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# GIORNATE CARDIOLOGICHE TORINESI



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

«CONS» - REBUTTAL

Eraldo Occhetta  
NOVARA - Italy



Azienda Ospedaliero-Universitaria  
Maggiore della Carità  
di Novara



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## OSCAR WILDE



*Non c'è una seconda occasione per far  
buona impressione la prima volta....*

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UNIVERSITÀ DEGLI STUDI DI TORINO



Europace (2009) **11**, 1129–1133  
doi:10.1093/europace/eup174

**EDITORIAL**

## Are complications of implantable defibrillators under-estimated and benefits over-estimated?

**Michele Brignole\***

Department of Cardiology, Arrhythmologic Centre, Ospedali del Tigullio, 16033 Lavagna, Italy

*Received 19 April 2009; accepted after revision 6 June 2009; online publish-ahead-of-print 4 July 2009*

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



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## Are complications of implantable defibrillators under-estimated and benefits over-estimated?

Michele Brignole\*

**Need to identify the patients who are likely to benefit more from an implantable cardioverter defibrillator**

be taken based on a careful risk-benefit evaluation. It is hopeful that future trials should focus on risk-benefit stratification and that future guidelines should consider to base their recommendations not only on crude cut-off, mainly based on values of EF, but rather on criteria of increasing probability of efficacy.





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## Are complications of implantable defibrillators under-estimated and benefits over-estimated?

Michele Brignole\*

Most patients currently implanted with an ICD never receive a therapeutic discharge but are exposed to the risks of ICDs outlined in this report. For example, in MADIT II trial,<sup>22</sup> 77% of patients did not receive appropriate shocks during 21 months and in SCD-HeFT trial,<sup>7</sup> 79% did not receive appropriate shocks at 5 years (annual rate of 5.1% of appropriate shocks). Similarly, three quarters to two-thirds of ICD recipients in the observational studies received no therapeutic ICD discharges.

**... too low specificity of EF indication criteria...**

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## Possible criteria to improve specificity (associated with low EF)

- Sustained inducible ventricular tachyarrhythmias (MADIT-MUSTT)
- Spontaneous non sustained ventricular arrhythmias
- Heart Rate Variability (HRV)
- Heart Rate Turbulence
- Baroreflex Response
- ECG Signal Averaging
- PCR/BNP
- **T Wave Alternans (TWA)**
- **MIBG (Scinti.....)**

**EXPEDITED PUBLICATIONS**

## **Prognostic Value of T-Wave Alternans in Patients With Heart Failure Due to Nonischemic Cardiomyopathy**

Results of the ALPHA Study

Jorge A. Salerno-Uriarte, MD,\* Gaetano M. De Ferrari, MD,† Catherine Klersy, MD,‡  
Roberto F. E. Pedretti, MD,§ Massimo Tritto, MD,|| Luciano Sallusti, BS,¶ Luigi Libero, MD,#  
Giacinto Pettinati, MD,\*\* Giulio Molon, MD,†† Antonio Curnis, MD,‡‡ Eraldo Occhetta, MD,§§  
Fabrizio Morandi, MD,\* Paolo Ferrero, MD,# Francesco Accardi, BS,¶ for the ALPHA Study  
Group Investigators

*Varese, Pavia, Tradate, Castellanza, Milano, Torino, Casarano, Negrar, Brescia, and Novara, Italy*

**High negative predictive value .....**



**But not considered for actual ICD indication!**



## Myocardial Iodine-123 Meta-Iodobenzylguanidine Imaging and Cardiac Events in Heart Failure

Results of the Prospective ADMIRE-HF (AdreView  
Myocardial Imaging for Risk Evaluation in Heart Failure) Study

Arnold F. Jacobson, MD, PhD,\* Roxy Senior, MD,† Manuel D. Cerqueira, MD,‡  
Nathan D. Wong, PhD,§ Gregory S. Thomas, MD, MPH,§ Victor A. Lopez, BS,§  
Denis Agostini, MD, PhD,|| Fred Weiland, MD,¶ Harish Chandna, MD,# Jagat Narula, MD, PhD,§  
on behalf of the ADMIRE-HF Investigators

*Princeton, New Jersey; London, United Kingdom; Cleveland, Ohio; Irvine, California; Caen, France;  
Roseville, California; and Victoria, Texas*

**Table 1** Clinical Characteristics of the Heart Failure Subjects

n	961
Sex, male (%)	80.1
Race, white (%)	74.9
Body mass index (kg/m <sup>2</sup> )	29.2 ± 6.1
ACE inhibitors/ARBs (%)	94.2
Beta-blockers (%)	91.9
Lipid-lowering agents (%)	74.6
Aldosterone antagonist (%)	38.9
Diabetes (%)	36.0
Hypertension (%)	64.5
Smoker, current or past (%)	73.9
Dyslipidemia (%)	72.4
Heart failure: NYHA functional class II, III (%)	82.7, 17.3
Heart failure: ischemic, nonischemic (%)	66.0, 34.0
LVEF (%)	27.1 ± 6.1

apply (29). ADMIRE-HF showed a highly significant relationship between time to HF-related events and the H/M, which was independent of other commonly measured parameters such as LVEF and BNP, as well as demographic parameters such as age and renal function, in an HF population on guidelines-based contemporary therapy. The

## Are complications of implantable defibrillators under-estimated and benefits over-estimated?

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Europace (2009) **11**, 1129–1133  
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In the MADIT II study,<sup>22</sup> the mortality rate of patients receiving therapy for ventricular fibrillation was over 50% at 2 years. The most common cause of death among patients who received any ICD shock was progressive heart failure. The authors speculated that successful abortion of sudden cardiac death merely shifted the mode of death to pump failure.

**... less benefits in too sick patients ....**

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## Composite Clinical Scores:

- US Coorte Study  
(Kramer DB, et al. Heart Rhythm 2012; 9:42-46)
- MADIT-II substudy  
(Goldenberg I, et al. JACC 2008; 51:288-296)
- **Seattle Heart Failure Model**  
**(Levy WC, et al. Circulation 2009; 120:835-842)**

**Circulation**  
JOURNAL OF THE AMERICAN HEART ASSOCIATION



**Maximizing Survival Benefit With Primary Prevention Implantable  
Cardioverter-Defibrillator Therapy in a Heart Failure Population**  
Wayne C. Levy, Kerry L. Lee, Anne S. Hellkamp, Jeanne E. Poole, Dariush Mozaffarian, David  
T. Linker, Aldo P. Maggioni, Inder Anand, Philip A. Poole-Wilson, Daniel P. Fishbein, George  
Johnson, Jill Anderson, Daniel B. Mark and Gust H. Bardy

*Circulation*. 2009;120:835-842; originally published online August 24, 2009;  
doi: 10.1161/CIRCULATIONAHA.108.816884  
*Circulation* is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231  
Copyright © 2009 American Heart Association, Inc. All rights reserved.  
Print ISSN: 0009-7322. Online ISSN: 1524-4539

# Sudden cardiac death and implantable cardioverter defibrillators: two modern epidemics?

**Demosthenes G. Katritsis<sup>1,2\*</sup> and Mark E. Josephson<sup>3</sup>**

<sup>1</sup>Athens Euroclinic, 9 Athanassiadou Street, Athens 11521, Greece; <sup>2</sup>St Thomas's Hospital, London, UK; and <sup>3</sup>Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA, USA

Received 19 October 2011; accepted after revision 30 December 2011; online publish-ahead-of-print 2 February 2012

Critical analysis of the existing evidence indicates that:

- (1) In patients with documented sustained ventricular arrhythmias and/or cardiac arrest, implantable cardioverter defibrillators (ICDs) confer a survival benefit. In several clinical settings this is rather transient, and might be lost when modern medical therapy including  $\beta$ -blockers is implemented.
- (2) In patients without sustained ventricular arrhythmias or cardiac arrest, ICDs confer a significant survival benefit only in high-risk patients with ischaemic cardiomyopathy and left ventricular ejection fraction of  $\leq 35\%$  due to a remote myocardial infarction.
- (3) Left ventricular ejection fraction alone is rather unlikely to be sufficient for effective sudden cardiac death risk prediction, due to low sensitivity and specificity.
- (4) The benefits of ICDs in the elderly as well as in women are not established.
- (5) With current prices, ICDs are probably cost-effective only when used in high-risk patients without associated comorbidities that limit the life expectancy to  $< 10$  years.

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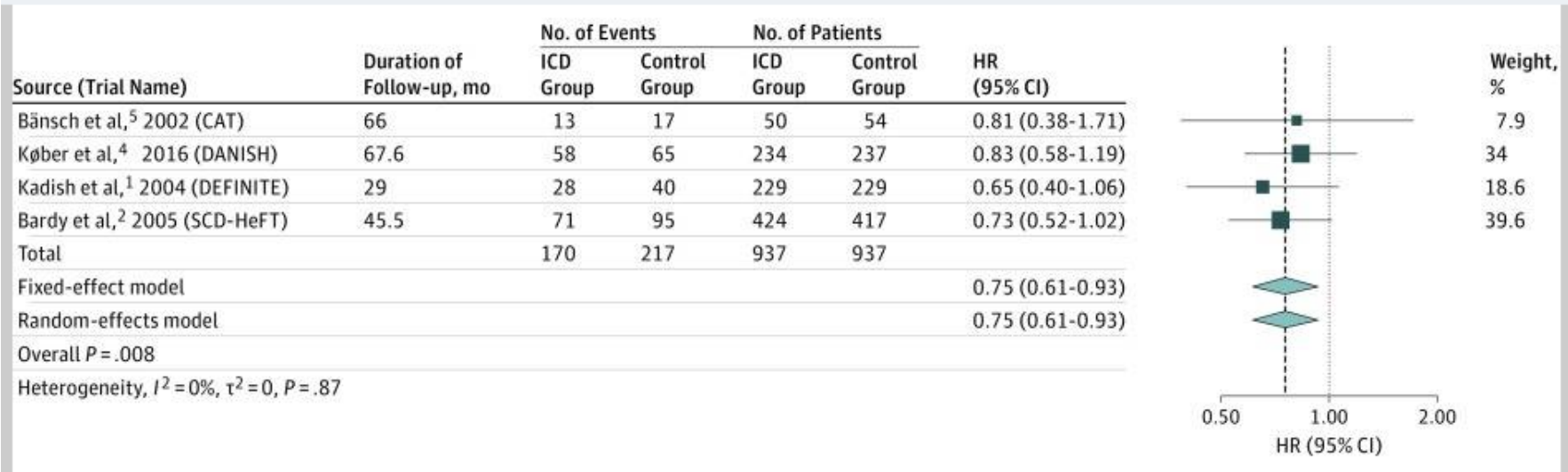


[JAMA Cardiol. 2017 Jun 1;2\(6\):685-688. doi: 10.1001/jamacardio.2017.0630.](#)

## Primary Prevention Implantable Cardioverter Defibrillators in Patients With Nonischemic Cardiomyopathy **A Meta-analysis.**

[Al-Khatib SM](#)<sup>1</sup>, [Fonarow GC](#)<sup>2</sup>, [Joglar JA](#)<sup>3</sup>, [Inoue LYT](#)<sup>4</sup>, [Mark DB](#)<sup>1</sup>, [Lee KL](#)<sup>5</sup>, [Kadish A](#)<sup>6</sup>, [Bardy G](#)<sup>7</sup>, [Sanders GD](#)<sup>8</sup>.

Drag image to reposition.



**CONCLUSIONS AND RELEVANCE:** Primary prevention ICDs are efficacious at reducing all-cause mortality among patients with nonischemic cardiomyopathy. These findings support professional guidelines that recommend the use of ICDs in such patients.



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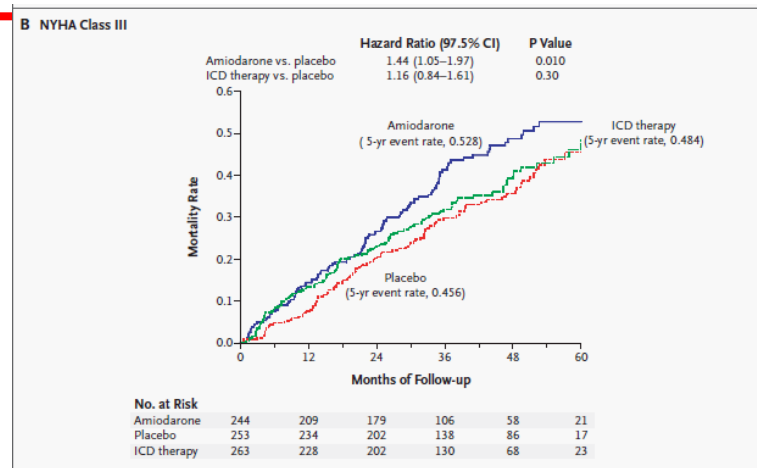
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## SCD-HeFT

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 did not vary according to either ischemic or nonischemic causes of CHF, but they did vary according to the NYHA class.



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## DANISH

### METHODS

In a randomized, controlled trial, 556 patients with symptomatic systolic heart failure (left ventricular ejection fraction,  $\leq 35\%$ ) 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.

### 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.)

**Positive role of CRT ???**

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## CONCLUSION

**PRIMARY PREVENTION OF SUDDEN  
CARDIAC DEATH IN NON ISCHEMIC  
CARDIOMYOPATHY:**

**INDICATION TO ICD ??**

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## CONCLUSION

PRIMARY PREVENTION OF SUDDEN  
CARDIAC DEATH IN NON ISCHEMIC  
CARDIOMYOPATHY:

INDICATION TO **ICD** ??



... OGGI NON TI DICO NO  
.... DOMANI NON LO SO !