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ORIGINAL REPORT

REHABILITATION OUTCOMES OF STROKE PATIENTS WITH LOW LEFT VENTRICULAR EJECTION FRACTION IN THE SUBACUTE REHABILITATION PHASE

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Objective: **To examine the left ventricular ejection fraction in patients with subacute stroke and compare rehabilitation outcomes between those with decreased left ventricular ejection fraction and those without.**

Design: **Retrospective chart review.**

Subjects: A total of 482 consecutive patients with stroke admitted to a convalescent rehabilitation hospital.

Methods: **Patients were assessed using transthoracic echocardiography within 7 days of admission. The patients were divided into a group with low left ventricular ejection fraction and a group with preserved left ventricular ejection fraction. Functional Independence Measure (FIM) scores at admission and discharge, FIM gain, FIM efficiency, and discharge disposition were compared between groups.**

Results: **The low left ventricular ejection fraction group had significantly lower cognitive and total FIM scores on admission than the preserved left ventricular ejection fraction group. The patients in the low left ventricular ejection fraction group tended to be transferred to acute hospitals more frequently. However, the total score of discharge FIM, FIM gain, and FIM efficiency did not differ significantly between the groups when rehabilitation was continued until discharge.**

Conclusion: **Stroke patients with low left ventricular ejection fraction in the subacute phase could achieve almost the same functional outcomes as those of patients with preserved left ventricular ejection fraction. Although the general medical condition should be considered, the finding of low left ventricular ejection fraction did not pose a barrier to successful rehabilitation after stroke.**

Key words: comorbidity; risk factor; convalescent hospital; cardiac function test; heart disease.

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MAIN MESSAGE

Cardiac problems could be inhibitory factors during the course of rehabilitation in patients with stroke. We evaluated the influence of the left ventricular ejection fraction (LVEF) on activity of daily living in 482 patients with subacute stroke. The patients with a low LVEF had lower activity of daily living on admission to subacute rehabilitation units and tended to be transferred to acute hospitals more frequently than those with the preserved LVEF. However, activity of daily living on discharge and the degree of improvement from admission to discharge did not differ between the patients with low LVEF and those with preserved LVEF. The general medical condition in patients with low LVEF should be carefully considered; however, a low LVEF did not pose a barrier to successful rehabilitation after stroke.

Impaired cardiac function increases the incidence of stroke (1–6); therefore, patients with stroke may have cardiac problems as comorbidities (7), which could be inhibitory factors in rehabilitation. Several previous studies have shown that cardiac abnormalities can be associated with poor rehabilitation outcomes in patients with stroke (8–14). Karataş et al. (9) and Giaquinto et al. (10) reported that the Functional Independence Measure (FIM) score at admission and discharge, as well as the gain in FIM score (FIM gain), were significantly lower among patients with atrial fibrillation than among those without. Roth et al. (11) found that improvement in the ability to perform mobility tasks, such as rolling, moving in bed, transferring from a wheelchair to a bed, and walking improvement was less among patients with coronary artery disease than among those without. Furthermore, cognitive heart failure has a significant impact on the course and outcome of patients undergoing rehabilitation for stroke (11, 12).

Systolic function is the fundamental cardiac function that maintains adequate circulation in the body. The prevalence of echocardiographic abnormalities in 750 consecutive patients with subacute stroke who were admitted to subacute rehabilitation units in Japan was studied previously (7). Among the various indices, the left ventricular ejection fraction (LVEF) was low in 12.2% of patients. The unfavourable effect of severely low LVEF (≤35%) on rehabilitation progress and outcome of patients with stroke has been reported in

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a few studies (13, 14). Kevorkian et al. reported that patients with low LVEF had a lower discharge FIM score, lower FIM gain, and lower FIM efficiency (13). Milionis et al. reported that patients with low LVEF had a higher modified Rankin scale during both acute and chronic phases of stroke (14).

In these studies, stroke patients with severely low LVEF in the acute phase were examined for the relationship between rehabilitation outcome and the presence of low LVEF. To the best of our knowledge, no study has examined whether low LVEF influences the outcomes of patients with stroke during subacute rehabilitation. Therefore, this study aimed to examine the LVEF in subacute stroke and compare rehabilitation outcomes between those with decreased LVEF and those without.

METHODS

Participants

A total of 767 consecutive Japanese patients with cerebral infarction or cerebral haemorrhage who were transferred from an acute hospital and admitted to a Kaifukuki Rehabilitation Ward (KRW) (15) in Tokyo Bay Rehabilitation Hospital within 60 days after onset from March 2007 to October 2009 were enrolled in the study.

Inclusion criteria for analysing discharge disposition were: (*i*) first stroke; and (*ii*) unilateral cerebral lesion. Exclusion criteria were: (*i*) incomplete echocardiographic findings due to inability to follow instructions; (*ii*) measurement difficulties due to severely irregular heartbeat; and (*iii*) missing echocardiographic findings and/or admission FIM (16) score because of early discharge. In addition to these criteria, the following exclusion criteria for selecting the patients for the analyses regarding functional outcomes were adopted: (*iv*) transferred to an acute hospital before the completion of rehabilitation due to medical conditions; and (*v*) insufficient data regarding impairments and functional outcomes. The study was approved by the ethics committee of Tokyo Bay Rehabilitation Hospital.

Study setting

The KRW system for intensive rehabilitation, a governmental insurance system for rehabilitation wards for patients during their convalescent period, was introduced in Japan in 2000 (15). Patients within 2 months after the onset of cerebral infarction or cerebral haemorrhage were eligible for admission to the KRW. Physical, occupational, and speech therapies lasting for a maximum of 3 h/day were provided as part of the intensive intervention. The KRW team provided patients and their families a comprehensive monthly rehabilitation plan, including information about achieved goals, planned goals, and rehabilitative approaches to the achieved goals; discharge planning; and social resources necessary for home discharge. Timing for discharge was set when patients reached a plateau in activities of daily living (ADL), and the maximum length of stay was 150 days for stroke and 180 days for stroke with severe disability and cognitive disorders. Thus, patients can stay in the KRW for a relatively longer time. The mean length of stay in the KRW for patients with stroke was 95.2 days in 2001 (15), while the median length of hospital stay for stroke rehabilitation was 16 days in the USA in the same year (17).

Basic information

The following demographic and background information about the patients were obtained from their medical records: age, sex, diagnosis, side of cerebral lesion, time elapsed from stroke onset until admission, length of stay, motor assessment items of the Stroke Impairment Assessment Set (18), aphasia, unilateral spatial neglect, Functional Independence Measure (FIM) score (16) upon admission and discharge, FIM gain (19), FIM efficiency (20), and discharge disposition (acute hospital, home, nursing home, and long-term care hospital).

Assessment of left ventricular ejection fraction

Patients were assessed with transthoracic echocardiography within 7 days of admission using an Aplio SSA-700A (Toshiba Medical Systems Corp., Tokyo, Japan). One medical technologist with more than 10 years of echocardiographic experience evaluated all the patients in the same manner. The LVEF evaluated in the long-axis view was measured using the Teichholz method (21), or modified Simpson's rule (22) if asynergy was present. In patients with atrial fibrillation, the mean values of LVEF during 3 consecutive heartbeats were analysed further. Echocardiograms with ambiguous findings were reassessed by a board-certified cardiologist.

Determination of abnormal values in left ventricular ejection fraction

The abnormal values in LVEF were determined and the patients with stroke were divided into a low LVEF group and a preserved LVEF group. Data for healthy Japanese persons described by Daimon et al. (23) were used as the normal reference. Values were considered abnormal when they deviated from mean –2 standard deviations (SD) of the healthy values for each age group (20–29, 30–39, 40–49, 50–59, 60–69, 70–79 years) and sex (see Appendix I for details). Because the age of healthy persons in the report by Daimon et al. (23) ranged from 20 to 79 years, we did not have normal references for patients aged ≤ 19 ($n=1$) and ≥ 80 ($n=66$) years; consequently, we used data for healthy persons aged 20–29 years and 70–79 years as the respective references for these patients.

Statistical analyses

The basic values between the low LVEF group and the preserved LVEF group were compared using χ^2 test and two-tailed Fisher exact test for categorical variables, unpaired *t*-tests for interval/ratio scale, and the Mann–Whitney *U* test for ordinal variables. Statistical analyses were performed with SPSS version 22 (IBM Corp., Armonk, NY, USA). Any p-values <0.05 were considered statistically significant.

RESULTS

Patients' characteristics

The flow of patients is shown in Fig. 1. A total of 482 patients were analysed for discharge disposition; and 416 underwent analysis of functional outcomes.

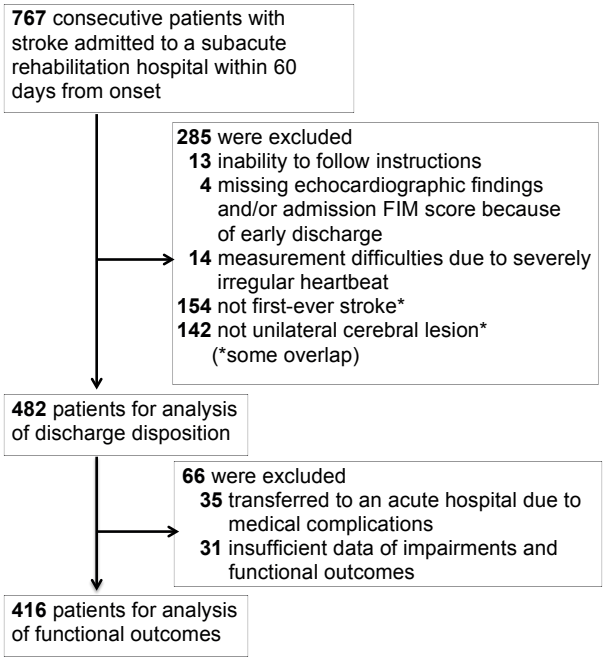

Fig. 1. Patient flow for analysis. The patients were selected for each analysis according the inclusion and exclusion criteria as shown in the figure. FIM: Functional Independence Measure.

Table I summarizes the patients' basic information: 53 (11.0%) were classified into the low LVEF group and the remaining 429 (89.0%) into the preserved LVEF group. Among the patients in the low LVEF group, 8 (1.6% of the total) had severely low LVEF (≤35%). The low LVEF group tended to be older and have a higher ratio of cerebral infarction patients and longer time after stroke; however, no statistical significance was observed. Other characteristics also showed no significant difference between the groups, except for the LVEF.

Table I. Patient characteristics ($n=482$)

	Low LVEF group ($n=53$)	Preserved LVEF group ($n=429$)	p-value
Age, years, mean (SD)	68.0 (12.6)	66.0 (12.6)	0.292
Female/male, n	20/33	178/251	0.600
Haemorrhage/infarction, n	18/35	200/229	0.081
Time from stroke, days, mean (SD)	38.7 (13.2)	35.3 (12.9)	0.074
Length of stay, days, mean (SD)	89.2 (40.6)	92.9 (41.9)	0.541
Lesion side, right/left, n	22/31	191/238	0.677
LVEF, %, mean (SD)	48.4 (8.4)	68.7 (7.3)	<0.001
Aphasia, none/mild/severe, n	28/6/12	258/63/67	0.314
Unilateral spatial neglect, absent/present, n	34/12	304/84	0.493
SIAS-m, median (interquartile range)			
Knee-mouth	3.0 (0.0–4.0)	2.0 (0.0–4.0)	0.740
Finger-function	1.0 (0.0–4.0)	1.0 (0.0–4.0)	0.697
Hip-flexion	3.0 (1.0–4.0)	3.0 (1.0–4.0)	0.879
Knee-extension	3.0 (1.0–4.0)	3.0 (1.0–4.0)	0.826
Foot-pat	3.0 (0.0–4.0)	2.0 (0.0–4.0)	0.822

LVEF: left ventricular ejection fraction; SIAS-m: motor assessment items of the Stroke Impairment Assessment Set.

Table II. Discharge dispositions

	Low LVEF group ($n=53$) n (%)	Preserved LVEF group ($n=429$) n (%)
Acute hospital	7 (13.2)	28 (6.5)
Home	34 (64.2)	322 (75.1)
Nursing home	12 (22.6)	74 (17.2)
Long-term care hospital	0 (0)	5 (1.1)
p-value for all 4 dispositions: 0.373		
p-value for acute hospital vs others: 0.076		

LVEF: left ventricular ejection fraction.

Discharge disposition

Table II shows the discharge disposition. Compared with the preserved LVEF group, the low LVEF group tended to be transferred to acute hospitals. There was a marginally significant difference in discharge dispositions between the groups. Table III shows medical complications during the stay in KRW, for which transfer to an acute hospital was required. In the preserved LVEF group, 4 patients had cardiovascular complications, while there were no transfers due to cardiovascular diseases in the low LVEF group.

Functional Independence Measure scores

Tables IV and V show the admission FIM score, discharge FIM score, FIM gain, and FIM efficiency. Compared with the preserved LVEF group, the low

Table III. Number of medical complications during subacute rehabilitation that required a transfer to an acute hospital

	Low LVEF group ($n=53$)	Preserved LVEF group ($n=429$)	All ($n=482$)
Gastrointestinal	2	8	10
Pulmonary	1	8	9
Neurological	2	3	5
Cardiovascular	0	4[a]	4[a]
Haematological	0	2	2
Orthopaedic	0	1	1
Others	1	1	2
Unknown	1	1	2
Total	7	28	35

[a]Cardiovascular problems: myocardial infarction ($n=1$), sick sinus syndrome ($n=1$), junctional rhythm ($n=1$), and spontaneous echo contrast that required further cardiac investigation ($n=1$). LVEF: left ventricular ejection fraction.

Table IV. Admission and discharge Functional Independence Measure (FIM) score

	Low LVEF group ($n=44$) Median (IQR)	Preserved LVEF group ($n=372$) Median (IQR)	p-value
FIM at admission			
Motor score	44.5 (20.5–66.0)	54.0 (32.0–69.0)	0.067
Cognitive score	22.5 (13.0–29.5)	27.0 (19.0–33.0)	0.017
Total score	71.0 (41.5–90.0)	82.0 (52.0–100.0)	0.032
FIM at discharge			
Motor score	76.5 (48.0–86.0)	78.0 (63.0–87.0)	0.252
Cognitive score	27.5 (23.0–33.0)	31.5 (25.0–35.0)	0.039
Total score	105.5 (74.0–116.0)	109.0 (88.5–119.0)	0.081

LVEF: left ventricular ejection fraction; IQR: interquartile range.

Table V. Functional Independence Measure (FIM) gain and FIM efficiency

	Low LVEF group ($n = 44$) Median (IQR)	Preserved LVEF group ($n = 372$) Median (IQR)	p-value
FIM gain			
Motor score	19.5 (8.0–32.5)	19.0 (9.0–27.0)	0.999
Cognitive score	2.0 (0.0–7.5)	2.0 (0.0–5.0)	0.640
Total score	20.5 (8.0–35.5)	21.0 (10.0–32.0)	0.971
FIM efficiency			
Motor score	0.19 (0.09–0.38)	0.20 (0.10–0.29)	0.631
Cognitive score	0.03 (0.00–0.09)	0.02 (0.00–0.05)	0.375
Total score	0.25 (0.11–0.42)	0.23 (0.12–0.34)	0.491

LVEF: left ventricular ejection fraction; IQR: interquartile range.

LVEF group tended to have a lower admission motor FIM score and significantly lower admission cognitive and total FIM scores. The discharge cognitive FIM score was also significantly lower in the low LVEF group than in the preserved LVEF group. However, the total score on discharge FIM showed no significant difference between groups. In addition, FIM gain and FIM efficiency did not differ significantly between groups.

DISCUSSION

To our knowledge, this is the first study to evaluate the longitudinal influence of LVEF on ADL level represented by FIM score in patients with subacute stroke. The patients in the low LVEF group tended to be transferred to acute hospitals more frequently. The low LVEF group had significantly lower cognitive and total FIM scores on admission than the preserved LVEF group. However, the total score on discharge FIM, FIM gain, and FIM efficiency showed no significant difference between the 2 groups.

Kevorkian et al. (13) and Milionis et al. (14) reported the relationships between LVEF at the acute phase and subsequent outcomes in patients with stroke. Kevorkian et al. investigated the LVEF in 262 patients admitted to a private tertiary acute general hospital. The patients were classified into 2 groups: low LVEF (≤35%) group (36 patients, 13.7%) and high LVEF (>35%) group (226 patients, 86.3%). Total FIM score, FIM gain, and FIM efficiency on admission and discharge after a mean of 13.7 days from admission were assessed. No significant difference in admission FIM score between the groups was noted; however, patients with low LVEF had a lower discharge FIM score, lower FIM gain, and lower FIM efficiency than patients with high LVEF. Discharge disposition was evaluated by comparing home with other situations; the high LVEF group was more likely to be discharged to home. Similarly, Milionis et al. investigated the association of low LVEF with long-term outcome of patients with acute ischaemic stroke. A total of 119 patients (4.9%) were categorized into the low LVEF (≤35%) group and the remaining 2,320 (95.1%) into the preserved LVEF (>35%) group based on echocardiographic assessment at the time of hospitalization or on a recent (within 12 months) evaluation. Patients with low LVEF were more likely to be male, older, and having higher rates of coronary artery disease and atrial fibrillation. Mortality rate and modified Rankin scale at 7 days, 3 months, and 12 months were higher among patients with low LVEF. Thus, patients with LVEF at the acute stage subsequently tended to have lower ADL. Discharge disposition was evaluated by comparing home/short recovery with any institution/hospital; the high LVEF group was more likely to be discharged to home/short recovery. In the present study, all the patients were in the subacute phase, and the lower admission FIM score in the low LVEF group could be attributed to the decline in ADLs due to low cardiac function at the acute phase, which is consistent with the findings in previous reports. Regarding the discharge disposition, the finding in the present study that the low LVEF group tended to be more likely to be discharged to acute hospitals compared with the preserved LVEF group, is also consistent with the findings in previous reports.

Our findings differed from those of previous studies in some aspects. Firstly, the number of patients with severely low LVEF (≤35%) was relatively lower in this study (1.4%) than in previous ones (13.7% and 4.9%). Selection bias is the most likely explanation. Patients in a poor condition in the acute phase, such as severe heart failure, might not survive until the subacute phase, or indication of rehabilitation in KRW may not be appropriate for a patient in a severely deteriorated condition, as the physical condition has to be sufficient for the patient to tolerate intensive rehabilitation. Secondly, total score on discharge FIM, FIM gain, and FIM efficiency showed no significant difference between the low LVEF group and the preserved LVEF group, although total FIM at admission was significantly lower in the low LVEF group. This suggests that the ADL decline due to decreased LV function during the acute phase could improve up to almost the same level of ADL as that in patients without LV dysfunction. This could be supported by the fact that mildly or moderately low LVEF does not necessarily restrict therapeutic exercise from the viewpoint of cardiac rehabilitation (24), and the metabolic cost of a comfortable speed of level walking is not extremely high in hemiplegic patients (25). In addition, the physiatrist, nurse, and therapist possibly considered the heart load sufficiently and thus provided rehabilitation carefully by taking into account the LVEF.

This study has several limitations. Firstly, the study was conducted at a single institution; therefore, our

patients might not accurately reflect the entire stroke population in subacute rehabilitation wards. Secondly, we used data for healthy individuals aged 70–79 years as a reference for patients aged ≥80 years because data for healthy Japanese people in this age group are unavailable; hence, overestimation of echocardiographic abnormalities is possible. Thirdly, the reference value used for determination of the abnormal values in LVEF was provided by using the data of healthy Japanese people (23). The traditional reference values by the American Society of Echocardiography in conjunction with the European Association of Echocardiography (26) were established from the data of American and European populations; thus, the values cannot be applied to a Japanese population, who are physically and racially different. This is one of the strengths of our report, as we used the data obtained from normal values of Japanese people. On the other hand, this is also what makes it difficult to compare our data with the data obtained from previous studies. Lastly, unlike previous studies (13, 14), we failed to analyse the effect of severely low LVEF on ADLs because there were only 6 cases with LVEF ≤35%. Further studies with a large sample size are warranted to clarify the effect of severely low LVEF on ADLs in the subacute phase.

Despite these limitations, the finding that rehabilitation of stroke patients with low LVEF in the subacute phase could result in almost the same outcomes as those in patients with preserved LVEF is a valuable piece of information for the patients as well as practitioners.

In conclusion, the general medical conditions in patients should be considered carefully, because discontinuation of rehabilitation due to medical complications tended to be higher in the low LVEF group than in the preserved LVEF group. However, the finding of low LVEF did not pose a barrier to successful rehabilitation after stroke.

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Appendix I. Cut-off values used to determine low left ventricular ejection fraction (LVEF) in each age group for each sex

	Age group, years							
Sex	≤19	20–29	30–39	40–49	50–59	60–69	70–79	80≤
Male	56[a]	56	54	55	52	56	54	54[a]
Female	56[a]	56	57	56	56	53	59	59[a]

Cut-off values determined as mean – 2 SD of healthy values in each age group (23) for low LVEF.
[a]Because the age of healthy persons in Daimon's report (23) ranged from 20 to 79 years, normal references for patients aged ≤19 ($n=1$) and ≥80 ($n=66$) years were unavailable. We therefore used data of healthy persons aged 20–29 years and 70–79 years for these comparisons, respectively.