Hindawi Publishing Corporation
Journal of Robotics
Volume 2011, Article ID 543060, 10 pages
doi:10.1155/2011/543060

Research Article

Stroke Rehabilitation in Frail Elderly with the Robotic Training Device ACRE: A Randomized Controlled Trial and Cost-Effectiveness Study

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Received 31 May 2011; Accepted 20 September 2011

Academic Editor: Ludovic Saint-Bauzel

The ACRE (ACtive REhabilitation) robotic device is developed to enhance therapeutic treatment of upper limbs after stroke. The aim of this study is to assess effects and costs of ACRE training for frail elderly patients and to establish if ACRE can be a valuable addition to standard therapy in nursing home rehabilitation. The study was designed as randomized controlled trial, one group receiving therapy as usual and the other receiving additional ACRE training. Changes in motor abilities, stroke impact, quality of life and emotional well-being were assessed. In total, 24 patients were included. In this small number no significant effects of the ACRE training were found. A large number of 136 patients were excluded. Main reasons for exclusion were lack of physiological or cognitive abilities. Further improvement of the ACRE can best be focused on making the system suitable for self-training and development of training software for activities of daily living.

1. Introduction

Stroke is the leading cause of long-term disability in the elderly in Western societies [1–3]. In The Netherlands, each year 41,000 people suffer a stroke for the first time, 19,000 of those are men and 22,000 are women. Twenty to twenty-five percent of these patients die within four weeks. At this moment, about 190,000 people in the Netherlands have suffered one or more strokes [4]. A large part of the patients who survive meet permanent disabilities and participation problems. Main physical consequences of a stroke are one-sided paralyses/paresis of upper and lower limbs, loss of sensibility, (partial) loss of speech or sight, and coordination problems. Also cognitive problems are reported like problems with orientation, attention, memory, concentration, information, and communication, still influencing the quality of life of the patients two years after stroke [5] and often the rest of their lives. No significant differences in the consequences of stroke are known related to age or gender of the patients. Right- and left-sided paralysis however relate to specific co-disorders. Right-handed paralysis relates to left hemisphere functions and may be accompanied by problems like communication, while left-handed paralysis may be accompanied by right hemisphere problems in the area of spatial awareness. Rehabilitation after stroke starts in the first week (acute phase) and ends in the chronic phase. Best practice in the Netherlands, as well as internationally, is the Stroke Service [6]. After a short stay of 7–10 days in the hospital, 60% of the stroke patients return home and, if necessary, receive day treatment in a rehabilitation centre. Around 10% of the patients die in hospital, 5% are discharged to a specialist rehabilitation centre, and 25%, mostly elderly people who are not able to return home, are discharged to a nursing home for a rehabilitation period up to 70 days average. This study focuses on this latter group. At this moment, standard treatment aiming at motor recovery of stroke patients in the nursing home consists of exercises under supervision of a physiotherapist or occupational therapist during their stay. A normal therapy session involves individual treatment by a therapist. It is evidence-based practice that a more intensive therapeutic treatment during the first period after stroke leads to earlier and better recovery [7]. However, economic reasons are limiting the number of therapy sessions of elderly people in a rehabilitation setting of the nursing home to two or three sessions of 30 minutes each week.

The ACRE (ACtive REhabilitation) device is developed to enhance therapeutic treatment of the upper limbs. A manipulator is attached to the user's forearm and provides a large 6 degrees of freedom motion range. In this study, one degree of freedom was limited by the arm/hand support (hand rotation around the forearm axis). The weight of the user's arm is balanced at all positions by an adjustable spring-based gravity compensation mechanism. This allows the user to move the arm through the whole motion range with very low muscle power (Figure 1).

An intrinsically safe impedance controller operates the back-driveable motorized joints to actively support the movements of the user's arm. It feels as a gentle force that helps you to go to the correct position. The level of support is adjustable from 0 to 100%. The system can be reversibly adapted from right- to left-handed use.

The position of the hand is shown on a computer screen in front of the user and is used to do training exercises or play games for rehabilitation purposes. Especially by the use of the games the patients are stimulated to train their affected arm more frequently and repetitively [7, 8]. The device is complementary to traditional arm-hand therapy and designed as an instrument for self-training. Eventually, a future version of the ACRE could even be placed at home for further rehabilitation and activation after stroke. A more detailed description of the current ACRE robot can be found in an article on the early pilot study with the ACRE prototype [8].

The conclusion of a first user pilot study from 2005 was that both the patient and the therapist found the ACRE suitable for rehabilitation after stroke [8].

The aim of the current study is to assess the effects and costs of the assisted use of an active rehabilitation self-training system (i.e., ACRE) for frail elderly stroke patients and to establish whether it can be a valuable addition to standard therapy within a nursing home rehabilitation program. The effect of additional ACRE training to standard therapy during rehabilitation was measured and related to the costs of adding ACRE training, with help of a therapist or in self-training, to standard therapy.

2. Method

2.1. Design. This study was designed as a two-arm pretest posttest randomized controlled trial in the nursing home setting. For this study with frail elderly persons, a review of medical-ethical aspects is mandatory, and permission of the Medical Ethical Trial Committee of the Leiden University was obtained before starting the inclusion of patients.

At the two participating nursing and rehabilitation centres, Pieter van Foreest (location De Bieslandhof) and Laurens (location Antonius Binnenweg), all consecutively admitted patients with main diagnosis stroke were asked to participate after meeting a set of inclusion criteria (see Section 2.2). Thereafter, they were assigned randomly to the ACRE training group or the control group, by drawing a closed envelope containing a participant number with a colour coding, indicating training or control group. The order of the colour coding was determined by a random number sequence generated using the software environment R version 2.12 [9]. To maintain good balance of the total number of patients assigned to each condition, permuted block randomization was used. The size of each block was set at 10. The randomization was stratified by training centre. Before treatment, a baseline measurement (pretest T0) was performed on functioning and emotional well-being. The control group received usual care including individual exercises and group physical therapy. Participants in the ACRE training group received usual care (including individual exercises and group physical therapy) plus 3 additional training sessions with ACRE per week for 6 weeks. The ACRE training varied from 10 to 30 minutes per session and consisted of various exercises chosen by the therapists according to progress and abilities of the patient. After this period of 6 weeks, the measurements were repeated for both ACRE training group and control group (posttest T1).

2.2. Participants. Patients arrived at the nursing and rehabilitation centre after a stay of approximately one week at the hospital. Patients were assessed and selected by the therapists taking into account the following inclusion criteria:

(i) adequate *physiological abilities* to endure the additional ACRE training, that is, being able to sit in a (wheel) chair for 30 minutes;

(ii) adequate *cognitive abilities* to comprehend and accomplish ACRE training, that is, being able to understand and perform a simple task;

(iii) impaired *motor function of upper limb* (right or left) as a result of the recent stroke as perceived by the physiotherapists as basis for the need for therapy;

(iv) no *other illnesses* impairing the ability to comply with ACRE training, such as aphasic disorder, delirium, low vision, pain, and tumor cerebri;

(v) *moment of stroke* less than 60 days prior to moment of inclusion, either first stroke or recurrence with no resulting impairments to the upper limbs from antecedent strokes;

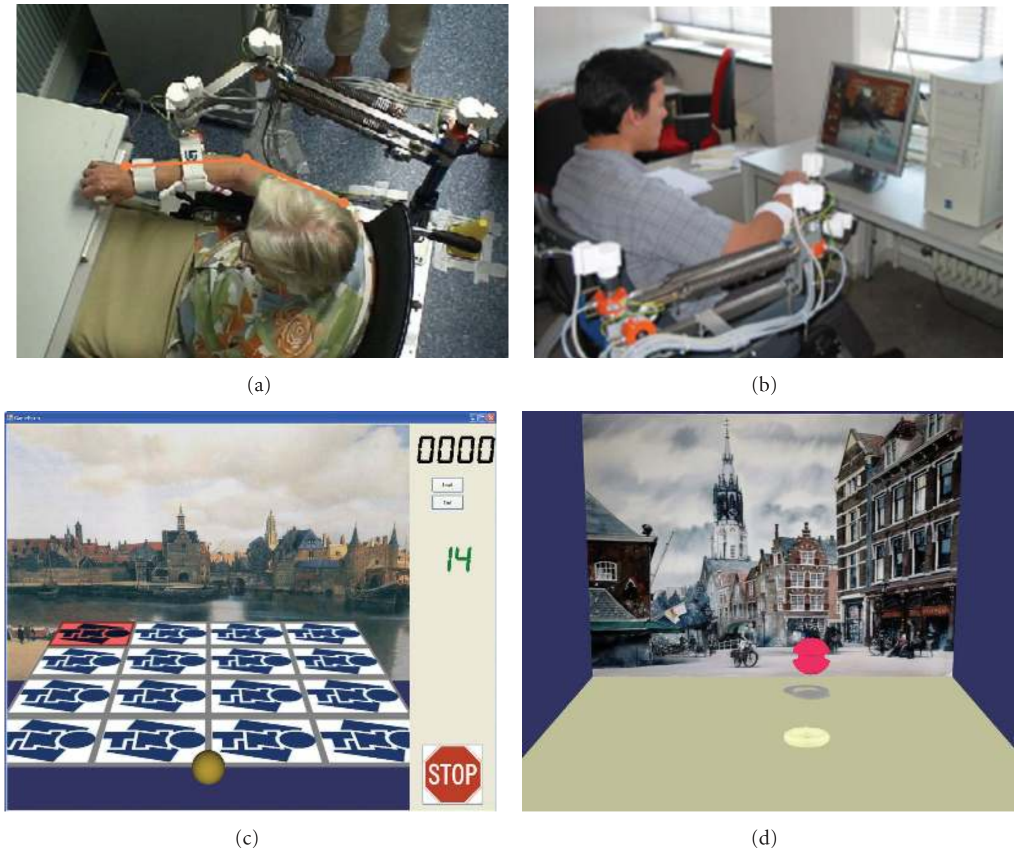

Figure 1: (a) The ACRE rehabilitation robot (top view). (b) Impedance controlled actuators help the patient to reach the desired positions. (c) "Go to the red tile" game. The ball represents the patients hand position. (d) "Follow the ball" game allows therapist to create custom movement for training. The red ball must stay close to the (moving) white ring.

A number of 64 patients for both the intervention group (receiving ACRE training) as well as the control group was aimed at, assuming a 6-point difference in the mean change on the Action Research Arm Test (ARAT) total score between the two groups to be clinically relevant. The power calculation was based on a two-sided α of .05, a power (1-β) of .80 and a correlation of 0.60 between the ARAT scores at T0 and T1. Standard deviations were derived from Van der Lee et al. [10].

2.3. Assessments and Outcome Parameters. At inclusion, patient characteristics were registered such as age, gender, preferred hand, and medical history. Primary and secondary outcomes were measured at base-line (T0) and at 6 weeks (T1) for all included patients in the ACRE training group and the control group. These assessments were made by two independent physiotherapists in training who were blind to the intervention.

2.3.1. Outcome Parameters. Primary outcome was motor recovery of the upper limb. Two tests with validated motor assessment instruments were used: The Action Research Arm Test (ARAT) and the Fugl-Meyer assessment for the arm. Although the Fugl-Meyer is widely used, the ARAT is considered to be more change-sensitive and related to functional recovery. The ARAT was used as a primary outcome measure in this study. The ARAT score is used to measure performance of movements and the ability to grasp, move, and release objects of different size, weight, and shape and will serve as a primary outcome measure in this study. The test consists of 19 items, rated on a 4-point ordinal scale (0 to 3). The ARAT has been shown to be valid, reliable, and responsive [11]. The ARAT-19 total score was computed as a sum score of the 19 items (range 0–57, 0 for no motor function and 57 for normal motor function). The minimal clinical importance difference is set at about 10% of the range of the total score, that is, 6 points [11]. In addition, an ARAT-15 total score was computed as a sum score of the 15 items recommended by Van der Lee et al. [12]. The Fugl-Meyer score for the upper extremities is a reliable and validated test of motor function in stroke patients [13]. This scale is a disease-specific objective impairment index designed specifically as an evaluative measure for assessment of recovery in the post stroke hemiplegic patient. The abilities (33 in total) are scored 0 for low, 1 for medium, and 2 for high. For upper limb functions, a maximum of 66 points can be reached, which means optimal function or no impairment. In the field of stroke rehabilitation, the Fugl-Meyer assessment is considered to be one of the most comprehensive quantitative measures of motor function following stroke, and its use has been recommended for clinical trials of stroke rehabilitation [14]. This test is widely used in intervention studies.

A set of secondary outcomes were measured to add insight into the patients' functionality both senso-motoric as well as psychological and social. To assess health-related quality of life, the generally applicable EuroQol-5 Dimensions (EQ-5D) was used [15], from which we calculated utilities using the Dutch tariff as assessed by Lamers et al. [16]. The utilities range from −.33 (worse than death) to 1 (completely healthy). We expected the quality of life to improve and the recovery to be faster, if patients have an active role in their recovery. The functionality of the paretic arm, as perceived by the patient, was scored with the Stroke Impact Scale version 3 in Dutch [17]. The Stroke Impact Scale consists of 8 subscales, and a Visual Analogue Scale measuring general recovery from stroke. A difference of 10% of the range is considered clinically relevant [17]. Disease specific aspects of emotional well-being, for example, depression, for patients with stroke were measured using the questionnaire Geriatric Depression Scale for mental state [18]. The assessment of the secondary outcomes was done per interview because most of the patients were not able to complete these questionnaires autonomously.

For the excluded patients age, gender and Barthel Index were registered at T0.

2.4. Analyses. In initial analyses, baseline characteristics were checked on significant differences by means of independent t-test. These t-test tells us if the two treatment groups (with or without ACRE) are comparable with respect to motor function, quality of life, daily functioning, depression and demographic variables, such as age, gender, and stroke characteristics before the start of the treatment. Also, the normality of the distribution of the outcome measures was checked.

Because of missing data at the posttest (T1), we performed multiple imputation with the method Multivariate Imputation via Chained Equations (MICE) [19, 20] to obtain 10 complete data sets. Several imputation models were used, because of the strong correlations between the functional measures (i.e., 0.86 between ARAT-19 and Fugl-Meyer total score); each imputation model included a functional measure and a quality of life measure (measured at both time points) and all background variables. The (cost-) effectiveness analyses were performed for these 10 sets, and the pooled results are reported.

To assess the short-term effectiveness of the ACRE treatment, an independent t-test was performed using as outcome variable the change scores on the ARAT from T0 to T1. The t-test indicates whether the mean change in the intervention group is significantly different from that of the control group. This type of analysis was repeated for the other outcome measures.

In the economic evaluation the cost of the additional effects of the ACRE on quality of life compared to standard treatment was assessed. In a cost utility analysis differences in costs at T1 were compared to differences in QALY (quality-adjusted life year) gain during the six week follow-up period. The cost analysis was performed from the perspective of the rehabilitation centre, therefore in this cost analysis only costs incurred by the rehabilitation centre are included. Costs were converted into 2011 price levels using the general Dutch consumer price index [21]. The costs included are the costs of activities aiming at the motor recovery. These are sessions with physiotherapists and occupational therapists, costs of volunteers taking patients to therapy sessions and the costs of ACRE. The costs of the ACRE consist of both the expected purchase price and the operating costs of the ACRE. Cost information was gathered during the six-week period of training. Information on the activities of the physiotherapists, occupational therapists, and volunteers was obtained from the patient logbook kept by the caregivers. Time spent by physiotherapists, occupational therapists, and volunteers was translated into costs by using standard costs [22]. Costs of ACRE were estimated at €30.000. Using a deprivation period of 10 years at 4.3% interest, 6.4% overhead costs and yearly cost of maintenance of 8.0% of the initial costs [22] result in yearly costs of €6394 for the ACRE. Assuming a yearly number of 2.000 ACRE sessions, results in a cost per ACRE session of €3.20. Depending on the willingness to pay for obtained effectiveness, a strategy is cost-effective compared with an alternative strategy if it has a better average net benefit (willingness to pay ∗ QALYs − costs). Given the statistical uncertainty of differences between costs and QALYs, cost-effectiveness acceptability curves graph the probability that a strategy is cost effective, as a function of willingness to pay. Group differences in QALY and costs were statistically analysed using standard t-tests for unequal variance.

In all analyses, a two-sided α of .05 was used as significance level. The analyses were performed using SPSS (version 17), R (version 2.12), and STATA (version 9.2).

3. Results

3.1. Participants. During the inclusion period of one year, a total of 24 persons were included and 136 exclusions were registered from the inflow of stroke patients. The 24 patients all gave their informed consent and complied with the baseline (T0) assessments. Six persons did not complete the training period of 6 weeks because of early leave of the nursing home or relapse and were not assessed at T1. They did not differ significantly from the patients who did not drop out on the background characteristics.

The baseline measurements showed no significant differences in patient characteristics between the ACRE training group and the control group (Table 1).

3.1.1. Characteristics of Exclusions. The total of 136 excluded patients consisted of 67 men and 66 women (gender of 3 patients unknown). The excluded patients varied in age from 35 to 98 years, with an average of 71.3 (age of 17 patients unknown). The Barthel Index of the excluded patients varied from 0 to 20 (Barthel Index of 19 patients unknown). Between the group of participants and the group of exclusions, no significant differences on age and gender

Table 1: Patient characteristics at baseline.

Variable	ACRE training group		Control group	
	n	mean (SD) or %	*n*	mean (SD) or %
Demographics				
Age (years)	10	73.4 (8.0)	14	76.5 (8.3)
Sex (female (%))	10	30.0	14	35.7
Right handed (%)	10	80.0	14	100.0
Barthel Index[a]	9	8.7 (4.4)	13	8.9 (6.0)
Characteristics of the stroke				
First stroke (%)	10	70.0	14	78.6
Ischemic cerebral vascular accident(%)	10	100.0	14	92.9
Consequences of the stroke				
Affected part of the brain	10		14	
Right hemisphere (%)		70.0		64.3
Left hemisphere (%)		30.0		35.7
Stroke-affected dominant arm (%)	10	30.0	14	35.7
Legs affected	10		14	
Left leg affected (%)		70.0		57.1
Right leg affected (%)		30.0		35.7
Legs not affected (%)		0.0		7.1
Swallow disorder (%)	10	30.0	14	64.3
Phatic disorder (%)	10	20.0	14	35.7
Neglect (%)	10	20.0	14	7.1
Apraxia (%)	10	0.0	14	28.6
Planning (%)	10	30.0	14	28.6
Attention (%)	10	30.0	14	21.4
Other neurological disorder (%)	10	57.2	14	50.0
Motor function[b]				
ARAT total score 19 items [0–57]	10	31.2 (27.0)	14	15.9 (14.6)
ARAT total score 15 items [0–45]	10	25.3 (21.6)	14	14.9 (13.3)
Fugl-Meyer total score [0–66]	10	40.7 (21.4)	14	37.2 (19.4)
Stroke impact score (SIS)[b]				
Strength [4–20]	9	11.0 (3.5)	13	11.5 (2.8)
Memory and thinking [7–35]	9	29.9 (6.7)	13	28.7 (3.4)
Emotion [9–45]	9	37.5 (5.5)	13	35.8 (5.8)
Communication [7–35]	9	32.7 (4.5)	13	31.1 (4.6)
Daily Activities (ADL) [10–50]	9	28.7 (7.2)	13	27.4 (8.3)
Mobility [9–45]	9	17.1 (4.1)	13	23.2 (10.2)
Hand function [5–45]	9	8.3 (2.9)	13	7.5 (3.5)
Participation [8–40]	9	32.2 (6.2)	13	28.4 (7.5)
Stoke recovery [0–100]	9	48.3 (26.5)	13	43.4 (27.7)
Quality of Life[b]				
EQ-5D [−0.33–1]	9	0.57 (0.25)	13	0.67 (0.19)
General health status [0–100]	9	59.6 (29.9)	13	61.9 (20.5)
Depression[b]				
Geriatric Depression Scale total score [0–15]	8	3.8 (2.6)	13	3.3 (2.5)

Note. None of the differences between groups were statistically significant ($P < 0.05$).
[a]Barthel Index is a standard assessment of the impact of an impairment on daily functioning (ADL).
[b]These assessments were part of the measurements of the effect study. Range is given between square brackets: [].

Table 2: Patient characteristics at baseline for included and excluded patients.

Variable	Participants (ACRE and control group)		Exclusions	
	n^b	mean (SD) or %	n^c	mean (SD) or %
Age (years)	24	75.2 (8.2)	119	71.3 (14.2)
Sex (female (%))	24	33.3	133	49.6
Barthel Index[a]	21	9.2 (5.0)	77	9.4 (6.7)

[a] Zero values were excluded.
[b] Total 24 participants, lower numbers for variable indicate missing values.
[c] Total 136 exclusions, lower numbers for variables indicate missing values.

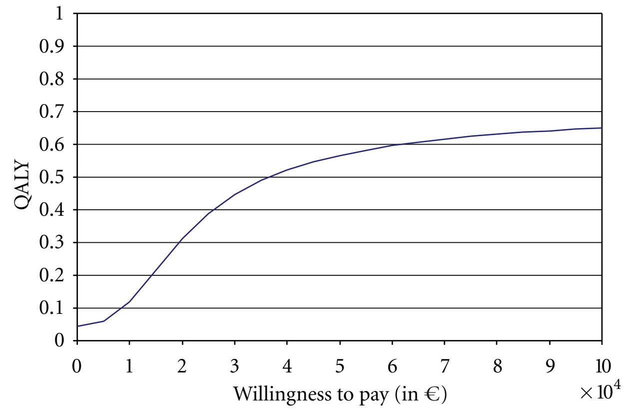

Figure 2: Cost-effectiveness acceptability curves for ACRE group in comparison with control group.

were found (Table 2). Also no significant differences in mean Barthel Index were found, when zero values were excluded (Table 2). However, 39 (34%) of the excluded patients had a Barthel Index of zero, whereas 1 (5%) of the participants ($P < 0.01$), implying that all but one of the most impaired patients were excluded.

Because of the large number of exclusions a qualitative analyses was made of the reasons for exclusion (Table 3). The reasons for exclusion were categorized into six groups:

(i) insufficient *physiological abilities*: low endurance, fatigue, condition problems, and balance problems;

(ii) insufficient *cognitive abilities*: low cognition, insufficient learning abilities, insufficient understanding, dementia, and neuropsychological impairments;

(iii) no *impaired functioning* to upper limbs: no arm/hand problems, that is, no rehabilitation for upper limbs needed;

(iv) *speech/communication problems*: aphasiac disorder, language barrier;

(v) *other illnesses* or medical reasons: fall incident, low vision, delirium, away for dialyses, bedridden, non stroke, subarachnoid haemorrhage, subdural hematoma, pain, subcomatose, tumor cerebri, deceased, and lower arm amputation;

(vi) *other reasons*: refused therapy, social problems, non cooperation, stroke over 60 days ago, and short stay only.

3.2. Effects. With regard to the motor recovery of the upper limb, our results were more favourable for the control group compared to the ACRE group. In the ACRE group an average decline in ARAT scores was found from T0 to T1, whereas an increase was found for the control group (Table 4). The same pattern was found for the Fugl Meyer and for the Stroke Impact Subscale Hand function. However, the differences in change scores between the groups were not statistically significant, due to the small sample size. Also, due the small sample size, the amount of uncertainty about the size of the effect was very large (see the confidence intervals given in the last column of Table 4). With regard to general health-related quality of life, our results were more favourable for the ACRE group compared to the control group. According to the EQ-5D, the improvement in quality of life from T0 to T1 in the ACRE group was larger than in the control group. Both groups showed an average decline on the general health status scale, but this decline was less in the ACRE group than in the control group. Again, the differences in change scores between groups were not significant, and the confidence intervals were large (Table 4).

3.3. Economic Evaluation

3.3.1. QALYs. According to the EQ-5D, an increase of 0.006 QALY (2.2 days) per patient in the ACRE group compared to the control group was found in the first six weeks after randomization. This difference between the groups was not significant ($P = 0.56$).

3.3.2. Costs. The average costs per patient in the intervention group were €220 (95% confidence interval €−33 to €474) higher than the average costs in the control group. This is mainly due to the costs of the additional ACRE training consisting of therapist cost and cost of the ACRE (Table 5).

3.3.3. Cost Utility Analysis. The combination of higher costs and more favourable QALY outcomes in the intervention group result in probability that the intervention is cost effective compared to the control group dependent of the willingness to pay (Figure 2). For values of the willingness to pay up to €40.0000 per QALY, the current Dutch threshold, usual care is preferred. For a willingness to pay higher than €40.000 per QALY, the intervention is preferred.

4. Discussion

4.1. Participants. Inclusion of participants from the target group of frail elderly turned out to be far more difficult than we expected. With an inclusion rate of 15% average the inclusion during one year only leveled approximately 20% of the number needed for statistical power of the results.

Analysis of the reasons for exclusion showed a wide variety of reasons for noncompliance, multiple reasons apparent

Table 3: Reasons for exclusion (♂/♀/total).

Location	Physical reasons			Cognitive reasons			No arm/hand problems			Communication problems			Other medical reasons			Other reasons		
	♂	♀	total	♂	♀	total	♂	♀	total	♂	♀	total	♂	♀	total	♂	♀	total
(1)	9	11	20	5	5	10	4	3	8	1	3	4	3	6	9	1	2	3
(2)	17	13	31	12	11	24	15	16	31	7	0	7	13	10	23	15	12	29
Total	26	24	51	17	16	34	19	19	39	8	3	11	16	16	32	16	14	32

Table 4: Means at baseline (T0) and posttest (T1) and change scores (T1-T0) for Motor function (ARAT/Fugl Meyer), Stroke Impact Scale, Quality of Life (EQ-5D), and Geriatric Depression Scale; results of independent t-test (change score was used as dependent variable) and the differences between the groups on the change scores.

Variable	Mean (SD)[1]				Change score (SD)[1]		Difference between groups[2] [95% CI]
	Acre group ($n = 10$)		Control group ($n = 14$)		Acre group ($n = 10$)	Control group ($n = 14$)	
	T0	T1	T0	T1			
ARAT-19	31.2 (27.0)	27.3 (24.9)	15.9 (14.6)	24.4 (20.7)	−4.0 (13.5)	8.4 (13.9)	−12.4 [−25.5, 0.8]
ARAT-15	25.3 (21.6)	24.8 (20.1)	14.9 (13.3)	22.8 (17.6)	−0.5 (8.4)	7.8 (9.8)	−8.3 [−17.6, 1.1]
Fugl-Meyer total score	40.7 (21.4)	36.8 (19.7)	37.2 (19.4)	39.1 (15.5)	−3.9 (13.1)	1.9 (18.1)	−5.8 [−20.3, 8.6]
Stroke impact Scale strength	10.8 (3.4)	12.4 (1.8)	11.4 (2.9)	13.1 (3.0)	1.6 (3.9)	1.7 (2.9)	−0.1 [−3.1, 2.9]
Stroke Impact Scale Memory/thinking	29.9 (6.4)	30.4 (3.2)	28.7 (3.4)	30.5 (2.7)	0.4 (6.7)	1.7 (3.7)	−1.3 [−5.9, 3.4]
Stroke impact Scale emotion	36.8 (5.6)	35.4 (3.9)	35.5 (5.8)	35.9 (5.4)	−1.5 (6.0)	0.4 (6.2)	−1.9 [−7.3, 3.5]
Stroke Impact Scale Communication	32.7 (4.3)	32.5 (4.2)	31.2 (4.4)	32.1 (3.9)	−0.2 (1.4)	0.9 (2.7)	−1.1 [−3.2, 1.0]
Stroke Impact Scale daily activities	28.2 (7.1)	28.4 (7.5)	27.2 (8.1)	31.4 (8.5)	0.2 (6.5)	4.3 (7.9)	−4.1 [−11.8, 3.6]
Stroke Impact Scale mobility	17.3 (3.9)	27.5 (9.6)	22.9 (9.9)	30.1 (10.0)	10.1 (7.1)	7.3 (7.5)	2.8 [−4.3, 10.0]
Stroke Impact Scale hand function	8.1 (2.9)	7.9 (4.0)	7.4 (3.5)	9.4 (5.8)	−0.2 (5.0)	2.0 (3.8)	−2.2 [−6.1, 1.8]
Stroke Impact Scale participation	32.4 (6.0)	27.3 (5.2)	28.7 (7.4)	30.8 (7.3)	−5.2 (8.7)	2.2 (11.7)	−7.3 [−16.6, 2.0]
Stroke Impact Scale stroke recovery	48.2 (25.0)	50.7 (18.2)	43.9 (26.7)	58.0 (22.7)	2.5 (22.9)	14.1 (18.2)	−11.7 [−29.7, 6.3]
EQ5-D-utilities	0.55 (0.26)	0.66 (0.16)	0.66 (0.20)	0.66 (0.25)	0.11 (0.32)	0.00 (0.30)	0.11 [−0.22, 0.44]
General health status	60.8 (29.5)	57.5 (20.4)	61.6 (20.9)	53.5 (21.4)	−3.3 (27.5)	−8.1 (30.2)	4.8 [−26.5, 36.2]
Geriatric Depression Scale Total score	3.5 (2.7)	4.7 (3.7)	3.4 (2.6)	5.1 (3.5)	1.2 (4.4)	1.7 (3.4)	−0.5 [−4.6, 3.6]

[1]Mean values are given of the statistic computed for the 10 imputed datasets.
[2]Pooled results are given of independent t-test for the 10 imputed datasets; CI: Confidence Interval.
None of the differences between the groups were significant (two-sided $P < 0.05$).

in half of the cases, the most important being insufficient physiological or cognitive abilities. Apparently, a large part of the patients who come to a nursing home, after their first week in hospital following the stroke, are not able to sit up for 30 minutes at a time or are not able to understand and perform a simple task. Also in almost a fourth part of the cases the stroke had not affected the upper limbs in such a way that arm-hand therapy was necessary. The most significant difference between the included and excluded patients was a 2-point lower Barthel Index, indicating a

Table 5: Mean cost per patient in the ACRE and control group in the first six weeks after randomization.

Cost item	ACRE group $N = 10$ Costs (€)	Control group $N = 14$ Costs (€)	Difference Costs (€)	P value*
Therapist	591.74 (346.21)	420.08 (208.21)	171.67	0.17
Volunteer	11.75 (21.30)	2.92 (9.36)	8.84	0.22
ACRE	40.64 (13.58)	0.75 (2.82)	39.89	0.00
Total costs	644.14 (361.01)	423.74 (204.75)	220.39	0.09

general lower state of ability in the excluded group. Due to early discharge from the hospital, the incoming patients in nursing homes are more impaired and frail than a few years ago [23, 24]. Because of evidence of motor-recovery ability being best at (and even limited to) the first period after the stroke [8, 11], guidelines for rehabilitation aim at starting rehabilitation training as soon as possible after the incident. This standpoint has led to our criterion for the moment of stroke being less than 60 days prior to the moment of inclusion. However, these frail elderly may benefit from ACRE training at a later stage of the rehabilitation, when they have regained a better physical condition.

4.2. Effects. Our results showed on the one hand a negative difference in the mean change scores (from pretest to posttest) between the ACRE training group and the control group for the primary outcome measures on motor recovery. On the other hand, our results showed a positive difference in change scores for general health-related quality of life. However, because of the low number of inclusions, no significant effects could be demonstrated for any of the variables.

Our negative result for motor recovery needs more reflection. The ACRE group showed a decline in motor functioning from T0 to T1, whereas the control group showed an improvement. In the ACRE group, four patients were included with an Action Research Arm Test (ARAT) baseline score at the upper extreme (i.e., 50 or higher). The physiotherapists had included these patients in the study, because they perceived that the patients still could improve the quality of their performance (i.e., speed, flexibility, reach). When we excluded these patients from the analysis, an improvement of the mean ARAT score from T0 to T1 was found for the remaining patients, but this improvement was still smaller than that of the control group. This result could be interpreted in two ways. Firstly, the result suggests a negative effect of the ACRE on motor recovery; however, the effect could be based merely on chance due to the small sample size. Alternatively, this result suggests that the ARAT was not sensitive enough to measure the effect of the ACRE training. Therefore, we recommend for future research that the quality of the performance should also be part of the assessment to gain a more complete representation of motor recovery.

Besides, the patients at the upper extreme of baseline ARAT scale, also three ACRE patients at the lower extreme were included, that is, an ARAT score of zero. Also, three control patients with a zero baseline score were included. All of these six patients scored zero on ARAT at the posttest. This result is in line with the conclusions of Kwakkel et al. [11] who found that highly impaired patients (ARAT scores less than ten) were not likely to benefit from intensive training aiming at motor recovery.

From the qualitative evaluation of the use of the ACRE in the study, it appeared that the training with ACRE using the games was fun and the robot training, as addition to standard therapy, was met by hardly any aversion from patients or therapists.

4.3. Economic Evaluation. The costs of ACRE therapy are currently primarily determined by the costs of the supervising therapists. The cost-utility analyses showed that for acceptable values for a QALY usual care is preferred if only the study period of six weeks is considered. However, if after the six weeks of the intervention the improvement in quality of life in the ACRE patients compared to usual care will be maintained, the additional costs per QALY will decrease, which will result in the ACRE being already preferred for values of the willingness to pay below €40.000 per QALY. Within this respect, further study with a longer follow-up period to prove its effectiveness. The attempt for a third assessment moment three months after inclusion within this study was met with too many practical problems.

4.4. Future Possibilities. To turn ACRE training for frail elderly after stroke to good account, use of ACRE at a later stage of the rehabilitation may be considered, when the patient has regained a better physical condition. Careful consideration must be given as to the subgroup benefitting from this kind of training, that is, patients with impairment of the upper limb, with a reasonable physical condition. Maybe the average nursing home patient may not fit this profile and beneficiaries of ACRE training will primarily be found in a polyclinical setting. Also the aim of ACRE training has to be reconsidered. ACRE training at a later stage may be aiming less at motor recovery as such, but more at improving general functioning of the patient in daily life, leading to greater independence of the patient and improvement of quality of life.

In a more structural use of ACRE in the nursing home setting, ACRE training is depicted with little or no therapist supervision at all, resulting in a low-cost alternative additional training possibility. Further development of the ACRE system is needed to make it suitable for autonomous use, with respect to functionality, adaptability to the patient, ease of use, feedback of training results, safety, and so forth, A more simplified ACRE could even be placed at the home for further training after discharge from the nursing home.

We still think that the use of additional ACRE training may be worthwhile for a select group of patients or at a later stage of the rehabilitation process. To prove (cost-) effectiveness for this select group additional research with a larger number of participants during a longer follow-up period is needed.

5. Conclusion

This study showed that for various reasons patients were not able to participate in the ACRE training. Based on this experience, expectations for the applicability of ACRE in regular stroke rehabilitation in frail elderly early in the rehabilitation process should be on the conservative side. Especially the target group recovering in the nursing home setting consists of fragile elderly with comorbidity who may have problems of physical or cognitive nature in early stages of recovery. In total, 24 patients were included. For this small sample no significant effects of the ACRE training were found. Because of the low inclusion numbers, caution in relation to the outcomes is justified. Further improvement of the ACRE can best be focused on making the system suitable for self-training and on development of training software for activities of daily living.

Acknowledgments

The authors thank Professor H. J. M. Cools, M.D., Ph.D., for making this study happen, because of his believe that also the frail elderly in nursing homes have the right to state-of-the art rehabilitation including robotic equipment. He retired from his function as a Medical Director of De Bieslandhof and Professor at Leiden University Medical Centre halfway this study. We also thank the staff involved at the two Dutch nursing homes and rehabilitation centres: De Bieslandhof, Pieter van Foreest at Delft and Antonius Binnenweg, Laurens at Rotterdam for their time. The study was partially funded by ZonMw, The Netherlands organisations for health research and development (Grant no. 17099109).

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