VARIANT-ICD Trial: ICD vs. Medical Therapy Alone in Variant Angina With Aborted SCD

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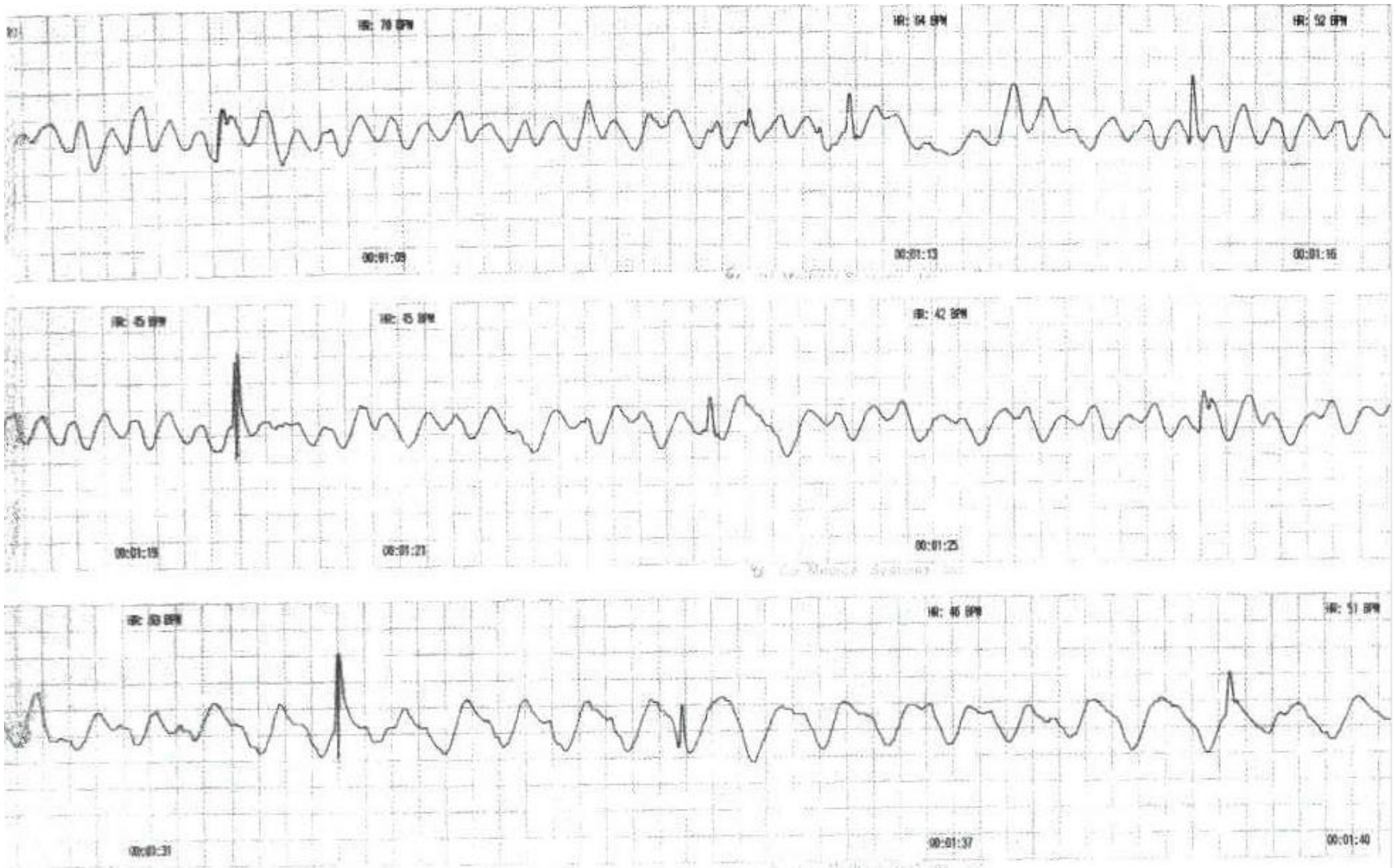
M/62 with Aborted Sudden Cardiac Death

M/62



Vasospastic Angina with Aborted SCD

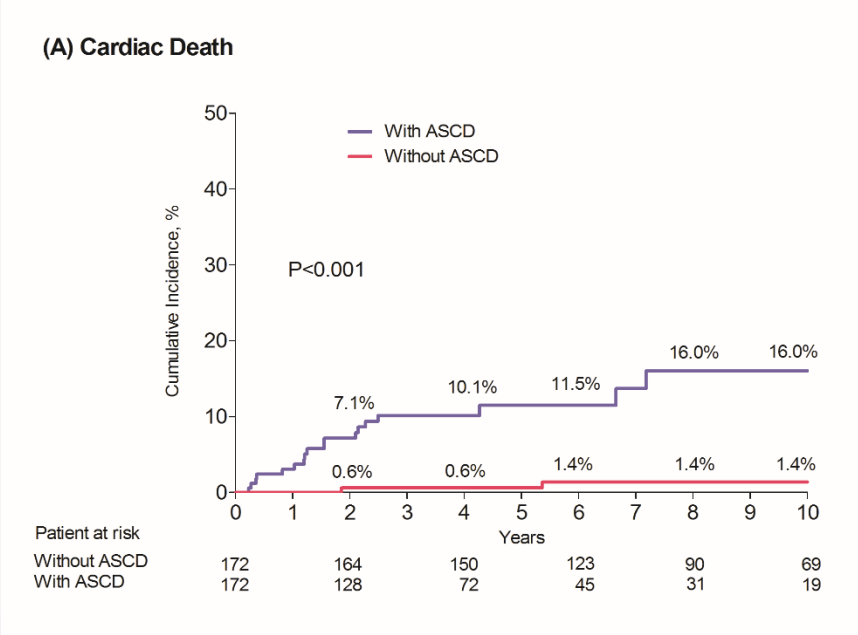
Guideline

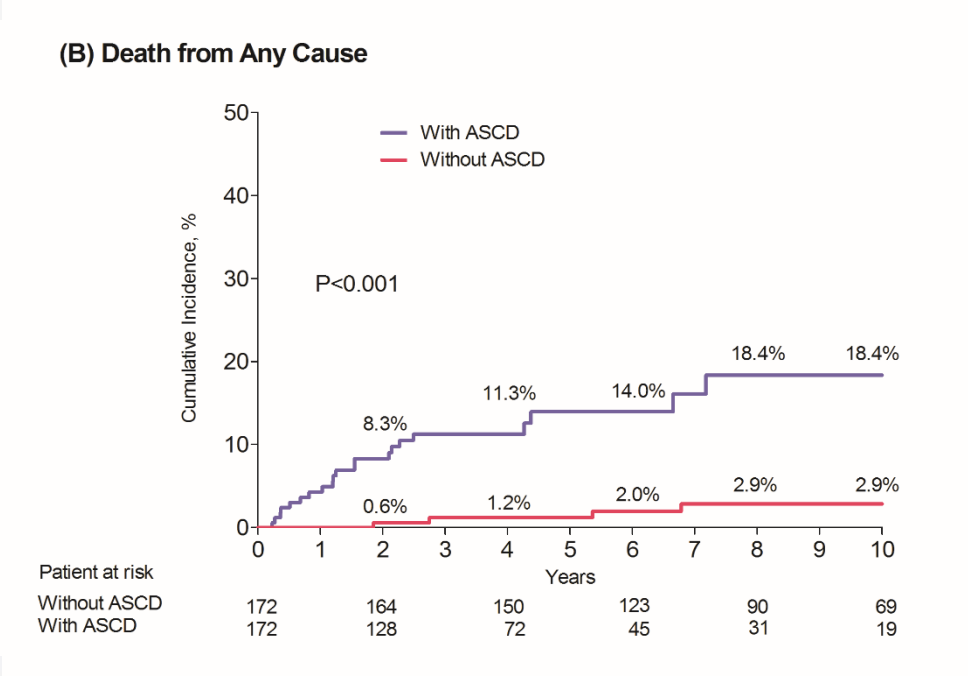
- ICD therapy is indicated in patients who are survivors of cardiac arrest due to ventricular fibrillation or hemodynamically unstable sustained ventricular tachycardia after evaluation to define the cause of the event and to exclude **any completely reversible causes**

- Coronary Spasm: Reversible Cause?

Guidelines for Device-Based Therapy of Cardiac Rhythm Abnormalities J Am Coll Cardiol 2008;51:e1-62

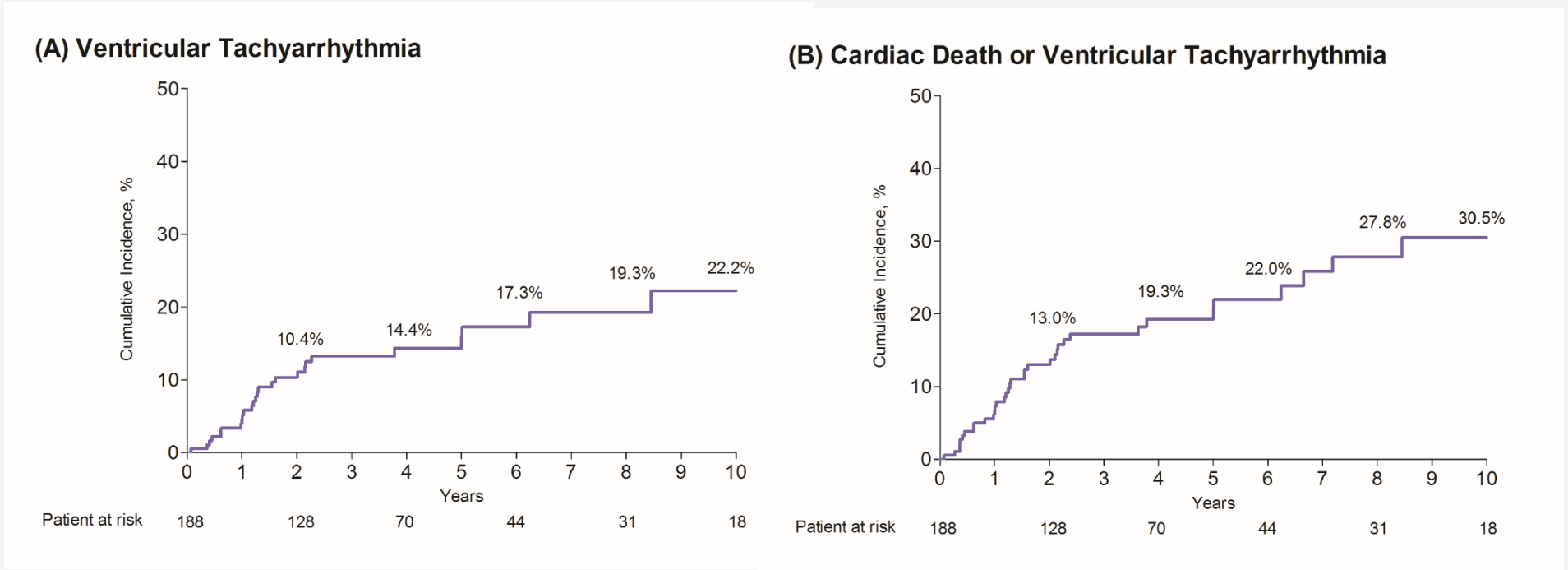
Variant Angina With ASCD





Ahn JM, Lee KH, Choi KJ, Park SJ et al. J Am Coll Cardiol. 2016 Jul 12;68(2):137-45

Variant Angina With ASCD



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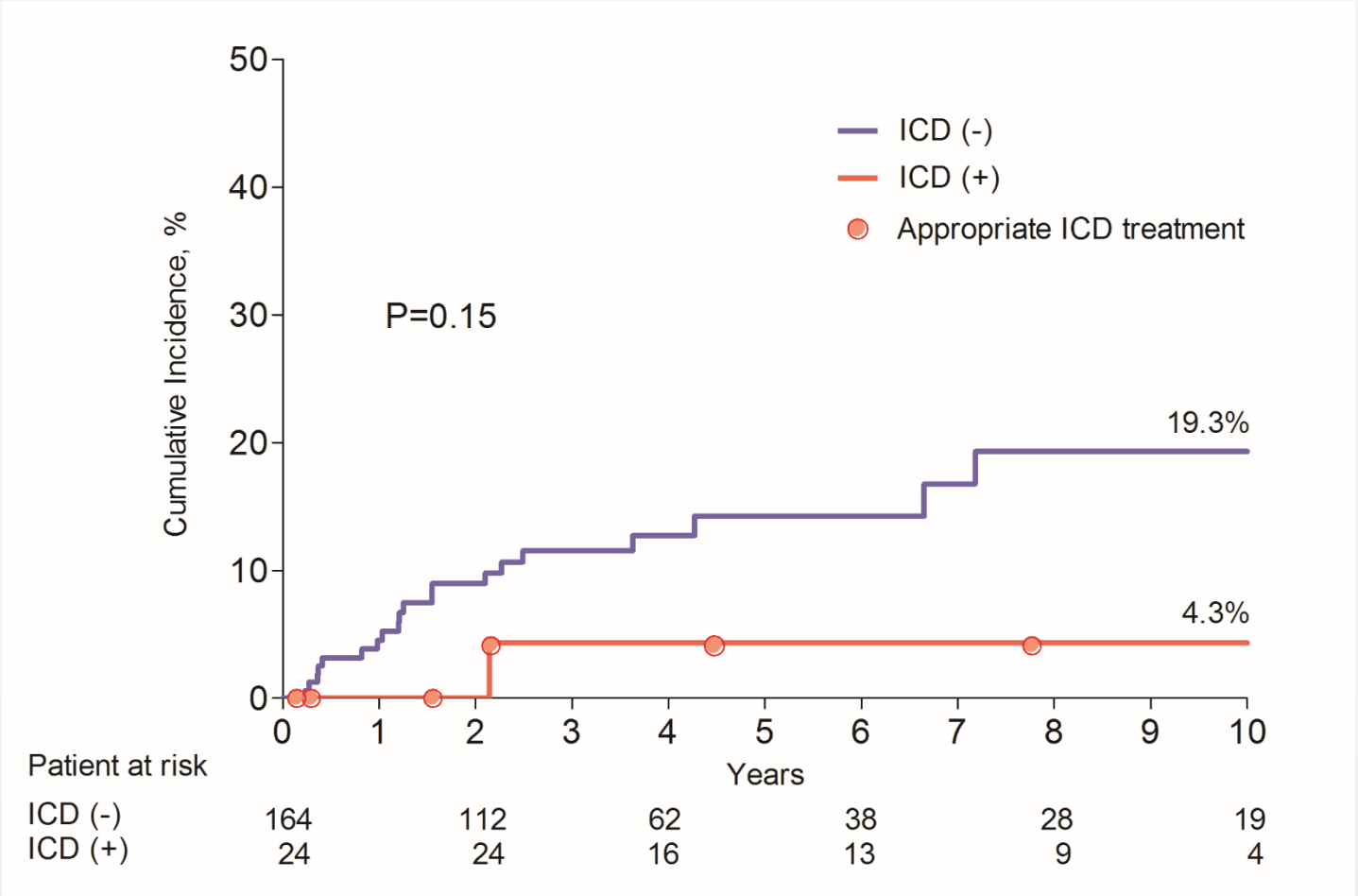
VA With ASCD and ICD ?



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Update from Korean Health Insurance Data

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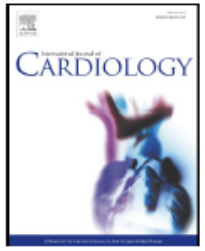

Differential prognosis of vasospastic angina according to presentation with sudden cardiac arrest or not: Analysis of the Korean Health Insurance Review and Assessment Service

Taek Kyu Park [a], Hye Bin Gwag [a], So Jin Park [b], Hyejeong Park [d], Danbee Kang [d], Jinkyeong Park [c], Joongbum Cho [c], Chi Ryang Chung [c], Kyeongman Jeon [c], Gee Young Suh [c,d], Eliseo Guallar [d,e,f], Juhee Cho [d,e], Jeong Hoon Yang [a,c,*]

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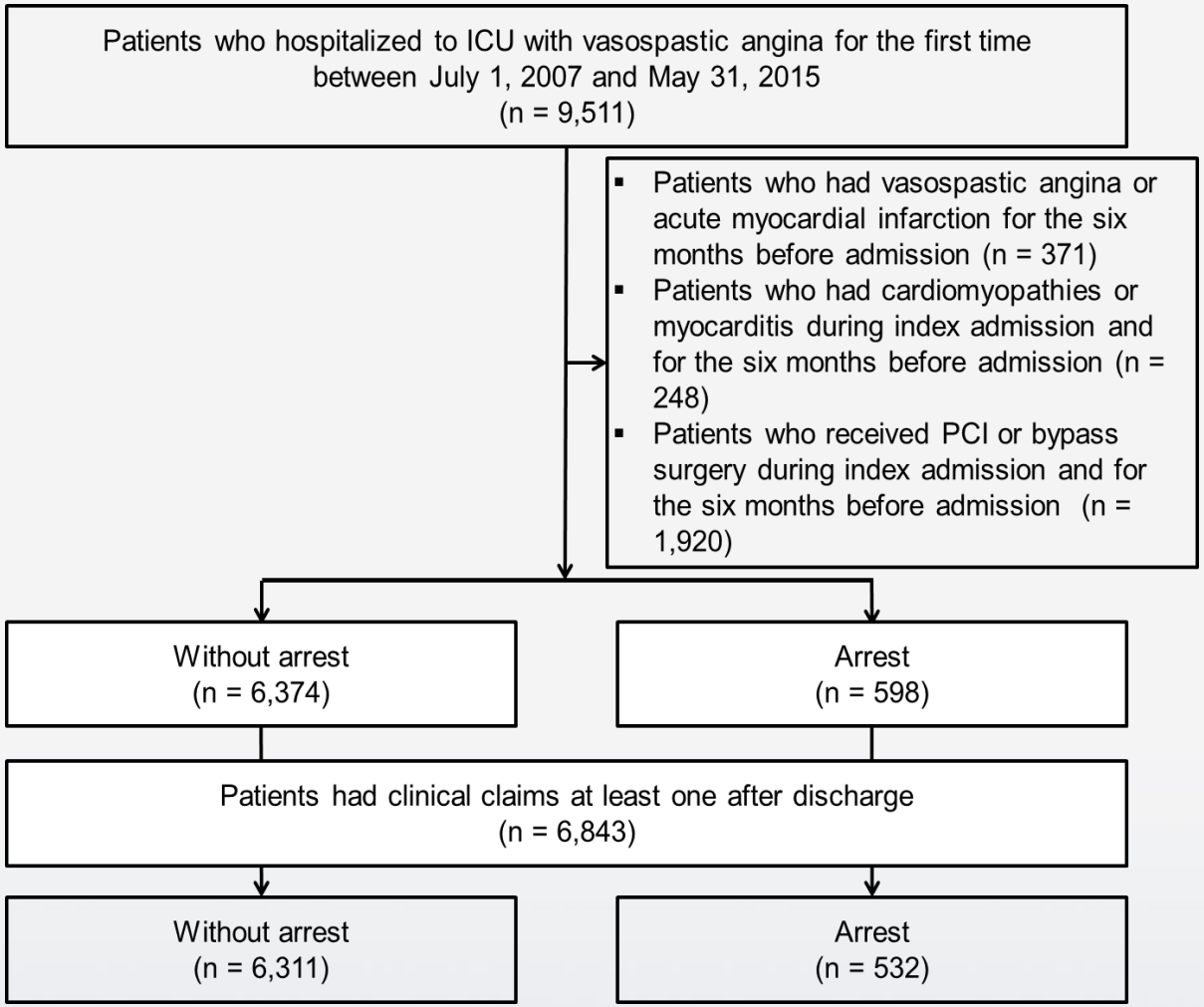
Update from Korean Health Insurance Data



Park TK, Yang JH et al. Int J Cariol. 2018;273:39-43

ASCS patients are Younger, More likely to be Male

	Overall (N = 6972)	Without arrest (N = 6374)	With arrest (N = 598)	p value
Age, years	55.9 ± 11.9	56.2 ± 11.9	52.9 ± 11.1	<0.001
Age ≥ 65 years	1774 (25.4)	1603 (25.2)	171 (28.6)	<0.001
Male	4907 (70.4)	4419 (69.3)	488 (81.6)	<0.001
Hypertension	3891 (55.8)	3568 (56.0)	323 (54.0)	0.355
Diabetes mellitus	2705 (38.8)	2440 (38.3)	265 (44.3)	0.004
Chronic kidney disease	82 (1.2)	73 (1.2)	9 (1.5)	0.435
Charlson index	1.3 ± 1.7	1.3 ± 1.7	2.0 ± 1.8	<0.001
Tertiary referrer hospital	3551 (50.9)	3203 (50.3)	348 (58.2)	<0.001
Admission from ER	5345 (76.7)	4815 (75.5)	530 (88.6)	<0.001
Spasm provocation test	2380 (34.1)	2124 (33.3)	256 (42.8)	<0.001
Year				<0.001
July 2007–2009	1787 (25.6)	1726 (27.1)	61 (10.2)	
2010–2012	2679 (38.4)	2460 (38.6)	219 (36.6)	
2013–2015	2506 (35.9)	2188 (34.3)	318 (53.2)	
Medication at discharge				
Aspirin	6339 (90.9)	5840 (91.6)	499 (83.4)	<0.001
Statin	4147 (59.5)	3839 (60.2)	308 (51.5)	<0.001
Calcium-channel blocker	5983 (85.8)	5407 (84.8)	576 (96.3)	0.021
Nitrate	6205 (89.0)	5661 (88.8)	544 (90.0)	0.107
Nicorandil	3322 (47.7)	3024 (47.4)	298 (49.8)	0.263
Trimetazidine	1244 (17.8)	1157 (18.2)	87 (14.6)	0.028
ACE inhibitor	1401 (20.1)	1276 (20.0)	125 (20.9)	0.606
Angiotensin receptor blocker	1180 (16.9)	1006 (15.8)	174 (29.1)	0.145
ECMO	27 (0.4)	7 (0.1)	20 (3.3)	<0.001
CRRT	42 (0.6)	14 (0.2)	28 (4.7)	<0.001

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ASCD Patients Had Poorer Outcome

	Without arrest ($n = 6374$)	With arrest ($n = 598$)	Univariable		Multivariable[a]		IPTW[b]	
			HR (95% CI)	*p* value	HR (95% CI)	*p* value	HR (95% CI)	*p* value
In-hospital death	47 (0.7)	58 (9.7)	5.83 (3.42–9.97)	<0.001	6.58 (3.98–10.89)	<0.001	6.79 (3.94–11.72)	<0.001
Post ICU outcome	($n = 6311$)	($n = 532$)						
Cardiac arrest	129 (2.0)	31 (5.8)	3.65 (2.56–5.22)	<0.001	4.22 (2.90–6.14)	<0.001	3.18 (2.00–5.04)	<0.001
Myocardial infarction	339 (5.4)	38 (7.1)	1.65 (1.10–2.47)	0.016	1.93 (1.28–2.91)	0.002	2.17 (1.34–3.51)	0.002
Cardiac arrest or myocardial infarction	432 (6.9)	64 (12.0)	2.23 (1.67–2.96)	<0.001	2.61 (1.95–3.49)	<0.001	2.52 (1.72–3.67)	<0.001

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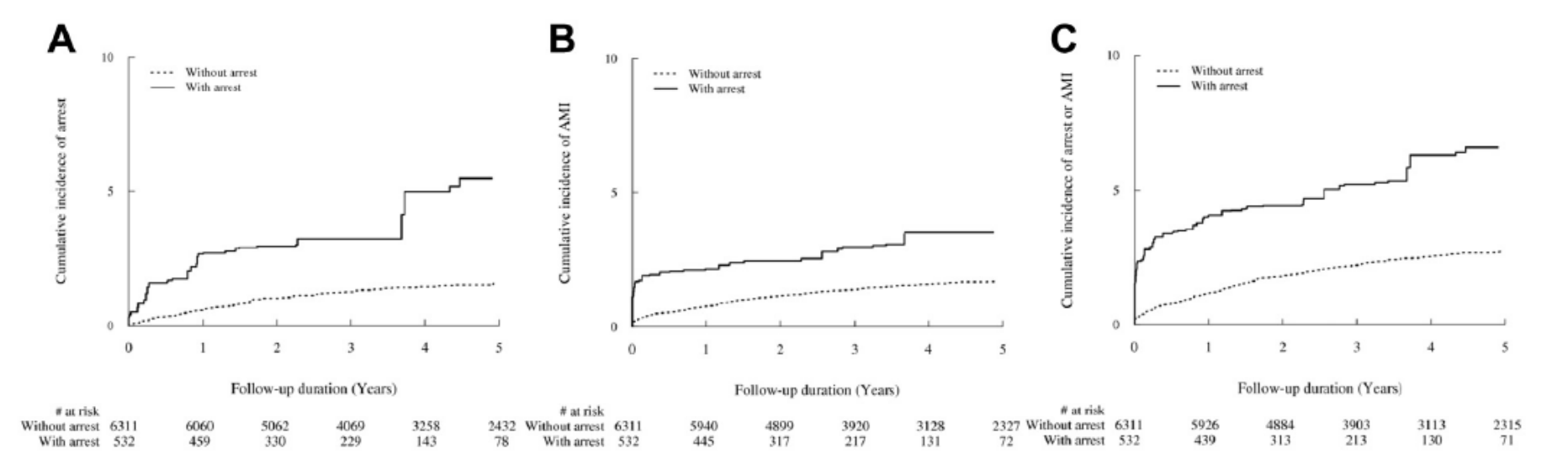
ASCD Patients Had More Arrest or MI

Cardiac Arrest *AMI* *Arrest or MI*



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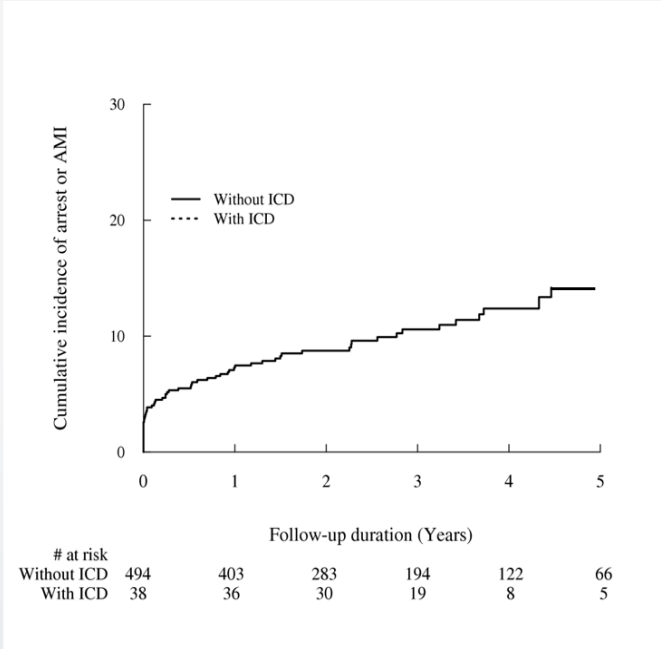
ICD Impact

- 38 ASCD Patients received ICD during index Hospitalization.
- None of these patients suffered from cardiac arrest or AMI.
- 12.1% (64) w/o ICD experienced cardiac arrest or AMI (P=0.009).

A



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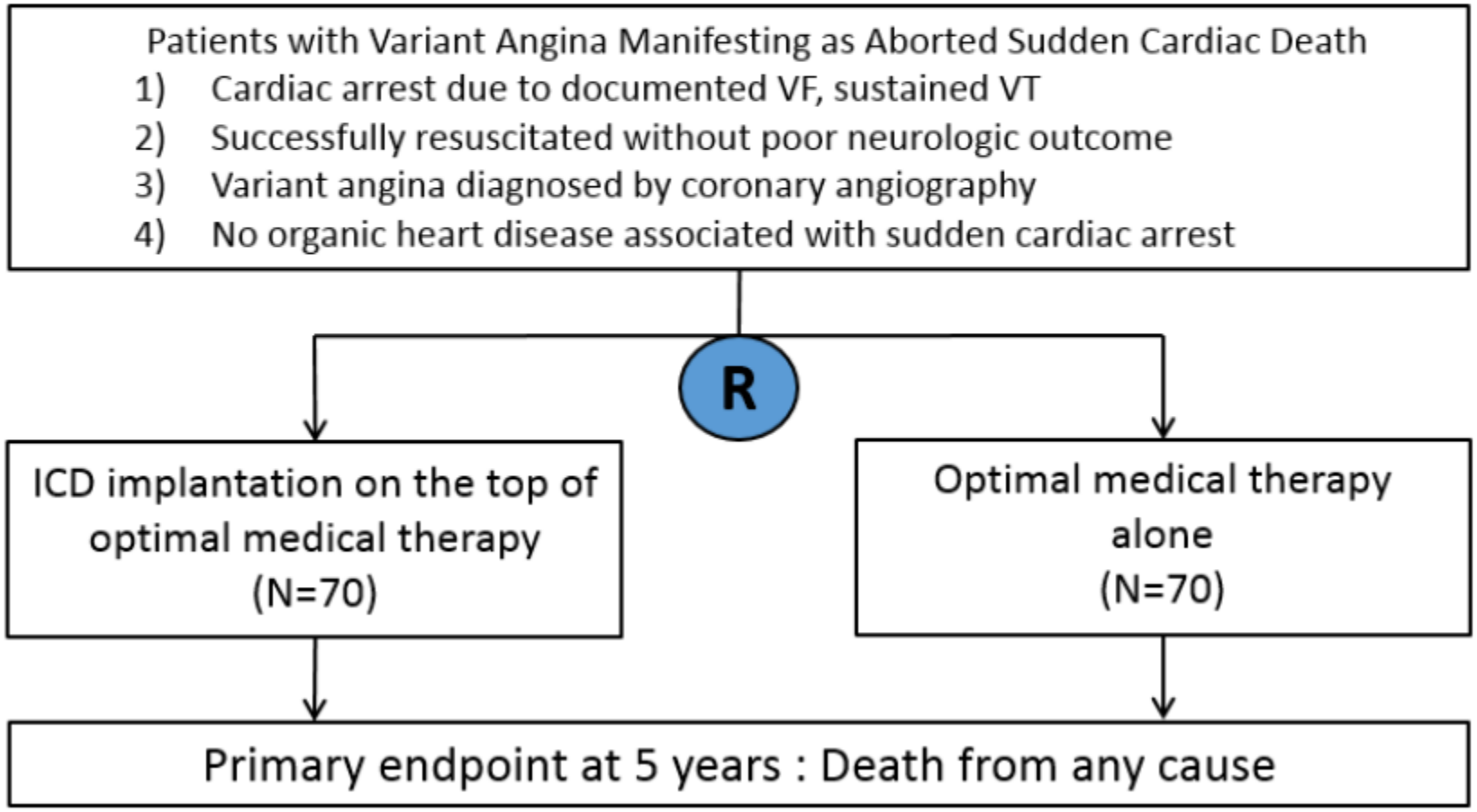
ICD + OMT versus OMT In Patients with Variant Angina Manifesting as Aborted Sudden Cardiac Death

VARIANT-ICD Trial



Eligible For the Trial

- <6months of randomization
- Documented VF or rapid VT
- Documented coronary spasm
    - Spontaenous spasm with STE
    - Positive provocation CAG
- No other heart diseases associated with sudden cardiac death

Ergonovine CAG

- To definitely rule out significant coronary artery disease, all ASCD patients will receive coronary angiography
- When coronary angiogram shows normal coronary artery, patients will receive ergonovine provocation test
- The definition of positive result is total or subtotal (>90% luminal diameter narrowing) occlusion in ergonovine provocation coronary angiography.

Primary Outcome

- Death from any cause at the 5 years of follow-up

Secondary Outcome

- Cardiac death
- Death from arrhythmia
- Cardiac arrest defined as sudden loss of consciousness requiring direct-current
- cardioversion or defibrillation to restore consciousness or a stable blood pressure and rhythm.
- Recurrence of ventricular tachyarrhythmia (ventricular tachycardia or fibrillation)
- Hospitalization due to unstable angina, acute myocardial infarction, heart failure, cardiac arrhythmia
- Appropriate ICD therapies defined as device-administered antitachycardia or defibrillation treatment for ventricular tachyarrhythmia that had not terminated spontaneously
- Inappropriate ICD therapies
- Major device-related complications
- Stroke

Inclusion Criteria

- Age 18 years or older
- Patients experienced successfully resuscitated cardiac arrest due to documented ventricular fibrillation or sustained rapid ventricular tachycardia within 6 months of randomization
- Diagnosed as variant angina, defined by spontaneous coronary spasm with ST elevation (≥0.1mV) in the coronary angiogram and/or documented coronary spasm on ergonovine provocation coronary angiography

Exclusion Criteria

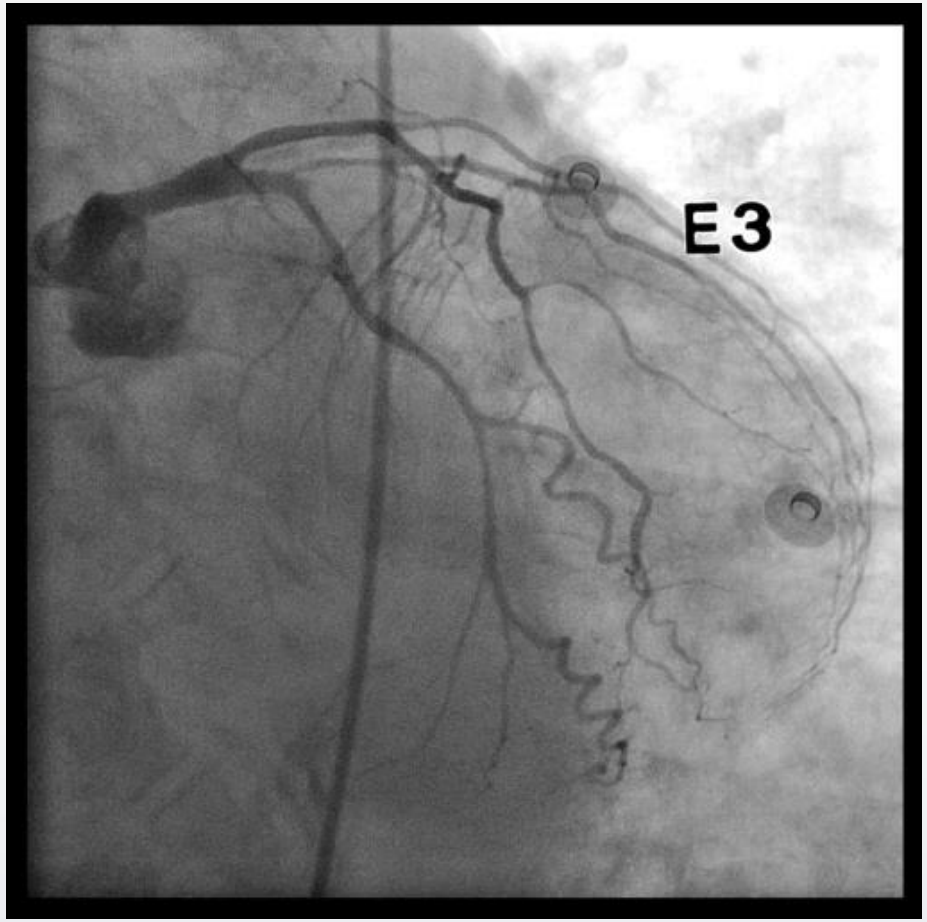
- Significant (>50%) coronary artery stenosis on coronary angiography
- Organic heart disease known to be associated with sudden cardiac arrest.
  - Heart failure with reduced ejection fraction (LV EF < 35%)
  - Presence of LV akinesia or aneurysm
  - Hypertrophic cardiomyopathy
  - Arrhythmogenic right ventricular dysplasia
- CHF New York Heart Association functional class III or IV
- prior history of atrial or ventricular arrhythmia requiring class I or III antiarrhythmic drugs (flecainide, propafenone, amiodarone, sotalol and dronedarone)
- Prior catheter ablation for ventricular arrhythmia
- Primary cardiac electrical diseases (long QT syndrome, Brugada syndrome, catecholaminergic polymorphic ventricular tachycardia)
- Prior pacemaker or ICD
- 2nd or 3rd degree AV block not related to coronary ischemia, requiring permanent pacemaker
- Patients with poor neurologic outcome (defined as cerebral performance category scale ≥3)
- Life expectancy <2years
- Psychiatric illnesses that may be aggravated by device implantation or that may

Ergonovine CAG

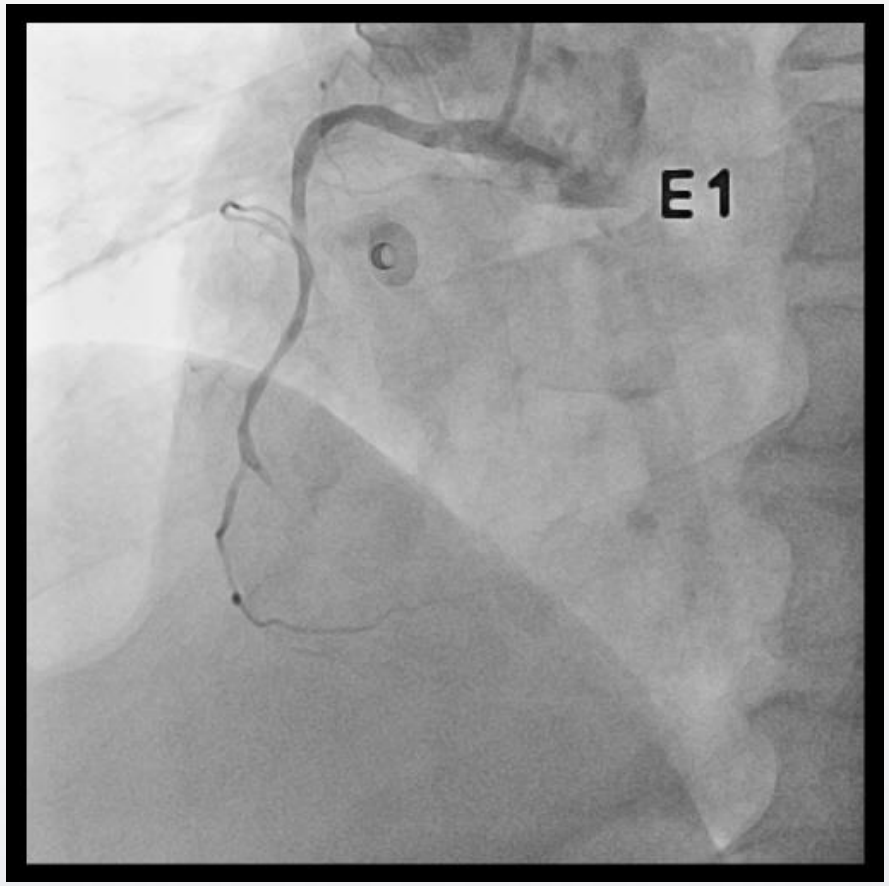
- Total
- Subtotal (90% luminal diameter narrowing)

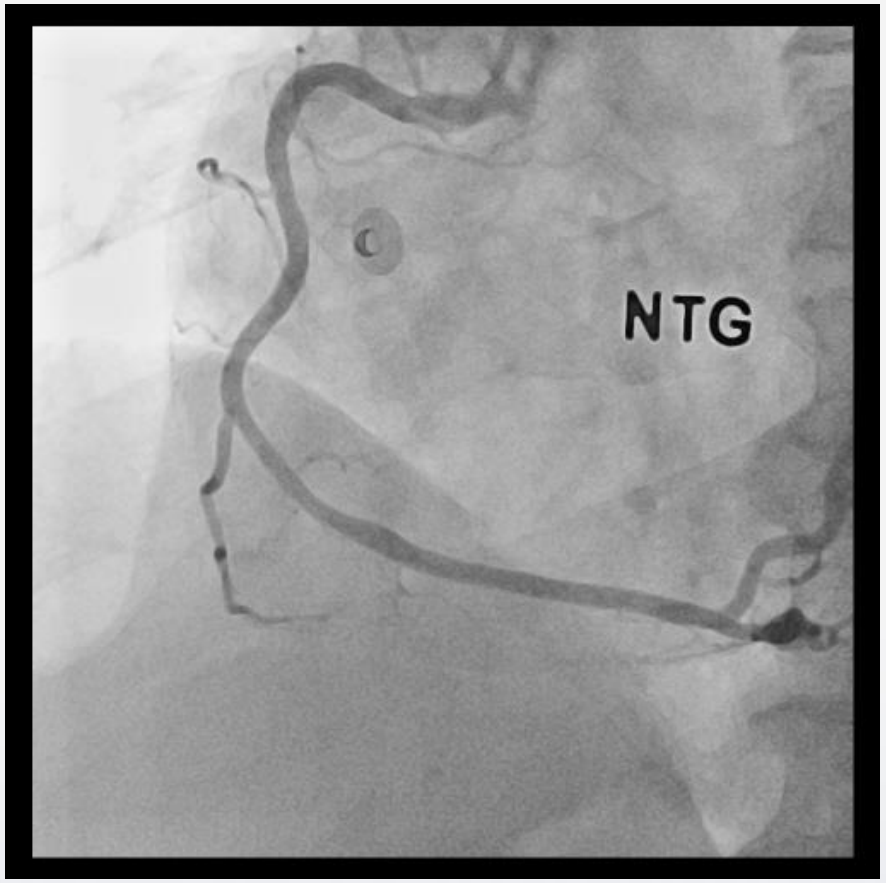
Diffuse Intermediate Narrowing (X)

Ergonovine CAG



Ergonovine CAG





OMT

- Management of daily life (correction of risk factors)
  - ✓Smoking cessation, no or moderate drinking
  - ✓Maintenance of ideal body weight, avoidance of excessive fatigue and mental stress
  - ✓Blood pressure control, correction of impaired glucose tolerance and lipid abnormalities
- Calcium-channel blockers
- Long-acting nitrates
- Nicorandil

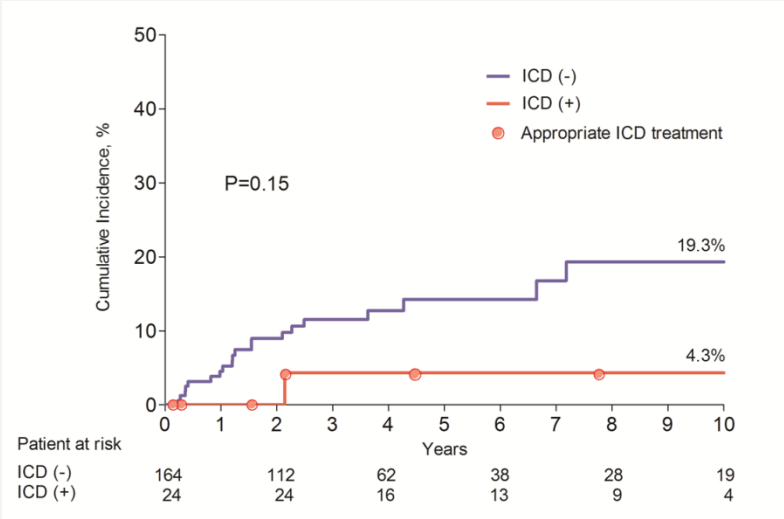
ICD implantation

- A single-coil ICD will be implanted according to available clinical practice guideline within 30 days after randomization.

- Patients receiving ICD therapy will be followed up every 3-6 months for clinical review, device interrogation, and capacitor reform or in the event of symptom onset or device discharge.

- **Cost**

Sample size calculation



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- A two-sided log-rank test with an overall sample size of ***140*** subjects (***70*** in the control group and ***70*** in the treatment group) achieves 80.0% power at a 0.05 significance level to detect a hazard ratio of 0.187 when the proportion of the surviving in the control group is 0.85. The study lasts for 2 time periods of which subject accrual (entry) occurs in the first time period. The assumed event rates are 3% in ICD plus OMT arm and 15% in OMT arm at 5 years.

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