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Exercise therapy for arm function in stroke patients: a systematic review of randomized controlled trials

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Objective: Assessment of the available evidence for the effectiveness of exercise therapy to improve arm function in patients who have suffered from a stroke.
Methods: A systematic search of bibliographical databases and reference checking were performed to identify publications on randomized controlled trials (RCTs) which evaluated the effect of exercise therapy on arm function in stroke patients. The methodological quality was assessed systematically by two raters, based on a standardized list of methodological criteria. Study characteristics, such as the chronicity and severity of impairment of the patient population, the amount and duration of interventions, and specific methodological criteria, were related to reported effects.
Results: Thirteen RCTs were identified, six of which reported positive results on an arm function test. In five of these six studies there was a contrast in amount or duration of exercise therapy between groups. Methodological scores ranged from 5 to 15 (maximum possible score: 19 points).
Conclusion: Insufficient evidence made it impossible to draw definitive conclusions about the effectiveness of exercise therapy on arm function in stroke patients. The difference in results between studies with and without contrast in the amount or duration of exercise therapy between groups suggests that more exercise therapy may be beneficial.

Introduction

Impaired arm function in patients who have suffered from a stroke is a common problem. In the population-based Copenhagen Stroke Study, it was found that on admission 32% of the stroke patients had severe arm paresis and 37% had mild arm paresis.[1] In 64 (13%) out of 491 surviving patients, the affected arm remained entirely a-functional, despite the efforts of a comprehensive rehabilitation programme. These patients accounted for 25% of the total number of bed-days for all 491 patients.[2] In recent

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decades, a number of articles have been published in which the effect of various rehabilitation methods to improve arm function after stroke has been evaluated. Apart from the many clinical studies which have been carried out, the designs of which range from case studies to randomized controlled trials, there have also been several attempts to synthesize the findings from different studies in reviews or meta-analyses. Most of these focus on one specific intervention, such as EMG biofeedback,[3–9] or electrostimulation.[10,11]

With regard to exercise therapy, many literature reviews do not present separate results for the upper and lower extremity.[12–21] However, this has been done in two recent reviews, which address different interventions. One of these reviews presents separate results for the arm,[22] and the other focuses entirely on interventions to improve arm function.[23] In both these reviews the conclusion is that exercise therapy, and in particular extensive practice, is beneficial. However, the validity of these two reviews remains uncertain, since they did not specify the methods used for the retrieval and selection of studies, and no explicit criteria were used to make the review process clear and replicable. The main objective of the present review was to use explicit, systematic methods to answer the following research question: 'Is there any evidence of the effectiveness of exercise therapy to improve the arm function of patients with a hemiparesis following stroke?' The term 'evidence' pertains to level I or level II evidence, i.e. resulting from large randomized trials with clear-cut results (level I), or small randomized trials with uncertain results (level II).[24,25]

A second objective of this review is to relate differences in reported results to differences in characteristics of the study populations, interventions, outcome measures or other methodological issues.

Methods

A literature search up to August 2000 was conducted in the following databases: Medline, Embase, CINAHL, the database of the Knowledge Centre for Professions Allied to Health, and the Database of the Cochrane Field 'Rehabilitation and Related Therapies', which includes the RCTs in this field. The keywords used were: stroke, cerebrovascular disorders, hemiplegia, hemiparesis, upper extremity, arm, rehabilitation, therapy, exercise therapy, physical therapy, physiotherapy and occupational therapy. Selection of articles was based on the title and the abstract. In case of uncertainty, the entire text of an article was read. A great deal of attention was paid to retrieving relevant references. The following inclusion criteria were applied: (1) studies concerning exercise therapy aimed at amelioration of the motor function of the hemiparetic/hemiplegic arm in stroke patients; (2) only studies designed and reported as randomized clinical trials (RCTs); (3) outcomes measured at impairment and/or disability level; (4) separate results presented for the affected arm; (5) published, full-length articles; (6) language: English, German, French or Dutch; (7) published after 1966. Studies concerning pharmacological interventions, biofeedback techniques or electrical stimulation were not included.

The methodological quality of the selected studies was assessed independently by two raters (JHvdL and IAKS), based on a list of 19 methodological criteria, recommended by Van Tulder *et al*., which comprises 11 internal validity criteria, six descriptive criteria and two statistical criteria (see Appendix).[26] Blinding of the reviewers was not considered to be feasible, because both reviewers already had considerable knowledge of the literature included in the review. Any disagreements were resolved by discussion, or, if necessary, by consulting a third reviewer (HB).

The result of each trial was summarized as either '+' (positive for the experimental group or the group receiving the greatest amount of exercise therapy) or '0' (no difference), according to the results presented in the original articles. Positive results were defined by a p-value <0.05. An attempt was made to identify a relationship between reported effects and the following variables: patient characteristics (acute or chronic, severity of impairment), study design (contrast in amount or duration of exercise therapy between experimental and control treatment), and two methodological characteristics that have been shown to cause bias in the results of earlier

reviews (concealed allocation of treatment and blinding of the outcome assessor).[27,28]

Results

The systematic search of the literature resulted in the identification of 72 articles, 57 of which were excluded because the study did not concern exercise therapy for the affected arm or because the study design was not a randomized controlled trial. (A list of the excluded articles can be obtained on request from the first author.)

In the 15 articles included in the review, 13 RCTs were described, involving a total of 939 patients.[29–43] The number of patients included in the trials ranged from nine[33,38] to 282.[40,41] In all studies, except for one in which no statistical test was applied,[38] positive results were defined by a p-value <0.05. The study characteristics, results (summarized as either '+' (positive for the experimental group or the group receiving the greatest amount of exercise therapy) or '0' (no difference), according to the presentation in the original article), conclusions reported in the original articles, and the methodological scores rated by the present reviewers are presented in Table 1.

In each study, two or more outcome measures were applied (Table 1). The most frequently used outcome measures were the Barthel Index (seven studies),[29–31,36,37,39,40] the Action Research Arm test (four studies),[37,39,40,42] and the Fugl-Meyer assessment scale (four studies).[36,37,42,43] It was not always clear what the primary outcome measures were. In all studies the outcomes were measured both at impairment level and at disability level.

In six of the 13 RCTs, positive short-term results were reported for arm function tests (Table 1).[31,33,38,39,42,43] In three of these six studies the effect was still positive after a follow-up period of six weeks,[39] one year[42] or two years.[33] In only two of the 12 studies which used ADL questionnaires were positive results on these questionnaires reported for both the short-term and the long-term follow-up.[33,35]

Nine studies included acute or subacute patients who had severe or mild to severe impairments, whereas the majority of studies concerning chronic patients included mild to moderately impaired patients (Table 2). It is not possible to show a relationship between a positive effect of exercise therapy and chronicity or severity of the arm paresis.

The relationship between three study characteristics and reported short-term effects on an arm function test is presented in Table 3. These study characteristics are presence or absence of a contrast in amount or duration of exercise therapy between groups, and the methodological criteria concerning concealed allocation of treatment and blinding of the outcome assessor. In eight studies there was a difference in the amount or duration of the exercise treatment between the experimental and control interventions (Table 3). In one of these studies, this difference was effectuated by immobilization of the affected arm in the control group,[39] and in another study the patients in the control group received fake short-wave therapy on the shoulder.[37] In a third study, both groups received an equal amount of treatment, but because the unaffected arm was immobilized in the experimental group, the amount of exercise of the affected arm was greater than in the control group.[42] In a fourth study the contrast between interventions was qualitative as well as quantitiative.[43] The control treatment (once a week) consisted of mere 'exposure' to the robotic device, which delivered sensorimotor exercise to the patients in the experimental group five times a week. In the other four studies in which there was a contrast in the amount or duration of exercise therapy, patients in the experimental group simply received more treatment.[31,33,35,40] In the remaining five studies, the amount of exercise was equal between groups, but the type of intervention differed (see Table 1 for details).[29,30,34,36,38] In five of the eight studies in which there was a contrast in the amount or duration of exercise therapy, the reported short-term result for the arm function test was positive, in favour of the more intensive treatment. In only one out of five studies without such a contrast in the amount or duration of therapy, was a positive result reported (Table 3).

The methodological assessment yielded disagreement on 15.8% of the items. On four of the 39 items which caused dissent the two reviewers could not reach a consensus, so the third reviewer made the final decision. The methodological

Table 1 Characteristics and methodological scores of 13 RCTs investigating the effect of exercise therapy to improve arm motor function in stroke patients

Author, year	Patients	Comparison of interventions	Long-term follow-up	Relevant outcome measures[a]	Reported effect[b]		Authors' conclusions	Methodological score (max. 19)
					Short-term	Long-term		
Kwakkel 1999[39] [c]	33 E / 37 C[d] Acute (mean 7.2–7.5 days) Mean age 64.1 (C) to 69 (E) Median ARA: 0	E half an hour extra arm training, 5 times a week for 20 weeks + basic rehab programme C half an hour immobilization of arm and leg by airsplints, 5 times a week for 20 weeks + basic rehab programme	6 weeks post intervention	BI ARA	BI: 0 ARA: +	0 +	Greater intensity of arm rehabilitation leads to small improvements in dexterity	15
Feys 1998[37]	50 E / 50 C Acute Mean 21.4 (E) and 24 (C) days Mean age 65.6 (E) and 62.8 (C) FMA <46 Mean FMA 14	E Rocking chair, inflatable arm splint, arm used to push backwards (sensorimotor stimulation) + usual rehab procedures C Rocking chair + fake short-wave therapy + usual rehab procedures 30 minutes, 5 times a week for 6 weeks	12 months post stroke	FMA ARA BI	FMA: 0 ARA and BI: 0	+ 0	Significant difference on FMA only at follow-up; no differential effect measured with ARA and BI	14
Van der Lee 1999[42]	31 E / 31 C (66 at the start) Chronic (Median 3 years) Median age 59 (E) and 62 (C) At least 20° wrist extension	E Forced use (immobilization of unaffected arm + intensive arm function training) C Intensive bimanual arm function training 5 days a week, 6 hours a day for 2 weeks	1 year post intervention	ARA RAP FMA MAL Problem score	ARA: + RAP: 0	+ 0	Small but lasting effect on dexterity (ARA); no effect on ADL (RAP)	14
Lincoln 1999[40] Parry 1999[41]	94 E QPT 93 E APT 95 C Acute (1–5 weeks) Median age 73 Median ARA: 0	E 2 hours a week additional therapy from a senior research PT (QPT) or physiotherapy assistant (APT) for 5 weeks + daily routine PT C Daily routine PT only	3 and 6 months post stroke	RMA arm scale ARA THPT Grip strength BI Extended ADL scale	0	0	No significant effect on arm function	13

Table 1 Continued

Author, year	Patients	Comparison of interventions	Long-term follow-up	Relevant outcome measures[a]	Reported effect[b]		Authors' conclusions	Methodological score (max. 19)
					Short-term	Long-term		
Duncan 1998[36]	10 E / 10 C Subacute (66 (E) and 56 (C) days) Mean age 67.3 (E) and 67.8 (C) Mean FMA 37	E Home-based exercise programme for 1.5 hours 3 times a week for 8 weeks C Usual care: variable content, frequency (average 39 visits in 12 weeks) and duration (average 44 minutes)	None	FMA Jebsen hand function test BI Lawton IADL MOS-36	0		Differences in motor recovery (FMA) were only significant for the lower extremity; no significant differences in upper extremity functional performance	12
Jongbloed 1989[30]	43 E / 47 C Subacute (average 40 days) Mean age 71.3 Brunnström stage 1–5	E Sensorimotor integrative treatment C Functional treatment 5 times a week 40 minutes for 8 weeks	None	BI Meal preparation 8 subtests of the Sensorimotor Integration Test Battery	0		No statistically significant differences between the two treatment groups	11
Sunderland 1992[31] 1994[32]	65 E / 67 C Acute (median 8–10 days) Median age 65 (E, severe) to 70 (C, mild) Inability to complete 9-hole peg test <18 s	E Enhanced therapy C Conventional therapy E more than twice the amount of arm therapy per week, during a longer period	6 months post stroke; Sunderland 1994: follow-up until 1 year post stroke	Extended Motricity Index Subtests of the Motor Club Assessment Resistance to and pain from passive movement Frenchay Arm Test Nine-hole Peg Test Tests of sensory loss BI	6 months: +	1 year: 0	Small but statistically significant difference in favour of E group after 6 months; effect lost at follow-up	11
Taub 1993[33]	4 E / 5 C (10 at the start) Chronic (median 4 years) Median age 65 (E) and 63 (C) At least 20° wrist extension	E Restraint of unaffected arm for over 90% of waking hours + 6 hours of supervised task practice on each weekday for 2 weeks C Procedures to focus attention on the involved extremity	2 years post intervention	Emory Motor Function Test Arm Motor Activity Test MAL	+	+	Restraint and practice was effective in restoring substantial motor function; effect was maintained during follow-up	10

Werner 1996[35]	28 E/ 12 C (49 at the start; 14 dropped out and 5 added) Chronic (mean 2.9 (E) and 3.3 (C) years) Mean age 59 (E) and 66 (C) Initial (mean?) FIM-MM 70 (C) to 75 (E)	E 1 hour PT and 1 hour OT on 4 days a week for 12 weeks C no treatment	6 months post intervention	FIM-MM Jebsen hand function test	FIM-MM: + Jebsen: 0	+ 0	Treatment had a lasting effect	10
Volpe 2000[43]	30 E / 26 C Acute Mean 22.5 (E) and 26 (C) days Mean age 62 (E) and 67 (C) Median FMA <7	E 5 times a week 1 hour sensorimotor exercise delivered by a robotic device + standard therapy C once a week one hour 'exposure' to the robotic device + standard therapy	None	FMA MP MS-SE MS-WH FIM Motor score	FMA, MS-WH: 0 MP, MS-SE, FIM Motor: +		Robot-delivered sensorimotor training enhanced motor performance of the trained shoulder and elbow as well as functional outcome	10
Gelber 1995[34]	15 E / 12 C Acute (11.3 (E) and 13.8 (C) days) Mean age 73.8 (E) and 69.8 (C) Residual arm function?	E Neurodevelopmental technique, frequency / duration not stated C Traditional functional retraining, frequency / duration not stated Interventions for the duration of inpatient and outpatient rehabilitation	6 and 12 months	Length of stay Total inpatient rehabilitation hospital costs FIM Time to ADL milestones Box & Block test Nine-hole Peg Test	0	0	No significant differences in effectiveness	9
Altschuler 1999[38]	4 E first; 5 C first (crossover design) Chronic Mean 4.8 years Age range 53–73 Mild to extremely severe; Severely decreased to absent proprioception	E symmetric movements using a mirror C symmetric movements using a transparent plastic sheet 15 min twice a day, 6 days a week for 4 weeks	None	Subjective comments from patients Rating of improvement based on video-tapes of 'cardinal movements of the upper limb'	+		'Mirror therapy may be beneficial for at least some patients with hemiparesis following stroke'	8

Table 1 Continued

Author, year	Patients	Comparison of interventions	Long-term follow-up	Relevant outcome measures[a]	Reported effect[b]		Authors' conclusions	Methodological score (max. 19)
					Short-term	Long-term		
Logigian 1983[29]	E + C = 42 Acute (within 7 weeks) Mean age 61.6 Mean MMT score 22–34	E Facilitation techniques C Traditional techniques 1 to 1.5 hours a day + range of motion group therapy for half an hour per day	None	MMT BI	0		No significant differences between both approaches	5

[a]Outcome measures not concerning the upper extremity are omitted.
[b]Results are summarized as reported in the original studies (see Methods). '+' refers to a positive difference in favour of the experimental group; '0' means no difference between groups.
[c]Leg training group ($n = 31$) not presented.
[d]E: experimental; C: control.
ARA, Action Research Arm test; BI, Barthel Index; FMA, upper extremity motor section of the Fugl-Meyer assessment scale; RAP, Rehabilitation Activities Profile; MAL, Motor Activity Log; QPT, qualified physiotherapist; APT, assistant physiotherapist; RMA, Rivermead Motor Assessment; THPT, Ten-hole Peg Test; Lawton IADL: Lawton Instrumental Activities of Daily Living; MOS-36, Medical Outcomes Study-36 Health Status Measurement; FIM-MM: FIM (Functional Independence Measure) Motor Measure; MP, Motor Power score; MS-SE, Motor Status score for shoulder and elbow; MS-WH, Motor Status score for wrist and hand; MMT, Manual Muscle Test.

Table 2 Categorization of 13 RCTs based on the patient characteristics of chronicity and severity (studies which reported positive short-term effects on an arm function test are indicated with +)

Acute		Chronic	
Severe	Mild to severe	Mild to severe	Moderate to mild
Feys 1998[37] Kwakkel 1999[39] + Lincoln 1999[40] Volpe 2000[43] +	Duncan 1998[36] Gelber 1995[34] [a] Jongbloed 1989[30] Logigian 1983[29] Sunderland 1992[31] +	Altschuler 1999[38] +	Taub 1993[33] + Van der Lee 1999[42] + Werner 1996[35]

[a]Severity not stated; therefore in broadest category.

Table 3 Relationship between three study characteristics (presence or absence of a contrast in amount or duration of exercise therapy between groups, and two methodological criteria) and reported short-term effect on an arm function test in 13 RCTs

	Contrast in amount or duration of exercise therapy	Concealed allocation[a]	Blinding of the outcome assessor[a]	Reported short-term effect on arm function test[b]
Altschuler 1999[38]	–	–	+	+
Kwakkel 1999[39]	+	+	+	+
Sunderland 1992[31]	+	–	+	+
Taub 1993[33]	+	–	–	+
Van der Lee 1999[42]	+	–	+	+
Volpe 2000[43]	+	–	+	+
Duncan 1998[36]	–	+	–	0
Feys 1998[37]	+	–	+	0
Gelber 1995[34]	–	–	–	0
Jongbloed 1989[30]	–	–	+	0
Lincoln 1999[40]	+	+	+	0
Logigian 1983[29]	–	–	–	0
Werner 1996[35]	+	–	+	0

[a] + means 'yes'; – means 'no / don't know'.
[b] + refers to a positive difference in favour of the experimental group or the group receiving the greatest amount or duration of exercise therapy; 0 means no difference between groups.

scores (maximum 19) ranged from 5[29] to 15.[39] In all studies the elegibility criteria were specified, a method of randomization was performed (although concealed allocation was only reported in three studies),[36,39,40] and a short-term follow-up measurement was performed. In none of the studies was the care-provider blinded. Other items that were less common were: blinding of the patients (three studies),[30,37,43] description of adverse effects (three studies),[31,33,42] and intention-to-treat analysis (three studies).[36,39,42]

Based on the distribution of the 13 RCTs according to the methodological criteria of concealed allocation and blinding of the outcome assessor (Table 3), there is no indication of bias towards more positive results in studies in which concealed allocation and blinding of the outcome assessor was not explicitly stated.

Discussion

Two recent literature reviews concerning various types of treatment for the arm in stroke patients concluded that more intensive exercise therapy is beneficial.[22,23] However, these reviews are

Clinical messages

- Trials comparing different types of exercise therapy for the arm function in stroke patients have shown no difference in effectiveness.
- More intensive exercise therapy appears to be beneficial.
- Stroke patients should be encouraged to continue exercising the affected arm.

authority-based, and not based on replicable, transparent methods. A similar conclusion in favour of more intensive exercise therapy was drawn in two recent meta-analyses which were not limited to the arm.[19,21] In the present review, the selection and assessment of studies was performed systematically. It was not possible to perform a meta-analysis of the findings of different RCTs resulting in a single summary effect size. Attempts to extract data which could be used to calculate effect sizes were hampered by insufficient data presentation in some studies. In several other studies the data were skewed, and only nonparametric tests were presented. No attempt was made to calculate effect sizes by using different formulas, depending on the available data, because such a procedure was not considered to produce meaningful, comparable results.[44] A 'best evidence synthesis' would merely have led to an unsatisfactory conclusion of 'insufficient evidence,' due to the small number of RCTs.[45] For these reasons, the results of individual studies have been summarized as they were presented by the original authors, which allows readers to re-evaluate the conclusions drawn.

The findings of this systematic review do not enable a definitive conclusion to be drawn about the effectiveness of exercise therapy to improve the arm motor function in stroke patients. Trials comparing different types of exercise therapy have shown no difference in effectiveness. However, the difference in results between studies with and without contrast in the amount or duration of exercise therapy between groups (presented in Table 3) suggests that more intensive exercise therapy may be beneficial. Identification of groups of patients who might be more likely to benefit was not possible.

The assessment of the methodological quality of the included studies was made by raters who were not blinded. Blinding was not considered to be feasible, because both raters already had considerable knowledge of the literature included in the review, and would recognize most of the studies, even if blinded. There is no consensus about the possible implications of the blinding of assessors, which is a time-consuming activity if done properly.[28,46–48] No weights were assigned to the methodological criteria, because these would be entirely arbitrary.[26] It is not always clear whether failure to meet a criterion is due to imperfections in the conduct of the study or to incomplete reporting.[49] In this review, no relationships were found between methodological quality and reported results.

The relative lack of positive findings in the literature on stroke rehabilitation has been ascribed to various factors, among which are the use of outcome measures of limited responsiveness, the heterogeneity of the study population,[50] and the low statistical power of studies.[51,52] The small amount of positive results measured by means of ADL questionnaires in the studies included in this review may be due to inadequate responsiveness of these questionnaires to changes in arm function.[1] Positive results were defined by most authors as statistically significant below a certain p-value (0.05). How large these effects should be in order to be considered clinically relevant, remains undecided.

Although it is not always possible to estimate the degree of heterogeneity of the study population, based on the description of patients, the difference in findings between two recent RCTs which were of good methodological quality may be an illustration of this principle. Kwakkel *et al.*, who included a very homogeneous patient sample, found a small effect of extra arm therapy on dexterity,[39] whereas Lincoln *et al.* did not find any effect in a much larger, but less homogeneous patient sample.[40]

Although no firm evidence of effectiveness was found in this review, this does not imply evidence of no effect.[53] The conclusion of this review, i.e. that more intensive exercise therapy may be beneficial, is in accordance with the conclusions of earlier reviews and meta-analyses.[19,21–23] Therefore, it is recommended that in daily practice

stroke patients should be offered extensive opportunity and encouragement to exercise the affected arm.

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Appendix 1 – Criteria list for the methodological quality assessment[26]

Patient selection

a)	Were the eligibility criteria specified?	Yes / No / Don't know
b)	Treatment allocation	
	1) Was a method of randomization performed?	Yes / No / Don't know
	2) Was the treatment allocation concealed?	Yes / No / Don't know
c)	Were the groups similar at baseline with regard to the most important prognostic indicators?	Yes / No / Don't know

Interventions

d)	Were the index and control interventions explicitly described?	Yes / No / Don't know
e)	Was the care-provider blinded for the intervention?	Yes / No / Don't know
f)	Were co-interventions avoided or comparable?	Yes / No / Don't know
g)	Was the compliance acceptable in all groups?	Yes / No / Don't know
h)	Was the patient blinded for the intervention?	Yes / No / Don't know

Outcome measurement

i)	Was the outcome assessor blinded for the intervention?	Yes / No / Don't know
j)	Were the outcome measures relevant?	Yes / No / Don't know
k)	Were adverse effects described?	Yes / No / Don't know
l)	Was the withdrawal/drop-out rate described and acceptable?	Yes / No / Don't know
m)	Timing of follow-up measurements	
	1) Was a short-term follow-up measurement performed?	Yes / No / Don't know
	2) Was a long-term follow-up measurement performed?	Yes / No / Don't know
n)	Was the timing of the outcome assessment in both groups comparable?	Yes / No / Don't know

Statistics

o)	Was the sample-size in each group described?	Yes / No / Don't know
p)	Did the analysis include an intention-to-treat analysis?	Yes / No / Don't know
q)	Were point estimates and measures of variability presented for the primary outcome measures?	Yes / No / Don't know