Hémodynamique :

Physiologie normale
Conséquences de la Stimulation Conventionnelle

Frédéric Anselme

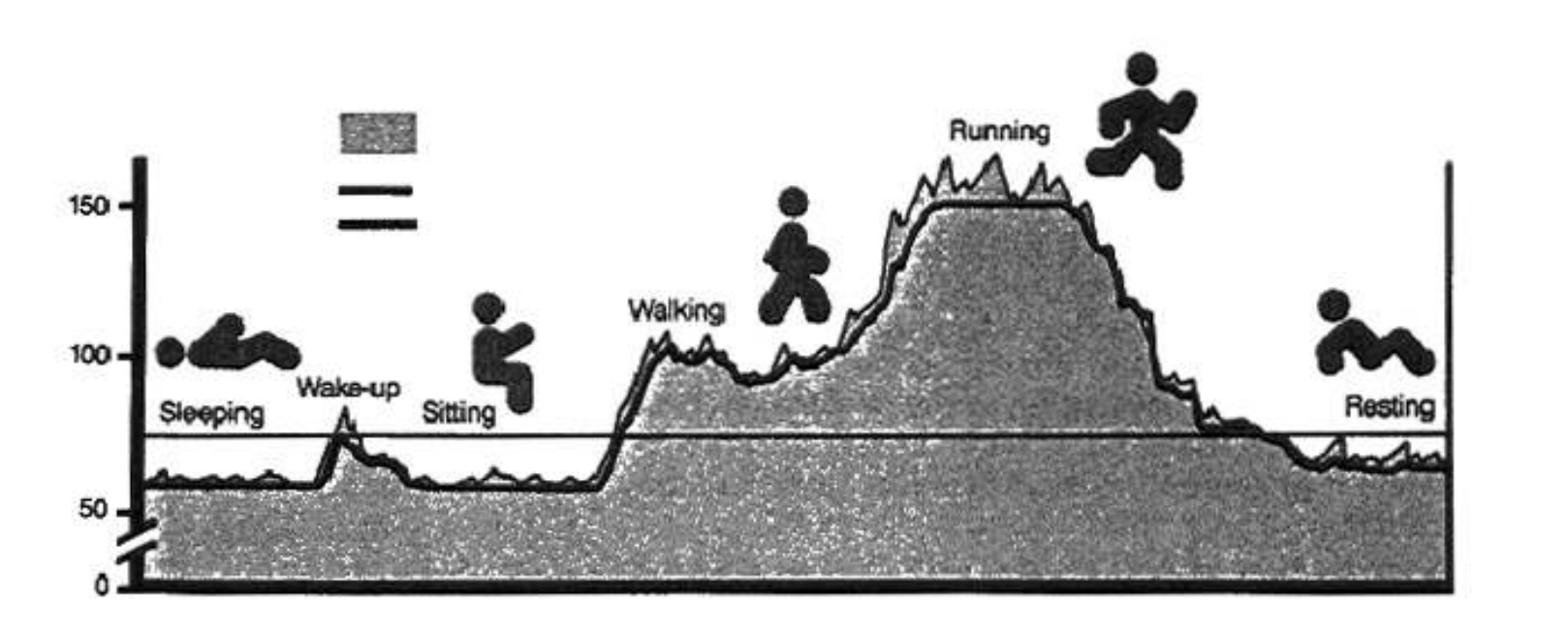
Éléments contribuant à l'hémodynamique cardiaque

QC = VES X FC

• Fréquence cardiaque	⟷	• Asservissement
• Systole auriculaire	⟷	• Mode de stimulation
• Synchronisme auriculo-ventriculaire	⟷	• Délai AV optimal
• Fonction ventriculaire syst. et diast.	⟷	• La stimulation V

A l'effort

- La réserve de VE systolique rend compte de 50% de l'augmentation du débit cardiaque
- La réserve en fréquence cardiaque peut permettre de tripler le débit cardiaque



Effets Hémodynamiques de la Systole Auriculaire

- Ventricular preload and filling
- Inotropism

In the adult at rest, an average of 20% of the stroke volume is caused by atrial contraction

Facteurs modifiants le rôle de la systole Atriale

- Age: atrial contribution increases with age
- Functional status of the atrium (dilatation)
- Physical exercise: up to 30% of stroke volume

  but rate acceleration plays a major role
- Atrioventricular delay: «optimal » AV delay
- LV systolic function:+++ if LV dysfunction
- LV relaxation and compliance (hypertrophy)

Synchronisme AV

« PACEMAKER SYNDROME »

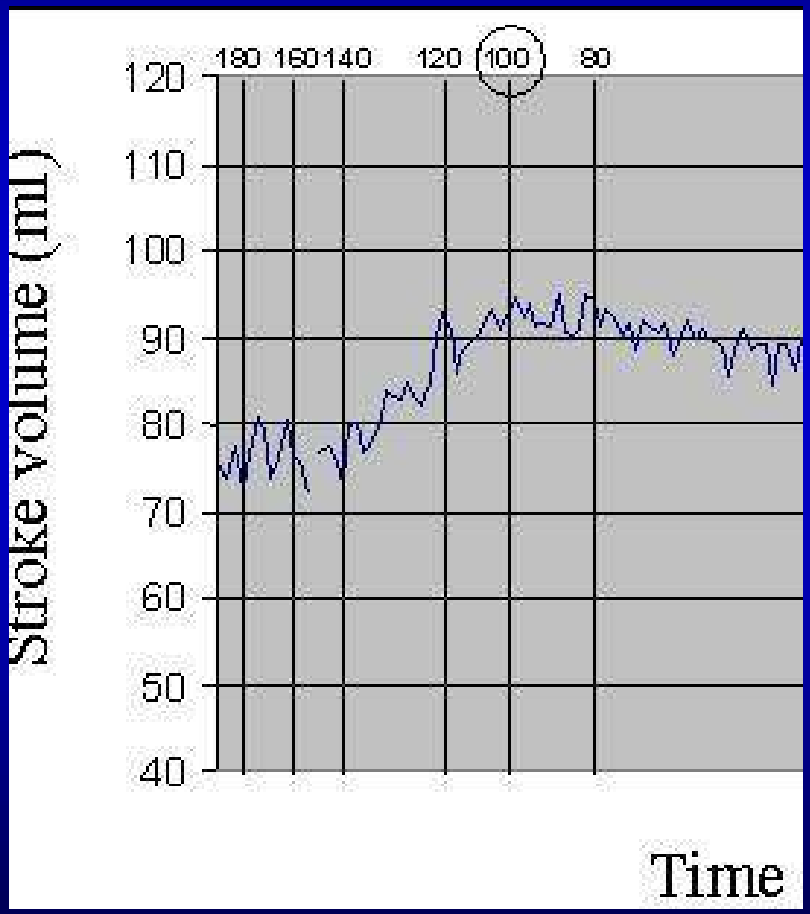
- Definition: presence of suggestive signs and/or symptoms associated with AV dyssynchrony (atrial contraction against closed A-V valves)
- Diagnosis: requires a high degree of suspicion and a willingness to evaluate patient 's complaints
- Exclusion of pacing system dysfunction
- Correlation symptoms - cardiac rhythm
- Incidence: 5-15% up to 70% depending on the diagnostic criteria

- May occur with ventricular (VVI / VVI-R) pacing and lack of AV sequential filling
- Symptoms usually resolve with a dual chamber (DDD / DDD-R / VDD) pacing system and appropriate AV delay

« PACEMAKER SYNDROME SYMPTOMS

- **Mild:** venous pulsation in neck, fatigue, tiredness, palpitations, vertigo, cough
- **Moderate:** chest pain, dizziness, dyspnea, headaches, confusion
- **Severe:** presyncope, syncope

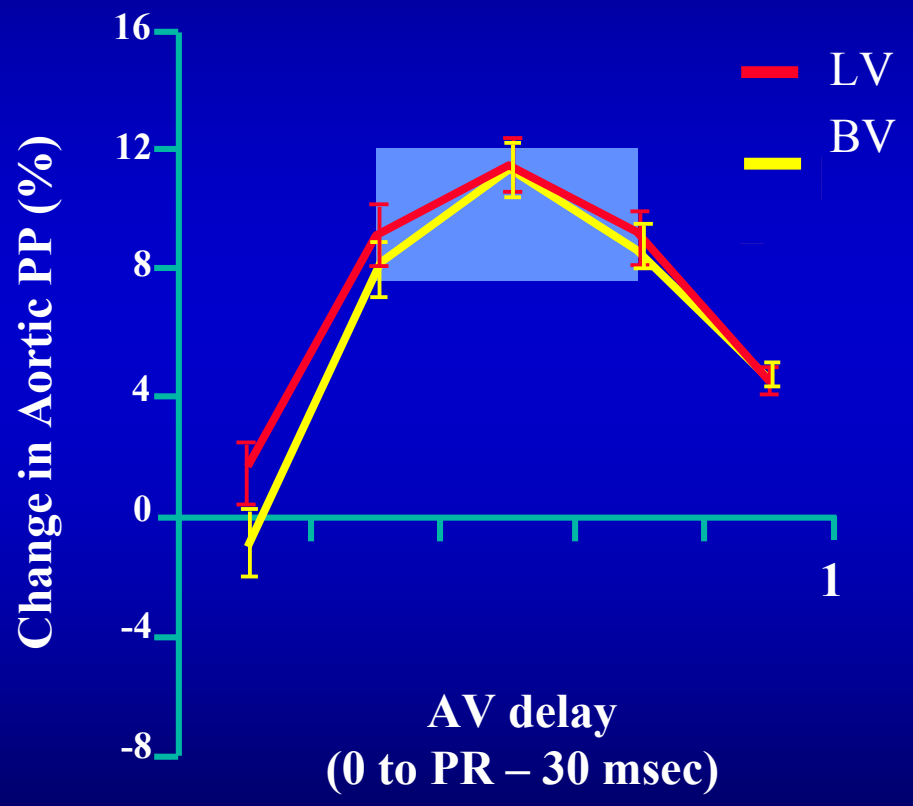
AV interval optimization

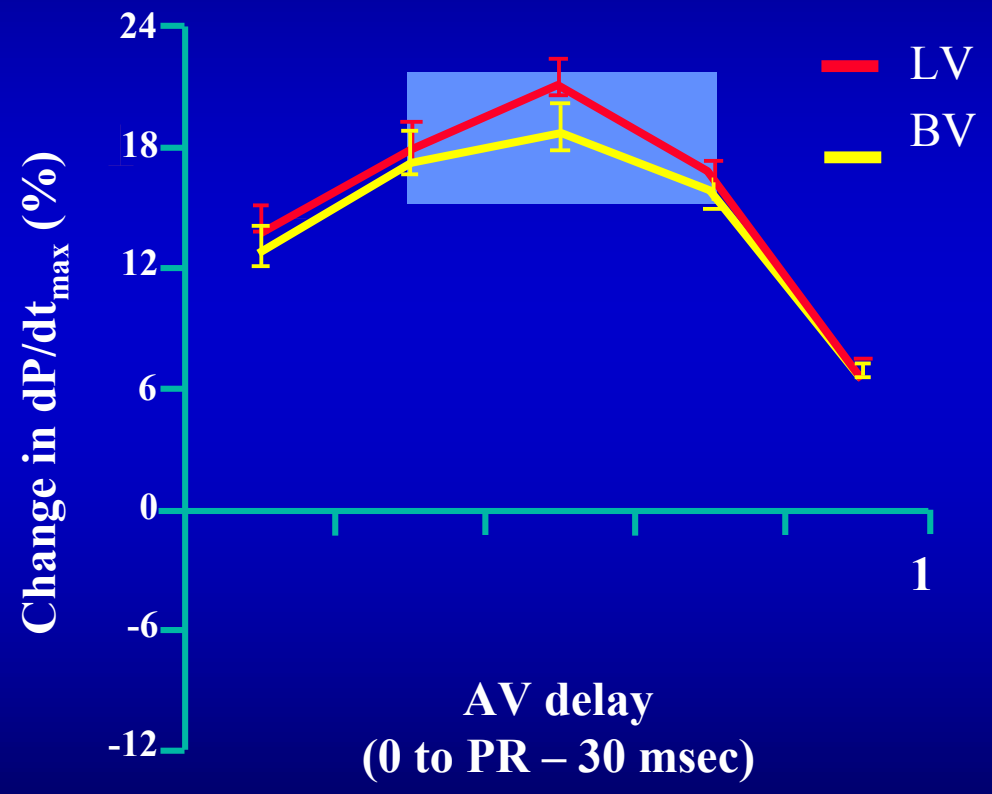


Stroke volume by bio-impedance measurement

Synchronisme AV

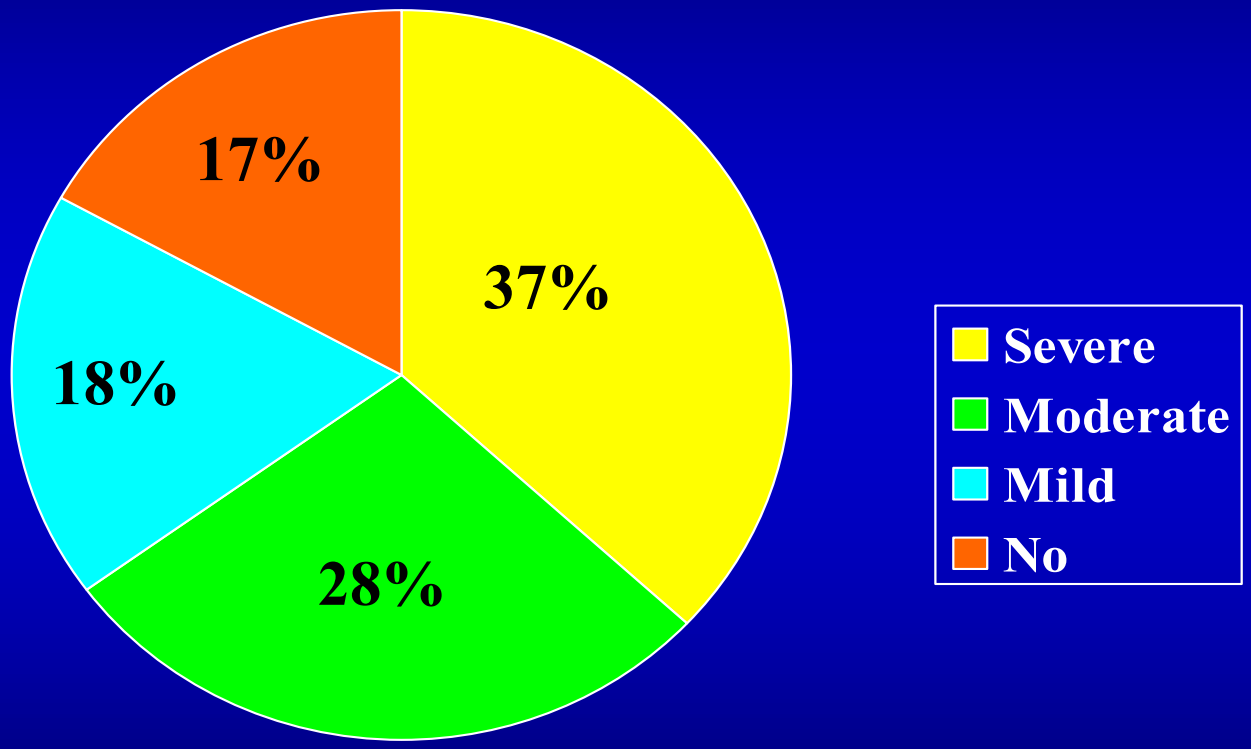
AV Interval Optimization





Adapted from Auricchio A, et al. Circulation. 1999;99:2993-3001.

PACEMAKER SYNDROME



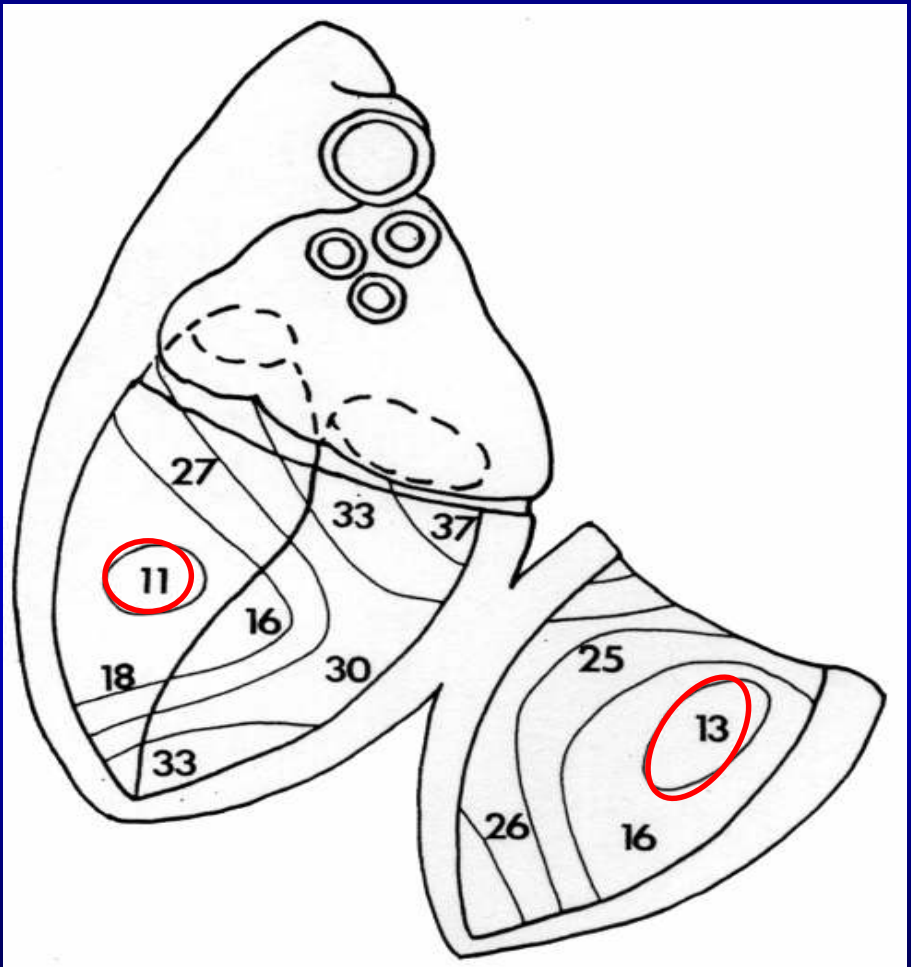
N= 40 pts

From Heldman, PACE,1990

La fonction Ventriculaire

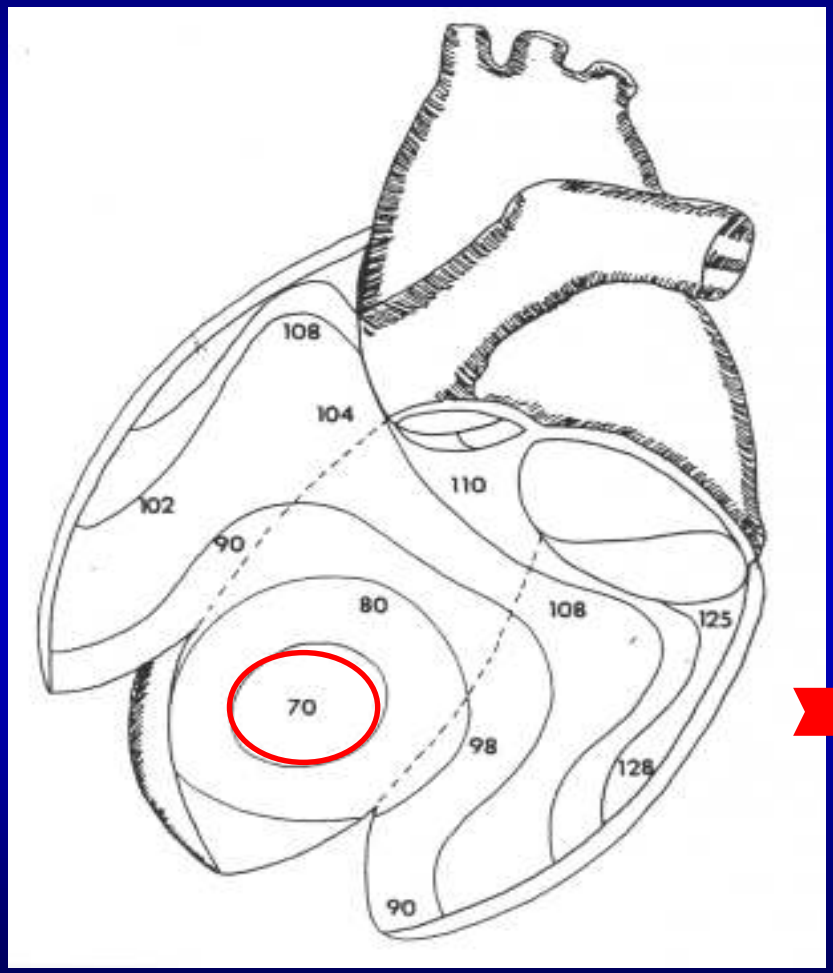
Physiologie normale

Rythme sinusal



Cassidy DM, et al. Circ 1984;70:37-42

Conséquences Électrique de la stimulation apicale VD



- **Single break-out location on LV endocardium**
  - Similar to left bundle branch block
- **Latest activation**
  - Similar to intrinsic : Infero-posterior base

Augmentation du temps d'activation VG : asynchronisme

Vassallo JA, et al. JACC 1986;7:1228-33

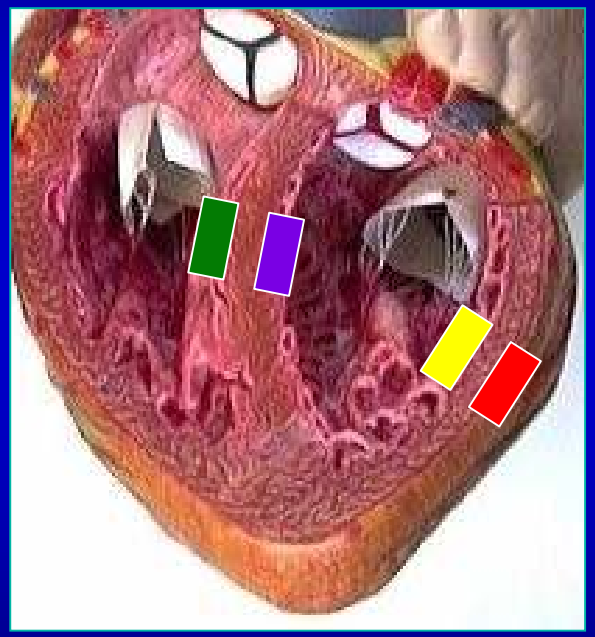
Effet délétère de la stimulation apicale VD: « From cell to bedside »

- Conséquences moléculaire
- Conséquences histologique
- Conséquences myocardique
- Conséquences fonctionnelles sur le VG
- Conséquences cliniques

Conséquences Moléculaires

- Experimental HF models
- Western blot of inner and outer myocardial layers from LV septum and lateral free wall

➡ Regional protein expression



Septum - RV

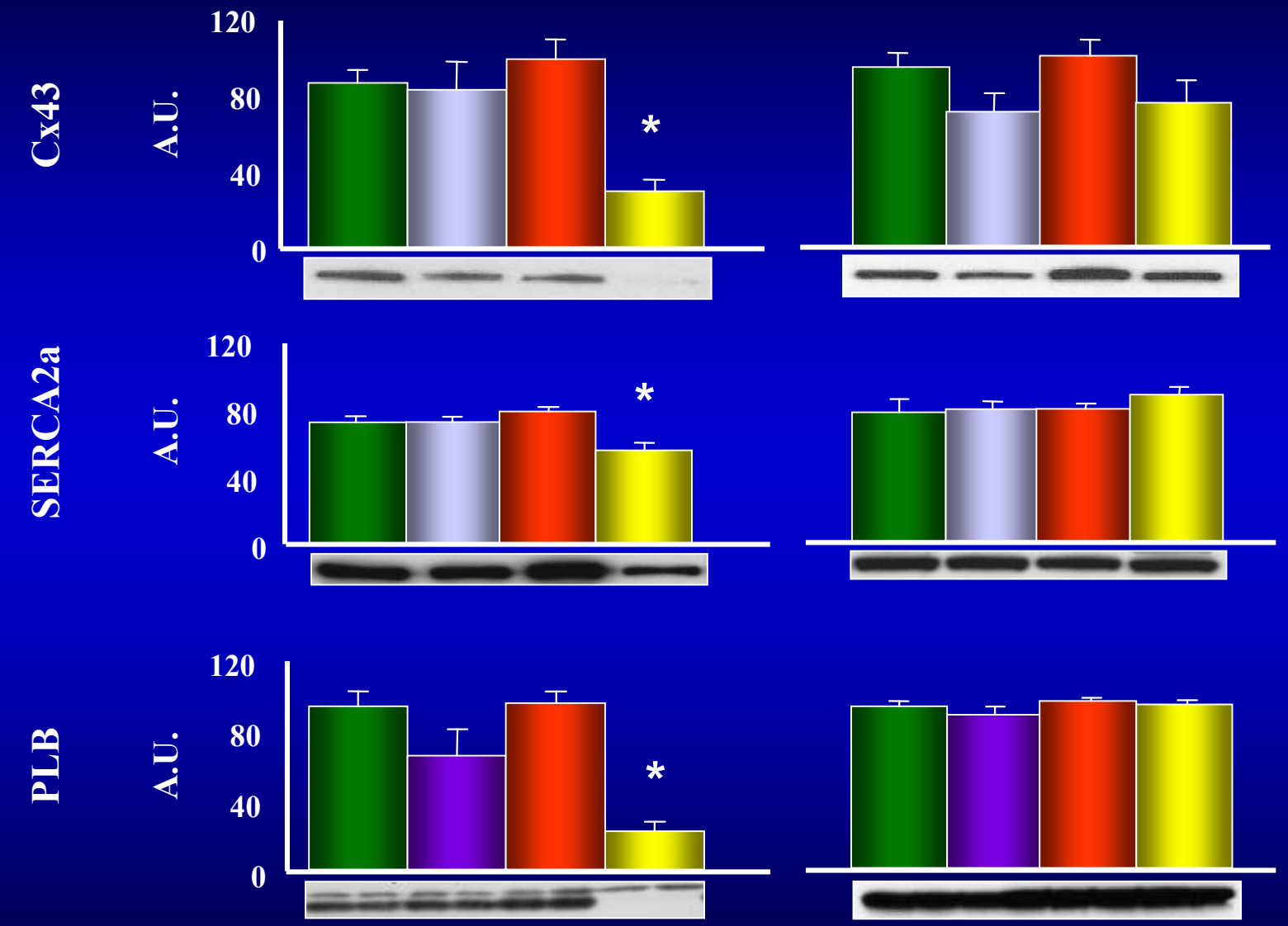
Septum - LV

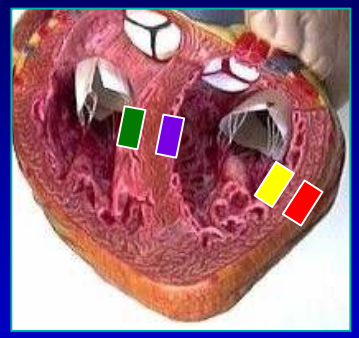
Lateral Epi.

Lateral Endo.

Spragg, Leclercq, Kass et al Circulation 2003;108:929-32

Altération de l'Expression Protéinique Régionale





Sep - RV

Sep - LV

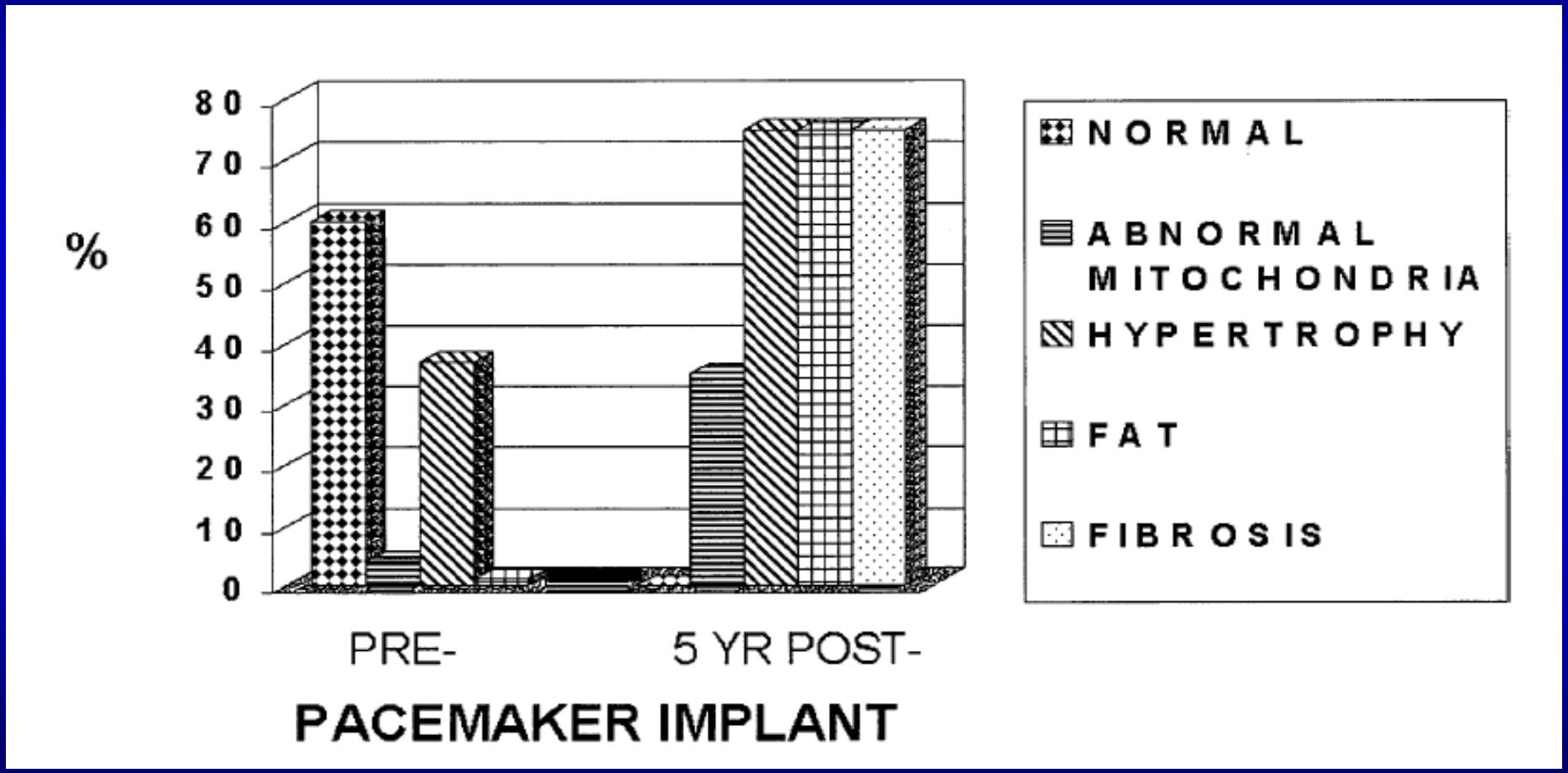
Lat Epi.

LatEndo.

* $p < 0.02$ v. all other segments

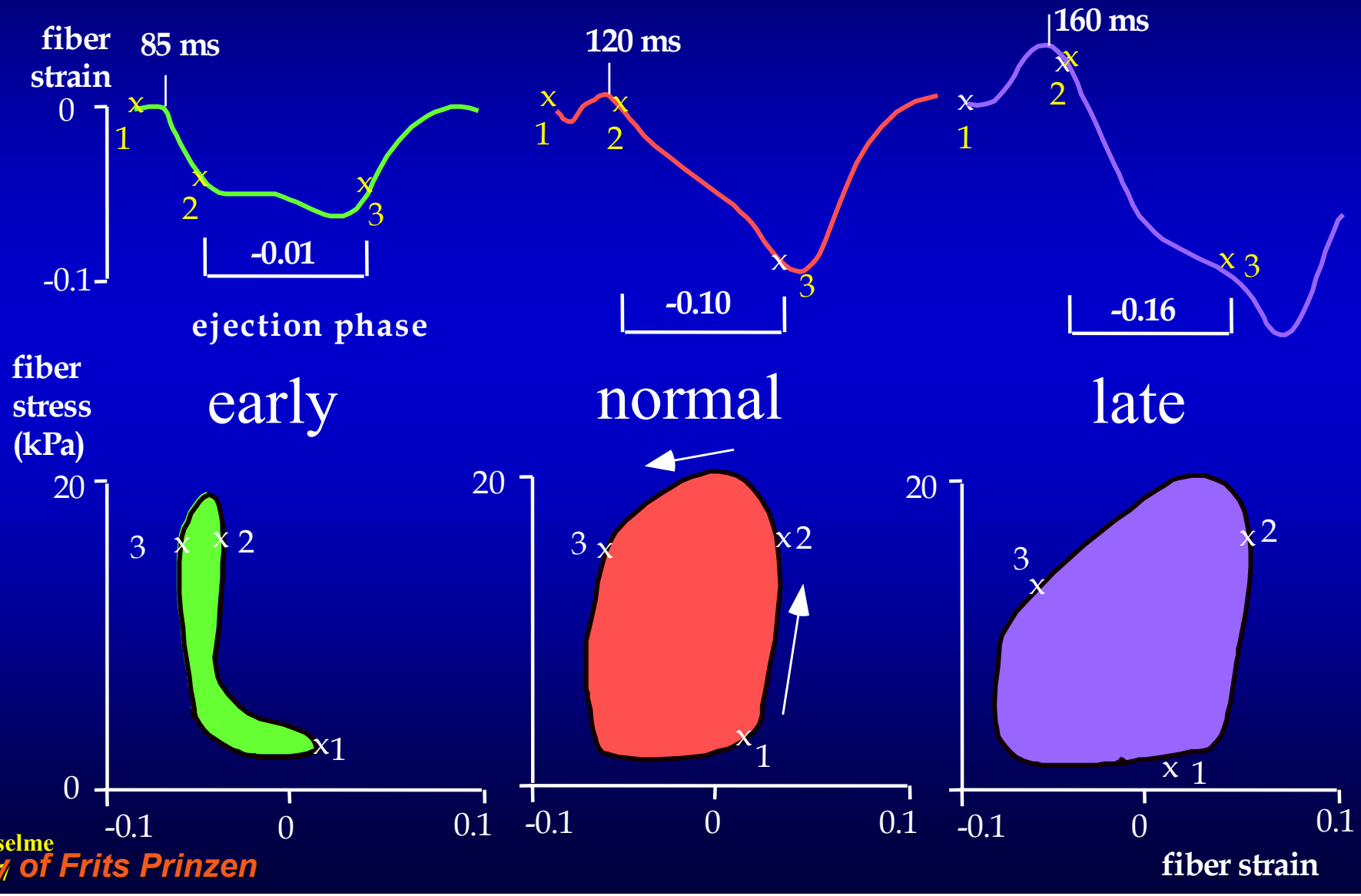
Frédéric Anselme
DIU 2007

Conséquences Histologiques



Karpawich. PACE 2004;27: 844-9

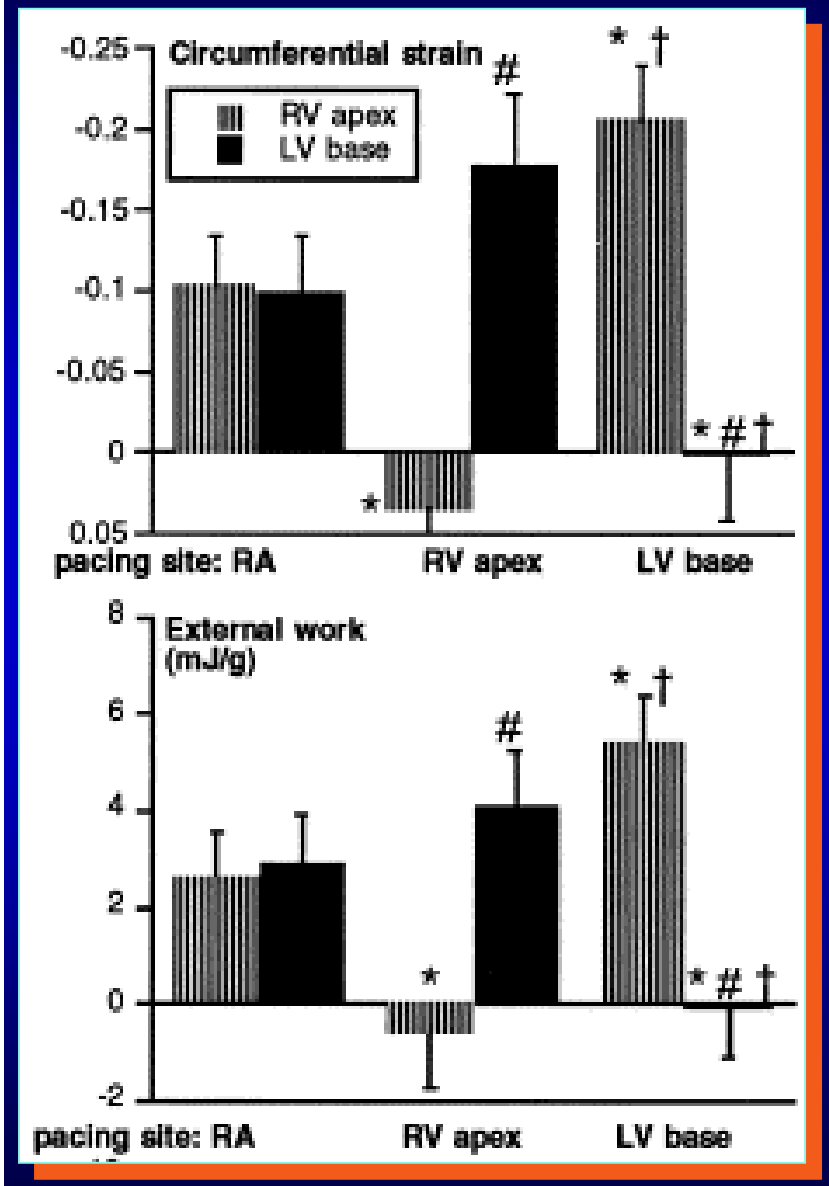
Regional wall motion with pacing-induced dyssynchrony



Frédéric Anselme

Courtesy of Frits Prinzen

VP Alters regional myocardial work



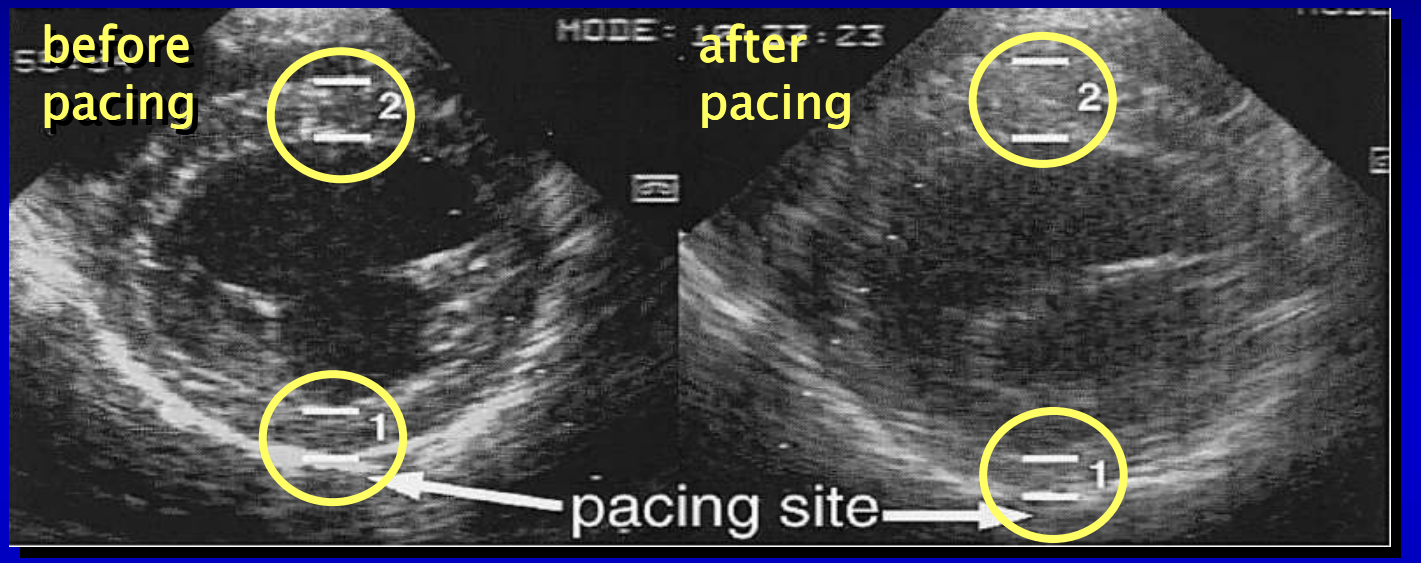
- High spatial and temporal resolution magnetic resonance-tagged images performed in 12 anesthetized dogs during RA, RVA, LV base pacing

- Systolic fiber strain and external work:
  - = O in regions near the pacing site
  - = twice the normal value at regions remote from the pacing site

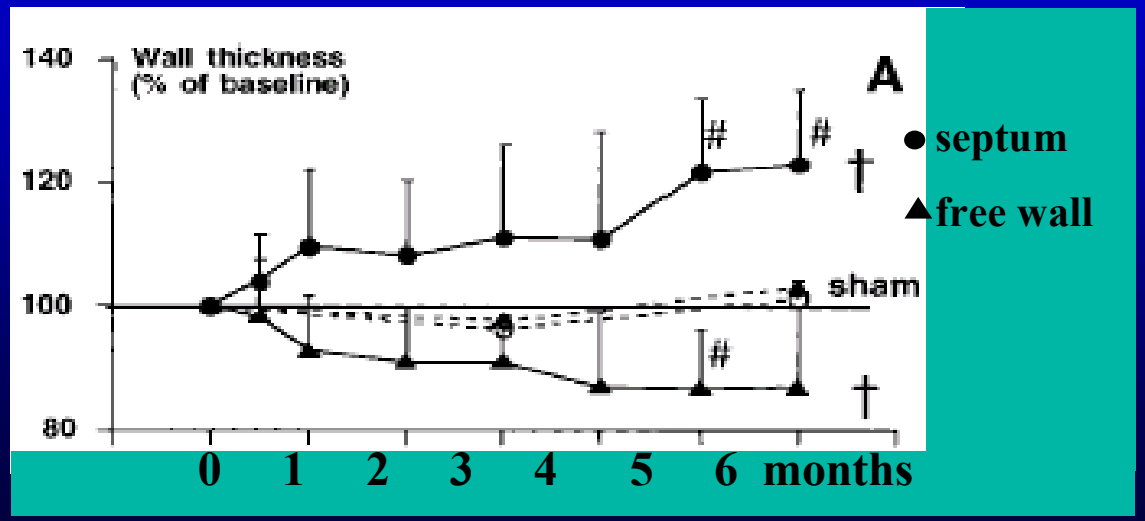
Prinzen FW, et al. JACC 1999;33:1735-42

Conséquences myocardiques: anatomiques

8 mongrel dogs paced at LV free wall for 6 months (5 controls)



- early activated regions 17% thinner
- late activated septum 23% thicker
- myocyte diameter 18% larger in septum than free wall



van Oosterhout et al., Circulation 1998

Conséquences myocardiques: Altération de la perfusion

- 43 pts with complete AV Block and DDDR pacing

- High Incidence of Myoc. Perf. Defects On Th. 201 Exercise Scinti.: 28 pts (65%)

- Radionucleotide Ventriculography

- inferior: 78%
- Apical: 67%
- septum: 21%
- anterior: 7%
- lateral: 3%

} 19% of significant CAD on Coronary Angio.

Overall: LVEF: 52.4±10.8%; Regional WM abnormalities: 63%

	Pts with perfusion defect	Pts without perfusion defect	
LVEF	48.5 ± 9.9%	59.6 ± 8.9%	p<0.001
Reg. WM Abn.	73%	33%	p=0.007
Duration of Pacing	43.9 ± 49.7 mths	20.1 ± 9.8 mth	p=0.05

- Regional myocardial defects, WM abnormalities more pronounced as pacing duration increases

Tse HF, et al. JACC 1997:29:744-9

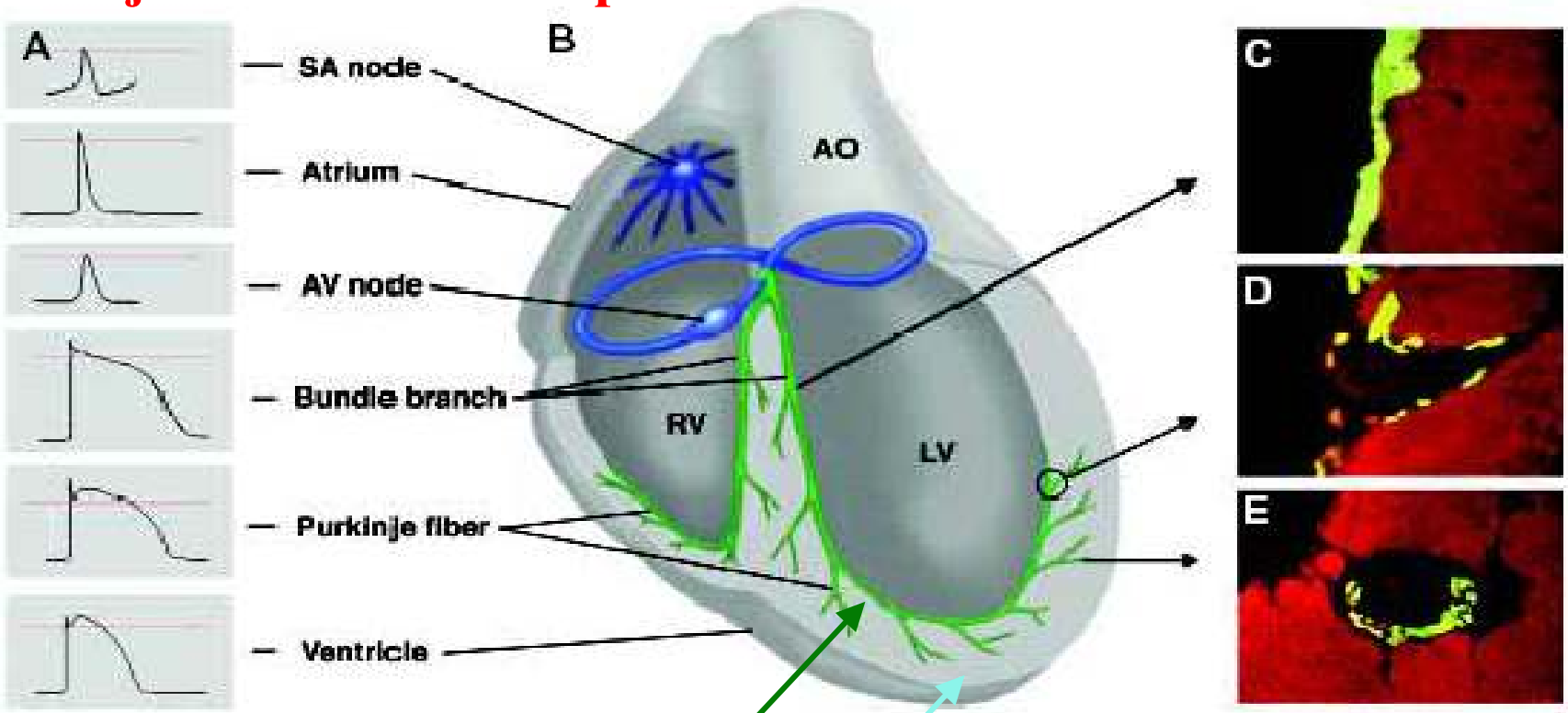
Conséquences Fonctionnelles : Altération de la performance VG

- **Wiggers (1925): Various epicardial pacing sites (dogs)**
  - "The initial rise of intraventricular pressure is prolonged, isometric contraction phase is lengthened, the gradient is not so steep, the pressure maximum is lower, and the duration of systole is increased."
  - Conclusion : The site of stimulation exerts a considerable influence on LV function and the degree of impairment is inversely related to the proximity of the stimulation site to the His-Purkinje system

- **Lister (1964)**
  - Greater reduction in cardiac output when pacing from ventricular sites associated with longest total activation time → muscle conduction
    - » **Conduction velocity differences**
      - **Purkinje = 2-4 m/s**
      - **Muscle = 0.2-1 m/s**

The Purkinje System

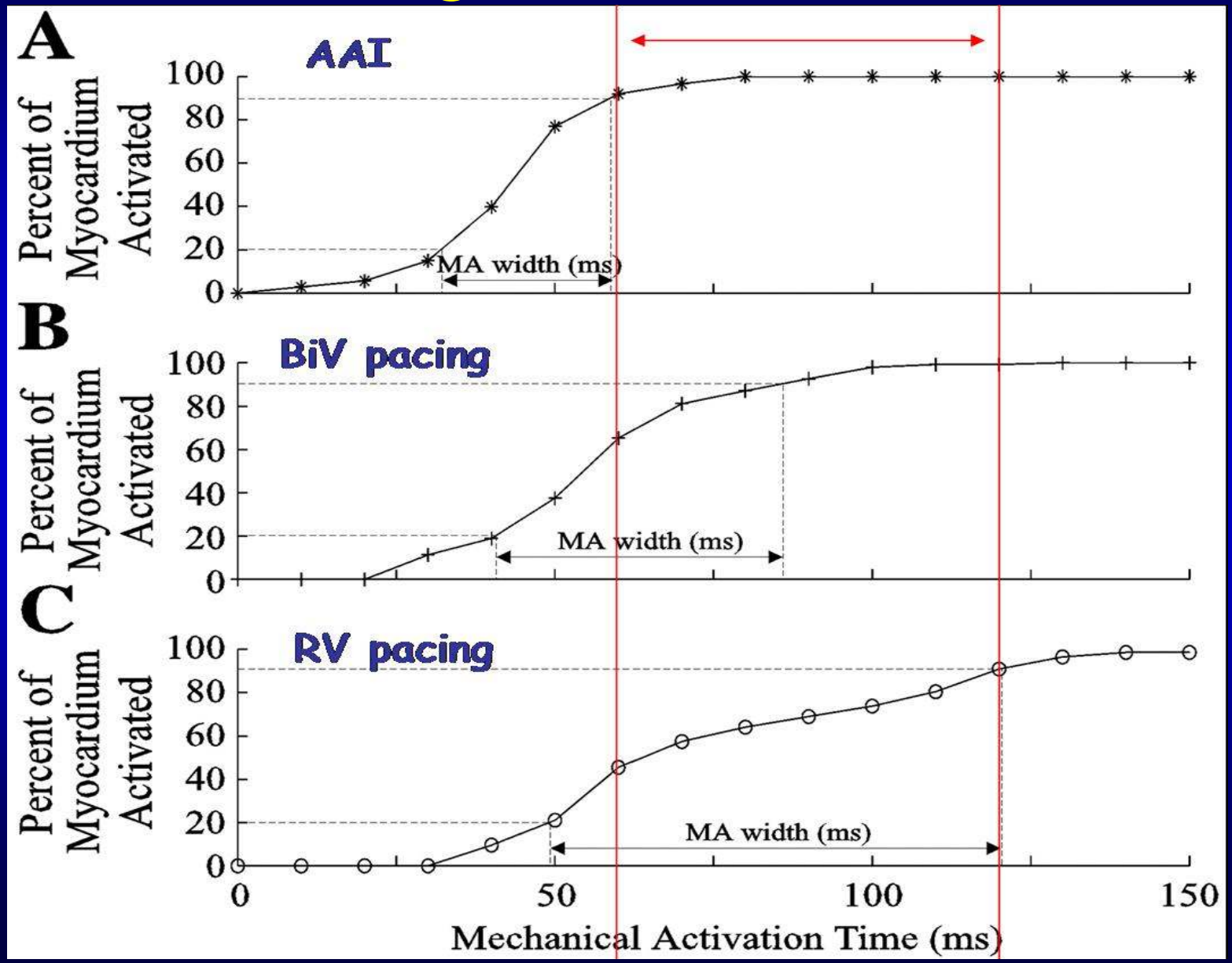
Purkinje fibers allow a rapid ventricular activation



Conduction velocity : 3-4 m/s

Conduction velocity : 0,3-1 m/s

By-pass the “normal” conduction system : => lengthens activation time



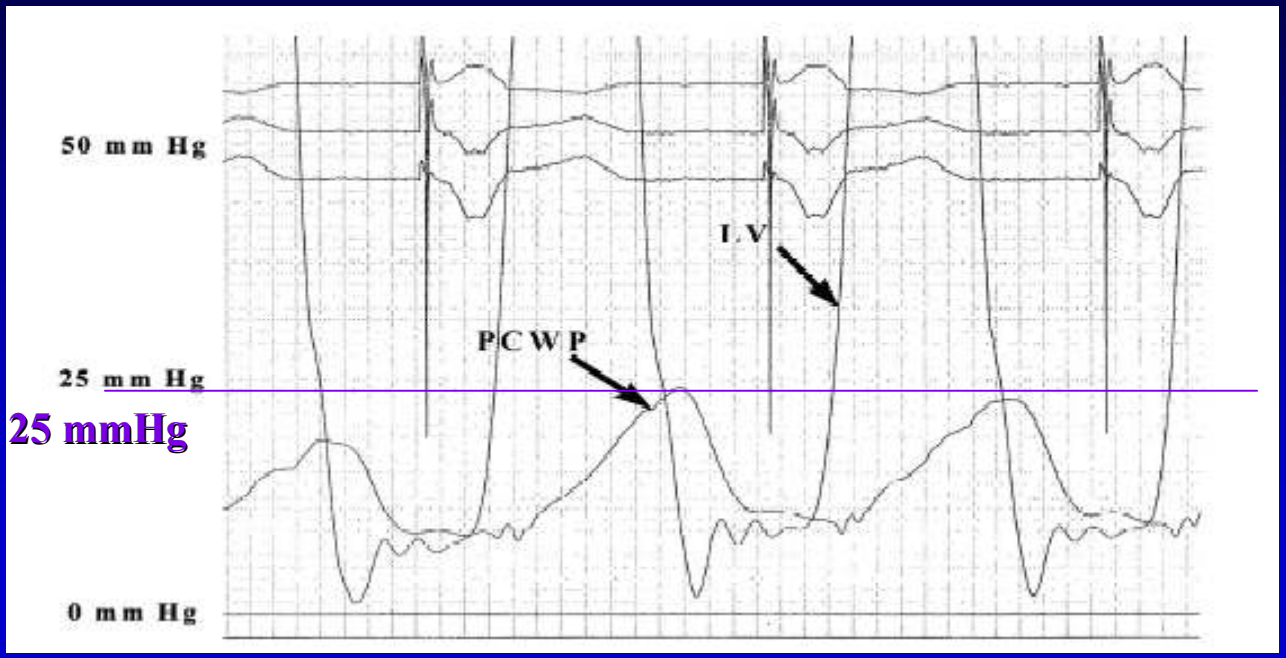
Frédéric Anselme
DIU 2007

MR increases after AV node ablation and PM implant

- Le Tourneau T, et al. *Heart* 1996;76:457
- Cannan CR, et al. PACE 1997;20:735-8
- Hanna SR, et al. Worsening of mitral regurgitation secondary to ventricular pacing. *J Heart Valve Dis*. 2000;9:273-5
- Nunez A, et al. PACE 2002;25:226-30

RV apical pacing worsens MR

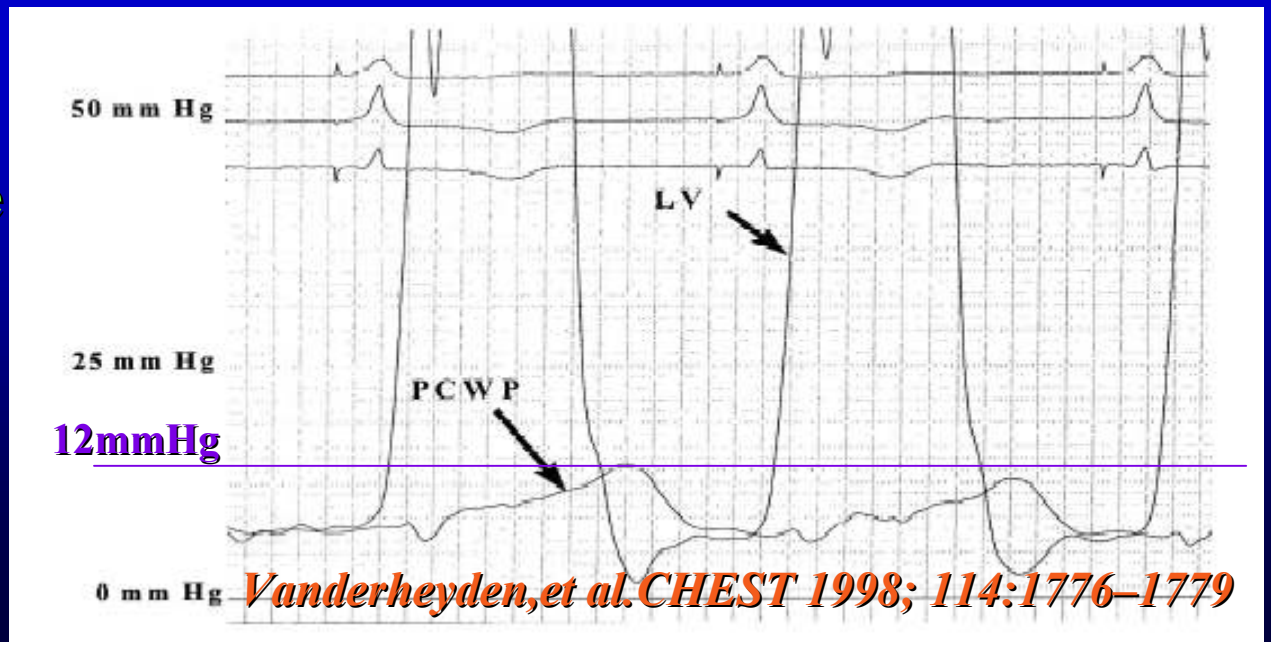
RV apical pacing



MR jet area
14.5 cm2

PCWP
25 mm Hg

His-bundle pacing

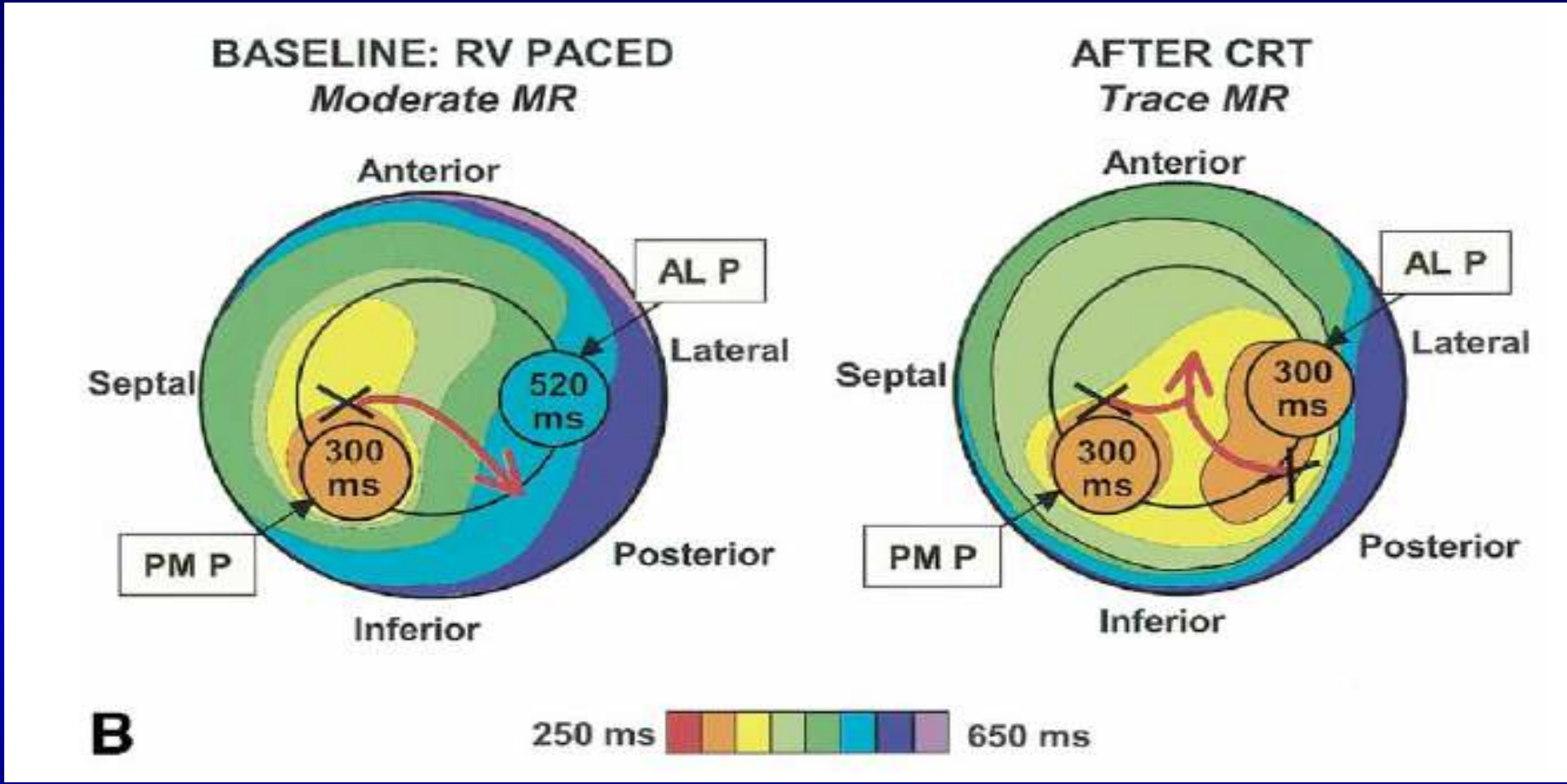


MR jet area
7.7 cm2

PCWP
12 mmHg

Vanderheyden,et al.CHEST 1998; 114:1776–1779

CRT reduces MR : Strain mechanical activation maps in the "bull's eye" projection

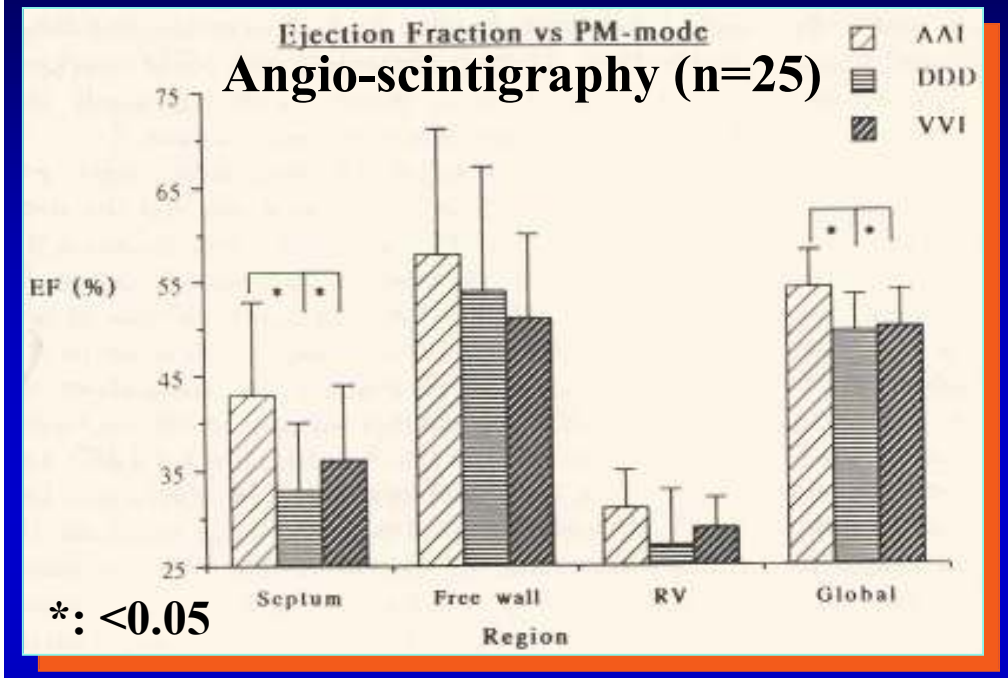


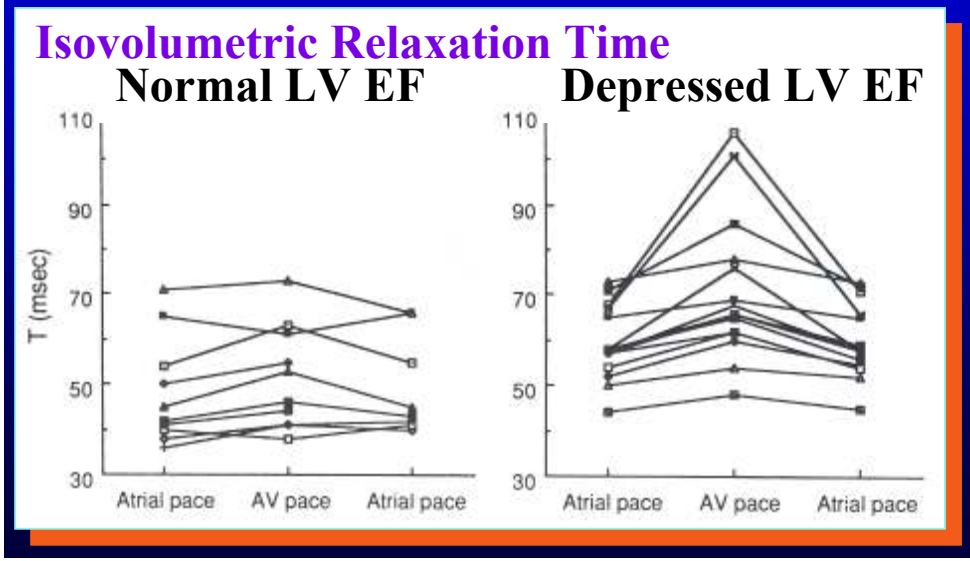
X = lead placement; ↗ = direction of the propagating activation

Decrease in papillary muscle time delay → decreased MR

Kanzaki et al. JACC 2004; 44: 1619-25

RV Pacing Alters Global LV function

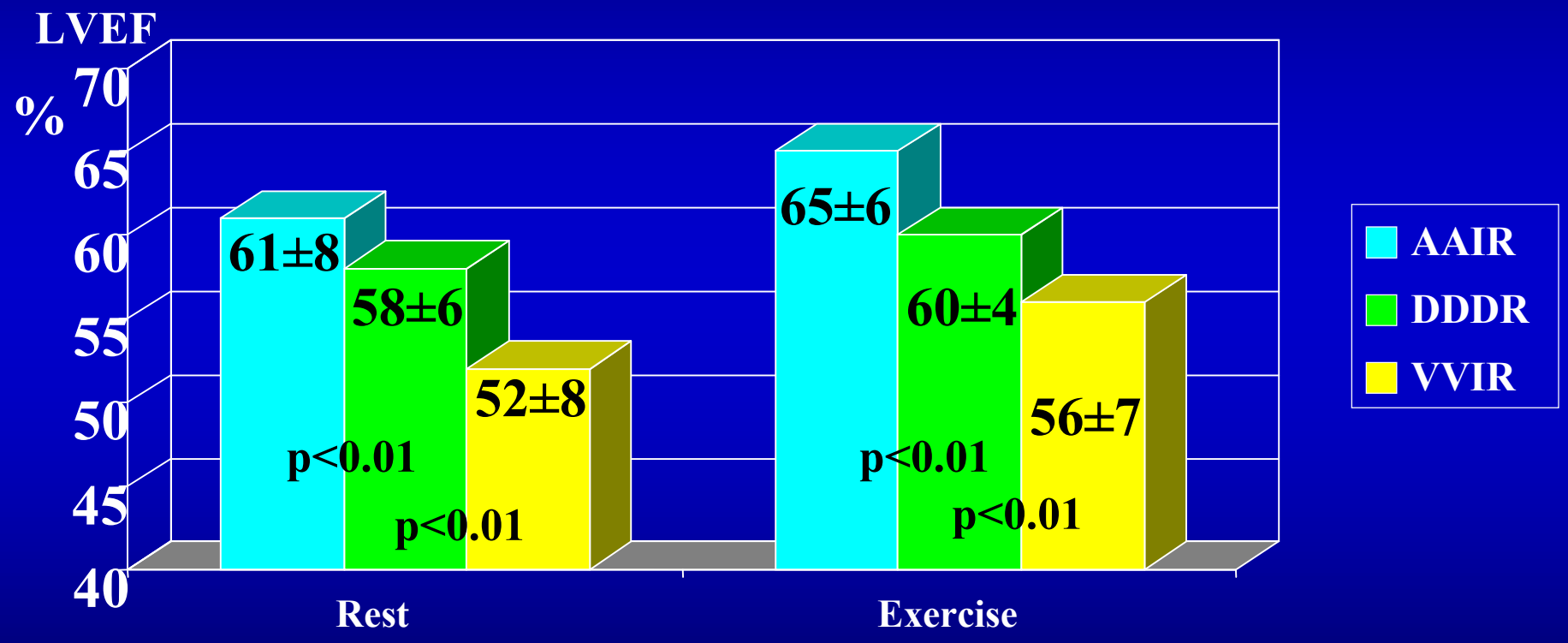




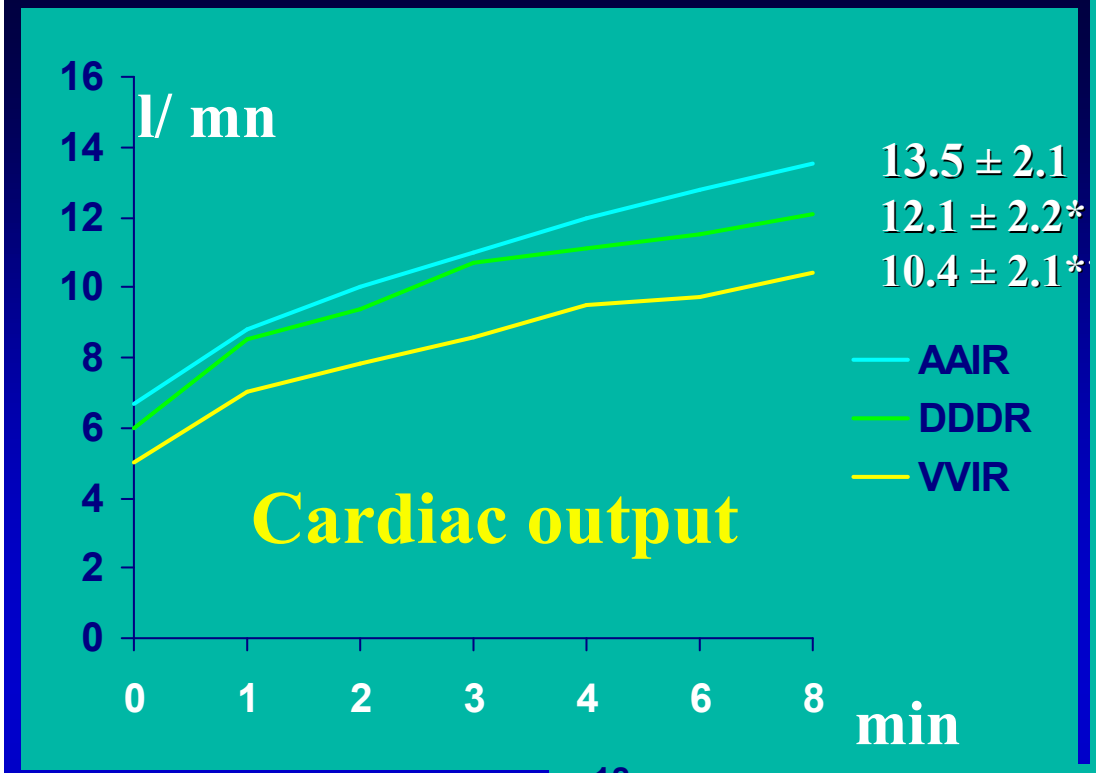
- As compared to atrial pacing, RV pacing (VVI and DDD modes) reduces systolic LV function *1*
- RV pacing alters LV relaxation in patients with abnormal systolic LV function *2*

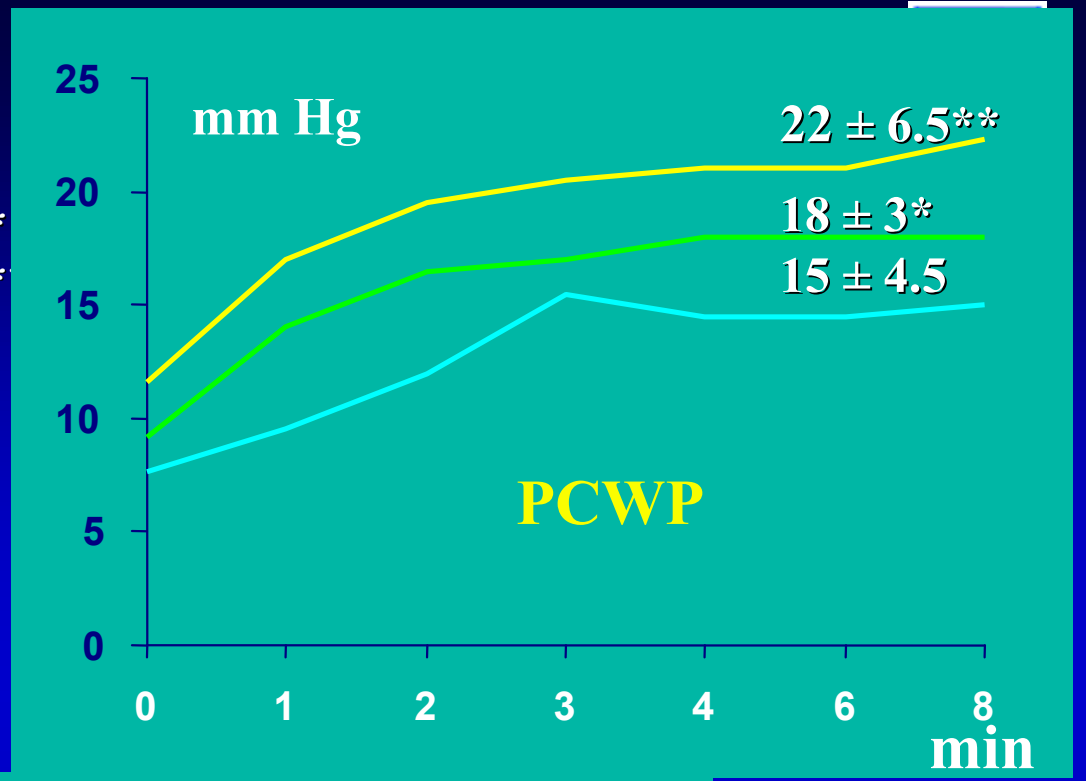
1 Rosenquist M, et al. AJC 1991;67:148-56
2 Bedotto JB et al. JACC 1990;15:658-64

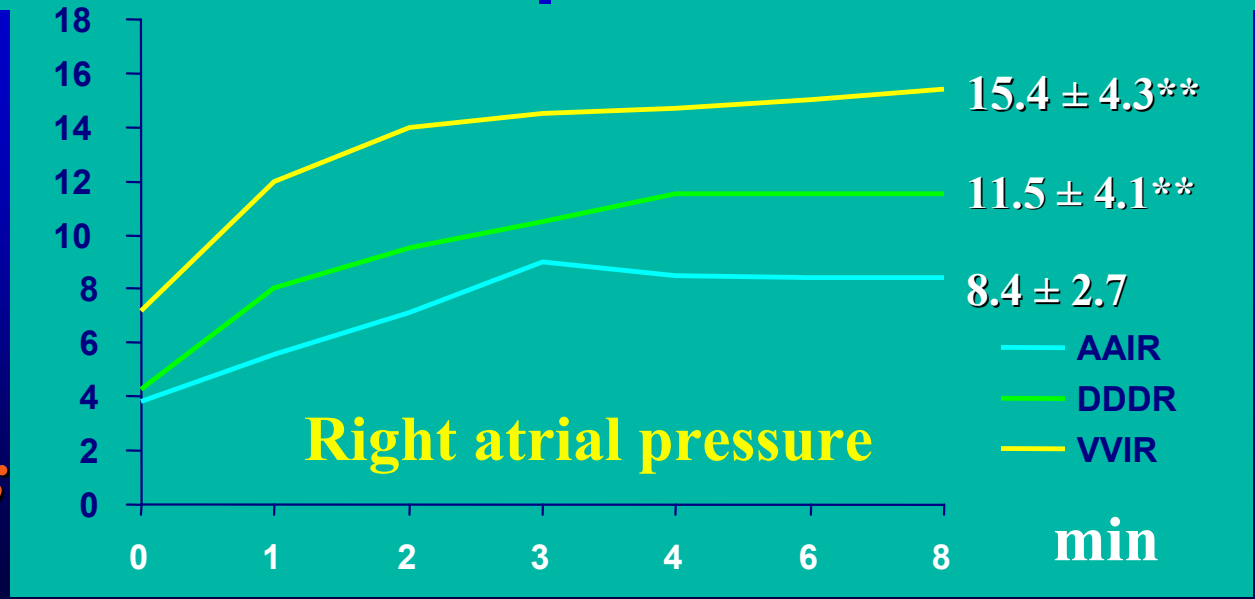
Conséquences Fonctionnelles : FE VG au repos et à l'effort



Leclercq. Am Heart J. 1995;129:1133-41







Leclercq.
Am Heart J. 1995;
129:1133-41

* : p<0.01
** : p <0.01

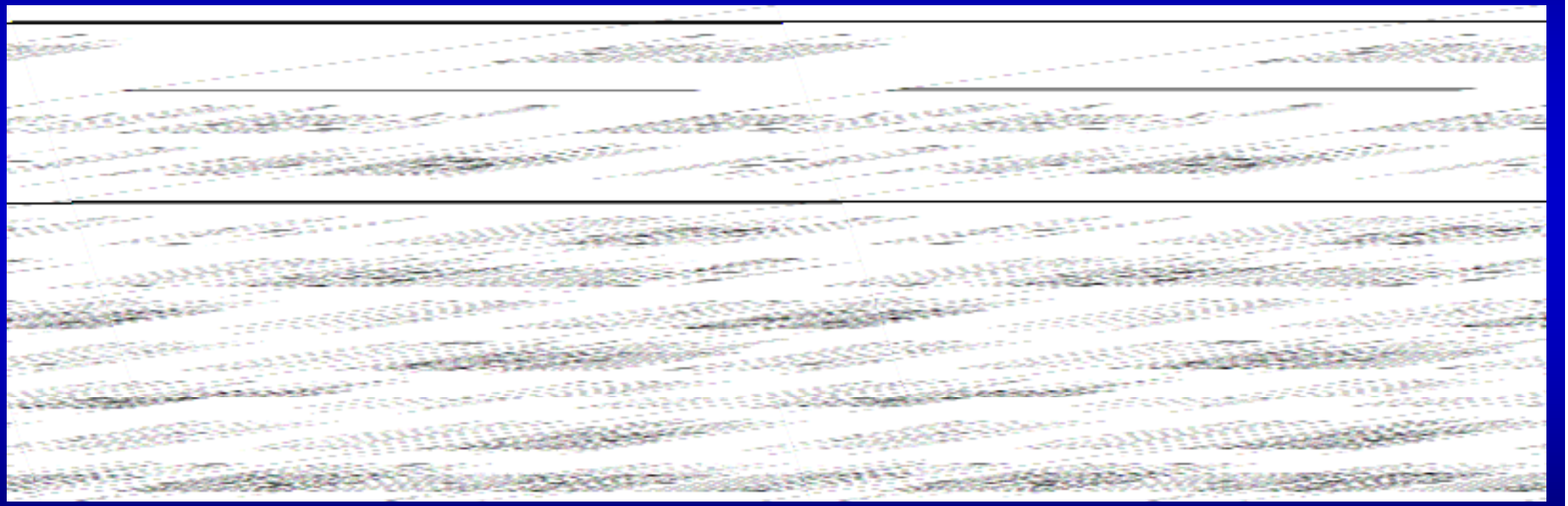
Conséquences Fonctionnelles : Altération de la FE VG chez des pts à FE altérée

- Retrospective study evaluating the determinants of improvement or deterioration in LVEF assessed by SPECT.

- Baseline LVEF $\geq$ 25% and $\leq$ 40%
- Second LVEF at least 6 months after
- 2 groups of pts : increase of $\geq$ 1O%
  decrease of $\leq$ 7%

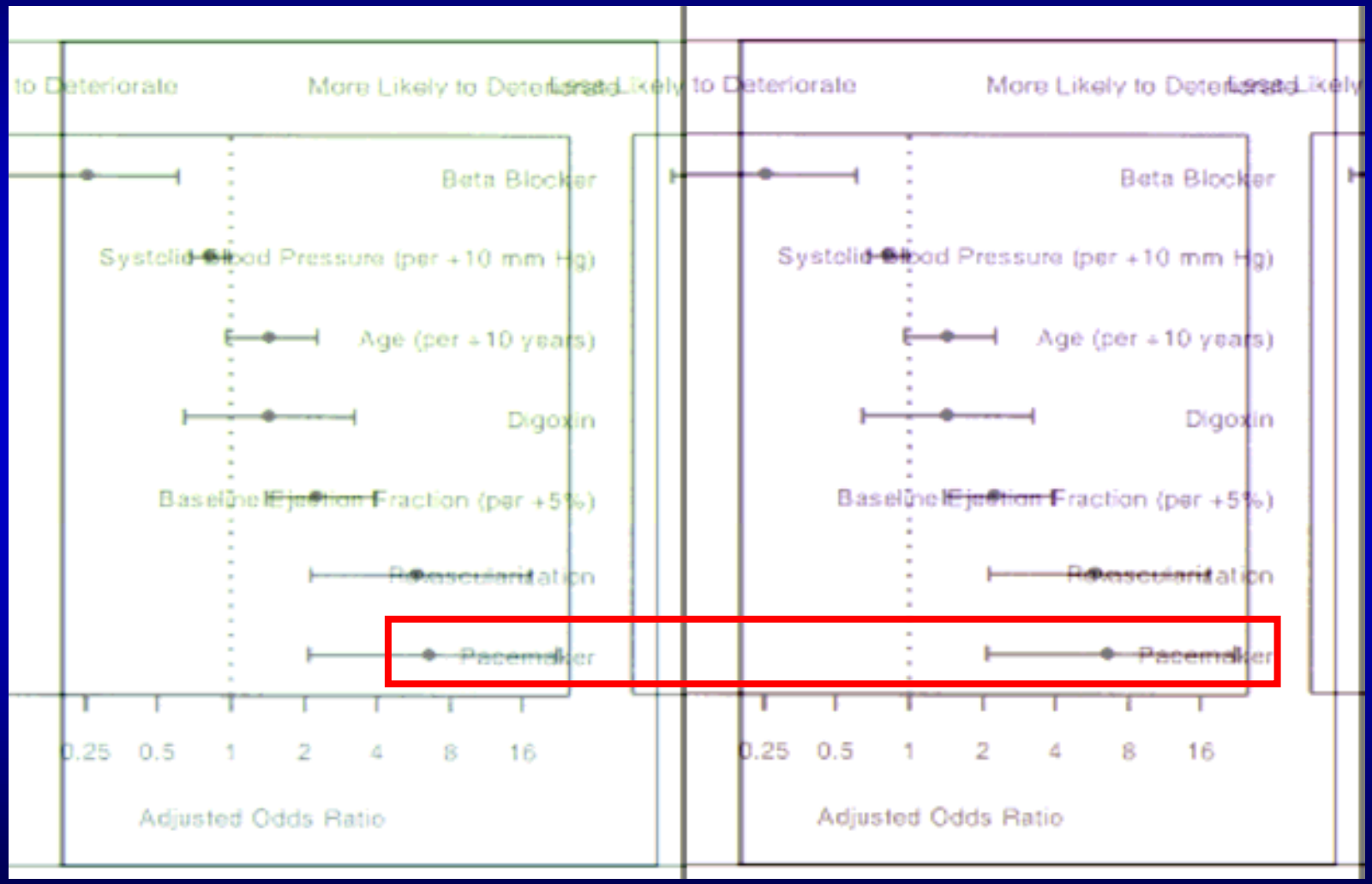
O'Keefe. Am J Cardiol 2005; 95: 771-3

Conséquences Fonctionnelles :
Altération de la FE VG chez des pts à FE altérée



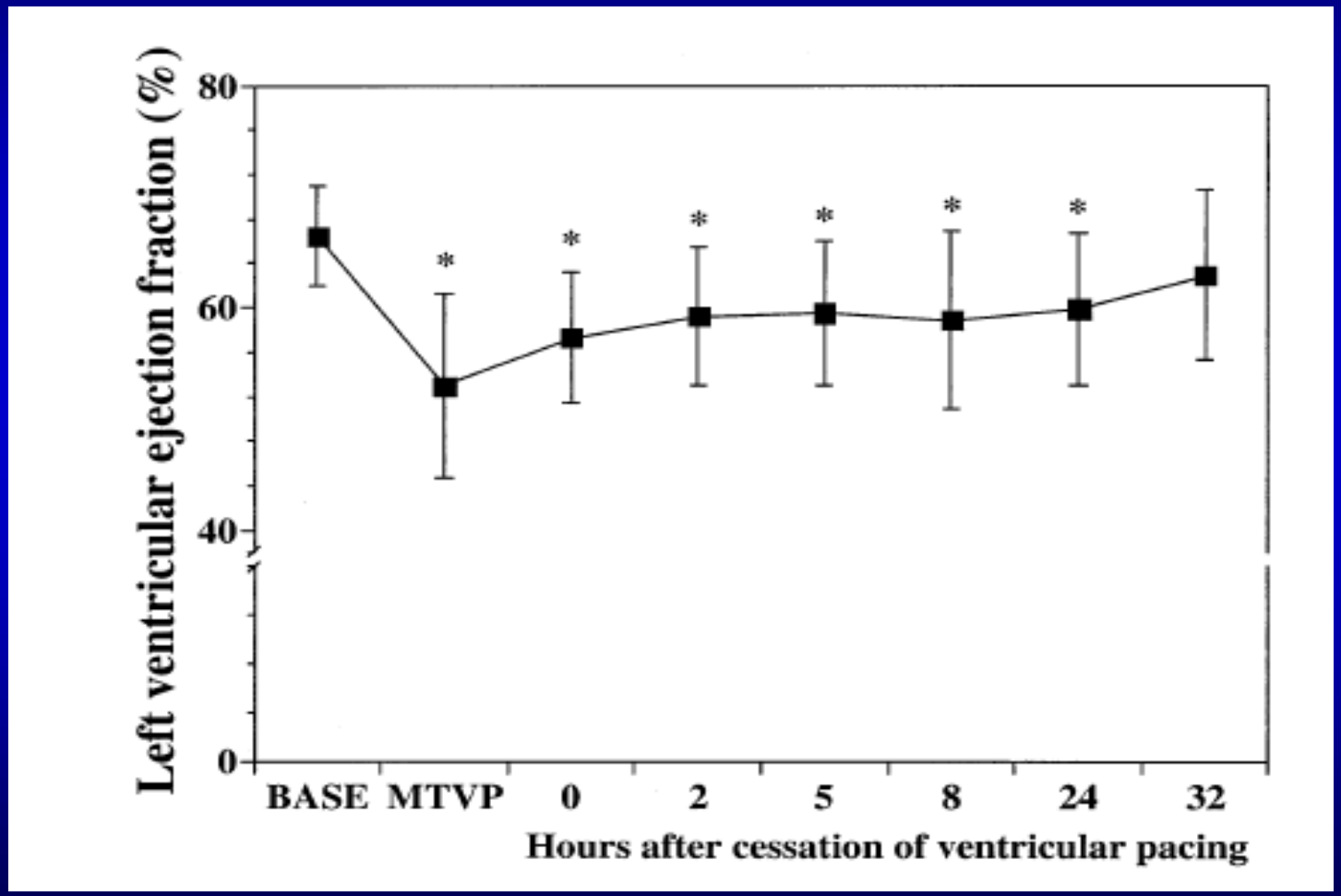
O'Keefe. Am J Cardiol 2005; 95: 771-3

Conséquences Fonctionnelles : Altération de la FE VG chez des pts à FE altérée



O'Keefe. Am J Cardiol 2005; 95: 771-3

Récupération de la FEVG après arrêt de la stim apicale VD



Nahlavi. J Am Coll Cardiol 2004;44:1883-8

Conséquences Fonctionnelles : Altération de la FE VG chez des pts à FE nle

- 33 CCAVB Vs 30 healthy subjects
- FU : 10 ± 3 years

	Long-Term RV Pacing	Controls
Cardiac output, L/min	3.8±0.6*	4.9±0.8
Mean LV EDD, mm	55±7*	46±6
Pathological LV EDD, %	52†	0
Ratio posterior/septal wall	1.3±0.2†	1±0.1
Ratio mitral regurgitation/left atrium	16±8*	5±2
LV filling time, ms	415±39*	477±51
Interventricular dyssynchrony, ms	55±18†	18±11
Intra-LV delay, ms	59±18†	19±9
Septal/posterior wall delay, ms	84±26†	18±9
DLC, %	39±15†	10±7
Exercise, W	123±24†	185±39

EDD indicates end-diastolic diameter.
*$P<0.05$; †$P<0.01$.

Thambo. Circulation 2004;110:3766-72

Désynchronisation en DTI

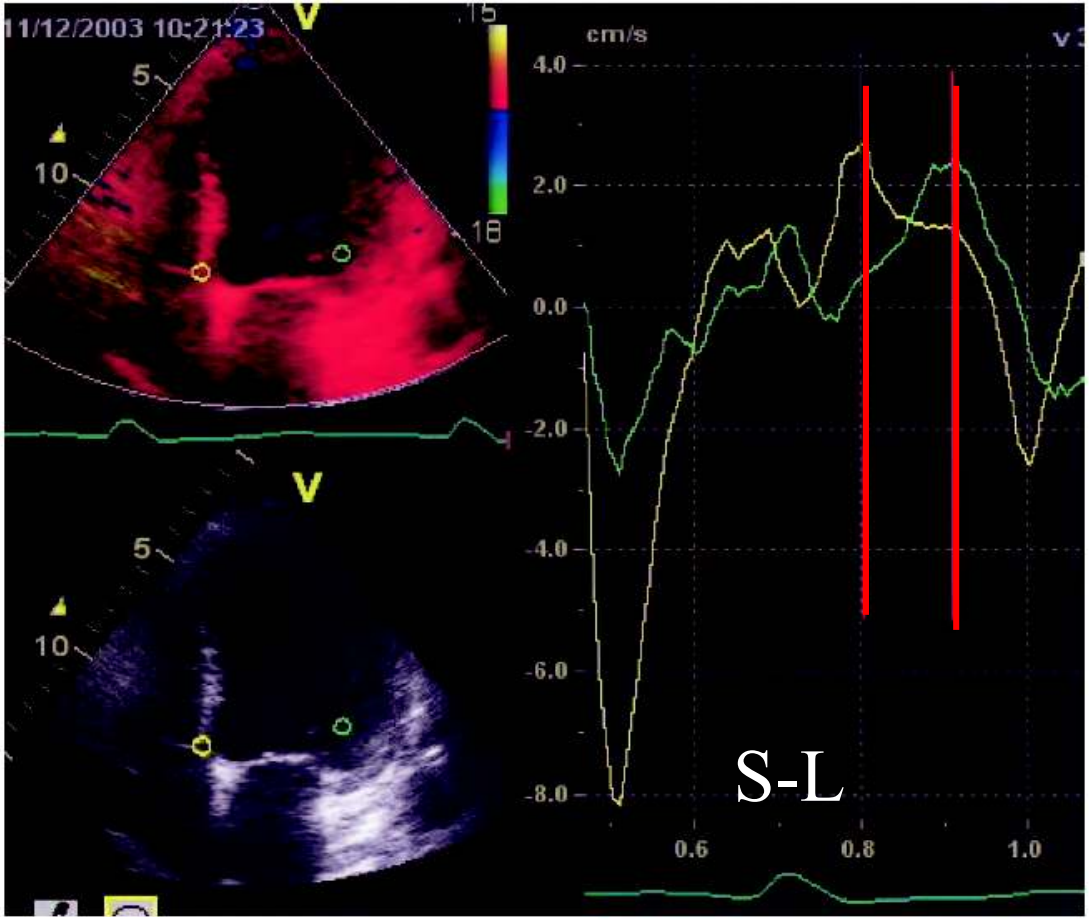


Figure 1. TDI. Important delay (>80 ms) between peak of systolic contraction (first line) of septo-basal segment (yellow curve) and peak of systolic contraction (second line) of lateral-basal segment (green curve).

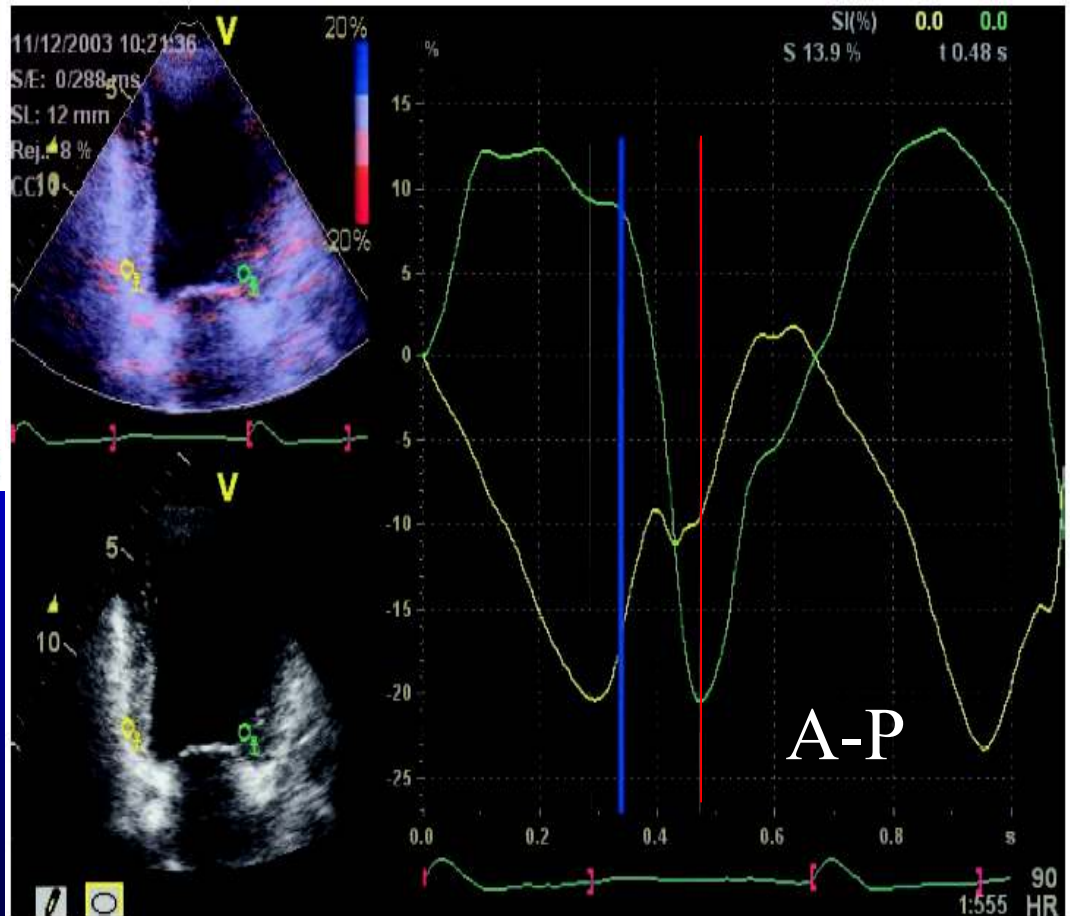


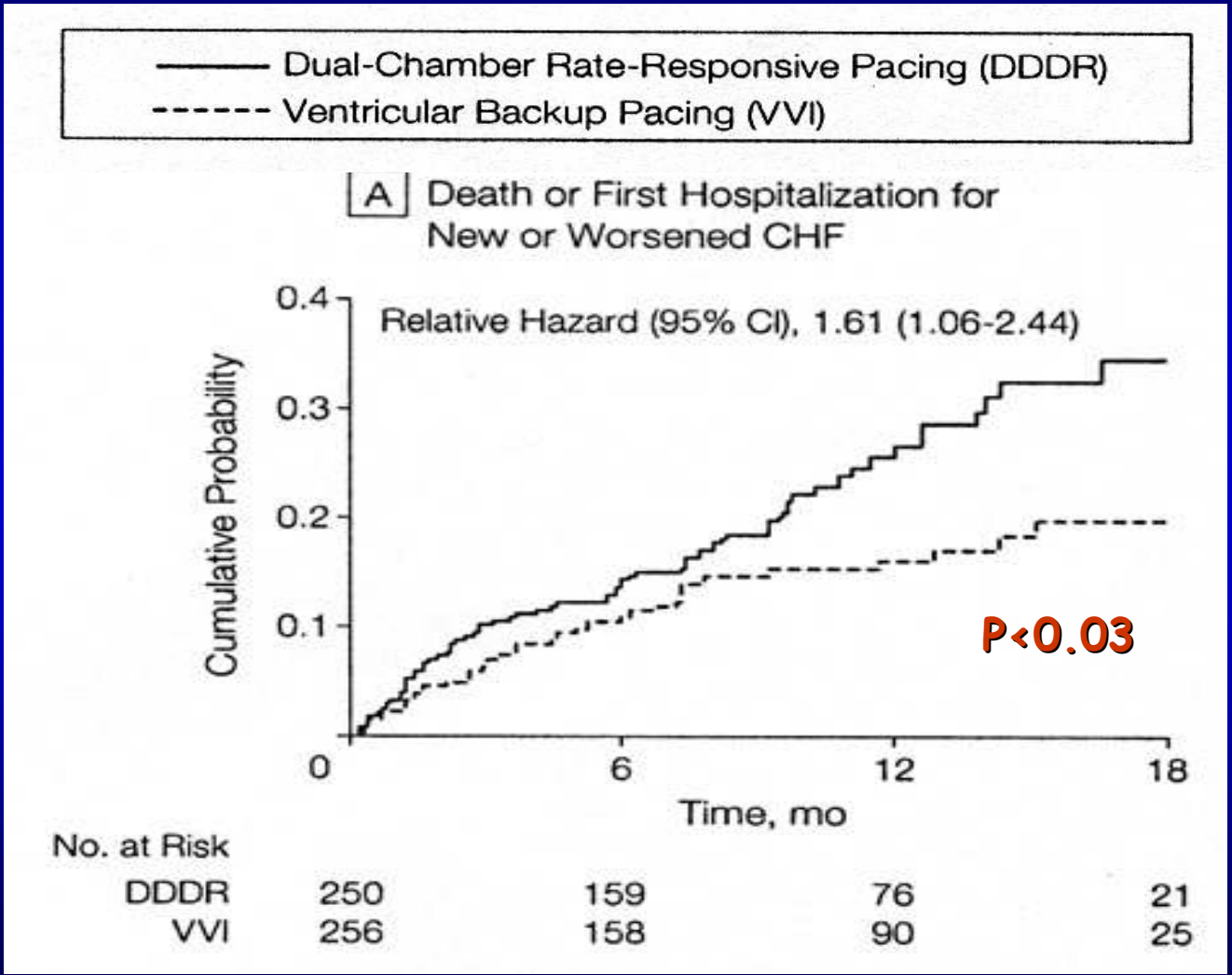
Figure 2. Strain rate analysis. Important delay (>100 ms) between end of systolic contraction (gray line) of inferobasal segment (yellow curve) and end of systolic contraction (red line) of anterobasal segment (green curve). This segment presents with major delayed longitudinal contraction; aortic closure is indicated with blue line.

Thambo et al., Circulation 2004

Frédéric Anselme
DIU 2007

Conséquences Cliniques
Mortalité, insuf. Card.

- 506 patients
- ICD indication
- VVI 40
  vs
  DDDR 70



DAVID Trial. JAMA 2002;288:3115-23

Conséquences Cliniques

SSS: deleterious effect of ventricular apex pacing
MOST Sub-study

- 1339 out of 2010 pts had a baseline QRS <120 ms
  - 707 (52.8%) pts in DDDR with 120 ms to 200 ms AV delay
  - 632 (47.2%) pts in VVIR

→ Cumulative % ventricular paced (Cum % VP) is greater in DDDR vs. VVIR (median 90% vs 58%)

→ Cum % VP is a strong predictor of *HF hospitalization*

→ DDDR: 2,6 x increased risk for Cum% VP > 40%

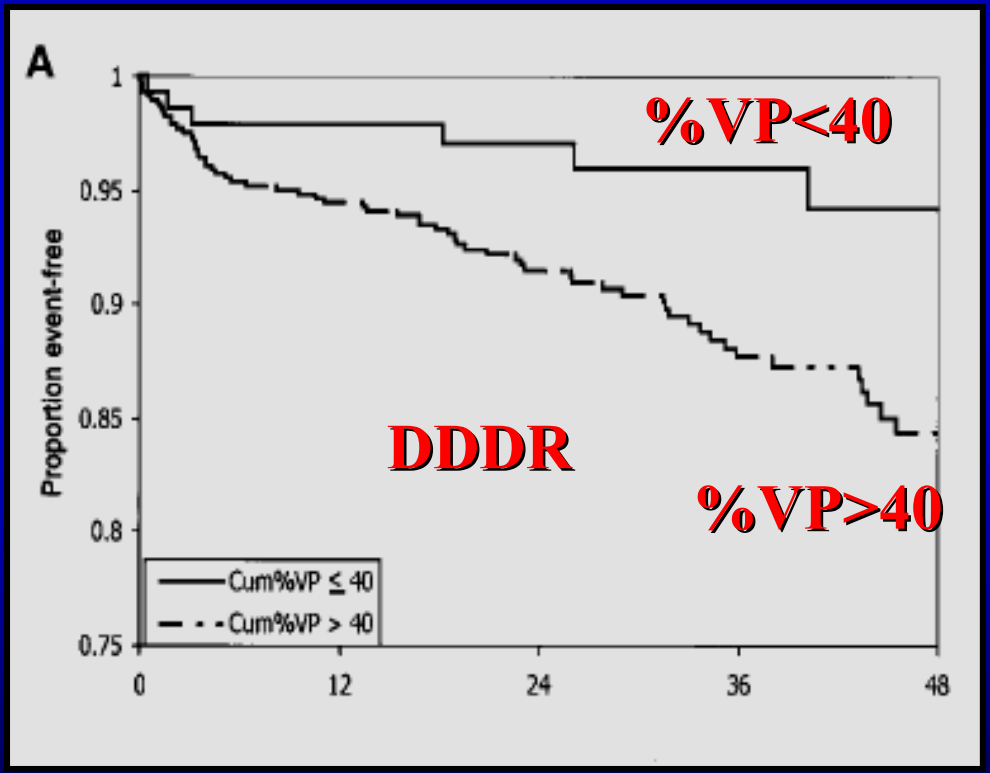
→ VVIR: 2,5 x increased risk for Cum% VP > 80%

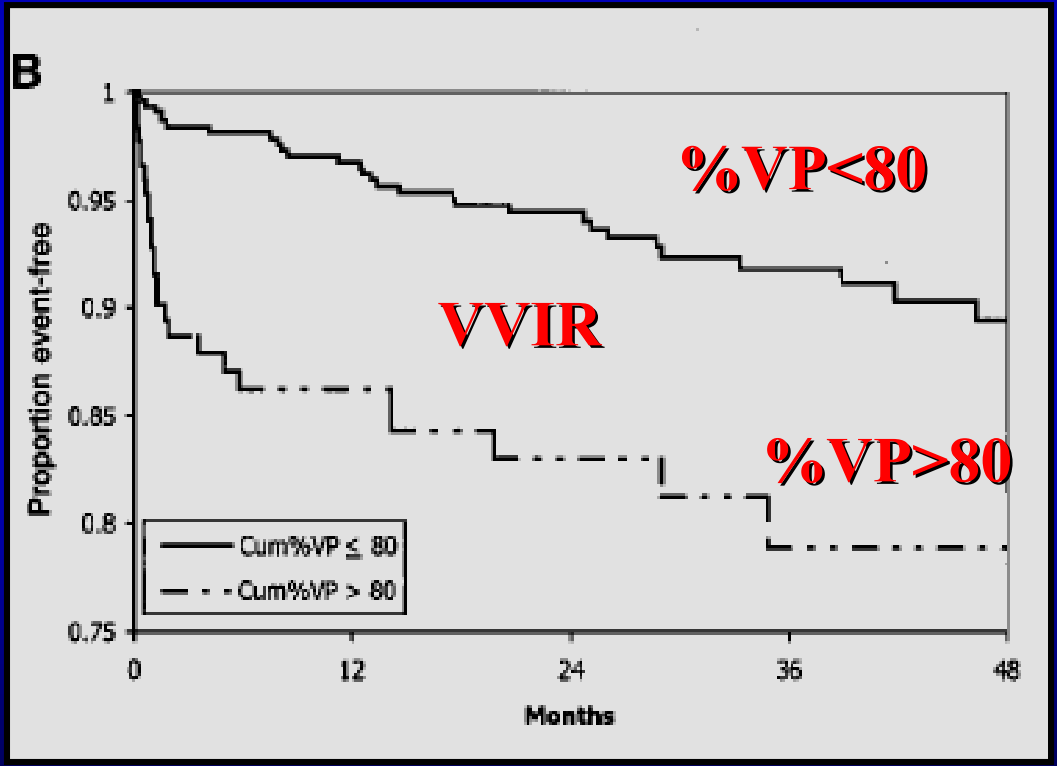
→ *Risk of AF* increase linearly with Cum% VP in both group

Sweeney. Circulation 2003; 107: 2932-7

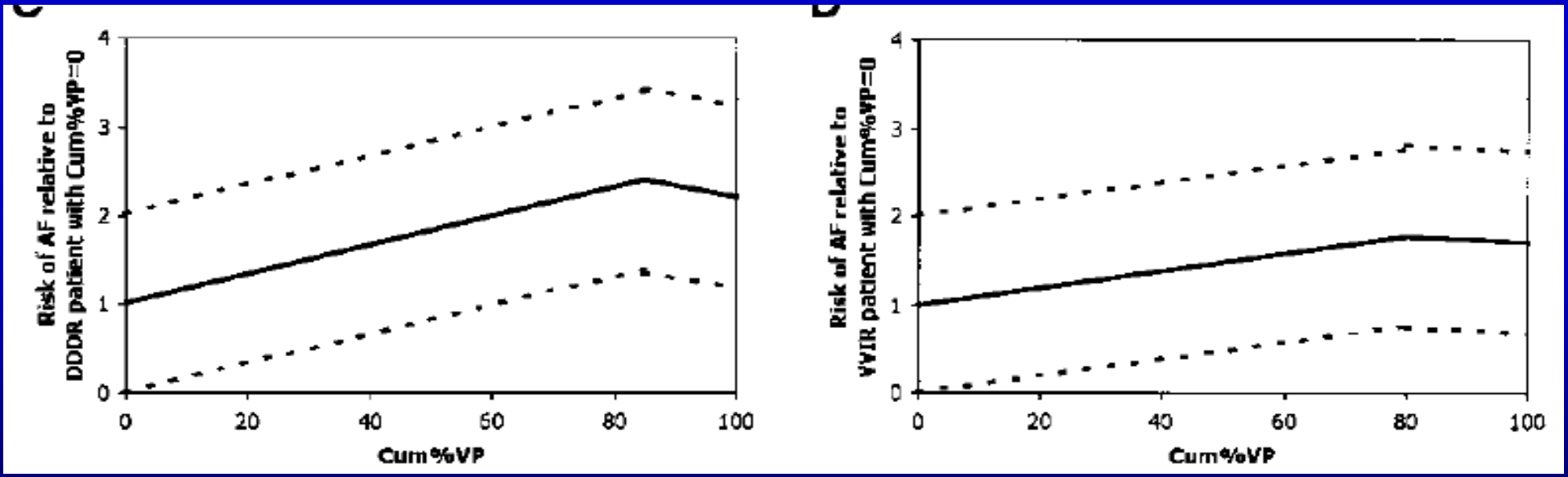
Conséquences Cliniques : Importance du % de stim apicale VD

Hospitalisation pour Insuf. Card.



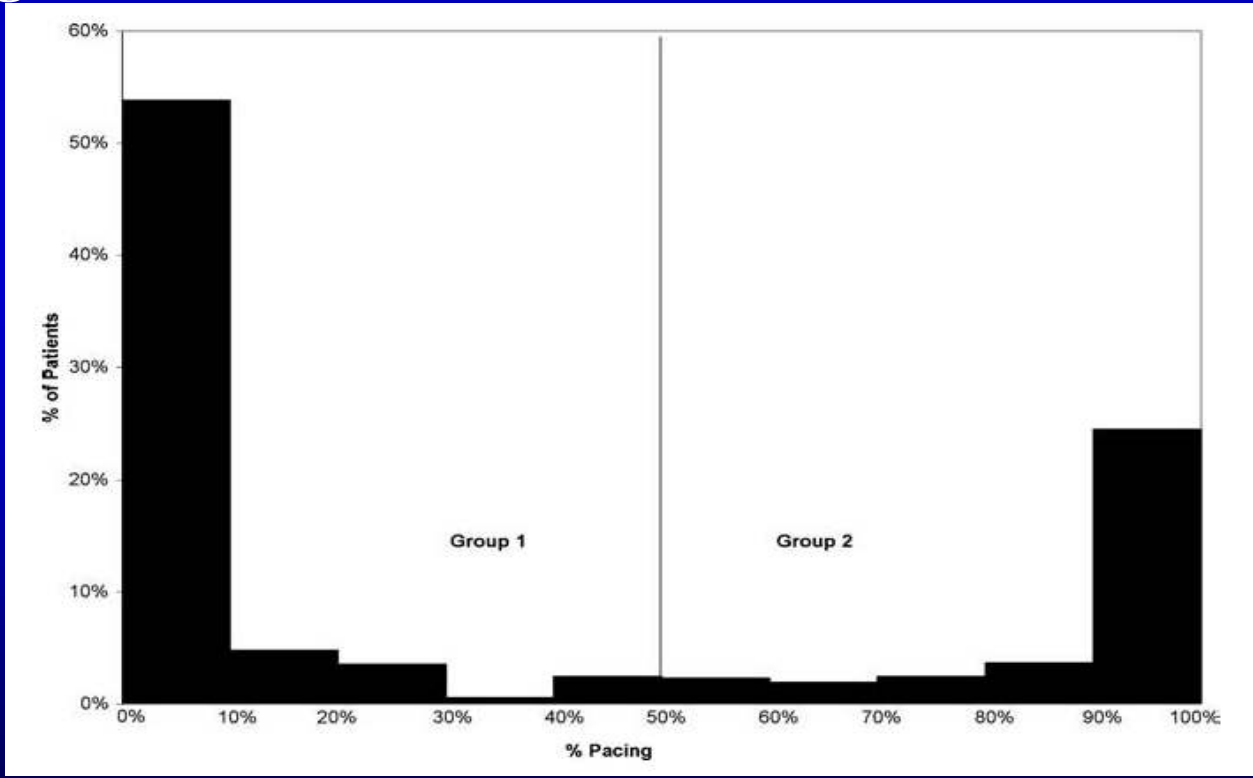


Sweeney, MOST Trial, Circulation 2003


C
Risk of AF relative to DDDR patient with Cum%VP=0
0
1
2
3
4
0
20
40
60
80
100
Cum%VP
D
Risk of AF relative to VVIR patient with Cum%VP=0
0
1
2
3
4
0
20
40
60
80
100
Cum%VP

Conséquences Cliniques : FE < 31%

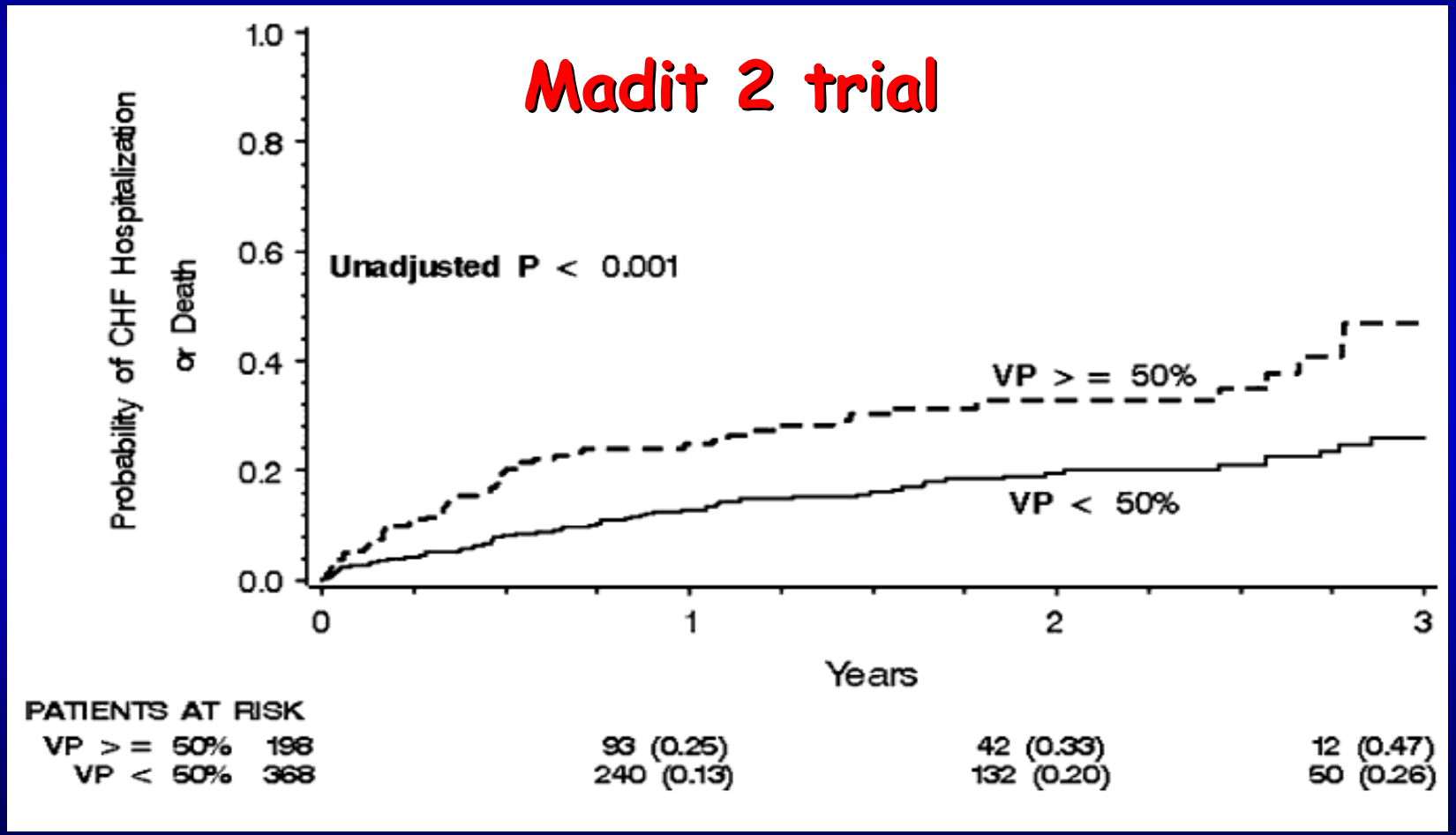
- Sub-study of the MADIT II trial
- Evaluation of the ventricular paced beats over the total number of beats: cumulative ventricular pacing
- 2 groups: Cum VP 0-50%
  Cum VP 50-100%
- Interrogation available in 76% of the 742 ICD pts



Steinberg. J Cardiol Electrophysiol 2005; 16: 359-65

Conséquences Cliniques : FE < 31%

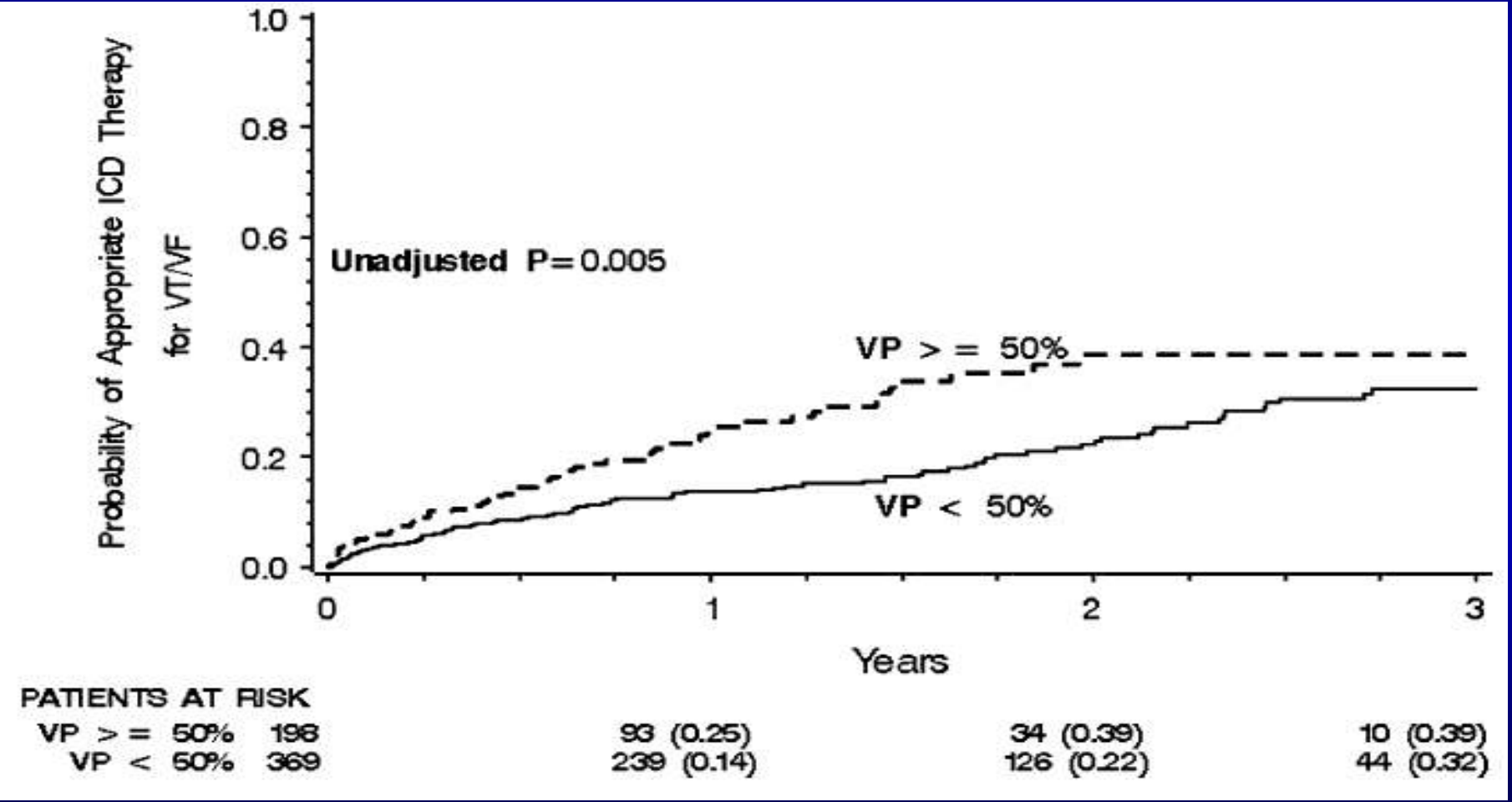
Augmentation du risque d'hospitalisation pour insuf. Card.



Steinberg. J Cardiol Electrophysiol 2005; 16: 359-65

Conséquences Cliniques : FE < 31%

Augmentation du risque de ttt par le DAI



Steinberg. J Cardiol Electrophysiol 2005; 16: 359-65

Conséquences Cliniques : FE < 31%

Augmentation du risque de IC, mortalité par IC, ttt par le DAI

Relationship of Ventricular Pacing to Outcome Events

Outcome Event	Hazard Ratio (95% CI)	P Value
Heart failure*	1.93 (1.28–2.90)	0.002
HF/death*	1.77 (1.21–2.60)	0.025
ICD therapy†	1.50 (1.05–2.14)	0.025
Death‡	1.47 (0.72–3.01)	0.29

HF = heart failure; ICD = implantable cardioverter defibrillator; CI = confidence interval.

*Covariates: heart rate ≥80 bpm, blood urea nitrogen ≥25 mg/dL, NYHA Class ≥2, age ≥65 yrs, QRS ≥120 msec.

†Covariates: blood urea nitrogen >25 mg/dL, NYHA Class ≥2.

‡Covariates: blood urea nitrogen ≥25 mg/dL.

Steinberg. J Cardiol Electrophysiol 2005; 16: 359-65

Conclusion

La stimulation conventionnelle apicale VD:

- ♥ Altère la séquence de dépolarisation VG
- ♥ Prolonge les temps d'activation des deux ventricules
- ♥ Crée un asynchronisme de contraction VG
- ♥ Altère le fonctionnement de la valve mitrale
- ♥ Favorise le développement de la fibrillation atriale
- ♥ Favorise la dysfonction VG et le développement de l'insuffisance cardiaque

Haemodynamics - Pacing Mode Synthesis

- **Restaurer une variabilité « physiologique » de la fréquence cardiaque**
  - Le rythme sinusal est souvent le mieux
  - Déterminer de valeurs appropriées de fréquence de base et max d'effort
  - Choix du capteur d'asservissement ?
- **Maintenir le synchronisme AV**
  - Différentier le délai AV stimulé et détecté
  - Programmer un délai AV adaptable
- **Préserver une séquence d'activation ventriculaire normale**