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First-Ever Acute Stroke in the Very Elderly: A Retrospective Study in Akita Prefecture, Japan, 1996-1998

Abstract

Background: The highest life expectancy is registered in Japan for both women and men at the present. The stroke of the very elderly has different features than the younger's' one, but published data is still scarce on this topic. The very elderly seem to receive fewer vascular protection interventions that have been shown to be effective in younger individuals. Although there has been an under-representation of the very elderly in studies of stroke therapy, these treatments might be of benefit to this group of patients.

Subjects and Methods: The subjects were selected from the Akita Stroke Registry with first-ever acute stroke from 1996 to 1998.

Results: 8,046 cases were recorded, 7362 patients aged <85 years, and 684 patients aged ≥85 years. Sex ratio (w/m) was 0.84 and 1.89 in the two age groups. In the population of Akita the crude incidence of first-ever stroke was 222/100,000/year, and 1,085/100,000/year in the very elderly, who were characterized with significantly lower prevalence of stroke risk factors, except that of atrial fibrillation and cardiac diseases. The stroke subtype distribution in the two age groups (young/old) was significantly different (intracerebral haemorrhage 26.7% vs. 20.6%, infarction 60.0% vs. 73.2%, SAH 13.3% vs. 6.2%). Severity at onset was higher in the very elderly patients (consciousness disturbance 29.9% vs. 45.5% and severe motor deficit 75.6% vs. 86.4%). Both 28 day case fatality (10, 1% vs. 22.3%) and 1 year mortality rates (17.8% vs. 48.8%) were poorer in the very elderly. The most powerful prognostic factor of death was consciousness level at onset in both age groups. The following in order was the SAH stroke subtype. In the elder group the risk factors were not independent predictors of death, except diabetes for death within 28 days.

Conclusion: The very elderly had lower prevalence of traditional cardiovascular risk factors, however they suffered stroke with very high frequency, the endured stroke event caused very severe symptoms and resulted in death with high rate.

Keywords: First-ever stroke; Stroke; Very elderly; Epidemiology

Research Article

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Introduction

Stroke is the 3rd leading cause of mortality and one of the main causes of long-term intellectual, psychological, and physical disability in Japan as well as in the other industrialized countries [1]. It is well known that the incidence of stroke increases with age [1-4]. In most of the developed countries the mean age of the population increased significantly in the last few decades due to the decreasing in birth rate and the increasing in life expectancy [5]. In Akita Prefecture of the highly industrialized Japan where the highest expected lifespan is measured for the time being, the number of people above 85 year in 2003 (25,378) was more than ten times higher than in 1970 (2,403) based on census data. Although stroke mortality declined during the last decades in most of the Western societies [6,7], stroke incidence is very high in the elderly, especially in the very elderly (≥85year) [8]. For rearranging the stroke prevention and treatment strategies, new epidemiological evaluations are needed to unfold the stroke characteristics of the very elderly people [9]. The very elderly seem to receive fewer vascular protection interventions that have been shown to be effective in younger individuals. Although there has been an under-representation of the very elderly in studies of stroke therapy, these treatments might be of benefit to this group of patients, too. Unfortunately only a few studies are engaging in this topic, most of the stroke epidemiological studies are dealing only with the younger population up to age 65, 75, maximum 85 years [10-12]. Even the most extensive comparison study, the MONICA Project, covers only a limited age range up to 75 years, but mainly up to 65 years [11]. Although some articles are available, they have only a very limited number of stroke patients above 85 year age [2,8,12]. Our purpose is to increase the data available on stroke of the very elderly people for planning adequate risk factor management and acute stroke care.

Subjects and Methods

Akita Prefecture, a rural area, is located in the northern part of Honshu Island, the main island of Japan and it had a population in 1997 of 1,205,621, including 21,009 people above

85 year, based on census data and yearly records of demographic changes. The study subjects were selected from the Akita Stroke Registry [13] with first-ever-acute-stroke onset [14] from 1996 to 1998. The registry was started in 1973 and it contains 27 hospitals of Akita Prefecture which deal with stroke patients. Its centre is located in the Department of Epidemiology, Research Institute of Brain and Blood Vessels Akita. All consecutive stroke cases are registered. From 1983 the diagnosis of stroke for case ascertainment was based on not only clinical data but on computer tomography (CT) as well in every case, or if it was necessary on magnetic resonance imaging (MRI) [13,14]. Stroke was defined as the onset of rapidly developing clinical signs of focal or global disturbance of cerebral function, lasting more than 24 hours or leading to death, with no apparent cause other than a vascular origin, according to the MONICA stroke criteria [11,14]. Therefore cases with transient ischemic attack (TIA) or "silent infarcts" with no associated symptomatic episode were excluded from the registry [14]. Although the Akita Stroke Registry is hospital based, it may be considered as a population based register because practically every suspected stroke cases are referred to hospital, the proportion of stroke cases are not hospitalised is estimated about 2% [13]. However, the proportion of stroke patients admitted to hospital varies widely in the different countries [4]. In our case this 2% probably contains the rapidly fatal cases, a few very mild events and a few very old patients [15]. Inhabitants' data encompasses basic demographic and detailed clinical characteristics, such as date of birth, sex, date of onset, date of admission, main clinical symptoms between onset and admission, presence of cerebrovascular risk factors, hospital of treatment features, date of performing CT (/MRI) scan, first-ever or recurrent stroke, stroke subtype, localisation of lesion. For stroke subtype classification we divided the inhabitants into three groups, cerebral haemorrhage, cerebral ischemia, and subarachnoideal haemorrhage. In order to use a simple and widely accepted method for classification of ischemic stroke subtypes [16,17] we reclassified the cases by the localisation of ischemic events into five subgroups, as follows: total anterior circulation infarcts (TACI), partial anterior circulation infarcts (PACI), posterior circulation infarcts (POCI), lacunar infarcts (LACI), and undetermined type, based on the Bamford classification [17].

Statistical methods

The hospitals involved in the registry send stroke case reporting forms regularly to the centre which contain patient demographic and clinical data. For the calculation of incidence rates the population of Akita Prefecture in 1997 was used as the denominator [18]. The incidence of stroke is expressed as the number of first-ever-in-a-lifetime stroke events per 100,000 persons per year. For statistical analysis we used Statistical Package of Social Sciences (SPSS) 12.0 software. We divided the first-ever stroke events into 2 groups by age, one for the patients younger than 85 year (henceforward Group 1, <85y; younger group; first group), and one for the patients above 85 year (henceforth Group 2, ≥85y; elderly group; second group). The two groups were compared. Survival rates were counted with timetable method. Risk factor distributions were calculated with two by two crosstabulation method, estimating of significance level was made by χ^2 test. For the continuous variables Mann-Whitney test was used. Relationship between outcome and different factors were analysed with Cox regression model. A value of $p<0.05$ was considered as significant. Considering that data on risk factors, consciousness level was missing in some cases, for the calculations in which these were used only 6,362 patients (5,830 and 532 patients in the two age groups, sex ratio (w/m) was 0.84 and 1.81, $p<0.001$, respectively) were included out of the 8,046. This means 20.9% data loss, which is acceptable in a retrospective study.

Results

In the three-year time period, from 1996-1998, 10,022 certain stroke cases occurred in Akita Prefecture, 8,046 (80.3%) of them were considered as first-ever-in-a-lifetime stroke cases. As it was mentioned above, we divided them into two groups by age. The first group contained 7,362 (91.5%) stroke patients, and the second one had 684 (8.5 %) patients. The sex ratio (women/men) in the two groups was 0.84 in Group 1, and 1.89 in Group 2 ($p<0.001$). The mean ages for the two groups were 67.9±10.9 and 88.2±2.8 years ($p<0.001$). In the studied period the crude annual stroke incidence rate in Akita Prefecture was 222/100,000 capita, 201/100,000 and 246/100,000 for women and men, respectively. The age-adjusted rate, standardized to the European population [14] was 137/100,000, for women it was 108/100000 and for men it was 174/100,000, as shown in Table 1. The stroke incidence rate in the very elderly was 1,085/100,000 per year. The incidence rates of the different stroke subtypes were much higher in the older group [19], respectively, as it is show in Table 2. In the younger group the proportion of ICH, CI and SAH were 26.7%, 60.0% and 13.3%. In the older group these ratios were remarkably different (ICH 20.6%, CI 73.2%, and SAH 6.1%, $p<0.001$). Symptoms at onset were more severe in the older age group.

The traditional risk factors were more frequent in the younger group ($p <0.001$ for each) except for atrial fibrillation and cardiovascular diseases ($p <0.001$ for each) as totalized in Table 3. The frequency of AF in the very elderly was 26.9% (in the younger group it was 15.0%, $p<0.001$). We examined the risk factor distributions in the two age groups by sex, because of the very different sex ratios in the two age groups. In the younger group men had significantly higher frequency of diabetes mellitus and atrial fibrillation (18.3% vs. 16.3%, $p=0.045$, and 16.2% vs. 13.7%, $p=0.008$), significantly lower frequency of hypertension and hyperlipidemia (54.8% vs. 59.2%, $p=0.001$, and 9.0% vs. 12.2%, $p<0.001$) than women, and there was no significant difference for the prevalence of heart disease. In the elderly group there were no significant differences in the prevalence of the different risk factors at all between women and men.

Regarding the ischemic stroke subtypes distribution, the proportions of total and partial anterior circulation infarcts were very high in the very elderly, much higher than in the younger group (8.8% vs. 3.3%, $p<0.001$, and 34.9% vs. 24.9%, $p<0.001$), while the proportions of posterior circulation infarcts and lacunar infarcts were significantly lower (7.6% vs. 13.3%, $p<0.001$, and 28.7% vs. 37.9%, $p<0.001$).

The 28 day case fatality (CF) and 1 year mortality rates were dramatically higher in the second group, mortality rates are given details in Table 4. Outcome in the aspect of survival after first-ever stroke in the very elderly was much poorer than in the younger group. The 7 and 28 day case fatality rates were about twice higher in the elder group (13.4% and 22.3%) than in the younger one (7.2% and 10.1%). The overall 28 day case fatality was 11.4%. The poorest outcome was found in patients with SAH in the group aged ≥85year (57.2%). In the CI subgroup the 28 day CF rates were 5.4% in the very elderly and 17.3% for the young patients, respectively.

We found higher severity at onset in the very elderly patients, consciousness level disturbance rate was 29.9% vs. 45.5%, the frequency of severe motor symptoms were 75.6% vs. 86.4%. Consciousness level disturbance proved to be the strongest predictor of death in the older group (HR=20.43, p<0.001 for 28 day fatality, HR=6.93, p<0.001 for 1 year mortality), and the younger group (HR=8.56 p<0.001 for 28 day fatality, 4.50, p<0.001 for 1 year mortality), too. For long-term mortality age was an independent predictor for stroke mortality in both age groups (HR=1.04, p<0.001 and HR=1.06, p=0.004 for 1 year, and HR=1.05, p<0.001 and HR=1.04, p=0.017 for 3 year mortality). Women aged less than 85 year had a lower 28 day mortality risk (HR=0.78, p=0.005) than men of the same age. This difference between the genders in the younger group could be seen in the 1- and 3-year mortality as well (HR=0.72, p<0.001 and HR=0.67, p<0.001). In the elderly group there was no significant difference in the mortality risk of men and women, although the gender difference remained as a non-significant trend. Our findings were that ICH meant a higher mortality risk (HR=1.56, p=0.001 for 28 day, HR=1.29, p=0.002 for 1 year, and HR=1.26, p=0.094 for 3 year mortality) than CI. In the older age group the risk of death was lower in patients with ICH than in the CI group (HR=0.92, p=0.761, HR=0.77, p=0.153, and HR=0.94, p=0.713), but these results were not significant, either. SAH was a strong, independent predictor of mortality in each age groups for both short and long term mortality (HR=2.76, p<0.001, HR=2.31, p<0.001 and HR=1.40, p<0.001 in the younger group, and HR=5.46, p=0.001, HR=3.75, p=0.001 and HR=1.91, p=0.010 in the elderly group). Regarding the main risk factors of stroke, like hypertension, AF, etc., none of them had significant influence on 28 day stroke mortality in neither of the age groups. In the respect of 1- and 3-year long-term mortality, none of these risk factors were associated with significantly higher or lower risk for mortality in the very elderly (p>0.05 for all). In the younger age group AF and diabetes were independent risk factors for death within 1 and 3 year (HR=1.31, p=0.016, HR=1.46, p<0.001 for 1 year, and HR=1.27, p=0.009, HR=1.35, p<0.001 for 3 year mortality). Hypertension and hyperlipidemia were associated with lower risk for 1-year mortality (HR=0.85, p<0.015 and HR=0.70, p<0.013) and for 3 year mortality as well (HR=0.83, p<0.001 and HR=0.68, p<0.001).

Table 1: Age and Sex Specific Incidence Rates.

Age group, y	Women		Men		All	
	Rate	±SD	Rate	±SD	Rate	±SD
0-4	0	0.0	0	0.0	0	0.0
5-9	0	0.0	0	0.0	0	0.0
10-14	2.0	4.7	1.9	4.5	1.9	3.2
15-19	1.8	4.4	0.9	2.9	1.3	2.6
20-24	4.6	7.8	1.1	3.6	2.8	4.2
25-29	2.1	5.1	10.9	11.7	6.5	6.3
30-34	9.4	10.7	19.5	15.6	14.4	9.4
35-39	15.9	12.7	43.4	21.3	29.5	12.3
40-44	35.8	17.7	61.5	23.3	48.6	14.6
45-49	77.2	23.9	127.8	30.8	102.5	19.5
50-54	116.6	33.6	237.9	49.4	175.4	29.6
55-59	164.7	38.4	323.2	58.4	237.5	33.9
60-64	252.2	44.5	457.6	65.6	345.6	38.5
65-69	374.1	54.7	685.8	82.0	514.1	47.6
70-74	541.9	71.7	825.7	102.9	662.5	60.1
75-79	772.6	100.8	994.5	148.2	855.4	84.0
80-84	973.0	139.1	1194.0	205.2	1052.6	115.7
85≤	1016.7	163.1	1244.5	275.0	1085.2	140.9
Total*	201	11	246	13	222	8
Adjusted**	174	9	108	6	137	5

Table 2: Incidence Rates of the Different Stroke Subtypes, /100000 per year.

Stroke Subtypes	Overall*	Aged ≥85year
Intracerebral Haemorrhage	58 (95% CI ± 4)	224 (95% CI ± 63)
Cerebral Ischemia	135 (95% CI ± 6)	795(95% CI ± 120)
Subarachnoideal Haemorrhage	28 (95% CI ± 3)	66 (95% CI ± 34)

*Crude annual rates

Table 3: Distribution of Main Risk Factors.

Risk Factors	Group 1 (<85y)	Group 2 (85y<=)	Significance level, p, CI 95%
Sex ratio (women/men)	0.84	1.89	<0.001
Mean age ± SD, year	67.9 ± 10.9	88.2 ± 2.8	<0.001
Hypertension	56.8%	47.0%	<0.001
Diabetes mellitus	17.4%	8.3%	<0.001
Atrial fibrillation	15.0%	26.9%	<0.001
Cardiovascular diseases	22.8%	34.2%	<0.001
Hyperlipidemia	10.5%	4.1%	<0.001
Smoking*	33.7%	8.2%	<0.001
Alcohol consumption*	43.4%	17.4%	<0.001

*For these calculations we had information of fewer cases, but after best case/worst case analysis the difference remained the same and significant (p<0.001).

Table 4: 28 Day Case Fatality and 1 Year Mortality Rates.

	28 Day Case Fatality				1 Year Mortality
	All Stroke	ICH	CI	SAH	
Younger group	10.4%	14.3%	5.4%	25.2%	17.7%
Older group	22.2%	22.8%	17.3%	78.5%	48.7%
Overall	11.4%	14.8%	6.7%	27.4%	20.4%

Discussion

Although this is a retrospective study, which has a high data quality [9,12], in Japan and in the Asian countries, this is the first study analysing the stroke characteristics of the very elderly and has a considerable number of cases in the mentioned age group. We found an 8.5% proportion of patients aged 85 years or more, which is lower than previously reported in other publications [2,8,12,20]. However, this value depends on the structure of the examined population. In the future the proportion of the very elderly is expected to increase due to the further increase in life expectancy and the further aging of the population in Japan.

In our study the incidence of first-ever stroke increased consistently with age from age 25 years in both sexes, and the rate was higher in men than in women in every age group above 25 year age, including the very elderly (≥85year), being in accord with other studies [2,12]. Although there are some studies reporting higher incidence rate in women than in men aged 85 year or older [2,4]. We found that the incidence rates of different main stroke subtypes were much higher in the very elderly than in the overall population of the prefecture.

We found substantial differences in the stroke subtype distributions between the two age groups in our study. In the younger group the distribution corresponded to the stroke subtype distribution throughout Japan [21] and China [1]. The high proportion of ischemic stroke events is prominent in the very elderly. The higher frequency of AF and heart disease, and lower frequency of hypertension in this age group can explain the shift toward the higher frequency of CI, and the lower frequency of ICH.

Regarding the ischemic stroke subtypes distribution, the proportions of total and partial anterior circulation infarcts were very high in the very elderly. The high frequencies of AF and heart disease in this age group support these findings, because TACI and PACI ischemic stroke subtypes are highly associated with embolic pathomechanism. The significantly lower proportions of posterior circulation infarcts and lacunar infarcts in the older group can be explained with the facts that the previous one is caused mainly by in situ thrombosis developed in the posterior circulation's large or middle size arteries, and the latter one is strongly associated with hypertension.

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The frequencies of controllable risk factors of stroke were relevantly lower in the elderly group, except that of atrial fibrillation and heart disease, which were much higher in patients aged 85 year or more. These results suggest that the very elderly people seem to be healthier than the younger ones, considering the risk factors, probably this is why they reached such a high age. Atrial fibrillation is a very important predictor of first-ever stroke, stroke severity, mortality and recurrence [22]. The frequency of atrial fibrillation is increasing with age [22], and this was very well demonstrated in the elderly group in our study. The frequency of AF in the very elderly was much higher than expected. We examined the risk factor distributions in the two age groups by sex, because of the very different sex ratios in the two age groups. In the younger group men had significantly higher frequency of diabetes mellitus and atrial fibrillation, significantly lower frequency of hypertension and hyperlipidemia than women, and there was no significant difference for the prevalence of heart disease. In the elderly group there were no significant differences in the prevalence of the different risk factors at all between women and men.

Outcome in the aspect of survival after first-ever stroke in the very elderly was much poorer than in the younger group. These fatality rates reported above are considerably lower than reported in other studies, both in hospital and population based ones [3,4,6,7,12,21,23], mainly due to the very high standard of stroke care in Japan. These very remarkable differences in the two groups in the respect of mortality cannot be explained with suboptimal treatment alone in the elderly group, as it was given details before. Our idea is that the cardio-respiratory and other life threatening complications occurred much more frequently in the elderly group, and this is a very important factor of short-term fatality [24] besides the higher severity of the disease in this age group in our study. Our data is consistent with the very high frequency of AF and heart disease. Furthermore, the pre-stroke functional status might be better in the patients aged less than 85 year as suggested in some publications [24-26], but unfortunately data on pre-stroke functional status is not available in our registry. The poorest outcome was found in patients with SAH, in the group aged ≥85year, more than the half of the patients died at the end of the first week. The best 28 day CF rates were found in the CI subgroup in both age groups. Not just the 28 day case fatality rates were much worse in the elderly group, but also the 1-year mortality rates, in accordance with the poorer post-stroke functional status and with the very high mean age in this group.

Severity at onset was higher in the very elderly patients due to probably due to the higher rate of cardiac embolism, high frequency of cardiac disease in the medical history.

We found that the level of consciousness at stroke onset, what is a good indicator of severity, had the most powerful effect on both short- and long-term mortality rates in both age groups, and this is in agreement with other studies on predictors for stroke mortality [26]. The relationship was stronger in the younger group. As reported in many studies, the patients with CI are at the lowest risk of death, and the patients with ICH or SAH were at higher risk [26,27]. Our findings were the same in the younger group. In the older age group the risk of death was lower in patients with ICH than in the CI group, but these results were not significant, either. This is likely because of selection bias, probably some patients aged 85 year or more with very severe ICH died before admission. SAH was a strong, independent predictor of mortality in each age groups for both short and long term mortality as expected.

Conclusion

We found very remarkable differences between the two age groups regarding the features of stroke. In the younger group the frequencies of the different stroke risk factors are still very high, stricter risk factor control is needed. The very elderly aged people had lower prevalence of traditional cardiovascular risk factors, notwithstanding they were the ones who suffered stroke with very high frequency, the endured cerebrovascular event caused very severe symptoms and resulted in death with high rate. This is highlighting the complexity of the course of aging, and it follows that it's valorising the importance of primary prevention, stroke care in the acute stage and rehabilitation in this high age group instead of the near nihilistic approach of the past.

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