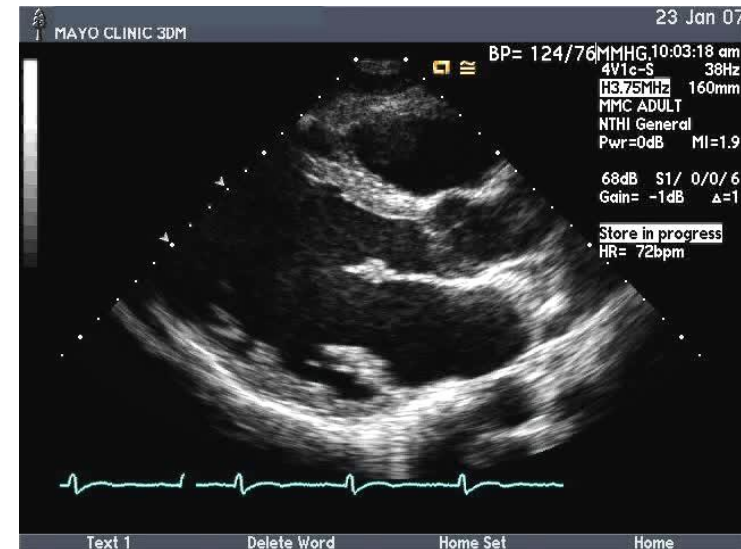


Mitral Valve Prolapse and Sudden Death



JF Avierinos
Hôpital Timone
Marseille
January 27th, 2017



Mitral Valve Prolapse

Between Benign and Malignant the Long Story of an Ongoing Controversy

... of a Pathologic disease ... defined by echo



JF Avierinos
Hôpital Timone
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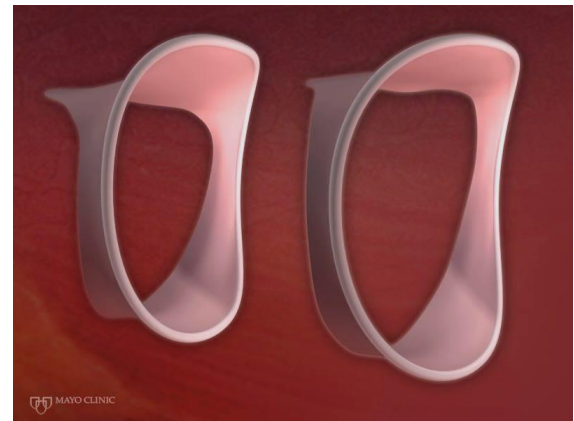
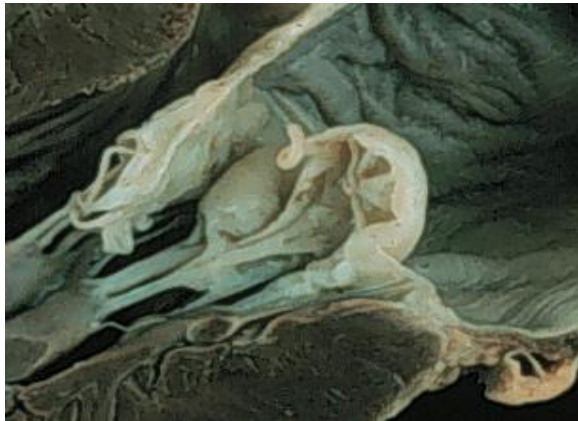


MVP : Four decades of controversy

From Pathology to stethoscope

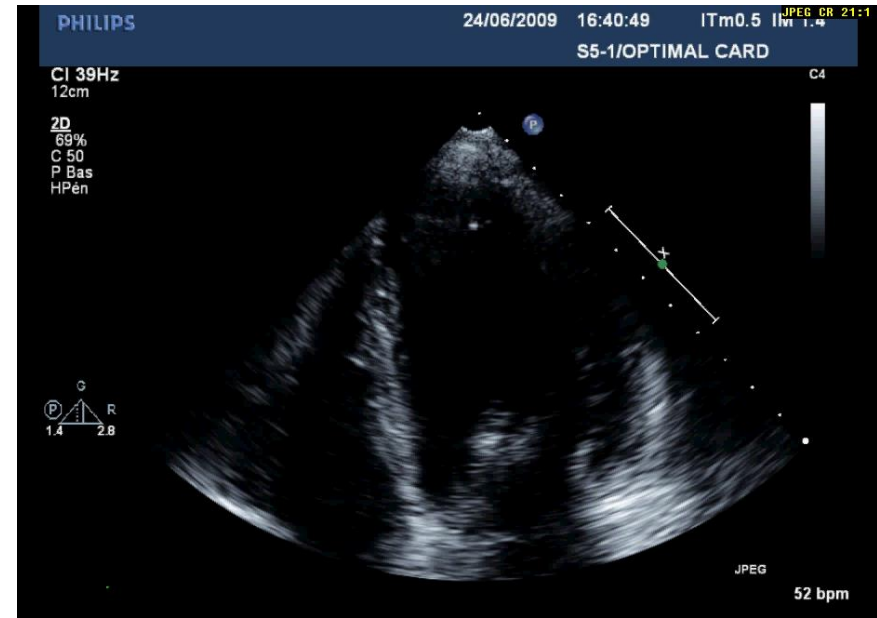
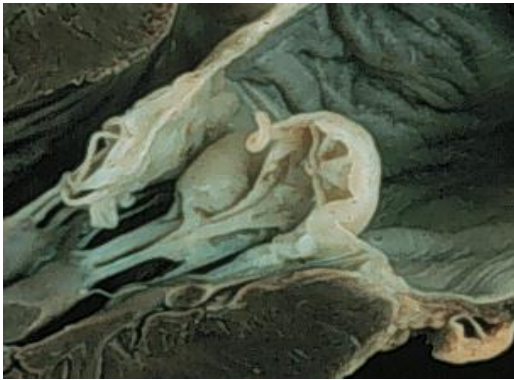
Dr Barlow

“The significance of late systolic murmurs and mid-late systolic clicks”
Am Heart J. **1963**;66:443.



MVP : Four decades of controversy

From stethoscope to echo

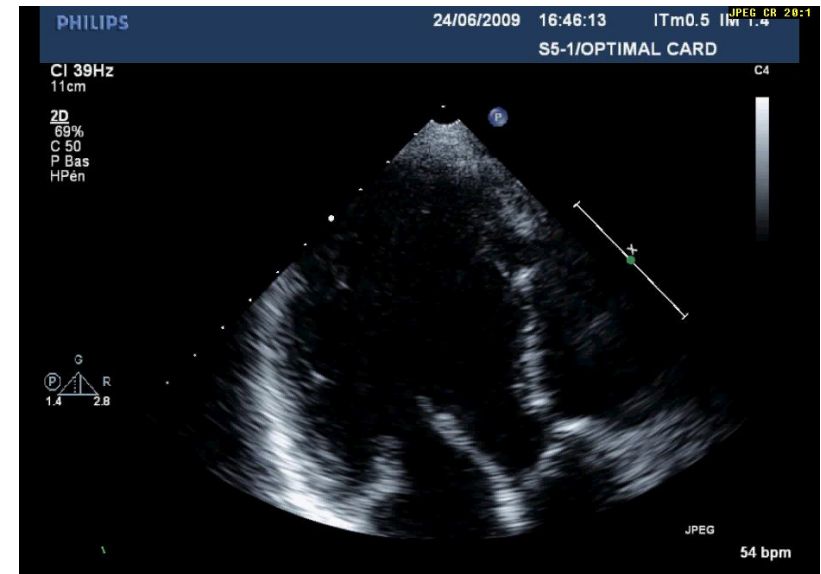
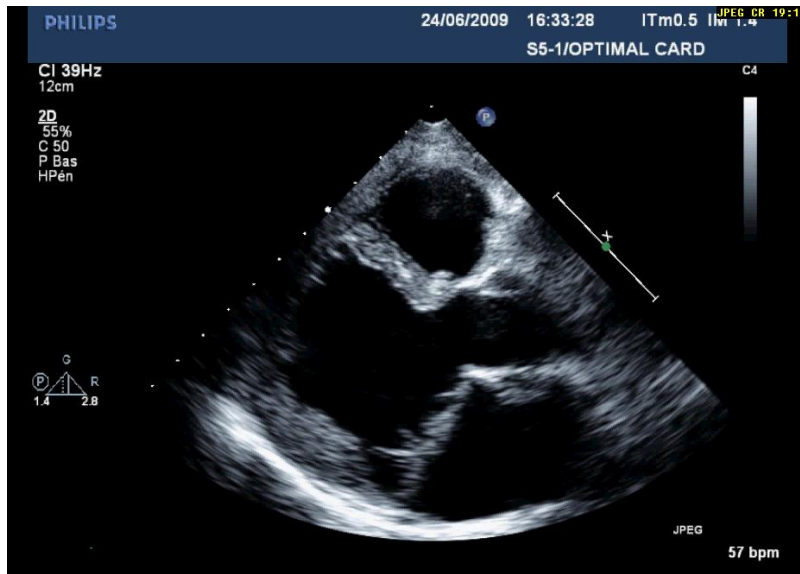


Prevalence : 5% to 17% ???

Savage, Am Heart J. 1983

MVP Prevalence

with current diagnostic criteria



0.6% to 2.4%

150 Million subjects worldwide

MVP : Four decades of controversy

Outcome

	Nishimura 1985	Duren 1988	Marks 1989	Zuppirolli 1995	Kim 1996	Freed 1999
N°	237	300	456	316	229	84
Age	44	42	47	42	51	56
Follow-up	6.2	6.1	Backwards	8.5	?	Backwards
Patients with Complic. (%)	22	39	17	10	44	5
Linearized Rates (%/year)	3.4	6.4	?	1.2	?	?

MVP : Four decades of controversy

Sudden Death

Sudden Death in the Mitral Valve Prolapse-Click Syndrome

ROBERT M. JERESATY
Hartford, Connecticut

Am J Cardiol, 1976

Sudden death in mitral valve prolapse with Holter monitoring-
documented ventricular fibrillation: evidence of coexisting
arrhythmogenic right ventricular cardiomyopathy
Martini, Int J Cardiol, 1994

Life-Threatening Arrhythmias in the Mitral Valve Prolapse Syndrome

Am J Med, 1976

Arrhythmias in the Mitral Valve Prolapse Syndrome

Prevalence, Nature, and Frequency

ANTHONY N. DeMARIA, M.D.; EZRA A. AMSTERDAM, M.D.; LOUIS A. VISMARA, M.D.;
ALEXANDER NEUMANN, B.S.; and DEAN T. MASON, M.D.; Davis, California

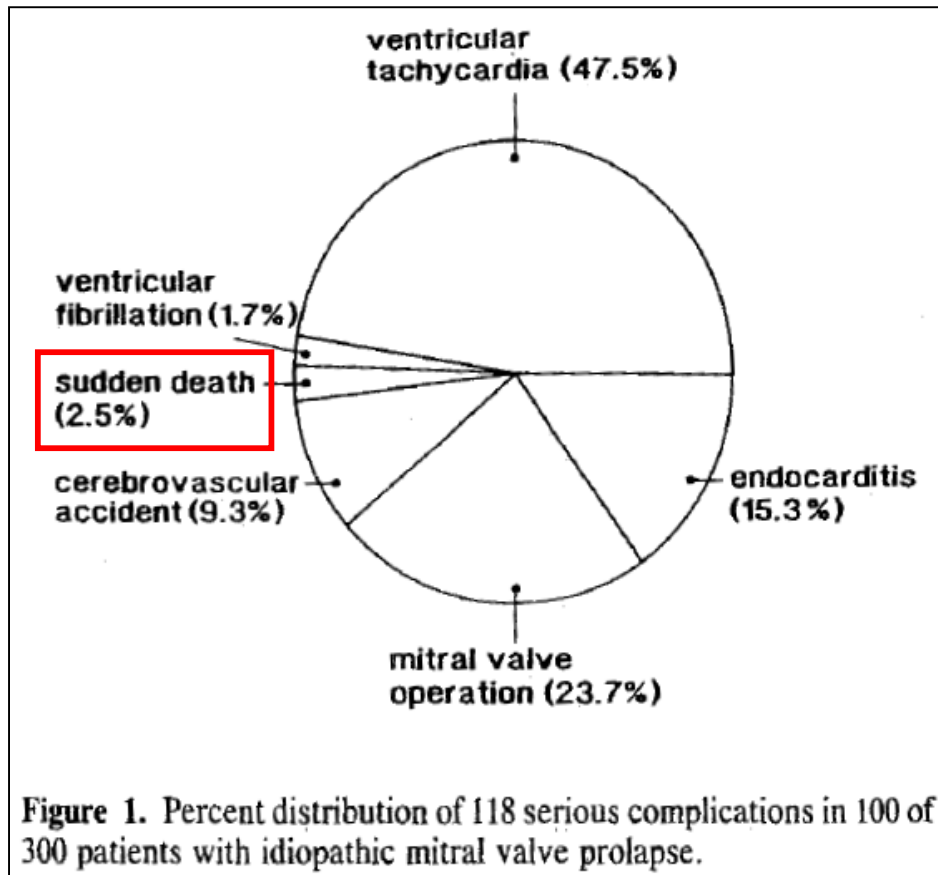
Arrhythmias in mitral valve prolapse: Relation
to anterior mitral leaflet thickening, clinical
variables, and color Doppler
echocardiographic parameters

Zuppiroli, Am H J 1994

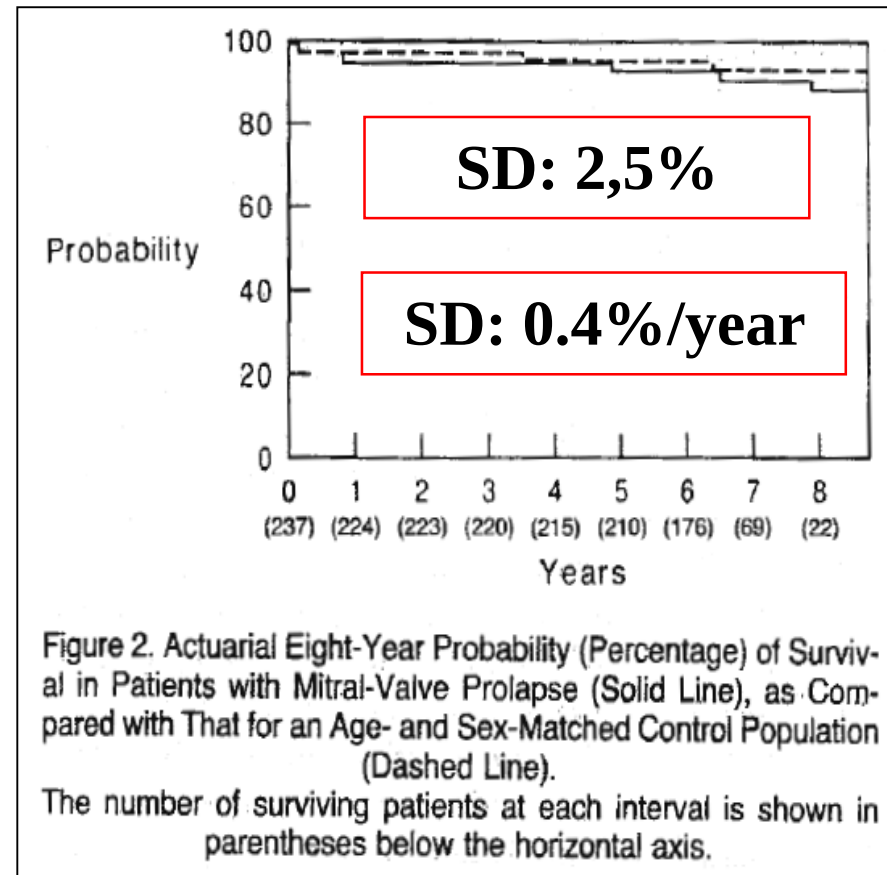
DeMaria, Ann Int Med, 1976

MVP : Four decades of controversy

Sudden Death



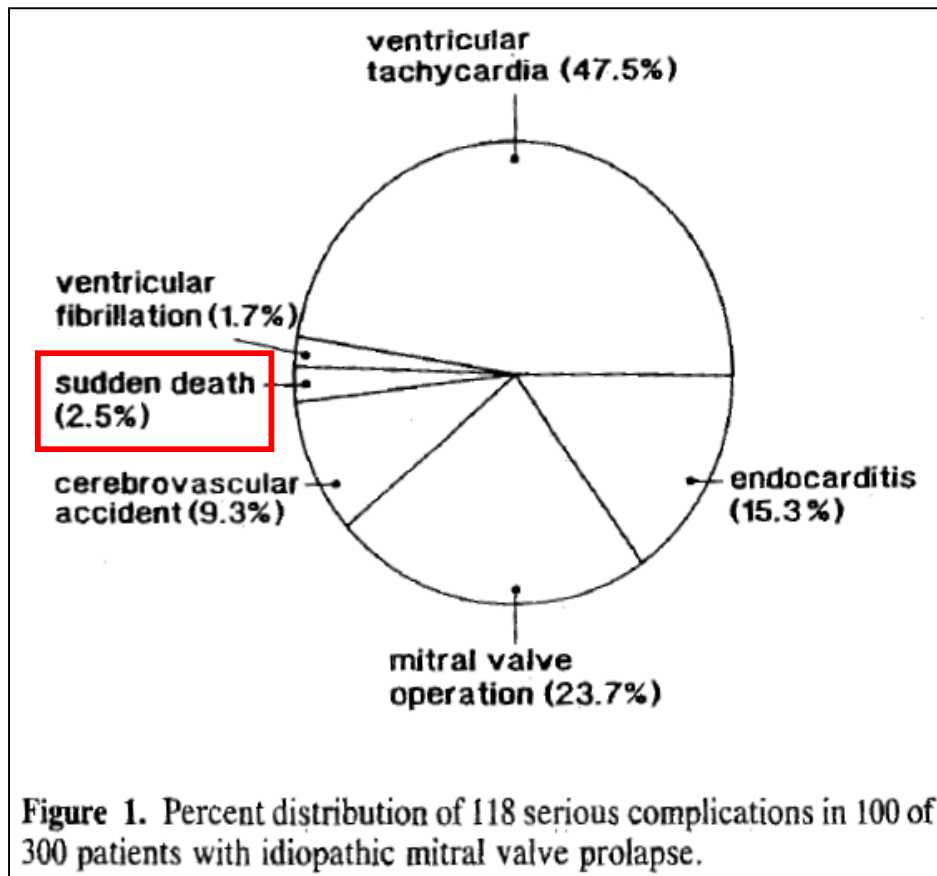
Düren DR, *et al.* Long-term follow-up of idiopathic mitral valve prolapse in 300 patients: a prospective study. *J Am Coll Cardiol.* 1988 Jan;11(1):42-7.



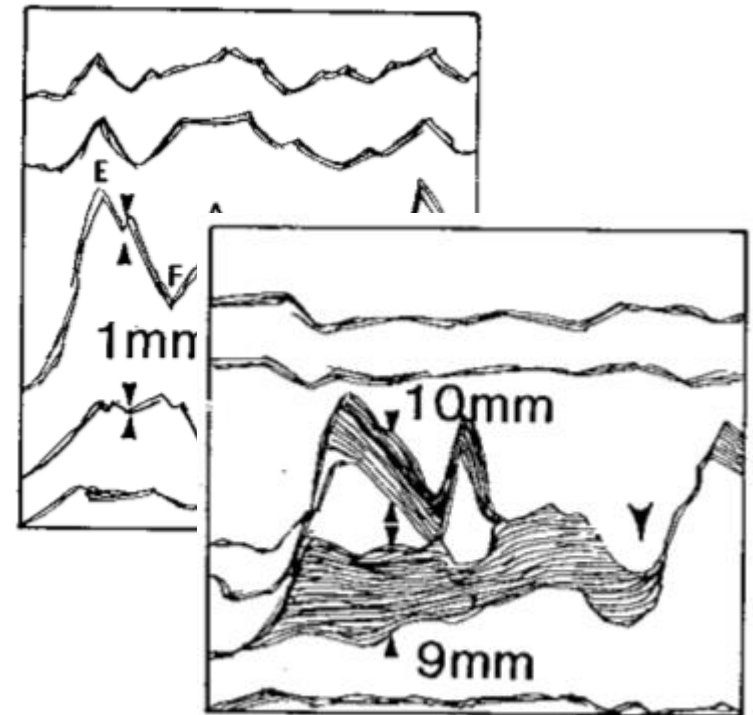
Nishimura RA, *et al.* Echocardiographically documented mitral-valve prolapse. Long-term follow-up of 237 patients. *N Engl J Med.* 1985 Nov 21;313(21):1305-9.

MVP : Four decades of controversy

Sudden Death



Düren DR, *et al.* Long-term follow-up of idiopathic mitral valve prolapse in 300 patients: a prospective study. *J Am Coll Cardiol.* 1988 Jan;11(1):42–7.



Nishimura RA, *et al.* Echocardiographically documented mitral-valve prolapse. Long-term follow-up of 237 patients. *N Engl J Med.* 1985 Nov 21;313(21):1305–9.

Prevalence and Clinical Outcome of Mitral Valve Prolapse

The New England Journal of Medicine July 1st, 1999

TABLE 2. PREVALENCE OF VARIOUS CLINICAL FINDINGS ACCORDING TO THE PRESENCE OR ABSENCE OF MITRAL-VALVE PROLAPSE.

CLINICAL FINDING	MITRAL- VALVE PROLAPSE (N=84)	NO MITRAL- VALVE PROLAPSE (N=3407)
	no. (%)	
Congestive heart failure	0	25 (0.7)
Atrial fibrillation	1 (1.2)	58 (1.7)
Cerebrovascular disease*	1 (1.2)	52 (1.5)
Syncope	3 (3.6)	103 (3.0)

*Cerebrovascular disease refers to stroke or transient ischemic attack.

MVP : a benign condition

THE NEW YORK TIMES, SUNDAY, JULY 4, 1999

Mitral Valve Problems Are Not So Serious After All

As many as 28 million Americans who were told they are in danger of stroke, heart failure and other problems because of mitral-valve prolapse **probably do not have to worry**. A new study showed that about 2.4 percent of the population — not the 5 percent to 15 percent previously estimated — have the condition, an abnormally long, floppy valve that can cause blood leakage in the heart. And in those who do

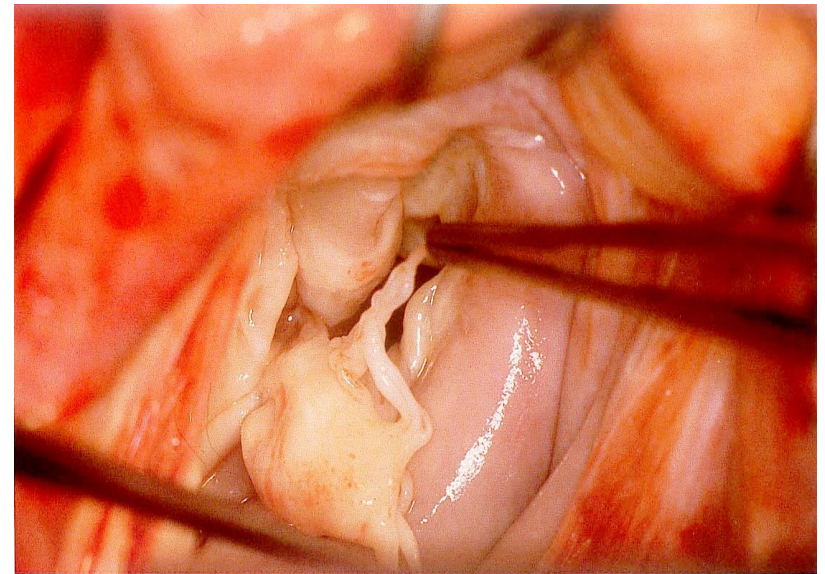
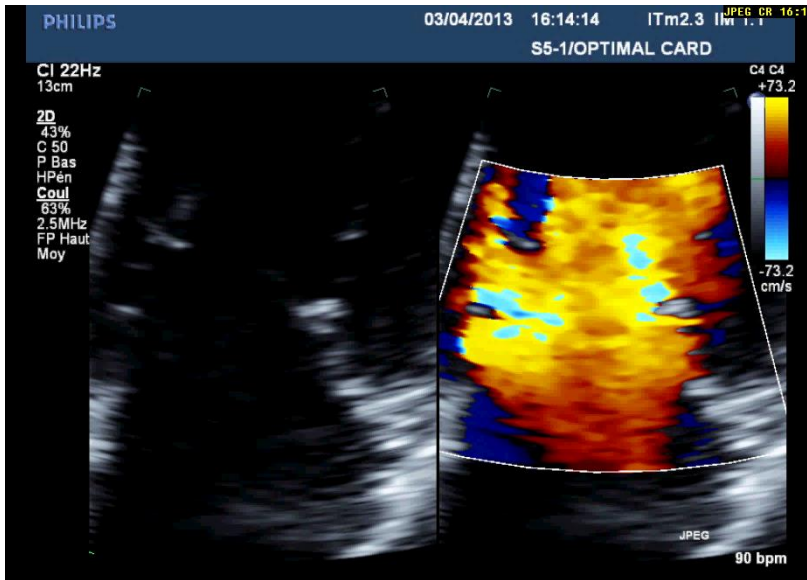
have it, it was found no more likely to cause the feared complications than those who do not.

HOLCOMB B. NOBLE



And in those who do have it, it was found no more likely to cause the feared complications than those who do not.

MVP : a benign condition ?

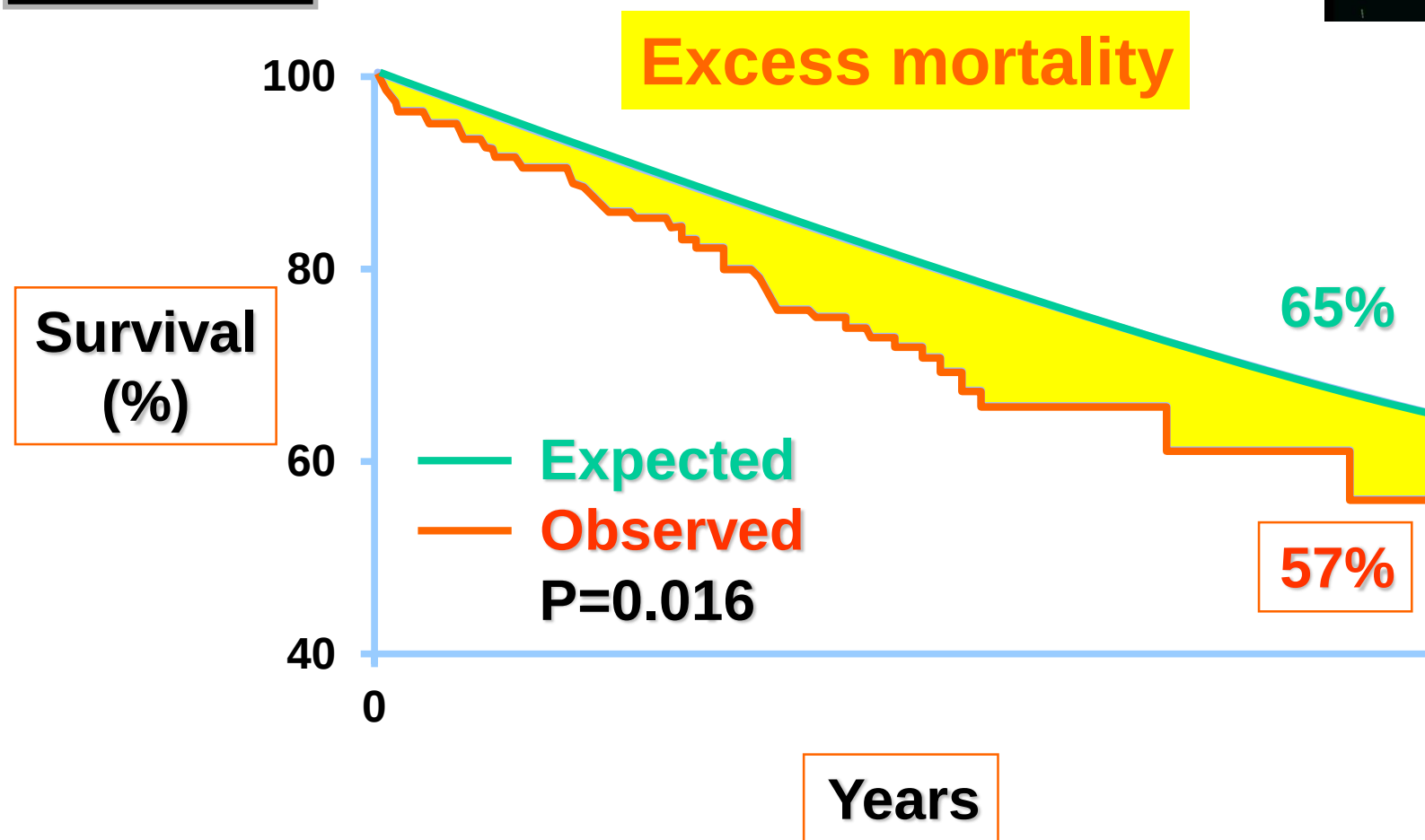


MVP = 70% surgical severe MR
in western countries

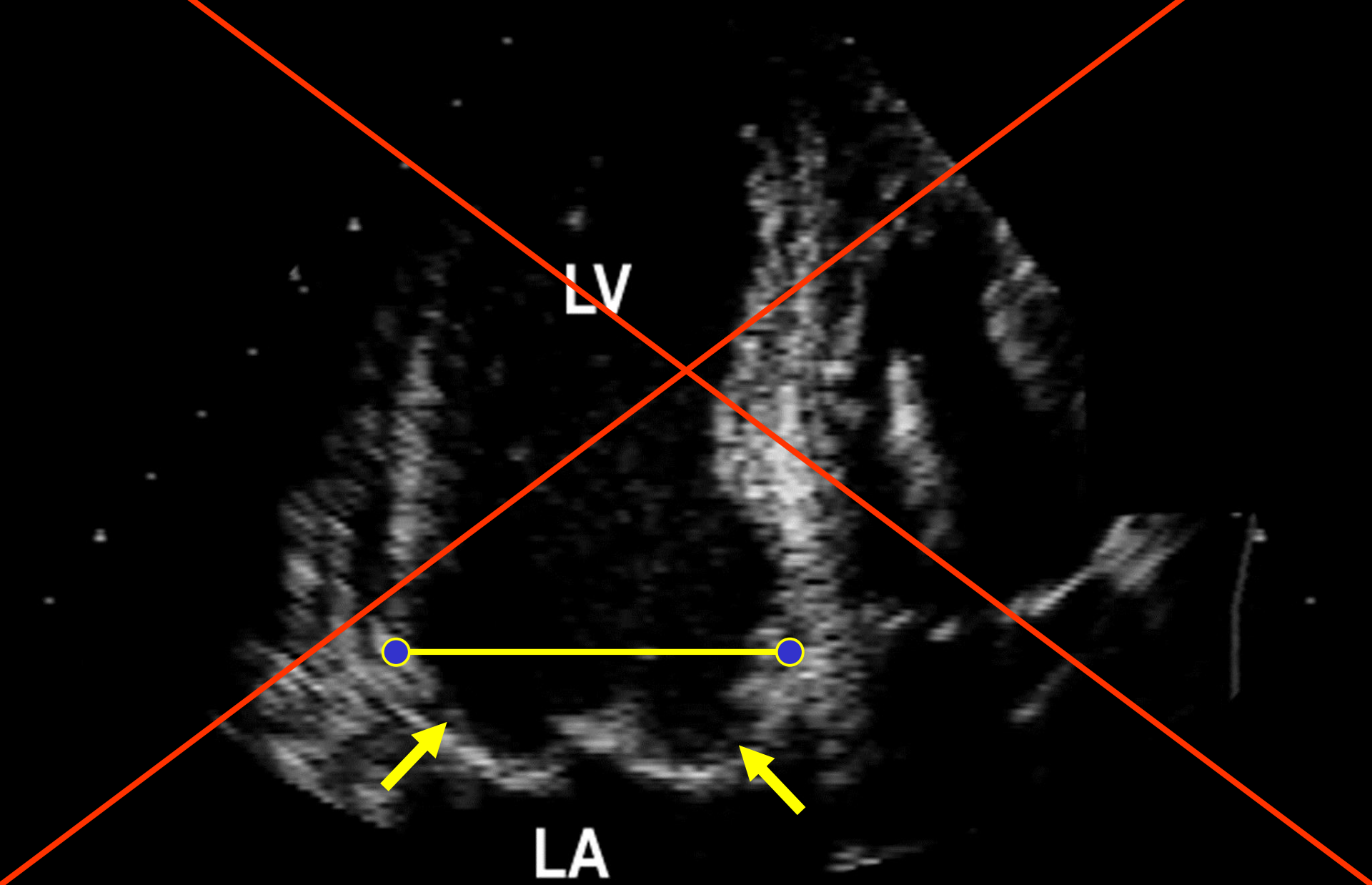


MVP with flail leaflet

Clinical outcome



Changes in Diagnostic criteria



MVP : Four decades of controversy

Outcome

	Series from referral centers (n=1538)	Population-based study (n=84)
Prognosis	Variable, often severe	Benign
Complications (%)	10 to 44	5
Linearized rates of complications (%/year)	1.2 to 6.4	?
Predictor	Mitral thickening	None
Criticism	Outdated criteria Referral bias	Small sample size No FU

MVP: Clinical outcome in the community

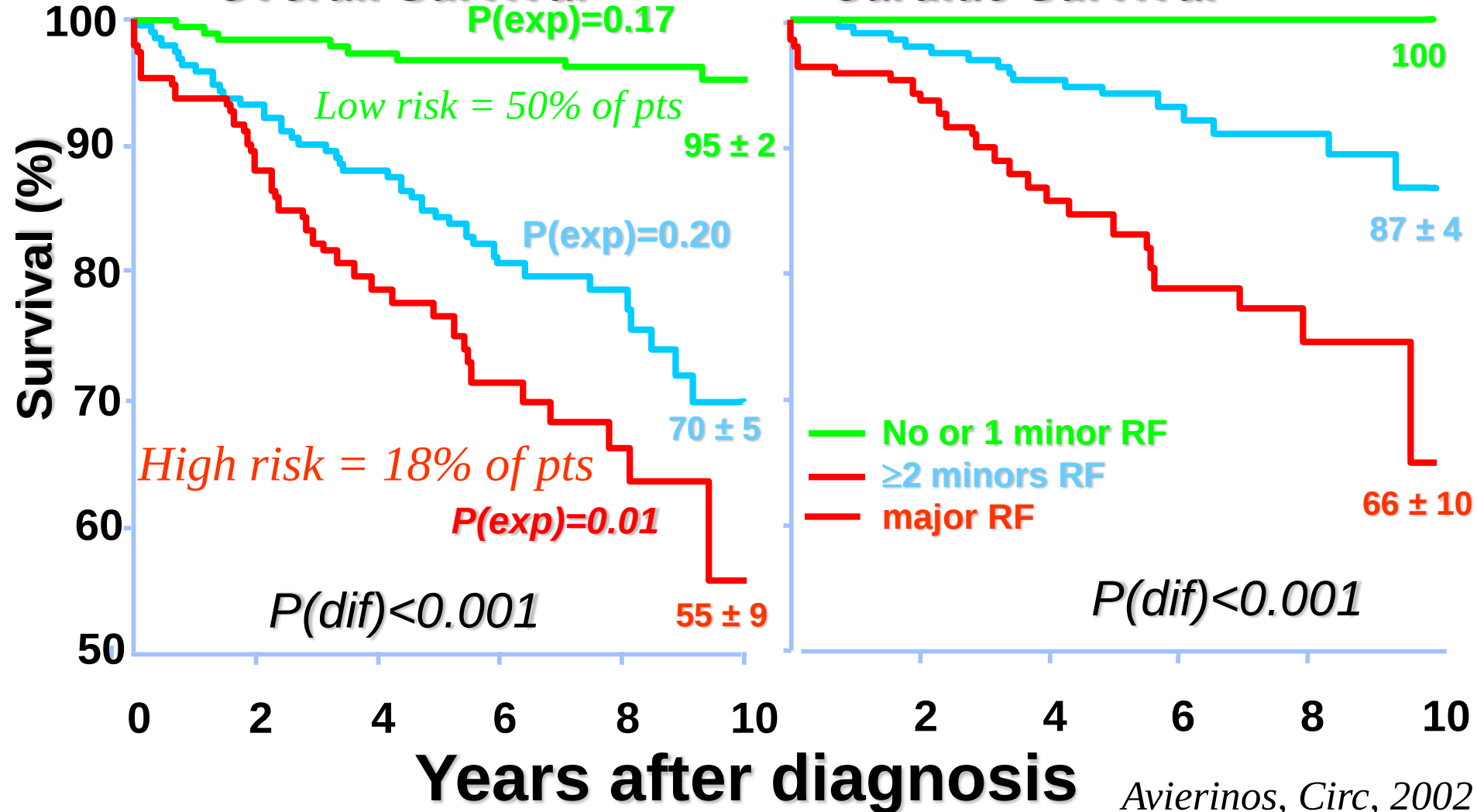
Risk Stratification

833 Community MVP



Overall Survival

Cardiac Survival

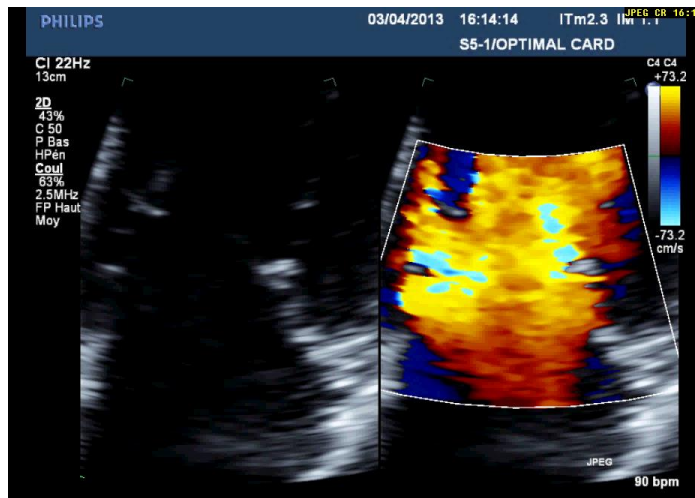


MVP: Clinical outcome in the community

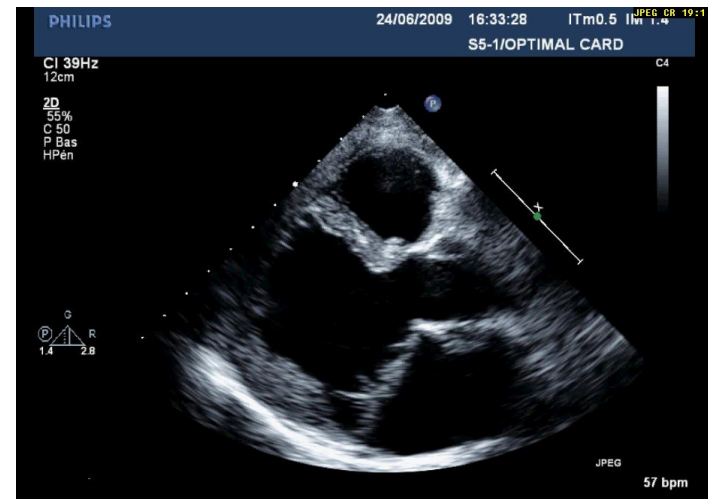
Sudden Death



Does it exist ?



Is it the leak ?



Is it MVP ?

MVP : Sudden Death and severe MR due to Flail Leaflet

348 Flail, 67yo, FU=48±41 months, 99 deaths

25 SD

1.8%/year

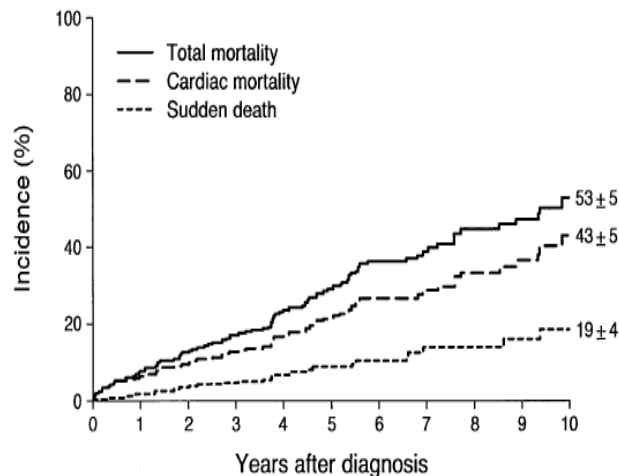
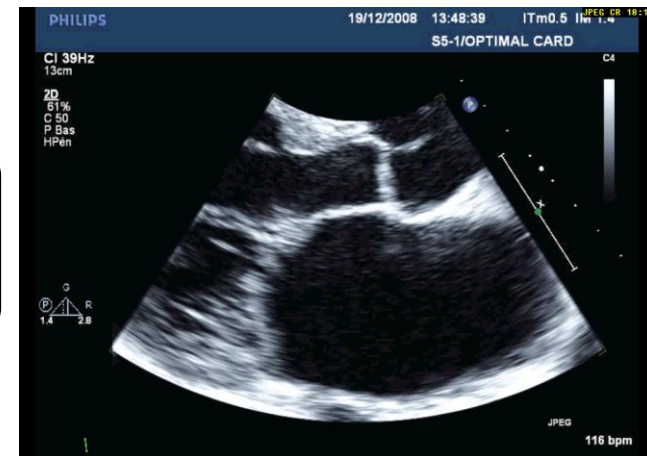
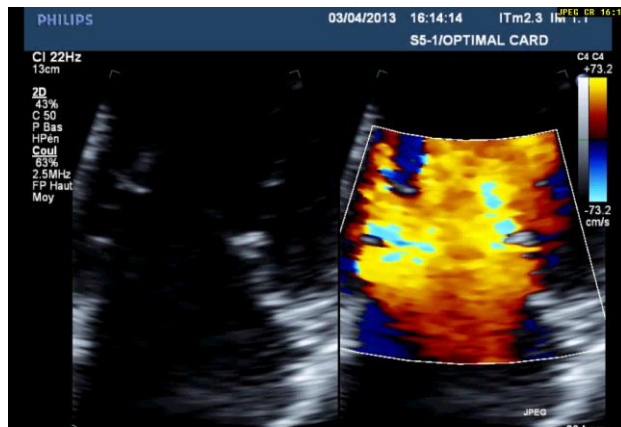
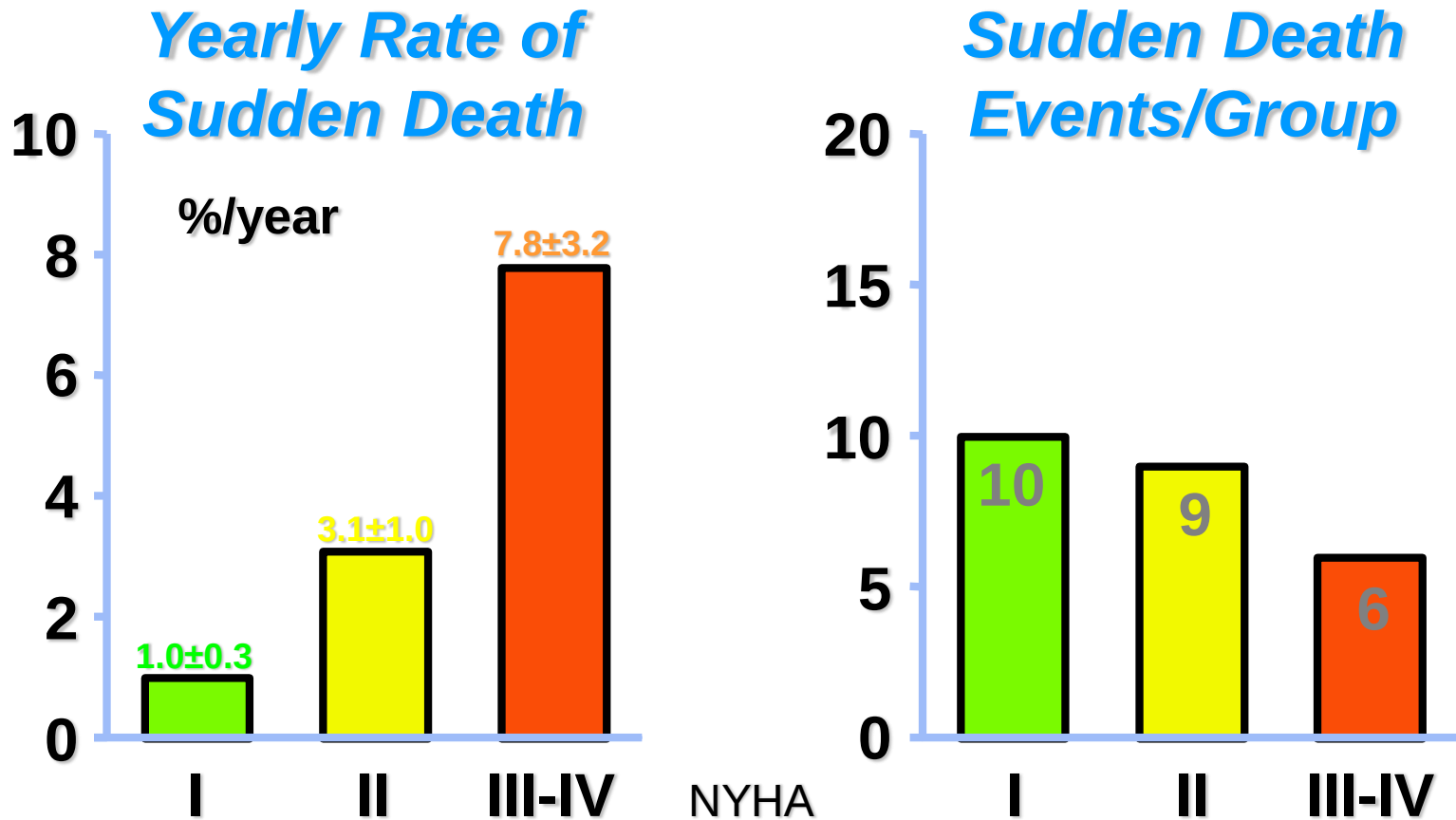


Table 2. Multivariate Predictor of Sudden Death*

	Unit	Risk Ratio	95% CI	p Value
EF (%)	Per percent	0.94	0.91-0.97	0.0001
NYHA functional class	Per class	1.91	1.20-3.04	0.006
AF	Per AF present	2.40	0.97-5.95	0.059

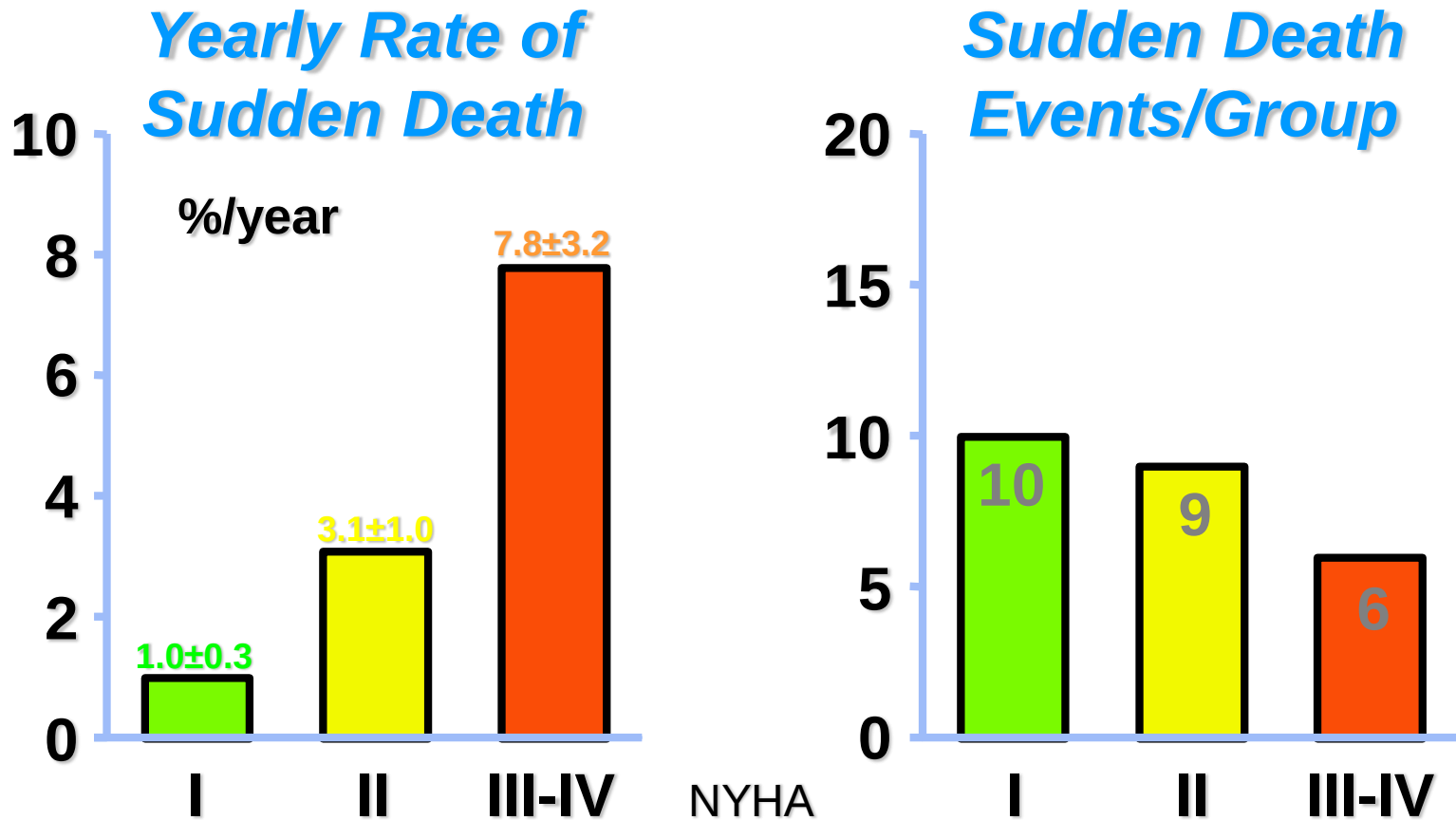
Grigioni, JACC, 1999

MVP : Sudden Death and severe MR due to Flail Leaflet



10 / 25 SD in asymptomatic patients
17 / 25 SD in patients with normal EF

MVP : Sudden Death and severe MR due to Flail Leaflet

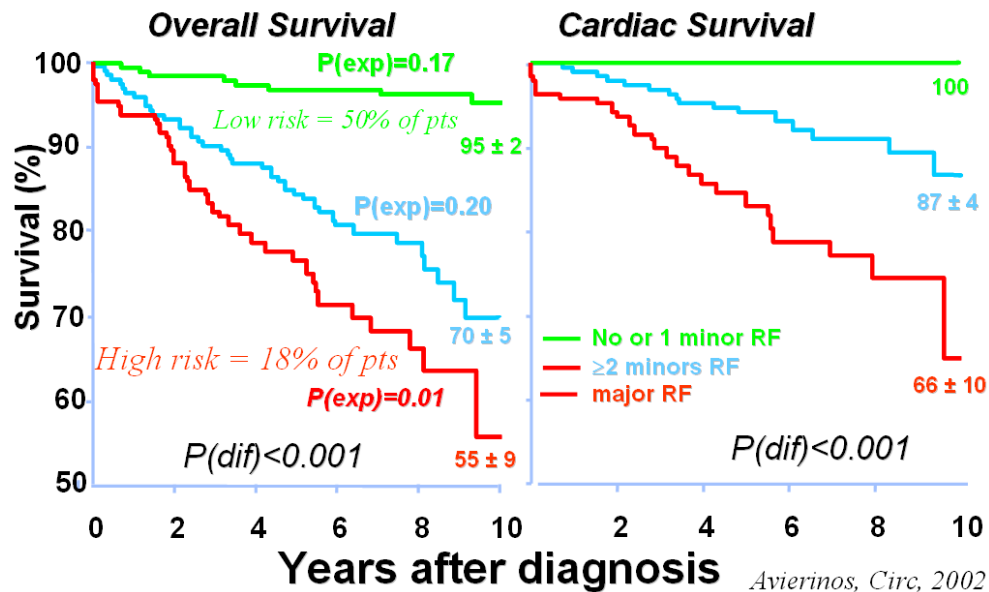
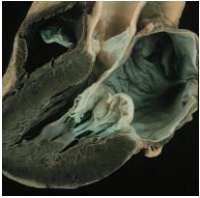


*There is probably more than just
the hemodynamic consequences of MR*

MVP: Clinical outcome in the community

Risk Stratification

833 Community MVP



16 sudden deaths

$3 \pm 0.9\%$ at 10 years

0.35%/year

NS from expected
rates of SD

70% belonging to the low risk group ????

There is more than just MR to explain SD

MVP : Sudden Death without severe MR

1200 Out-of-hospital SD with documented arrhythmia

24 unexplained SD after initial assessment –

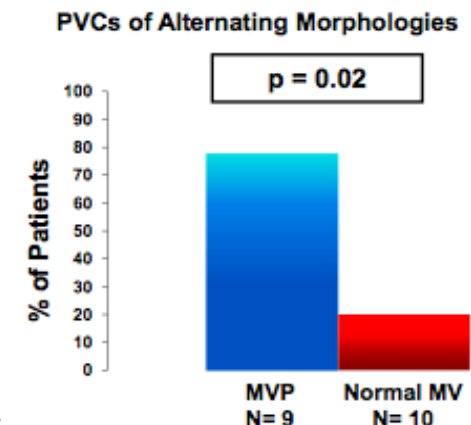
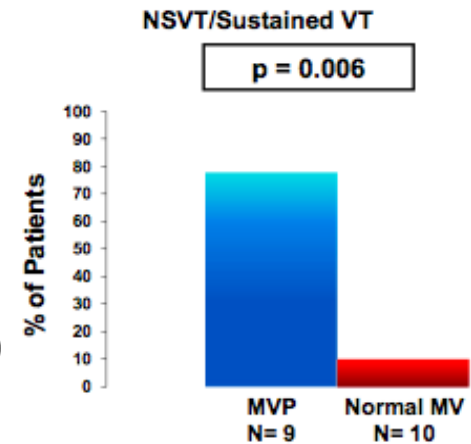
10/24 with MVP - 0.83% of all OH SD; 50% of unexplained SD

* Female (90%)

* Frequent/complex ventricular arrhythmias
(Outflow tract/Papillary Muscles/Fascicular Origin)

* Inverted T waves in inferior leads

* **Bileaflet MVP** (100%)
only 1 with severe MR

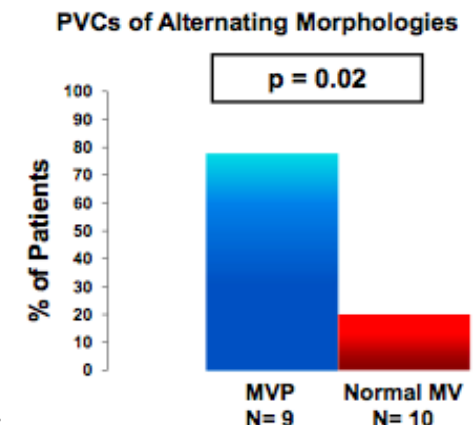
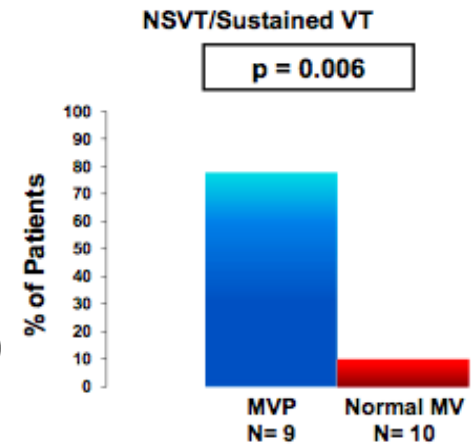


MVP : Sudden Death without severe MR

Malignant MVP ?

- * Female (90%)
- * Frequent/complex ventricular arrhythmias (Outflow tract/Papillary Muscles/Fascicular Origin)
- * Inverted T waves in inferior leads

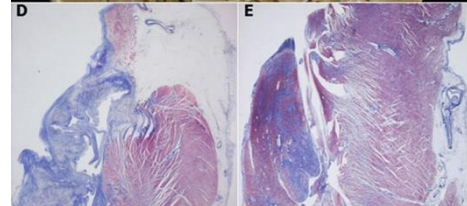
* **Bileaflet MVP** (100%)
only 1 with severe MR



MVP : Sudden Death without severe MR : impact of fibrosis

650 SD with autopsy (North Italy), 43 with isolated MVP
(MVP=7% of all SD)

- 60% females, 32 yo, 21% with BBLOCKERS
- 70% with Bileaflet MVP
- 100% with replacement-type fibrosis
 - at PM level
 - & 90% under posterior leaflet



MVP : Sudden Death without severe MR ; impact of fibrosis

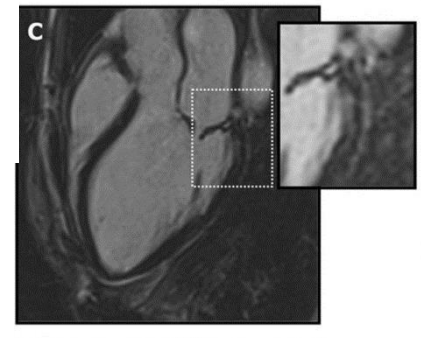
30 MVP alive patients with complex arrhythmia
(VF & VT, including 2 resuscitated SD)

* 73% **Female**, 41 yo

* 70% with **Bileaflet MVP**

* 93% with MRI **Late Gadolinium Enhancement** at PM level and under post leaflet

Arrhythmic MVP ?

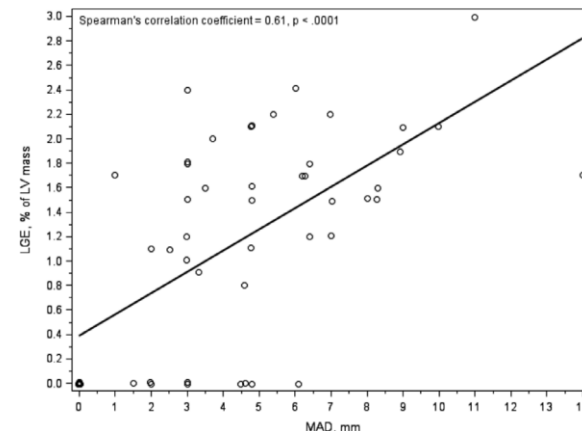
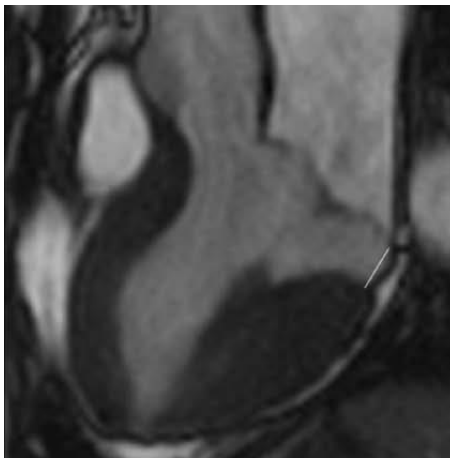


MVP : Sudden Death without severe MR: origin of Fibrosis

36 arrhythmic MVP with no or mild MR + LGE
(27females, 44yo)

Vs. 16 MVP without LGE (6females, 40 yo)

Annulus disjunction correlates with Fibrosis

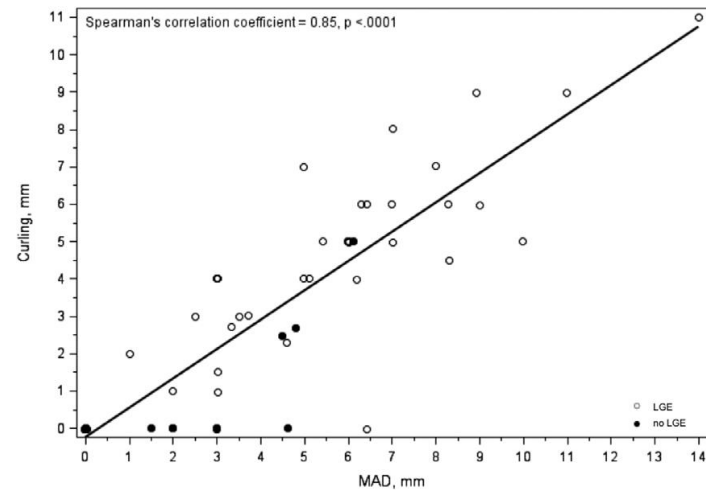
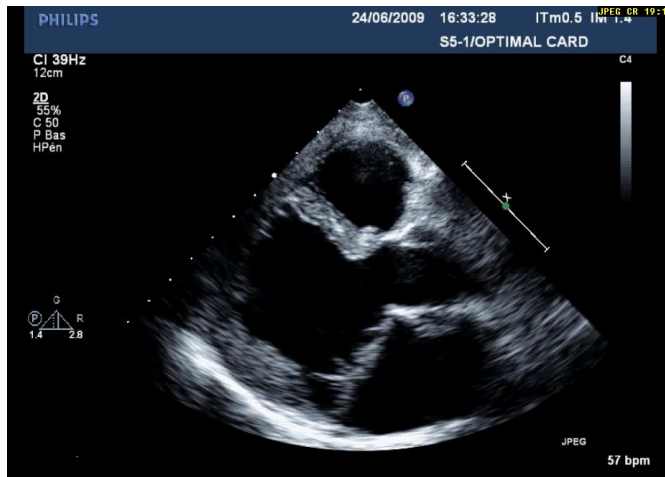


MVP : Sudden Death without severe MR: origin of Fibrosis

36 arrhythmic MVP with no or mild MR + LGE
(27females, 44yo)

Vs. 16 MVP without LGE (6females, 40 yo)

Annulus curling correlates with MAD & Fibrosis

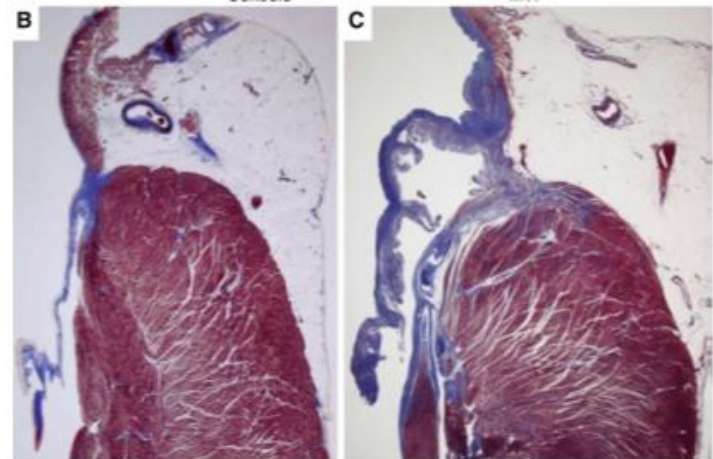


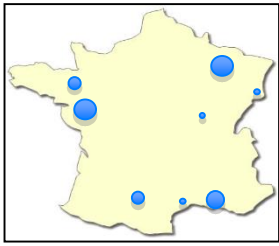
MVP : Sudden Death without severe MR: origin of Fibrosis

36 arrhythmic MVP with no or mild MR + LGE
(27females, 44yo)

Vs. 16 MVP without LGE (6females, 40 yo)

MAD creates curling which creates fibrosis





MVP : Sudden Death



- **Multi-center Case-control study** (8 french academic centers + Mayo Clinic)
- **Inclusion Criteria**
 - ICD for Secondary Prevention after idiopathic aborted cardiac arrest
 - MVP: only abnormality found after initial assessment
- **MVP with SUD vs. matched MVP without SUD**

42 Patients with MVP and SUD
Ventricular Fibrillation in all

Frequency Matched

1:2

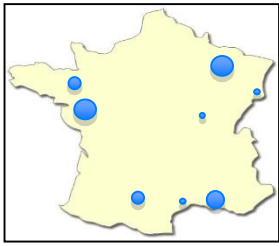


84 Controls
with MVP Alive at Last Follow up

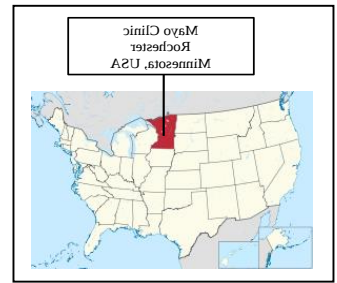


Matched for Age, sex, **MR**, Afib and EF

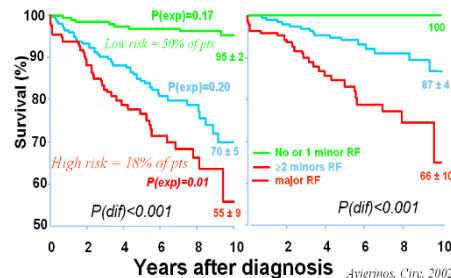
Hourdain, Enriquez Sarano...



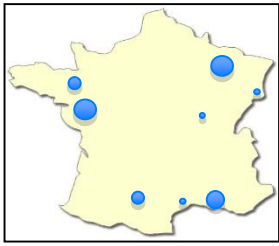
MVP : Sudden Death



	Sudden Death patients (n=42)	Control patients (n=84)	P
Gender, Female, n	28	56	1
Age, years	53.36±14.4 44 at SD	53.88±14.2	0.85
LVEF, %	62.2±5.2	62.2±5.0	0.98
Mitral Regurgitation, n (%)			1
1: None or trivial	8	16	
2: Mild or Mild-Moderate	29	58	
3: Moderate or Moderate-Severe	3	6	
4: Severe	2	4	
History of Atrial Fibrillation, n	7*	15	1



Most SUD patients belong to the low risk group !!!



MVP : Sudden Death

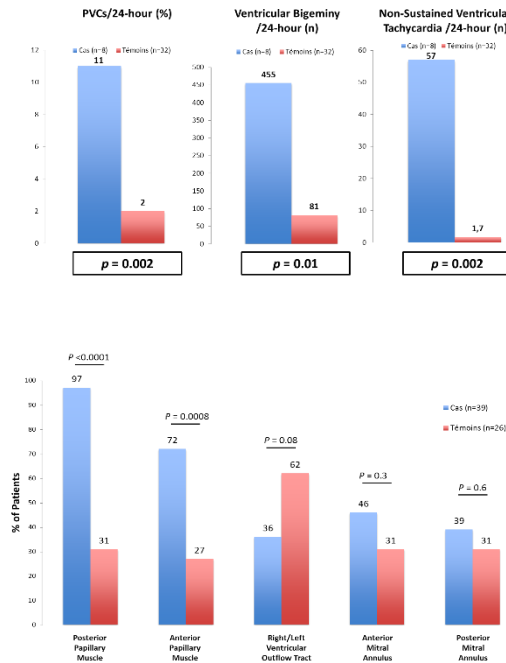


Cases vs. Controls

Clinical

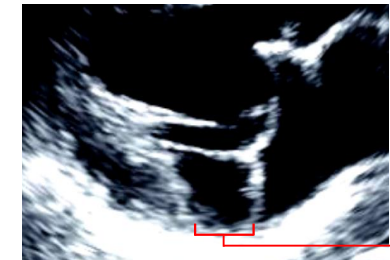
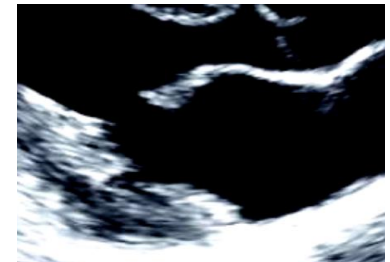
- Syncope (60%)
- Pre syncope (95%)
- Family Hx of SUD

ECG

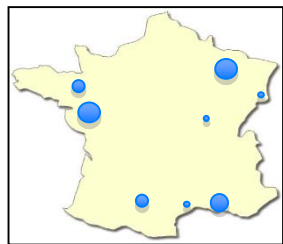


Echo

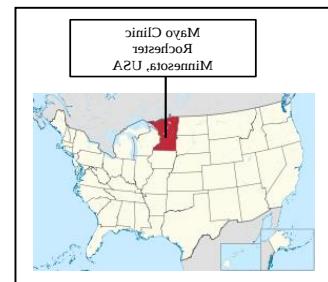
↑ LVED; ↑ LVES



Hourdain, Enriquez Sarano...



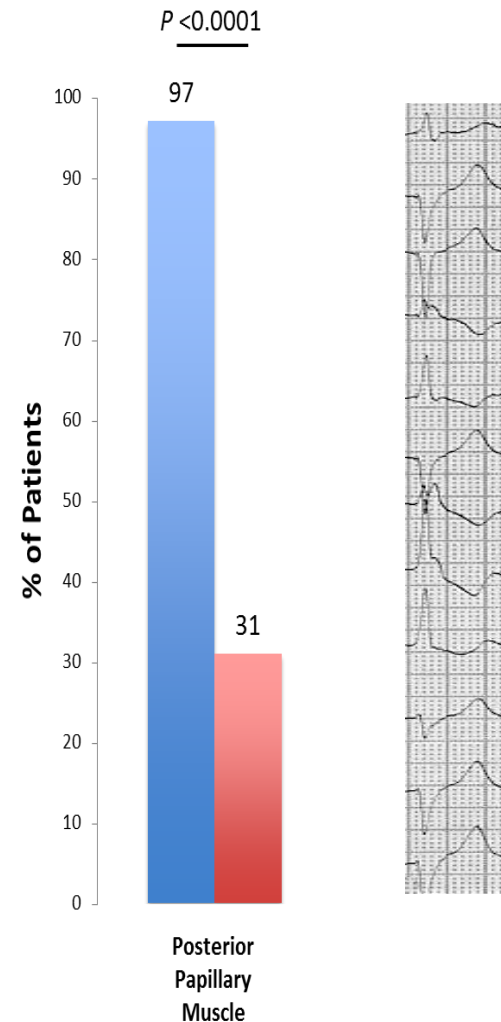
MVP : Sudden Death Determinants



- Past History of Syncope
- % of Posterior PM PVCs
- Severe Myxomatous Disease



Mitral Annulus Disjunction



Hourdain, Enriquez Sarano...

Conclusion

MVP: benign or malignant ?

- * Heterogeneous, not uniformly benign or malignant
- * A same diagnosis for different diseases:
single vs. bileaflets, flail vs. no flail, non thickened vs. severe myxomatous changes, no MR vs. severe MR
- * Most complications driven by severe MR and its consequences on LA and LV
- * Small subset at risk of Sudden Death despite no MR

Conclusion

MVP: Sudden Death Risk Profile

* Clinical :

Young females, Syncope, palpitations, familial history of SD

* Electrocardiographic:

Complex and frequent ventricular arrhythmia from posterior papillary Muscle

* Echocardiographic:

Thickened bileaflet MVP, annulus disjunction, curling

Potential role of mechanical traction by deep MVP on PPM generating **localized fibrosis**

Conclusion

MVP: proposed pathway for SD in MVP

