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The trends in cerebral infarction in Yamagata Prefecture, Japan

—A study based on 10 years of stroke registry data—

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ABSTRACT

We studied ten years of stroke data registered with the Yamagata Society on Treatment for Cerebral Stroke (YSTCS). The subjects included 16,407 cases of acute-phase cerebral infarction that were registered with the YSTCS during the ten years between 2002 and 2011. The cases were divided into two groups: the early phase group (2002-2006) and the late phase group (2007-2011).

The clinical diagnoses included atherothrombotic cerebral infarction (AT) (n=7,196; 43.9%), cardiogenic cerebral embolism (CE) (n=4,011; 24.4%), and lacunar infarction (LI) (n=4,703; 28.7%). The average age of the early phase group was 72.7±11.43 years, while that of the late phase group was 75.0±11.35 years; the difference was statistically significant. The proportion of CE cases increased in the late phase, while that of LI decreased. This phenomenon was more marked in cases involving patients of ≥80 years of age. In both the early and late phase groups, the AT and CE cases showed a significantly high proportion of poor outcomes. However, when age adjustment was implemented in the late phase group, the treatment outcomes improved across all clinical entities. A multiple logistic regression analysis revealed a significant association between old age, female sex, severe symptoms at onset, CE, a previous history of stroke, and a poor prognosis.

It is clear that developments in medicine have not kept pace with the advancement in the age at onset. The improvement of the outcomes of treatment for cerebral infarction requires further developments in acute-phase therapies and the primary prevention of cardiogenic cerebral embolism, many cases of which are severe.

Key words: Cerebral infarction, Yamagata prefecture, cardiogenic cerebral embolism

Introduction

According to data from the Ministry of Health, Labour and Welfare of Japan in 2011, cerebrovascular disorder or stroke, is－by a very narrow margin－the fourth most common cause of death in Japan, after cancer, cardiac disease and pneumonia. Furthermore, they are the most common cause of patients requiring care. Thus, the improvement of the outcomes of treatment for stroke is an issue that demands attention at the national level. It is well-known that strokes can be broadly divided into ischemic and hemorrhagic cerebrovascular disorders; however, the proportion of cerebral infarctions, which account for approximately three quarters of all strokes, is far higher, both in Japan and other countries[1)-3)]. In other words, an increasing number of patients is considered to require improved treatment results, especially for cerebral infarction.

A further notable change occurring in recent years has been the change in the clinical categorization of the subtypes of cerebral infarction based on the NINDS (National Institute of Neurological Disorders and Stroke) Classification Edition III[4)]; specifically, the proportion of atherothrombotic cerebral infarction, cardiogenic stroke, and lacunar infarction. Conventionally, lacunar infarction has been the most common form of stroke in Japan; however, in recent years the proportion of lacunar stroke has fallen, and the incidence rates of atherothrombotic cerebral infarction and cardiogenic stroke have been increasing[5),6)].

There is a wide range of factors that impact the effects of treatment for cerebral infarction. It is necessary to clarify these factors in order to improve the treatment results. In Yamagata Prefecture, the Yamagata Society on Treatment for Cerebral Stroke (YSTCS) was founded in 1998 for the purpose of eradicating stroke. This research group includes not only neurosurgeons, neurologists and radiologists specializing in stroke treatment, but also nurses, therapists, emergency and public sector workers, and the participating facilities include major hospitals throughout the prefecture. This facilitates a comprehensive understanding of the features of acute-phase stroke in the prefecture. Many reports have used community-based registries and hospital-based registries to ascertain the incidence of stroke and to analyze risk factors and prognosis[5)-7)]. However, it is difficult to cover all medical facilities within a community using a community-based registry, and since it is not guaranteed that patients will receive a specialist diagnosis and treatment, there are problems with accuracy and comprehensiveness of such reports. At the same time, while the use of hospital-based registries provides a high level of accuracy and data that can be precisely analyzed, their scope－in terms of the facilities that they cover－is narrow and since they tend to include minor cases and do not reflect the state of strokes in a particular region, they are thought to lack comprehensiveness. The data registered in the YSTCS registry consists of acute-phase patients who underwent neuroradiological examinations and who were diagnosed, treated, and evaluated by specialists. Furthermore, almost all of the facilities to which patients with acute-phase stroke are admitted participate in the registry. Thus, although the YSTCS registry is hospital-based registry, it is considered highly comprehensive and is thought to provide an accurate picture of the state of strokes within Yamagata Prefecture, where 1% of Japan's population resides[8)].

We studied the data on strokes that were registered with the YSTCS over the past ten years in order to investigate the factors associated with a worse prognosis in cerebral infarction and to clarify the factors that are in its treatment, with the aim of improving the outcomes of cerebral infarction in the future.

Patients and Methods

[**Patients**] The study population included 16,407 patients (male, n=9,567; female, n=6840; average age, 74.0±11.44 years) with acute-phase cerebral infarction whose cases were registered with the YSTCS during the ten years between 1st January 2002 and 31st December 2011. The clinical diagnoses included atherothrombotic cerebral infarction (AT) (n=7,196; 43.9%), cardiogenic cerebral embolism (CE) (n=4,011; 24.4%), and lacunar infarction (LI) (n=4,703; 28.7%); 497 (3.0%) cases were classed as "other" (OT). The characteristics of the patients are shown in Table 1.

The factors that were analyzed included age, gender, severity at onset, final outcome (time to discharge or ADL at one month after onset), risk factors (hypertension, atrial fibrillation, diabetes, hyperlipidemia and a history of smoking), and a history of stroke.

[**Diagnosis of clinical categories**] Stroke specialists in each facility used computed tomography (CT) and magnetic resonance imaging (MRI), as well as medical history, blood tests and a detailed cardiac examination by a cardiovascular specialist, in order to provide an integrated decision based on the

Table 1. The patient characteristics

characteristics	2002-2011	2002-2006	2007-2011
Patient (no.)	16407	7565	8842
≥80 yr	*5626*	*2158*	*3468*
<80yr	10781	5407	5374
Age, yr	74.0±11.44	72.7±11.43	75.0±11.35*
≥80 yr(%)	*34.3*	*28.5*	*39.2*
<80yr (%)	65.7	71.5	60.8
Male sex(%)	58.3	58.1	58.5
≥80 yr(%)	*41.5*	*40*	*42.4*
<80yr (%)	67.1	65.3	68.9
subtype of infarction (%)			
Atherothrombotic	43.9	44.4	43.4
≥80 yr	*44*	*45*	*43.5*
<80yr	43.8	44.1	43.4
Cardioembolic	24.4	22.6	26
≥80 yr	*30.6*	*28.5*	*31.9*
<80yr	21.2	20.3	22.2
Lacunar infarction	28.7	30.5	27.1
≥80 yr	*23.3*	*25*	*22.3*
<80yr	31.4	32.7	30.3
Other	3	2.5	3.4
≥80 yr	*2*	*1.5*	*2.4*
<80yr	3.6	2.9	4.1
Medical history			
Hypertension (%)			
yes	66.5	64.3	68.3
≥80 yr	*66.6*	*64.6*	*67.9*
<80yr	66.4	64.2	68.6
Atrial fibrillation(%)			
yes	22.3	20.5	23.9
≥80 yr	*29.6*	*27.8*	*30.7*
<80yr	18.5	17.6	19.5
Diabetes mellitus (%)			
yes	33.6	32.5	34.6
≥80 yr	*28.8*	*28.4*	*29.1*
<80yr	36.1	34.1	38.1
Hyperlipidemia (%)			
yes	17.9	16.3	19.3
≥80 yr	*14.1*	*11.4*	*15.9*
<80yr	19.9	18.3	21.5
Smoking(%)			
yes	25.5	24.2	26.5
≥80 yr	*13.8*	*12.2*	*14.8*
<80yr	31.6	29	34.1
Previous stroke(%)			
yes	24.4	22.2	26.3
≥80 yr	*27.8*	*25*	*29.6*
<80yr	22.6	21.1	24.2

*P<0.01

definitions in NINDS Classification Edition III[4].

The evaluation of the severity at onset and the final outcome (time to discharge or ADL at one month after onset) was made using the following five categories: E (excellent: almost fully recovered, with no impediment to working or household tasks); G (good: some symptoms remain, but working or household tasks, and independent daily living, are possible), F (fair: clear symptoms remain, and some assistance is required for activities of daily living), P (poor: assistance is required for most activities of daily living), and D (dead). E and G were defined as good prognoses, while F, P and D were defined as poor prognoses. The risk factors and the patient' s history of stroke were confirmed by interviewing either the patient or his/her family when they attended the hospital.

[**Categories evaluated**] (1) The proportions of cases in each clinical category, (2) the treatment results according to the final outcome, and (3) factors associated with a poor prognosis (final outcomes F, P and D). Furthermore, the data from the ten-year study period were divided into two groups, the early phase group (2002-2006) and the late phase group (2007-2011), and analyzed in order to clarify recent trends. Additionally, in order to consider the contribution of age, the age distribution of the late phase group was adjusted in line with that of the early phase group, and then the same categories were studied.

[**Statistical analysis**] The clinical entities and treatment outcomes in both the early and late phases were compared using a chi-squared test and a residual test, while age was compared using a t-test. The factors associated with good or poor prognoses were considered using a good or poor prognosis as objective variables, and performing univariate and multivariate logistic regression analyses. Atrial fibrillation, which is believed to be strongly correlated with CE, was omitted as an explanatory variable in the multivariate logistic regression analysis. In all cases, p values of <0.05 were considered to indicate statistical significance.

This research project was implemented with the approval of the ethical committees of Yamagata University and the cooperating facilities.

Results

[**Age distribution**]

The average age of the late phase group (75.0±

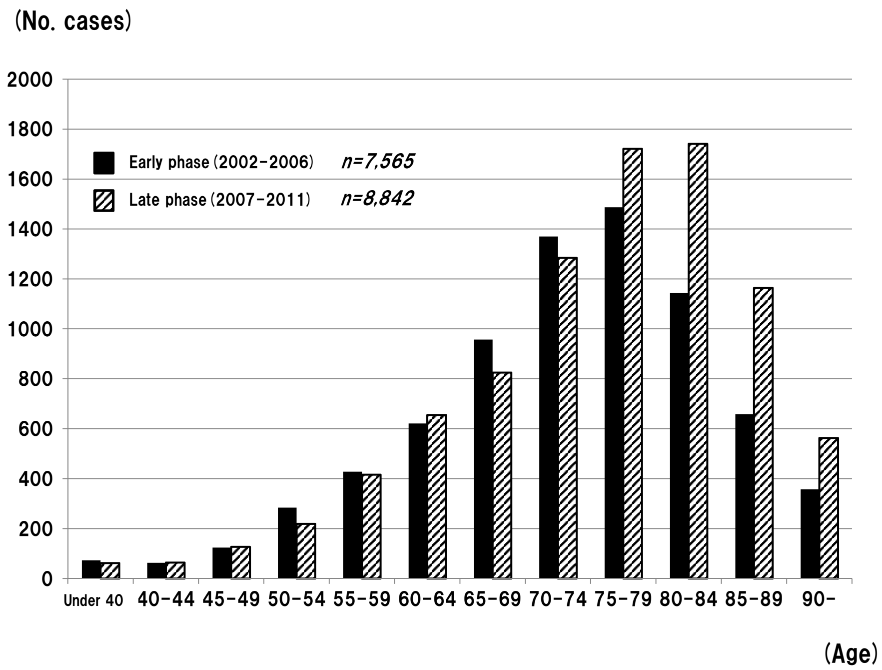


Figure 1 . The age distribution in the early phase (2002-2006) and late phase (2007-2011) groups. The number of patients in the late phase group was increased in comparison to the early phase group, which depended mainly on the difference in the number of patients aged 75 years and older.

11.35 years) was significantly higher than that of the early phase group at 72.7±11.43 (t-test, p<0.01). Figure 1 shows the distribution of cases in each age group, in the early and late phases. The total number of cases in the late phase group was greater than that of the early phase group, which depended mainly on the difference in the number of patients aged 75 years and older. Furthermore, in terms of the clinical categories, the total number of cases in the late phase group was greater than that of the early phase group in all categories, especially in CE cases, which depended mainly on the difference in the number of patients aged 75 years and older (Figure 2).

Clinical categories

A comparison of the proportions of each type of cases in the early and late phase groups showed that in the early phase group, there were 3,357 cases of AT (44.4%), 1,711 cases of CE (22.6%), 2,305 cases of LI (30.5%) and 192 OT cases (2.5%), while in the late phase group there were 3,839 cases of AT (43.4%), 2,300 cases of CE (26%), 2,398 cases of LI (27.1%), and 305 OT cases (3.4%). The proportion of CE cases increased during the late phase, while the proportion of LI cases decreased. This phenomenon was more marked in the cases involving patients of ≥80 years of age (Table 1). When adjusted for age, the incidence rates in the late phase group were as follows: AT, 43.4%; CE, 24.7%; LI, 28.1%; and OT, 3.8%; the proportion of CE cases was slightly reduced, which brought the distribution closer to that of the early phase group.

Treatment outcomes

The prognoses of all cases from 2002 to 2011 were as follows: (E: n=4,494, 27.4%; G: n=4,956, 30.2%); F (n=3,280, 20%); P (n=2,726, 16.6%); and D (n=951, 5.8%). The classifications during the early phase (2002-2006) were as follows: E (n=2,153, 28.5%); G, (n=2,325, 30.7%); F (n=1,621, 21.4%); P (n=1,034, 13.7%); and D (n=432, 5.7%). The classifications during the late phase (2007-2011) were as follows: E (n=2,341, 26.5%); G (n=2,631, 29.8%); F (n=1,659;

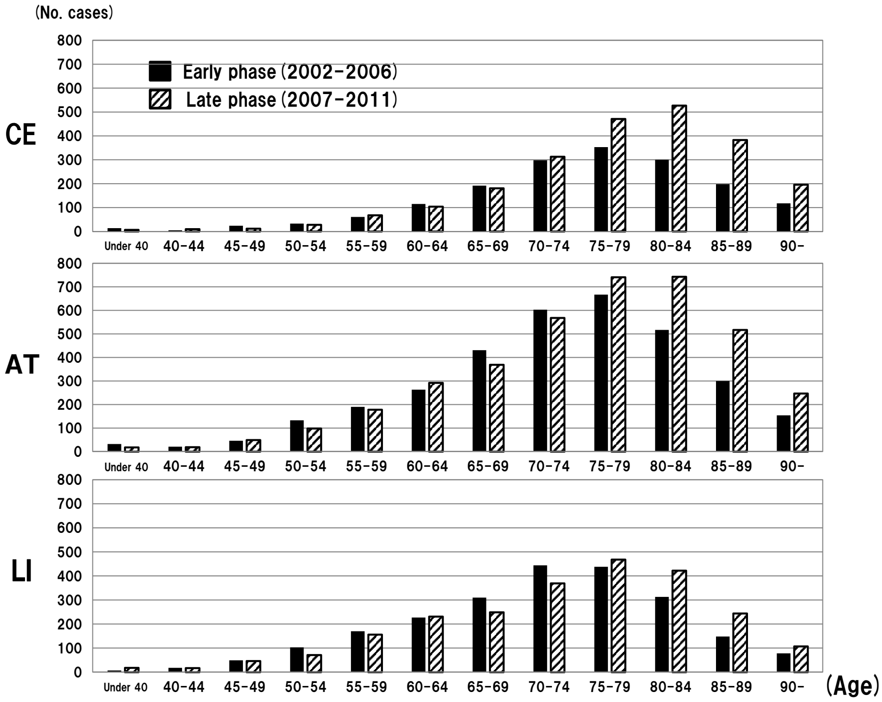
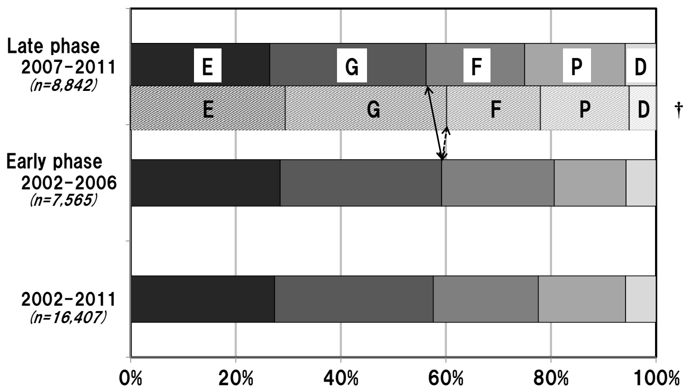


Figure 2. The age distribution in each clinical category of the early phase (2002-2006) and late phase (2007-2011) groups.
The number of patients in the late phase group was increased in comparison to the early phase group, which depended mainly on the difference in the number of patients aged 75 years and older, especially patients with cardiogenic cerebral embolism (CE).



E: excellent, G: good, F: fair, P: poor, D: dead

Figure 3. The rates of each outcome in the early phase (2002-2006) and late phase (2007-2011) groups.
The graph shows that in the late phase group, the proportions of E and G cases were lower, while the proportion of P cases was higher in comparison to the early phase group (chi-squared test and residual test, p<0.01).
When the late phase was adjusted for age to match the early phase †, the proportion of combined E and G cases increased in comparison to the early phase group.

18.8%); P (n=1,692; 19. 1%); and D (n=519; 5.9%). Thus, the proportions of E and G cases in the late phase were lower than those in the early phase; the proportion of P cases in the late phase was higher than that in the early phase (chi-squared test and residual test, p<0.01). When the late phase was adjusted for age, the proportions were as follows: E, 29.4%; G, 30.7%; F, 17.9%; P, 16.8% and D, 5.1%. The

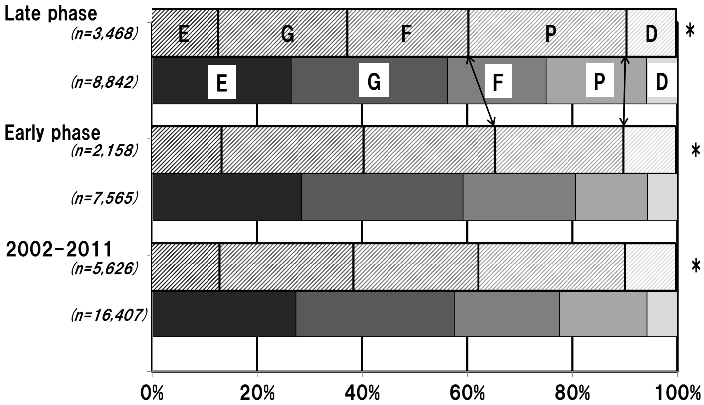


Figure 4. The rates of each outcome in the early phase (2002-2006) and late phase (2007-2011) groups.
Striped columns show each outcome in over 80 years of age*.
The proportions of E, G and F cases among patients of ≥80 years of age in the late phase group were low, and the proportion of P cases was high in comparison to the early phase group (chi-squared and residual test, p<0.01).

combined proportion of E and G cases was higher in comparison to the early phase (Figure 3). At the same time the proportion of E, G and F cases among patients of ≥80 years of age in the late phase group was low, and the proportion of P cases was high in comparison to the early phase group (chi-squared test and residual test, p<0.01) (Figure 4).

[The treatment outcomes according to the clinical categories]

In both treatment groups, among the clinical categories, the AT and CE cases showed a significantly high proportion of poor outcomes, while the LI cases showed a significantly high proportion of good outcomes (chi-squared test, p<0.05). The late phase group tended to show lower proportions of good outcomes (E and G), and higher proportions of P and D (considered to be poor outcomes) in comparison to the early phase group. The average age was significantly higher across all clinical entities in the late phase group (t-test, p<0.01). Furthermore, when the late phase group was adjusted for age, the treatment outcomes improved across all clinical entities, with a higher proportion of good outcomes (E and G) in comparison to the early phase cases (Figure 5).

[The factors associated with poor outcomes]

Table 2 shows the results of the univariate analysis of the factors associated with poor outcomes, which investigated the correlations between the risk factors, stroke history, age, gender, severity at onset and CE or non-CE, and a poor prognosis. Old age, female sex, severe symptoms at onset, atrial fibrillation, a history of smoking, CE and a previous history of stroke were significantly correlated with a poor prognosis. The results of a multiple logistic regression analysis that included these factors using explanatory variables other than the presence of atrial fibrillation – which is strongly correlated with CE – are shown in Table 3. Significant associations were observed between old age, female sex, severe

Table 2. The factors significantly associated with a poor prognosis (univariate logistic regression analysis)

	2002-2011	(n=16407)	
	Odds ratio	95% CI	p value
Age	1.067	(1.064-1.071)	<0.01
Sex (female)	1.795	(1.686-1.912)	<0.01
Severity of stroke	11.043	(10.291-11.849)	<0.01
Hypertension	0.919	(0.860-0.981)	0.0111
Atrial fibrillation	2.455	(2.227-2.646)	<0.01
Diabetes mellitus	0.965	(0.903-1.030)	0.283
Hyperlipidemia	0.643	(0.592-0.699)	<0.01
Smoking	0.599	(0.557-0.645)	<0.01
Previous stroke	1.808	(1.683-1.943)	<0.01
CE or non-CE	2.763	(2.567-2.973)	<0.01

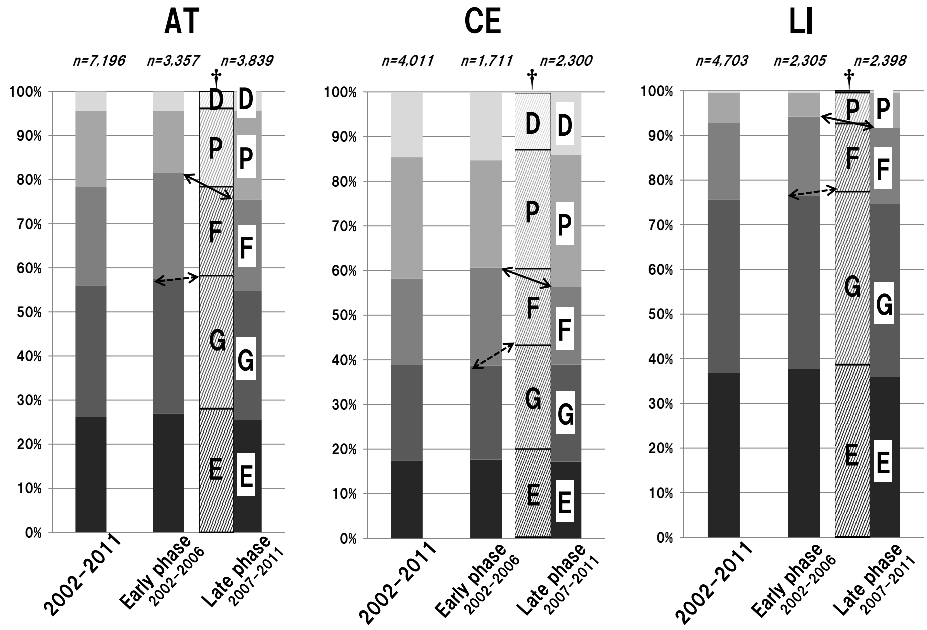


Figure 5. The rates of each outcome in the early phase (2002-2006) and late phase (2007-2011) groups according to the clinical category.
In the late phase group, the proportions of P and D increased in all clinical categories in comparison to the raw data of the early phase group (chi-squared and residual test, p<0.01). However, after adjusting the late phase group for age † (to match the early phase group), the proportions of E and G in all clinical categories were higher in comparison to the early phase group.
AT: atherothrombotic infarction, CE: cardiogenic cerebral embolism, LI: lacunar infarction

Table 3. The factors significantly associated with a poor prognosis (multiple logistic regression analysis)

	2002-2011 (n=16407)			2002-2006 (n=7565)			2007-2011 (n=8842)		
	Odds ratio	95% CI	p value	Odds ratio	95% CI	p value	Odds ratio	95% CI	p value
age	1.044	(1.04-1.049)	<0.01	1.04	(1.034-1.047)	<0.01	1.049	(1.043-1.055)	<0.01
sex (female)	1.322	(1.204-1.453)	<0.01	1.234	(1.071-1.421)	<0.01	1.402	(1.235-1.591)	<0.01
severity of stroke	9.766	(9.075-10.509)	<0.01	12.123	(10.804-13.602)	<0.01	8.289	(7.534-9.120)	<0.01
hypertension	0.908	(0.829-0.995)	0.039	0.909	(0.793-1.043)	0.175	0.991	(0.805-1.031)	0.138
hyperlipidemia	0.819	(0.730-0.918)	<0.01	0.882	(0.737-1.056)	0.171	0.781	(0.673-0.907)	<0.01
smoking	0.983	(0.882-1.096)	0.787	0.883	(0.749-1.042)	0.135	1.079	(0.934-1.248)	0.302
previous stroke	1.696	(1.538-1.871)	<0.01	1.787	(1.534-2.081)	<0.01	1.642	(1.444-1.866)	<0.01
CE or non-CE	1.36	(1.190-1.553)	<0.01	1.459	(1.188-1.793)	<0.01	1.288	(1.081-1.535)	<0.01

symptoms at onset, CE, a previous history of stroke, and a poor prognosis.

Discussion

Almost all of the facilities to which acute-phase stroke are admitted in Yamagata were registered their data with the YSTCS. Thus, despite the fact that this is a hospital-based registry, the results are highly comprehensive. However, there is a limitation in that some patients with minor or asymptomatic stroke might have been excluded. A study[9] from Akita prefecture (2004 population: 1,159,000), which is located next to Yamagata (2004 population: 1,223,000), reported that 18,018 cases of cerebral infarction (CI) occurred over a 10-year period (1995-2004). Thus, the comprehensiveness of the results is almost comparable to the results of the Akita study.

The present study showed that in the late phase group, the proportion of cases that were categorized as lacunar infarction was smaller, and the number of cardiogenic cerebral embolism cases was increased in comparison to the early phase group. This reflects findings from a study in Hisayama town[5], and might indicate a reduction in lacunar infarction due to recent improvements in blood pressure control. At the same time, the Westernization of both diet and lifestyle has led to increased rates of obesity, diabetes and hyperlipidemia, and this is considered to be a factor in the increasing numbers of both cardiogenic cerebral embolism and atherothrombotic cerebral infarction cases[10]. The proportions of patients with diabetes and hyperlipidemia in the late phase were higher than those in the earlier phase of the present study (Table 1), and the issue of preventing the onset of future cerebral infarction needs to be considered in light of these findings.

In terms of the treatment outcomes, the late phase included a higher proportion of cases with a poor prognosis in comparison to the earlier phase. A recent report on the outcomes of cerebral infarction treatment provided the largest stroke databank from a hospital-based registry in Japan. The results from that study also showed that in 2005 to 2007, the proportions of cases with good outcomes were decreased across all categories (atherothrombotic cerebral infarction, cardiogenic cerebral embolism and lacunar infarction) in comparison to the data registered from 2000 to 2004[11,12]. In other words, the results were similar to those of the present study, in which no improvement in the treatment outcomes was seen over the latter part of the study. However, after adjustment for age, the treatment outcomes in the late phase were better than those in the early phase, and it is considered that age may have had a significant impact on this result. In the present study, the average age at onset in the early phase was 72.7 ± 11.43 years, while that in the late phase was 75.0 ± 11.35; the difference was statistically significant ($p<0.01$). According to the National Census data from 2000, 3.82% of the national population and 5.11% of the population of Yamagata Prefecture was ≥80 years of age, while in 2010 these proportions had almost doubled to 6.35% nationwide and 9.38% in Yamagata Prefecture.

One more issue that should be noted is the fact that the proportion of lacunar infarction (which has a good prognosis) in the late phase group fell in comparison to the early phase group, while the proportion of cardiogenic cerebral embolism (which has a poor prognosis), rose. Despite the fact that the proportion of cardiogenic cerebral embolism fell when adjusted for age, patients become more likely to develop non-valvular atrial fibrillation, which is the greatest risk factor for cardiogenic cerebral embolism, with advancing age[13,14]. It is likely that this contributed to the increased proportion of cardiogenic cerebral embolism cases. In other words, diagnosis and treatment of cerebral infarction have definitely advanced because of the results in the late phase group after age adjustment has improvement tendency, but the current situation is that medical advancements can hardly keep up with the higher age at onset of stroke.

The multiple logistic regression analysis revealed that age, female sex, severe symptoms at onset, CE, and a previous history of stroke were significantly associated with a poor prognosis in cases of cerebral infarction. Previous studies of female patients did not clearly explain the biological reasons associated with the sex differences, and many reports seem to suggest that social factors (i.e., living alone or admittance to a residential facility) may contribute to this result[15,16].

The results of the present study have implications when considering how to improve treatment outcomes for cerebral infarction in the future. Firstly, severe symptoms at onset are associated with a poor prognosis; thus the treatment outcomes of acute-phase cerebral infarction require further improvement. rt-PA infusion treatment is still only used in the treatment of 5.2% of cerebral infarction patients[17], even in studies reporting its use in the treatment of a high proportion of cases, and a good prognosis was reported to have been achieved in 33.1–39.0% of rt-PA-treated cases[18,19]. A good prognosis was reported in 42% of cases in which mechanical thrombus collection therapy was performed in the hyper acute-phase[20], and further improvements are anticipated. These methods have only just been approved and the number of institutions implementing them is still relatively small; thus, there is an issue with regard to ensuring that the number of cases to which these treatment modalities are applied increases in the future. For this reason, further developments in acute-phase therapies are required. In particular, the primary prevention of cardiogenic cerebral embolism, which has a particularly poor prognosis, is believed to be an extremely important issue.

When considering the primary prevention of cardiogenic cerebral embolism, the main target becomes patients with non-valvular atrial fibrillation. To date, treatment has consisted of the administration of the anticoagulant warfarin; however, 2–6.6% of patients who receive warfarin suffer from the complication of intracranial hemorrhage[21)–23)]. As such, warfarin is not been widely used in primary prevention. More recently direct oral anticoagulants that are associated with a lower incidence of intracranial hemorrhage in comparison to warfarin[24),25)] have been approved, and physicians no longer need to be hesitant in administering these drugs as a means of primary prevention. The application of anticoagulant therapy in the treatment of non-valvular atrial fibrillation, the major risk factor in cardiogenic cerebral embolism, has previously been determined based on the patient's CHADS2[26)] score (one point each for C [congestive heart failure], H [hypertension], A [age≥75 years]and D [diabetes mellitus], and two points for S [stroke]). Recently, however, the more accurate CHA2DS2-VASc[27)] score (in which one point is awarded for V [vascular disease]A [age 65-74 years]and S [female sex]) has been recommended for identifying cases in which the additional use of anticoagulants is considered to be associated with less risk. The stricter application of primary prevention methods for cardiogenic cerebral embolism will be necessary in the future.

Conclusions

The analysis of the stroke data registered in YSTCS revealed that in the late phase (2007-2011) there was a reduction in the incidence of lacunar infarction and an increase in the incidence of cardiogenic cerebral embolism in comparison to the early phase (2002-2006). However, after adjustment for age, the outcomes tended to improve in the late phase. In other words, while definite progress has been made in the diagnosis and treatment of cerebral infarction, it is clear that developments in medicine have not kept pace with the advance in age at the onset of stroke. Furthermore, the present study clarified that female sex, old age, severe symptoms at onset, cardiogenic cerebral embolism and a previous history of stroke were independently associated with a poor prognosis in patients with cerebral infarction.

Improving the outcomes of treatment for cerebral infarction will require further developments in acute-phase therapies and the primary prevention of cardiogenic cerebral embolism, many cases of which were severe. In other words, it will be necessary to thoroughly and strictly administer anticoagulant treatment to patients with non-valvular atrial fibrillation, which is the main cause of cardiogenic cerebral embolism.

Addendum

Yamagata Society on Treatment for Cerebral Stroke

Kitamurayama Municipal Hospital Department of Neurology, Kitamurayama Municipal Hospital Department of Neurosurgery, Yamagata Prefectural Kahoku Hospital Department of Neurology, Yamagata Prefectural Kahoku Hospital Department of Internal Medicine, Yamagata Prefectural Kahoku Hospital Department of Neurosurgery, Yamagata Prefectural Shinjo Hospital Department of Brain Surgery, Yamagata Prefectural Central Hospital Department of Neurology, Yamagata Prefectural Central Hospital Department of Neurosurgery, Okitama Public General Hospital Department of Neurology, Okitama Public General Hospital Department of Neurosurgery, NHO Yamagata National Hospital Department of Neurology, Yonezawa National Hospital Department of Neurology, Sanyudo Hospital Department of Neurosurgery, Shinoda General Hospital Department of Neurosurgery, Tsuruoka Municipal Shonai Hospital Department of Neurosurgery, Nihonkai

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