

Ablation should be the first line therapy for
patients with appropriate ICD shocks

Jun Kim MD

University of Ulsan College of Medicine

Asan Medical Center

If (catheter) ablation is *highly effective (curative)* in *treatment of ventricular arrhythmias (tachycardia or fibrillation)* leading to ICD shocks irrespective of underlying heart disease (*ischemic, nonischemic or electrical disorders*), ablation should be the first line therapy.

1.

ICD shocks

(in 24 hours)

=

electrical storm

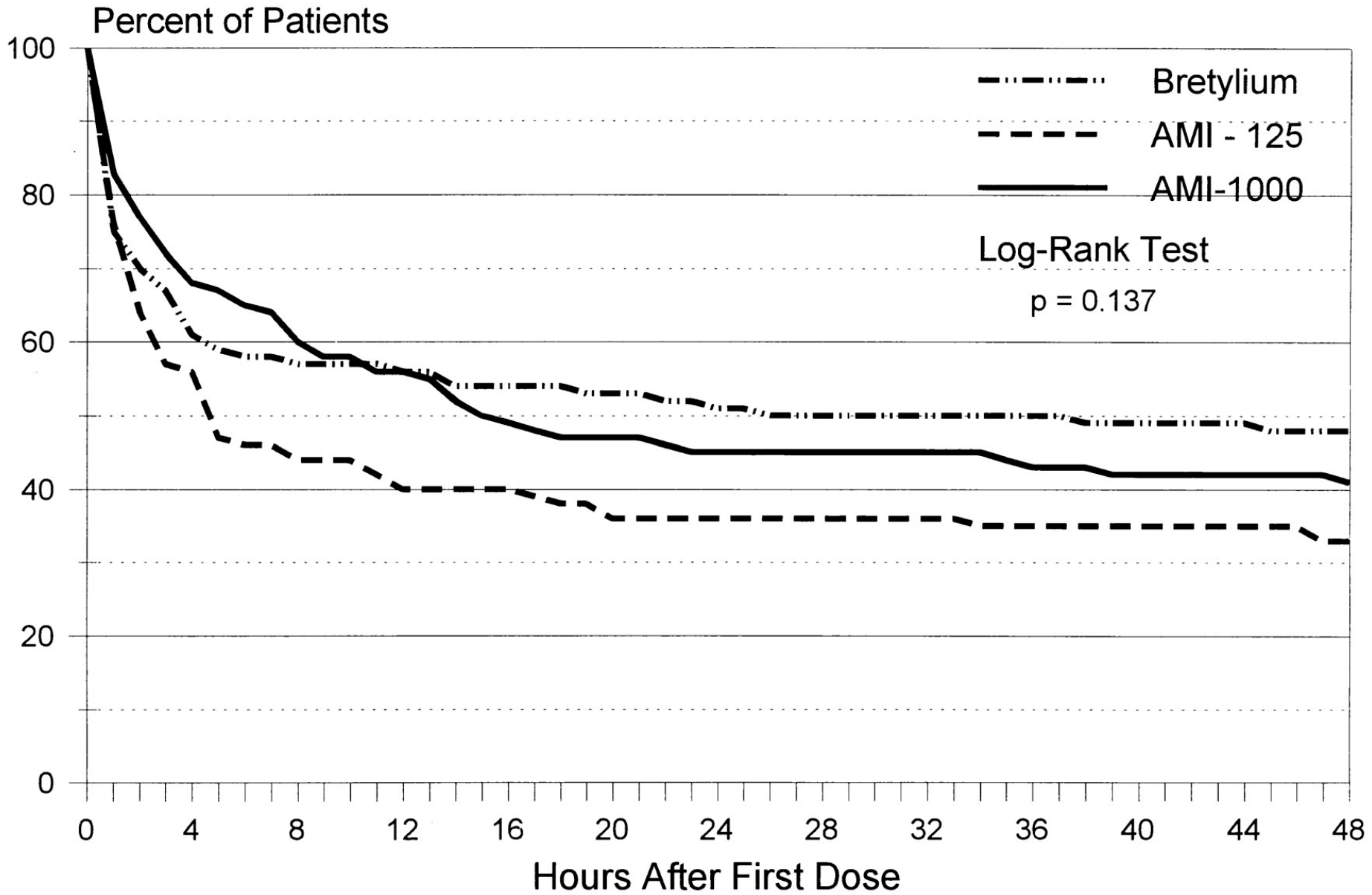
Electrical storm

Occurrence of highly malignant, hemodynamically destabilizing ventricular tachycardia or fibrillation, that recurs frequently or incessantly. (Kowey, PR, Can J Cardiol, 1996)

Ventricular tachycardia or fibrillation resulting in ICD intervention ≥ 3 times a single 24-hr period (Credner SC, Hohnloser SH, JACC, 1998)

Inclusion criteria of Randomized, double-blind comparison of intravenous amiodarone and bretylium in the treatment of patients with recurrent, hemodynamically destabilizing ventricular tachycardia or fibrillation. The Intravenous Amiodarone Multicenter Investigators Group

if they had *incessant (recurring immediately after termination) VT, VF, or at least 2 (mean, 4.93) episodes of hemodynamically destabilizing VT or VF in the 24 hours before enrollment. Hemodynamic instability* was defined as a loss of consciousness or a systolic blood pressure of <80 mm Hg with signs or symptoms of shock.



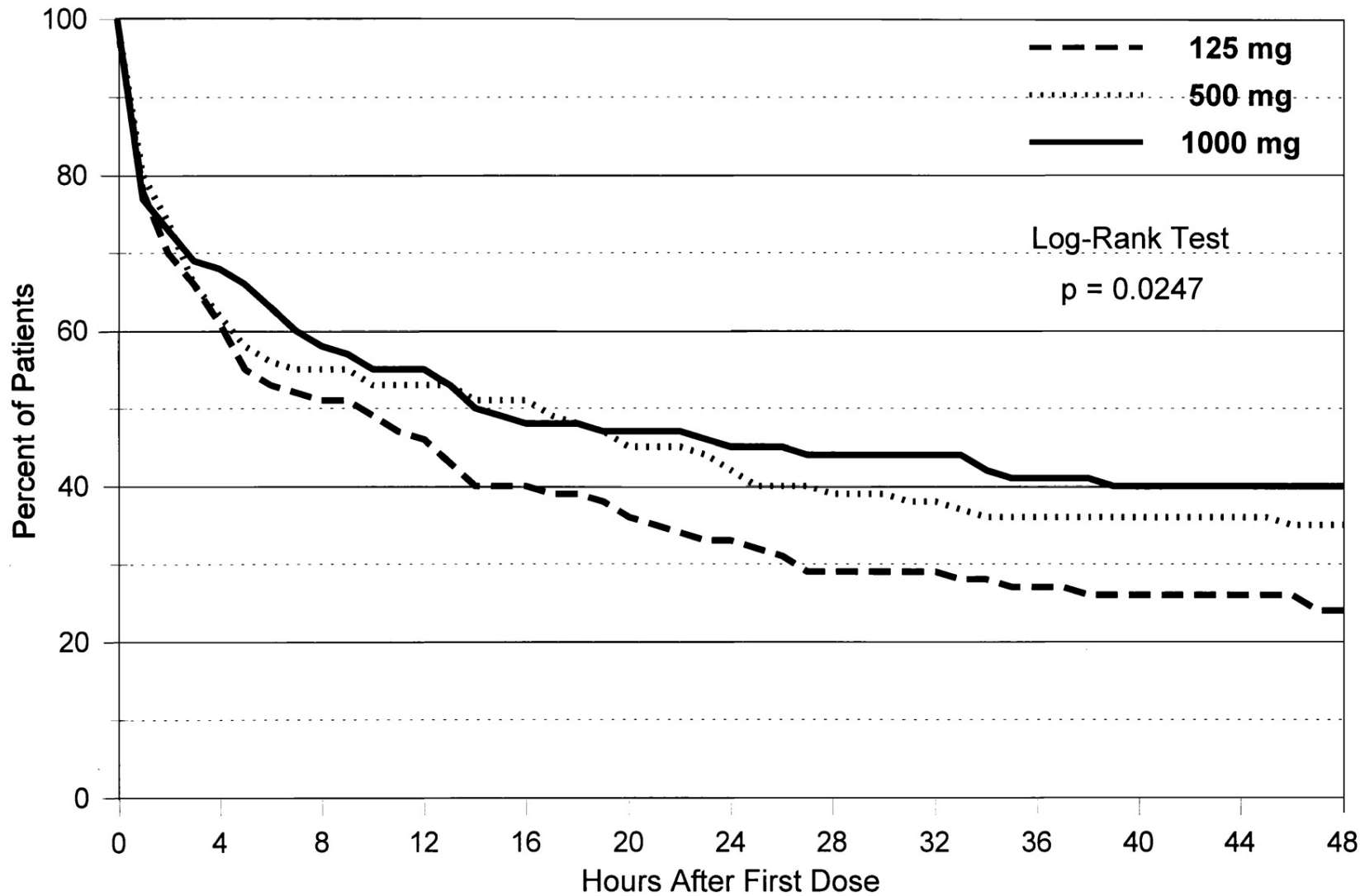
Dose-Ranging Study of Intravenous Amiodarone in Patients With Life-Threatening Ventricular Tachyarrhythmias

incessant (recurrent, despite attempted cardioversion), hemodynamically destabilizing VT or **at least two episodes** of hemodynamically destabilizing *VT or VF within the 24 hours* before enrollment.

Hemodynamically destabilizing was defined as a fall in systolic blood pressure to <80 mm Hg and/or clinical signs and *symptoms of shock* requiring immediate nonpharmacological intervention.

They were also required to be refractory to or intolerant of standard doses of lidocaine, procainamide, and bretylium within the 72 hours before enrollment.

time to first event analysis



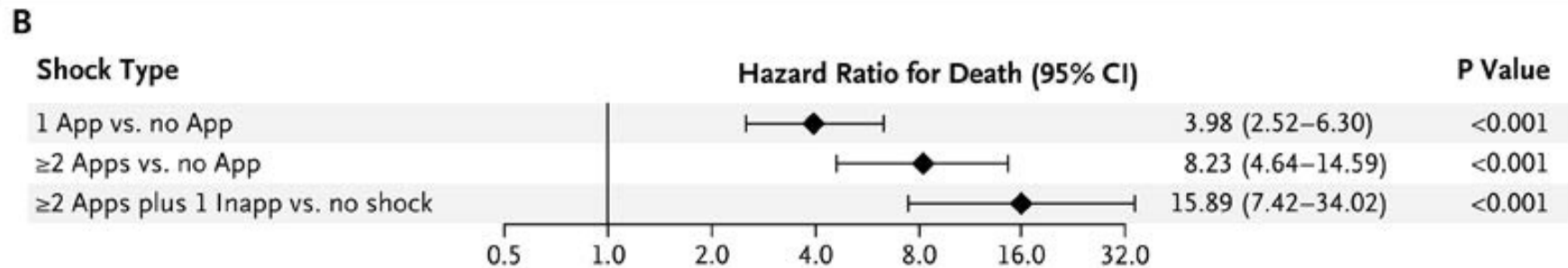
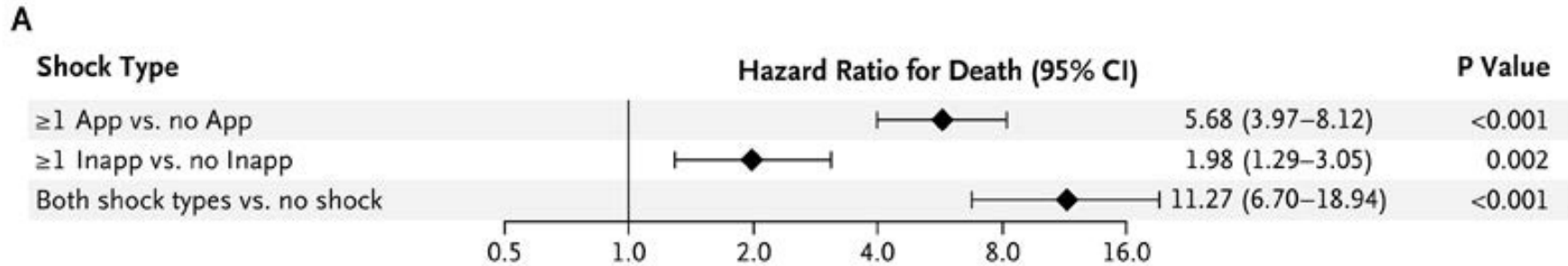
Electrical storm

- 61 ± 14 years, male (81%)
- Coronary artery disease (69%), DCM (21%)
- LVEF $36 \pm 14\%$
- 10% (14/136) patients at average 133 ± 135 days after ICD implantation
- Arrhythmia episode 17 ± 17 (3-50)
- Beta-blocker + amiodarone
- Not related to mortality

2.

- No increased mortality (Greene M, Europace, 2000)
- Increased mortality (Exner DV, Circulation, 2001)
 - AVID (The antiarrhythmics versus implantable defibrillators) Trials
 - Electrical storm (N=90), 9.2 ± 11.5 months post ICD implant
 - Independent risk factor of mortality RR 2.4
 - Increased mortality within 3 months of ES RR 5.4

Prognostic importance of defibrillator shocks in patients with heart failure



Meta-analysis of 13 studies involving 5912 patients (857 with electrical storm) (Guerra F, Europace, 2014)

- RR of all-cause mortality 3.15[2.22,4.48]
- RR of all-cause mortality 2.51[1.38,4.58] with history of VT/VF but no ES
- RR of all-cause mortality 3.41[1.52,7.31] with no history of VT/VF
- RR of all-cause mortality, heart transplantation, hospitalization for decompensated HF or cardiogenic shock 3.39[2.31,4.97)

2.

- Catheter ablation of electrical storm after myocardial infarction (Bänch D, Circulation, 2003)
- Many other report on catheter ablation
- 3 RCT demonstrating superiority of catheter ablation over medical treatments
- So, catheter ablation of VT or VPC triggering VF should be the first line therapy.

Conclusions

In patients with **ischemic** cardiomyopathy and an ICD who had ventricular tachycardia **despite antiarrhythmic drug therapy**, there was a significantly lower rate of the **composite primary outcome** of death, ventricular tachycardia storm, or appropriate ICD shock among patients undergoing catheter ablation than among those receiving an escalation in antiarrhythmic drug therapy.

(Funded by the Canadian Institutes of Health Research and others;

VANISH ClinicalTrials.gov number, [NCT00905853](https://clinicaltrials.gov/ct2/show/study/NCT00905853).)

(From Sapp JL, N Eng J Med 2016;375:111-121)

- MI
- ICD
- VT during RX with amiodarone or class I or III within 6 Mo
 - ≥ 3 episodes of VT treated with ATP (1 symptomatic)
 - ≥ 1 appropriate ICD shock
 - ≥ 3 episode of VT within 24 hours
 - Sustained VT at a rate below ICD detection rate
 - All VT; monomorphic, rate < 250 bpm

Escalated therapy

- amiodarone 400 mg BD for 2 w \rightarrow 400 mg QD for 4 w \rightarrow 200 mg QD
- amiodarone 400 mg BD for 2 w \rightarrow 400 mg QD for 1 w \rightarrow 300 mg QD
- amiodarone ≥ 300 mg + mexiletine 200 mg TID

Ablation

- stable VT; entrainment mapping
- unstable VT; substrate mapping
- Fast VT (< 300 ms), polymorphic VT not targeted

Primary endpoint : composite of death, VT storm, and appropriate ICD shock after a 1 month treatment period

Outcome	Escalated Therapy N=127	Catheter Ablation N=132	Hazard Ratio (95% CI)	P value
Primary outcome	87(68.5)	78(59.1)	0.72(0.53-0.98)	0.04
Death	35(27.6)	36(27.3)	0.96(0.60-1.53)	0.86
from cardiovascular cause				
from noncardiovascular cause				
from unknown cause				
Appropriate ICD shock after 30 days	54(42.5)	50(37.9)	0.77(0.53-1.14)	0.19
Ventricular tachycardia storm after 30 days	42(33.1)	32(24.2)	0.66(0.42-1.05)	0.08
~~~~~				
Sustained VT below ICD detection limit				
at any time	13(10.2)	4(3.0)	0.27(0.09-0.84)	0.02
after 30 days	8(6.3)	3(2.3)	0.33 (0.09-1.25)	0.09

*(From Sapp JL, N Eng J Med 2016;375;111-121)*



# VTACH

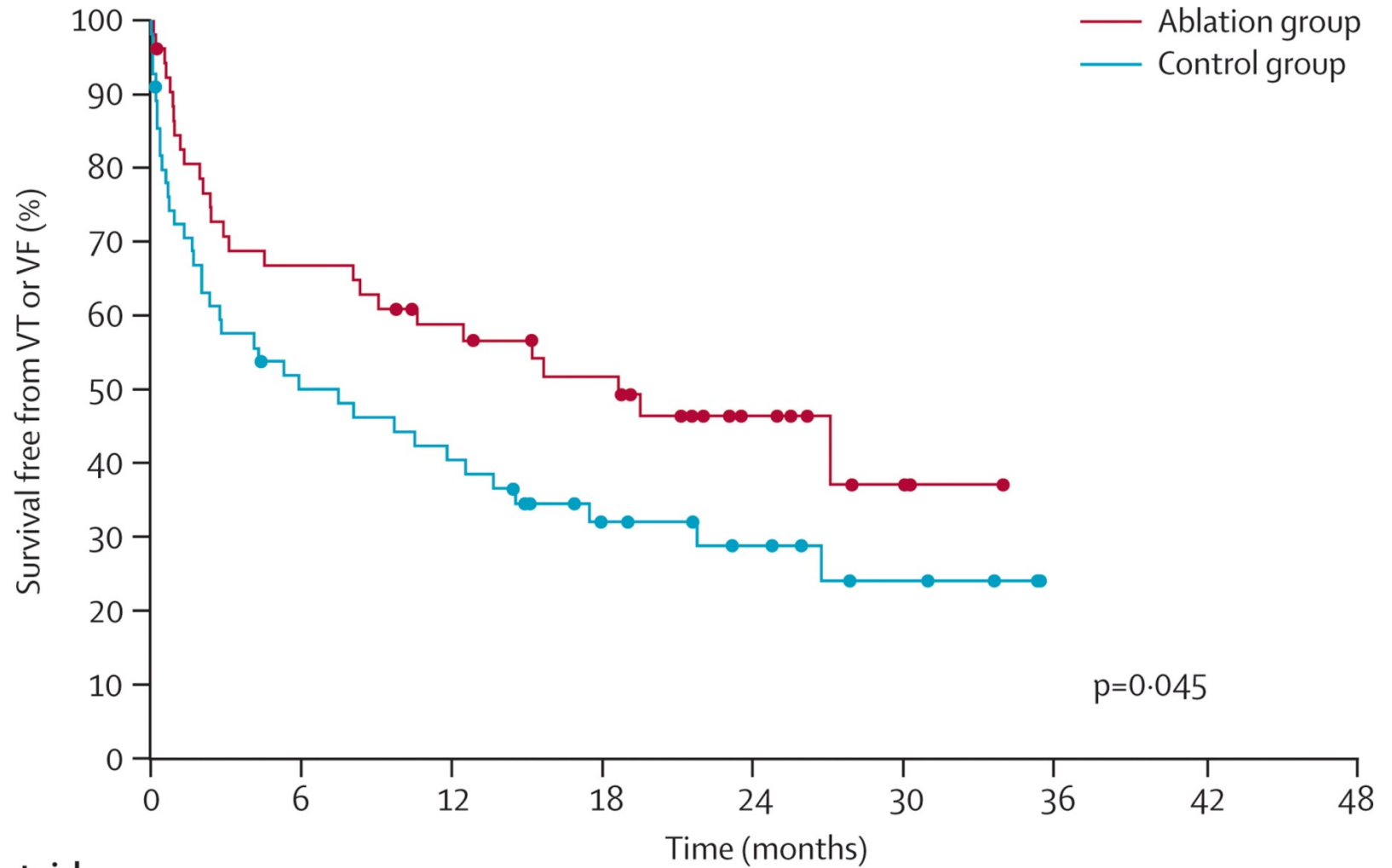
- Stable clinical VT
  - not related to cardiac arrest, syncope
  - SBP > 90 mmHg
- CAD, previous MI
- LVEF ≤ 50%

Electrophysiologic study to induce VT

Ablation → ICD  
3D EAM  
Entrainment mapping  
Substrate mapping

ICD

Primary endpoint : time from ICD implant to recurrence of any Sustained VT or VF



**Number at risk**

Ablation group	52	34	28	21	9	3	0
Control group	55	26	21	12	8	4	0

	Ablation (N=52)	Control (N=55)	HR (95%CI)	P value
Time to 1 st VT or VF	15.9(1.7)	11.3(1.5)	0.61(0.37,0.99)	0.045
24-month event-free survival(%)				
VT(EGM documented)	46.6%	28.8%	0.61(0.37-0.99)	0.045
Hospital admission for cardiac reasons	67.4%	45.4%	0.55(0.30-0.99)	0.044
<b>VT storm</b>	<b>75%</b>	<b>69.4%</b>	<b>0.73(0.36-1.50)</b>	<b>0.395</b>
Death	91.5%	91.4%	1.32(0.35-4.94)	0.677

## SMASH-VT

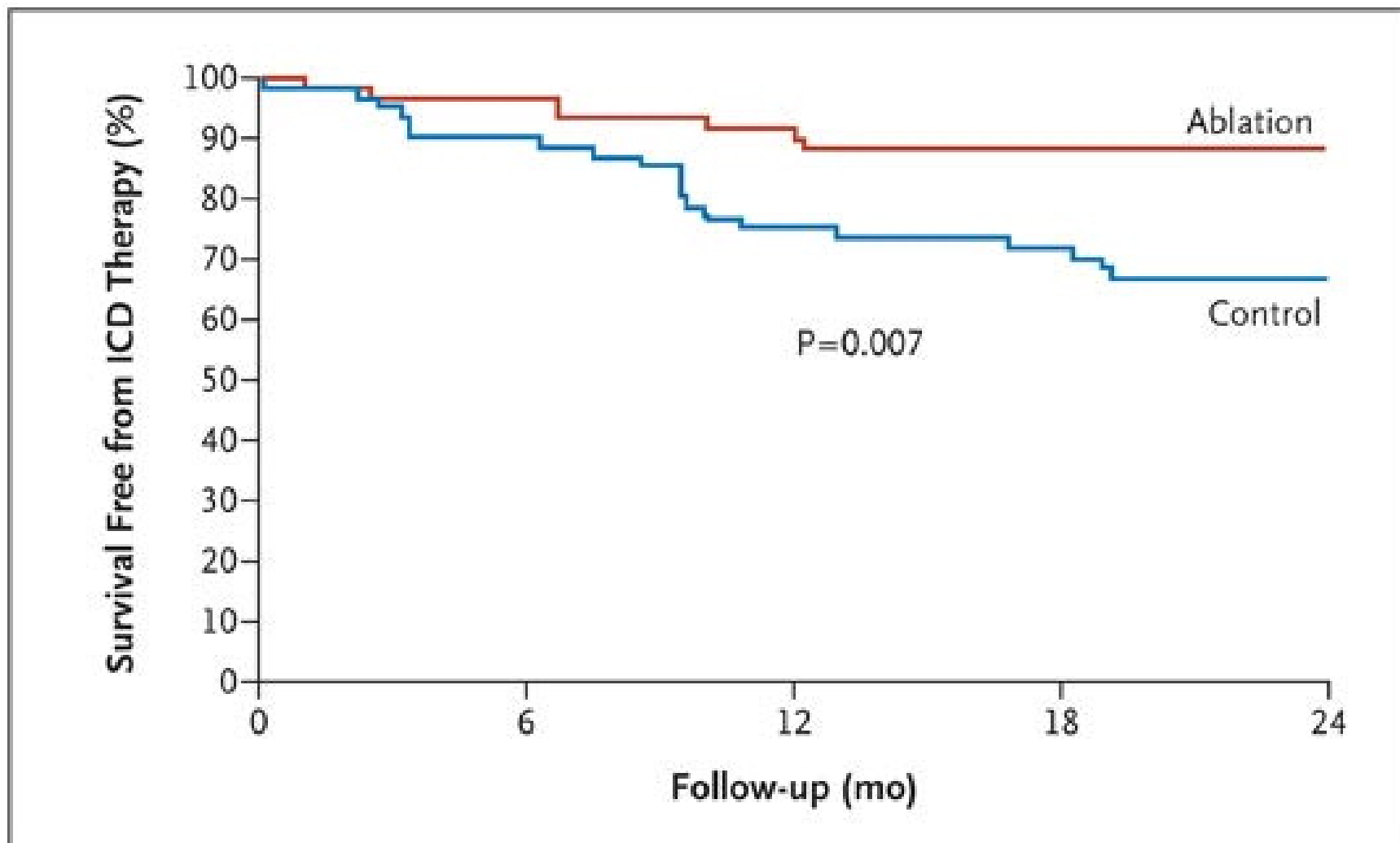
- MI
- planned ICD
  - for VF, unstable VT, syncope and inducible VT
- prior ICD (<6 mo)
  - Appropriate ICD Tx

**Exclusion: class I/III AAD, incessant/multiple VTs**

Ablation  
3D EAM  
Substrate mapping

Control

**Primary endpoint : survival free from any appropriate ICD therapy**



	Ablation (N=64)	Control (N=64)	HR (95%CI)	P value
ICD events (shock+ATP)	8(12)	21(33)	0.35 (0.15,0.78)	0.007
ICD shocks	6(9)	20(31)	0.27(0.11-0.67)	0.003
<b>ICD storms</b>	<b>4(6)</b>	<b>12(19)</b>	<b>0.30(0.09-1.00)</b>	<b>0.06</b>
Death	6(9)	11(17)	0.59	0.29
CHF	3(5)	6(9)		
<b>VT storm</b>	<b>0</b>	<b>1(2)</b>		
cancer	1(2)	0		
pulm embolism	1(2)	0		
unknown	1(2)	4(6)		

	Non-ablation Tx	Ablation Tx
Trial 1	42/127	32/132
Trial 2	17/55	13/52
Trial 3	12/64	4/64
Electrical storm	71	49
No electrical storm	175	199

Chi-square statistic 5.5654

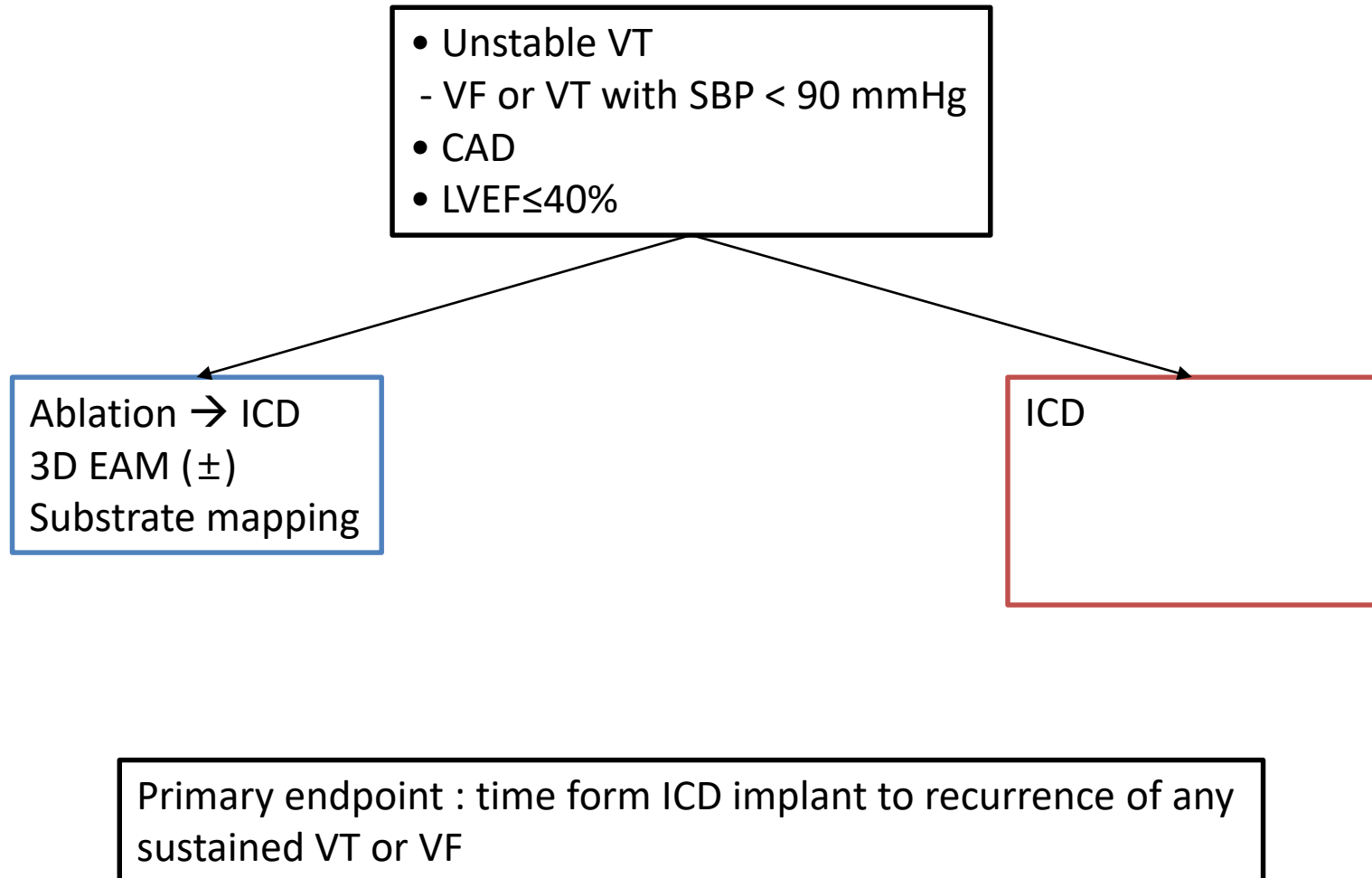
P <0.05

Catheter ablation is superior in preventing electrical storm

In patients with prior MI, VT/VF either on AAD or off AAD

Compared with non-ablation treatment.

## SMS (Substrate modification study)





## Adverse events related to catheter ablation

3 rd degree AV block	(2)
Cardiac tamponade	(2)
Pneumothorax	(0)
Lead dislodgement/repositioning	(3)

NO difference in 1st VT occurrence  
Freedom free VT/VF: 49% (RFCA)  
vs 52.4% (ICD)

NO difference in electrical storm

# Successful ventricular tachycardia ablation in patients

with electrical storm *reduces recurrences and improves survival.*

From International VT Ablation Center Collaborative group (IVTCC)

*Vergara P et al. Heart Rhythm 2017 Accepted*

Patients with ES

- more inducible VT ( $2.5 \pm 1.8$  vs  $1.9 \pm 1.9$ )
- higher in-hospital mortality (6.2% vs 1.4%)
- higher VT recurrence (32.1% vs 22.6%)
- higher 1-year mortality (20.1% vs 8.5%)

Patients without any inducible VT after RFA (N=394)

- better survival (86.3%) vs others (N=220, nonclinical VT, clinical VT, not done)

# ESC GUIDELINES

Level of  
evidence **B**

Data derived from a single randomized  
clinical trial or large non-randomized  
studies.

Urgent catheter ablation in specialized or experienced centres is recommended in patients presenting with incessant VT or electrical storm resulting in ICD shocks.

**I**

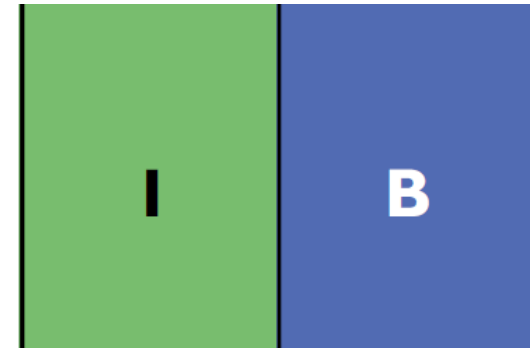
**B**

183

183. Carbucicchio C, Santamaria M, Trevisi N, Maccabelli G, Giraldi F, Fassini G, Riva S, Moltrasio M, Cireddu M, Veglia F, Della Bella P. Catheter ablation for the treatment of electrical storm in patients with implantable cardioverter-defibrillators: short- and long-term outcomes in a prospective single-center study. *Circulation* 2008;**117**:462–469.

# ESC GUIDELINES

Amiodarone or catheter ablation is recommended in patients with recurrent ICD shocks due to sustained VT.



64,156,  
184–  
186

184. Calkins H, Epstein A, Packer D, Arria AM, Hummel J, Gilligan DM, Trusso J, Carlson M, Luceri R, Kopelman H, Wilber D, Wharton JM, Stevenson W. Catheter ablation of ventricular tachycardia in patients with structural heart disease using cooled radiofrequency energy: results of a prospective multicenter study. Cooled RF Multi Center Investigators Group. *J Am Coll Cardiol* 2000;**35**: 1905–1914.
185. Stevenson WG, Wilber DJ, Natale A, Jackman WM, Marchlinski FE, Talbert T, Gonzalez MD, Worley SJ, Daoud EG, Hwang C, Schuger C, Bump TE, Jazayeri M, Tomassoni GF, Kopelman HA, Soejima K, Nakagawa H. Irrigated radiofrequency catheter ablation guided by electroanatomic mapping for recurrent ventricular tachycardia after myocardial infarction: the multicenter thermocool ventricular tachycardia ablation trial. *Circulation* 2008;**118**:2773–2782.
186. Tanner H, Hindricks G, Volkmer M, Furniss S, Kuhlkamp V, Lacroix D, C DEC, Almendral J, Caponi D, Kuck KH, Kottkamp H. Catheter ablation of recurrent scar-related ventricular tachycardia using electroanatomical mapping and irrigated ablation technology: results of the prospective multicenter Euro-VT-study. *J Cardiovasc Electrophysiol* 2010;**21**:47–53.

## CALYPSO

(The Catheter Ablation for VT in Patients with an Implantable Cardioverter Defibrillator )

PILOT Trial

- ICD
- ischemic heart disease
- LVEF $\leq$ 40%
- appropriate ICD Rx  
- $\geq$  1 shock OR  $\geq$  3 ATP
- no reversible causes

4 US centers  
 $\geq$  50 ischemic VT ablation

Pharmacologic  
therapy

Catheter ablation

Primary endpoint : Feasibility

secondary endpoints: recurrent VT, time to first recurrent Rx for VT, death etc

## Reasons of screening failure

## Number of patients

**N=216**

Already on antiarrhythmic medication for VT	88 (41)
VT with a reversible cause	23 (11)
Incessant VT	20 (9)
LVAD	17 (8)
>30 days of amiodarone treatment in past 3 months	16 (7)
Inability to provide informed consent	12 (6)
Contraindication to VT catheter ablation	7 (3)
Presence of other exclusion criteria	23 (11)

Patie

Othe

**27 patients enrolled**

[†]These include: physician refusal, prior VT ablation, history of noncompliance with medications, advanced illness with a poor prognosis, and poor social support.

# 3.

## Catheter ablation of VT in patients with Non-ischemic cardiomyopathy

1. Higher recurrence of VT rate compared with patients with ICM

2. ***NO Randomized Clinical Trial on VT ablation***
3. ***in patients with nonischemic CM***

*(Dinov B, CAE, 2015)*

# ESC GUIDELINES

Catheter ablation may be considered in patients with DCM and VA not caused by bundle branch re-entry refractory to medical therapy.

**IIb**

**C**

355

355. Proietti R, Essebag V, Beardsall J, Hache P, Pantano A, Wulffhart Z, Jutta R, Tsang B, Joza J, Nascimento T, Pegoraro V, Khaykin Y, Verma A. Substrate-guided ablation of haemodynamically tolerated and intolerated ventricular tachycardia in patients with structural heart disease: effect of cardiomyopathy type and acute success on long-term outcome. *Europace*. 2015;**17**:461–467.



# 4.

Catheter ablation of ventricular substrate  
in patients with Brugada syndrome

1. Single center, limited number of patients  
*(Nademanee K, Circ, 2001)*

***NO Randomized Clinical Trial  
on substrate ablation  
in patients with Brugada syndrome***

# ESC GUIDELINES

Catheter ablation may be considered in patients with a history of electrical storms or repeated appropriate ICD shocks.

**IIb**

**C**

201,  
455

201. Haissaguerre M, Extramiana F, Hocini M, Cauchemez B, Jais P, Cabrera JA, Farre J, Leenhardt A, Sanders P, Scavee C, Hsu LF, Weerasooriya R, Shah DC, Frank R, Maury P, Delay M, Garrigue S, Clementy J. Mapping and ablation of ventricular fibrillation associated with long-QT and Brugada syndromes. *Circulation* 2003;**108**: 925–928.
455. Nademanee K, Veerakul G, Chandanamattha P, Chaothawee L, Ariyachaipanich A, Jirasirojanakorn K, Likittanasombat K, Bhuripanyo K, Ngarmukos T. Prevention of ventricular fibrillation episodes in Brugada syndrome by catheter ablation over the anterior right ventricular outflow tract epicardium. *Circulation* 2011;**123**:1270–1279.

Ablation should be the first line therapy for patients with appropriate ICD shocks.

regardless of underlying heart disease  
regardless of use of amiodarone

False

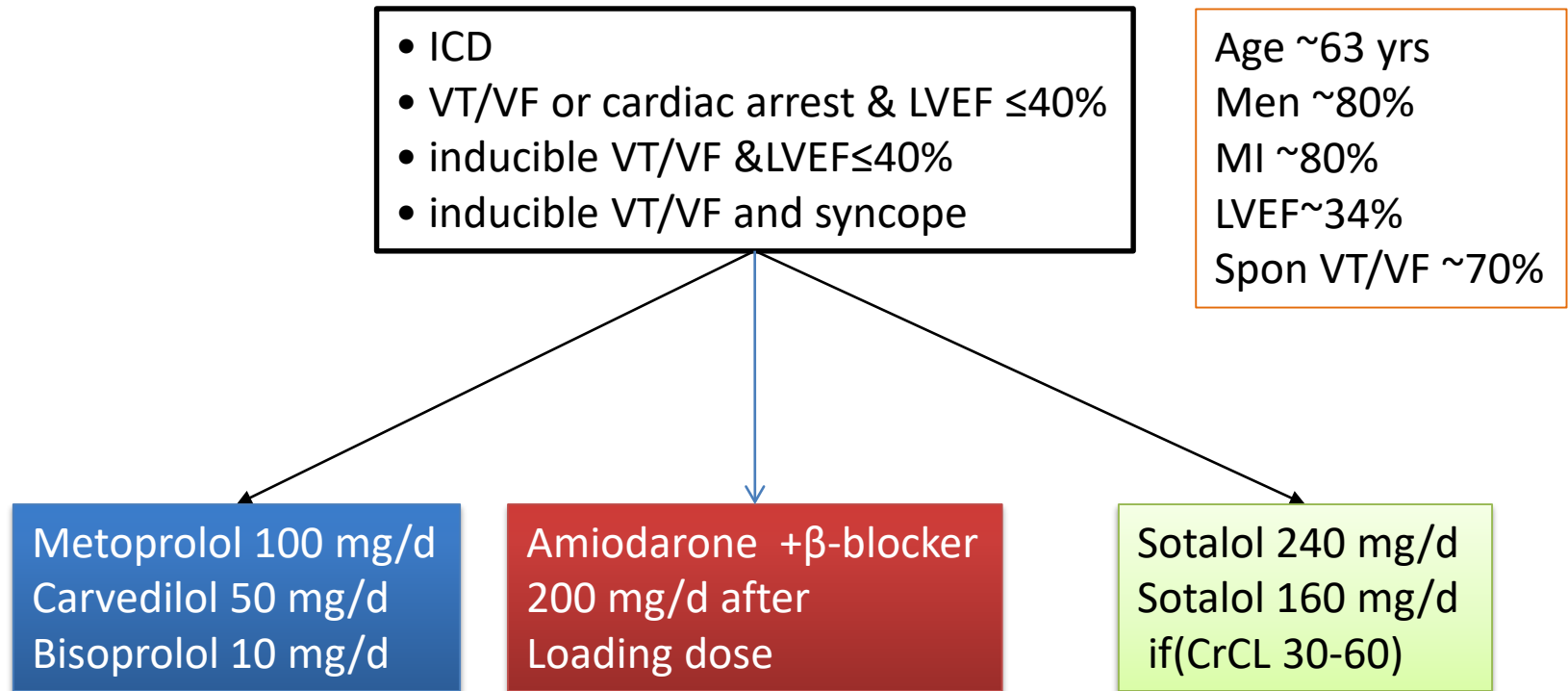
Considering result of (catheter) ablation is *highly variable* *depending on* underlying heart disease (*ischemic, nonischemic or electrical disorders*), (catheter) ablation are recommended in post MI patients with appropriate ICD shocks refractory to/contraindicated to/ or intolerable to amiodarone therapy.

Rebuttal

1. We should monitor side effects of antiarrhythmic drugs.

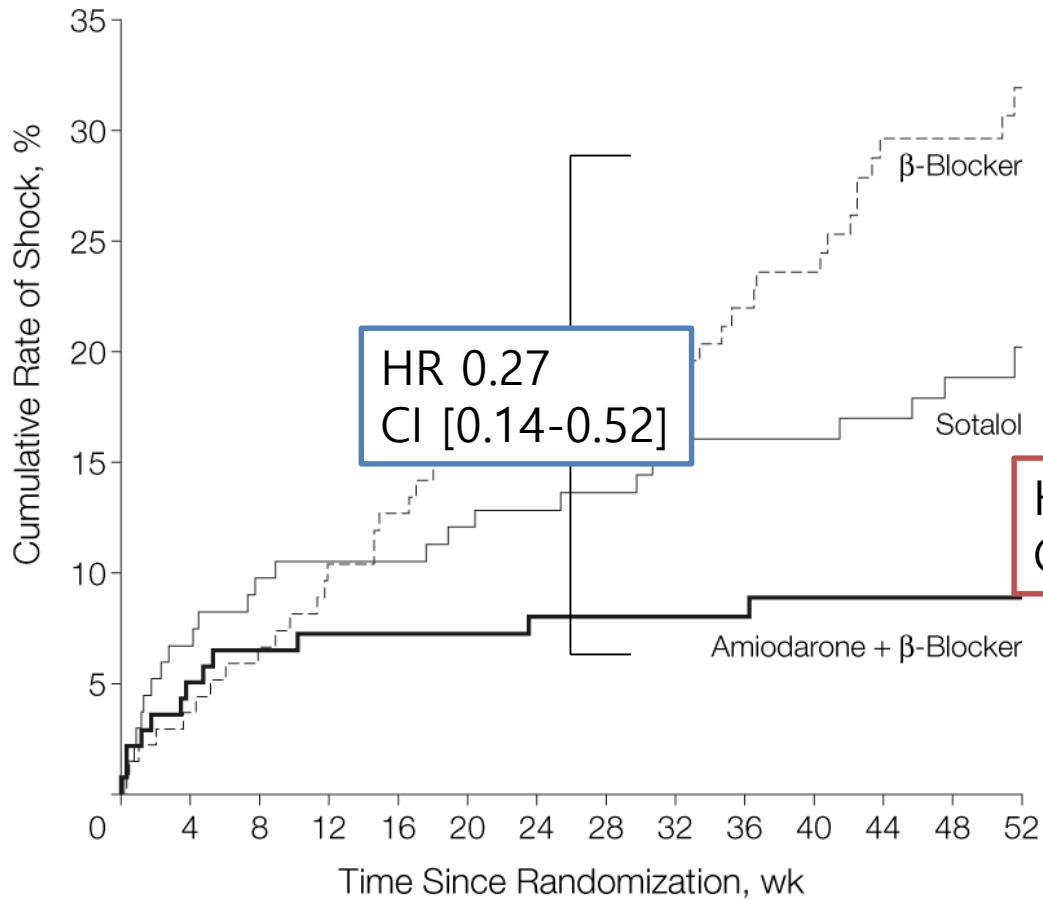
2. It is unknown whether Korean patients can tolerate high dose amiodarone therapy as in VANISH trial.

## Optimal Pharmacological Therapy In Implantable Defibrillator Patients (OPTIC)



Primary endpoint : first occurrence of any shock delivery by the ICD

Age ~63 yrs  
 Men ~80%  
 MI ~80%  
 LVEF~34%  
 Spon VT/VF ~70%



No. at Risk					
β-Blocker	138	119	109	91	42
Sotalol	134	118	108	94	35
Amiodarone + β-Blocker	140	124	115	106	56



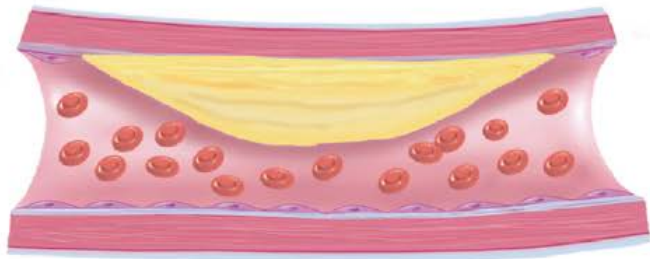
Adverse event	$\beta$ -blocker N=138	amiodarone+ $\beta$ -blocker N=140	sotalol N=134	P value
Death	2(1.4)	6(4.3)	4(3.0)	0.36
Arrhythmic death	1(0.7)	2(1.4)	1(0.8)	0.60
MI	1(0.7)	1(0.7)	0	0.62
Heart failure	9(6.5)	12(8.6)	14(13.4)	0.14
AF	6(4.4)	1(0.7)	6(4.5)	0.13
<b>Pulmonary adverse event</b>	<b>0</b>	<b>7(5.0)</b>	<b>4(3.0)</b>	<b>0.03</b>
<b>Hypothyroidism</b>	<b>0</b>	<b>6(4.3)</b>	<b>1(0.8)</b>	<b>0.01</b>
Hyperthyroidism	0	2(1.4)	0	0.14
<b>Symp Brady</b>	<b>1(0.7)</b>	<b>8(6.4)</b>	<b>2(1.5)</b>	<b>0.009</b>
TdP	0	0	0	>0.99
skin adverse event	2(1.5)	4(2.9)	3(2.2)	0.72
Hospitalization	60(43.3)	49(34.9)	40(30.1)	0.32

Loading 400 mg bid * 2 w  
→ 400 mg qd * 4 w

*Connolly SJ, JAMA, 2006;295:165-171*

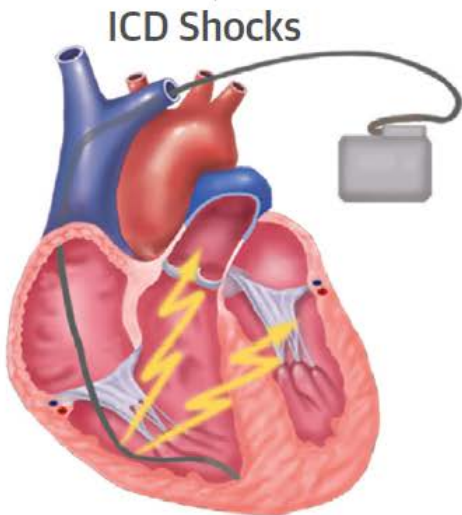
Event	AAD group	Ablation group	P
<b>Catheter ablation related</b>			
vascular injury		3(2.3)	0.25
major bleeding	1(0.8)	3(2.3)	0.62
cardiac perforation	1(0.8)	2(1.5)	1.00
endocarditis	1(0.8)		0.49
heart block	1(0.8)		0.49
<b>Antiarrhythmic drug related</b>			
<b>death</b>			
<b>pulmonary toxicity</b>	<b>2(1.6)</b>		0.24
<b>liver toxicity/MOF</b>	<b>1(0.8)</b>		0.49
pulmonary infiltrate	2(1.6)		0.24
Shortness of breath	3(2.4)	1(0.8)	0.36
HF admission	1(0.8)	3(2.3)	0.62
Hyperthyroidism	5(3.9)	3(2.3)	0.49
Hypothyroidism	5(3.9)	2(1.5)	0.27
Hepatic dysfunction	6(4.7)		0.013
Tremor/ataxia	6(4.7)		0.013
Drug therapy change	6(4.7)		0.013
other adverse events	6(4.7)	4(3.0)	0.53
<b>Total Patients</b>	<b>39(30.7%)</b>	<b>20(15.2%)</b>	<b>0.0031</b>
<b>Total Events</b>	<b>51</b>	<b>22</b>	<b>0.0023</b>

(From Sapp JL, N Eng J Med 2016;375;111-121)



Coronary Artery Disease

+ Recurrent VT

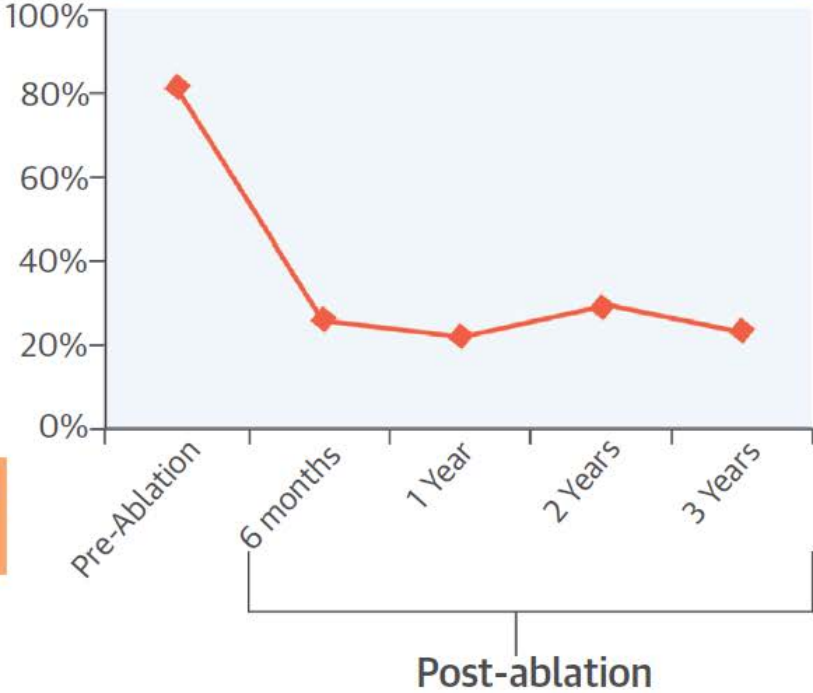


ICD Shocks

Open-Irrigated VT  
Catheter Ablation  
(249 Patients)

No Procedure-Related  
Strokes

Long-Term Outcome  
Percentage with ICD Shocks

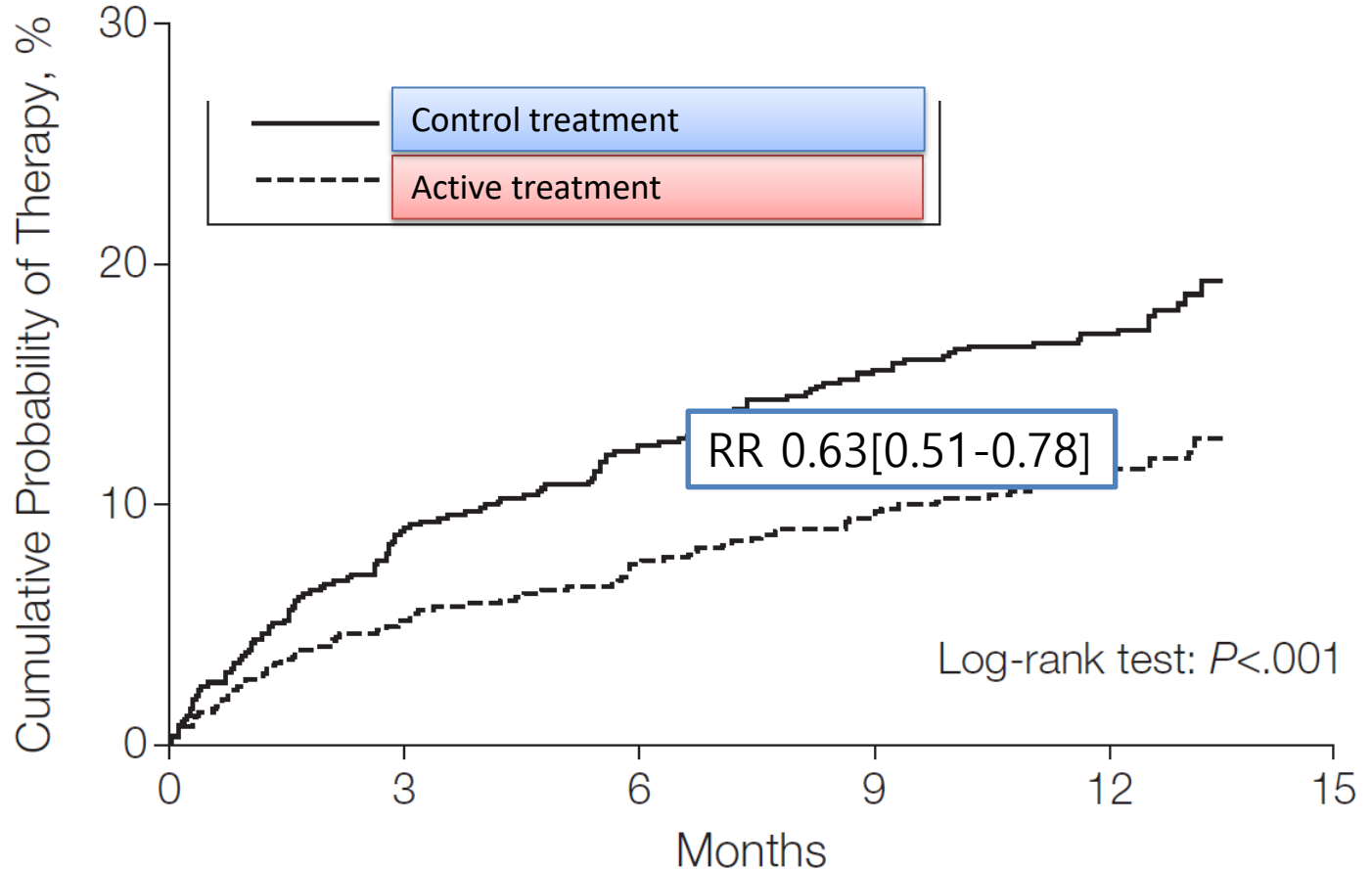


- ↓ Anxiety Score (6 Months)
- ↓ Amiodarone Requirement (6 Months-3 Years)
- ↓ Hospitalizations (6 Months-3 Years)

*Catheter ablation is  
the only treatment  
of  
reducing (or preventing)  
ICD therapy.*

# Which treatment reduced 1st ICD therapy?

- 65 years
- VT/VF 25%
- CAD 60%
- LVEF 30%



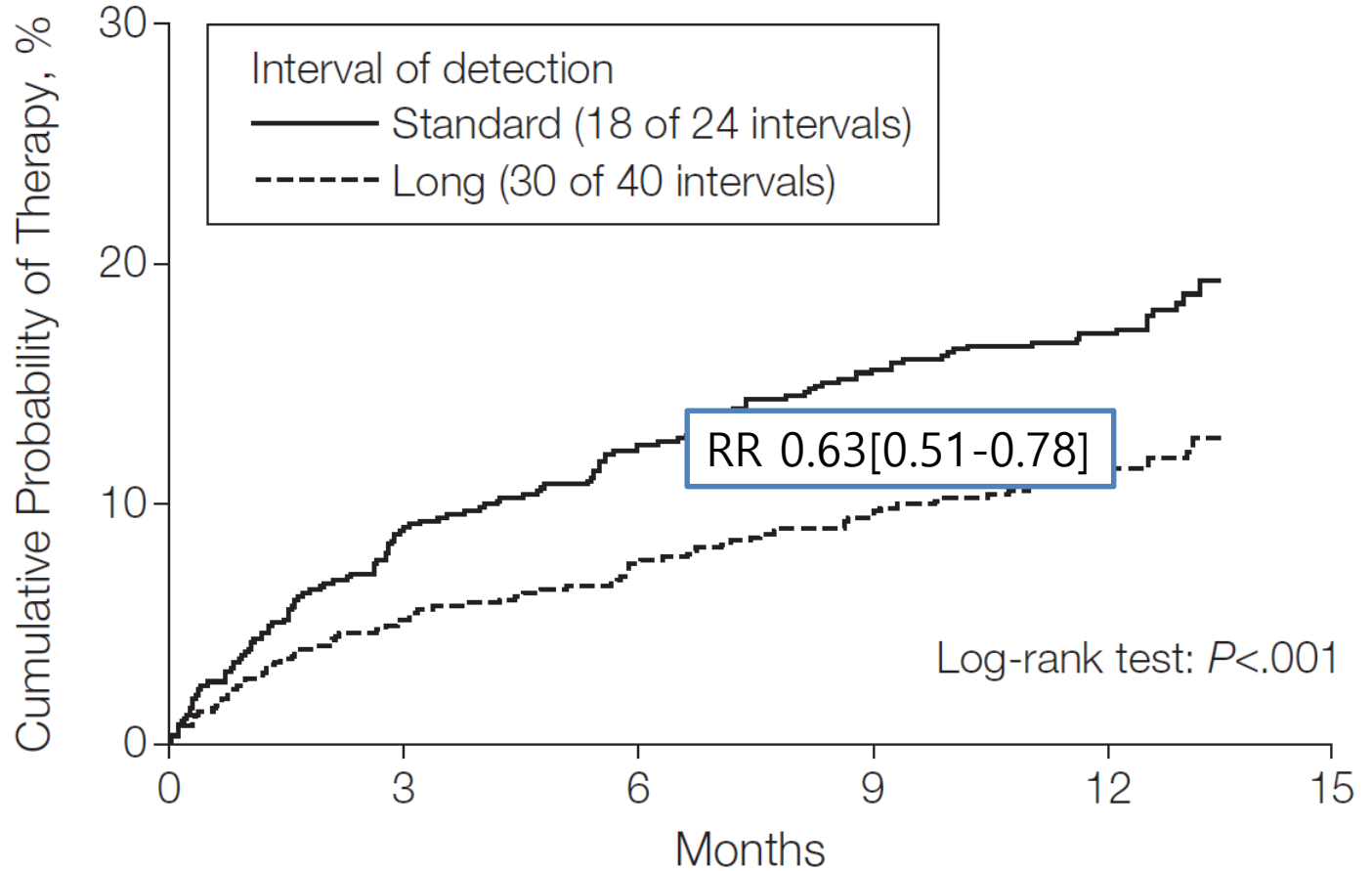
No. at risk

Standard Rx	891	777	707	639	438
Active Rx	876	812	752	686	462

(1) Amiodarone (2) Amiodarone +  $\beta$ -blocker (3) Ablation (4) Other

**A** Time to first therapy

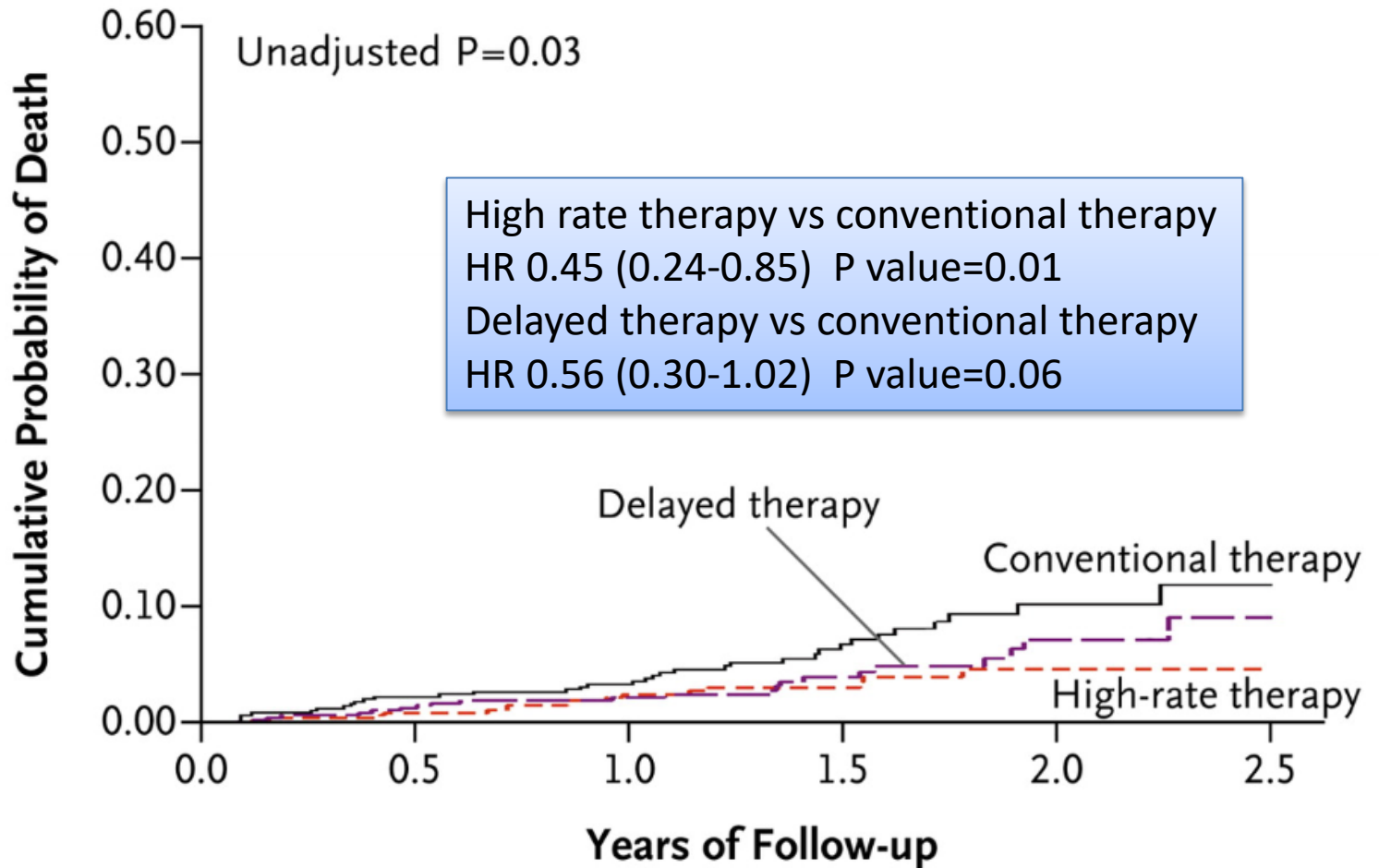
- 65 years
- VT/VF 25%
- CAD 60%
- LVEF 30%



No. at risk

Interval of detection	0	3	6	9	12
Standard	891	777	707	639	438
Long	876	812	752	686	462

(4) Other



**No. at Risk**

Conventional therapy	514	490 (0.02)	392 (0.03)	219 (0.07)	89 (0.10)	14 (0.12)
High-rate therapy	500	478 (0.01)	372 (0.02)	221 (0.03)	90 (0.05)	21 (0.05)
Delayed therapy	486	471 (0.01)	375 (0.02)	205 (0.04)	99 (0.07)	14 (0.09)

- Electrical storm in familial long QT syndrome (Saxon LA, Am Heart J, 1996)
- Short QT syndrome (Bun SS, Heart Rhythm, 2012)
- Short-coupled variant of torsades de pointes (Takeuchi, T, PACE, 2003)
- Fatal electrical storm due to pneumonia in Brugada syndrome (Dickal MH, Europace, 2003)
  
- PMS and variant angina (Li, Calin Res Cardiol, 2011)
  
- Electrical storm due to jet-lag (**Han SW**, IJC, 2005)
- Hypothermia (Takahiro T, Heart Rhythm 2015)
- Electrical storm due to amiodarone-induced thyrotoxicosis in a man with DCM (Marketou, PACE, 2001)
- Electrical storm due to abrupt beta-blocker interruption (Fragakis, ANE, 2017)
  
- T-wave pacing induced electrical storm (Jaoude SA, JICEP, 2003)
- Managed ventricular pacing (Mansour, F, Heart Rhythm, 2012)
- Electrical storm after CABG due to a kinked left internal mammary artery graft (Pezannowski, 2004)



## Causes of death according to types of shock

type of shock	all patients	patients who died	cause of death		
			sudden arrhythmia number of patients	Heart Failure	other cardiac causes
Any shock	269	77	16	33	9
any appropriate shock	182	67	14	<b>29</b>	8
inappropriate shock only	87	10	2	4	1
No Shock	542	86	13	34	6

**Table 2.** Time from ICD Shock to Death among Patients Who Received at Least One Shock.*

Type of Shock	All Patients	Patients Who Died	Time from Shock to Death			Kaplan–Meier Survival Rate 1 Year after Shock
			Median	Interquartile Range	Full Range	%
Any shock	269	77	204	1–630	0–1872	82.5±2.4
One or more inappropriate shocks only	87	10	294	28–509	0–735	94.9±2.5
One or more appropriate shocks	182	67	168	1–797	0–1872	76.9±3.2
NYHA class II	117	31	206	1–977	0–1872	84.0±3.5
NYHA class III	65	36	168	7–626	0–1343	64.2±6.1
Ischemic heart failure	93	49	96	0–443	0–1872	62.6±5.2
Nonischemic heart failure	89	18	622	204–908	1–1785	91.6±3.0
First shock for ventricular fibrillation	77	33	3	0–622	0–1872	74.6±5.0
First shock for ventricular tachycardia	105	34	258	59–797	0–1785	78.5±4.2

* Plus–minus values are survival rates ±SE. ICD denotes implantable cardioverter–defibrillator, and NYHA New York Heart Association.

## What we know

1. Electrical storm occurs in ICD patients
2. Electrical storm increase mortality.
3. Catheter ablation in ES patients reduced combined endpoints.
4. No sufficient data in patients with NICM, BS.

## What we don't know

1. What is precipitating factors of ES?
  - (1) deterioration of heart failure
  - (2) progression of coronary artery disease
  - (3) acute MI
  - (4) change of autonomic nervous system
  - (5) non-cardiac medical conditions
2. role of other treatment such as LVAD