

SUPPLEMENTAL MATERIAL

Data S1. METHODS

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Table S1 Baseline and Angiographic Characteristics According to Various Vasodilator

	No vasodilator (n = 359)	Vasodilator			p Value†
		Non-nitrate vasodilator* (n = 1,187)	Conventional nitrate (n = 209)	Combination (n = 140)	
Demographics					
Age, years	55.6 (11.5)	55.4 (11.2)	52.9 (11.3)	53.8 (11.9)	0.012
Male	199 (55.4)	753 (63.4)	138 (66.0)	81 (57.9)	0.018
Medical history					
Ischemic heart disease	42 (11.7)	150 (12.6)	18 (8.6)	26 (18.6)	0.049
Stable CAD	21 (5.8)	69 (5.8)	8 (3.8)	16 (11.4)	0.028
History of PCI	3 (0.8)	28 (2.4)	3 (1.4)	6 (4.3)	0.077
Hypertension	136 (37.9)	448 (37.7)	86 (41.1)	50 (35.7)	0.747
Diabetes mellitus	28 (7.8)	117 (9.9)	20 (9.6)	13 (9.3)	0.710
Dyslipidemia	50 (13.9)	188 (15.8)	40 (19.1)	32 (22.9)	0.063
AF or AFL	6 (1.7)	10 (0.8)	1 (0.5)	1 (0.7)	0.439
Cerebrovascular accident	8 (2.2)	18 (1.5)	3 (1.4)	3 (2.1)	0.778
Thyroid disease	13 (3.6)	45 (3.8)	1 (0.5)	6 (4.3)	0.097
Hyperthyroidism	2 (0.6)	21 (1.8)	0	2 (1.4)	0.100
Hypothyroidism	9 (2.5)	14 (1.2)	0	3 (2.1)	0.064

Chronic airway disease	5 (1.4)	17 (1.4)	3 (1.4)	1 (0.7)	0.922
Familial history of CAD	15 (4.2)	76 (6.4)	15 (7.2)	3 (2.1)	0.082
Current or ex-smoking	136 (37.9)	484 (40.8)	110 (52.6)	56 (40.0)	0.005
Past medication					
Aspirin	66 (18.4)	257 (21.7)	34 (16.3)	27 (19.3)	0.226
Thienopyridine	15 (4.2)	34 (2.9)	13 (6.2)	8 (5.7)	0.048
Calcium-channel blocker	50 (13.9)	248 (20.9)	31 (14.8)	38 (27.1)	0.001
ACE inhibitor or ARB	69 (19.2)	213 (17.9)	30 (14.4)	19 (13.6)	0.280
Beta-blocker	36 (10.0)	92 (7.8)	9 (4.3)	8 (5.7)	0.074
Statin	49 (13.6)	200 (16.8)	25 (12.0)	17 (12.1)	0.121
Initial presentation					
Chest pain	318 (88.6)	1,095 (92.2)	196 (93.8)	131 (93.6)	0.073
Angina class >2	252 (70.2)	752 (63.4)	176 (84.2)	104 (74.3)	<0.001
Dyspnea	23 (6.4)	77 (6.5)	5 (2.4)	5 (3.6)	0.073
Syncope	7 (1.9)	12 (1.0)	4 (1.9)	1 (0.7)	0.391
Cardiac arrest	10 (2.8)	7 (0.6)	5 (2.4)	5 (3.6)	0.001
VT or VF	6 (1.7)	4 (0.3)	1 (0.5)	1 (0.7)	0.048
STE during chest pain	15 (4.2)	58 (4.9)	19 (9.1)	13 (9.3)	0.012
STD during chest pain	4 (1.1)	6 (0.5)	4 (1.9)	3 (2.1)	0.068
TWI during chest pain	7 (1.9)	22 (1.9)	12 (5.7)	6 (4.3)	0.004

Fixed stenosis	136 (37.9)	409 (34.5)	76 (36.4)	50 (35.7)	0.678
Left main	3 (0.8)	12 (1.0)	3 (1.4)	2 (1.4)	0.882
LAD or diagonal	100 (27.9)	280 (23.6)	50 (23.9)	38 (27.1)	0.358
LCX or OM	37 (10.3)	119 (10.0)	23 (11.0)	15 (10.7)	0.973
RCA	61 (17.0)	209 (17.6)	43 (20.6)	20 (14.3)	0.488
Significant stenosis‡	20 (5.6)	47 (4.0)	7 (3.3)	5 (3.6)	0.499
LAD or diagonal	13 (3.6)	28 (2.4)	4 (1.9)	4 (2.9)	0.535
LCX or OM	2 (0.6)	10 (0.8)	2 (1.0)	1 (0.7)	0.946
RCA	7 (1.9)	14 (1.2)	2 (1.0)	0	0.325
Other finding					
Myocardial bridge	13 (3.6)	82 (6.9)	20 (9.6)	8 (5.7)	0.035
Slow flow	12 (3.3)	67 (5.6)	10 (4.8)	9 (6.4)	0.320
Spasm provocation test					
Spasm positive arteries					
Left main	1 (0.3)	9 (0.8)	0	8 (5.7)	<0.001
LAD or diagonal	178 (49.6)	573 (48.3)	106 (50.7)	80 (57.1)	0.250
LCX or OM	101 (28.1)	273 (23.0)	38 (18.2)	35 (25.0)	0.048
RCA	192 (53.5)	593 (50.0)	116 (55.5)	64 (45.7)	0.199
Multivessel spasm	103 (28.7)	280 (23.6)	44 (21.1)	38 (27.1)	0.121
Spontaneous spasm	49 (13.6)	175 (14.7)	24 (11.5)	28 (20.0)	0.158

Diffuse spasm	234 (65.2)	755 (63.6)	120 (57.4)	76 (54.3)	0.045
Focal spasm	134 (37.3)	427 (36.0)	102 (48.8)	67 (47.9)	<0.001
Mixed spasm	41 (11.4)	111 (9.4)	13 (6.2)	5 (3.6)	0.021
Spasm on fixed stenosis	77 (21.4)	248 (20.9)	56 (26.8)	36 (25.7)	0.184
Chest pain during spasm	207 (57.7)	692 (58.3)	149 (71.3)	93 (66.4)	0.001
Result of provocation test					0.806
Definite positive	132 (36.8)	459 (38.7)	81 (38.8)	58 (41.4)	
Intermediate positive	227 (63.2)	728 (61.3)	128 (61.2)	82 (58.6)	
ECG change					
STE	29 (8.1)	99 (8.3)	15 (7.2)	14 (10.0)	0.824
STD	16 (4.5)	48 (4.0)	11 (5.3)	6 (4.3)	0.877
TWI	15 (4.2)	55 (4.6)	11 (5.3)	11 (7.9)	0.349
Medication at discharge					
Calcium-channel blocker	301 (83.8)	1,088 (91.7)	191 (91.4)	125 (89.3)	<0.001
ACE inhibitor or ARB	68 (18.9)	218 (18.4)	32 (15.3)	21 (15.0)	0.533
Antiplatelet	166 (46.2)	558 (47.0)	96 (45.9)	61 (43.6)	0.886
Statin	161 (44.8)	592 (49.9)	97 (46.4)	66 (47.1)	0.353
Beta-blocker	21 (5.8)	86 (7.2)	6 (2.9)	8 (5.7)	0.109
Alpha blocker	5 (1.4)	15 (1.3)	0	2 (1.4)	0.420

Values are expressed as mean (SD) or n (%). *Non-nitrate vasodilator includes nicorandil, molsidomine and trimetazidine. †The p Values are derived from the chi-square test for categorical variables, when appropriate, and from one-way analysis of variance F-test or Kruskal-Wallis test for continuous variables for between-group comparison. ‡There was no significantly fixed coronary artery stenosis in left main.

ACE = angiotensin-converting enzyme; AF = atrial fibrillation; AFL = atrial flutter; ARB = angiotensin II receptor blocker; CAD = coronary artery disease; ECG = electrocardiography; LAD = left anterior descending artery; LCX = left circumflex artery; LVEF = left ventricular ejection fraction; OM = obtuse marginal; PCI = percutaneous coronary intervention; RCA = right coronary artery; SMD = standardized mean difference; STD = ST-segment depression; STE = ST-segment elevation; TWI = T-wave inversion; VF = ventricular fibrillation; VT = ventricular tachycardia.

Table S2 Detailed Characteristics of the VSA Patients With All-Cause Deaths

	Sex	Age (yrs)	JCSA score	DL	AF or AFL	Smoking	Significant fixed stenosis	ERGT positive type	Spasm type	MS	Involved vessel	Medication Change	Time to death (days)
1	Female	77	5	Yes	No	Yes	No	Definite	Mixed	Yes	LAD, LCX	Yes	242
2	Female	72	3	No	No	Yes	No	Definite	Diffuse	No	RCA	No	259
3	Male	65	6	No	No	Yes	No	Definite	Diffuse	No	LAD	Yes	570
4	Male	46	8	No	No	Yes	No	Definite	Diffuse	No	RCA	No	572
5*	Male	61	4	Yes	No	Yes	No	Definite	Diffuse	Yes	LAD/RCA	No	169
6	Female	60	9	No	No	No	No	Intermediate	Diffuse	Yes	LAD/RCA	No	439
7*	Male	45	2	No	No	Yes	No	Definite	Mixed	No	RCA	No	19
8	Male	55	2	No	No	Yes	No	Definite	Diffuse	No	LAD	No	418
9*	Male	56	2	No	No	Yes	No	Definite	Focal	No	RCA	Yes	119
10*	Male	60	2	No	No	No	No	Definite	Focal	No	RCA	Yes	529
11	Female	60	0	No	No	No	No	Intermediate	Diffuse	No	LAD	Yes	173
12	Female	68	2	No	No	No	No	Intermediate	Diffuse	Yes	LAD, LCX	No	858
13	Female	62	2	Yes	No	Yes	No	Intermediate	Diffuse	No	LCX	No	1,280

*Cardiac death.

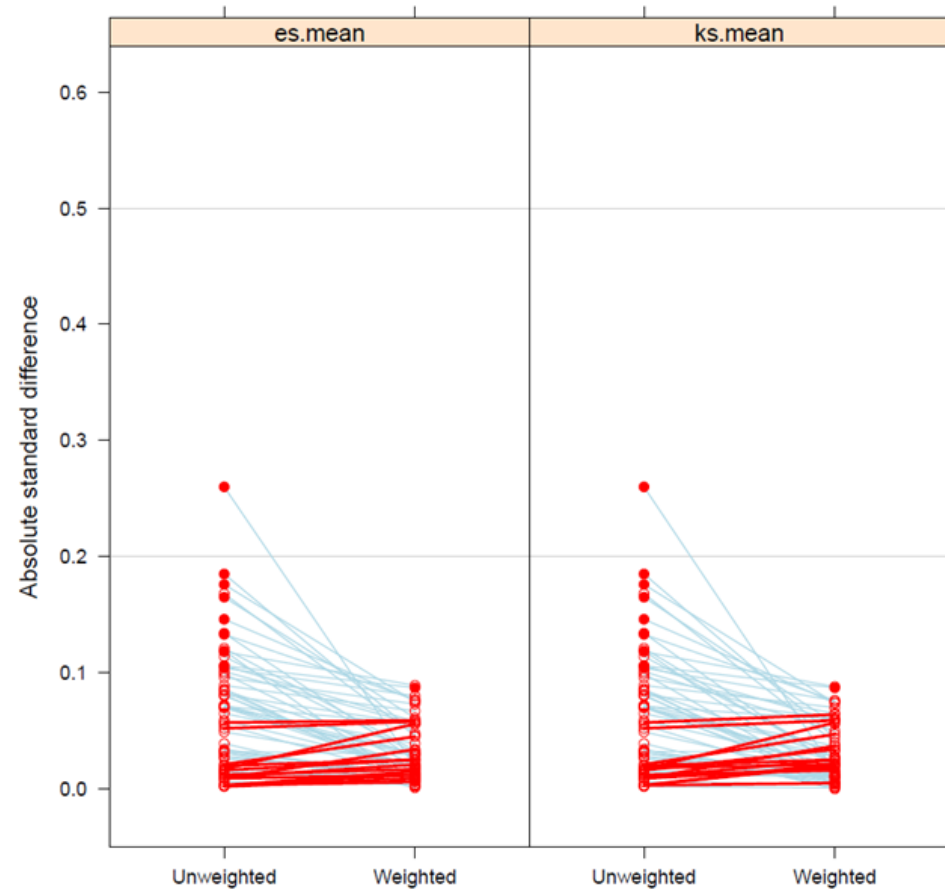
AF = atrial fibrillation; AFL = atrial flutter; DL = dyslipidemia; JCSA = Japanese Coronary Spasm Association; LVEF = left ventricular ejection fraction; MS = multivessel spasm.



Table S3 Independent Predictors for Primary Endpoint or Acute Coronary Syndrome

	Hazard Ratio	95% Confidence Interval	p Value*
Primary endpoint*			
Non-nitrate vasodilator (no vasodilator group as a reference)	0.74	0.42-1.31	0.301
Conventional nitrate (no vasodilator group as a reference)	1.25	0.61-2.56	0.539
Combination (no vasodilator group as a reference)	1.48	0.69-3.18	0.320
Atrial fibrillation or flutter	3.22	1.13-9.19	0.029
Significantly fixed coronary artery stenosis†	2.58	1.33-4.99	0.005
ACS			
Non-nitrate vasodilator (no vasodilator group as a reference)	0.92	0.40-2.11	0.842
Conventional nitrate (no vasodilator group as a reference)	2.31	0.91-5.86	0.077
Combination (no vasodilator group as a reference)	3.18	1.22-8.28	0.018
Dyslipidemia	1.89	1.05-3.38	0.033
Atrial fibrillation or flutter	4.91	1.45-16.70	0.011
Significantly fixed coronary artery stenosis	3.04	1.33-6.98	0.009
*The primary endpoint was a composite of cardiac death, acute coronary syndrome, and new-onset arrhythmia. †The definition was more than 50% diameter stenosis in left main and more than 70% stenosis in non-left main coronary artery.			
ACS= acute coronary syndrome.			

Figure S1 Absolute Standardized Difference for Multinomial Propensity Score



Standardized effect size plot for estimating the propensity scores. ES = effect size; KS = Kolmogorov-Smirnov.