Noniskemik KMP'de primer korunmada ICD'nin rolü

Dr. İlyas ATAR
Güven Hastanesi, Ankara

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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*

ABSTRACT

BACKGROUND

The benefit of an implantable cardioverter–defibrillator (ICD) in patients with symptomatic systolic heart failure caused by coronary artery disease has been well documented. However, the evidence for a benefit of prophylactic ICDs in patients with systolic heart failure that is not due to coronary artery disease has been based primarily on subgroup analyses. The management of heart failure has improved since the landmark ICD trials, and many patients now receive cardiac resynchronization therapy (CRT).

The authors' affiliations are listed in the Appendix. Address reprint requests to Dr. Køber at the Department of Cardiology, Rigshospitalet, University Hospital, Blegdamsvej 9, Copenhagen, Denmark, or at lars.koeber@regionh.dk.

*A complete list of investigators in the Danish Study to Assess the Efficacy of ICDs in Patients with Non-ischemic Systolic Heart Failure on Mortality (DANISH)

2013 ACCF/AHA Guideline

- **Class I**
- **ICD therapy is recommended for primary prevention of SCD to reduce total morta[lity] in patients with nonischemic DCM or ischemic h[eart disease] at least 40 days post-MI with LVEF of 35% or less and NYHA class II or III symptoms on chronic GDMT, who have reasonable expectation of meaningful survival for more than 1 year.†[355],[593] *(Level of Evidence: A)***

SCD HEFT

- **CRT is indicated for patients who have LVEF of 35% or less, sinus rhythm, left bundle-branch block (LBBB) with a QRS duration of 150 ms or greater, and NYHA class II, III, or ambulatory IV symptoms on GDMT. *(Level of Evidence: A for NYHA class III/IV* [38],[78],[116],[594]*; Level of Evidence: B for NYHA class II*[595],[596]**)**

2013 ACCF/AHA guideline for the management of heart failure. Circulation 2013; 128: e240-327.

2013 ACCF/AHA Guideline

- **There are no trials that support CRT-pacing (without ICD) in NYHA class I and II patients**. Thus, it is anticipated these patients would receive CRT-D unless clinical reasons or personal wishes make CRT-pacing more appropriate. **In patients who are NYHA class III and ambulatory class IV, CRT-D may be chosen but clinical reasons and personal wishes may make CRT-pacing appropriate to improve symptoms and quality of life when an ICD is not expected to produce meaningful benefit in survival**.

2013 ACCF/AHA guideline for the management of heart failure. Circulation 2013; 128: e240-327.

2016 ESC Guideline

Recommendations for implantable cardioverter-defibrillator in patients with heart failure

Recommendations	Class [a]	Level [b]	Ref [c]
Secondary prevention An ICD is recommended to reduce the risk of sudden death and all-cause mortality in patients who have recovered from a ventricular arrhythmia causing haemodynamic instability, and who are expected to survive for >1 year with good functional status.	I	A	223–226
Primary prevention An ICD is recommended to reduce the risk of sudden death and all-cause mortality in patients with symptomatic HF (NYHA Class II–III), and an LVEF ≤35% despite ≥3 months of OMT, provided they are expected to survive substantially longer than one year with good functional status, and they have:			
• IHD (unless they have had an MI in the prior 40 days – see below).	I	A	149, 156, 227
• DCM.	I	B	156, 157, 227

SCD HEFT,
DEFINITE, META-ANALİZ

2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure. Eur Heart J 2016; 37:2129-200.

2016 ESC Guideline

- If the primary reason for implanting CRT is to improve prognosis, then the majority of evidence lies with **CRT-D for patients in NYHA Class II and with CRT-P for patients in NYHA Classes III–IV**.

2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure. Eur Heart J 2016; 37:2129-200.

Çalışmaların karşılaştırılması

NYHA Sınıfı	SCD-HeFT[1] N = 2521	DEFINITE[2] N = 458	COMPANION[3] N = 1520	CARE-HF[4] N = 813
I	0%	22%	0%	0%
II	70%	57%	0%	0%
III	30%	21%	85%	93%
IV	0%	0%	15%	7%

[1] Bardy GH. *N Engl J Med.* 2005;352:225-237.
[2] Kadish A. *N Engl J Med.* 2004;350:2151-2158.
[3] Bristow M. *N Engl J Med*. 2004;350:2140-2150.
[4] Cleland JGF. *N Engl J Med.* 2005;352:1539-1549.

Çalışmaların karşılaştırılması

	SCD-HeFT[1] N = 2521	DEFINITE[2] N = 458	COMPANION[3] N = 1520	CARE-HF[4] N = 813
Çalışma Tedavileri*	ICD Plasebo Amiodaron	ICD Medikal tdv	CRT CRT-D Medikal tdv	CRT Medikal tdv
Takip süresi	45.5 ay Median	29 ay Mean	11.9 - 16.2 ay Median	29.4 ay Mean

[1] Bardy GH. *N Engl J Med.* 2005;352:225-237.
[2] Kadish A. *N Engl J Med.* 2004;350:2151-2158.
[3] Bristow M. *N Engl J Med*. 2004;350:2140-2150.
[4] Cleland JGF. *N Engl J Med.* 2005;352:1539-1549.

Çalışmaların karşılaştırılması

	% Noniskemik KKY NYHA Class	LVEF	QRS süresi	Age (ort)	% ölümde azalma
SCD-HeFT[1] N = 2521	%48 Noniskemik klas II/III	%25 Median	< 111.5 ms	60 yaş	**%23** ICD vs. Placebo
DEFINITE[2] N = 458	%100 Noniskemik klas I/II/III	%21 Mean	115 ms Mean	58 yaş	**%35** ICD vs. OPT (ns)
COMPANION[3] N = 1520	%44 Noniskemik III/IV	%21 Mean	160 ms Mean	67 yaş	**%36** CRT-D vs. OPT **%24** CRT vs. OPT
CARE-HF[4] N = 813	%62 Noniskemik III/IV	%25 Median	160 ms Mean	67 yaş	**%33** CRT-D vs. OPT

[1] Bardy GH. *N Engl J Med.* 2005;352:225-237.
[2] Kadish A. *N Engl J Med.* 2004;350:2151-2158.
[3] Bristow M. *N Engl J Med*. 2004;350:2140-2150.
[4] Cleland JGF. *N Engl J Med.* 2005;352:1539-1549.

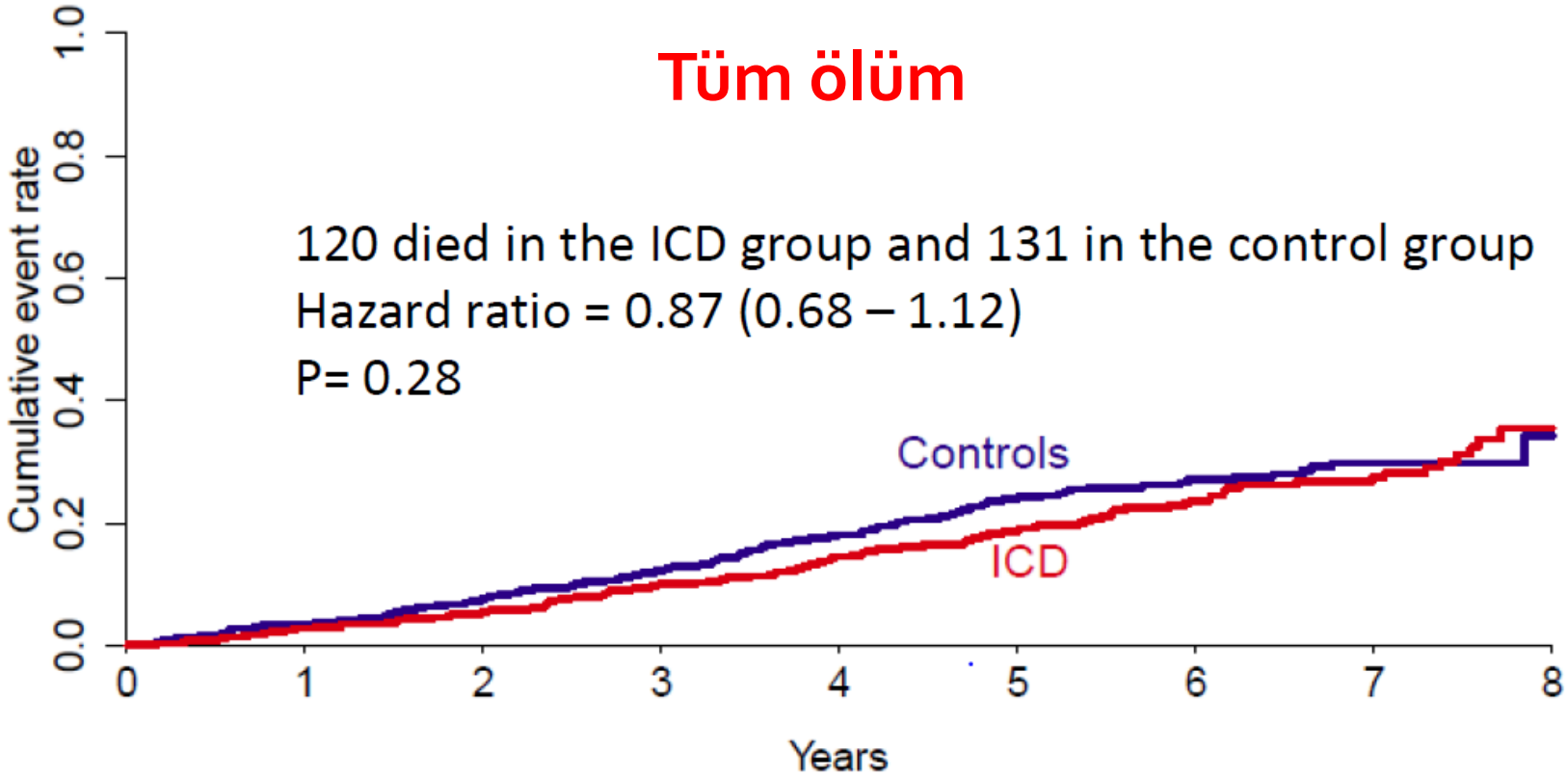
DANISH çalışması

	ICD (N=556)	Control (N=560)
Age (years)	64 (56-72)	63 (56-70)
Female gender (%)	151 (27)	156 (28)
NT-proBNP (pg/ml)	1244 (616-2321)	1110 (547-2166)
LVEF (%)	25 (20-30)	25 (20-30)
Medications (%)		
ACEi/ARB	533 (96)	544 (97)
Beta-blocker	509 (92)	517 (92)
MRA	326 (59)	320 (57)
Planned CRT (%)	322 (58)	323 (58)

Kober L. Et al. N Engl J Med 2016;375:1221-

DANISH çalışması

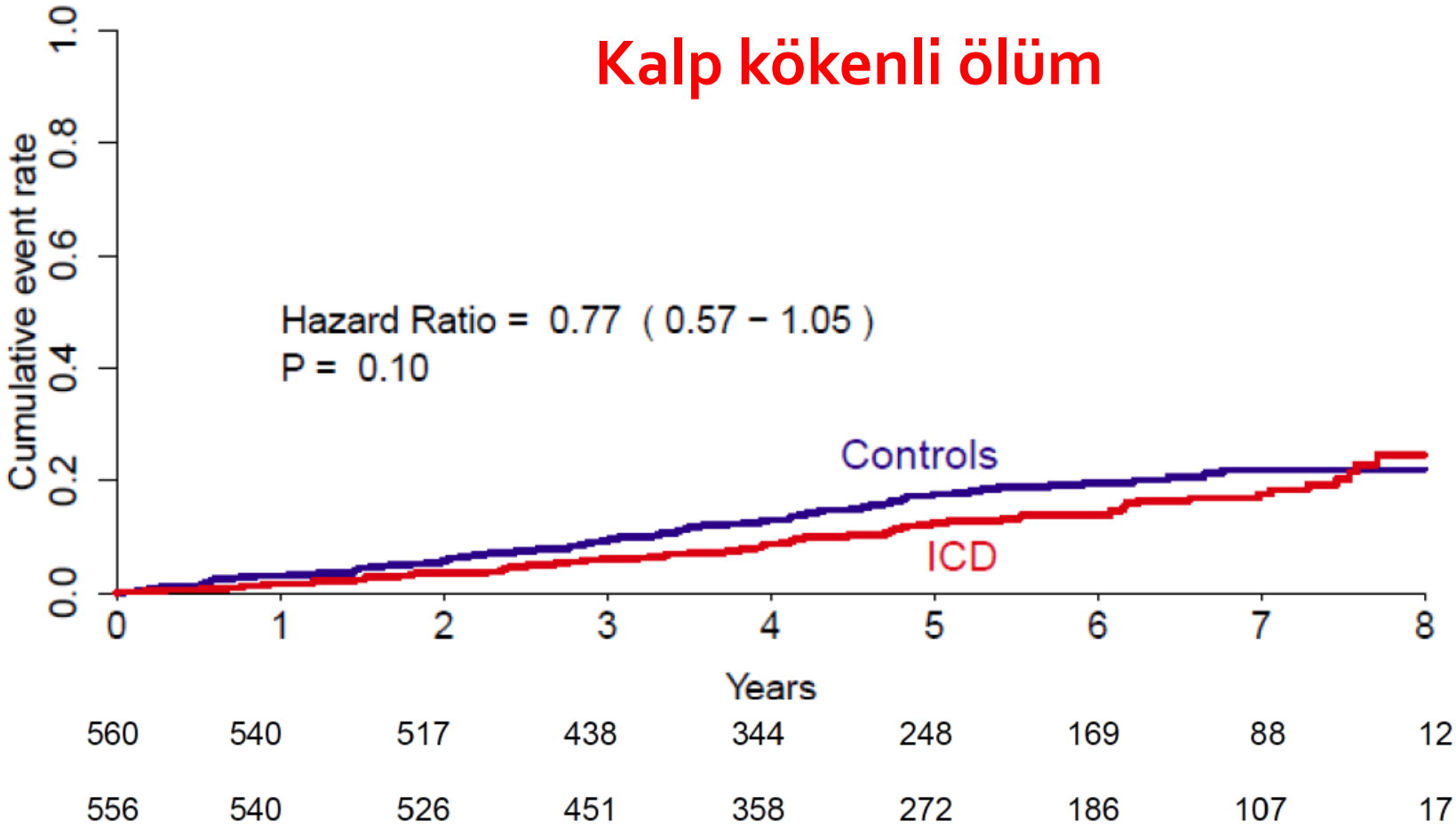
Tüm ölüm



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

Kober L. Et al. N Engl J Med 2016;375:1221-

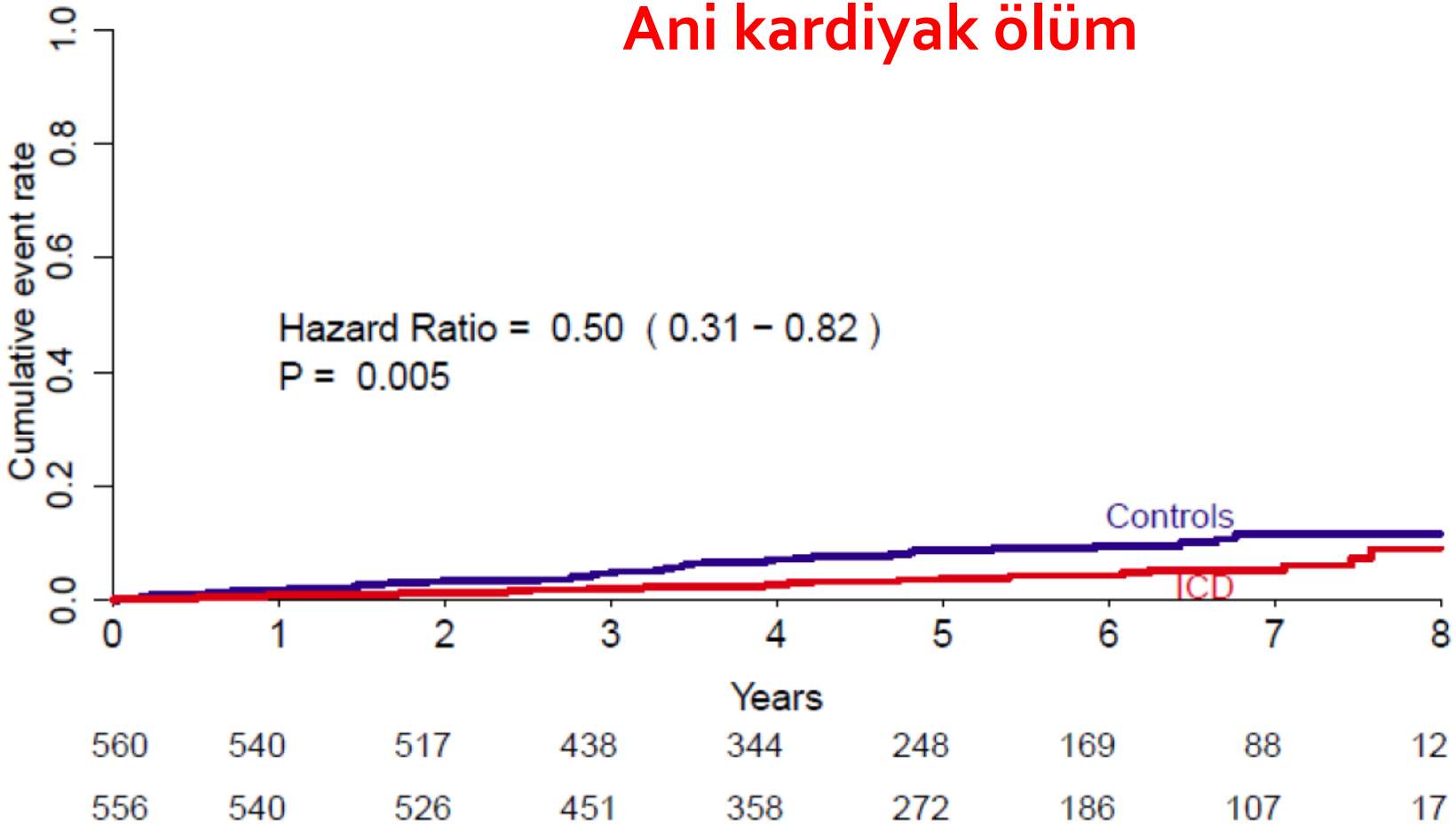
DANISH çalışması



Kober L. Et al. N Engl J Med 2016;375:1221-

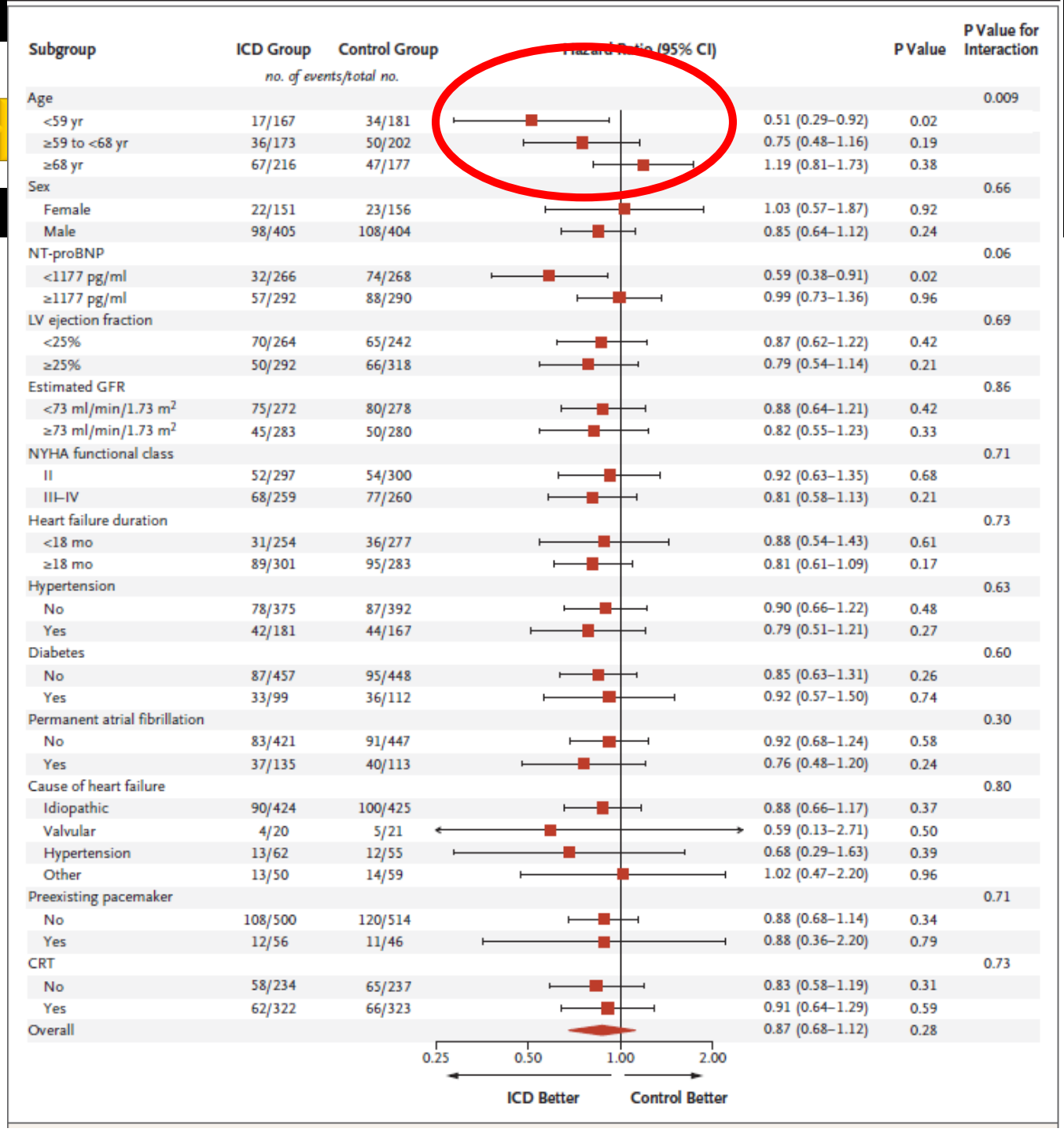
DANISH çalışması

Ani kardiyak ölüm



Kober L. Et al. N Engl J Med 2016;375:1221-

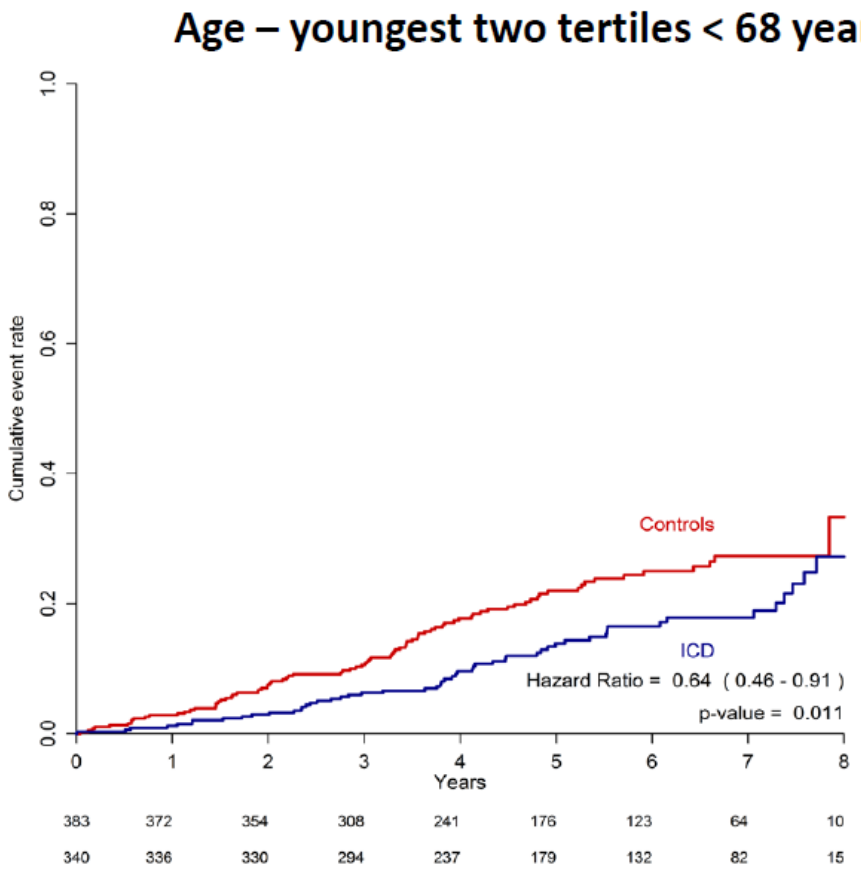
DANISH

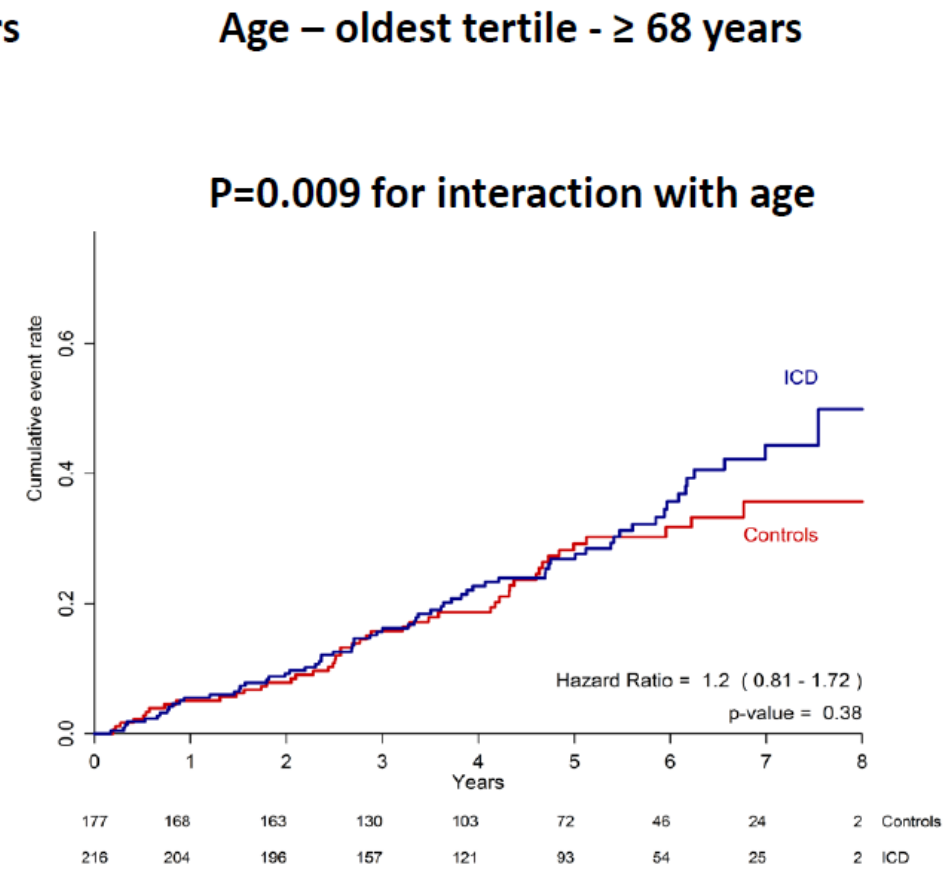


Subgroup	ICD Group	Control Group	Hazard Ratio (95% CI)	P Value	P Value for Interaction
	no. of events/total no.				
Age					0.009
<59 yr	17/167	34/181	0.51 (0.29–0.92)	0.02	
≥59 to <68 yr	36/173	50/202	0.75 (0.48–1.16)	0.19	
≥68 yr	67/216	47/177	1.19 (0.81–1.73)	0.38	
Sex					0.66
Female	22/151	23/156	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	

Kober L. Et al. N Engl J Med 2016;375:1221-30.

DANISH çalışması





Kober L. Et al. N Engl J Med 2016;375:1221-

Olgu

- 68 yaş erkek hasta,
  - 6 ay önce efor dispnesi ve bacaklarda şişlikle başvurmuş
  - Ağır alkol kullanım öyküsü var, 5 yıldır bırakmış
  - EKO: EF %30, KAG: Normal
  - Tanı: Alkole bağlı? NIKMP
  - Tedavi:
    - Lisinopril 20 mg/gün
    - Karvedilol 2 * 25 mg
    - Spironolakton 1*25 mg/gün
    - Furosemide 20 mg/gün

.

- Hastanın tedavi uyumu iyi,
- Ek sağlık problemi yok
- Klas 2 efor kapasitesi, istirahatte asemptomatik
- EKG: NSR, QRS süresi: 90 msn
- Kontrol eko: EF aynı

.

- 6 ay önce taburcu olunca bahsedilmiş olan ICD implantasyonun gerekliliğini sorguluyor
  - Mutlak gerekli değilse invaziv işlemlerden hoşlanmıyor
  - ICD'lerin uygunsuz şok verebildiğini duymuş
  - Yakınlarda bi arkadaşında ICD takılırken hematom gelişmiş
  - İyi kalitede, hastaneye yatış olmaksızın, yaşayabildiği kadar uzun yaşamak istiyor.

- Ne dersiniz?
- Hastaya medikal tedavisine ilave olarak ICD önerirmisiniz?

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CLINICAL DECISIONS

INTERACTIVE AT NEJM.ORG

Implantable Cardioverter–Defibrillators in Nonischemic Cardiomyopathy

This interactive feature addresses the approach to a clinical issue. A case vignette is followed by specific options, neither of which can be considered either correct or incorrect. In short essays, experts in the field then argue for each of the options. Readers can participate in forming community opinion by choosing one of the options and, if they like, providing their reasons.

CASE VIGNETTE

A Man with Nonischemic Cardiomyopathy Who Is Considering an ICD

Rebecca E. Berger, M.D.

Mr. Gregory is a 68-year-old man with nonischemic cardiomyopathy who has come to your office to discuss possible placement of an implantable cardioverter–defibrillator (ICD). Six months ago, he was admitted to the hospital with progressive exercise intolerance and new onset of edema in his legs. He has a history of heavy alcohol use but has been abstinent for the past 5 years. During his hospital stay, an echocardiogram showed an ejection fraction of 30%; cardiac catheterization revealed no clinically significant coronary artery disease. He received a diagnosis of nonischemic cardiomyopathy, which was presumed to be due to alcohol use. At discharge, medical therapy was prescribed that included lisinopril (20 mg daily), carvedilol (25 mg twice daily), spironolactone (25 mg daily), and furosemide (20 mg daily).

visit is unchanged from the prior one. He is otherwise in good health, with no other major medical problems.

During Mr. Gregory's hospital stay 6 months ago, you had discussed with him the possibility of implanting an ICD. He is concerned about invasive procedures and hesitant to proceed with interventions unless he is convinced that they are necessary. He has heard that ICDs sometimes deliver inappropriate shocks, and he mentions a friend who recently had a hematoma after pacemaker placement. He wants to live as long as possible, with a good quality of life, and would like to avoid hospitalizations. Mr. Gregory is seeking your advice and is eager to accept your recommendation.

TREATMENT OPTIONS

In addition to continuing medical therapy, which of the following treatment options would you recommend for this patient?

1. **Undergo placement of an ICD.**
2. **Do not undergo placement of an ICD.**

Berger RE, Ellenbogen KA, Stevenson WG. N Engl J Med. 2016 ;375:2290-2292.

- 1 ay süre
- 32000 kişi okumuş
- 55 ülkeden 472 kişi oylamış (%39 ABD veya Kanada)
  - ICD takılsın: %41
  - ICD takılmasın: %59
- Her iki fikirde 29'ar kişi yorum yapmış
  - Angiotensin reseptor–neprilysin inhibitorü (PARADIGM-HF çalışması)
  - MRI'da fibrozis varlığı? Holterde aritmi varlığı?

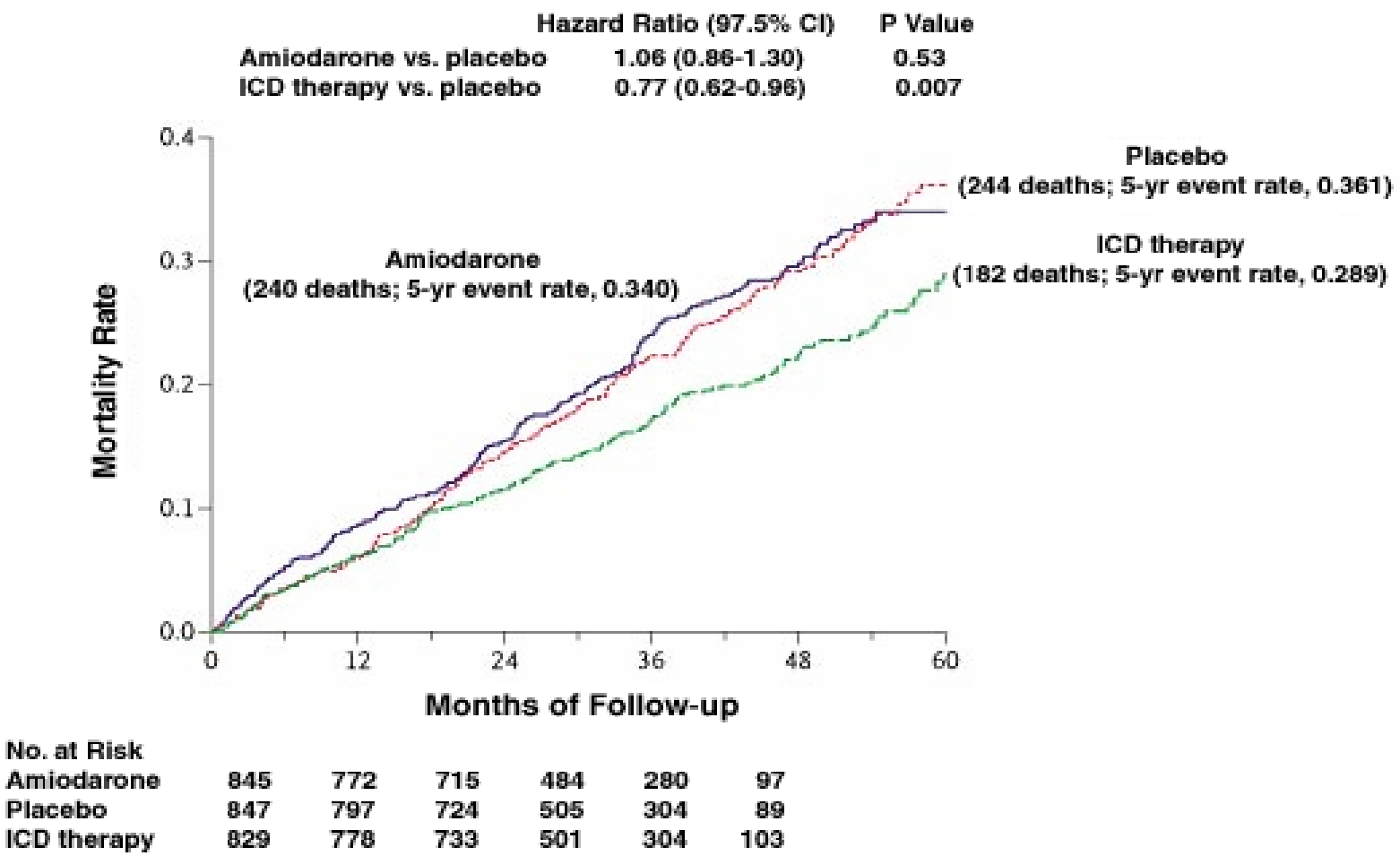
Berger RE, Ellenbogen KA, Stevenson WG. N Engl J Med. 2016 ;375:2290-2292.

Sonuç

- Kılavuz önerilerini tüm NIDKMP hastalarına uygulamak ?
  - DANISH çalışma verileri
  - CARE-HF verileri
- Hastaya göre bireysel yaklaşım?
  - Genç çoklu risk faktörü olmayan hastada ICD
  - Yaşlı ve/veya çoklu risk faktörü olan hastada
    - CRT endikasyonu varsa CRT-P
    - ICD takılmaması?
      - Hukuk?

- Bitti .....

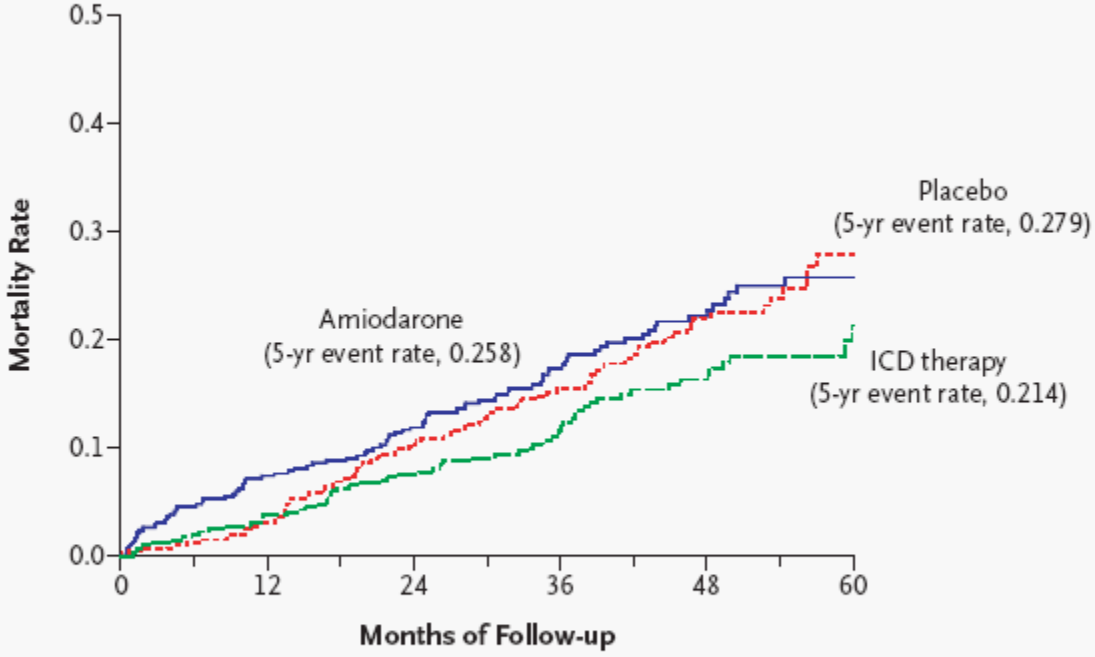
SCD –HEFT çalışması



Bardy et al. , et al. New Engl J Med. 352 (3): 225

B Nonischemic CHF

	Hazard Ratio (97.5% CI)	P Value
Amiodarone vs. placebo	1.07 (0.76–1.51)	0.65
ICD therapy vs. placebo	0.73 (0.50–1.07)	0.06

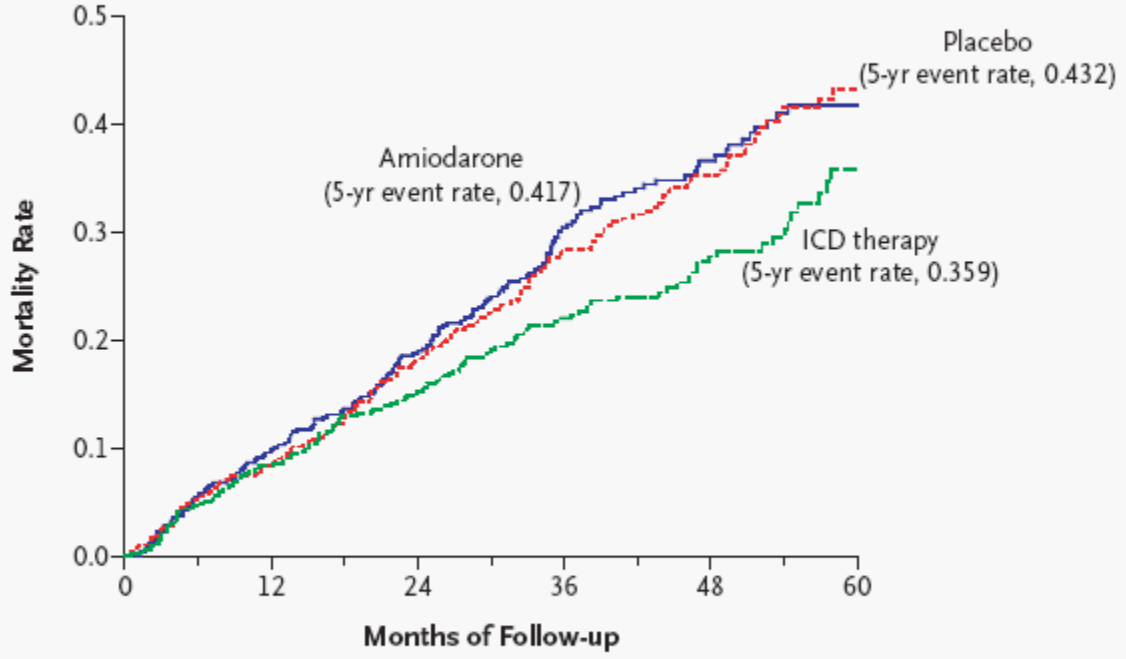


No. at Risk						
Amiodarone	419	388	369	257	150	51
Placebo	394	382	354	261	152	41
ICD therapy	398	383	368	257	160	55

Bardy et al. , et al. New Engl J Med. 352 (3): 225

A Ischemic CHF

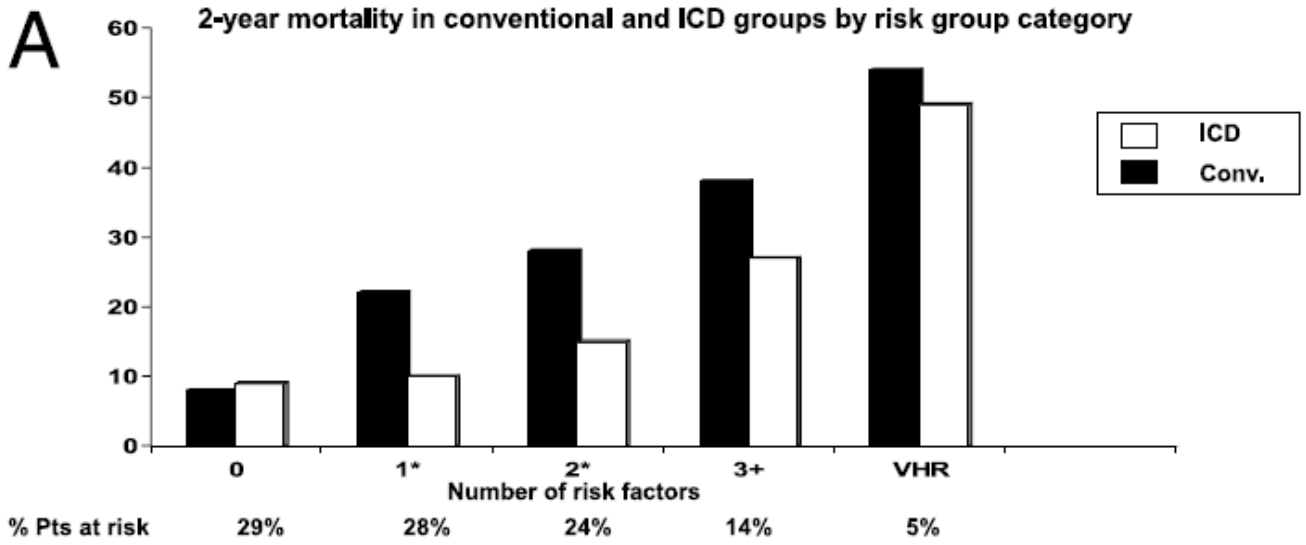
	Hazard Ratio (97.5% CI)	P Value
Amiodarone vs. placebo	1.05 (0.81–1.36)	0.66
ICD therapy vs. placebo	0.79 (0.60–1.04)	0.05

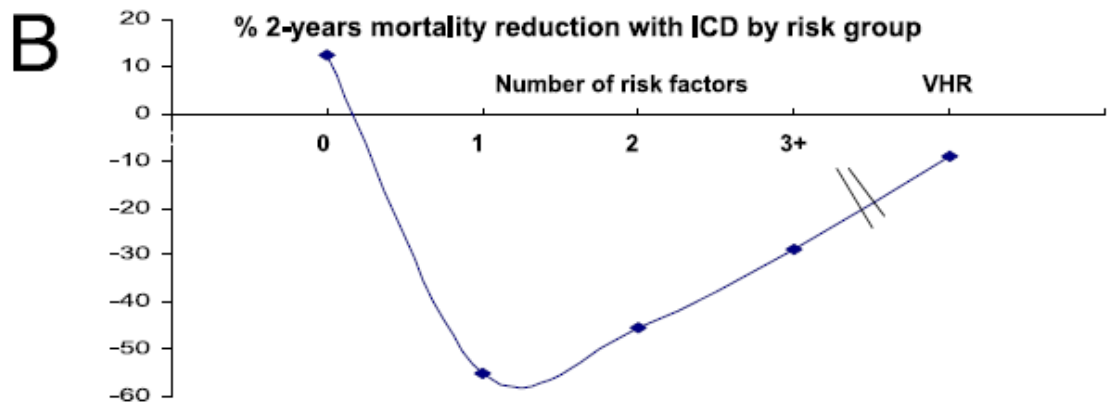


No. at Risk						
Amiodarone	426	384	346	227	130	46
Placebo	453	415	370	244	152	48
ICD therapy	431	395	365	244	144	48

Bardy et al. , et al. New Engl J Med. 352 (3): 225

MADIT 2 hastaları: Risk faktörü sayısı ve mortalite faydası ilişkisi



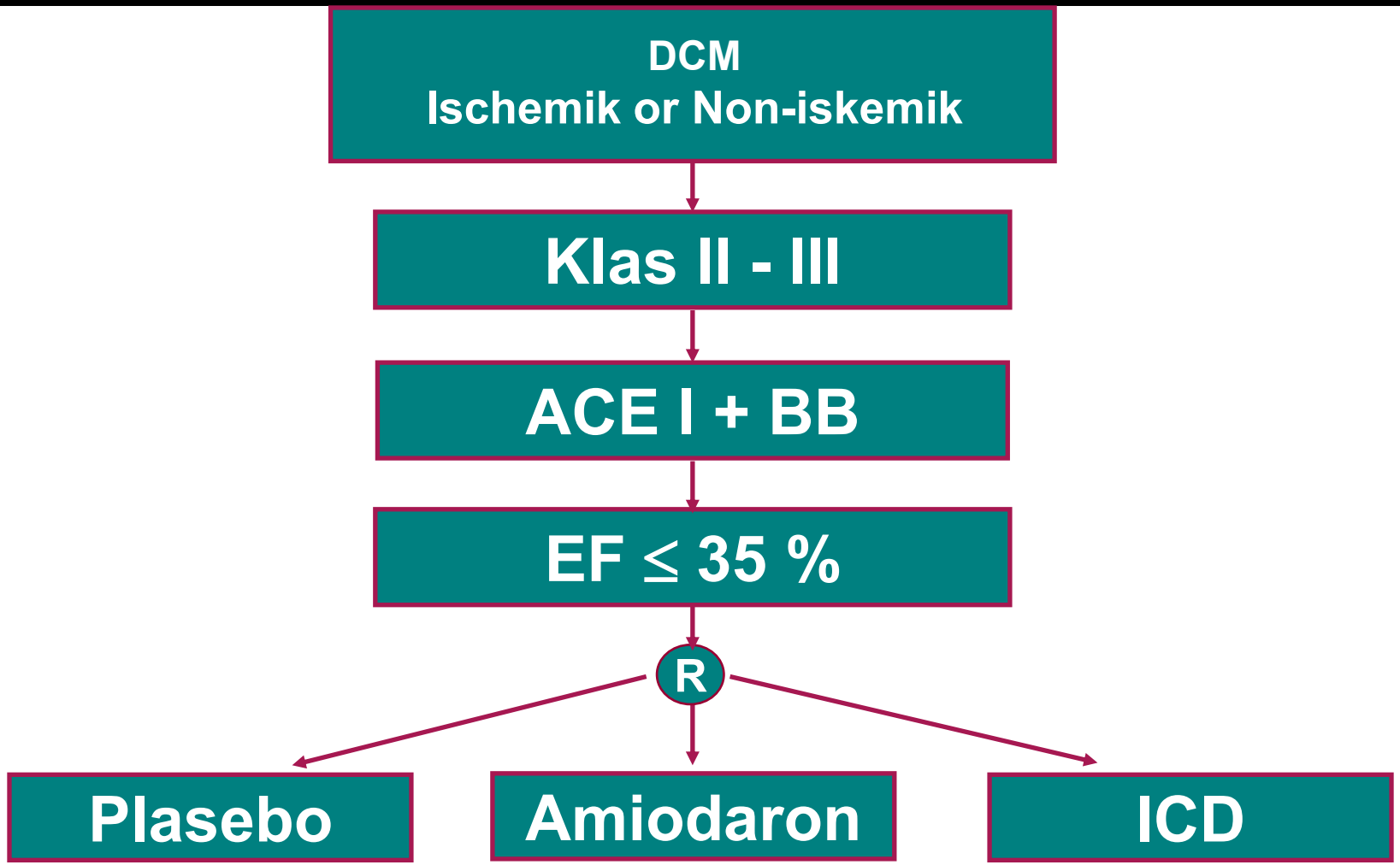


Risk Faktörleri

- NYHA klas >2
- Yaş >70
- BUN >26 mg/dl
- QRS süresi > 0.12 sn
- Atriyal Fibrilasyon

Goldenberg I, et al J Am Coll Cardiol 2008;51:288–96

SCD-HeFT: Sudden Cardiac Death in Heart Failure Trial
Çalışma dizaynı

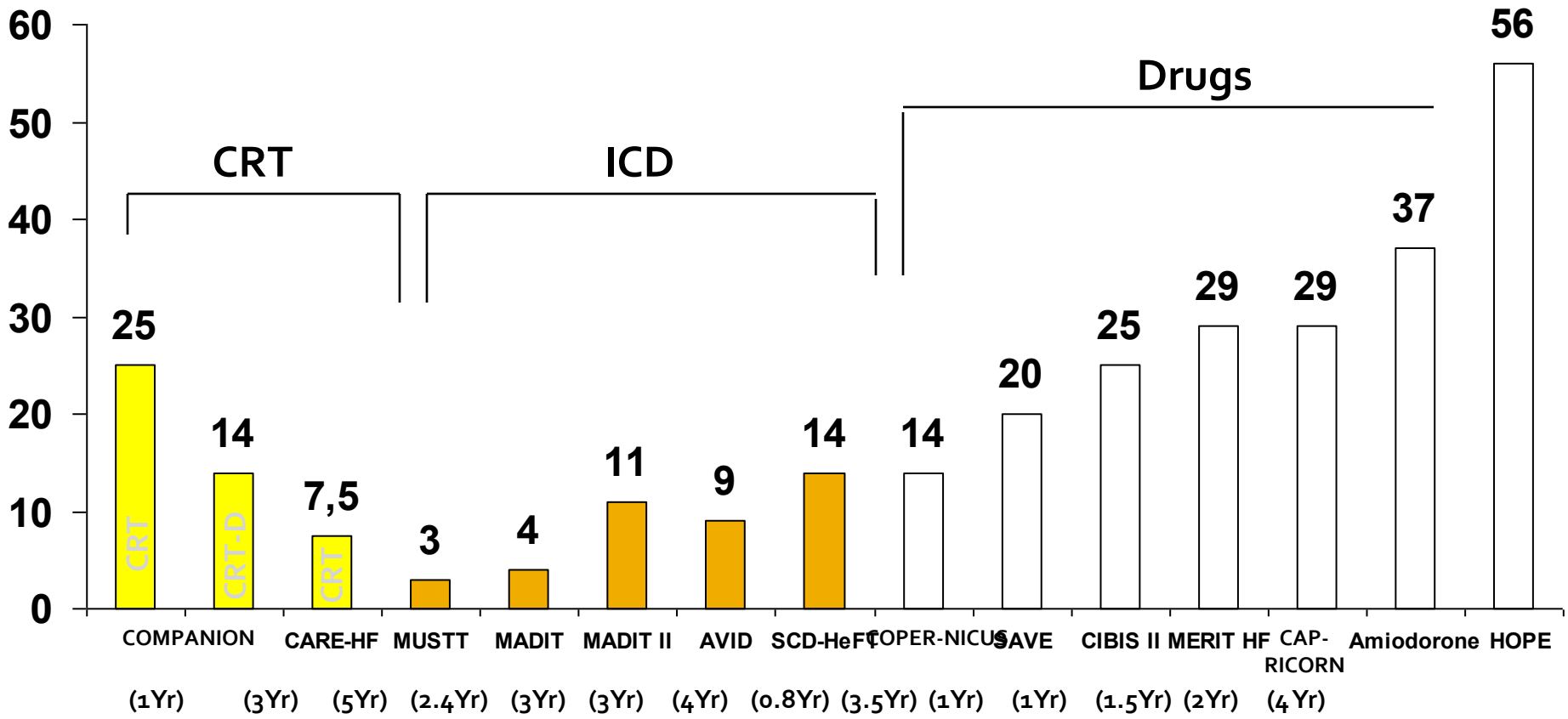


SCD-HeFT Patient Characteristics

- Patients enrolled: 2521
- NYHA Class: 70% NYHA II, 30% NYHA III
- Median follow-up: 45.5 months
- Median age: 60 years
- % female: 23%
- Median EF: 25%
- Concomitant Rx: ACE 72%, beta blocker 78%

Number Needed to Treat To Save A Life

$NNT_{x\ years}$ = 100 / (% Mortality in Control Group – % Mortality in Treatment Group)



Adapted from Auricchio A, Abraham W. Circulation 2004; 109; 300-307.

2016 ESC Guideline

Recommendations for cardiac resynchronization therapy implantation in patients with heart failure

Recommendations	Class [a]	Level [b]	Ref [c]
CRT is recommended for symptomatic patients with HF in sinus rhythm with a QRS duration ≥150 msec and LBBB QRS morphology and with LVEF ≤35% despite OMT in order to improve symptoms and reduce morbidity and mortality.	I	A	261–272
CRT should be considered for symptomatic patients with HF in sinus rhythm with a QRS duration ≥150 msec and non-LBBB QRS morphology and with LVEF ≤35% despite OMT in order to improve symptoms and reduce morbidity and mortality.	IIa	B	261–272
CRT is recommended for symptomatic patients with HF in sinus rhythm with a QRS duration of 130–149 msec and LBBB QRS morphology and with LVEF ≤35% despite OMT in order to improve symptoms and reduce morbidity and mortality.	I	B	266, 273
CRT may be considered for symptomatic patients with HF in sinus rhythm with a QRS duration of 130–149 msec and non-LBBB QRS morphology and with LVEF ≤35% despite OMT in order to improve symptoms and reduce morbidity and mortality.	IIb	B	266, 273
CRT rather than RV pacing is recommended for patients with HFrEF regardless of NYHA class who have an indication for ventricular pacing and high degree AV block in order to reduce morbidity. This includes patients with AF (see Section 10.1).	I	A	274–277
CRT should be considered for patients with LVEF ≤35% in NYHA Class III–IV[d] despite OMT in order to improve symptoms and reduce morbidity and mortality, if they are in AF and have a QRS duration ≥130 msec provided a strategy to ensure bi-ventricular capture is in place or the patient is expected to return to sinus rhythm.	IIa	B	275, 278–281
Patients with HFrEF who have received a conventional pacemaker or an ICD and subsequently develop worsening HF despite OMT and who have a high proportion of RV pacing may be considered for upgrade to CRT. This does not apply to patients with stable HF.	IIb	B	282
CRT is contra-indicated in patients with a QRS duration < 130 msec.	III	A	266, 283–285

2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure. Eur Heart J 2016; 37:2129-200.