



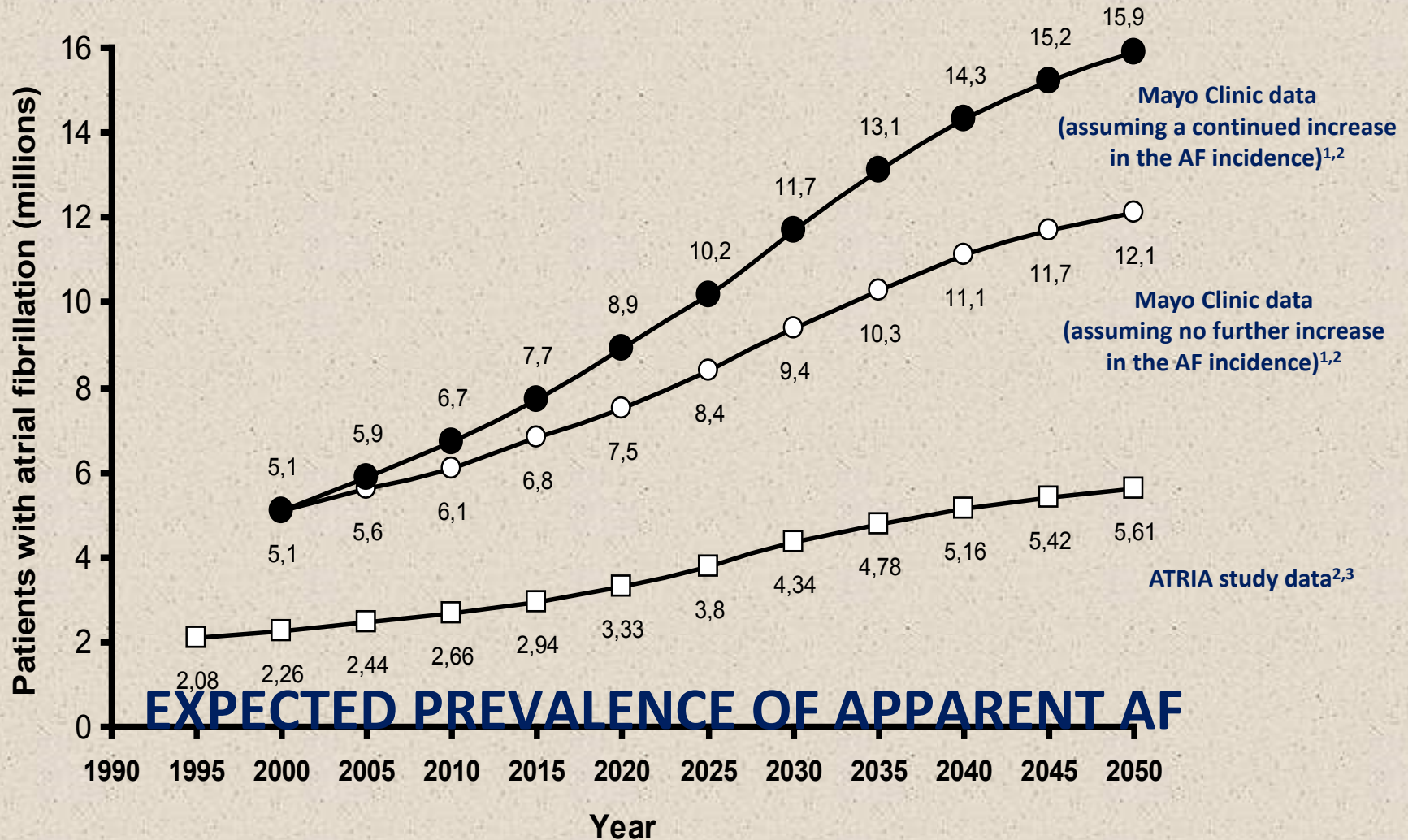
# Interplay between AF and sudden death

**Prof. Dr. Martin Borggrefe**  
Mannheim

**ADVANCES IN CARDIAC  
ARRHYTHMIAS**  
and  
**GREAT INNOVATIONS  
IN CARDIOLOGY**

**Turin**  
**October 13-15, 2016**

# Management of atrial fibrillation

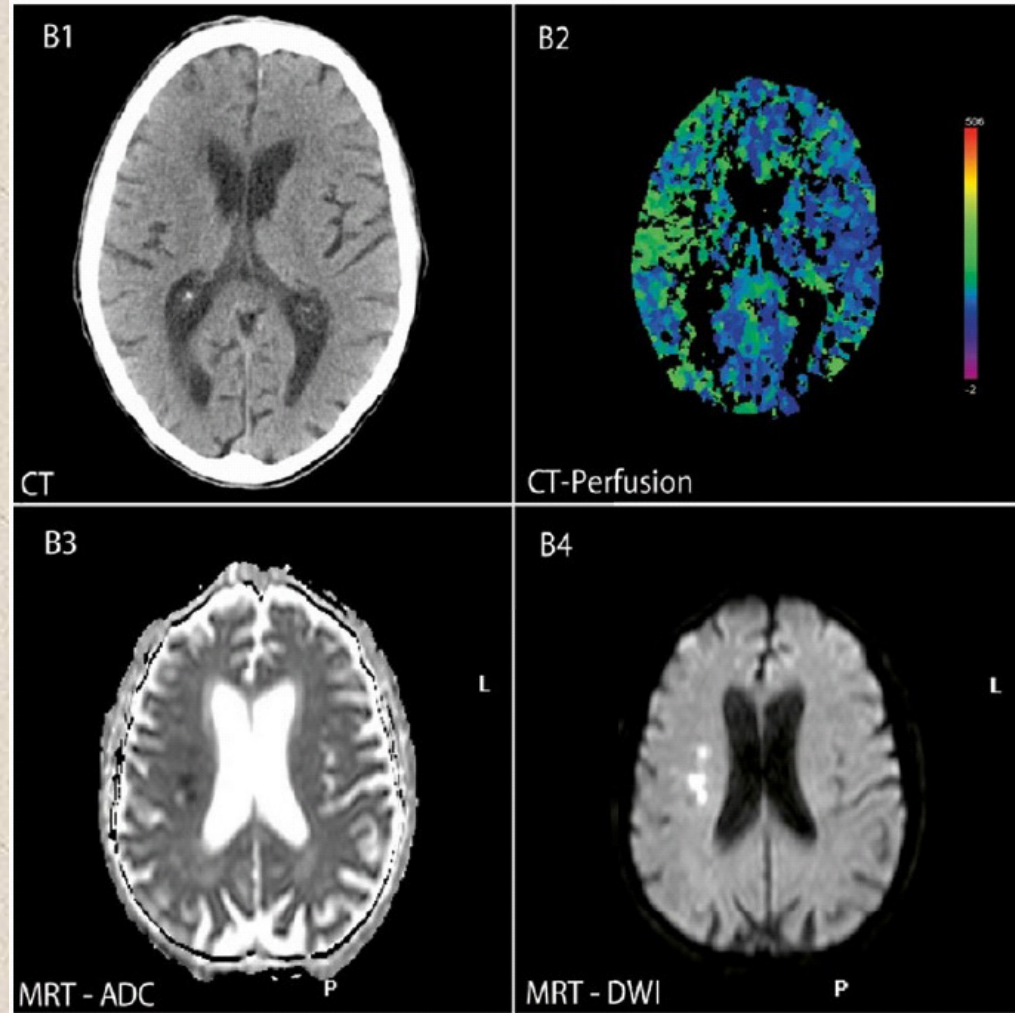
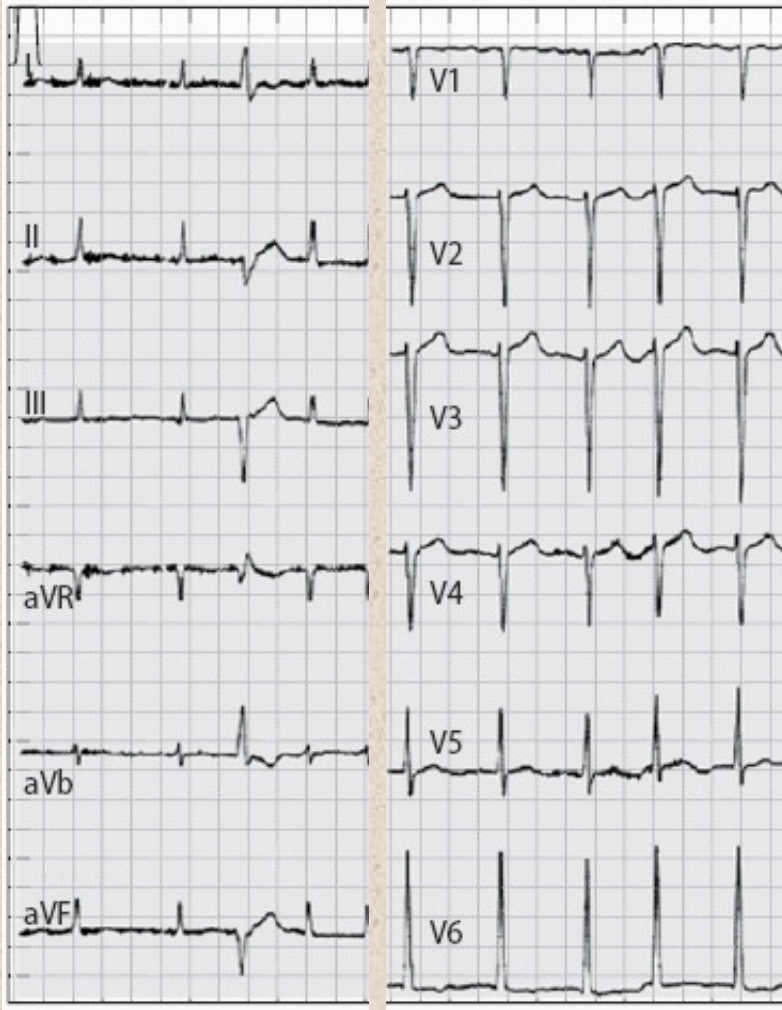


1. Miyasaka Y et al. Circulation 114:119-125 (2006), 2. Savelieva I, Camm J. Clin Cardiol 31:55-62 (2008), 3. Go AS et al. JAMA 285:2370-2375 (2001)



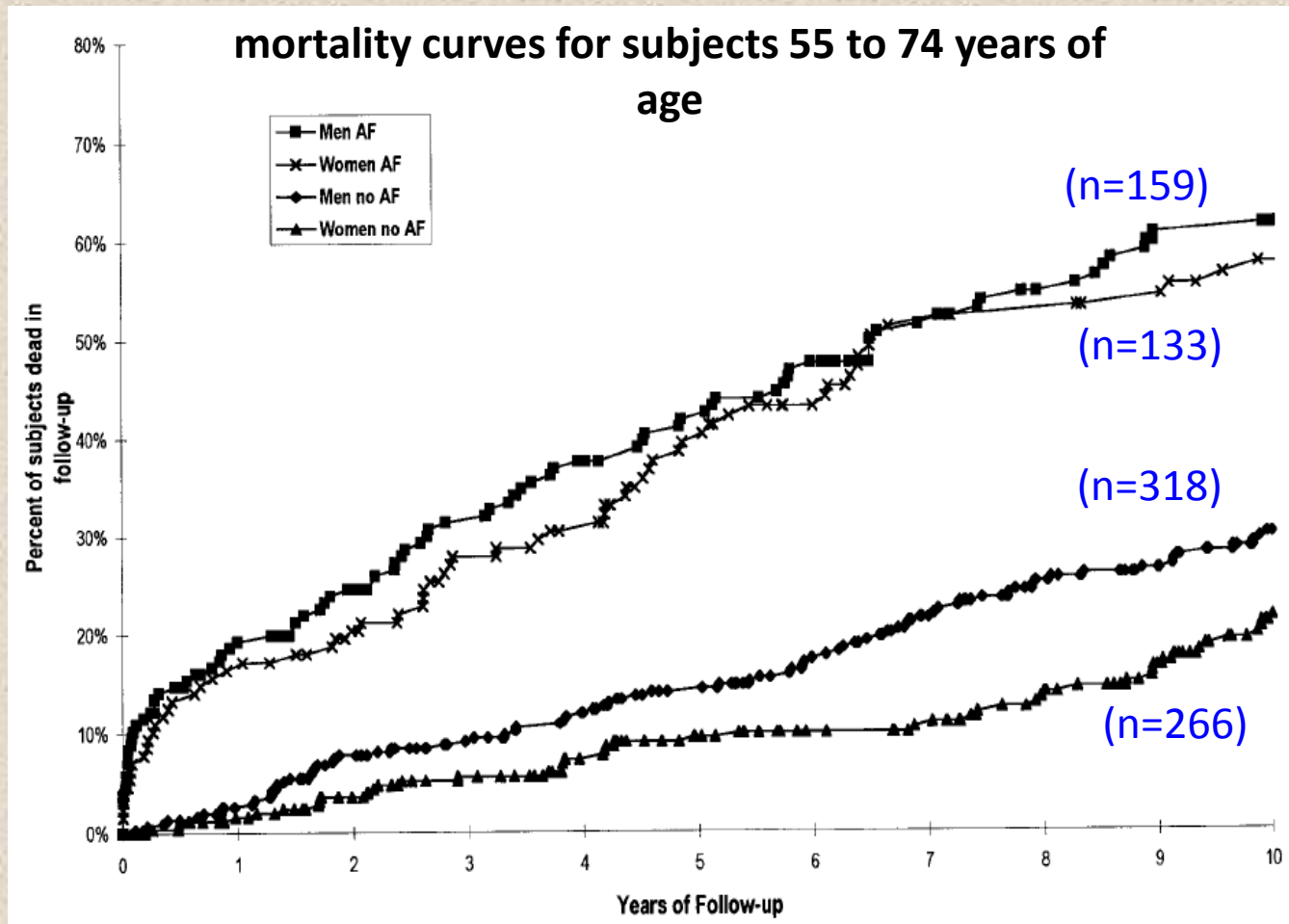
# Stroke as a first sign of AF

75 yr-old male patient with acute hemi-paresis preceding dyspnea NYHA for 7 days



# Management of atrial fibrillation

## Burden of disease : AF The Framingham Heart Study



Benjamin et al, Circulation 1998;98:946-952

# The interplay between AF and SCD

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## Atrial Fibrillation and the Risk of Sudden Cardiac Death

*The Atherosclerosis Risk in Communities Study and Cardiovascular Health Study*

Lin Y. Chen, MD, MS; Nona Sotoodehnia, MD, MPH; Petra Bůžková, PhD; Faye L. Lopez, MS, MPH;  
Laura M. Yee, MS; Susan R. Heckbert, MD, PhD; Ronald Prineas, MB, BS, PhD;  
Elsayed Z. Soliman, MD, MSc, MS; Selcuk Adabag, MD, MS; Suma Konety, MD, MS;  
Aaron R. Folsom, MD, MPH; David Siscovick, MD, MPH; Alvaro Alonso, MD, PhD

**JAMA Intern Med. 2013;173(1):29-35**

# The interplay between AF and SCD

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## ARIC

n: 15439 pts  
(1987-89  $\Rightarrow$  2001)

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## CHS

n: 5479 pts  
(1989-90  $\Rightarrow$  2006)

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# The interplay between AF and SCD

## ARIC Study

Risk of SCD and nonSCD by AF using time-dependent covariates

Characteristic	Incident AF through 2001, HR (95% CI)		PValue
	No	Yes	
<b>Sudden cardiac death</b>			
Model 1	1 [reference]	2.87 (1.88-4.40)	<.001
Model 2	1 [reference]	2.03 (1.30-3.17)	.002
<b>Nonsudden cardiac death</b>			
Model 1	1 [reference]	2.16 (1.39-3.35)	<.001
Model 2	1 [reference]	1.48 (0.94-2.34)	.09

# The interplay between AF and SCD

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## Relationship of Sudden Cardiac Death to New-Onset Atrial Fibrillation in Hypertensive Patients With Left Ventricular Hypertrophy

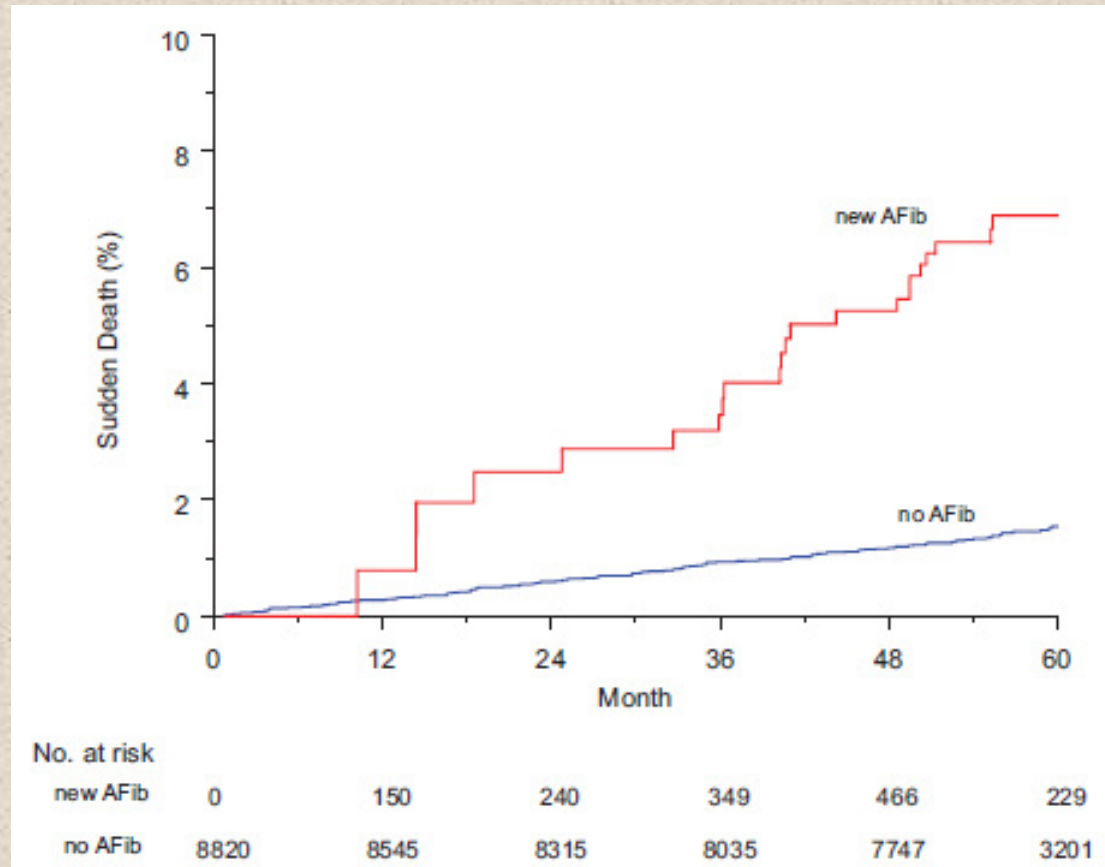
Peter M. Okin, MD; Casper N. Bang, MD; Kristian Wachtell, MD, PhD; Darcy A. Hille, MSEMBA; Sverre E. Kjeldsen, MD, PhD; Björn Dahlöf, MD, PhD; Richard B. Devereux, MD

**Circ Arrhythm Electrophysiol. 2013; 6: 243-251**



# The interplay between AF and SCD

Survival curves illustrating the rate of sudden cardiac death in relation to development of new-onset atrial fibrillation (AFib) over time



Okin et al. *Circ Arrhythm Electrophysiol.* 2013; 6: 243-251

# The interplay between AF and SCD

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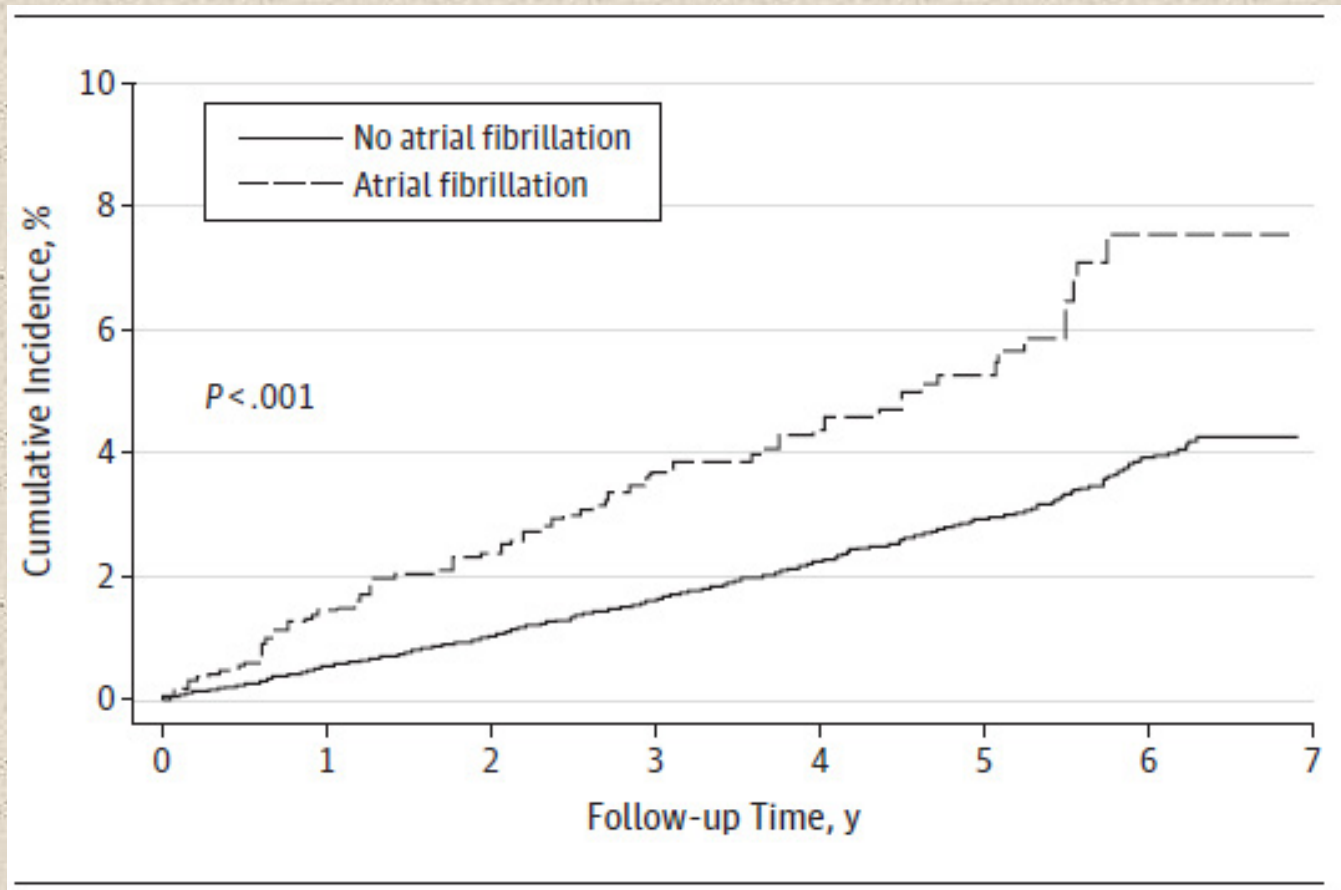
## Atrial Fibrillation and the Risk of Myocardial Infarction

Elsayed Z. Soliman, MD, MSc, MS; Monika M. Safford, MD; Paul Muntner, PhD; Yulia Khodneva, MD, PhD;  
Farah Z. Dawood, MD; Neil A. Zakai, MD; Evan L. Thacker, PhD; Suzanne Judd, PhD; Virginia J. Howard, PhD;  
George Howard, DrPH; David M. Herrington, MD, MHS; Mary Cushman, MD, MSc

**JAMA Intern Med. 2014;174:107-114**

# The interplay between AF and SCD

## Unadjusted Cumulative Incidence of Myocardial Infarction by Baseline Atrial Fibrillation Status



Soliman et al. JAMA Intern Med. 2014;174:107-114

# The interplay between AF and SCD

## Risk of Incident MI Associated With Baseline AF Stratified by the Level of CHADS2 Score

CHADS2 level	Participants, No.	MI Events, No.	Model	
			HR (95% CI)	Pvalue
No AF	22 297	570	1 [reference]	NA
AF and CHADS2 score $\leq 1$	983	30	1.40 (0.91-2.17)	.13
AF and CHADS2 score $>1$	648	48	1.95 (1.33-2.86)	<.001

Soliman et al. JAMA Intern Med. 2014;174:107-114

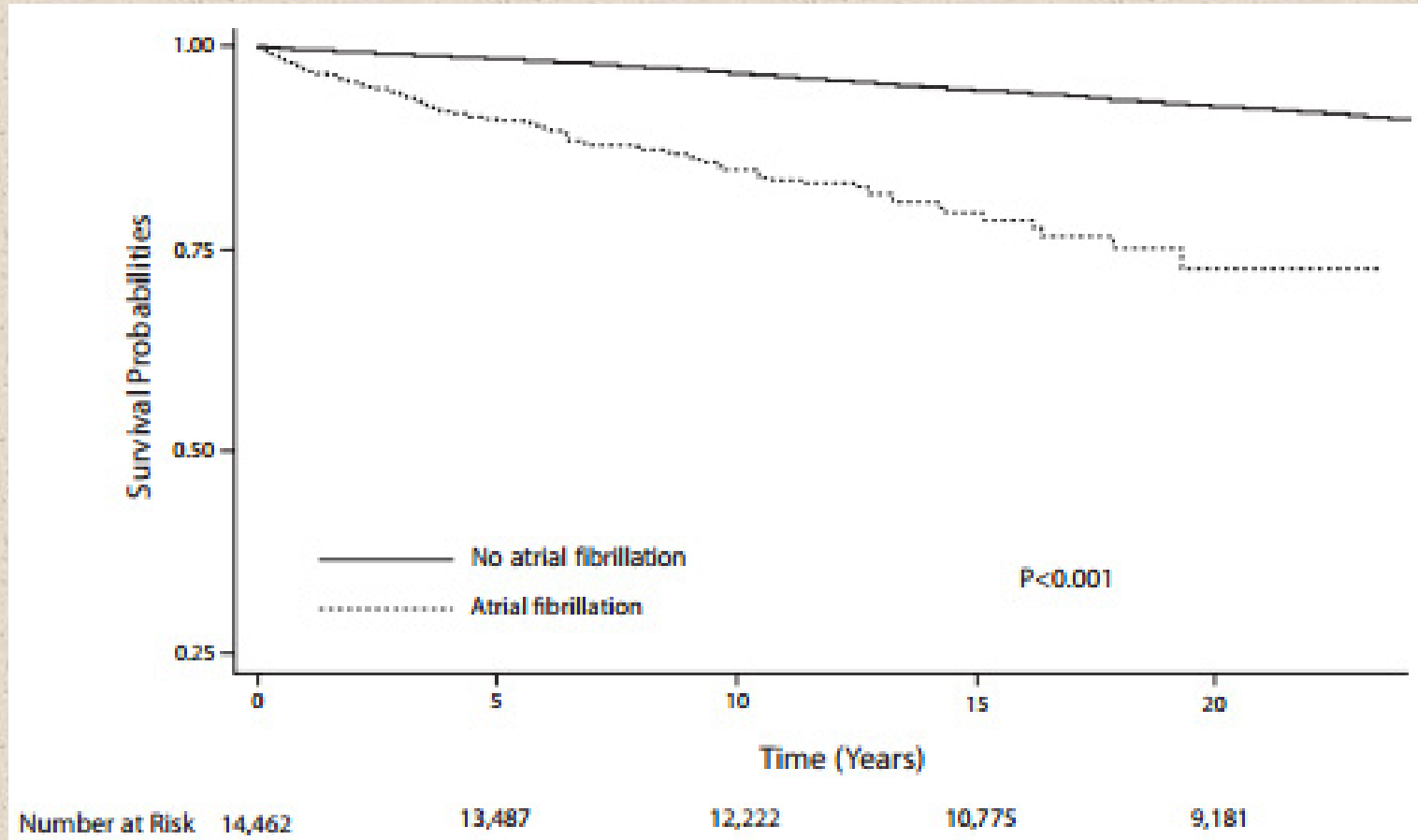
# **Atrial Fibrillation and Risk of ST-Segment–Elevation Versus Non–ST-Segment–Elevation Myocardial Infarction The Atherosclerosis Risk in Communities (ARIC) Study**

Elsayed Z. Soliman, MD, MSc, MS; Faye Lopez, MS, MPH; Wesley T. O’Neal, MD, MPH;  
Lin Y. Chen, MD; Lindsay Bengtson, PhD; Zhu-Ming Zhang, MD, MPH;  
Laura Loehr, MD, PhD; Mary Cushman, MD, MSc; Alvaro Alonso, MD, PhD

**Circulation 2015; 131: 1843-1850**

# AF and Risk of MI by Type

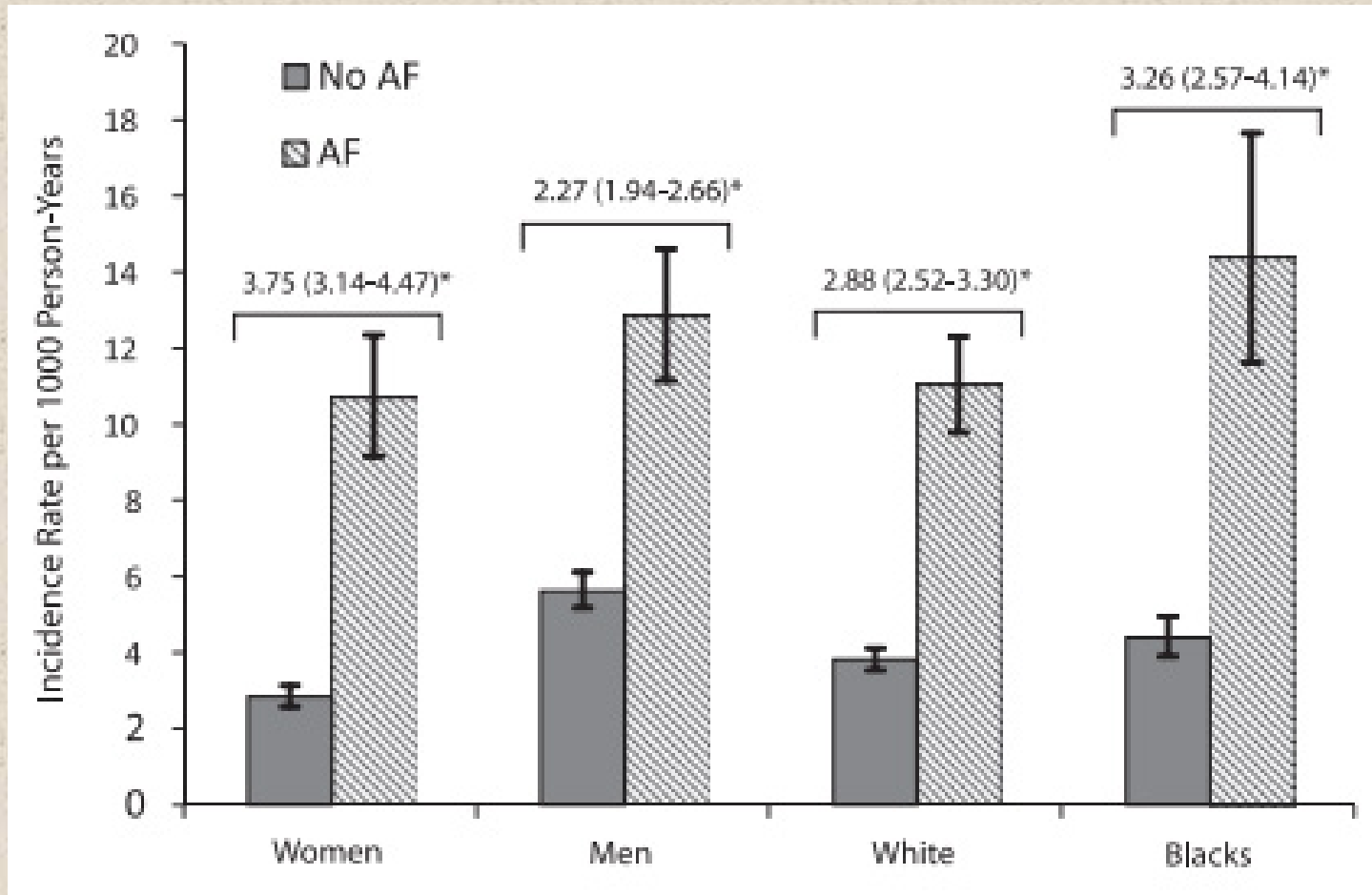
## Myocardial infarction-free survival curves by AF status



Soliman et al. Circulation 2015; 131: 1843-1850

# AF and Risk of MI by Type

Sex- and race-stratified age-adjusted incidence rates and incidence rate ratios of myocardial infarction by AF status



Soliman et al. *Circulation* 2015; 131: 1843-1850

# The interplay between AF and SCD

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## Prevalence, Clinical Features, and Prognosis of Acute Myocardial Infarction Attributable to Coronary Artery Embolism

Tatsuhiro Shibata, MD; Shoji Kawakami, MD; Teruo Noguchi, MD; Tomotaka Tanaka, MD;  
Yasuhide Asaumi, MD; Tomoaki Kanaya, MD; Toshiyuki Nagai, MD; Kazuhiro Nakao, MD;  
Masashi Fujino, MD; Kazuyuki Nagatsuka, MD; Hatsue Ishibashi-Ueda, MD;  
Kunihiro Nishimura, MD; Yoshihiro Miyamoto, MD; Kengo Kusano, MD; Toshihisa Anzai, MD;  
Yoichi Goto, MD; Hisao Ogawa, MD; Satoshi Yasuda, MD

**Circulation 2015; 132:241-250**



# The interplay between AF and SCD

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## Prevalence, Clinical Features, and Prognosis of Acute Myocardial Infarction Attributable to Coronary Artery Embolism

**52 / 1776 pts with AMI (2.9%)**

Tatsuro Shihata, MD; Shoji Kaneko, MD; Hiroo Noguchi, MD; Tomoaki Kanaya, MD;  
Yasuhide Asaumi, MD; Tomoaki Kanaya, MD; Toshiyuki Nagai, MD; Kazuhiro Nakao, MD;  
Masashi Fujino, MD; Kazuyuki Nagatsuka, MD; Hatsue Ishibashi-Ueda, MD;  
Kunihiro Nishimura, MD; Yoshihiro Miyamoto, MD; Kengo Kusano, MD; Toshihisa Anzai, MD;  
Yoichi Ito, MD; Kyoji Ueda, MD; Satoshi Yasuda, MD

**AF most common causes**

Circulation 2015; 132:241-250  
**(73%)**

# The interplay between AF and SCD

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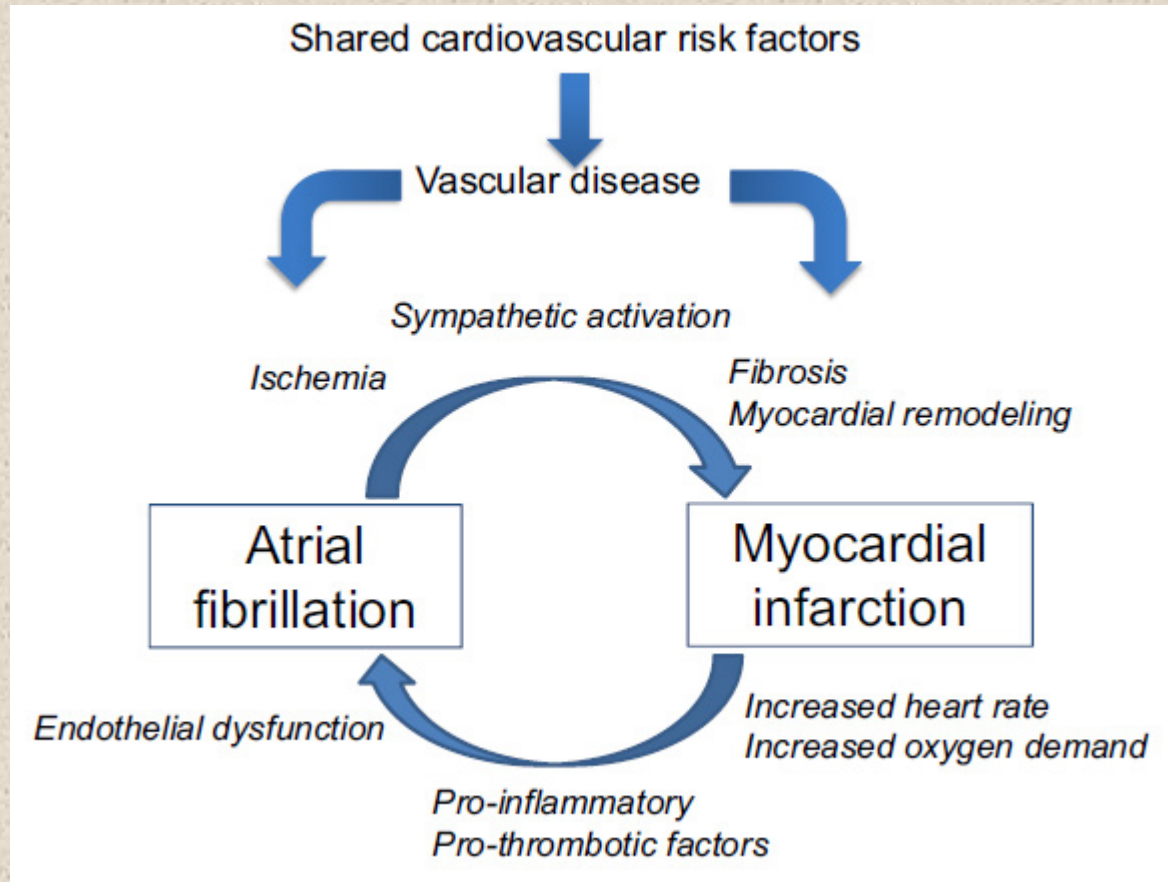
## **Acute Onset Human Atrial Fibrillation Is Associated With Local Cardiac Platelet Activation and Endothelial Dysfunction**

Joseph G. Akar, MD, PHD, Walter Jeske, PHD, David J. Wilber, MD  
*Maywood, Illinois*

**J Am Coll Cardiol 2008; 51: 1790–3**

# AF and Risk of MI by Type

Conceptual figure of the bidirectional relation between atrial fibrillation and myocardial infarction



Vermond et al. Circulation 2015; 131: 1824-1826

# The interplay between AF and SCD

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## Does Atrial Fibrillation Beget Ventricular Fibrillation in Patients with Acute Myocardial Infarction?

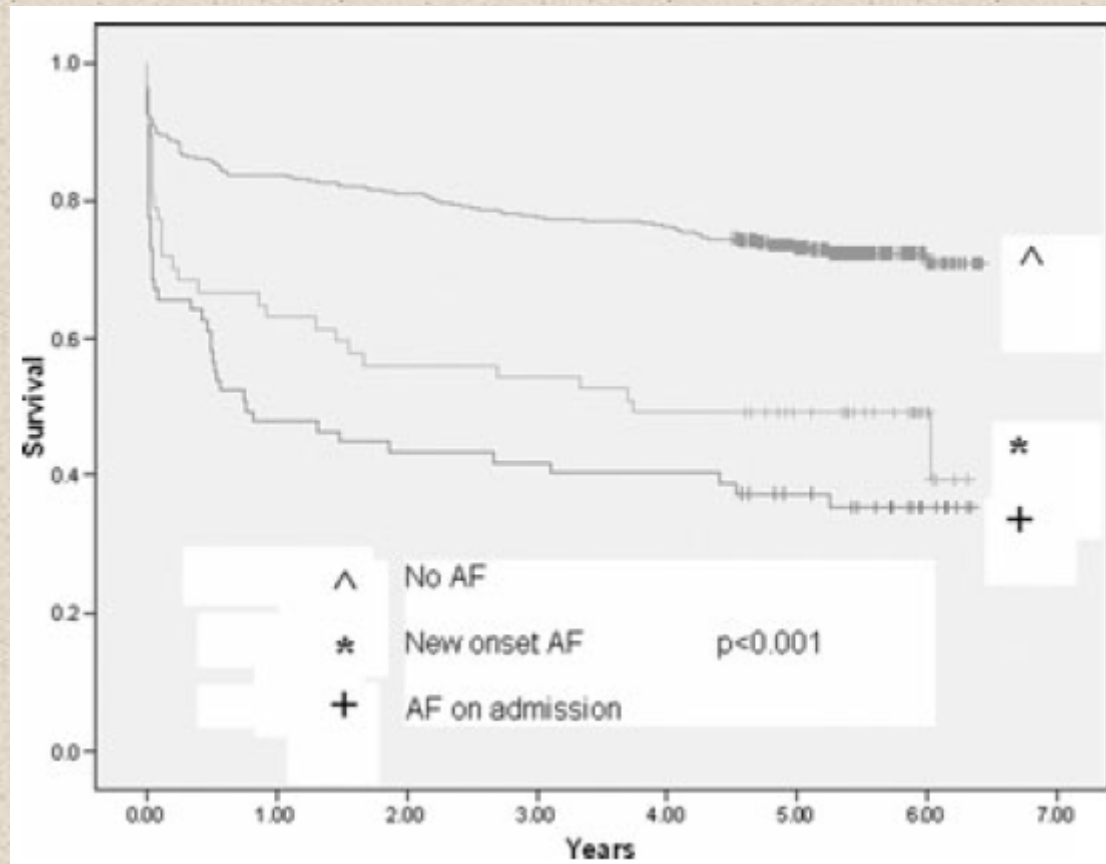
RAJIV SANKARANARAYANAN, M.B.B.S, M.R.C.P.,\* MICHAEL A. JAMES, M.D., F.R.C.P.†  
BOGDAN NUTA, M.R.C.P.,‡ MANDIE TOWNSEND M.B.B.Ch., M.R.C.P.,§ SUJATA KESAVAN,  
M.B.B.S., M.R.C.P.,¶ STEPHANIE BURTCHAELL, B.Sc., R.N.,\*\* RUSSELL HOLLOWAY,††  
and PAUL EWINGS, B.Sc., M.Sc., Ph.D., C.Stat., F.R.S.S., Hon.M.F.P.H.M.‡‡

**PACE 2008; 31:1612-1619**

# The interplay between AF and SCD

## Survival

n = 500 pts with AMI



# The interplay between AF and SCD

## Outcomes of the Various Subsets of Patients in the Study Population with Respect to Mortality and Ventricular Arrhythmias

	AF on Admission, n=67	New-onset AF n=57	All patients with AF n=124	Patients without AF, n=376
<b>Mortality In-pt</b>	<b>23 (34%) P &lt; 0.001</b>	<b>13 (23%) P = 0.005</b>	<b>36 (29%) P &lt; 0.001</b>	<b>38 (10%)</b>
<b>1 year</b>	<b>35(52%) P &lt; 0.001</b>	<b>21 (37%) P = 0.0001</b>	<b>56 (45%) P &lt; 0.001</b>	<b>61 (16%)</b>
<b>5.5 year</b>	<b>43 (64%) P &lt; 0.001</b>	<b>30 (53%) P &lt; 0.001</b>	<b>73 (59%) P &lt; 0.001</b>	<b>103 (27%)</b>
<b>Ventricular tachycardia</b>	<b>13 (19%) P = 0.73</b>	<b>12 (21%) P = 0.46</b>	<b>25 (20%) P = 0.50</b>	<b>65 (17%)</b>
<b>Ventricular fibrillation</b>	<b>11 (16%) P = 0.01</b>	<b>5 (9%) P = 0.57</b>	<b>16 (13%) P = 0.03</b>	<b>24 (6%)</b>

# The interplay between AF and SCD

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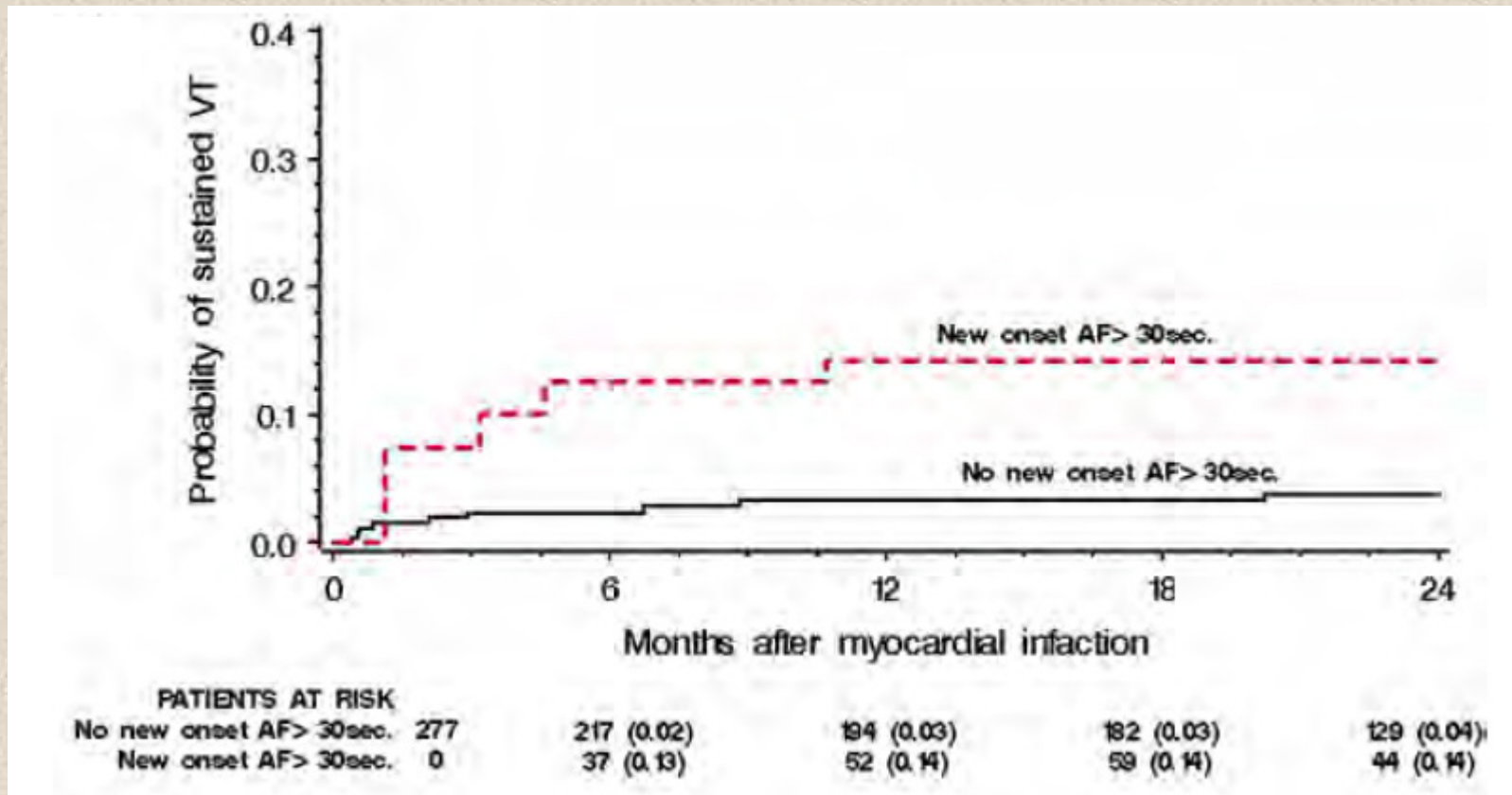
## **New-onset atrial fibrillation predicts malignant arrhythmias in post-myocardial infarction patients— A Cardiac Arrhythmias and Risk Stratification after acute Myocardial infarction (CARISMA) substudy**

Anne-Christine Huth Ruwald, MD,<sup>a,b</sup> Poul Erik Bloch Thomsen, MD, PhD,<sup>c</sup> Uffe Gang, MD, PhD,<sup>a</sup> Rikke Mørch Jørgensen, MD, PhD,<sup>d</sup> Heikki V. Huikuri, MD, PhD,<sup>c</sup> and Christian Jons, MD, PhD,<sup>a</sup>

**Am Heart J 2013; 166:855-863.e3**

# The interplay between AF and SCD

## Risk of ventricular tachycardia and AF



Ruwald et al. Am Heart J 2013; 166:855-863.e3



# The interplay between AF and SCD

## The association between new-onset AF and specific subtypes of ventricular tachyarrhythmic events

End point	Events	All AF			AF >30 s		
		HR	95% CI	P	HR	95% CI	P
Non-sustained ventricular tachycardia*	38	3.83	1.91-7.70	<.001	3.48	1.69-7.16	<.001
Sustained ventricular tachycardia *	13	6.71	1.83-24.62	.004	4.16	1.10-15.66	.035
VF <sup>†</sup>	10	1.34	0.31-5.77	.697	1.14	0.22-5.78	.877

Ruwald et al. Am Heart J 2013; 166:855-863.e3



# The interplay between AF and SCD

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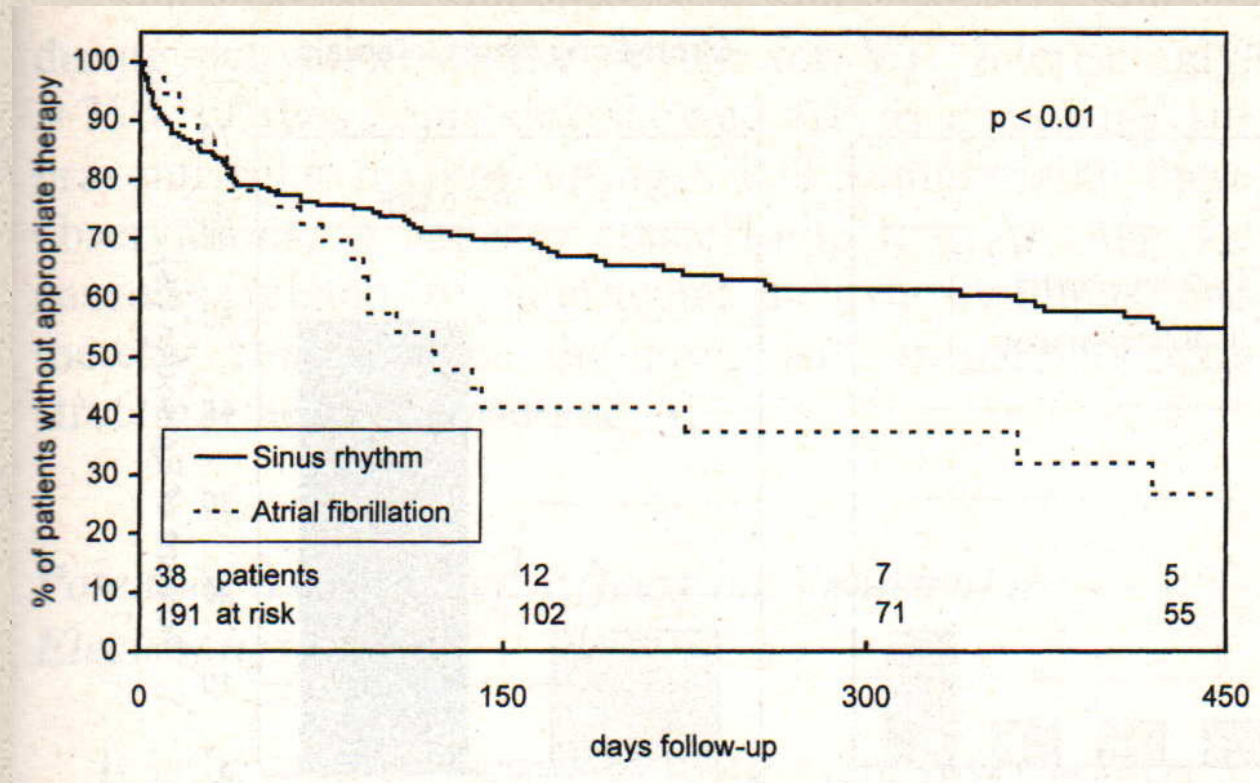
## Association Between Atrial Fibrillation and Appropriate Implantable Cardioverter Defibrillator Therapy: Results from a Prospective Study

GERIAN C. GRÖNEFELD, M.D., OLIVER MAUSS, M.SC., YI-GANG LI, M.D.,  
THOMAS KLINGENHEBEN, M.D., and STEFAN H. HOHNLOSER, M.D., FACC

**J Cardiovasc Electrophysiol 2000;11: 1208-1214**

# The interplay between AF and SCD

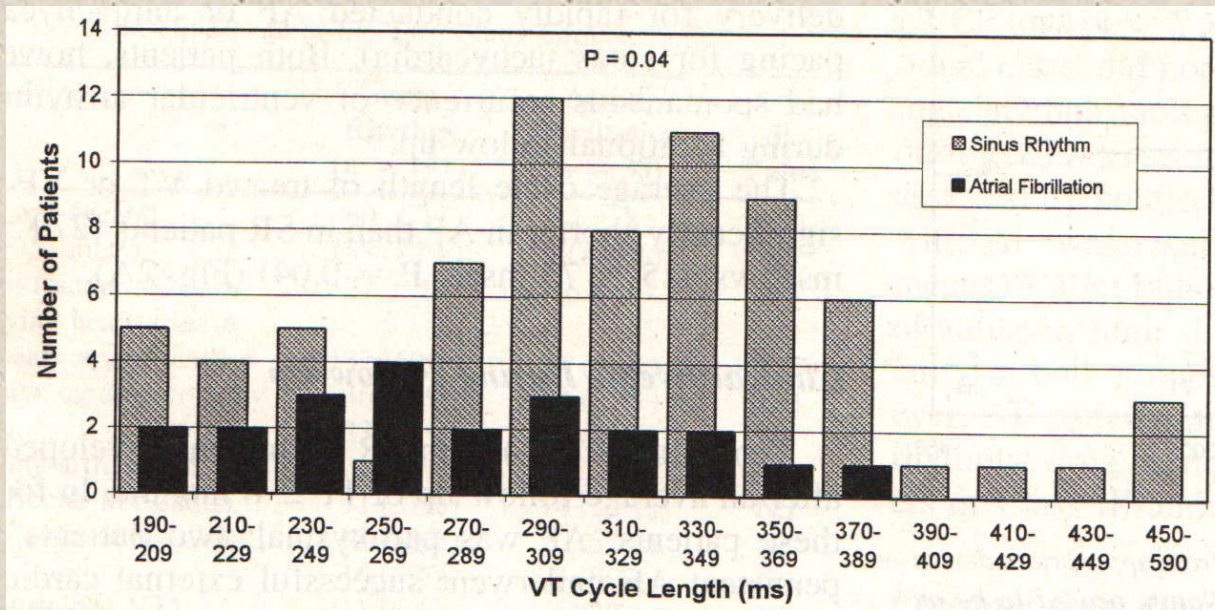
## Freedom from appropriate device therapy



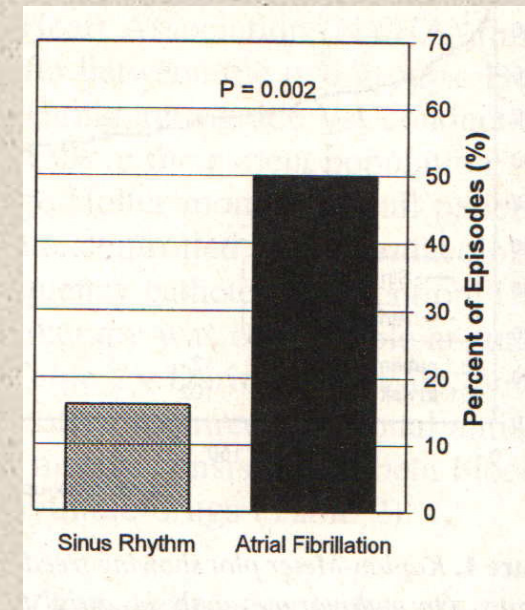
# The interplay between AF and SCD

## Cycle lengths of the ventricular arrhythmia

Tachycardia Cycle Length (ms) Distribution



Short-Long-Short Intervals



# The interplay between AF and SCD

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## **Atrial Fibrillation Is an Independent Risk Factor for Ventricular Fibrillation**

### **A Large-Scale Population-Based Case-Control Study**

Abdennasser Bardai, MD; Marieke T. Blom, MA; Daniel A. van Hoeijen, MSc; Hanneke W.M. van Deutekom, PhD; Henk J. Brouwer, MSc; Hanno L. Tan, MD, PhD

**Circ Arrhythm Electrophysiol. 2014; 7: 1033-1039**

# The interplay between AF and SCD

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## AF and sudden death

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1397 VF cases



AF : 215 pts (15,4%)

3774 controls



AF : 90 pts (2.6%)

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## AF increases risk for VF: OR 3.1

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Bardai et al. Circ Arrhythm Electrophysiol. 2014; 7: 1033-1039



# The interplay between AF and SCD

## AF and sudden death

### Possible mechanisms (I)

- Embolic
- Cerebral bleeding
- AF facilitates VT/VF
- AF = marker of more severe disease
- Antiarrhythmic drugs

AF intrinsically increases VF risk  
(genetic mutations for both AF/VF)

AF → coronary perfusion ↓ → ischemia → EMD (VF)

Bardai et al. Circ Arrhythm Electrophysiol. 2014; 7: 1033-1039

# The interplay between AF and SCD

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## AF and sudden death

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### Possible mechanisms (II)

- AV begets MI
- New-onsets AF leads to platelet activation and thrombin generation
- AF-mediated inflammation
- Coronary artery embolism

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 **Increased risk of sudden death**

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Bardai et al. Circ Arrhythm Electrophysiol. 2014; 7: 1033-1039



# The interplay between AF and SCD

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## **Patients With Supraventricular Tachycardia Presenting With Aborted Sudden Death: Incidence, Mechanism and Long-Term Follow-Up**

YINSHI WANG, MD, MELVIN M. SCHEINMAN, MD, FACC, WALTER W. CHIEN, MD, TODD J. COHEN, MD, MICHAEL D. LESH, MD, FACC, JERRY C. GRIFFIN, MD, FACC

**J Am Coll Cardiol 1991; 18:1711-9**

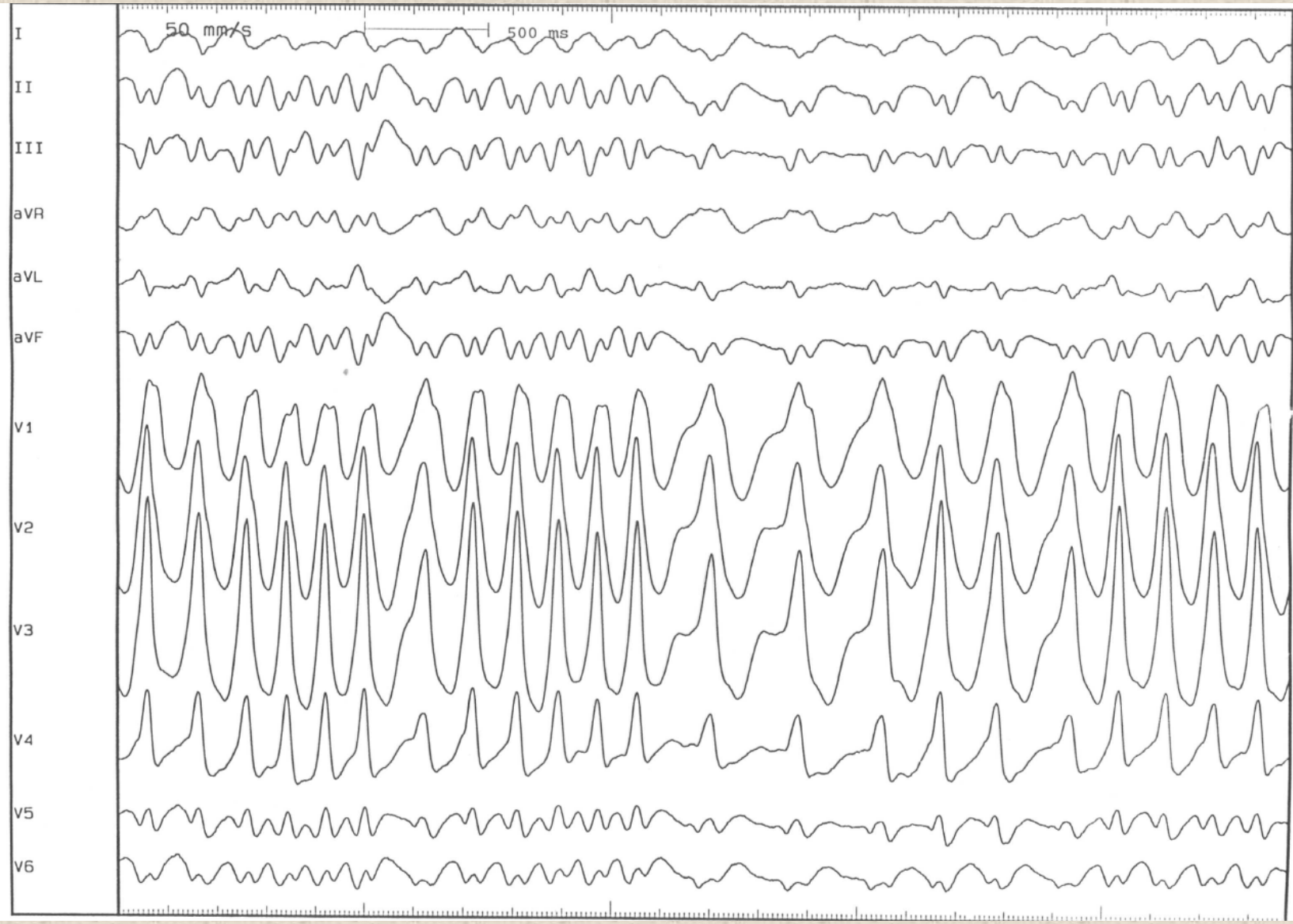
### *Editorial Comment*

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## **Supraventricular Tachyarrhythmias: Not Always So Benign\***

JEFFREY L. ANDERSON, MD, FACC

**J Am Coll Cardiol 1991; 18:1720-1**



# The interplay between AF and SCD

## SVT and sudden death

13/290 pts with aborted SD

SVT  VF

➤ WPW syndrome	n = 6	}	4.5%
➤ AVN RT	n = 3		
➤ AF + EANC	n = 4		

# The interplay between AF and SCD

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## AF and sudden death

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### Possible mechanisms (III)

- Enhanced AV nodal conduction  
(pts with DCM + LSB)
  - Rapid heart rate
  - Increased sympathetic flow
  - Hemodynamic compromise  
(LVEDP↑ → Stretch → VF)
  - Irregularity of HP activation
- 

Bardai et al. Circ Arrhythm Electrophysiol. 2014; 7: 1033-1039

# The interplay between AF and SCD

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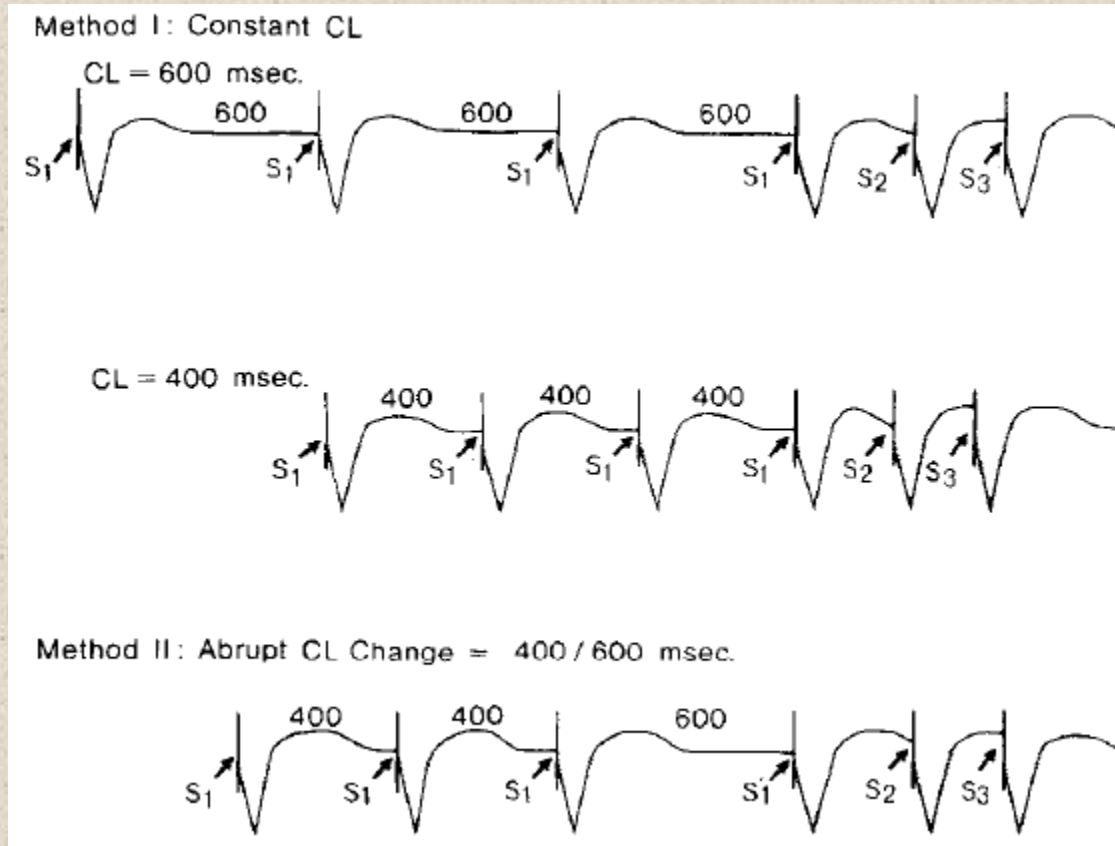
## Facilitation of Ventricular Tachycardia Induction with Abrupt Changes in Ventricular Cycle Length

STEPHEN DENKER, MD, MICHAEL LEHMANN, MD, REHAN MAHMUD, MD,  
CAROL GILBERT, RN, and MASOOD AKHTAR, MD

**AM J Cardiol 1984; 53: 508-515**

# The interplay between AF and SCD

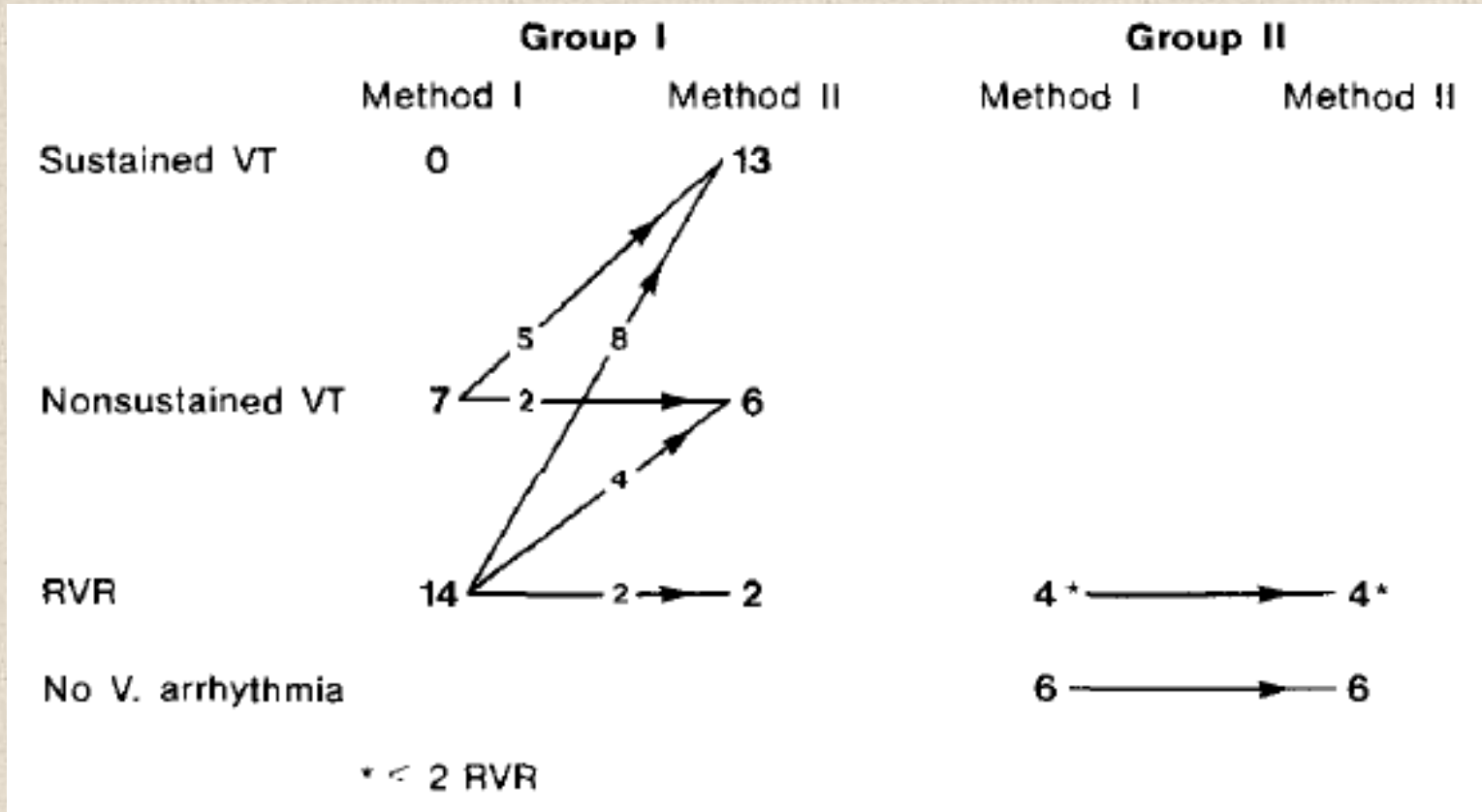
## Stimulation protocols



Denker et al. Am J Cardiol 1984; 53: 508-515

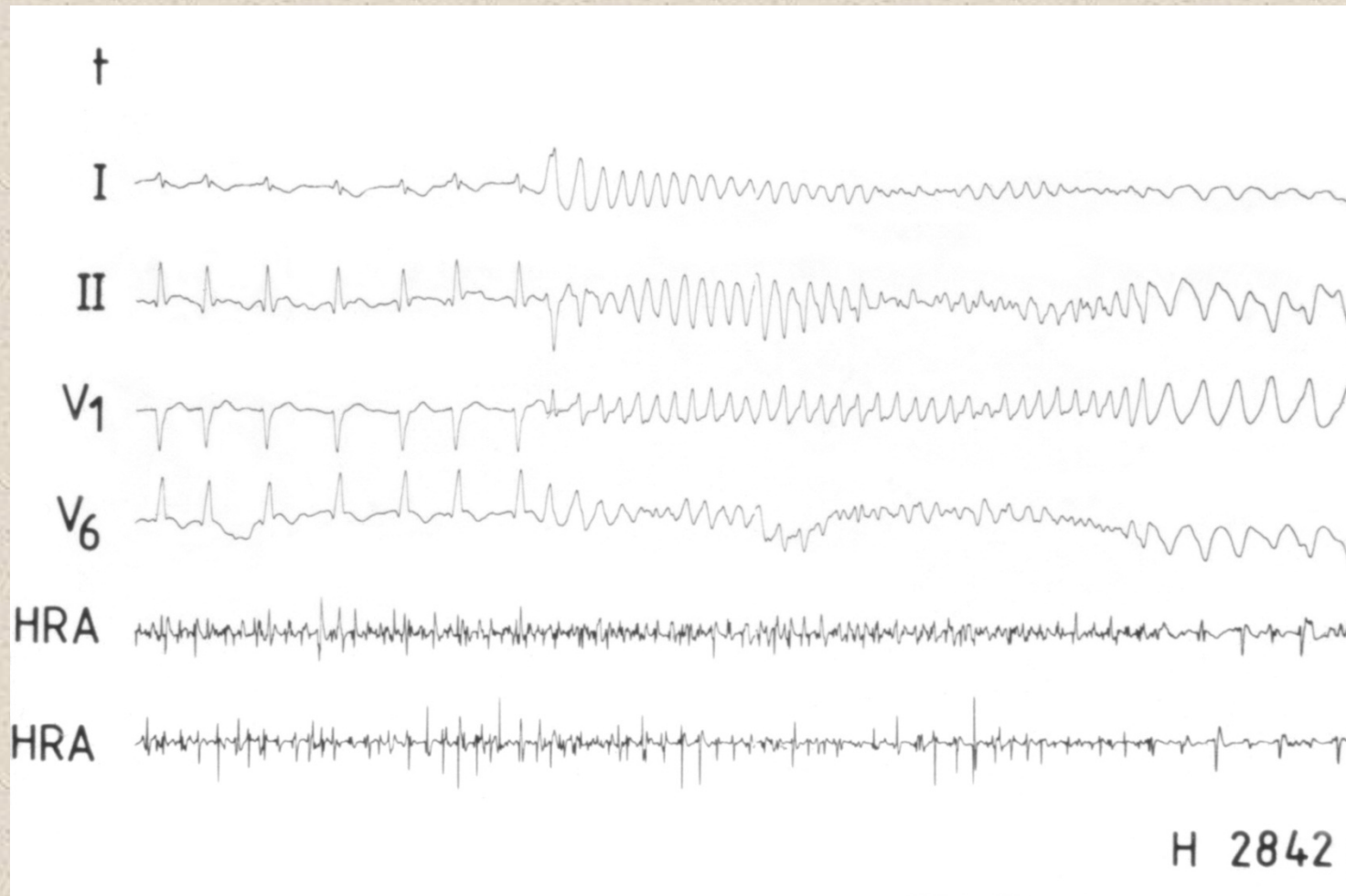
# The interplay between AF and SCD

## Incidence of ventricular tachycardia induction



Denker et al. Am J Cardiol 1984; 53: 508-515

# The interplay between AF and SCD





# The interplay between AF and SCD



# The interplay between AF and SCD

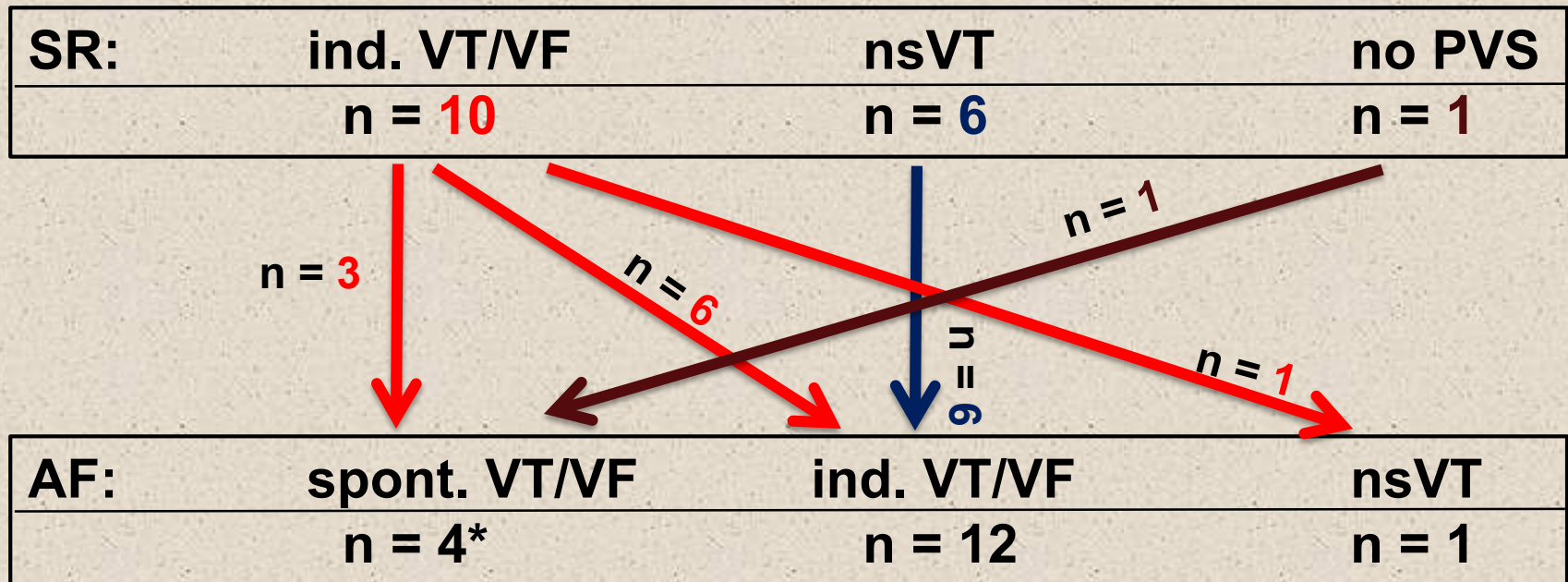


# The interplay between AF and SCD



# The interplay between AF and SCD

## VF/VT during sinus rhythm / AF Inducibility during SR vs AF



\*n = 1 spont. and ind.



# The interplay between AF and SCD

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## An Intersection of Atrial Fibrillation With Sudden Death

*Look Both Ways, and Proceed With Caution*

**Kyndaron Reinier et Sumeet S. Chugh**

**JAMA INTERN MED 2013; 173: 35-37**