# SECONDARY PREVENTION of Sudden Death: in which patients ?

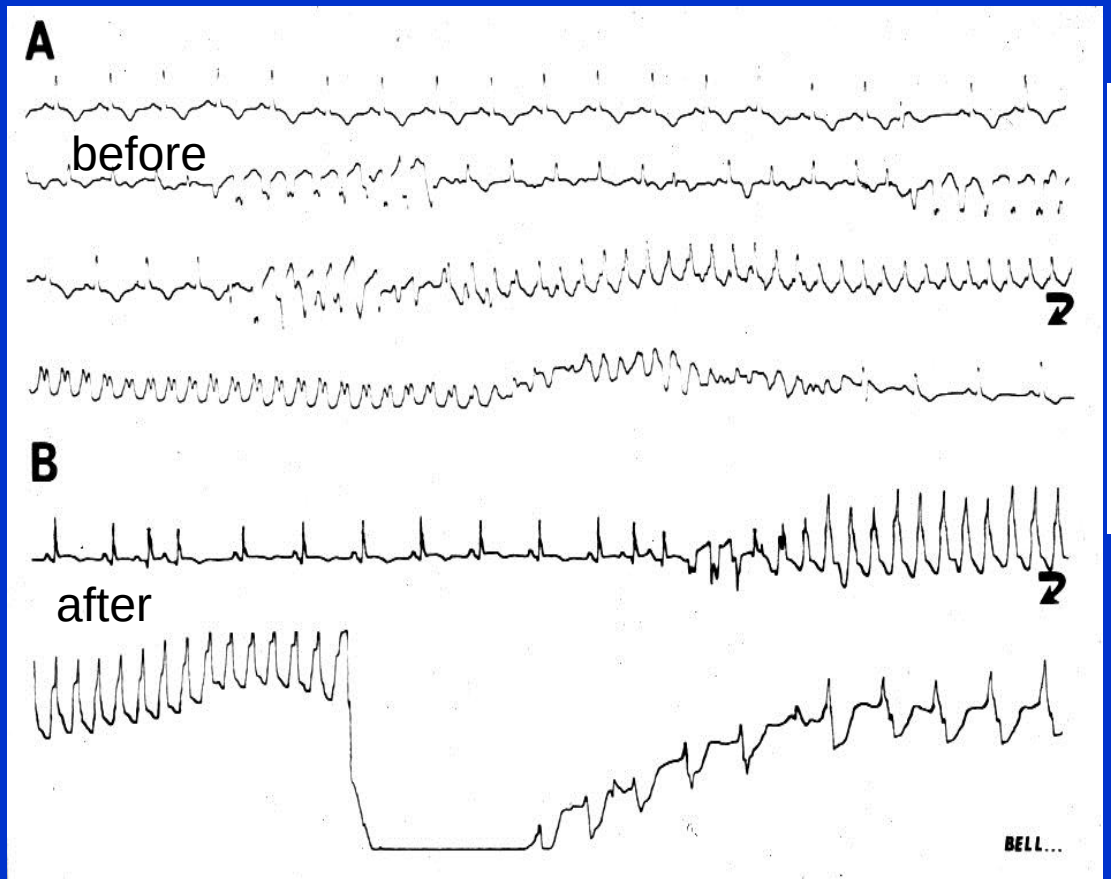
**Jean François Leclercq**

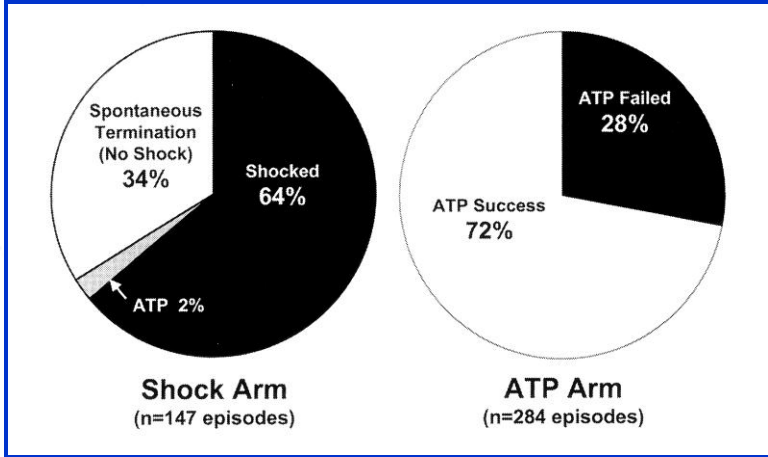
**Department of Rythmology**

**Private Hospital of Parly 2 - Le Chesnay F**

# Why an AID is effective ?

- Because it stoppes a VT very quickly, almost always before its transformation into VF.




Even better with ATP before Shock delivering

# AID indications in France

- **Class I:**

- **Circulatory arrest by VF or VT**, without acute or reversible cause *proof level* **A**
- Spontaneous symptomatic **sustained VT** with heart disease impairing cardiac function *proof level* **B**
- Nonsustained VT with old MI, LVEF<35% and **VT/VF inducible** *proof level* **A**

JF Leclercq & S Lévy Arch Mal Cœur 2000;93:1227

# AID indications in France

- **Class II:**
  - **Genetic disease** with high risk of SD and no other efficient therapy *proof level* **B**
  - **Syncope** without cause and **VT/VF inducible** *proof level* **C**
  - Bad tolerated **sustained VT** in waiting list for heart transplant *proof level* **C**

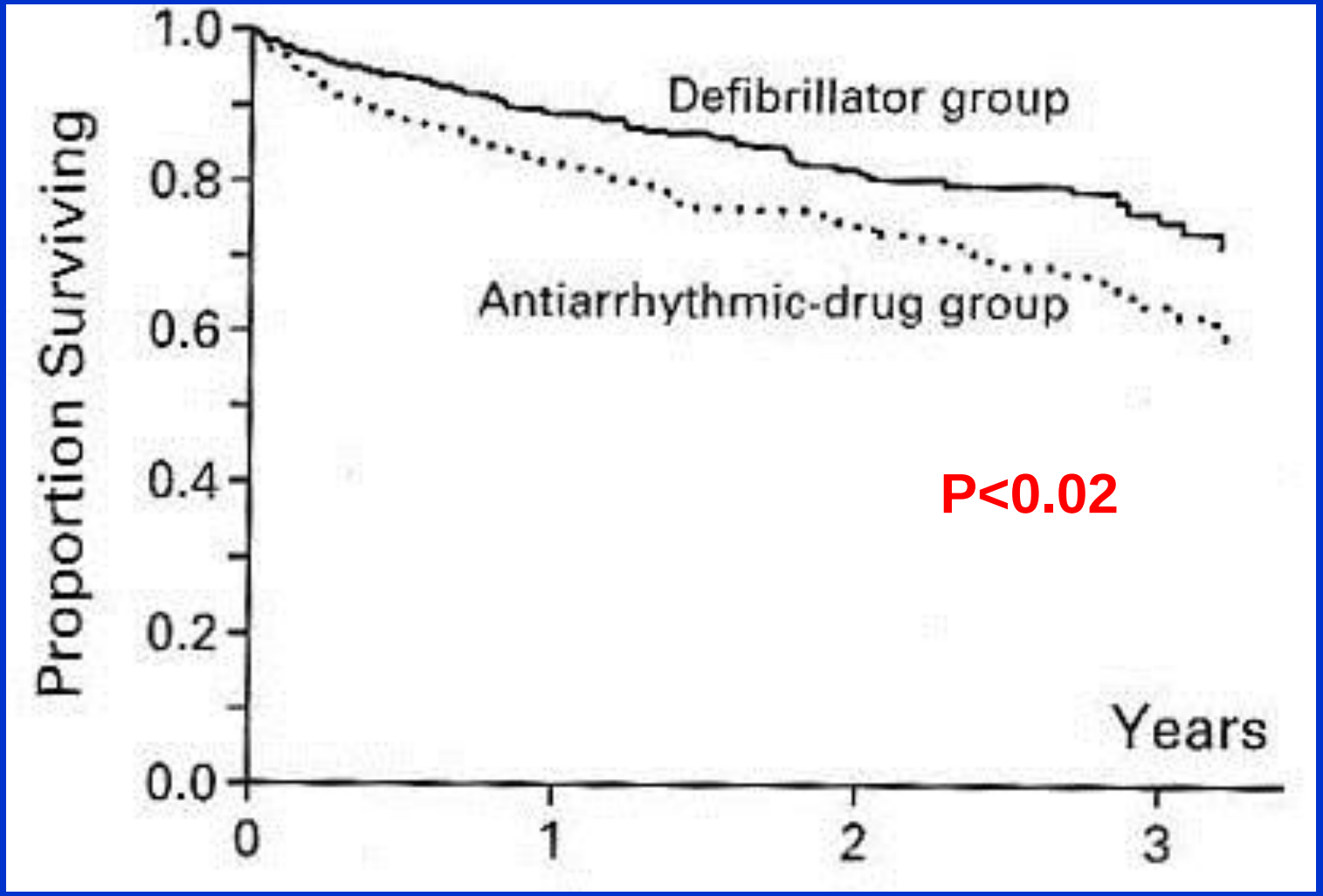
JF Leclercq & S Lévy Arch Mal Cœur 2000;93:1227

# CONTROLLED STUDIES: AVID

- Inclusion criteria:
  - Resuscitated VF (45% of cases)
  - VT with syncope or bad tolerance and LVEF <40%
- 1,016 pts randomized 1/1 between AID and antiarythmics (amiodarone in 96% of cases)

**N Engl J Med 1997;337:1576**

# CONTROLLED STUDIES: AVID




- 3-year survival: 75.4% (AID) vs 64.1% (amiodarone) i.e. a 31% decrease in mortality.

N Engl J Med 1997;337:1576

# CONTROLLED STUDIES: AVID

- Problem: more patients treated with beta-blockers in the AID group (42%) than in the amiodarone group (16.5%).
- However, the rate of appropriate shock delivered by AID is high: 64% during the 3-year F-U in the implanted group.
- The maximal benefit in survival was seen for LVEF between 20 and 34%.

# CONTROLLED STUDIES: CASH

- Inclusion criteria: mainly resuscitated VF (84%) or syncopal VT (only 16%) by mobile care units.
- Randomization into 4 groups:
  - AID
  - Amiodarone
  - Metoprolol
  - Propafenone

**Kuck & al Circulation 2000;102:748**

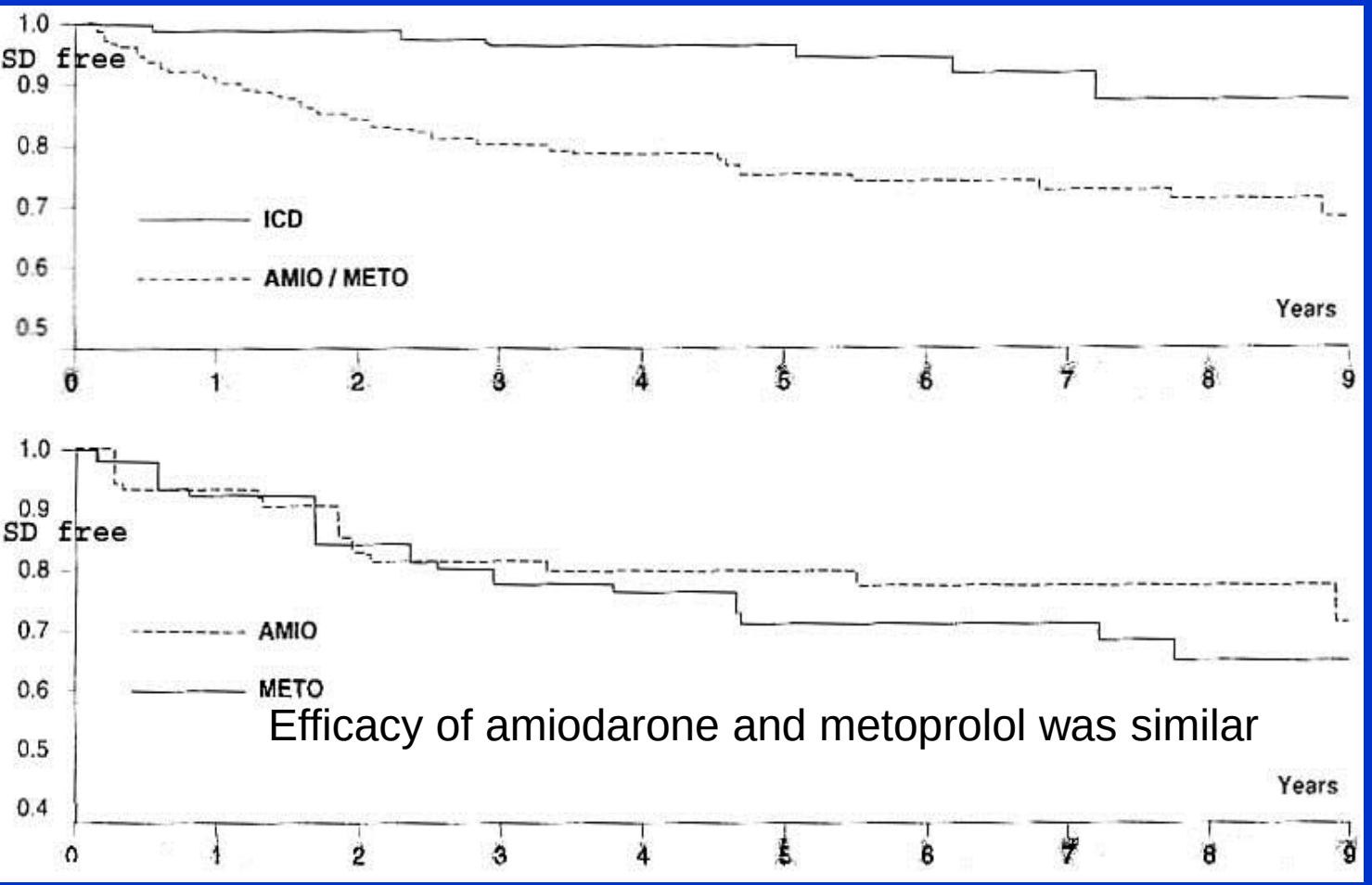
# CONTROLLED STUDIES: CASH

- The group randomized to propafenone had a much higher mortality and this arm was stopped very early by the survey comitee.
- The 3 other arms were continued for a very long period of inclusion (beginning in 1987, results in 1999).
- Many of AID implanted by thoracotomy.

**Kuck & al Circulation 2000;102:748**

# CONTROLLED STUDIES: CASH

288 pts, 10% without underlying heart disease, mean LVEF 46% (high percentage of primary ischaemic VF). Mean F-U: 4.7 years.



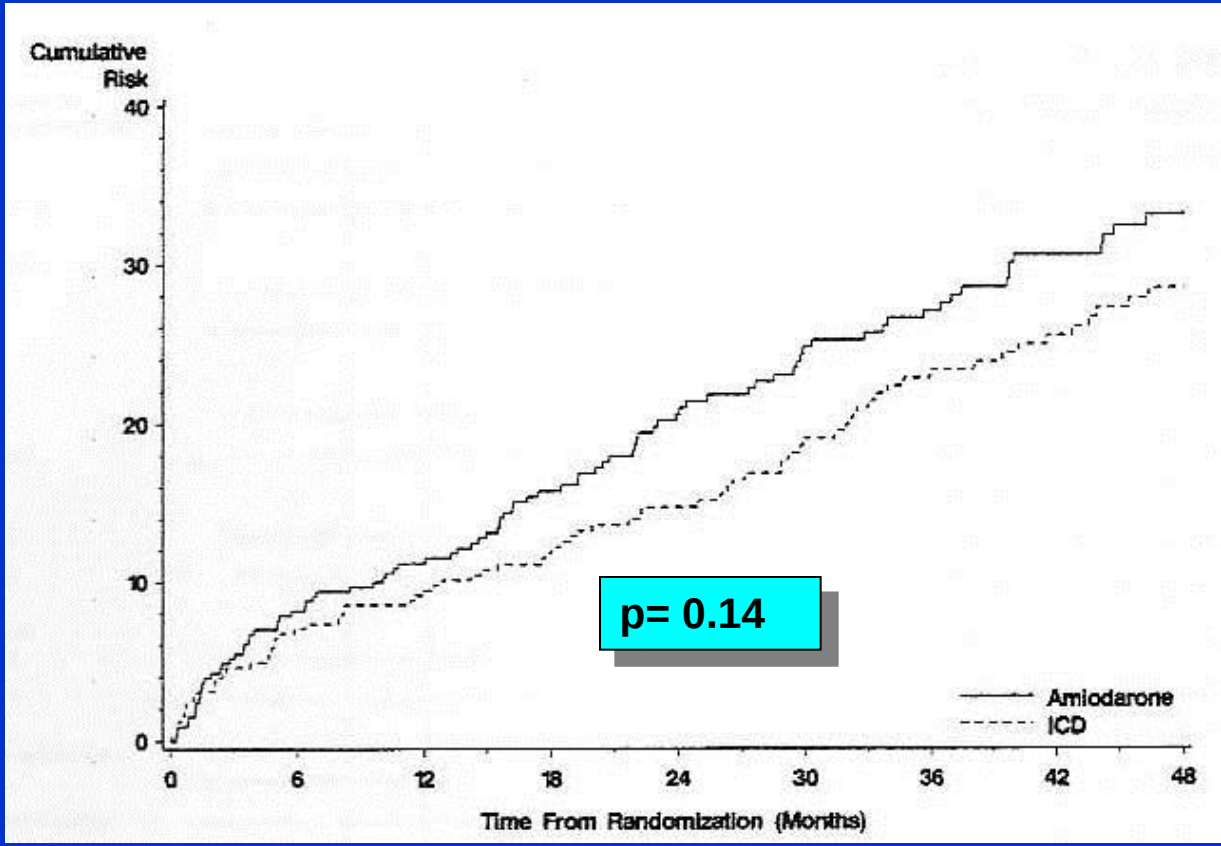

Efficacy of amiodarone and metoprolol was similar

**By comparison to the 2 groups amiodarone & metoprolol, AID decreases total mortality of 23% (p=0.08) and sudden death of 60% (p<0.01)**

**Kuck & al Circulation 2000;102:748**

# CONTROLLED STUDIES: CIDS

- 659 pts with VF, syncopal or sustained VT, or syncope and inducible VT, randomized between AID and amio



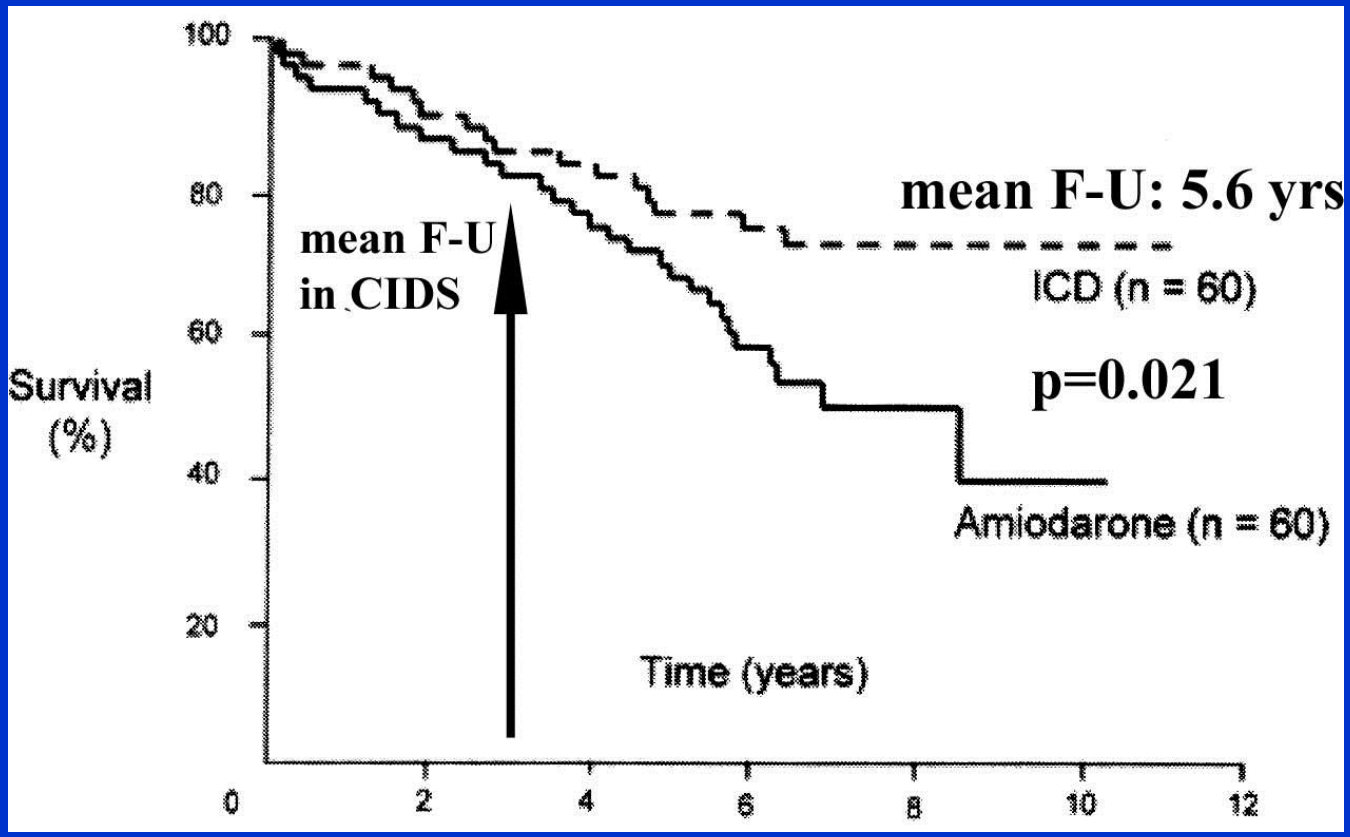

**Decrease in total Mortality: 20% (NS) in sudden death : 33% (NS).**

The trial was stopped early after the publication of AVID.

**Connolly & al Circulation 2000;101:1297**

# CONTROLLED STUDIES: CIDS

- A single center prolonged F-U up to 5.6 years: the difference became significant despite the small number of pts (120).

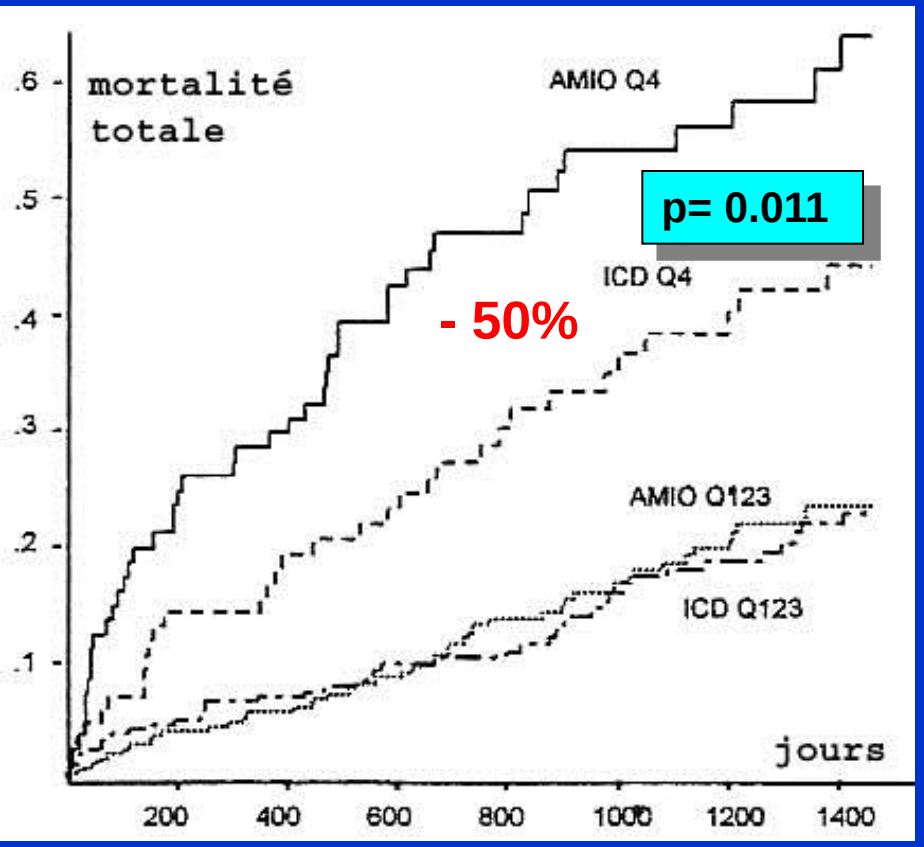



Benefit from AID Is not linear: it Increases with time.

**Bokhari & al Circulation 2004;110:112**

# CONTROLLED STUDIES: CIDS

## Subgroup analysis




3 parameters predict mortality in the amiodarone group: LVEF, age, and NYHA class.

In the AID group, a decrease in mortality is obvious in the 4th quartile of pts classified according to these criteria (50% reduction). Mortality in the 3 other quartiles is similar.

Authors conclude that AID may be useful in pts with **2** of these factors:

- Age >70 yrs
- LVEF <35%
- class NYHA III or IV

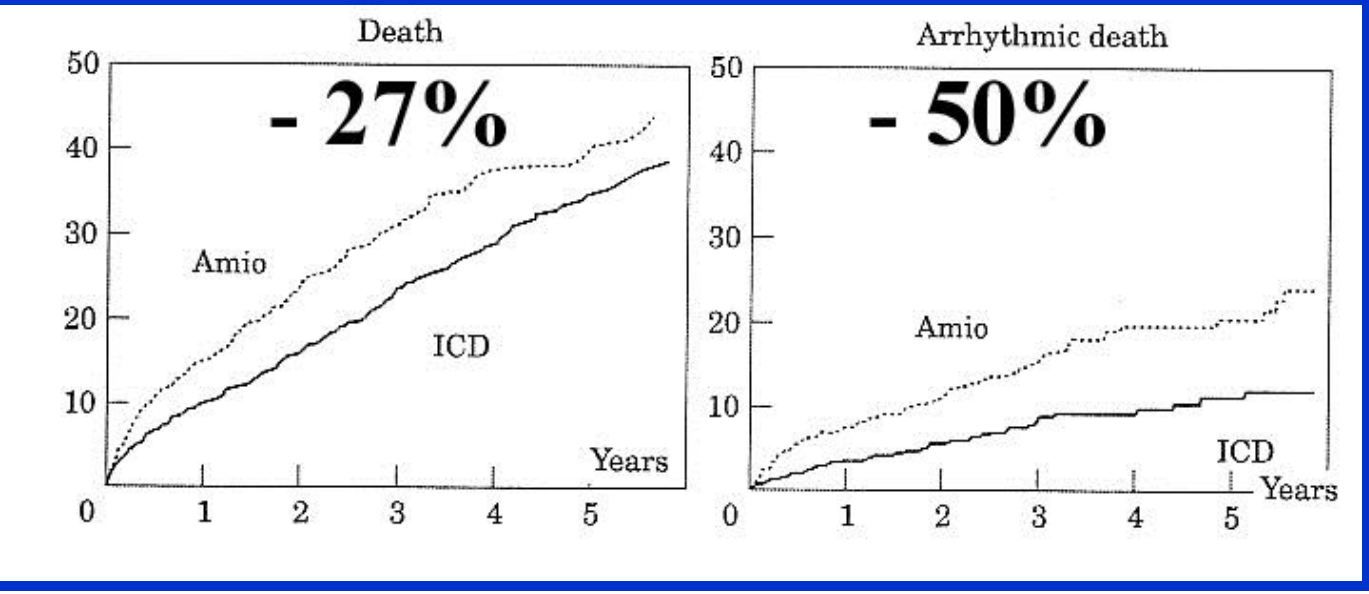
**Sheldon & al Circulation 2000;101:1660**

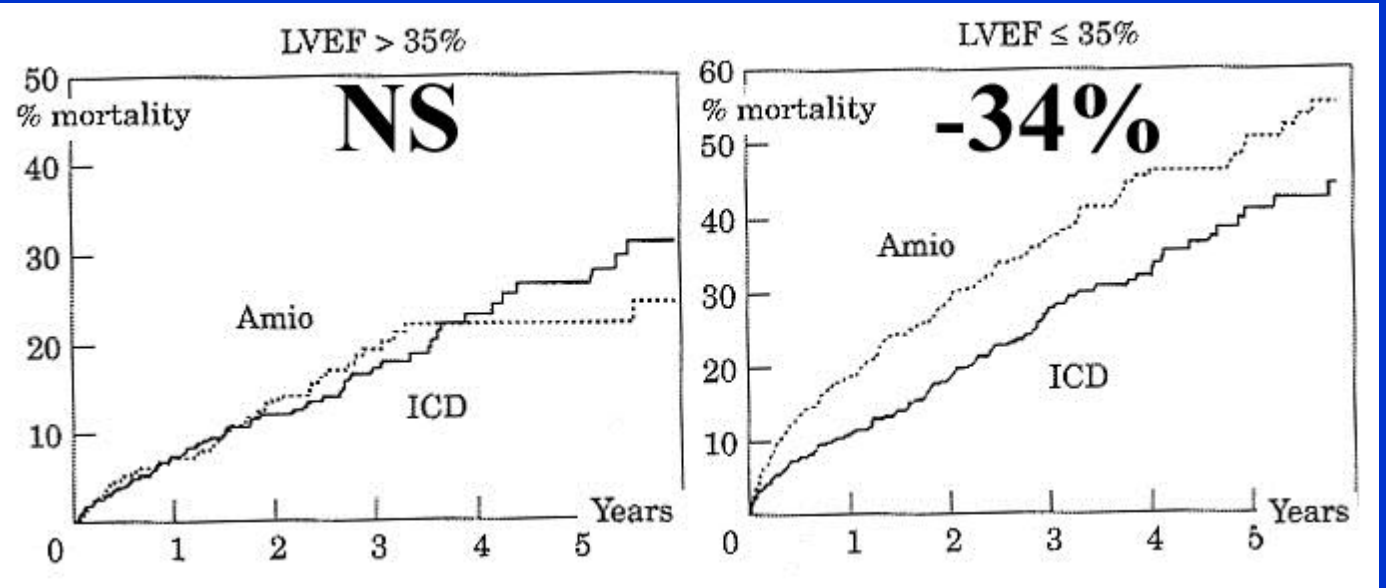
# CONTROLLED STUDIES: AVID Subgroup analysis

- Retrospective analysis of the AVID study using the same subgroup as in CIDS:
- In pts with 2 or 3 risk factors (age>70yrs, LVEF <35%, class NYHA III-IV), the benefit of AID was significant (RR=0.57, p<.01), whereas it is less in those with no or 1 risk factor (RR=0.70, p=.07).
- However, all deaths prevented by AID occured in pts with LVEF<0.35 ++++

**Exner & al Am Heart J 2001;141:99**

# CONTROLLED STUDIES:



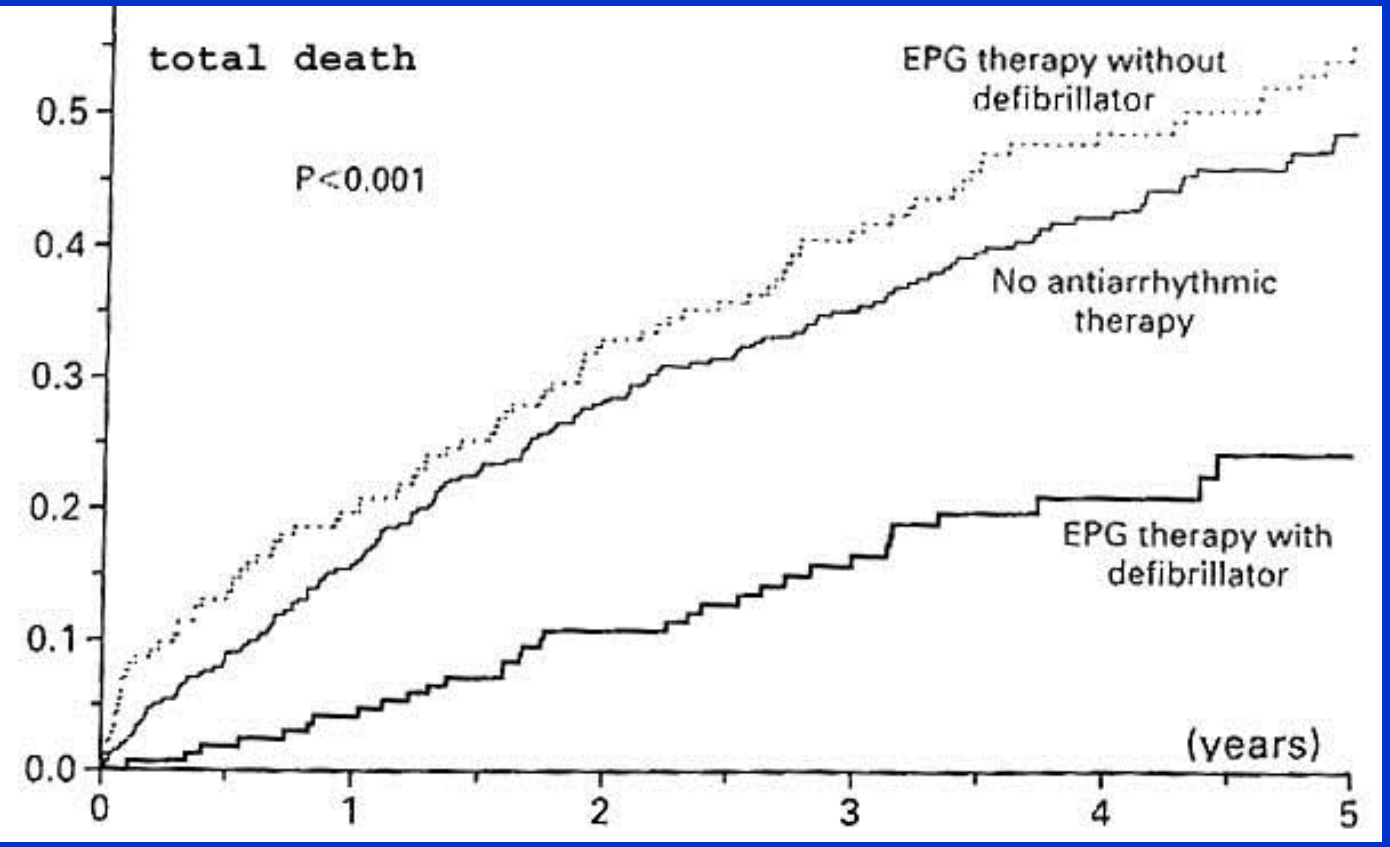

Meta-analysis of the 3 studies (AVID, CIDS & CASH)

Obvious benefit only for pts with **LVEF < 35%**

**Connolly et al Eur Heart J 2000;21:2071**

# CONTROLLED STUDIES:
# VT substrate **MUSTT**

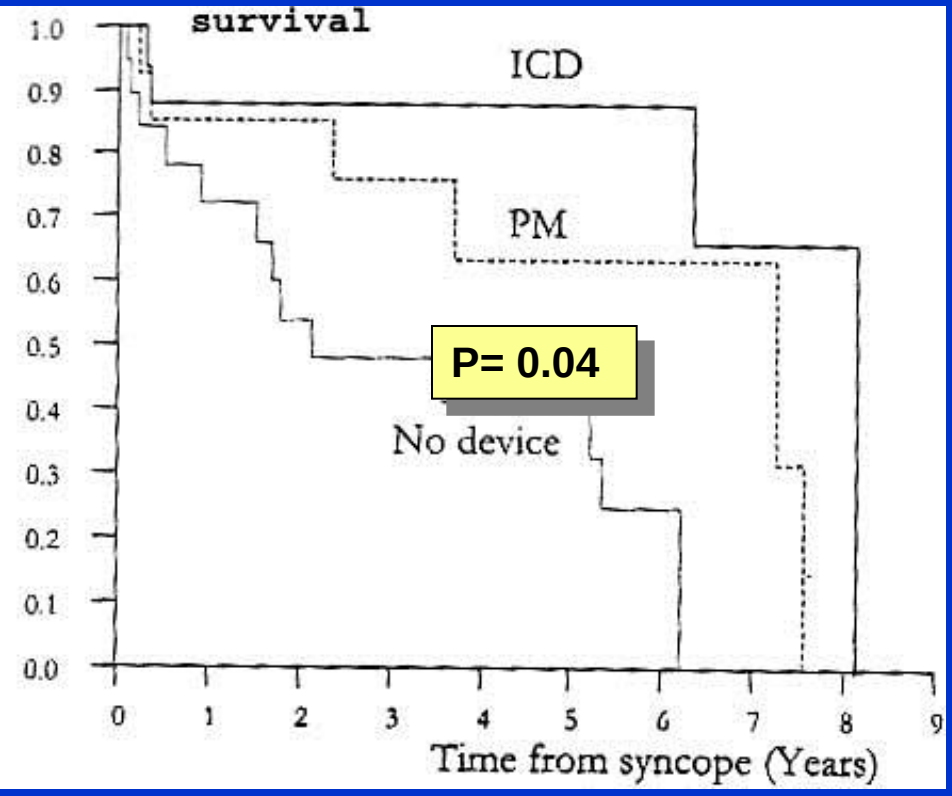
704 pts with CAD, LVEF<40%, NSVT and inducible VT/VF




Final trt:
Class-I 26%,
Amiodarone 10%,
Sotalol 9%,
AID alone 46%

**Buxton & al N Engl J Med 1999.341:1882**

# CONTROLLED STUDIES: Syncope and VT substrate




Brilakis & al. PACE 2001;24:1623

VT/VF inducibility in DCM

54 pts with DCM & syncope: better survival with AID.

Inducibility did not predict the occurrence of spontaneous VT/VF (47% vs 40% at 1 yr)

So DCM with syncope requires AID implant without EPS.

# AID: particular indications

- Pts with **non-compacted cardiomyopathy** ?
- 12 pts implanted for secondary prevention (7 VF, 5 VT)
- After 33±24 months, a recurrence was observed in 1/3 of cases.

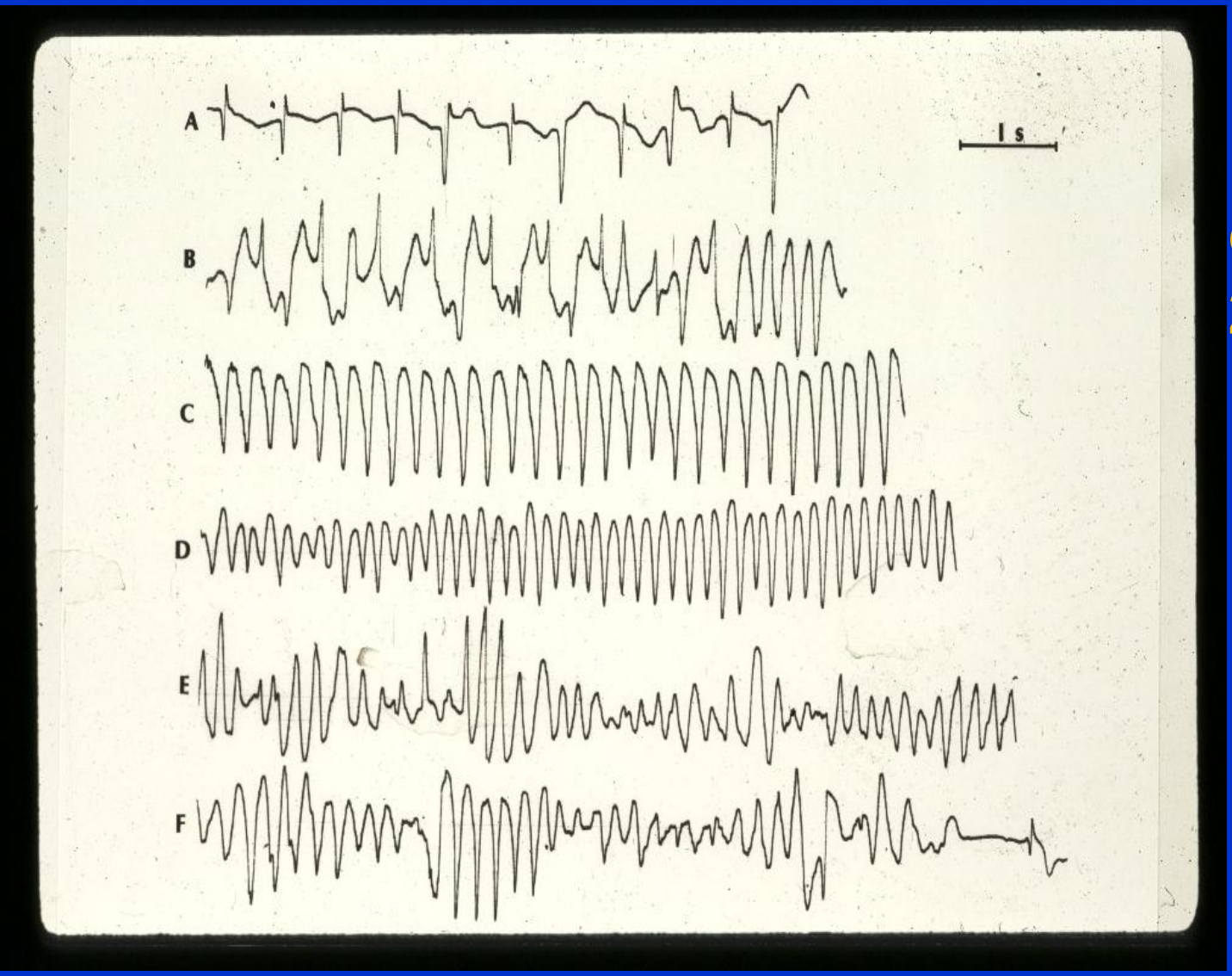
**Caliskan & al J Cardiovasc Electrophysiol 2011;22:898**

# Particular indications of AID: LQTS

## Risk of events on beta-blocker therapy


Priori et al. JAMA 2004

# Particular indications of AID: PCVT



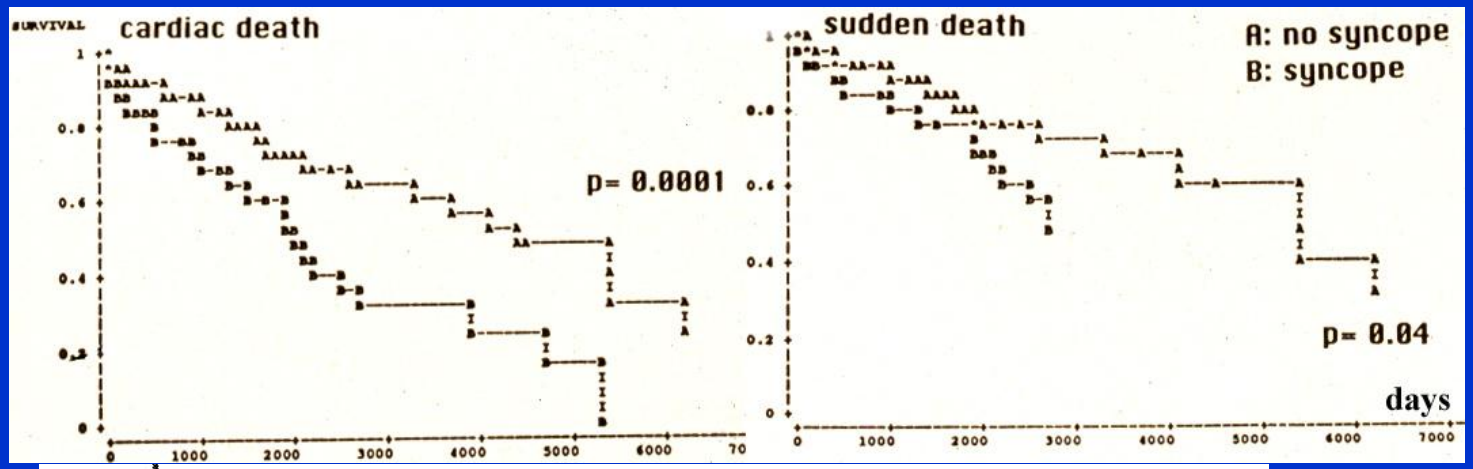

**Risk of SD on β-blocker: 24 to 27%**

**Leenhardt & al Circulation 1995;91:1512**

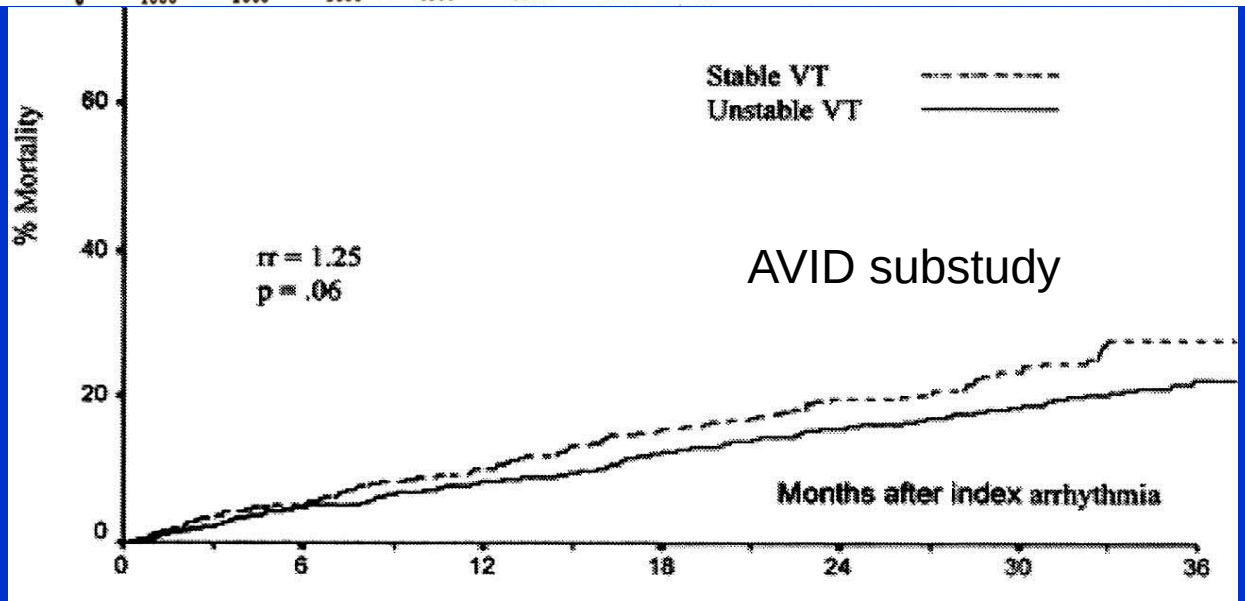
**Scheinman & al Am J Cardiol 1995;75:687**

# Risk of SD after sustained VT

- High in CAD or DCM, even if VT is well tolerated



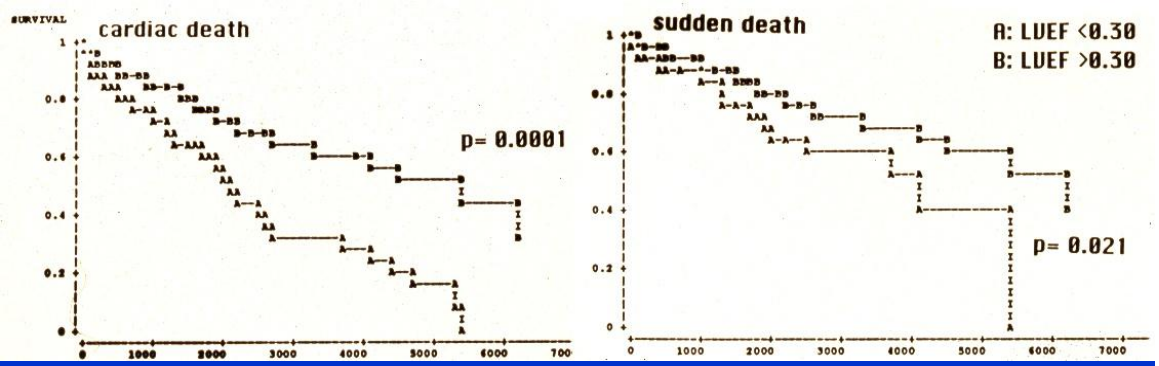

**Leclercq et al Am Heart J 1991;121:1685**



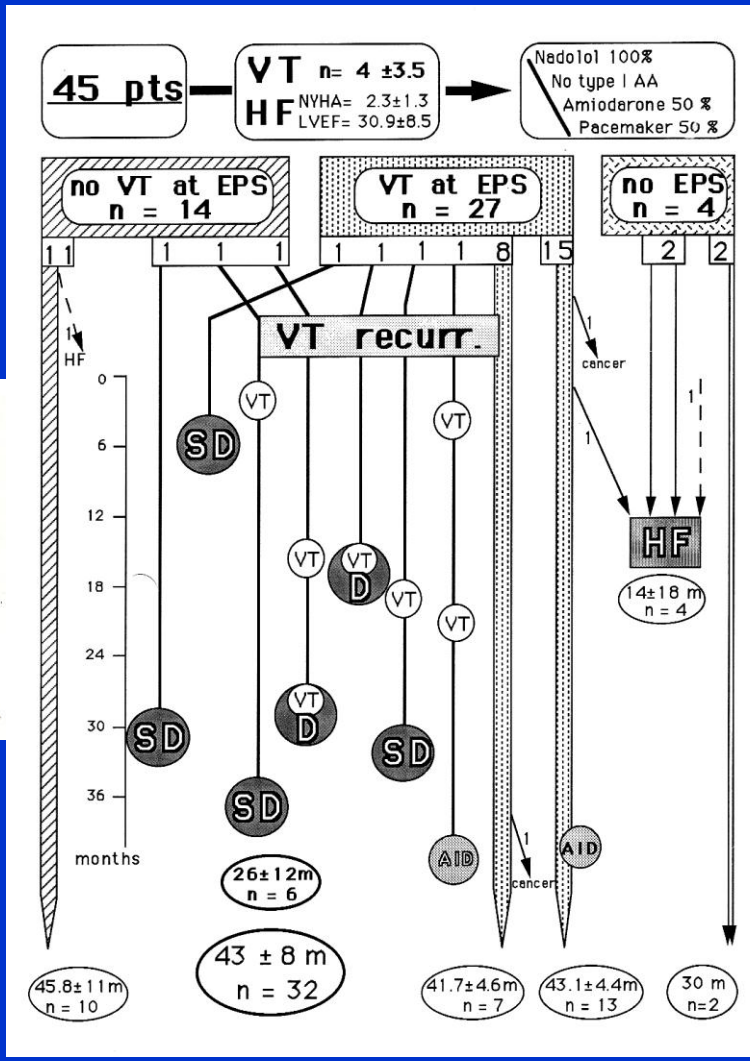

**Raitt & al Circulation 2001;103:244**

# Risk of SD after sustained VT

- High risk on optimal treatment (β-blocker + amio)
- Risk significant even in pts with LVEF>0.30

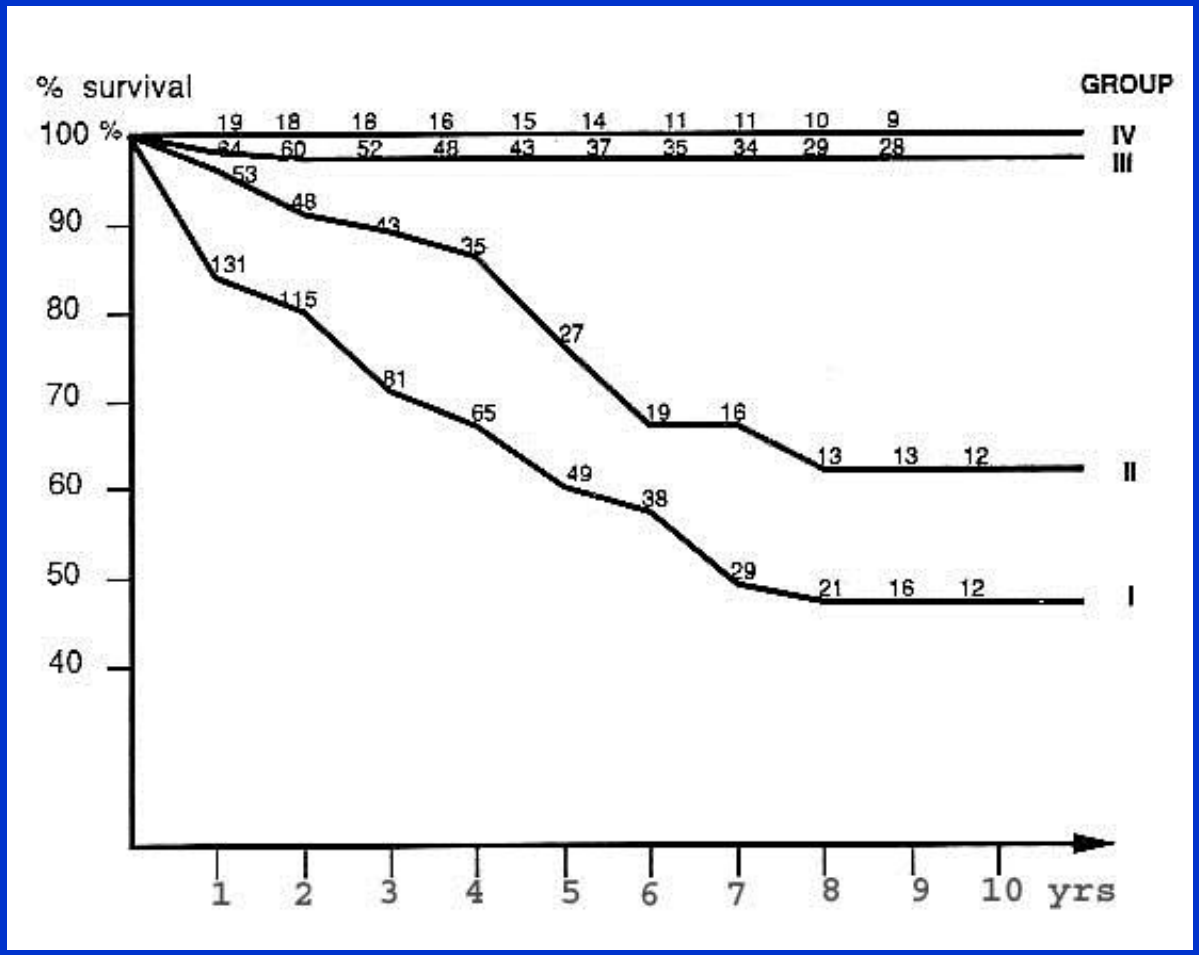



**Leclercq et al Am Heart J 1991;121:1685**



# Risk of SD after sustained VT

- However, low risk of SD in pts with normal LV




**Idiopathic VT**
**ARVD**

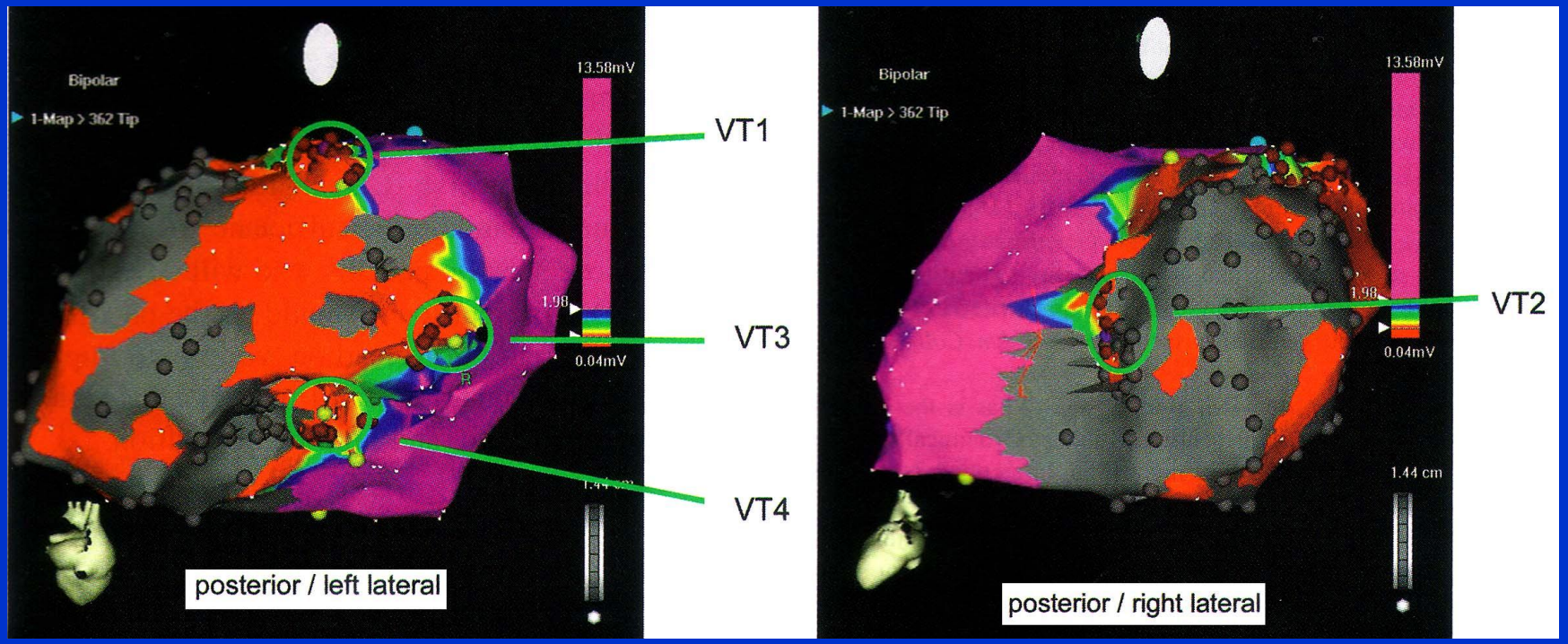
**DCM**

**CAD**

**Leclercq et al**
**Am Heart J**
**1991;121:1685**

# Risk of SD after sustained VT

- VT ablation is a good alternative therapy for idiopathic VT (fascicular of infundibular)
- It has a place for ARVD
- In CAD or DCM, it is difficult (complex substrate)



# Syncope and VT/VF induction: primary or secondary prevention?

- 50 pts with Syncope and VT/VF inducibility (66% had underlying heart disease)

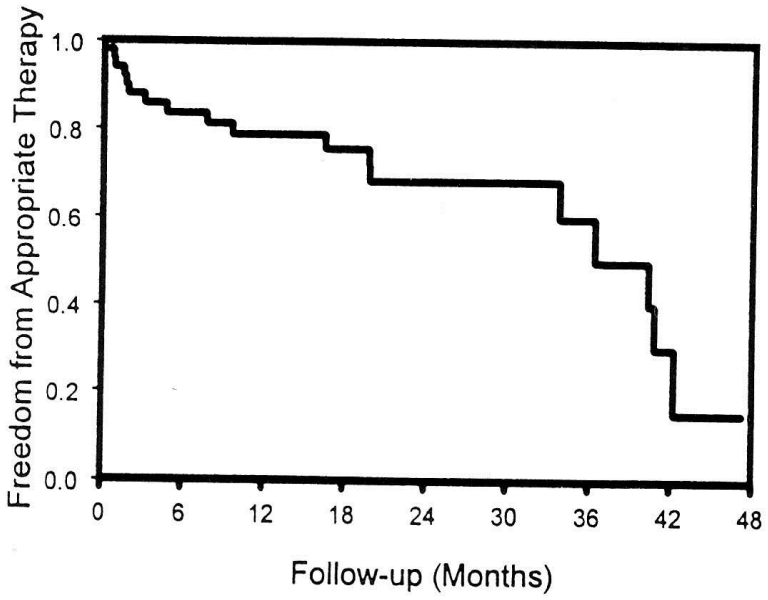



**Table 2.** Predictors of Appropriate Implantable Cardioverter-Defibrillator Therapy

| Variable | p Value | RR |
|---|---|---|
| Shorter cycle length of induced arrhythmia | 0.03 | 1.17/10 ms* |
| Fewer extrastimuli to induce arrhythmia | 0.07 | 0.36 |
| Q waves on admission ECG | 0.07 | 0.43 |
| Discharge without AAD | 0.09 | 0.39 |
| SAECG abnormalities | 0.11 | 4.6 |
| Left ventricular ejection fraction | 0.60 | 0.99 |
| Etiology of heart disease | 0.77 | 0.99 |
| Type of arrhythmia induced | | |
| NSVT | | 1.0 |
| SMVT | 0.93 | 1.48 |
| VF | | 1.50 |

**High incidence of shocks**

**Fast VT/VF and LP predictive**

**Link & al J Am Coll Cardiol 1997;29:370**

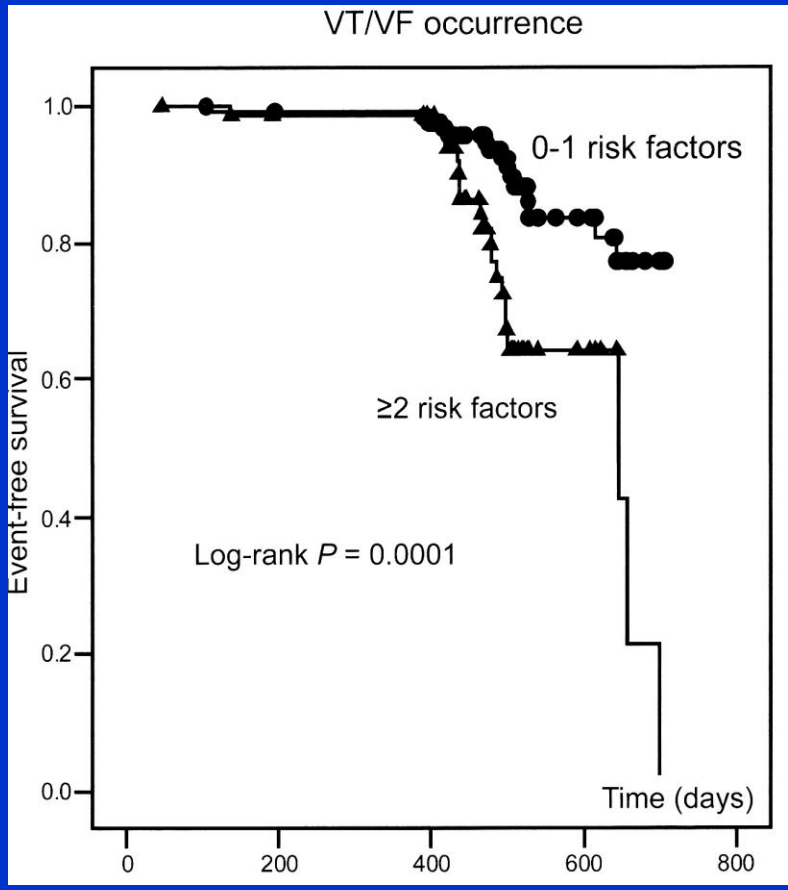
# Predictors of appropriate shocks

- 250 pts (92% for 2ary prevention); PROFIT study
- Multivariate analysis: LVEF<40%, QRS>150ms, permanent AF.

Cox regression analysis for VT/VF occurrence

| Parameter | Univariate | Multivariate Analysis | |
|---|---|---|---|
| | *P* | *P* | |
| NT-proBNP | 0.005 | 0.490 | |
| EF | 0.002 | 0.019 | ← |
| QRS | 0.018 | 0.020 | ← |
| Atrial fibrillation | 0.011 | 0.042 | ← |
| NYHA | 0.044 | 0.265 | |

**Klein & al Europace 2006;8:618**



# Primary and Secondary prevention of SD by AID: is it different ?

- 2,134 pts implanted (61% for primary and 39% for secondary prevention). After 3.4 ± 2.8 years, 20% died. The 5-year incidence of mortality was identical: 25% for primary prevention patients and 23% for secondary prevention patients.
- Secondary prevention patients had an increased risk for appropriate therapy (HR=1.7; p<.001). A comparable risk for inappropriate shocks was observed (HR=1.0; p= 0.9)

**Van Welsenes et al Europace 2011;13:389**

# Class-I indications of AID

| Clinical status | Proof |
|---|---|
| **Cardiac arrest by VF/VT after exclusion of any totally reversible cause** | A |
| **Spontaneous sustained VT with underlying heart disease, whatever the tolerance** | B |
| **Syncope of unknown cause and VT/VF induction at EPS** | B |
| **LVEF<35% & NYHA II or III, more than 40 days after MI** | A |
| **LVEF<35% & NYHA II or III, non-ischaemic DCM** | B |
| **LVEF<30% & NYHA I, more than 40 days after MI** | A |
| **NSVT, LVEF< 40% post-MI, and VT/VF induction at EPS** | B |

**ACC/AHA/HRS 2008 Guidelines Circulation 2008;117:2820 JACC 2008;51:2085**

# Class-II A indications of AID

| Clinical status | Proof |
|---|---|
| **Syncope of unknown cause and non-ischaemic DCM with LV dysfonction** | C |
| **Spontaneous sustained VT without underlying heart disease** | C |
| **LQTS and syncope or VT under β-blocker therapy** | B |
| **CPVT and VT or syncope under β-blocker therapy** | C |
| **Brugada syndrome and syncope or non-syncopal VT** | C |
| **Patients at home waiting for heart transplantation** | C |
| **HCM with 1 or more risk factor of SD** | C |
| **ARVD with 1 or more risk factor of SD** | C |

**ACC/AHA/HRS 2008 Guidelines Circulation 2008;117:2820 JACC 2008;51:2085**

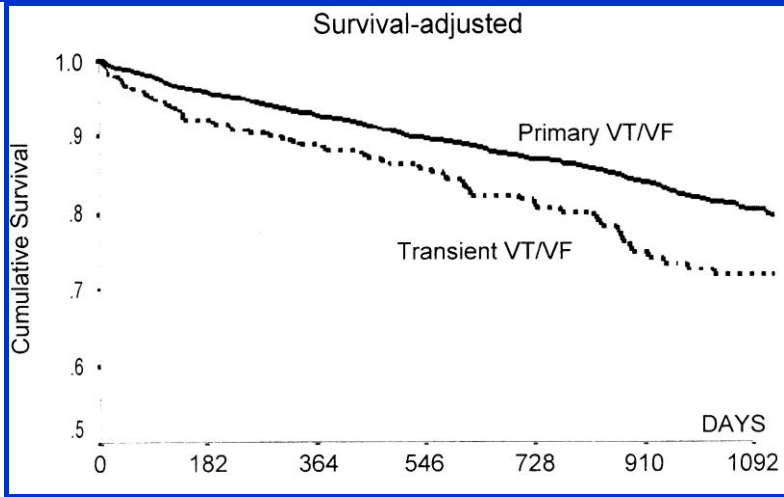
# VF due to transient or correctable cause: AID not indicated ?

- AVID registry (4,450 pts). « Transient » VT/VF in 278, caused mainly by ischemia.
- Survival egal or worse than in other pts.

**Table 2.** Putative Transient or Correctable Causes of VT/VF (n = 278)

| | n | % |
|---|---|---|
| Ischemic events | 183 | 65.8% |
| New MI | 161 | 57.9% |
| Non–Q-wave | 83 | 29.9% |
| Q-wave | 78 | 28.0% |
| Transient ischemia, no MI | 22 | 7.9% |
| Other or unknown* | 50 | 17.9% |
| Electrolyte imbalance | 27 | 9.7% |
| Antiarrhythmic drug reaction | 18 | 6.5% |

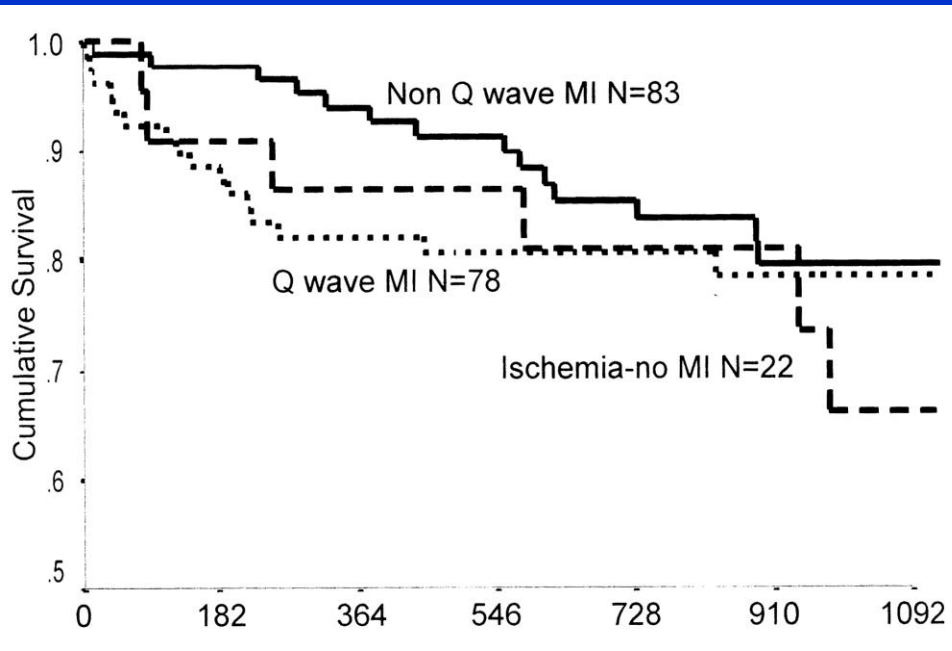
*For example, cocaine or illicit drug use, sepsis, hypoxia, electrocution, drowning.

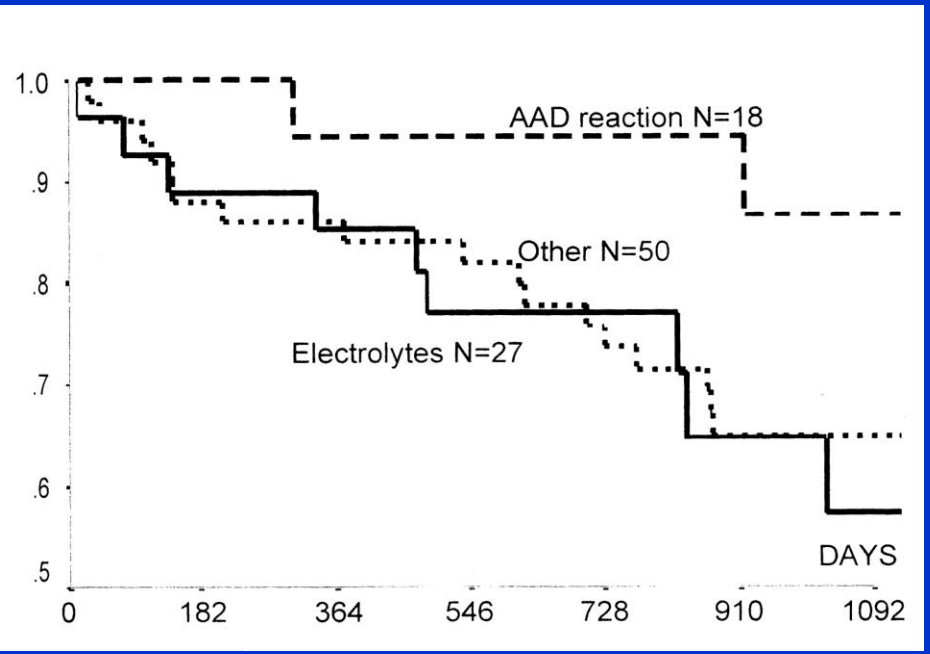



**Wyse & al J Am Coll Cardiol 2001;38:1718**

# VF due to transient or correctable cause: AID not indicated ?

- It depends probably of the cause:
- OK for proarrhythmic effect of drugs
- Other causes, especially ischaemia ???

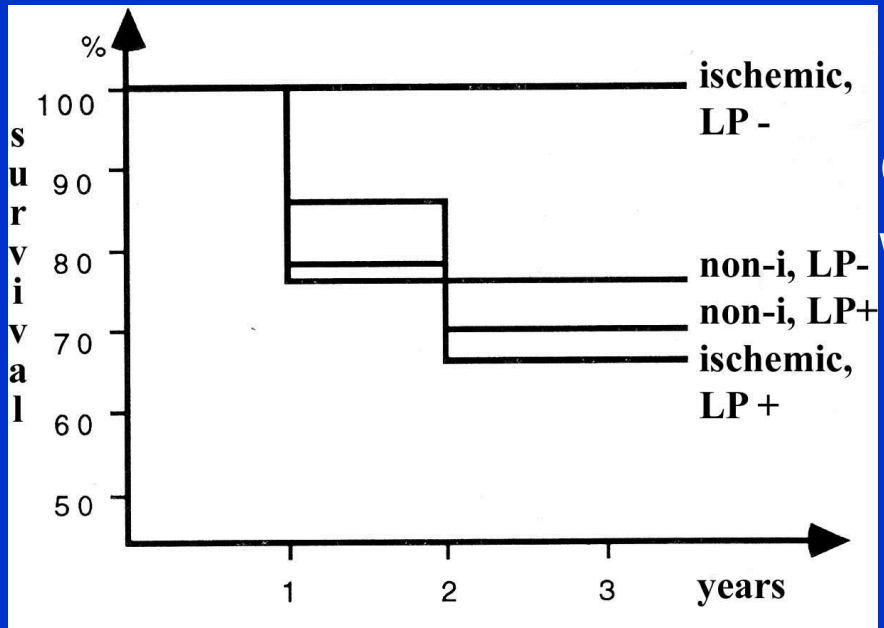



Wyse & al J Am Coll Cardiol 2001;38:1718

# VF due to transient or correctable cause: AID not indicated ?

- 38 pts with CAD and resuscitated VF, free of antiarrhythmic drugs before event.
- 22 during documented ischaemia (acute MI), 16 without pain or ECG changes.




**Only pts with ischaemic VF and without LP have good prognosis**

Leclercq & all Arch Mal Cœur 1994;87:57

# Conclusions

- AID indications increased with time, of course for primary but also for secondary prevention. It could still increase.
- It is logical, because it seems preferable to stop a VT as soon as possible.
- VT ablation represents more a combined treatment than an alternative: implant first, but think after…