Effectiveness of Stroke Rehabilitation Compared between Intensive and Nonintensive Rehabilitation Protocol: A Multicenter Study

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> Background and aim: Stroke is one of the leading causes of death, physical disability, and economic burden. Nowadays, various types of rehabilitation are available. Rehabilitation centers in Thailand provide services in different ways, including starting time, duration, and frequency of each therapy. In addition, many rehabilitation wards have a standing policy to reduce length of stay (LOS) due to economic considerations. This study aimed to compare the effectiveness and efficiency between intensive and nonintensive rehabilitation protocol for stroke patients. Methods: This prospective, multicenter cohort study was conducted among stroke patients who admitted to rehabilitation wards at 14 centers. All participants received either intensive or non-intensive rehabilitation program. Barthel Index (BI) at admission (BIad), BI at discharge (BIdc), and LOS were recorded. The effectiveness was difference in BIdc and BIad score (Δ BI), and the efficiency was Δ BI divided by LOS (Δ BI/LOS). *Results:* Seven hundred and eighty stroke patients were included. Mean age was 61.9 ± 13.3 years, and 59.7% were male. The majority of patients (79.5%) were admitted for intensive rehabilitation. Effectiveness and efficiency were significantly higher in the intensive group than in the nonintensive group (4.5 \pm 3.4 versus 2.6 \pm 3.2 and .24 \pm .30 versus .18 \pm .33, respectively). LOS, intensive rehabilitation, and quality of life were significantly positively correlated with effectiveness; whereas, age, onset to admission interval (OAI), and Blad were significantly negatively correlated with the effectiveness of stroke rehabilitation. Conclusions: Stroke patients admitted for intensive rehabilitation had better effectiveness and efficiency than those admitted for non-intensive rehabilitation. Younger patients with shorter OAI, lower BIad, and longer LOS realized significantly enhanced effectiveness.

Key Words: Stroke—Rehabilitation—Effectiveness—Efficiency © 2020 Elsevier Inc. All rights reserved.

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Introduction

Stroke is one of the leading causes of death, physical disability, and economic burden.^{1,2} Most stroke survivors have enduring motor disability, which often results in activity limitation and participation restriction.³ Approximately 40% of stroke patients were discharged to inpatient rehabilitation services.⁴ Well-organized postacute care with interdisciplinary rehabilitation would help to improve the ability of stroke survivors.^{5,6} Rehabilitation programs are designed on a patient-to-patient basis according to each patient's level of disability and learning ability. Although there are fundamental principles of rehabilitation for each type of disability, rehabilitation protocols can vary from center to center. Stroke recovery outcome depends on many factors, including age, severity of stroke, comorbidity, cognitive function, duration of disease, and family support.^{7,8} Rehabilitation service, which provides an effective rehabilitation program using organized and accepted practice guidelines, is one of the factors that contributes to good functional recovery in stroke survivors.²

There are currently many types of rehabilitation service available, including very early rehabilitation, early intensive rehabilitation, extended rehabilitation service, and home-based rehabilitation. Many studies have been conducted to evaluate the effectiveness of rehabilitation after stroke. Previous studies reported that early mobilization of acute stroke patients reduces complications related to immobility and decreases hospital length of stay.^{9,10} Biernaskie, et al reported that early rehabilitation after stroke enhances brain recovery, but that this effect declines over time.¹¹ In contrast, Langhorne, et al conducted a multicenter, randomized controlled trial study to evaluate the effect of routine care (the normal poststroke care protocol at each center) compared to very early rehabilitation after stroke (defined as starting less than 24 hours after onset, and performed 3 sessions each day in addition to usual care). Their results showed that routine stroke care had more favorable outcomes at 3 months.¹² Yaqi et al retrospectively collected data from the national acute care inpatient database in Japan relative to ischemic stroke patients that received post-stroke rehabilitation during April 2012 to March 2014. They found that early rehabilitation (starting within 3 days after admission) and intensive rehabilitation (more than 5 rehabilitation units/day, 1 unit = 20 minutes) both associated with good functional recovery.¹³ Similarly, Kinoshita, et al found rehabilitation with a frequency of 7 days per week to be associated with favorable functional recovery in patients with acute stroke.14

Rehabilitation centers in Thailand provide services in different ways, including starting time, duration, and frequency of each therapy. Nowadays, only 14 rehabilitation centers in Thailand have provided the inpatient rehabilitation. After acute stroke care, most of stroke patients are

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referred back to community hospital which could not provide intensive rehabilitation, only few patients are transferred to rehabilitation ward for rehabilitation in the same admission. Due to limitation of rehabilitation bed in each center, some stroke patients receive rehabilitation program late, may be 2-3 months after the onset of stroke. In addition, many rehabilitation wards have a standing policy to reduce length of stay due to economic considerations. Thus, these factors have an effect on the outcome of rehabilitation program, the aim of this study was to determine the effectiveness and efficiency of rehabilitation in stroke patients in Thailand compared between intensive and non-intensive rehabilitation admission protocol.

Methods

This prospective, multicenter cohort study enrolled stroke patients admitted for inpatient rehabilitation at 14 different rehabilitation units located across Thailand. This study was part of a Key Performance Indicator project that aimed to report the effectiveness of inpatient rehabilitation at 2 rehabilitation centers, 7 university hospitals, and 5 general hospitals.¹⁵ The protocol for this study was approved by the Institutional Review Board of each participating center, and complied with the principles set forth in the Declaration of Helsinki (1964) and all of its subsequent amendments. Written informed consent was obtained from all participating subjects.

Type of admission was categorized as either intensive or nonintensive rehabilitation. Patients admitted for intensive program could tolerate rehabilitation at least 3 hours per day, 5 days per week. Patients admitted for nonintensive satisfied 1 or more of the following criteria: (1) patient could tolerate less than 2 hours per day; (2) patients admitted for investigation; (3) patients admitted so that their caregiver could receive caregiver skills training; and/or, (4) patients admitted to be treated for complications.

Patient characteristics, such as age, gender, onset to admission interval (OAI), type of admission, rehabilitation impairment category, and comorbidities were collected and recorded. Complications that developed during rehabilitation were also recorded, including urinary tract infection, musculoskeletal pain, deep vein thrombosis, pressure ulcer, and spasticity. Quality of life (QoL) was assessed both at admission and at discharge using EQ-5D-3L.¹⁶ This tool consists of 5 dimensions, including mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Each dimension has 3 response options, as follows: no problems, some/moderate problems, and unable/extreme problems. The higher the overall QoL score, the higher the patient's QoL. Functional outcomes were evaluated using Barthel Index (BI) score at admission (BIad) and at discharge (BIdc). BI score ranges from 0-20, with a higher score indicating a greater degree of patient independence.¹⁷ Length of stay (LOS) was also recorded. Effectiveness was

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calculated using the following equation: $\Delta BI = BIdc$ minus BIad. Efficiency was calculated using the following equation: ΔBI divided by LOS. Factors related to effectiveness were also analyzed by univariate and multivariate analysis.

Statistical Analysis

Data analysis was performed using PASW Statistics (SPSS) 18.0 (SPSS Inc., Chicago, IL). Demographic data were summarized using descriptive statistics. Categorical data was presented as number and percentage, and continuous data was presented as mean \pm standard deviation or median and range. Student's t test was used to compare effectiveness and efficiency of stroke patients during rehabilitation between intensive and nonintensive types of admission. Univariate analysis was performed to individually evaluate the significance of each factor. The factors related to the effective of rehabilitation were analyzed using Student's t test and 1-way analysis of variance for categorical data. Pearson's and Spearman's rank correlation were applied for continuous data. All factors with a P value of less than .05 in univariate analysis were included in multiple linear regression analysis. A P value less than .05 was regarded as being statistically significant.

Results

Seven hundred and eighty stroke patients from 14 rehabilitation centers were included. Mean age was 61.9 ± 13.3 years, and 59.7% were male. The median OAI was 2.0 months (range: 0.03-360). Left and right side of body was involved in 45.8% and 44.0% of cases, respectively. Most patients (79.5%) were admitted for intensive rehabilitation program. Approximately one-fourth of patients developed complications during the rehabilitation period (Table 1).

Effectiveness and efficiency of stroke patients during rehabilitation by type of admission is shown in Table 2. Mean effectiveness (Δ BI) of stroke patients after rehabilitation was 4.1 ± 3.5, with a mean LOS of 27.9 ± 17.3 days.

 Table 1. Demographic and clinical data of 780 stroke patients

 admitted for rehabilitation

Variables	(N = 780)
Gender, n (%)	
Male	466 (59.7%)
Female	314 (40.3%)
Age, mean \pm SD	61.9 ± 13.3
Onset admission interval (months),	2.0 (.03-360)
median (range)	
Onset admission interval (months),	8.5 ± 25.7
mean \pm SD	
Rehabilitation impairment category, n (%)	
Left body	357 (45.8%)
Right body	343 (44.0%)
Bilateral	67 (8.6%)
Other stroke	13 (1.7%)
Type of admission, n (%)	
Intensive	620 (79.5%)
Less intensive	64 (8.2%)
Investigation	3 (.4%)
Caregiver training	44 (5.6%)
Treat complication	4 (.5%)
Others	45 (5.8%)
Having complication during	182 (23.3%)
rehabilitation, n (%)	

Abbreviation: SD, standard deviation.

Mean efficiency was $.23 \pm .31$ per day of admission. Stroke patients admitted for intensive program had significantly higher BIad, BIdc, effectiveness, and efficiency scores than patients admitted for nonintensive program. LOS was longer in the intensive program group, but the difference between groups was not statistically significant.

Relative to the effectiveness of rehabilitation services for stroke patients, LOS, intensive rehabilitation admission, and increased QoL were found to be significantly positively correlated with effectiveness; whereas, age, OAI, and Blad were significantly negatively correlated with the effectiveness of stroke rehabilitation (Table 3).

Variables	Total cases (N = 780) Mean \pm SD	Types of	P value	
		Intensive $(n = 620)$ Mean \pm SD	Nonintensive* $(n = 160)$ Mean \pm SD	
BI admission	7.6 ± 4.7	8.0 ± 4.5	6.2 ± 5.4	<.001
BI discharge	11.7 ± 5.5	12.5 ± 5.0	8.8 ± 6.2	<.001
Effectiveness [†]	4.1 ± 3.5	4.5 ± 3.4	2.6 ± 3.2	<.001
Length of stay	27.9 ± 17.3	28.5 ± 17.1	25.9 ± 18.0	0.099
Efficiency [‡]	$.23 \pm .31$	$.24 \pm .30$	$0.18 \pm .33$.032

Table 2. Effectiveness and efficiency of stroke patients during rehabilitation by type of admission

Abbreviations: \triangle , change/difference; BI, Barthel Index; LOS, length of stay; SD, standard deviation.

A P value < .05 indicates statistical significance.

The bold and italic values indicates statistical significance.

*Nonintensive included less-intensive, investigation, caregiver training, and treat complications.

[†]Effectiveness = \triangle BI.

[‡]Efficiency = (\triangle BI/LOS).

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Table 3. I	Factors related to	the effectiveness	(mean $\triangle BI$) o	f rehabilitation in stroke	patients $(N = 780)$
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Variables	Ν	Univariate analysis		М	ultivariate analy	ysis
		Change in BI score				
		Mean \pm SD	P value	b	SE (b)	P value
Gender			.290			
Female	314	3.93 ± 3.25				
Male	466	4.20 ± 3.59				
Age (years)	780	r =152	<.001	042	.011	<.001
LOS (days)	780	r = .138	<.001	.025	.007	.001
OAI (months)	767	r=368	<.001	010	.005	.027
Type of admission			<.001			
Nonintensive	160	2.58 ± 3.24				
Intensive	620	4.48 ± 3.41		1.203	.332	<.001
complication during admission			.619			
No	598	4.12 ± 3.44				
Yes	182	3.98 ± 3.51				
BI _{ad}	780	r =126	<.001	177	.030	<.001
\triangle QoL (EQ-5D)			<.001			
No change or decreased	189	2.73 ± 2.96				
Increased	372	5.05 ± 3.54		2.235	.284	<.001
Type of medical facility			.993			
University hospital	233	4.08 ± 3.69				
Rehabilitation center	354	4.08 ± 3.49				
General hospital	193	4.11 ± 3.10				

Abbreviations: BI, Barthel Index; EQ-5D, Euro quality of life 5 dimensions; LOS, length of stay; OAI, onset to admission interval; QoL, quality of life; SD, standard deviation; SE, standard error.

A P value < .05 indicates statistical significance.

The bold and italic values indicates statistical significance.

Discussion

The results of this study show that stroke patients admitted for intensive program had better outcomes than those admitted for nonintensive program, including functional score, effectiveness, and efficiency. This difference between groups may be explained by the fact that intensive program patients could tolerate at least 3 hours of rehabilitation per day, which is longer than the duration of daily rehabilitation received by nonintensive group patients. Chan, et al reported that higher-intensity rehabilitation program reduced costs and improved outcomes in stroke patients.¹⁸ Imura, et al found that early and intensive rehabilitation program had a positive effect on functional improvement in stroke patients with no increase in adverse events.¹⁹ A 2014 Cochrane Review in functional recovery of stroke after rehabilitation revealed that highdose rehabilitation consisting of 30-60 minutes per day, 5-7 days per week yielded more benefit.⁶ Nonintensive rehabilitation program is suitable for patients who are thought to have a low potential for rehabilitation, such as patients that require more time for recovery. This lowpotential patient population is also at higher risk for development of complications that could interfere with the intended rehabilitation outcome. Especially in limited resource settings, the appropriate selection and allocation of cases admitted for inpatient rehabilitation into high

and low-intensity programs is cost-effective and yields better functional outcomes. In 2017, Pattanasuwanna and Kuptniratsaikul performed a retrospective study of outcomes of stroke patients receiving rehabilitation program during 2010-2014. They found that patients admitted for intensive program gained more effectiveness and efficiency than those who received non-intensive program.²⁰

Concerning factors related to effectiveness or mean change in BI score, this study found LOS, intensive type of admission, and increased QoL score to be significantly positively correlated with effectiveness; while, age, OAI, and BIad were significantly negatively correlated with effectiveness of rehabilitation in stroke patients. BI score at admission was the most informative predictor of rehabilitation outcomes.⁸ A 2017 study found that patients with a higher BI at admission had less change in BI score between admission and discharge.²⁰ This may be due to the ceiling effect of BI,^{21,22} and may not reflect actual improvement (Δ BI) compared with potential improvement after completion of rehabilitation (BI_{max}-BI_{ad}).²⁰

Specific to LOS, a 2009 multicenter study by Kuptniratsaikul, et al in 327 stroke patients receiving rehabilitation at 9 tertiary hospitals of Thailand found a longer LOS to be positively correlated with effectiveness of treatment during the rehabilitation period.²³ Teasell, et al reported that severe stroke patients with a functional independence measure score below 40 and an inability to ambulate were

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admitted to a specialized multidisciplinary rehabilitation program for a period of close to 3 months. After rehabilitation, 43% of those patients were able to return home, and 28% were no longer wheelchair dependent.²⁴

Age is an important determinant of stroke outcome. Meyer, et al found age to be strongly correlated with functional outcomes in stroke patients.⁸ Stroke during older age may have more pathology in different brain regions, so it can cause more deficits and result in more comorbidity compared to younger stroke patients.²⁵ In addition, the process of neuroplasticity is slower and poorer in an older brain than in a younger brain.²⁶ Moreover, cognitive function, particularly memory function, declines with increasing age,²⁷ so more time is needed for adaptation and for learning new information.

Regarding OAI, we found significant correlation between shorter OAI and higher effectiveness of rehabilitation treatment. Many studies demonstrated association between early admission to rehabilitation and better functional outcomes. Paolucci, et al conducted a prospective study in the outcomes of stroke patients who were admitted to rehabilitation at different times after stroke onset.²⁸ They found that stroke patients who received rehabilitation early did better functionally than those whose rehabilitation was delayed. Maulden, et al found early rehabilitation admission to be significantly associated with better functional outcomes in severe stroke, and shorter LOS in rehabilitation wards.²⁹

Another factor related to the effectiveness of rehabilitation treatment was increased QoL score after completion of rehabilitation. Many studies reported better QoL as a result of improvement in function. A 2008 multicenter study by Manimmanakorn, et al that included 9 tertiary hospitals in Thailand studied QoL after stroke rehabilitation and found that QoL evaluated by WHO-QOL-BREF questionnaire improved after inpatient rehabilitation program.³⁰ Madden, et al examined changes in functions and QoL during rehabilitation period, and found that both functional status and QoL substantially improved during the rehabilitation period.³¹ A study by Hopman and Verner assessed QoL during rehabilitation using SF-36, and found considerable gains in QoL during inpatient stroke rehabilitation. However, those improvements were not sustained, as the score declined within 6 months after discharge.32

This study is limited by the fact that we included patients treated only at centers with dedicated inpatient rehabilitation wards. As such, our findings may not be generalizable to other levels of care or other hospitals that do not offer inpatient rehabilitation services. The other limitation is the difference in characteristics of participants in each group (intensive versus intensive rehabilitation) such as Barthel's index score at the admission which influences the outcome of rehabilitation program. Moreover, this study recruited stroke patients in all stages, the high standard deviation of the onset admission interval showed the variability of the participants. The strengths of this study include its prospective design, the fact that a range of types of centers were included (7 medical schools, 5 general hospitals, and 2 rehabilitation centers), and that 4 of 6 regions of Thailand were represented. Moreover, all study participants were recruited within the same 1-year period (2012), so this data can be considered representative of the effectiveness of rehabilitation services for stroke patients in Thailand.

Summary and Conclusion

Stroke patients admitted for intensive rehabilitation had better effectiveness and efficiency than those admitted for non-intensive rehabilitation. Younger patients with shorter OAI, lower BIad, increased QoL score, and longer LOS realized significantly enhanced effectiveness.

Conflict of Interest

All authors declare no personal or professional conflicts of interest regarding any aspect of this study.

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References

- 1. Mozaffarian D, Benjamin EJ, Writing Group Members. Heart disease and stroke statistics-2016 update: a report from the American Heart Association. Circulation 2016;133:e38-360.
- Miller EL, Murray L, Richards L, et al. Comprehensive overview of nursing and interdisciplinary rehabilitation care of the stroke patient: a scientific statement from the American Heart Association. Stroke 2010;41:2402-2448.
- Anderson CS, Linto J, Stewart-Wynne EG. A populationbased assessment of the impact and burden of caregiving for long-term stroke survivors. Stroke 1995;26:843-849.
- Tian W. An All-Payer View of Hospital Discharge to Postacute Care, 2013: Statistical Brief #205. In: Healthcare Cost and Utilization Project) HCUP) Statistical Briefs [Internet], RockvilleMD: Agency for Healthcare Research and Quality) US; 2006. [cited 2017 Aug 21]. Available at: http://www.ncbi.nlm.nih.gov/books/NBK373736/ Accessed 21 August 2017.
- Hachinski V, Donnan GA, Gorelick PB, et al. Stroke: working toward a prioritized world agenda. Int J Stroke 2010;5:238-256.
- Pollock A, Baer G, Campbell P, et al. Physical rehabilitation approaches for the recovery of function and mobility following stroke. Cochrane Database Syst Rev 2014;4. CD001920.
- Denti L, Artoni A, Casella M, et al. Validity of the modified Charlson Comorbidity Index as predictor of shortterm outcome in older stroke patients. J Stroke Cerebrovasc Dis 2015;24:330-336.

- 8. Meyer MJ, Pereira S, McClure A, et al. A systematic review of studies reporting multivariable models to predict functional outcomes after post-stroke inpatient rehabilitation. Disabil Rehabil 2015;37:1316-1323.
- 9. Langhorne P, Pollock A. Stroke Unit Trialists' Collaboration. What are the components of effective stroke unit care? Age Ageing 2002;31:365-371.
- **10.** Abilleira S, Ribera A, Sánchez E, et al. The second stroke audit of catalonia shows improvements in many, but not all quality indicators. Int J Stroke 2012;7:19-24.
- Biernaskie J, Chernenko G, Corbett D. Efficacy of rehabilitative experience declines with time after focal ischemic brain injury. J Neurosci 2004;24:1245-1254.
- 12. Langhorne P, Wu O, Rodgers H, et al. A very early rehabilitation trial after stroke (AVERT): a phase III, multicentre, randomised controlled trial. Health Technol Assess 2017;21:1-120.
- **13.** Yagi M, Yasunaga H, Matsui H, et al. Impact of rehabilitation on outcomes in patients with ischemic stroke: a nationwide retrospective cohort study in Japan. Stroke 2017;48:740-746.
- 14. Kinoshita S, Momosaki R, Kakuda W, et al. Association between 7 days per week rehabilitation and functional recovery of patients with acute stroke: A retrospective cohort study based on the Japan Rehabilitation Database. Arch Phys Med Rehabil 2017;98:701-706.
- **15.** Kuptniratsaikul V, Wattanapa P, Wathanadilokul U, et al. The effectiveness and efficiency of inpatient rehabilitation services in Thailand: a prospective multicenter study. Rehabilitation Process Outcome 2016;5:13-18.
- **16.** Tongsiri S, Cairns J. Estimating population-based values for EQ-5D health states in Thailand. Value Health 2011;14:1142-1145.
- **17.** Wade DT, Hewer RL. Functional abilities after stroke: measurement, natural history and prognosis. J Neurol Neurosurg Psychiatry 1987;50:177-182.
- Chan B. Effect of increased intensity of physiotherapy on patient outcomes after stroke: an economic literature review and cost-effectiveness analysis. Ont Health Technol Assess Ser 2015;15:1-43.
- **19.** Imura T, Nagasawa Y, Fukuyama H, et al. Effect of early and intensive rehabilitation in acute stroke patients: retrospective pre-/post-comparison in Japanese hospital. Disabil Rehabil 2018;40:1452-1455.

- Pattanasuwanna P, Kuptniratsaikul V. Inpatient rehabilitation outcomes in patients with stroke at Thailand's largest tertiary referral center: a 5-year retrospective study. J Scientific Res Studies 2017;4:208-216.
- Balu S. Differences in psychometric properties, cut-off scores, and outcomes between the Barthel Index and Modified Rankin Scale in pharmacotherapy-based stroke trials: systematic literature review. Curr Med Res Opin 2009;25:1329-1341.
- 22. Kwon S, Hartzema AG, Duncan PW, et al. Disability measures in stroke: relationship among the Barthel Index, the Functional Independence Measure, and the Modified Rankin Scale. Stroke 2004;35:918-923.
- Kuptniratsaikul V, Kovindha A, Dajpratham P, et al. Main outcomes of stroke rehabilitation: a multi-centre study in Thailand. J Rehabil Med 2009;41:54-58.
- 24. Teasell RW, Foley NC, Bhogal SK, et al. A rehabilitation program for patients recovering from severe stroke. Can J Neurol Sci 2005;32:512-517.
- 25. Di Carlo A, Lamassa M, Baldereschi M, et al. European BIOMED Study of Stroke Care Group. Risk factors and outcome of subtypes of ischemic stroke. Data from a multicenter multinational hospital-based registry. The European Community Stroke Project. J Neurol Sci 2006;244:143-150.
- 26. Jones S, Nyberg L, Sandblom J, et al. Cognitive and neural plasticity in aging: general and task-specific limitations. Neurosci Biobehav Rev 2006;30:864-871.
- 27. Ruth P. Ageing and the brain. Postgrad Med J 2006;82:84-88.
- 28. Paolucci S, Antonucci G, Grasso MG, et al. Early versus delayed inpatient stroke rehabilitation: a matched comparison conducted in Italy. Arch Phys Med Rehabil 2000;81:695-700.
- 29. Maulden SA, Gassaway J, Horn SD, et al. Timing of initiation of rehabilitation after stroke. Arch Phys Med Rehabil 2005;86(12 Suppl 2):S34-S40.
- Manimmanakorn N, Vichiansiri R, Nuntharuksa C, et al. Quality of life after stroke rehabilitation among urban vs. rural patients in Thailand. J Med Assoc Thai 2008;91:394-399.
- **31.** Madden S, Hopman WM, Bagg S, et al. Functional status and health-related quality of life during inpatient stroke rehabilitation. Am J Phys Med Rehabil 2006;85:831-838.
- **32.** Hopman WM, Verner J. Quality of life during and after inpatient stroke rehabilitation. Stroke 2003;34: 801-805.