Comparison of Two-Year Outcomes of Acute Myocardial Infarction Caused by Coronary Artery Spasm Versus that Caused by Coronary Atherosclerosis

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The study compared the 2-year outcomes of patients diagnosed with acute myocardial infarction (AMI) triggered by coronary artery atherosclerosis and AMI caused by coronary artery spasm. A total of 36,797 patients in the Korea AMI Registry were grouped into 2 categories—(1) AMI due to coronary artery spasm without stenotic lesion (CAS-AMI, n = 484); and (2) AMI induced by coronary artery atherosclerosis (CAA-AMI, n = 36,313). The major clinical outcomes of the 2 groups were compared over a 2-year clinical follow-up period. Major adverse cardiac events (MACE) were defined as the composite of total death, nonfatal myocardial infarction, and repeat revascularization. The incidence of MACE (7.1% vs 11.1%; p = 0.007) and repeat revascularization (0.4% vs 4.2%; p <0.001) in the CAS-AMI group were significantly lower than in the CAA-AMI group at 2 years. However, the incidence of total death and nonfatal myocardial infarction was similar in both the groups. Aborted cardiac arrest was strongly associated with 2-year mortality in the CAS-AMI group (hazard ratios 13.5, 95% confidence interval 5.34 to 34.15, p <0.001) The incidence of MACE in CAS-AMI patients was significantly lower than in the CAA-AMI group of patients up to 2 years due to the relatively lower rate of repeat revascularization in CAS-AMI patients. However, the incidence of total death or nonfatal myocardial infarction in CAS-AMI patients was not different from that of patients with CAA-AMI. **(Am J Cardiol 2019;124:1493−1500)**

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Coronary artery spasm (CAS) is known to trigger acute myocardial infarction (AMI).[1−3] In patients with vasospastic angina, AMI occurs not only in those diagnosed with atherosclerotic coronary artery disease, but also in those without coronary stenosis.[4] A previous study[5] reported aggravated vasospastic angina as a risk factor for myocardial infarction and cardiac death. However, persistent vasospastic activity is closely associated with progressive atherosclerosis in 49,345 patients with vasospastic angina.[6,7] However, in non-Asian patients, acute coronary syndrome triggered by CAS is associated with a favorable prognosis for cardiac events after a 3-year follow-up.[8] Relatively few cases of cardiac death or nonfatal myocardial infarction have included patients without culprit lesions compared with acute coronary syndrome outcomes in those with culprit lesions. Such discrepancies in AMI clinical outcomes triggered by CAS in Asian and non-Asian patients have been reported.[9−11] Therefore, the objective of the present study was to analyze the clinical outcomes in Koreans diagnosed with AMI induced by coronary artery atherosclerosis compared with those triggered by CAS without stenotic lesions over a 2-year follow-up period.

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Methods

We consecutively selected 49,345 patients with AMI who successfully underwent coronary angiography and/or percutaneous coronary intervention from the database of the Korea Acute Myocardial Infarction Registry-National Institutes of Health. This national registry is a prospective, multicenter, web-based observational cohort study that was established to develop prognostic and surveillance indices of Koreans diagnosed with AMI at numerous centers within Korea. It was supported by grants awarded by the Korea Centers for Disease Control and Prevention from 2005 to 2015.

The diagnosis of AMI was based on variation in cardiac biomarker profiles (creatinine kinase-myocardial band, troponin I, or troponin T) with at least one value above the 99th percentile of the upper reference limit combined with at least one of the following criteria: ischemia, new or presumed new significant ST-segment-T wave changes or new left bundle branch block, development of pathological Q waves in electrocardiogram, and imaging evidence suggesting recent loss of viable myocardium or new regional wall motion abnormalities.[12]

We categorized the 43,071 patients based on AMI due to coronary artery atherosclerosis (CAA-AMI, 36,313 patients) and those due to CAS without stenotic lesions (CAS-AMI, 484 patients). We excluded 6,274 patients diagnosed with myocardial infarction due to coronary myocardial bridge and recent or healed myocardial infarction. Patients with a past history of myocardial infarction were also excluded from this study. All the patients were angiographically confirmed based on CAA or CAS. CAS was confirmed using a spasm provocation test during coronary angiography. Absence of stenotic lesion during coronary angiography prompted investigation for spasm in the segment with ischemic insults consistent with the electrocardiogram. A spasm provocation test was performed either during primary catheterization or during a second session, depending on the patient's condition and the medication administered. During the test, incremental doses of 20, 50, and 100 μg acetylcholine chloride or 10, 20, and 40 μg ergonovine were injected into the left coronary artery, and 20, and 50 μg acetylcholine or 5, 10, and 20 μg ergonovine into the right coronary artery through the diagnostic catheter every 3 minutes. The test was not performed under the following conditions: patient refusal, suspected myocarditis, Takotsubo cardiomyopathy, severe chronic obstructive pulmonary disease, severe renal insufficiency, and allergy to iodinated contrast. Any culprit lesions were

Table 1
Baseline clinical characteristics

Variables	Total (n = 36,797)	CAS-AMI (n = 484)	CAA-AMI (n = 36,313)	p Value
Age (years)	63 ± 12.7	55.4 ± 12.4	63.1 ± 12.7	<0.001
Men	26826 (72.9%)	334 (69.0%)	26492 (73.0%)	0.052
LV ejection fraction (%)	52.4 ± 11.5	60 ± 10	52.3 ± 11.5	<0.001
Body mass index (kg/m^2)	24 ± 3.2	23.9 ± 3.2	24 ± 3.2	0.297
Hypertension	17443 (47.4%)	192 (39.7%)	17251 (47.5%)	0.001
Diabetes mellitus	9421 (25.6%)	54 (11.2%)	9367 (25.8%)	<0.001
Medical treatment	7600 (20.7%)	42 (8.7%)	7558 (20.8%)	<0.001
Insulin	693 (1.9%)	4 (0.8%)	689 (1.9%)	0.085
Dyslipidemia	3544 (9.6%)	30 (6.2%)	3514 (9.7%)	0.010
Cerebrovascular accidents	2240 (6.1%)	11 (2.3%)	2229 (6.1%)	<0.001
Heart failure	386 (1.0%)	2 (0.4%)	384 (1.1%)	0.167
Smoker	21663 (58.9%)	278 (57.4%)	21385 (58.9%)	0.519
Current smoker	16101 (43.8%)	208 (43.0%)	15893 (43.8%)	0.727
Ex-smoker	5562 (15.1%)	70 (14.5%)	5492 (15.1%)	0.687
Family history of coronary artery disease	2686 (7.3%)	38 (7.9%)	2648 (7.3%)	0.639
STEMI	22031 (59.9%)	189 (39.0%)	21842 (60.1%)	<0.001
NSTEMI	14766 (40.1%)	295 (61.0%)	14471 (39.9%)	<0.001
Aborted cardiac arrest at admission	1285 (3.5%)	26 (5.4%)	1259 (3.5%)	0.023
Killip Class				
I	26594 (72.3%)	385 (79.5%)	26209 (72.2%)	<0.001
II	4310 (11.7%)	42 (8.7%)	4268 (11.8%)	0.037
III	2401 (6.5%)	14 (2.9%)	2387 (6.6%)	0.001
IV	1819 (4.9%)	27 (5.6%)	1792 (4.9%)	0.516
Total cholesterol (mg/dl)	185 ± 45	173 ± 54	185 ± 45	<0.001
Triglyceride (mg/dl)	134 ± 111	135 ± 185	134 ± 110	0.779
HDL-Cholesterol (mg/dl)	44 ± 18	48 ± 14	44 ± 18	<0.001
LDL-Cholesterol (mg/dl)	118 ± 42	101 ± 38	118 ± 42	<0.001
CK-MB (ng/ml)	136 ± 236	49 ± 91	137 ± 238	<0.001
Troponine (ng/ml)	48.9 ± 193.8	15.5 ± 50.1	49.3 ± 195.7	<0.001
high-sensitive C-reactive peptide (mg/dl)	11.4 ± 58.9	12 ± 81.1	11.4 ± 58.6	0.862
Glucose (mg/dl)	170 ± 80	143 ± 63	170 ± 80	<0.001
Hemoglobin A1c (%)	6.6 ± 2.2	6.1 ± 1.2	6.6 ± 2.2	<0.001
NT-pro B-type natriuretic peptide (pg/ml)	2260 ± 5948	1337 ± 4014	2271 ± 5971	<0.001
B-type natriuretic peptide (pg/ml)	482 ± 2152	723 ± 3708	478 ± 2131	0.516

managed with percutaneous coronary intervention, coronary artery bypass grafting or conservatively.

Study protocols were approved by the ethics committee of each participating center based on the principles of the Declaration of Helsinki. All patients provided written, informed consent for participation in the registry. Trained study coordinators at each participating institution collected data using a standardized case report format. Standardized definitions of all variables were provided by the steering committee of Korean AMI registry.

The primary end point was major adverse cardiac events (MACE) defined as the composite of total death, nonfatal myocardial infarction, and repeat revascularization at 2-year follow-up.

The statistical analysis was performed using categorical variables expressed as frequencies and percentages, and continuous variables presented as means ± standard deviations of the means. Categorical variables were analyzed with a Chi-square test or Fisher's exact test as appropriate, whereas continuous variables were analyzed with Student's *t* test. Baseline covariates between the 2 groups were compared with paired *t* tests for continuous variables, whereas a Chi-square test or Fisher's exact test was used as appropriate for categorical variables. Cumulative event rates of the 2 groups were estimated using the Kaplan-Meier method. Time-to-event curves were compared using log-rank tests.[13,14] Multiple logistic regression analysis with an "enter" method was used to identify independent predictors of 30-day total death in both groups.

Results

Patients in the CAA-AMI group reported a history of diabetes, dyslipidemia, or cerebrovascular events higher than in the CAS-AMI group. In addition, the CAA-AMI group manifested higher Killip class II-III, ST-segment elevation myocardial infarction, total and low-density lipoprotein cholesterol levels, and maximal serum levels of creatine kinase myocardial band, troponin, glucose, hemoglobin A1c, and N-terminal pro B-type natriuretic peptide compared with those in the CAS-AMI group. However, patients in the CAS-AMI group manifested a higher incidence of elevated left ventricular ejection fraction, non-ST segment elevation myocardial infarction, aborted cardiac arrest, and carried higher levels of high-density lipoprotein cholesterol than those in the CAA-AMI group (Table 1). All angiographic and procedural characteristics in the CAA-AMI group were absolutely higher than those in the CAS-AMI group (Table 2). In addition, patients in the CAA-AMI group were treated with a significantly greater number of medications, both during hospitalization and at discharge and (Table 3).

Table 2
Baseline angiographic and procedural characteristics

Variables	Total (n = 36,797)	CAS-AMI (n = 484)	CAA-AMI (n = 36,313)	p Value
Left main disease	1,336 (3.6%)	0 (0.0%)	1,336 (3.7%)	<0.001
Multivessel coronary disease	19,120 (52.0%)	0 (0.0%)	19,120 (52.7%)	<0.001
1	17,572 (47.8%)	0 (0.0%)	17,572 (48.4%)	<0.001
2	10,958 (29.8%)	0 (0.0%)	10,958 (30.2%)	<0.001
3	7,565 (20.6%)	0 (0.0%)	7,565 (20.8%)	<0.001
Treated lesion				
Left main	942 (2.6%)	0 (0.0%)	942 (2.6%)	<0.001
Left arterial descending	19,763 (53.7%)	0 (0.0%)	19,763 (54.4%)	<0.001
Left circumflex	8,732 (23.7%)	0 (0.0%)	8,732 (24%)	<0.001
Right	13,798 (37.5%)	0 (0.0%)	13,798 (38%)	<0.001
Infarct related artery				
Left main	729 (2.0%)	0 (0.0%)	729 (2%)	0.002
Left arterial descending	17,304 (47.0%)	0 (0.0%)	17,304 (47.7%)	<0.001
Left circumflex	6,007 (16.3%)	0 (0.0%)	6,007 (16.5%)	<0.001
Right coronary artery	11,984 (32.6%)	0 (0.0%)	11,984 (33%)	<0.001
TIMI flow (Preprocedural)				
0	16,518 (44.9%)	0 (0.0%)	16518 (45.5%)	<0.001
1	4,056 (11.0%)	0 (0.0%)	4056 (11.2%)	<0.001
2	4,913 (13.4%)	0 (0.0%)	4913 (13.5%)	<0.001
3	8,612 (23.4%)	0 (0.0%)	8,612 (23.7%)	<0.001
Lesion type (B2/C)	26,421 (71.8%)	0 (0.0%)	26,421 (72.8%)	<0.001
A	1,171 (3.2%)	0 (0.0%)	1,171 (3.2%)	<0.001
B1	5,489 (14.9%)	0 (0.0%)	5,489 (15.1%)	<0.001
B2	10,852 (29.5%)	0 (0.0%)	10,852 (29.9%)	<0.001
C	15,569 (42.3%)	0 (0.0%)	15,569 (42.9%)	<0.001
Stents type				
Sirolimus-eluting	5,318 (14.5%)	0 (0.0%)	5,318 (14.6%)	<0.001
Paclitaxel-eluting	4,638 (12.6%)	0 (0.0%)	4,638 (12.8%)	<0.001
Zotarolimus-eluting	7,157 (19.4%)	0 (0.0%)	7,157 (19.7%)	<0.001
Everolimus-eluting	9,070 (24.6%)	0 (0.0%)	9,070 (25%)	<0.001
Biolimus-eluting	2,661 (7.2%)	0 (0.0%)	2,661 (7.3%)	<0.001
Cilostazol-eluting	193 (0.5%)	0 (0.0%)	193 (0.5%)	0.189

TIMI = Thrombolysis In Myocardial Infarction.

Table 3
In-hospital and discharge medications

Variables. N	Total (n = 36,797)	CAS-AMI (n = 484)	CAA-AMI (n = 36,313)	p Value
In-hospital medications				
Aspirin	35,934 (97.7%)	427 (88.2%)	35,507 (97.8%)	<0.001
Clopidogrel	33,451 (90.9%)	332 (68.6%)	33,119 (91.2%)	<0.001
Cilostazol	8,115 (22.1%)	15 (3.1%)	8,100 (22.3%)	<0.001
Prasugrel	1,207 (3.3%)	16 (3.3%)	1,191 (3.3%)	0.975
Ticagrelor	1,992 (5.4%)	11 (2.3%)	1,981 (5.5%)	0.002
Discharge medications				
Aspirin	33,615 (91.4%)	313 (64.7%)	33,302 (91.7%)	<0.001
Clopidogrel	32,647 (88.7%)	286 (59.1%)	32,361 (89.1%)	<0.001
Cilostazol	7,755 (21.1%)	12 (2.5%)	7,743 (21.3%)	<0.001
Prasugrel	954 (2.6%)	0 (0.0%)	954 (2.6%)	<0.001
Ticagrelor	1,642 (4.5%)	0 (0.0%)	1,642 (4.5%)	<0.001
Calcium channel blockers	2,654 (7.2%)	347 (71.7%)	2,307 (6.4%)	<0.001
Beta blockers	27,509 (74.8%)	60 (12.4%)	27449 (75.6%)	<0.001
Angiotensin converting enzyme inhibitor	20,139 (54.7%)	116 (24.0%)	20,023 (55.1%)	<0.001
Angiotensin II receptor blocker	7,949 (21.6%)	69 (14.3%)	7,880 (21.7%)	<0.001
Statin	28,069 (76.3%)	311 (64.3)	27,758 (76.4%)	<0.001
Fibrate	193 (0.5%)	4 (0.8%)	189 (0.5%)	0.327
Ezetimibe	1,497 (4.1%)	7 (1.4%)	1,490 (4.1%)	0.003
Omega3	333 (0.9%)	1 (0.2%)	332 (0.9%)	0.140

In patients managed in the hospital and those with discharge medications, a higher number of patients in the CAS-AMI group were treated with calcium-channel blockers. By contrast, a higher number of patients in the CAA-AMI group was treated with antiplatelet agents, β-blockers, and renin-angiotensin system inhibitors and statins (Table 3).

In terms of primary outcome, patients in the CAS-AMI group showed a lower incidence of MACE at 2-year follow-up, compared with those manifesting CAA-AMI (7.1% vs 11.2%, log rank p = 0.007; Figure 1). However, the incidence of total death or nonfatal myocardial infarction in the CAS-AMI group was not significantly different from that of the CAA-AMI group (total death: 5.6% vs 6.4%, log rank p = 0.503; myocardial infarction: 0.9% vs 1.5%, log rank p = 0.594; Figure 2). The incidence of repeat revascularization in patients included in the CAS-AMI group was significantly lower than in the CAA-AMI group (0.4% vs 4.2%, log rank p <0.001; Figure 2). No differences were found in 30-day total death or cardiac death between the 2 groups (total death: 4.6% in CAS-AMI vs 4.5% in CAA-AMI, p = 0.941; cardiac death: 4.1% in CAS-AMI vs 4.3% in CAA-AMI, p = 0.901). In patients included in the CAS-AMI group, total death was mostly observed during hospitalization. In terms of in-hospital complications, major bleeding events and atrioventricular blocks in the CAS-AMI group were significantly lower than in the CAA-AMI group (Tables 4 and 5).

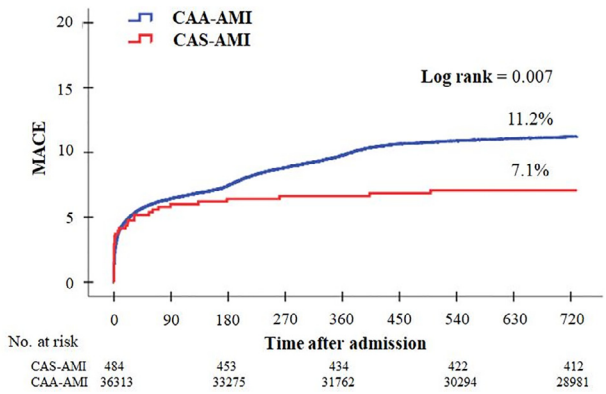

Figure 1. Kaplan–Meier curve for composite of MACE in patients with CAS-AMI and CAA-AMI.
The two-year incidence of MACE in the CAS-AMI group was significantly lower than in the CAA-AMI group. CAS-AMI = Acute myocardial infarction caused by coronary artery spasm without stenotic lesion; MACE = major adverse cardiac events; CAA-AMI = Acute myocardial infarction due to coronary artery atherosclerosis.

Based on multivariate logistic regression analysis, age, ST-segment elevation myocardial infarction, aborted cardiac arrest, low left ventricular ejection fraction (<40%), shock, diabetes mellitus, current smoking status, multivessel disease, and left main disease were independent predictors of 2-year total death in patients with CAA-AMI. However, aborted cardiac arrest alone was significantly associated with 2-year total death in the CAS-MI group (Table 6).

Discussion

The following are the main findings of this study: (1) Overall, in Koreans diagnosed with AMI, the incidence of MACE in patients with CAS-AMI was significantly lower than in patients with CAA-AMI up to 2 years, which was attributed to the relatively lower rate of repeat revascularization (RR); (2) The incidence of total death and nonfatal myocardial infarction in patients with CAS-AMI was similar to that of patients with CAA-AMI; (3) Independent predictors of 2-year total death in the CAA-AMI group include age, ST-segment elevation myocardial infarction, aborted cardiac arrest, low left ventricular ejection fraction (<40%), shock, diabetes mellitus, current smoking status, multivessel disease and left main disease, whereas aborted

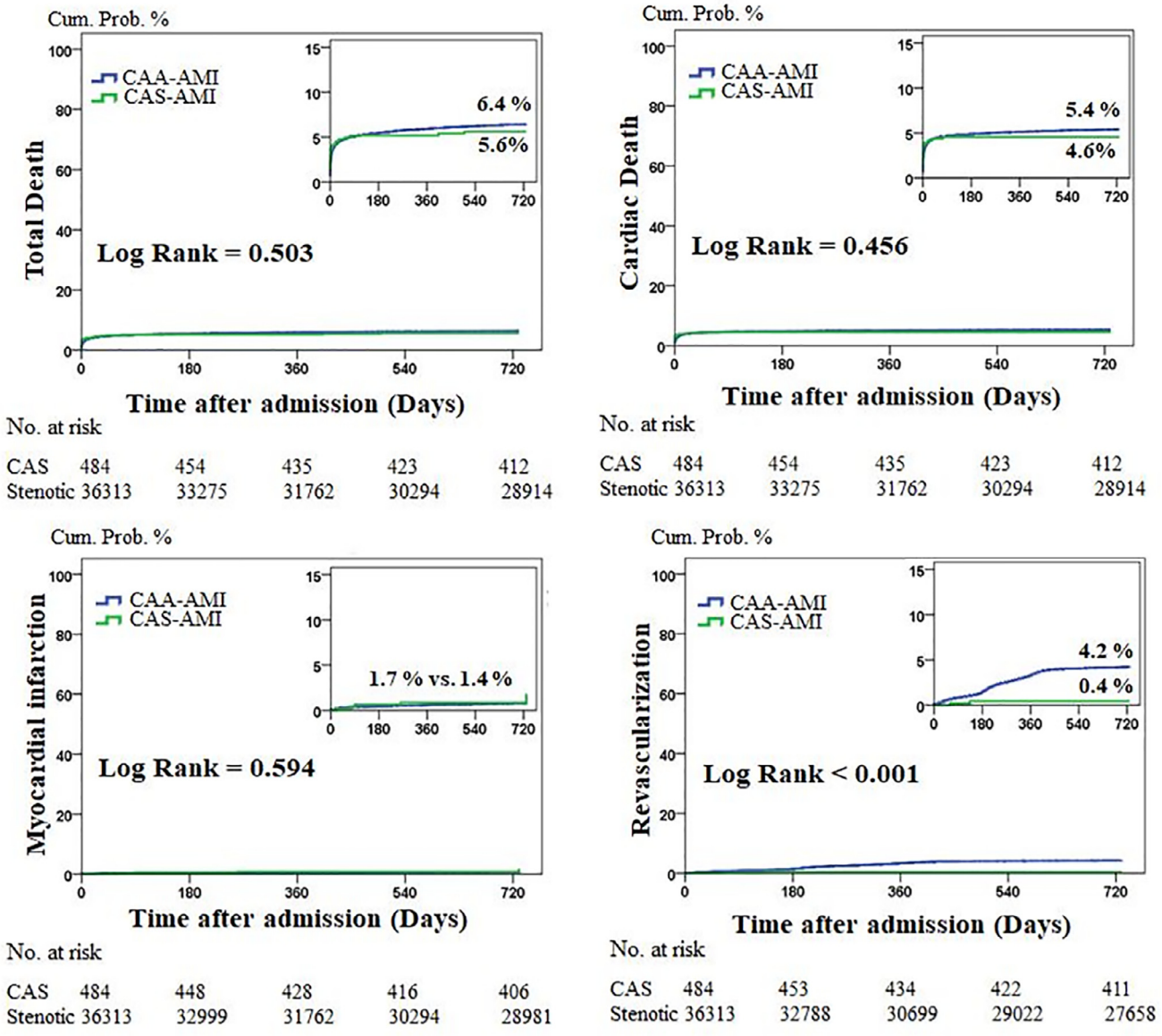

Figure 2. Kaplan−Meier curve for clinical outcomes in patients with CAS-AMI and CAA-AMI; (*A*) Total death, (*B*) Cardiac death, (*C*) Nonfatal myocardial infarction, (*D*) Repeat revascularization. The difference in MACE between the 2 groups was mainly attributed to the lower rate of RR in the group with CAA-AMI. However, the incidence of TD and MI was similar between the 2 groups. CAS-AMI = Acute myocardial infarction caused by coronary artery spasm without stenotic lesion; MACE = Major adverse cardiac events; RR = Repeat revascularization; CAA-AMI = Acute myocardial infarction due to coronary artery atherosclerosis.

cardiac arrest alone was significantly associated with 2-year total death in the CAS-AMI group.

Previously reports of clinical data involving AMI caused by CAS suggested varying findings. Patients with acute coronary syndrome without culprit lesions and evidence of CAS manifested excellent prognosis for survival compared with patients diagnosed with obstructive acute coronary syndrome.[8,15] However, other studies with a small study population reported higher incidence of cardiac death and nonfatal myocardial infarction in patients diagnosed with CAS-AMI[16,17]

Our findings differ from previous studies as follows.

First, the prognosis of CAS-AMI was far from benign. The present study showed that the 2-year incidence of cardiac death in the CAS-AMI group reached 4.6%, which was not significantly different compared with 5.4% in the CAA-AMI group. Second, the cardiac death in CAS-AMI group occurred mainly during admission. Interestingly, the incidence of aborted cardiac arrest was relatively higher than in CAA-AMI. Furthermore, the logistic regression analysis showed that aborted cardiac arrest due to CAS-AMI was strongly associated with 2-year total death. Previous studies suggested that the prognosis of patients with variant angina associated with aborted sudden cardiac arrest was worse than in patients without it.[17,18] All-cause mortality also occurred more frequently in patients suffering from aborted cardiac arrest due to coronary spasm over a median follow-up of 7.5 years.[18]

By contrast, our data showed that survivors of CAS-AMI following hospitalization showed excellent prognosis with appropriate management. Therefore, patients with severe

Table 4
In-hospital complications

Variables. N	Total (n = 36,797)	CAS-AMI (n = 484)	CAA-AMI (n = 36,313)	p Value
In-hospital complication				
Cardiogenic shock	1,806 (4.9%)	16 (3.3%)	1,790 (4.9%)	0.100
Acute renal insufficiency	213 (0.6%)	2 (0.4%)	211 (0.6%)	ns
Acute heart failure	546 (1.5%)	3 (0.6%)	543 (1.5%)	0.114
Major bleeding	447 (1.2%)	0 (0.0%)	447 (1.2%)	0.014
Atrioventricular block	724 (2.0%)	1 (0.2%)	723 (2%)	0.005
Atrial fibrillation	455 (1.2%)	3 (0.6%)	452 (1.2%)	0.217

Table 5
Two year clinical outcomes up to 2 years by Kaplan-Meier with Log-rank test and Cox-hazard ratio analysis

Variables, N	Incidence			p Value
	Total (n = 36,797)	CAS-AMI (n = 484)	CAA-AMI (n = 36,313)	
30-day clinical outcomes				
MACE	1,922 (5.2%)	23 (4.8%)	1,899 (5.2%)	0.639
Total death	1,649 (4.5%)	22 (4.6%)	1,627 (4.5%)	0.941
Cardiac death	1,564 (4.3%)	20 (4.1%)	1,544 (4.3%)	0.901
Myocardial infarction	194 (0.5%)	1 (0.2%)	193 (0.5%)	0.527
Revascularization	131 (0.4%)	0 (0.0%)	131 (0.4%)	0.424
Acute stent thrombosis	36 (0.1%)	0 (0.0%)	36 (0.1%)	0.99
Subacute stent thrombosis	84 (0.2%)	0 (0.0%)	84 (0.2%)	0.631

Variables	Incidence		HR (95% C.I)	p Value
	CAS-AMI (n = 484)	CAA-AMI (n = 36,797)		
2-year clinical outcomes				
MACE	34 (7.1%)	3,978 (11.2%)	0.639 (0.449 - 0.882)	0.007
Total death	27 (5.6%)	2,303 (6.4%)	0.879 (0.601 - 1.284)	0.503
Cardiac death	22 (4.6%)	1,940 (5.4%)	0.853 (0.560 - 1.298)	0.456
Myocardial infarction	8 (1.7%)	478 (1.4%)	1.244 (0.618 - 2.502)	0.540
Revascularization	2 (0.4%)	1391 (4.2%)	0.104 (0.026 - 0.415)	<0.001

Table 6
The independent predictors of total death up to 2 years

Variables	CAA-AMI		CAS-AMI	
	HR (95% CI)	p Value	HR (95% CI)	p Value
Age	1.04 (1.04 - 1.05]	<0.001	1.01 (0.97 - 1.05)	0.777
Men	0.90 (0.81 - 1.01]	0.073	0.66 (0.24 - 1.84)	0.429
STEMI	1.78 (1.59 - 2.00)	<0.001	0.77 (0.29 - 2.00)	0.586
Aborted cardiac arrest at admission	5.22 (4.60 - 5.92)	<0.001	13.5 (5.34 - 34.15)	<0.001
Low LVEF (<40%)	1.43 (1.28 - 1.61)	<0.001	1.47 (0.39 - 5.56)	0.574
Cardiogenic shock	2.63 (2.33 - 2.96)	<0.001	1.75 (0.48 - 6.29)	0.395
Hypertension	0.98 (0.88 - 1.08)	0.638	1.33 (0.52 - 3.42)	0.554
Diabetes mellitus	1.42 (1.28 - 1.58)	<0.001	1.80 (0.62 - 5.23)	0.277
LDL-Cholesterol	0.74 (0.60 - 0.90)	0.003	1.10 (0.20 - 6.19)	0.914
Current smoker	0.81 (0.72 - 0.92)	0.001	0.90 (0.30 - 2.70)	0.855
Multi-vessel disease	1.50 (1.35 - 1.68)	<0.001		
Left main disease	2.23 [1.90 - 2.62)	<0.001		
Failed coronary intervention	5.76 [4.80 - 6.91)	<0.001		

coronary spasm that resulted in aborted cardiac arrest might have poor prognosis with occasional fatal outcomes due to cardiac events within the admission period. Compared with non-Asian cases, severe CAS in Korean population may result in a higher incidence of AMI-induced cardiac death during hospitalization.

Our data suggest that the incidence of CAS-AMI without stenotic lesions was only 1.1% in the overall population

diagnosed with all-cause myocardial infarction, with approximately 4% of such patients manifesting cardiac death during a 2-year follow-up. Therefore, only a small proportion of patients in the overall population with all-cause myocardial infarction probably manifest fatal prognosis due to severe CAS. Furthermore, our data showed a higher incidence of aborted cardiac arrest due to CAS-AMI during admission correlated with significant short-term cardiac events in the CAS-AMI group, which influenced the 2-year prognosis. These patterns of clinical outcome involving CAS-induced AMI may be explained as follows:

First, compared with Caucasians, Asians diagnosed with variant angina appear to manifest diffusely hyperreactive coronary arteries based on segmental rather than focal CAS, and multivessel CAS vasomotor reactivity.[11] Second, cardiac deaths due to CAS may be triggered by sustained and overwhelming or multivessel spasm, resulting in transient myocardial ischemia or infarction. In addition, fatal ventricular arrhythmia may trigger cardiac arrest.[19] Third, nationwide Japanese multicenter registries revealed that out-of-hospital cardiac arrest events induced by CAS were significantly correlated with concomitant idiopathic ventricular fibrillation and long-term MACE of vasospastic angina.[20,21] In addition, cardiac arrest with vasospastic angina may occur in the left anterior descending coronary artery compared with the remaining patients diagnosed with noncardiac arrest.[22] In patients with vasospastic angina accompanied by cardiac arrest, the prevalence of QT dispersion was significantly higher than in those without complications.[23–25] In our study, the majority of cardiac death in the CAS-AMI group occurred during hospitalization. In patients surviving beyond 30 days, further events were sparse compared with the greater than approximately 1% cardiac deaths observed in the CAA-AMI group.

The study limitations are as follows. First, due to the retrospective and observational study design, inherent limitations were inevitable. Second, despite comprehensive analysis of prescription medications in both groups, the timing and mode of administration of medications to treat spasm, and the patient response during hospitalization were unknown. Therefore, the role of intensive management using vasodilators in patients with AMI or even unstable aborted cardiac arrest due to CAS could not be established.

In conclusion, data analyzing the prognosis of Asian patients diagnosed with CAS-AMI has been sparse until now. The present study demonstrated that the incidence of MACE in CAS-AMI patients was significantly lower than in patients with CAA-AMI up to 2 years. However, the incidence of total death or nonfatal myocardial infarction in CAS-AMI patients did not differ from that of patients diagnosed with CAA-AMI. Therefore, the impact of CAS-AMI in the Korean population clearly differed in MACE during short- and long-term prognosis when compared with previous studies involving non-Asian populations.

Disclosures

The authors have nothing to disclose.

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