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研究成果の刊行に関する一覧表

書籍

著者氏名	論文タイトル名	書籍全体の編集者名	書　籍　名	出版社名	出版地	出版年	ページ
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発表者氏名	論文タイトル名	発表誌名	巻号	ページ	出版年
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Effects of Public Education by Television on Knowledge of Early Stroke Symptoms Among a Japanese Population Aged 40 to 74 Years : A Controlled Study

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Effects of Public Education by Television on Knowledge of Early Stroke Symptoms Among a Japanese Population Aged 40 to 74 Years

A Controlled Study

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Background and Purpose—An educational campaign by mass media has been associated with great increases in the knowledge about early symptoms of stroke. However, few studies were conducted with a controlled community intervention study.

Methods—To clarify the effects of a 1-year television campaign for the whole population on improvement of knowledge about stroke symptoms in 2 cities, a campaign area and a control area in Japan were selected. Before and after the campaign, 1960 randomly selected residents aged 40 to 74 years answered a telephone survey regarding knowledge of early stroke symptoms. We calculated the percentage and 95% CIs of participants who correctly chose all 5 early symptoms of stroke in each area and in each year.

Results—Before the campaign, 53% of participants (95% CI, 50%–55%) in the campaign area and 46% (95% CI, 44%–49%) in the control area correctly chose 5 early symptoms. After the 1-year television campaign, knowledge was significantly improved only in the campaign area (campaign area, 63%; 95% CI, 60%–66%; control area, 51%; 95% CI, 48%–54%). After sex stratification, only women showed improved knowledge of early symptoms. The audience rate for the campaign television programs was found to be higher in women than in men.

Conclusions–A 1-year stroke educational television campaign effectively improved knowledge about early stroke symptoms among Japanese women aged 40 to 74 years. No impact was found among men in this age group. Future studies should examine the impact of this approach on stroke knowledge among younger individuals and whether there are any behavioral changes that contribute to earlier presentation for treatment. **(*Stroke*. 2012;43:545-549.)**

Key Words: acute stroke ■ educational campaigns ■ knowledge ■ prevention ■ symptoms ■ warning signs

Delayed access to medical care in patients with stroke is associated with poor outcome. Knowledge of the early symptoms of stroke and the need to call an ambulance should therefore be widespread. The importance of ensuring timely treatment has grown dramatically since the introduction of thrombolytic treatment with tissue-type plasminogen activator[1–3] for cerebral infarction.

Various strategies for community education have been examined in previous studies.[4–8] Some reports have noted that television campaigns show greater efficacy for public education than other media.[4,6] However, few controlled studies have evaluated the effects of community education by television on knowledge about the early symptoms of stroke.[7] Furthermore, to our knowledge, there is no community education by television for stroke in Asian countries, where mortality due to stroke is high.[9]

The purpose of this study was to verify that television campaign could improve knowledge about early symptoms of stroke.

Methods

Study Setting

A community intervention providing information on early symptoms of stroke was conducted by television. The preintervention survey was performed in April 2009 and the postintervention survey was performed in April 2010. Because mortality of stroke varies between

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Table 1. Exposure to Intervention During the Campaign Period Among Participants in the Campaign Area: Postintervention Telephone Survey 2010

	Exposure to Intervention, No. (%)			
		Sex Differential		
Educational Intervention by Television	Overall (n = 968)	Men (n = 484)	Women (n = 484)	*P**
1-min spots†	381 (39.8)	161 (33.3)	220 (45.5)	<0.001
Highlight programs‡	274 (28.3)	108 (22.3)	166 (34.3)	<0.001
Both of 1-min spots† and highlight programs‡	207 (21.4)	74 (15.3)	133 (27.5)	<0.001
At least 1 of 1-min spots† and highlight programs‡	447 (46.2)	195 (40.3)	252 (52.2)	<0.001

*P value for χ^2 test.

†One-min spots: approximately 900 times of TV spots about stroke, each airtime was 60 s.

‡Highlight programs: a total of 60 times of documentaries and reports about stroke, each airtime was 5–15 min.

western and eastern Japan, 2 cities were selected from adjoining prefectures located in western Japan: Okayama city in Okayama prefecture for the campaign area and Kure city in Hiroshima prefecture for the control area.

A local branch of Japan Broadcasting Corporation (NHK, the largest noncommercial broadcasting in Japan) produced a series of television programs for the present study and broadcast them throughout the 1-year campaign period from April 2009. Okayama city was located in the broadcasting area of this local branch (Okayama broadcasting station of NHK). Residents living in the control area had few chances to watch these educational contents, because contents of broadcasting of a local branch of NHK vary by prefectures, and 2 cities do not have a common border and are located far from each other (approximately 150 km).

Participants

Sample size was calculated based on our previous surveys without television programs.[10] The number of participants required was estimated to be 780 people for each area (α=0.05, β=0.8). We decided to recruit approximately 1000 people from both areas for each of pre- and postintervention surveys.

Potential participants were randomly selected from the telephone directory in each area in each survey. A telephone survey was then continued until 140 complete interviews had been obtained for both men and women in their 40s, 50s, and 60s; and 70 complete interviews had been obtained for both men and women at 70 to 74 years old. A total of 3920 citizens were surveyed to find 980 in the campaign area and 980 in the control area for each pre- and postintervention survey. Approximately two thirds of available contacts were nonrelevant contacts, representing contacts with individuals <40 years old or ≥75 years old. Because the population was aged 40 to 74 was 300 389 in the campaign area and 114 670 in the control area in 2009, the sampling rate was approximately 0.33% and 0.85%, respectively.

Community Education

Because television programs produced by NHK are systematically distributed, similar television programs are broadcast by all local branches of NHK. However, sometimes slots are at the discretion of the local branch, such as 1-minute spots before serial dramas or 15-minute slots for local news before national news programs. The television campaign in the present study was thus mainly performed using these time slots.

The major points of the campaign by television programs were as follows. The first point was to make broadcasting content based on accurate scientific evidence. The second point was to provide repeated audiovisual information, that is, 1-minute spots were broadcast at least twice almost everyday, whereas highlight programs were broadcast at least once a week. Both types of programs were continued throughout the study period from April 2009 to March 2010.

The Okayama broadcasting station for NHK, Kawasaki Medical School, and the Japan Stroke Association supervised the campaign programs. The 1-minute spots comprised a total of 10 versions covering stroke, both of early symptoms and risk factors, prevention, up-to-date medical treatments, and rehabilitation. Highlight programs featuring 33 topics were broadcast during the campaign period.

Main Outcome Measures

Participants were asked to choose which of 10 listed symptoms fit as early symptoms of stroke. The 10 symptoms listed consisted of 5 early symptoms of stroke[11] and 5 incorrect or atypical symptoms ("sudden nasal bleeding," "sudden hot flush," "sudden pain in the left shoulder," "numbness or palsy of both hands and/or fingers," and "sudden difficulty breathing").

At the postintervention survey in the campaign area, participants were also asked whether they had seen any of the television spots and special programs.

Statistical Analysis

We estimated 95% CIs of population proportions for those who correctly chose all 4 early symptoms of stroke in surveys according to F-distribution. Sex-specific analysis was also performed. Participants who chose all 10 symptoms (n=45) were excluded from these analyses.

Results

Response rates of telephone surveys were 31.6% and 34.7% for pre- and postintervention surveys in the campaign area and 30.3% and 35.5% in the control area, respectively. In the postintervention survey in the campaign area, approximately 40% of participants reported "I saw some of the 1-minute spots about stroke on NHK between April 2009 and March 2010," whereas 30% reported seeing the highlight programs (Table 1). These audience rates for both types of programs were significantly higher for women than for men.

Proportions of participants who correctly chose 5 early symptoms are shown in Table 2. In all groups, regardless of area or sex, we observed tendencies toward improvement in knowledge about early symptoms of stroke; however, 95% CIs of those proportions demonstrated that only the campaign area showed a significant improvement in stroke knowledge (Figure). After sex stratification, only women in the campaign area showed a significant improvement (Figure).

In addition, the participants who watched either program had better knowledge about early symptoms of stroke (age- and sex-adjusted ORs and 95% CIs, 1.41 and 1.07–1.86).

Table 2. Proportion of Participants Who Correctly Chose 5 Early Symptoms of Stroke

	Campaign Area		Control Area	
	Preintervention 2009	Postintervention 2010	Preintervention 2009	Postintervention 2010
Overall				
No. of participants	965	968	971	971
Correct answer about stroke symptoms (%)				
Sudden numbness or weakness of the face, arm, or leg	868 (89.9)	869 (89.9)	805 (82.9)	812 (83.6)
Sudden confusion or trouble speaking or understanding others	907 (94.0)	901 (93.1)	895 (92.9)	879 (90.5)
Sudden trouble seeing with 1 or both eyes	674 (69.8)	764 (78.9)	651 (67.0)	642 (66.1)
Sudden dizziness, walking difficulties, or loss of balance or coordination	806 (83.5)	815 (84.2)	756 (77.9)	787 (81.1)
Sudden severe headache with no known cause	810 (83.9)	821 (84.8)	773 (79.6)	812 (83.6)
No. of selected correct answer about stroke symptoms (%)				
None	24 (2.5)	41 (4.2)	34 (3.5)	47 (4.8)
1	13 (1.3)	14 (1.4)	33 (3.4)	33 (3.4)
2	43 (4.5)	23 (2.4)	44 (4.5)	35 (3.6)
3	83 (8.6)	59 (6.1)	129 (13.3)	89 (9.2)
4	293 (30.4)	222 (22.9)	283 (29.1)	273 (28.1)
5*	509 (52.7)	609 (62.9)	448 (46.1)	494 (50.9)
Men				
No. of participants	478	484	484	486
Correct answer about stroke symptoms (%)				
Sudden numbness or weakness of the face, arm, or leg	422 (88.3)	421 (87.0)	389 (80.4)	388 (79.8)
Sudden confusion or trouble speaking or understanding others	444 (92.9)	437 (90.3)	437 (90.3)	429 (88.3)
Sudden trouble seeing with 1 or both eyes	342 (71.5)	365 (75.4)	328 (67.8)	325 (66.9)
Sudden dizziness, walking difficulties, or loss of balance or coordination	386 (80.8)	386 (79.8)	350 (72.3)	373 (76.7)
Sudden severe headache with no known cause	399 (83.5)	400 (82.6)	364 (75.2)	399 (82.1)
No. of selected correct answer about stroke symptoms (%)				
None	14 (2.9)	28 (5.8)	23 (4.8)	28 (5.8)
1	7 (1.5)	12 (2.5)	25 (5.2)	19 (3.9)
2	23 (4.8)	14 (2.9)	23 (4.8)	24 (4.9)
3	50 (10.5)	30 (6.2)	65 (13.4)	47 (9.7)
4	130 (27.2)	121 (25.0)	138 (28.5)	134 (27.6)
5*	254 (53.1)	279 (57.6)	210 (43.4)	234 (48.1)
Women				
No. of participants	487	484	487	485
Correct answer about stroke symptoms (%)				
Sudden numbness or weakness of the face, arm, or leg	446 (91.6)	448 (92.6)	416 (85.4)	424 (87.4)
Sudden confusion or trouble speaking or understanding others	463 (95.1)	464 (95.9)	458 (94.0)	450 (92.8)
Sudden trouble seeing with 1 or both eyes	332 (68.2)	399 (82.4)	323 (66.3)	317 (65.4)
Sudden dizziness, walking difficulties, or loss of balance or coordination	420 (86.2)	429 (88.6)	406 (83.4)	414 (85.4)
Sudden severe headache with no known cause	411 (84.4)	421 (87.0)	409 (84.0)	413 (85.2)
No. of selected correct answer about stroke symptoms (%)				
None	10 (2.1)	13 (2.7)	11 (2.3)	19 (3.9)
1	6 (1.2)	2 (0.4)	8 (1.6)	14 (2.9)
2	20 (4.1)	9 (1.9)	21 (4.3)	11 (2.3)
3	33 (6.8)	29 (6.0)	64 (13.1)	42 (8.7)
4	163 (33.5)	101 (20.9)	145 (29.8)	139 (28.7)
5*	255 (52.4)	330 (68.2)	238 (48.9)	260 (53.6)

*This proportion was defined as "participants who have knowledge about early symptoms of stroke" in the present study.

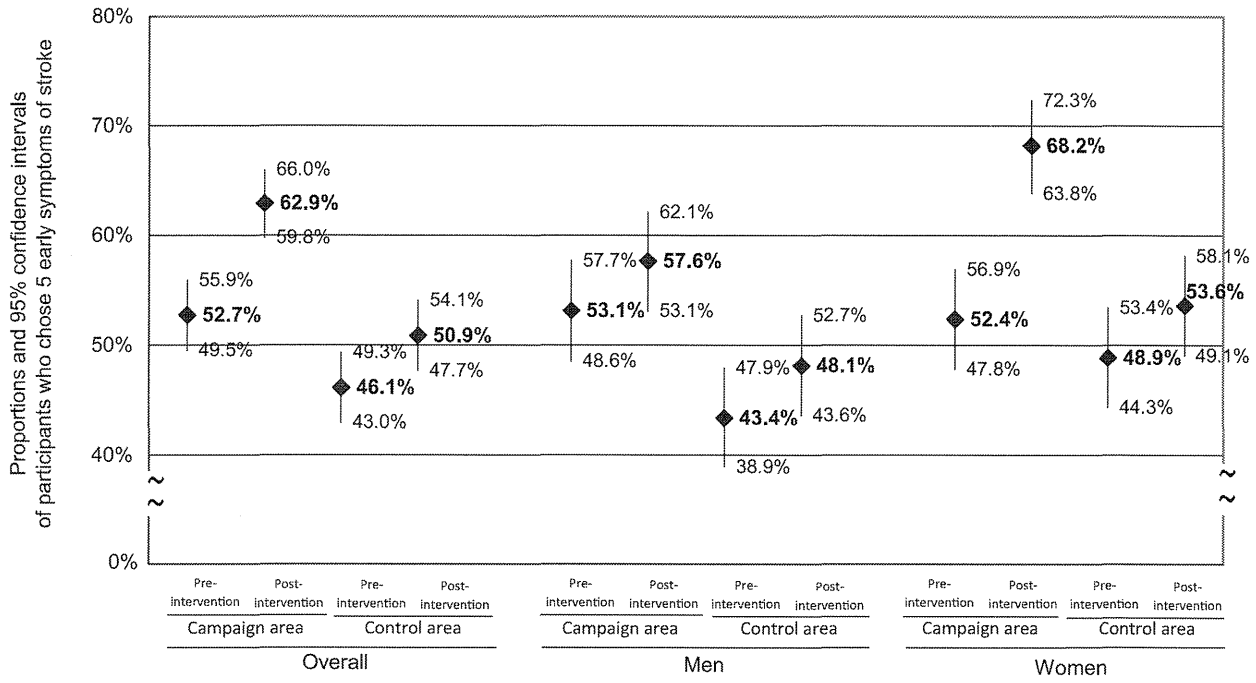

Figure. Overall and sex-stratified proportions and 95% confidence intervals (CIs) for participants who correctly chose 5 early symptoms of stroke before and after community education. Lozenge points indicate proportions of participants who correctly chose 5 early symptoms of stroke. Flickers indicate 95% CIs.

Discussion

This study is the first study of community education of stroke early symptoms in an Asian country. One advantage of the present study was the evaluation of the efficacy of television programs in the controlled trial with all participants randomly selected from the populations of the 2 areas. Another advantage was the use of a 1-year campaign, in which medically accurate contents were made by the collaboration of not only researchers and medical professionals, but also many staff from the largest noncommercial broadcasting corporation in Japan, that is, with mass media communication experts. As a result, this collaboration might have made the television programs more attractive for the audience, and many subjects reported that they had seen the 1-minute spots and the highlight programs during the campaign. In addition, our programs were repeated many times, which should have increased the likelihood of people seeing them, remembering them, and also remembering how to act if someone experiences early symptoms of stroke.

In previous studies that focused on public education about knowledge of stroke symptoms, the effectiveness of campaigns was assessed according to the ability to name ≥2 early symptoms of stroke without being shown multiple-choice items.[6,12] However, patients with stroke are unable to choose their own symptom at the time of onset, so people should be aware of all the typical early symptoms of stroke. Accordingly, the present study assessed improvements in knowledge about early symptoms of stroke based on the proportion of respondents who correctly chose all 5 early symptoms from a list of 10 symptoms.

We did not find significant improvements in knowledge about early symptoms of stroke among men. The improvement only in women may be explained by the greater exposure to television programs associated with the campaign, as suggested by the higher audience rates in women than in men. Furthermore, in previous studies of Western populations, knowledge about early symptoms of stroke was found to be better in women than in men during periods both with and without educational campaign.[12,13] Our results demonstrated not only similar sex differences to these previous studies, but also sex differences in the effects of the television campaign in a controlled trial. These results raise the possibility that men may have less general interest about health information compared with women. Therefore, it may be important to provide men various occasions to watch educational programs; for example, to increase a total number of on-air times, especially around programs that men are likely to watch such as sports, news, and action movies.

There are several limitations in the present study. First, we only evaluated the improvement in knowledge about early symptoms of stroke by broadcasting campaign; therefore, further study is necessary to assess its effectiveness in actual behaviors of patients with stroke; for example, the number of patients with stroke calling an ambulance, time from symptom onset to hospital presentation, how soon bystanders called the emergency center after having noticed early symptoms, and numbers of patients able to undergo therapy with tissue-type plasminogen activator should be evaluated. A previous cross-sectional study indicated that the knowledge about stroke symptoms was not associated with the intent to call 911 for stroke.[14] A gap may exist between the improvements in knowledge and actual changes in patient behavior. A second limitation is the lack of information about the costs involved in the campaign. The television programs were

made by NHK Okayama as its own project. Researchers thus did not need to worry about the costs of content production and broadcasting. Third, this study did not include individuals <40 years, who may be a person identifying a stroke onset of his or her family members and accessing the emergency medical services system. In addition, it is also important to distribute information about stroke to children and adolescent by television programs they are watching. They would probably advise their parents even if parents are not too interested about health information. This should be assessed in future studies.

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Disclosures

None.

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Brain Natriuretic Peptide Levels as a Predictor for New Atrial Fibrillation During Hospitalization in Patients With Acute Ischemic Stroke

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The aim of this study was to investigate the relation between brain natriuretic peptide (BNP) levels and the detection rate of new documented atrial fibrillation (AF) after ischemic stroke. Consecutive patients with ischemic stroke prospectively enrolled within 24 hours of onset. Patients with AF on admission electrocardiography or with histories of AF were excluded. The plasma BNP level was measured on admission, and the factors associated with new documented AF were investigated by multivariate logistic regression analysis. Furthermore, the detection rates of AF according to BNP level were evaluated. A total of 584 patients were enrolled. AF was detected in 40 patients (new AF group; 6.8%). The median BNP level of the new AF group was significantly higher than for the non-AF group (186.6 pg/ml [interquartile range 68.7 to 386.3] vs 35.2 pg/ml [interquartile range 15.9 to 80.1], p <0.0001). The cut-off level, sensitivity, and specificity of BNP levels to distinguish the new AF group from the non-AF group were 65.0 pg/ml, 80%, and 70%, respectively. Multivariate logistic regression analysis demonstrated that National Institutes of Health Stroke Scale score >7 (odds ratio 3.4, 95% confidence interval 1.685 to 7.006, p = 0.0007) and a plasma BNP level >65.0 pg/ml (odds ratio 6.8, 95% confidence interval 2.975 to 15.359, p <0.0001) were independently associated with new AF. The detection rates of AF according to BNP level were as follows: 2% of patients with <50 pg/ml, 4% of those with 50 to <100 pg/ml, 12% of those with 100 to <200 pg/ml, 26% of those with 200 to <400 pg/ml, and 38% of those with ≥400 pg/ml. In conclusion, BNP levels can predict new AF in patients with acute ischemic stroke. Elevated BNP levels result in an increase in the frequency of detection of new AF. (Am J Cardiol 2012;109:1303–1307)

Brain natriuretic peptide (BNP) is a 32–amino acid polypeptide containing a 17–amino acid ring structure that was isolated from porcine brain in 1988 and is a diuretic factor with vasodilator activity.[1] BNP is primarily released from ventricular myocardium and has been shown to be useful in the assessment of patients with cardiac dysfunction.[2] In addition, plasma BNP levels have also been shown to be elevated in patients with acute ischemic stroke,[3–13] in particular those with atrial fibrillation (AF).[5–13] Recently, several studies determined a BNP level threshold as a predictor of delayed AF after ischemic stroke or transient ischemic attack,[7,11] but the sample sizes of these studies were small. No previous study has examined the association between the detection rate of new AF and BNP level. In the present study, we investigated the relation between elevated BNP levels and the detection rate of new AF during hospitalization in patients with acute ischemic stroke.

Methods

From March 2006 to August 2010, we prospectively enrolled consecutive patients with acute ischemic stroke within 24 hours of onset. Patients with AF on admission 12-lead electrocardiography (ECG) or with histories of AF were excluded. Patients with dialysis-dependent chronic renal failure were also excluded from the present study, because plasma BNP levels are increased in these patients.[14] The plasma BNP level was measured on admission. This study complied with the Declaration of Helsinki with regard to investigations in humans, and the study protocol was approved by the ethics committee of Kawasaki Medical School Hospital.

Diagnosis of acute ischemic stroke was made by stroke neurologists and confirmed by computed tomography or magnetic resonance imaging. The following factors were assessed: age, gender, previous ischemic stroke, previous coronary artery disease, previous heart failure, vascular risk factors, treatment before ischemic stroke, stroke subtype, National Institutes of Health Stroke Scale (NIHSS) score[15] on admission, and blood testing (serum creatinine and plasma BNP).

To identify the mechanism of cerebral infarction, we performed duplex carotid ultrasonography, ECG, transthoracic echocardiography, transcranial Doppler, magnetic res-

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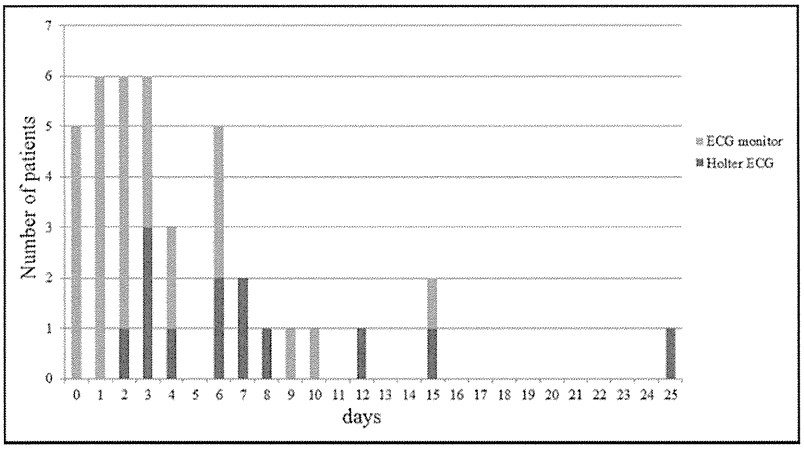

Figure 1. Interval to detection of AF and method of identifying AF.

Table 1
Clinical, radiographic, and laboratory variables

Variable	Non-AF Group (n = 544)	New AF Group (n = 40)	p Value
Age (years)	72 (62–80)	78 (71–84)	0.0007
Women	189 (35%)	20 (50%)	0.0520
Previous ischemic stroke	107 (20%)	10 (25%)	0.4162
Previous coronary artery disease	53 (10%)	4 (10%)	0.9578
Previous heart failure	1 (0.2%)	1 (2.5%)	0.1324
Hypertension	361 (66%)	24 (60%)	0.4127
Diabetes mellitus	139 (26%)	11 (28%)	0.7854
Hyperlipidemia	155 (28%)	8 (20%)	0.2478
Smoker	283 (52%)	15 (38%)	0.0762
Preadmission medications			
Warfarin	17 (3%)	1 (3%)	1.0000
Antiplatelet agents	114 (21%)	7 (18%)	0.6065
β blockers	23 (4%)	2 (5%)	0.6861
Angiotensin-converting enzyme inhibitors or angiotensin receptor blockers	93 (17%)	9 (23%)	0.3849
Calcium channel blockers	106 (19%)	9 (23%)	0.6435
Digitalis	7 (1%)	0 (0%)	1.0000
Diuretics	26 (5%)	0 (0%)	0.2456
Stroke subtype			<0.0001
Large artery atherosclerosis	125 (23%)	0 (0%)	
Small vessel occlusion	69 (13%)	0 (0%)	
Cardioembolism	38 (7%)	37 (93%)	
Others/undetermined	312 (57%)	3 (7%)	
NIHSS score on admission	4 (2–9)	14 (5–20)	<0.0001
Creatinine (mg/dl)	0.72 (0.57–0.90)	0.77 (0.59–0.91)	0.4296
BNP (pg/ml)	35.2 (15.9–80.1)	186.6 (68.7–386.3)	<0.0001

Data are expressed as median (IQR) or as number (percentage).

onance angiography, and/or computed tomographic angiography. Stroke subtype was classified according to the Trial of Org 10172 in Acute Stroke Treatment.[16]

We also evaluated the following vascular risk factors: hypertension (defined as the use of antihypertensive agents, systolic blood pressure ≥140 mm Hg, or diastolic blood pressure ≥90 mm Hg before stroke onset or 2 weeks after stroke onset), diabetes mellitus (defined as the use of oral hypoglycemic agents or insulin, fasting blood glucose level ≥126 mg/dl, or glycosylated hemoglobin level ≥6.4%), hyperlipidemia (defined as the use of antihyperlipidemic agents or serum total cholesterol level ≥220 mg/dl), current smoking habit (defined as a history of smoking during the preceding 3 months), and AF (diagnosed by 12-lead ECG, continuous electrocardiographic monitoring, or 24-hour Holter ECG).

Baseline blood samples of all patients were taken on admission. We prospectively measured plasma BNP for all patients on admission. Samples were collected from a peripheral vein into tubes containing aprotinin and ethylenediamine tetraacetic acid, and the plasma was isolated and then stored at −80°C until analysis. The plasma BNP concentration was measured using a chemiluminescence enzyme immunoassay for human BNP (Shionogi & Company,

Ltd., Osaka, Japan). Briefly, this assay uses 2 monoclonal antibodies against human BNP, 1 recognizing a carboxyl-terminal sequence and the other the ring structure of BNP, and measures BNP by sandwiching it between the 2 antibodies. BNP can be accurately quantified within 11 minutes. The normal value of BNP is ≤18.4 pg/ml in our hospital. The minimal detectable quantity of BNP is 3.9 pg/ml. The intra-assay coefficient of variation ranges from 1.6% to 3.6%, and the interassay coefficient of variation ranges from 1.3% to 4.5%. Investigators were not blinded to BNP results.

First, we investigated the detection rate of new AF, the method of identifying AF, and the interval to detection of AF during hospitalization. Second, we divided the patients into 2 groups according to the presence of AF: the new AF group, whose patients had newly documented AF during hospitalization, and the non-AF group. We compared the clinical characteristics, including BNP level, between the 2 groups using chi-square tests and Mann-Whitney U tests, and linear regression analysis was used to examine factors associated with plasma BNP level. The optimal cut-off points for each continuous variable to distinguish the new AF group from the non-AF group were determined from receiver-operating characteristic curves. Then, the factors with p values <0.10 on univariate analysis and the optimal level of plasma BNP were entered into a multivariate analysis to determine adjusted odds ratios. Finally, we evaluated the frequency of new AF detection for the following BNP levels: <50, 50 to <100, 100 to <200, 200 to <400, and ≥400 pg/ml. Data were statistically analyzed using StatView version 5 (SAS Institute Inc., Cary, North Carolina) and SPSS version 11 (SPSS Japan, Inc., Tokyo, Japan). Differences were considered statistically significant at p <0.05.

Results

During the study period, 844 patients were admitted to our hospital <24 hours after the onset of acute ischemic stroke. We excluded 260 patients with AF on admission ECG or with histories of AF or dialysis-dependent chronic renal failure. Finally, 584 patients were included in the present study (mean age 71.1 years, 209 women). The mean NIHSS score on admission was 7.1 ± 7.4.

All patients underwent continuous electrocardiographic monitoring, and 24-hour Holter ECG was performed in 536 patients (91.8%) (large artery atherosclerosis 91%, small vessel occlusion 100%, cardioembolism 81%, and other or undetermined findings 91%). AF was documented in 40 patients (6.8%) during hospitalization (new AF group). Delayed AF was detected in 28 patients by ECG and in 12 by 24-hour Holter ECG. The median interval from admission to the appearance of AF was 3 days (range 0 to 25; Figure 1). The non-AF group consisted of 544 patients (93.2%).

The baseline characteristics of the patients in the present study are listed in Table 1. The median age in the new AF group (78 years, interquartile range [IQR] 71 to 84) compared to the non-AF group (72 years, IQR 62 to 80) (p = 0.0007) and the median NIHSS score on admission (14 [IQR 5 to 20] vs 4 [IQR 2 to 9], p <0.0001) were significantly higher in the new AF group than in the non-AF group. There were no differences in the other variables.

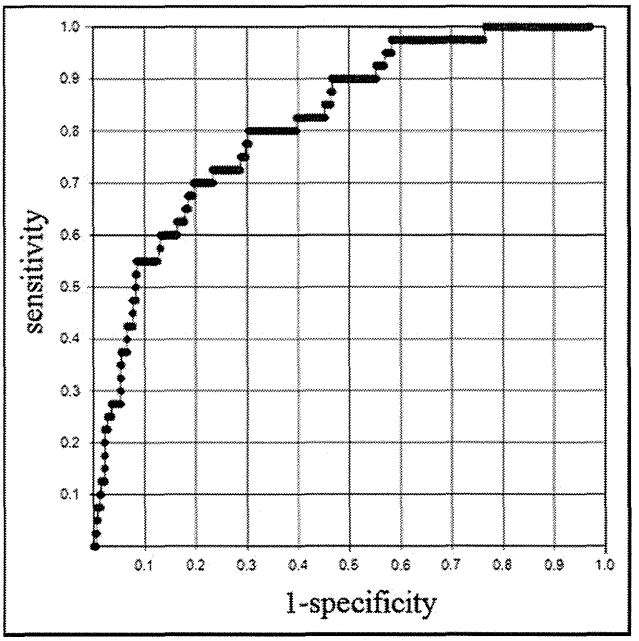

Figure 2. Receiver-operating characteristic curve analysis. The optimal cut-off value, sensitivity, and specificity required to distinguish new AF from non-AF were 65.0 pg/ml, 80.0% and 70.0%, respectively. The area under the curve using BNP to predict new AF was 0.82 (95% confidence interval 0.753 to 0.881).

Table 2
Multivariate logistic regression analysis models for probability of new atrial fibrillation

Variable	Odds Ratio	95% Confidence Interval	p Value
Age >75 years	1.4	0.693–2.987	0.3290
Female gender	1.2	0.595–2.493	0.5895
NIHSS score on admission >7	3.4	1.685–7.006	0.0007
BNP >65.0 pg/ml	6.8	2.975–15.359	<0.0001

The mean interval from stroke onset to blood sample collection was 8.2 ± 6.9 hours. The median plasma BNP level of the new AF group was significantly higher than that of the non-AF group (186.6 pg/ml [IQR 68.7 to 386.3] vs 35.2 pg/ml [IQR 15.9 to 80.1], p <0.0001). Plasma BNP level was significantly associated with female gender (p <0.0001) and previous coronary artery disease (p = 0.0013). Furthermore, plasma BNP level was correlated with age (r = 0.194, p <0.0001) and NIHSS score (r = 0.260, p <0.0001).

Age, female gender, NIHSS score on admission, and plasma BNP level were chosen as possible admission factors associated with delayed AF. The ability of BNP to identify the new AF group was assessed using receiver-operating characteristic curve analysis. A BNP level of 65.0 pg/ml had sensitivity of 80% and specificity of 70% (Figure 2). The area under the curve when BNP was used to differentiate the new AF group from the non-AF group was 0.82 (95% confidence interval 0.753 to 0.881). The cut-off levels

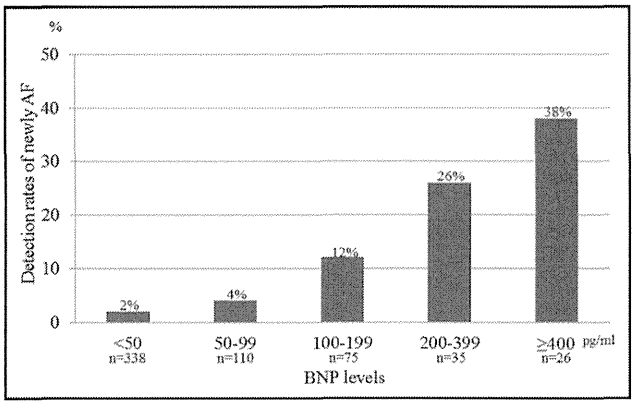

Figure 3. Detection rates of new AF according to the plasma BNP levels. The detection rates of new AF were increased with elevation of BNP levels.

of other variables that identified new AF with high sensitivity and high specificity were age >75 years (60% and 63%, respectively) and NIHSS score >7 (68% and 60%, respectively). On multivariate logistic regression analysis using these variables, NIHSS score >7 (odds ratio 3.4, 95% confidence interval 1.685 to 7.006, p = 0.0007) and plasma BNP >65.0 pg/ml (OR 6.8, 95% confidence interval 2.975 to 15.359, p <0.0001) were found to be independently associated with new AF (Table 2). The detection rates of new AF according to BNP levels were as follows: 2% of patients with BNP <50 pg/ml, 4% of those with 50 to <100 pg/ml, 12% of those with 100 to <200 pg/ml, 26% of those with 200 to <400 pg/ml, and 38% of those with ≥400 pg/ml (Figure 3).

Discussion

A plasma BNP level >65.0 pg/ml in acute ischemic stroke was an independent predictor of new AF. Furthermore, elevated BNP levels increased the frequency of detection of new AF.

A previous smaller study identified a BNP threshold level of >66.0 pg/ml with sensitivity of 92.3% and specificity of 97.5% as a predictor of cardioembolic stroke with paroxysmal AF,[7] and our larger population study supports this threshold. Therefore, in patients with acute ischemic stroke without AF on admission ECG or without histories of AF with plasma BNP levels >65.0 pg/ml, new AF should be considered and a diagnostic workup performed.

There are a few possible explanations for why elevated BNP levels increased the frequency of detection of new AF after ischemic stroke. It has been reported that plasma BNP is elevated in patients with congestive heart failure, and therefore, BNP is regarded as a hallmark of disease severity. Congestive heart failure is usually absent at BNP levels <100 pg/ml and usually present in patients with BNP levels >400 pg/ml.[17] The Framingham Heart Study demonstrated that congestive heart failure was significantly associated with the development of AF.[18] Tsang et al[19] demonstrated that the presence and severity of diastolic dysfunction are independently predictive of first documented nonvalvular AF in the elderly. Therefore, the presence and severity of congestive heart failure may induce the onset of AF because of an increase in atrial pressure, atrial stretch, and neurohormonal activation, including the release of atrial natriuretic factor.

In the present study, the total detection rate of new AF was 6.8%, which is compatible with previous studies.[20] However, we found that the detection rate of new AF increased accordingly as the BNP level increased, as follows: 2% of patients with BNP <50 pg/ml, 4% of those with 50 to <100 pg/ml, 12% of those with 100 to <200 pg/ml, 26% of those with 200 to <400 pg/ml, and 38% of those with ≥400 pg/ml. Douen et al[21] reported that serial electrocardiographic assessments within the first 72 hours of an acute stroke significantly improve the detection of AF (17.5%). Furthermore, Rizos et al[22] demonstrated that continuous bedside ECG monitoring for >48 hours diagnosed new AF (21.3%). We propose routine BNP measurement as screening for AF in acute ischemic stroke patients without either AF on admission ECG or histories of AF, and in patients with high plasma BNP levels, a more intensive diagnostic examination, such as serial ECG or continuous bedside ECG, should be performed.

Stroke severity is known to be associated with AF,[23] and our data by multivariate logistic regression analysis support this previous finding. In contrast, factors that commonly predict the risk to develop AF, such as older age, hypertension, and diabetes mellitus, were not independently associated with AF in our study.

The present study had some limitations. First, continuous ECG and 24-hour Holter ECG might have failed to diagnose AF in a small number of patients. Second, we did not evaluate cardiac function on admission. Further detailed investigation into cardiac function, such as left atrial diameter, mitral valve disorder, the ejection fraction, and E/E′ ratio, should be performed.

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Hypertension Research (2012) 35, 975–979

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ORIGINAL ARTICLE

Stroke patients with cerebral microbleeds on MRI scans have arteriolosclerosis as well as systemic atherosclerosis

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Cerebral microbleeds (CMBs) are recognized as a manifestation of arteriolosclerosis in cerebral small vessels. However, little is known regarding whether stroke patients with CMBs often have systemic atherosclerosis. The aim of the present study was to elucidate this issue using the cardio–ankle vascular index (CAVI), a new index of systemic atherosclerosis, in acute ischemic stroke patients. We prospectively studied 105 patients (71 males, median age = 70.0 years) with acute ischemic stroke. All of the patients were examined using T2*-weighted gradient echo magnetic resonance imaging (MRI) to look for and assess the CMBs and using fluid-attenuated inversion recovery to evaluate white matter hyperintensity (WMH). We assigned the patients into CMB and non-CMB groups and compared the clinical characteristics of these groups. The factors associated with CMBs were investigated using multivariate logistic regression analysis. T2*-weighted gradient echo MRI revealed CMBs in 47 patients (44.8%) and no CMBs in 58 patients (55.2%). The CAVI was significantly higher in the CMBs group (10.5 *vs.* 8.6, $P<0.001$). In the multivariate logistic regression analysis, CAVI per one point increase (odds ratio (OR), 1.50; 95% confidence interval (CI), 1.12–2.00; $P=0.006$), advanced WMH (OR, 4.78; 95% CI, 1.55–14.74; $P=0.006$) and impaired kidney function (OR, 3.31; 95% CI, 1.16–9.81; $P=0.031$) were independent factors associated with the presence of CMBs. A high CAVI was independently associated with CMBs in patients with acute ischemic stroke. Our results indicated that ischemic stroke patients with CMBs may have cerebral arteriolosclerosis as well as systemic atherosclerosis.
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Keywords: arteriolosclerosis; cardio–ankle vascular index; cerebral microbleeds; ischemic stroke; systemic atherosclerosis

INTRODUCTION

Cerebral microbleeds (CMBs), represented on T2*-weighted gradient echo magnetic resonance imaging (MRI) scans as spotty low-intensity areas, are found in 33.5–40.0% of patients with ischemic stroke,[1,2] and the presence of CMBs is recognized as a risk factor for subsequent intracerebral hemorrhage in such patients.[3] Histopathological analyses of the small cerebral vessels associated with CMBs have generally identified vascular pathological changes indicative of hypertensive arteriolosclerosis.[4,5]

Atherosclerosis of the systemic medium or large arteries is caused mainly by aging[6] and hypertensive wall damage.[7] Pulse wave velocity (PWV) is typically determined in the clinical setting to assess the grade of systemic atherosclerosis. Recently, the novel cardio–ankle vascular index (CAVI) was developed as an indicator of atherosclerosis.[8] A previous study showed that a CAVI $\geqslant 9.0$ was associated with the presence of carotid plaques, increased intima media thickness and coronary artery disease.[9] Furthermore, Suzuki *et al.*[10] reported that CAVI was statistically greater in ischemic stroke patients with leukoaraiosis and small-vessel occlusion. However, no evidence has yet indicated that CAVI is associated with CMBs in patients with ischemic stroke. The present study examined the association between CMBs and CAVI and determined whether ischemic stroke patients with CMBs exhibited not only cerebral arteriolosclerosis but also systemic atherosclerosis.

METHODS

Patients

We prospectively enrolled consecutive patients with acute cerebral infarction or transient ischemic attack within 7 days after onset between October 2009 and September 2010. All of the patients underwent diffusion-weighted imaging, fluid-attenuated inversion recovery (FLAIR) and T2*-weighted gradient echo MRI imaging. Cerebral infarction was diagnosed as an acute neurological event lasting $\geqslant 24$ h, which was explained by representative lesions on the MRI scan, including diffusion-weighted imaging. A transient episode of neurological dysfunction caused by focal brain ischemia lasting $\leqslant 24$ h was defined as transient ischemic attack. We examined blood biochemistry, blood count, electrocardiogram, MRI and chest X-rays upon admission, and CAVI was determined within 14 days thereafter. Patients with heart valve replacements,

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pacemakers or clipped cranial arteries were excluded from this study, as MRI is contraindicated for such patients.

The following clinical data were collected from all of the patients: (1) age and gender; (2) National Institutes of Health Stroke Scale (NIHSS) score upon admission; (3) vascular risk factors, including hypertension, diabetes mellitus and hyperlipidemia; (4) atrial fibrillation; (5) impaired kidney function; (6) previous illness, such as stroke, ischemic heart disease or peripheral artery disease; (7) current smoking status and history of alcohol consumption; (8) pre-admission use of antithrombotic agents, such as antiplatelet agents and warfarin; (9) CAVI; and (10) ischemic stroke subtype, using Trial of Org 10172 in the Acute Stroke Treatment (TOAST) criteria.[11]

Risk factors

We assessed vascular risk factors based on the following definitions: (1) hypertension was defined as a history of using antihypertensive agents, a systolic blood pressure >140 mm Hg, or a diastolic blood pressure >90 mm Hg 14 days after the stroke; (2) diabetes mellitus was defined as the use of oral hypoglycemic agents or insulin, a fasting blood glucose of $>126\,mg\,dl^{-1}$, or a glycosylated hemoglobin level $>6.4\%$; (3) hyperlipidemia was defined as the use of antihyperlipidemic agents or a serum cholesterol level $>220\,mg\,dl^{-1}$; (4) impaired kidney function was defined as a serum estimated glomerular filtration rate of $<60\,ml^{-1}$ min per $1.73\,m^2$; (5) previous stroke was defined as a history of cerebral infarction or intracranial hemorrhage; (6) previous ischemic heart disease was defined as a history of angina pectoris or myocardial infarction; and (7) peripheral artery disease was defined as an ankle–brachial index of <0.9 on at least one side.

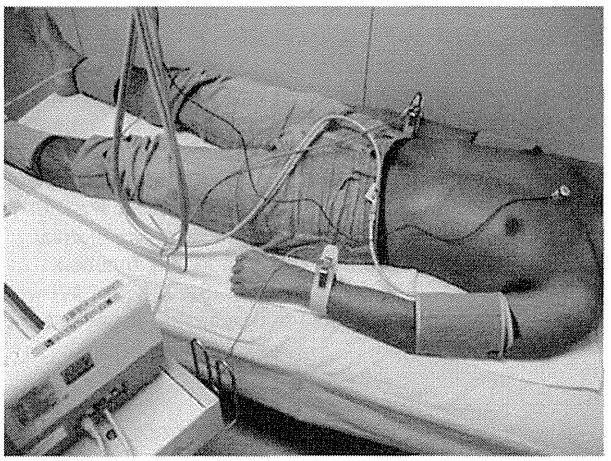

Figure 1 Measurement of the CAVI. The CAVI was automatically calculated from the pulse volume, blood pressure and vascular length from heart to ankle. CAVI, cardio–ankle vascular index.

Measurement of the CAVI

Technologists who were blinded to the clinical data measured the CAVI using an automated Vasera VS-1000 (Fukuda Denshi, Tokyo, Japan). Cuffs were applied to the four extremities, and electrocardiogram electrodes were attached to the upper arm. A microphone was placed on the sternal angle to obtain phonocardiograms. The patients rested in the supine position for 5 min (Figure 1). The PWV was calculated by dividing the distance from the aortic valve to the ankle artery by the sum of the time between the sound of the aortic valve closing and the notch of the brachial pulse wave and the time between the increase in the brachial and ankle pulse waves.

The CAVI was calculated from blood pressure and the PWV using the following equation:

$$CAVI = 2\rho \times 1/(Ps - Pd) \times \ln(Ps/Pd) \times PWV^2$$

(Ps, systolic blood pressure; Pd, diastolic blood pressure; ρ, blood density).

The higher CAVI obtained from either the left or right side was included in the analysis.

Neuroimaging of CMBs and white matter hyperintensity

We examined all of the patients by MRI within 7 days of admission using a Symphony Vision 1.5-T system (Siemens, Munich, Germany). The imaging protocol consisted of T2*-weighted gradient echo sequences (TR/TE, 484 ms/40 ms; field of view, 26 cm; acquisition matrix, 163×260; section thickness, 5.0 mm with a 0.5-mm intersection gap); a FLAIR sequence (TR/TE, 8550 ms/111 ms; field of view, 23 cm; acquisition matrix, 208×230; section thickness, 5.0 mm with a 0.5-mm intersection gap); and a diffusion-weighted imaging sequence (TR/TE, 2600 ms/79 ms; *b* values, 1000 and $50\,s\,mm^{-2}$; field of view, 23 cm; acquisition matrix, 230×230; section thickness, 5.0 mm with a 0.5-mm intersection gap). We defined CMBs as hypointense lesions 2–5 mm in diameter in the brain parenchyma identified in T2*-weighted gradient echo images (Figure 2a).

Patients with probable cerebral amyloid angiopathy according to the Boston criteria (multiple CMBs restricted to the cortical/corticosubcortical regions)

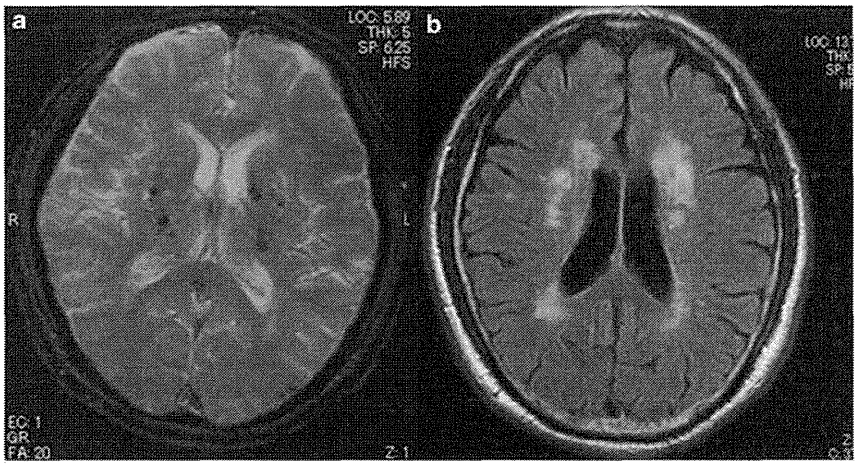

Figure 2 MRI scan of the brain of a 73-year-old male patient with lacunar infarction and a CAVI of 11.5. (**a**) A T2*-weighted gradient echo image shows multiple CMBs in the bilateral basal ganglia. (**b**) A FLAIR image shows advanced WMH. CAVI, cardio–ankle vascular index; CMBs, cerebral microbleeds; FLAIR, fluid-attenuated inversion recovery; WMH, white matter hyperintensity.

Table 1 Baseline clinical background of groups with and without CMBs

	All (n = *105*)	*CMBs* (n = *47*)	*Non-CMBs* (n = *58*)	P-*value*
Age, years; median (IQR)	70.0 (68.0–76.5)	72.0 (65.0–80.0)	66.5 (53.8–76.0)	0.017
Male, *n* (%)	71 (67.6)	36 (76.6)	35 (60.3)	0.095
NIHSS score; median (IQR)	3 (2–8)	3 (2–5)	2 (1–6)	0.461
Classification of stroke, n (%)				
Transient ischemic attack	9 (8.6)	3 (6.4)	6 (10.3)	
Large artery atherosclerosis	23 (21.9)	15 (31.9)	8 (13.8)	
Cardioembolism	26 (24.8)	9 (19.1)	17 (29.3)	
Small-vessel occlusion	18 (17.1)	11 (23.4)	7 (12.1)	
Other or undetermined cause	29 (27.6)	9 (19.1)	20 (34.5)	
Risk factors, n (%)				
Hypertension	79 (75.2)	42 (89.4)	37 (63.8)	0.003
Diabetes mellitus	39 (37.1)	17 (36.2)	22 (37.9)	1.000
Hyperlipidemia	52 (49.5)	21 (44.7)	31 (53.4)	0.434
Atrial fibrillation	21 (20.0)	5 (10.6)	16 (27.6)	0.048
Impaired kidney function	41 (39.0)	24 (51.1)	17 (29.3)	0.028
Previous stroke	24 (22.9)	17 (36.2)	7 (12.1)	0.005
Previous ischemic heart disease	11 (10.5)	7 (14.9)	4 (6.9)	0.213
Peripheral artery disease	23 (21.9)	13 (27.7)	10 (17.2)	0.239
Smoking	54 (51.4)	25 (53.2)	29 (50.0)	0.845
Alcohol	54 (51.4)	24 (51.1)	30 (51.7)	1.000
Antithrombotic agents	45 (42.9)	24 (51.1)	21 (36.2)	0.165
Advanced WMH, *n* (%)	47 (44.8)	32 (68.1)	15 (25.9)	<0.001
CAVI; median (IQR)	9.3 (8.1–10.7)	10.5 (9.2–11.7)	8.6 (7.6–10.2)	<0.001

Abbreviations: CAVI, cardio–ankle vascular index; CMBs, cerebral microbleeds; IQR, interquartile range; NIHSS, National Institute of Health Stroke Scale; WMH, white matter hyperintensity.
Advanced WMH was defined as WMH of grades 2 or 3 using scoring system of Fazekas *et al.*

were excluded from this study.[12] Hypointense lesions within the subarachnoid space were regarded as pial blood vessels. Symmetric hypointense lesions in areas of the globus pallidus were regarded as calcification, and intracerebral lesions with a hemorrhagic component were excluded.

The severity of white matter hyperintensity (WMH) in the FLAIR images was scored as described by Fazekas *et al.*[13] into grades of 0, absent; 1, punctuate; 2, early confluent; and 3, confluent. Grade 2 or 3 WMH was regarded as advanced WMH (Figure 2b). One neurologist (TS) who was blinded to the clinical information evaluated the MRI images. The medical ethics committee of the Jikei University School of Medicine approved the study.

Statistical analysis

All of the patients were assigned to groups based on the presence or absence of CMBs, and their clinical characteristics were compared. Univariate analysis was performed using Fisher's exact test and the Mann–Whitney *U* test. Receiver operating characteristic curves analysis was performed to determine the cut-off values of CAVI to differentiate the two groups. Variables with *P*-values of <0.1 were included in the multivariate logistic regression analyses to determine factors that are independently associated with the presence of CMBs.

Then, linear regression analysis was used to test the association between the number of CMBs and the CAVI. Moreover, we also compared the clinical characteristics between the patients with single and multiple ($\geqslant 2$) CMBs. The data were statistically analyzed using the Statistical Package for the Social Sciences (SPSS ver. 17.0) software for Windows (SPSS Inc., Chicago, IL, USA).

RESULTS

A total of 113 patients were admitted to the Jikei University Hospital with acute ischemic stroke during the study period. We excluded two patients who were diagnosed with cerebral amyloid angiopathy, three with pacemakers and three who did not undergo CAVI determination because of a leg fracture ($n=1$) or death soon after admission ($n=2$). We therefore enrolled 105 patients (median age, 70.0 years; male, $n=71$; median NIHSS score, 3).

T2*-weighted gradient echo MRI revealed CMBs in 47 patients (44.8%) and no CMBs in 58 patients (55.2%). The characteristics of the two groups are shown in Table 1. The CMB group was significantly older than the non-CMB group (72.0 *vs.* 66.5 years; $P=0.017$). Hypertension, impaired kidney function and advanced WMH were more frequent (89.4% *vs.* 63.8%, $P=0.003$; 51.1% *vs.* 29.3%, $P=0.028$ and 68.1% *vs.* 25.9%, $P<0.001$), whereas atrial fibrillation was less frequent, in the CMB group than in the non-CMB group (10.6% *vs.* 27.6%, $P=0.048$). The use of antithrombotic agents before admission did not significantly differ between the two groups. The CAVI was significantly higher in the CMB group (10.5 *vs.* 8.6, $P<0.001$).

The factors with representative values of $P<0.1$ in the univariate analysis were age per 10 year increase, male sex, hypertension, previous stroke, atrial fibrillation, impaired kidney function, advanced WMH and CAVI per one point increase; these factors were included in the multivariate logistic regression analysis (Table 2, Model 1). CAVI per one point increase (odds ratio (OR), 1.50; 95% confidence interval (CI), 1.12–2.00; $P=0.006$), advanced WMH (OR, 4.78; 95% CI, 1.55–14.74; $P=0.006$) and impaired kidney function (OR, 3.31; 95% CI, 1.16–9.81; $P=0.031$) were independent factors associated with the presence of CMBs. Using receiver operating characteristic curves, the cut-off level for the CAVI in the presence of CMBs was 9.2

Table 2 Multivariate logistic analysis model to evaluate independent factors for the presence of CMBs

	Model 1			*Model 2*		
	OR	*95% CI*	P-*value*	*OR*	*95% CI*	P-*value*
Male	1.15	0.39–3.40	0.806	1.12	0.38–3.32	0.842
Age (per 10 years)	0.98	0.93–1.03	0.806	0.98	0.93–1.03	0.842
Hypertension	1.11	0.29–4.18	0.880	1.28	0.34–4.74	0.715
Impaired kidney function	3.31	1.16–9.81	0.031	2.81	0.97–8.20	0.058
Previous stroke	1.96	0.53–7.24	0.310	1.79	0.50–6.36	0.376
Atrial fibrillation	0.16	0.04–0.70	0.015	0.18	0.05–0.73	0.017
CAVI (per one point increase)	1.50	1.12–2.00	0.006	—	—	—
CAVI ⩾9.2	—	—	—	5.46	1.59–18.75	0.007
Advanced WMH	4.78	1.55–14.74	0.006	3.92	1.30–11.84	0.016

Abbreviations: CAVI, cardio-ankle vascular index; CI, confidence interval; CMBs, cerebral microbleeds; OR, odds ratio; WMH, white matter hyperintensity.
Advanced WMH is defined as grade 2 or 3 WMH using the scoring system of Fazekas *et al.*
Impaired kidney function is defined as serum estimated glomerular filtration rate $<60\,ml^{-1}\,min$ per $1.73\,m^2$.
Model 1: male, age (per 10 years), hypertension, impaired kidney function, previous stroke, atrial fibrillation, CAVI (per one point increase) and advanced WMH.
Model 2: male, age (per 10 years), hypertension, impaired kidney function, previous stroke, atrial fibrillation, CAVI ⩾9.2 and advanced WMH.

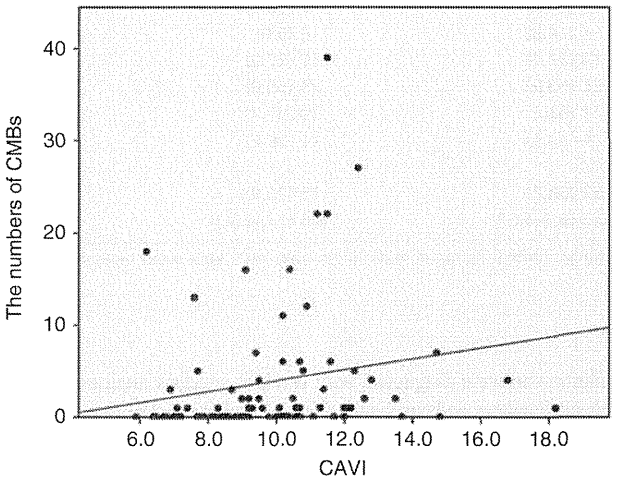

Figure 3 Linear regression analysis of the number of CMBs and the CAVI. There was a weak but statistically significant relationship between the number of CMBs and the CAVI ($R^2 = 0.040$, $P = 0.041$). CAVI, cardio-ankle vascular index; CMBs, cerebral microbleeds.

(sensitivity, 78.7%; specificity, 65.5%). We also tested two categories (CAVI⩾9.2 or <9.2) with the same adjustment applied (Table 2, Model 2). A CAVI⩾9.2 was independently associated with CMBs (OR, 5.46; 95% CI, 1.59–18.75; $P = 0.007$).

There was a weak but statistically significant relationship between the number of CMBs and the CAVI ($R^2 = 0.040$, $P = 0.041$; Figure 3). Thirty-one patients (29.5%) had multiple CMBs on T2*-weighted gradient echo MRI scans. No significant differences in age, sex or any risk factors were observed between the two groups. There was no difference in the CAVI between the patients with single and multiple CMBs (10.4 *vs.* 10.5, $P = 0.613$).

DISCUSSION

The present study found that the CAVI is independently associated with the presence of CMBs. It also found that advanced WMH and impaired kidney function are associated with the presence of CMBs. However, there was no factor, including the CAVI, that significantly distinguished patients with single CMBs from those with multiple CMBs.

We found a correlation between the CAVI (the new index of atherosclerosis) and CMBs in patients with acute ischemic stroke. Our results were partially in line with the previous findings of a close association between the PWV and CMBs.[14–16] However, the PWV is affected by changes in blood pressure during measurement and might not accurately reflect atherosclerosis in hypertensive patients.[8] In contrast, the CAVI is less influenced by blood pressure during measurement than is the PWV.[8] However, the mechanisms linking the CAVI and CMBs are complex and therefore not well understood. One possibility is that the CAVI reflects atherosclerosis in systemic large arteries, including the carotid, coronary and peripheral arteries.[8] Moreover, atherosclerosis in large extracranial[17] or intracranial arteries[18] also leads to arteriolosclerosis in small cerebral vessels and to the development of CMBs. Thus, systemic atherosclerosis may have a key role in the occurrence of cerebral arteriolosclerosis and CMBs. Indeed, the presence of CMBs is a risk factor not only for subsequent intracerebral hemorrhage in patients with ischemic stroke[3] but also for antithrombotic-related intracerebral hemorrhage.[19,20] Therefore, patients with a history of ischemic stroke and an elevated CAVI should be evaluated for CMBs and appropriately treated with antihypertensive and antithrombotic drugs to avoid intracerebral hemorrhage.

The present study demonstrated a significant relationship between advanced WMH and CMBs, which supports the results of other studies indicating a higher frequency of CMBs in patients with ischemic stroke accompanied by severe leukoaraiosis.[21,22] Pathologically, WMH and CMBs are attributed to cerebral small-vessel disease, such as the loss of smooth muscle cells, lumen restriction, vessel wall thickening, vessel wall damage and microaneurysms.[4,5] Interestingly, Suzuki *et al.*[10] showed that WMH was also correlated with the CAVI in ischemic stroke patients. Moreover, previous studies have established a strong association between the CAVI and small-vessel disease of other organs.[23,24] Kubozono *et al.*[23] reported a relationship between the CAVI and a low estimated glomerular filtration rate. Kim *et al.*[24] identified a correlation between the CAVI and microvascular complications in type 2 diabetes mellitus patients without a history of macrovascular disease. The CAVI may thus be a marker of small-vessel disease of various organs, including the brain.