Deborah Heart and Lung Center

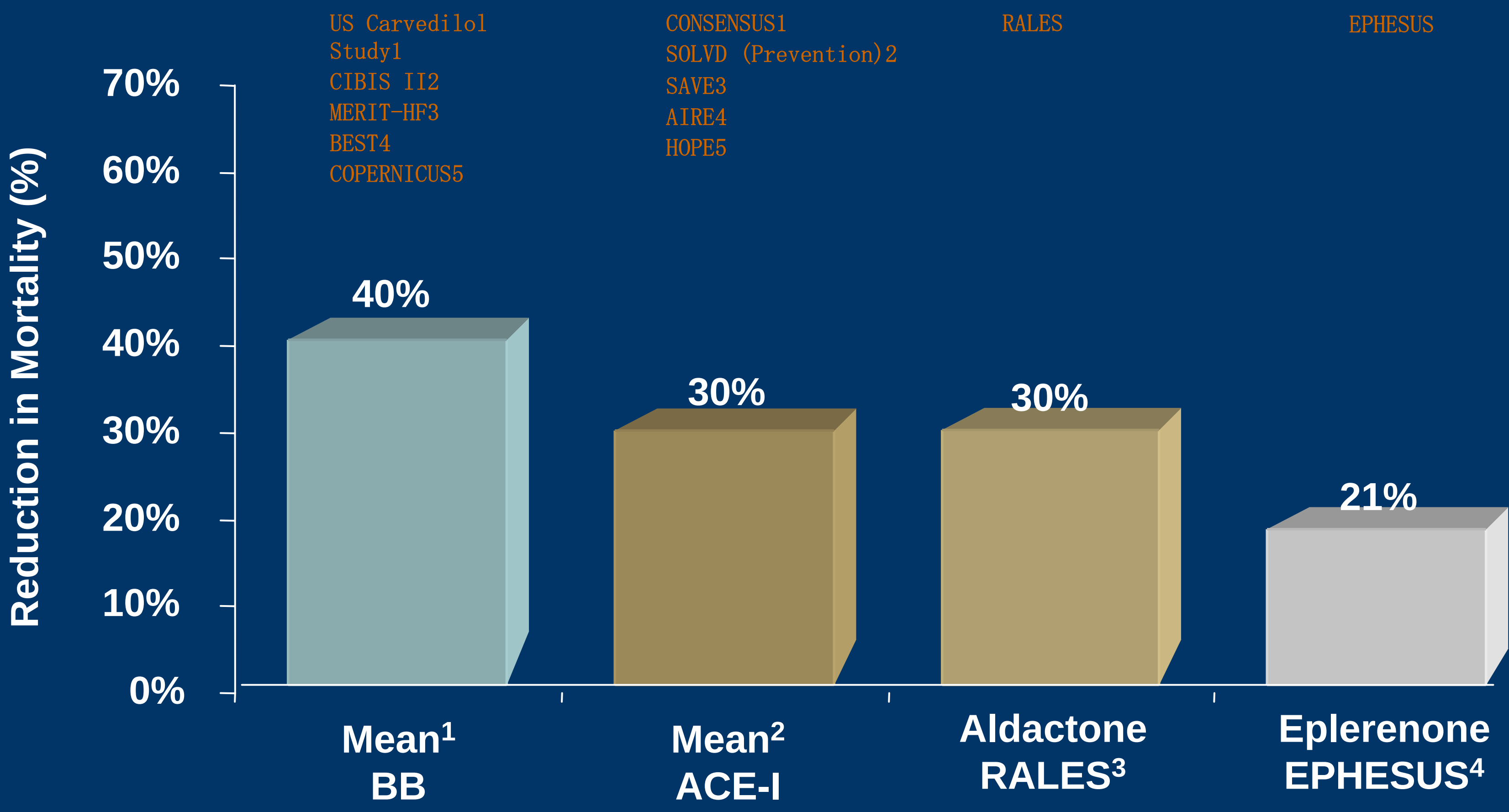
Heart Failure, From an Electrophysiological Perspective Device Therapy in the Failing Heart

Raffaele Corbisiero MD
Director of Electrophysiology
Deborah Heart & Lung Center

Quote from DeDoer 1935

Fibrillation, especially atrial, has become important in the clinic. Since Ventricular fibrillation usually results in sudden cardiac death, it is, of course, of much less importance

Expected Mortality Reduction with Drugs

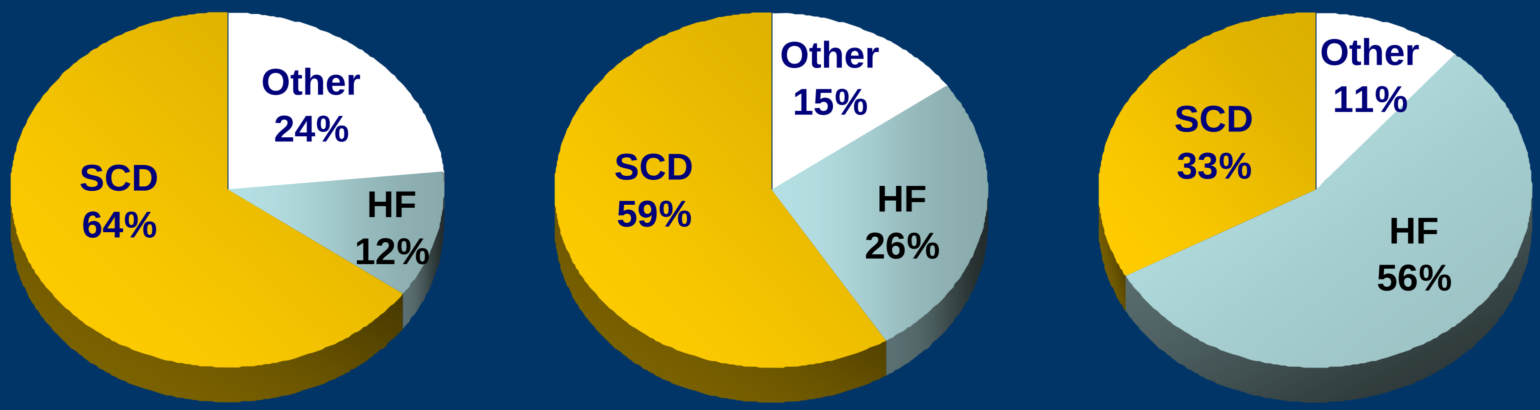


1. Mean of major beta blocker trials
2. Mean of major ACE inhibitor trials
3. *N Engl J Med* 1999 Sep 2; 341(10):709-17.
4. *N Engl J Med* 2003; 348:1309-1321.

This slide demonstrates that the benefits of medical therapy are clear, however, we must remember that compliance is an issue with these patients and is sometimes as low as 50%.

1 The AVID Investigators. *N Engl J Med.* 1997;337:1576-1583.
2 Connolly SJ. *Circulation.* 2000; 101; 1297-1302.
3 Moss AJ. *N Engl J Med.* 1996;335;1933-1940.
4 Buxton AE. *N Engl J Med.* 1999; 341:1882-1890.
5 Moss AJ. *N Engl J Med.* 2002;346:877-883.

Mechanism of Death in HF



NYHA II

No. of deaths
n=103

NYHA III

No. of deaths
n=232

NYHA IV

No. of deaths
n=27

HF = mortality secondary to worsening heart failure
SCD = sudden cardiac death

MERIT-HF Study Group. *Lancet* 1999;353:2001-2007.

The MERIT-HF study evaluated the effects of metoprolol on mortality in patients with decreased ejection fraction and symptoms of HF.

A post-hoc analysis of the MERIT-HF study looked at the total mortality and mode of death relative to the NYHA functional classification.

The proportion of sudden cardiac deaths decreased with increasing severity of NYHA functional class.

Sudden death occurred in nearly 60% of patients.

The proportion of patients who died from worsening HF increased with increasing functional class.

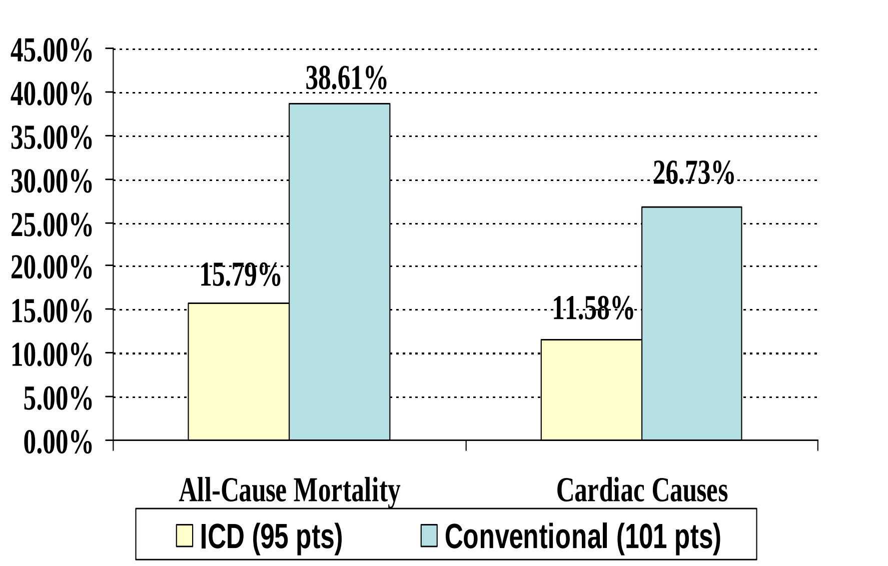
Ventricular dysrhythmias, not controlled by medical therapy, are often the cause of SCD in HF.

Clearly, there are unmet needs in the management of patients with HF.

MERIT-HF Study Group. *Lancet* 1999;353:2001-2007.

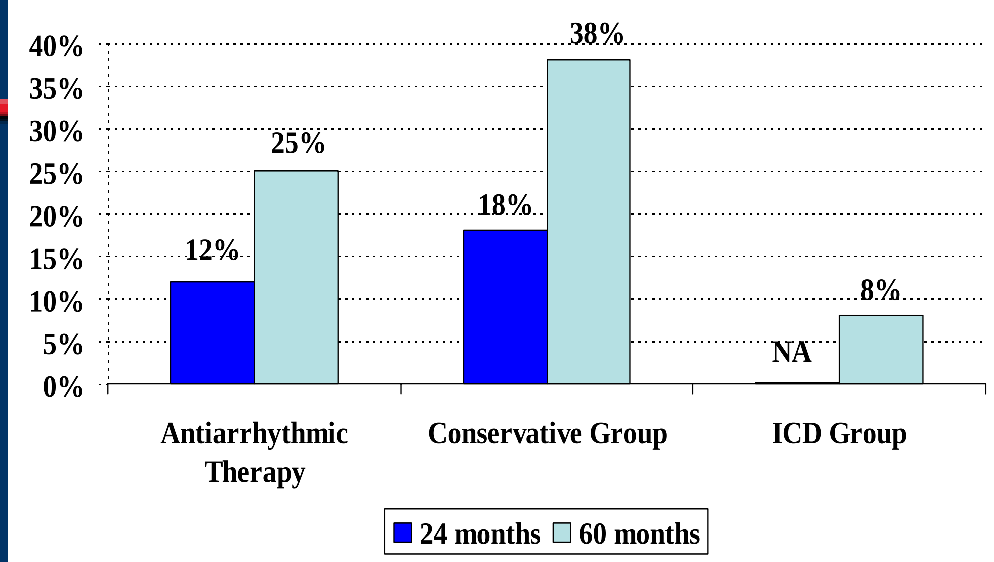
MADIT

The New England Journal of Medicine 1996;335:1933-40



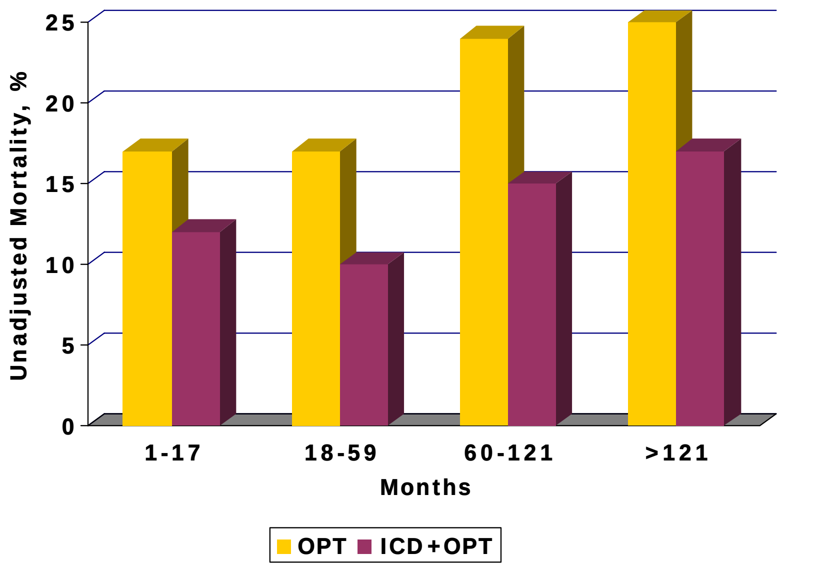
MUST

N Engl J Med. 1999;341:1882-90



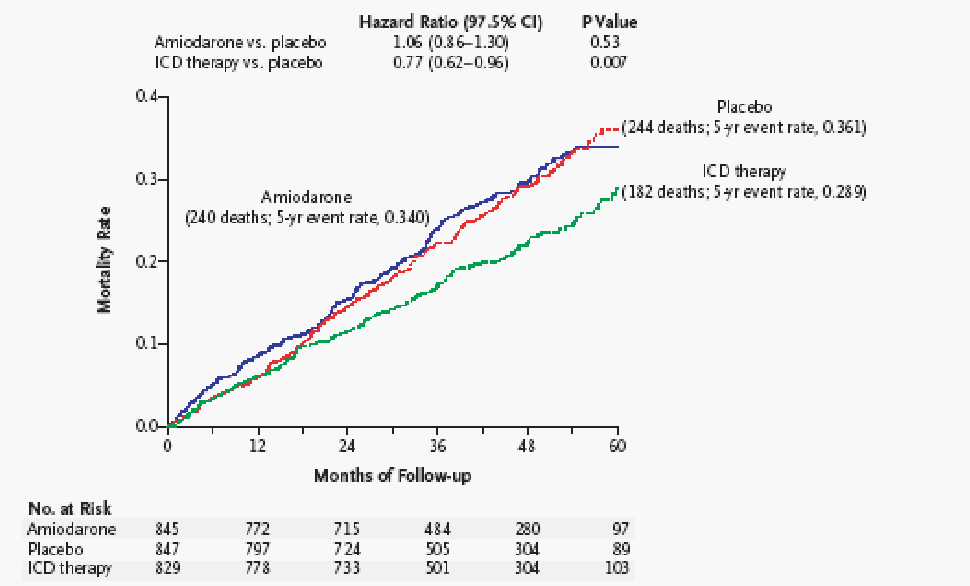
MADIT II

Wilber DJ, et al. NASPE, 24th Scientific Session



SCD HeFT

Bardy, et al. NEJM 2005

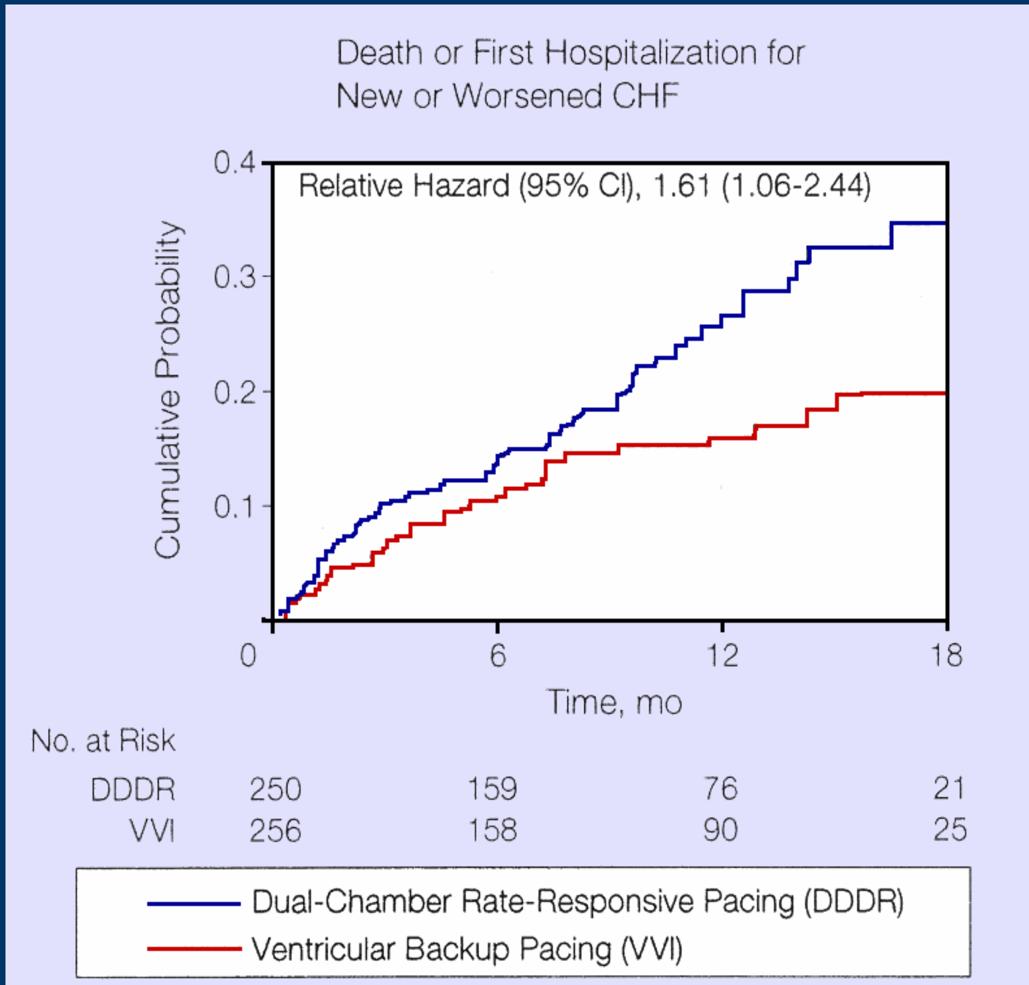


A summary of the major clinical trials showing the benefit of prophylactic ICD’s. The MADIT, MUSTT and MADIT II trial had patient populations with ischemic cardiomyopathy. Of note, around two thirds of these patients carried a diagnosis of CHF. The SCD HeFT trial included all etiologies of LV dysfunction.

Death or First Hospitalization for New or Worsening Heart Failure

- VVI-40 patients had fewer occurrences (p≤.03)

- 1 year survival free of composite
  - VVI-40 83.9%
  - DDDR-70 73.3%



Clearly, ICD’s can help in sudden cardiac death risk prevention, however, the deleterious effects of ventricular pacing in an abnormal heart must be kept in mind.

Baseline to One month CPX

CARDIOPULMONARY EXERCISE TEST RESULTS

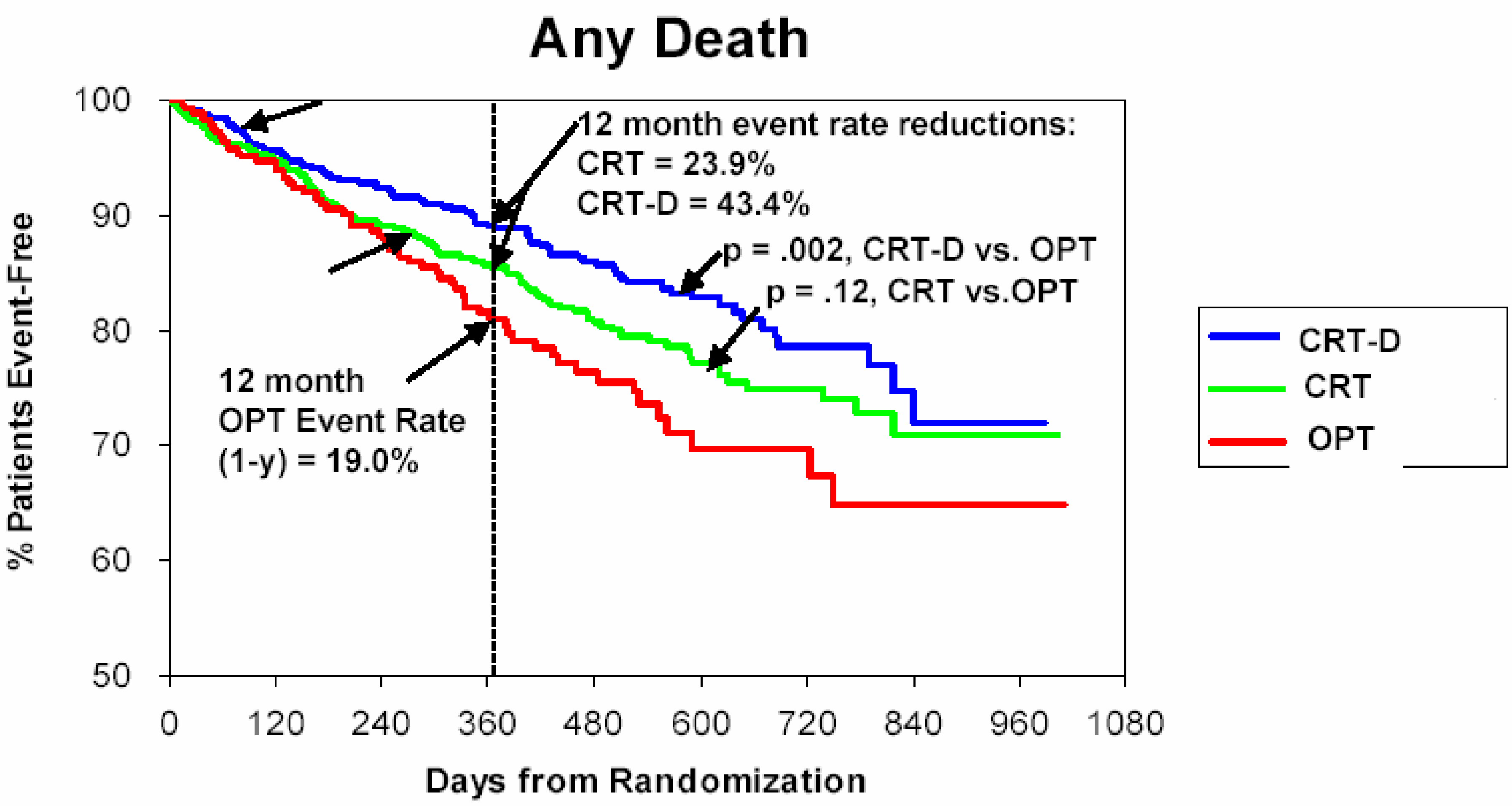
		REST	MAX	PRED	%PRED
Time Min	Min	0.4	3.4		
VO2	L/min	0.538	0.947	1.544	(61)
VO2/kg					
METS					
VCO2					
VE(BTPS					
BR					
Vt					
RR					
RQ					
VEO2					
VECO2					
PetO2					
PetCO2					
SpO2					
VD/Vt E					
VD/Vt A					
HR					
O2 Puls					
Speed					

CARDIOPULMONARY EXERCISE TEST RESULTS

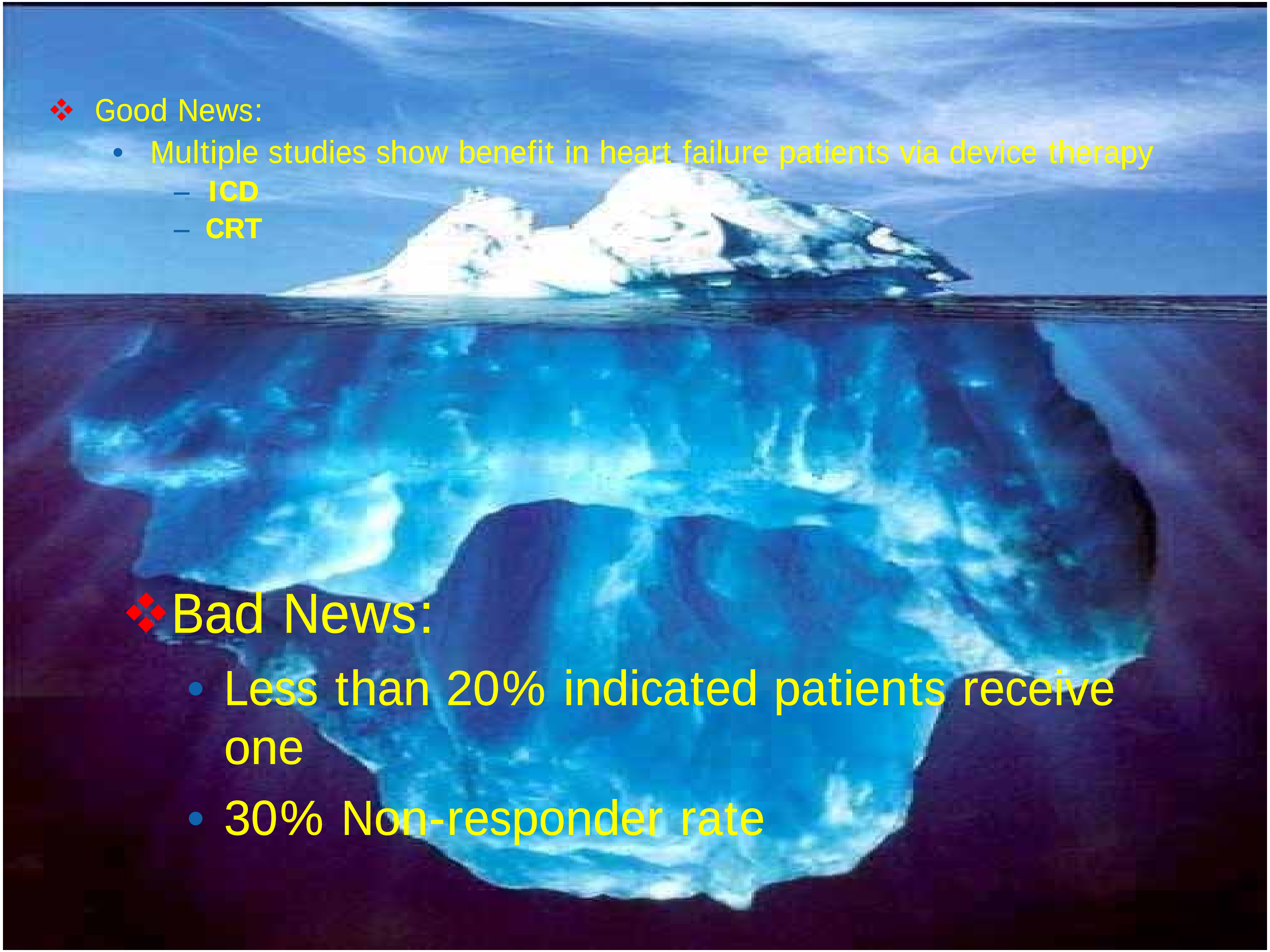
		REST	MAX	PRED	%PRED
Time Min	Min	0.4	12.9		
VO2	L/min	0.244	1.434	1.512	95
VO2/kg	mL/kg/min	3.4	19.7	13.8	143
METS		1.0	5.6		
VCO2	L/min	0.201	1.547		
VE(BTPS)	L/min	10.3	62.8	97.7	64
BR	%	25	25		
Vt	Liters	0.642	2.068	1.852	112
RR	BPM	16	30		
RQ		0.82	1.08		
VEO2		42	44		
VECO2		51	41		
PetO2	mmHg	105.9	120.1		
PetCO2	mmHg	35.7	30.0		
SpO2	%				
VD/Vt Est		0.43	0.19	0.18	105
VD/Vt ABG				0.18	
HR	BPM	107	165		

Personal experience of first patient with biventricular pacemaker. Dramatic improvement in symptoms were noted, however, patient did die of VF.

COMPANION: *Secondary Endpoint of All-Cause Mortality*



The results of COMPANION, to date, are the most important resynchronization therapy trial.



- Good News:
  - Multiple studies show benefit in heart failure patients via device therapy
    - **ICD**
    - **CRT**
- Bad News:
  - Less than 20% indicated patients receive one
  - 30% Non-responder rate

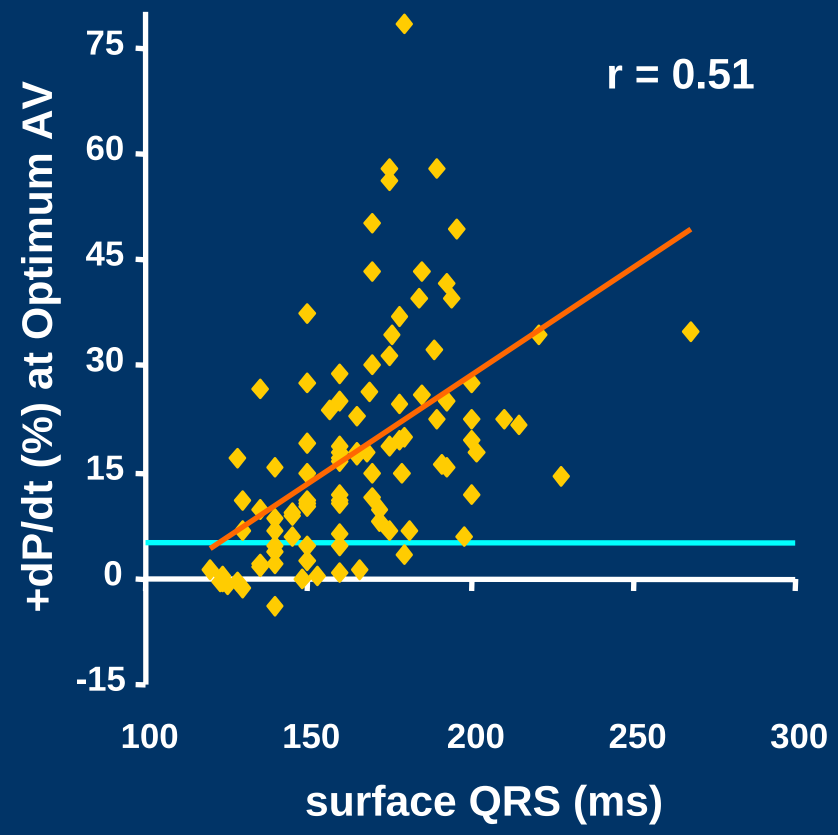
Despite the promising benefit of device therapy, we must keep in mind two key points:

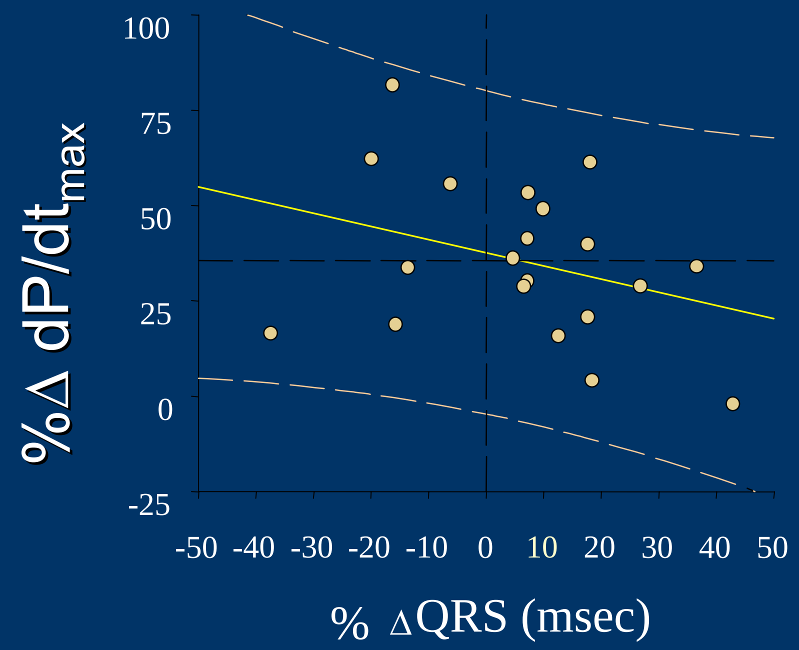
1. In the USA, only one out of every five persons who need an ICD are receiving one.

2. The non-responder rate in CRT therapy is over 30%.

QRS duration is only weakly correlated with acute improvement [1,2]

However, change in QRS duration does not correlate with acute improvement[2]





[1] Kadhiresan et al., PACE, 23:II12, 2000

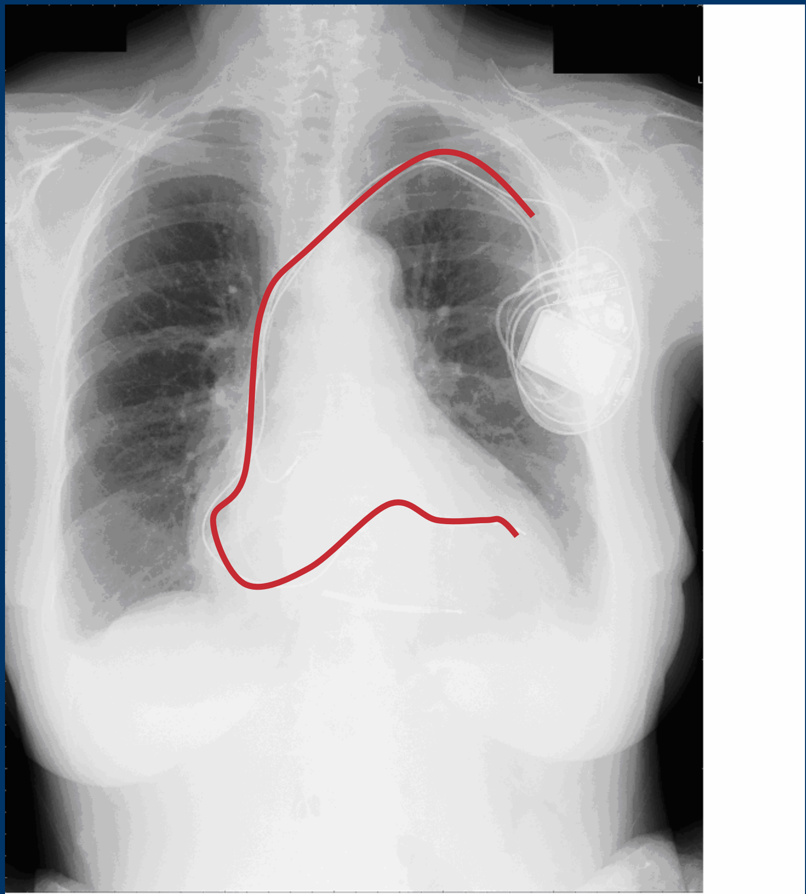
[2] Nelson et al., Circulation, 101:2703-9, 2001

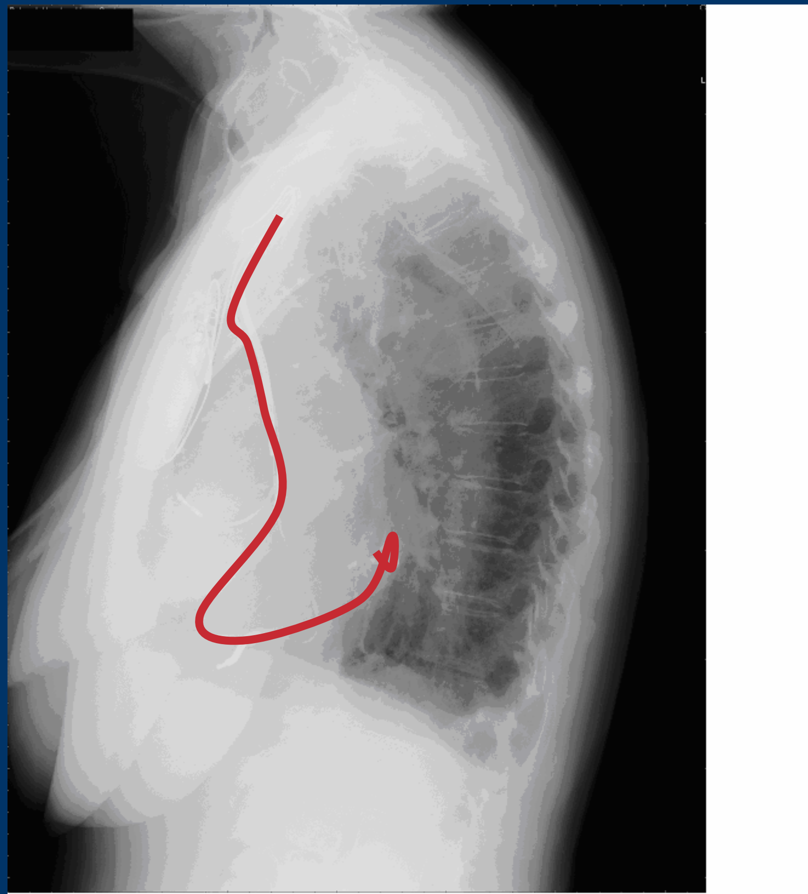
The ECG is only the beginning in determining CRT candidate. The post CRT ECG is of little use or value.

Non-responder

- Dyssynchrony
  - ECG is only the start
  - Post CRT ECG is of little value
  - More direct measure of dyssynchrony is needed, such as echo or more sophisticated imaging, CT/MRI
  - We are underutilizing CRT using a wide QRS as an diagnosis criteria. 40% of narrow QRS CHF patients may have dyssynchrony

Case study 2

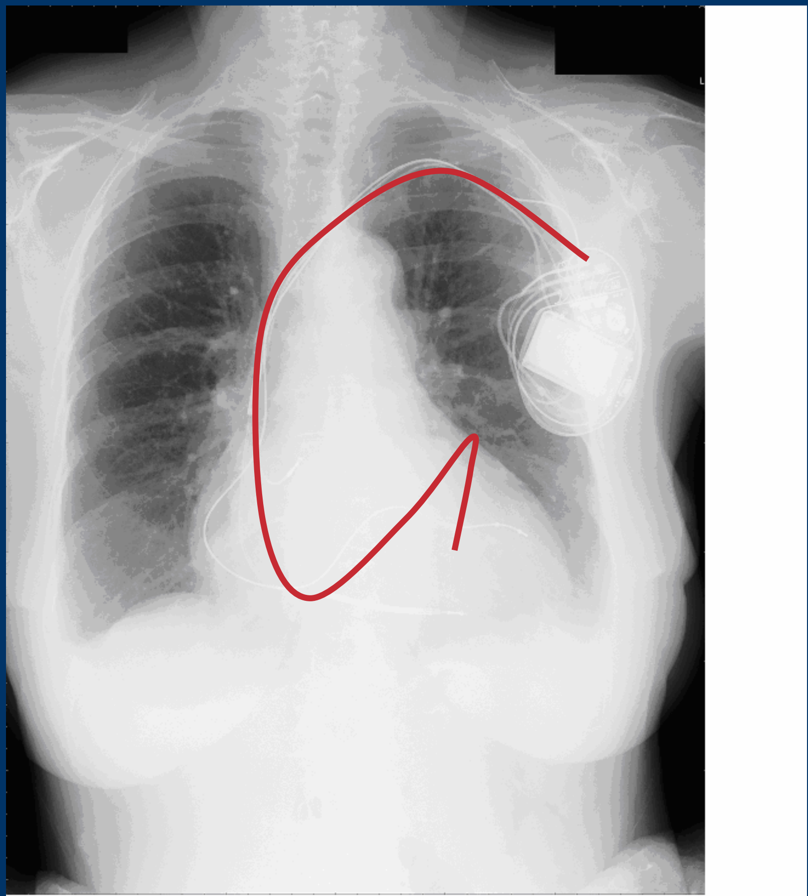




Post-op PA / LAT

Once you have selected a patient for CRT, the most important area of concern is lead placement. Here we see a chest x-ray of a "responder". Note the lateral lead position is important.

Case study 2

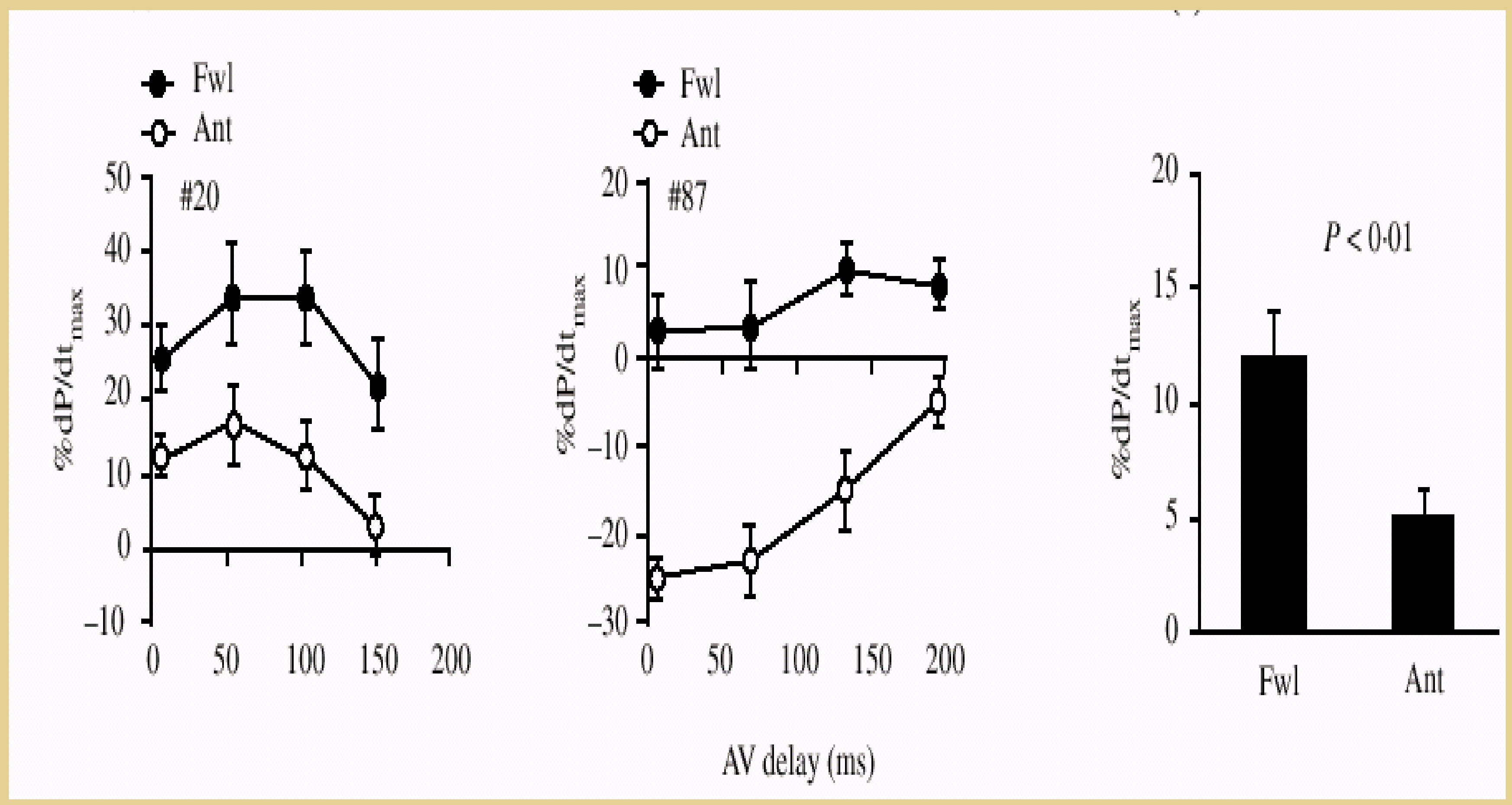


Follow-up PA / LAT

Spontaneous dislodgement of the lead is noted in the chest x-ray. The lead was still capturing the LV, however, the patient’s CHF symptoms worsened.

Pacing Site Matters:

Opimal Site For LV Lead is Generally the Lateral free Wall

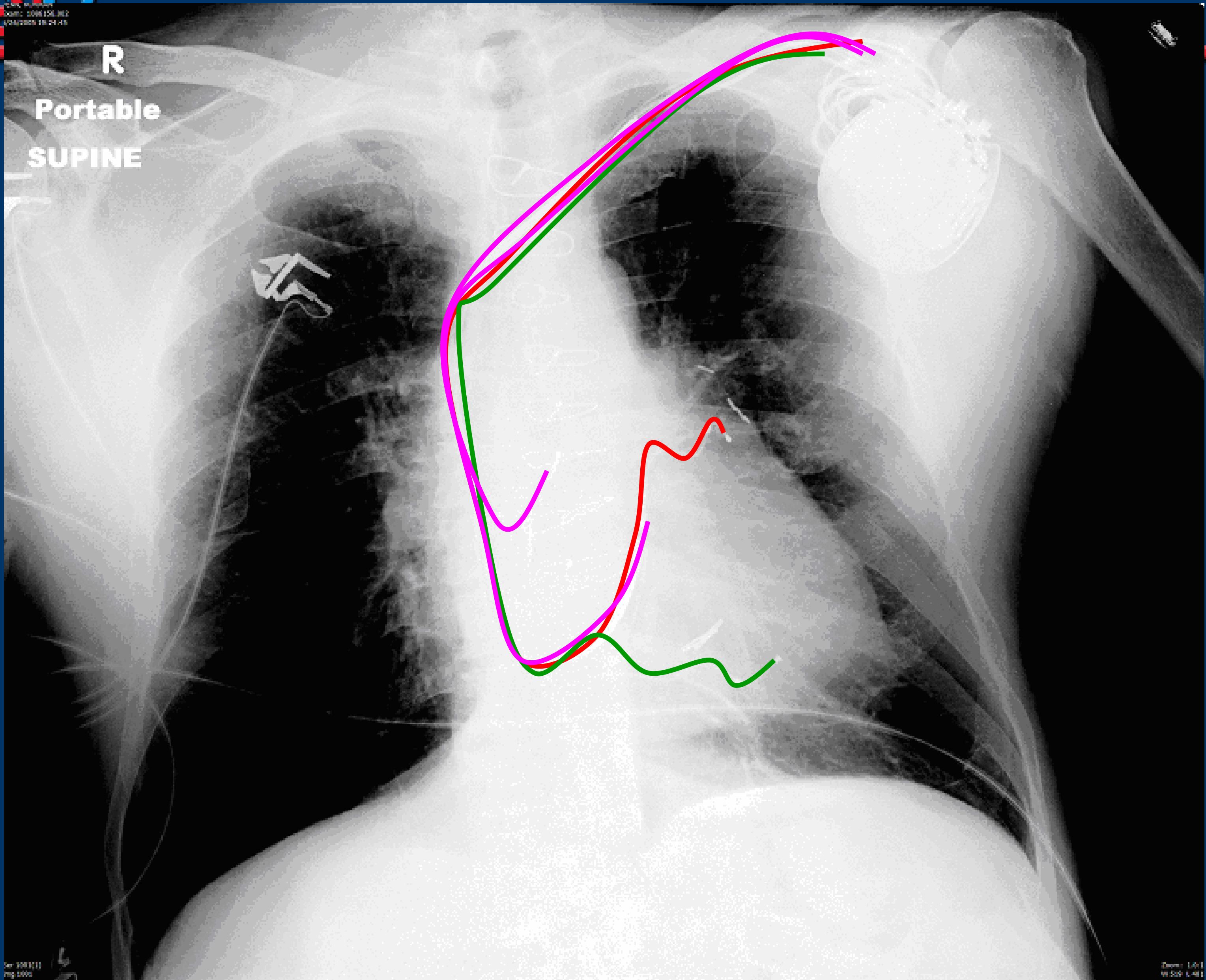


Butter et. Al. *Circulation 2001; 104:3026*

Non-responders

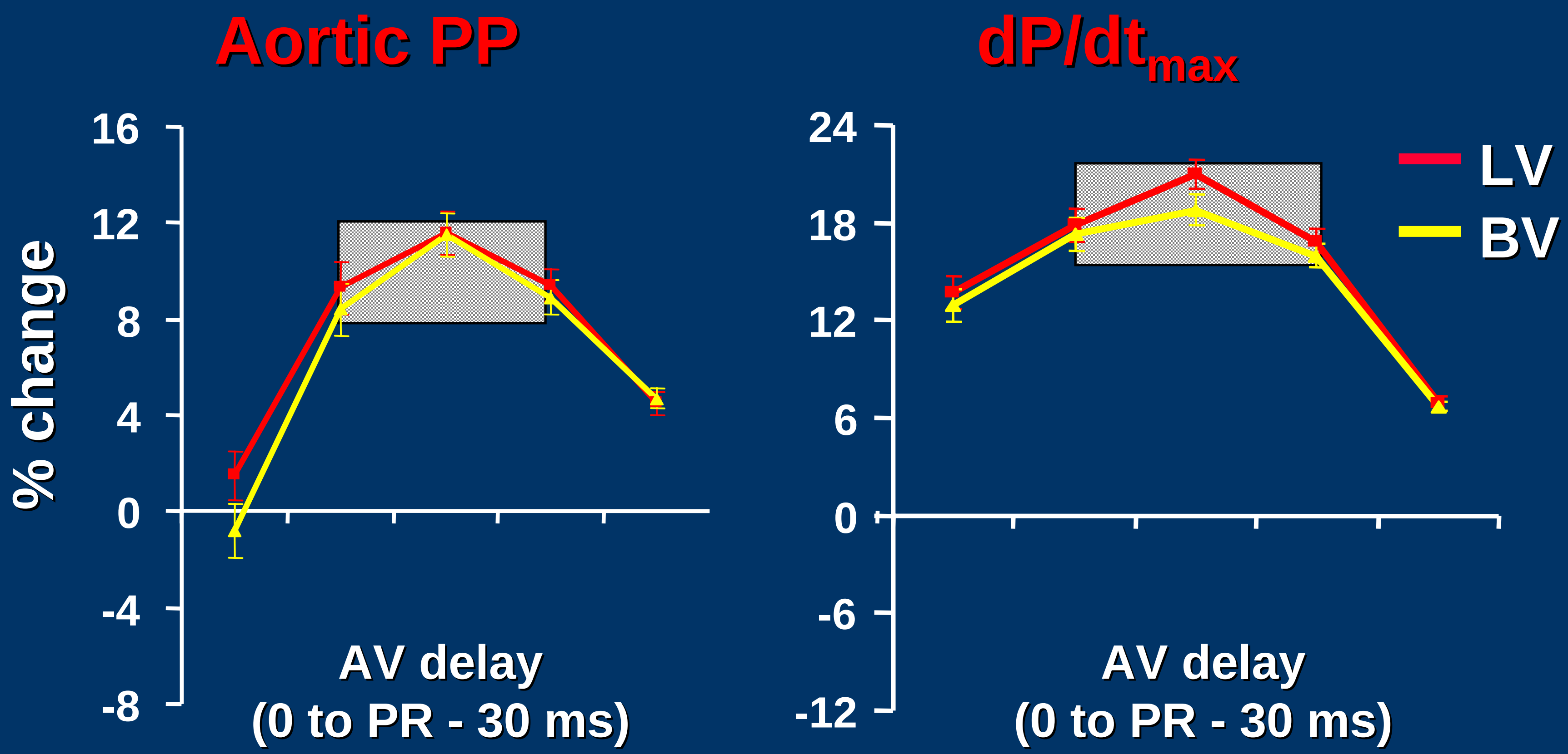
- 1. Dyssynchrony
- 2. Lead placement
  - Lateral wall is good
  - Anterior wall probably not good
  - Specific site difficult to determine
  - Multiple site

Multi-site



There has been research to determine responders versus non-responders and optimal pacing sight but little effort has looked into the efficiency of CRT based on a cellular and cardiac architecture perspective. Multiple studies have shown cardiac motion as a wringing out effect, such as simultaneous clockwise and counter clockwise rotation of the LV apex and base. Pacing from two locations in the LV is showing improved cardiac function in CT.

AV interval optimization:
Generally less critical than getting right site



Auricchio et al, (1999) *Circulation 99;2993*

AV delay may not be as critical as LV lead placement, however, still needs to be addressed in non-responders. Many CHF patients have intra-atrial conduction abnormalities which sometimes lead to simultaneous left atrial and left ventricular contractions or biventricular pacemaker syndrome. In our experience, we have not found an ECG criteria that has helped in the programming of the AV delay. We used intracardiac electrogram with success.

Use of intra-cardiac electrograms for programming of optimal sensed and paced AV delays in CRT devices in an attempt to prevent "Bi-ventricular pacing syndrome."

Raffaele Corbisiero, MD, David Muller RN, Leonard Polak

BACKGROUND: During participation in the RHYTHM Trial (St. Jude Medical), it was noted that some patients were non-respondent to CRT therapy. A subset was noted to have long intra-atrial conduction deficits with or without surface ECG evidence resulting in premature ventricular systole via pacing with shorter AV/PV cycles.

METHODS: Seven patients (7 men and 0 women) were studied with ages of 71.1 ± 14.1 years, NYHA class III (n = 6) and class IV (n = 1) heart failure, LV ejection fraction <30% (21.4 ± 4.6%) and a prolonged QRS duration of 151.85 ± 11.15 ms. These patients were implanted with a V-338 Epic HF (n = 6) or aV-340 Atlas+ HF (n = 1). An electrogram (A-tip to Can configuration) derived from the device was utilized to program AV/PV delays and LVOT Vti at this AV/PV delay was compared to that using echocardiography optimization via a General Electric Vivid 7 system.

RESULTS: The proposed AV/PV delay using the electrogram was in the range of 160-190 ms for 7 patients, and the Vti at this proposed AV/PV delay was 14.6 ± 4.6 ms; in comparison, optimized AV/PV delay and Vti using echocardiograph were 140-225 ms and 14.9 ± 4.3 ms, correspondingly. The correlation coefficient between Vti values obtained by these two methods was 0.99.

CONCLUSION: Vti obtained by the electrogram derived AV/PV delay is a good estimation of the Vti optimized by echocardiography. It may reduce time and expense related to echocardiography for CRT patients. Further analysis should be performed with a larger sample size.

Non-responders

- 1. Dyssynchrony
- 2. Lead placement
- 3. AV optimization
  - Echo – Ritter , VTi
  - Non - echo

AF in LV Dysfunction

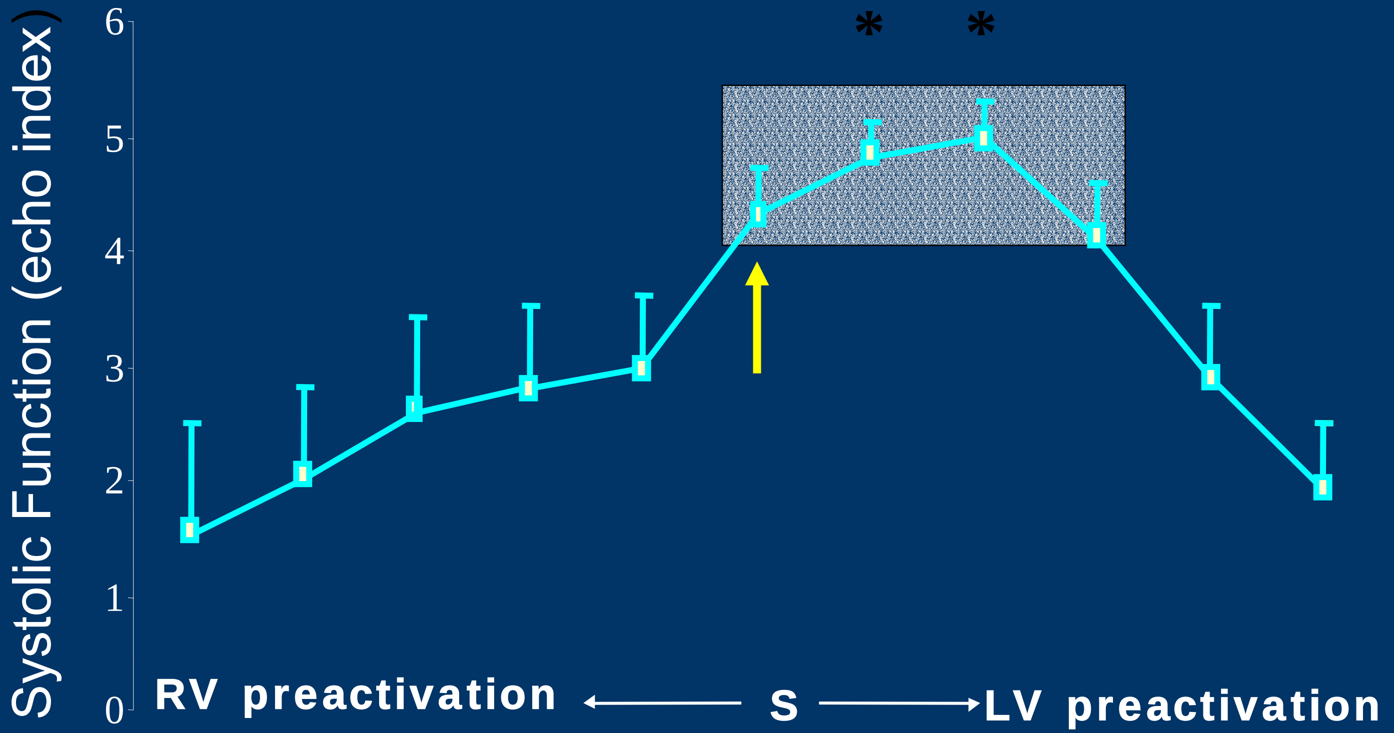
Incidence of Atrial Fibrillation in Patients with LV dysfunction

Predominant NYHA Type	Prevalence of AF, %	Study, y
I	4	SOLVD-prevention (1992)
II–III	10–26	SOLVD-treatment (1991)
		CHF-STAT (1995)
		MERIT-HF (1999)
		Diamond (1999)
III–IV	20–29	Middlekauff (1991)
		Stevenson (1996)
		GESICA (1994)
IV	50	CONSENSUS (1987)

NYHA, New York Heart Association; AF indicates atrial fibrillation; SOLVD, Studies of Left Ventricular Dysfunction; CHF-STAT, Survival Trial of Antiarrhythmic Therapy in Congestive Heart Failure; MERIT-HF, Metoprolol CR/XL Randomized Intervention Trial in Congestive Heart Failure; GESICA, Grupo Estudio de la Sobrevida en la Insufficienca Cardiaca en Argentina (V); and CONSENSUS, Co-operative North Scandinavian Enalapril Survival Study.

The optimal AV delays require sinus rhythm which is sometimes hard to maintain in the CHF patient. Studies are forthcoming the will shed light on the question of sinus rhythm and CHF patients. If beneficial, sinus can be maintained through a variety of methods including one of a combinations of drugs, pacing and ablation. If atrial fibrillation persists or is poorly controlled, AV node ablation with pacing (biventricular as per PAVE) is clearly an option.

Synchronous vs non-Synchronous BiV Pacing
Is RV-LV delay important?



Sogaard P, et al; Circulation 2002; 106:2078

Timing between the ventricles is now available in certain CRT-D devices and is useful in non-responders.

V-V Supporting Data

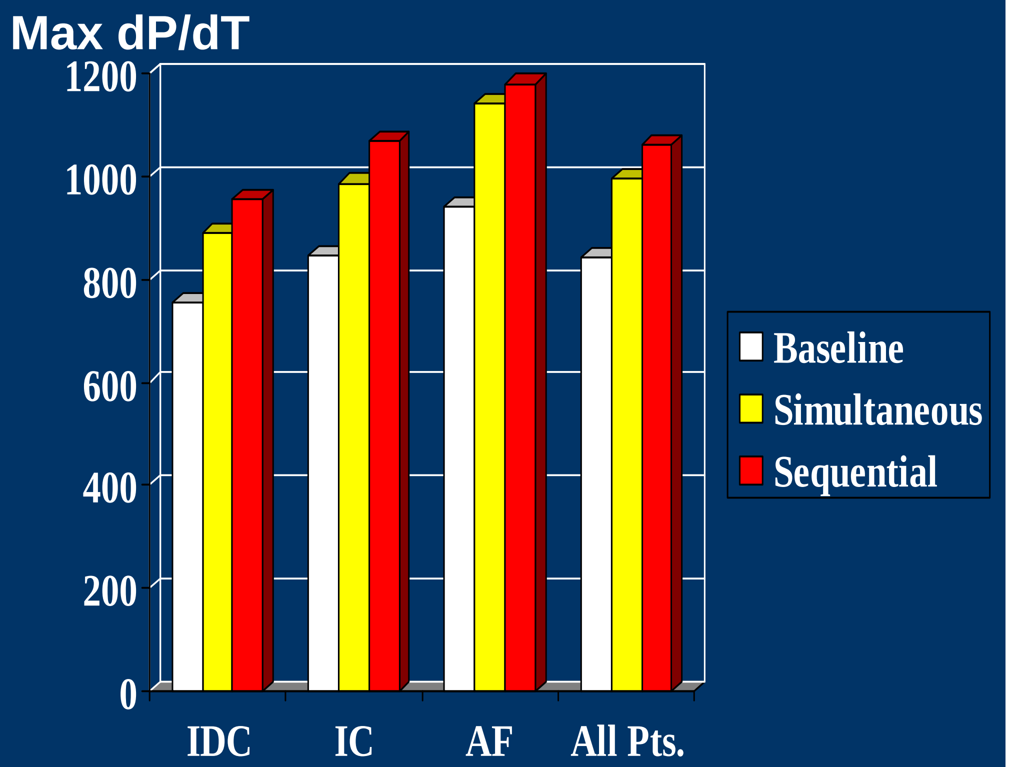
Chan et al. "Tissue Doppler Guided Optimization of A-V and V-V Delay of Biventricular Pacemaker Improves Response to Cardiac Resynchronization Therapy in Heart Failure Patients" *J of Cardiac Failure 2004; 10, 4 (suppl.): S72 (abstract 199)*

- ❖ 45 patients classified as "non-responders" following implant
- ❖ A-V & V-V delay optimized using Echo TDI
- ❖ 85% of patients improved significantly after optimization as shown by QOL and EF

V-V Supporting Data

Van Gelder et al. "Effect of Optimizing the VV Interval on Left Ventricular Contractility in Cardiac Resynchronization Therapy" *Am J Cardiol 2004; 93, 1500-1503*

- 53 patients
  - 41 patients in sinus rhythm
    - 26 patients w/ischemic cardiomyopathy (IC)
    - 15 patients w/idiopathic dilated cardiomyopathy (IDC)
  - 12 patients in AF
- Maximum dP/dT measured
  - Baseline (prior to BiV implant)
  - Simultaneous BiV pacing
  - V-V Optimized

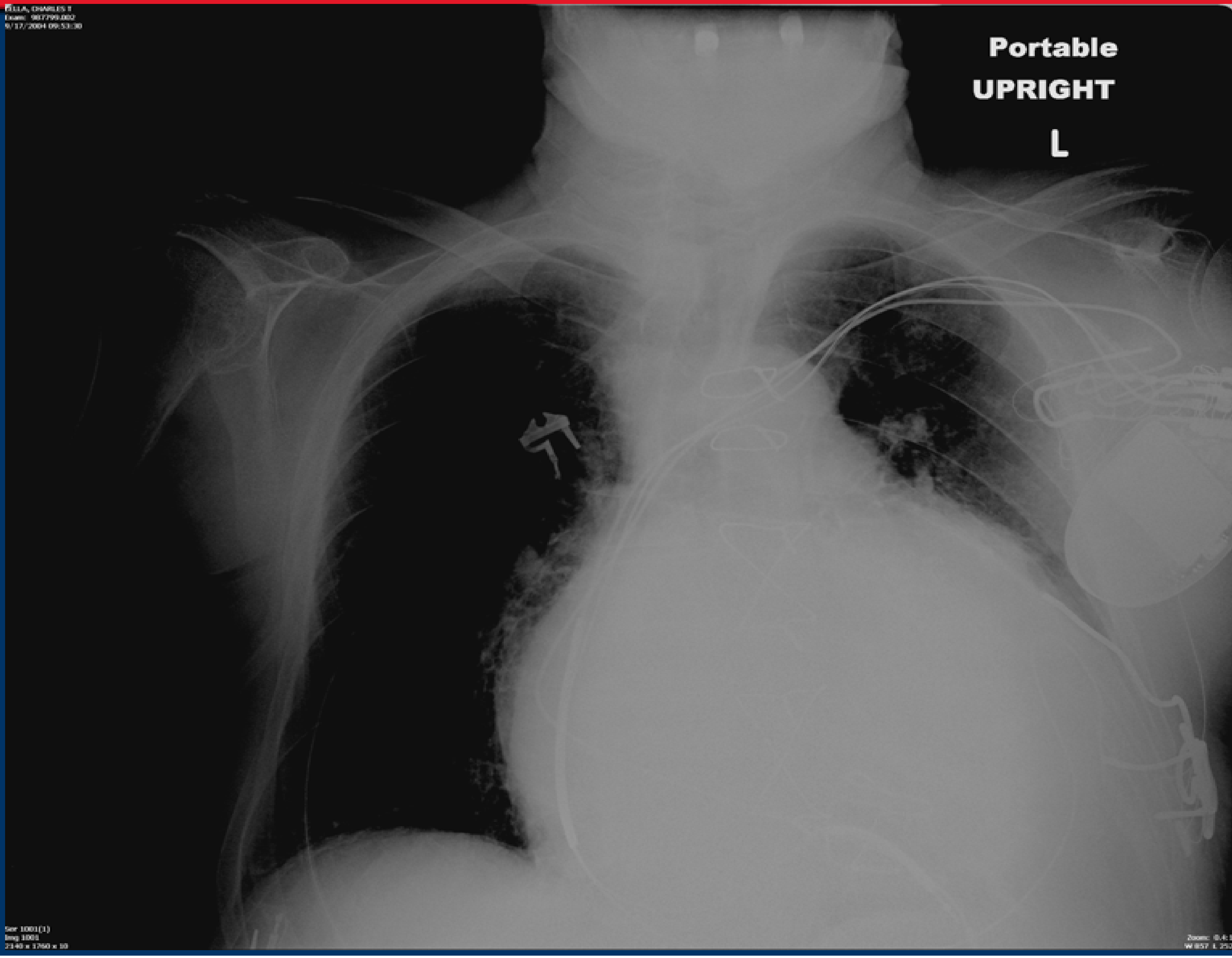


	n	Baseline	Simultaneous	% Increase	Optimized V-V	% Increase
AF	12	941 ± 240	1,142 ± 207	21	1,180 ± 196	25
Sinus Rhythm	41	814 ± 178	952 ± 271	17	1,027 ± 297	26
IDC	15	754 ± 220	890 ± 245	18	955 ± 267	27
IC	26	846 ± 249	987 ± 232	17	1,069 ± 252	26
All Patients	53	842 ± 231	995 ± 247	18	1,061 ± 259	26

Non-responders

- 1. Dyssynchrony
- 2. Lead placement
- 3. AV optimization
- 4. Atrial arrhythmia's
- 5. V-V optimization

Too Late



The chest x-ray represents a class IV CHF patient with little hope of benefit from CRT-D.

MADIT-CRT

Can CRT inhibit or slow progression of LV dysfunction and heart failure in minimally symptomatic patients (NYHA I-II) with low ejection fraction and wide QRS?

Madit-CRT asks an extremely important questions here. Could devices be used prophylactically for CHF as they are for ICD’s.