Prevention of Sudden Cardiac Death in Postinfarct Patients

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Case: M, 74 yr (Shin DC)

C. C.: Acute-onset severe chest pain

Present Illness:

2004. 4. 13 새벽에 acute-onset chest pain으로 종합병원에서 unstable angina로 치료하던 도중 BP하강, dyspnea 심하여져 전원됨

Past Hx: HTN(-), DM(-), smoker (2 p/40yrs)

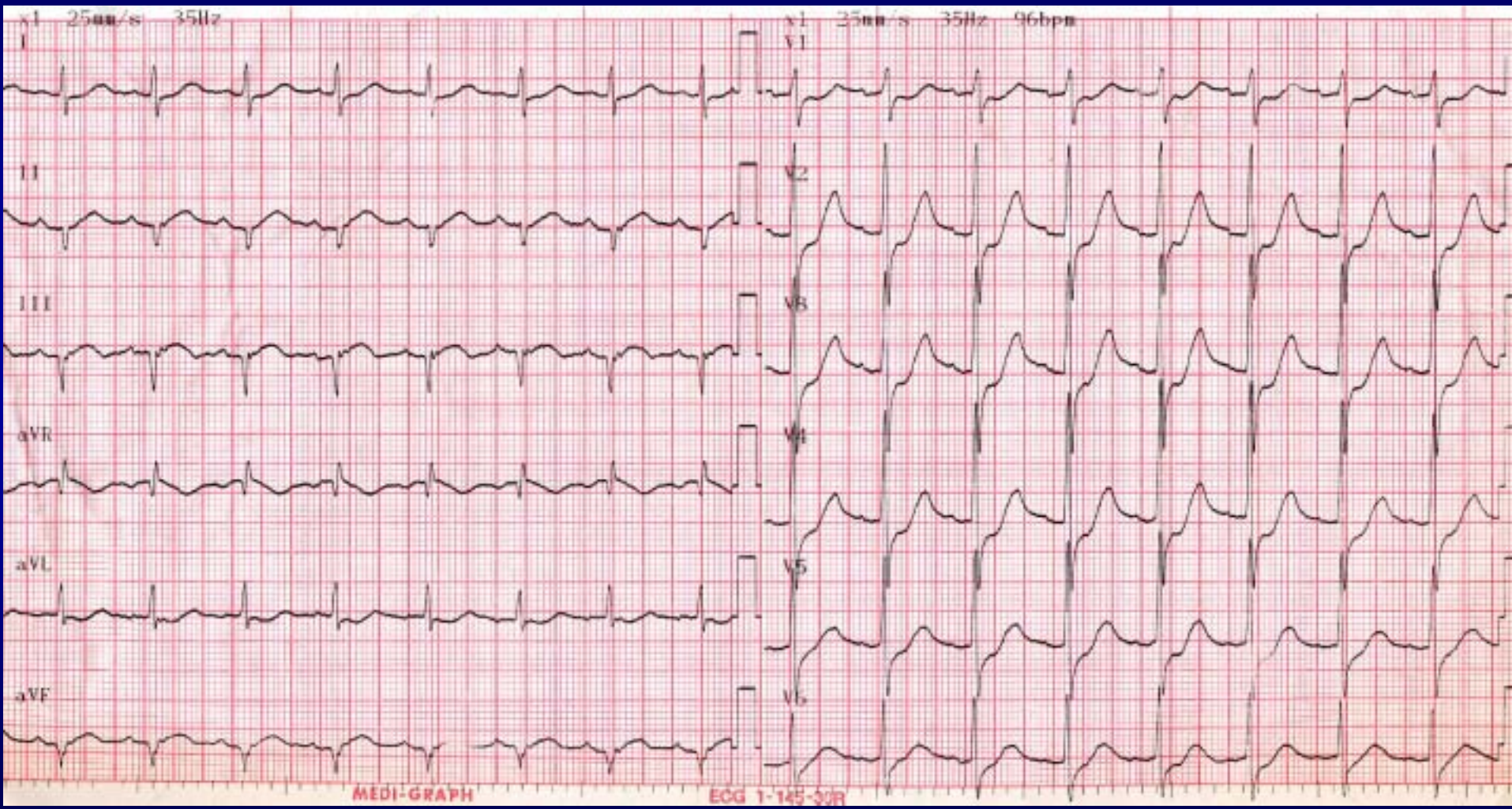
COPD & Bronchiectasis (?)

V/S: 120/80 mmHg, 86 bpm, 36.6 ºC, 16 RR

(with inotropic agents)

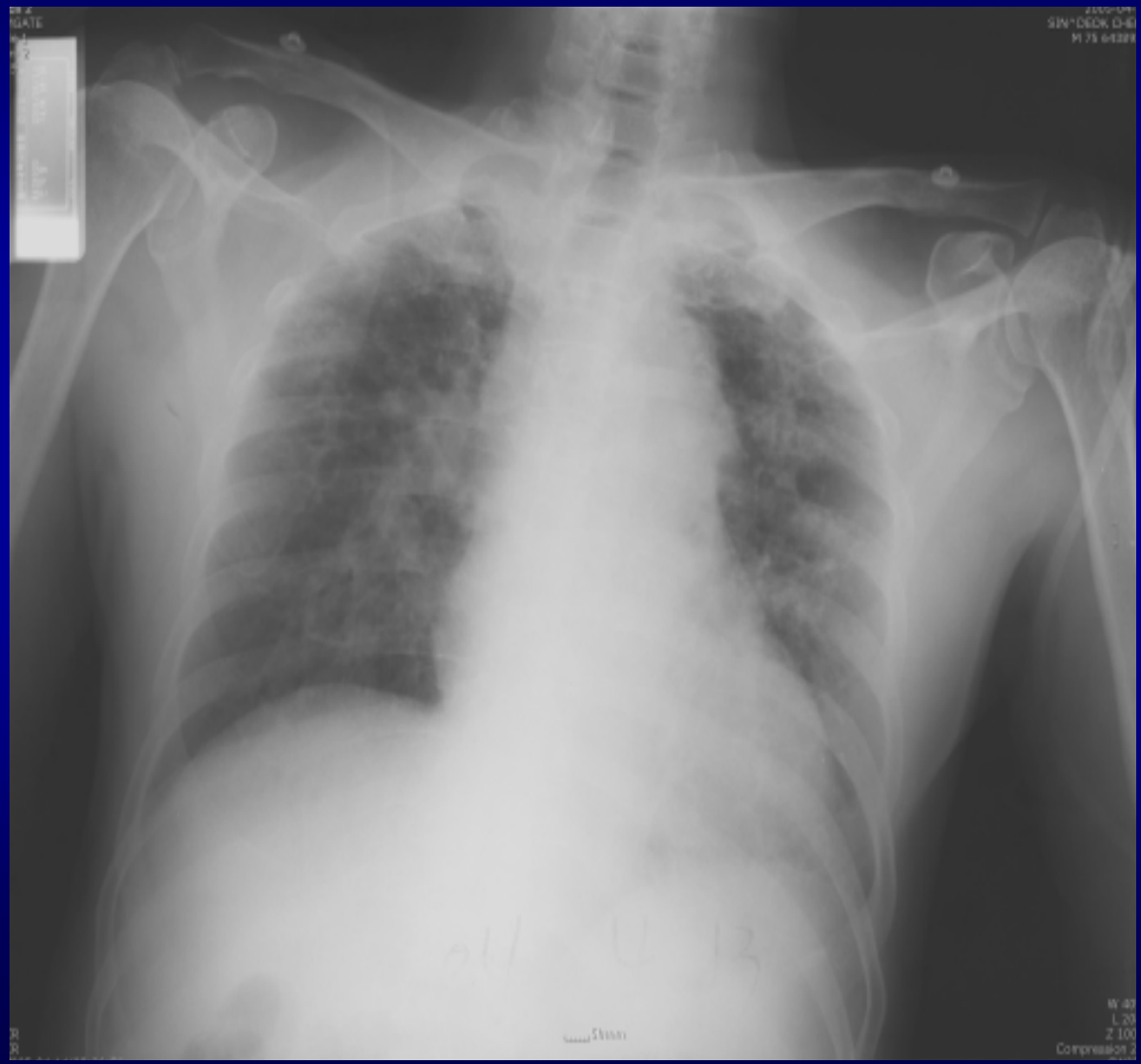
Chest: crackle on both lower lungs

ECG

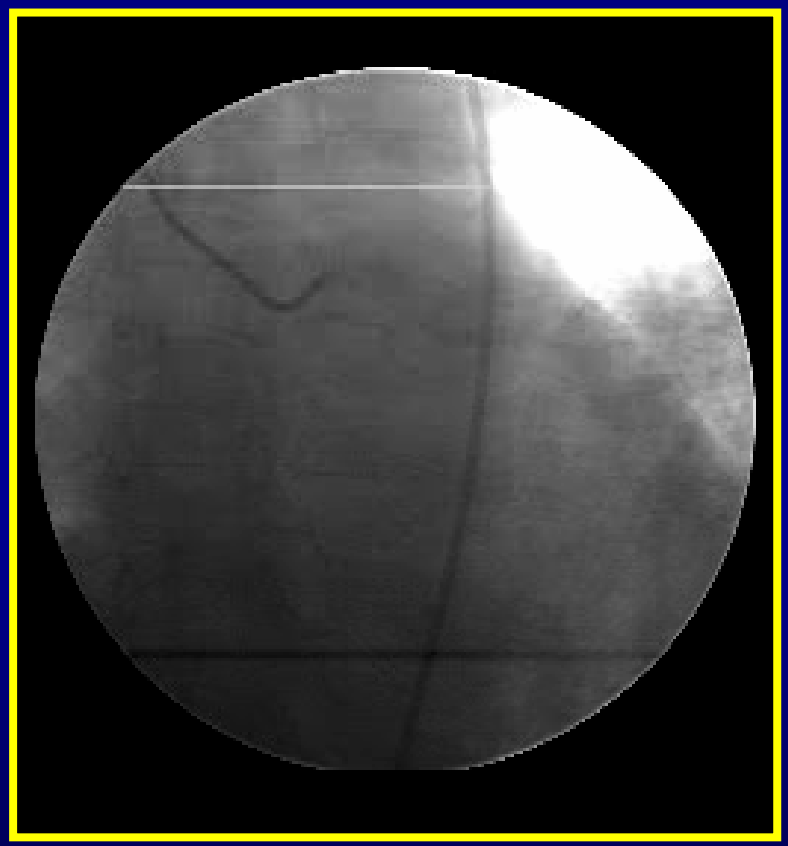


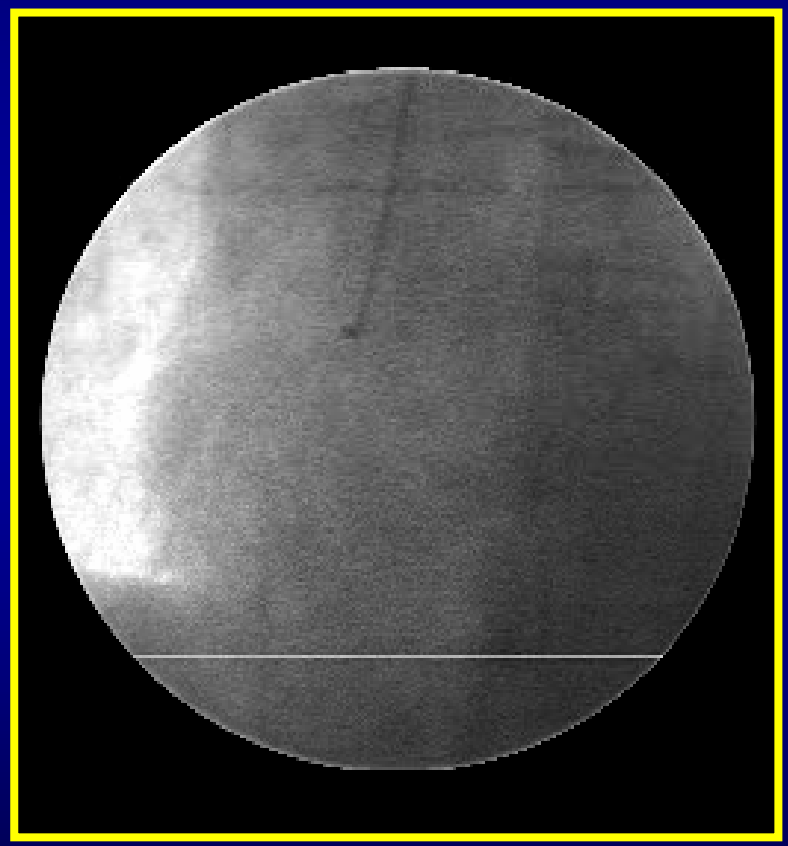
Acute STEMI, inferoposterior wall

Chest X-Ray



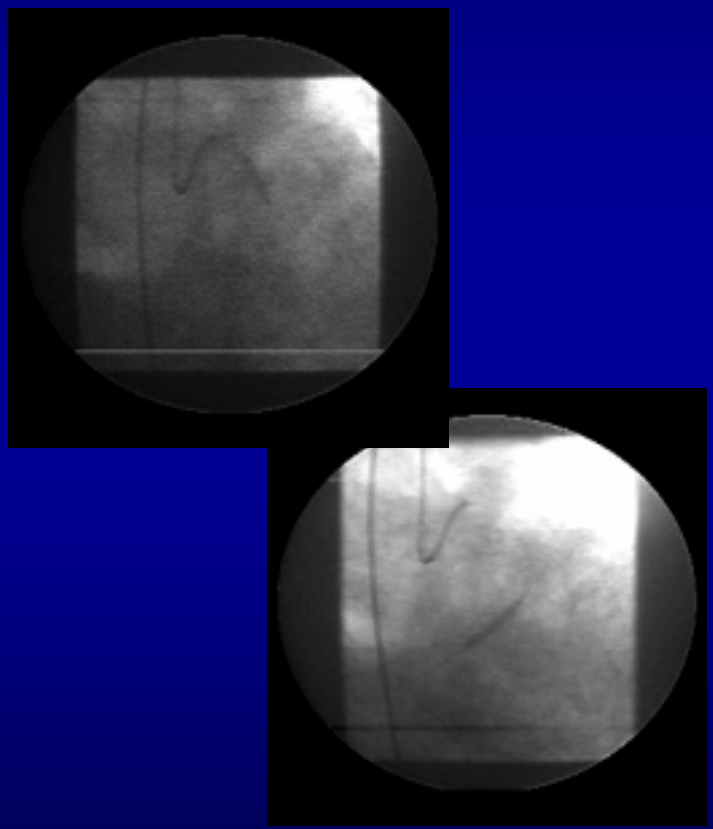
Coronary Angiograms

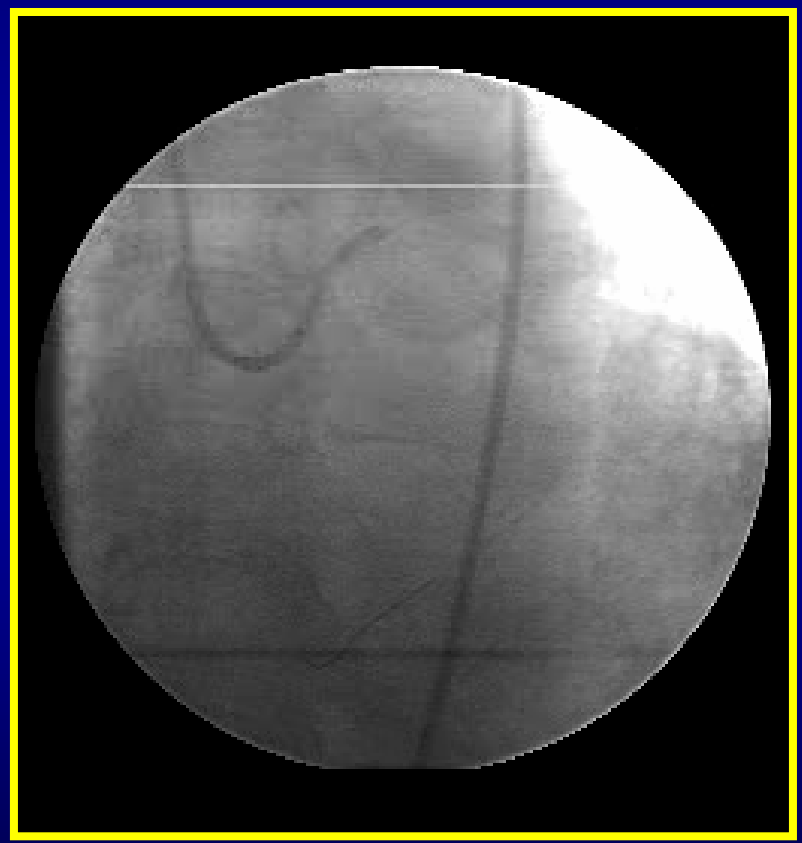




After Primary Stenting

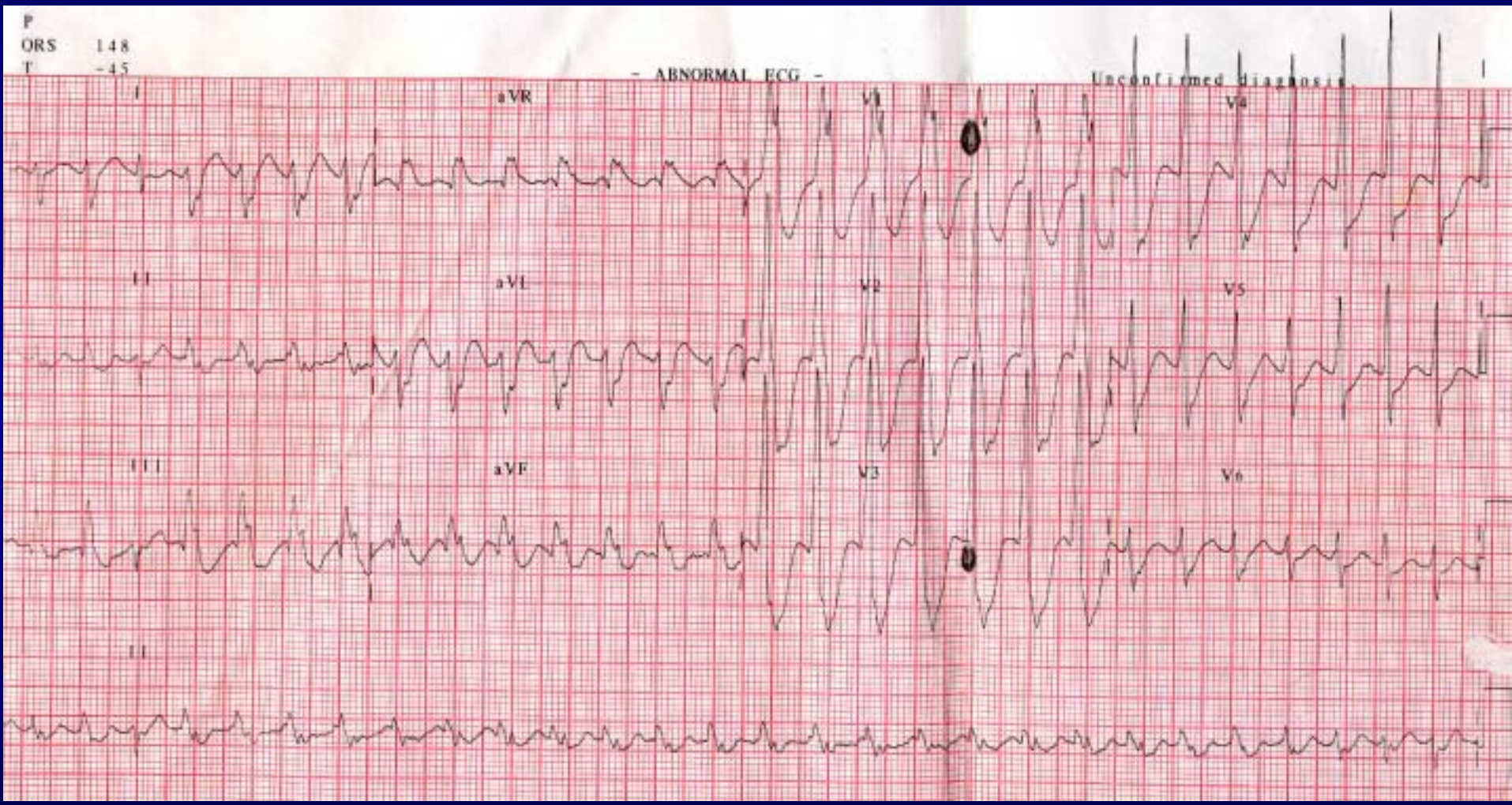
Cypher 3.0x18 mm at p-LCx





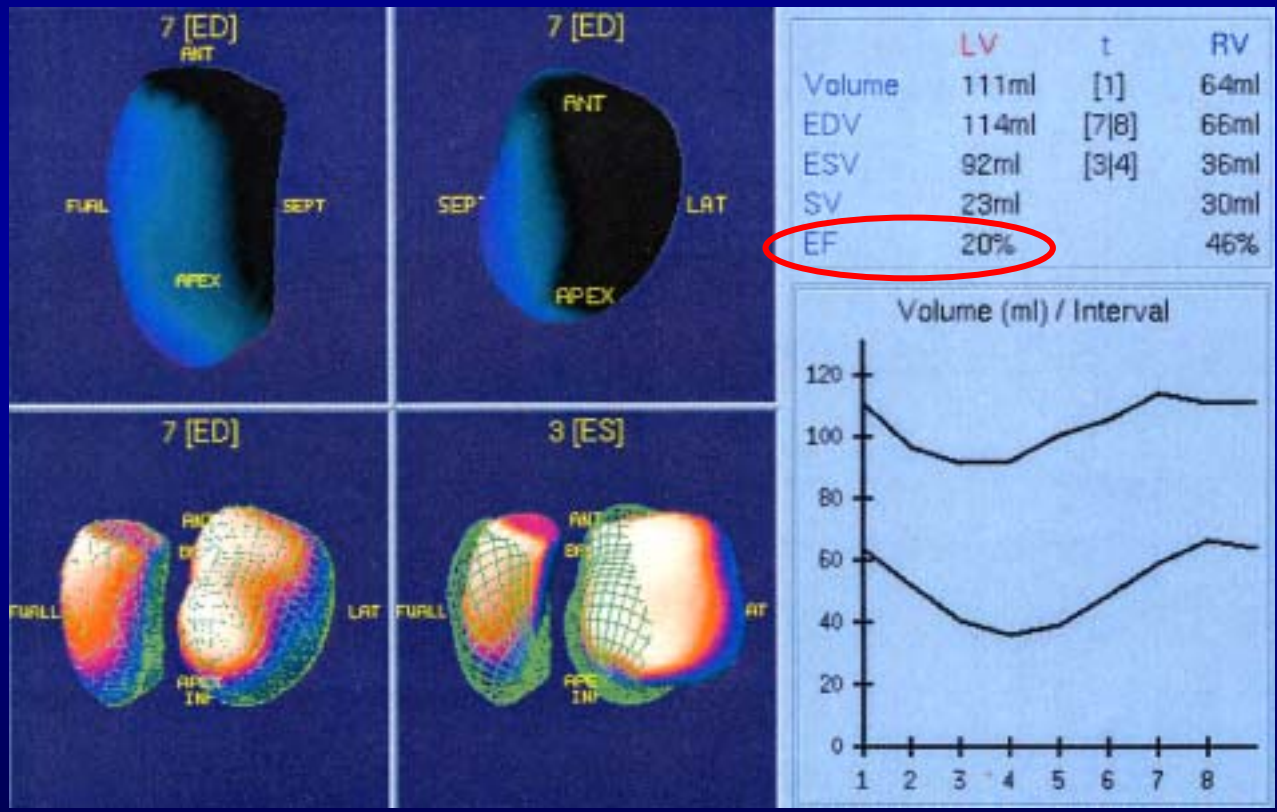
Cypher 2.75x18 mm at d-LCx

2 Days After Stenting



Sustained VT

Gated Blood Pool SPECT After 2 Weeks



Follow-up Without Event

- **The patient is stable for over 1 year**
- Astrix 100 mg qd
  Plavix 75 mg qd
  Tritace 2.5 mg qd
  Lasix 20 mg bid
  Aldactone 25 mg bid
  Dilatrend 6.25 mg qd
  Digoxin 0.125 mg bid
  Cordarone 200 mg qd
  Mevalothin 40 mg qd

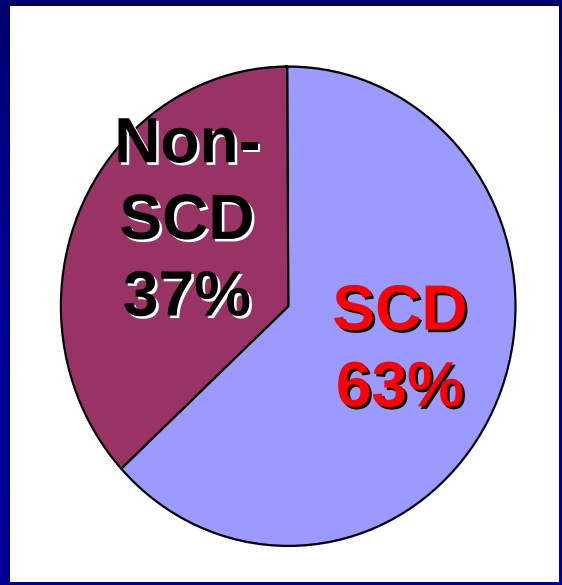
Do I recommend him a prophylactic ICD to prevent sudden cardiac death ?

Cardiac Mortality

- In 1999 US,

  Total cardiac mortality 730,000

  SCD 460,000



- 80% of SCD victims → not survive to discharge

  50% of those who do survive → die within 3 yrs

  ⇒ the importance of primary and secondary prevention of SCD

SCD: Etiology (Substrate and Triggers)

39 (38.2%) → evidence of acute MI or ischemia

Cardiac (n = 102)	
Coronary artery disease	72 (70.6%)
Cardiomyopathy	13 (12.7%)
Primary arrhythmic diseases	13 (12.7%)
Valvular heart diseases	7
Hypertension	3
Noncardiac (n = 58)	
Respiratory failure	24
Sepsis	14
Gastrointestinal diseases	9
Cerebrovascular accidents	7
Drug intoxication	3

김영훈 외
SCD in Korea Multicenter Trial
순환기 2001

Prevention of SCD in CAD

- Pharmacologic treatments

- Primary prevention of SCD in CAD
  - MADIT II and SCD-HeFT
  - DINAMIT
  - ICDs for all patients after MI ?

Medications to Reduce SCD

- **β-blockers** (Lancet 2001;357:1385-90)
- **ACE inhibitors** (JACC 1999;33:598-604)
- **Angiotensin II-receptor blockers** (Circ 2004;110:2618-26)
- **Aldosterone antagonists** (NEJM 1999;341:709)
- **Statins** (Arch Intern Med 2005;165:62-7)

β-Blockers on SCD

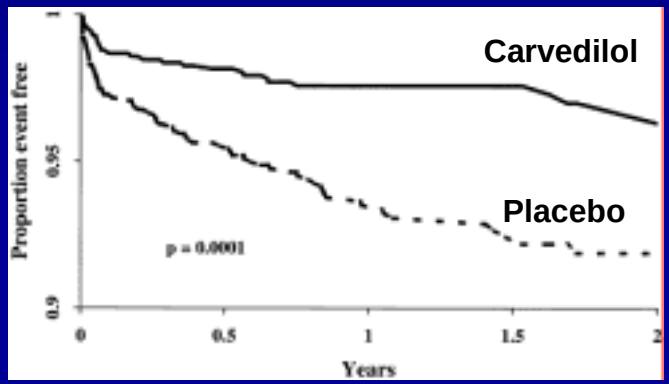
	No. of Deaths/Patients			
	Control	β Blocker	Reduction (%)	p Value
Total mortality				
All long-term studies (n = 24)[1]	1,199/12,431	1,027/13,815	20	< 0.0001
All short-term studies (n = 28)	586/13,721	513/13,815	13	< 0.02
Sudden deaths				
All studies (n = 16)	480/9,441	333/9,887	34	< 0.0001

[1]2-Year follow-up.

Hjalmarson A, AJC 1997;80:35J-39J

Carvedilol on SCD after AMI

CAPRICORN trial (Carvedilol Post-Infarct Survival Control in Left Ventricular Dysfunction)



	Placebo	Carvedilol	HR	*p*
Any VAs	7.0%	2.7%	0.37	<0.0001
VT or VF	3.9%	0.9%	0.24	<0.0001

JACC 2005;45:525-30

Spironolactone on SCD: RALES trial

CHF & EF ≤35%

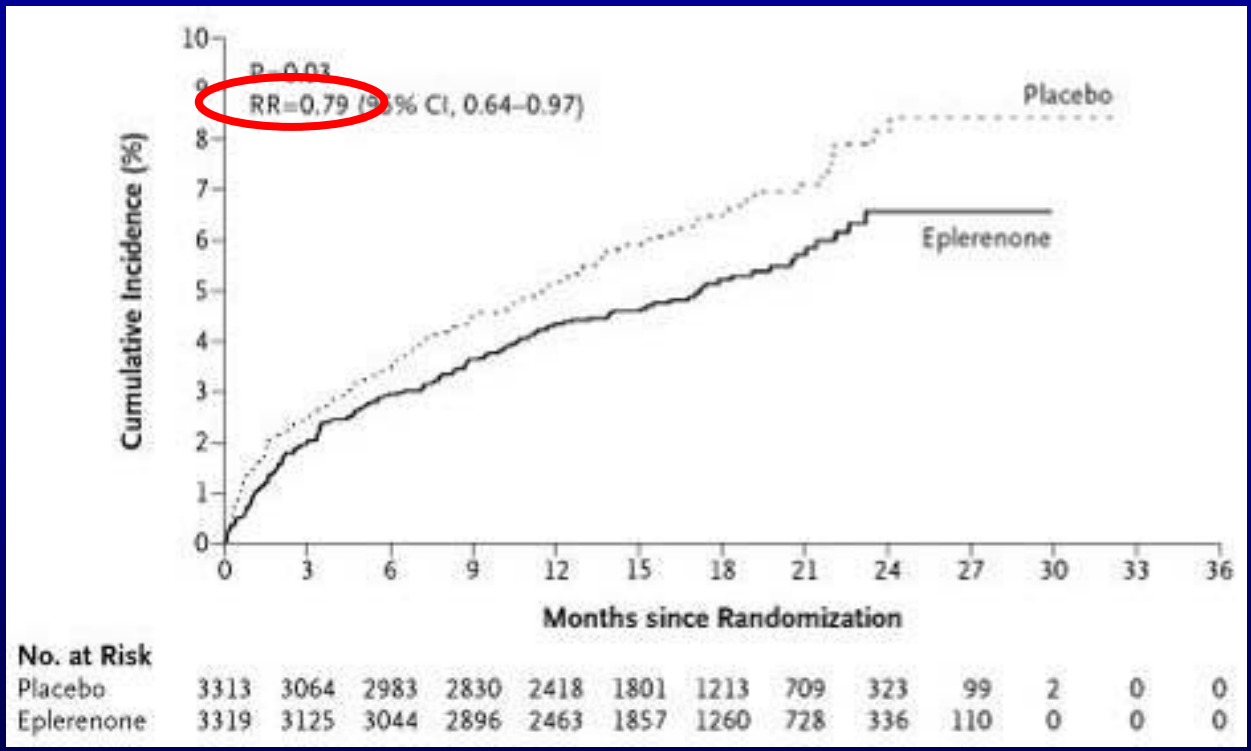
Variable	Placebo Group (N=841)	Spironolactone Group (N=822)	Relative Risk (95% CI)*	P Value
	no. of patients			
Cause of death				
Cardiac causes	314	226	0.69 (0.58–0.82)	<0.001
Progression of heart failure†	189	127	0.64 (0.51–0.80)	<0.001
Sudden death‡	110	82	0.71 (0.54–0.95)	0.02
Myocardial infarction	15	17		
Other cardiovascular causes	13	12		
Stroke	11	8		
Noncardiovascular causes	41	29		
Unknown	7	9		
Total	386	284	0.70 (0.60–0.82)	<0.001

NEJM 1999;341:709-17

Eplerenone (selective aldosterone blocker) on SCD

Ephesus trial (Eplerenone Post–Acute Myocardial Infarction Heart Failure Efficacy and Survival Study)

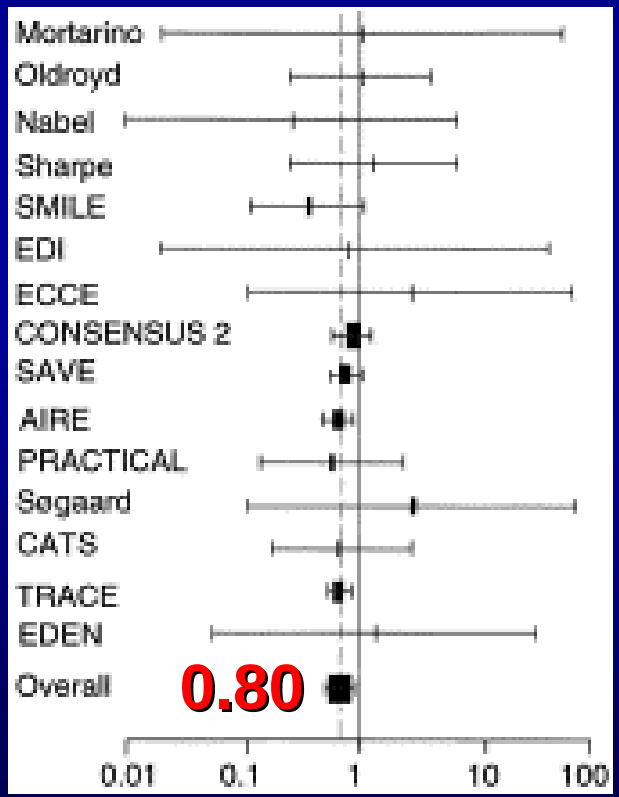
Eplerenone vs. placebo in MI survivor (3-14 days after AMI, EF ≤40%, CHF)



Pitt B, NEJM 2003;348:1309-21

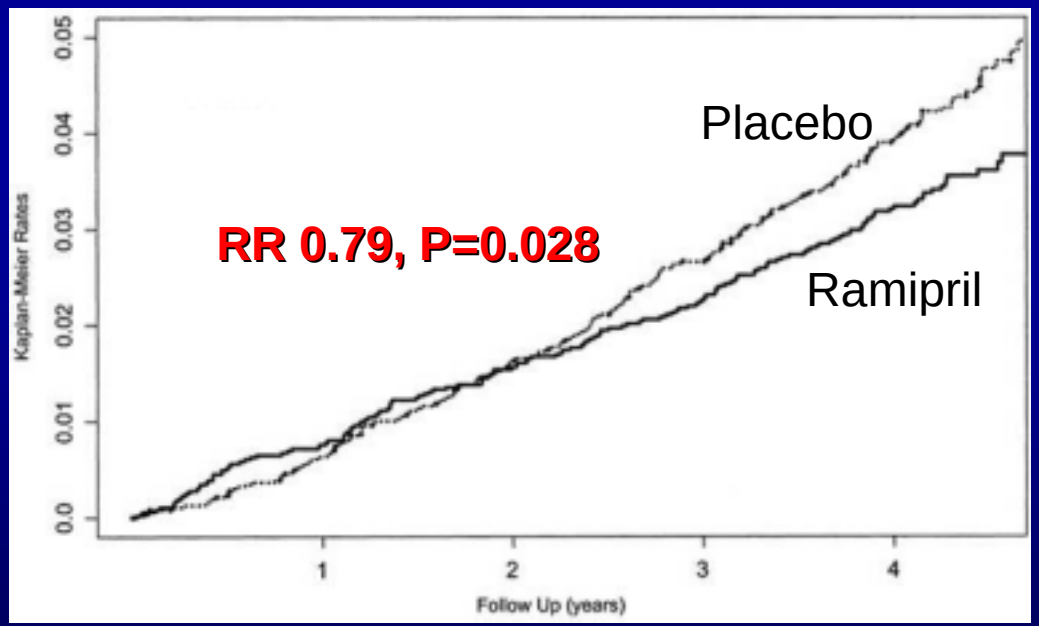
ACE Inhibitors on SCD after AMI

CHF
Depressed LV function



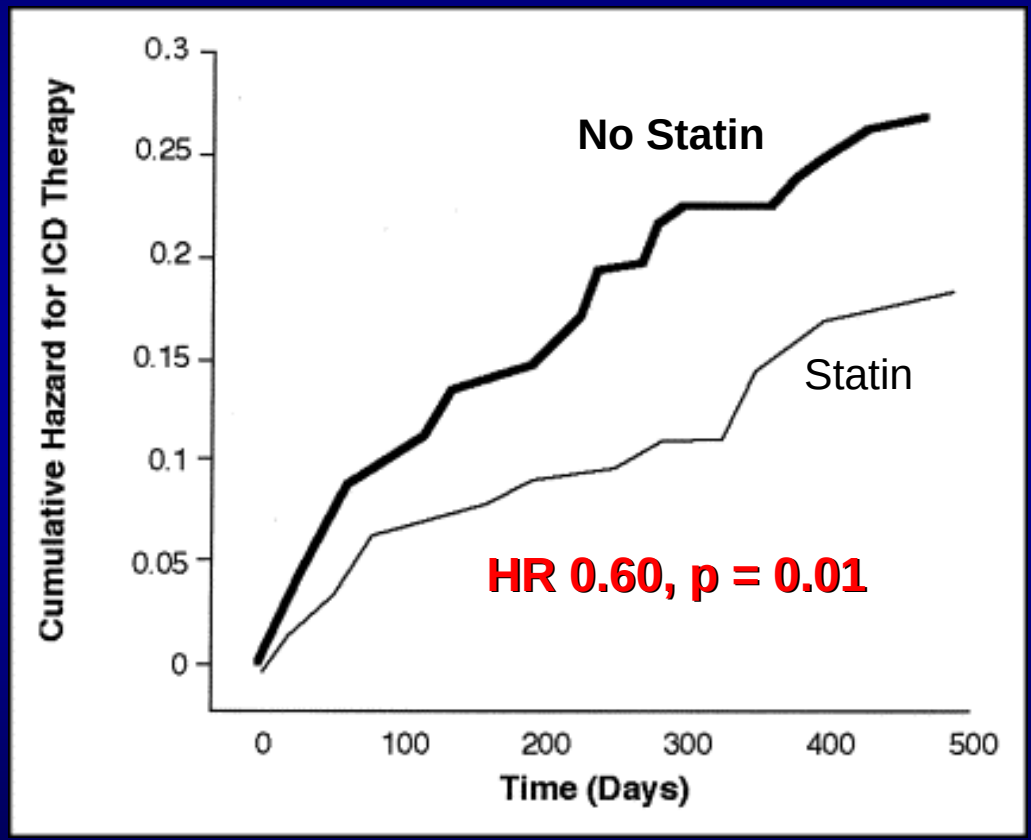
JACC 1999;33:598-604

Without CHF or overt LV dysfunction (HOPE)



Circulation 2004;110:1413-7

Statins on Ventricular Arrhythmias



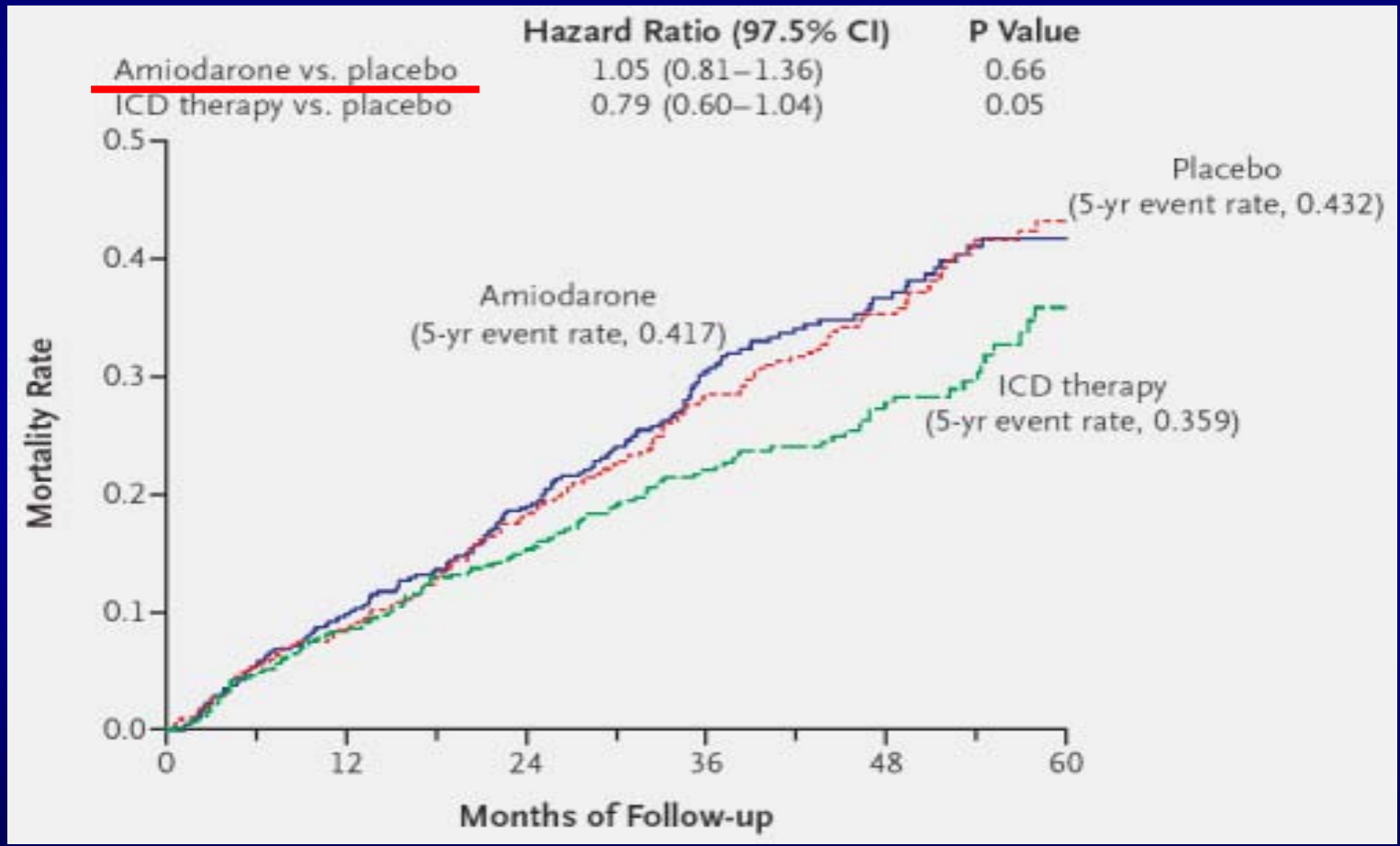
N = 281 pts with CAD after ICD

Mean f/u = 10 mo

Chiu, AJC 2005;95:490-1

Amiodarone on SCD in Ischemic CHF

SCD-HeFT (Sudden Cardiac Death in Heart Failure Trial)



NEJM 2005;352:225-37

Prevention of SCD in CAD

- Pharmacologic treatments

- Primary prevention of SCD in CAD
  - MADIT II and SCD-HeFT
  - DINAMIT
  - ICDs for all patients after MI ?

MADIT II (Multicenter Automatic Defibrillator Implantation Trial)

Inclusion Criteria

- Pts with a prior MI 1 month or more before entry
- EF <30%
- No requirement of NSVT or EPS

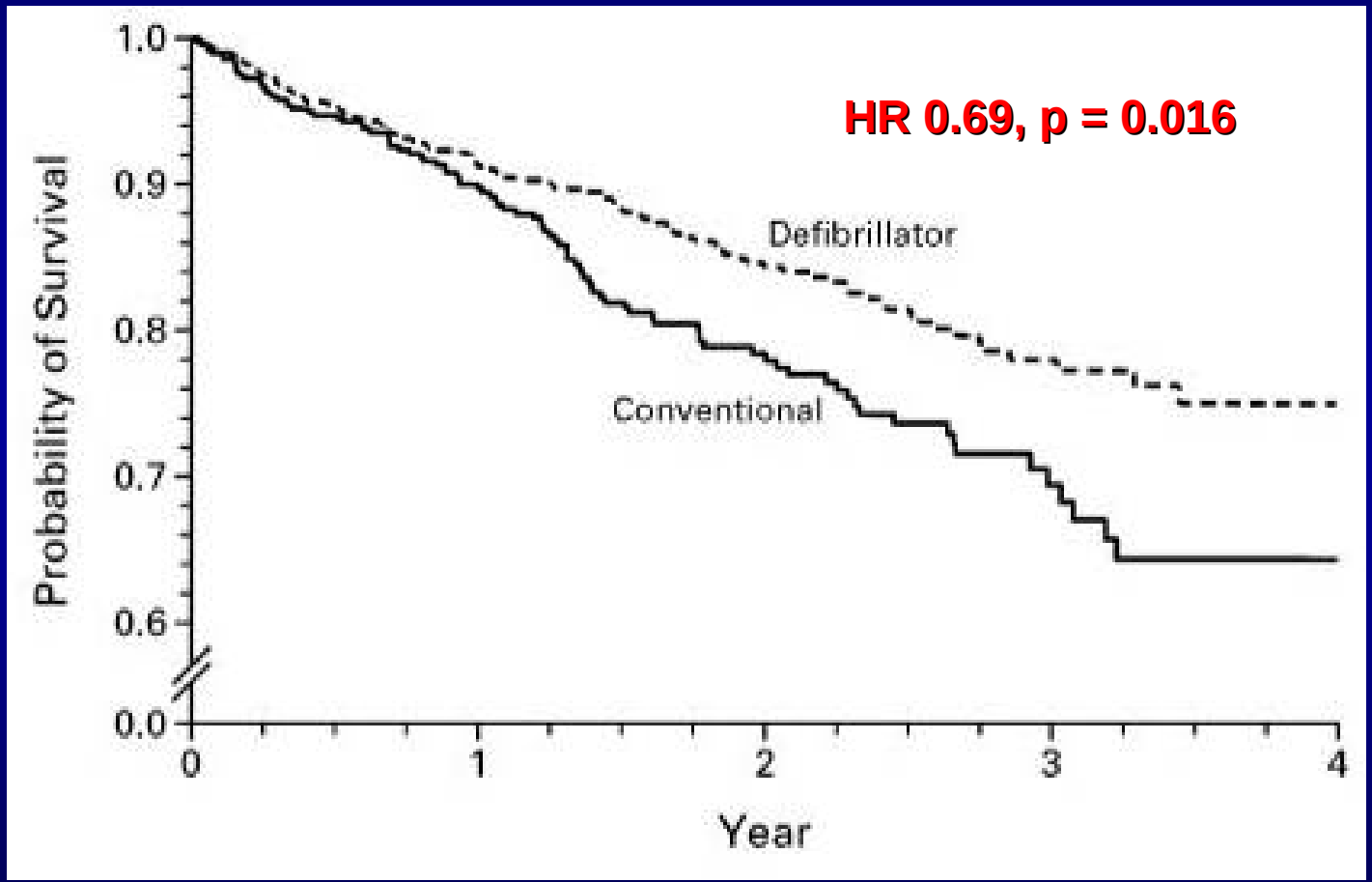
Moss, NEJM 2002;346:877-83

Characteristic	Defibrillator Group (N=742)	Conventional-Therapy Group (N=490)
Age (yr)	64±10	65±10
Male sex (%)	84	85
NYHA functional class (%)†		
I	35	39
II	35	34
III	25	23
IV	5	4
Treatment for hypertension (%)	53	53
Diabetes (%)	33	38
Current or former cigarette smoker (%)	80	82
Coronary bypass surgery (%)	58	56
Coronary angioplasty (%)	45	42
Interval of >6 mo between most recent myocardial infarction and enrollment (%)	88	87
Cardiac findings at enrollment (%)		
Blood urea nitrogen >25 mg/dl (8.92 mmol/liter)	29	32
Atrial fibrillation	9	8
QRS interval ≥0.12 sec	50	51
Nonspecific conduction defect	22	26
Right bundle-branch block	9	7
Left bundle-branch block	19	18
Left ventricular ejection fraction	23±5	23±6
Medications at last contact (%)‡		
Amiodarone	13	10
Angiotensin-converting–enzyme inhibitors	68	72
Beta-blockers	70	70
Calcium-channel blockers	9	9
Class I antiarrhythmic agents	3	2
Digitalis	57	57
Diuretics	72	81
Lipid-lowering statin drugs	67	64

MADIT II:
Patients Characteristics

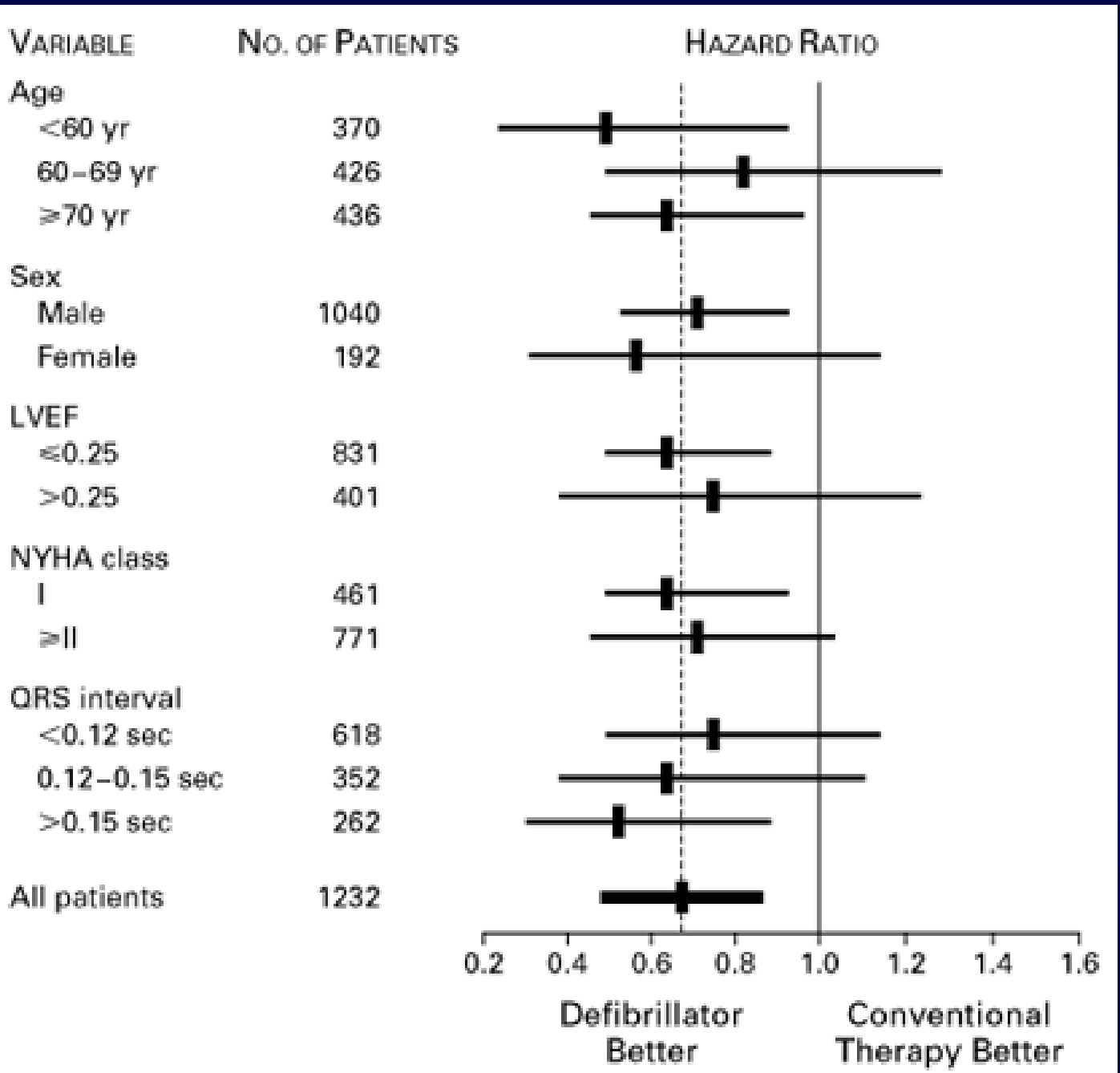
Moss, NEJM 2002;346:877-83

MADIT II: All-cause Mortality



Moss, NEJM 2002;346:877-83

MADIT II: Subgroup Analyses



Moss, NEJM 2002;346:877-83

SCD-HeFT (Sudden Cardiac Death in Heart Failure Trial)

DCM ± CAD and CHF

↓

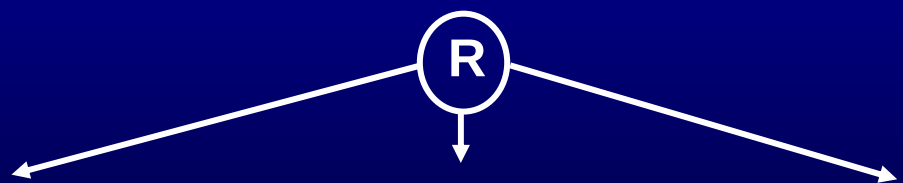
EF ≤ 35%

↓

NYHA Class II or III

↓

6 minute walk, Holter



Placebo Amiodarone ICD

Bardy, NEJM 2005;352:225-37

SCD-HeFT

Baseline Enrollment Characteristics

• CHF duration	24.5 mo (8.1, 59.4)
• LV EF	25.0 (20.0, 30.0)
• NYHA II, III	70%, 30%
• Ischemic, non-ischemic	52%, 48%
• 6 minute walk	1130 ft (840, 1360)
• Diabetes	30%

Bardy, NEJM 2005;352:225-37

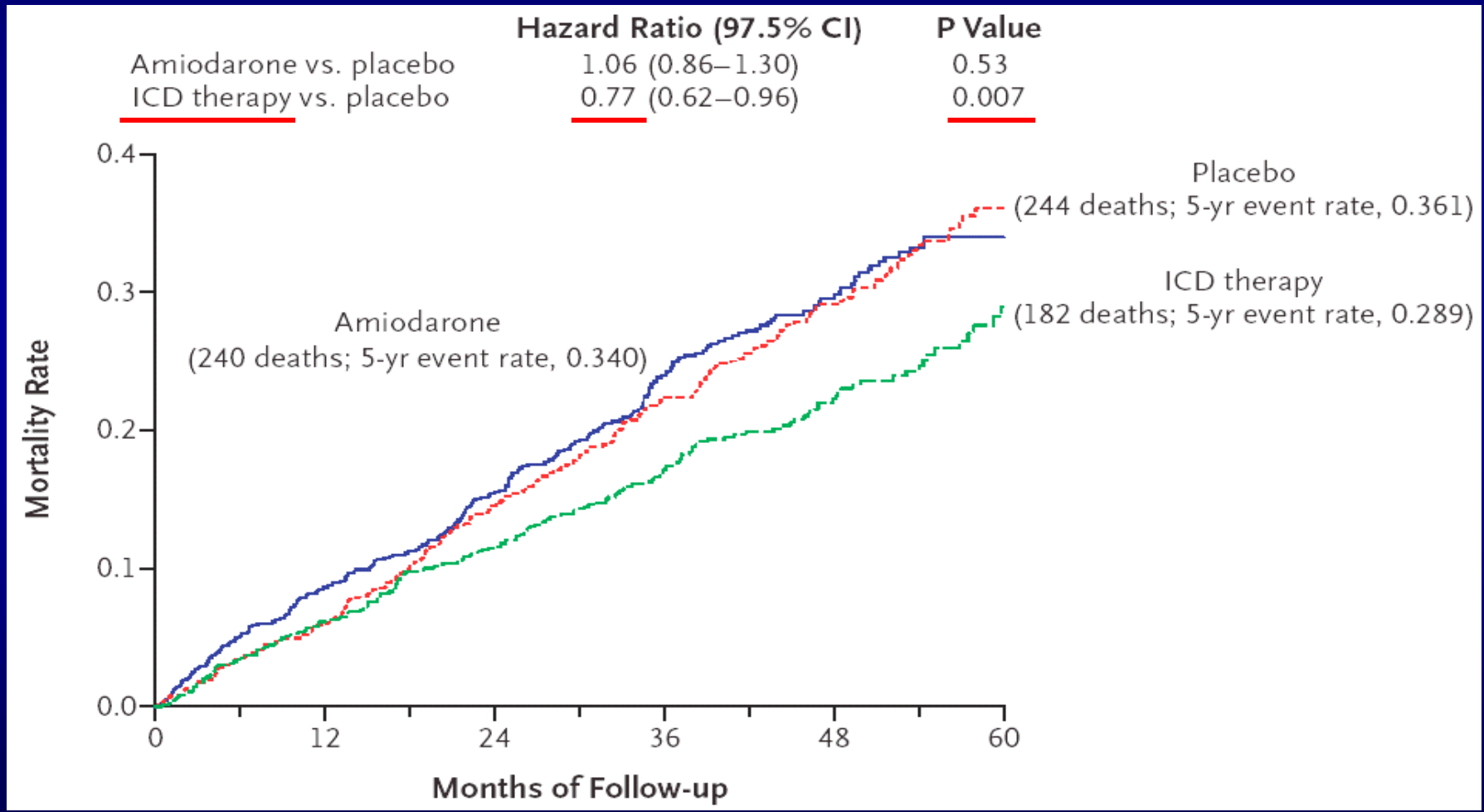
SCD-HeFT

Background Medications

	Baseline	Last F/U
ACE I	85%	72%
ACE I or ARB	96%	87%
β-Blockers	69%	78%
Spironolactone	19%	31%
Loop diuretics	82%	80%
Aspirin	56%	55%
Statin	38%	47%

Bardy, NEJM 2005;352:225-37

SCD-HeFT: All-cause Mortality



Bardy, NEJM 2005;352:225-37

SCD-HeFT: Primary Conclusions

1. In class II or III CHF pts with EF ≤ 35% on good background drug therapy, the mortality rate for placebo-controlled patients is 7.2% per year over 5 years
2. Simple, single lead, shock-only ICDs decrease mortality by 23%
3. Amiodarone, when used as a primary preventative agent, does not improve survival

Bardy, NEJM 2005;352:225-37

Should all patients after AMI with depressed LV function receive ICDs ?

DINAMIT (Defibrillator in Acute Myocardial Infarction Trial)

Inclusion Criteria

- Recent MI (6 ~ 40 days)
- EF <35% & abnormal HRV (SDNN ≤ 70 ms or 24-hr RR ≤ 750 ms)
- Age 18 ~ 80 yrs

Hohnloser SH, NEJM 2004;351:2481-8

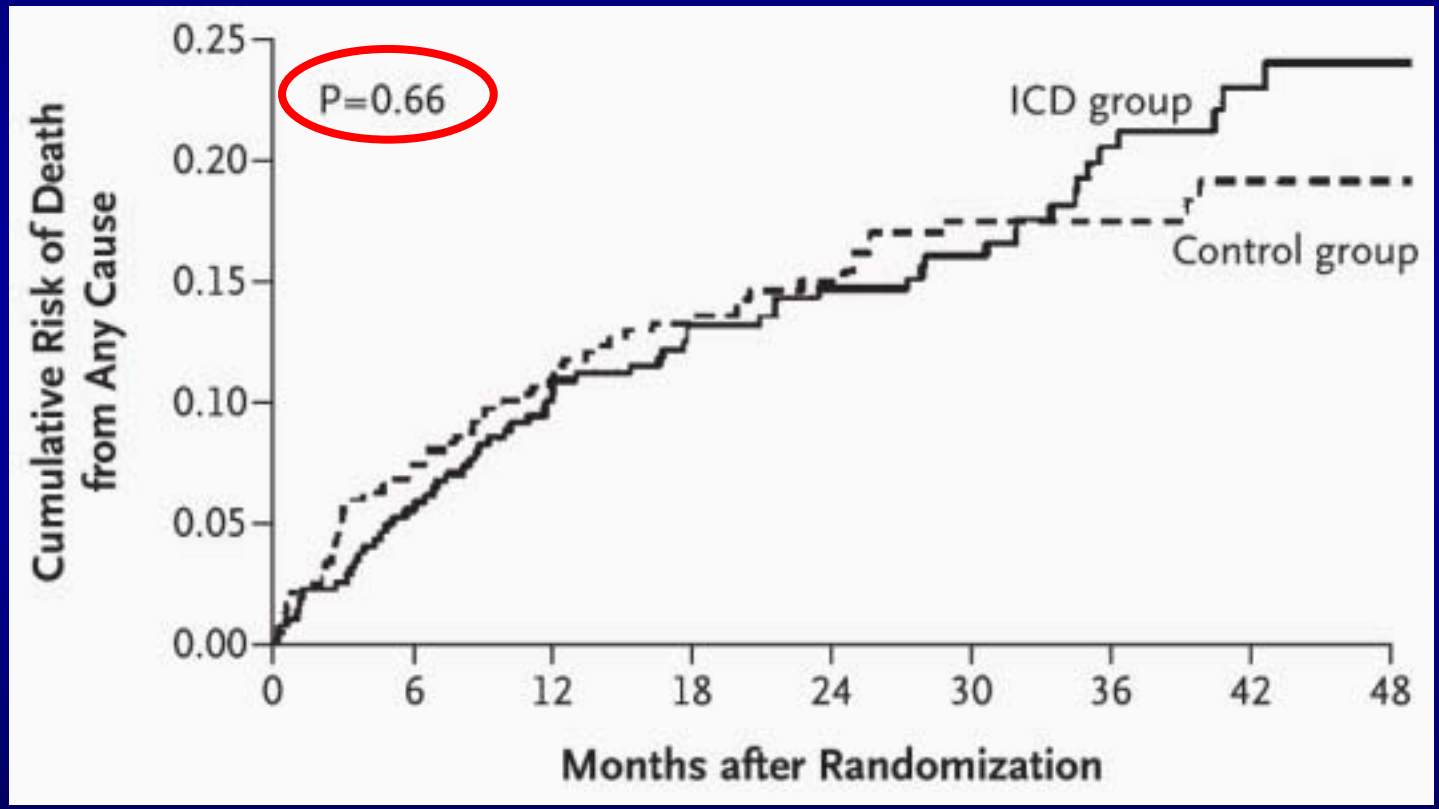
DINAMIT

Key Baseline Criteria

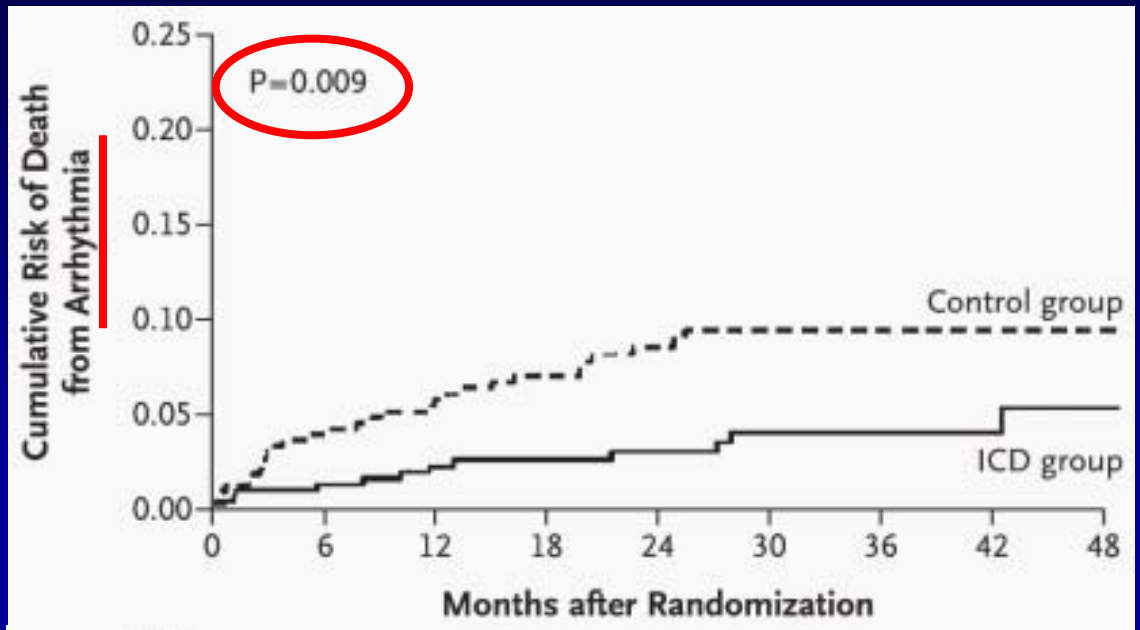
	ICD	Control
LVEF	28%	28%
SDNN	61 ms	61 ms
24-hr RR	745 ms	747 ms

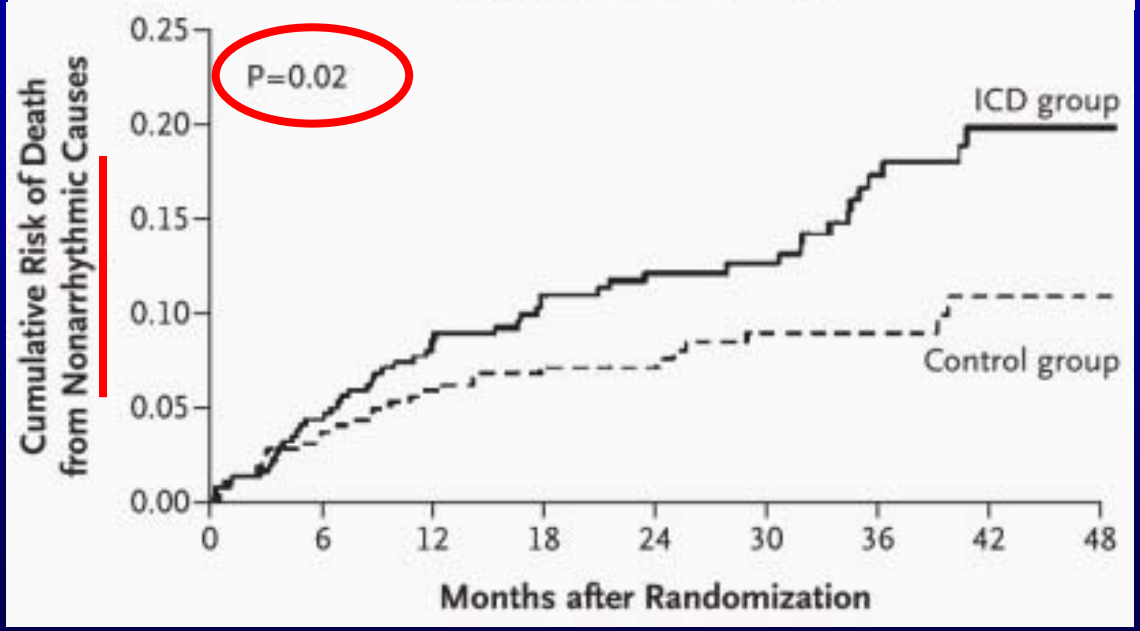
Hohnloser SH, NEJM 2004;351:2481-8

DINAMIT: All-cause Mortality



Hohnloser SH, NEJM 2004;351:2481-8





DINAMIT:
Arrhythmic and Nonarrhythmic Death

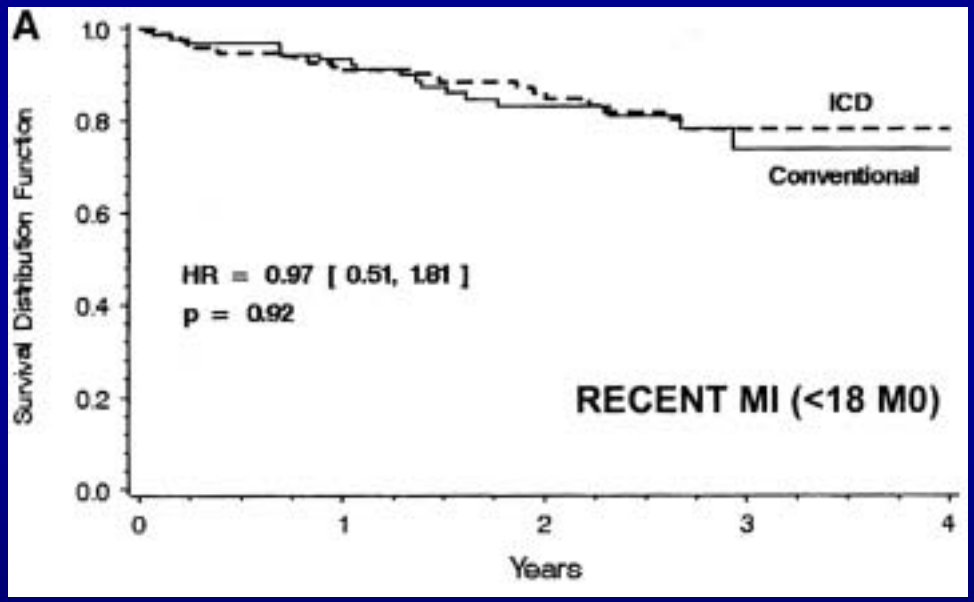
Hohnloser SH
NEJM 2004;351:2481-8

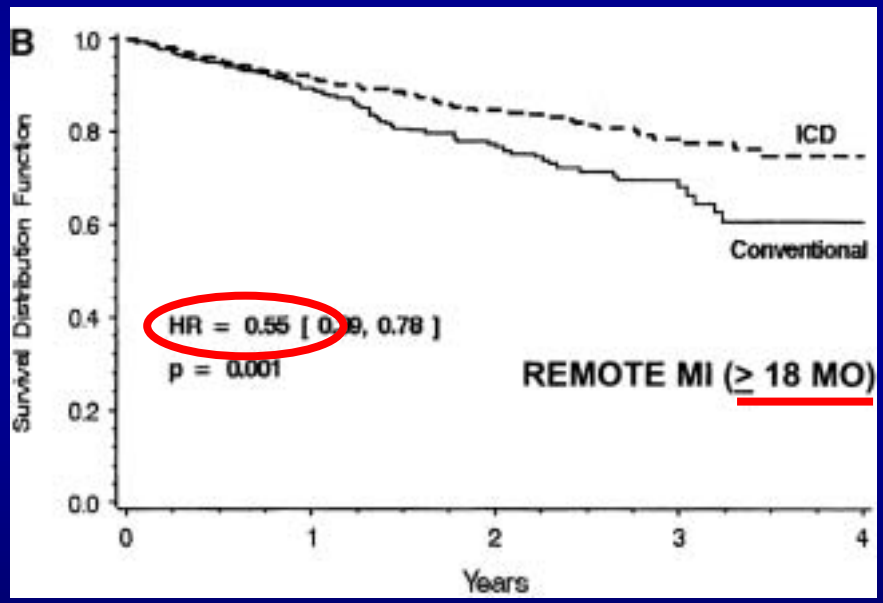
Differences on 1º Prevention Trials

	MADIT II	SCD-HeFT	DINAMIT
Patients	1,232	2,521	674
Age	64	60	61
Time from most recent MI	6.5 yr	24.4 mo	18 day
LVEF	23%	25%	28%
NYHA III	25%	30%	40%
Follow-up	20 mo	45.5 mo	30 mo

MADIT II:

Survival in pts with recent MI vs. remote MI





Wilber, Circulation 2004;109:1082-4

MADIT II:

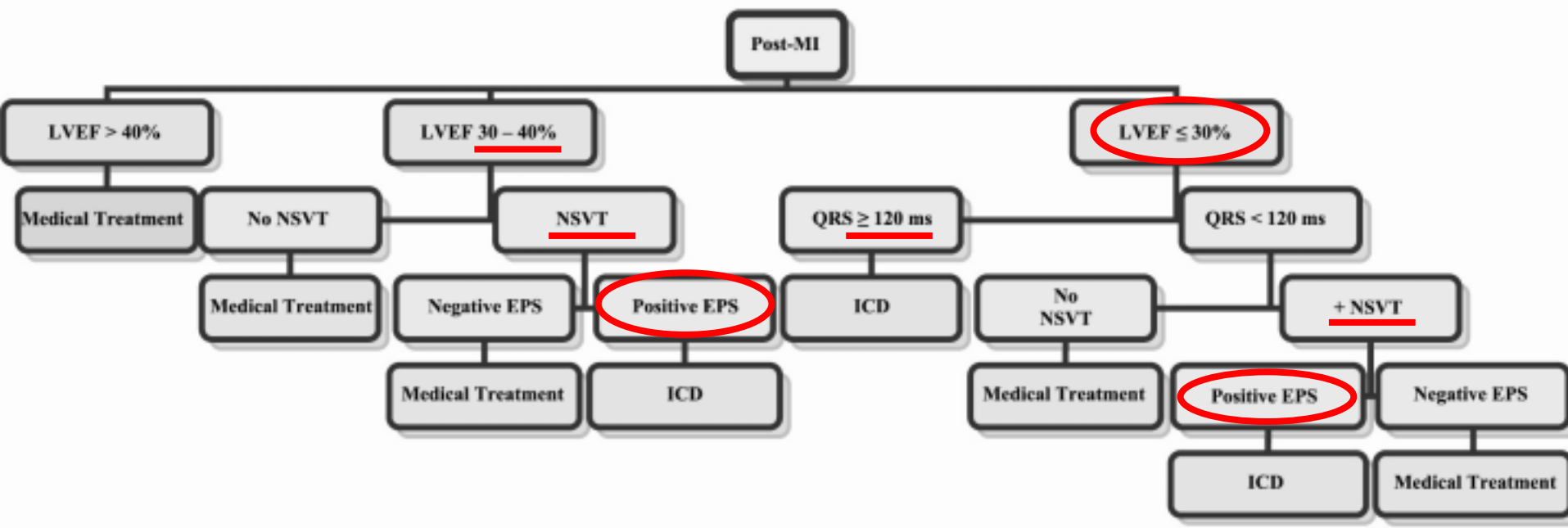
Effect of the ICD by Elapsed Time From MI

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

Wilber, Circulation 2004;109:1082-4

DINAMIT & MADIT II fail to demonstrate survival benefit during 18 mo after MI

Triaging Patients for 1º Preventive ICD Therapy



Insurance Coverage

이전의 심근경색환자, 관상동맥질환자 또는 좌심기능부전환자 중에서 아래의 세가지 모두에 해당되는 경우

(1) 30% 이하의 low EF

(2) 비지속성 심실빈맥

(3) 임상전기생리학적검사(EPS)상 심실세동이나 지속성 심실빈맥이 유발되는 경우

All DINAMIT Patients

- had an indicator of autonomic dysfunction (abnormal heart-rate variability, elevated HR at rest) → possibility that presence of marker of autonomic dysfunction identified a patient cohort at high risk for death due to progressive HF
- Further studies to determine whether pts with impaired autonomic function late after MI do not obtain a survival benefit from ICD therapy

MADIT II Criteria

- Only 50% of pts with MADIT II indications for ICD tx received tx for VTAs within 3 yrs after implantation
- As compared with 74% of pts with a prior MI who received an ICD for 2º prevention of sudden death

Better Risk-stratification Techniques

- To identify the pts at high risk for sudden death who are most likely to benefit from prophylactic ICD use. (for cost-effective use of ICD tx)
- Prophylactic ICD tx needs to be individualized according to pt's risk of sudden cardiac death and the competing risk of death from other causes