Effect of Comorbidity on Functional Recovery in Patients with Stroke

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Original Article

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Objectives: Stroke is a vital cause of acute neurological dysfunction. This study evaluated the prevalence of comorbidities and their effects on functional recovery in patients with stroke.

Methods: This was a prospective study. The participants were 105 patients with acute stroke with moderate to severe functional disability who were admitted for comprehensive rehabilitation. The participants were 76 patients who underwent the Post-acute Care-Cerebrovascular Diseases program and 29 participants who accepted a regular rehabilitation program within 6 months after stroke. The effect of each comorbidity on the patients' post-hospitalization daily living activities was analyzed based on the Charlson Comorbidity Index (CCI).

Results: For each 1-point increase in a patient's CCI score, there was a 0.97-point decrease in the patient's score on the Barthel Index (BI) after discharge (p = 0.013). An analysis of 19 comorbidities showed that the order of highest prevalence was diabetes (21%), prior cerebrovascular accident with mild or no residual or transient ischemic attack (17.1%), and diabetes with end-organ damage (14.3%). An analysis of the effect of the various comorbidities on the patients' daily living activities indicated that the most harmful disease was chronic pulmonary disease (leading to a decrease of discharge BI scores by 35.50 points; p = 0.004), followed by prior history of hemiplegia (leading to a decrease of discharge BI scores by 18.51 points; p = 0.002).

Conclusions: Comorbidities, especially chronic pulmonary disease and hemiplegia, can affect the functional recovery and daily living activities of patients with stroke. Other comorbidities, including osteoarthritis and arrhythmia, need to be investigated. A comorbidity index should be established for patients with stroke. (Tw J Phys Med Rehabil 2018; 46(1): 27 - 35)

Key Words: acute cerebrovascular disease, comorbidity, functional recovery

INTRODUCTION

Ischemic and hemorrhagic strokes are vital causes of acute neurological dysfunction. Approximately 15 million people experience from stroke worldwide annually. Of

those, approximately 5 million die and another 5 million are left permanently disabled, placing a burden on families and communities.[1] Stroke is the third most common cause of death in developed countries, exceeded only by coronary heart disease and cancer. Stroke is the second leading cause of death in people older than 60 years, and the fifth leading cause in people aged 15–59 years.[2] Numerous studies have examined stroke-related clinical symptoms, complications, and potential physiological responses. However, researches on factors that influence functional recovery have mainly focused on age, stroke type/severity, depression, nutrition, and cognitive functions.[3,4] Little systematic research has been conducted on the effects of comorbidities on functional recovery in patients with stroke.[5,6] Stroke cases are often accompanied by comorbidities.[7] Although the relationship between comorbidities and post-stroke functional outcomes can be directly intuited, few studies have evaluated the independent influencing factors of comorbidities.[8,9] Most studies have focused on the relationship between comorbidities and the stroke survival rate.[10-15] A 2016 study indicated that the comorbidity index is a poor predictor of the community discharge and functional status of patients following post-acute rehabilitation (including patients with stroke).[16]

The use of different methods and samples may produce different results, and related research is lacking in Taiwan. Regarding comorbidity, different evaluation, selection, and weighting methods can be applied. No comorbidity evaluation scale has yet been developed specifically for patients with stroke, and most studies have applied Charlson Comorbidity Index (CCI) scores.[8,9,17] Furthermore, the effect of comorbidities on functional recovery after stroke has not been studied. Therefore, this study investigated the effects of different comorbidities on the progress of daily living activities in patients with stroke after comprehensive rehabilitation.

MATERIAL AND METHODS

Participants

This was a prospective observational cohort study. Participants in this study were patients with acute stroke with moderate to severe functional disability (modified Rankin Scale, mRS: 3–5) who underwent comprehensive rehabilitation at the Yangming Branch of Taipei City Hospital in Taipei, Taiwan. Data from 105 patients were collected between July 2014 and December 2015. Seventy-six participants participated in the Post-acute Care-Cerebrovascular Diseases (PAC-CVD) program promoted by the National Health Insurance Administration. These participants demonstrated a stable medical condition within 1 month after an acute exacerbation of stroke as well as the potential for effective rehabilitation and active participation in the rehabilitation program. Patients with adequate family support were preferred. Another 29 participants were hospitalized and underwent a regular rehabilitation program within 6 months after stroke. All the participants accepted comprehensive rehabilitation, which included the daily administration of physical therapy and occupational therapy for 1 hour, 5 days a week and speech therapy for 30 minutes, 2 days a week. The two groups differed in their disease onset and days of hospitalization. The participants signed a consent form approved by an ethics committee.

Research Design

Each participant's age, days since disease onset, days of hospitalization, overall functional disabilities, comorbidities, cognitive function (based on the Mini-Mental State Examination [MMSE] at admission), and depression (based on the 5-item Brief Symptom Rating Scale (BSRS-5) at admission) were recorded. Furthermore, we recorded whether tubing, including nasogastric (NG) tubes and urinary catheters, was removed during each patient's hospital stay. Overall functional disabilities were assessed using the mRS, wherein overall functional states are divided into seven levels, with 0 indicating no symptoms, 3 indicating moderate disability (requiring some help, but able to walk without assistance), 4 indicating moderately severe disability (unable to walk and attend to bodily needs without assistance), 5 indicating severe disability (bedridden, incontinent, and requiring constant nursing care and attention), and 6 indicating death. This study focused on patients with acute stroke with moderate to severe functional disability (mRS: 3–5).

Barthel Index (BI) scores at hospital admission and at discharge were used to evaluate the degree of recovery of daily living activities, and to assess whether each patient could live independently. The BI is widely used in rehabilitation and geriatrics. The scale consists of 10 evaluation items, of which eight are related to self-care (feeding, transfers, grooming, bathing, dressing, toilet use, and the presence or absence of fecal or urinary incontinence) and two are related to mobility (walking and climbing stairs). The participants' capacities to engage in these daily living activities were studied through direct observation during their hospital stay. A score of 100 points indicated that the patient did not require care and was independent in daily life. Because the Barthel scale has a substantial ceiling effect,[18] a recovery percentage (%) was added as [(BI score improvement/BI at admission) x 100%]. For example, if the BI at admission = 30 and the BI at discharge = 75, then the improvement = 45 and % recovery = 45/30, or 150%, indicating that based on the comparison of daily living function at admission and at discharge, the patient had recovered by 150%. This value indicates the patient's degree of recovery in comparison with the patient's daily living function at the moment of hospital admission.

Comorbidities

The CCI was used to evaluate the comorbidities,[19] and records were made according to the International Classification of Diseases, Ninth Revision, Clinical Modification code. Drawing from the literature, 19 diseases were selected for the CCI. Overall scores were obtained by assigning a weighted score of 1, 2, 3, or 6 depending on the associated risk of death. The CCI is widely used in research on multiple diseases related to stroke. The diseases among the sample in this study were cerebrovascular accident (CVA) with mild or no residual or transient ischemic attack (TIA) and hemiplegia, which were recorded by prior history before the stroke.

Statistical Analyses

This study utilized the SPSS Statistics software package (Version 21). An independent t test and linear regression were used for analyzing the predictors of functional improvement and the relationship between comorbidities and the performance of daily living activities (discharge BI) in the patients. Statistical significance was indicated by $p < 0.05$.

Table 1: Characteristics of the participants in the two groups

	post-acute care(n=76)	Control(n=29)	p value
Age	65.6±13.5	60.8±13.8	0.891
Onset weeks	2.5±0.8	15.4±12.0	<0.001[c]
Stay days	58.9±22.9	32.5±21.0	0.001[c]
mRS on admission	3.8±0.5	3.9±0.8	0.229
Charlson Comorbidity score (CCI)	3.4±1.4	3.7±1.4	0.941
MMSE at admission	24.0±6.2	21.1±9.7	0.016c
BSRS-5 at admission	2.9±3.1	2.1±3.0	0.252
Tract remove %[a]	78(n=9) ±44.1	33(n=3) ±57.7	0.543
BI admission [b]	41.8±24.5	37.2±26.5	0.311
BI discharge	75.5±20.5	47.2±27.1	0.008[c]
BI improvement	33.75±19.7	10±11.4	<0.001[c]
% recovery	140%±170%	40%±60%	0.015[c]

[a] Tracts refer to NG and Foley

[b] % recovery: improvement/BI admission × 100%

[c] p < 0.05: statistical significance

Abbreviations: BI, Barthel Index

Table 2. Effect of comorbidities on the patients' performance in daily living activities

Comorbidity			95% Wald CI		
	Prevalence (%)	beta	Lower	Upper	p value
Myocardial infarct	11.4	10.60	-9.50	30.60	0.301
Congestive heart failure	8.6	-2.30	-24.80	20.30	0.845
Peripheral vascular disease	11.4	9.98	-5.78	25.73	0.210
CVA with mild or no residua or TIA	17.1	-12.04	-24.33	0.24	0.060
Dementia	2.9	-5.88	-30.45	18.70	0.640
Chronic pulmonary disease	2.9	-35.50	-52.86	-18.13	0.004 [a]
Connective tissue disease	1.0	27.30	16.08	38.52	0.001 [a]
Peptic ulcer disease	7.6	-9.49	-31.05	12.06	0.390
Mild liver disease	1.0	-1.21	-8.69	6.26	0.750
Diabetes	21.0	4.91	-5.95	15.77	0.380
Hemiplegia	2.9	-18.51	-30.11	-6.92	0.002 [a]
Moderate or severe renal disease	3.8	16.63	-7.13	40.38	0.170
Diabetes with end-organ damage	14.3	11.31	-8.68	31.29	0.267
Tumor without metastasis	1.9	41.37	16.75	65.99	0.001 [a]
Leukemia	0.0	0.00			
Lymphoma	0.0	0.00			
Moderate or severe liver disease	0.0	0.00			
Metastatic solid tumor	0.0	0.00			
AIDS (not just HIV positive)	0.0	0.00			

Prevalence: disease item detection rate in the patients with stroke

Dependent variable: Barthel Index score at discharge

Beta value: every point that the effective factor can increase or decrease the independent variable

[a] $p < 0.05$: statistical significance

Abbreviations: CI, confidence interval

RESULTS

The post-acute care group included 76 patients with stroke who participated in the PAC-CVD program. The control group included 29 patients who underwent regular rehabilitation within 6 months after acute stroke. The average number of weeks since stroke onset for each group was 2.5 and 15.4 for the post-acute care group and control group, respectively; the average age was 65.6 and 60.8 years, respectively; the average mRS score indicating overall functional condition was 3.8 and 3.9 points, respectively; the average CCI score was 3.4 and 3.7, respectively; and the average BSRS-5 score indicating depression was 3.1 and 2.1, respectively. No significant difference was observed in these results (Table 1). The removal rate of indwelling tubes, namely NG tubes, Foley catheters, and tracheostomy tubes, was recorded. Due to a lack of participants with tracheostomy tubes, only the removal of NG and Foley tubes was studied, and no significant difference was observed between the two groups.

After the PAC-CVD program intervention, the average BI scores increased from 41.8 at admission to 75.5 at discharge (the average progress was 33.7 points). The patients in the control group had an average BI score of 37.2 at admission and 47.2 at discharge (the average progress was 10 points). The results indicated no significant difference between the admission BI scores of the two groups (post-acute care:control = 41.8:37.2; p = 0.311), whereas their discharge BI scores (post-acute care:control = 75.5:47.2; p = 0.008) showed a significant

difference. The functional recovery rate of daily living activities in the post-acute care group was equal to [(BI score improvement/BI at admission) x 100%] and was significantly higher than that of the control group (post-acute care:control = 140%:40%; p = 0.015). The post-acute care group outperformed the control group in terms of cognitive function at admission, with average MMSE scores equal to 24.0 and 21.1 points, respectively (p = 0.016).

The variables used to evaluate the factors influencing the patients' performance in activities of daily living (discharge BI) were based on items from the CCI. The results revealed that for each 1 point increase in the patients' degree of comorbidity (CCI score), their daily living ability score decreased by 0.97 points (p = 0.013), indicating that comorbidity affected post-hospital daily living activities. Therefore, the 19 comorbidities included in the CCI were further analyzed. No participants had the following five comorbidities in the CGI: leukemia, lymphoma, moderate or severe liver disease, metastatic solid tumor, and acquired immune deficiency syndrome. Therefore, the prevalence of such diseases was equal to 0. The diseases with the highest prevalence among the sample were diabetes (21%), CVA with mild or no residual or TIA (17.1%), and diabetes with end-organ damage (14.3%). An analysis of the effects of the comorbidities on the patients' performance in activities of daily living revealed that the most harmful disease was chronic pulmonary disease (leading to a 35.50 point decrease in discharge BI scores; p = 0.004), followed by hemiplegia (leading to a 18.51 point decrease in discharge BI scores; p = 0.002). A prior history of CVA was found to affect the patients' post-hospitalization daily living activities. In comparison with those without a prior history of CVA, their discharge BI scores were 12.04 points lower (p = 0.06). Although these results were not statistically significant, they indicated a certain tendency (Table 2). Connective tissue disease and tumor without metastasis were found to be related to an improvement in the patients' post-hospitalization daily living activities (discharge BI scores increased by 27.3 in the post-acute care group and 41.37 points in the control group).

A two-tailed bivariate correlation analysis of the patients' weeks since disease onset and discharge BI scores (*one tail: p < 0.05; **two tail: p < 0.001) indicated a significantly moderate negative correlation between the number of weeks from disease onset to hospitalization and discharge BI scores (Pearson r = −0.319, p < 0.001). The statistical analysis revealed that the longer the time from disease onset to hospitalization was, the worse the patient's living function.

DISCUSSION

In this study, 76 patients with stroke participated in a post-acute care program. Twenty-nine patients underwent regular rehabilitation within 6 months after acute stroke. No difference was found between the two groups in terms of background factors, namely age, daily living ability (BI at admission), disability (mRS), comorbidity (CCI), and depression (BSRS-5). This study found that discharge BI scores were higher in patients with a longer hospital stay, indicating a higher improvement in their independent daily living activities. The average BI scores in the post-acute care group increased from 41.8 to 75.5 points; this progress was significantly higher than that in the group of patients who underwent regular rehabilitation within 6 months after stroke (p = 0.008). The patients' degree of recovery at discharge compared with their condition at admission was higher in the post-acute care group (post-acute care:control = 1.4:0.4; p = 0.015) (Table 1). No significant difference was found in terms of indwelling tube removal (the removal of NG tubes and urinary catheters).

Comorbidities affected the patients' post-hospitalization daily living activities, with discharge BI scores decreasing by 0.97 with each 1 point increase in CCI scores (p = 0.013). This indicated that higher CCI scores were related to a decrease in post-hospitalization daily living activities. Among the 19 diseases, the two that had the greatest effect on the performance of daily living activities were chronic pulmonary disease (which reduced discharge BI scores by 35.50 points) and hemiplegia (which reduced discharge BI scores by 18.51 points) (Table 2). Comorbidities such as diabetes, CVA with mild or no residual or TIA, and diabetes with end-organ damage were characterized by highest prevalence rates and strong correlations with stroke. Patients with connective tissue disease and tumor without metastasis had a relatively high improvement in daily

living function after discharge. An analysis of the reasons for such findings revealed the following. Only one participant had connective tissue disease (specifically, rheumatoid arthritis), and it was well controlled using immunosuppressive drugs. Only two participants had tumors without metastasis; one had nasopharyngeal cancer and the other had tongue cancer. In both patients, the tumor was completely removed, and both received treatment and underwent regular follow-up checks for recurrence. Because the number of these cases was small, and because they had effective control over their corresponding diseases, and a positive personality, high motivation to recover, and adequate family support, these patients were able to show considerable progress in their daily living activities after comprehensive rehabilitation.

Furthermore, this study found longer periods from disease onset to hospitalization resulted in a decrease in the BI scores at discharge. This indicated that, under a stable condition, earlier post-acute rehabilitation was associated with a higher chance of the patients recovering their performance in daily living activities.

The CCI was originally developed in acute medicine to predict mortality and morbidity rates. Thus, its use in assessing the prognosis of functional recovery is often questioned. An earlier study found that the CCI can be applied in short-term prognosis for patients with stroke; higher CCI scores indicated a worse prognosis,[17] and the comorbidities with the highest prevalence were cerebrovascular disease, diabetes, and chronic heart failure, findings which were similar to the results in this study. However, the previous study did not indicate which comorbidity was the main factor affecting functional recovery.

This study is the first to analyze the effects of comorbidities on functional recovery after comprehensive rehabilitation in patients with stroke in Taiwan. Comorbidities were found to negatively influence the performance in daily living activities at discharge. Moreover, based on CCI scores, the functional recovery of the patients with stroke was strongly correlated to chronic pulmonary disease and prior hemiplegia. One study applied the Liu Comorbidity Index to evaluate comorbidity and found that the most common comorbidity suffered by patients with stroke was hypertension; however, the Liu Comorbidity Index scores

and performance were negatively related.[20] Mohamed investigated the relationship between comorbidity and duration of hospital stay and disabilities in cases of patients with ischemic stroke. The most common comorbidity among patients with ischemic stroke was hypertension, followed by smoking and diabetes. Patients with congestive heart failure, chronic kidney disease, atrial fibrillation, or other arrhythmia had a longer hospital stay, but this was not correlated with the degree of disability.[21] Disabilities in that study were evaluated using mRS, whereas the current study used the BI to evaluate independent daily living activities at discharge. However, arrhythmia is a potential factor that could influence disability. Roth found that functional recovery in patients with a history of congestive heart failure is limited.[22] Piernik-Yoder found that patients with stroke and diabetes demonstrated a relatively poor rehabilitation outcome; however, the influence of diabetes decreased with age.[23] Apart from the 19 comorbidities listed in the CCI, the functional recovery of patients with ischemic stroke is also affected by cardiac autonomic dysfunction.[24]

This study has several limitations. First, not all comorbidities that potentially relate to stroke—such as anemia, hypertension, hyperlipidemia, arrhythmia (especially atrial fibrillation), cardiac autonomic dysfunction, osteoarthritis, peripheral nerve disease, and osteoporosis, all of which may be related to progress in functional recovery—were included in the CCI. Second, the sample—particularly of patients with connective tissue disease, tumors, moderate to severe liver disease, and acquired immune deficiency syndrome—was small. Thus, their relationships to the improvement of daily living activities were difficult to examine. Third, the participants in the post-acute care group who accepted comprehensive rehabilitation were generalized earlier than in the control group, and cognition function in the post-acute care group was higher than that in the control group; therefore, the progress may have been higher, and not only related to hospital stay. Fourth, we did not evaluate the correlations among the outcome and severity of stroke, lesion site, or management. Perhaps, the stroke type and lesion site affect the relationship between the comorbidities and functional recovery. Fifth, discharge BI scores were used in this study to evaluate daily living

activities. However, the effects on long-term function were not investigated. Future studies should consider recruiting more participants, examining more comorbidities and their relationships to functional recovery, and conducting follow-up checks for long-term function.

CONCLUSION

Living function deteriorated as the number of weeks from disease onset increased. Therefore, it is strongly suggested that patients with stroke undergo post-acute rehabilitation as early as possible to ensure a sounder functional recovery. Furthermore, comorbidities, especially chronic pulmonary disease and prior history of hemiplegia, were found to affect the functional recovery and the performance of daily living activities of the patients. The effects of other comorbidities, such as osteoarthritis and arrhythmia, remain to be studied. The comorbidity index for patients with stroke should be developed to predict their rehabilitation results.

DISCLOSURE

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腦中風病患共病症與功能恢復之影響

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　　目的：腦中風是導致急性神經功能障礙的重要原因，本研究探討腦中風患者共病症盛行率和功能恢復之影響。

　　方法：本研究為前瞻性研究，研究對象為中度至重度功能障礙急性腦中風患者，共收集 105 位病患接受高強度復健，根據察爾森共病症嚴重度指數分析每項共病症與患者出院生活能力之影響。

　　結果：腦中風患者其察爾森共病症嚴重度指數每增加一分，出院時巴氏量表會減少 0.97 分(p=0.013)。在 19 項共病症之中，盛行率最高的依序是糖尿病(21%)、曾經腦中風或是暫時性腦缺血病史(17.1%)和糖尿病合併終端器官損壞(14.3%)。共病症對腦中風患者生活能力的影響分析中，發現影響最大的是慢性肺部疾病，之前有偏離病史次之。

　　結論：腦中風患者共病症會影響功能恢復及生活能力，尤其是慢性肺部疾病與中風之前有過半側偏癱病史，其他相關的共病症像是退化性關節炎或是心律不整等問題則需要再研究，期許未來可以建立一個屬於腦中風病人的共病症指標。（台灣復健醫誌 2018；46(1)：27 - 35）

關鍵詞：急性腦血管疾病(acute cerebrovascular disease)，共病症(comorbidity)，功能恢復(functional recovery)