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Difference in prognoses among subtypes after first-ever ischemic stroke

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ABSTRACT

Stroke has been a leading cause of death in Japan and given a heavy burden on public health due to its high prevalence and associated disabilities. The high recurrence rate of stroke is also a struggling heath issue, resulting in cumulative disabilities and cognitive dysfunction.

In order to verify factors affecting prognosis after initial stroke, including stroke recurrence, we investigated post-stroke patients who were admitted to the stroke centers with

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first-ever ischemic stroke, and analyzed the relationship between characteristics of the patients and their prognoses, retrospectively.

In this study we examined the influences of various factors on the prognosis of post-stroke patients, and found that clinical subtypes of ischemic stroke gave much impact on the prognosis, in addition to conventional risk factors. It may probably caused by different etiology of stroke among subtypes.

These findings suggest that appropriate treatment and persistent health education for post-stroke patients, according to their subtypes, are essential to prevent recurrence and cumulative disabilities.

Key words: ischemic stroke, prognosis, subtype, mRS, nursing care

INTRODUCTION

Stroke has been a leading cause of death in Japan[1] and given a heavy burden on public health due to its high prevalence and associated disabilities. The high recurrence rate of stroke is also a struggling heath issue, resulting in cumulative disabilities and cognitive dysfunction. Stroke, then, accounts for about one fourth of the causes of the long-term nursing care in Japan[2].

Stroke is classified into ischemic type (cerebral infarction) and hemorrhagic type (cerebral hemorrhage). Ischemic stroke is further divided into several clinical subtypes, including lacunar, atherothombotic, cardioemboric strokes, and transient ischemic attack (TIA). Considerable differences in prognosis of patients with first-ever ischemic stroke were reported by several studies[3-8]. Various risk factors, such as age, gender, hypertension, diabetes mellitus (DM), dyslipidemia, atrial fibrillation (AF), were assumed to affect the difference in prognosis of post-stroke patients. We have previously reported that the disability level of patients at discharge well correlated with the level at about two years after discharge[9]. Thus it could be a predictor of prognosis after stroke. Furthermore, a number of articles have been published which give additional knowledge on difference in outcomes by ischemic stroke subtypes[10-13]. In these articles, subtypes of ischemic stroke are assumed to be an important determinant of long-term prognosis.

The purpose of the present study is to examine the influences of subtypes of first-ever ischemic stroke on the prognosis of post-stroke patients. We focused on discharged patients who were admitted to the high-volume stroke centers at Aichi and Hiroshima prefectures in Japan with first-ever ischemic stroke, including TIA.

METHODS

Participants of this study were 2, 052 patients who had suffered from first-ever ischemic stroke, including TIA, and were admitted to the two high-volume stroke centers at Aichi and Hiroshima prefectures in Japan, and discharged between December 2006 and January 2009. Under approval of the ethical committees of these two hospitals, survey questionnaires were sent to the above 2, 052 patients by mail. We were able to associate the clinical data of 1, 087 patients (53. 0%) with their useable returned questionnaires.

Clinical data obtained were the day of stroke onset, subtypes of ischemic stroke, records of admission and discharge, disability level evaluated by modified Rankin Scale (mRS), severity level assessed by National Institute of Health Stroke Score (NIHSS), and conventional risk factors, such as hypertension, diabetes mellitus (DM), dyslipidemia, atrial fibrillation (AF), family history and so forth. Survey questionnaires include recurrence of stroke, present status of health care, prescribed medications and the required level of long-term nursing care. Information on personal identification of the participants was deleted after assignment of optical numbers.

We used mRS and NIHSS for assessing function or severity level of the patients. The mRS is a widely applied measure for evaluating the degree of disability of stroke patients[14]. NIHSS was developed to measure the overall degree of neurological impairment of stroke patients[15].

In order to examine factors affecting the prognosis of post-stroke patients, we analyzed the relationship between ischemic stroke subtypes of the participants and their prognoses. Prognostic factors analyzed were: disability levels evaluated by mRS, status of health care, regular outpatient visit, and required levels of the long-term nursing care.

STATISTICS

Chi-square test was performed to investigate the association between stroke subtypes and their prognoses, such as disability level, status of health care, regular ambulatory care, and required levels of the long-term nursing care.

All statistical analyses were carried out with IBM SPSS Statistics Ver. 19. 0. All significant levels were set at p value of less than 0. 05 on two-sided testing.

RESULTS

1. Characteristics of participants

Participants were 1, 087 post-stroke patients (70. 4 ± 11. 7 years), consisted of 719

(66.1%) male patients (68.5±11.2 years) and 368 (33.9%) female patients (74.2±11.6 years). Distribution of the age peaked at 65-69 years for male, and 80-84 for female. Their averag period after discharge was 704.3±211.1 days.

Clinical subtypes of initial stroke on the participants were lacunar 352 (32.4%), atherothrombotic 324 (29.8%), cardioemobolic 239 (22.0%), TIA 91 (8.4%) and others 81 (7.5%), respectively. Proportion of the male subjects on each subtypes was highest in atherothrombotic (69.8%), followed by TIA (68.1%) and lacunar (65.1%). The average age of the patients was highest in cardioembolic (73.7±11.4 years), succeeded by atherothrombotic (71.3±10.7 years) and lacunar infarction (69.9±10.3 years).

The functional levels of the patients at discharge evaluated by mRS and NIHSS were described in Table 1 and Table 2. As shown in Table 1, the distribution of mRS grades of the participants was "grade 0 (no symptom)" 26.0%, "grade 1 (no significant disability)" 26.1%, "grade 2 (slight disability)" 19.0%, "grade 3 (moderate disability)" 11.4%, "grade 4 (moderately severe disability)" 12.2%, and "grade 5 (severe disability)" 5.2%. The proportion of the participants with mRS grade over 3 by subtypes was highest in cardioembolic 41.0%, followed by atherothrombotic 36.7%, lacunar 20.2%, and lowest in TIA 5.5%. Statistically significant difference in the distribution of mRS grade was observed across ischemic stroke subtypes ($p<0.001$).

The distribution of the severity levels of the participants measured by NIHSS was indi-

Table 1 Distribution of mRS grades at discharge by ischemic stroke subtypes

Subtype	N	mRS grade at discharge (%)						Average (Mean±SD)
		0	1	2	3	4	5	
Lacunar	352 (100.0%)	66 (18.8%)	132 (37.5%)	83 (23.6%)	37 (10.5%)	28 (8.0%)	6 (1.7%)	1.57±1.23
Atherothrombotic	324 (100.0%)	74 (22.8%)	68 (21.0%)	63 (19.4%)	48 (14.8%)	53 (16.4%)	18 (5.6%)	1.98±1.56
Cardioembolic	239 (100.0%)	52 (21.8%)	52 (21.8%)	37 (15.5%)	27 (11.3%)	40 (16.7%)	31 (13.0%)	2.18±1.74
TIA	91 (100.0%)	69 (75.8%)	10 (11.0%)	7 (7.7%)	4 (4.4%)	1 (1.1%)	0 (0.0%)	0.44±0.90
Others	81 (100.0%)	22 (27.2%)	22 (27.2%)	17 (21.0%)	8 (9.9%)	11 (13.6%)	1 (1.2%)	1.57±1.34
Total	1,087 (100.0%)	283 (26.0%)	284 (26.1%)	207 (19.0%)	124 (11.4%)	133 (12.2%)	56 (5.2%)	1.73±1.52

The distribution of mRS grade was significantly different across subtypes by chi-square test ($p<0.001$).

Table 2 Distribution of NIHSS scores of the patients by ischemic stroke subtypes

Subtype	N	NIHSS score at discharge (%)					Average (Mean±SD)
		0-4	5-10	11-16	17-22	23-	
Lacunar	352 (100.0%)	322 (91.5%)	25 (7.1%)	2 (0.6%)	1 (0.3%)	2 (0.6%)	1.83±2.71
Atherothrombotic	324 (100.0%)	241 (74.4%)	47 (14.5%)	20 (6.2%)	11 (3.4%)	5 (1.5%)	3.64±5.41
Cardioembolic	239 (100.0%)	157 (65.7%)	26 (10.9%)	26 (10.9%)	12 (5.0%)	18 (7.5%)	6.01±8.64
TIA	91 (100.0%)	87 (95.6%)	4 (4.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0.62±1.49
Others	81 (100.0%)	72 (88.9%)	9 (11.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1.72±1.96
Total	1,087 (100.0%)	879 (80.9%)	111 (10.2%)	48 (4.4%)	24 (2.2%)	25 (2.3%)	3.18±5.58

The distribution of NIHSS score was significantly different among subtypes by chi-square test ($p<0.001$).

cated in Table 2. The average NIHSS score at discharge was highest in cardioembolic, followed by atherothrombotic, lacunar stroke and TIA. The proportion of the patients with NIHSS score under 4 (mild level) was 95.6% in TIA, 91.5% in lacunar, 74.4% in atherothrombotic, and lowest (65.7%) in cardioembolic. On the other hand, the proportion of the patients with NIHSS score over 11 (severe level) was, 23.4% in cardioembolic, 11.1% in atherothrombotic stroke. This tendency was similar to that of mRS, and statistically significant difference in the distribution of NIHSS score was observed among subtypes of ischemic stroke ($p<0.001$).

2. Prognoses of the participants after discharge

1) Recurrence rate

In the present study, 21.3% recurrence rate of ischemic stroke within two years after discharge was observed for all the participants. Recurrence rates of individual subtype were: cardioemobolic 26.4%, lacunar 22.4%, TIA 19.8% and atherothrombotic 17.9%, respectively. There was difference in recurrence rates among subtypes, but it was not at significant level ($p=0.09$).

2) Functional level

The distribution of mRS grade about two years after discharge is shown in Table 3. The distribution of mRS grade after discharge was almost consistent with the grade at discharge. The average mRS score of the patients with caridioembolic stroke was highest, followed by atherothrombotic and lacunar stroke. The proportion of the patients with mRS grade 6 (dead) had reached 10% for cardioembolic patients. The distribution of mRS grade was significantly different among stroke subtypes ($p<0.001$).

3) Status of health care after discharge

As indicated in Table 4, status of health care for all the participants at about 2 years af-

Table 3 Distribution of mRS grades after discharge by ischemic stroke subtypes

Subtype	N	mRS grade after discharge (%)							Average
		0	1	2	3	4	5	6	(Mean±SD)
Lacunar	335 (100.0%)	108 (32.2%)	86 (25.7%)	76 (22.7%)	35 (10.4%)	11 (3.3%)	14 (4.2%)	5(1.5%)	1.45±1.45
Atherothrombotic	305 (100.0%)	78 (25.6%)	71 (23.3%)	56 (18.4%)	36 (11.8%)	24 (7.9%)	22 (7.2%)	18(5.9%)	1.98±1.81
Cardioembolic	229 (100.0%)	53 (23.1%)	39 (17.0%)	30 (13.1%)	28 (12.2%)	20 (8.7%)	36 (15.7%)	23(10.0%)	2.54±2.08
TIA	87 (100.0%)	54 (62.1%)	18 (20.7%)	10 (11.5%)	3 (3.4%)	0 (0.0%)	1 (1.1%)	1(1.1%)	0.67±1.12
Others	78 (100.0%)	21 (26.9%)	22 (28.2%)	18 (23.1%)	9 (11.5%)	5 (6.4%)	1 (1.3%)	2(2.6%)	1.56±1.45
Total	1,034 (100.0%)	314 (30.4%)	236 (22.8%)	190 (18.4%)	111 (10.7%)	60 (5.8%)	74 (7.2%)	49 (4.7%)	1.79±1.77

The distribution of mRS grade was significantly different across subtypes by chi-square test ($p<0.001$).

Table 4 Status of health care after discharge

Subtype	N	Status of health care after discharge (%)				
		Home care	Hospitalized	Nursing home	Died	Uncertain
Lacunar	352 (100.0%)	324 (92.0%)	7 (2.0%)	15 (4.3%)	5 (1.4%)	1 (0.3%)
Atherothrombotic	324 (100.0%)	264 (81.5%)	14 (4.3%)	26 (8.0%)	18 (5.6%)	2 (0.6%)
Cardioembolic	239 (100.0%)	170 (71.1%)	14 (5.9%)	32 (13.4%)	23 (9.6%)	0 (0.0%)
TIA	91 (100.0%)	90 (98.9%)	0 (0.0%)	0 (0.0%)	1 (1.1%)	0 (0.0%)
Others	81 (100.0%)	77 (95.1%)	1 (1.2%)	1 (1.2%)	2 (2.5%)	0 (0.0%)
Total	1,087 (100.0%)	925 (85.1%)	36 (3.3%)	74 (6.8%)	49 (4.5%)	3 (0.3%)

Significant difference ($p<0.01$) was observed among stroke subtypes by chi-square test.

ter discharge were, "home care" 85.1%, "hospitalized" 3.3%, "residential care at nursing home" 6.8%, and 4.5% of the patients had "died". Nearly all of TIA patients and more than 90% of the patients with lacunar stroke had received home care, while 9.6% of cardioembolic patients and 5.6% of atherothrombotic patients had died within two years after discharge. Concerning cardioembolic patients, 4.3% had hospitalized and 13.4% were receiving residential care at nursing homes. The health care status of participants were significantly different among stroke subtypes ($p<0.01$).

4) Regular ambulatory care

Nearly 80% of all the participants received the regular ambulatory care after discharge from the stroke centers (Table 5). The proportion of the patients receiving the regular ambulatory care was highest in TIA 93.4%, followed by lacunar 84.4%, athrothrombotic 75.6%, and lowest in cardioembolic stroke 69.0%. In addition, three fourth of the patients visited a physician more than once a month.

5) Required levels of the long-term nursing care after discharge.

The distribution of required levels of the long-term nursing care after discharge were significantly different among subtypes of ischemic stroke ($p<0.001$). The required nursing care levels of the patients with cardioembolic stroke were relatively higher than those with

Table 5 Regular ambulatory care

	N	Regular ambulatory care (%)		
		+	−	Uncertain
Lacunar	352 (100.0%)	297 (84.4%)	25 (7.1%)	30 (8.5%)
Atherothrombotic	324 (100.0%)	245 (75.6%)	19 (5.9%)	60 (18.5%)
Cardioembolic	239 (100.0%)	165 (69.0%)	3 (1.3%)	71 (29.7%)
TIA	91 (100.0%)	85 (93.4%)	4 (4.4%)	2 (2.2%)
Others	81 (100.0%)	68 (84.0%)	9 (11.1%)	4 (4.9%)
Total	1,087 (100.0%)	860 (79.1%)	60 (5.5%)	167 (15.4%)

Table 6　Required levels of the long-term nursing care after discharge

Subtype	NC *	Required levels of the long-term nursing care **							Total
		S1	S2	C1	C2	C3	C4	C5	
Lacunar	238 (71.9%)	31 (9.4%)	15 (4.5%)	15 (4.5%)	10 (3.0%)	8 (2.4%)	6 (1.8%)	8 (2.4%)	331 (100%)
Atherothrombotic	173 (59.7%)	21 (7.2%)	16 (5.5%)	16 (5.5%)	20 (6.9%)	18 (6.2%)	13 (4.5%)	13 (4.5%)	290 (100%)
Cardioembolic	106 (51.2%)	14 (6.8%)	8 (3.9%)	13 (6.3%)	15 (7.2%)	14 (6.8%)	12 (5.8%)	25 (12.1%)	207 (100%)
TIA	73 (83.9%)	5 (5.7%)	5 (5.7%)	2 (2.3%)	1 (1.1%)	1 (1.1%)	0 (0.0%)	0 (0.0%)	87 (100%)
Others	57 (74.0%)	3 (3.9%)	3 (3.9%)	7 (9.1%)	3 (3.9%)	3 (3.9%)	1 (1.3%)	0 (0.0%)	77 (100%)
Total	647 (65.2%)	74 (7.5%)	47 (4.7%)	53 (5.3%)	49 (4.9%)	44 (4.4%)	32 (3.2%)	46 (4.6%)	992 (100%)

*NC: not certified

**S: levels needed support, C: levels needed nursing care

The distribution of required levels of the long-term nursing care was significantly different among subtypes by chi-square test ($p<0.001$).

other subtypes (Table 6).

DISCUSSION

Stroke has been a substantial health issue in Japan due to its high prevalence, recurrence and associated disabilities. In order to clarify factors affecting outcomes or prognoses of post-stroke patients, we analyzed the data of 1, 087 participants who were admitted to the two high volume stroke centers in Japan, suffering from first-ever ischemic stroke. The characteristics of the participants in our study were almost consistent with those of previous studies and the Japan Standard Registry Study[16].

The average recurrence rate of the participants within about two years after discharge was 21. 3%, and higher recurrence was observed in the patients with cardioembolic 26. 4% and lacunar stroke 22. 4%. As we reported previously[9], mRS grade as well as age, gender and family history had statistically significant impact on stroke recurrence, and magnitude of impact of each factors varied across ischemic stroke subtypes. Our data also suggested that the mRS grade of stroke patients at discharge might be a predictive indicator of the prognosis, and patients with higher mRS grade have much worse prognosis than those with lower mRS grade. Kimura K et al. reported from a multi-institutional research that functional disability as well as gender, age, DM, AF, and history of stroke were independent predictors of death[17].

It is also suggested from previous studies[10-13] that subtypes of ischemic stroke might be a predictor of prognosis, in addition to the above mentioned factors. As described in the results, distribution of mRS and NIHSS scores at discharge were significantly different across stroke subtypes (see Table 1, Table 2). The proportion of the patients with NIHSS score

over 11 (severe level) was highest in cardioembolic stroke, followed by atherothrombotic stroke, and lowest in TIA. The distribution of mRS had similar tendency with that of NIHSS. The population-based Minnesota study revealed, by functional assessment using mRS, that patients with lacunar stroke had better post-stroke function than those with other subtypes, while patients with cardioembolic stroke was the poorest survival[12]. The results of our study were almost consistent with them. The functional status and disability level of the patients was associated with mRS grade and NIHSS score at discharge, depending on stroke subtypes.

The present study also shows that one tenth of cardioembolic patients had died, and about 20% of them hospitalized or received residential care at nursing homes, while more than 90% of patients after lacunar stroke and almost all of the TIA patients were independent and living at home. Then, the proportion of patients who received regular ambulatory care was higher in the subtypes with low disability, such as lacunar stroke and TIA. It is assumed that etiology of stroke may relate to the difference in prognoses among clinical subtypes.

On the other hand, Bo Norrving described in the review on the long-term prognosis after lacunar stroke[18], that the risk of recurrence of lacunar stroke is similar to that after other subtypes, and the patients have increased risk of cognitive decline and dementia. Then, he insisted that more studies on mechanisms, prevention and treatment are needed to provide specific guidance on long-term management of risk factors of the patients. This suggests the importance of appropriate and persistent health care of post-stroke patients, regardless of stroke subtypes.

Besides its high mortality and morbidity, stroke is the first leading cause of the long-term nursing care in Japan and accounted for 25% of all causes[2]. In our study, proportion of the patients who required nursing care after discharge was about 35% and one fifth of them needed intensive nursing care. The disability level of the patients measured by mRS was well associated with the level of required nursing care, and it could be a predictor of dependency on nursing care after stroke[19].

As Coull et al. suggested[20], we would like to emphasize that adequate treatment and risk factor management by persistent health education for post-stroke patients is necessary to prevent stroke recurrence and associated disabilities effectively, according to their stroke subtypes and disability levels.

There were some limitations on this study. Participants for analyses were limited to the patients who were admitted to the two stroke centers in Japan, and useable information was obtained from about half of the stroke patients who were sent questionnaires. The accuracy

of the information from the participants was insufficient and there may be some biases, because this study was retrospective.

CONCLUSION

The number of stroke patients is expected to increase, as the aging society advances in Japan. Various factors were assumed to affect the prognosis of stroke patients independently or mutually. Ischemic stroke subtypes and severity level of post-stroke patients might be important predictors of prognosis.

Therefore, adequate management of the disease and risk factors, from the early stage of onset throughout the course are aspired, especially for patients with low functional level or severe disability. We would like to emphasize the necessity of persistent health education and organization of health care services towards post-stroke patients.

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