Daily Functioning and Quality of Life in a Randomized Controlled Trial of Therapeutic Exercise for Subacute Stroke Survivors

Stephanie Studenski, MD, MPH; Pamela W. Duncan, PhD, FAPTA; Subashan Perera, PhD; Dean Reker, RN, PhD; Sue Min Lai, PhD; Lorie Richards, PhD, FAOTA

Background and Purpose—The ability of therapeutic exercise after stroke to improve daily functioning and quality of life (QOL) remains controversial. We examined treatment effects on these outcomes in a randomized controlled trial (RCT) of exercise in subacute stroke survivors.

Methods—This is a secondary analysis of a single-blind RCT of a 12-week program versus usual care. Baseline, post-treatment and 6-month post-treatment daily functioning and QOL were assessed by Barthel index, Functional Independence Measure, instrumental activities of daily living, Medical Outcomes Study short-form 36-item questionnaire (SF-36), and Stroke Impact Scale (SIS).

Results—Of 100 randomized subjects, 93 completed the postintervention assessment, (mean age 70; 54% male; 81% white; mean Orpington Prognostic Score 3.4), and 80 had 6-month post-treatment assessment. Immediately after intervention, the intervention group improved more than usual care in SF-36 social function (14.0 points; \( P = 0.0051 \)) and in SIS (strength [9.2 points; \( P = 0.0003 \)], emotion [5.6 points; \( P = 0.0240 \)], social participation [6.6 points; \( P = 0.0488 \)], and physical function [5.0 points; \( P = 0.0145 \)]). Treatment was marginally more effective on Barthel score (3.3 points; \( P = 0.0510 \)), SF-36 (physical function [6.8 points; \( P = 0.0586 \)], physical role function [14.4 points; \( P = 0.0708 \)], and SIS upper extremity function (7.2 points; \( P = 0.0790 \)). Effects were diluted 6 months after treatment ended.

Conclusion—This rehabilitation exercise program led to more rapid improvement in aspects of physical, social, and role function than usual care in persons with subacute stroke. Adherence interventions to promote continued exercise after treatment might be needed to continue benefit. (Stroke. 2005;36:1764-1770.)

Key Words: disability ■ exercise ■ quality of life ■ rehabilitation ■ stroke

Poststroke exercise interventions should improve functional status and quality of life (QOL).1–3 Evidence supporting the clinical impact of therapeutic exercise after stroke is limited and equivocal with the quality constrained by heterogeneity of participants, interventions, and outcome measures and by methodological concerns.1–3 Interventions may be offered in the acute, subacute, or chronic phase of stroke and may include aerobic training, strength training, functional activities, or other strategies. Exercise studies in stroke survivors and older adults in general tend to capture effects on intermediate outcomes such as strength and physical abilities rather than on more integrated indicators such as functional status and QOL.4 Common methodological limitations in stroke rehabilitation trials include failure to implement concealed allocation, blinding of the assessors, and intention to treat analyses, all of which help reduce bias in the findings.1–3,5 To examine the benefits of a structured, progressive, physiologically based exercise intervention on recovery in persons with subacute stroke using trial methods recommended to overcome previous concerns, we designed and completed a randomized single-blind clinical trial.6 This study used a reproducible intervention of strength, endurance, balance, and upper extremity and functional training, and incorporated the key aspects of research methodology noted above. It targeted persons during natural recovery <6 months after stroke. The study found significant benefits on primary outcomes of impairments and functional limitations such as endurance, balance, and mobility. The purpose of this report.
was to describe the effects on daily functioning and QOL. Effects immediately and 6 months after treatment are examined.

Methods
The design and methods for this trial have been published previously and are summarized here.

Design
This is a prospective, randomized, single-blind clinical intervention trial. The University of Kansas institutional review board, and each participating facility approved the study.

Subjects
The source of trial participants was the Kansas City Stroke Registry, made up of 17 participating facilities. Registry eligibility criteria included clinical stroke diagnosis consistent with the World Health Organization definition, confirmed by clinical assessment or imaging, age ≥50, stroke onset within 3 to 28 days, and residence within 50 miles. Trial eligibility criteria were: (1) stroke within 30 to 150 days; (2) independently ambulates 25 feet; and (3) mild-to-moderate stroke deficits by Fugl-Meyer Score of 27 to 90,11 Orpington Prognostic Score (OPS) of 2.0 to 5.2, and palpable wrist extension, and Mini-Mental Status Exam score ≥16. Each subject’s primary care physician approved participation in the study.

Measures
Stroke severity was assessed using the OPS.8 Outcome measures of daily functioning included the Functional Independence Measure (FIM),10 Barthel index,11 Lawton and Brody instrumental activities of daily living (ADL),12 and gait speed thresholds (0.8 m/s) for community ambulation.13 Measures of QOL included subscales of the Stroke Impact Scale (SIS)14 and the Medical Outcomes Study short-form 36-item questionnaire (SF-36).15 Potential cofactors included demographics, stroke severity by OPS at entry to the Stroke Registry within 2 weeks of the event, and previous functional status as covariates to obtain adjusted group differences. A covariance analysis was performed, with treatment group as the primary factor and baseline measurement, stroke severity, and comorbidity between completers and noncompleters (n = 7) or between intervention and usual care groups (Table 1). Six months after treatment, noncompleters (n = 20) were more likely to be receiving Medicare and entered the study sooner after their stroke than continued participants (n = 80) (data not shown). Subject screening, exclusion, and dropout are reported in the Figure.

Results
Participants were diverse in gender, ethnicity, and socioeconomic status, had mild-to-moderate deficits, prevalent comorbidity conditions, and no differences in demographics, stroke severity, or comorbidity between completers and noncompleters (n = 7) or between intervention and usual care groups (Table 1). Six months after treatment, noncompleters (n = 20) were more likely to be receiving Medicare and entered the study sooner after their stroke than continued participants (n = 80) (data not shown). Subject screening, exclusion, and dropout are reported in the Figure.

The intervention and usual care groups demonstrated recovery of function over the 3 months between study entry and postintervention assessment. Each group increased the proportion of participants who were independent in basic ADLs (Barthel score) and who were independent in community ambulation. Both groups demonstrated increasing scores in motor FIM, SF-36, and SIS scales. Immediate post-treatment outcomes are shown in Table 2. Multiple imputation is used to account for missing data attributable to losses to reduce bias attributable to differences between noncompleters and persisters. The gains in the intervention group were greater than in usual care in every domain and were significantly greater for SF-36 social function, SIS strength, emotion, social participation, and physical function. Treatment was marginally more effective for Barthel score, SF-36 physical function, physical role

Statistical Analysis
A covariance analysis was performed, with treatment group as the primary factor and baseline measurement, stroke severity, and previous functional status as covariates to obtain adjusted group differences. The effect of adjusting for other covariates on main comparisons was investigated in additional analyses. Standardized means differences (SMDs) were computed by dividing group differences by within-group SD to quantify the effect size.17 For dichotomous outcomes, similar analyses were performed using logistic models instead of general linear models. To account for possible missing value bias, multiple imputation was performed.18 Five imputations for each missing value were generated, resulting in 5 imputed data sets. Next, each data set was analyzed using the above-described methods. Finally, results from the 5 analyses were combined to obtain intervention effects, SIs, and P values. Sensitivity analyses (data not shown) suggested no significant differences in effects based on various approaches to missing data.
function, and SIS upper extremity function. There were no detectable effects on the motor or cognition scales of the FIM or on instrumental ADL (IADL) score.

Effect sizes are presented in Table 2. The effect size (SMD) was 0.31, 0.43, and 0.61 for physical function, physical role, and social function (SF-36), respectively, and 0.59, 0.39, 0.27, 0.32, and 0.35 for strength, emotion, upper extremity, social participation, and physical function (SIS), respectively. The proportion of participants considered independent in self-care (Barthel index ≥95) after the interven-
tion period was 29 of 44 (67.4%) in the intervention arm and 21 of 49 (45.7%) in the usual care arm, for a difference of 21.7%. Community ambulation (gait speed ≥0.8 m/s) was achieved in 25 of 44 (56.8%) of the intervention and 20 of 49 (42.6%) of usual care participants, for a benefit attributable to the treatment alone of 14%.

Longer-term benefit was assessed in 80 participants 6 months after intervention (Table 3). Participants in the intervention group were given written guidelines for a structured home program and were encouraged to exercise but without supervision or ongoing effort to promote adherence. The benefits of the intervention were dissipated by 9 months, largely because of continued recovery among the usual care participants. For example, average SF-36 physical function score improved only slightly from 56 to 58.9 in the intervention group, whereas it increased from 43.7 to 51.0 in the usual care group.

**Discussion**

This therapeutic exercise intervention for stroke survivors in the subacute phase of recovery appears to accelerate gains in function and QOL in the early months after completing usual acute rehabilitation. The intervention produced greater gains and higher rates of independence immediately after the intervention than did usual care. Much of the benefit appeared to have dissipated by 6 months after intervention, largely because of continued recovery in the usual care group and a plateau in functioning in the intervention group.

The effect of therapeutic exercise on function and QOL is much less clear than its effect on impairments and physical
TABLE 2. Immediate Effects of the Intervention Adjusted for Age, Prestroke Physical Function, and Stroke Severity, and Baseline Measurement of Outcome With Multiple Imputation for Dropouts

<table>
<thead>
<tr>
<th>Intervention Group (n=44) Mean (SD)</th>
<th>Usual Care Group (n=49) Mean (SD) or n (%)</th>
<th>Adjusted Comparison of Intervention vs Usual Care</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Intervention Group</td>
<td>Usual Care Group</td>
</tr>
<tr>
<td>Lawton IADL score</td>
<td>22.8 (3.2)</td>
<td>21.8 (3.9)</td>
</tr>
<tr>
<td>Barthel ADL index</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total score</td>
<td>94.4 (6.7)</td>
<td>89.6 (10.4)</td>
</tr>
<tr>
<td>Achieved 95+</td>
<td>29 (67.4)</td>
<td>21 (45.7)</td>
</tr>
<tr>
<td>Community ambulation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.8+ m/s</td>
<td>25 (56.8)</td>
<td>20 (42.6)</td>
</tr>
<tr>
<td>FIM</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cognitive score</td>
<td>33.7 (1.1)</td>
<td>33.6 (1.2)</td>
</tr>
<tr>
<td>Motor score</td>
<td>84.5 (5.8)</td>
<td>81.9 (8.3)</td>
</tr>
<tr>
<td>SF-36</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Physical function</td>
<td>56.0 (22.1)</td>
<td>43.7 (21.2)</td>
</tr>
<tr>
<td>Role-physical</td>
<td>44.2 (33.6)</td>
<td>27.2 (33.3)</td>
</tr>
<tr>
<td>Social function</td>
<td>79.9 (21.0)</td>
<td>62.8 (24.6)</td>
</tr>
<tr>
<td>SIS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Strength</td>
<td>66.1 (14.4)</td>
<td>56.1 (16.7)</td>
</tr>
<tr>
<td>Memory and thinking</td>
<td>85.6 (15.7)</td>
<td>78.2 (22.0)</td>
</tr>
<tr>
<td>Emotion</td>
<td>83.0 (12.1)</td>
<td>76.5 (16.2)</td>
</tr>
<tr>
<td>Communication</td>
<td>85.4 (17.9)</td>
<td>81.3 (18.3)</td>
</tr>
<tr>
<td>ADL/IADL</td>
<td>79.2 (16.3)</td>
<td>73.0 (16.1)</td>
</tr>
<tr>
<td>Mobility</td>
<td>76.3 (16.2)</td>
<td>71.7 (16.4)</td>
</tr>
<tr>
<td>Upper extremity</td>
<td>66.7 (27.0)</td>
<td>57.7 (26.7)</td>
</tr>
<tr>
<td>Social participation</td>
<td>66.6 (22.9)</td>
<td>58.2 (18.5)</td>
</tr>
<tr>
<td>Physical function</td>
<td>72.1 (15.0)</td>
<td>64.6 (14.0)</td>
</tr>
<tr>
<td>SIS-16</td>
<td>81.3 (14.2)</td>
<td>75.3 (14.5)</td>
</tr>
</tbody>
</table>

*p<0.05; †p<0.01; ‡p<0.001.

performance. In a recent meta-analysis of home-based stroke rehabilitation intervention trials, substantial heterogeneity of populations and interventions was found.19 Overall benefit, estimated using the SMD, was 0.14 for basic ADL and 0.17 for IADL compared with our estimate of 0.38 for basic daily functioning by Barthel score and 0.10 for IADL. None of the 3 recent pooled analyses of stroke rehabilitation based on studies completed by 2002 reported effect sizes for QOL indicators; whereas our estimates range from 0.31 to 0.61 for SF-36 and 0.12 to 0.59 for stroke-specific SIS scales.1,3 More recent intervention studies have had mixed results. Aerobic training during the subacute phase of stroke recovery produced gains in performance and conditioning but did not directly impact daily function and social activities at 6 months after stroke.20,21 A treadmill and overground walking program for persons with chronic stroke produced gain in walking but not handicap using the sickness impact profile.22 An early intensive intervention based on increased daily duration of exercise during the first 2 weeks after hospitalization did not produce gains in ADL by Barthel index at 2 weeks or 6 months.23 A high-intensity strength training program compared with stretching in chronic stroke survivors produced significant differences in lower extremity strength and in 3 of 10 subscales of the late life disability index, with treatment differences attributable to improvements in the exercisers and declines in the comparison group.24 Our multimodal exercise program produced gains in impairments and functional limitations such as endurance, balance, and mobility,6 which may have influenced aspects of daily functioning and QOL. The main differences between our intervention and that offered in the usual care group were the inclusion of aerobic training, the explicit progression of all types of exercise, and the increased attention. We do not know what combination of these treatment differences produced the observed effects. Our results contribute to the evidence supporting the benefit of supervised exercise for daily functioning and QOL after stroke.

Our intervention appears to accelerate recovery in the subacute phase compared with usual postrehabilitation community care but did not provide sustained benefit 6 months later. More rapid return to community ambulation and improved QOL may provide additional months of reduced caregiver stress and personal satisfaction that have societal and personal value. Most of the eventual loss of treatment effect by 9 months after randomization was attributable to the continued recovery of the usual care group, with little additional change in the intervention group. We do not know whether the intervention group reached a plateau of functional...
TABLE 3. Six-Month Posttreatment Effects of the Intervention Adjusted for Age, Prestroke Physical Function, Stroke Severity, and Baseline Measurement of Outcome With Multiple Imputation for Dropouts

<table>
<thead>
<tr>
<th>Intervention Group (n=40) Mean (SD) or n (%)</th>
<th>Usual Care Group (n=40) Mean (SD) or n (%)</th>
<th>Adjusted Comparison of Intervention vs Usual Care</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lawton IADL Score</td>
<td></td>
<td>Difference (SE)/OR 95% CI SMD</td>
</tr>
<tr>
<td>23.2 (3.7)</td>
<td>22.4 (4.3)</td>
<td>0.26 (0.69) −1.12 to 1.63 0.06</td>
</tr>
<tr>
<td>Barthel ADL Index</td>
<td></td>
<td>−1.50 (2.13) −5.97 to 2.97 −0.17</td>
</tr>
<tr>
<td>Total score</td>
<td></td>
<td>0.46</td>
</tr>
<tr>
<td>Achieved 95+</td>
<td></td>
<td>0.16 to 1.35</td>
</tr>
</tbody>
</table>

Community ambulation

0.8+ m/s

20 (54.1) 14 (38.9) 1.09 0.32 to 3.68...

FIM

Cognitive score 33.9 (6.0) 33.5 (2.00) 0.33 (0.35) −0.37 to 1.03 0.22

Motor score 84.5 (6.2) 82.6 (10.5) 0.83 (1.47) −2.13 to 3.80 0.10

SF-36

Physical function 58.9 (22.7) 51.0 (22.9) 2.74 (4.30) −5.83 to 11.32 0.12

Role-physical 50.0 (37.6) 40.0 (32.9) 12.4 (7.66) −2.71 to 27.57 0.35

Social function 80.6 (19.2) 70.0 (26.2) 8.29 (4.97) −1.63 to 18.21 0.36

SIS

Strength 61.1 (14.4) 62.4 (14.7) −0.39 (2.77) −5.90 to 5.12 −0.03

Memory and thinking 82.4 (17.3) 78.1 (20.2) 0.16 (2.63) −5.39 to 5.08 0.01

Emotion 81.1 (14.1) 80.2 (16.8) −1.18 (2.99) −7.12 to 4.75 −0.08

Communication 84.7 (15.5) 81.8 (19.2) 0.41 (2.12) −4.62 to 3.80 0.07

ADL/IADL 79.6 (14.8) 73.1 (18.3) 0.71 (2.49) −4.22 to 5.64 0.04

Mobility 75.7 (15.8) 73.5 (18.2) 1.80 (2.63) −7.03 to 3.43 0.11

Upper extremity 64.9 (25.6) 58.9 (28.7) 4.15 (4.38) −4.55 to 12.85 0.15

Social participation 72.0 (20.2) 66.5 (22.4) 2.41 (4.00) −5.54 to 10.37 0.11

Physical function 70.3 (14.2) 67.0 (16.0) 0.50 (2.12) −3.72 to 4.70 0.03

SIS-16 80.9 (13.7) 75.9 (15.7) 0.18 (2.01) −3.81 to 4.17 0.01

*0.05 < P < 0.10; †0.01 < P < 0.05; ‡P < 0.01

capacity earlier than the usual care group or whether explicit support for continued exercise might have sustained a treatment benefit. Our intervention did not support participants during the transition to self-maintained exercise or record adherence to exercise in the postintervention phase. Self-maintenance of exercise after a supervised program may require explicit attention to motivational and cognitive behavioral strategies that we did not incorporate into our program.25

The effects of spontaneous recovery on outcomes, observed mostly in acute and subacute stroke and less in chronic stroke, must be considered when evaluating clinical trials of exercise in stroke. In clinical trials of stable chronic stroke patients, the lack of spontaneous gains in the comparison group makes between-group treatment effects easier to detect because controls are not improving. Chronic stroke trials are less relevant to real-world poststroke rehabilitation services. Interventions are probably best tested in populations still in the recovery phase and should expect to detect spontaneous gains in controls.

This study has numerous strengths. It is fairly large and offers a physiologically based and highly reproducible intervention that could be implemented by others using our protocols. Outcome assessment was blinded, as was treatment allocation, and primary analyses were performed with multiple imputation to reduce missing data bias. The participants represent a clinically relevant group of stroke survivors: those who return to the community with significant stroke deficits after completing acute rehabilitation. The study also has limitations. Participants could not be blinded to treatment assignment. Because virtually all measures of daily functioning and QOL are based on self-report, knowledge of treatment assignment could bias findings. There were also differences in the amount of attention paid to participants in the 2 arms; treatment participants had more direct contact time from research staff than did usual care participants. We attempted to reduce the attention effect by providing structured visits with tangible benefits to the usual care group. By the final 9-month assessment, we had lost 20% of participants because of medical and nonmedical causes. Losses create missing data, which can bias findings. We attempted to examine potential bias through sensitivity analyses.

Summary

A structured exercise intervention during the subacute phase of stroke recovery resulted in accelerated gains in daily
functioning and QOL compared with usual care, but additional benefit of the intervention had dissipated by 6 months after the intervention. Earlier recovery of function may have benefit to stroke survivors. Effective exercise interventions in rehabilitation, as in other types of exercise programs, might need to be more explicitly coupled to a motivational adherence intervention for continued benefit.

Acknowledgments

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