Blood pressure and stroke risk in a regional network for general practitioners with regular specialist consultation

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Abstract : *Objective*— The Shizuoka Stroke Network (SSN) is a stroke prevention system that enables general practitioners to manage patients at high risk of stroke with regular specialist consultation. We evaluated blood pressure control, and compared risk of stroke among the SSN and three recent cohort studies of patients treated by specialists.
Methods— Blood pressure obtained in 389 patients registered in the SSN were retrospectively investigated (at the time of enrollment, and after 1-, 2- and 3-years of follow-up). The stroke rate in SSN patients was compared with that in the Japanese Reduction of Atherothrombosis for Continued Health (REACH) Registry (n = 5193), Japan Thrombosis Registry of Atrial Fibrillation, Coronary and Cerebrovascular Events (J-TRACE) (n = 8,093), and Effective Vascular Event Reduction after Stroke Registry (EVEREST) (n = 3,411).
Results— Systolic and diastolic blood pressure in SSN patients at 1-, 2-, and 3-year follow-up were significantly lower ($p < 0.001$ for each) than at enrollment (135.5, 134.4, 132.2 vs. 146.8 mmHg ; 76.2, 75.6, 73.6 vs. 81.2 mmHg). The stroke rate in primary prevention SSN patients (0.99 events per 100 person-years, confidence interval ; 0.98-1.00) was lower than that in the Japanese REACH Registry (1.28-2.07). The stroke rate in secondary prevention SSN patients (3.23, confidence interval ; 3.18-3.29) was higher than that in the Japanese REACH Registry and J-TRACE (2.95), but lower than that in EVEREST (3.81).
Conclusion— Our stroke prevention system might help general practitioners to manage blood pressure and prevent stroke onset as well as specialists.

Key words : stroke, blood pressure, cholesterol, risk factor, prevention, regional network

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Ⅰ. Introduction

Stroke causes nearly 10% of all deaths worldwide, and is the most common disease leading to patients becoming bedridden in Japan[1,2]. The management of stroke risk factors is important for reducing the risk of stroke[3,4]. Although general practitioners play an important role in managing these risk factors, certain impediments to such management have been pointed out, such as inadequate follow-up and monitoring, inadequate prescribing of prevention therapies, poor information provision, and inadequate self-management of risk factors by patients[5~9].

With the aim of providing for a division of roles and cooperation through community-based, critical cooperative paths, the Japanese government has promoted a concrete medical cooperation system for individual programs within medical care plans including stroke, cancer, and pediatric emergency medical services[10]. The cooperation system for stroke has been promoted in each community, but the promoting of division of roles for stroke prevention between general practitioners and stroke specialists is not easy in comparison with the cooperation system. Inadequate management by practitioners, anxiety of patients and their families about leaving the general hospital, and lack of a cooperation system between general hospital and general practitioners hinder promotion of division of roles. Since late 2006, we have managed the Shizuoka Stroke Network (SSN), a local stroke network in Shizuoka City (population, approximately 720,000)[11]. The SSN comprises six general hospitals which treat 88% of all emergency patients in the area, four rehabilitation facilities, and approximately 220 general practitioners. The SSN consists of two connected networks : a network for acute stroke (NAS) and a network for stroke prevention (NSP). NAS has the aim of rapidly transferring patients to a general hospital to receive intravenous tissue plasminogen activator or other treatments, and to realize the smooth referral of stroke patients from general hospitals to rehabilitation facilities and general practitioners. After hospital or rehabilitation facility discharge, registration in the network shifts from NAS to NSP. NSP is concerned with primary and secondary prevention of stroke, and is termed a circulating referral prevention system. This system involves recurring, scheduled referrals of registered patients to general hospitals from general practitioners. The aim of the circulating referral prevention system is to maintain highquality management of stroke prevention and to provide a sense of security to patients and their families.

Hypertension is the major risk factor for both ischemic and hemorrhagic stroke[12,13]. Blood pressure (BP) is positively associated with risk of stroke[14] and reduction of BP diminishes the risk of stroke[15,16]. Management targets for hypertension have been provided by various guidelines[17~21], but it is not uncommon for BP to be refractory to control, and the frequency of patients with such uncontrolled BP varies among countries[8]. The rate of adequate BP control is reported at less than 50% for general practitioners[22], compared with more than 70% for specialists[23,24].

Reductions in stroke recurrence rate have been seen in a recent study of Western countries[25,26] and have also been seen in Japan[27~29]. Recent cohort studies in Japan have demonstrated less than 4.0 stroke events per 100 person-years[27~29], about one-third the rate found in a previous population-based cohort study[30]. The patients in these studies were recruited from August 2004 to July 2009.

Progress in management of risk factors might have contributed to this reduction in stroke recurrence rate.

The purpose of the present study was to evaluate the efficacy of the SSN for control of BP and for prevention of stroke. BP was the strongest risk factor for any subtype of stroke[2]. Our hypothesis was that if the rate of adequate BP control achieved by the SSN, the rate of stroke onset in the SSN would be the same as that in patients under the care of stroke specialists. Because our study did not have a control group, the rate of stroke in our study was compared with that in recent cohort studies of patients treated by specialist cardiologists and/or neurologists in Japan as a benchmark. These studies were the Japanese Reduction of Aterothrombosis for Continued Health (REACH) Registry[27], Japan Thrombosis Registry of Atrial Fibrillation, Coronary and Cerebrovascular Events(J-TRACE)[28], and Effective Vascular Event Reduction after Stroke (EVEREST) Registry[29].

The findings of the present study may help to promote the development of prevention systems in other regional stroke networks.

Ⅱ. Methods

1. Study design

This was a retrospective multicenter cohort study. All subjects were patients registered in a network for high-risk patients in the SSN involving four general hospitals to which almost all stroke patients in this emergency services area were transferred. The registration period was between September 2006 and March 2008. This study protocol conformed to the ethical standards described in the Declaration of Helsinki and was approved by an institutional review board at each site.

2. Outline of the network for stroke prevention (NSP) in the SSN

The NSP has primary prevention and secondary prevention components. The aim of the primary prevention component is for general practitioners to be able to easily consult stroke special-ists at a general hospital regarding stroke risk for patients with coronary artery disease, peripheral artery disease, or multiple risk factors for atherothrombosis. When a general practitioner refers a patient to a stroke specialist, the stroke specialist evaluates : the history of cerebrovascular events ; BP ; current smoking ; presence of obesity (body mass index≥25); activities of daily living ; pulse wave velocity ; ankle-brachial pressure index ; neuroimaging findings (usually magnetic reso-nance imaging (MRI) and magnetic resonance angiography (MRA) ; and risk score. HbA1c, creatinine, triglyceride (TG), low density lipoprotein cholesterol (LDL-C), and high density lipoprotein cholesterol (HDL-C) were measured as necessary in accordance with the patients' risk factors. The stroke specialist evaluates the risk of stroke using these data and the clinical examination, decides on the schedule for the next consultation, and provides feed-back to general practitioners on a clinical pathway. The administration staff at the general hospital gives notice of scheduled referral to the general practitioner, who then make an appointment for their patient to see a specialist at the general hospital. At the next consultation, the stroke specialist reevaluates the risk of stroke using data from the clinical pathways and the clinical examination, and provide feedback to the general practitioner on new clinical pathway. In the network for secondary prevention, stroke specialists assess the risk of stroke and record the data on the clinical pathway in the same way as in the

network for primary prevention. This system is unique in that stroke specialists can intervene in the management of primary prevention, whereas they do not usually manage risk factors until stroke has occurred.

3. Study data and outcome

At the time of enrollment, patients were assessed for demographic variables, medical history, and risk factors using the clinical pathways. BP values were obtained from the clinical pathways for the time of enrollment, and for 1-, 2-, and 3-year follow-up visits. Adequate BP cont-rol was defined as <140/90 mmHg, and rates of adequate BP control were calculated at the time of enrolment, and at 1-, 2-, and 3-year follow-up visits.

Study outcome was all strokes occurring during the follow-up period of 3 years. Stroke was diagnosed when a patient had acute onset of focal neurological manifestations and the responsible lesion was confirmed by brain computed tomography or MRI. To allow comparison with other studies, the rate of stroke onset was calculated as events per 100 person-years. This definition is the same as that of J-TRACE and EVEREST. The REACH Registry calculated TIA and stroke separately. To compare with the stroke rate of the present study and that of previous studies, TIA was not recorded.

4. Study supervision

This study had a steering committee consisting of 7 members and a surveillance committee consisting of 4 members. The steering committee members were responsible for the study design, study progress management, statistical analysis, and preparation for publication. The surveillance committee monitored the works of the steering committee.

5. Data management

We collected all patient data from each hospital on recordable compact discs or other digital media. For security purposes, all investigators used the same forms, which did not include the hospital identification number, name, date of birth, or other information that could identify patients.

6. Published cohort studies used for comparison

The REACH Registry is a large, international, prospective cohort of patients with cerebrovascular disease (CVD), peripheral artery disease (PAD), or multiple (≥3) risk factors (MRFs) for atherothrombosis[27]. In the Japanese REACH registry, 5193 patients were enrolled between August and December 2004, and l-year follow-up data were available for 5,021 patients (69.25% male, average age 70.31 years). The number of patients with CVD, PAD, and MRFs was 1962, 603, and 2252, respectively. The 1-year event rate in patients with CVD was compared with that of patients with symptomatic atherothrombosis at other sites. J-TRACE is a nationwide multicenter cooperative cohort of Japanese patients with myocardial infraction (MI), stroke, or atrial fibrillation (AF). Baseline characteristics of 8087 Japanese patients (5804 male, average age 68.7 years) with a history of stroke (n = 3554), MI (n = 2291), or AF (n = 2242) were analyzed[28]. The manority of referring clinicians were cardiologists and neurologists, who referred 58.8% and 27.9% of participants, respectively. The EVEREST registry was conducted to investigate 1-year rates of atherothrombotic vascular events in patients with recent noncardioembolic ischemic stroke receiving at least one oral antiplatelet agent, and to assess the risk factors for recurrent

ischemic stroke in this population[29]. At 9-15 months after enrollment, data on presence/absence of atherothrombotic vascular events were collected.

7. Statistical analysis

We used descriptive statistics and reported mean and standard deviation (SD) for all measures. Changes in systolic and diastolic BP were analyzed using one-factor analysis of variance (ANOVA) with $P < 0.05$ indicating statistical significance. If ANOVA showed a significant difference, the Bonferroni/Dunn procedure was used as a posthoc test. The event rate was expressed as number of events per 100 person-years. When multiple events occurred in the same patient during the follow-up period, those events were regarded as multiple independent events. Statistical analysis was conducted with IBM SPSS Statistics 20.0 (IBM-Armonk, NY). The 95% confidence interval was calculated by the normal approximation for the Poisson distribution that the number of events per year was assumed to follow.

Ⅲ. Results

During this study period, 389 patients registered in the network for high-risk patients were available for assessment. Patient demographic variables are shown in Table 1. Primary prevention strategies were provided to 131 (34%) patients and secondary prevention strategies to 258 (66%). For the secondary prevention patients, initial stroke type was cerebral infarction in 173 (according to the TOAST classification[31], large-artery atherosclerosis was diagnosed in 38%, cardioembolism in 18%, small-artery occlusion in 26%, and other determined or undetermined etiology in 18%), cerebral hemorrhage in 39, subarachnoid hemorrhage in 9, transient ischemic attack in 9, and other in 28. Systolic and diastolic BP values at the time of enrollment and at the 1-, 2- and 3-year follow-up visits are shown in Table 2. SBP and DBP showed significant changes ($p < 0.001$ for each ; one-factor ANOVA), and SBP/DBP at 1-, 2-, 3-year follow-up visits decreased significantly compared with at the

Table 1. Baseline characteristics of patients in the SSN study

Number of patients	389
Age (years), mean ± SD	71.8 ± 10.5
Men (%)	46
Risk factors for stroke	
Hypertension (%)	80
Diabetes (%)	22
Dyslipidemia (%)	44
Atrial fibrillation (%)	12
Current smoker (%)	11
Obesity (%)	13

SSN= Shizuoka Stroke Network

Table 2. Time course of blood pressu

	Enrollment (n=389)	1-year follow-up (n=257)	2-year follow-up (n=220)	3-year follow-up (n=165)
Blood pressure				
SBP (mmHg)	146.8 (22.0)	135.5 (16.0)*	134.4 (14.9)*	132.2 (16.9)*
DBP (mmHg)	81.3 (13.6)	76.7 (10.5)*	75.6 (10.4)*	73.6 (10.6)*

SBP, systolic blood pressure; DBP, diastolic blood pressure; data are means (SD). SBP and DBP show significant changes ($p < 0.001$ for each; one-factor ANOVA), and SBP/DBP at 1-, 2-, and 3-year follow-up visits decrease significantly compared with at the time of enrolment (by 11.4/4.6, 12.5/5.7, and 14.6/7.7 mmHg, respectively; $p < 0.001$ for each; Bonferroni multiple-comparison test).

time of enrolment ($p < 0.001$ for each ; Bonferroni multiple-comparison test). SBP/DBP showed no significant differences between primary prevention patients and secondary prevention patients at the time of enrolment, or at 1-, 2-, and 3-year follow-up visits (primary prevention : 146/79.4, 135.5/75.2, 134.1/73.9, 131.7/71.7 mmHg, respectively ; secondary prevention : 147/82.6, 135.4/77.4, 134.5/76.4, 132.6/74.8 mmHg). The rates of adequate BP control were 40%, 64%, 68%, and 76% at the time of enrolment, and at 1-, 2-, and 3-year follow-up visits, respectively.

During this study period, two primary prevention patients and 14 secondary prevention patients experienced stroke, and the respective rates of stroke in these two patient groups were 0.99 (confidence interval, 0.98-1.00), and 3.23 (3.18-3.29) events per 100 person-years. In comparison to the recent published cohort studies, the SSN patients were older and less likely to be male or current smokers than the J-TRACE and EVEREST populations (SSN vs. Japanese REACH Registry, J-trace, EVEREST ; mean age, 72 vs. 70, 69, 69 years old ; male, 46% vs. 69%, 72%, 67% ; current smokers ; 11% vs. 17%, 22%, 23%). The rates of hypertension, diabetes and dyslipidemia in the SSN patients were similar to those in the other studies. The rate of stroke in the SSN primary prevention patients was lower than that in the REACH Registry (Table 3). The rate of stroke in the SSN secondary prevention patients was higher than that of subsequent stroke in the REACH Registry and J-TRACE, but lower than that in EVEREST (Table 3).

Ⅳ. Discussion

The rate of adequate BP control at 3-years' follow-up in the SSN patients was 76%, similar to rates reported for patients under the care of specialists in recent Japanese studies[23,24]. As mentioned in the results, the rates of stroke onset in the SSN patients were also equivalent to those in other studies of patients under specialist care. These findings might support our hypothesis that if the rate of adequate BP control in SSN patients could be achieved, the rate of stroke

Table 3. Comparison of stroke rates between the present study and recent cohort studies in Japan

	Stroke events per 100 person-years	
	Primary prevention	Secondary prevention
REACH Registry		
Patients with CVD (n = 1962)		2.77
Patients with CAD (n = 2252)	1.28	
Patients with PAD (n = 603)	2.07	
Patients with MRFs (n = 831)	1.56	
J-TRACE (n = 8093)		2.95
EVEREST (n = 3411)		3.81
Present study (n = 389)		
Primary prevention (n = 131)	0.99	
Secondary prevention (n = 258)		3.23

REACH = The REduction of Atherothrombosis for Continued Health; CVD = cerebrovascular disease; CAD = coronary artery disease; PAD = peripheral artery disease; MRFs = multiple (≥3) risk factors for atherothrombosis other than CVD, CAD, and PAD; J-TRACE = Japan Thrombosis Registry of Atrial Fibrillation, Coronary and Cerebrovascular Events; EVEREST = Effective Vascular Event Reduction after Stroke registry.

onset in SSN patients would be the same as in patients under the care of specialists.

The rate of adequate BP control in the present study was only 40% at enrolment, but it increased to 64% at the 1-year follow-up visit and eventually reached 76% at 3 years. This improvement might result from the circulating prevention system, which provided patients with regular specialist consultation. Regular evaluation by an external clinician might help maintain motivation regarding risk control, not only for practitioners but also for patients[32]. We speculate that the present patients maintained their motivation because they could receive advice from the specialists and because the importance of risk management was reaffirmed at follow-up visits. The low rate of adequate BP control at enrolment in the present study might be explained as follows. First, the purpose of our network for primary prevention is to manage high-risk patients, and many patients with uncontrolled BP were enrolled in this study. Second, patients who developed stroke were usually enrolled at discharge in our network for secondary prevention, and many ischemic stroke patients were managed with only moderate antihypertensive treatment because they were in the acute or sub-acute phase.

Although the SSN practice of regularly performing MRI and MRA might seem excessive, it is common practice in Japan. This might relate to the facts that 1) Japan has more MRI units per hospital than do other countries[33], and 2) approximately one-quarter of Japanese patients with atherosclerotic thrombosis have intracranial atherosclerotic stenosis or occlusion[34].

Some limitations of the present study should be considered. First, we enrolled outpatients who could visit practitioners with or without assistance, and most patients had mild to moderate ischemic stroke. As a result, our study findings are not generalizable to patients with severe ischemic stroke. However, as other recent cohort studies have the same limitation, comparison of the rate of stroke between these studies and the present would be reasonable. Second, adequate BP control was defined as <140/90 mmHg in this study, but this definition did not consider the difference between primary and secondary prevention. The guidelines suggest maintaining a normal BP, which is defined as 120/80 mmHg or lower for primary prevention and 140/90 mmHg or lower for secondary prevention)[17–21]. The benefit of maintaining a normal BP in secondary prevention is controversial. The J-shaped curve applies largely to the cardiovascular arterial bed rather than the cerebrovascular bed[35,36] ; however, a recent study demonstrated that among patients with recent non-cardioembolic ischemic stroke, SBP levels during follow-up in the very low-normal (<120 mm Hg) range were associated with increased risk of recurrent stroke[37]. Hence adequate BP control may differ among stroke types. Third, the present cohort study started out with fewer males and with lesser smokers than the published cohort studies. This may have resulted in better stroke rates. However. patients in the SSN were older that in published cohort studies. Aging raises the risk of the stroke far more than smoking and sex difference[2]. We believe that the main results is unaffected by the differences in patients' baseline characteristics.

Ⅴ. Conclusions

The SSN stroke prevention system might have a possibility to achieve risk factors management and stroke prevention equivalent to those achieved by specialists. We believe that

a circulating stroke prevention system can help general practitioners to manage risk factors and prevent stroke as well as specialists, and promote the division of roles for stroke prevention between general practitioners and specialists.

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References

1) Shinohara Y, Yanagihara T, Abe K, et al. Stroke in general. J Stroke Cerebrovasc Dis 2011 ; 20 : S7-30.
2) Suzuki K, Izumi M, Sakamoto T, et al. Blood pressure and total cholesterol level are critical risks especially for hemorrhagic stroke in Akita, Japan. Cerebrovasc Dis 2011 ; 31 : 100-6.
3) Harmsen P, Lappas G, Rosengren A, et al. Long-term risk factors for stroke : twenty-eight years of follow-up of 7457 middle-aged men in Goteborg, Sweden. Stroke 2006 ; 37 : 1663-7.
4) Candelise L, Bianchi F, Galligoni F, et al. Italian multicenter study on reversible cerebral ischemic attacks : III-Influence of age and risk factors on cerebrovascular atherosclerosis. Stroke 1984 ; 15 : 379-82.
5) Jorgensen HS, Nakayama H, Reith J, et al. Stroke recurrence : predictors, severity, and prognosis. The Copenhagen Stroke Study. Neu-rology 1997 ; 48 : 891-5.
6) Bak S, Sindrup SH, Alslev T, et al. Cassation of smoking after first-ever stroke : a follow-up study. Stroke 2002 ; 33 : 2263-9.
7) Kaplan RC, Tirschwell DL, Longstreth WT JR, et al. Vascular events, mortality, and preventive therapy following ischemic stroke in the elderly. Neurology 2005 ; 65 : 835-42.
8) Wolfe CD, Redfern J, Rudd AG, et al. Cluster randomized controlled trial of a patient and general practitioner intervention to improve the management of multiple risk factors after stroke : stop stroke. Stroke 2010 ; 41 : 2470-6.
9) Bushnell CD, Olson DM, Zhao X, et al. Secondary preventive medication persistence and adherence 1 year after stroke. Neurology 2011 ; 77 : 1182-90.
10) Overview of the Law to Amend the Medical Care Law in Establishing a System that Provides High Quality Medical Care (revised in 2006). Ministry of Health, Labour and Welfare, Japan web site. [publication date 2008. accessed 2014-05-30]. http://www.mhlw.go.jp/english/wp/wp-hw4/dl/health_and_medical_services/P38.pdf.
11) Kobari M, Imai N, Fukuchi Y, et al. Comprehensive referral system for stroke and high-risk patients : Shizuoka Stroke Network. Jpn J Stroke 2010 ; 32 : 647-53. (in Japanese,Abstract in English)
12) Kannel WB, Wolf PA, McGee DL, et al. Systolic blood pressure, arterial rigidity, and risk of stroke. The Framingham study. JAMA 1981 ; 245 : 1225-9.
13) Tanaka H, Ueda Y, Hayashi M, et al. Risk factors for cerebral hemorrhage and cerebral infarction in a Japanese rural community. Stroke 1982 ; 13 : 62-73.
14) MacMahon S, Peto R, Cutler J, et al. Blood pressure, stroke, and coronary heart disease. Part 1, Prolonged differences in blood pressure : prospective observational studies corrected for the regression dilution bias. Lancet 1990 ; 335 : 765-74.
15) Staessen JA, Wang JG, Thijs L.Cardiovascular protection and blood pressure reduction :

a meta-analysis. Lancet 2001 ; 358 ; 1305-15.
16) Law MR, Morris JK, Wald NJ. Use of blood pressure lowering drugs in the prevention of cardiovascular disease : meta-analysis of 147 randomised trials in the context of expectations from prospective epidemiological studies. BMJ. 2009 ; 338 : b1665.
17) Chobanian AV, Bakris GL, Black HR, et al. Seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. Hypertention 2003 ; 42 : 1206-52.
18) Furie KL, Kasner SE, Adams RJ, et al. Guidelines for the prevention of stroke in patients with stroke or transient ischemic attack : a guideline for healthcare professionals from the American Heart Association/ American Stroke Association. Stroke 2011 ; 42 : 227-76.
19) Goldstein LB, Bushnell CD, Adams RJ, et al. Guidelines for the primary prevention of stroke : a guideline for healthcare professionals from the American Heart Association/American Stroke Association. Stroke 2011 ; 42 : 517-84.
20) Japanese Society of Hypertension. Japanese Society of Hypertension guidelines for the management of hypertension (JSH 2004). Hypertens Res 2006 ; 29 : Suppl : S1-105.
21) Ogihara T, Kikuchi K, Matsuoka H, et al. The Japanese Society of Hypertension Guidelines for the Management of Hypertension (JSH 2009). Hypertens Res 2009 ; 32 : 3-107.
22) Mori H, Ukai H, Yamamoto H, et al. Current status of antihypertensive prescription and associated blood pressure control in Japan. Hypertens Res 2006 ; 29 : 143-51.
23) Hasegawa E, Tsuchihashi T, Ohta Y. Prevalence of chronic kidney disease and blood pressure control status in elderly hypertensive patients. Intern Med 2010 ; 51 : 1473-8.
24) Ohta Y, Tsuchihashi T, Kiyohara K, et al. Trend of blood pressure control status in hypertensive outpatients : with special reference to elderly hypertensives. Clin Exp Hypertens 2012 ; 34 : 258-63.
25) Girot M, Mackowiak-Cordoliani MA, Deplanque D, et al. Secondary prevention after ischemic stroke. Evolution over time in prac-tice. J Neurol 2005 ; 252 : 14-20.
26) Lewsey J, Jhund PS, Gillies M, et al. Temporal trends in hospitalisation for stroke rerecurrence following incident hospitalisation for stroke in Scotland. BMC Med 2010 ; 8 : 23.
27) Uchiyama S, Goto S, Matsumoto M, et al. Cardiovascular event rates in patients with cerebrovascular disease and atherothrombosis at other vascular locations : results from 1-year outcomes in the Japanese REACH Registry. J Neurol Sci 2009 ; 287 : 45-51.
28) Goto S, Ikeda Y, Shimada K, et al. One-year cardiovascular event rates in Japanese outpatients with myocardial infarction, stroke, and atrial fibrillation. -Results From the Japan Thrombosis Registry for Atrial Fibrillation, Coronary, or Cerebrovascular Events(-TRACE). Circ J 2011 ; 75 : 2598-604.
29) Suzuki N, Sato M, Houkin K, et al. One-year atherothrombotic vascular events rates in outpatients with recent non-cardioembolic ischemic stroke : the EVEREST (Effective Vascular Event REduction after STroke) registry. J Stroke Cerebrovasc Dis 2012 ; 21 : 245-53.
30) Hata J, Tanizaki Y, Kiyohara Y, et al. Ten year recurrence after first ever stroke in a Japanese community : the Hisayama study. J Neurol Neurosurg Psychiatry 2005 ; 76 : 368-72.
31) Adams HP Jr, Bendixen BH, Kappelle LJ, et al. Classification of subtype of acute ischemic stroke. Definitions for use in a multicenter

clinical trial. TOAST. Trial of Org 10172 in Acute Stroke Treatment. Stroke 1993 ; 24 : 35-41.

32) Heart Care Network Groups.Current trends in lifestyle-related disease management by general practitioners : a report from the "Heart Care Network" groups. J Atheroscler Thromb 2009 ; 16 : 799-806.

33) Health care resources ; MRI units per million population. OECD Health Statistics 2013-Frequently Requested Data. OECD web site. [acce-ssed 2014-5-30] http://www.oecd.org/els/health-systems/oecdhealthdata2013-frequentlyrequesteddata.htm

34) Akiyama Y, Haruki Y, Kobayashi S.Severity and prognosis of patients with cerebrovascular stenosis classified by the stroke type. in : Stroke data bank 2009. Kobayashi S ed. Nakayamashoten, Tokyo, 2009 : 72-3 (In Japanese).

35) Arima H, Chalmers J, Woodward M, et al. Lower target blood pressures are safe and effective for the prevention of recurrent stroke : the PROGRESS trial. J Hypertens 2006 ; 24 : 1201-8.

36) Chrysant SG, Chrysant GS. Effectiveness of lowering blood pressure to prevent stroke versus to prevent coronary events. Am J Cardiol2010 ; 106 : 825-9.

37) Ovbiagele B, Diener HC, Yusuf S, et al. Level of systolic blood pressure within the normal range and risk of recurrent stroke. JAMA 2011 ; 306 : 2137-44.