



ICD Therapy/Biventricular Pacers: New Stratification in 2007

Hakan Oral, MD

Associate Professor
Director, Cardiac Electrophysiology
University of Michigan, Ann Arbor, MI



Cardiac Resynchronization Therapy

- Eliminates the delay in activation of LV free wall
- Improves mechanical synchrony
- Increases LV filling time
- Reduces mitral regurgitation
- Reduces septal dyskinesia



CRT may improve

- NYHA class
- Quality of life
- 6-min walk test
- VO₂ consumption
- LV size
- LV EF
- Hospital admissions due to CHF
- Mortality



Patient Selection 2005

- Sinus rhythm / AF
- LV EF \leq 35%
- Ischemic or nonischemic cardiomyopathy
- QRS duration \geq 120 ms
- NYHA functional class III or IV
- Optimal pharmacological therapy

AHA Science Advisory 2005 endorsed by the ACCF and the Heart Failure Society of America



Cardiac Resynchronization Therapy in Heart Failure with Narrow QRS Complexes (*RETHINQ*)

- Double-blind RCT
- Standard indication for an ICD
- LV EF $\leq 35\%$
- NYHA class III
- QRS < 130 ms
- Mechanical dyssynchrony on echocardiography
- Optimal medical therapy

Beshai J et al. N Engl J Med 2007.



Echo Criteria for LV Dyssynchrony

- M-Mode

- Septal posterior wall mechanical delay (SPWMD) \geq 130 ms

OR

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

- Septal to lateral delay \geq 65ms

OR

- Antero-septal to posterior delay \geq 65ms



Study Design

CRT-ICD implant in 172 patients



At 2 weeks:

Randomized 1:1 to CRT and no CRT



At 6 months:

Increase in peak VO₂ at 6 months

Improvement in QOL

Improvement in NYHA class



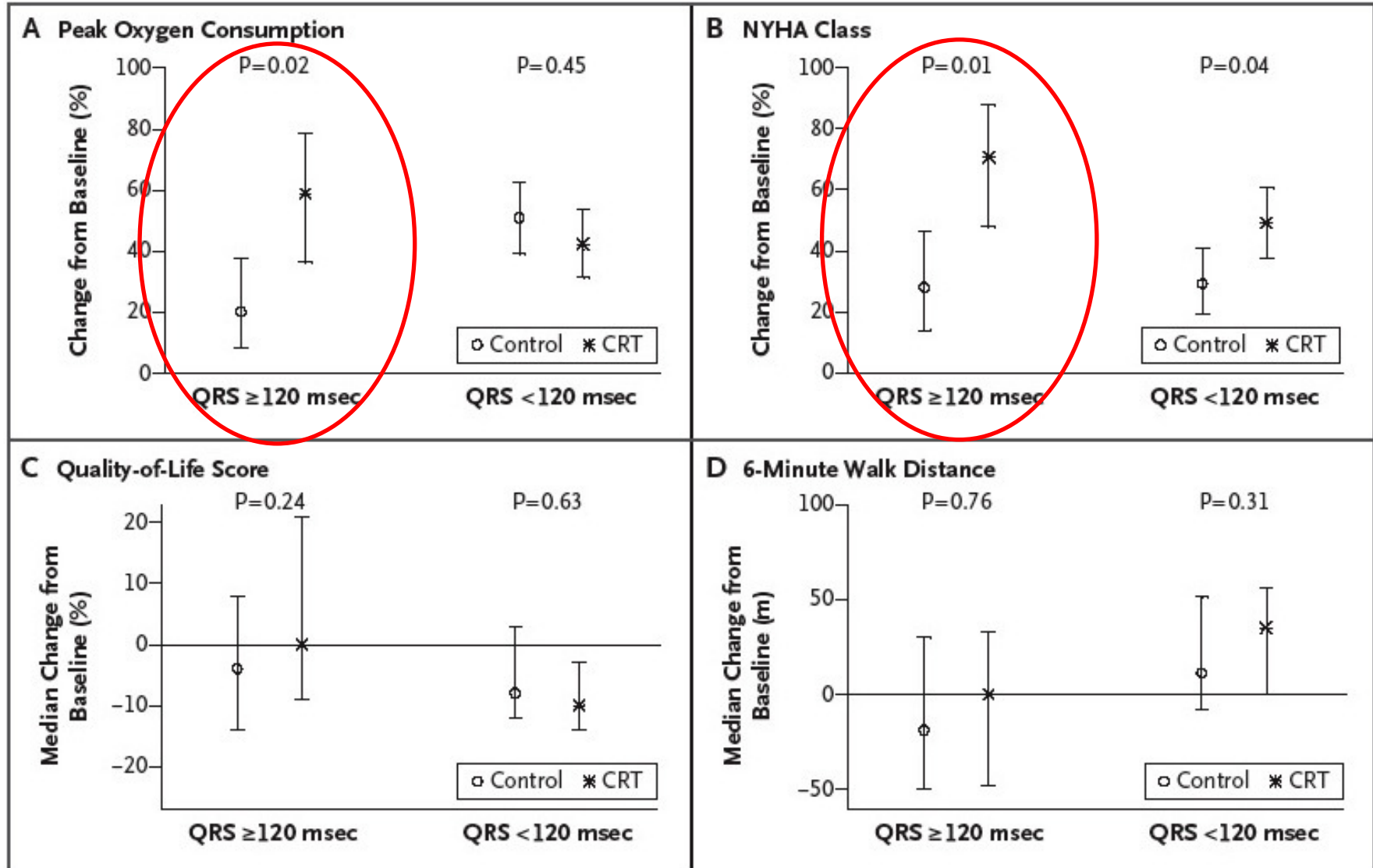
Effect of CRT on Primary and Secondary End Points

Variable	Control Group	CRT Group	P Value
Primary end point			
<u>Change in peak oxygen consumption</u>			0.63
No. of patients	80	76	
Median change (95% CI) — ml/kg/min	0.5 (-0.3 to 1.1)	0.4 (-0.6 to 1.2)	
Increase of ≥ 1.0 ml/kg/min — no. (%)	33 (41)	35 (46)	
Secondary end points			
<u>Change in quality-of-life score[†]</u>			0.91
No. of patients	80	76	
Median change (95% CI)	-7 (-11 to 3)	-8 (-10 to -1)	
<u>Change in NYHA class</u>			0.006
No. of patients	80	76	
Improved by 1 class or more — no. (%)	23 (29)	41 (54)	
No change — no. (%)	51 (64)	31 (41)	
Worsened — no. (%)	6 (8)	4 (5)	

*No difference in survival at 6 months (98% vs 99%, $P=0.58$)
Improvement in peak VO_2 if QRS >120 and <130 ms.*

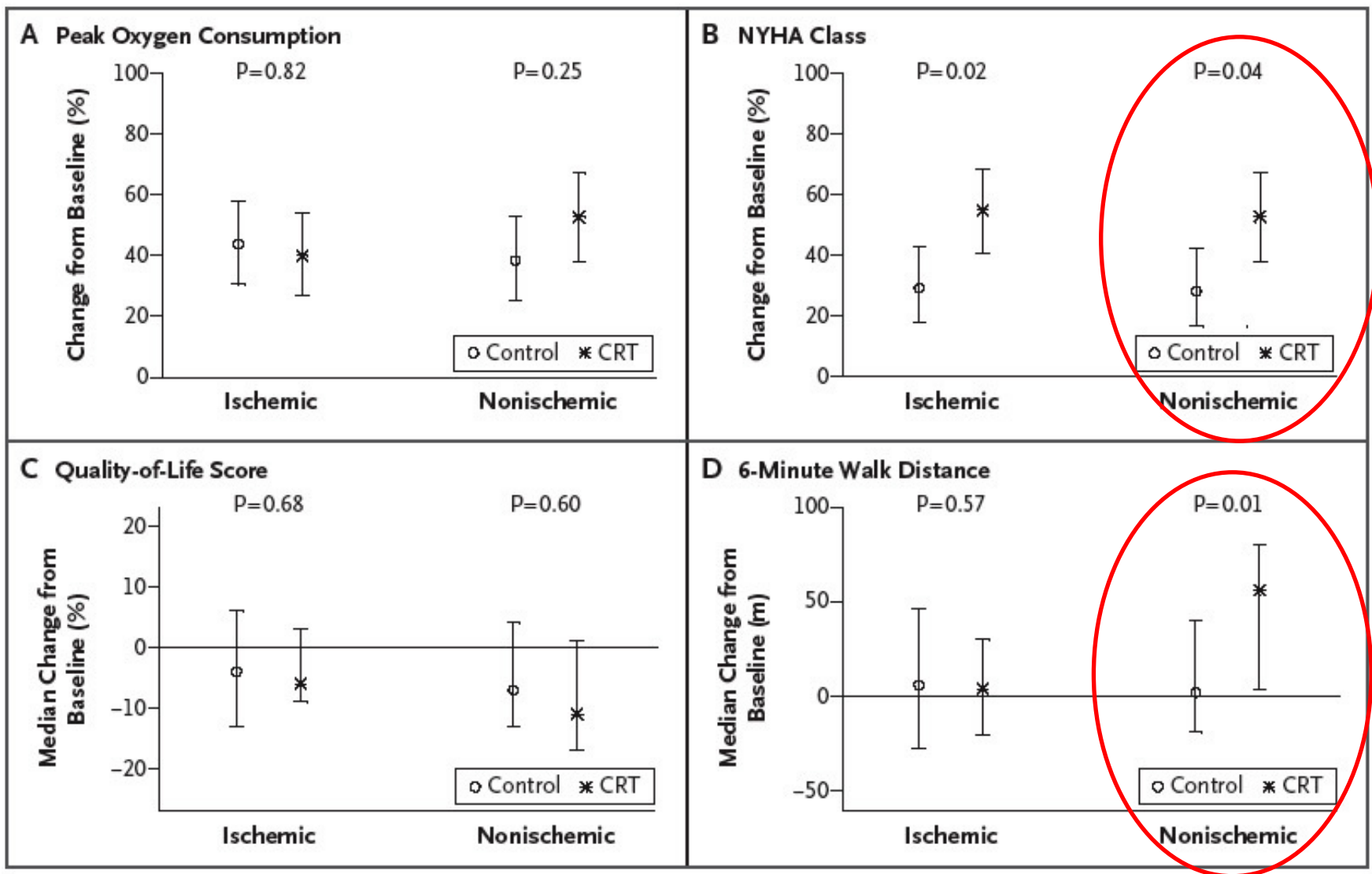


Subgroup Analysis According to the QRS Interval at 6 Months





Subgroup Analysis According to Cardiomyopathy at 6 Months





CRT for Patients with CHF and Narrow QRS

- CRT is not associated with an improvement in peak VO_2 during exercise in patients with NYHA Class III heart failure, QRS duration <130 ms, $EF \leq 35\%$ and mechanical dyssynchrony.
- Except for an improvement in NYHA class, CRT is not associated with an improvement in quality-of-life, 6-minute walking test, or echocardiographic measures of reverse LV remodeling.
- Patients with a QRS duration >120 ms and <130 had an improvement in peak VO_2 in response to CRT.



Predictors of Response to CRT Therapy (PROSPECT Study)

- 426 patients with stable heart failure
- Echo indicators of ventricular dyssynchrony
- Composite clinical endpoint at 6 months
 - Heart failure free survival
 - NYHA class improvement
 - QOL
 - LV ESV



Assessment of Dyssynchrony

- Echocardiographic parameters
 - SPWMD 72%
 - IVMD 92%
 - LVFT/RR 85%
 - LPEI 95%
- High inter-laboratory variability



Response to CRT

- At 6 months
- Clinical composite score
 - 69% improvement :
 - 76% in nonischemics vs 64% in ischemics (P=0.01)
- Reverse remodeling:
 - 56% improvement:
 - 63% in nonischemics vs 50% in ischemics (P=0.03)



Predictors of Response to CRT

- Slight however significant predictors of an improvement in clinical response:
 - IVMD
 - LVFT/RR
 - LVPEI
- Significant predictors of reverse remodeling
 - IVMD
 - LVFT/RR
 - SPWMD



Predictors of Response to CRT (PROSPECT Study)

- Disagreement on echo parameters 50-90%
- No single measure of mechanical dyssynchrony predicts response to CRT.
- QRS width remains as the primary criterion for patient selection.



CRT in Mildly Symptomatic Heart Failure (*MIRACLE ICD II*)

- Double-blind RCT
- NYHA class II
- LV EF $\leq 35\%$
- QRS ≥ 130 ms
- 186 patients
 - 101 to control group
 - 85 to CRT



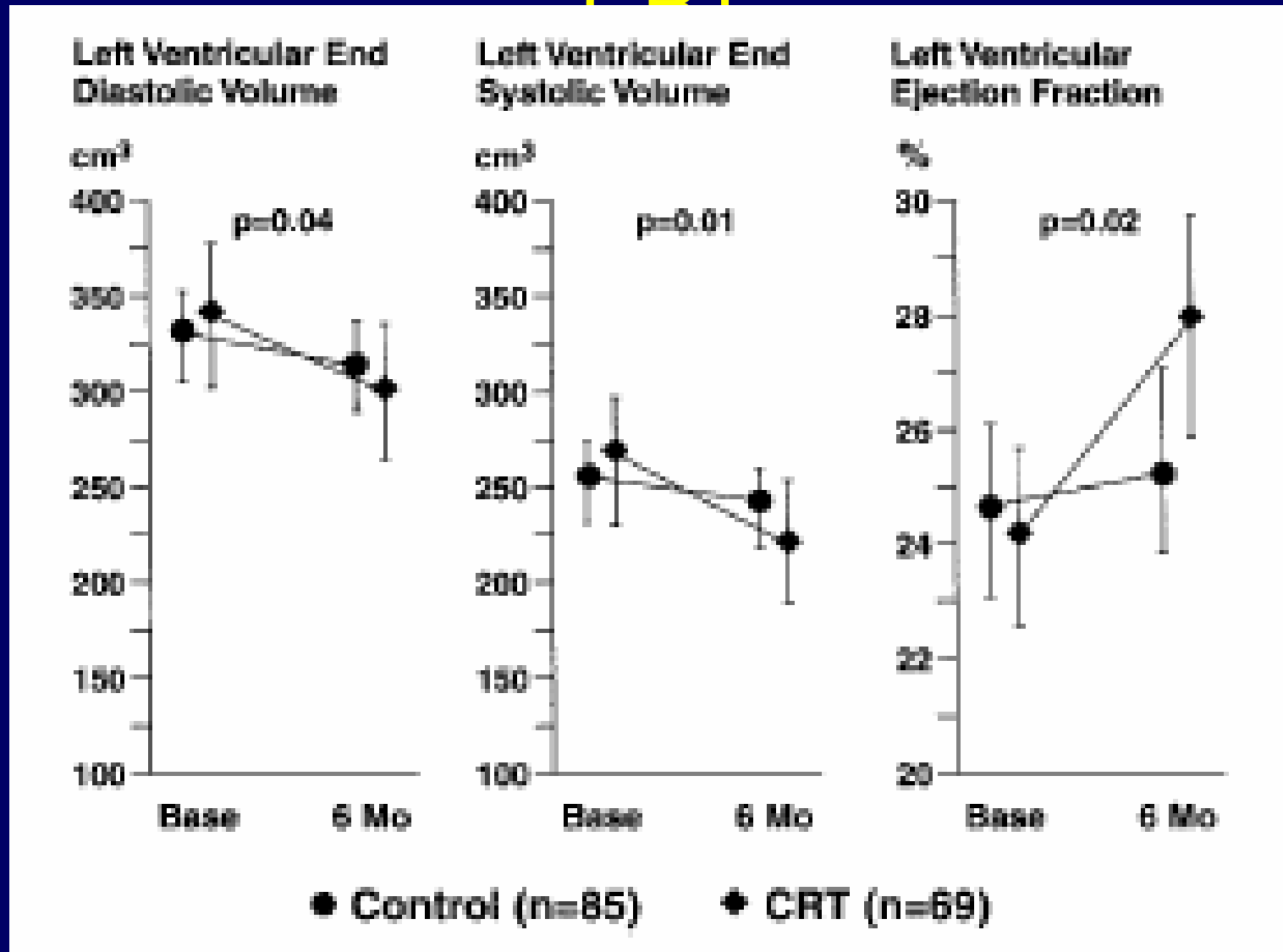
CRT in Mildly Symptomatic Heart Failure (*MIRACLE ICD II*)

- At 6 months, CRT was associated with:
 - *No improvement in peak VO₂*
 - *No improvement in 6-min walk test*
 - *No improvement in QOL*
 - Improvement in LV diastolic and systolic volumes
 - Improvement LV EF
 - Improvement NYHA class
 - Improvement Clinical composite response

Abraham et al, Circulation, 2004



Reverse Remodeling in Response to CRT



Abraham et al, Circulation, 2004



CRT for NYHA Class II vs III/IV Heart Failure (InSync/InSync ICD Italian Registry)

- 952 patients
 - 188 NYHA Class II
 - 764 NYHA Class III or IV
- Observational registry
- LV EF \leq 35%
- QRS $>$ 130 ms
- Ischemic \sim 45%



CRT for NYHA Class II vs III/IV Heart Failure (InSync/InSync ICD Italian Registry)

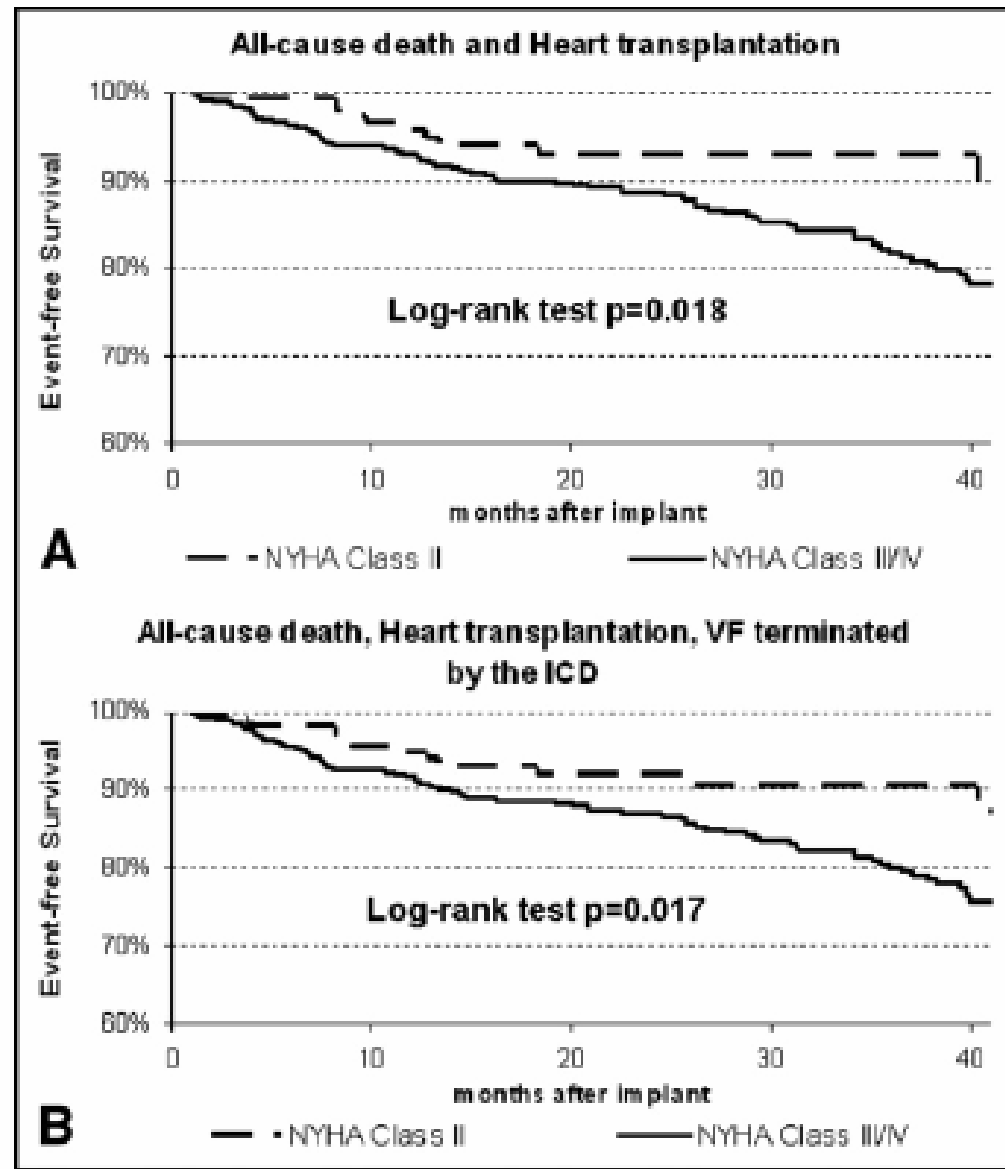
Parameter	NYHA Class			
	II (n = 188)		III or IV (n = 764)	
	Baseline	Follow-Up	Baseline	Follow-Up
Hospitalizations for HF (n/yr)	1.1 ± 1.3	0.2 ± 0.5 [†]	1.8 ± 1.4	0.4 ± 0.9 [†]
QRS duration (ms)	163 ± 29	148 ± 27*	168 ± 32	144 ± 29*
EF (%)	29 ± 7	37 ± 11*	27 ± 8	36 ± 11*
End-diastolic diameter (mm)	69 ± 10	65 ± 11*	69 ± 9	65 ± 10*
End-systolic diameter (mm)	57 ± 12	53 ± 12*	59 ± 10	53 ± 12*
Mitral regurgitation (grade)	1.9 ± 1.0	1.8 ± 0.9	2.3 ± 1.0	1.9 ± 0.9*

* p < 0.01 versus baseline (paired Student's *t* test).

[†] p < 0.01 versus baseline (Wilcoxon's nonparametric test).



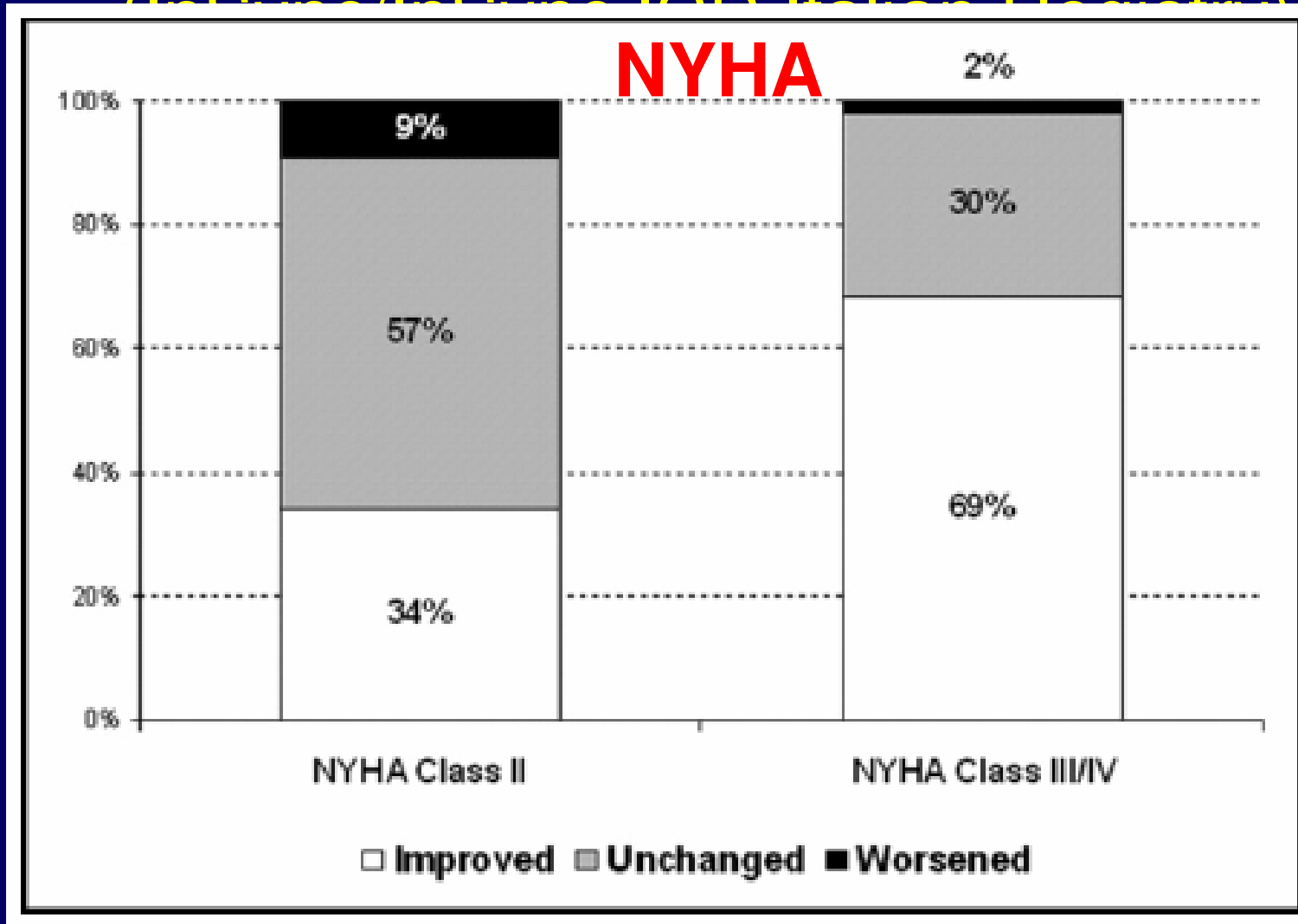
CRT for NYHA Class II vs III/IV Heart Failure (InSync/InSync ICD Italian Registry)





CRT for NYHA Class II vs III/IV Heart Failure

(In-Cycle/In-Cycle ICD Utilization Registry)





Patient Selection 2007

- QRS width (≥ 120 ms) remains as the gold standard.
- There is a need to identify practical and reproducible parameters of dyssynchrony to precisely identify patients who are more likely to respond to CRT.
- There are insufficient objective data to justify routine CRT in patients with NYHA class II heart failure.

