Sudden cardiac death early post MI: Are we barking up the wrong tree?

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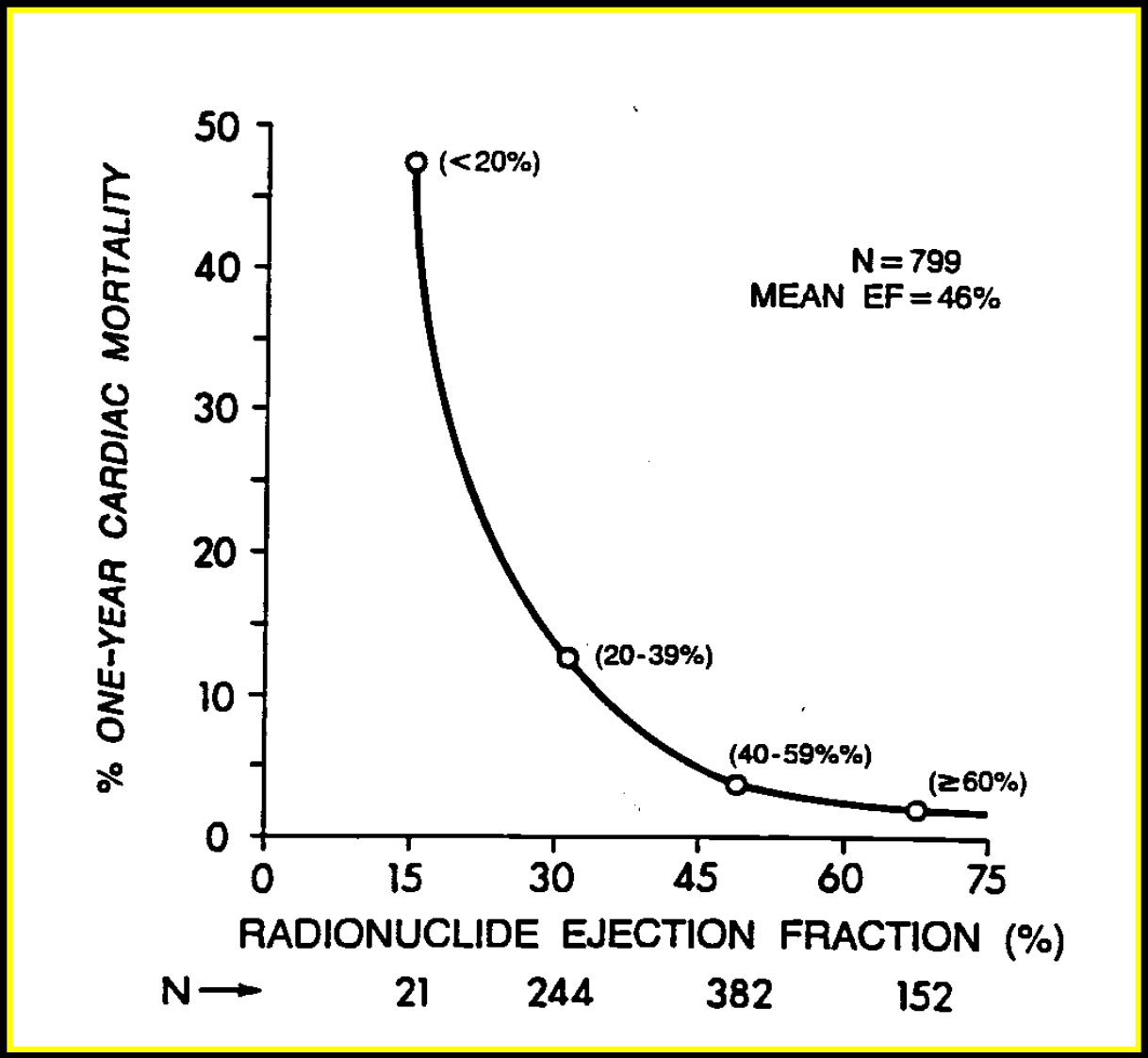
Director, Cardiac Electrophysiology Research

Professor of Medicine

Disclosures

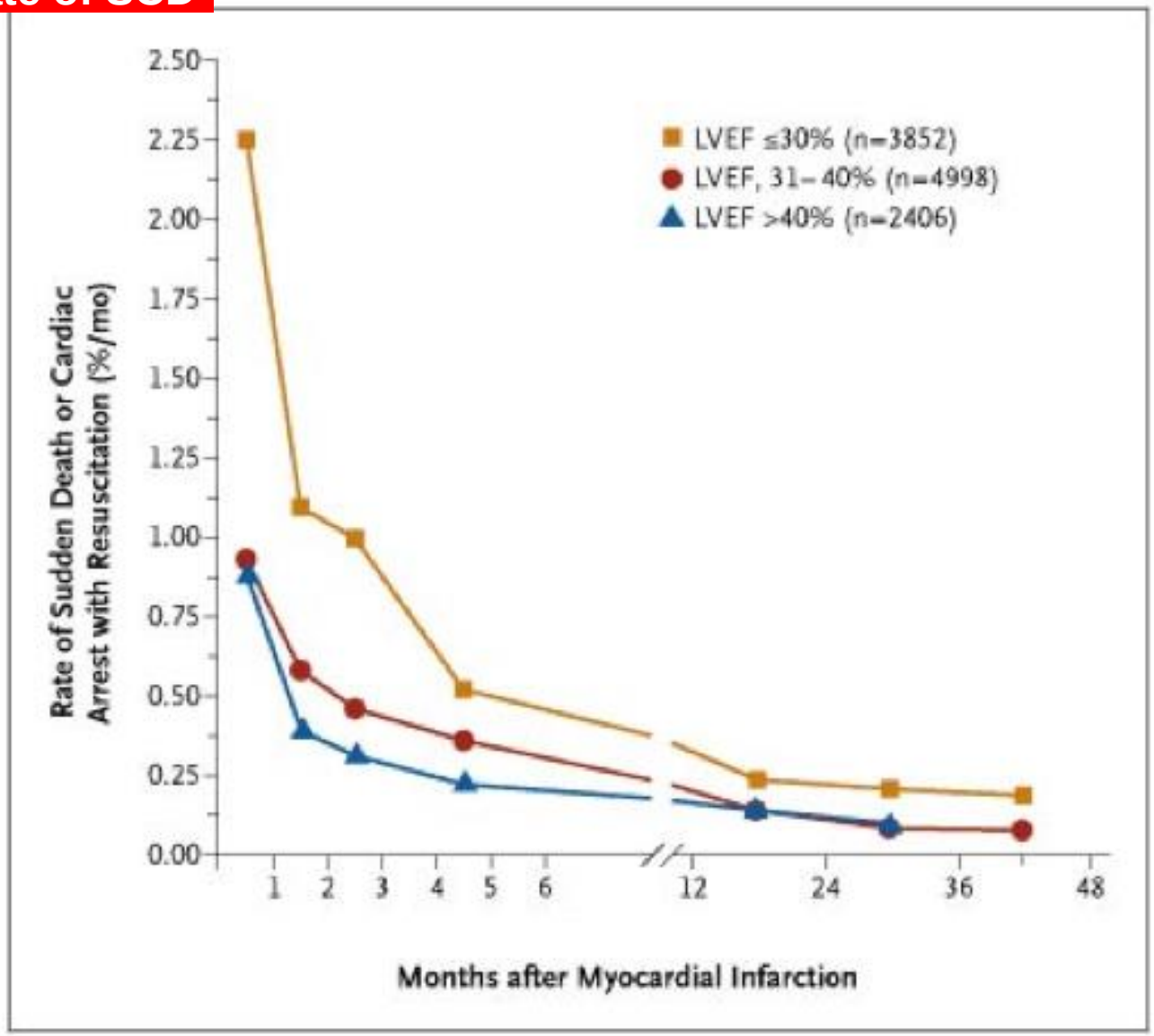
- **Research/Lectures - Boston Scientific, Medtronic. St. Jude**

Can we identify patients after acute MI who are at high risk for SCD and need early intervention?



Multicenter Postinfarction Research Group NEJM 1983

Monthly rate of SCD 1.4% 0.5% 0.27% 0.18% 0.14%



VALIANT, Solomon et al N Engl J Med 2005

Questions

- **After an MI, when do VT/VF events occur?**
- **Is better definition of the substrate for VT/VF likely to result in better risk stratification?**

“The electrophysiologic substrate for VT gradually develops in the first 2 weeks after MI, and once established, appears to remain indefinitely”

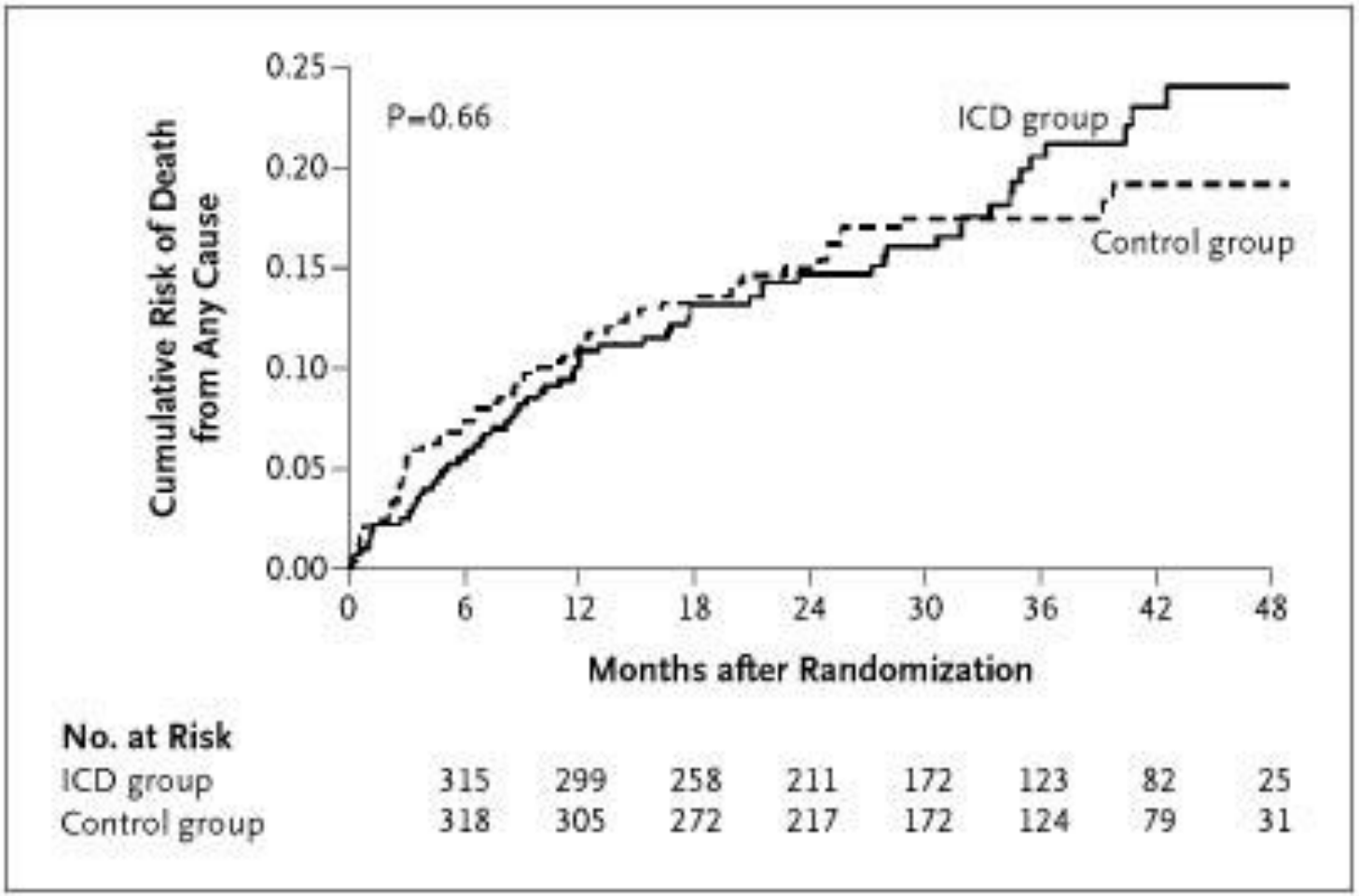
Zipes, Jalife: Cardiac Electrophysiology: From Cell to Bedside: 2004

Defibrillator in Acute MI Trial

- N=674, 76% male, age 62±11 years
- 6-40 days after acute MI (mean 18 days)
- LVEF ≤ 35% (actual 28 ± 5 %)
- SDNN ≤ 70 ms or mean RR ≤ 750 ms
- 87% on ß-blockers
- 95% on ACE inhibitos
- 78% on lipid lowering agents

Hohnloser et al N Engl J Med 2004

DINAMIT



Hohnloser et al N Engl J Med 2004

The NEW ENGLAND JOURNAL of MEDICINE

Study Hypothesis

Immediate **R**isk-Stratification **I**mproves **S**urvival (IRIS) study

High-risk patients after acute MI will show a better survival when treated early with an ICD compared to patients receiving optimal medical therapy (OMT) alone

Steinbeck et al N Engl J Med 2009

Methods Used for Risk-Stratification

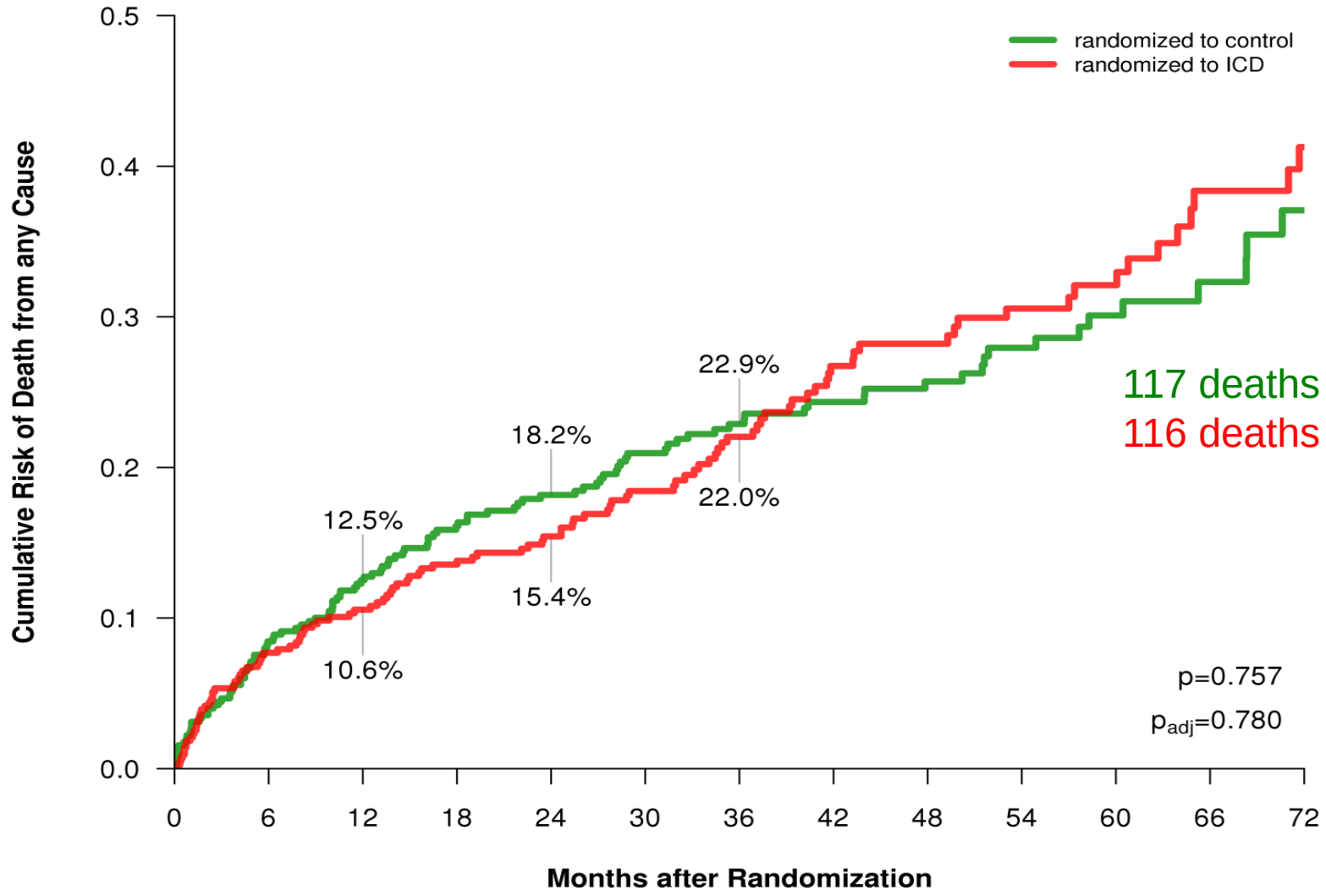
Criterion I Left ventricular ejection fraction (EF) ≤ 40% on day 5–31, together with heart rate ≥ 90 beats per minute (bpm) on the first available electrocardiogram

and/or

Criterion II Non-sustained ventricular tachycardia at a rate ≥ 150 bpm during Holter-ECG on day 5-31

Steinbeck et al N Engl J Med 2009

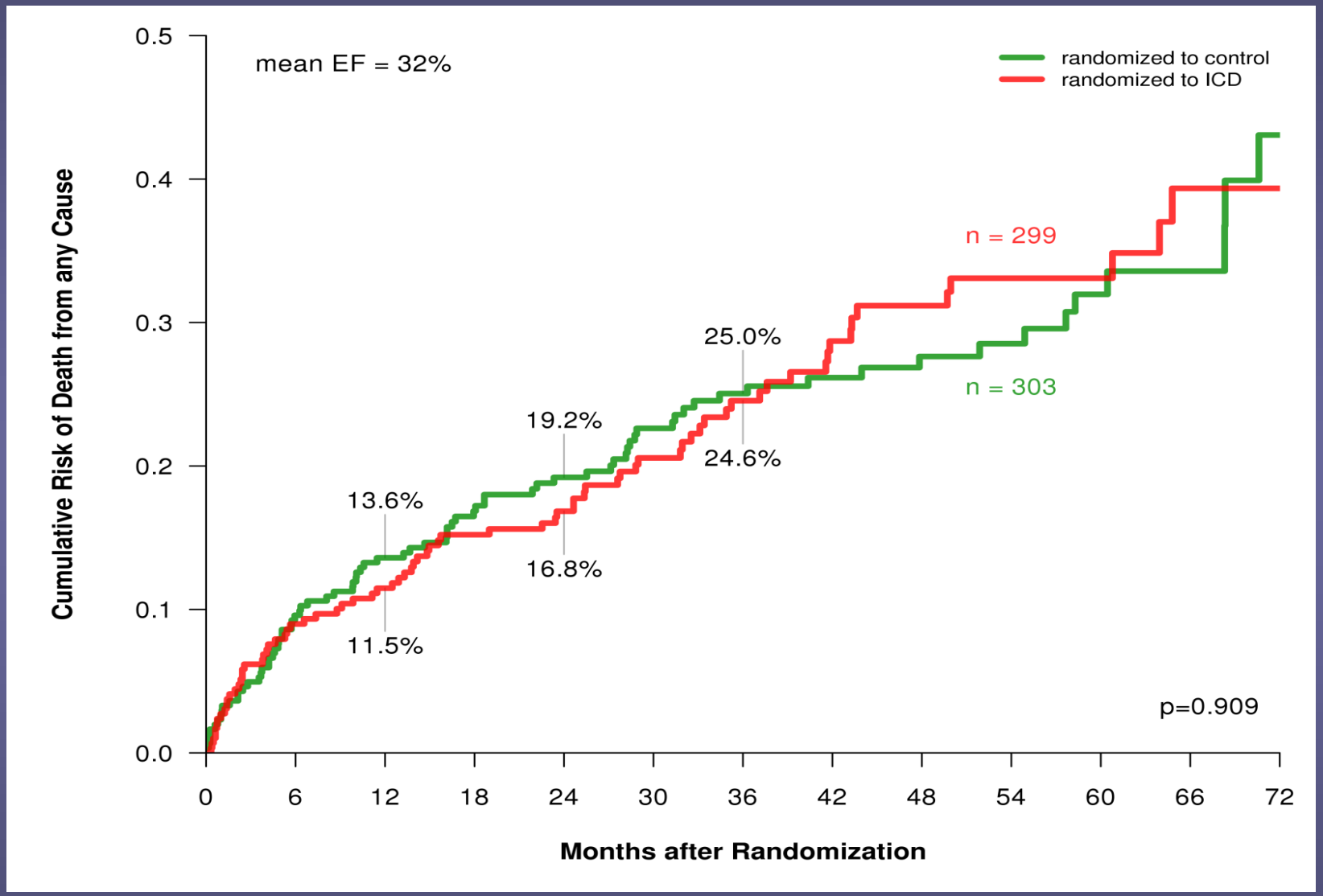
All Cause Mortality



No. at Risk

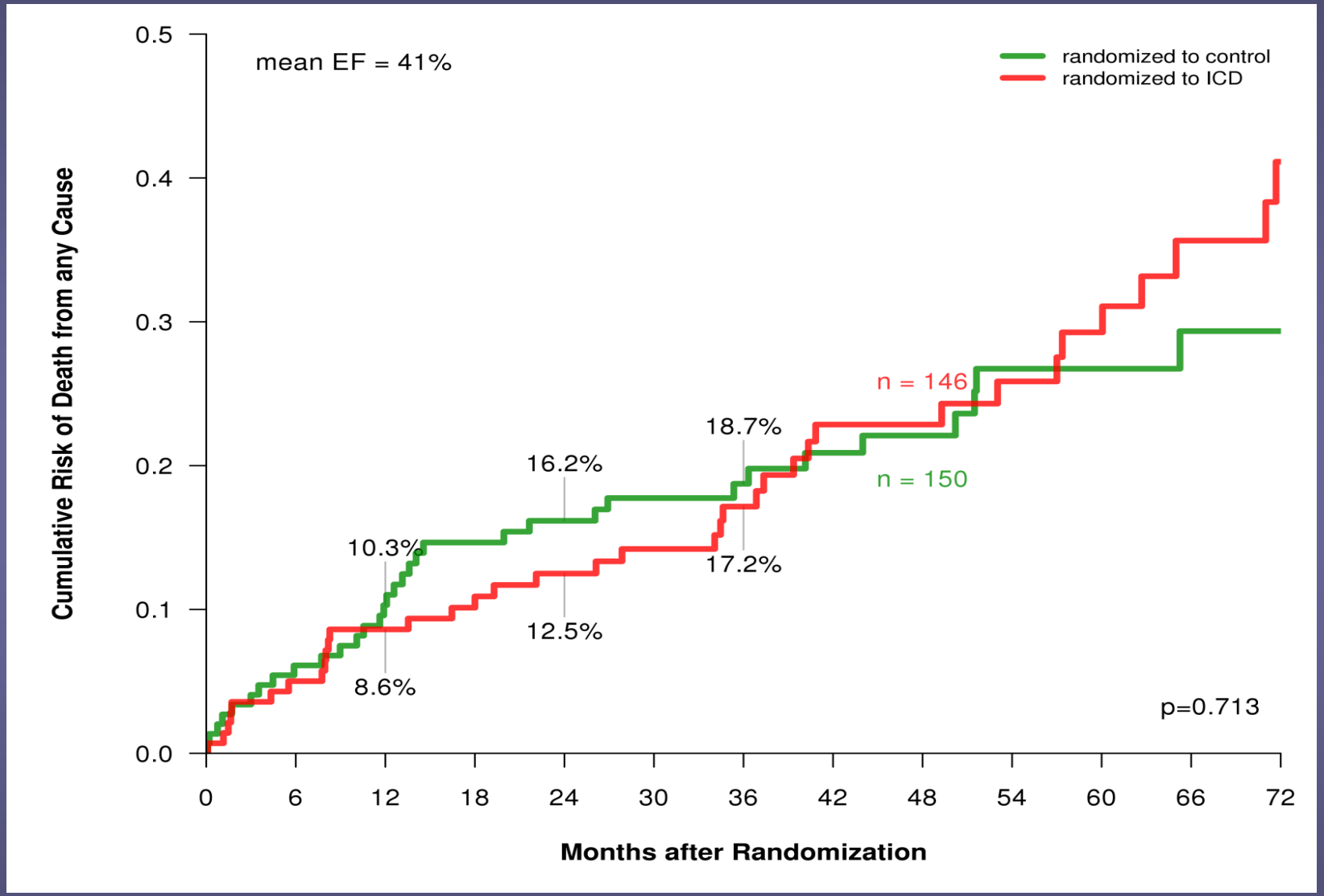
Control group	453	410	380	336	307	267	230	187	151	118	79	49	36
ICD group	445	390	366	338	303	253	207	163	137	106	78	48	40

EF ≤ 40%, Heart Rate ≥ 90 bpm



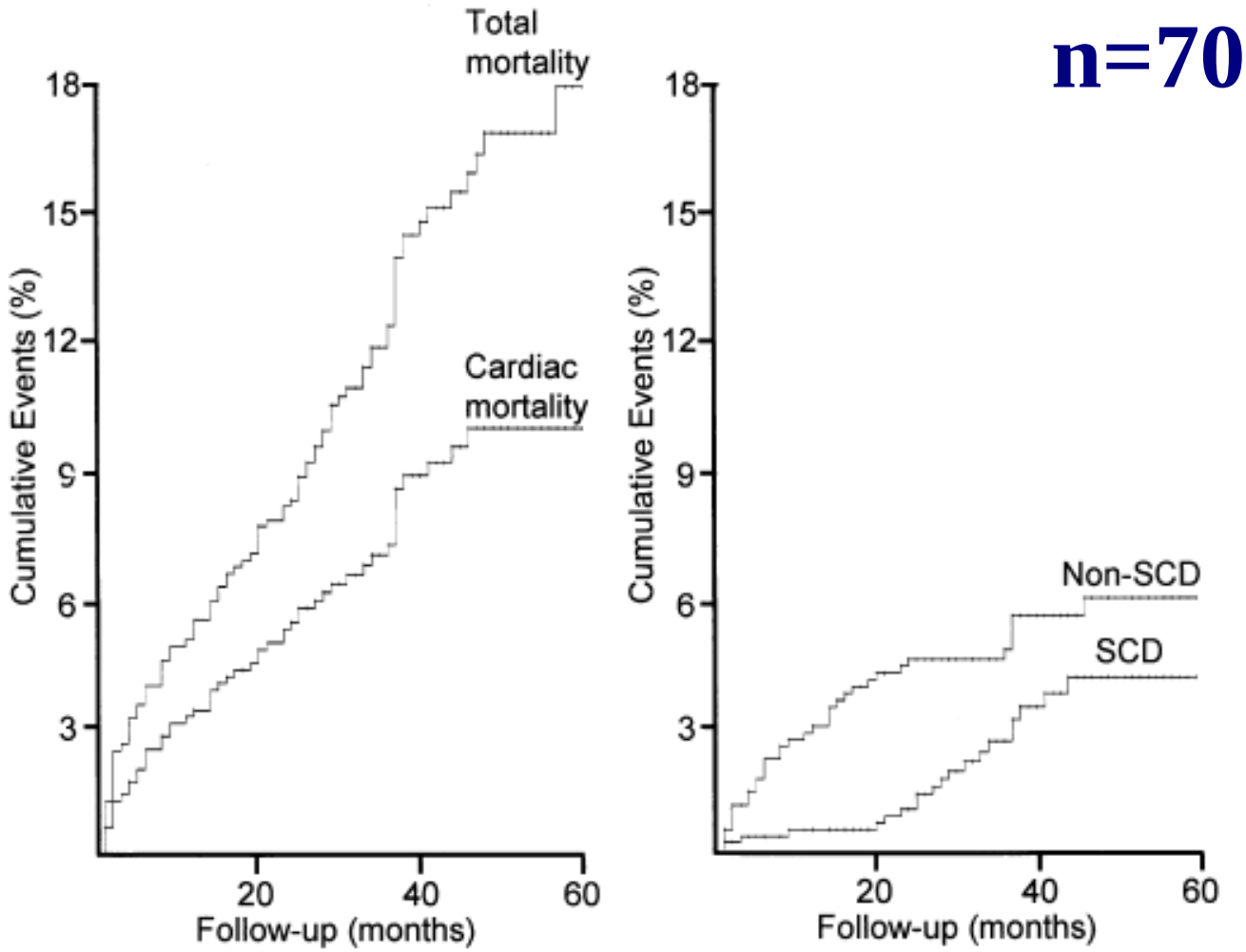
Steinbeck et al N Engl J Med 2009

Rapid Non-sustained Ventricular Tachycardia



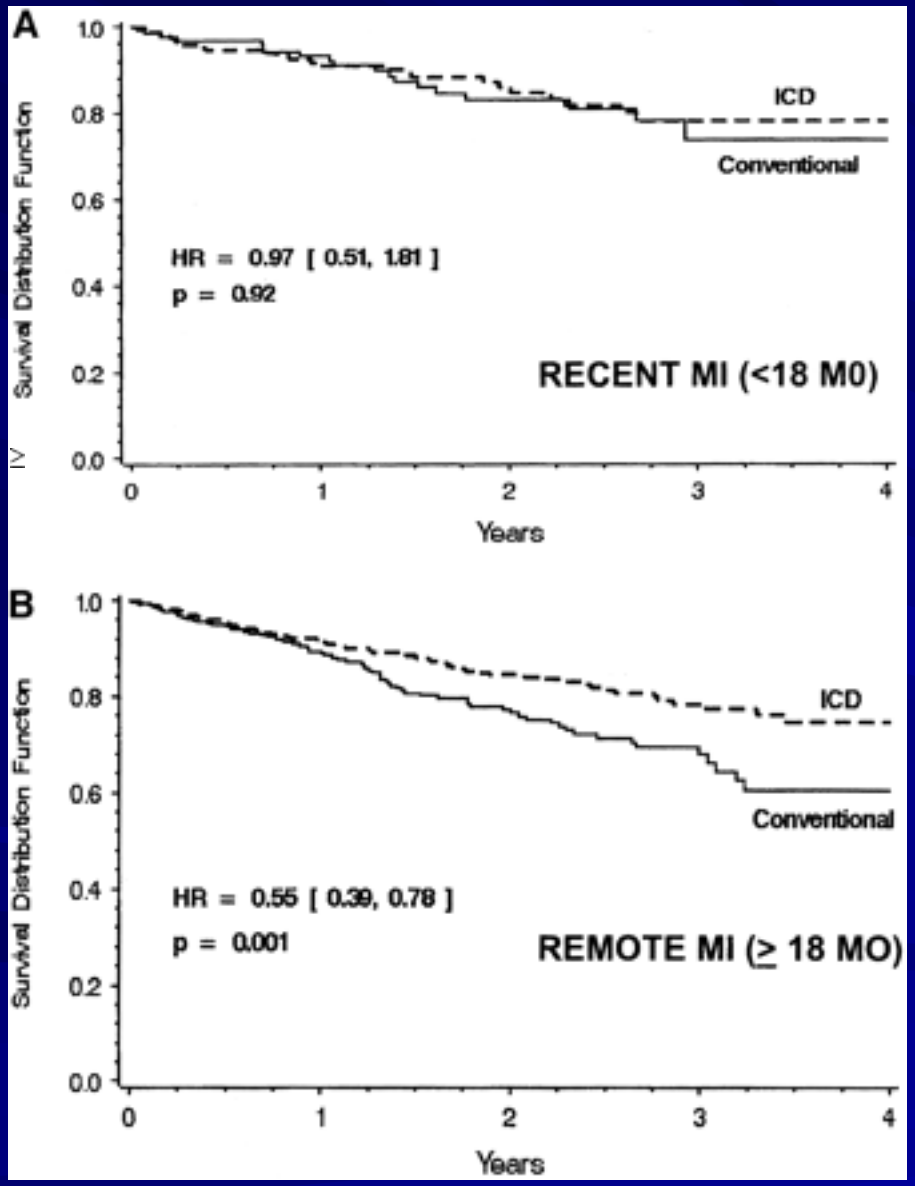
Steinbeck et al N Engl J Med 2009

Sudden Death After MI



Huikuri et al JACC 2003

MADIT II



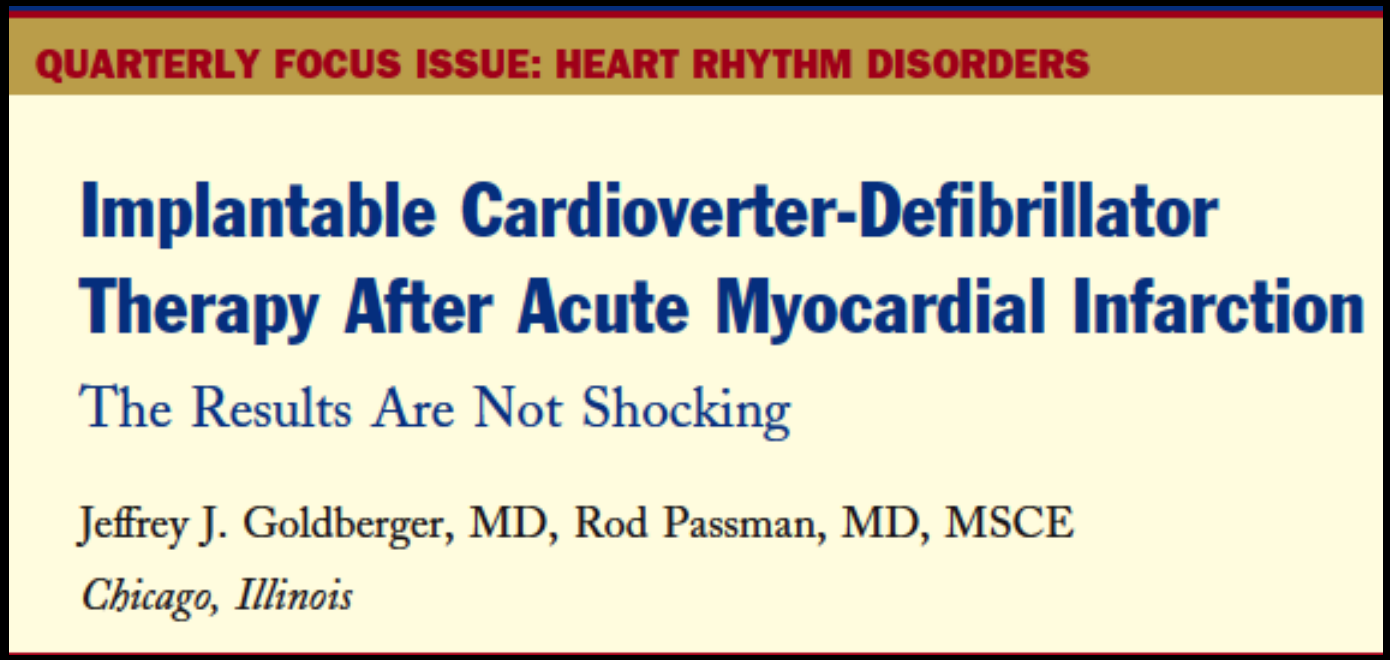
MI ≥ 1 month
LVEF ≤ 30%

MI Time (mo)	HR	95% CI	P
<18	0.98	0.52–1.84	0.95
18–59	0.52	0.26–1.05	0.07
60–119	0.50	0.28–0.91	0.02
120	0.62	0.36–1.08	0.09

HR indicates hazard ratio for ICD vs conventional therapy.

Wilber et al Circulation 2004

Explaining the Acute MI - SCD Paradox



QUARTERLY FOCUS ISSUE: HEART RHYTHM DISORDERS

Implantable Cardioverter-Defibrillator Therapy After Acute Myocardial Infarction

The Results Are Not Shocking

Jeffrey J. Goldberger, MD, Rod Passman, MD, MSCE

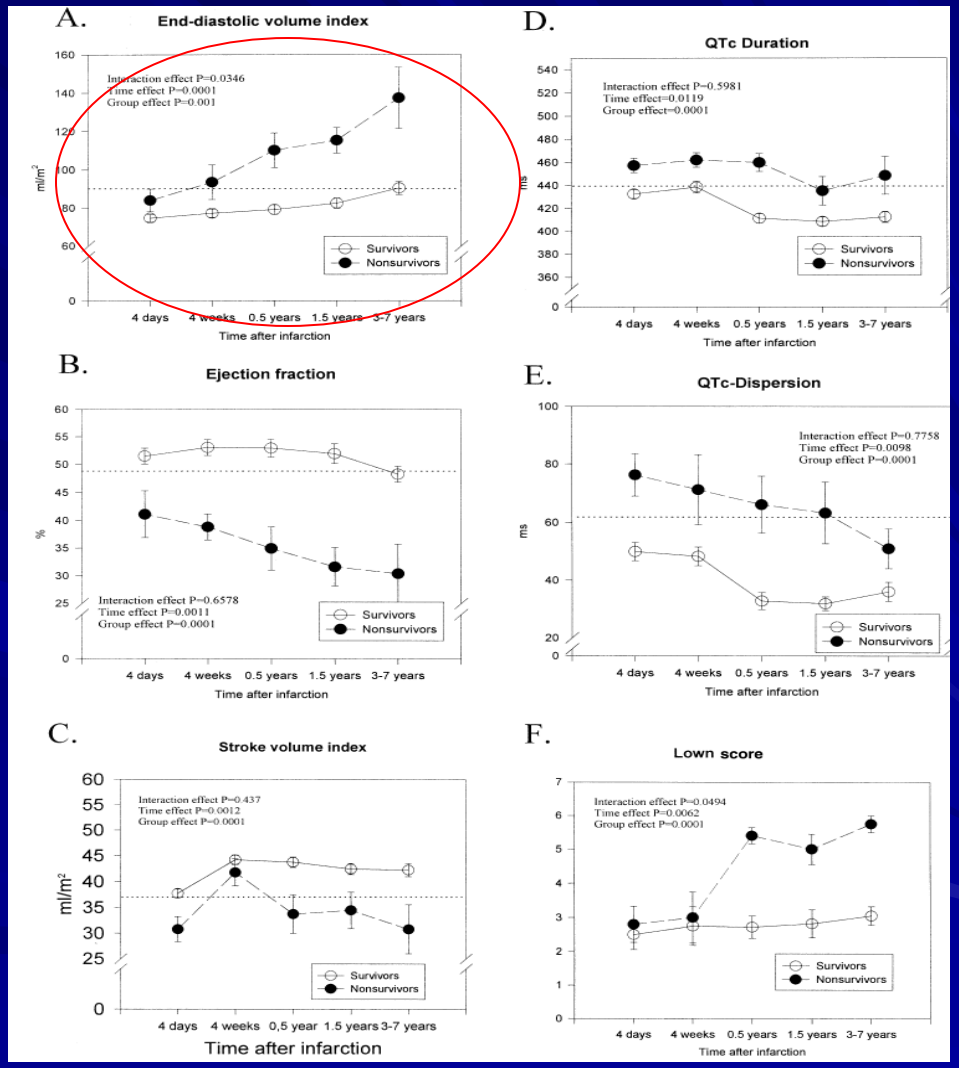
Chicago, Illinois

- **Pathogenesis of SCD immediately after acute MI is different than later post-MI**
- **Different risk stratifiers are needed after acute MI**
- **ICD implantation after acute MI may have deleterious effects**

JACC 2009; 54:2001-5

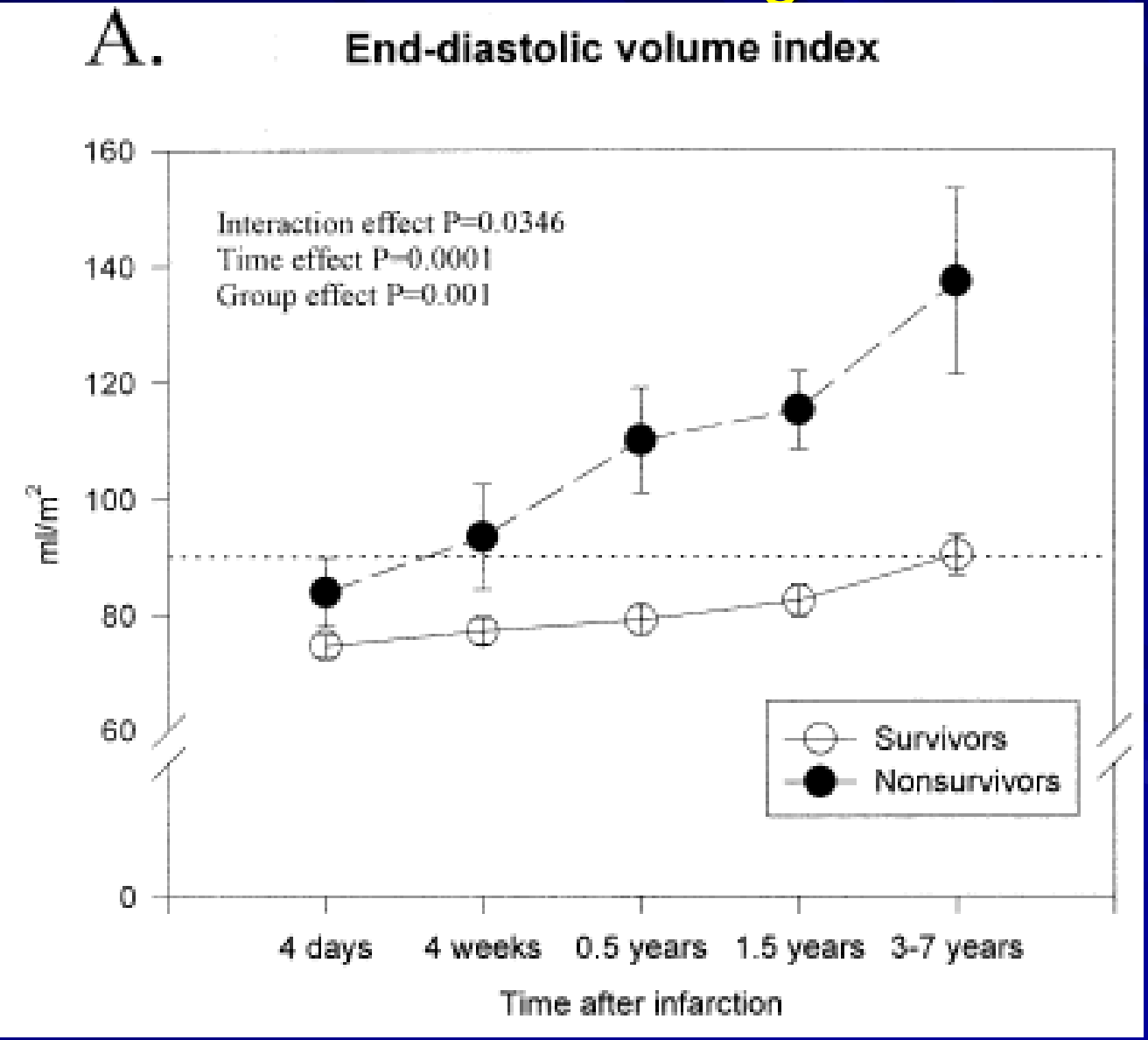
Time Course of Structural, Functional and Electrical Changes

- 134 asymptomatic post-MI patients
- MUGA, RH cath, ECG, Holter
  - 4 days
  - 4 weeks
  - 6 months
  - 1.5 years
  - 3-7 years



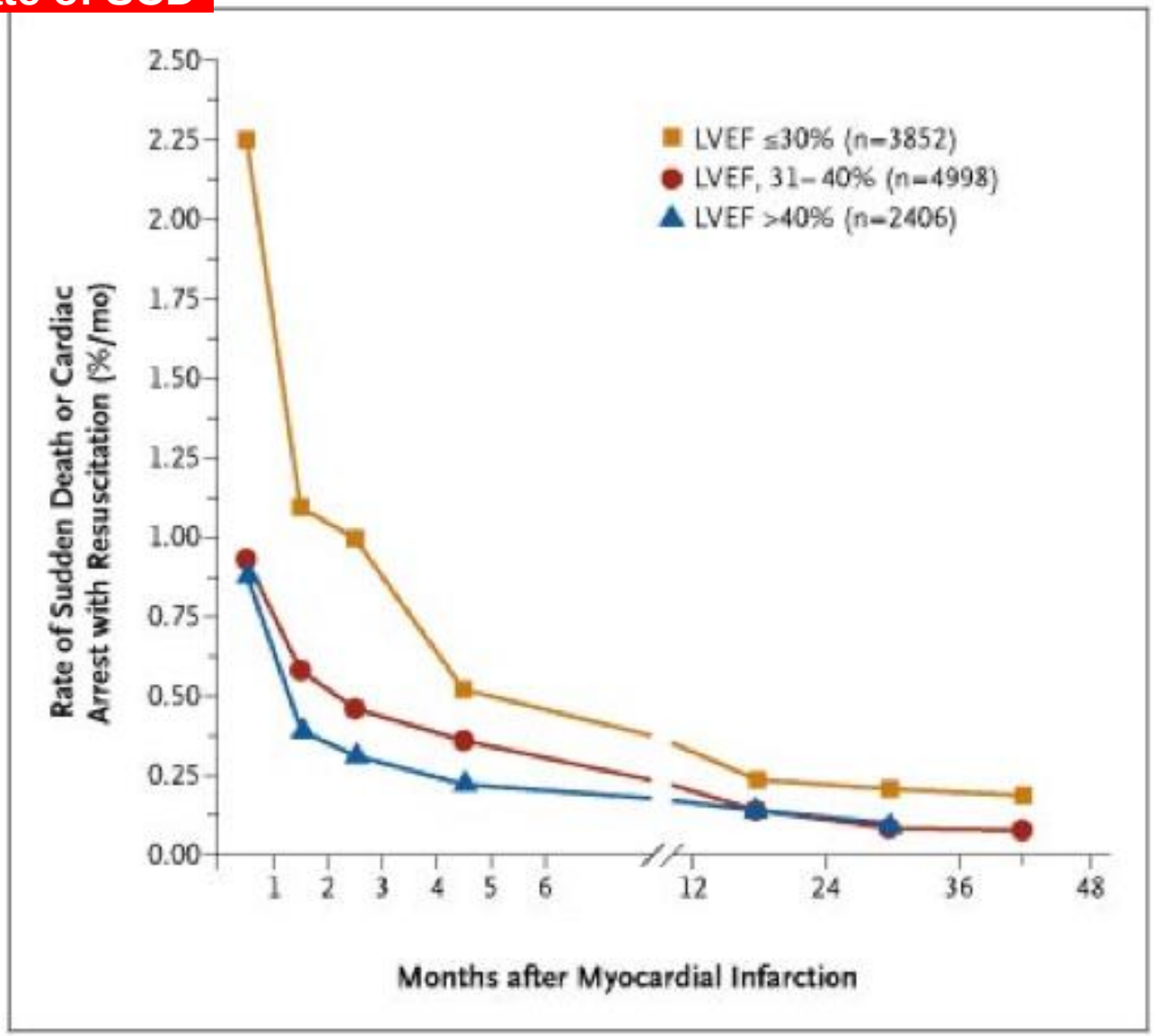
Gaudron et al; JACC 38; 2001

Time Course of Structural, Functional and Electrical Changes



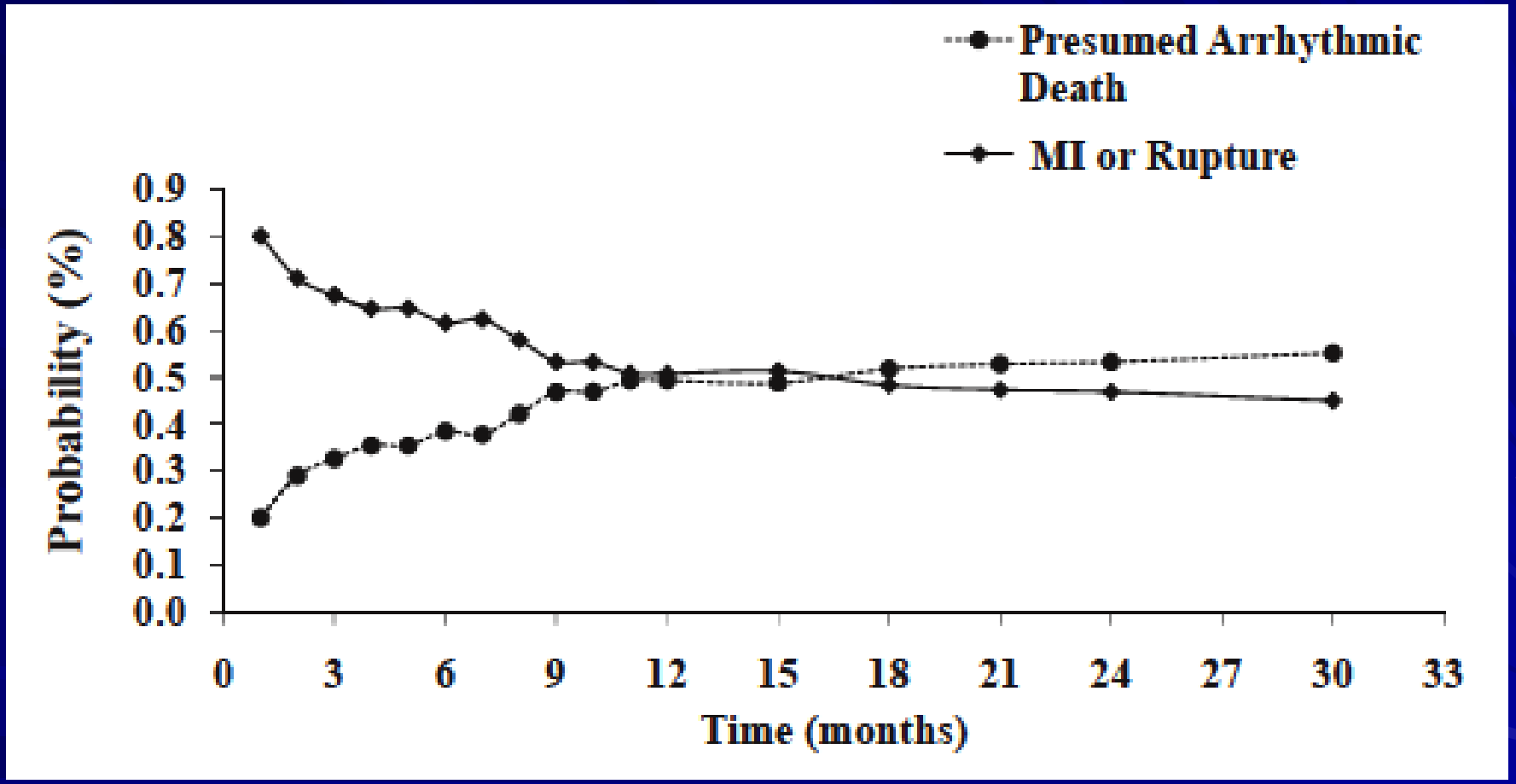
Gaudron et al; JACC 38; 2001

Monthly rate of SCD 1.4% 0.5% 0.27% 0.18% 0.14%



VALIANT, Solomon et al N Engl J Med 2005

Results of Autopsy Adjudication in 105 Clinical Cases of SCD

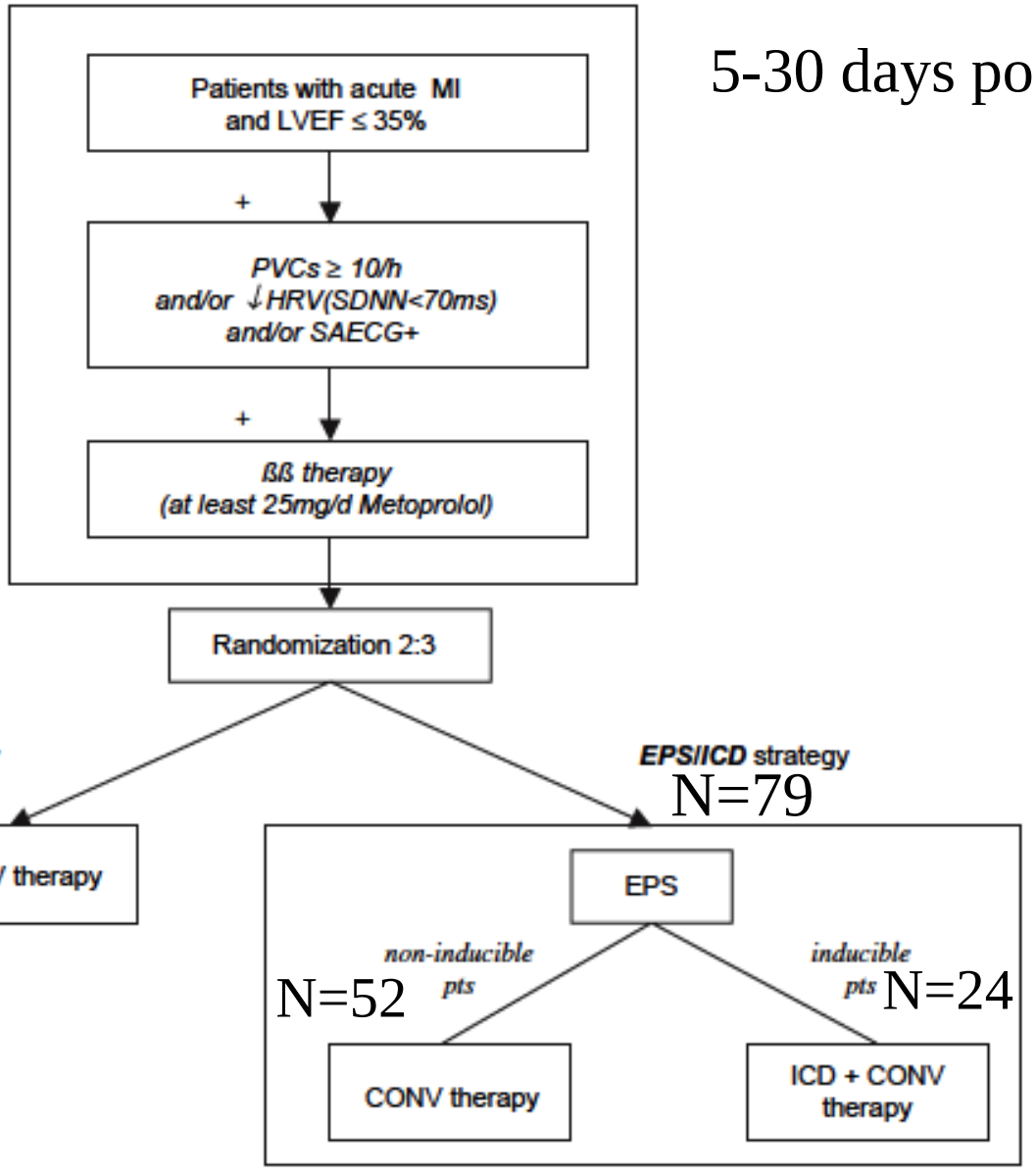


VALIANT, Pouleur et al Circulation 2010

Explaining the Acute MI - SCD Paradox

- Pathogenesis of SCD immediately after acute MI is different than later post-MI
- **Different risk stratifiers are needed after acute MI**
- ICD implantation after acute MI may have deleterious effects

BEta-blocker STrategy Plus ICD Trial



5-30 days post-MI

	1-yr	2-yr
CONV	18%	29.5%
EPS	11%	20%

Ravielle et al Europace 2005

Early Risk Stratification after STEMI

Table 1. Baseline Patient Characteristics by Group*

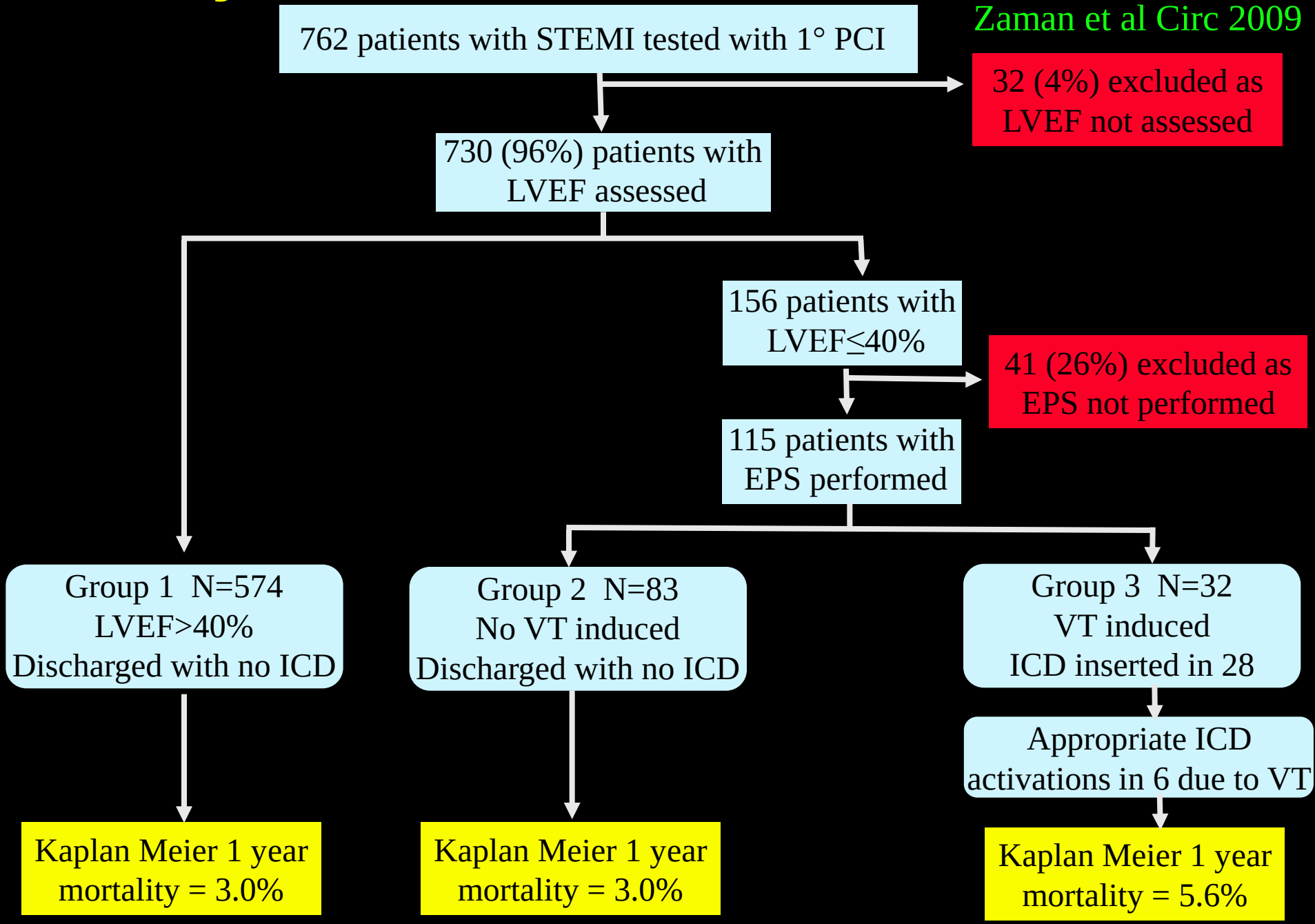
Characteristic	Group 1 (n=574)	Group 2 (n=83)	Group 3 (n=32)	*P*
Men, n (%)	453 (79)	62 (75)	30 (94)	0.077
Age, mean±SD, y	60±13	58±11	57±11	0.224
Diabetes mellitus, n (%)	149 (26)	13 (16)	11 (34)	0.225
Hypertension, n (%)	320 (56)	32 (39)	14 (44)	0.007
Hyperlipidemia, n (%)	332 (58)	40 (48)	22 (69)	0.097
Family history, n (%)	308 (54)	41 (49)	20 (63)	0.482
History of coronary artery disease, n (%)	130 (23)	16 (19)	10 (31)	0.405
Previous coronary artery surgery, n (%)	25 (4)	2 (2)	2 (6)	0.598
Previous PCI, n (%)	54 (9)	5 (7)	6 (19)	0.113
Current smoker, n (%)	237 (41)	45 (54)	11 (34)	0.089
Previous stroke, n (%)	24 (4)	4 (5)	1 (3)	0.919
Q-wave development, n (%)	348 (61)	55 (66)	20 (63)	0.643

*Group 1, LVEF >40% and no EPS; group 2, LVEF ≤40%, no VT, and no ICD; group 3, LVEF ≤40%, VT induced, and ICD.

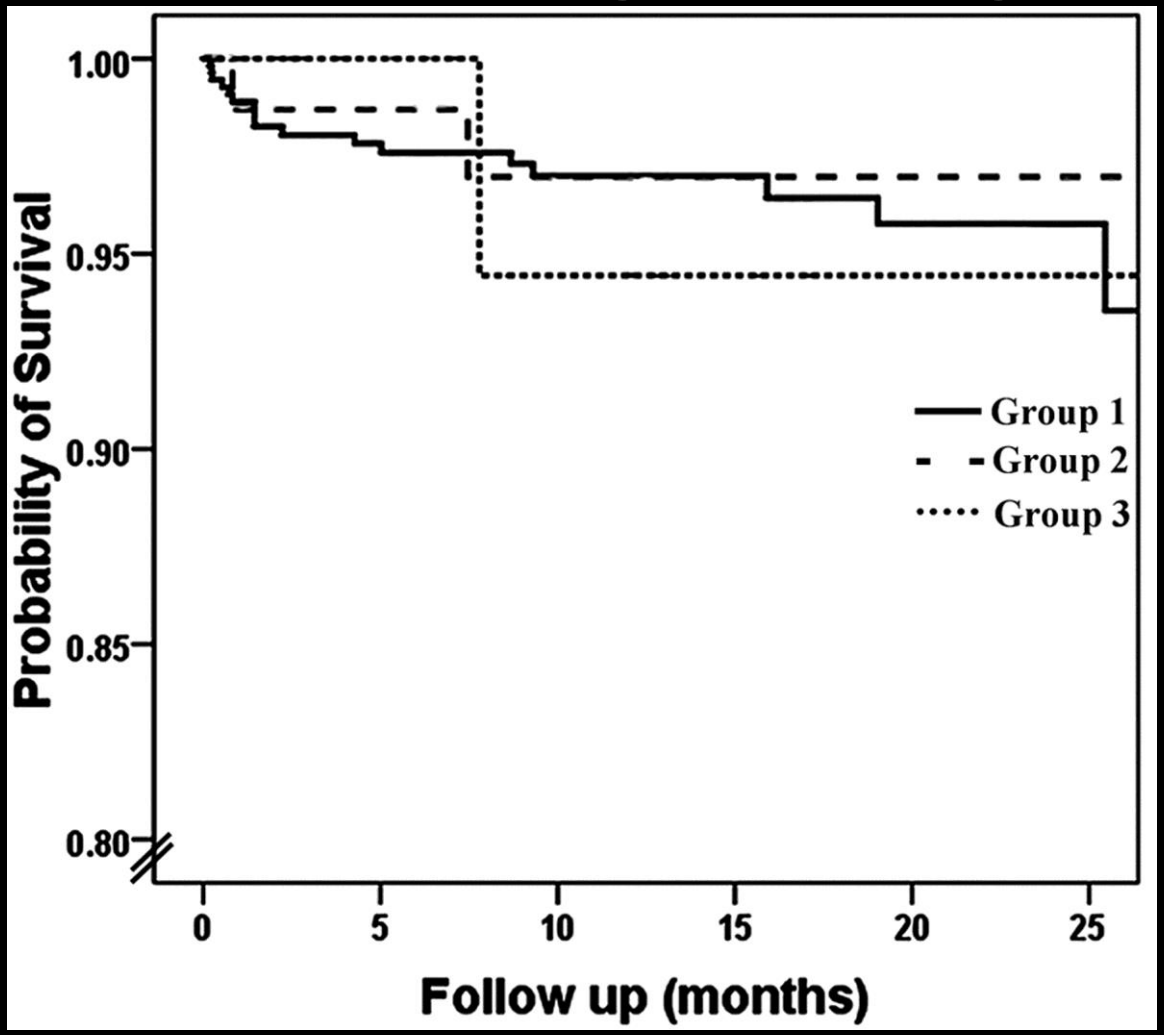
Zaman et al Circulation 2009

Early Risk Stratification after STEMI

Zaman et al Circ 2009



Kaplan-Meier estimates of the probability of survival according to study group



Circulation

Zaman, S. et al. Circulation 2009;120:194-200

Questions

- After an MI, when does substrate for VT/VF form? When do VT/VF events occur?
- Is better definition of the substrate for VT/VF likely to result in better risk stratification?

GUSTO 2-YEAR SURVIVAL

EF>40%

N=1701

2 year mortality 6.8%

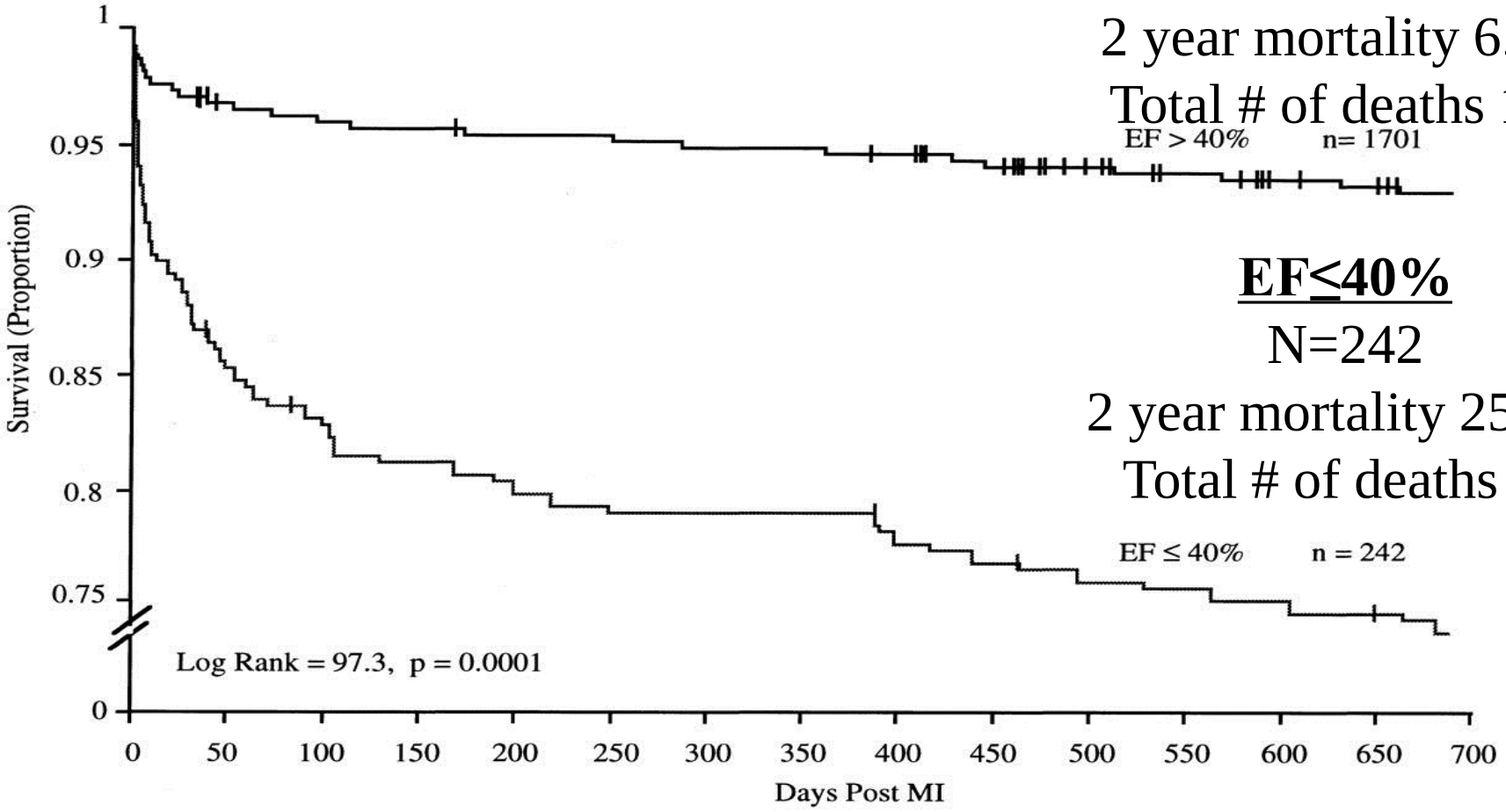
Total # of deaths 116

EF≤40%

N=242

2 year mortality 25.2%

Total # of deaths 61

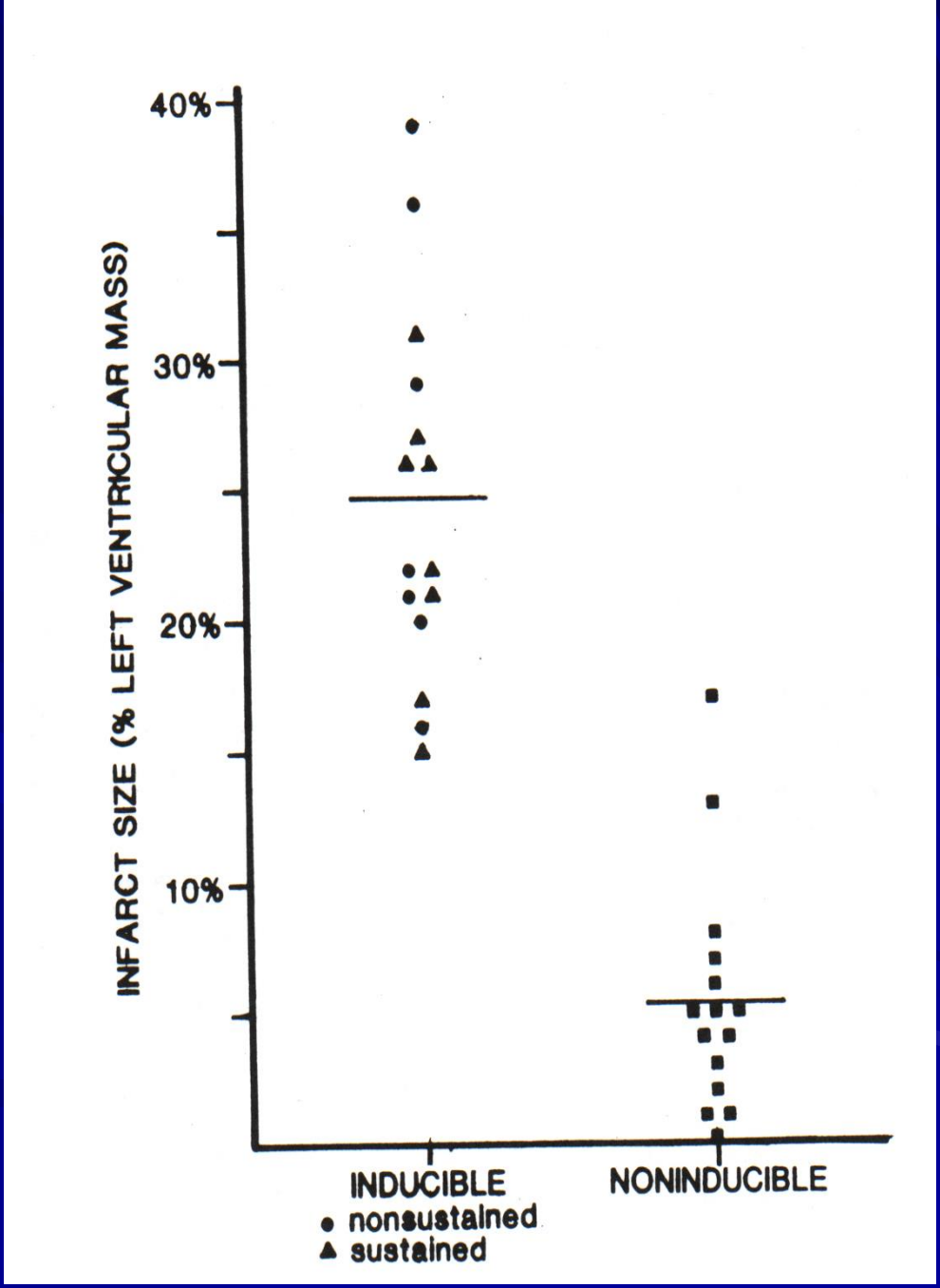


Cumulative Deaths per interval													
EF > 40%	60	11	6	4	2	6	0	6	7	4	2	5	3
EF ≤ 40%	36	5	4	3	2	1	0	2	2	2	2	1	1

Ross AM Circulation 1998; 97: 1549-1556

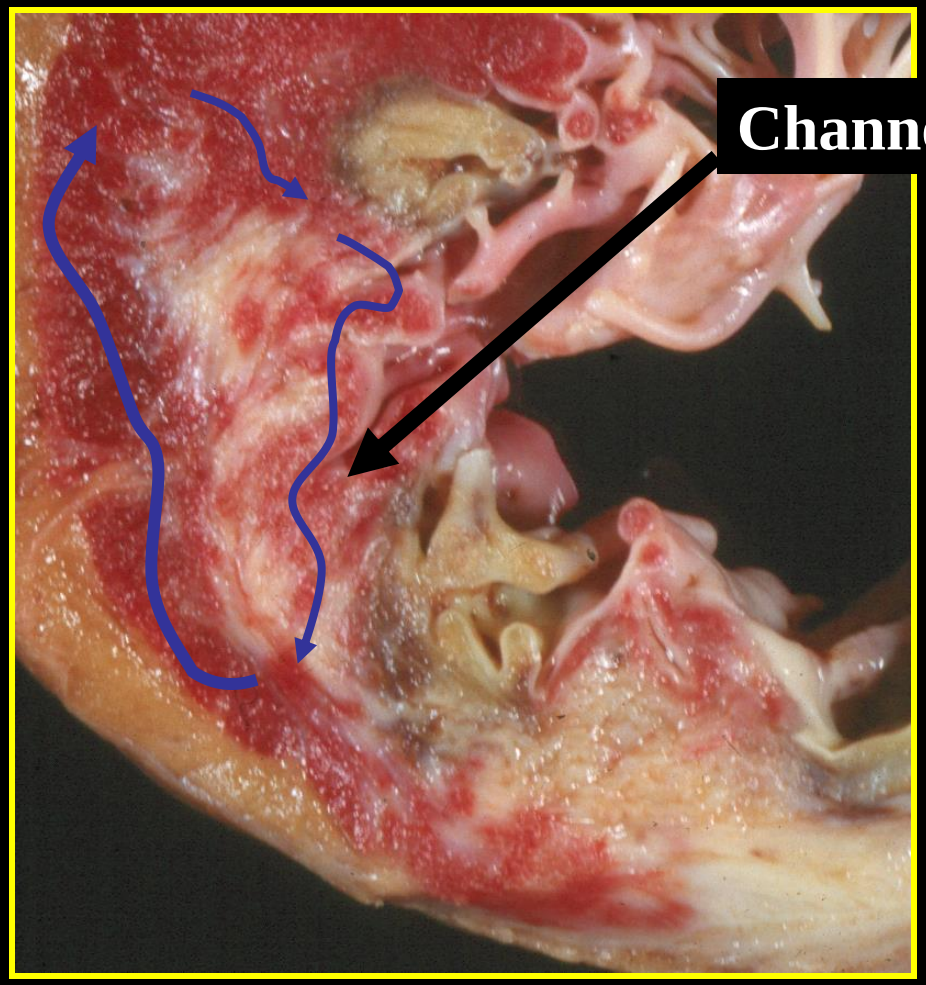
Canine Model

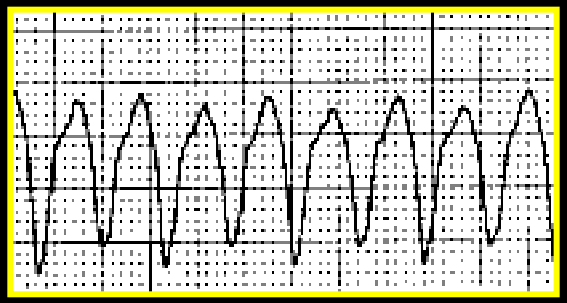
Extent of myocardial scar is related to inducibility of VT



Wilber et al *Am Heart J* 1985

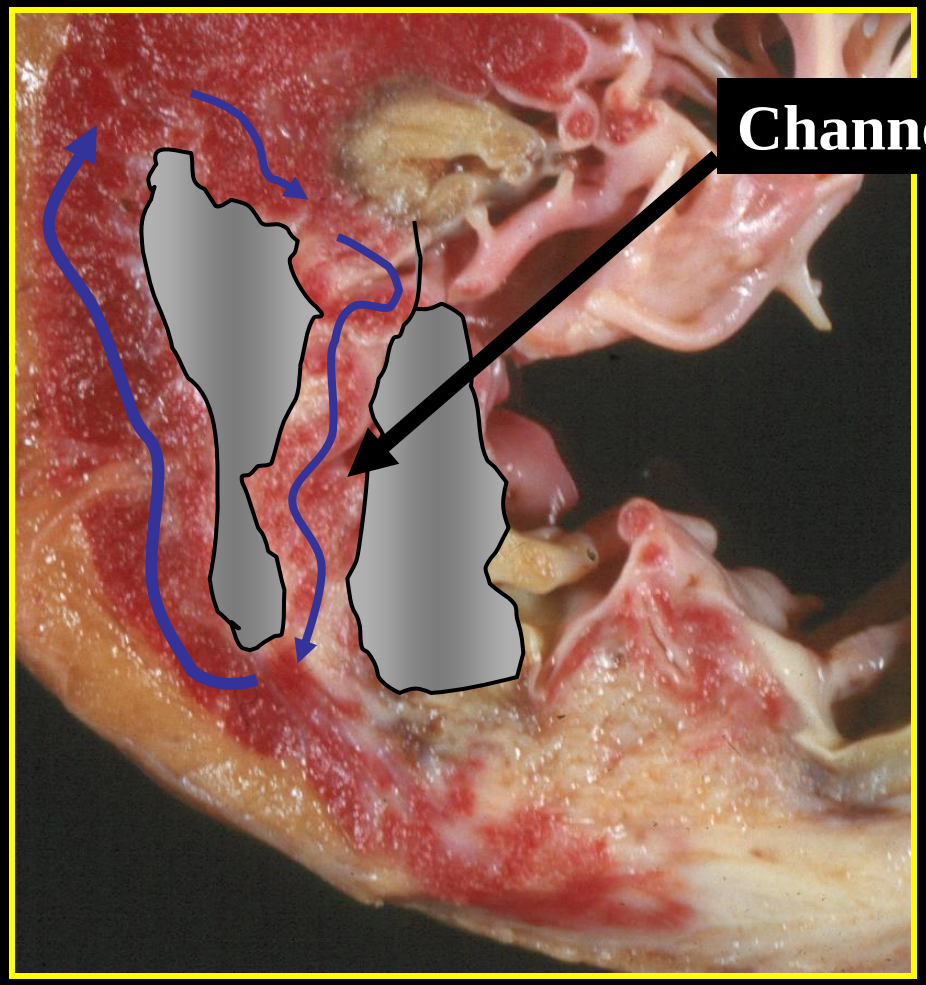
Sustained Monomorphic VT: Reentry in an infarct scar

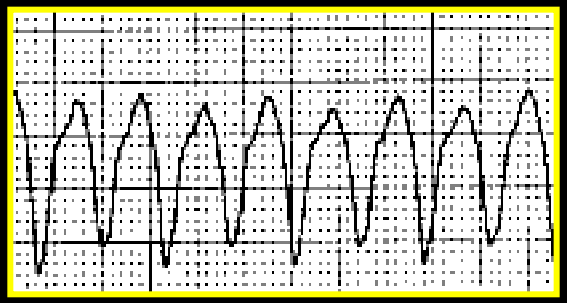




Courtesy of Bill Stevenson

Sustained Monomorphic VT: Reentry in an infarct scar





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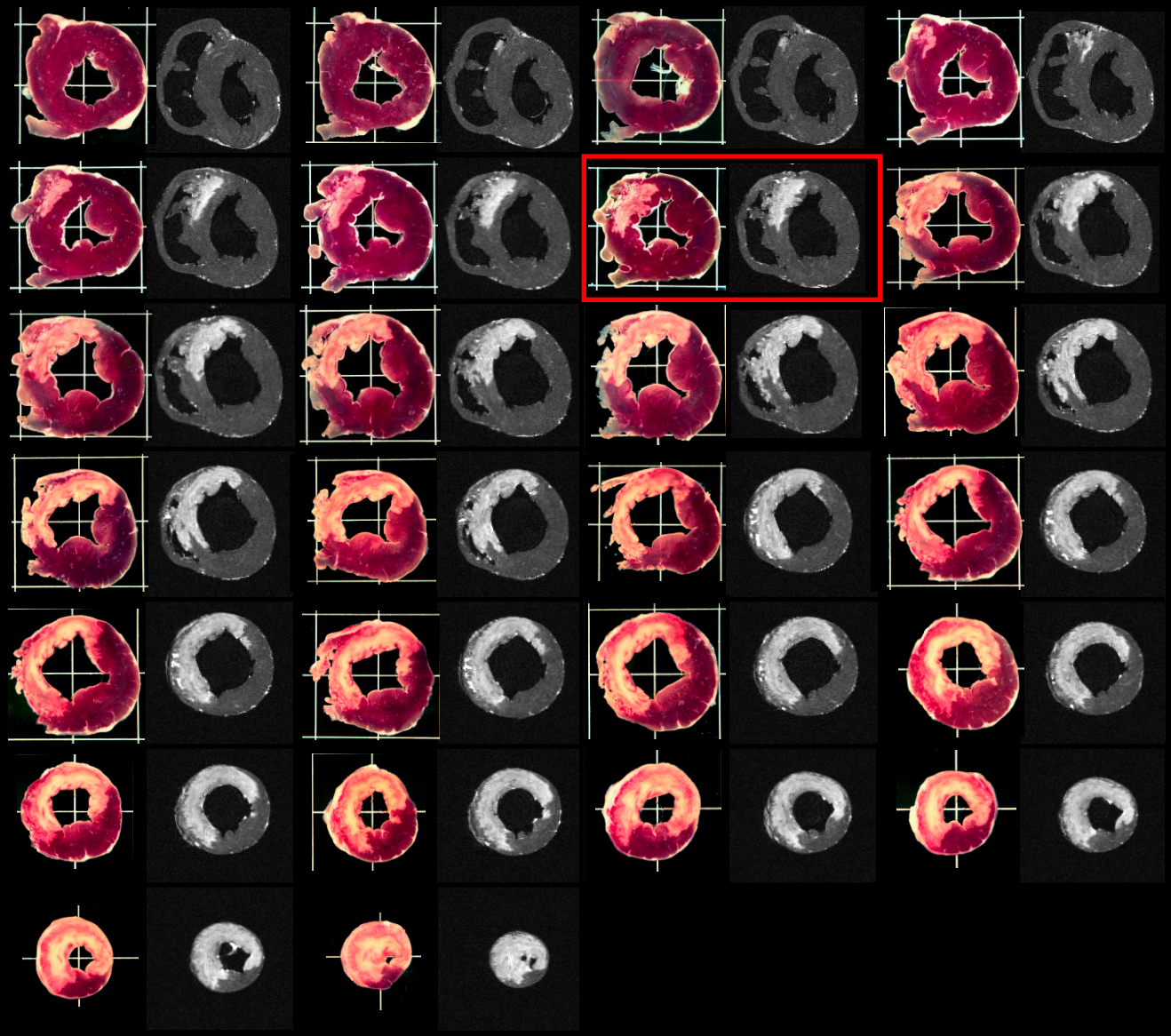
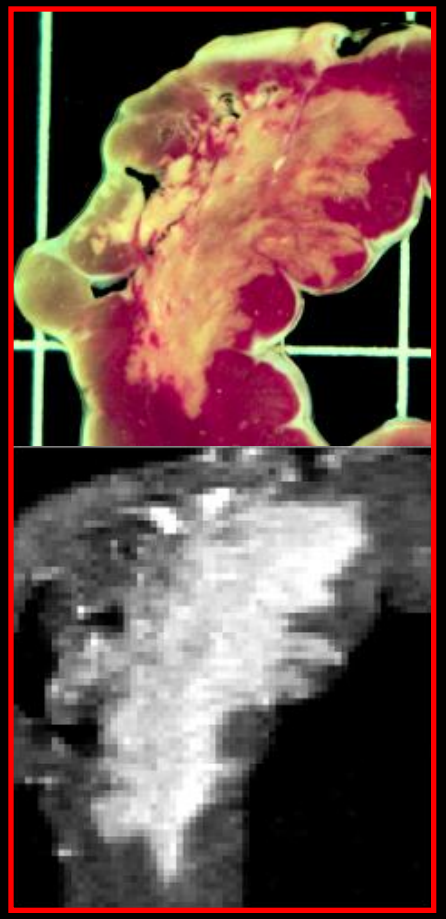




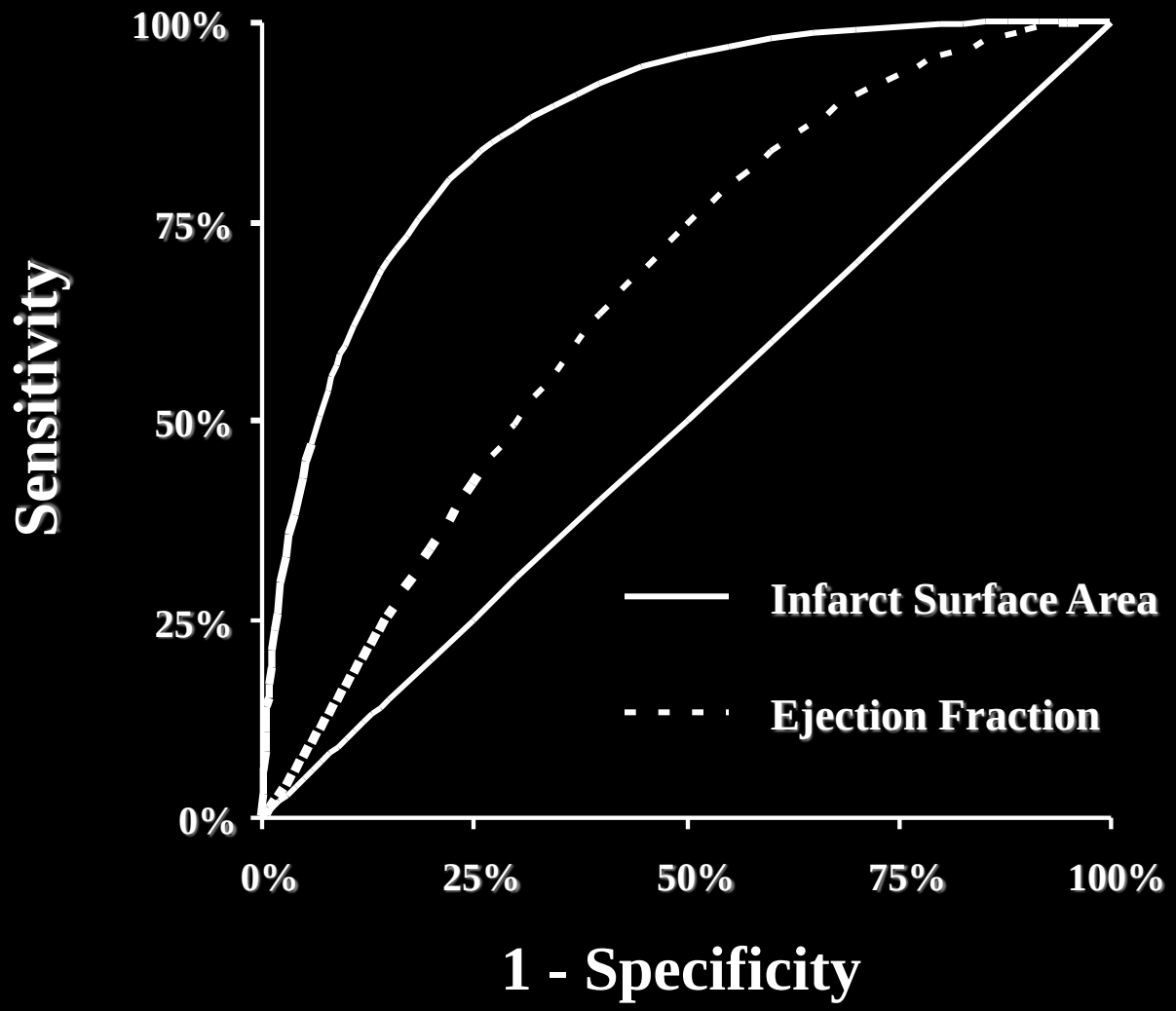
Infarct Morphology Identifies Patients With Substrate for Sustained VT

- **48 pts with CAD undergoing EPS**
  - **21 not inducible** **EF 35 ± 3 %**
  - **18 MVT** **EF 28 ± 2 %**
  - **9 PVT/VF** **EF 34 ± 6 %**
- **MRI results**
  - **21 NI:** **Inf mass 14 ± 3%** **SA 93 ± 14 cm^2**
  - **18 MVT:** **Inf mass 26 ± 3%** **SA 172 ± 15 cm^2**

<0.009 **<0.002**

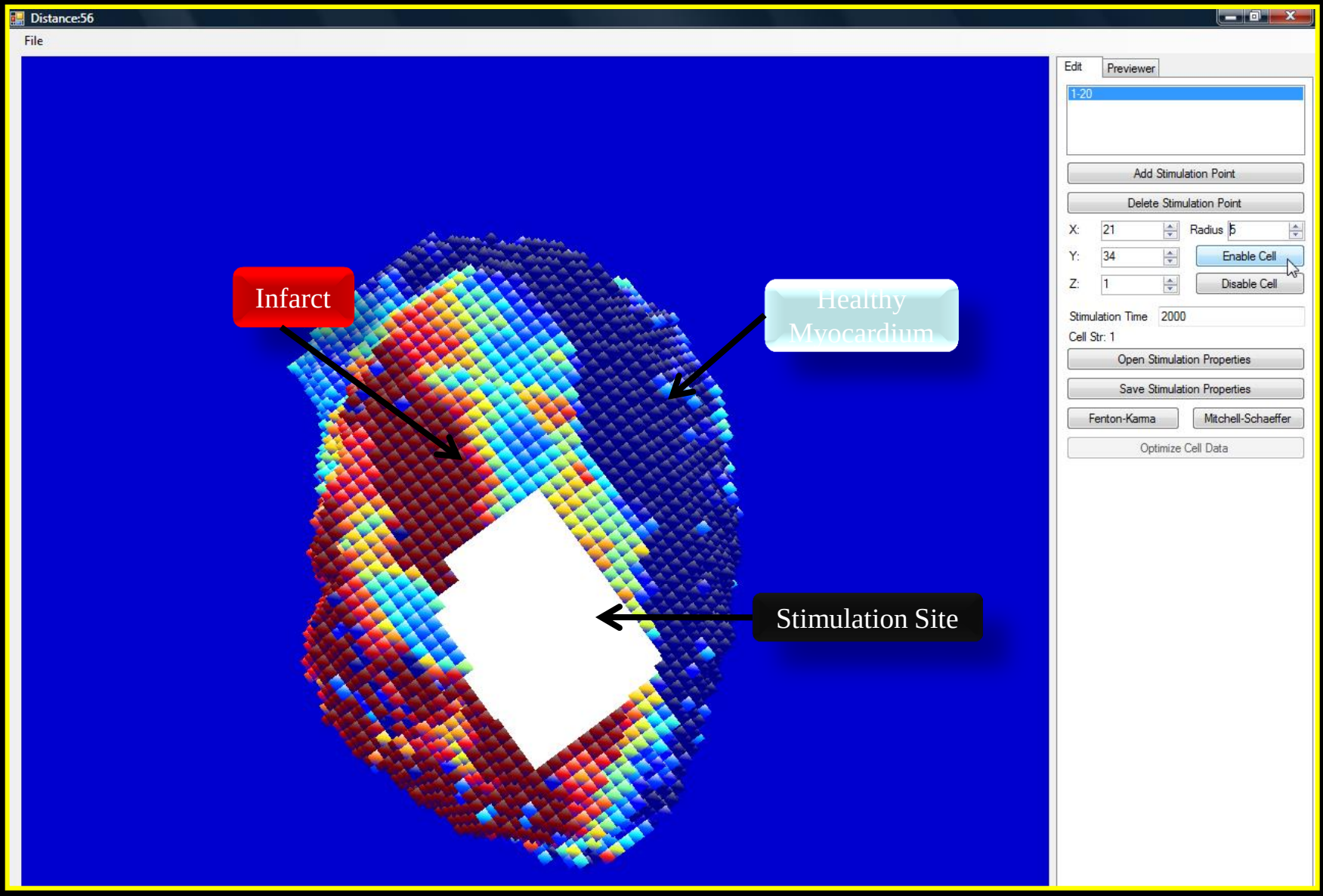
Bello, Goldberger JACC 2005

ROC Curves


100%
75%
50%
25%
0%
Sensitivity
0%
25%
50%
75%
100%
1 - Specificity
Infarct Surface Area
Ejection Fraction

Virtual Electrophysiologic Testing Using Cardiac MRI

- 3D ceMRI to reconstruct LV and define scar
- At sites of normal LV - normal conduction
- At sites of scar - no conduction
- At border zone - slowed conduction
- Model propagation


Distance:56
File
Infarct
Healthy Myocardium
Stimulation Site
Edit
Previewer
1-20
Add Stimulation Point
Delete Stimulation Point
X:
21
Radius
5
Y:
34
Enable Cell
Z:
1
Disable Cell
Stimulation Time
2000
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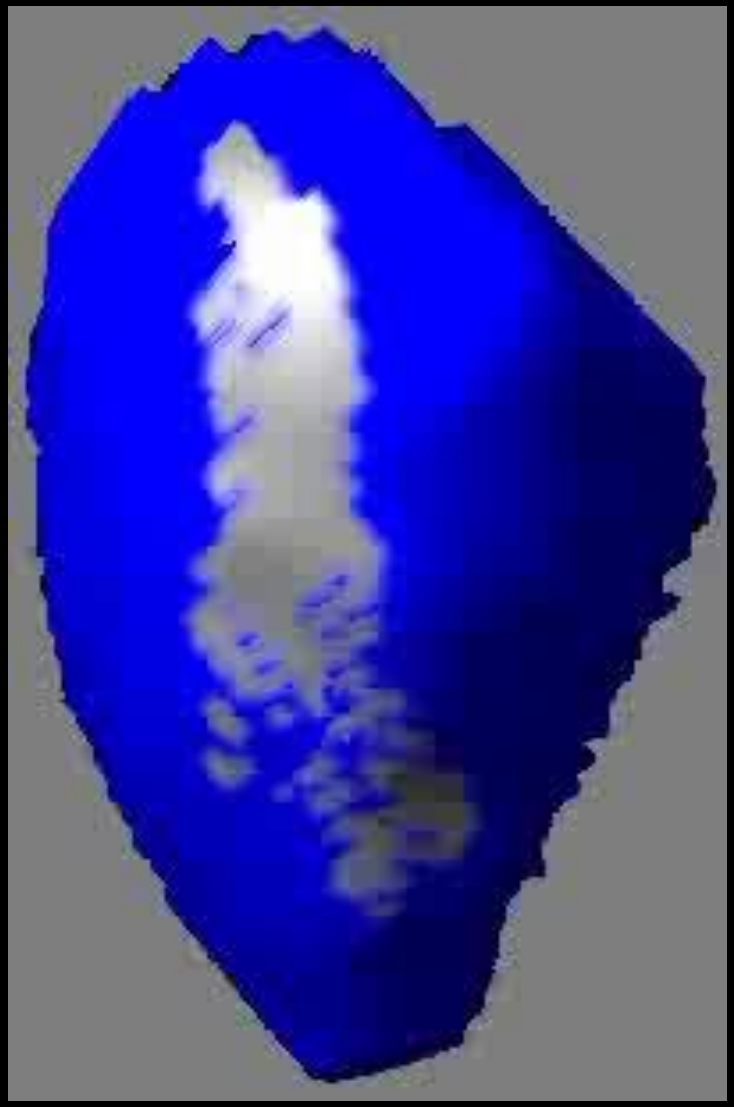
Open Stimulation Properties
Save Stimulation Properties
Fenton-Karma
Mitchell-Schaeffer
Optimize Cell Data

VT Induction Example



Can we identify patients after acute MI who are at high risk for SCD and need early intervention?

- **? Lower risk of arrhythmic SCD than previously thought**
- **EF is NOT a good discriminator**
- **EPS has promising potential**
- **Novel imaging approaches may be complementary**