The Role of AICDs in Nonischemic Cardiomyopathy

Are they really necessary ?

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Disclosures: Consultant, Zoll Lifevest

Understanding the Risk
LV Systolic Dysfunction and SCD Risk

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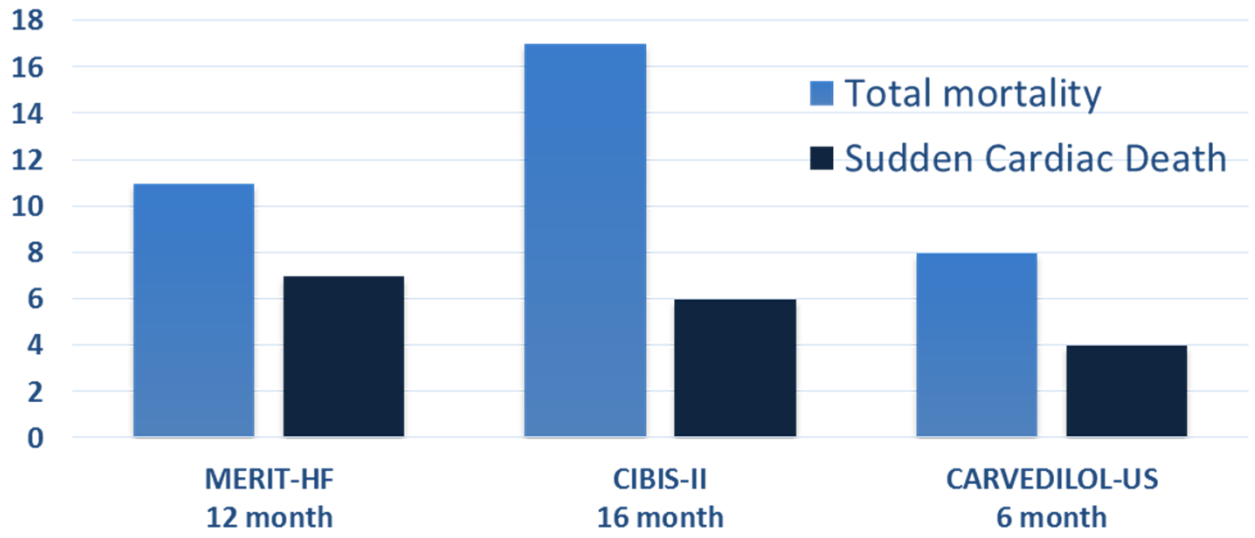
- SCD accounted for ~50% (35-64%) of total mortality
  - EF was the single most important risk factor for SCD



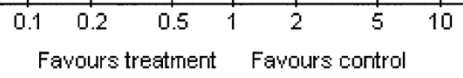
Prophylactic Implantable Cardioverter-Defibrillator Therapy in Patients With Left Ventricular Systolic Dysfunction:
A Pooled Analysis of 10 Primary Prevention Trials

Death from all causes in all available primary prevention trials.

Comparison: 01 ICD vs. Control (Overall)
Outcome: 01 All-Cause Mortality

Study or sub-category	Treatment n/N	Control n/N	RR (random) 95% CI	Weight %	RR (random) 95% CI
AMIOVIRT	6/51	7/52		2.76	0.87 [0.32, 2.42]
CABG Patch	101/446	95/454		12.79	1.08 [0.84, 1.39]
CAT	13/50	17/54		5.93	0.83 [0.45, 1.52]
COMPANION	105/595	131/617		13.19	0.83 [0.66, 1.05]
DEFINITE	28/229	40/229		8.46	0.70 [0.45, 1.09]
DINAMIT	62/332	58/342		11.00	1.10 [0.80, 1.52]
MADIT 1	15/95	39/101		7.12	0.41 [0.24, 0.69]
MADIT 2	105/742	97/490		12.71	0.71 [0.56, 0.92]
MUSTT	35/161	255/537		11.42	0.46 [0.34, 0.62]
SCD HeFT	182/829	244/847		14.62	0.76 [0.65, 0.90]
Total (95% CI)	3530	3723		100.00	0.75 [0.63, 0.91]

Total events: 652 (Treatment), 983 (Control)
Test for heterogeneity: Chi² = 29.67, df = 9 (P = 0.0005), I² = 69.7%
Test for overall effect: Z = 3.00 (P = 0.003)



Nanthakumar K, et al. J Am Col Cardiol 2004;44:2166-2172.

2015 ESC Guidelines:Risk Stratification and Management of Patients with Dilated Cardiomyopathy

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Recommendations	Class[a]	Level[b]	Ref.[c]
Optimal medical therapy (ACE inhibitors, beta-blockers and MRA) is recommended in patients with DCM to reduce the risk of sudden death and progressive HF.	I	A	8
Prompt identification and treatment of arrhythmogenic factors (e.g. pro-arrhythmic drugs, hypokalaemia) and co-morbidities (e.g. thyroid disease) is recommended in patients with DCM and VA.	I	C	8
A coronary angiography is recommended in stable DCM patients with an intermediate risk of CAD and new onset VA.	I	B	8
An ICD is recommended in patients with DCM and haemodynamically not tolerated VT/VF, who are expected to survive for >1 year with good functional status.	I	A	151–154
An ICD is recommended in patients with DCM, symptomatic HF (NYHA class II–III) and an ejection fraction ≤35% despite ≥3 months of treatment with optimal pharmacological therapy who are expected to survive for >1 year with good functional status.	I	B	64, 313, 316, 317, 354
Catheter ablation is recommended in patients with DCM and bundle branch re-entry ventricular tachycardia refractory to medical therapy.	I	B	8,208, 345, 346
An ICD should be considered in patients with DCM and a confirmed disease-causing *LMNA* mutation and clinical risk factors.[d]	IIa	B	71
Amiodarone should be considered in patients with an ICD that experience recurrent appropriate shocks in spite of optimal device programming.	IIa	C	229
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
Invasive EPS with PVS may be considered for risk stratification of SCD.	IIb	B	115
Amiodarone is not recommended for the treatment of asymptomatic NSVT in patients with DCM.	III	A	313, 354
Use of sodium channel blockers and dronedarone to treat VA is not recommended in patients with DCM.	III	A	129, 356, 357

Eur Heart J 2015:2793-2867.

DEFINITE

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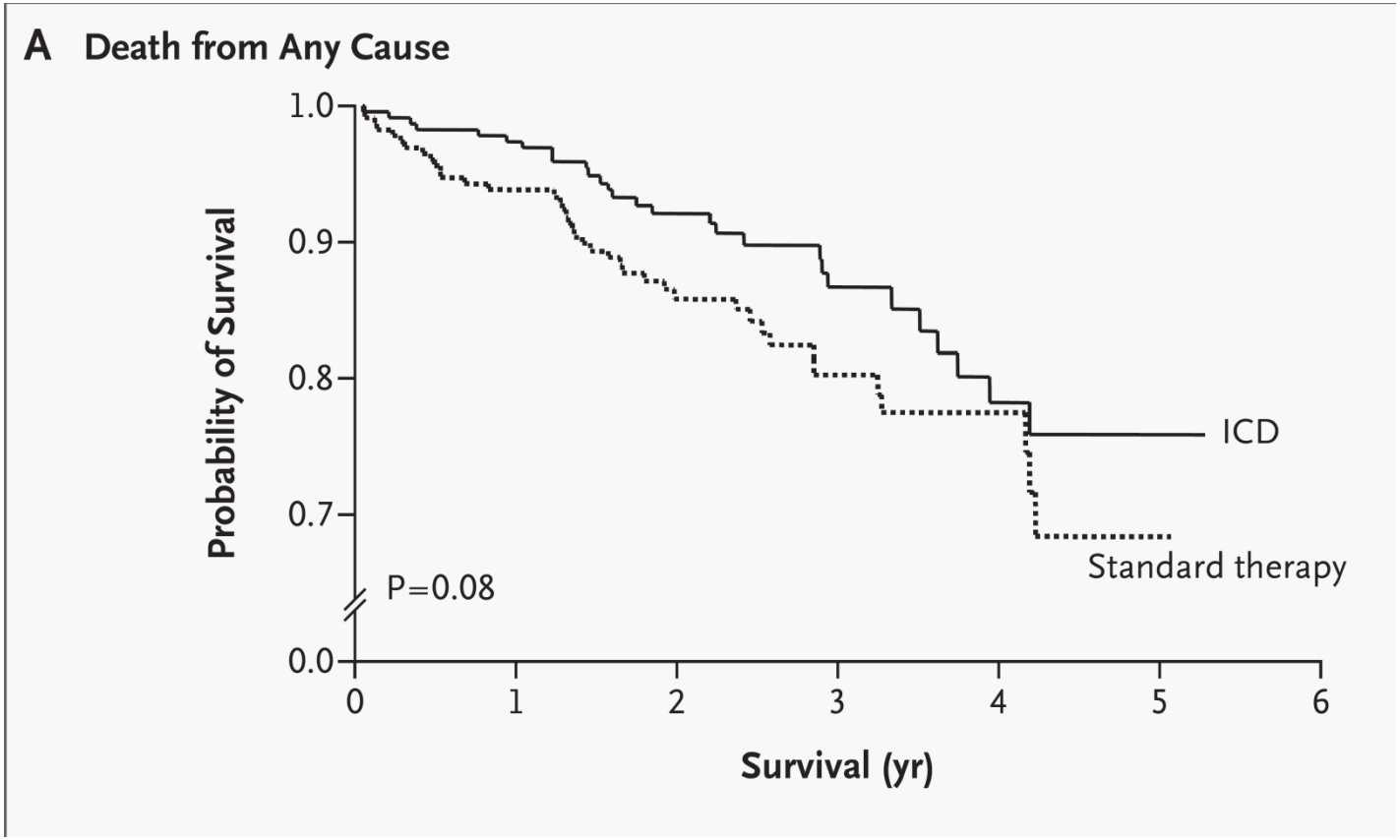
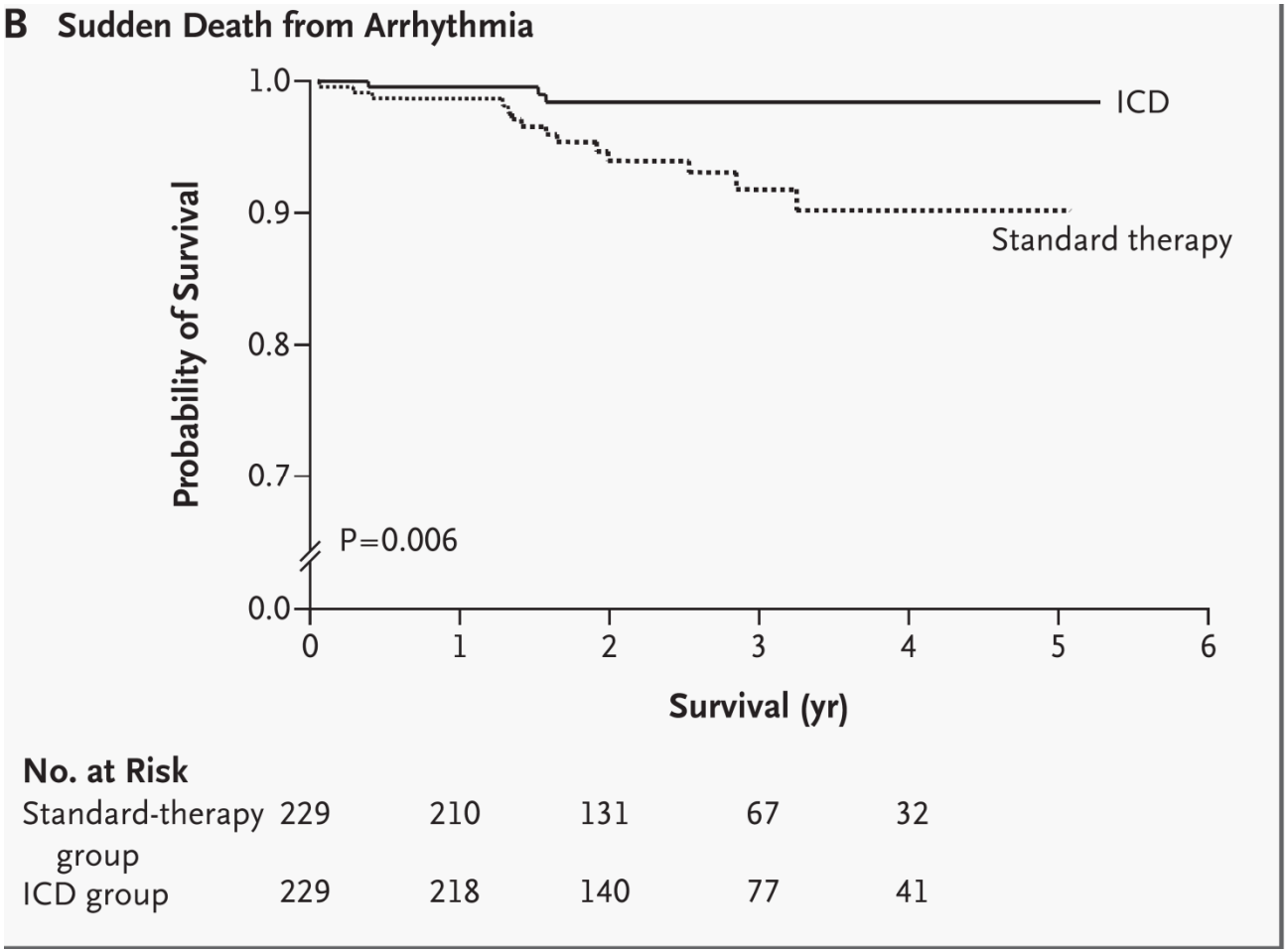
Death from any cause among patients who received an ICD and patients who received standard therapy (N=458, HF 2.8 years)



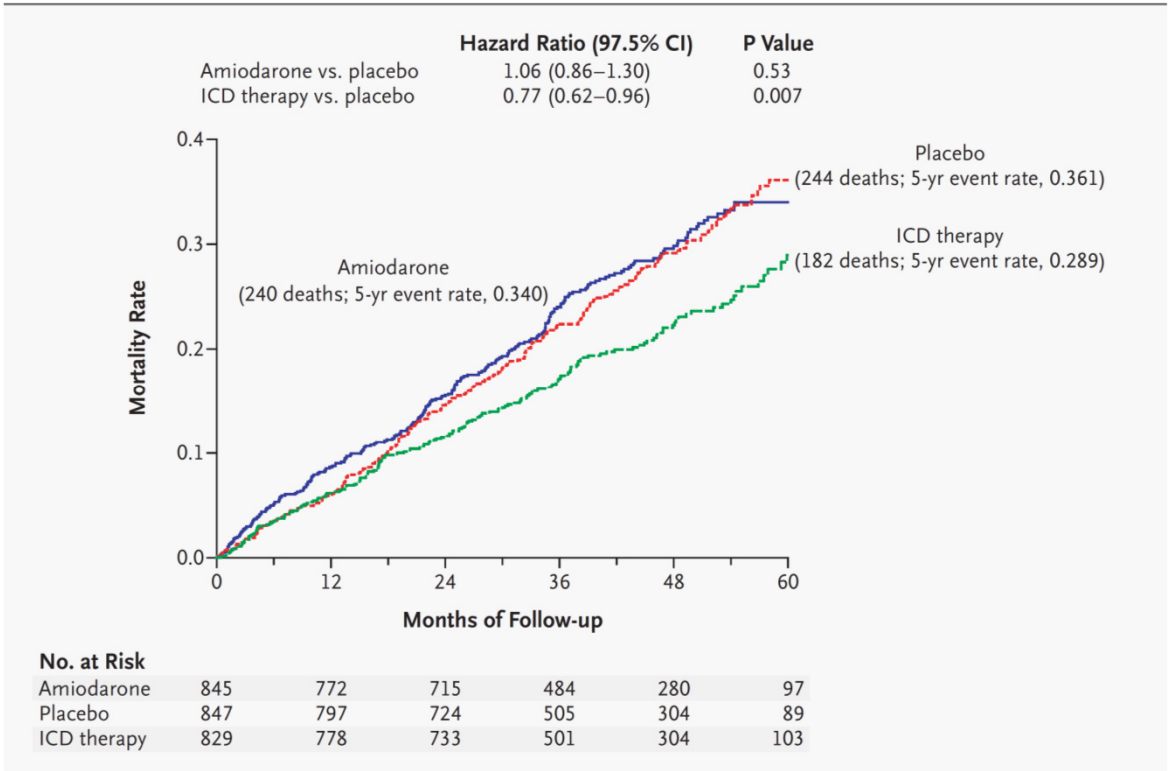
Kadish A, et al. New Engl J Med 2004;350:2151-2158.

Death from Arrhythmia Among Patients who Received Standard Therapy and Patients who Received an ICD



Kadish A, et al. N Engl J Med 2004;350:2151-2158.

SCD-HeFT: Amiodarone or an Implantable Cardioverter-Defibrillator for CHF – Death from Any Cause (n=2521, 48% nonischemic)



Bardy GH, et al. N Engl J Med 2005; 352:225-237.

Amiodarone or an AICD for CHF – Death from Any Cause in Subgroup with Ischemic CHF

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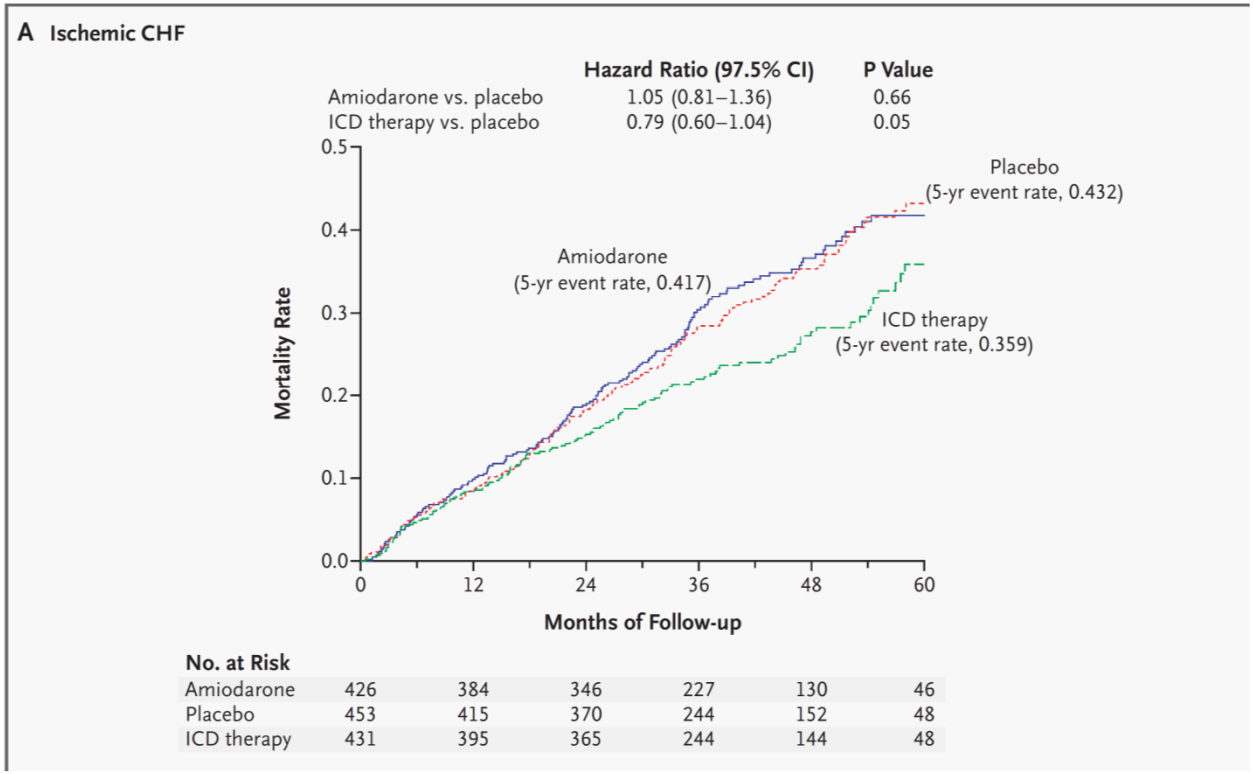

Bardy GH, et al. N Engl J Med 2005; 352:225-237.

Amiodarone or an AICD for CHF – Death from Any Cause in Subgroup with Nonischemic CHF

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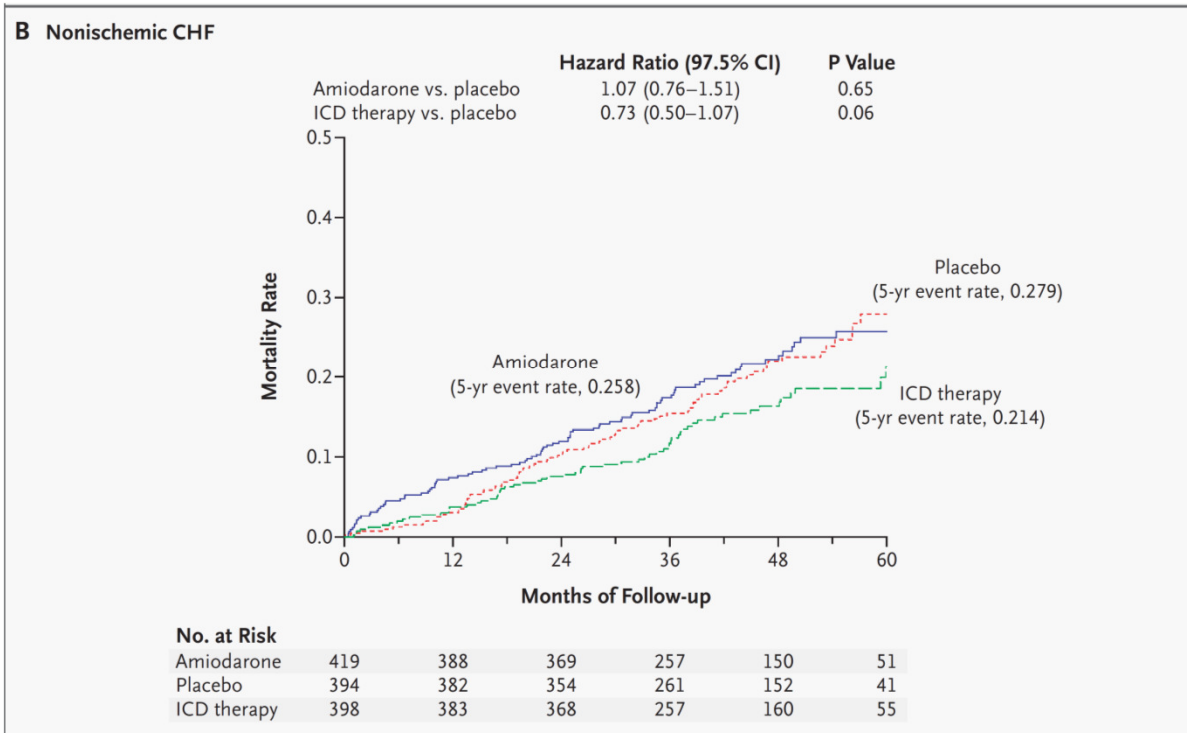

Bardy GH, et al. N Engl J Med 2005; 352:225-237.

Amiodarone or an AICD for CHF – Death from Any Cause in Subgroup with NYHA Class III

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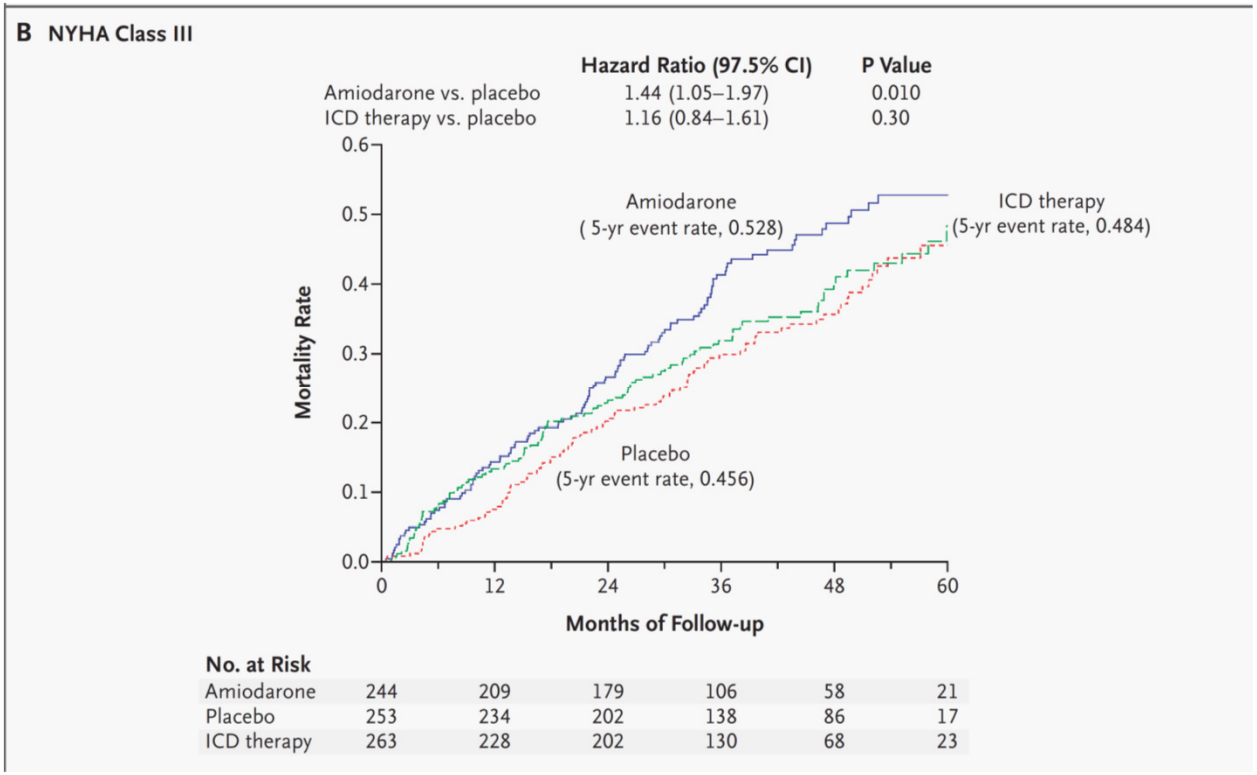

Bardy GH, et al. N Engl J Med 2005; 352:225-237.

Nonischemic Cardiomyopathy: A Complex Process

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- Inflammatory process
- Various forms of myocarditis
- Idiopathic structural changes
- Genetic abnormalities
- Toxic, hormonal
- Auto-immunological and metabolic disturbances

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Defibrillator Implantation in Patients with Nonischemic Systolic Heart Failure

Lars Køber, M.D., D.M.Sc., Jens J. Thune, M.D., Ph.D., Jens C. Nielsen, M.D., D.M.Sc., Jens Haarbo, M.D., D.M.Sc., Lars Videbæk, M.D., Ph.D., Eva Korup, M.D., Ph.D., Gunnar Jensen, M.D., Ph.D., Per Hildebrandt, M.D., D.M.Sc., Flemming H. Steffensen, M.D., Niels E. Bruun, M.D., D.M.Sc., Hans Eiskjær, M.D., D.M.Sc., Axel Brandes, M.D., Anna M. Thøgersen, M.D., Ph.D., Finn Gustafsson, M.D., D.M.Sc., Kenneth Egstrup, M.D., D.M.Sc., Regitze Videbæk, M.D., Christian Hassager, M.D., D.M.Sc., Jesper H. Svendsen, M.D., D.M.Sc., Dan E. Høfsten, M.D., Ph.D., Christian Torp-Pedersen, M.D., D.M.Sc., and Steen Pehrson, M.D., D.M.Sc., for the DANISH Investigators*

NEJM 2016 Aug 28

Characteristics of the Patients at Baseline (n=1,116)

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Characteristic	ICD Group (N=556)	Control Group (N=560)
Median age (IQR) — yr	64 (56–72)	63 (56–70)
Female sex — no. (%)	151 (27)	156 (28)
Median blood pressure (IQR) — mm Hg		
Systolic	123 (110–139)	124 (111–138)
Diastolic	74 (65–81)	74 (66–82)
Median body-mass index (IQR)†	26.8 (23.9–30.5)	26.8 (23.8–30.1)
Median NT-proBNP level (IQR) — pg/ml	1244 (616–2321)	1110 (547–2166)
Median QRS duration (IQR) — msec	146 (114–166)	145 (110–164)
Median left ventricular ejection fraction (IQR) — %	25 (20–30)	25 (20–30)
Median estimated GFR (IQR) — ml/min/1.73 m^2	74 (58–91)	73 (58–92)
NYHA class — no. (%)		
II	297 (53)	300 (54)
III	252 (45)	253 (45)
IV	7 (1)	7 (1)
Median duration of heart failure (IQR) — mo	20 (8–72)	18 (8–60)
Coexisting conditions — no. (%)		
Hypertension	181 (33)	167 (30)
Diabetes	99 (18)	112 (20)
Permanent atrial fibrillation	135 (24)	113 (20)
Means of exclusion of ischemic cause of heart failure — no. (%)		
Nuclear study	5 (1)	8 (1)
CT angiogram	18 (3)	11 (2)
Catheterization	533 (96)	541 (97)
Cause of heart failure — no. (%)		
Idiopathic	424 (76)	425 (76)
Valvular	20 (4)	21 (4)
Hypertension	62 (11)	55 (10)
Other	50 (9)	59 (11)
Medications — no. (%)		
ACE inhibitor or ARB	533 (96)	544 (97)
Beta-blocker	509 (92)	517 (92)
Mineralocorticoid-receptor antagonist	326 (59)	320 (57)
Amiodarone	34 (6)	32 (6)
CRT — no. (%)	322 (58)	323 (58)
Preexisting pacemaker or CRT pacemaker — no. (%)	56 (10)	46 (8)

Time-to-Event Curves for Death from Any Cause, Cardiovascular Death, and Sudden Cardiac Death

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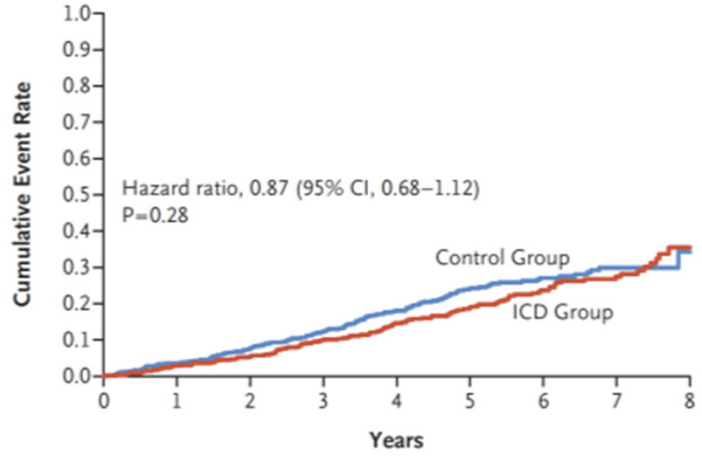
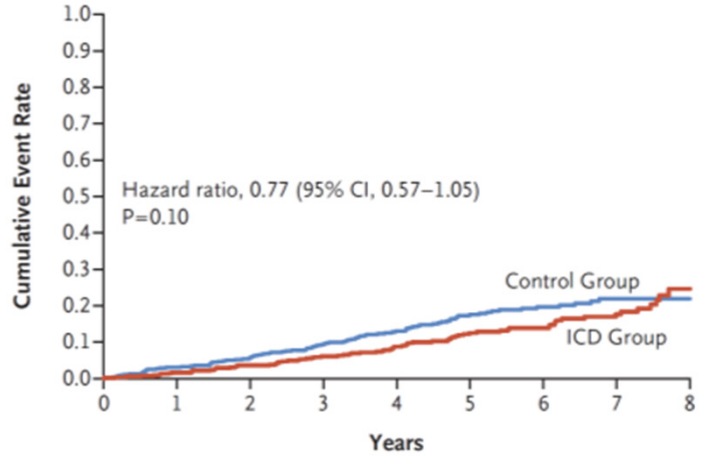
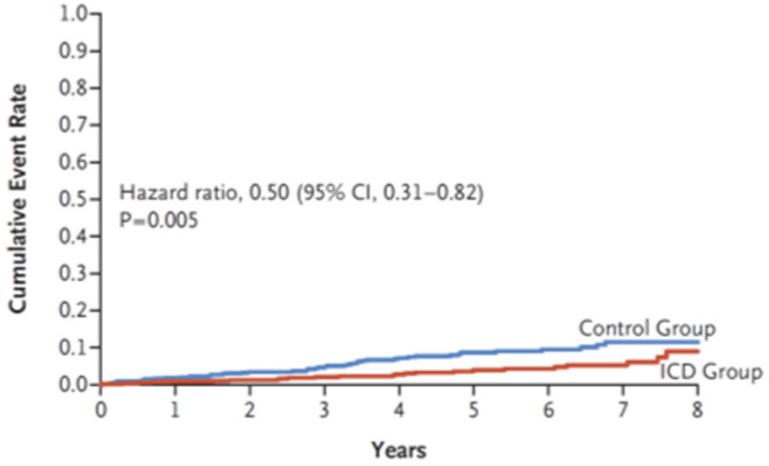
A Death from Any Cause



B Cardiovascular Death



C Sudden Cardiac Death



No. at Risk

Control Group	560	540	517	438	344	248	169	88	12
ICD Group	556	540	526	451	358	272	186	107	17

Rate of Death from Any Cause (Primary Outcome) in Prespecified Subgroups

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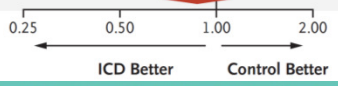
Subgroup	ICD Group	Control Group	Hazard Ratio (95% CI)	P Value	P Value for Interaction
	no. of events/total no.				
Age					0.009
<59 yr	17/167	34/181	0.51 (0.29–0.92)	0.02	
≥59 to <68 yr	36/173	50/202	0.75 (0.48–1.16)	0.19	
≥68 yr	67/216	47/177	1.19 (0.81–1.72)	0.38	
Sex					0.66
Female	22/151	23/156	1.03 (0.57–1.87)	0.92	
Male	98/405	108/404	0.85 (0.64–1.12)	0.24	
NT-proBNP					0.06
<1177 pg/ml	32/266	74/268	0.59 (0.38–0.91)	0.02	
≥1177 pg/ml	57/292	88/290	0.99 (0.73–1.36)	0.96	
LV ejection fraction					0.69
<25%	70/264	65/242	0.87 (0.62–1.22)	0.42	
≥25%	50/292	66/318	0.79 (0.54–1.14)	0.21	
Estimated GFR					0.86
<73 ml/min/1.73 m^2	75/272	80/278	0.88 (0.64–1.21)	0.42	
≥73 ml/min/1.73 m^2	45/283	50/280	0.82 (0.55–1.23)	0.33	
NYHA functional class					0.71
II	52/297	54/300	0.92 (0.63–1.35)	0.68	
III–IV	68/259	77/260	0.81 (0.58–1.13)	0.21	
Heart failure duration					0.73
<18 mo	31/254	36/277	0.88 (0.54–1.43)	0.61	
≥18 mo	89/301	95/283	0.81 (0.61–1.09)	0.17	
Hypertension					0.63
No	78/375	87/392	0.90 (0.66–1.22)	0.48	
Yes	42/181	44/167	0.79 (0.51–1.21)	0.27	
Diabetes					0.60
No	87/457	95/448	0.85 (0.63–1.31)	0.26	
Yes	33/99	36/112	0.92 (0.57–1.50)	0.74	
Permanent atrial fibrillation					0.30
No	83/421	91/447	0.92 (0.68–1.24)	0.58	
Yes	37/135	40/113	0.76 (0.48–1.20)	0.24	
Cause of heart failure					0.80
Idiopathic	90/424	100/425	0.88 (0.66–1.17)	0.37	
Valvular	4/20	5/21	0.59 (0.13–2.71)	0.50	
Hypertension	13/62	12/55	0.68 (0.29–1.63)	0.39	
Other	13/50	14/59	1.02 (0.47–2.20)	0.96	
Preexisting pacemaker					0.71
No	108/500	120/514	0.88 (0.68–1.14)	0.34	
Yes	12/56	11/46	0.88 (0.36–2.20)	0.79	
CRT					0.73
No	58/234	65/237	0.83 (0.58–1.19)	0.31	
Yes	62/322	66/323	0.91 (0.64–1.29)	0.59	
Overall			0.87 (0.68–1.12)	0.28	



Prognostic Importance of Defibrillator Shocks in Patients with Heart Failure (SCD-HeFT)

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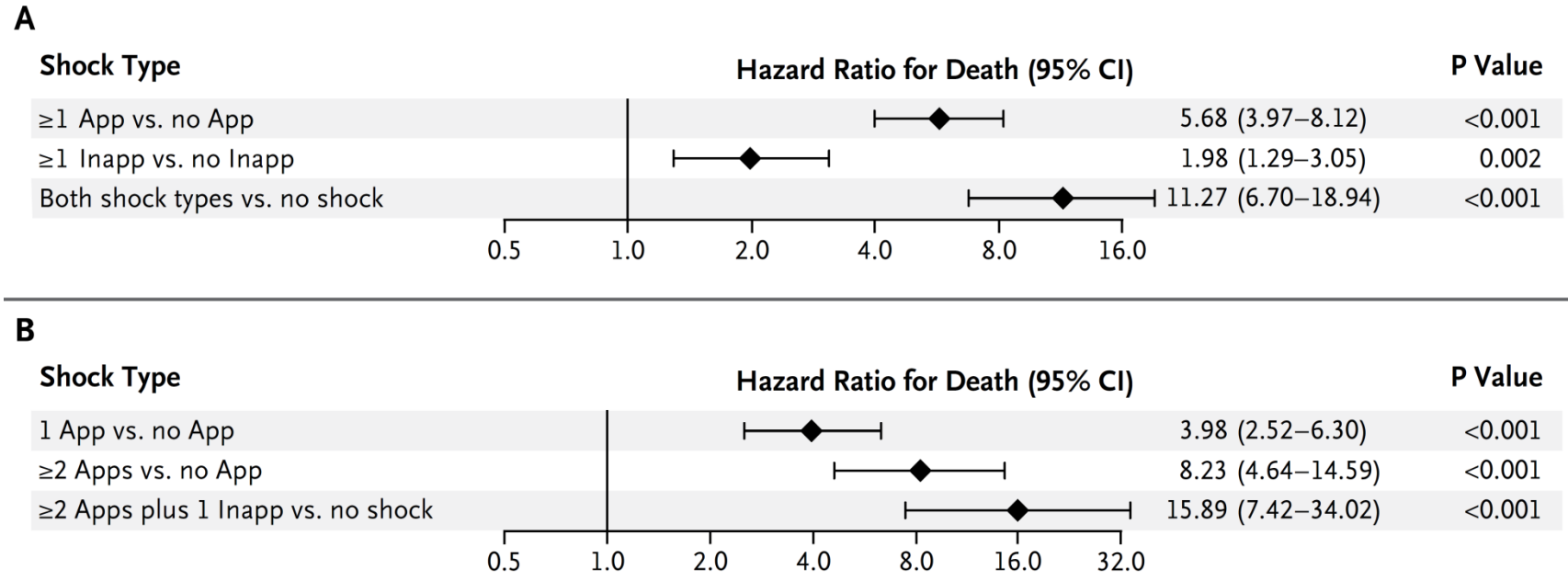

Figure 1. Hazard Ratios for the Association of ICD Shock with the Risk of Death, According to Shock Type.

Poole JE, et al. N Engl J Med 2008;359:1009-17.

Time-to-Event Curves for Death from Any Cause, Cardiovascular Death, and Sudden Cardiac DeathCHF

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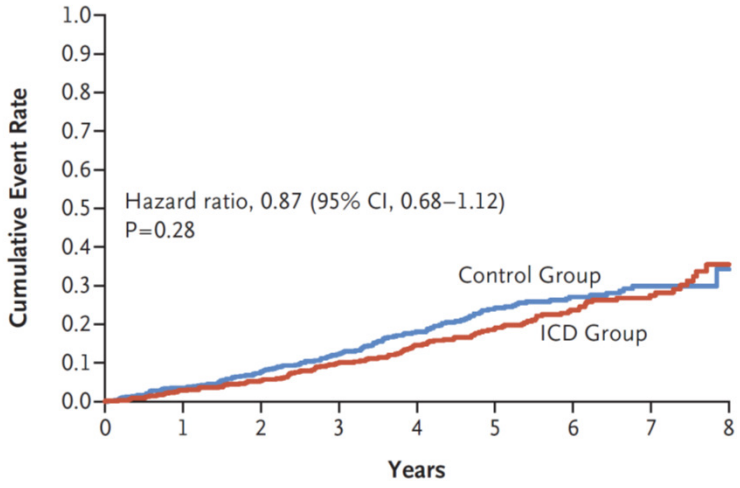
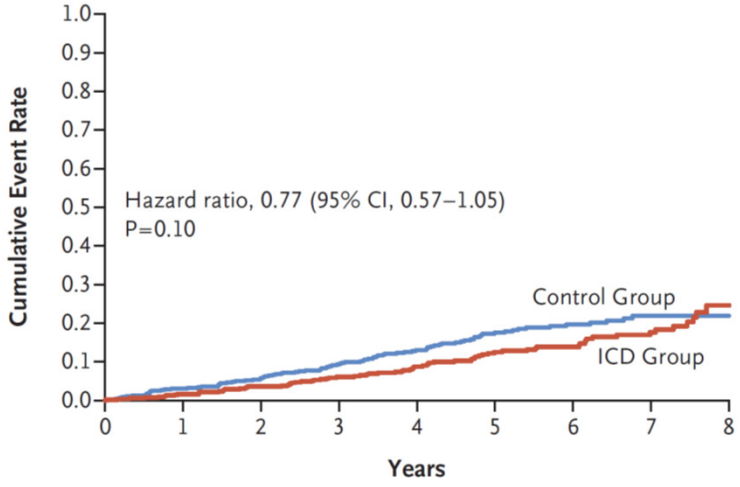
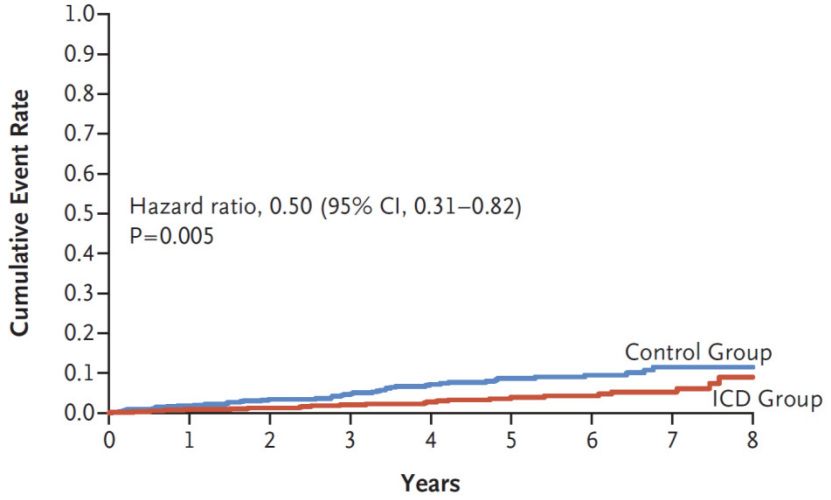
A Death from Any Cause



B Cardiovascular Death



C Sudden Cardiac Death



No. at Risk

Control Group	560	540	517	438	344	248	169	88	12
ICD Group	556	540	526	451	358	272	186	107	17

Noninvasive Arrhythmia Risk Stratification in Idiopathic Dilated Cardiomyopathy

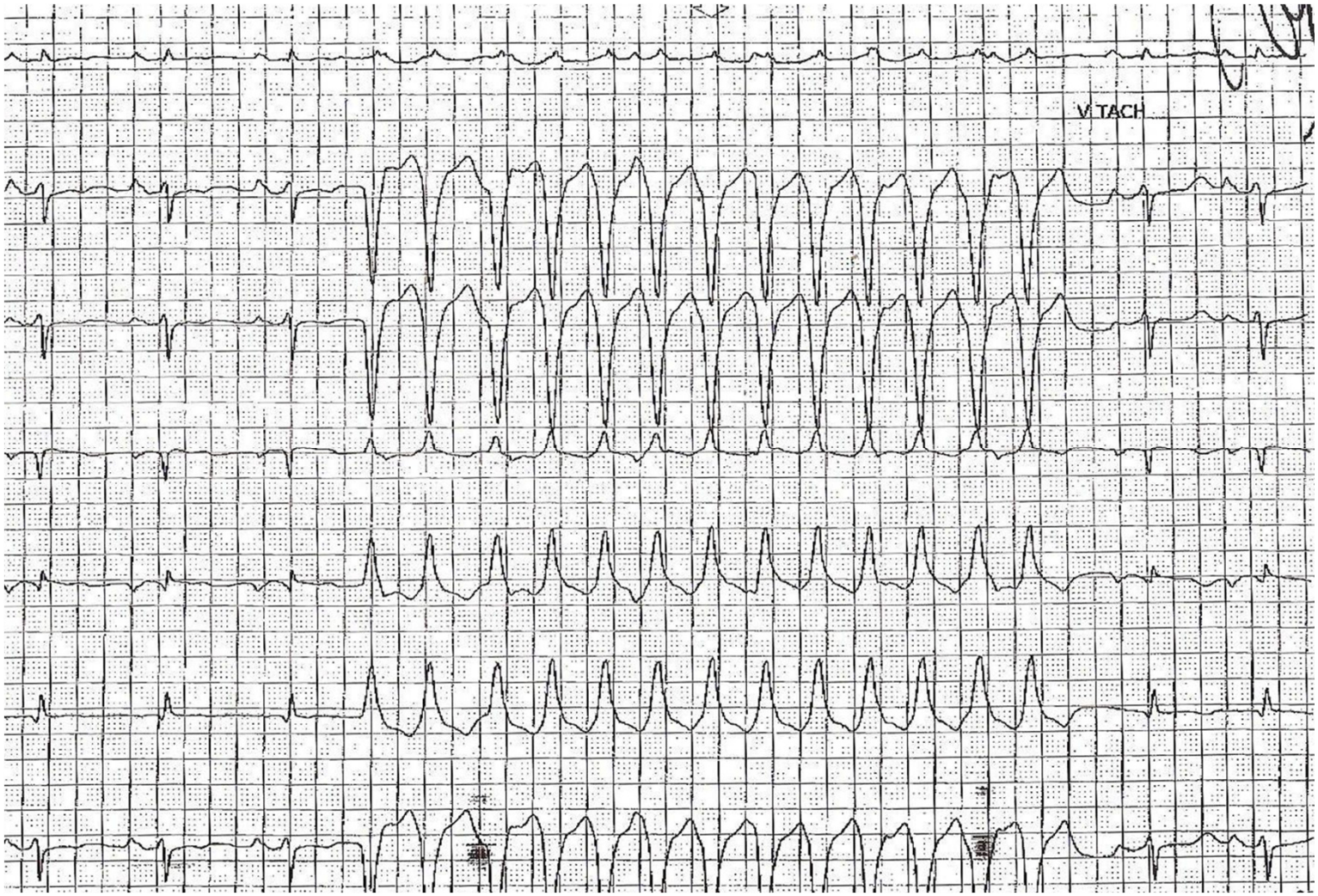
Results of the Marburg Cardiomyopathy Study

Wolfram Grimm, MD; Michael Christ, MD; Jennifer Bach, MD;
Hans-Helge Müller, PhD; Bernhard Maisch, MD

Background—Arrhythmia risk stratification with regard to prophylactic implantable cardioverter-defibrillator therapy is a completely unsolved issue in idiopathic dilated cardiomyopathy (IDC).

Methods and Results—Arrhythmia risk stratification was performed prospectively in 343 patients with IDC, including analysis of left ventricular (LV) ejection fraction and size by echocardiography, signal-averaged ECG, arrhythmias on Holter ECG, QTc dispersion, heart rate variability, baroreflex sensitivity, and microvolt T-wave alternans. During 52±21 months of follow-up, major arrhythmic events, defined as sustained ventricular tachycardia, ventricular fibrillation, or sudden death, occurred in 46 patients (13%). On multivariate analysis, LV ejection fraction was the only significant arrhythmia risk predictor in patients with sinus rhythm, with a relative risk of 2.3 per 10% decrease of ejection fraction (95% CI, 1.5 to 3.3; $P=0.0001$). Nonsustained ventricular tachycardia on Holter was associated with a trend toward higher arrhythmia risk (RR, 1.7; 95% CI, 0.9 to 3.3; $P=0.11$), whereas β-blocker therapy was associated with a trend toward lower arrhythmia risk (RR, 0.6; 95% CI, 0.3 to 1.2; $P=0.13$). In patients with atrial fibrillation, multivariate Cox analysis also identified LV ejection fraction and absence of β-blocker therapy as the only significant arrhythmia risk predictors.

Conclusions—Reduced LV ejection fraction and lack of β-blocker use are important arrhythmia risk predictors in IDC, whereas signal-averaged ECG, baroreflex sensitivity, heart rate variability, and T-wave alternans do not seem to be helpful for arrhythmia risk stratification. These findings have important implications for the design of future studies evaluating prophylactic implantable cardioverter-defibrillator therapy in IDC. **(*Circulation*. 2003;108:2883-2891.)**


V. TACH

ORIGINAL CONTRIBUTION

Association of Fibrosis With Mortality and Sudden Cardiac Death in Patients With Nonischemic Dilated Cardiomyopathy

Gulati A, et al. JAMA 2013; 309:896-908.

Estimates of Time to Events by Midwall Fibrosis Status (n=472)

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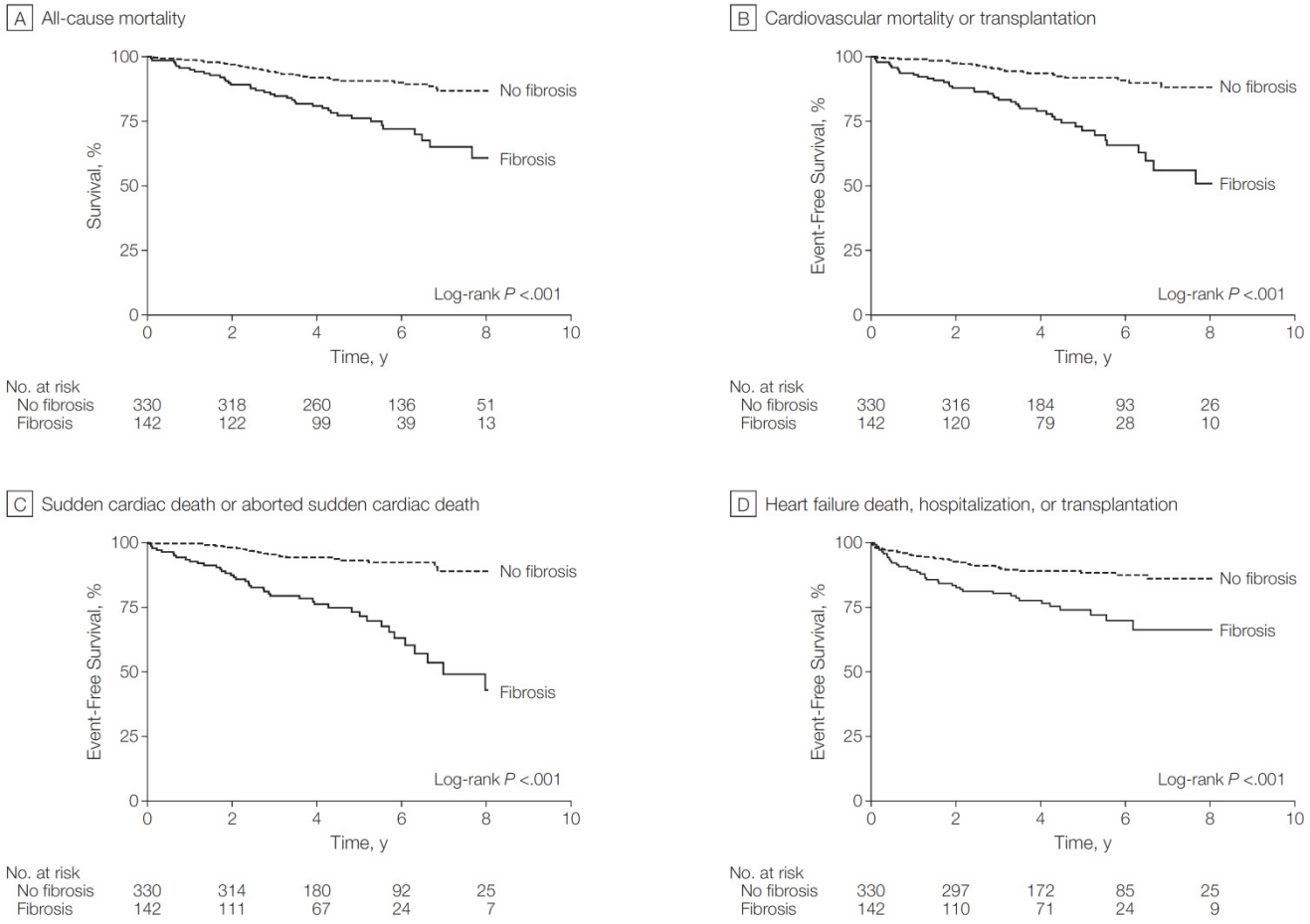

Gulati A, et al. JAMA 2013; 309:896-908.

Conclusions

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- Nonischemic cardiomyopathy is related to multifactorial issues that alter the patter of sudden cardiac death.
- Younger age, lower BNP, Fibrosis may enhance the need for AICD for primary prevention.
- Latest guidelines 2015 ESC guideline (class I, level of evidence B)
- Individual patient discussions are required to determine risk and need for AICD for primary prevention