercise instructor recorded patient attendance at sessions and whether each exercise station was performed according to the protocol (i.e., adherence).

Follow-Up Assessments

Patients were reassessed as soon as possible after completion of the interventions (3-month assessment) and then 4 months after completion of the interventions (7-month assessment).

Analysis of Outcome Data

Raw data with skewed distributions were appropriately transformed to a normal or near-normal distribution when possible (Table 1). Outcome measures with large ceiling or floor effects (i.e., a large proportion of measures reached the maximum or minimum possible score) could not be transformed and so were omitted from the main analyses. Comparison of the exercise and relaxation groups was by intention to treat (ITT), missing outcome data at the 3- and 7-month assessments being replaced using the last observation carried forward method. Baseline measurements of the outcome variables were occasionally missing for different reasons (e.g., pain or dizziness in the patient, equipment failure). This affected 2.7% of these data points. Where possible, these missing data were replaced using the next measurement to preserve the ITT design as closely as possible.[22] Sensitivity analyses applied to the original data and to data with missing values replaced produced similar results.

Analysis of covariance (ANCOVA) was used to test whether, and by how much, the outcome measures at 3 and at 7 months differed between the groups, controlling for their baseline levels. Adjustment was also made for age, sex, and time from stroke to baseline. Other patient characteristics were also considered for inclusion as independent variables, including hospital of origin, but none was sufficiently influential. Possible reasons for outliers were investigated, but none was excluded. All models used the Type III sum-of-squares method. All two-way interactions were tested for significance.

Results are expressed as means of the outcome measures, adjusted for the influence of independent variables, and the significance of the difference between the exercise and relaxation groups (Table 1). Effect size is also given as a standardized measure of the size of the treatment effect, independent of sample size. For this unbalanced ANCOVA design, partial eta-squared is the appropriate effect size index (intervention effect sum of squares (SS) divided by error SS plus intervention SS). This measure of effect size is small at 0.01, medium at 0.09, and large at 0.25.[23]

For each intervention, baseline assessments were also compared with the 3- and 7-month assessments using univariate analysis to determine the effect of each intervention on the outcome measures (paired *t* tests for normally distributed and transformed data and sign tests for nonnormal data).

RESULTS

Patients

Baseline characteristics are shown in Table 2. Progress of patients through the trial is shown in Figure 1.

Feasibility

Interventions

Nineteen of 32 (59%) patients allocated to exercise and 17 of 34 (50%) allocated to relaxation achieved full attendance ($\geq$36 sessions). The timing of absences was variable but infrequent; hence, the median number of sessions attended was 36 (interquartile range (IQR) 30.00–36.75) for exercise, and 36 (IQR 30.50–37.00) for relaxation. Adherence to the exercise stations ranged from 94% (cycle ergometry) to 99% (pole raise) of the total of all patients' attendances.

Assessments

Sixty-four (97%) patients attended the 3-month assessment and 62 (94%) the 7-month assessment (Figure 1). In total, 192 assessments were performed, and data were obtained for the majority of outcome measures. Less than 3% of data were missing for outcome measures using questionnaires (i.e., FIM, NEADL, RMI, SF-36, HADS), whereas the amount of missing data was higher for physical measurements (timed up-and-go (8/192, 4%), sit-to-stand (9/192, 5%), functional reach (10/192, 5%), EMS (12/192, 6%), extensor power of unaffected leg (15/192, 8%), extensor power of affected leg (10/192, 5%), walking speed (14/192, 7%), and walking economy (21/192, 11%)). The most common reasons for noncompletion of the physical tests were limb pain or illness.

Analysis

Although it was possible to satisfactorily transform most of the outcome variables to a normal or near-normal distri-

Table 1. Outcome Measurements* 3 and 7 Months After Baseline Assessment, Adjusted for Patient Characteristics

Outcome Measure	Months	Exercise Group (n = 32) Adjusted Mean (95% Confidence Interval)		Relaxation Group (n = 34) Adjusted Mean (95% Confidence Interval)		Effect Size (Partial Eta^2)	*P*-value for Difference Between Intervention Groups†
Functional Independence Measure (range 18–126)	3	118.2	(116.9–119.3)	118.3	(117.1–119.4)	0.001	.84
	7	117.9	(116.3–119.4)	117.7	(116.1–119.1)	0.001	.82
Nottingham Extended ADLs (range 0–22)	3	16.5	(15.8–17.1)	16.7	(16.1–17.4)	0.004	.61
	7	16.7	(15.7–17.5)	16.4	(15.5–17.3)	0.002	.70
Rivermead Motor Index (range 1–15)	3	13.2	(12.7–13.6)	13.0	(12.5–13.4)	0.007	.50
	7	13.3	(12.8–13.7)	13.1	(12.6–13.5)	0.007	.53
Functional Reach, cm‡	3	28.8	(26.3–31.1)	26.3	(23.7–28.7)	0.032	.16
	7	28.3	(25.7–30.7)	25.8	(23.1–28.3)	0.030	.18
SF-36 (range 0–100)							
Physical functioning§	3						
	7	55.8	(49.9–61.7)	57.8	(52.1–63.5)	0.004	.63
Role physical	3	90.8	(85.1–95.2)	75.5	(66.8–82.8)	0.16	.002
	7	84.2	(76.1–90.7)	71.7	(61.4–80.3)	0.07	.04
General health	3	76.2	(69.9–81.8)	68.1	(60.0–74.4)	0.052	.08
	7	65.0	(57.8–71.5)	71.5	(65.1–77.2)	0.032	.16
Vitality	3	59.0	(53.6–64.3)	57.5	(52.3–62.7)	0.003	.69
	7	55.2	(49.2–61.2)	51.9	(46.1–57.7)	0.01	.44
Mental health	3	80.4	(74.4–85.5)	82.5	(77.1–87.2)	0.006	.56
	7	77.3	(71.4–82.5)	79.9	(74.6–84.7)	0.008	.48
HADS score (range 0–21)							
Anxiety	3	3.65	(2.63–4.82)	3.99	(2.96–5.17)	0.003	.67
	7	3.95	(2.89–5.16)	4.20	(3.15–5.41)	0.002	.75
Depression	3	4.05	(2.99–5.27)	3.51	(2.56–4.61)	0.008	.49
	7	4.21	(3.18–5.37)	4.03	(3.07–5.13)	0.001	.82
Leg extensor power (affected leg)	3	1.11	(1.01–1.23)	1.04	(0.95–1.15)	0.014	.37
W/kg‖	7	1.11	(0.99–1.22)	1.09	(0.98–1.20)	0.001	.82
Leg extensor power (unaffected leg)	3	1.25	(1.13–1.36)	1.23	(1.12–1.33)	0.001	.81
W/kg‖	7	1.29	(1.19–1.40)	1.25	(1.16–1.36)	0.005	.61
Walking speed, m/sec¶	3	0.735	(0.697–0.773)	0.735	(0.697–0.773)	$<$0.001	1.0
	7	0.698	(0.662–0.735)	0.736	(0.701–0.772)	0.037	.14
Walking economy (oxygen uptake)	3	0.112	(0.103–0.121)	0.126	(0.116–0.136)	0.065	.05
mL/kg per meter¶	7	0.118	(0.108–0.129)	0.120	(0.110–0.136)	0.002	.72
Timed Up-and-Go, seconds	3	10.4	(9.8–11.1)	11.5	(10.8–12.3)	0.076	.03
	7	11.2	(10.6–11.8)	11.5	(10.9–12.2)	0.011	.41
Sit-to-stand, seconds	3	0.94	(0.85–1.06)	1.01	(0.90–1.14)	0.01	.43
	7	1.02	(0.93–1.13)	1.09	(1.00–1.21)	0.017	.31

* Back-transformed, if necessary, after analysis of transformed data (square root of reflected data: Functional Independence Measure, Nottingham Extended Activities of Daily Living (ADLs), Rivermead Motor Index; functional reach, Medical Outcomes Study 36-item Short Form Questionnaire (SF-36) (role physical, general health, and mental health); square root: Hospital Anxiety and Depression Scores, leg extensor power; reciprocal: Timed Up-and-Go and sit-to-stand; logarithmic: walking economy).

† From analysis of covariance effects table.

‡ Time from stroke to baseline omitted from both models because of strong interaction with other covariates.

§ Analysis of the 3-month assessment not done because of heterogeneity of regression slopes.

‖ One subject in exercise group omitted because no extensor power data were available for either leg at any stage. One subject in exercise group omitted because no extensor power data were available for unaffected leg at any stage.

¶ One subject in relaxation group omitted because no walking data were available at any stage.

Table 2. Characteristics of Patients at Baseline

Characteristic	Exercise Group (n = 32)	Relaxation Group (n = 34)
Age, mean ± SD	72.0 ± 10.4	71.7 ± 9.6
Men, n (%)	18 (56)	18 (53)
Required inpatient treatment for stroke, n (%)	27 (84)	29 (85)
Length of inpatient stay, median (IQR)	19 (7–39)	16 (6.5–48.5)
	n = 27	n = 29
Outpatient treatment only, n (%)	5 (16)	5 (15)
Subtype of stroke (Oxfordshire Community Stroke Project Classification), n (%)		
Total anterior circulation	1 (3)	1 (3)
Partial anterior circulation	16 (50)	16 (47)
Lacunar	10 (31)	9 (26)
Posterior circulation or uncertain	5 (16)	8 (24)
Pathological type, n (%)		
Ischemic	28 (88)	32 (94)
Hemorrhagic or unknown	4 (12)	2 (6)
Side of brain lesion, n (%)		
Right	12 (38)	15 (44)
Left	19 (59)	18 (53)
Bilateral or unknown	1 (3)	1 (3)
Days between stroke and baseline, median (IQR)	171 (55–287)	147.5 (78.8–235.5)
	n = 31	n = 34
Days between discharge and baseline, median (IQR)	106 (50–230)	80 (49–154)
	n = 27	n = 29
Days between stroke and start of intervention, median (IQR)	178 (86–307)	161.5 (91.8–242.8)
	n = 31	n = 32
Smoking, n (%)		
Nonsmoker	13 (41)	15 (44)
Ex-smoker	6 (19)	6 (18)
Smoker	13 (41)	12 (35)
Drugs, n (%)*†		
Antiplatelets or anticoagulants	30 (97)	34 (100)
Antihypertensives	13 (42)	18 (53)
Statins	18 (58)	26 (77)
Other	29 (94)	31 (91)
Comorbid disease, n (%)*‡		
Hypertension	12 (46)	19 (56)
Ischemic heart disease or left ventricular failure	10 (39)	15 (44)
Cancer (prior or current)	4 (15)	2 (6)
Prior stroke or transient ischemic attack	7 (27)	8 (24)
Other	21 (81)	18 (53)
Sitting blood pressure, mmHg, mean ± SD		
Systolic	140.6 ± 18.6	139.5 ± 17.9
	n = 31	n = 32
Diastolic	74.7 (10.0)	71.7 (8.9)
	n = 31	n = 32
Speech, n (%)		
Normal	22 (69)	24 (71)
Dysarthria	9 (28)	7 (21)
Expressive dysphasia	1 (3)	3 (9)
Weakness (score <5 on Medical Research Council motor scale), n (%)		
Arm	9 (28)	13 (38)
Leg	7 (22)	8 (24)
Inattention, n (%)	2 (6)	2 (6)
Functional Ambulation Category score, n (%)		
4	3 (9)	4 (12)
5	29 (91)	30 (88)

* Multiple response variable; percentages do not add to 100.
† There were no medications for one patient (exercise group); excluded from calculation of percentages.
‡ There were no comorbidities for six subjects (all exercise group); excluded from calculation of percentages.
IQR = interquartile range; SD = standard deviation.

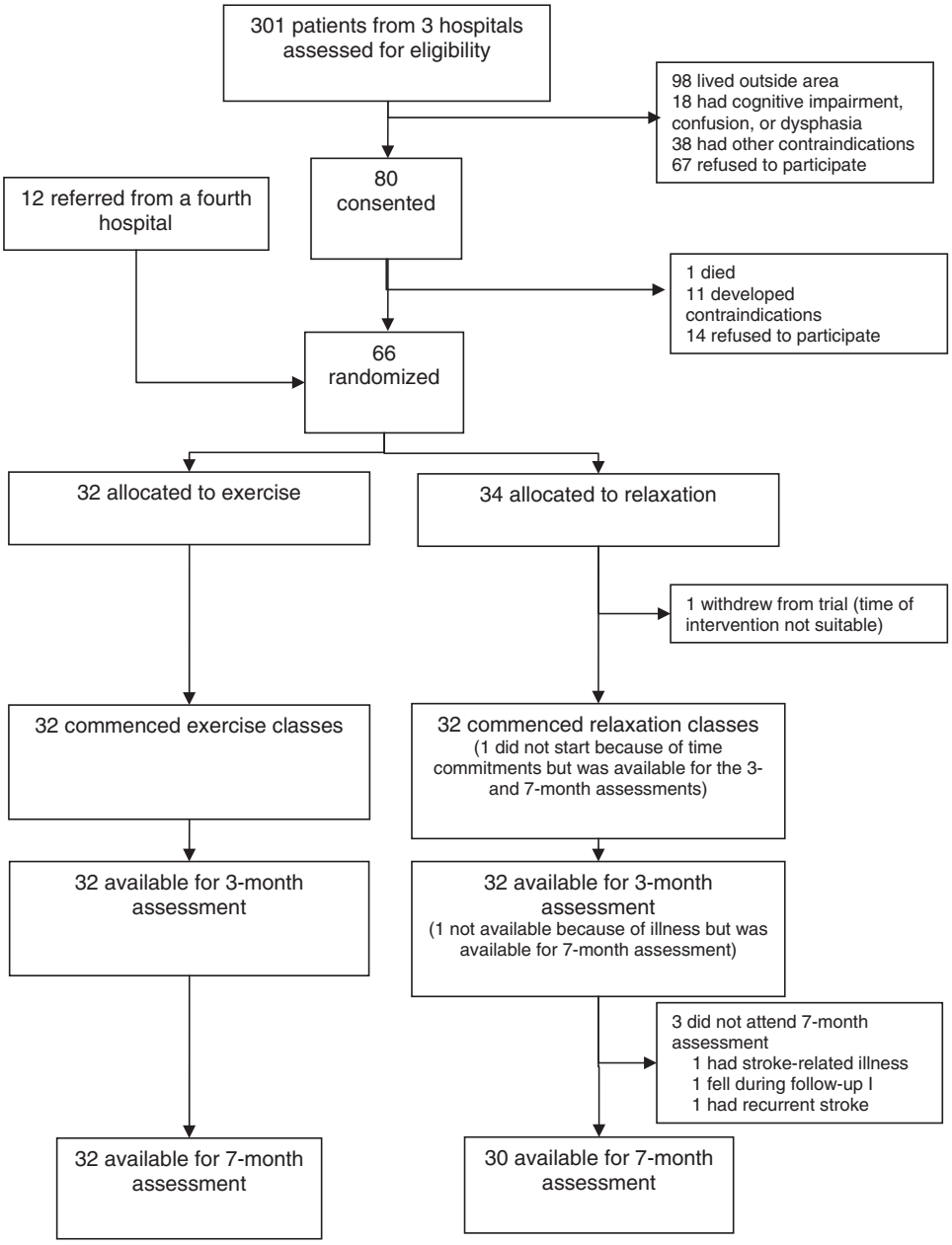

Figure 1. Patient flow through the trial.

bution, this was not possible for EMS or SF-36 social functioning, bodily pain, or role-emotional, because many of the data (77%, 54%, 46%, and 43%, respectively, at baseline) reached the maximum possible score for that particular variable (i.e., ceiling effect). Therefore, these measurements had to be excluded from ANCOVA.

Outcomes

Comparison of Exercise and Relaxation

At 3 months, SF-36 role-physical, timed up-and-go and walking economy were significantly better for exercise than relaxation (Table 1), although by 7 months, only role-physical remained significantly better in the exercise group.

Changes Between Baseline and 3- and 7-Month Assessments for Each Group

In the exercise group, there were statistically significant improvements between baseline and 3 months for SF-36 role-physical, sit-to-stand time, extensor power of the affected lower limb, and comfortable walking speed (all $P<.001$); SF-36 general health, SF-36 mental health, timed up-and-go, and HADS anxiety (all $P<.01$); SF-36 vitality, SF-36 role-emotional, functional reach, extensor power of the unaffected lower limb, and walking economy (all $P<.05$). At 7 months, significant improvements were maintained only in the extensor power of both lower limbs ($P<.01$), HADS anxiety, and sit-to-stand (both $P<.05$).

In the relaxation group, there were statistically significant improvements between baseline and 3 months in walking speed ($P<.001$), SF-36 mental health and extensor power of the lower unaffected limb (both $P<.05$). Significant improvement was maintained in all of these outcomes at 7 months ($P<.05$, $P<.01$, and $P<.001$, respectively), but SF-36 bodily pain was significantly worse ($P<.01$) (all data available on request).

Adverse Events

During the 3-month period of the interventions, eight of 32 patients in the exercise group reported 11 falls, and four of 34 patients in the relaxation group reported five falls (P = ns); all falls occurred outside the sessions. One patient allocated to relaxation fell at the 3-month assessment.

DISCUSSION

This is the largest randomized trial to compare in detail the feasibility and effect of mixed exercise training performed in a group setting with that of a nonexercise "attention control" intervention for ambulatory stroke patients.

The interventions were feasible, with high rates of attendance at both classes and, for patients attending the exercise classes, excellent adherence to individual exercises. The battery of outcome measures was feasible, particularly the questionnaires. The rate of missing data from even the least-well-tolerated measurement (walking economy) was only 11%. The analysis was feasible, although the EMS and some items of the SF-36 could not be used in the multivariate analysis because of ceiling effects (i.e., a large proportion of scores reached the maximum possible). Generally, floor or ceiling effects greater than 20% are likely to cause problems with data analysis.

The between-group comparison demonstrated that, at the 3-month assessment, patients allocated to exercise performed significantly better than those allocated to relaxation on the timed up-and-go test, one item on the SF-36, and walking economy. The effect sizes were small for timed up-and-go and walking economy and medium for role-physical.[23] At the 7-month assessment, the only significant difference between groups was in role-physical (small effect), suggesting that benefits of exercise training are lost after the exercise sessions cease.

There were many statistically significant improvements between baseline and 3 months in the exercise group and a few also in the relaxation group. Social interaction may have mediated some of these.[24]

There were several methodological strengths to the study. First, particular attention was paid to problems such as bias (e.g., the Internet randomization service ensured that the investigator randomizing patients had no prior knowledge of likely treatment allocation, and the outcome assessors could not obtain information about treatment allocation). Second, an attention-control intervention rather than usual care was used, which means that between-group differences were due to the exercise training per se, rather than social interaction. Third, a 7-month assessment was performed to investigate whether any benefits were maintained in the long term.

There are some limitations. First, like with previous studies,[2–4] patients unable to mobilize independently had to be excluded, because a single instructor taught the classes. Groups of more severely impaired patients would require a higher instructor–patient ratio and safe transport. Second, prestroke function or severity of stroke was not measured. This information was not available in standardized format from the hospital records, and the study personnel who recruited patients could not obtain these data retrospectively. However, stroke subtype, which provides an indication of stroke severity, was similarly distributed between the groups.

This exploratory study will inform the design of a definitive study. The same methods of recruitment and randomization and the same exercise program will be used. The assessments will be simplified by excluding scales with a large proportion of ceiling values. It had been expected that a definitive trial would determine the effect of exercise training on disability, but preliminary power calculations using data from this study have demonstrated that several hundred patients would be required in each group for a primary endpoint of the NEADL scale. Therefore, a definitive trial may need to focus on functionally relevant physical measures and indices of fitness. Disability data from a definitive trial could be incorporated into a meta-analysis of data from other trials. The data from the 7-month assessment suggest that the benefits of exercise training are not retained long term, so a definitive trial should also evaluate strategies to facilitate long-term participation in physical activity.

In summary, a randomized, controlled trial of physical fitness training in ambulatory poststroke patients is feasible. This exploratory study suggests significant benefits that justify a larger clinical trial to evaluate the effectiveness of an endurance and resistance exercise intervention on measures of physical functioning.

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Approval was obtained from Lothian Research Ethics Committee.

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Author Contributions: All authors except Ms. Cunningham and Ms. Fitzsimons devised the protocol and obtained funding. Dr. Mead was the principal investigator, led the study, and recruited patients. Ms. Dinan designed and quality assured the exercise intervention. Mr. Saunders advised on the incremental progression and recording of the exercises. Dr. Greig, Mr. Saunders, and Ms. Fitzsimons performed the baseline assessments and postintervention assessments. Ms. Cunningham assisted with recruitment and delivered the interventions. Dr. Lewis advised on the trial design and performed the statistical analysis. Professor Young assisted with recruitment of patients. All authors were involved in preparation of the manuscript. Dr. Mead is the guarantor.

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