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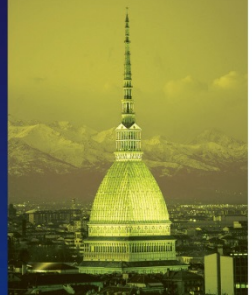

UNIVERSITÁ DEGLI STUDI DI TORINO

AZIENDA OSPEDALIERO - UNIVERSITARIA
Città della Salute e della Scienza di Torino

PRIMARY PREVENTION OF SUDDEN CARDIAC DEATH IN NON ISCHEMIC CARDIOMYOPATHY: INDICATION TO CARDIAC DEFIBRILLATOR

«CONS»

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NOVARA - Italy

Azienda Ospedaliero-Universitaria
Maggiore della Carità
di Novara

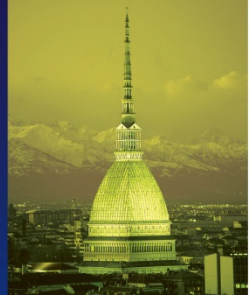
UPO
UNIVERSITÀ DEL PIEMONTE ORIENTALE

Sudden cardiac death risk in ISCHEMIC and IDIOPATIC substrate of CARDIOMYOPATHY

Common point:
LOW LV-EF (<35%)

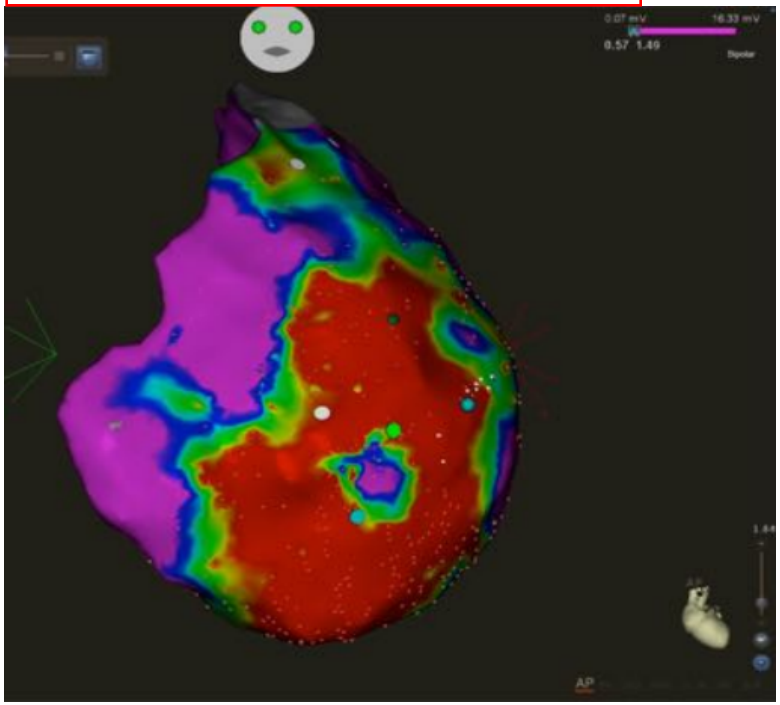
BUT ……

Is left ventricular Ejection Fraction enough to identify the Heart Failure patients at high risk for Sudden Cardiac Death ?

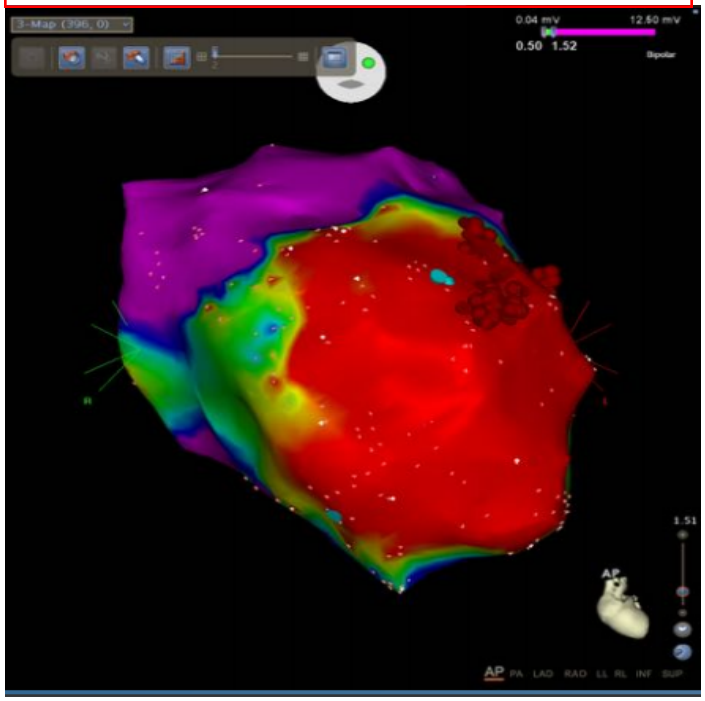


There are some different physiopathological mechanisms to trigger life threathening ventricular tachyarrhythmias ….

Ischemic cardiomyopathy
Disomogeneous mapping



Idiopatic cardiomyopathy
More omogeneous mapping



Ischemic cardiomyopathy

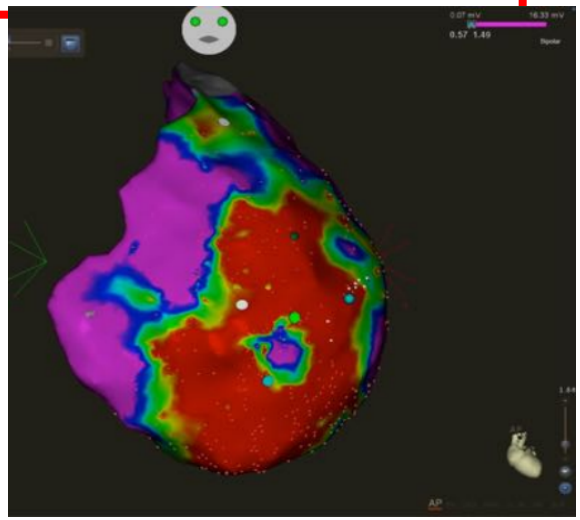
–> post-necrotic/fibrotic areas

–> REENTRY CIRCUITS

Not or partially revascularized Myocardial Infarction

-> wider necrotic area = lower Ejection Fraction

-> more risk of reentry ventricular tachyarrhythmias



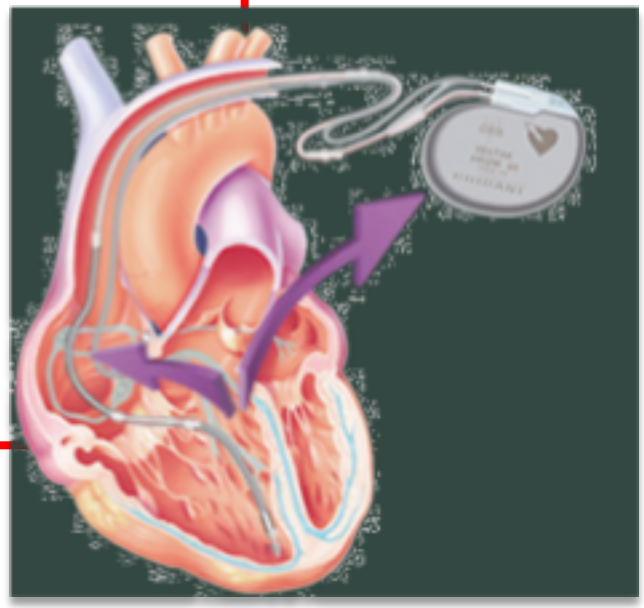
REENTRY CIRCUITS prevention

Sooner revascularization (PTCA/CABG) may reduce myocardial necrotic area with EF increasing

Later revascularization -> Persistent low EF

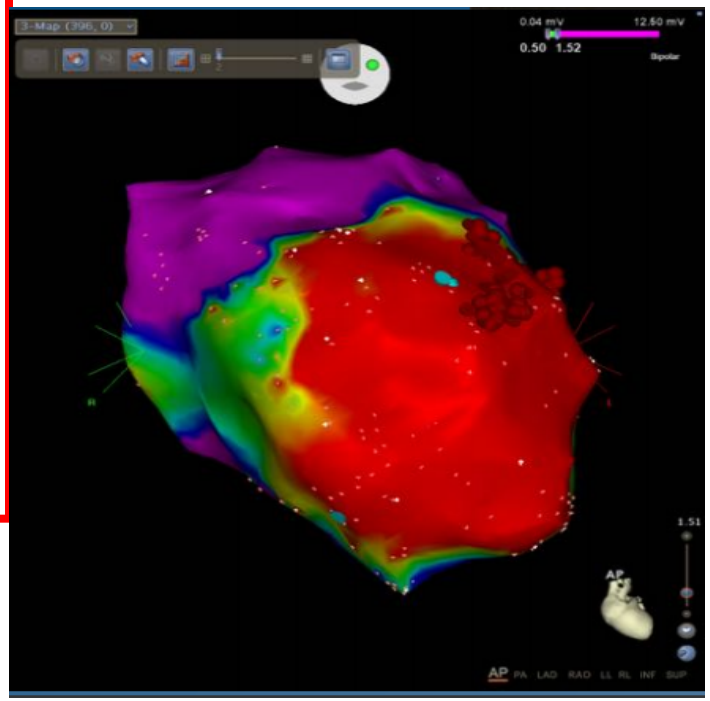
-> higher reentry/ventricular tachyarrythmias

ICD



Idiopatic Cardiomyopathy (non ishemic)
-> «Functional» Reentry
- **Parietal dyssynchronia/distress**
- **Microfibrosis**

Physiopathlogical arrhythmia mechanisms could be modified by:
- **Pharmacological therapy (ACE/ARVB/BetaBlockerd/Sicubitril/…)**
- **Not pharmacological therapy:**
  - **CRT**
  - **CCM**
  - **….**

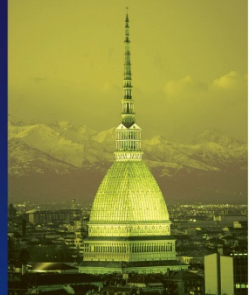


Cardiomyopahy therapy rational….

- Ischemic substrate:
  - -> Rivascolarization
  - -> Low EF (< 35%) -> ICD

- Non ischemic substrate:
  - -> wait for
    - drugs therapy effect
    - CRT/CCM effect

ICD only is low EF (< 35%) after long time
(Life Vest back up?)

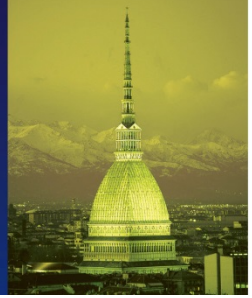


Besides rational….

What about Licterature
for ICD for Primary Prevention in non ischemic cardiomyopathy with low EF (<35%) ?

2 preliminary studies
- **-> CAT (2002 – 104 pts) -> no ICD favour**
- **-> DEFINITE (2004 – 458 pts): ICD possible**

More recent larger studies:
- **-> SCD-HeFT (2005 – 2521 pts): ICD positive**
- **-> DANISH (2016 – 1116 pts): no ICD favour**



Circulation. 2002 Mar 26;105(12):1453-8.

Primary prevention of sudden cardiac death in idiopathic dilated cardiomyopathy: the Cardiomyopathy Trial (CAT).

Bänsch D[1], Antz M, Boczor S, Volkmer M, Tebbenjohanns J, Seidl K, Block M, Gietzen F, Berger J, Kuck KH.

Author information

Abstract

BACKGROUND: Patients with idiopathic dilated cardiomyopathy (DCM) and impaired left ventricular ejection fraction have an increased risk of dying suddenly.

METHODS AND RESULTS: Patients with recent onset of DCM (< or =9 months) and an ejection fraction < or =30% were randomly assigned to the implantation of an implantable cardioverter-defibrillator (ICD) or control. The primary end point of the trial was all-cause mortality at 1 year of follow-up. The trial was terminated after the inclusion of 104 patients because the all-cause mortality rate at 1 year did not reach the expected 30% in the control group. In August 2000, the vital status of all patients was updated by contacting patients, relatives, or local registration offices. One hundred four patients were enrolled in the trial: Fifty were assigned to ICD therapy and 54 to the control group. Mean follow-up was 22.8+/-4.3 months, on the basis of investigators' follow-up. After 1 year, 6 patients were dead (4 in the ICD group and 2 in the control group). No sudden death occurred during the first and second years of follow-up. In August 2000, after a mean follow-up of 5.5+/-2.2 years, 30 deaths had occurred (13 in the ICD group and 17 in the control group). Cumulative survival was not significantly different between the two groups (93% and 80% in the control group versus 92% and 86% in the ICD group after 2 and 4 years, respectively).

CONCLUSIONS: This trial did not provide evidence in favor of prophylactic ICD implantation in patients with DCM of recent onset and impaired left ventricular ejection fraction.

The NEW ENGLAND JOURNAL of MEDICINE

N Engl J Med 2004;350:2151-8.

ORIGINAL ARTICLE

Prophylactic Defibrillator Implantation in Patients with Nonischemic Dilated Cardiomyopathy

Alan Kadish, M.D., Alan Dyer, Ph.D., James P. Daubert, M.D., Rebecca Quigg, M.D., N.A. Mark Estes, M.D., Kelley P. Anderson, M.D., Hugh Calkins, M.D., David Hoch, M.D., Jeffrey Goldberger, M.D., Alaa Shalaby, M.D., William E. Sanders, M.D., Andi Schaechter, B.S.N., R.N., and Joseph H. Levine, M.D., for the Defibrillators in Non-Ischemic Cardiomyopathy Treatment Evaluation (DEFINITE) Investigators*

BACKGROUND

Patients with nonischemic dilated cardiomyopathy are at substantial risk for sudden death from cardiac causes. However, the value of prophylactic implantation of an implantable cardioverter–defibrillator (ICD) to prevent sudden death in such patients is unknown.

METHODS

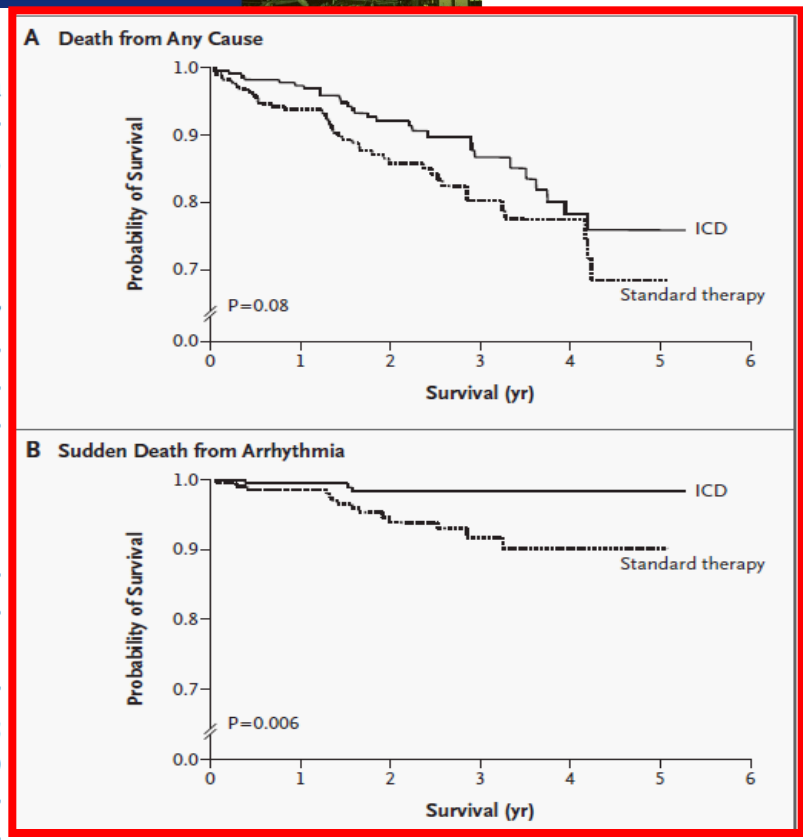
We enrolled 458 patients with nonischemic dilated cardiomyopathy, a left ventricular ejection fraction of less than 36 percent, and premature ventricular complexes or nonsustained ventricular tachycardia. A total of 229 patients were randomly assigned to receive standard medical therapy, and 229 to receive standard medical therapy plus a single-chamber ICD.

RESULTS

Patients were followed for a mean (±SD) of 29.0±14.4 months. The mean left ventricular ejection fraction was 21 percent. The vast majority of patients were treated with angiotensin-converting–enzyme (ACE) inhibitors (86 percent) and beta-blockers (85 percent). There were 68 deaths: 28 in the ICD group, as compared with 40 in the standard-therapy group (hazard ratio, 0.65; 95 percent confidence interval, 0.40 to 1.06; P=0.08). The mortality rate at two years was 14.1 percent in the standard-therapy group (annual mortality rate, 7 percent) and 7.9 percent in the ICD group. There were 17 sudden deaths from arrhythmia: 3 in the ICD group, as compared with 14 in the standard-therapy group (h

CONCLUSIONS

In patients with severe, nonischemic dilated cardiomyopathy who were treated with ACE inhibitors and beta-blockers, the implantation of a cardioverter–defibrillator significantly reduced the risk of sudden death from arrhythmia and was associated with a nonsignificant reduction in the risk of death from any cause.



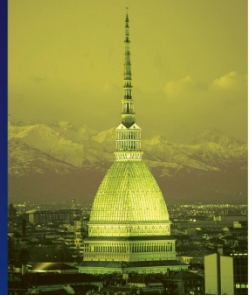
The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JANUARY 20, 2005 VOL. 352 NO. 3

N Engl J Med 2005;352:225-37.

Amiodarone or an Implantable Cardioverter–Defibrillator for Congestive Heart Failure

Gust H. Bardy, M.D., Kerry L. Lee, Ph.D., Daniel B. Mark, M.D., Jeanne E. Poole, M.D., Douglas L. Packer, M.D., Robin Boineau, M.D., Michael Domanski, M.D., Charles Troutman, R.N., Jill Anderson, R.N., George Johnson, B.S.E.E., Steven E. McNulty, M.S., Nancy Clapp-Channing, R.N., M.P.H., Linda D. Davidson-Ray, M.A., Elizabeth S. Fraulo, R.N., Daniel P. Fishbein, M.D., Richard M. Luceri, M.D., and John H. Ip, M.D., for the Sudden Cardiac Death in Heart Failure Trial (SCD-HeFT) Investigators*



SCD-HeFT

BACKGROUND

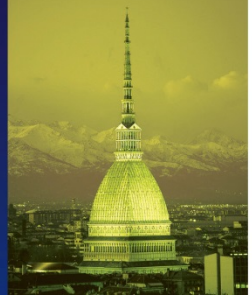
Sudden death from cardiac causes remains a leading cause of death among patients with congestive heart failure (CHF). Treatment with amiodarone or an implantable cardioverter–defibrillator (ICD) has been proposed to improve the prognosis in such patients.

METHODS

We randomly assigned 2521 patients with New York Heart Association (NYHA) class II or III CHF and a left ventricular ejection fraction (LVEF) of 35 percent or less to conventional therapy for CHF plus placebo (847 patients), conventional therapy plus amiodarone (845 patients), or conventional therapy plus a conservatively programmed, shock-only, single-lead ICD (829 patients). Placebo and amiodarone were administered in a double-blind fashion. The primary end point was death from any cause.

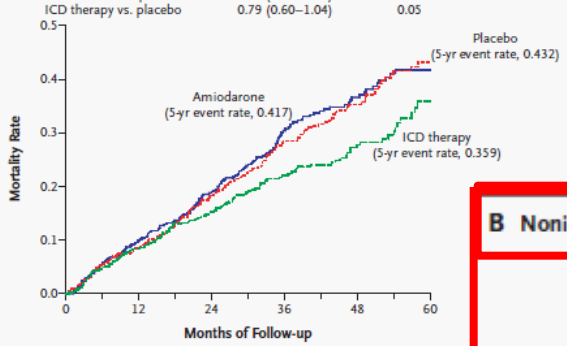
RESULTS

The median LVEF in patients was 25 percent; 70 percent were in NYHA class II, and 30 percent were in class III CHF. The cause of CHF was ischemic in 52 percent and nonischemic in 48 percent. The median follow-up was 45.5 months. There were 244 deaths (29 percent) in the placebo group, 240 (28 percent) in the amiodarone group, and 182 (22 percent) in the ICD group. As compared with placebo, amiodarone was associated with a similar risk of death (hazard ratio, 1.06; 97.5 percent confidence interval, 0.86 to 1.30; P=0.53) and ICD therapy was associated with a decreased risk of death of 23 percent (0.77; 97.5 percent confidence interval, 0.62 to 0.96; P=0.007) and an absolute decrease in mortality of 7.2 percentage points after five years in the overall population. Results did not vary according to either ischemic or nonischemic causes of CHF, but they did vary according to the NYHA class.



A Ischemic CHF

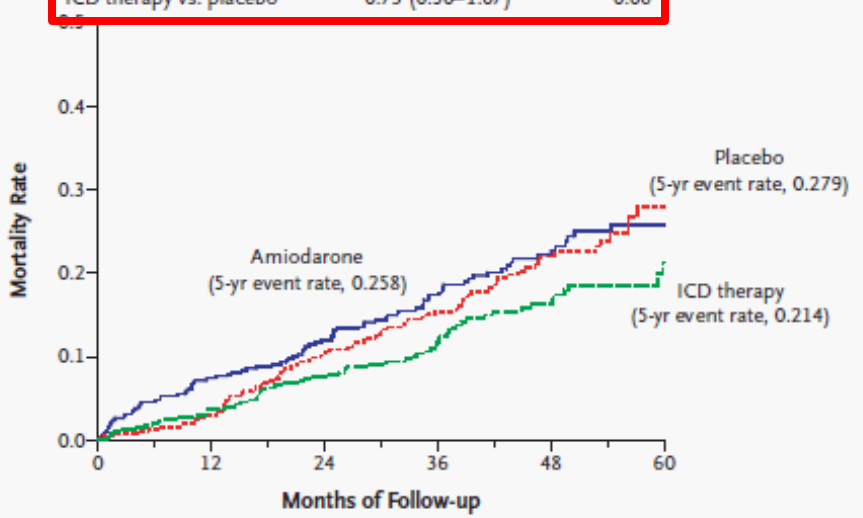
	Hazard Ratio (97.5% CI)	P Value
Amiodarone vs. placebo	1.05 (0.81–1.36)	0.66
ICD therapy vs. placebo	0.79 (0.60–1.04)	0.05



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

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

SCD-HeFT

CONCLUSIONS

In patients with NYHA class II or III CHF and LVEF of 35 percent or less, amiodarone has no favorable effect on survival, whereas single-lead, shock-only ICD therapy reduces overall mortality by 23 percent.

Not distinction between ischemic and non ischemic etiology

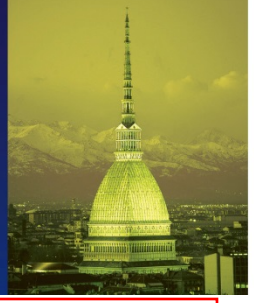
The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 SEPTEMBER 29, 2016 VOL. 375 NO. 13

N Engl J Med 2016;375:1221-30.
DOI: 10.1056/NEJMoa1608029

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*



DANISH

BACKGROUND

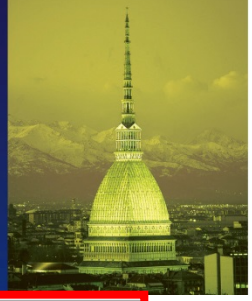
The benefit of an implantable cardioverter–defibrillator (ICD) in patients with symptomatic systolic heart failure caused by coronary artery disease has been well documented. However, the evidence for a benefit of prophylactic ICDs in patients with systolic heart failure that is not due to coronary artery 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).

METHODS

In a randomized, controlled trial, 556 patients with symptomatic systolic heart failure (left ventricular ejection fraction, ≤35%) not caused by coronary artery disease were assigned to receive an ICD, and 560 patients were assigned to receive usual clinical care (control group). In both groups, 58% of the patients received CRT. The primary outcome of the trial was death from any cause. The secondary outcomes were sudden cardiac death and cardiovascular death.

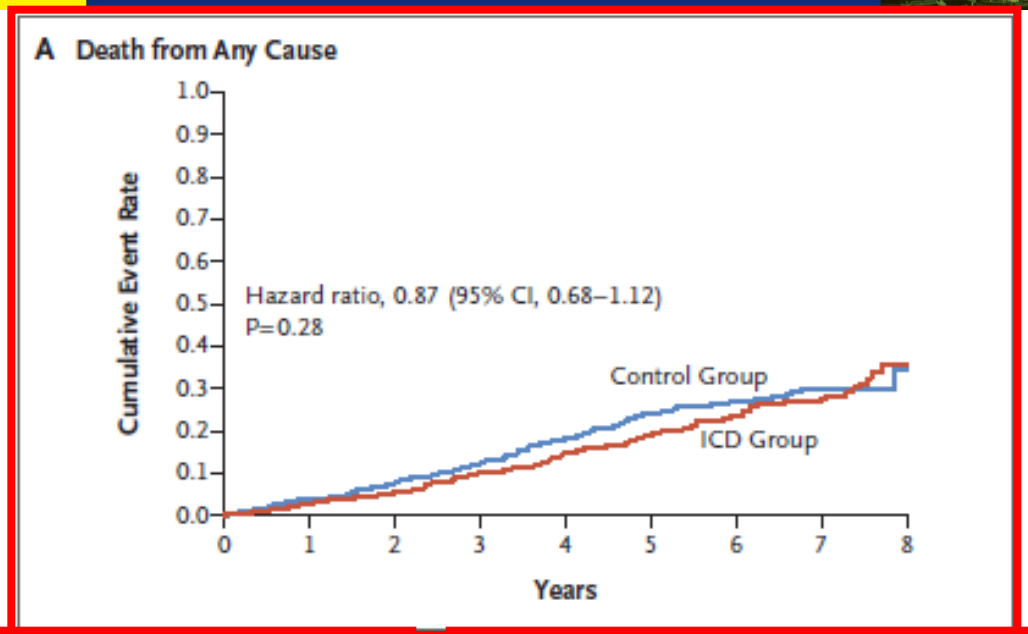
RESULTS

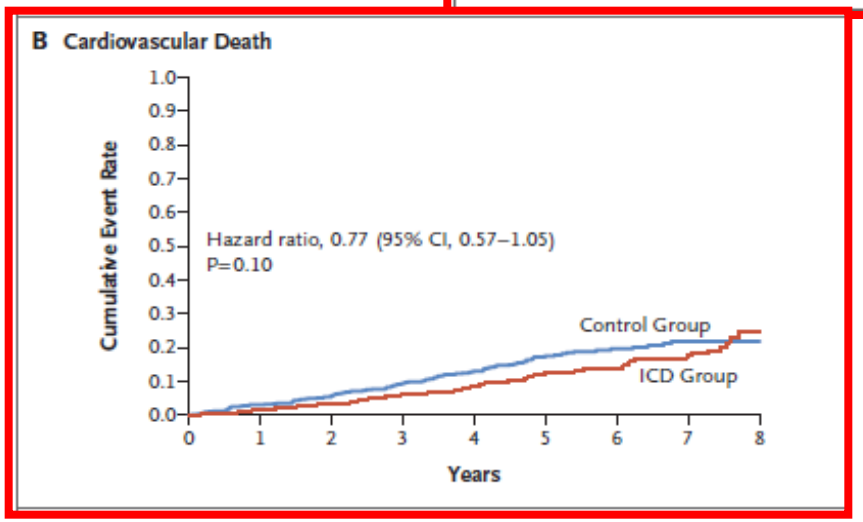
After a median follow-up period of 67.6 months, the primary outcome had occurred in 120 patients (21.6%) in the ICD group and in 131 patients (23.4%) in the control group (hazard ratio, 0.87; 95% confidence interval [CI], 0.68 to 1.12; P=0.28). Sudden cardiac death occurred in 24 patients (4.3%) in the ICD group and in 46 patients (8.2%) in the control group (hazard ratio, 0.50; 95% CI, 0.31 to 0.82; P=0.005). Device infection occurred in 27 patients (4.9%) in the ICD group and in 20 patients (3.6%) in the control group (P=0.29).

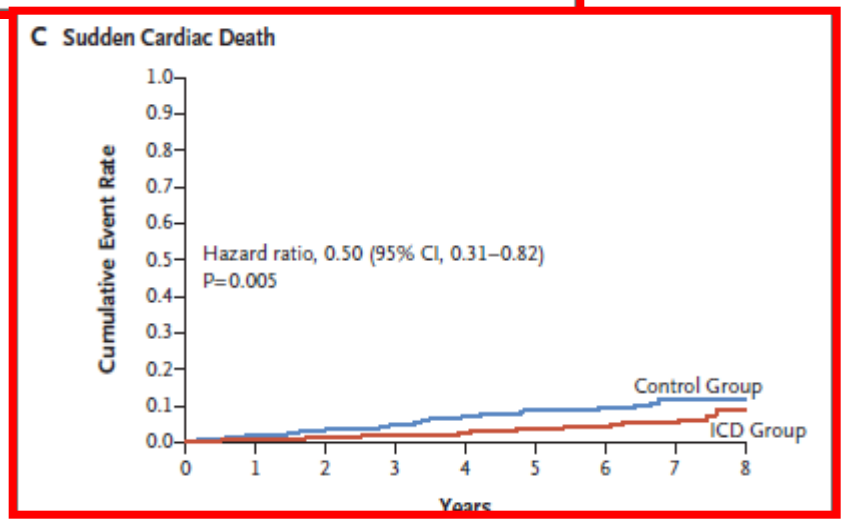


DANISH

2016


A Death from Any Cause
Cumulative Event Rate
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0.0
Hazard ratio, 0.87 (95% CI, 0.68–1.12)
P=0.28
Control Group
ICD Group
0
1
2
3
4
5
6
7
8
Years


B Cardiovascular Death
Cumulative Event Rate
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0.0
Hazard ratio, 0.77 (95% CI, 0.57–1.05)
P=0.10
Control Group
ICD Group
0
1
2
3
4
5
6
7
8
Years


C Sudden Cardiac Death
Cumulative Event Rate
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0.0
Hazard ratio, 0.50 (95% CI, 0.31–0.82)
P=0.005
Control Group
ICD Group
0
1
2
3
4
5
6
7
8
Years

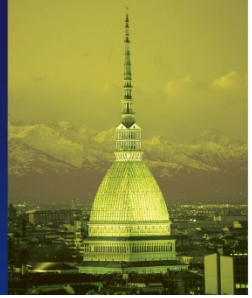
DANISH - 2016

CONCLUSIONS

In this trial, prophylactic ICD implantation in patients with symptomatic systolic heart failure not caused by coronary artery disease was not associated with a significantly lower long-term rate of death from any cause than was usual clinical care. (Funded by Medtronic and others; DANISH ClinicalTrials.gov number, NCT00542945.)

TURIN, October 25th-27th 2018 Starhotels Majestic

GIORNATE CARDIOLOGICHE TORINESI 30



UNIVERSITÁ DEGLI STUDI DI TORINO

AZIENDA OSPEDALIERO - UNIVERSITARIA Città della Salute e della Scienza di Torino

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World Journal of Cardiovascular Diseases, 2017, 7, 79-90
http://www.scirp.org/journal/wjcd
ISSN Online: 2164-5337
ISSN Print: 2164-5329

Clinical Predictors of Appropriate Implantable Cardioverter-Defibrillator Therapies in Primary Prevention: A Retrospective Study

Chiara Devecchi[1,2], Eraldo Occhetta[1], Vincenzo Alessandro Galiffa[1], Gabriele Dell'Era[1] Andrea Magnani[1], Francesco Rametta[2], Paolo Nicola Marino[1]

[1]AOU Maggiore della Carità, Novara, Italy
[2]Presidio Ospedaliero S. Andrea, Vercelli, Italy
Email: devchiara@gmail.com

Abstract

Implantable cardioverter-defibrillator (ICD) in heart failure with reduced ejec tion fraction (EF) patients reduces risk for sudden cardiac death (SCD). Pre vious data suggest that the benefit of ICD therapy in real life may be lowe than expected from the results of controlled studies and only about one-thir of ICD patients receive appropriate therapies. Nevertheless, all ICD patient are at risk of perioperative complications and inappropriate shocks. We re trospectively studied 613 patients undergoing ICD for primary prevention i 2002-2015; we excluded inherited arrhythmogenic syndromes. Patients un derwent 12-leads ECG, echocardiography, laboratory tests and quality of lif questionnaire. We evaluated comorbidities, appropriate therapies, complica tions and all-cause mortality. Consecutive patients (age 67 ± 10 years, 81% males, 59% ischaemic aetiology) were followed for 51 ± 31 months. 198 pa tients (32%) received appropriate ICD therapy, 93 (15%) had inappropriat shocks, 53 (8%) had at least one complication (electrode dysfunction, infec tion and pocket related) and 191 (33%) died. Multivariate analysis showe atrial fibrillation (OR = 1.8, CI = 1.27 - 2.53; $p < 0.01$), diabetes (OR = 1.8, C = 1.27 - 2.53; $p = 0.041$) and vasculopathy (OR = 1.8, CI = 1.27 - 2.53; p = 0.031) as predictors of appropriate therapy. Logistic regression, considerin atrial fibrillation, diabetes, vasculopathy, EF, NYHA class, left atrial diamete and natremia, identified SCD low risk group (probability < 0.1258). Ventricu lar arrhythmias necessitating ICD therapy are common, but complication and inappropriate therapies are frequent. Many parameters should be consi dered for a better selection of ICD candidates, to reduce ineffective implants Our multifactorial score may eventually reduce about 10% ICD implantation.

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World Journal of Cardiovascular Diseases, 2017, 7, 79-90
http://www.scirp.org/journal/wjcd
ISSN Online: 2164-5337
ISSN Print: 2164-5329

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Table 1. Baseline characteristics before implantation.

	Baseline
Age and gender	
Mean age (years)	67.4 ± 10.1
Male (%)	496 (80.9)
Aetiology	
Ischemic (%)	360 (58.7)
Previously AMI (%)	313 (51.1)
Previous coronary bypass surgery (%)	181 (29.5)
Valvular aetiology (%)	57 (9.3)
Idiopathic cardiomyopathy (%)	196 (32)

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Andrea Magnani[1], Francesco Rametta[2], Paolo Nicola Marino[1]**

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Email: devchiara@gmail.com

Table 5. Difference in baseline characteristic between patients with and without appropriate ICD therapy

	Appropriate therapy (n=198)	Without appropriate therapy (n=415)	P-value
Ischemic aetiology (%)	113 (57,1)	247 (59,5)	
Previously AMI (%)	98 (49,[illegible])	215 (51,8)	0,592
Previous coronary bypass surgery (%)	65 (32,[illegible])	116 (28,0)	0,216
Valvular aetiology (%)	20 (10,[illegible])	37 (8,9)	
Idiopathic cardiomyopathy (%)	65 (32,8)	131 (31,6)	

European Heart Journal Advance Access published August 29, 2015

European Heart Journal
doi:10.1093/eurheartj/ehv316

ESC GUIDELINES

2015 ESC Guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death

The Task Force for the Management of Patients with Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death of the European Society of Cardiology (ESC)

7.1 Dilated cardiomyopathy

Risk stratification and management of patients with dilated cardiomyopathy

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

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

64 ->SCD-HeFT 2004
313 -> Companion 2004
316 -> Definite 2004
317 -> Metanalisi 2004
354 -> AMIOVIRT 2003

2015 ESC GUIDELINES …. On 2004 Studies

After 2016 DANISH Study

In conclusion, in our trial, prophylactic ICD implantation in patients with symptomatic systolic heart failure that was not caused by coronary artery disease was not found to reduce long-term mortality.

… could GUIDELINES for ICD primary prevention indication in non ischemic cardiomyopathy CHANGE ???

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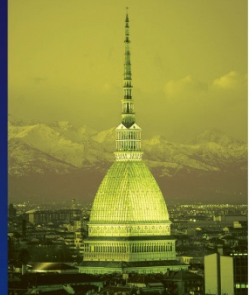

UNIVERSITÁ DEGLI STUDI DI TORINO

AZIENDA OSPEDALIERO - UNIVERSITARIA
Città della Salute e della Scienza di Torino

PRIMARY PREVENTION OF SUDDEN CARDIAC DEATH IN NON ISCHEMIC CARDIOMYOPATHY: INDICATION TO CARDIAC DEFIBRILLATOR

…. DISCUSSION AFTER REBUTTAL…

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