18th Joint Meeting of Coronary Revascularization (JCR 2018)
December 7-8, 2018, in Busan, Korea

Atherosclerotic and Non-Atherosclerotic Coronary Artery Diseases, Coronary dissection, embolism and ectasia; Lessons from NCVC Registry

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Presenter Disclosure Information

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Atherosclerotic and Non-Atherosclerotic Coronary Artery Diseases, Coronary dissection, embolism and ectasia; Lessons from NCVC Registry

FINANCIAL DISCLOSURE:

Remuneration for lecture: Takeda, Daiichi-Sankyo, Bristol-Myers

Trust research/joint research funds: Takeda, Abbott

Background; Atherosclerotic and non-atherosclerotic coronary artery disease

- The most common, clinically significant cause of acute myocardial infarction (AMI) is an angiographically demonstrable (sub-)occlusive disease due to atherosclerotic changes in coronary artery.

- Occasionally, we experience AMI patients who have other causes for their luminal compromise than atherosclerosis.

Purpose

- We investigated the prevalence, clinical features, and long-term outcomes of the uncommon atherosclerotic (CAE; Coronary artery ectasia) and non-atherosclerotic coronary artery disease (CE; Coronary artery embolism and SCAD; Spontaneous coronary artery dissection) in the National Cerebral and Cardiovascular Center (NCVC) registry.

National Cerebral and Cardiovascular Center
NCVC Database (1977-)

NCVC database collected
the data of patients admitted as AMI over past 40years

6000
5000
4000
3000
2000
1000
0

1977 1978 1979 1980 1981 1982 1983 1984 1985 1986 1987 1988 1989 1990 1991 1992 1993 1994 1995 1996 1997 1998 1999 2000 2001 2002 2003 2004 2005 2006 2007 2008 2009 2010 2011

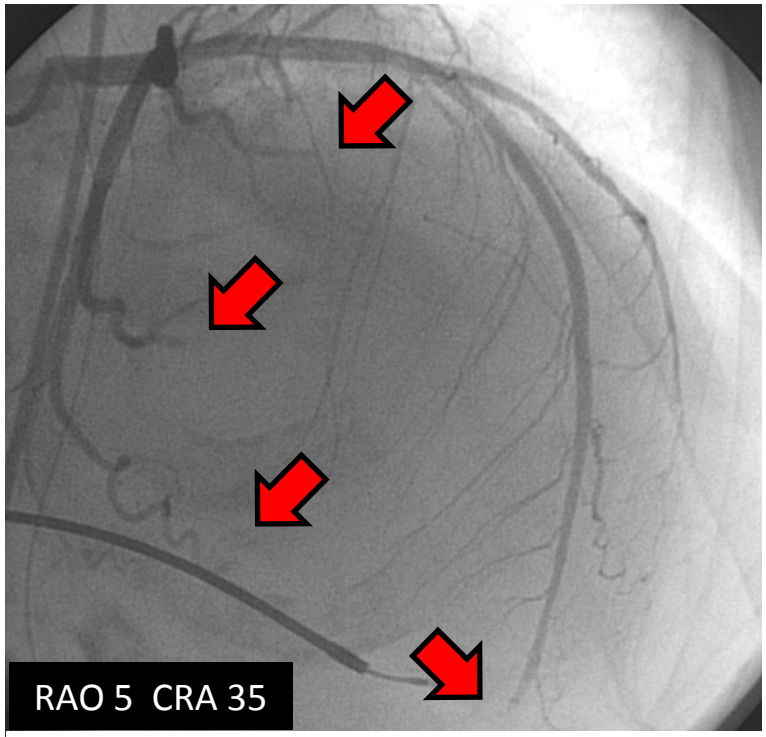
2011 2010 2009 2008 2007 2006 2005 2004 2003 2002 2001 2000 1999 1998 1997 1996 1995 1994 1993 1992 1991 1990 1989 1988 1987 1986

Non-atherosclerotic coronary artery disease

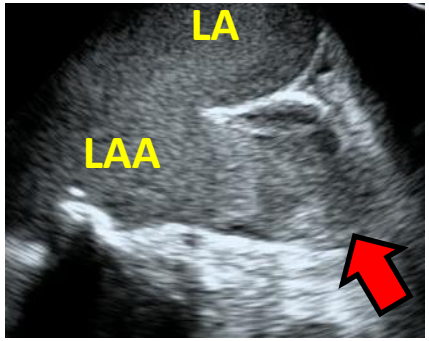
1. Coronary artery embolism

Shibata T, Yasuda S, et al. Circulation. 2015 Jul 28;132(4):241-50.

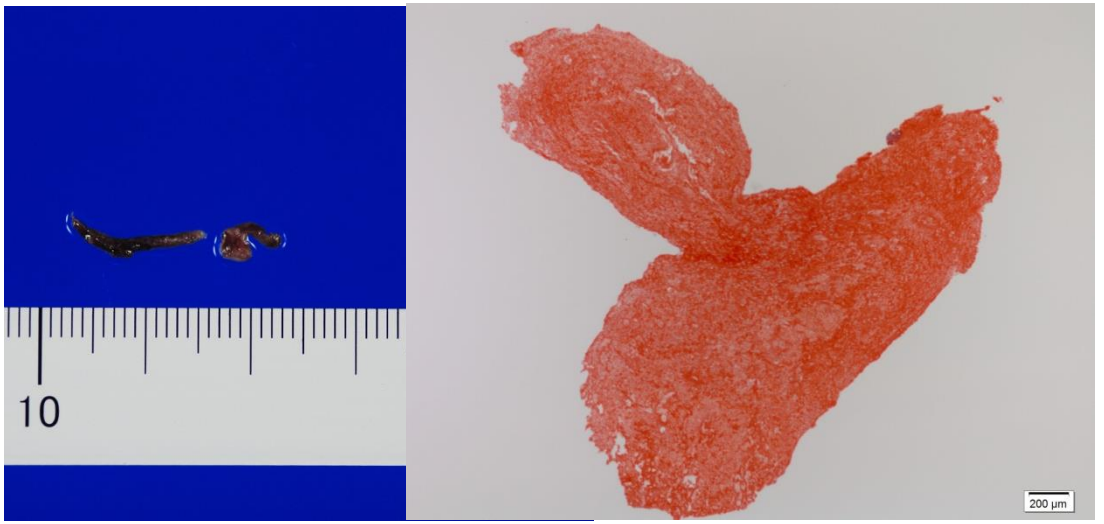
Coronary artery embolism (CE) is recognized as an important non-atherosclerotic cause of acute myocardial infarction (AMI); 64 yo female, AF + post MVR, major criteria: 3 minor criteria: 2



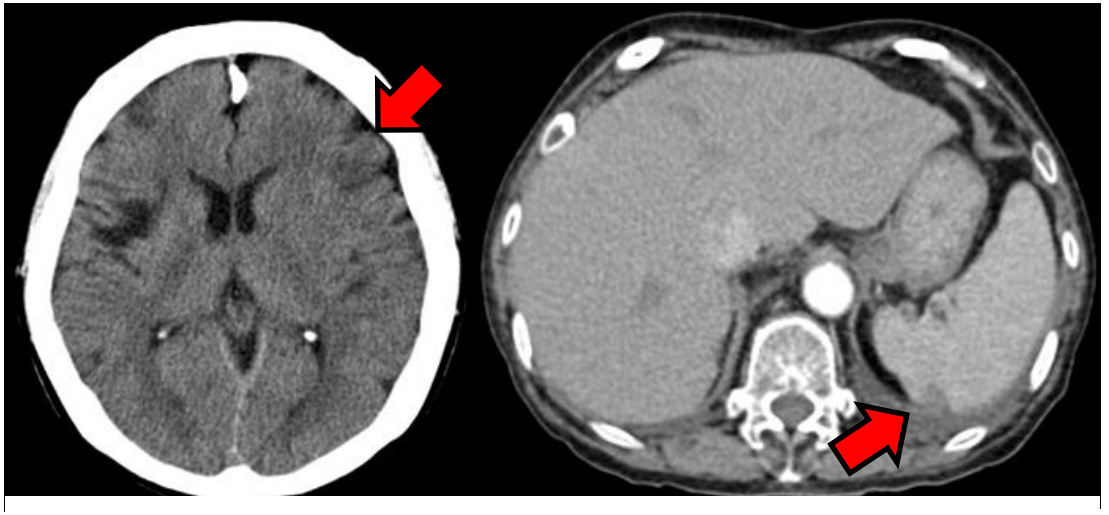
Simultaneous total occlusion of the distal portion of LAD and LCX (major criterion + minor criterion)



Thrombus in the left atrial appendage by TEE (minor criterion)



Fresh red thrombus without evidence of atherosclerotic components (major criterion)



Simultaneous cerebral and splenic infarction (major criterion)

Figure 2. Proposed NCVC criteria for the clinical diagnosis of coronary artery embolism

Major criteria

- ■ Angiographic evidence of embolic coronary artery occlusion and thrombus without atherosclerotic components
- ■ Concomitant coronary artery embolization at multiple sites*
- ■ Concomitant systemic embolization without left ventricular thrombus due to acute myocardial infarction

Minor Criteria

- □ ≤ 25% stenosis on coronary angiography, except for the culprit lesion
- □ Evidence of an embolic source based on transthoracic echocardiography, transesophageal echocardiography, computed tomography, or magnetic resonance imaging
- □ Presence of embolic risk factors: atrial fibrillation, cardiomyopathy, rheumatic valve disease, prosthetic heart valve, patent foramen ovale, atrial septal defect, history of cardiac surgery, infective endocarditis, or hypercoagulable state

Definite CE

- Two or more major criteria, or
- One major criterion plus two or more minor criteria, or
- Three minor criteria

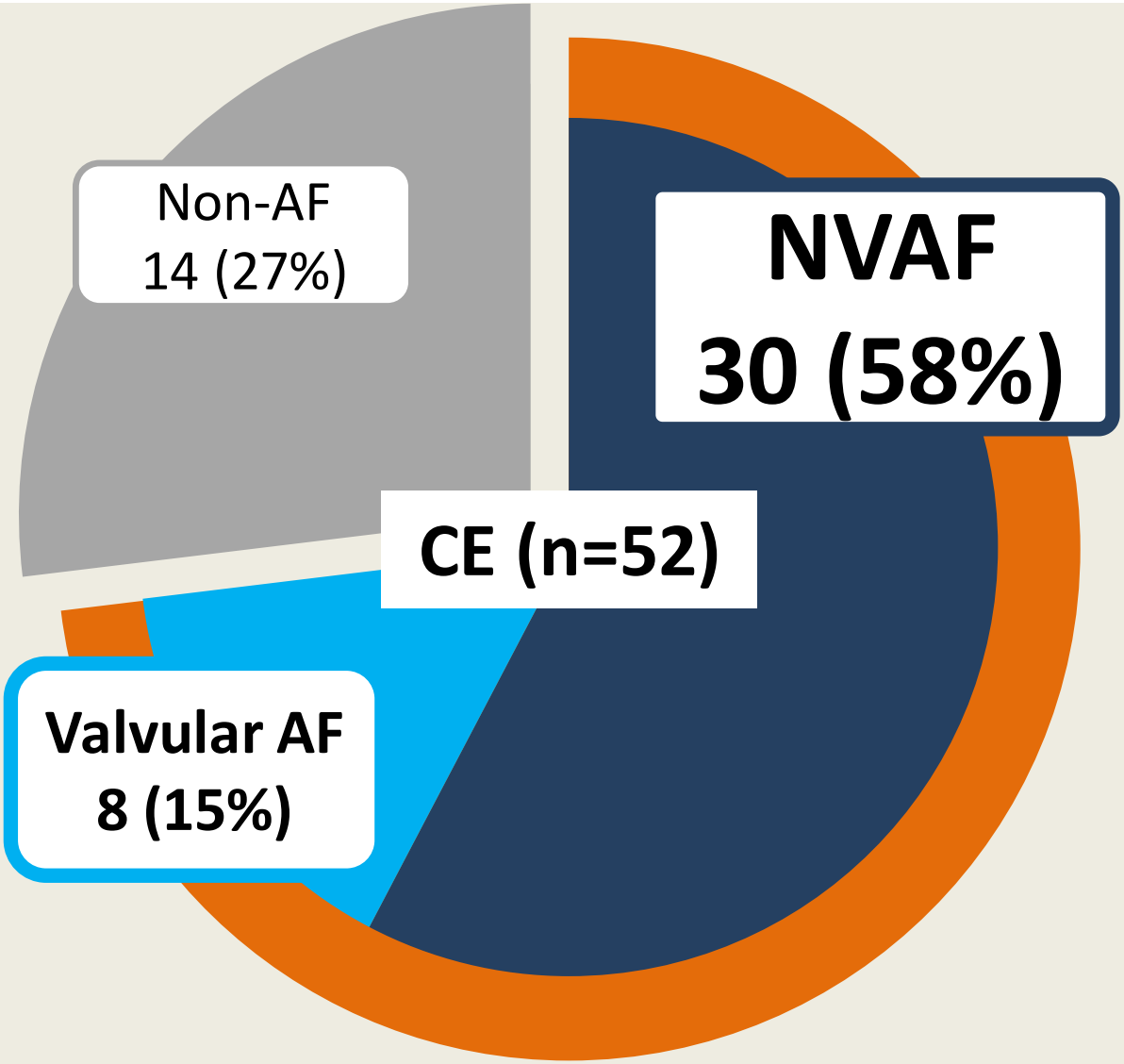
Probable CE

- One major criterion plus one minor criterion, or
- Two minor criteria

A diagnosis of CE should not be made if there is

- Pathological evidence of atherosclerotic thrombus
- History of coronary revascularization
- Coronary artery ectasia
- Plaque disruption or erosion detected by intravascular ultrasound or optic coherence tomography at the proximal site of the culprit lesion

*indicates multiple vessels within one coronary artery territory or multiple vessels in the coronary tree



The most common cause was AF (73%), 38 of 52 CE patients

Circulation. 2015 Jul 28;132(4):241-50.

Prevalence, Clinical Features, and Prognosis of Acute Myocardial Infarction Attributable to Coronary Artery Embolism

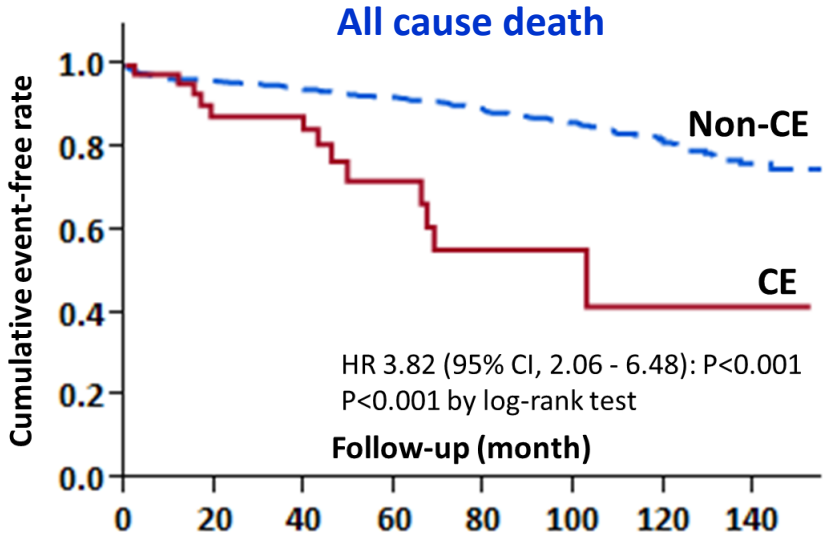
Tatsuhiro Shibata, MD; Shoji Kawakami, MD; Teruo Noguchi, MD; Tomotaka Tanaka, MD; Yasuhide Asaumi, MD; Tomoaki Kanaya, MD; Toshiyuki Nagai, MD; Kazuhiro Nakao, MD; Masashi Fujino, MD; Kazuyuki Nagatsuka, MD; Hatsue Ishibashi-Ueda, MD; Kunihiro Nishimura, MD; Yoshihiro Miyamoto, MD; Kengo Kusano, MD; Toshihisa Anzai, MD; Yoichi Goto, MD; Hisao Ogawa, MD; Satoshi Yasuda, MD

- We screened 1776 consecutive patients who presented with de novo acute myocardial infarction between 2001 and 2013.
- The overall prevalence of CE in new-onset AMI was 2.9% (n=52) and the most common cause was AF (73%). 21 (40%) were female, with a mean age of 66 ± 14 years.
- Simultaneous systemic emboli were observed in 12 patients (23%), especially cerebral infarction occurred in 8 patients (15%).
- Only 39% CE with AF patients have received VKA therapy at the onset of AMI, and were all inadequate INR values; median 1.42 (range, 0.95–1.80) .

Circulation. 2015 Jul 28;132(4):241-50.

Comparison of long-term outcomes between CE and non-CE

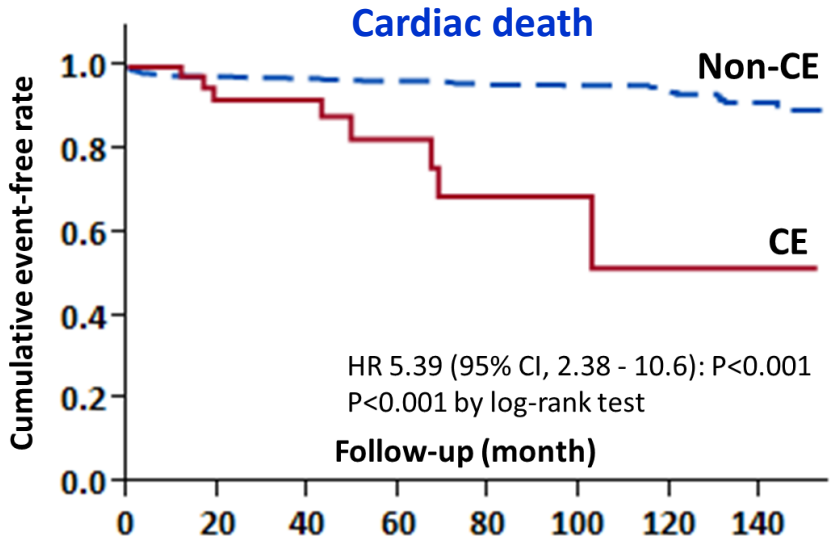
A



Number at risk

CE	48	33	27	14	6	5	3	3
Non-CE	1,623	1,209	957	693	518	354	215	79

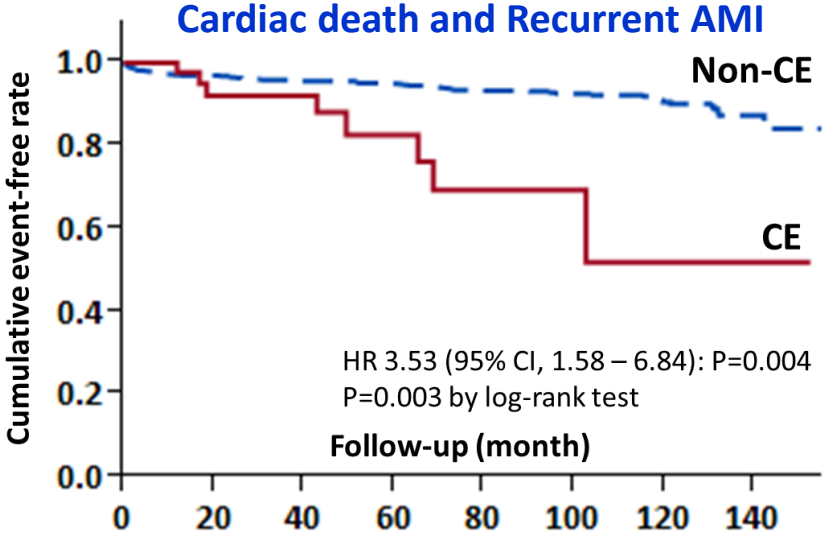
B



Number at risk

CE	48	33	27	14	6	5	3	3
Non-CE	1,623	1,209	957	693	518	354	215	79

C



Number at risk

CE	48	33	27	14	6	5	3	3
Non-CE	1,623	1,198	937	677	499	337	204	73

Median follow-up: 49 months (IQR, 19-93)

Kaplan-Meier analysis indicated a significantly higher incidence of cardiac death and re-AMI in CE patients compared with non-CE patients (Log-rank, P=0.003).

Non-atherosclerotic coronary artery disease

2. Spontaneous coronary artery dissection

Nakashima T, Yasuda S, et al. Int J Cardiol. 2016 Mar 15;207:341-8.

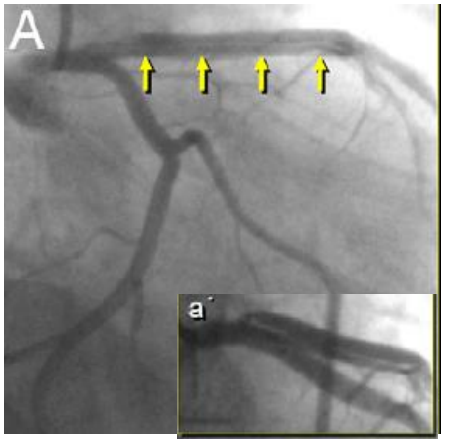
SPONTANEOUS CORONARY ARTERY DISSECTION (SCAD)

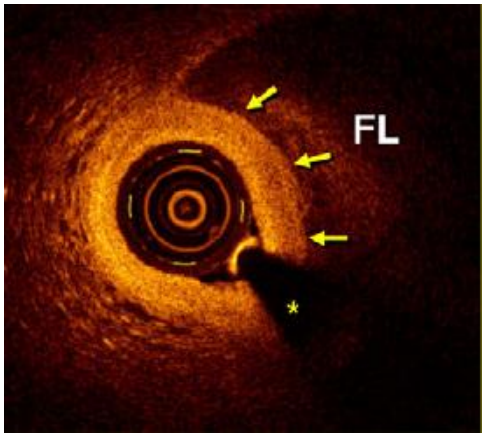
SCAD has been traditionally considered to occur in young females with minimal atherosclerotic risk factors and not as part of a broader clinical spectrum that includes older patients with coronary artery disease (CAD).

SCAD was defined as follows;

I. CAG (NHBLI classification) ; radiolucent area, double lumen, extraluminal cap, spiral luminal filling defect

II. Medial dissection or intramural hematoma without atherosclerotic changes detected by intravascular ultrasonography (IVUS), or optical coherence tomography (OCT)

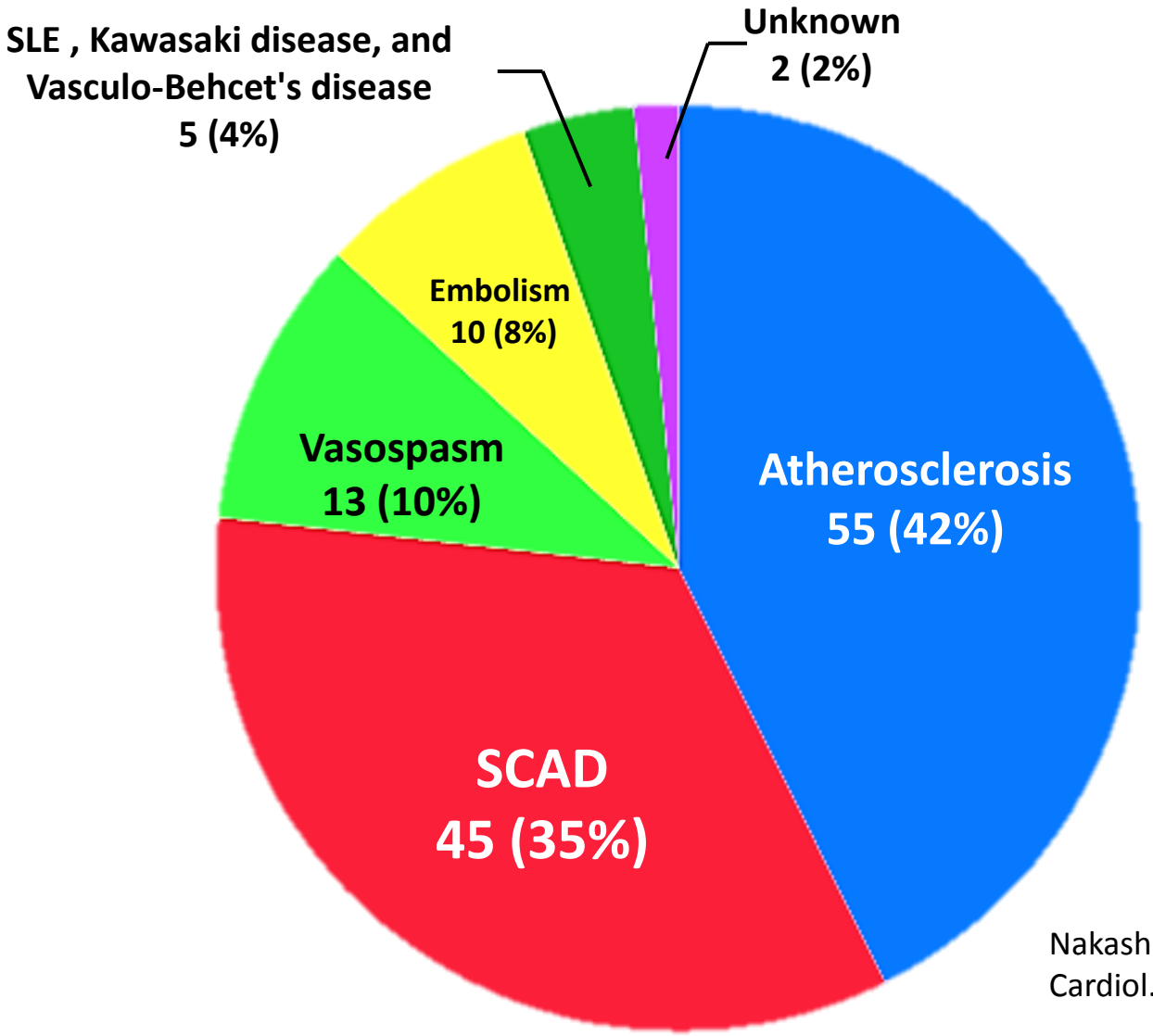




Alfonso F, et al. J Am Coll Cardiol 2012;59:1073-9.
Maehara A, et al. Am J Cardiol 2002;89:466-8.
Huber MS, et al. Am J Cardiol 1991;68:467-71.

Causes of AMI in females aged 50 years or younger

Of the overall 20,195 AMI patients, the prevalence of AMI in female aged 50 years or younger was 0.64% (n=130). While atherosclerosis was the most frequent cause of AMI (n=55, 42%), SCAD was the second most frequent cause (n=45, 35%).

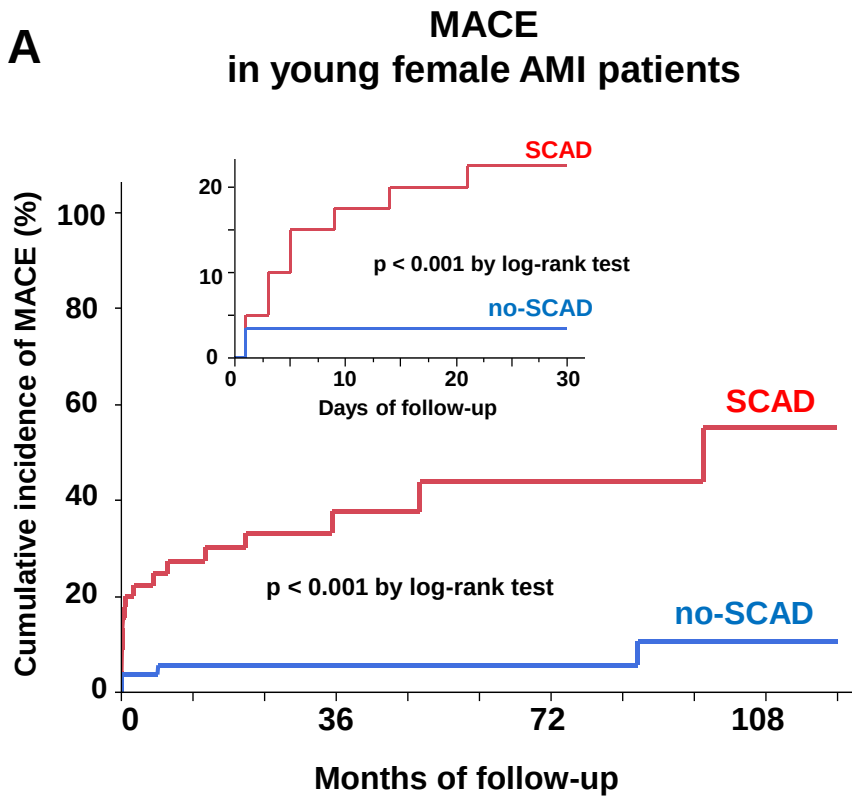


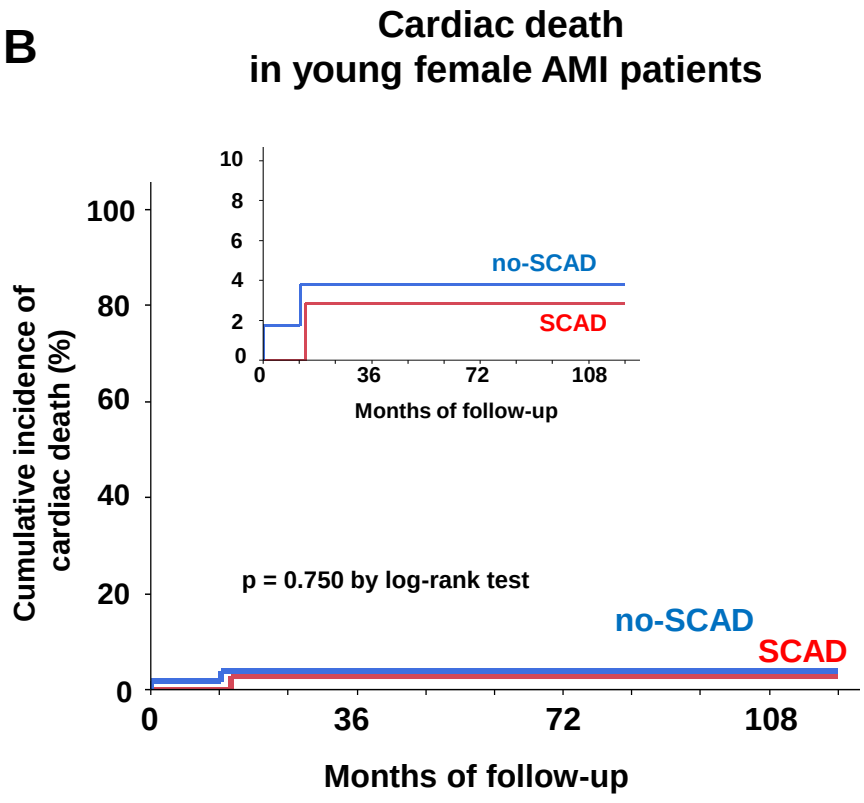
Nakashima T, Yasuda S, et al. Int J Cardiol. 2016 Mar 15;207:341-8.

Long-term outcomes in young female AMI patients in the SCAD and no-SCAD (atherosclerosis) groups; Young female patients with SCAD represent a high-risk subgroup of young female patients with AMI.

(A) Kaplan-Meier analysis showed a significantly higher incidence of MACE in the SCAD group compared with the no-SCAD group .

(B)There were no significant differences in the rate of cardiac death between the 2 groups





Number of patients at risk				
SCAD	45	15	7	4
no-SCAD	55	32	26	13

Number of patients at risk				
SCAD	45	24	9	7
no-SCAD	55	36	27	14

Nakashima T, Yasuda S, et al. Int J Cardiol. 2016 Mar 15;207:341-8.

Atherosclerotic coronary artery disease

3. Coronary artery ectasia

Doi T, Yasuda S, et al. Arterioscler Thromb Vasc Biol. 2017 Dec;37(12):2350-2355.

Coronary artery ectasia (CAE); an infrequently observed vascular phenotype characterized by abnormal vessel dilatation and disturbed coronary flow. its association with cardiac events has not been fully characterized.

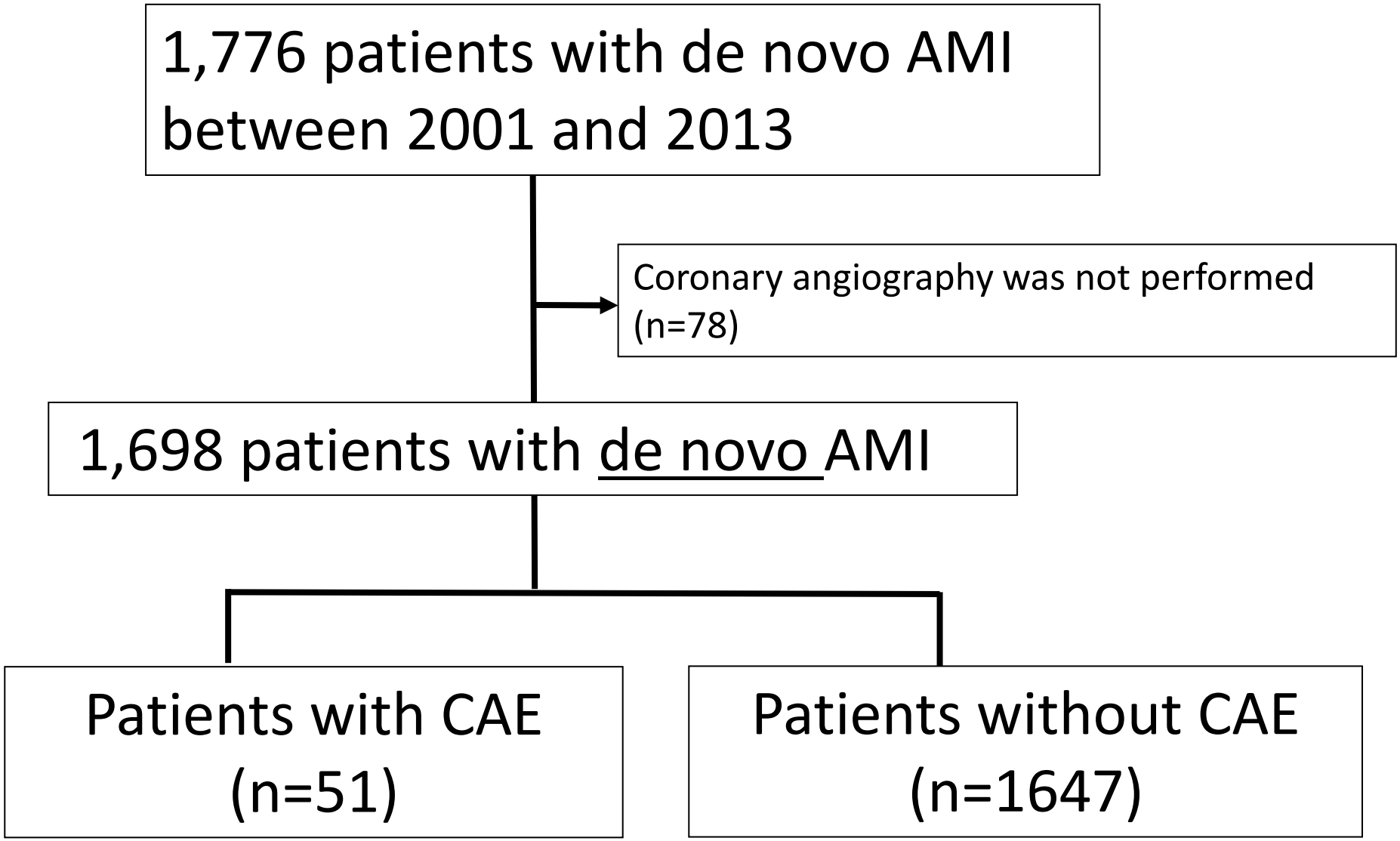
CAE patient with adjacent normal segment.

Segmental CAE: Coronary segment dilatation of more than 1.5-fold diameter of adjacent normal coronary segments.

CAE patient without adjacent normal segment.

Diffuse CAE: Normal reference value of corresponding segment was used from data in age-sex-matched patients without heart disease.

Analysis of CAE in AMI cases



CAE was identified in 3.0% of study subjects.

Doi T, Yasuda S, et al. Arterioscler Thromb Vasc Biol. 2017 Dec;37(12):2350-2355.

Clinical Demographics

	CAE (+) (n=51)	CAE (-) (n=1647)	P value
Age (year±SD)	63±13	68±12	0.005
Male, n(%)	43(84)	1382(71)	0.04
Hypertension, n(%)	38(75)	1087(66)	0.20
Diabetes, n(%)	15(29)	659(40)	0.14
Dyslipidemia, n(%)	24(47)	889(54)	0.30
Smoking, n(%)	44(86)	1169(71)	0.02
BMI≧30kg/m^2, n(%)	6(12)	66(4)	0.008
Numbers of coronary risk (mean ±SD)	2.9±1.1	2.7±1.2	0.04
STEMI, n(%)	43(84)	1317(80)	0.45
Initial Killip class≧2, n(%)	4(8)	296(18)	0.07
Three vessel disease, n(%)	10(20)	362(22)	0.64
Primary PCI, n(%)	42(82)	1219(74)	0.17
Peak CK, units/L, median (IQR)	2109(1089-3694)	2142(1114-3924)	0.66
LVEF (mean±SD)	49±8	45±10	0.003

Doi T, Yasuda S, et al. Arterioscler Thromb Vasc Biol. 2017 Dec;37(12):2350-2355.

PCI Procedures

	CAE(+) (n=38, 83%)	CAE(-) (n=1218, 73%)	P value
Stent implantation, n(%)	24(62)	1108(91)	<0.001
BMS, n(%)	21(55)	974(80)	<0.001
DES, n(%)	3(7)	114(11)	0.38
Non-stent PCI, n(%)	14(38)	110(9)	
POBA, n(%)	12(31)	85(7)	<0.001
Thrombectomy, n(%)	12(31)	24(2)	<0.001
Final TIMI flow grade 3, n(%)	17(45)	1072(88)	<0.001
Mechanical circulatory support			
IABP, n(%)	11(29)	170(14)	0.01

Doi T, Yasuda S, et al. Arterioscler Thromb Vasc Biol. 2017 Dec;37(12):2350-2355.

Summary of MACE

MACE : cardiac death＋non-fatal myocardial infarction

Observational period : median 4.0 years (1.6-7-7)

	CAE (+) (n=51)	CAE（-） (n=1647)	P value
MACE, n(%)	14(28)	132(8)	<0.001
Cardiac death, n(%)	7(14)	82(5)	<0.001
Non-fatal myocardial infarction, n(%)	8(15)	33(2)	<0.001

Patients with CAE more frequently developed nonfatal MI and cardiac death.

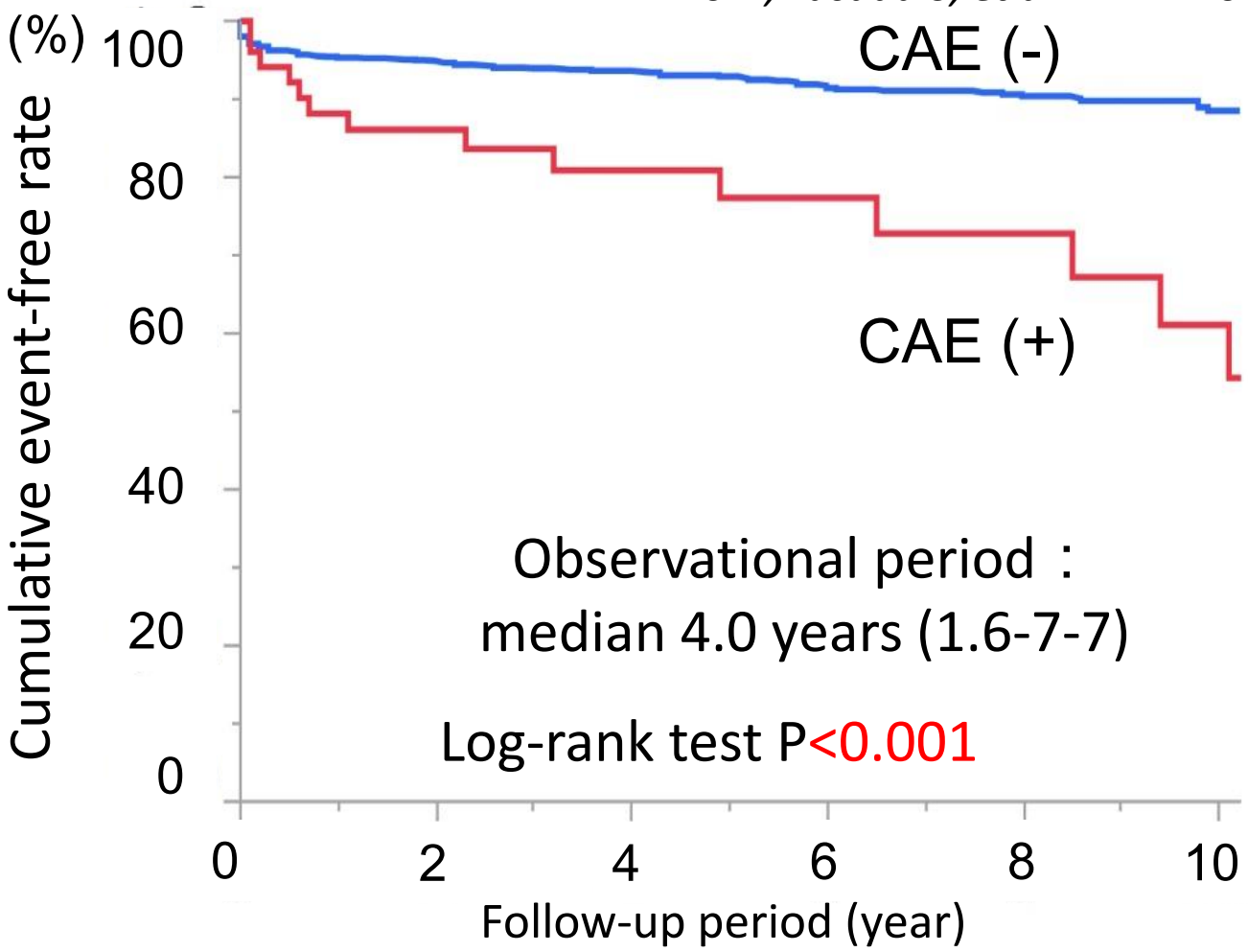
Doi T, Yasuda S, et al. Arterioscler Thromb Vasc Biol. 2017 Dec;37(12):2350-2355.

Long-term Prognosis

MACE (cardiac death＋non-fatal myocardial infarction)

During the observation period, CAE was associated with 3.25-fold greater likelihoods of experiencing MACE (95% confidence interval [CI], 1.88–5.66; *P*<0.001).

Doi T, Yasuda S, et al. ATVB. 2017;37:2350-2355



Long-term Prognosis

Cardiac risks of CAE were consistently observed in a multivariate Cox proportional hazards model.

	Univariate			Multivariate		
	HR	95% CI	P value	HR	95% CI	P value
CAE	3.25	(1.87-5.66)	<0.001	4.50	(2.16-9.36)	<0.001

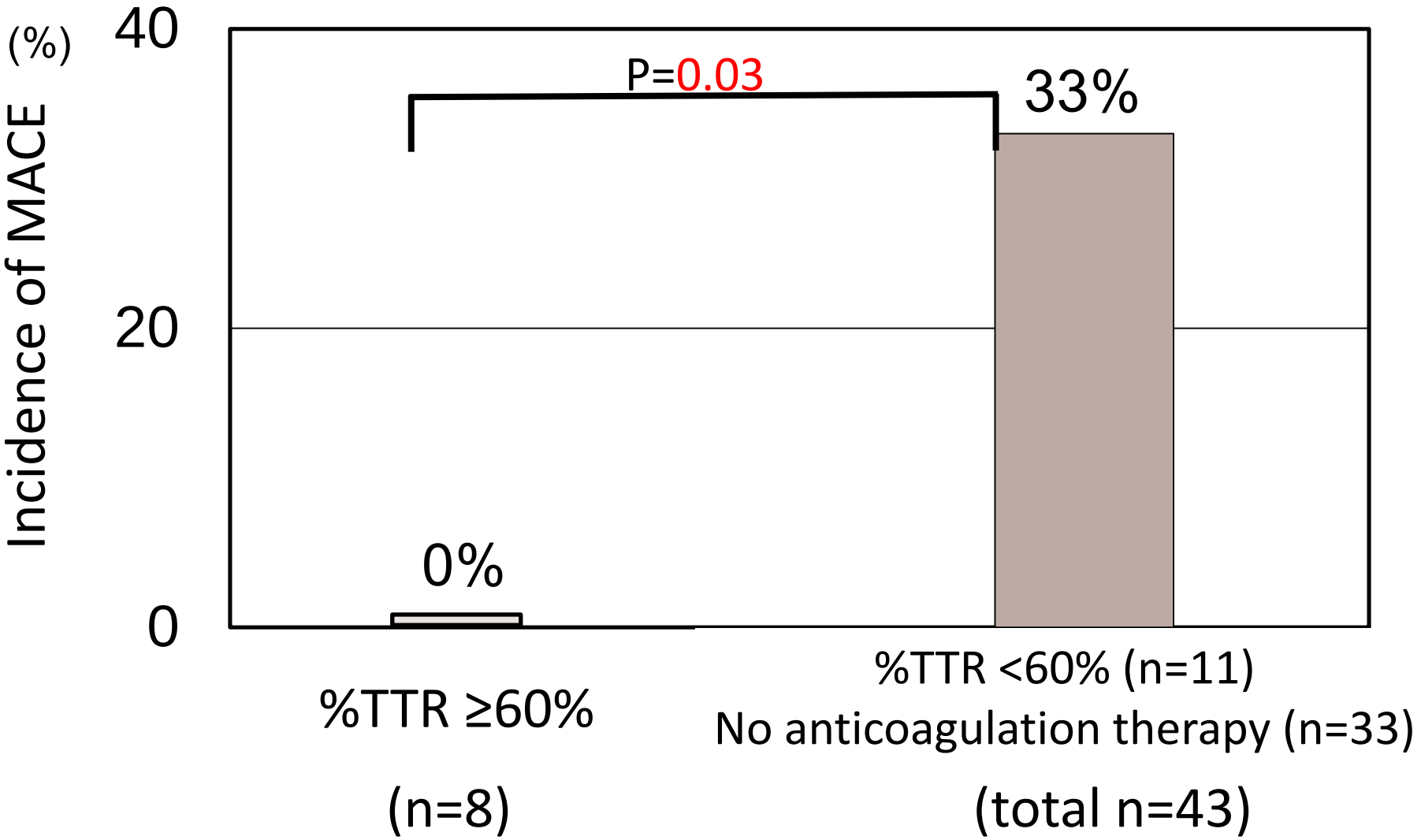
Covariates：

age, sex, BMI≧30, smoking, LVEF, STEMI, peak CK, three vessel disease, Killip class on admission, and CAE

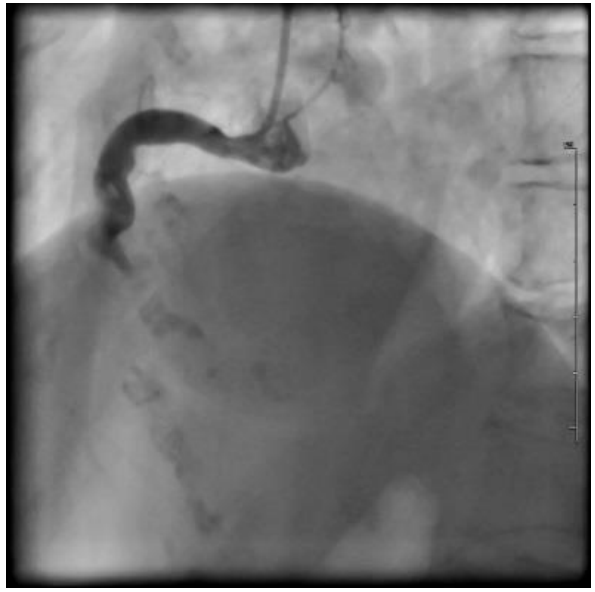
Doi T, Yasuda S, et al. Arterioscler Thromb Vasc Biol. 2017 Dec;37(12):2350-2355.

Anti-coagulation therapy and MACE in Patients with CAE

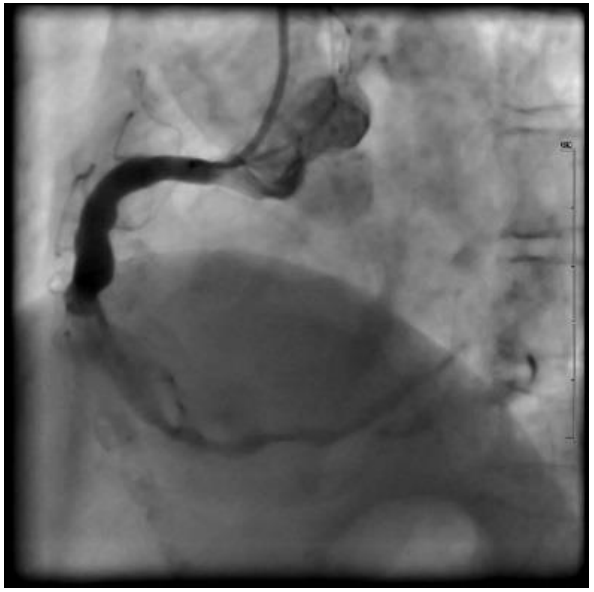
Patients who achieved %TTR (Time in Therapeutic Range) ≥60% with warfarin therapy exhibited a lower occurrence of MACE compared with those with %TTR <60% or without anticoagulation therapy.



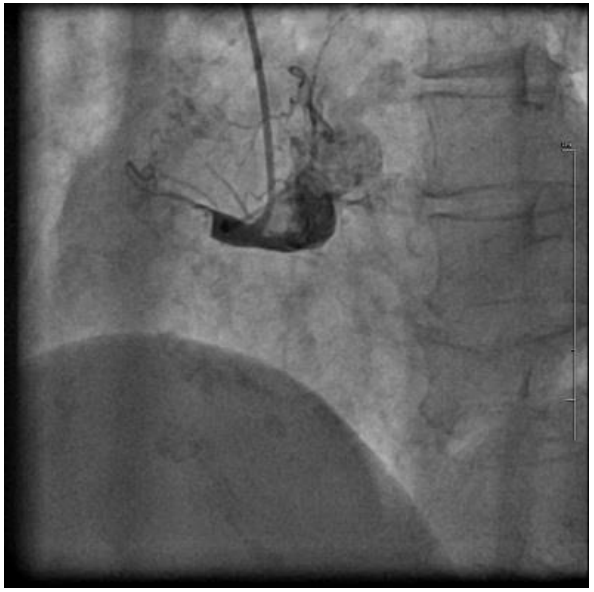
Summary: CAE Predicts Future Cardiac Events in Patients With AMI



Total occlusion of dilated RCA.



PCI (with thrombectomy and POBA) with IABP.



5 years later, RCA occluded again.

Our findings highlight CAE as a high-risk vascular phenotype requiring additional pharmacological approaches to optimally control the coagulation cascade.

Doi T, Yasuda S, et al. Arterioscler Thromb Vasc Biol. 2017 Dec;37(12):2350-2355.

Conclusions

- There has been accumulation of data to guide the identification and management of patients with uncommon atherosclerotic and non-atherosclerotic diseases who are at risk for cardiovascular events.
- The institutional registry will be a major source of data that answer the unmet need in this area.

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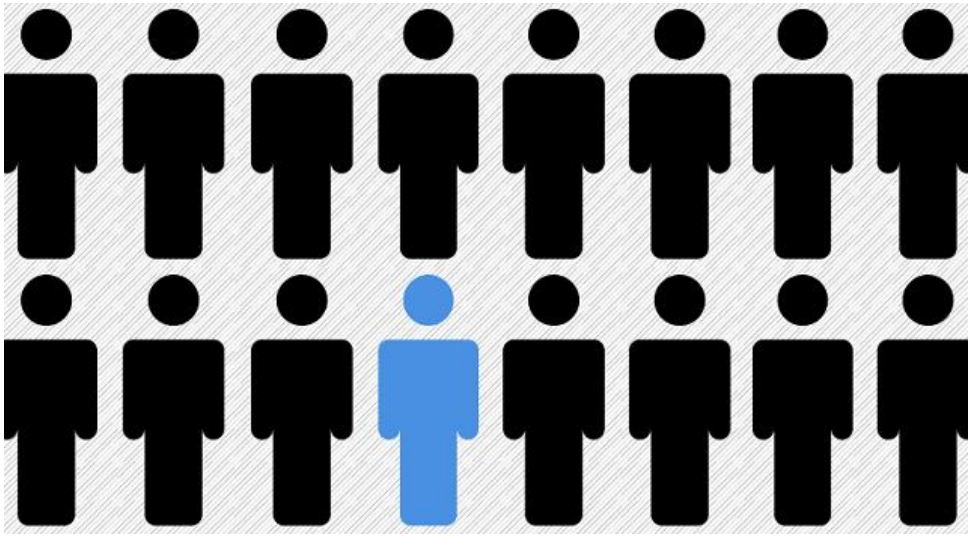

끝까지 경청해 주셔서 감사합니다

May 2, 2018; Department of Cardiovascular Medicine, NCVC