Comparison of the $CHADS_2$, CHA_2DS_2-VASc and R_2CHADS_2 Scores in Japanese Patients with Non-valvular Paroxysmal Atrial Fibrillation not Receiving Anticoagulation Therapy

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Abstract

Aim: It remains unclear whether the $CHADS_2$, CHA_2DS_2-VASc, or R_2CHADS_2 score is the most useful for the risk stratification of ischemic stroke/systemic thromboembolism (IS/SE) in Japanese patients with paroxysmal non-valvular atrial fibrillation (PNVAF).

Methods and Results: We investigated the incidence of IS/SE on the basis of the $CHADS_2$, CHA_2DS_2-VASc, and R_2CHADS_2 scores in 332 consecutive PNVAF patients (224 men, mean age: 65±13 years) who had not been administered anticoagulation therapy but who were administered antiarrhythmic drug therapy to maintain sinus rhythm between August 1995 and July 2008 before the 2008 Japanese Circulation Society guideline was issued (mean follow-up period: 53±35 months). The annual rates of IS/SE without underlying antiarrhythmic drug therapy are shown in the table included in this article. Higher $CHADS_2$, CHA_2DS_2-VASc, and R_2CHADS_2 scores were associated with greater annual rates of IS/SE ($P<0.001$). In a multivariate logistic regression analysis adjusted for potentially confounding variables, the $CHADS_2$ scores (odds ratio [OR]: 4.74, 95% confidence interval [CI]: 2.80–8.00, $p<0.001$), CHA_2DS_2-VASc scores (OR: 4.15, 95% CI: 2.57–6.71, $p<0.001$), and R_2CHADS_2 scores (OR: 1.94, 95% CI: 1.48–2.53, $p<0.001$) were significant independent predictors of IS/SE. The area under the receiver-operator characteristic curve for predicting IS/SE was 0.89 for CHA_2DS_2-VASc scores, 0.87 for $CHADS_2$ scores, and 0.85 for

R_2CHADS_2 scores (all, $P<0.001$), with no significant difference among the three scores.

Conclusion: In Japanese patients with PNVAF, the $CHADS_2$, CHA_2DS_2-VASc, and R_2CHADS_2 scores are all useful for the risk stratification of IS/SE cases.

Key words: $CHADS_2$ score, CHA_2DS_2-VASc score, R_2CHADS_2 score, Japanese patients, non-valvular paroxysmal atrial fibrillation

Introduction

According to recent epidemiological studies in Europe and the United States, the prevalence of atrial fibrillation (AF) is about 4% in individuals in their 70s and about 10% in those over 80 years of age, showing a significant increase with age. In Japan, where the elderly population is increasing rapidly, the prevalence of AF in the elderly population is also high, occurring in about 2%-3% of those in their 70s, and is expected to reach 1000 per 100,000 population in 2010-2030[1)], with further increases in the future. AF is thus considered an important condition that will significantly affect the healthcare system in Japan.

AF is the most common sustained clinical arrhythmia in humans and not only impairs the quality of life but also causes serious complications, such as embolism and hemodynamic dysfunction. It also generates arrhythmia that worsens the cardiovascular prognosis in cases of left ventricular dysfunction[2)].

The R_2CHADS_2 score has been newly proposed for stratifying patients with non-valvular atrial fibrillation (NVAF) according to the risk of stroke[3)]. We previously demonstrated that the $CHADS_2$ and CHA_2DS_2-VASc scores were useful for risk stratification of cardiovascular events in Japanese patients with paroxysmal AF[4)5)]. However, it remains unclear whether the $CHADS_2$, CHA_2DS_2-VASc, or R_2CHADS_2 score is the most useful for

the risk stratification of ischemic stroke/systemic thromboembolism (IS/SE) in Japanese patients with paroxysmal non-valvular atrial fibrillation (PNVAF).

We therefore investigated the incidence of IS/SE on the basis of the $CHADS_2$, CHA_2DS_2-VASc, and R_2CHADS_2 scores in patients with PNVAF who did not receive anticoagulation therapy before the Japanese Circulation Society (JCS) guidelines were issued in 2008.

Methods

A total of 548 patients had paroxysmal AF confirmed based on symptoms and 12-lead surface electrocardiograms (ECG) and/or ambulatory 24-h monitoring findings at Iwate Medical University School of Medicine between August 1995 and July 2008 before the publication of the JCS guidelines in 2008. Our database, which was established in August 1995, contains data on all new patients admitted to Iwate Medical University School of Medicine in Morioka, Japan. The principle aim for establishing this hospital-based database is to monitor the prevalence and prognosis of cardiovascular diseases in a local area of Japan. The registry started in August 1995, and patients have been continually registered in the database annually. The study sample was drawn from this group and comprised 332 patients (224 men and 108 women; mean age: 65 ± 13 years) who were not receiving anticoagulation therapy and in whom transthoracic echocardiography (TTE) had ruled out cardiac valvular disease. Valvular AF was defined as AF with mitral stenosis and/or a history of valvular surgery (both biological and mechanical valve). All subjects were treated on an outpatient basis every two to four weeks, underwent rhythm control therapy using antiarrhythmic drugs, and were followed for at least one year. All patients were screened for diabetes mellitus using fasting glucose and hemoglobin A_1c levels. All patients also underwent a medical interview, chest

X-ray, exercise tolerance test, and TTE or other appropriate noninvasive examinations for underlying cardiopulmonary diseases, and the investigators performed a pulmonary function test, chest computed tomography (CT), and cardiac catheterization whenever necessary.

Patients with congestive heart failure; serious bradyarrhythmia (e.g. sick sinus syndrome, atrioventricular block, bi-fascicular block or more); thyroid, hepatic, or renal dysfunction; child-bearing potential during the study period; a history of drug allergy; and receiving warfarin anticoagulation therapy were excluded from the study. In this study, the mean observation period was 53 ± 35 months (range: 12 to 127 months).

Definition

Paroxysmal AF was defined as AF terminating spontaneously within seven days of onset[6]. Permanent (chronic) AF was defined as AF refractory to antiarrthythimc drug therapy or electrical cardioversion and where a sinus rhythm could not be maintained for more than 12 months, as assessed by ECG. Ischemic stroke was confirmed based on typical neurological symptoms and the presence of a ≥ 3 mm infarct area, as obtained by brain CT or magnetic resonance imaging (MRI), which was performed in all patients. The diagnosis of hypertension followed the 2009 JSH guidelines[7]. Dyslipidemia was defined as fasting serum

cholesterol of ≥ 220 mg/dl and triglycerides of ≥ 150 mg/dl[8]. AF was divided into three types depending on the time of onset: diurnal type (7:00 to 17:00), nocturnal type (17:00 to 7:00), and mixed type (any time)[9]. Chronic obstructive pulmonary disease was defined as a forced expiratory volume in one second of <70%, as measured by a pulmonary function test. Systemic embolism was defined as an acute vascular occlusion of an extremity or organ, documented by means of imaging or surgery.

$CHADS_2$ and CHA_2DS_2-VASc scores were defined according to 2006 the American Heart Association (AHA) guidelines[10] and 2010 the European Society of Cardiology (ESC) guidelines[11], respectively. The R_2CHADS_2 score[3] awards one point each for the presence of congestive heart failure, hypertension, age ≥75 years old, and diabetes mellitus and two points for prior stroke or transient ischemic attack and renal dysfunction (estimated glomerular filtration rate [eGFR] <60 ml/min/m^2).

Protocol for antiarrhythmic drug therapy

In patients in whom TTE revealed a left ventricular ejection fraction ≥40% after spontaneous or pharmacological/electrical cardioversion, Class I or III antiarrhythmic drugs were administered based on the judgment of the outpatient attending physician. When TTE by

contrast showed a left ventricular ejection fraction <40% after spontaneous or pharmacological/electrical cardioversion, aprindine, bepridil, or amiodarone was administered based on the judgment of the outpatient attending physician.

To confirm recurrence of AF, we performed a subjective assessment through history taking. We also obtained recordings from a standard 12-lead ECG and a portable monitor at the time of the medical examination after 2-4 weeks of administration or a change in antiarrhythmic drugs. Furthermore, ambulatory 24-h ECG monitoring was performed every 3 months to detect recurrence of AF if considered necessary by the outpatient attending physician.

If AF became permanent despite antiarrhythmic therapy, β-blockers, Ca antagonists, or digitalis was administered orally to control the ventricular rate.

Protocol for antiplatelet therapy

Before publication of the Japanese Circulation Society guidelines [12] in November 2001, the attending physicians administered antiplatelet therapy at their own discretion. After November 2001, antiplatelet therapy was generally performed in accordance with the guidelines, but the decision to administer antiplatelet therapy was left to the physician. Doses

of aspirin were 81 to 100 mg/day.

The subjects of the present study had not received anticoagulation therapy or had received only aspirin. We examined the patient distributions with regard to the $CHADS_2$, CHA_2DS_2-VASc, and R_2CHADS_2 scores; patient background factors; ischemic stroke; and systemic embolism in patients with PNVAF in whom anticoagulant therapy was not administered before the JCS guideline issued in 2008.

Statistical analyses

The obtained values were expressed as the mean and standard deviation. The patient characteristics were compared between subgroups with the Mann-Whitney U test, and patient percentages were compared with the chi-squared test. The percentage of patients without IS/SE was evaluated using the Kaplan-Meier method, and differences between subgroups were tested for significance using the log-rank test. A multivariate logistic analysis was used to identify predictive factors for ischemic stroke and systemic embolism, and the Hosmer-Lemeshow goodness-of-fit test was used to validate the model. All statistical analyses were performed using the SPSS 13.0 statistical software package. A p-value <0.05 was considered statistically significant.

Ethical issues

The ethical committee at Iwate Medical University School of Medicine granted approval for this study, and all of the patients gave their informed consent.

Results

Patient characteristics

All patient characteristics are shown in Tables 1A, 1B and 1C.

Distribution of $CHADS_2$, CHA_2DS_2-VASc, and R_2CHADS_2 scores in patients with PNVAF

The $CHADS_2$, CHA_2DS_2-VASc, and R_2CHADS_2 score distributions are shown in Figure 1. The mean $CHADS_2$ score was 1.2 ± 1.2 points, the mean CHA_2DS_2-VASc score was 2.0 ± 1.6 points, and the mean R_2CHADS_2 score was 1.6 ± 1.6 points.

The survival rate free from IS/SE among the $CHADS_2$, CHA_2DS_2-VASc, and R_2CHADS_2 score groups

The respective survival rates free from IS/SE on the basis of the $CHADS_2$ score at 12, 36, 60, 90, and 120 months of follow-up were as follows: score value 0: 100%, 100%, 100%, 99%, and 99%; score value 1: 100%, 100%, 99%, 99%, and 99%; score value 2: 98%, 94%, 89%, 87%, and 85%; score value 3: 93%, 77%, 60%, 50%, and 47%; and score value ≥4: 90%, 80%, 65%, 60%, and 50% (Fig. 2A). There was a significant difference in the survival rate during the follow-up period among the 5 groups (p<0.001).

The respective survival rates free from IS/SE on the basis of the CHA_2DS_2-VASc score at 12, 36, 60, 90, and 120 months of follow-up were as follows: score value 0: 100%, 100%, 100%, 100%, and 100%; score value 1: 100%, 100%, 98%, 98%, and 97%; score value 2 group: 99%, 99%, 97%, 97%, and 97%; score value 3: 99%, 94%, 91%, 91%, and 90%; score value 4: 96%, 93%, 89%, 79%, and 75%; score value 5: 96%, 78%, 70%, 52%, and 48%; and score value ≥6: 86%, 71%, 57%, 43%, and 43% (Fig. 2B). Here as well, there was a significant difference in the survival rate during the follow-up period among the 7 groups (p<0.001).

The respective survival rates free from IS/SE on the basis of the R_2CHADS_2 score at 12, 36, 60, 90, and 120 months of follow-up were as follows: score value 0: 100%, 100%, 100%, 99%, and 99%; score value 1: 100%, 100%, 98%, 98%, and 98%; score value 2: 98%, 92%, 87%, 85%, and 83%; score value 3: 98%, 91%, 79%, 77%, and 77%; score value 4: 91%, 91%, 83%, 70%, and 70%; and score value ≥5: 95%, 75%, 70%, 60%, and 55% (Fig. 2C). Here as well, there was a significant difference in the survival rate during the follow-up period among the 6 groups (p<0.001).

Annual incidence of IS/SE on the basis of the $CHADS_2$, CHA_2DS_2-VASc, and R_2CHADS_2

scores

Table 2 shows the annual rates of IS/SE by $CHADS_2$, CHA_2DS_2-VASc, and R_2CHADS_2 score. In each category, the higher value groups had higher annual rates of IS/SE. In total patients, the annual rates of IS/SE in the no anticoagulant therapy group and in the aspirin group were 2.6%/year and 3.1%/year, respectively.

Predictors of IS/SE in patients with PNVAF

In a multivariate logistic regression analysis adjusted for other potentially confounding variables, the $CHADS_2$ score (odds ratio [OR]: 4.735, 95% confidence interval [CI]: 2.803-7.998, P<0.001), CHA_2DS_2-VASc score (OR: 4.152, 95% CI: 2.570-6.709, P<0.001), R_2CHADS_2 score (OR: 1.937, 95% CI: 1.481-2.533, P<0.001), and mixed type onset (OR: 3.380, 95% CI: 1.133-10.08, P = 0.003 in Table 3A; OR: 3.120, 95% CI: 1.018-9.565, P = 0.046 in Table 3B; and OR: 2.782, 95% CI: 1.021-7.584, P = 0.045 in Table 3C) were significant independent predictors of IS/SE.

Predictability of IS/SE by $CHADS_2$, CHA_2DS_2-VASc, and R_2CHADS_2 score using a receiver operating characteristic (ROC) curve

When the predictability of IS/SE was compared based on the area under the ROC curve, the $CHADS_2$ score was 0.865 ($P<0.001$), the CHA_2DS_2-VASc score was 0.899 ($P<0.001$), and the R_2CHADS_2 score was 0.851 ($P<0.001$). All of the parameters were useful for predicting the occurrence of IS/SE. The area under the ROC curve for the CHA_2DS_2-VASc score was higher than that for the $CHADS_2$ and R_2CHADS_2 scores, but not to a significant degree (Fig. 3).

Discussion

Major findings of the present study

During antiarrhythmic drug therapy to maintain sinus rhythm in patients with PNVAF, higher $CHADS_2$, CHA_2DS_2-VASc, and R_2CHADS_2 scores were associated with higher annual rates of IS/SE in patients with PNVAF not receiving anticoagulant therapy. All three parameters were independent predictors for IS/SE. In addition, the discriminative ability for the incidence of IS/SE in patients with PNVAF was compared by ROC. No significant differences were observed among the parameters, indicating that all score schemes were useful for risk stratification.

A comparison of the $CHADS_2$, CHA_2DS_2-VASc, and R_2CHADS_2 scores in NVAF patients

NVAF is a risk factor for IS/SE. The annual rate of ischemic stroke among patients with NVAF (approximately 5%) has been shown to be 2- to 7-fold higher than in subjects without AF[13)14)15)]. In general, the $CHADS_2$ score is recommended for the risk stratification of IS/SE or determining whether or not to introduce anticoagulant therapy in patients with NVAF[16)17)18)]. The $CHADS_2$ score was estimated as the sum of points obtained after assigning one point each for age ≥75 years, hypertension, diabetes mellitus, and heart failure and two

points for previous IS/SE.

The CHA_2DS_2-VASc score was established in the 2010 European Society of Cardiology (ESC) guidelines and incorporated other risk factors in addition to those mentioned in the $CHADS_2$ score, such as cardiomyopathy, age 65 to 74 years, a history of myocardial infarction, aortic plaque, vascular disease, and gender (female). The CHA_2DS_2-VASc score was estimated as the sum of points obtained after assigning one point each for age 65 to 74 years, hypertension, diabetes mellitus, heart failure, vascular disease, and gender (female) and two points each for previous IS/SE and age ≥75 years[19].

The R_2CHADS_2 score, which accounts for renal dysfunction (Crr <60 ml/min/m^2), has also been proposed for the risk stratification of IS/SE[3]. Piccini et al. found that the R_2CHADS_2 score enhanced the stroke risk assessment on the basis of the net reclassification index by 8.2% compared with the $CHADS_2$ score and by 6.2% compared with the CHA_2DS_2-VASc score[1].

To our knowledge, there have been no studies comparing the $CHADS_2$, CHA_2DS_2-VASc and R_2CHADS_2 scores in Japanese patients with PNVAF not receiving anticoagulation therapy. However, our study showed that the $CHADS_2$, CHA_2DS_2-VASc, and R_2CHADS_2 scores were all useful for the risk stratification of IS/SE in Japanese patients with

PNVAF with no significant differences among the three scores. These results may reflect ethnic differences in stroke risk assessment in patients with NVAF.

Chronic renal failure and cardiovascular complications

Chronic kidney disease (CKD) is usually considered a risk factor for cardiovascular complications. In patients with chronic renal failure, arteriosclerosis is enhanced[20)21)] by vascular inflammation and protein catabolism as well as by poor nutrition. In addition, patients with chronic renal failure have high oxidative stress. It has been reported that oxidative stress can activate several complements, increase vascular endothelial adhesion molecules, deteriorate endothelial NO production via reactive oxygen species, and induce the development of vascular endothelial dysfunction[22)23)]. Serum concentrations of asymmetric dimethylarginine (asymmetric dimethyl arginine [ADMA]), an endogenous NOS inhibitor of the release of NO from arginine, have been shown to be increased in patients with not only renal dysfunction but also cerebral infarction[24) -26)]. However, the structure of the brain blood vessels is similar to that of the renal ones from an anatomical perspective[27)], which may help analyze the mechanisms underlying the onset of stroke in patients with renal dysfunction. We therefore investigated the relationship between the R_2CHADS_2 score and IS/SE in patients

with NVAF, as the above findings suggest that the R_2CHADS_2 score, which accounts for renal dysfunction, may be more useful than the $CHADS_2$ score for the risk stratification of IS/SE in patients with NVAF.

Association of chronic renal failure with AF

The 2013 Japanese guideline of chronic renal failure recommend renal dysfunction be considered a risk factor for cardiovascular disease, and a number of previous reports have described the close relationship between AF and chronic renal failure [28)29)30)31)]. Soliman et al. reported that the incidence of AF increased in patients ≥70 years of age with moderate renal dysfunction (average eGFR 43.6 ml/min/m^2) when their eGFR was ≤45 ml/min/m^2 [32)]. Furthermore, Watanabe et al. reported that the incidence of AF was newly found in 2,947 of 235,818 patients with chronic renal failure during 4.5 years of follow-up. They further found that the hazard ratio of patients with eGFR 30-59 ml/min/m^2 was 1.32 (95% CI: 1.08-1.62), and the hazard ratio of patients with eGFR <30 ml/min/m^2 was 1.52 (95% CI: 0.89-2.77)[33)]. However, the Atherosclerosis Risk in Communities (ARIC) study, which compared the cardiovascular prognosis between patients with and without a history of AF during 10.1 years of follow-up, found that an impaired renal function was not an independent predictor in

patients with AF[36], and Roldán et al. reported that the addition of renal dysfunction to the $CHADS_2$ and CHA_2DS2-VASc score as a risk factor of cardiovascular events did not improve the predictive probability in patients with AF[37]. In the present study, no significant difference was observed among the $CHADS_2$, CHA_2DS_2-VASc, and R_2CHADS_2 scores for discriminative ability of IS/SE in Japanese patients with PNVAF, and our results were consistent with those of previous studies.

However, it constitutes the R2 CHADS 2 score is moderate to severe renal dysfunction, so further examination is particularly important in patients with mild renal dysfunction.

Study limitations

Several limitations associated with the present study warrant mention. First, the patient background likely did not conform to the current AF status because the follow-up period in this study was from August 1995 to July 2008. According to a large-scale epidemiological study conducted from 2000 to 2010, the incidence of AF in the Japanese population increased by 1.4, and it is suspected that the incidence of female AF patients may be rapidly increasing in Japan[1]. Second, the present study was conducted only in patients with paroxysmal AF, and

it is unclear whether or not the same findings would be obtained in patients with persistent and permanent AF. Third, there are a number of methodological limitations hindering physicians from determining when AF actually recurred, and none of the currently available monitoring methods can make a correct evaluation, except for dedicated devices. Finally, the number of patients was relatively small. A large-scale multicenter study should be performed in Japanese patients with NVAF to further evaluate the utility of the $CHADS_2$, CHA_2DS_2-VASc, and R_2CHADS_2 scores in risk stratification.

Conclusion

In Japanese patients with PNVAF, the $CHADS_2$, CHA_2DS_2-VASc, and R_2CHADS_2 scores were all found to be useful for risk stratification of IS/SE.

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Figure and Table Legends

Table 1-A: Patient characteristics

Table 1-B: Details of underlying heart disease

Table 1-C: Selected antiarrhythmic drugs

Fig. 1: Distribution of PNVAF patients on the basis of $CHADS_2$, CHA_2DS_2-VASc, and R_2CHADS_2 scores.

Fig. 2-A: Survival curve free from ischemic stroke/systemic embolism on the basis of the $CHADS_2$ score.

Fig. 2-B: Survival curve free from ischemic stroke/systemic embolism on the basis of the CHA_2DS_2-VASc score

Fig. 2-C: Survival curve free from ischemic stroke/systemic embolism on the basis of the R_2CHADS_2 score

Table 2: Incidences and annual rates of ischemic stroke/systemic embolism on the basis of the $CHADS_2$, CHA_2DS_2-VASc, and R_2CHADS_2 scores

Table 3-A: Predictors of ischemic stroke/systemic embolism in patients with PNVAF not receiving antithrombotic therapy

Abbreviations: AF, atrial fibrillation; RAAS, renin-angiotensin-aldosterone system; LVDd,

left ventricular end-diastolic dimension; LAD, left atrial dimension; LVEF, left ventricular ejection fraction

Table 3-B: Predictors of ischemic stroke/systemic embolism in patients with PNVAF not receiving antithrombotic therapy

Abbreviations: AF, atrial fibrillation; RAAS, renin-angiotensin-aldosterone system; LAD, left atrial dimension; LVEF, left ventricular ejection fraction; LVDd, left ventricular end-diastolic dimension

Table 3-C: Predictors of ischemic stroke/systemic embolism in patients with PNVAF not receiving antithrombotic therapy

Abbreviations: AF, atrial fibrillation; RAAS, renin-angiotensin-aldosterone system; LAD, left atrial dimension; LVDd, left ventricular end-diastolic dimension; LVEF, left ventricular ejection fraction

Fig. 3: Predictive ability of the $CHADS_2$, CHA_2DS_2-VASc, and R_2CHADS_2 scores for ischemic stroke/systemic embolism based on the receiver operating characteristic curve

Table.1A

Number	332		
Follow-up period (months)	53±35	LVDd (mm)	46±5
Age (years)	65±13	LAD (mm)	34±6
Male : female	224:108	LVEF (%)	69±10
Hypertension	142 (43%)	RAAS inhibitors	80 (24%)
Diabetes Mellitus	42 (13%)	Statins	45 (14%)
Dyslipidemia	44 (13%)	Antithrombotic therapy ;	
Smoking habits	89 (27%)	None	223 (67%)
Alcohol habits	134 (40%)	Aspirin	109 (33%)
Hyperuricemia	19 (6%)	ANP during SNR (pg/ml)	38±37
Underlying heart disease	65 (20%)	Onset of AF	
Underlying pulmonary disease	18 (5%)	diurnal : nocturnal : mixed	65:129:138
AF history (months)	18±32		

Table.1B

Underlying heart disease	Number (%)	
Old myocardial infarction	15 (19%)	Ischemic heart disease (57%, N=37)
Angina pectoris	20(25%)	
Syndrome X	2 (3%)	
Dilated cardiomyopathy	5 (6%)	Non-Ischemic heart disease (43%, N=28)
Hypertrophic cardiomyopathy	13 (16%)	
Myocarditis	1 (1%)	
Atrial septal defect	2 (3%)	
Sick sinus syndrome	7 (9%)	

Table.1C

Antiarrhythmic drugs	Number (%)	
Disopyramide	80 (24%)	Class I antiarrhythmic drugs (94.5%, N=314)
Aprindine	51 (15%)	
Cibenzoline	101 (30%)	
Pilsicainide	40 (12%)	
Flecainide	25 (8%)	
Propafenone	6 (2%)	
Pirmenol	11 (3%)	
Bepridil	14 (4%)	other antiarrhythmic drugs (4.5%, N=15)
Amiodarone	1 (0.3%)	
Verapamil	2 (0.7%)	
β-blockers	1 (0.3%)	

Figure 1

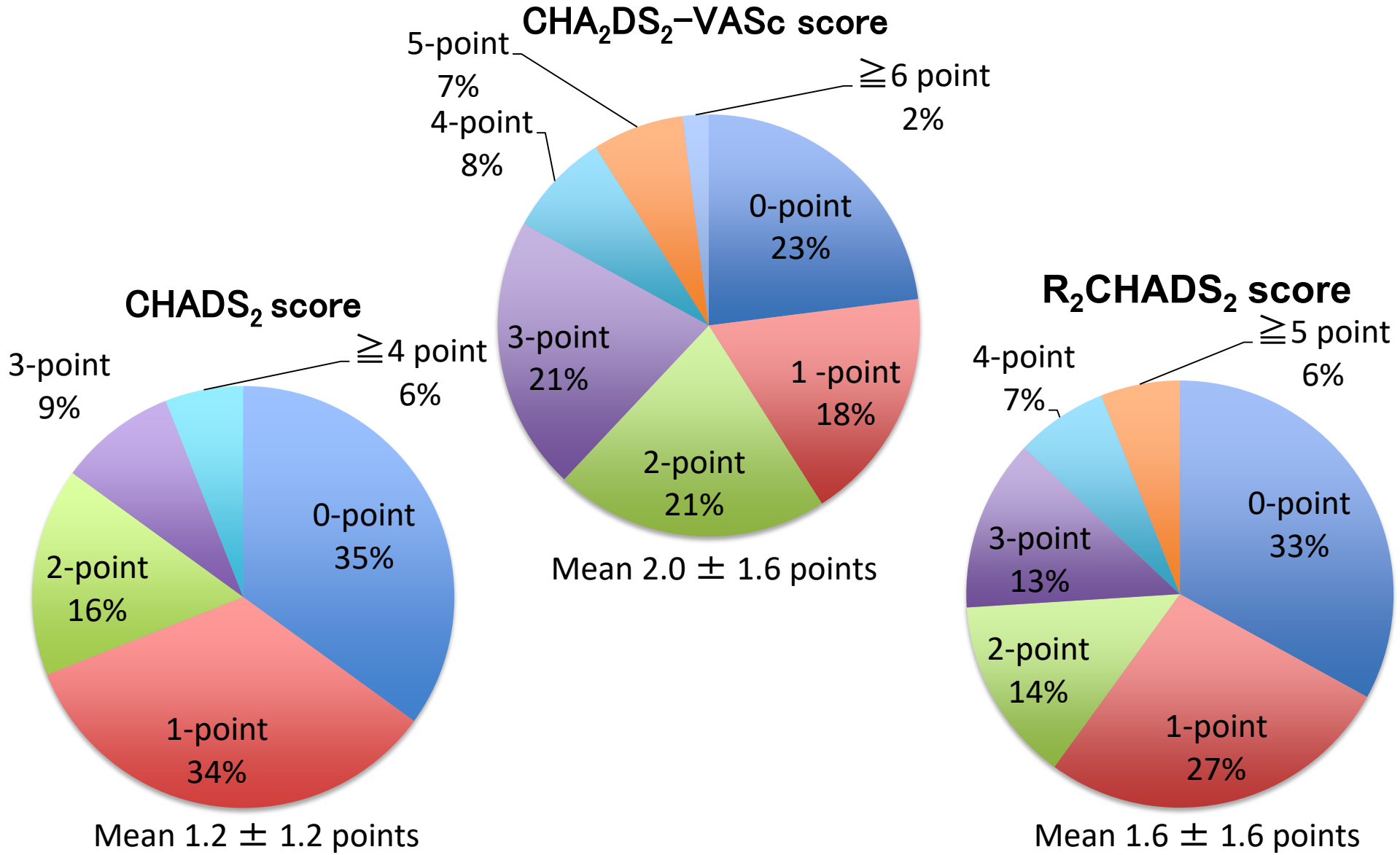
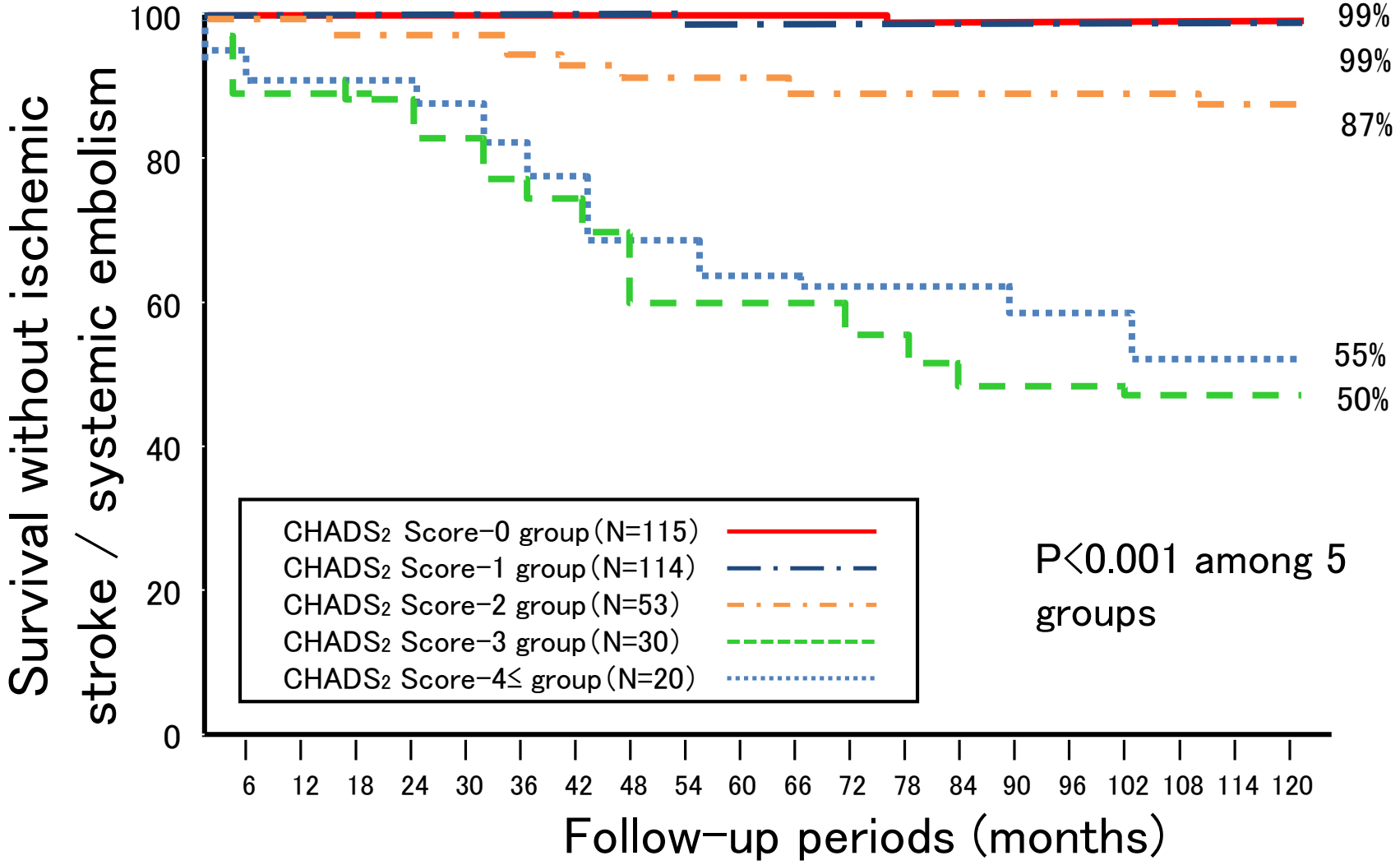

CHA2DS2–VASc score
5-point 7%
≧6 point 2%
4-point 8%
0-point 23%
3-point 21%
1 -point 18%
2-point 21%
Mean 2.0 ± 1.6 points
CHADS2 score
3-point 9%
≧4 point 6%
0-point 35%
2-point 16%
1-point 34%
Mean 1.2 ± 1.2 points
R2CHADS2 score
4-point 7%
≧5 point 6%
0-point 33%
3-point 13%
2-point 14%
1-point 27%
Mean 1.6 ± 1.6 points

Figure 2-A



(Komatsu T, et al. J Cardiol 2012;59: 321-328.)

Figure 2-B

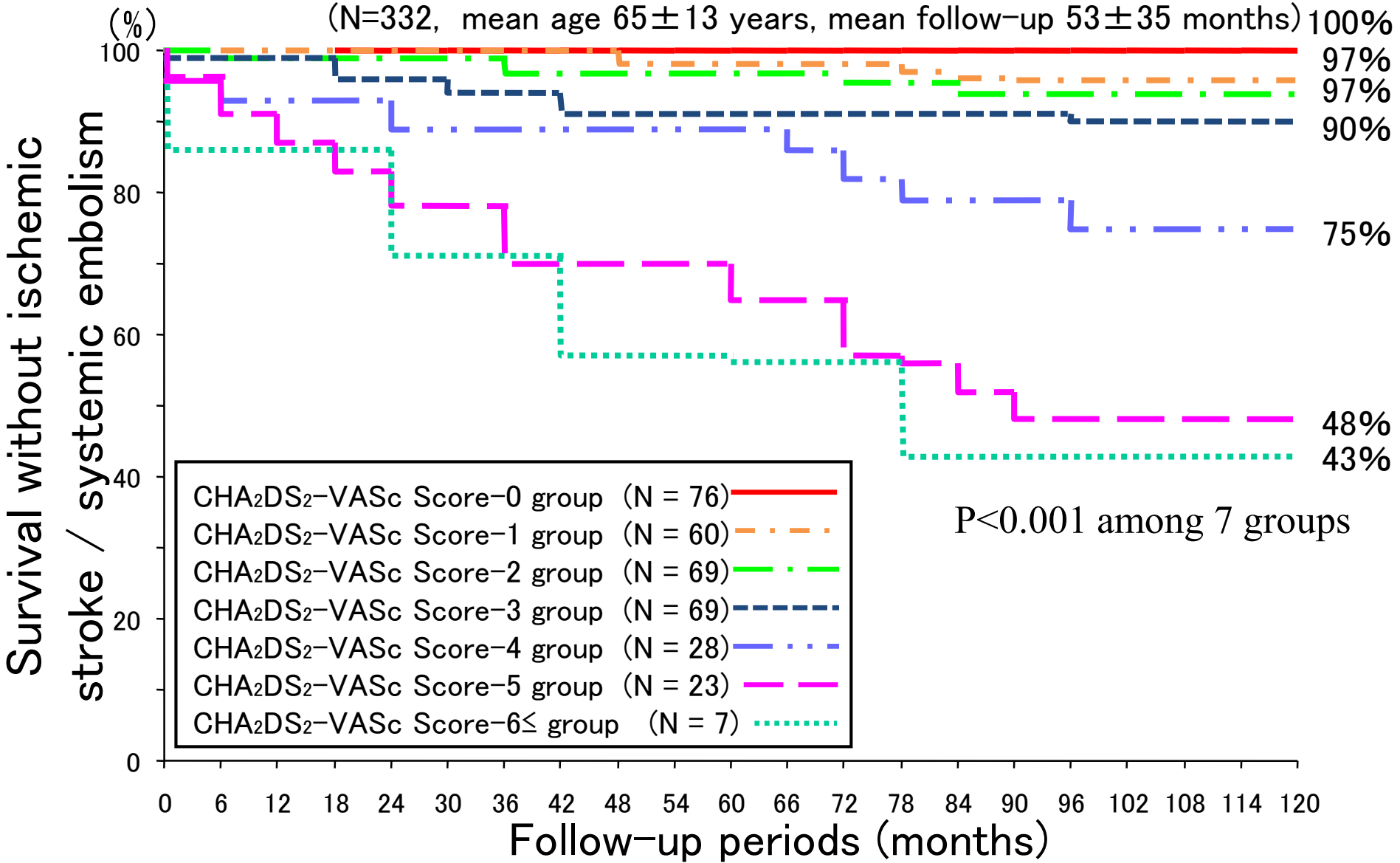

(%)
(N=332, mean age 65±13 years, mean follow-up 53±35 months)
100%
97%
97%
90%
75%
48%
43%
Survival without ischemic stroke / systemic embolism
100
80
60
40
20
0
CHA2DS2-VASc Score-0 group (N = 76)
CHA2DS2-VASc Score-1 group (N = 60)
CHA2DS2-VASc Score-2 group (N = 69)
CHA2DS2-VASc Score-3 group (N = 69)
CHA2DS2-VASc Score-4 group (N = 28)
CHA2DS2-VASc Score-5 group (N = 23)
CHA2DS2-VASc Score-6≤ group (N = 7)
P<0.001 among 7 groups
0 6 12 18 24 30 36 42 48 54 60 66 72 78 84 90 96 102 108 114 120
Follow-up periods (months)

Figure 2-C

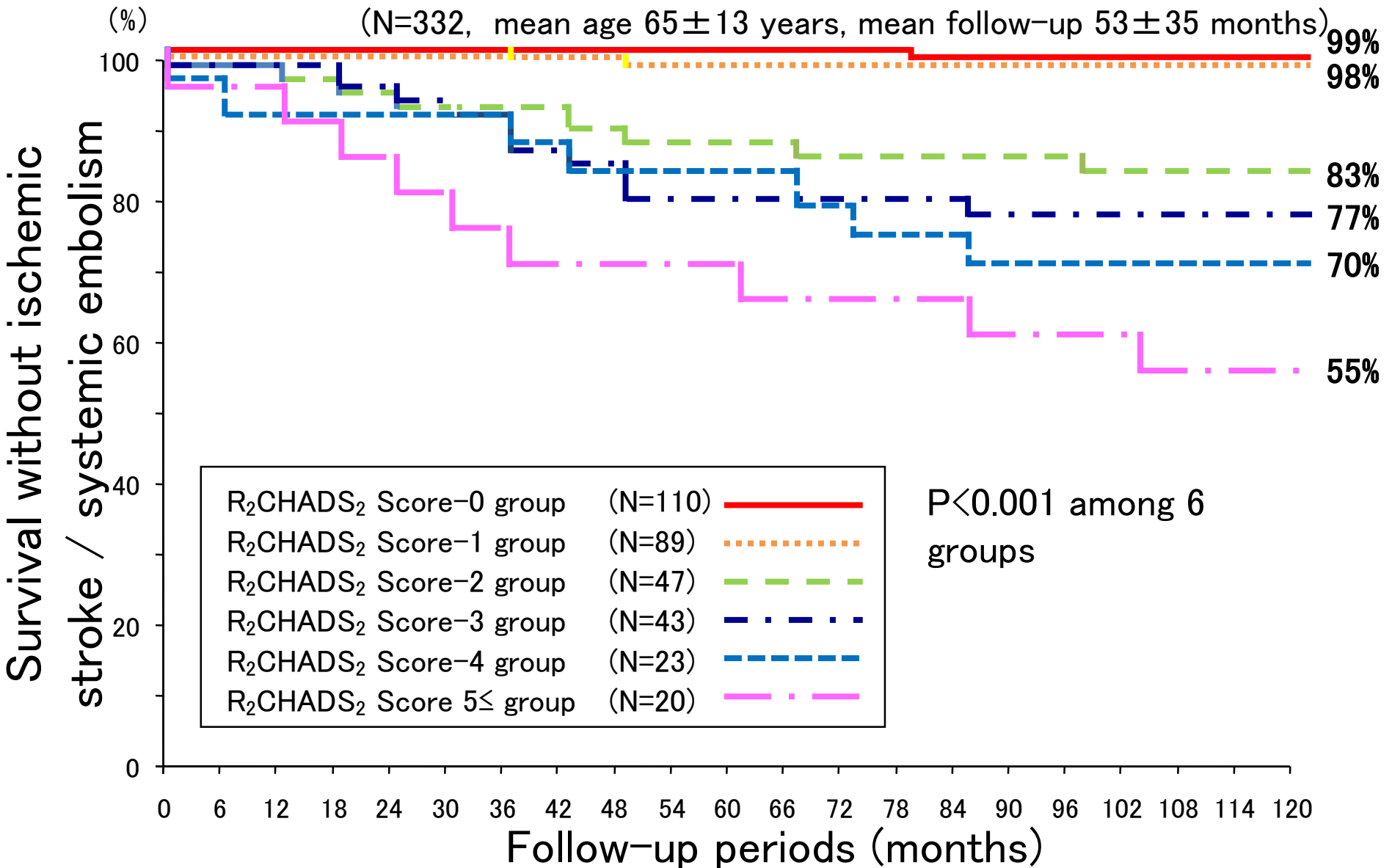

(%)
(N=332, mean age 65±13 years, mean follow-up 53±35 months)
Survival without ischemic stroke / systemic embolism
100
80
60
40
20
0
99%
98%
83%
77%
70%
55%
R2CHADS2 Score-0 group (N=110)
R2CHADS2 Score-1 group (N=89)
R2CHADS2 Score-2 group (N=47)
R2CHADS2 Score-3 group (N=43)
R2CHADS2 Score-4 group (N=23)
R2CHADS2 Score 5≤ group (N=20)
P<0.001 among 6 groups
0 6 12 18 24 30 36 42 48 54 60 66 72 78 84 90 96 102 108 114 120
Follow-up periods (months)

Table.2

$CHADS_2$ score	Number	Follow up period (months)	Annual rate (%/year;95%CI)
Score 0	(N=115)	46±32	0.21 (0.10-0.33)
Score 1	(N=114)	51±35	0.93 (0.79-1.07)
Score 2	(N=53)	65±39	2.78 (2.61-2.96)
Score 3	(N=30)	68±39	9.41 (8.98-9.85)
Score 4 ≤	(N=20)	55±30	10.90 (10.18-11.67)
CHA_2DS_2-VASc score	Number	Follow up period (months)	Annual rate (%/year;95%CI)
Score 0	(N=76)	45±33	0
Score 1	(N=60)	42±31	0.60 (0.45-0.76)
Score 2	(N=69)	58±34	0.95 (0.73-1.18)
Score 3	(N=69)	62±39	1.96 (1.65-2.28)
Score 4	(N=28)	55±32	5.45 (5.06-5.85)
Score 5	(N=23)	69±33	9.06 (8.41-9.72)
Score 6≤	(N=7)	50±29	13.70 (11.79-15.62)
R_2CHADS_2 score	Number	Follow up period (months)	Annual rate (%/year;95%CI)
Score 0	(N=110)	47±33	0.23 (0.12-0.35)
Score 1	(N=89)	49±35	0.56 (0.36-0.77)
Score 2	(N=47)	62±39	3.29 (3.00-3.58)
Score 3	(N=43)	56±32	4.98 (4.57-5.40)
Score 4	(N=23)	53±37	5.80 (5.13-6.47)
Score 5 ≤	(N=20)	70±32	7.71 (5.81-9.61)

Non-valvular paroxysmal AF (N=332, mean age 65±13years, mean follow-up 53±35months)

Table 3A

Variables	Odds ratio (95%CI)	P-value
$CHADS_2$ score	4.735 (2.803 – 7.998)	<0.001
Mixed type (time of AF onset)	3.380 (1.133 – 10.08)	0.003
Statins	3.185 (0.978 – 13.72)	0.068
Age (years)	0.956 (0.908 – 1.007)	0.091
RAAS inhibitors	2.106 (0.667 – 6.648)	0.145
Chronic AF	1.420 (0.490 – 4.116)	0.204
Underlying Heart Disease	1.662 (0.244 – 11.30)	0.518
Underlying Pulmonary Disease	0.801 (0.231 – 2.771)	0.604
AF recurrence	0.984 (0.899 – 1.077)	0.726
LVDd (mm)	1.005 (0.974 – 1.038)	0.726
AF history (months)	0.988 (0.908 – 1.074)	0.739
LAD (mm)	1.007 (0.960 – 1.056)	0.770
LVEF (%)	0.988 (0.908 – 1.074)	0.788
Male	1.150 (0.394 – 3.357)	0.799

— A multivariate logistic regression analysis —

Table 3B

(N=332, mean age 65±13 years, mean follow-up 53±35 months)

Variables	Odds ratio (95%CI)	P-value
CHA_2DS_2-VASc score	4.152 (2.570 – 6.709)	<0.001
Mixed type (time of AF onset)	3.120 (1.018 – 9.565)	0.046
Male	2.907 (0.991 – 8.530)	0.052
Age (years)	0.965 (0.901 – 1.012)	0.098
Statins	2.743 (0.892 – 11.41)	0.113
RAAS inhibitors	2.095 (0.752 – 5.837)	0.157
Chronic AF	1.871 (0.586 – 5.972)	0.290
Underlying Pulmonary Disease	0.537 (0.279 – 11.61)	0.537
AF history (months)	1.003 (0.989 – 1.016)	0.702
AF recurrence	1.256 (0.379 – 4.161)	0.709
LAD (mm)	0.985 (0.904 – 1.075)	0.739
LVEF (%)	0.993 (0.949 – 1.039)	0.765
LVDd (mm)	0.988 (0.903 – 1.082)	0.795
Underlying Heart Disease	1.119 (0.388 – 3.225)	0.835

— A multivariate logistic regression analysis —

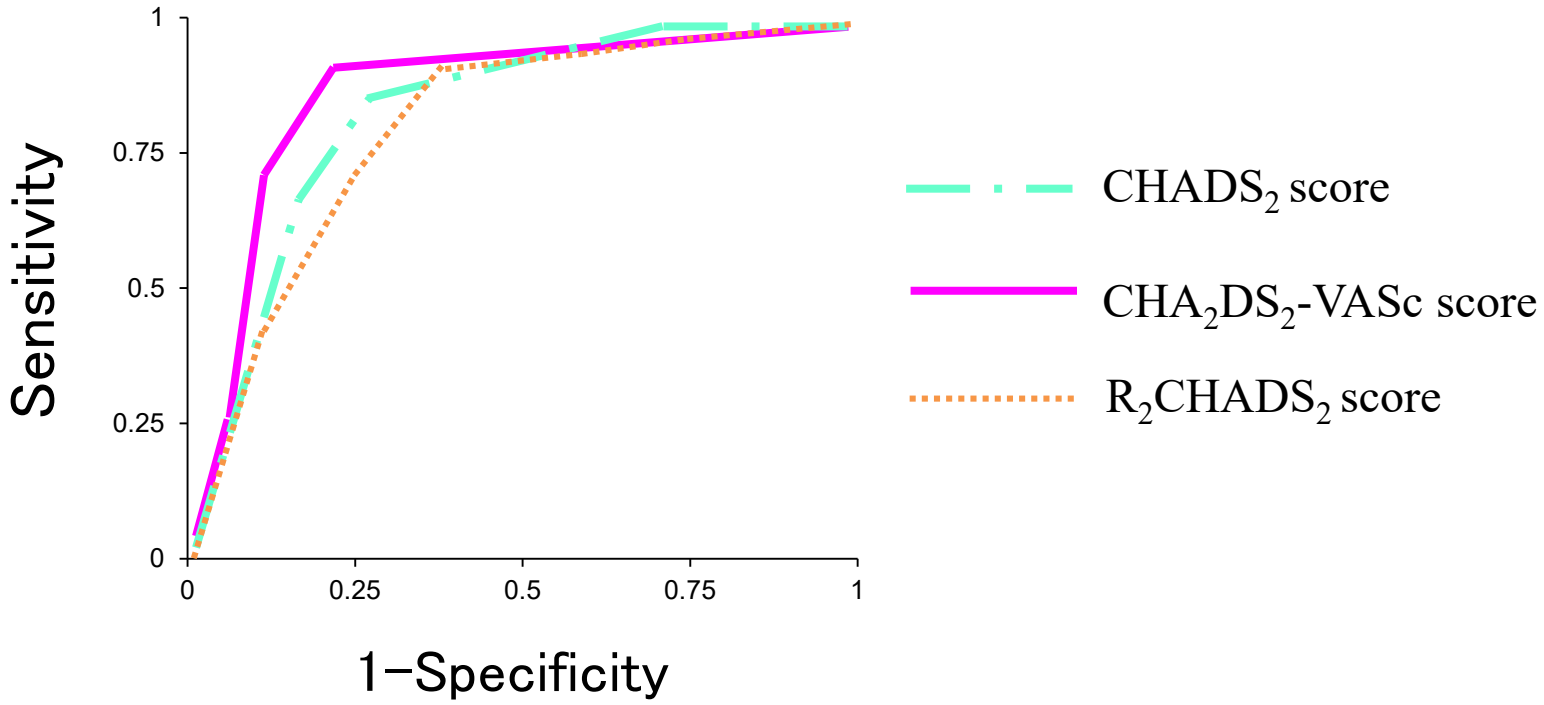
Table 3C

(N=332, mean age 65±13 years, mean follow-up 53±35 months)

Variables	Odds ratio (95%CI)	P-value
R_2CHADS_2 score	1.937 (1.481 – 2.533)	< 0.001
Mixed type (time of AF onset)	2.782 (1.021 – 7.584)	0.045
Statins	2.920 (0.922 – 9.246)	0.068
Chronic AF	1.778 (0.643 – 4.918)	0.268
RAAS inhibitors	1.610 (0.659 – 3.933)	0.296
LAD (mm)	1.031 (0.962 – 1.105)	0.385
Symptomatic AF	0.634 (0.225 – 1.738)	0.388
AF history (months)	1.003 (0.991 – 1.015)	0.651
Male	1.199 (0.471 – 3.051)	0.704
Underlying Pulmonary Disease	1.336 (0.252 – 7.081)	0.734
LVDd (mm)	1.011 (0.934 – 1.094)	0.789
LVEF (%)	0.934 (0.957 – 1.037)	0.846
Underlying Heart Disease	1.015 (0.406 – 2.539)	0.974
AF recurrence	1.005 (0.335 – 3.019)	0.993

— A multivariate logistic regression analysis —

Figure 3



Receiver-operator characteristic (ROC) curve	Area (95% CI)	P-value	
CHA_2DS_2-VASc score	0.894 (0.846-0.951)	P<0.001	
$CHADS_2$ score	0.866 (0.807-0.925)	P<0.001	N.S.
R_2CHADS_2 score	0.851 (0.794-0.908)	P<0.001	