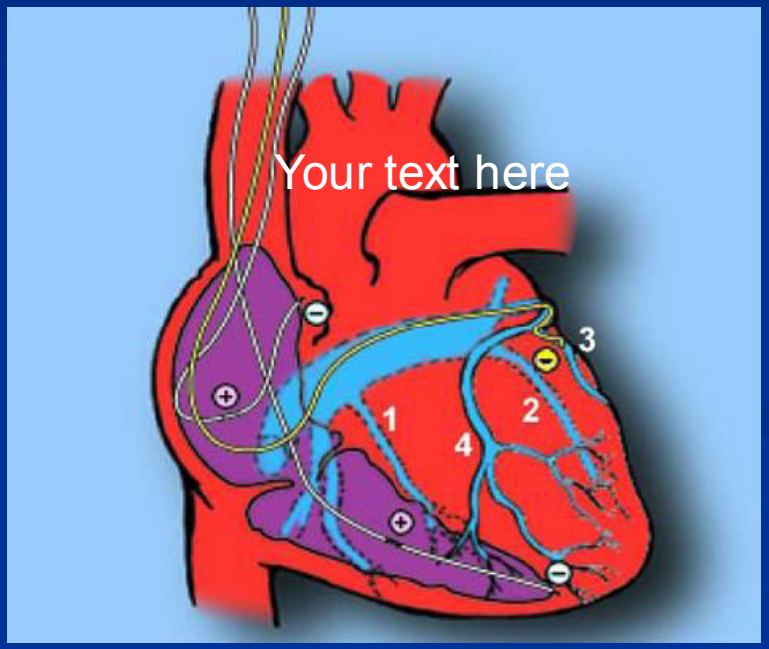
CARDIAC RESYNCHRONIZATION THERAPY (CRT)



BS Đỗ Văn Bửu Đan
Trưởng khoa Điện sinh lý tim
BV Tim Tâm Đức

HF Incidence and Prevalence

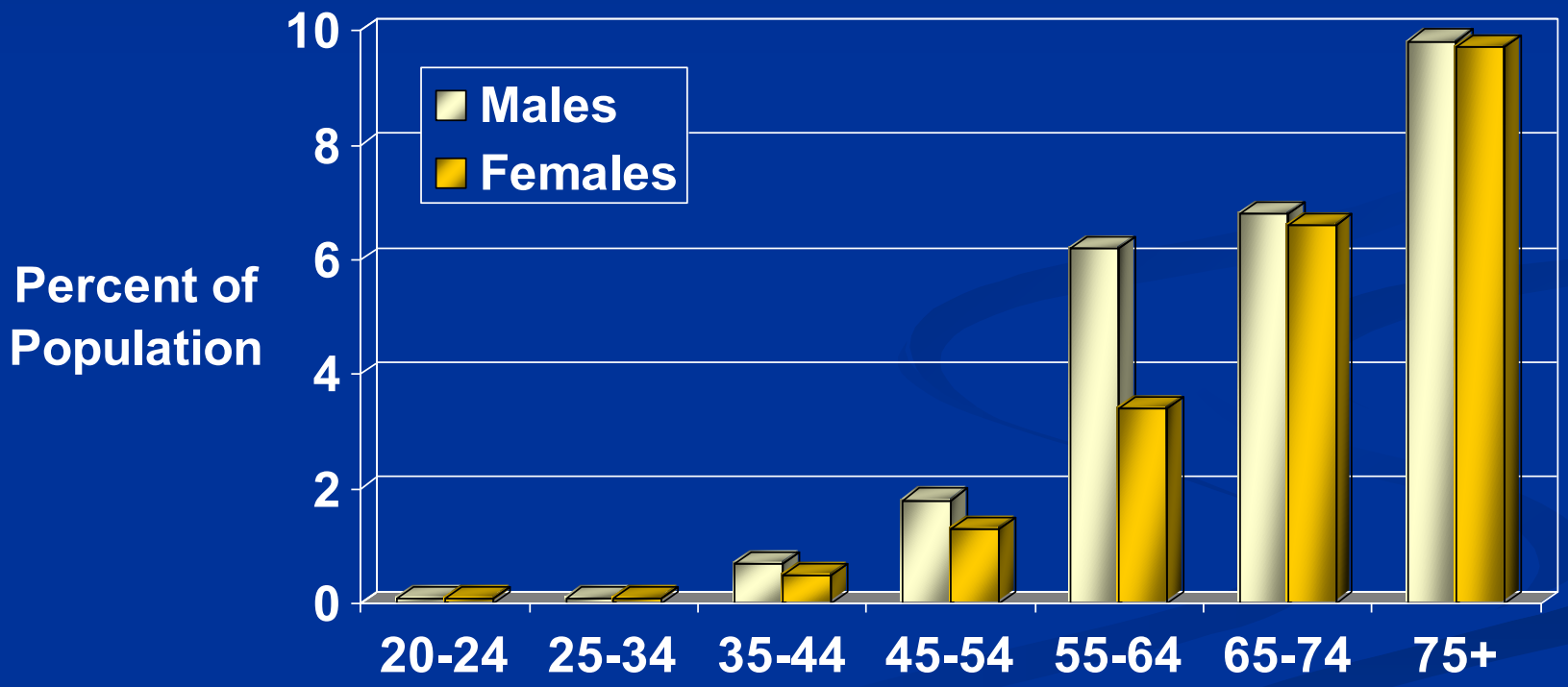
- Prevalence
  - Worldwide, 22 million[1]
  - United States, 5 million[2]
- Incidence
  - Worldwide, 2 million new cases annually[1]
  - United States, 500,000 new cases annually[2]
- HF afflicts 10 out of every 1,000 over age 65 in the U.S.[2]

1 World Health Statistics, World Health Organization, 1995.

2 American Heart Association, 2002 Heart and Stroke Statistical Update.

Prevalence of HF by Age and Gender

United States: 1988-94



Source: NHANES III (1988-94), CDC/NCHS and the American Heart Association

New York Heart Association Functional Classification

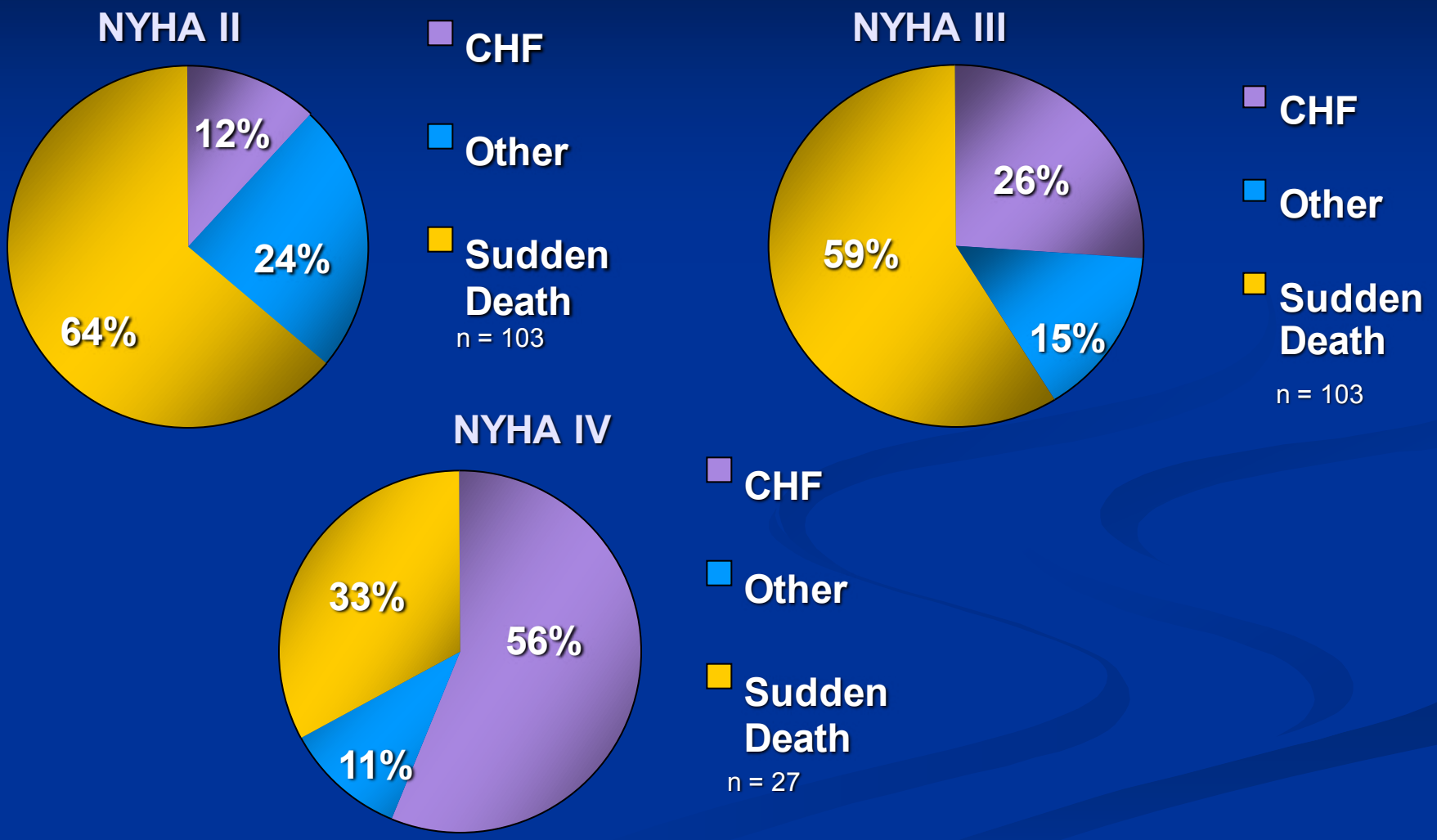
Class I: No symptoms with ordinary activity

Class II: Slight limitation of physical activity. Comfortable at rest, but ordinary physical activity results in fatigue, palpitation, dyspnea, or angina

Class III: Marked limitation of physical activity. Comfortable at rest, but less than ordinary physical activity results in fatigue, palpitation, dyspnea, or anginal pain

Class IV: Unable to carry out any physical activity without discomfort. Symptoms of cardiac insufficiency may be present even at rest

Severity of Heart Failure
Modes of Death



MERIT-HF Study Group. Effect of Metoprolol CR/XL in chronic heart failure: Metoprolol CR/XL randomized intervention trial in congestive heart failure (MERIT-HF). *LANCET.* 1999;353:2001-07.

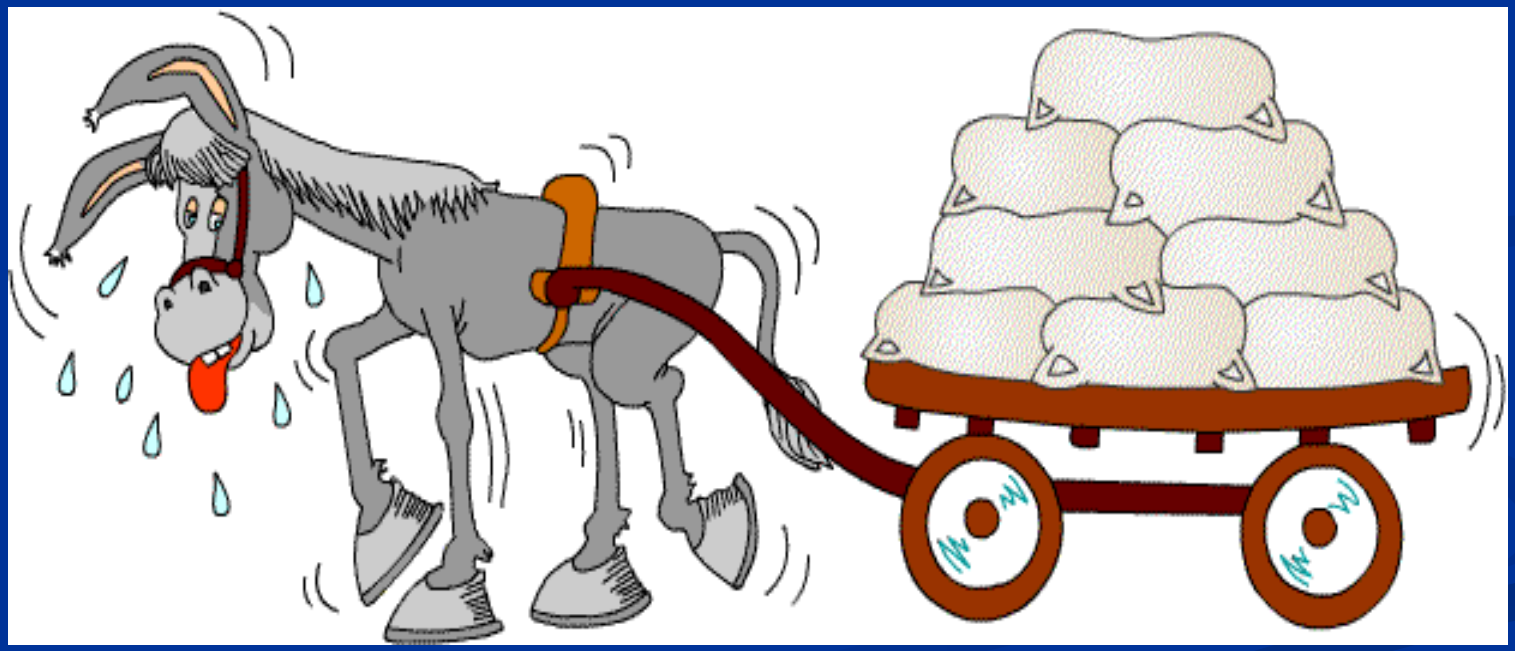
Etiology of Heart Failure

What causes heart failure?

- The loss of a critical quantity of functioning myocardial cells after injury to the heart due to:
  - Ischemic Heart Disease
  - Hypertension
  - Idiopathic Cardiomyopathy
  - Infections (e.g., viral myocarditis, Chagas' disease)
  - Toxins (e.g., alcohol or cytotoxic drugs)
  - Valvular Disease
  - Prolonged Arrhythmias

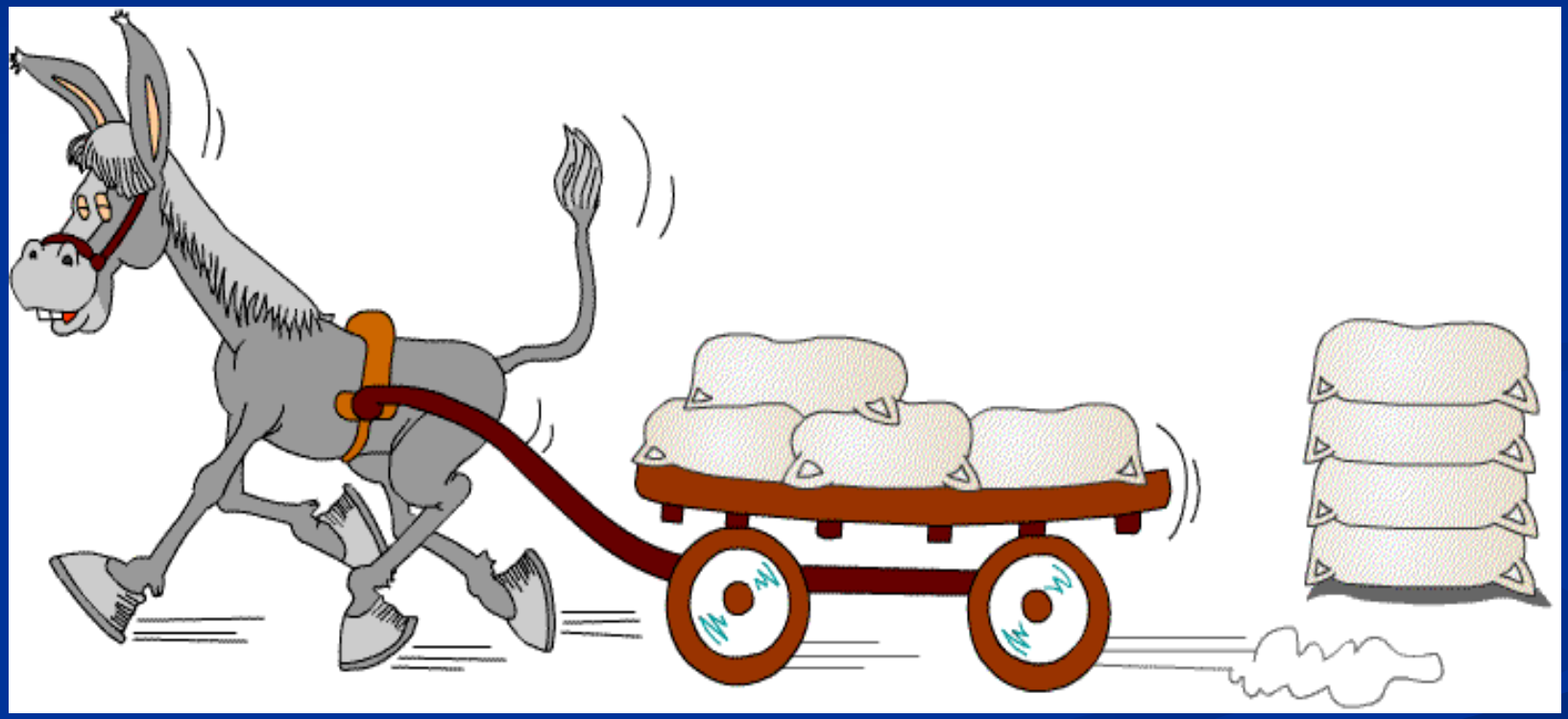
The Donkey Analogy

Ventricular dysfunction limits a patient's ability to perform the routine activities of daily living…



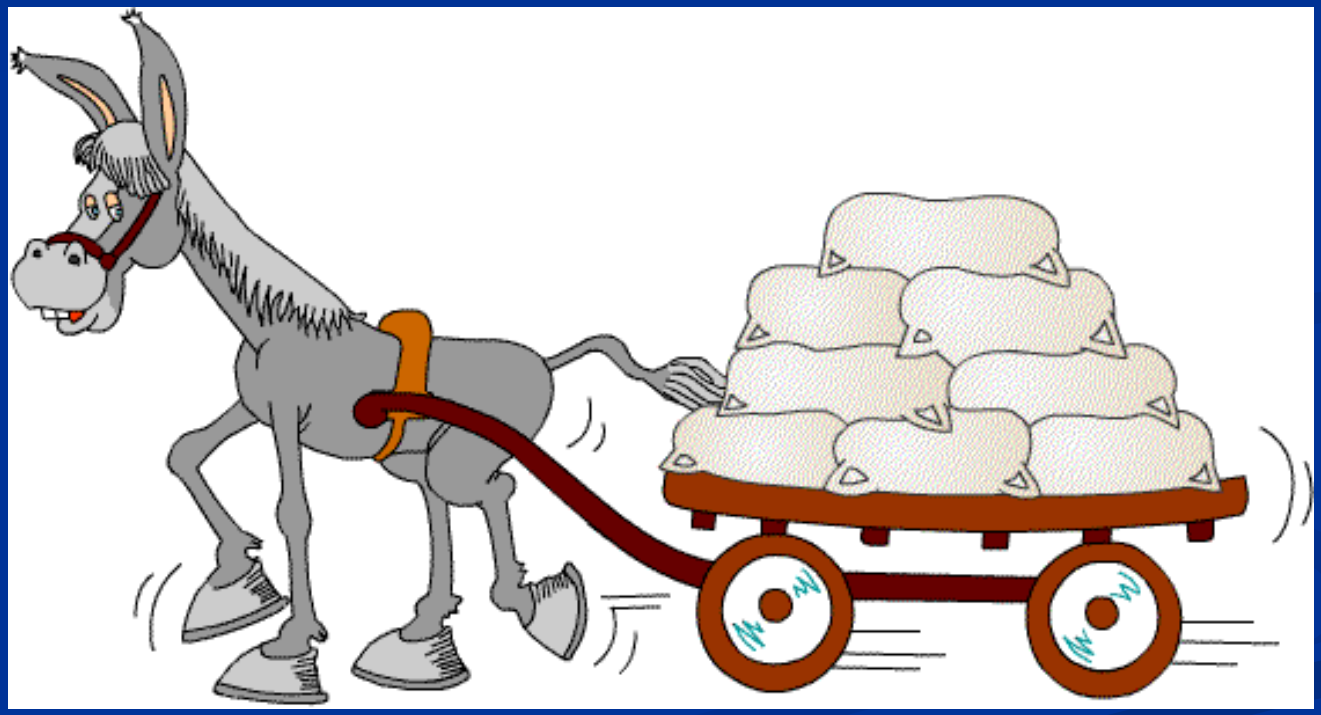
Diuretics, ACE Inhibitors

Reduce the number of sacks on the wagon



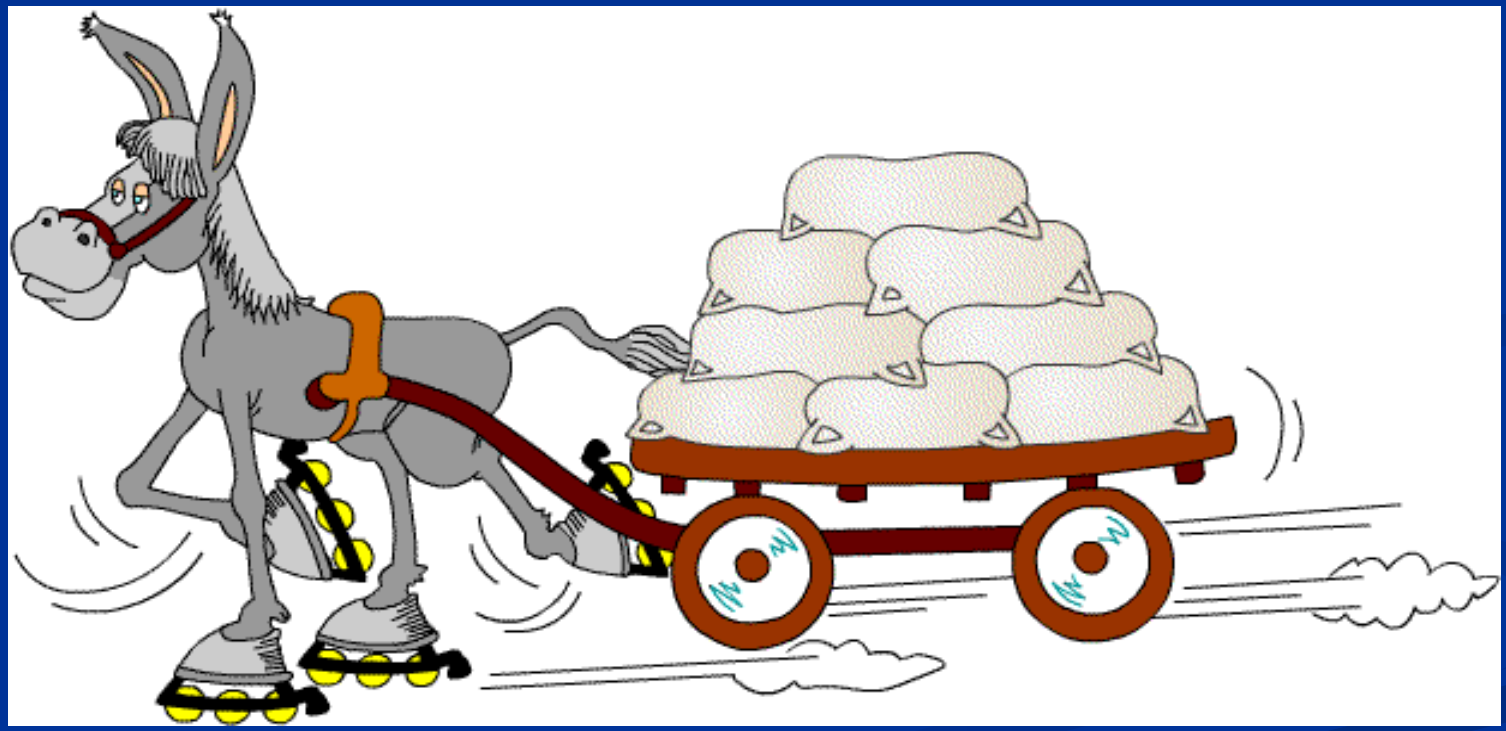
ß-Blockers

Limit the donkey's speed, thus saving energy



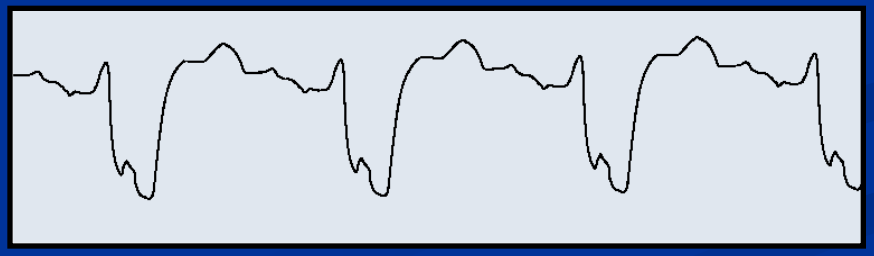
Cardiac Resynchronization Therapy

Increase the donkey's (heart) efficiency

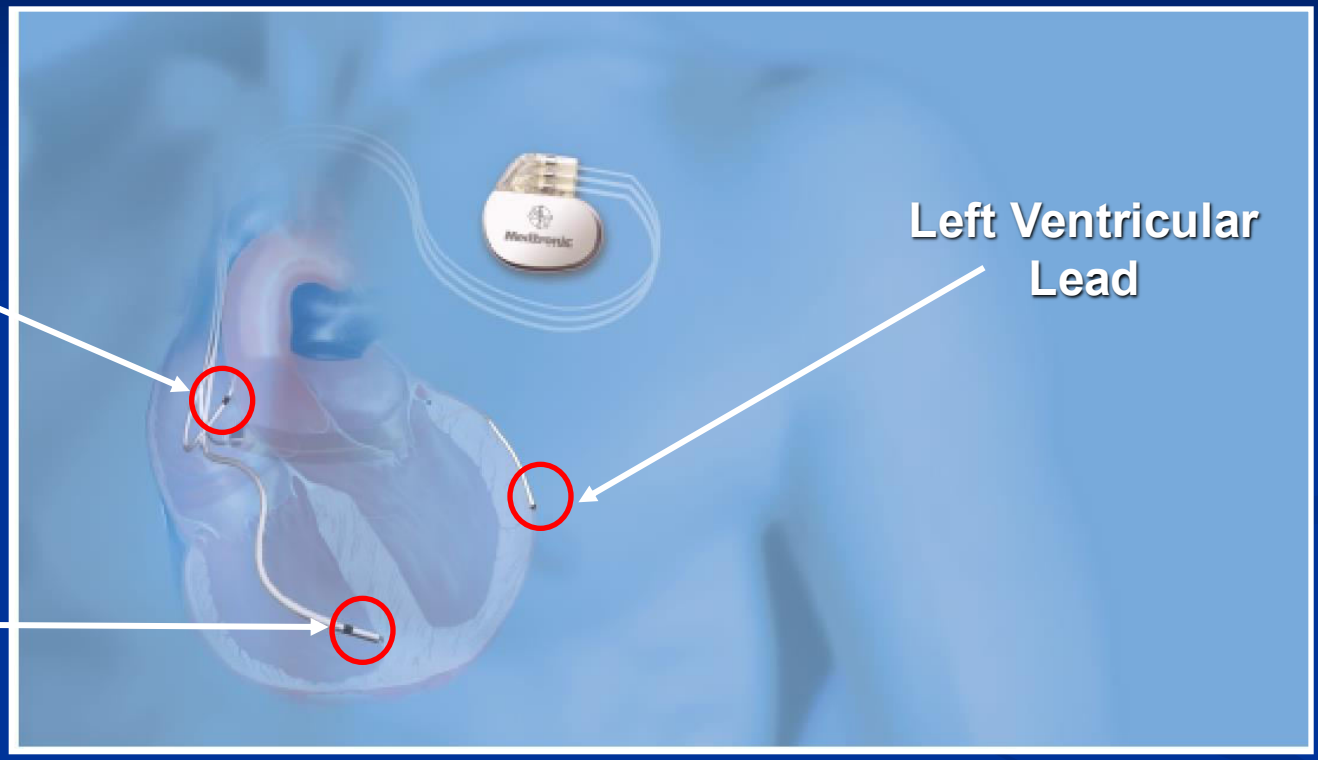


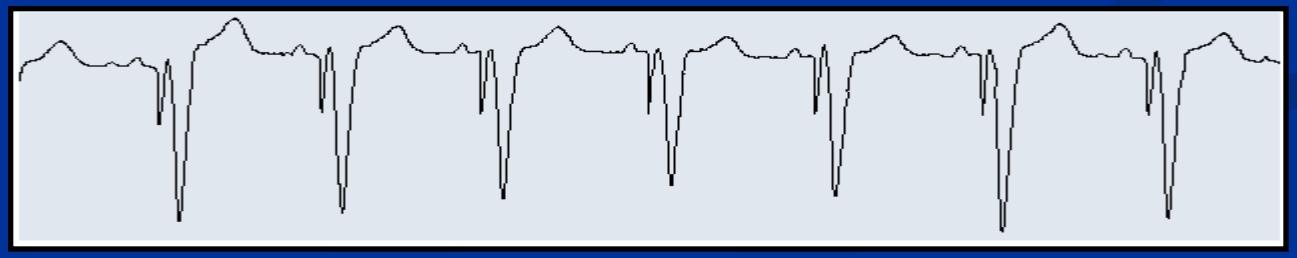
Cardiac dysynchrony

- Loss of homogeneous segmental LV contraction
- Delayed conduction through diseased myocardium
- Manifested by LBBB.
- Decreased EF, increased intracavitary pressures and wall tension, MR, shortened diastolic filling period

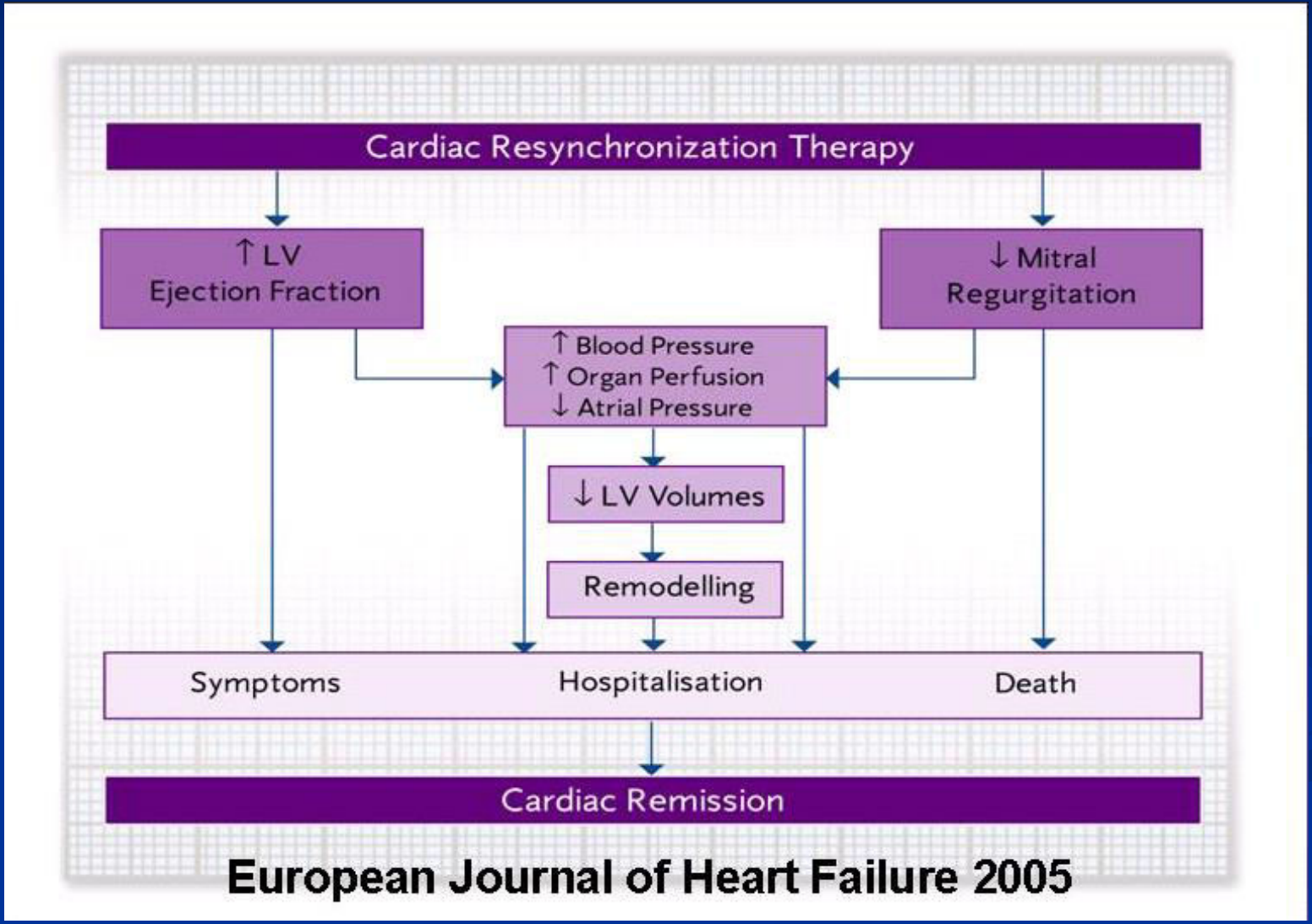


Achieving Cardiac Resynchronization





Effects of CRT

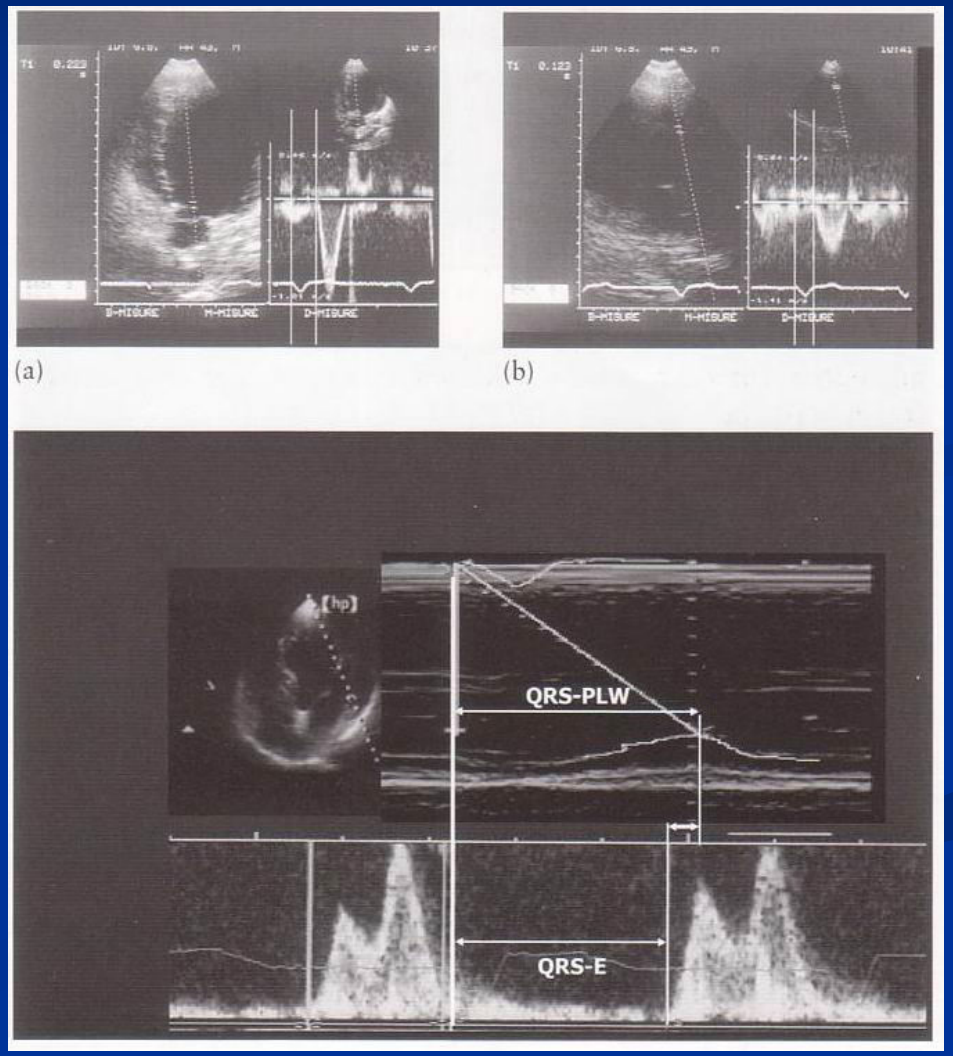


Candidates for CRT

- CARE-HF trial (N Engl J Med 2005;352:1539-49)
  - Dilated cardiomyopathy: EF ≤ 35%, LVEDD ≥ 55mm
  - NYHA III/IV
  - Optimal medical treatment: ACEI, diuretics, betablocker, spironolactone
  - Ventricular dyssynchrony
    - QRS ≥ 150ms
    - QRS 120-149ms: 2 of 3 echo criteria.

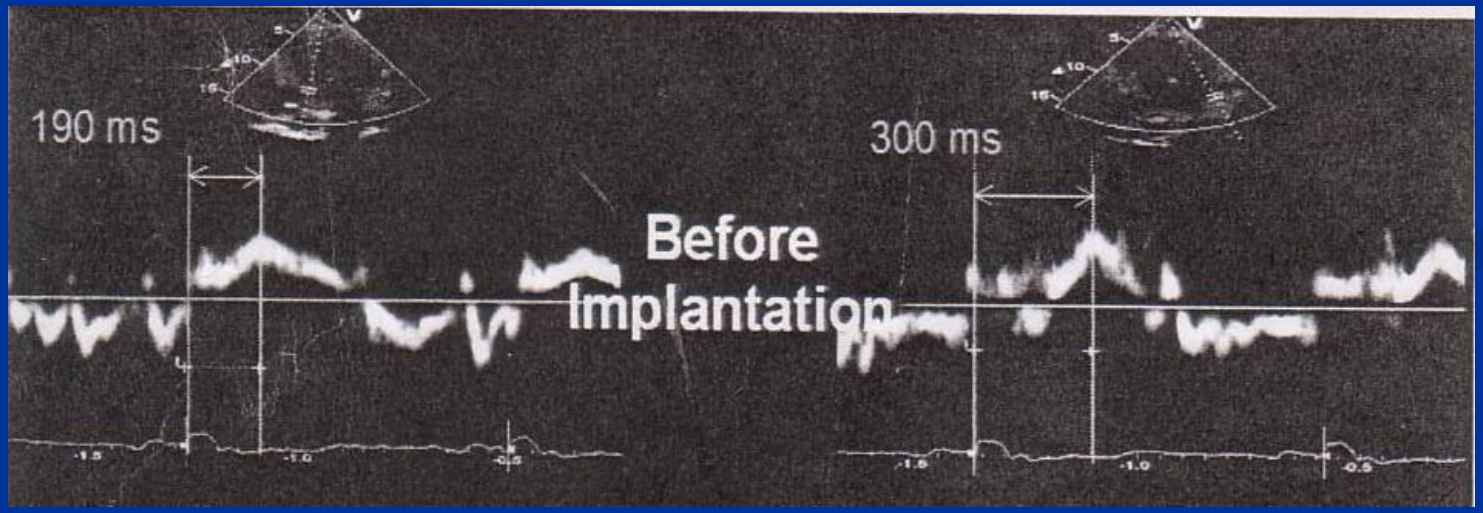
Conventional echocardographic criteria

- Aortic pre-ejection delay ≥ 140ms
- Interventricular mechanical delay ≥ 40ms
- Delayed activation of the posterolateral left ventricular wall (systolic-diastolic overlap)



New echocardiographic techniques

- Tissue Doppler imaging (TDI)
  - Intraventricular delay>60ms*

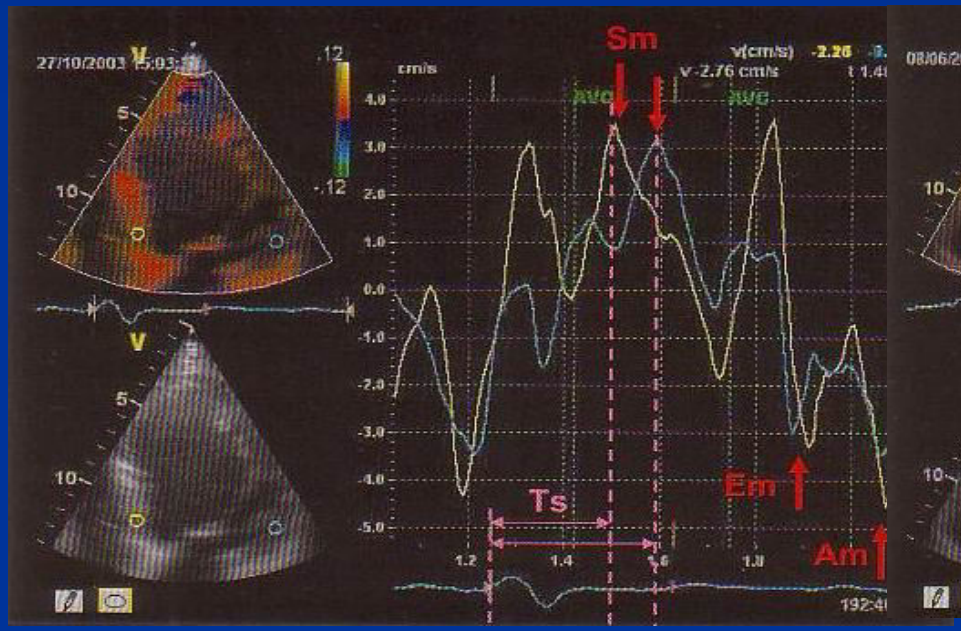


Spectral pulse

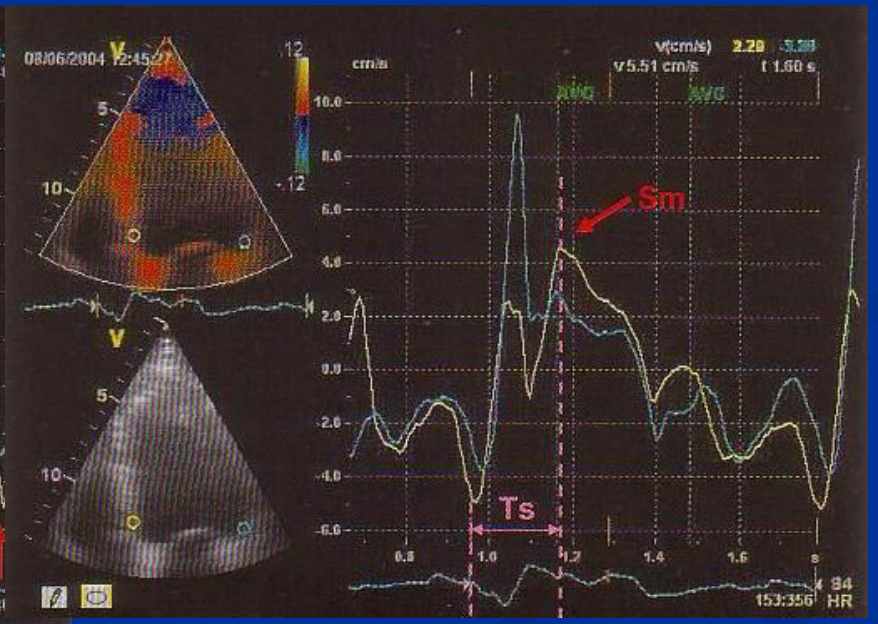
*Bax JJ et al. Left ventricular dyssynchony predicts benefit of cardiac resynchronization therapy . Am J Cardiol 2003;92:1238-40

New echocardiographic techniques

- 2D-color TDI



Before CRT



After CRT

Cardiac Resynchronization Therapy, 2006 Blackwell Publishing, p 93.

Clinical situations unfavored of CRT

- Unstable coronary artery disease
- Severe MR due to structural abnormalities
- Severe AS
- Advanced RV dysfunction due to chronic lung disease

CRT and RBBB

- No definite data about CRT on RBBB patients
- MIRACLE study*: RBBB respond less well than LBBB
- Garrigue et al. **: RBBB + LV intraventricular dyssynchrony (TDI) benefits from CRT more than RBBB without dyssynchrony

* N Engl J Med 2002;346:1845-53

** Am J Cardiol 2001;88:1436-1441

What is the evidence of clinical improvement with resynchronization therapy?

NYHA CLASS

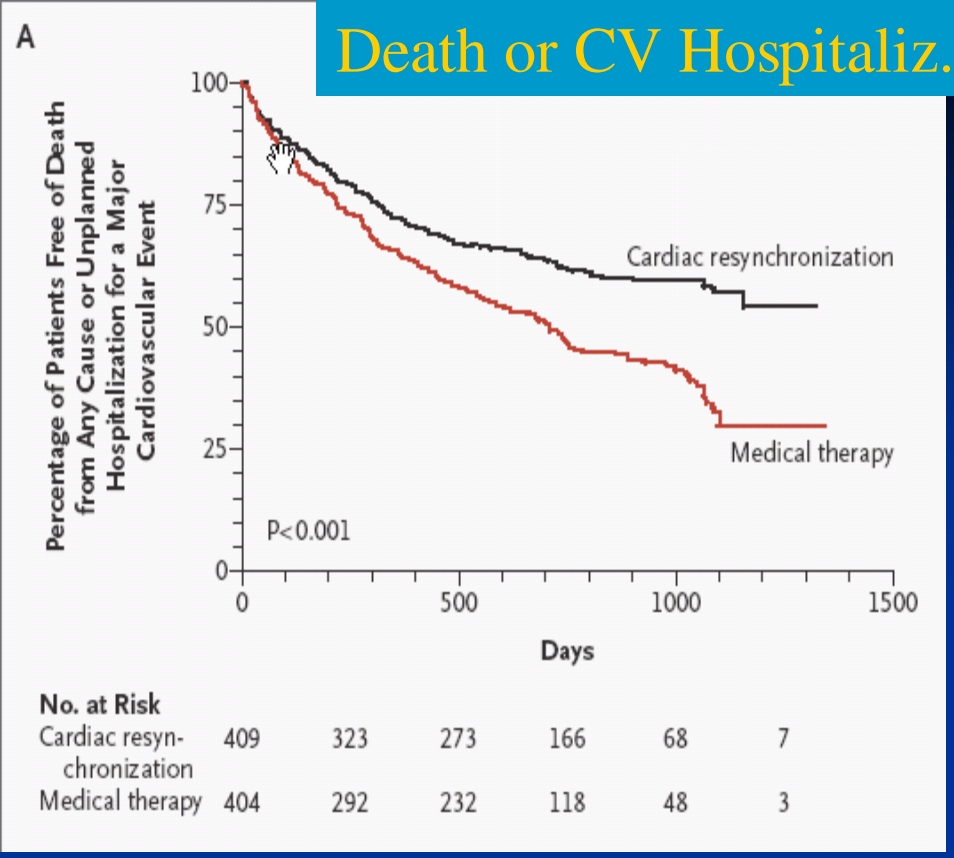
*CRT vs. Non CRT

Quality-of-life Score

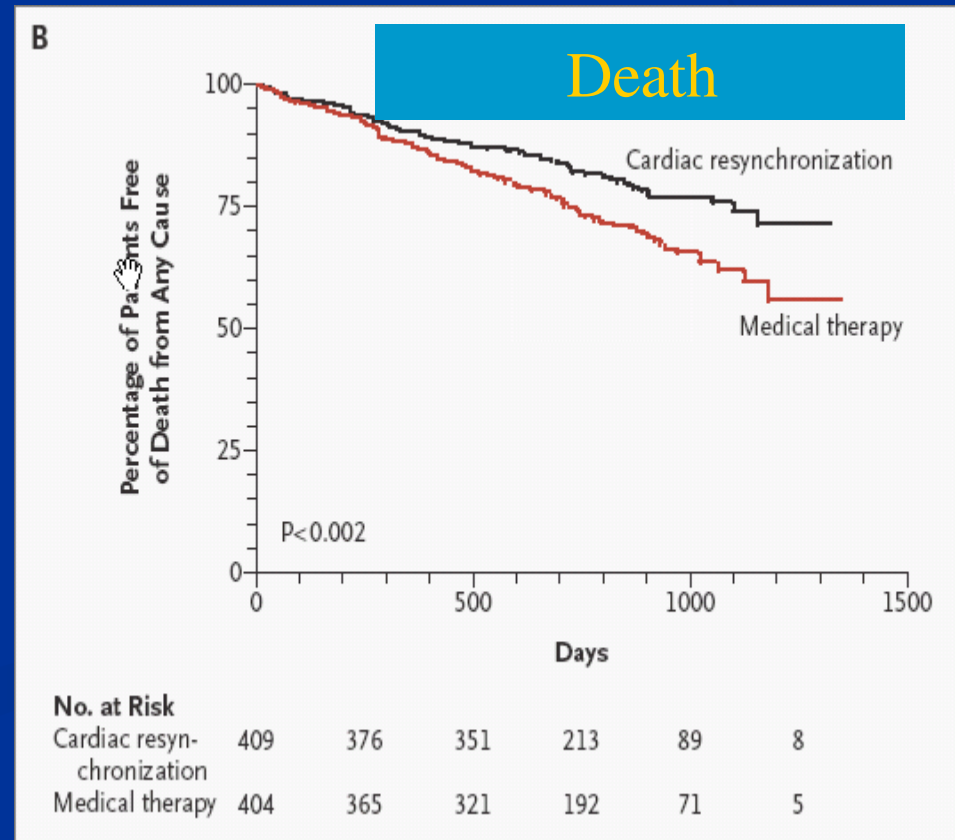
*CRT vs. Non CRT

CARE CHF

Death or CV Hospitaliz.



Death



N Engl J Med 2005;352:1539-49

CRT-P vs CRT-D

- COMPANION trial*
- 1520 pts
- OMT, OMT + CRT-P, OMT + CRT-D
- Primary endpoints: all-cause mortatily + all-cause hospitalizations
- CRT-P > OMT, CRT-D> OMT
- CRT-P vs CRT-D → no significant difference

* N Engl J Med 2004;350:2140-50

CRT-P vs CRT-D

Table 17 Clinical guidance to the choice of CRT-P or CRT-D in primary prevention

Factors favouring CRT-P	Factors favouring CRT-D
Advanced heart failure	Life expectancy >1 year
Severe renal insufficiency or dialysis	Stable heart failure, NYHA II
Other major co-morbidities	Ischaemic heart disease (low and intermediate MADIT risk score)
Frailty	Lack of comorbidities
Cachexia	

How about CRT in narrow QRS?

The Resynchronization Therapy in Normal QRS (RethinQ) Study

John F. Beshai, MD, Richard A. Grimm, DO, Sherif F. Nagueh, MD, James H. Baker II, MD, Scott L. Beau, MD, Steven M. Greenberg, MD, Luis A. Pires, MD, Patrick J. Tchou, MD
for the RethinQ study investigators

Study Design

Overall Objective

Determine CRT safety and efficacy in patients who are candidates for an ICD with NYHA Class III, narrow QRS duration (<130 ms) and evidence of mechanical dyssynchrony as measured by echocardiography/Tissue Doppler Imaging

Primary Endpoint

Improvement in Peak VO_2 during CPET of at least 1.0ml/kg/min at 6 months.

Secondary Endpoints

Improvement in quality of life score at 6-months

Improvement in NYHA classification at 6-months

Inclusion and Exclusion Criteria

Inclusion Criteria

- NYHA class III HF
- LVEF ≤ 35%
- Evidence of mechanical dyssynchrony
- QRS duration < 130ms

Exclusion Criteria

- NYHA class I, II, or IV
- Permanent Atrial Fibrillation
- Recent MI, unstable angina or cardiac revascularization
- Prior cardiac resynchronization therapy

Echo Criteria for LV Dyssynchrony

Mechanical dyssynchrony considered present if either

M-Mode

- Septal posterior wall mechanical delay (SPWMD) ≥ 130 ms

OR

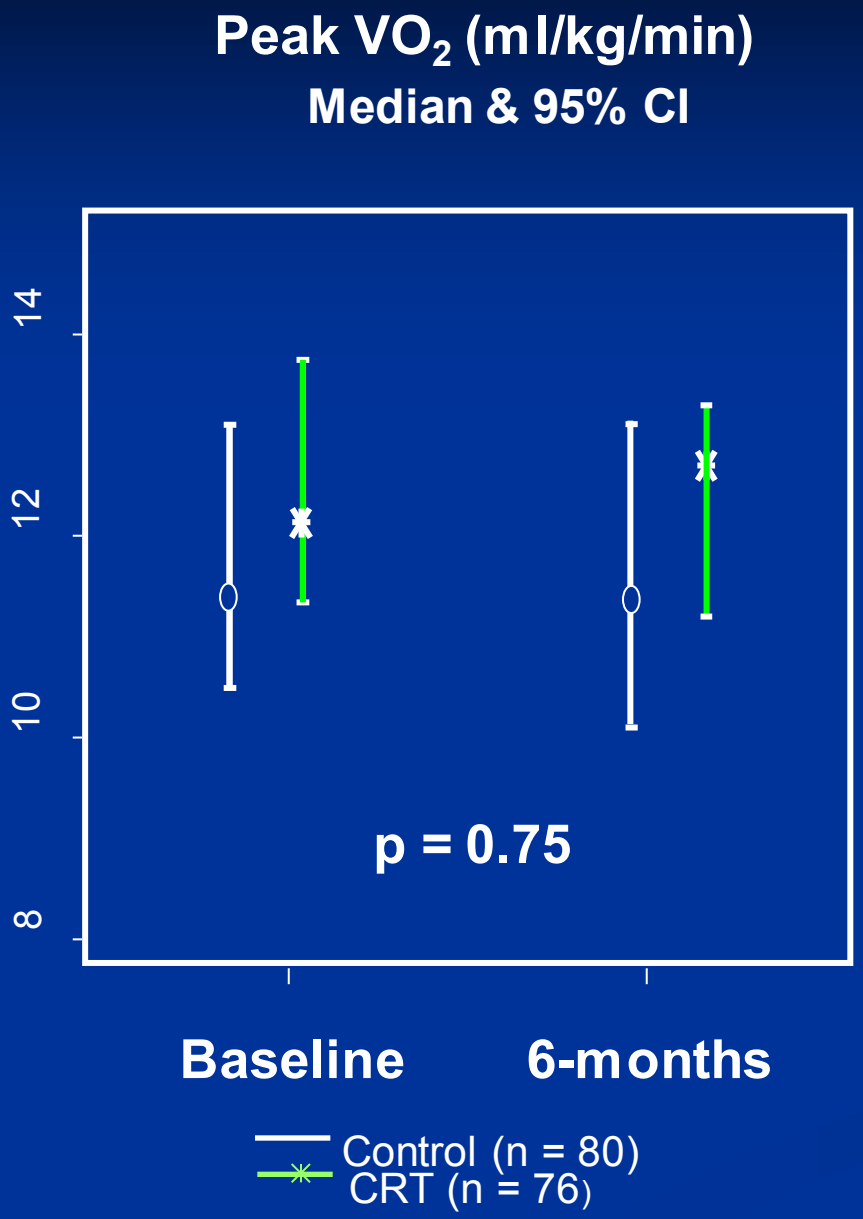
Tissue Doppler Imaging (TDI) of the basal ventricular segments in apical 4/2/3 chamber views

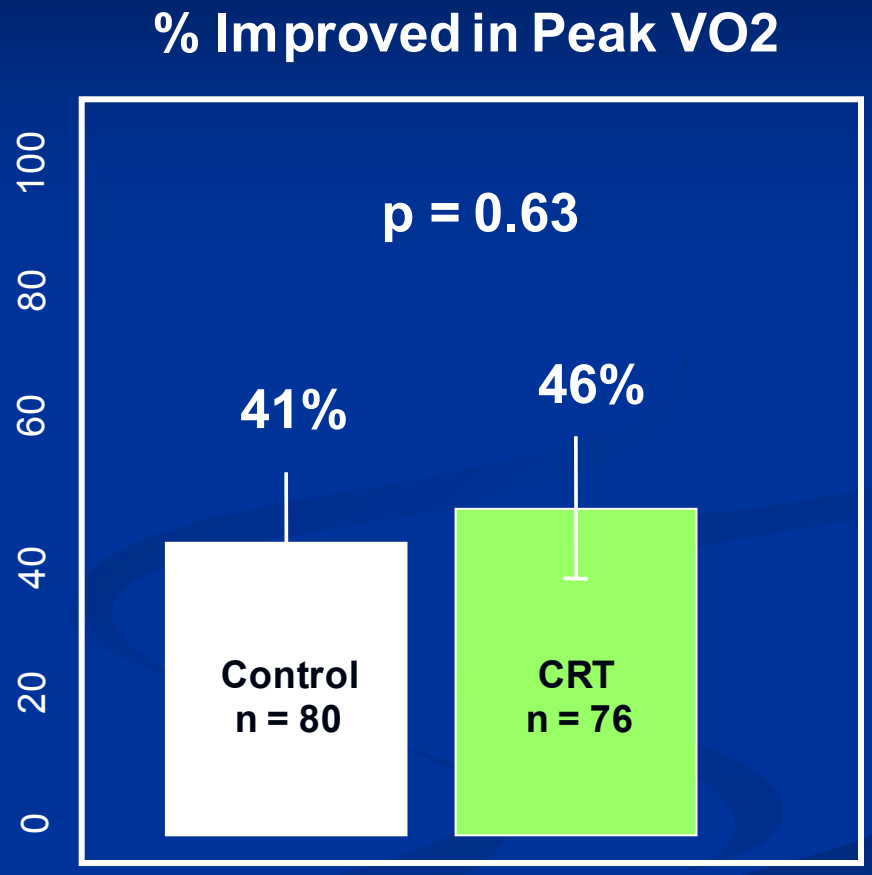
- Septal to lateral delay ≥ 65ms

OR

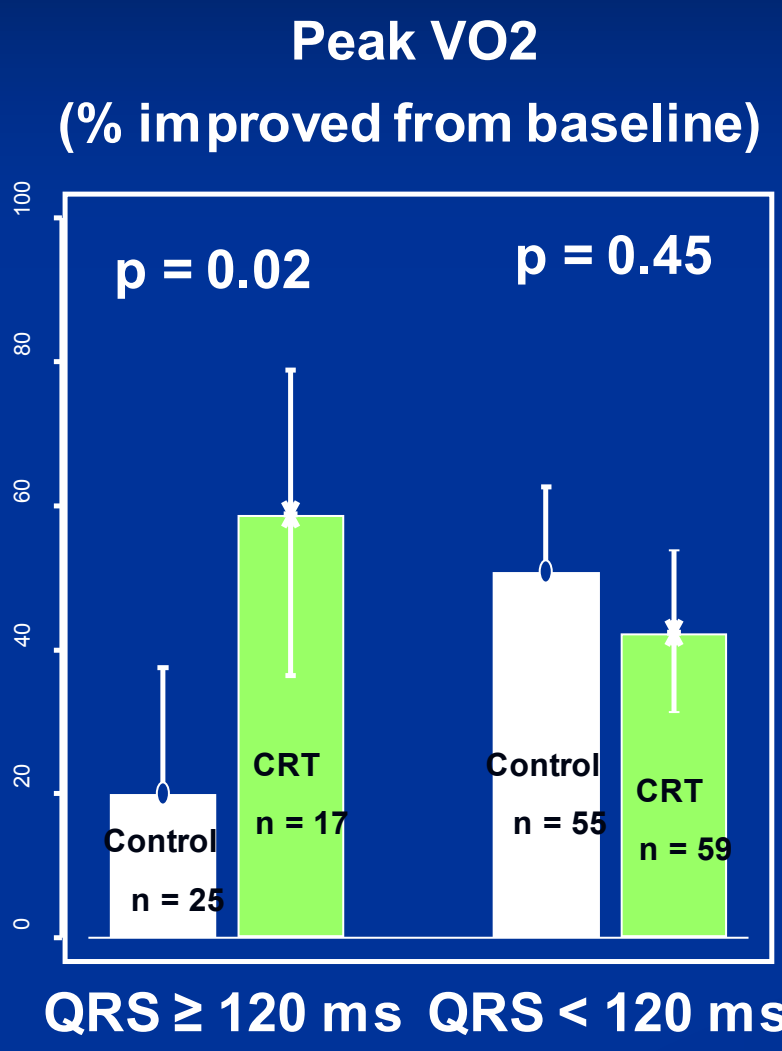
- Antero-septal to posterior delay ≥ 65ms

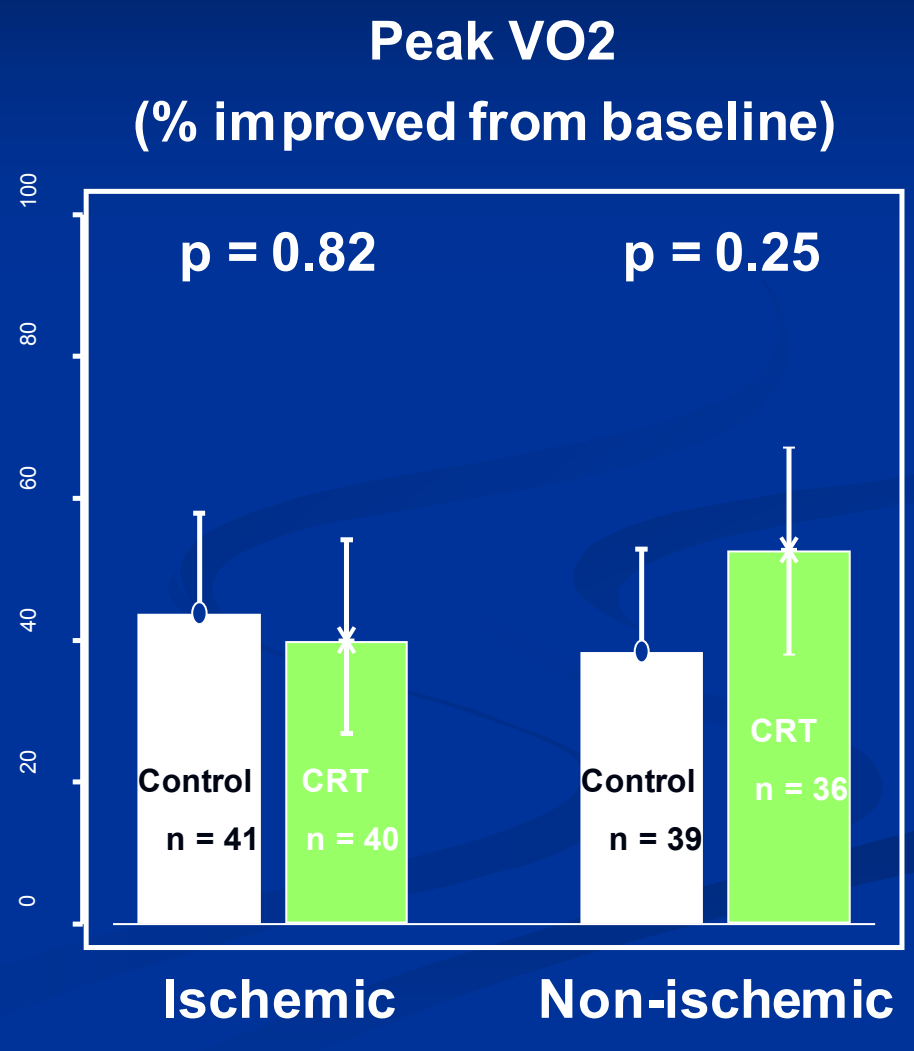
Results - Primary Endpoint





Peak VO_2 by sub-group





Conclusion

- CRT did not improve Peak VO_2 during exercise in patients with NYHA Class III heart failure, QRS duration <130ms, EF ≤ 35% and mechanical dyssynchrony as specified in this trial.

- While there was a statistically significant improvement of NYHA class, a secondary endpoint, there was no improvement in quality-of-life, 6-minute walking test, or echocardiographic measures of reverse LV remodeling.

- A subgroup of patients with QRS duration between 120 ms and 130 ms demonstrated an improvement from CRT, however patients with QRS duration < 120 ms did not demonstrate improvement.

Value of echocardiography?

Results of the Predictors of Response to CRT (PROSPECT) Trial

Eugene S. Chung, MD; Angel R. Leon, MD; Luigi Tavazzi, MD; Jing-Ping Sun, MD; Petros Nihoyannopoulos, MD; John Merlino, MD; William T. Abraham, MD; Stefano Ghio, MD; Christophe Leclercq, MD; Jeroen J. Bax, MD; Cheuk-Man Yu, MD, FRCP; John Gorcsan III, MD; Martin St John Sutton, FRCP; Johan De Sutter, MD, PhD; Jaime Murillo, MD

Background—Data from single-center studies suggest that echocardiographic parameters of mechanical dyssynchrony may improve patient selection for cardiac resynchronization therapy (CRT). In a prospective, multicenter setting, the Predictors of Response to CRT (PROSPECT) study tested the performance of these parameters to predict CRT response.

Methods and Results—Fifty-three centers in Europe, Hong Kong, and the United States enrolled 498 patients with standard CRT indications (New York Heart Association class III or IV heart failure, left ventricular ejection fraction ≤35%, QRS ≥130 ms, stable medical regimen). Twelve echocardiographic parameters of dyssynchrony, based on both conventional and tissue Doppler–based methods, were evaluated after site training in acquisition methods and blinded core laboratory analysis. Indicators of positive CRT response were improved clinical composite score and ≥15% reduction in left ventricular end-systolic volume at 6 months. Clinical composite score was improved in 69% of 426 patients, whereas left ventricular end-systolic volume decreased ≥15% in 56% of 286 patients with paired data. The ability of the 12 echocardiographic parameters to predict clinical composite score response varied widely, with sensitivity ranging from 6% to 74% and specificity ranging from 35% to 91%; for predicting left ventricular end-systolic volume response, sensitivity ranged from 9% to 77% and specificity from 31% to 93%. For all the parameters, the area under the receiver-operating characteristics curve for positive clinical or volume response to CRT was ≤0.62. There was large variability in the analysis of the dyssynchrony parameters.

Conclusion—Given the modest sensitivity and specificity in this multicenter setting despite training and central analysis, no single echocardiographic measure of dyssynchrony may be recommended to improve patient selection for CRT beyond current guidelines. Efforts aimed at reducing variability arising from technical and interpretative factors may improve the predictive power of these echocardiographic parameters in a broad clinical setting. (*Circulation*. **2008;117: 2608-2616.**)

How about CRT in NYHA II?

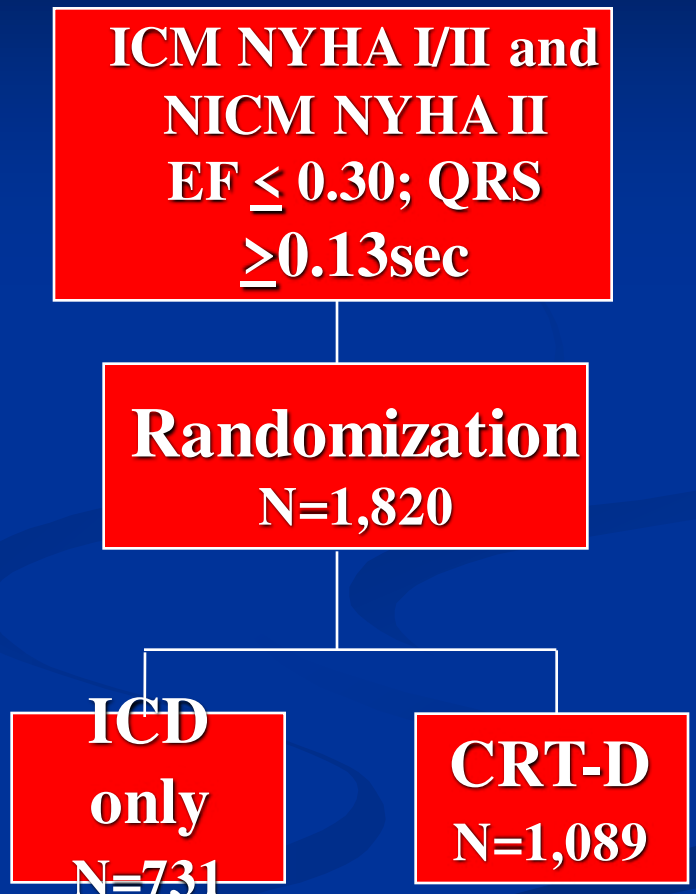
MADIT-CRT

Entry Criteria:

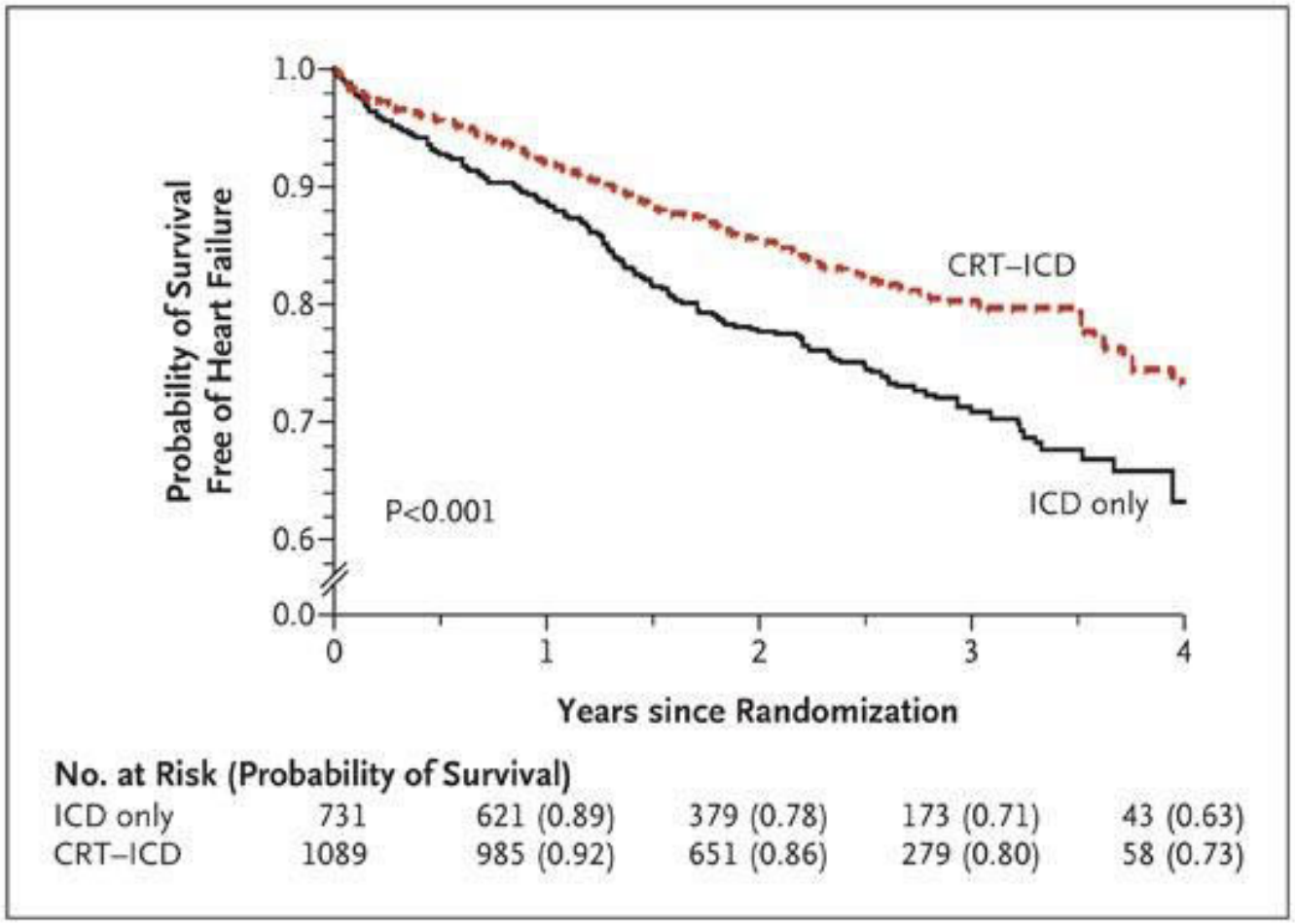
- Ischemic NYHA I-II or non-ischemic NYHA class II
- EF≤0.30
- QRS ≥0.13sec
- Sinus Rhythm
- Optimal pharmacologic therapy: B-b (>3 mo.); ACE/ARB (>1 mo.); statins in IHD

Exclusions:

- NYHA III-IV <90 days PTE
- Acute MI, CABG, PCI <3 months
- Existing ICD or CRT device
- AF; PR≥250ms; 2nd or 3rd degree HB
- BUN >70mg/dl or creatinine >3.0mg/dl



Kaplan-Meier Estimates of the Probability of Survival Free of Heart Failure



No. at Risk (Probability of Survival)					
ICD only	731	621 (0.89)	379 (0.78)	173 (0.71)	43 (0.63)
CRT–ICD	1089	985 (0.92)	651 (0.86)	279 (0.80)	58 (0.73)

Moss AJ et al. N Engl J Med 2009;361:1329-1338

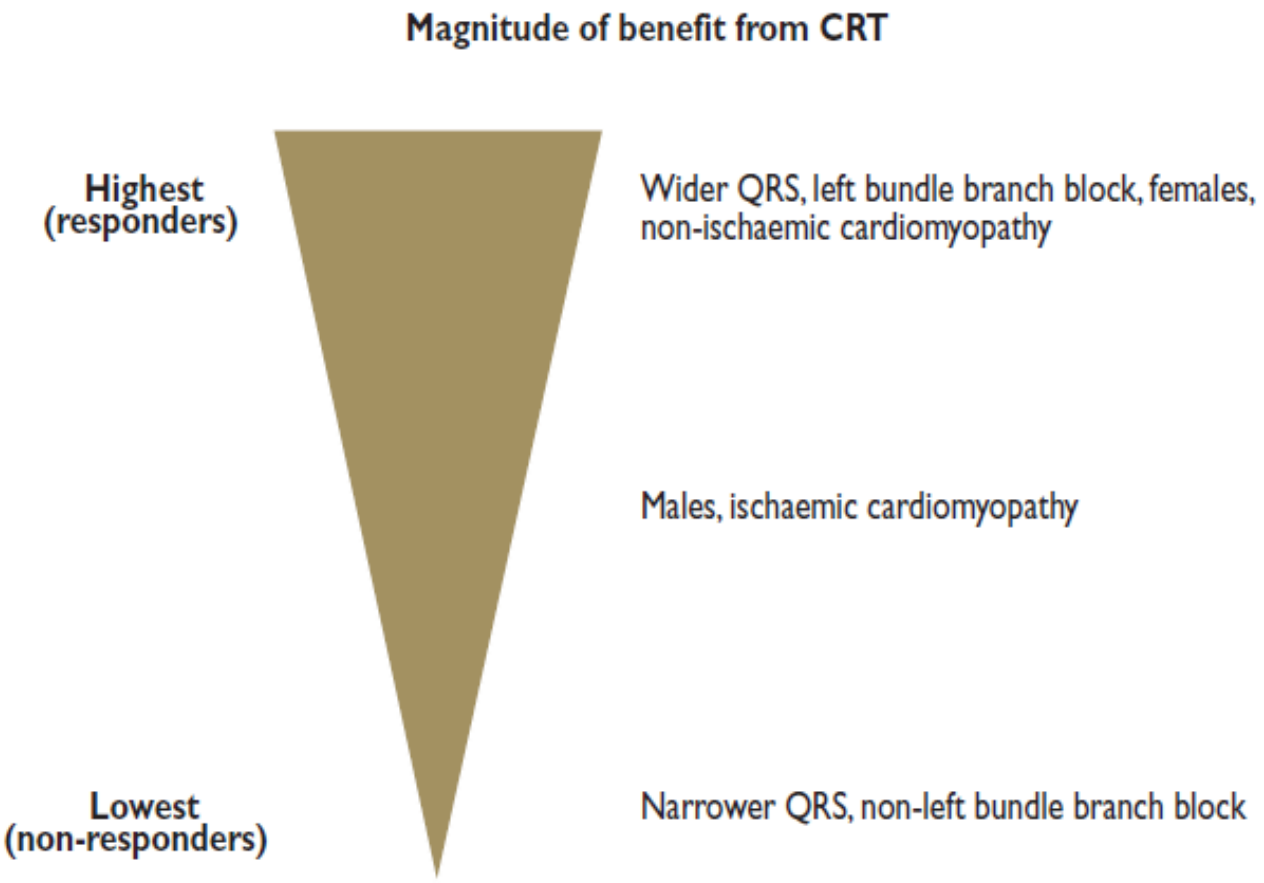


Figure 8 Clinical factors influencing the likelihood to respond to CRT.

Indications for CRT in pt with SR

Recommendations	Class [a]	Level [b]
1) LBBB with QRS duration >150 ms. CRT is recommended in chronic HF patients and LVEF ≤35% who remain in NYHA functional class II, III and ambulatory IV despite adequate medical treatment. [d]	I	A
2) LBBB with QRS duration 120–150 ms. CRT is recommended in chronic HF patients and LVEF ≤35% who remain in NYHA functional class II, III and ambulatory IV despite adequate medical treatment. [d]	I	B
3) Non-LBBB with QRS duration >150 ms. CRT should be considered in chronic HF patients and LVEF ≤35% who remain in NYHA functional class II, III and ambulatory IV despite adequate medical treatment. [d]	IIa	B
4) Non-LBBB with QRS duration 120–150 ms. CRT may be considered in chronic HF patients and LVEF ≤35% who remain in NYHA functional class II, III and ambulatory IV despite adequate medical treatment. [d]	IIb	B
5) CRT in patients with chronic HF with QRS duration <120 ms is not recommended.	III	B

CRT and AF

- AF + Fast ventricular rate → No CRT
- AF + Slow ventricular rate (spontaneous or AV node ablation)
  - MUSTIC-AF
  - PAVE
  - Gasparini et al. JACC 2006;48:734–43

CRT in AF patients

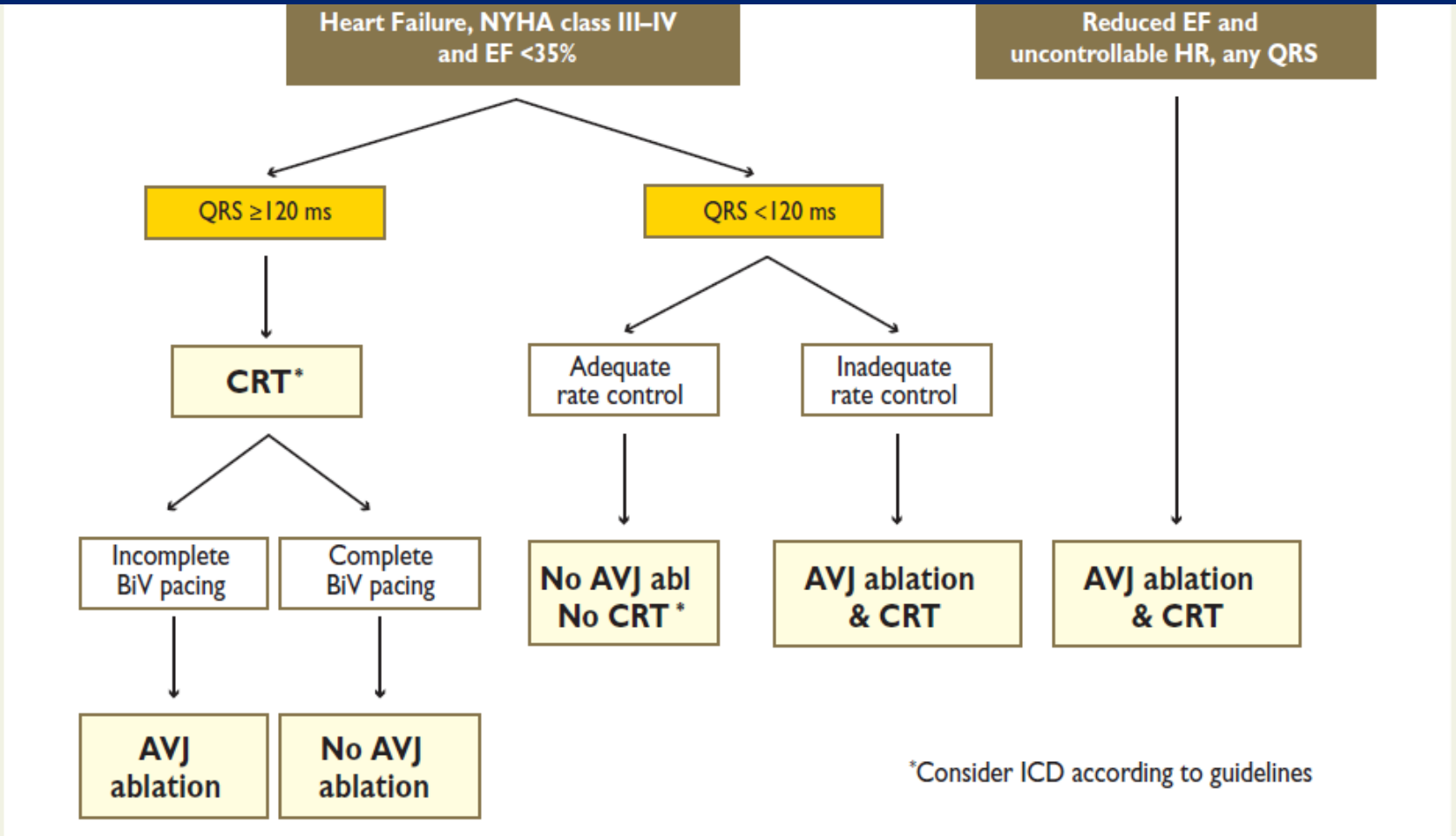


Figure 10 Indication for atrioventricular junction (AVJ) ablation in patients with symptomatic permanent atrial fibrillation (AF) and optimal pharmacological therapy. BiV = biventricular; CRT = cardiac resynchronization therapy; EF = ejection fraction; HR = heart rate; ICD = implantable cardioverter defibrillator; NYHA = New York Heart Association.

Indications for CRT in AF pts

Recommendations	Class [a]	Level [b]	Ref. [c]
1) Patients with HF, wide QRS and reduced LVEF: **1A)** CRT should be considered in chronic HF patients, intrinsic QRS ≥120 ms and LVEF ≤35% who remain in NYHA functional class III and ambulatory IV despite adequate medical treatment[d], provided that a BiV pacing as close to 100% as possible can be achieved.	IIa	B	62, 89–95
1B) AV junction ablation should be added in case of incomplete BiV pacing.	IIa	B	67–69, 90, 96–105
2) Patients with uncontrolled heart rate who are candidates for AV junction ablation. CRT should be considered in patients with reduced LVEF who are candidates for AV junction ablation for rate control.	IIa	B	89, 94, 105–107

Indication for upgraded or *de novo* cardiac resynchronization therapy in patients with conventional pacemaker indications and heart failure

Recommendations	Class [a]	Level [b]	Ref. [c]
1) Upgrade from conventional PM or ICD. CRT is indicated in HF patients with LVEF <35% and high percentage of ventricular pacing who remain in NYHA class III and ambulatory IV despite adequate medical treatment. [d]	I	B	47, 108–122
2) *De novo* cardiac resynchronization therapy. CRT should be considered in HF patients, reduced EF and expected high percentage of ventricular pacing in order to decrease the risk of worsening HF.	IIa	B	123–130

Implant procedure

Implant Procedure

- Venous access
- Cannulation
- Venograms
- LV lead placement
- LV lead testing
- Removal of delivery equipment

Right atrial anatomy

Crista Terminalis

Tricuspid Annulus

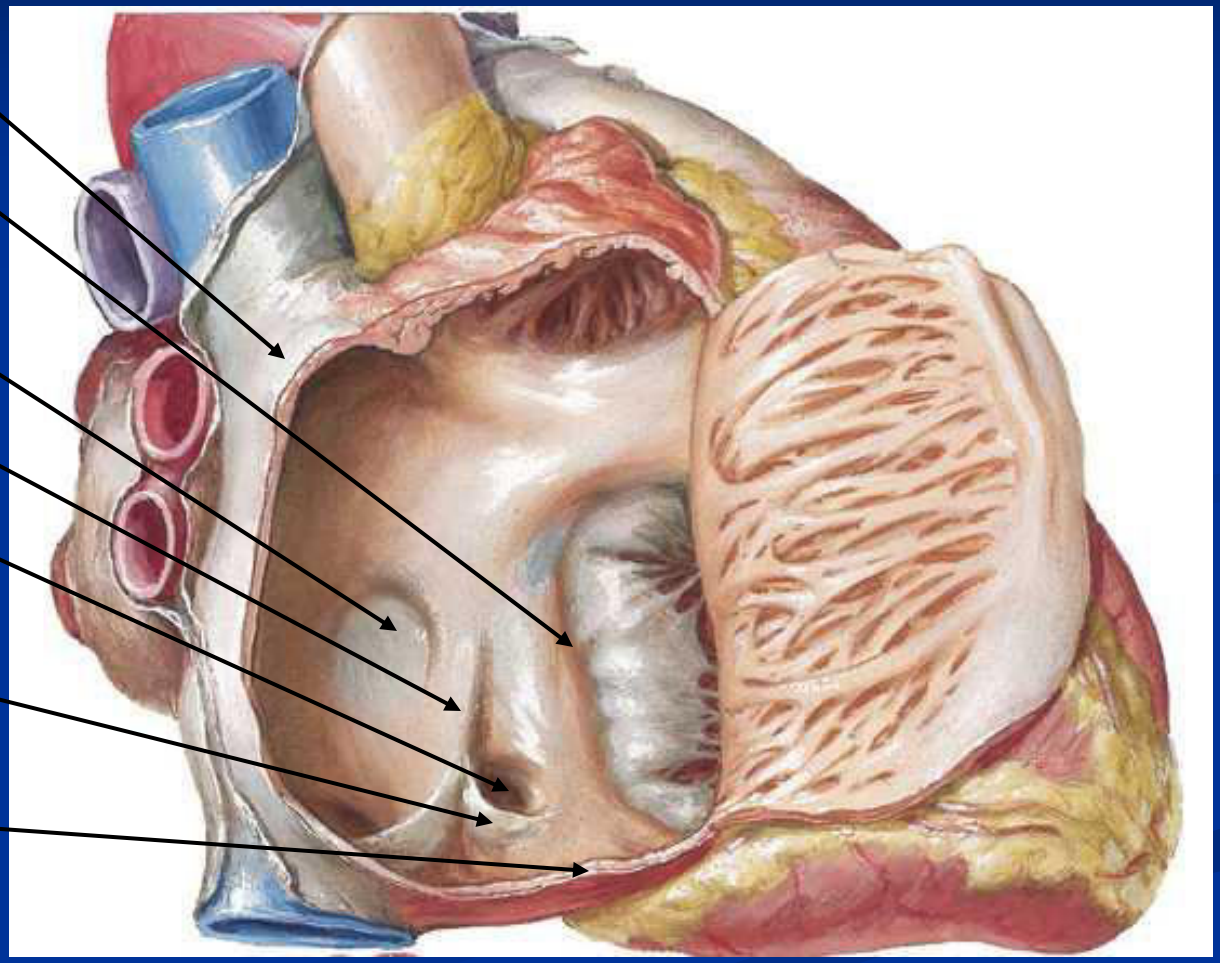
Foramen Ovale

Eustachian Ridge

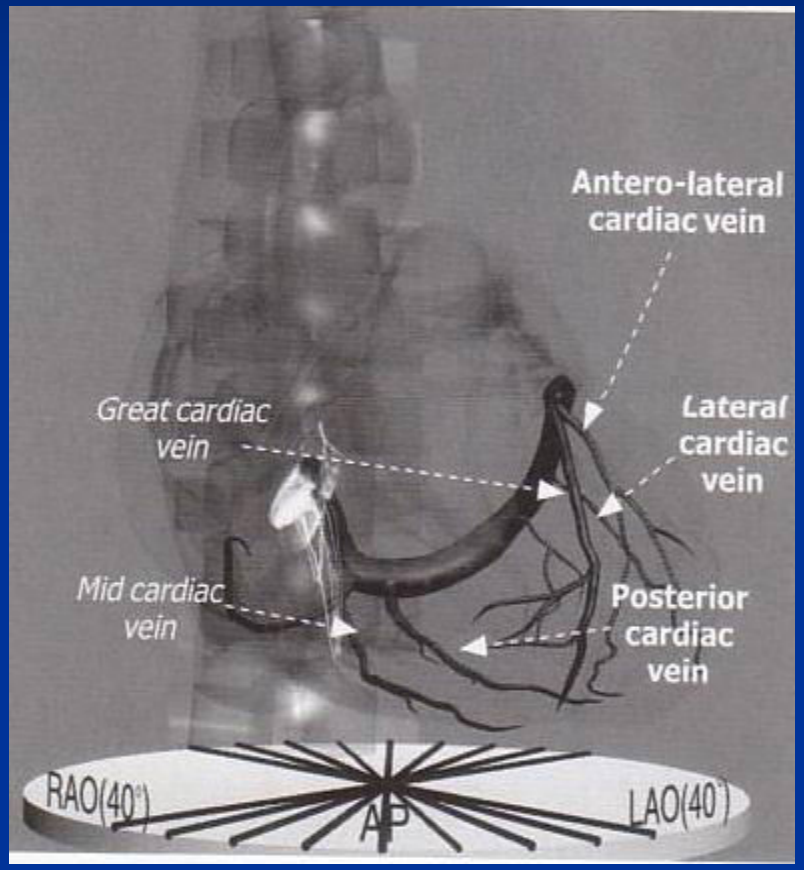
OS Coronary Sinus

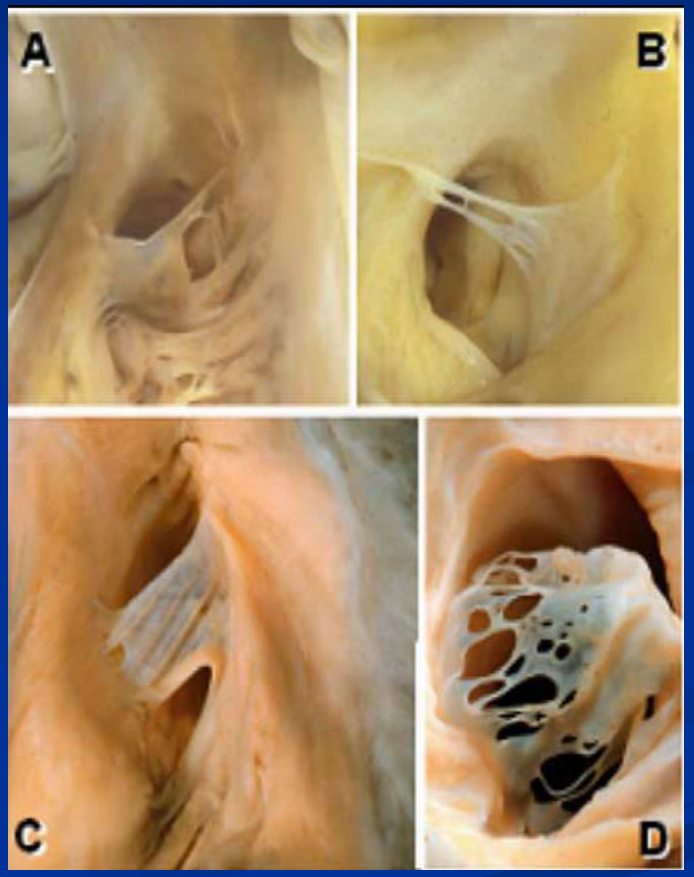
Thebesian Valve

Isthmus



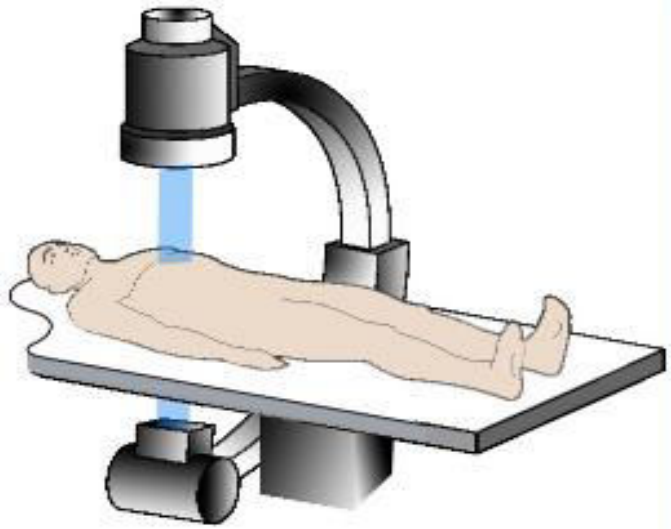
Coronary sinus anatomy



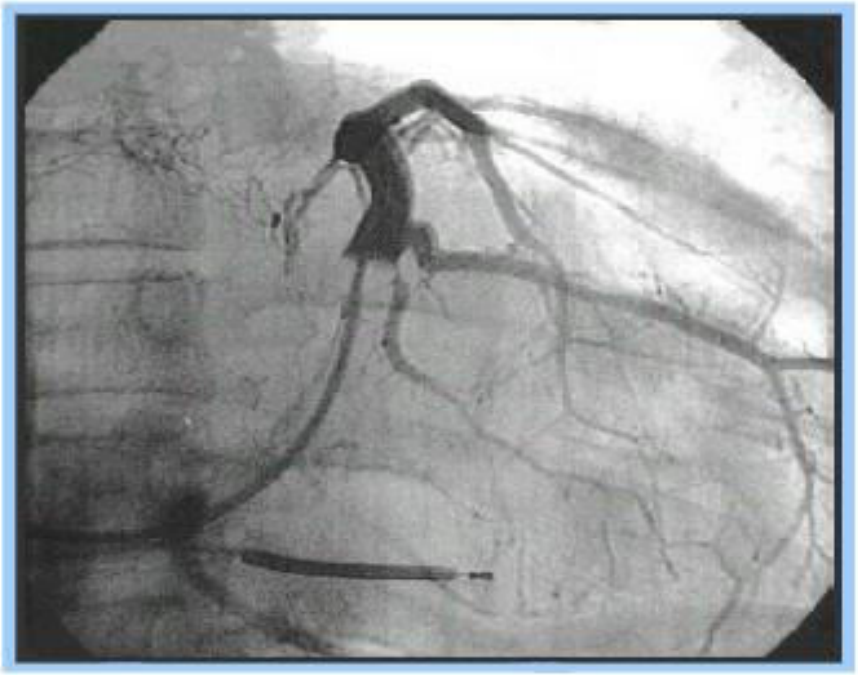


AP Fluoroscopy

AP Orientation

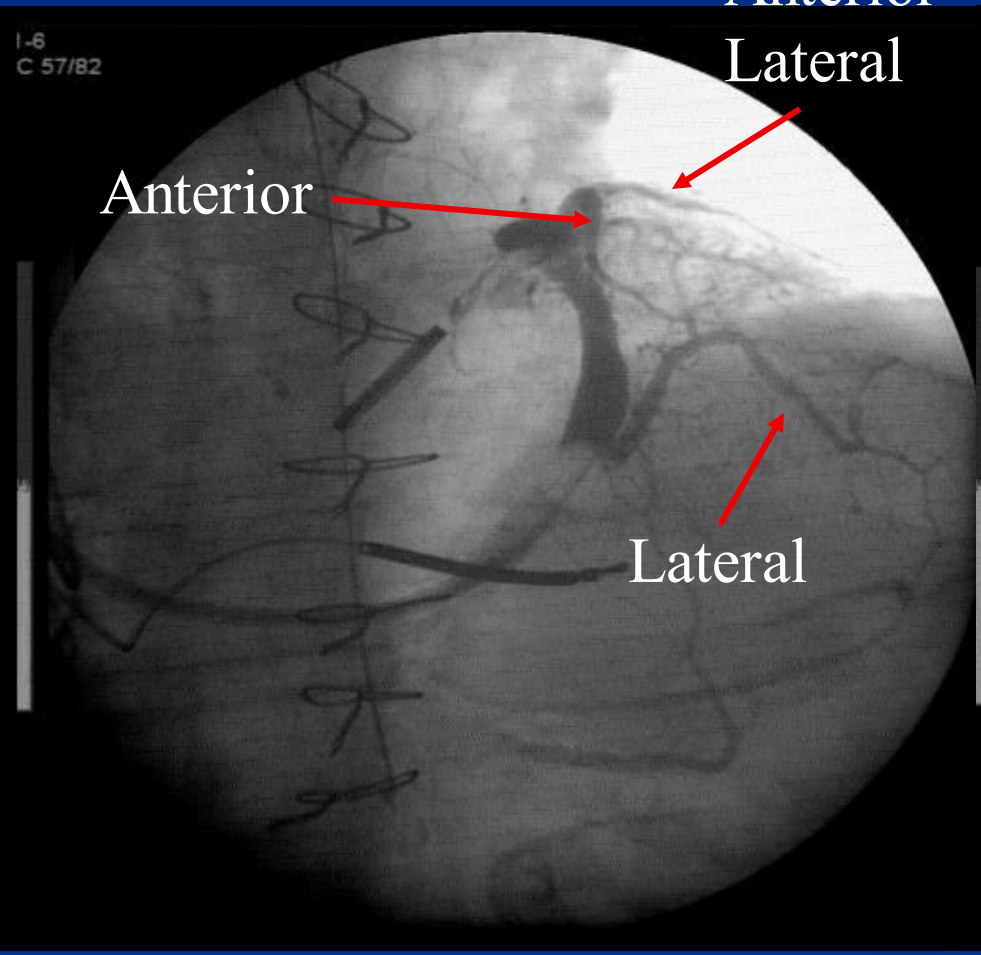


AP Venogram



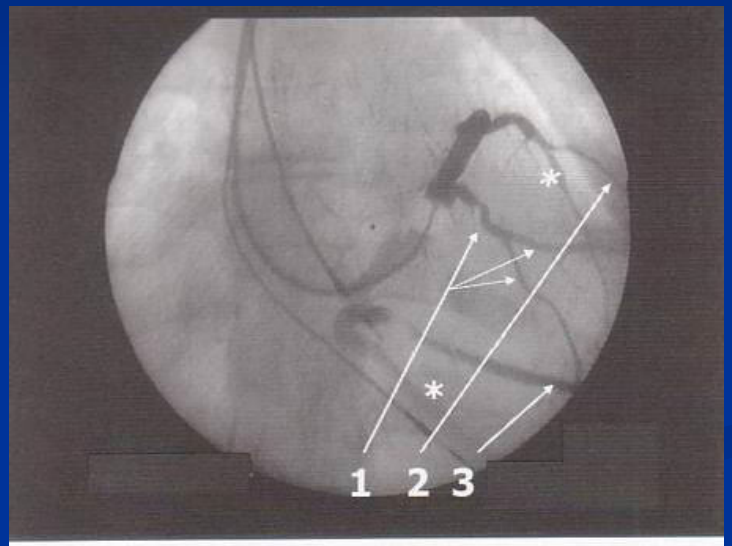
AP

Venogram



Final LV Lead Placement

Optimal LV pacing sites



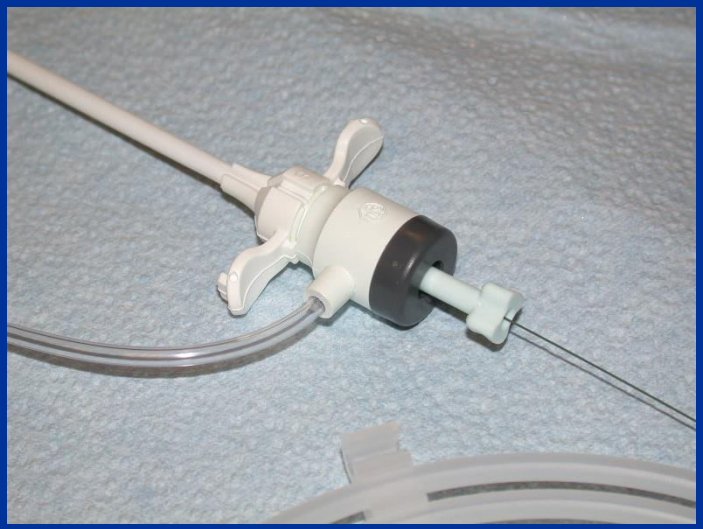
Various optimal LV pacing sites

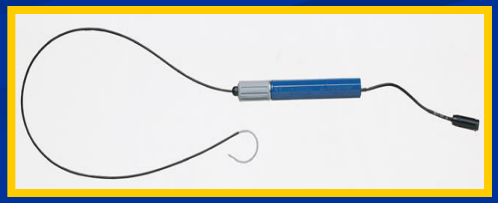
1. Lateral vein
2. Anterior lateral vein
3. Posterior vein

* Non optimal LV pacing site

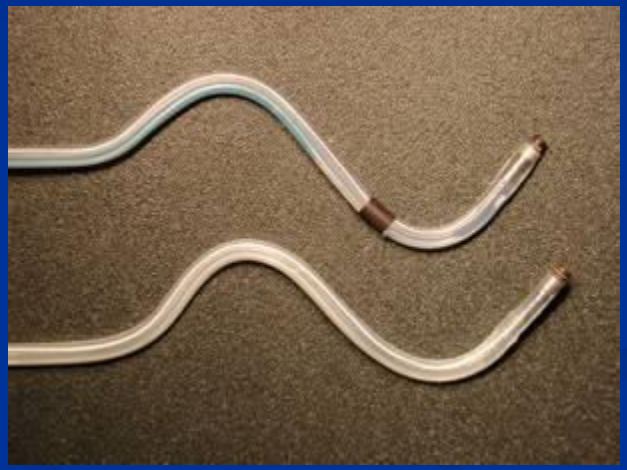
- Great cardiac vein
- *Middle cardiac vein*

Delivery system

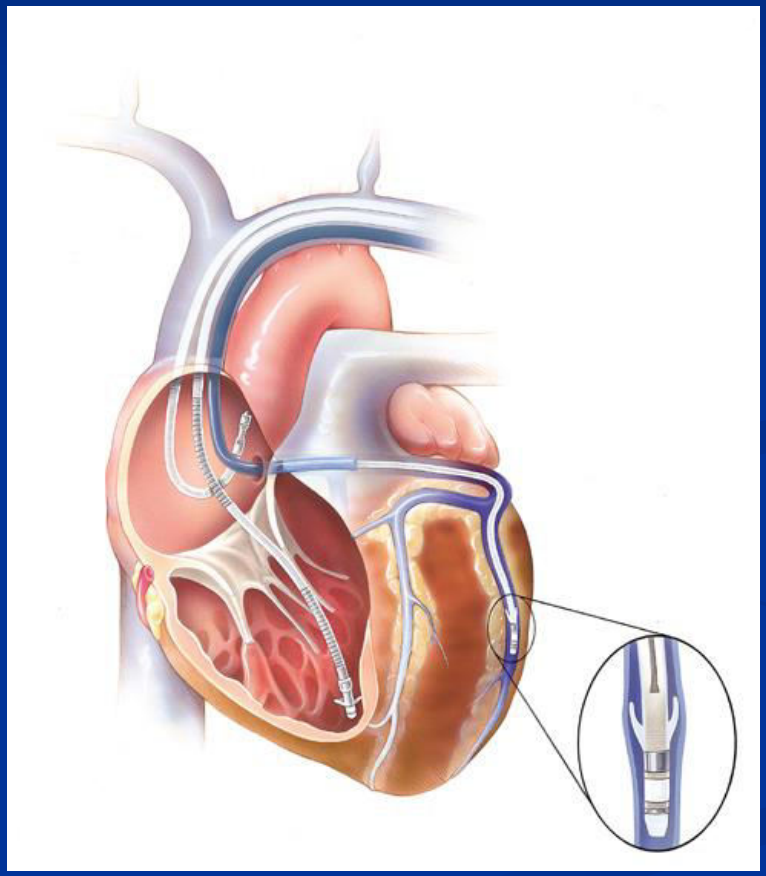




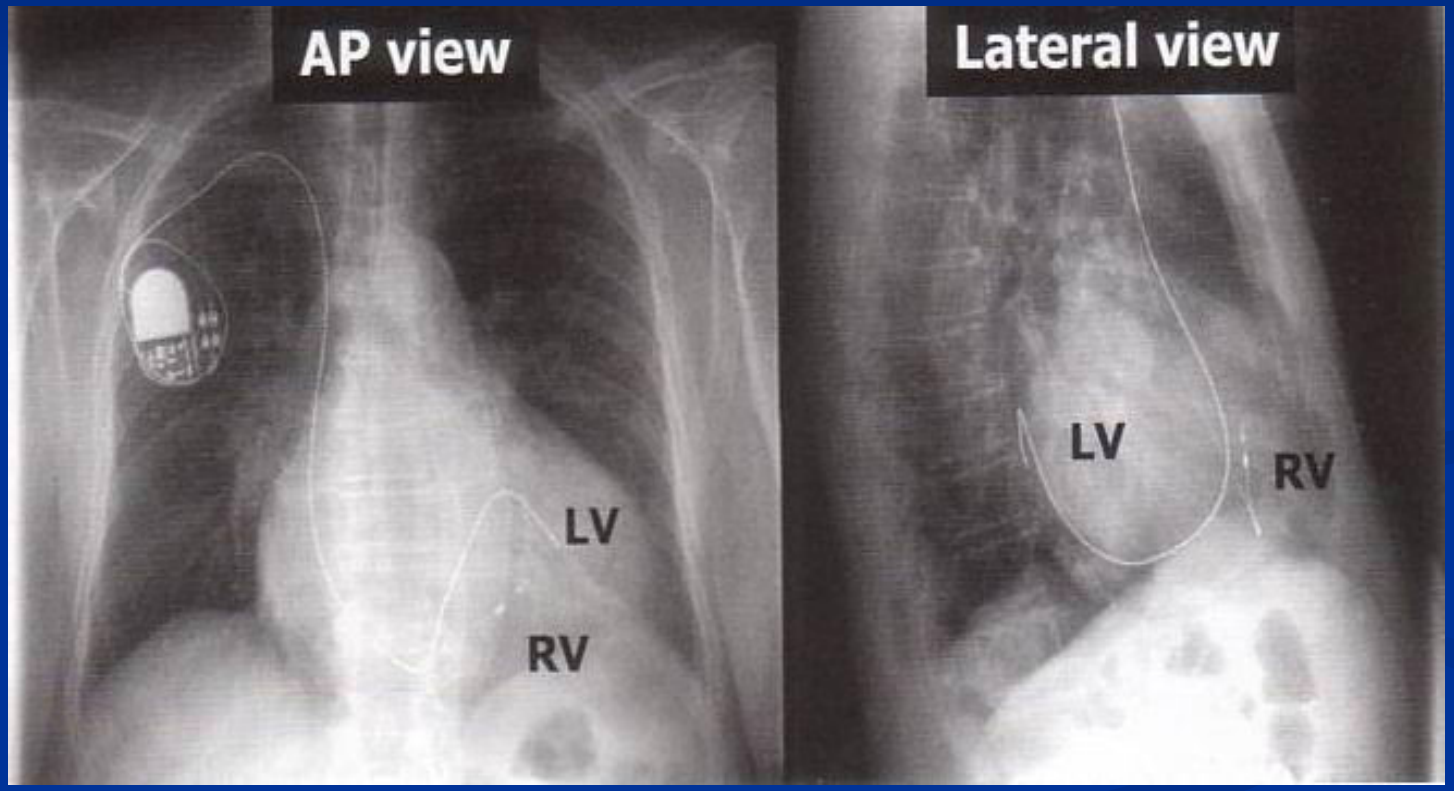
Pacemaker and LV lead



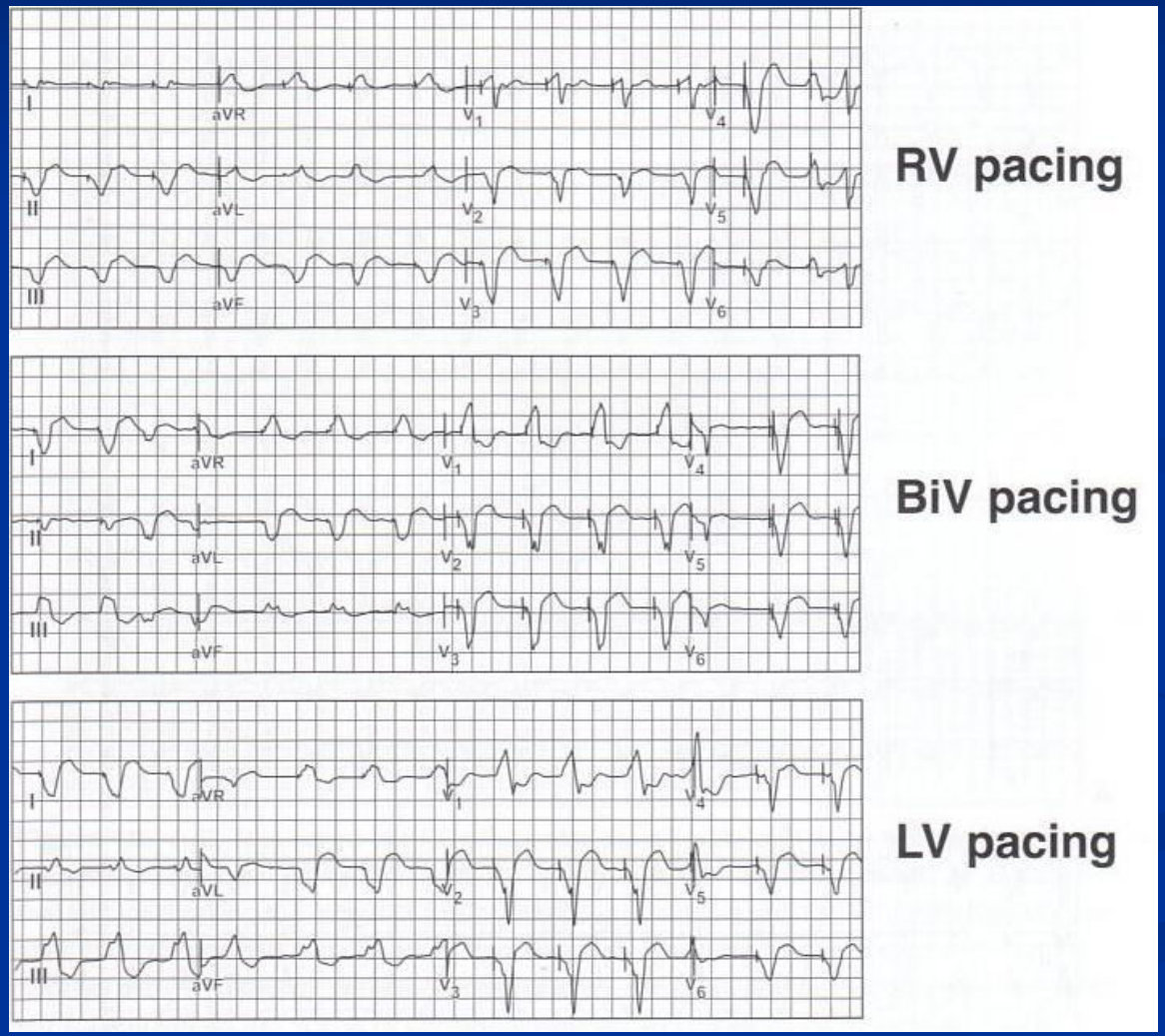
Leads in place



CRT X-rays



CRT ECG


I
aVR
V1
V4
II
aVL
V2
V5
III
aVF
V3
V6
RV pacing
BiV pacing
LV pacing

Complications of CRT

- Pacemaker's complication
- Coronary sinus dissection
- Coronary vein perforation
- Renal failure

Thank you for your attention!