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CLINICAL RESEARCH — Coronary Artery Disease

Prognostic Stratification of Patients With Vasospastic Angina

A Comprehensive Clinical Risk Score Developed by the Japanese Coronary Spasm Association

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Objectives The present study aimed to develop a comprehensive clinical risk score for vasospastic angina (VSA) patients.

Background Previous studies demonstrated various prognostic factors of future adverse events in VSA patients. However, to apply these prognostic factors in clinical practice, the assessment of their accumulation in individual patients is important.

Methods The patient database of the multicenter registry study by the Japanese Coronary Spasm Association (JCSA) (n = 1,429; median 66 years; median follow-up 32 months) was utilized for score derivation.

Results Multivariable Cox proportional hazard model selected 7 predictors of major adverse cardiac events (MACE). The integer score was assigned to each predictors proportional to their respective adjusted hazard ratio; history of out-of-hospital cardiac arrest (4 points), smoking, angina at rest alone, organic coronary stenosis, multivessel spasm (2 points each), ST-segment elevation during angina, and beta-blocker use (1 point each). According to the total score in individual patients, 3 risk strata were defined; low (score 0 to 2, n = 598), intermediate (score 3 to 5, n = 639) and high (score 6 or more, n = 192). The incidences of MACE in the low-, intermediate-, and high-risk patients were 2.5%, 7.0%, and 13.0%, respectively ($p < 0.001$). The Cox model for MACE between the 3 risk strata also showed prognostic utility of the scoring system in various clinical subgroups. The average prediction rate of the scoring system in the internal training and validation sets were 86.6% and 86.5%, respectively.

Conclusions We developed a novel scoring system, the JCSA risk score, which may provide the comprehensive risk assessment and prognostic stratification for VSA patients. (J Am Coll Cardiol 2013;62:1144–53) © 2013 by the American College of Cardiology Foundation

Vasospastic angina (VSA) is one of the important functional cardiac disorders characterized by transient myocardial ischemia due to epicardial coronary artery spasm (1–3). The terms for VSA are basically synonymous with the terms *Prinzmetal's angina* and *variant angina*, and is known to be associated with a wide variety of cardiac conditions, including stable angina, acute coronary syndrome, and life-threatening arrhythmic events (4,5).

A number of studies have elucidated patient characteristics, outcomes, and prognostic factors of VSA (6–12), which led to a better understanding and management for this disorder. We have also recently reported the prognostic importance of the history of out-of-hospital cardiac arrest (OHCA) (13) and specific angiographic findings during diagnostic testing (14) in VSA patients from the multicenter registry study with more than 1,400 patients. However, because the patient characteristics and the number of prognostic factors present in individual patients may vary and the potential interaction between each prognostic factor may exist, it is difficult to accurately evaluate risk stratification of VSA patients in the current clinical practice. Thus, the comprehensive assessment tool

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that provides a valid risk prediction in individual patients needs to be developed. As one of the useful means to assess the comprehensive risk, simple scoring models, in which the prognostic factors identified by multivariable analysis are combined, have been developed for several disorders (15), although there is currently no tool available for VSA patients.

In the present study, we thus aimed to develop a comprehensive clinical risk scoring system that provides the prediction of future adverse cardiac events and the prognostic stratification for VSA patients in the nationwide multicenter registry study conducted by the Japanese Coronary Spasm Association (JCSA).

Abbreviations and Acronyms

AIC = Akaike Information Criterion
ECG = electrocardiography
HR = hazard ratio
ICD = implantable cardioverter-defibrillator
IQR = interquartile range
JCSA = Japanese Coronary Spasm Association
MACE = major adverse cardiac event
OHCA = out-of-hospital cardiac arrest
SD = standard deviation
VSA = vasospastic angina

Methods

The JCSA was founded in 2006 and currently consists of 81 institutes in Japan. The present study was conducted as an investigator initiated observational clinical research. The study was approved by the institutional review boards or ethics committees of all participating institutes.

Study patients. The VSA patients diagnosed between April 1, 2003, and December 31, 2008 were enrolled. The registration was made between September 1, 2007, and December 31, 2008. The data collection was conducted in a retrospective fashion for patients seen before September 2007 and in a prospective manner for those seen after that date. The diagnosis of VSA was made based on the spasm provocation tests and/or spontaneous angina attack defined by the Guidelines for Diagnosis and Treatment of Patients with Vasospastic Angina of the Japanese Circulation Society (16). The positive diagnosis of the provocation tests was defined as a total or subtotal (>90%) coronary artery narrowing induced by pharmacological (e.g., acetylcholine and ergonovine) or nonpharmacological (e.g., hyperventilation) challenge during coronary angiography, accompanied by chest pain and/or ischemic electrocardiography (ECG) changes. The definition of spontaneous attack was angina at rest and/or effort, accompanied by a transient ST-segment elevation or depression of more than 0.1 mV, or a new appearance of negative U-wave on ECG (16). The criterion of spontaneous attack was applied when the patients did not have significant organic coronary stenosis that can explain their angina attacks.

Data collection. The demographic and clinical data were submitted to a central database system, including age, sex, coronary risk factors, types of angina episodes, ST-segment changes and arrhythmias during spontaneous angina attack, angiographic findings of the spasm provocation tests, medications, and device therapy such as implantable cardioverter defibrillator (ICD). The clinical outcomes during the follow-up period were also collected. Follow-up data were obtained from each participating or cooperating hospital records and patients' regular visits to physicians in the outpatient clinic. The outcomes of the retrospective population were evaluated retrospectively. The prospective cohort was followed up until December 31, 2008.

Hypertension, dyslipidemia, and diabetes mellitus were diagnosed based on the guidelines of the Japanese Society of Hypertension, Japan Atherosclerosis Society, and Japan Diabetes Society, respectively (17–19). The OHCA was defined as the cessation of cardiac mechanical activity, as confirmed by the absence of signs of circulation that occurred outside of the hospital setting (20). Organic coronary stenosis was assessed as either nonsignificant (25% to 50% luminal narrowing) or significant (more than 50% luminal narrowing) by coronary angiography.

Endpoints. The primary endpoint was defined as major adverse cardiac events (MACE), including cardiac death, nonfatal myocardial infarction, hospitalization due to unstable angina pectoris, heart failure, and the appropriate ICD shocks during the follow-up period that began at the date of the diagnosis of VSA. In particular, cardiac death, nonfatal myocardial infarction and ICD shocks were categorized as hard MACE. The secondary endpoint was all-cause mortality. The definition of these events was previously described (13).

Statistical analysis. Continuous variables are presented as medians and interquartile ranges (IQR) or means and standard deviations (SD) and categorical variables as numerals and percentages. Group comparisons were performed with the Kruskal-Wallis test for continuous variables, the chi-square test for categorical variables, and the log-rank test for survival curves. Survival free from MACE and death were analyzed by the Kaplan-Meier method. A value of $p < 0.05$ was considered to be statistically significant.

The clinical variables included in our JCSA risk score and respective scoring points were determined based on their prognostic contribution for VSA patients. Univariable and multivariable Cox proportional hazard model were applied to select the demographic and angiographic characteristics and treatments that correlated with MACE. The variables showing statistical significance or a trend ($p < 0.1$) in univariable Cox model were subjected to multivariable analysis with a forced-entry method. The Akaike Information Criterion (AIC) was used to select appropriate explanatory variables (21). Missing data were handled using a multiple imputation procedure with 20 resampling replications. The proportional hazards assumption for the Cox model was examined with the log minus log plot. Significant variables selected from multivariable Cox model were assigned integer score proportional to their adjusted hazard ratio (HR) for MACE. The variables with

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a statistical trend were uniformly defined as 1 point. Then the score was calculated in individual patients by the sum of weighted variables present. The differences in the incidence of MACE and death for increasing the JCSA risk score were assessed by the chi-square test for trend. Relative hazard for MACE between 3 risk strata defined by the range of risk score was estimated by the univariable Cox model. The interaction between the risk strata and predefined clinical subgroups in their effects on MACE was assessed by the Cox model with interaction terms.

The validity of the scoring system was assessed by the simulation study, which was formed with the iteration of random partition of the data into training and validation sets (22). First, we divided the whole population data of 1,429 patients into 1,286 training (90%) and 143 validation (10%) sets, the latter of which was completely set aside during training. To train the model, the Cox proportional hazard model was applied to the training set with the clinical variables that were included in the JCSA risk score. Adjusted HR and respective scoring points for each variable were determined by exactly the same method for the aforementioned full model. The JCSA risk score obtained from the training data was applied to the samples in the validation set and the corresponding risk strata were predicted for each sample. This process was iterated 1,000 times and the average prediction rate and its SD predicting correct risk strata were calculated. We also calculated the average incidence of MACE in each predicted risk stratum.

Results

Patient characteristics and treatments. Among the 1,528 patients registered from 47 participating hospitals, 99 were excluded because they did not meet the inclusion criteria. Finally, 1,429 VSA patients, including retrospective (n = 1,276) and prospective populations (n = 153), were analyzed in the present study. The demographic and angiographic characteristics and treatments of the study patients are summarized in Table 1 and Online Table 1. The median age was 66 years. Angina attack occurred at rest alone was noted in 634 patients. The ST-segment changes were documented in 393 patients during spontaneous angina attacks. The arrhythmic events were observed in 107 patients, of which 52 suffered from life-threatening events including ventricular tachycardia, ventricular fibrillation, and OHCA. All the patients underwent coronary angiography, and the spasm provocation tests were performed in 1,244 patients. Significant organic coronary stenosis was found in 201 patients. Of those, 180 patients were diagnosed by performing the provocation test, and the remaining 21 patients were diagnosed based on spontaneous attacks. For the treatment of VSA, calcium channel blockers were used in 1,331 patients, whereas the use of beta-blockers was limited to 61. In 35 patients with a history of OHCA, 14 underwent ICD implantation for the secondary prevention of sudden cardiac death.

Table 1 Demographic and Angiographic Characteristics and Treatments of VSA Patients (N = 1,429)

Demographic characteristics	
Age, yrs	66 (58, 73)
Male	1,090 (76)
Coronary risk factor	
Hypertension	666 (47)
Dyslipidemia	647 (45)
Diabetes mellitus	233 (16)
Smoking	848 (59)
Previous myocardial infarction	91 (6)
Clinical situation of angina attack*	
Rest	634 (50)
Effort	113 (9)
Rest and effort	513 (41)
ST-segment change during angina attack†	
ST-segment elevation	272 (21)
ST-segment depression	121 (9)
Arrhythmic event during angina attack	
PVC	14 (1)
VT/VF	43 (3)
AV block	21 (1)
Bradycardia/sinus pause	28 (2)
OHCA	35 (2)
Angiographic characteristics	
Organic coronary stenosis	
Without stenosis	878 (61)
Nonsignificant stenosis	350 (25)
Significant stenosis	201 (14)
Spasm-positive artery induced by provocation test‡	
LAD	666 (56)
LCx	317 (27)
RCA	693 (59)
Multivessel	374 (32)
Medical treatments	
Calcium-channel blocker	1,331 (93)
Long-acting nitrate	695 (49)
Antiplatelet	669 (47)
Statin	472 (33)
ACEI/ARB	340 (24)
Beta-blocker	61 (4)

Values are median (IQR) or n (%). *Data of clinical situation of angina attacks were available for 1,260 patients. †Data of ST-segment changes were available for 1,317 patients. ‡The spasm provocation test was performed on 1,244 patients, and the data of spasm-positive artery were available for 1,184 patients.

ACEI = angiotensin-converting enzyme inhibitor; ARB = angiotensin receptor blocker; AV = atrioventricular; IQR = interquartile range; LAD = left anterior descending artery; LCx = left circumflex coronary artery; OHCA = out-of-hospital cardiac arrest; PVC = premature ventricular contraction; RCA = right coronary artery; VF = ventricular fibrillation; VSA = vasospastic angina; VT = ventricular tachycardia.

Long-term outcomes and correlated factors of MACE. During the median follow-up period of 32 months (IQR: 17 to 46 months), 85 patients (5.9%) reached the primary endpoint (Table 2), of those 14 patients (1.0%) suffered from hard MACE. All-cause death as the secondary endpoint occurred in 19 patients (1.3%). Kaplan-Meier analysis demonstrated that the 5-year survival rate free from MACE and all-cause death were 91% and 98%, respectively. The

Table 2 Primary and Secondary Outcomes During the Follow-Up Period (N = 1,429)

MACE	85 (6)
Cardiac death	6 (0.4)
Nonfatal myocardial infarction	9 (1)
Unstable angina	68 (5)
Heart failure	4 (0.3)
Appropriate ICD shock	2 (0.1)
All-cause death	19 (1)

Values are n (%).

ICD = implantable cardioverter-defibrillator; MACE = major adverse cardiac event; other abbreviations as in Table 1.

primary and secondary endpoints in patients with organic coronary stenosis are summarized in Online Table 2.

The patient characteristics and the treatments associated with the primary endpoint at univariable and multivariable analysis are shown in Table 3. Multivariable Cox model demonstrated 5 significant predictors of MACE, including smoking, angina at rest alone, history of OHCA, significant organic coronary stenosis, and multivessel spasm. The ST-segment elevation during angina attack and the use of beta-blockers also tended to have a prognostic impact, although statistical significance was not derived. The covariates included in the final multivariable model were determined by reference to AIC. At first, a model was considered with 9 variables including diabetes mellitus and previous myocardial infarction. However, exclusion of these 2 variables resulted in a reduction of AIC from 1,155.08 to 1,153.15 ($p = 0.037$), indicating the adequacy of the final model consisting of 7 variables (Table 3).

Derivation of the JCSA risk score. Five significant predictors selected from the multivariable Cox model were assigned integer score proportional to their respective HR for MACE (Table 3). The variables with a statistical trend, such as ST-segment elevation during angina attack and the use of beta-blockers were uniformity assigned 1 point. Subsequently, these 7 predictors were integrated into the JCSA risk scoring system. The risk score was then calculated based on the sum of weighted predictors present in individual patients. The distribution of the scoring points and corresponding incidence of MACE is shown in Figure 1. The score ranged from 0 to 9 points among the study patients. The incidence of MACE was progressively increased with an increase in the risk score.

For simplicity, 3 risk strata were defined in accordance with the scoring points; low (score 0 to 2, n = 598), intermediate (score 3 to 5, n = 639) and high (score 6 or more, n = 192). The incidence of MACE in the low-, intermediate-, and high-risk patients were 2.5%, 7.0%, and 13.0%, respectively ($p < 0.001$) (Fig. 2A). The Kaplan-Meier curve for MACE between the 3 risk groups showed clear prognostic utility of the scoring system throughout the follow-up period (low vs. intermediate [$p < 0.001$]; low vs. high [$p < 0.001$]; intermediate vs. high [$p = 0.007$]) (Fig. 3). Even when the endpoint was limited to hard MACE (cardiac death, nonfatal myocardial infarction, and ICD shocks), the 3 risk strata showed their predictive capacity (Fig. 2B). In contrast, as expected, the stratification

Table 3 Correlated Factors for MACE in VSA Patients and Assigned Score

	Univariable Analysis			Multivariable Analysis			
	HR	95% CI	p Value	HR	95% CI	p Value	Assigned Score
Age	0.99	0.97–1.01	0.38				
Male	1.07	0.64–1.79	0.79				
Hypertension	0.90	0.58–1.38	0.62				
Dyslipidemia	1.17	0.76–1.79	0.48				
Diabetes mellitus	1.57	0.94–2.61	0.09				
Smoking	1.96	1.21–3.19	0.006	1.71	1.04–2.79	0.034	2
Previous myocardial infarction	2.19	1.10–4.38	0.026				
Angina at rest alone	1.49	0.95–2.35	0.09	1.71	1.08–2.72	0.023	2
ST-segment elevation during angina attack	1.50	0.93–2.42	0.09	1.54	0.95–2.50	0.08	1
History of OHCA	3.98	1.73–9.13	0.001	3.79	1.61–8.94	0.002	4
Significant organic stenosis	2.28	1.39–3.73	0.001	2.24	1.33–3.78	0.002	2
LAD spasm	1.28	0.81–2.02	0.29				
LCx spasm	1.16	0.75–1.80	0.50				
RCA spasm	1.05	0.68–1.61	0.83				
Multivessel spasm	1.51	0.94–2.45	0.09	1.69	1.03–2.78	0.039	2
Calcium-channel blocker	0.73	0.35–1.51	0.39				
Long-acting nitrate	1.35	0.89–2.07	0.17				
Antiplatelet	1.43	0.94–2.20	0.10				
Beta-blocker	2.34	1.08–5.06	0.032	2.00	0.88–4.54	0.09	1

CI = confidence interval; HR = hazard ratio; other abbreviations as in Table 1.

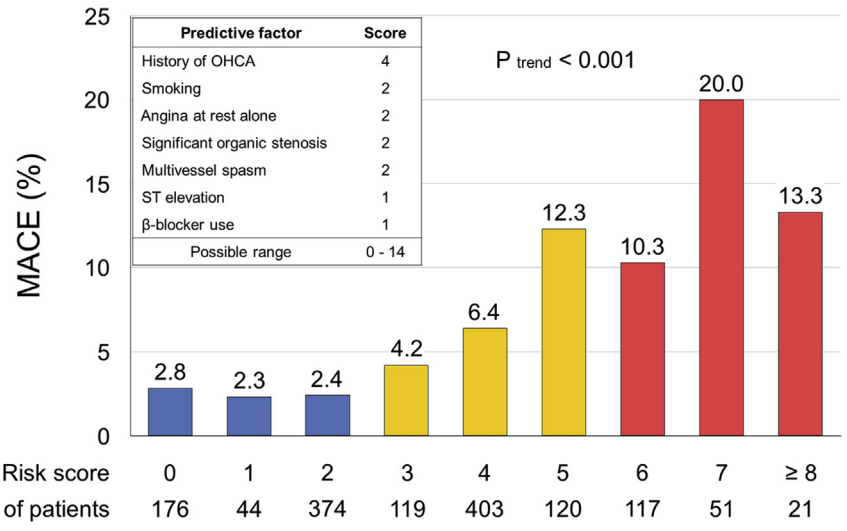

Figure 1 The JCSA Risk Scoring System and Corresponding Incidence of MACE

The scoring system consisted of 7 predictors of major adverse cardiac events (MACE). The total score was positively correlated with the incidence of MACE. JCSA = Japanese Coronary Spasm Association.

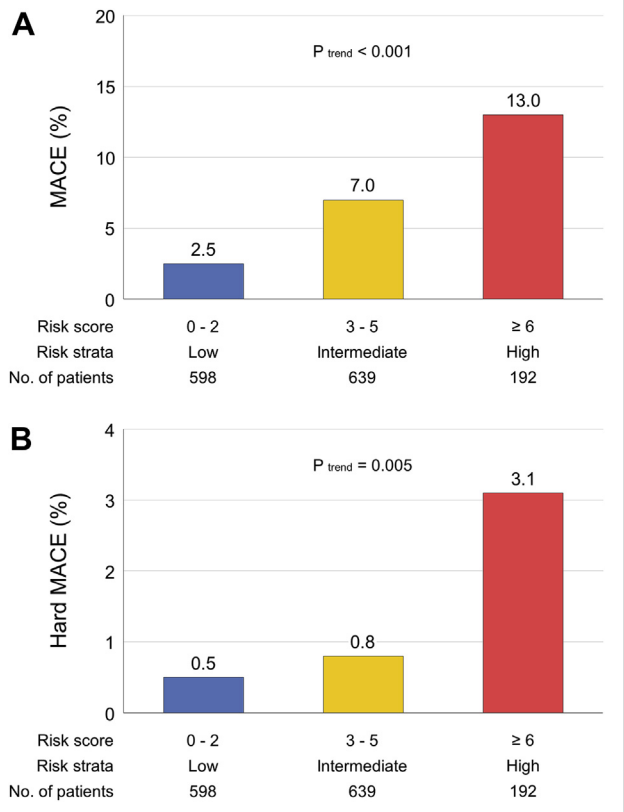

Figure 2 The 3 Risk Strata Classified Based on the JCSA Risk Score and Corresponding Incidence of MACE

(A) The incidence of MACE. **(B)** The incidence of hard MACE, including cardiac death, nonfatal myocardial infarction, and appropriate implantable cardioverter defibrillator shocks. Abbreviations as in Figure 1.

by the JCSA risk score did not predict all-cause mortality (low-risk 1.2% vs. intermediate-risk 1.1% vs. high-risk 2.6%; p = 0.25).

Application of the JCSA risk score to clinical subgroups. The JCSA risk score was also applied to clinical subgroups identified by patient characteristics and treatments. Importantly, the Cox proportional hazard model for

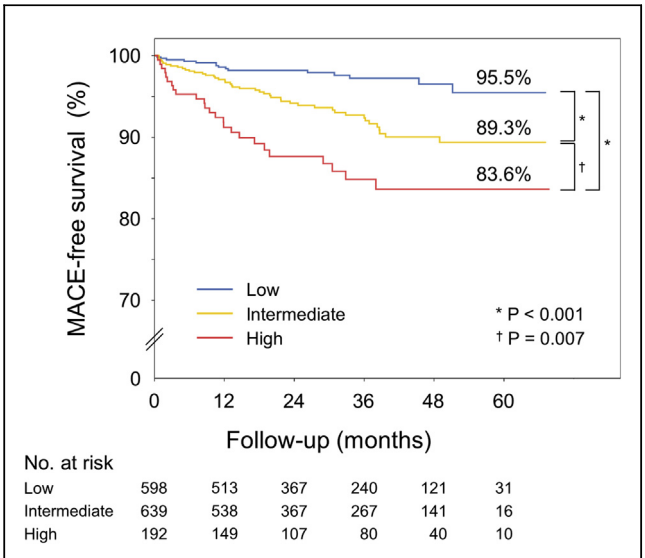

Figure 3 Kaplan-Meier Curve for MACE Between the 3 Risk Strata

Kaplan-Meier analysis demonstrated the prognostic difference between low-, intermediate-, and high-risk patients throughout the follow-up period. Abbreviations as in Figure 1.

MACE between the 3 risk strata demonstrated that the JCSA risk score is useful among various subgroups (Fig. 4).

Validation of the JCSA risk score. The JCSA risk score was validated in the internal training and validation sets. The random data partition was conducted 1,000 times, and the rate for the prediction of risk strata was calculated with each iteration. On average, the prediction rate was 86.6% (SD 10.0%) in the training set and 86.5% (SD 10.4%) in the validation set. The average incidence of MACE was 3.0% for validation samples predicted to be low-risk, 7.6% for intermediate-risk, and 13.0% for high-risk (Fig. 5).

Discussion

The major findings of the present study were that: 1. the JCSA risk score, in which 7 predictive factors derived from the multivariable Cox model were integrated, showed a significant correlation with the prognosis of VSA patients; 2. the 3 risk categories were classified based on the JCSA score and provided clear risk stratification of cardiac events, even among various VSA subgroups; and 3. the JCSA risk score showed an acceptable predictive capacity in the internal validation. To the best of our knowledge, this is the first study that has developed the useful clinical risk score for VSA patients.

Need for risk prediction tools for VSA. Since Prinzmetal et al. (23) first described VSA as a "variant angina" in 1959, a number of studies have revealed the clinical characteristics and outcomes of this disorder. The prognostic studies with hundreds of VSA patients were performed in the 1980s demonstrating that 5-year survival rate free from death or myocardial infarction were 77% to 97% and 60% to 83%, respectively (7–9), whereas the patient outcomes appear to have improved in the 2000s (5,11,12,24). Several prognostic factors for VSA, such as smoking, organic coronary stenosis, and multivessel spasm, have been established (6–10,12). Recently, we have also confirmed the importance of these well-known predictors, and newly identified the prognostic impact of history of OHCA (13) and specific angiographic findings during the diagnostic provocation tests (14) from the multicenter registry study, which shares the same population with the present study. These lines of evidence have contributed to a better understanding of VSA. However, to apply such prognostic findings to clinical practice, the accumulation of various prognostic factors in individual patients should be taken into consideration. In addition, it is conceivable that potential interactions among those prognostic factors exist, making it difficult to assess individual prognosis. Thus, the comprehensive assessment tool that provides the valid risk prediction in individual patients needs to be developed. As a useful tool for clinical risk prediction, simple scoring systems have been devised for several disorders (15). The well-established scoring systems include the TIMI (Thrombolysis In Myocardial Infarction) risk score and the CADILLAC (Controlled Abciximab and Device Intervention to Lower Late Angioplasty Complications) risk score (25,26), in which the weighted clinical variables selected from multivariable logistic regression model provide an estimation of 30-day and 1-year mortality of patients with myocardial infarction. The present study demonstrates that the JCSA risk score provides the useful risk assessment for VSA patients.

The JCSA risk score for VSA patients. Although VSA patients are often thought to have relatively favorable outcomes, their clinical risk varies considerably depending on patient characteristics and treatments. The accurate risk stratification for future adverse events may contribute to an appropriate patient management, which could be provided by the JCSA risk scoring system. In the present study, the risk score had a good correlation with patient outcome (Fig. 1). The 3 risk strata defined in accordance with the scoring points found that there were 2- to 3-fold relative increases in risk for MACE for each rise in the stratum. In addition, the 3 risk strata provided the prognostic stratification, even for various clinical subgroups (Fig. 4), suggesting the wide applicability of the scoring system.

The JCSA scoring system consisted of 7 predictive factors for MACE identified by the multivariable Cox model (Table 3). The clinical significance of these predictors for VSA patients has been consistently shown in the previous studies (6–10,12,27), suggesting its adequacy. Interestingly, rather than indicating the importance of common cardiovascular risks or structural abnormalities, the scoring system emphasizes the significance of characteristic clinical findings reflecting or affecting disease activity of VSA. This is especially the case with angina at rest alone and ST-segment elevation during an attack that may represent the occurrence of serious occlusive spasm, and thereby may be one of the indicators that reflect the severity of this disorder. Meanwhile, the use of beta-blockers could be an avoidable risk (28–30). The beta-blockers are thought to have an aggravating effect on VSA due to inhibition of beta-adrenergic receptor-mediated coronary vasodilatation, unmasking alpha-adrenoceptor-mediated coronary vasoconstriction, and increasing vascular permeability to calcium (31). Although beta-blockers could be considered when combined with structural disorder or other conditions, its tolerability may need to be measured by reference to the present risk score.

When applying the JCSA risk score to clinical practice, it may be a major concern whether the scoring system sufficiently predicts the outcomes of VSA patients. Because the comparable external dataset were not available in the present study, we alternatively validated the scoring system in the internal training and validation sets as the second best policy. The average prediction rate of the scoring system in the validation set was approximately 90%. Although the rigorous validation should be performed in the independent datasets, the present scoring system appears to have an acceptable reliability for clinical use.

It should be noted that the JCSA risk score was derived from the study population in whom adequate medical treatments were provided. As first-line therapy for VSA

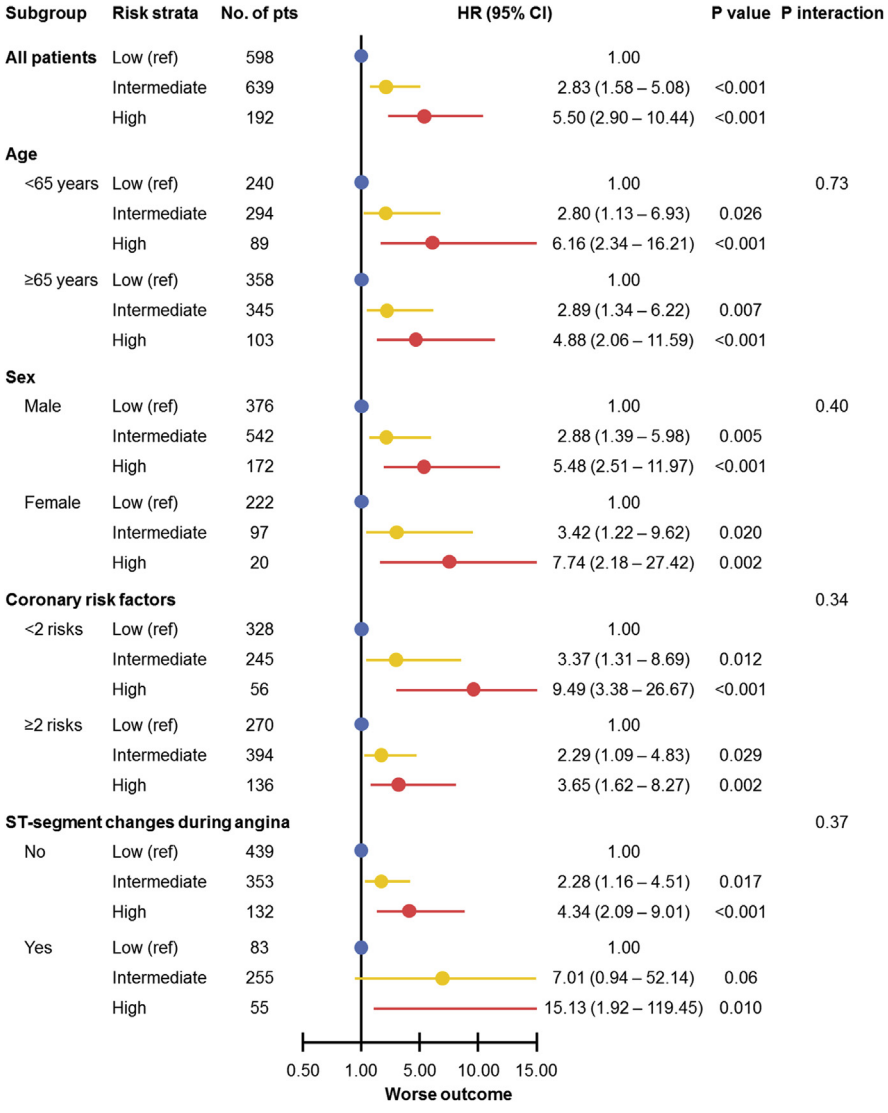

Figure 4 **Hazard Ratios for MACE Between the 3 Risk Strata According to Clinical Subgroups**

Coronary risk factor includes hypertension, dyslipidemia, diabetes mellitus, and smoking. Organic coronary stenosis includes nonsignificant and significant stenosis. ACEI = angiotensin-converting enzyme inhibitor; ARB = angiotensin receptor blocker; CI = confidence interval; pts = patients; ref = reference; other abbreviations as in Figure 1. *Continued on the next page.*

(2,16,32), calcium channel blockers were used in more than 90% of the patients (Table 1). Also, about one-half of the patients were additionally treated with long-acting nitrates and antiplatelets For this reason, the present risk score should be applied on the premise that the patients receive standard treatment for this disorder.

Clinical implications. The JCSA risk scoring system assembled multiple prognostic factors and estimates future adverse cardiac events in individual VSA patients. The clinical information required for the present scoring system may be readily available from routine practice, which helps clinicians predict patient outcomes easily. The information on prognostic stratification may lead to personalized management, including the judgment of necessity for intensive medical treatment and close follow-up. In addition, because the outcomes of VSA patients could be aggravated by a rebound phenomenon after careless discontinuation of medications (13,33,34), it is of clinical significance that the adherence in high-risk patients could be enhanced through the awareness raised by the risk score.

Study limitations. First, the present study was conducted as an observational study and consisted of retrospective and prospective designs. Because the retrospective population accounted for the majority of study patients, the cause-result relationship was not established. Furthermore, the follow-up periods varied in individual patients and management

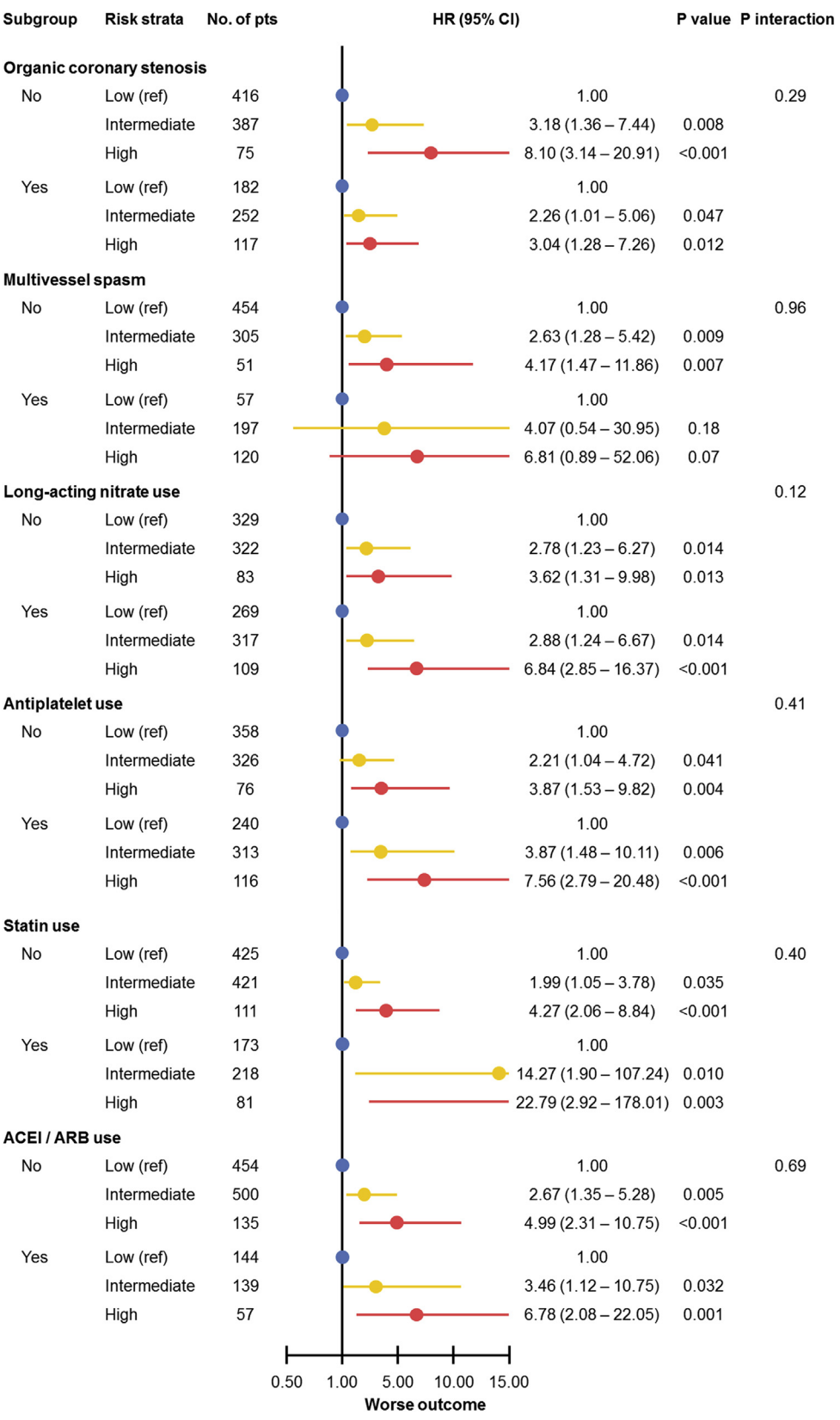

Figure 4 Continued

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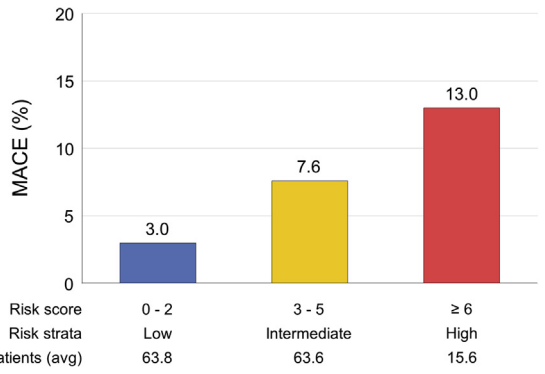

Figure 5 **Average Incidence of MACE Between the 3 Risk Strata in the Validation Set**

The incidence of MACE was calculated in each random partition of the validation process, and the average incidence was derived through the 1,000 times iteration. Avg = average; other abbreviations as in Figure 1.

decisions were left to the discretion of each attending physician. Second, the composite primary endpoint was used. Third, the means for capturing ST-segment changes or arrhythmias during angina attacks were not standardized. Because coronary spasm develops transiently and the frequency of attack markedly varies in individual patients, it is conceivable that the prevalence of these ECG findings was underestimated. Fourth, the prognostic impact of patient adherence to medications during the follow-up period was not evaluated. Fifth, the scoring system consisted of only clinical variables that were available in the present registry data. Thus, some important predictors may possibly be missed. Sixth, the scoring system was not validated in the independent external datasets; its usefulness should be examined in future studies. Seventh, the prediction of all-cause mortality is not sufficient. The present scoring system did not show the predictive capacity of this endpoint. However, despite these limitations, the present JCSA risk score should merit emphasis for better understanding and management of VSA patients.

Conclusions

The present multicenter study by the Japanese Coronary Spasm Association developed the novel clinical risk prediction score for VSA patients. The JCSA risk score, in which established prognostic factors are integrated provides the comprehensive risk assessment and prognostic stratification for VSA patients.

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Key Words: angina ■ arrhythmia ■ coronary vasospasm ■ ischemia ■ prognosis.

APPENDIX

For a listing of the members of the Japanese Coronary Spasm Association, and supplemental tables, please see the online version of the article.