

ORIGINAL REPORT

COMORBIDITY IN PATIENTS AFTER STROKE: IMPACT ON FUNCTIONAL OUTCOME

Altınay Goksel Karatepe, MD, PhD, Rezzan Gunaydin, MD, PhD, Taciser Kaya, MD, PhD and Gul Turkmen, MD

From the Izmir Training and Research Hospital, Department of Physical Medicine and Rehabilitation, Izmir, Turkey

**Objective:** To evaluate the incidence of comorbid diseases and their impact on functional outcome in patients after stroke.

**Design:** A prospective study.

**Subjects:** A total of 140 patients after stroke.

**Methods:** Comorbidities were assessed with the Liu comorbidity index. Functional independence was evaluated using the Functional Independence Measure (FIM™). The relationship between comorbidities and functional outcomes were investigated. The impact of comorbidities on functional outcome was examined with multiple stepwise regression analysis.

**Results:** Ninety-four (67%) of 140 patients completed the study. The most frequent comorbid condition was hypertension at the initial visit. The weighted comorbidity index at baseline was negatively correlated with the follow-up FIM™ score and functional gain. Multiple regression analysis revealed that follow-up FIM™ score could be best explained by FIM™ at admission and the contribution of the weighted comorbidity index to functional outcome was 3.1%.

**Conclusion:** Comorbid diseases are common among patients after stroke. They were shown to have a negative correlation with functional outcome; however, their impact on functional outcome was not clear. The proper evaluation of comorbid conditions should be included in stroke outcome research.

**Key words:** comorbidity, functional outcome, stroke.

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*Correspondence address:* Altınay Goksel Karatepe, Izmir Eğitim ve Araştırma Hastanesi, Fizik Tedavi ve Rehabilitasyon Kliniği, Bozyaka, Izmir, Turkey. E-mail: altinaygoksel@yahoo.com

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INTRODUCTION

Stroke causes a considerable clinical, social and economic burden (1). There is a high incidence of coexisting medical disorders among patients recovering from stroke. If severe, or if poorly managed, these disorders may interfere with the patient's participation in the rehabilitation programme and may adversely affect the outcome of rehabilitation. Optimal management of comorbid conditions may accelerate recovery and reduce the cost of medical care (2).

Measuring comorbidity is an aspect of research that is receiving increasing attention in the current literature. Several authors

have discussed and compared the use of various selected methods to measure comorbidity (3–6). De Groot et al. (7) suggested that there were 13 different methods used to measure comorbidity; only 6 indices have been developed for clearly defined diagnoses. In this paper, it has been mentioned that there were 3 indices used to evaluate patients after stroke: the Charlson Index (8), the Shwartz Index (9), and the Liu Index (10). The Charlson Comorbidity Index (CCI) has been validated for ischaemic stroke outcome studies (11). However, it was originally developed for patients in acute hospital settings, and it focused on mortality, not functional impairment. The Shwartz Index consists of 21 weighted conditions and evaluates the negative influence of comorbid conditions on the treatment of the primary condition, including stroke, lung disease, heart disease, prostate disease, low back disorders, and hip fracture (9). The Liu Index was constructed specifically for use in stroke outcome research (10). Its validity and reliability for stroke outcome studies was shown in 2 different studies (10, 12). There are many studies that have investigated the relationship between comorbid conditions and survival of patients after stroke (13–17). However, the existence of prospectively collected data on comorbid conditions and their impact on stroke outcome are rare.

The aim of this study was to evaluate the incidence of comorbid diseases and their impact on functional outcome in patients after stroke. The Liu Index was selected for this purpose, which was specific for stroke and appeared to be advantageous and a valid indicator of stroke outcome research. We hypothesize that a negative correlation will be observed between the comorbid diseases and functional outcome.

METHODS

*Subjects*

A total of 140 patients participated in the study. All patients were seen within one week of a stroke event during the inpatient period at the neurology service. Stroke was defined according to World Health Organization (WHO) criteria (18); diagnosis was confirmed by clinical history, neurological examination, and imaging via computed tomography or magnetic resonance imaging. We excluded patients with bilateral hemiplegia, lack of motor involvement, and those with a history of stroke. All patients were taken through an exercise programme by a physiotherapist during the inpatient period at the neurology service. An appropriate home-based exercise programme was provided to each patient for 4 weeks after they were discharged from the hospital. The home-based exercise programme duration was 2–5 h a day, for 5 days a week. This conventional stroke rehabilitation programme consisted

of proper positioning of extremities, passive range of motion exercises, passive stretching, and muscle strengthening exercises. All patients and their primary caregivers were given detailed information and were instructed to perform an appropriate home-based exercise programme. Moreover, the patients and caregivers were given information about self-care activities and exercises designed to help perform activities of daily life. Patients who completed the exercise programme were invited for a control visit at the physical medicine and rehabilitation service.

#### Demographic variables and clinical outcome

At the baseline assessment, age, gender, and type and side of the cerebral lesion were documented for each patient. Stroke severity was determined using the Canadian Neurological Scale (CNS) (19), which is designed to assess neurological function in patients after stroke. The scale includes an assessment of level of consciousness, orientation, aphasia, and motor strength. Each domain is assigned both a score and total score from 0 to 11.5; a higher score indicates better neurological performance.

Functional disability was assessed using the Turkish version of the Functional Independence Measure (FIM<sup>TM</sup>) (20) at both the baseline examination and the follow-up visit. The FIM<sup>TM</sup> is an 18-item measurement that evaluates the following parameters: self-care, sphincter control, mobility, locomotion, communication, and social cognition. The items on the FIM<sup>TM</sup> are scored on a 7-point ordinal scale that ranges between 1 and 7. The minimum range of the scores on the FIM<sup>TM</sup> is 18, which indicates a low level of functioning; the maximum range of scores is 126, which indicates a very high level of functioning. Functional gain was recorded as the difference between the FIM<sup>TM</sup> score at baseline and the FIM<sup>TM</sup> score at follow-up visit (fu-FIM). Data were collected by direct observation of the patient and, when necessary, by interview with relatives.

#### Comorbidities

The type, incidence and severity of comorbidities were studied by patient's history, physical examination and a structured form to collect information. The comorbidities were assessed with the comorbidity index (CI) of Liu et al. (12) and the weighted comorbidity index (w-CI) calculated at both the initial and follow-up visits. The CI of Liu consists of 41 conditions that are arranged according to the 13 main diagnostic categories, and is specifically constructed for use in stroke outcome research. Each comorbid condition is rated on a 6-point scale, ranging from 0 to 5 according to the need for treatment and limitations on daily activities and/or exercise. We counted the total number of comorbidities, which gives the CI score, and calculated w-CI, which consists of the sum of the weighted scores. We also studied the changes of grading for individual comorbidities.

#### Statistical analysis

The Kolmogorov-Smirnov test was used to check for a normal distribution of data. Values were expressed as mean with standard deviation (SD) for the normal distribution or as median and range for the non-parametric data. The correlation between CI and w-CI, and their relationship with functional scores and CNS score were calculated with the Spearman's rank correlation coefficient. The frequencies of the comorbidities were tabulated. The Wilcoxon signed-ranks test was performed to determine the presence of FIM<sup>TM</sup> improvement and CI changes during the follow-up period. Multiple regression analysis using stepwise procedure was performed to examine the impact of comorbidities on the fu-FIM score and to determine the most predictive comorbid condition for the w-CI. In the fu-FIM model, selected independent variables were FIM<sup>TM</sup>, w-CI and CNS scores at the initial visit. In the w-CI model, independent variables were selected according to the results of the Spearman's correlation analysis. The SPSS statistical program was used in the analysis of data. Significance was set as  $p < 0.05$ .

All patients and primary caregivers were given detailed information concerning the purpose of the study and gave their verbal informed consent to participate in the study.

## RESULTS

Ninety-four (67%) of 140 patients who enrolled in the study completed a home-based exercise programme. Eighteen patients stated that they could not attend the control visit, due to their own (12 patients) and/or caregivers' (6 patients) health problems. We could not contact 7 patients, due to changed telephone numbers and/or postal address. We contacted 12 patients by telephone, but for various reasons they did not agree to attend the follow-up visit. Nine patients were excluded from the study due to death. A description of stroke characteristics of the 94 patients is provided in Table I.

The most frequent comorbid condition of our patients was hypertension, followed by constipation, hyperlipidaemia, diabetes mellitus and electrocardiographic (ECG) abnormalities at the initial visit. At the follow-up visit the most frequent comorbid condition was hypertension, followed by shoulder pain, hyperlipidaemia, constipation, diabetes mellitus and osteoarthritis. The list of comorbid conditions and their frequencies are given in Table II. The median number of comorbid conditions per person was 5, at both the baseline and the control visit. Most of our patients had comorbidities graded as 2 or below, 80.8% of our patients had a low comorbidity score.

It was observed that, in comparison with baseline assessment, there were statistically significant improvements in the FIM<sup>TM</sup> scores and CNS scores at the follow-up visit ( $p = 0.000$ ).

Table I. Characteristics of patients and changes of disease characteristics during the follow-up period

	Initial visit	Follow-up visit	p-value
Age, years, mean (SD)	66.5 (10.8)	–	–
Sex, men/women	43/51	–	–
Lesion side, right/left	47/47	–	–
Days from stroke onset, days, mean (SD)	32.7 (5.2)	–	–
Total FIM <sup>TM</sup> score, median (range)	45 (18–126)	79.5 (19–126)	0.000
Motor FIM <sup>TM</sup> score, median (range)	21 (13–91)	53 (13–92)	0.000
Cognitive FIM <sup>TM</sup> score, median (range)	22.5 (5–35)	30 (6–35)	0.000
CI, median (range)	5 (0–13)	5 (1–14)	>0.05
w-CI, median (range)	8 (0–22)	8 (0–22)	>0.05
CNS, mean (SD)	6.4 (2.5)	8.3 (2.7)	0.000

FIM: Functional Independence Measure; CI: Comorbidity Index; w-CI: weighted Comorbidity Index; CNS: Canadian Neurological Scale; SD: standard deviation.

Table II. Comorbid conditions and their frequencies

Comorbid conditions	Initial visit, %	Follow-up visit, %
Hypertension	79.8	83.0
Constipation	44.7	39.4
Hyperlipidaemia	34.0	40.4
Diabetes mellitus	27.7	27.7
ECG abnormality	26.6	23.4
Osteoarthritis	26.6	30.9
Visual impairment	25.5	20.2
Shoulder pain	24.5	44.7
Depression	21.3	27.7
Neurogenic bladder	18.1	11.7
Gastritis	13.8	20

ECG: electrocardiographic.

However, we did not find any significant changes in the CI and w-CI scores (Table I). Analysis of the individual comorbid conditions showed that there were statistically significant differences in the scores of the shoulder pain, gastritis, vision impairment and neurogenic bladder. There was an increase in the scores of patients with shoulder pain ( $p=0.001$ ) and those with gastritis ( $p=0.018$ ) and a decrease in the scores of patients with neurogenic bladder ( $p=0.045$ ) and those with vision impairment ( $p=0.020$ ). In the multiple stepwise regression analysis, the most important factor in explaining w-CI was ECG abnormalities; this was followed by myocardial infarction and hyperlipidaemia ( $w\text{-CI}=7.088+1.802\times\text{ECG abnormality}+1.542\times\text{myocardial infarction}+1.503\times\text{hyperlipidaemia}$ ) ( $r^2=0.317$ ,  $p=0.045$ ).

A negative correlation was found between the fu-FIM and w-CI scores at baseline. The fu-FIM scores were also correlated with the FIM<sup>TM</sup> scores at baseline and the CNS scores at baseline. Functional gain was negatively correlated with the w-CI, whereas the FIM<sup>TM</sup> scores at baseline were correlated neither with the comorbidities nor with the CNS score (Table III). Multiple stepwise regression analysis revealed that the fu-FIM could be best explained by FIM<sup>TM</sup> at admission; this variable explained 45% of the variation in fu-FIM scores. The contribution of the other independent variables, such as CNS score and w-CI, were 5.8% and 3.1%, respectively ( $r^2=0.553$ ,  $p=0.000$ ) (Table IV).

Table III. Correlations between comorbid conditions, functional outcomes and stroke severity

	fu-FIM	FIM <sup>TM</sup> baseline	FIM <sup>TM</sup> gain	CI	w-CI	CNS
fu-FIM	1	0.583†	0.706†	-0.139	-0.180*	0.685†
FIM <sup>TM</sup> baseline		1	-0.017	-0.041	-0.051	0.763†
FIM <sup>TM</sup> gain			1	-0.146	-0.173*	0.149
CI				1	0.938†	0.076
w-CI					1	0.106
CNS						1

\* $p<0.01$ , † $p<0.001$ .

FIM: Functional Independence Measure, fu-FIM: follow-up Functional Independence Measure, CI: Comorbidity index, w-CI: weighted comorbidity index, CNS: Canadian Neurological Scale.

Table IV. Results of multiple regression analysis with follow-up FIM<sup>TM</sup> as the dependent variable

	Estimated coeff			95% CI for regression coeff	
	$\beta$	SE	$p$ -value	Lower bound	Upper bound
Constant	33.675	7.874	0.000	18.033	49.317
FIM <sup>TM</sup> baseline	0.378	0.138	0.007	0.104	0.652
w-CI baseline	6.340	1.520	0.000	3.321	9.360
CNS baseline	-1.657	0.551	0.003	-2.751	-0.563

FIM: Functional Independence Measure; w-CI: weighted comorbidity index; CNS: Canadian Neurological Scale; 95% CI: 95% confidence interval; SE: standard error; coeff: coefficient.

## DISCUSSION

In this study, comorbidities were shown to have a negative correlation with functional outcome and functional gain in patients after stroke. The comorbid conditions seen most frequently in our patients were hypertension, constipation, and hyperlipidaemia at the initial visit; hypertension, shoulder pain, and hyperlipidaemia were seen at the control visit.

Although there are many comorbid conditions in patients after stroke, there have been few studies into the effects of comorbid conditions on functional outcome, and the results are contradictory. Giaquinto (21) investigated the relationship between comorbid conditions and functional outcome in patients after stroke. They used the Cumulative Illness Rating Scale to investigate comorbid diseases and found that there was a negative correlation between severity of comorbid conditions and FIM<sup>TM</sup> score, both at discharge and on admission. In another study, Goldstein et al. (11) investigated the effects of comorbid conditions on functional outcome in patients after stroke using modified Charlson Index-weighted scores. In this study, the authors stated that both functional outcomes at discharge and 1-year mortality rates were associated with the number and severity of comorbid diseases. In a prospective study in which patients with acute ischaemic stroke were assessed using CCI (22), the authors found that high stroke severity on admission, atrial fibrillation, and 2 CCI items (coronary artery disease and diabetes) predicted an unfavourable outcome; however, CCI itself was not a significant predictor. The authors noted that it was wiser to analyse individual comorbidities rather than a global comorbidity index. In Japanese studies, Liu et al. (10, 12) found that CI and w-CI correlated negatively with discharge FIM<sup>TM</sup> scores. In the regression model, the 6.6% of variance was explained by w-CI scores, while CI did not significantly relate to FIM<sup>TM</sup> discharge scores. Ferriero et al. (23) investigated the effects of comorbid conditions and complications on functional outcome by CI. The authors reported that there was a negative correlation between weighted scores and discharge FIM<sup>TM</sup> score, and admission FIM<sup>TM</sup> score was the most powerful predictor of the functional outcome. They also stated that the contribution of the weighted score to the functional outcome was 4% in a regression model. A negative correlation between the w-CI and fu-FIM scores has been found according to our results. In the multiple regression analysis, w-CI was negatively associated with the functional

outcome, explaining the 3.1% of variance. Nevertheless, the FIM™ score on admission has been determined as the best predictor of fu-FIM. In previous studies, it has been shown that functional status on admission was a stronger predictor of functional outcome (24–26).

The results of the studies that investigated the relationship between comorbid conditions and functional gain were uncertain. Although there were some studies (21, 27) that suggested no relationship between functional gain and comorbidities; there were others (23, 28) that showed a negative effect of comorbid conditions on functional gain. According to our results, a negative correlation between functional gain and comorbid diseases has been found.

Gresham et al. (29) reported hypertension, hypertensive cardiovascular disease, coronary heart disease, obesity, diabetes mellitus, arthritis, left ventricular hypertrophy by ECG, and congestive heart failure as more frequent comorbidities in stroke patients. Fisher et al. (22) prospectively followed up 266 patients with acute ischaemic stroke. In this study, it has been found that the most frequent comorbid condition was a previous cerebrovascular event, followed by coronary artery disease, diabetes and tumour. In another study, Studenski et al. (24) also reported musculoskeletal diseases, diabetes mellitus, and cardiovascular diseases as more frequent comorbid conditions. Giaquinto (21) showed that the most frequent impairments in the major organ groups were neurological and cardiovascular. In the study of Liu et al. (12), it has been observed that hypertension ranked first, followed by shoulder pain, diabetes mellitus, constipation, dental problems, and atrial fibrillation. Similar to these findings, the most frequent comorbid conditions we observed were hypertension, followed by constipation, hyperlipidaemia, diabetes, and ECG abnormalities. Common findings in all these studies were that the most frequent comorbid conditions in patients after stroke were cardiovascular diseases and diabetes mellitus. In our study it has been determined that the comorbid diseases that most frequently contributed to weighted comorbidity index were ECG abnormalities, myocardial infarction and hyperlipidaemia. These diseases were also determined risk factors for stroke.

It has been reported that the presence of comorbid diseases is one of the determinants of the final functional status achieved (30). Cardiovascular diseases, such as uncontrolled hypertension, angina, myocardial infarction, significant atrial or ventricular arrhythmia, and congestive heart failure, occur in 40% of patients after stroke during inpatient rehabilitation (31). Roth (32) has reported that patients with a history of congestive heart failure may have a more limited functional outcome, compared with patients without congestive heart failure. A transient reactive hyperglycaemia could appear in patients with diabetes mellitus during the acute stroke period. Many diabetic patients who were previously managed with diet or oral anti-hyperglycaemic agents require insulin to control glucose. This may make it more difficult to participate in stroke rehabilitation (31). However, Lew et al. (33) have stated that when the stroke risk factors were eliminated, other medical comorbidities did not significantly affect discharge

FIM™ score and FIM™ change. The authors also indicated that if the patients had only minor medical problems, they could continue therapy daily without interruption or delay. In another study, it has also been indicated that heart diseases could adversely affect patient's ability to participate in a therapeutic exercise programme and achieve favourable outcomes; however, for diabetes mellitus and hypertension it might not be accurate (34). Most of our patients (80.8%) had a low comorbidity score. The comorbid conditions that were seen most frequently in our patients were hypertension, constipation, hyperlipidaemia, diabetes mellitus, and ECG abnormalities. The percentage of patients who had comorbid conditions graded as 3 or 4 were 15%, 0%, 0.7% and 2.8% for hypertension, constipation and hyperlipidaemia, diabetes mellitus, and ECG abnormalities, respectively. Therefore, the degree of relationship between comorbidities and functional outcome might be low in our study.

Our study has some limitations that warrant consideration. Firstly, the CI, which is used to measure comorbid conditions in our study, has been developed originally in patients with post-acute stage who underwent an inpatient rehabilitation programme. However, patients after stroke in acute phase were recruited in this study and their functional statuses were evaluated after the short-term (4 weeks) home-based exercise programme. Secondly, our patients had a low comorbidity score. Thirdly, our sample size was slightly small. Fourthly, a relatively high drop-out rate (33%), primarily due to follow-up compliance was observed in our study. However, a comparison of baseline variables for individuals who dropped out vs those who remained in the study has been indicated that both groups shared similar baseline characteristics, including comorbid conditions. These limitations may reduce internal validity and limit the conclusions.

Despite these limitations, our results confirm those of previous studies, which indicated that comorbid conditions are frequent in patients after stroke and also showed that comorbidities have a negative relationship with the functional outcome of stroke. There is a need for more studies with long-term follow-up and with greater numbers of patients with different comorbidities. Nevertheless, we conclude that the results of our study will be helpful in stroke outcome studies because of its prospective nature.

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