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ORIGINAL ARTICLE
Acute Coronary Syndrome

Prognostic Impact of Peak Aortic Jet Velocity on Patients With Acute Myocardial Infarction

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Background: Aortic valve stenosis (AS) leads to increased cardiovascular mortality and morbidity, and recent studies reported that even mild-to-moderate AS was associated with poor prognosis in the general population. This study investigated the prognostic impact of mild or moderate AS, defined as 2.0 m/s ≤ peak aortic jet velocity (Vmax) ≤3.9 m/s using echocardiography in acute myocardial infarction (AMI) patients.

Methods and Results: This study enrolled 3,049 AMI patients using data from the Mie ACS registry. Patients were divided into 2 groups according to Vmax: Group 1: Vmax <2.0 m/s and/or visually intact aortic valve in which all 3 leaflets are fully and evenly open; Group 2: 2.0 m/s ≤ Vmax ≤ 3.9 m/s. There were 2,976 patients in Group 1and 73 patients in Group 2. The Group 2 patients were older, had a higher percentage of males and had lower body mass index and Killip ≥2 than the Group 1 patients. Angiographic data, door-to-balloon time, and mechanical support were not different between the 2 groups. The Group 2 patients demonstrated a significantly higher all-cause mortality rate (P<0.01) and composite of cardiovascular death and heart failure hospitalization (P<0.01), and Kaplan-Meier analysis showed the same tendency in propensity score-matched patients.

Conclusions: The present study revealed that mild or moderate AS based on Vmax is associated with poor prognosis following AMI.

Key Words: Acute myocardial infarction; Aortic valve stenosis; Prognosis

Acute myocardial infarction (AMI) represents one of the main causes of death worldwide.[1] A large number of risk assessment instruments have been developed to quantify the risk of mortality and morbidity among patients with AMI.[2] In contrast, aortic valve stenosis (AS) is the most common valvular heart disease in the elderly population,[3,4] and shares pathophysiological mechanisms and risk factors with coronary artery disease (CAD).[5] Although severe AS is a serious and potentially life-threatening condition, there is growing evidence that mild-to-moderate forms of AS are not as benign as commonly assumed both in patients with and without concurrent systolic dysfunction.[6–8] However, the prognostic impact of mild or moderate AS on AMI remains unknown. The assessment of AS severity usually relies on 3 key measurements, including peak aortic jet velocity (Vmax), mean pressure gradient, and aortic valve area. Vmax is a simple and reproducible parameter among them, and we hypothesized that this parameter can be used for risk identification in patients with AMI. This study investigated the prognostic impact of mild or moderate AS on AMI patients assessed by echocardiography-derived Vmax using data from the Mie ACS Registry.

Methods

Study Population

The Mie ACS Registry is a prospective, ongoing, multicenter

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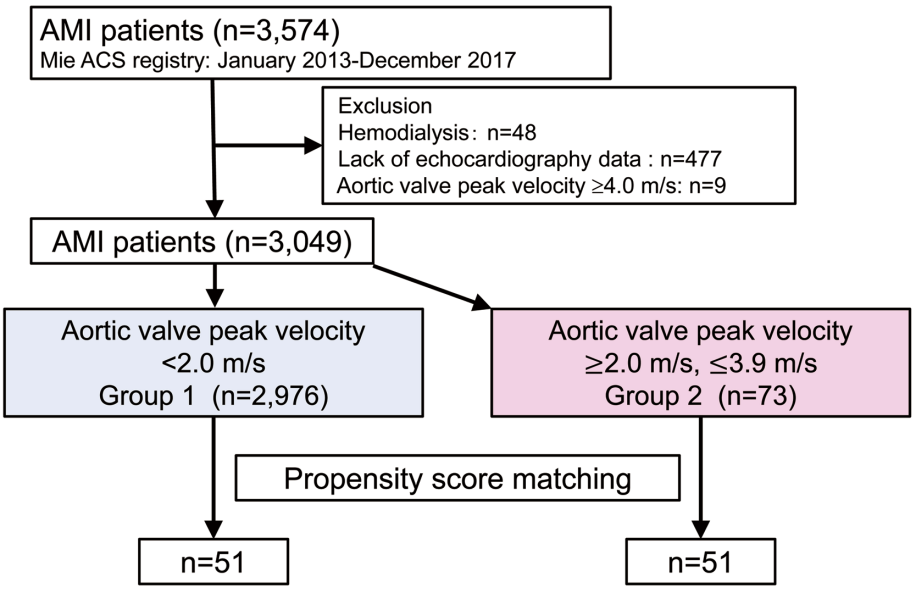

Figure 1. Flow chart of patient enrollment. ACS, acute coronary syndrome; AMI, acute myocardial infarction.

registry in Mie Prefecture in Japan.[9,10] All 15 participating centers registered ACS patients based on the research protocol. We consecutively evaluated 3,574 patients with AMI between January 2013 and December 2017 using data from the Mie ACS Registry. The exclusion criteria included: patients who were receiving hemodialysis (n=48), patients with a lack of sufficient echocardiography data (n=477), and patients with Vmax ≥4.0 m/s (n=9). A total of 3,049 AMI patients were included (**Figure 1**).

This registry study conformed to the principles of the Declaration of Helsinki and was approved by the Institutional Review Board of Mie University Graduate School of Medicine and each participating hospital's ethics committee (Reference number 2881). All patients gave their "opt-out" informed consent. This study was also registered in a clinical trial registry (URL: https://www.umin.ac.jp/ctr/index-j.htm, Unique identifier: UMIN 000036020).[9,10]

Definitions of Aortic Stenosis and AMI

All patients were classified into 2 groups according to Vmax assessed by Doppler echocardiography, which was performed during hospitalization: Group 1: Vmax <2.0 m/s and/or visually intact aortic valve in which all 3 leaflets were fully and evenly open; and Group 2: 2.0 m/s ≤ Vmax ≤ 3.9 m/s, which corresponds to mild or moderate aortic stenosis according to the current American College of Cardiology/American Heart Association (ACC/AHA) guidelines for Management of Patients with Valvular Heart Disease (**Figure 1**).[11] The diagnosis of AMI was based on the third universal definition of MI.[12] As a general rule, echocardiography was performed within a week after the onset of the index myocardial infarction and after percutaneous coronary intervention (PCI) or coronary artery bypass graft (CABG).[13]

Follow up and Outcomes

Outcome data were collected via patient interviews at the outpatient clinic, hospital chart reviews, or telephone interviews with the patient or close relatives, and clinical events were recorded in a Internet-based system. Patients who were lost to follow up were still included but that data from their last contact had to be used. The primary outcome was defined as 2-year all-cause mortality. Cardiovascular (CV) death was defined using the classification by the Academic Research Consortium as death from fatal MI, heart failure (HF), fatal arrhythmia, or sudden unexpected death occurring without another explanation. When a patient experienced the events several times, the first event was used for analysis.

Statistical Analyses

Continuous variables with normal distributions were expressed as the mean±standard deviation, and those without normal distributions were expressed as median and interquartile range. Categorical variables were expressed as a number and percentage. To assess differences between the 2 subgroups, a Student's t-test was performed for continuous variables. A Mann-Whitney U-test and Pearson's chi-squared test for non-normally distributed data and categorical data, respectively, were also performed. All-cause death and the composite events of HF admission and CV death were displayed using Kaplan-Meier survival curves and were compared using the log-rank test. In addition, survival curves for the time-to-event variables were constructed for patients who survived the first 730 days after hospital admission (landmark analysis) using Kaplan-Meier estimates. A Cox regression model was used to investigate the independent predictors of all-cause mortality. The propensity score was estimated using a multivariable logistic regression model that included the following variables: age, sex, body mass index, hypertension, diabetes mellitus, dyslipidemia, current smoker, Killip classification, hemoglobin, creatinine, triglyceride, high density lipoprotein (HDL) cholesterol, and low density

Table 1. Characteristics of Acute MI Patients

	All patients (n=3,049)	Group 1 (n=2,976)	Group 2 (n=73)	P value
Age, years	68.5 [60.0–77.0]	68.0 [59.0–76.0]	82.0 [73.5–85.0]	<0.01
Male	77.3	78.1	42.5	<0.01
Body mass index, kg/m^2	23.3 [21.1–25.5]	23.3 [21.2–25.5]	22.4 [20.8–24.5]	<0.01
Hypertension	63.2	62.8	76.7	0.02
Diabetes mellites	31.8	31.7	35.6	0.48
Dyslipidemia	47.9	46.7	49.3	0.80
Hyperuricemia	6.0	6.1	2.7	0.32
Current smoking	30.4	30.8	15.1	<0.01
Family history of CAD	5.2	5.1	11.0	0.05
Prior MI	8.5	8.4	13.7	0.11
Previous PCI	9.0	8.9	11.0	0.55
Previous CABG	0.8	0.7	2.7	0.10
Previous stroke	5.2	5.2	8.2	0.28
Previous HF hospitalization	1.6	1.6	4.1	0.12
Peripheral artery disease	1.2	1.1	4.1	0.05
STEMI	78.1	78.3	67.6	0.03
Killip class 1	76.9	77.2	64.4	0.01
Pre-hospital CPA	4.4	4.5	2.7	0.77
Laboratory data				
White blood cells, /μL	9,400 [7,488–11,900]	9,400 [7,500–11,900]	8,800 [6,600–10,450]	<0.01
Hemoglobin, g/dL	14.3 [13.0–15.6]	14.4 [13.1–15.6]	12.4 [11.1–14.2]	<0.01
Total cholesterol, mg/dL	193 [167–223]	193 [167–223]	190 [169–227]	0.14
Triglyceride, mg/dL	105 [72–164]	106 [73–166]	85 [55–112]	<0.01
HDL-C, mg/dL	48 [40–57]	48 [40–56]	57 [41–65]	<0.01
LDL-C, mg/dL	120 [97–146]	120 [97–146]	113 [83–140]	<0.01
Creatinine, mg/dL	0.83 [0.70–1.01]	0.83 [0.71–1.01]	0.93 [0.62–1.27]	0.75
Glucose, mg/dL	153 [127–198]	153 [127–197]	151 [125–219]	0.31
HbA1c, %	5.9 [5.6–6.6]	5.9 [5.6–6.6]	6.0 [5.7–6.4]	0.59
Uremic acid, mg/dL	5.7 [4.7–6.7]	5.7 [4.7–6.7]	5.4 [4.2–6.8]	0.47
Peak CK, IU/L	1,598 [607–3,259]	1,579 [597–3,254]	1,995 [785–3,887]	0.40
Echocardiography				
Atrial fibrillation, % (n)	2.4 (73)	2.4 (72)	1.4 (1)	0.73
IVST, mm	9.7 [9.0–10.8]	9.7 [9.0–10.8]	10.3 [9.3–11.0]	<0.01
LV PWT, mm	9.7 [9.0–10.4]	9.5 [9.0–10.3]	10.3 [9.2–11.0]	<0.01
LV end-diastolic dimension, mm	49.0 [45.4–53.0]	49.0 [45.5–53.0]	47.3 [45.0–51.0]	0.04
LV end-systolic dimension, mm	33.7 [29.2–38.1]	33.7 [29.2–38.2]	32.0 [28.8–34.8]	0.06
LV ejection fraction	55.8±12.3	55.8±12.3	57.3±12.7	0.33

Data are expressed as median [interquartile range] or percentage, unless otherwise stated. CABG, coronary artery bypass grafting; CAD, coronary artery disease; CK, creatine kinase; CPA, cardiopulmonary arrest; HbA1c, hemoglobin A1c; HDL-C, high-density lipoprotein cholesterol; HF, heart failure; IVST, interventricular septum thickness; LDL-C, low-density lipoprotein cholesterol; LV, left ventricular; MI, myocardial infarction; PCI, percutaneous coronary intervention; PWT, posterior wall thickness; STEMI, ST elevation myocardial infarction.

lipoprotein (LDL) cholesterol concentration to match the cases (**Figure 1**). Significance was defined as P<0.05. Statistical analyses were performed using SPSS version 27.0 (IBM Corp., Armonk, NY, USA).

Results

Baseline Characteristics of the Study Population

Baseline patient characteristics are summarized in **Table 1**. Among all 3,049 patients, the median age was 68.5 years, 77.3% were male, and the median body mass index was 23.3 kg/m^2. The prevalence of CV risk factors including hypertension, diabetes mellitus, dyslipidemia, and current smoking was 63.2%, 31.8%, 47.9%, and 30.4%, respectively. A history of prior myocardial infarction was present in 8.5% of patients. Furthermore, 78.1% of the patients developed ST-elevation myocardial infarction (STEMI), and 76.9% of the patients were classified as having Killip class 1 MI. Echocardiography was performed at a median of 2 days [IQR 1–6 days]. There were 2,976 patients (97.6%) in Group 1 and 73 patients (2.4%) in Group 2. The mean value of Vmax in Group 2 was 2.8±0.6 m/s, 50 patients had mildly increased Vmax between 2.0 m/s and 2.9 m/s, and 23 patients had moderately increased Vmax between 3.0 m/s and 3.9 m/s. The Group 1 patients were significantly younger (68.5 vs. 79.9 years, P<0.01) and had a higher prevalence of males and a higher BMI. In addition, Group 1 had a higher prevalence of a history of

Table 2. Post-PSM Characteristics of Acute MI Patients

	All patients (n=102)	Group 1 (n=51)	Group 2 (n=51)	P value
Age, years	81.0 [73.0–85.0]	80.0 [73.0–85.0]	81.5 [73.3–84.8]	0.51
Male	50.0	51.0	49.0	0.84
Body mass index, kg/m^2	22.9 [20.8–24.7]	22.9 [20.5–25.2]	22.8 [20.9–24.5]	0.75
Hypertension	83.3	88.2	78.4	0.18
Diabetes mellitus	43.1	52.9	33.3	0.07
Dyslipidemia	51.0	49.0	52.9	0.69
Hyperuricemia	2.9	3.9	2.0	1.00
Current smoking	20.6	21.6	19.6	0.81
Family history of CAD	7.8	3.9	11.8	0.27
Prior MI	11.8	7.8	15.7	0.22
Previous PCI	12.7	11.8	13.7	0.77
Previous CABG	2.9	2.0	3.9	1.00
Previous stroke	12.7	15.7	9.8	0.37
Previous HF hospitalization	2.0	0.0	3.9	0.50
Peripheral artery disease	2.9	0.0	5.9	0.24
STEMI, %	69.0	70.6	67.3	0.73
Killip class 1, %	60.8	62.7	58.8	0.69
Pre-hospital CPA, %	3.9	3.9	3.9	1.00
Laboratory data				
White blood cells, /μL	8,800 [6,600–11,000]	8,800 [6,100–11,300]	8,850 [6,600–10,475]	0.93
Hemoglobin, g/dL	12.4 [11.2–13.7]	12.3 [10.9–13.4]	12.4 [11.2–14.2]	0.56
Total cholesterol, mg/dL	190 [172–217]	155 [130–205]	150 [123–209]	0.92
Triglyceride, mg/dL	87 [51–123]	90 [46–127]	84 [55–112]	0.51
HDL-C, mg/dL	55 [40–65]	53 [39–68]	57 [40–64]	0.59
LDL-C, mg/dL	118 [104–140]	119 [105–140]	114 [86–141]	0.42
Creatinine, mg/dL	0.79 [0.64–1.18]	0.79 [0.64–0.98]	0.90 [0.62–1.24]	0.90
Glucose, mg/dL	152 [128–205]	155 [130–205]	150 [123–209]	0.33
HbA1c	6.0 [5.7–6.9]	6.1 [5.8–7.5]	6.0 [5.6–6.3]	0.13
Uremic acid, mg/dL	5.3 [4.1–6.2]	5.1 [4.0–6.0]	5.4 [4.1–6.5]	0.49
Peak CK, IU/L	1,815 [778–3,967]	1,618 [567–4,201]	2,063 [781–3,927]	0.85
Echocardiography				
Atrial fibrillation, % (n)	0 (0)	0 (0)	0 (0)	
IVST, mm	10.0 [8.8–9.0]	9.1 [8.1–10.0]	10.5 [9.5–11.0]	<0.01
LV PWT, mm	10.0 [9.0–10.6]	9.1 [8.5–10.1]	10.4 [9.8–11.3]	<0.01
LV end-diastolic dimension, mm	48.4 [44.6–52.0]	49.4 [42.8–53.3]	47.7 [45.0–51.0]	0.52
LV end-systolic dimension, mm	33.0 [29.0–38.0]	34.2 [29.3–40.0]	32.5 [28.6–35.1]	0.17
LV ejection fraction, %	54.4±12.6	52.4±12.3	56.3±12.6	0.13

Data are expressed as median [interquartile range] or percentage, unless otherwise stated. PSM, propensity score-matched. Other abbreviations as in Table 1.

hypertension, STEMI, and Killip classification 1. In contrast, current smokers were less frequent in Group 1 than in Group 2. There were no differences in the rate of pre-hospital cardiopulmonary arrest between both groups. White blood count, hemoglobin concentration level, and lipid profile were significantly different between the groups; however, there was a significant difference in peak creatine kinase. Atrial fibrillation (AF) was observed in 2.4% of the total patients at the time of echocardiography, and there were no statistical differences in its prevalence between the 2 groups. The Group 2 patients had significantly thicker interventricular septum thickness (IVST) and posterior wall thickness (PWT), and greater left ventricular (LV) end-diastolic dimension than Group 1 patients. However, there were no differences in LV end-systolic dimension and LV ejection fraction between the 2 groups. After propensity score matching with a 1:1 matching algorithm, 51 patients from each group were well matched, and there were no differences in the baseline characteristics between both groups except for IVST and PWT (**Table 2**).

Angiographic Data and the Treatment Strategy of AMI

Among all 3,049 patients, no significant differences were found in angiographic data or PCI procedures between the 2 groups (**Table 3**). The percentage of primary PCI, the percentage of patients with a door-to-balloon time within 90 min who underwent PCI <6 h, and mechanical support were not significantly different between the 2 groups. Medication at hospital discharge was similar between the 2 groups. **Table 4** shows that there were no significant differences in angiographic data or PCI procedures between both groups after propensity score matching.

Table 3. Angiographic Data and the Treatment Strategy of Acute MI

	All patients (n=3,049)	Group 1 (n=2,976)	Group 2 (n=73)	P value
Angiographic data				
LMT culprit	2.0	2.0	2.8	0.66
LAD culprit	45.6	45.7	40.3	0.36
LCX culprit	14.8	14.9	12.5	0.58
RCA culprit	35.9	35.8	41.7	0.31
Urgent PCI	86.8	80.8	86.7	0.14
DTB <90 min	60.1	60.3	49.1	0.09
Urgent CABG	3.5	3.4	5.6	0.05
IABP usage	13.9	13.8	17.8	0.33
VA-ECMO usage	2.1	2.0	2.7	0.66
Respiratory support usage	12.0	11.9	16.7	0.22
Medication at hospital discharge				
ACE-I or ARB	80.6	80.5	84.9	0.35
β-blocker	43.9	44.1	37.0	0.23
Calcium channel blocker	16.0	15.9	19.2	0.45
Statin	83.3	83.3	82.2	0.80
Ezetimibe	3.6	3.7	0.0	0.11
EPA/DHA	4.8	4.8	2.7	0.58
Insulin	6.7	6.7	6.8	0.82
Oral antidiabetic	20.0	20.0	21.9	0.68
Antiplatelet agent	97.7	97.7	95.9	0.23
Oral anticoagulation	11.5	11.6	11.0	0.87

Data are presented as percentages. ACE-I, angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blocker; CABG, coronary artery bypass grafting; ECMO, extracorporeal membrane oxygenation; DTB, door-to-balloon time; EPA/DHA, eicosapentaenoic acid/docosahexaenoic acid; IABP, intra-aortic balloon pumping; LAD, left anterior descending artery; LCX, left circumflex artery; LMT, left main trunk; MI, myocardial infarction; PCI, percutaneous coronary intervention; RCA, right coronary artery.

Table 4. Post-PSM Angiographic Data and the Treatment Strategy of Acute MI

	All patients (n=102)	Group 1 (n=51)	Group 2 (n=51)	P value
Angiographic data				
LMT culprit	3.0	2.0	4.0	0.62
LAD culprit	46.5	49.0	44.0	0.61
LCX culprit	12.9	9.8	16.0	0.35
RCA culprit	36.6	39.2	34.0	0.59
Urgent PCI	96.1	51.0	49.0	0.62
DTB <90 min	47.3	45.7	48.9	0.76
Urgent CABG	5.0	6.0	3.9	0.68
IABP usage	19.0	19.6	19.6	1.00
ECMO usage	2.0	2.0	2.0	1.00
Respiratory support usage	16.8	11.8	22.0	0.17
Medication at hospital discharge				
ACE-I or ARB	84.3	78.4	90.2	0.10
β-blocker	37.3	47.4	52.6	0.68
Calcium channel blocker	25.5	31.4	19.6	0.17
Statin	88.2	88.2	88.2	1.00
Ezetimibe	2.9	5.9	0.0	0.24
EPA/DHA	2.0	2.0	2.0	1.00
Insulin	9.8	9.8	9.8	1.00
Oral antidiabetic	28.4	35.3	21.6	0.12
Antiplatelet agent	99.0	100.0	98.0	1.00
Oral anticoagulation	15.7	17.6	13.7	0.59

Data are presented as percentages. PSM, propensity score-matched. Other abbreviations as in Table 3.

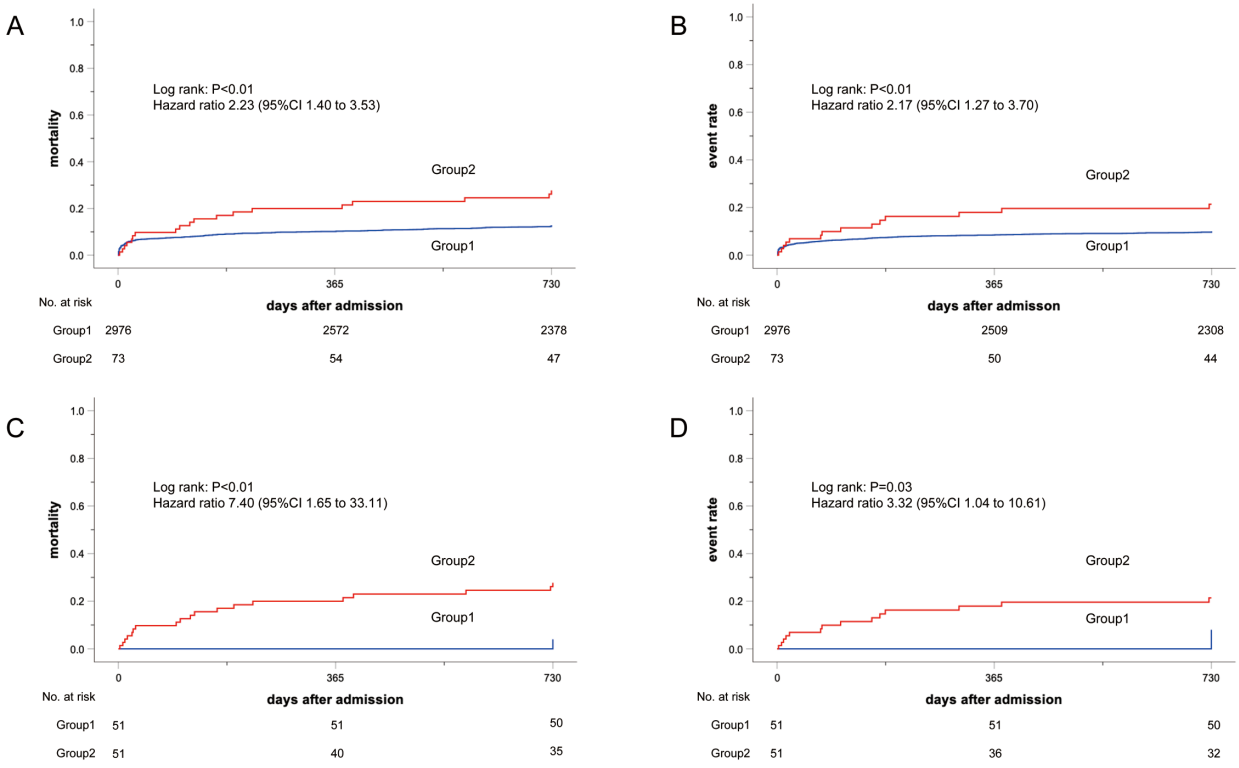

Figure 2. Kaplan-Meier curves for the cumulative incidence of 2-year all-cause death (**A**), the event of CV death, and HF admission (**B**) in patients from Group 1 and Group 2. Kaplan-Meier survival curve for the propensity score-matched patients for the cumulative incidence of 2-year all-cause death (**C**) and the event of CV death and HF admission (**D**) in patients in Group 1 and Group 2. CV, cardiovascular; HF, heart failure.

Patient Outcomes

During the follow-up periods, 390 (12.8%) patients experienced all-cause death. The Kaplan-Meier curves for all-cause mortality, and CV death and hospitalization for HF stratified by Vmax for Groups 1 and 2 are shown in **Figure 2A** and **B**, respectively. The Group 2 patients had a higher 2-year all-cause death rate (12.5% vs. 26.0%, P<0.01, Hazard ratio 2.23 [95% CI 1.40–3.53]) and CV death and hospitalization for HF rate (9.5% vs. 19.2%, P<0.01, Hazard ratio 2.17 [95% CI 1.27–3.70]) than Group 1 patients. After propensity score matching, there was a significant difference in 2-year all-cause death rate (3.9% vs. 23.5%, P<0.01, Hazard ratio 7.40 [95% CI 1.65–33.1]) and CV death and hospitalization for HF rate (7.8% vs. 19.6%, P=0.03, Hazard ratio 3.32 [95% CI 1.04–10.61]) between the groups (**Figure 2C** and **D**). Group 2 patients were divided into 2 subgroups according to the Vmax: Group 2A: 2.0 m/s ≤ Vmax ≤ 2.9 m/s (n=50) and Group 2B: 3.0 m/s ≤ Vmax ≤ 3.9 m/s (n=23). There were 10 deaths in Group 2A and 9 deaths in Group 2B during the 2-year follow up, and 8 events in Group 2A and 6 events in Group 2B for CV death or HF hospitalization. The Kaplan-Meier curves for all-cause mortality, and CV death and hospitalization for HF stratified by Vmax for Groups 1, 2A and 2B are shown in **Supplementary Figure A** and **B**, respectively. There were no significant differences in the 2-year all-cause death rate (12.5% vs. 20.0%, P=0.11, Hazard ratio 1.67 [95% CI 0.89–3.13]) and CV death and hospitalization for HF rate (9.5% vs. 16.0%, P=0.11, Hazard ratio 1.76 [95% CI 0.87–3.56]) between Group 1 and Group 2A. In contrast, Group 2B had a higher 2-year all-cause death rate (12.5% vs. 39.1%, P<0.01, Hazard ratio 3.53 [95% CI 1.82–6.83]) and CV death and hospitalization for HF rate (9.5% vs. 26.1%, P<0.01, Hazard ratio 3.12 [95% CI 1.39–7.00]) than Group 1. There were no significant differences in the 2-year all-cause death rate (20.0% vs. 39.1%, P=0.10, Hazard ratio 0.47 [95% CI 0.19–1.17]) and CV death and hospitalization for HF rate (16.0% vs. 26.1%, P=0.29, Hazard ratio 0.56 [95% CI 0.20–1.63]) between Group 2A and Group 2B.

Discussion

The present study found that AMI patients having mild or moderate AS stratified by Vmax had a poorer 2-year prognosis, including all-cause mortality and composite of CV death and hospitalization for HF, than those without AS, even after propensity matching analysis using data from the Mie ACS registry.

The prevalence of AS in an aging population increases rapidly for those aged >65 years, particularly women. A Japanese multicenter registry revealed that patients with severe AS included a much higher proportion of women than men, with the sex ratio of females to males increasing with age.[14] In the present study, AMI patients with mild or moderate AS were older, had a higher prevalence of females, and had a lower median body mass index com-

pared with those without AS. In addition, there was a strong association between conventional coronary risk factors and the development of AS. Hypertension has been identified as the highest population-attributable risk factor,[15] and the present study also found that AMI patients with mild or moderate AS had a higher prevalence of hypertension than those patients without AS.

There is growing evidence that mild-to-moderate AS is not as benign as commonly assumed, both in patients with and without concurrent systolic dysfunction.[6–8] Strange et al reported that moderate AS (mean gradient 20.0–39.0 mmHg or peak systolic flow velocity 3.0–3.9 m/s) is associated with reduced 5-year survival after adjusting for age, sex, and other potential confounders, including concurrent left heart disease or LV dysfunction, using the National Echocardiographic Database of Australia, with a large and unselected patient group.[16] The present study also found a poorer composite of CV death and hospitalization for HF for AMI patients with a Vmax between 2.0 m/s and 3.9 m/s than those without AS even after propensity matching analysis using the ACS registry, whereas the severity of AS was assessed based on a single parameter (Vmax). The majority of patients underwent primary PCI or CABG, and the 2-year prognosis of non-AS patients was satisfactory. Nevertheless, patients with mild or moderate AS had a poorer 2-year prognosis after suffering an AMI. Although patients with AS had different clinical characteristics from non-AS patients, the findings of the Kaplan-Meier curves showed the same tendency in propensity score-matched patients. A recent meta-analysis reported that aortic valve sclerosis, calcification, and thickening of the aortic valve in the absence of obstruction with Vmax <2.0 m/s, were identified as the highest risk factors for CAD, stroke, and CV mortality.[17] It is worth noting that some patients have a risk for the rapid progress of AS and might require aortic valve replacement (AVR).[18] In the present study, no patients underwent surgical or transcatheter AVR during a limited 2-year follow-up period. Based on these results, the presence of mild-to-moderate AS is a good candidate for a surrogate marker of poor clinical outcomes rather than the therapeutic target. In other words, the results obtained from the present study are not supportive data for a recommendation of concomitant AVR for AMI patients undergoing emergent CABG even if they had mild or moderate AS. A study using registry data about STEMI obtained between February 2004 and May 2013 in the Netherlands showed similar results to the present study regarding the prevalence and prognostic impact of AS in a total of 2,041 patients.[19] In their study, the prevalence of AS, defined as an aortic valve area $\leq 2.0\,cm^2$, was 2.7% in the total population and it increased with age after excluding patients with prior myocardial infarction, prior AVR, or incomplete echocardiographic data to determine the severity of AS. They also showed that patients with AS had a significantly higher death rate than those with aortic valve sclerosis and a normal aortic valve, and that AS was independently associated with all-cause mortality. As there were no significant differences in the 2-year all-cause death rate and a composite of CV death and hospitalization for HF rate between non-AS and mild AS patients in the present study, which involved low numbers of AS patients, the prognostic impact of mild AS with $2.0\,m/s \leq Vmax \leq 2.9\,m/s$ among AMI patients warrants further investigation with a larger study population.

In the present study, the severity of AS was assessed based on Vmax among 3 key measurements, including mean pressure gradient and aortic valve area calculated using the continuity equation. The discordance among these parameters may be observed in some clinical settings; these include measurement errors, small body size, and reduced LV function or low cardiac output. For example, Vmax may underestimate the severity of AS in patients with reduced LV function or low cardiac output; therefore, there is a possibility that there were some patients in Group 2 with true severe AS despite their Vmax being <4.0 m/s. Nevertheless, Vmax is a simple and reproducible parameter, and the present study successfully showed that this parameter can be used for risk identification in patients with AMI.

Study Limitations

The present study had some limitations. First, this was an observational study with potential for biases and unmeasured confounders. Furthermore, there was a lack of information on the transition of medical therapies after discharge.[20] Second, the timing of comprehensive echocardiography was decided by each attending physician based on a comprehensive consideration of the patient's condition during hospitalization. Third, calcium scoring of the aortic valve and/or coronary artery using cardiac computed tomography was not performed, which can help predict the risk of a future CV event.[21–24] Fourth, although the prevalence of AF was low, echocardiography has its challenges and limitations in assessing the severity of AS and LV function in the presence of AF because of the variability in cycle length. Fifth, there was no information regarding the progression of AS during the follow-up period after hospital discharge. Finally, the sample size was relatively small, and the follow-up duration was relatively short; thus, the evaluation of long-term outcomes and prognostic factors was difficult.[25]

Clinical Implication

The present study revealed that the presence of AS, even in its mild-to-moderate forms, had a prognostic impact on AMI patients. Vmax, an easy and reproducible parameter for the assessment of AS, may be routinely used for risk stratification in AMI patients.

Conclusions

Mild or moderate AS, assessed by echocardiography-derived Vmax, was associated with poor prognosis in patients with AMI.

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IRB Information

This study was approved by the Mie University Hospital Institutional Review Board (Reference number 2881).

Data Availability

(1) Individual de-identified participant data (including data dictionaries) will be shared.
(2) Microsoft Excel data used for analysis will be shared. The data of each table and figure will be shared upon request. The study protocol will also be shared.
(3) Data will be available during the review process and 1 year after acceptance.
(4) Data will be available to reviewers and anyone else who is interested in this article after acceptance if they contact the corresponding author.
(5) The data will be shared as Microsoft Excel or CSV files via E-mail.

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Supplementary Files

Please find supplementary file(s);
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