Seminars of the Hellenic Working Groups
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Bi-Ventricular pacing after the most recent studies

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ACC/AHA/HRS Guidelines 2008

Recommendations for CRT-D/P in Patients With Severe Systolic CHF (LVEF ≤ 35%)

Class I:
- QRS duration ≥ 120 ms
- Sinus rhythm
- NYHA III/ambulatory IV

Class IIa:
- QRS duration ≥ 120 ms; AF; NYHA III/ambulatory IV
- NYHA III/ambulatory IV; Frequent dependence on ventricular pacing

Class IIb:
- NYHA I/II; implantation of permanent pacing or ICD with anticipated frequent ventricular pacing

LVEF = left ventricular ejection fraction

ACC/AHA/HRS Guideline Committee. *J Am Coll Cardiol.* 2008;51:2085-2105.

Italian guidelines AIAC 2006

Cardiac Resynchronisation Therapy	
Class I Indication	**Synus Rhythm, Reduced EF (≤ 35%)** **Ventricular Dyssynchrony (QRS > 120ms)** **NYHA III-IV despite Optimal Medical Therapy**
Class II Indications	Synus Rhythm, Reduced EF (≤ 35%) Ventricular Dyssynchrony (QRS > 120ms) **Symptomatic (NYHA II) and with pacing indication or Primary Prevention ICD indication**
	Chronic Right Ventricular Pacing, Reduced EF (≤ 35%) Severe Ventricular Dyssynchrony NYHA III-IV despite Optimal Medical Therapy
	Pts In Atrial Fibrillation, Reduced EF (≤ 35%) Ventricular Dyssynchrony (QRS > 120ms) NYHA III-IV despite Optimal Medical Therapy
	Reduced EF (≤ 35%), **QRS ≤ 120 ms** **Ventricular Dyssynchrony** (Echo assessment) NYHA III-IV despite Optimal Medical Therapy

CRT: Open issues

- ✓Patients in **I/II NYHA** functional class
- ✓Patients with indication to **chronic right ventricular pacing**
- ✓Patients with **chronic atrial fibrillation**
- ✓Patients without **electrical dyssynchrony**

CRT: Open issues

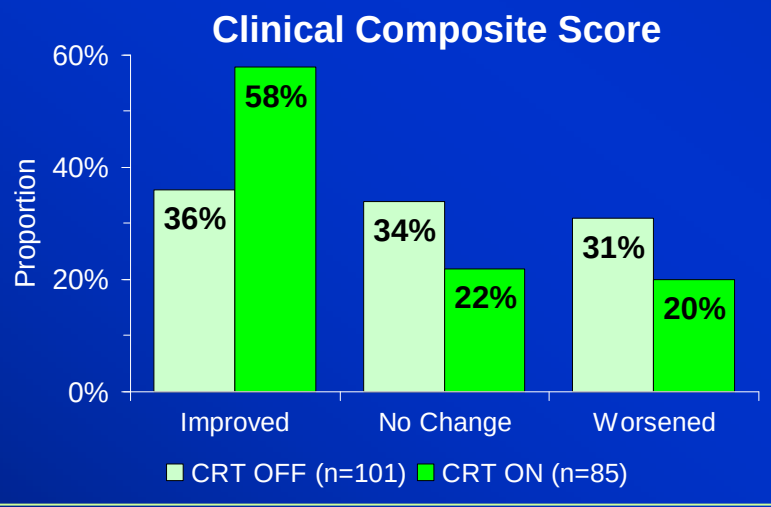
- ✓Patients in **I/II NYHA** functional class
- ✓Patients with indication to chronic right ventricular stimulation
- ✓Patients with chronic atrial fibrillation
- ✓Patients without electrical dyssynchrony

Effects of Cardiac Resynchronization on Disease Progression in Patients With Left Ventricular Systolic Dysfunction, an Indication for an Implantable Cardioverter-Defibrillator, and Mildly Symptomatic Chronic Heart Failure

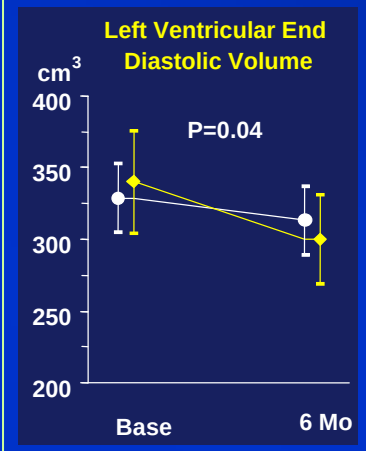
William T. Abraham, MD; James B. Young, MD; Angel R. León, MD; Stuart Adler, MD; Alan J. Bank, MD; Shelley A. Hall, MD; Randy Lieberman, MD; L. Bing Liem, DO; John B. O'Connell, MD; John S. Schroeder, MD; Kevin R. Wheelan, MD; on behalf of the Multicenter InSync ICD II Study Group

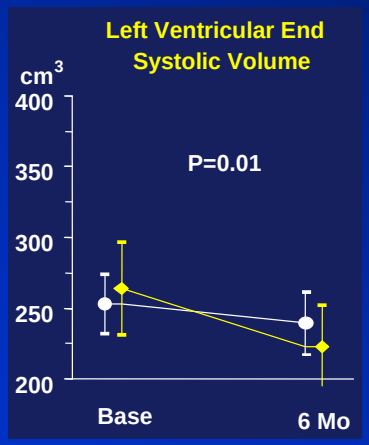
CRT in NYHA II

186 pts in NYHA II, FE ≤ 35% and QRS > 130ms randomized CRT ON vs CRT OFF



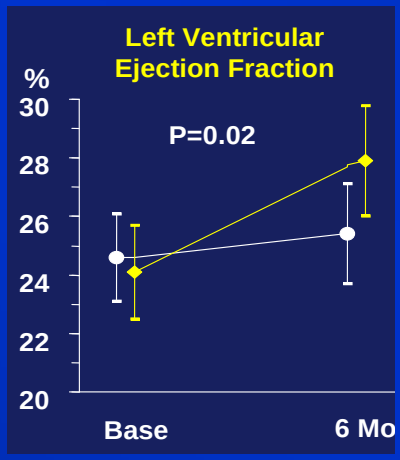
End Point	CRT OFF	CRT ON	P
Change in peak VO2	0.2±3.2	0.5±3.2	0.87
Change in exercise duration, s	37±186	42±167	0.56
Change in NYHA	0.01±0.63)	0.18±0.61	0.05
Change in QOL	10.7±21.7	13.3±25.1	0.49
Change in 6MHWT, m	33±98	38±109	0.59





•CRT (n=69)

•CRT OFF (n=85)



Abraham et al., MIRACLE ICD II, Circulation 2004

Cardiac Resynchronization Therapy
for the Treatment of Heart Failure in
Patients With Intraventricular Conduction
Delay and Malignant Ventricular Tachyarrhythmias

Steven L. Higgins, MD, FACC,* John D. Hummel, MD, FACC,† Imran K. Niazi, MD, FACC,‡ Michael C. Giudici, MD, FACC,§ Seth J. Worley, MD, FACC,‖ Leslie A. Saxon, MD, FACC,¶ John P. Boehmer, MD, FACC,# Michael B. Higginbotham, MD,** Teresa De Marco, MD, FACC,¶ Elyse Foster, MD, FACC,¶ Patrick G. Yong, MSEE††

CRT in NYHA II

132 pts in NYHA I-II and QRS > 120ms (study subgrup)

End Point	NYHA Class I/II at Randomization		
	CRT	No CRT	p Value
Peak VO_2 (ml/kg/min)	0.2 ± 0.3 (n = 120)	0.0 ± 0.3 (n = 121)	0.77
6 MW (m)	17 ± 9 (n = 125)	10 ± 9 (n = 130)	0.55
QOL (points)	−1 ± 2 (n = 127)	−4 ± 2 (n = 129)	0.26
NYHA class (%)	(n = 64)	(n = 68)	
Improved 2 classes	—	—	
Improved 1 class	9	16	0.84
No change	72	60	
Worsened	19	24	
$LVID_d$ (mm)	−2.4 ± 0.8 (n = 124)	0.0 ± 0.8 (n = 117)	0.024
$LVID_s$ (mm)	−3.2 ± 0.8 (n = 124)	−0.5 ± 0.8 (n = 117)	0.014
LVEF (%)	4.7 ± 0.9 (n = 123)	2.9 ± 0.9 (n = 125)	0.16

Higgins SL et al JACC 2003

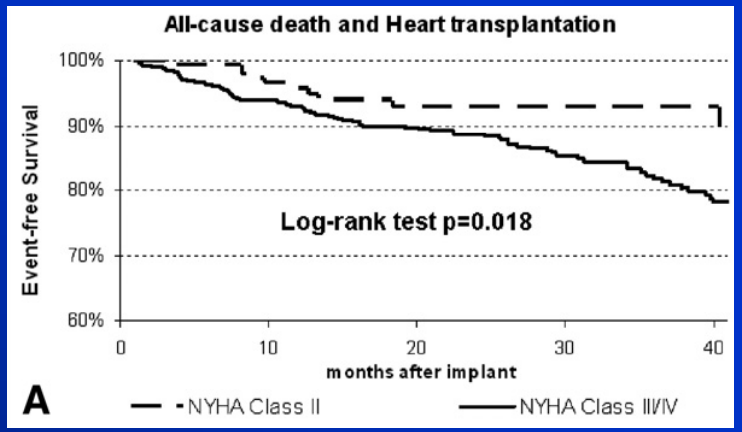
Comparison of the Effects of Cardiac Resynchronization Therapy in Patients with Class II Versus Class III and IV Heart Failure (From the InSync/InSync ICD Italian Registry)

Maurizio Landolina[a] MD, Maurizio Lunati[b] MD, Maurizio Gasparini[c] MD, Massimo Santini[d] MD, Luigi Padeletti[e] MD, Augusto Achilli[f] MD, Stefano Bianchi[g] MD, Francesco Laurenzi[h] MD, Antonio Curnis[i] MD, Antonio Vincenti[j] MD, Sergio Valsecchi[k] MS, Alessandra Denaro[k]

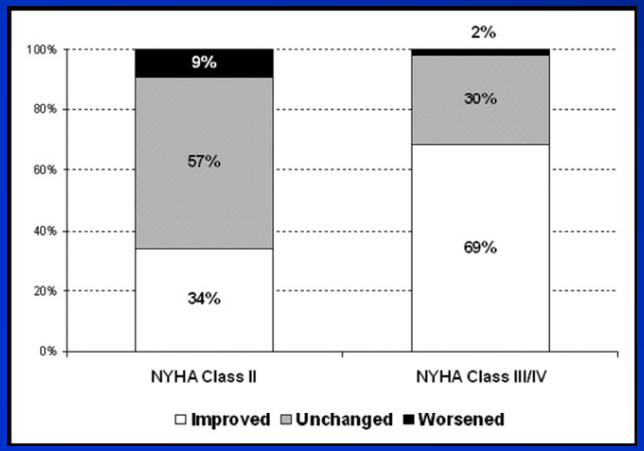
CRT for NYHA II

952 pts analyzed: NYHA II (188 pts) vs NYHA III-IV (764)

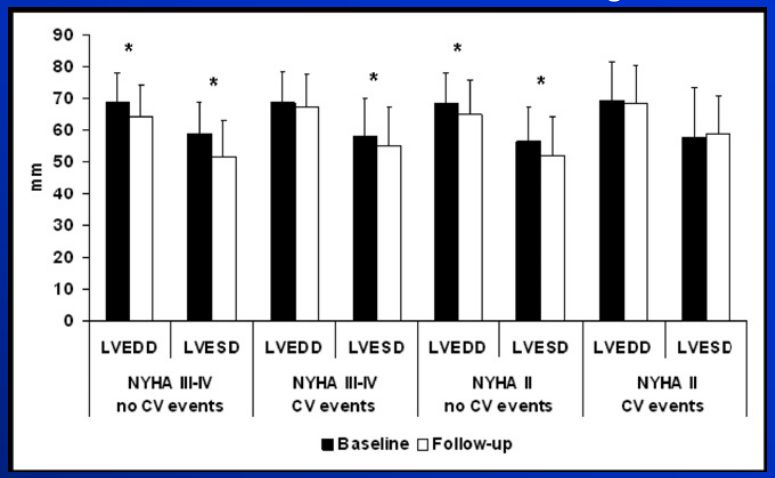
Reduction of major CV events



NYHA class improvement with different %



Same reverse remodeling



Landolina M et al. AJC 2007

CRT in NYHA I-II:
REVERSE & MADIT CRT

2009:

The evidence!

CRT in NYHA II:
REVERSE & MADIT CRT

REVERSE

presented at ACC09

262 patients (Europe) followed for 24 months

Age (mean) yrs	61.3 ± 10.4
Ischemic	44%
NYHA II	83%
EF	27.1 ± 6.8
LVEDD (mm)	68.8 ± 9.2
QRS (ms)	156 ± 23
ICD therapy optional	68%

CRT OFF 82 Patients | **CRT ON 180 Patients**

Daubert et al JACC 2009

MADIT-CRT

presented at ESC 09

1820 patients (US&Europe) >30 months

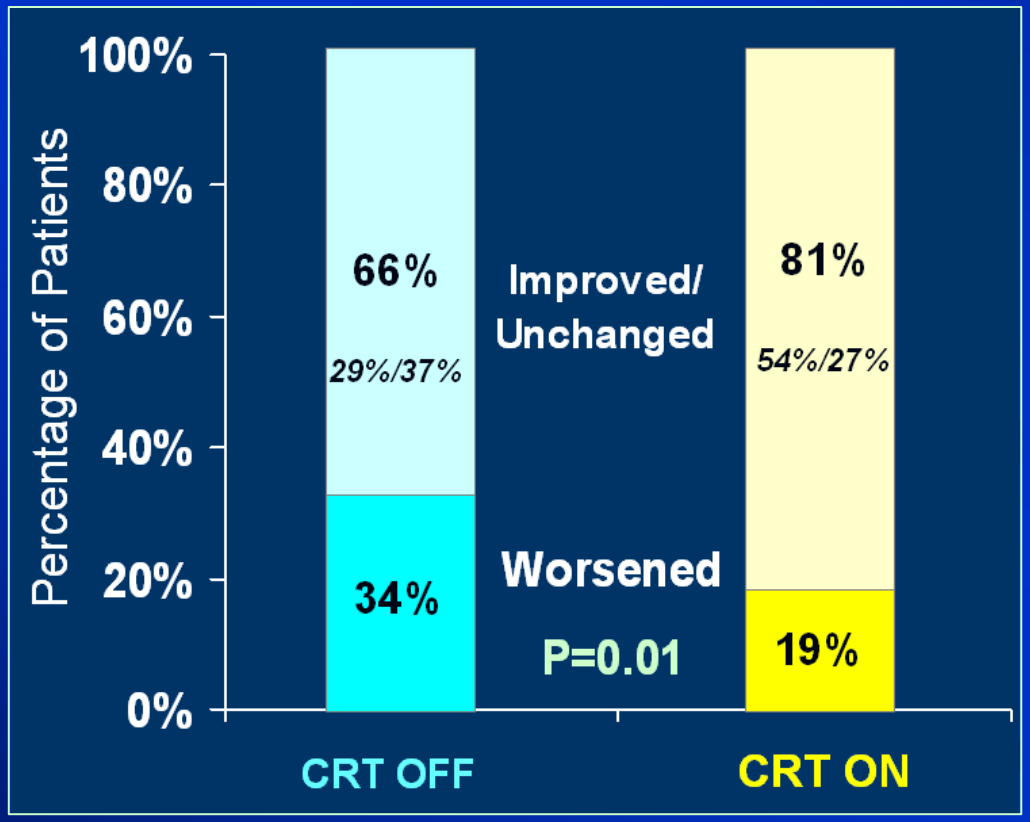
Age (mean) yrs	N.A.
Ischemic	N.A.
NYHA	I+II
EF	≤30%
LVEDD (mm)	>55
QRS (ms)	>130
ICD therapy mandatory	100%

CRT OFF ~728 Patients | **CRT ON ~1092 Patients**

Moss et al NEJM 2009

CRT in NYHA II: REVERSE

Primary End Point: Clinical Composite Response at 24-month % worsened

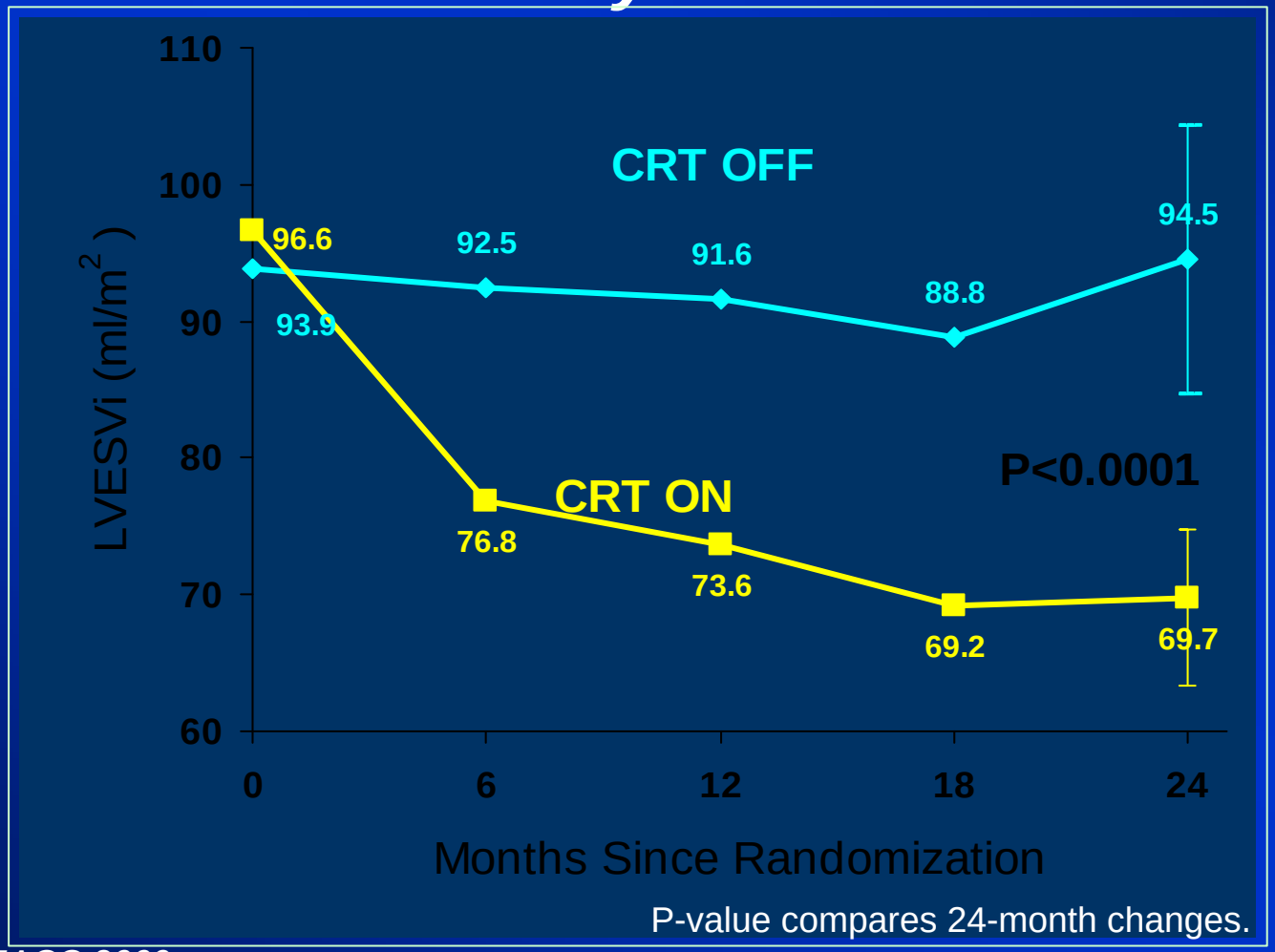


Daubert et al JACC 2009

Entire distribution analysis of worsened, unchanged and improved: P=0.0006

CRT in NYHA II: REVERSE

Powered Secondary End Point: LVESVi

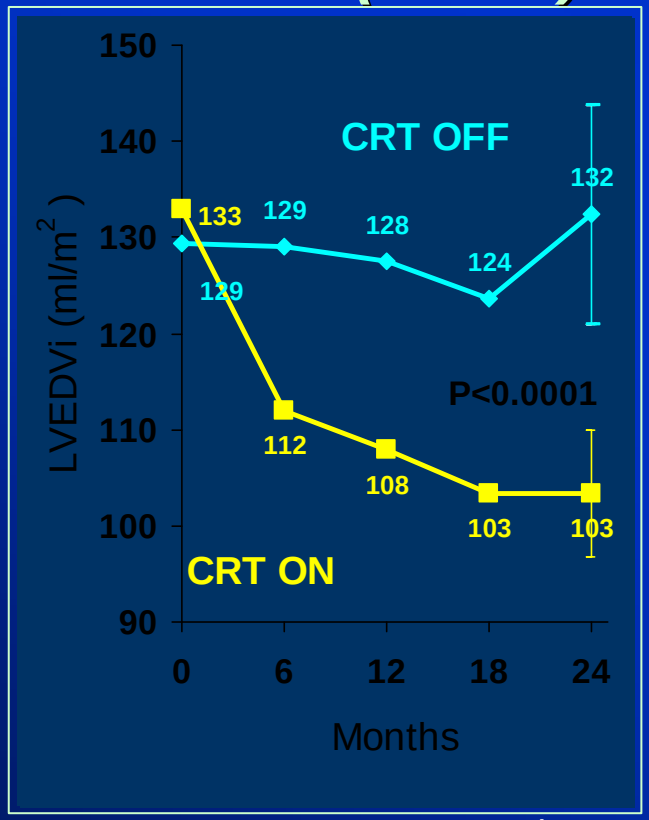


Daubert et al JACC 2009

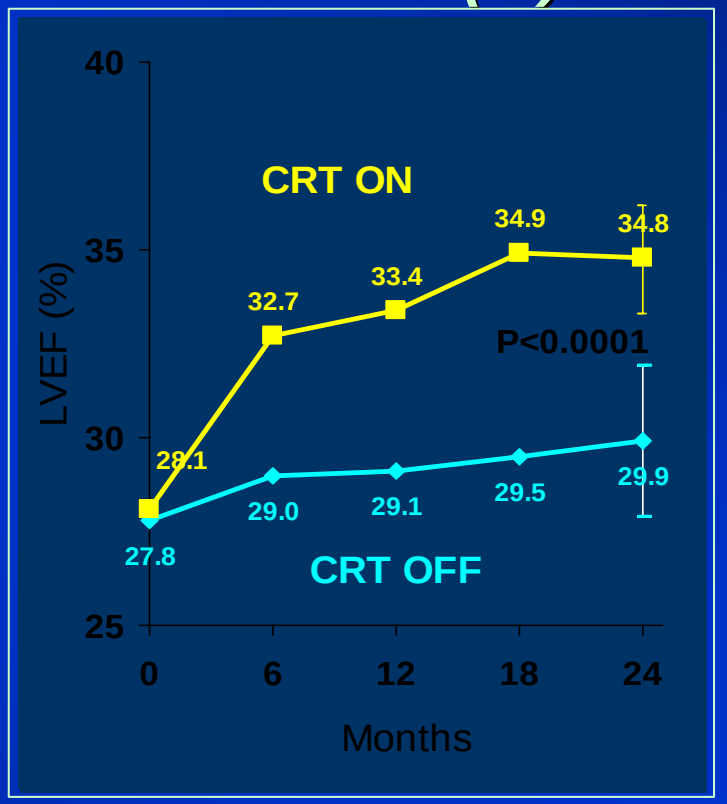
CRT in NYHA II: REVERSE

Other Remodeling Parameters

LVEDVi (ml/m2)



LVEF (%)



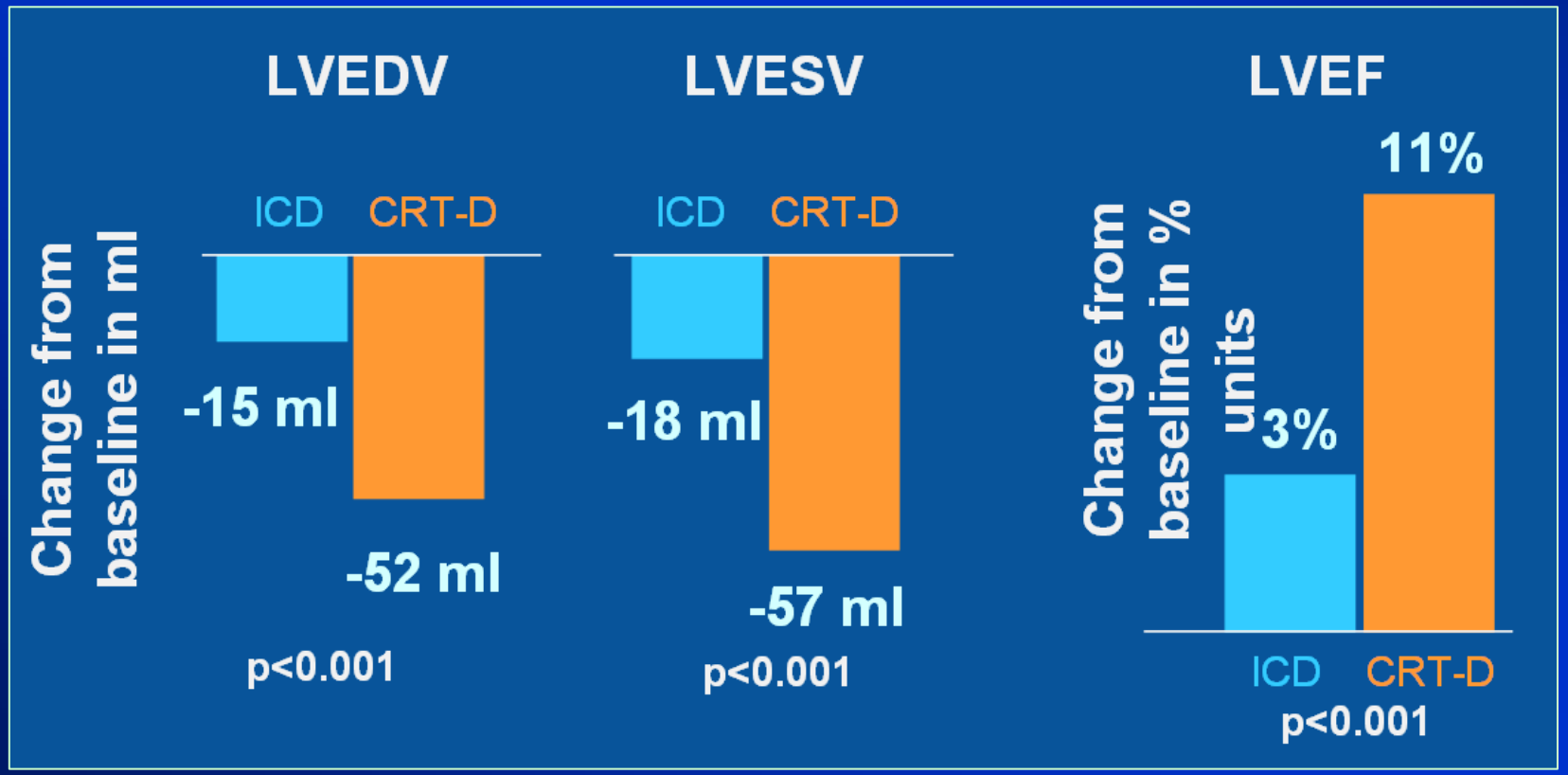
P-value compares 24-month changes.

Daubert et al JACC 2009

CRT in NYHA II:
MADIT CRT confirms REVERSE

Improvements in LV function with CRT-D

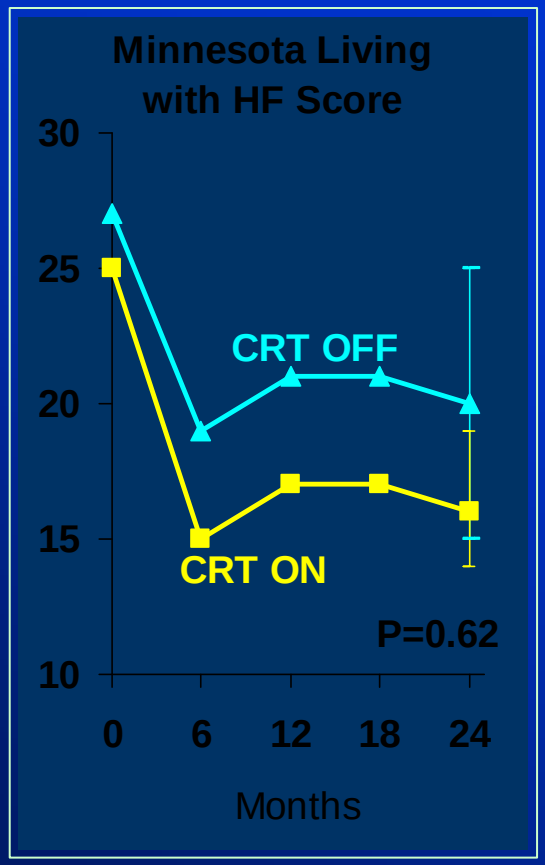
Changes from baseline to 1-year follow-up

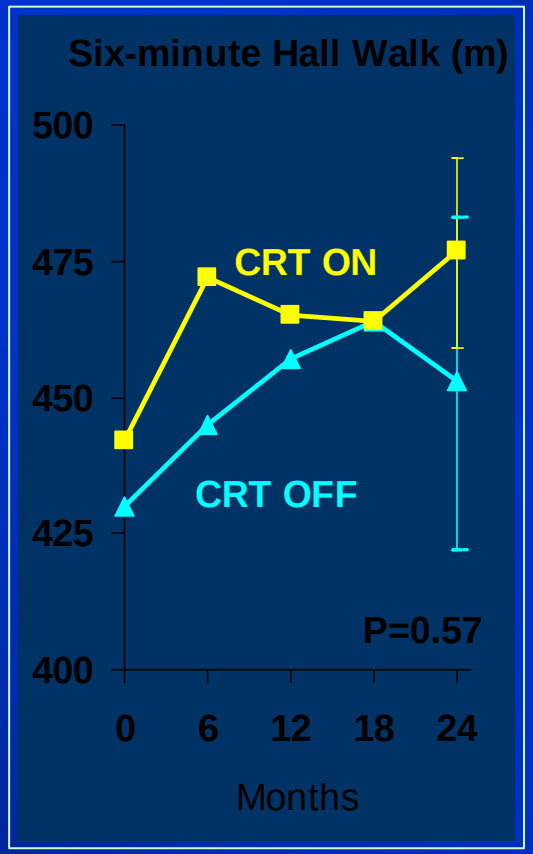


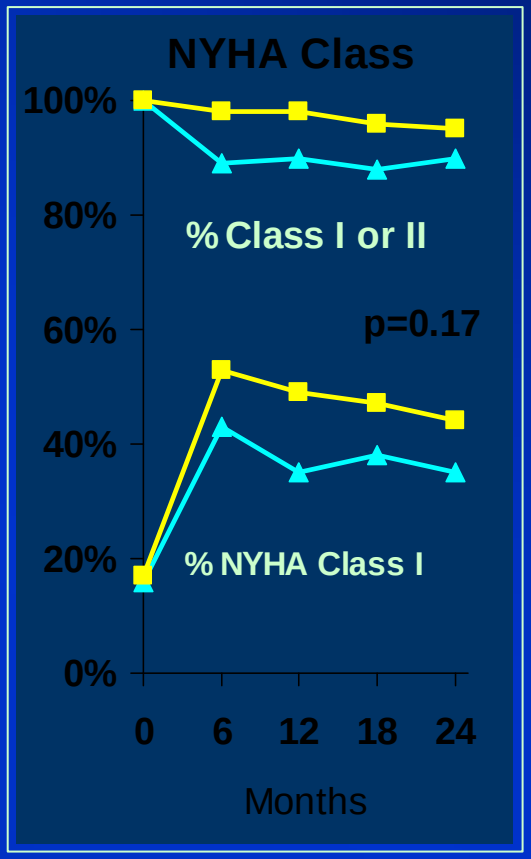
Moss et al NEJM 2009

CRT in NYHA II: REVERSE

Other Secondary Endpoints: Functional Paramaters







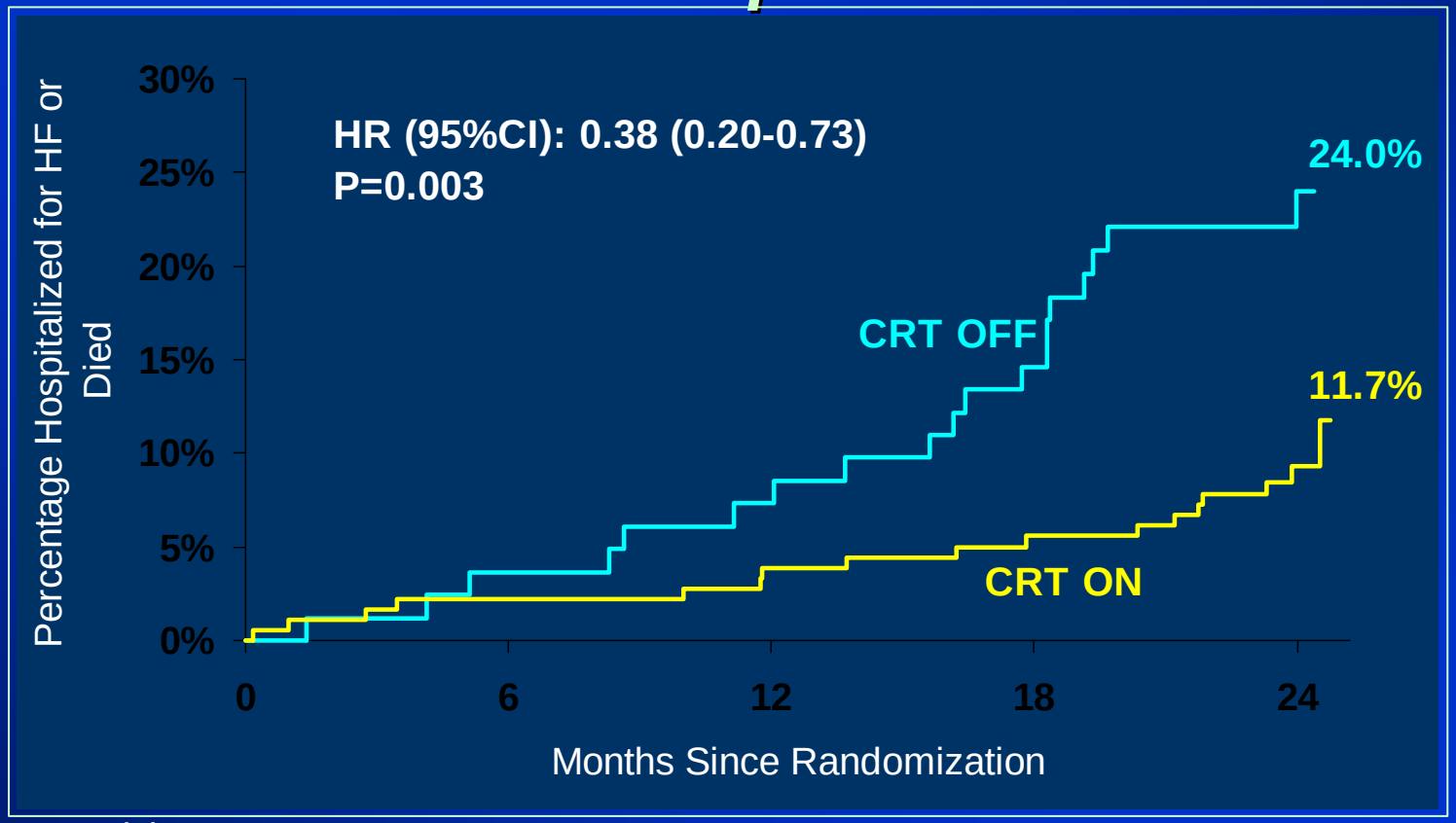
P-values compares 24-month changes.

P-value compares 24-month NYHA.

Daubert et al JACC 2009

CRT in NYHA II: REVERSE

Time to First HF Hospitalization or Death

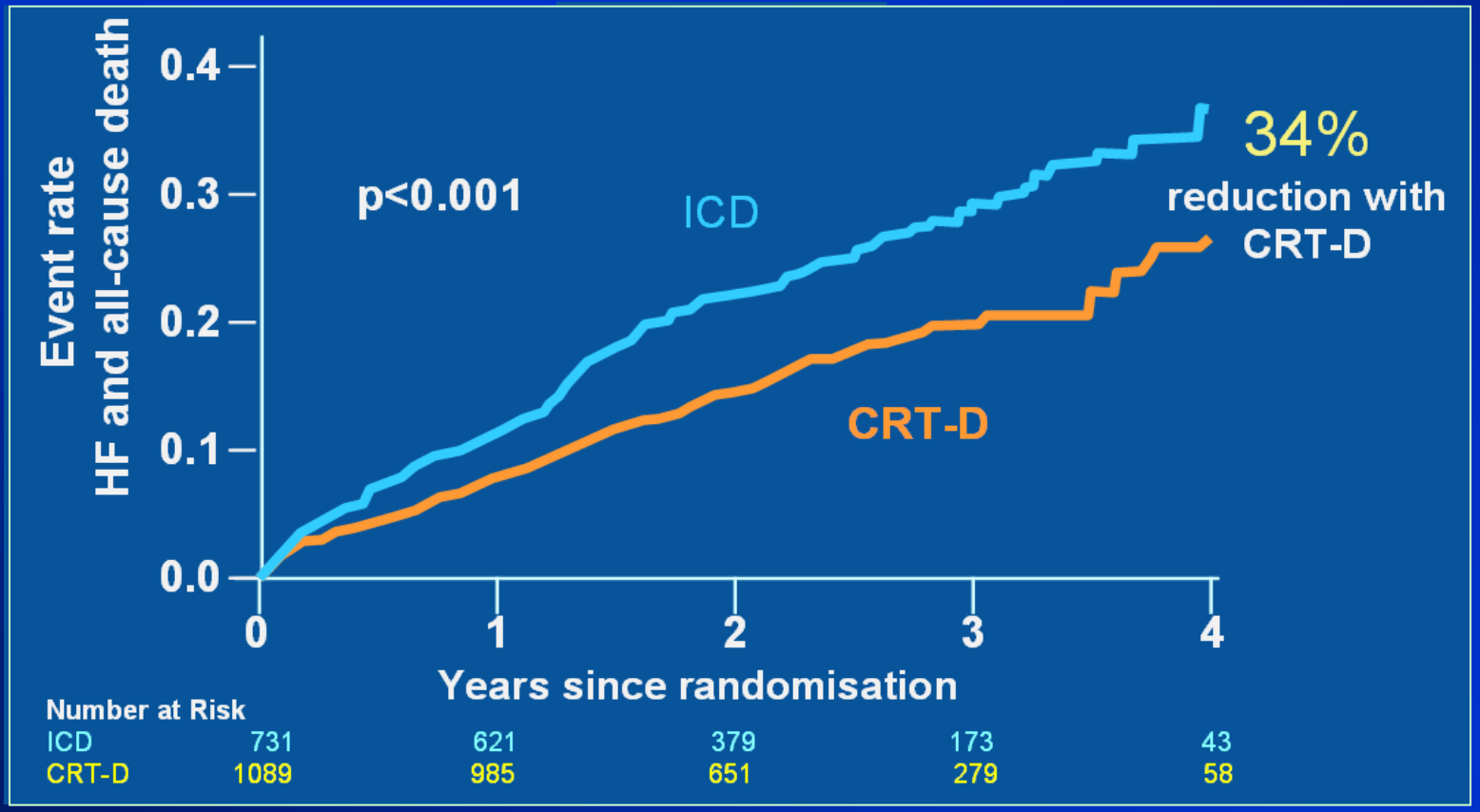


Number at Risk					
CRT OFF	82	79	76	70	39
CRT ON	180	176	173	168	77

Daubert et al JACC 2009

CRT in NYHA II:
MADIT CRT confirms REVERSE

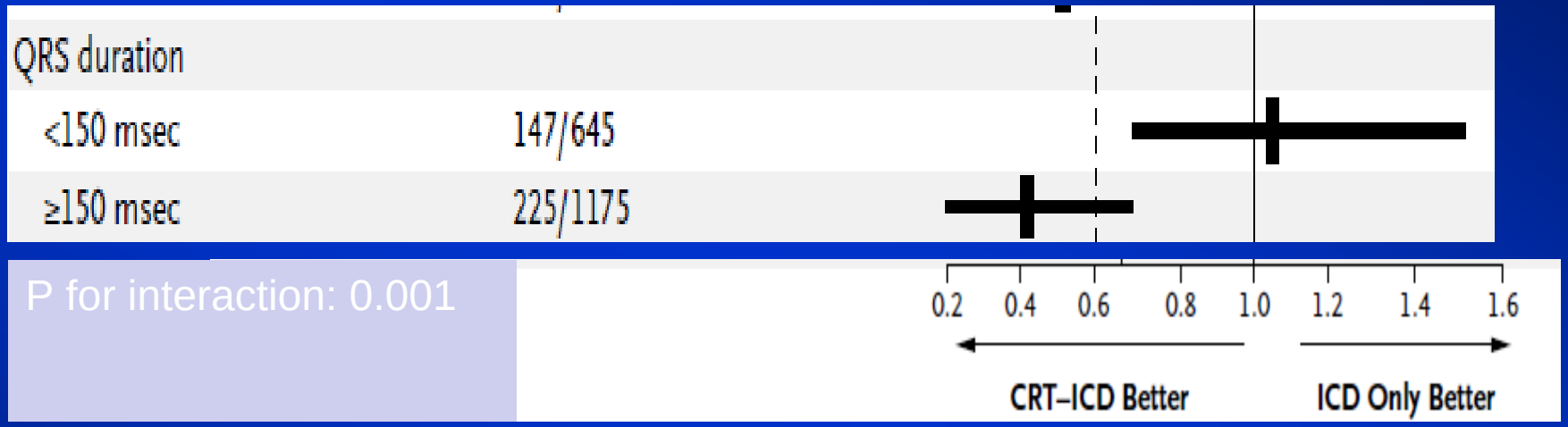
Primary endpoint:
Heart Failure or Death



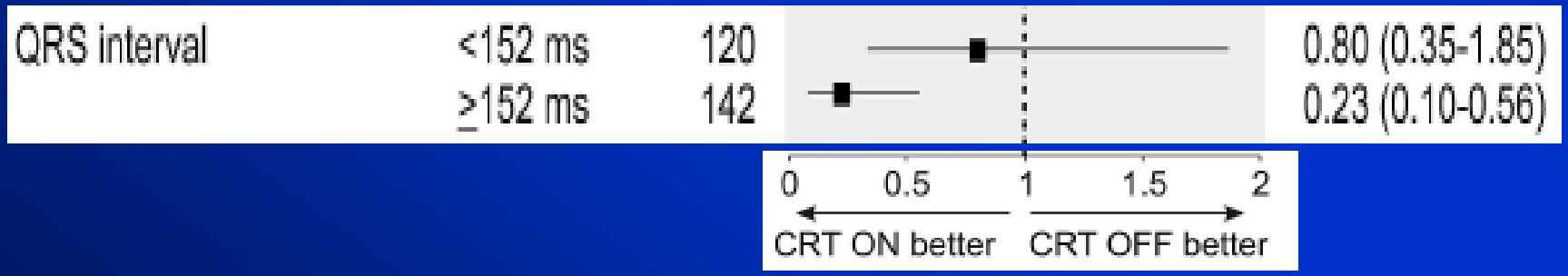
Moss et al NEJM 2009

Predictive value of QRS: *MADIT CRT-REVERSE*

MADIT CRT



REVERSE 24-months



CRT in NYHA II:
REVERSE & MADIT CRT

CRT reduces Morbidity and Mortality in asymptomatic HF Patients with LVD and wide QRS

REVERSE
Presented at ACC09

Presented results show that CRT

Significanty reduces time to first HF hospitalization or death[1] by 62 percent (HR 0.38 (0.20-0.73) p=0.003 within 24 months

[1] Note:ime to First HF hospitalization or death" was not the primary endpoint

When compared to OMT, ICD optional

Daubert et al JACC 2009

MADIT-CRT
Presented at ESC

Presented results show that CRT is associated with a

Significant 34 percent reduction (p<0.001) in death or heart failure interventions within 33 months

When compared to OMT, ICD mandatory

Moss et al NEJM 2009

There is clear and solid evidence of the benefits of "Prophylactic CRT" in terms of clinical outcome and verntricular remodeling

CRT: Open issues

- ✓Patients in I/II NYHA functional class
- ✓Patients with indication to **chronic right ventricular pacing**
- ✓Patients with chronic atrial fibrillation
- ✓Patients without electrical dyssynchrony

Advanced Biventricular Pacemakers to all Patients with AV-block?

A E Albertsen, J.C. Nielsen*, S.H. Poulsen*, H. Egeblad*, A.K. Pedersen*, P.S. Hansen*, H.K. Jensen*, P.T. Mortensen*
From the *Skejby University Hospital - Aarhus N - Denmark

CRT in pts with AV block

- 50 pts with complete A-V block and normal pump function
- randomized single site RV pacing or BIV pacing

Conclusions:

✓BIV pacing preserved LV pump function and minimized LV dyssynchrony as compared to conventional RV pacing;

✓LV pump function decreased significantly and LV dyssynchrony was more pronounced in the RV pacing group

Albertsen AE et al Europace 2008

Biventricular Pacing in Patients with Bradycardia and Normal Ejection Fraction

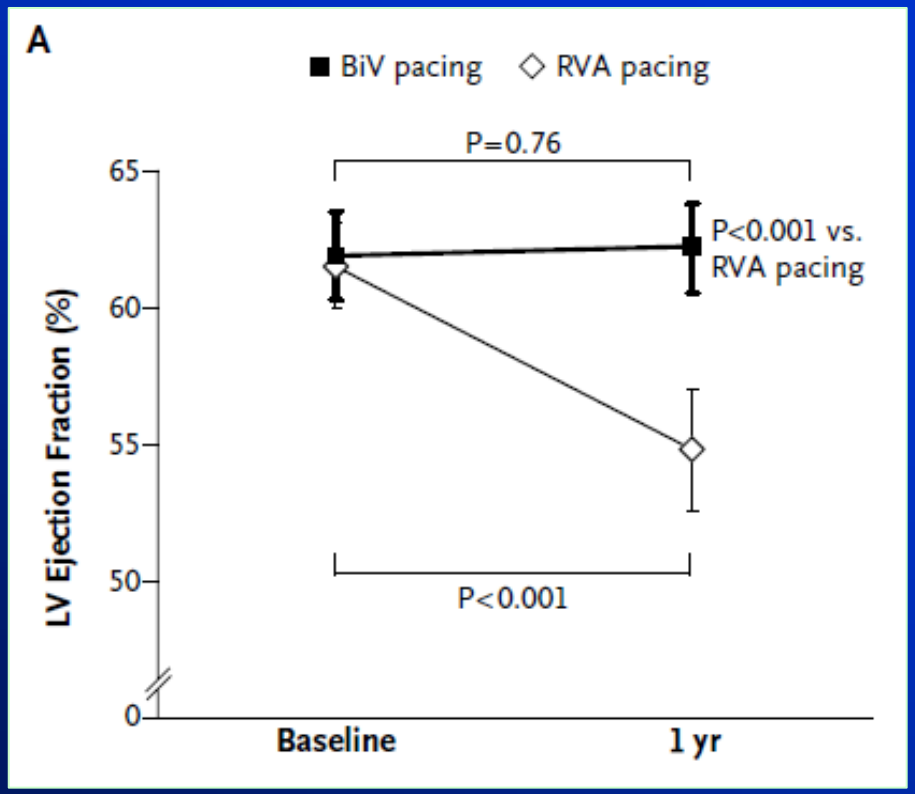
Cheuk-Man Yu, M.D., F.R.C.P., Joseph Yat-Sun Chan, F.H.K.A.M., Qing Zhang, M.M., Ph.D., Razali Omar, M.D., Gabriel Wai-Kwok Yip, M.D., F.A.C.C., Azlan Hussin, M.D., Fang Fang, Ph.D., Kai Huat Lam, M.B., B.S., Hamish Chi-Kin Chan, F.R.C.P., and Jeffrey Wing-Hong Fung, M.D., F.R.C.P.

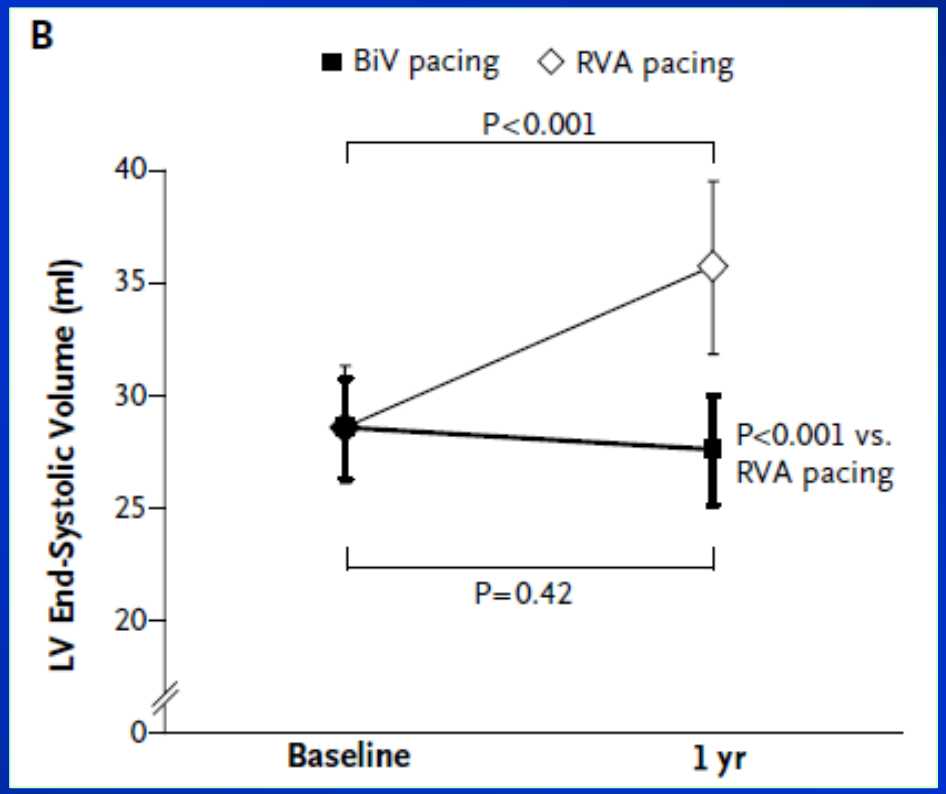
CRT in pts with bradycardia

177 pts with bradycardia and normal EF implanted with a CRT device

Randomization 1:1 Biventricular pacing versus Right Ventricular Apical pacing

Primary end-point: LVEF and LVESV at 12 mos FU





Yu et al NEJM Nov 2009

Biventricular Pacing in Patients with Bradycardia and Normal Ejection Fraction

Cheuk-Man Yu, M.D., F.R.C.P., Joseph Yat-Sun Chan, F.H.K.A.M., Qing Zhang, M.M., Ph.D., Razali Omar, M.D., Gabriel Wai-Kwok Yip, M.D., F.A.C.C., Azlan Hussin, M.D., Fang Fang, Ph.D., Kai Huat Lam, M.B., B.S., Hamish Chi-Kin Chan, F.R.C.P., and Jeffrey Wing-Hong Fung, M.D., F.R.C.P.

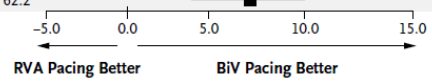
CRT in pts with bradycardia

177 pts with bradycardia and normal EF implanted with a CRT device

Randomization 1:1 Biventricular pacing versus Right Ventricular Apical pacing

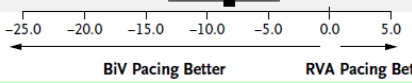
Subgroup analysis of LVEF

Subgroup	No. of Patients	LV Ejection Fraction (%) RVA	BiV	P Value for Interaction
Diastolic dysfunction				0.46
No	66	54.4	63.1	
Yes	107	55.0	61.6	
Pacing indication				0.53
Heart block	102	54.5	62.6	
Sinus-node dysfunction	71	55.3	61.7	
Age				0.20
<70 yr	86	54.8	60.4	
≥70 yr	87	54.8	63.9	
Sex				0.62
Male	95	53.2	61.1	
Female	78	57.0	63.5	
Hypertension				0.53
No	60	56.1	62.3	
Yes	113	54.0	62.1	
Diabetes				0.67
No	125	56.3	62.5	
Yes	48	51.2	61.0	
Coronary heart disease				0.93
No	135	55.4	62.6	
Yes	38	53.1	60.6	
QRS duration				0.24
<110 msec	113	56.2	62.5	
≥110 msec	60	52.2	61.8	
All patients	173	54.8	62.2	



and LVESV

Subgroup	No. of Patients	LV End-Systolic Volume (ml) RVA	BiV	P Value for Interaction
Diastolic dysfunction				0.39
No	66	36.9	26.4	
Yes	107	34.9	28.4	
Pacing indication				0.16
Heart block	102	38.6	28.0	
Sinus-node dysfunction	71	31.2	27.1	
Age				0.17
<70 yr	86	37.4	31.8	
≥70 yr	87	33.8	23.4	
Sex				0.83
Male	95	39.4	31.1	
Female	78	30.6	23.3	
Hypertension				0.10
No	60	32.2	29.4	
Yes	113	37.7	26.8	
Diabetes				0.53
No	125	33.5	26.6	
Yes	48	40.8	30.6	
Coronary heart disease				0.52
No	135	34.0	27.0	
Yes	38	40.1	29.6	
QRS duration				0.94
<110 msec	113	34.3	25.9	
≥110 msec	60	38.1	29.2	
All patients	173	35.7	27.6	



Yu et al NEJM Nov 2009

BioPace study

- **Randomized, multicentric, prospective, single-blind, parallel-group-design**
- **International (EMEAC + Australia)**
  - **1st large scaled randomized study looking at the prevention of mechanical desynchronization**
  - **Extend the benefit of BiV pacing to a broader patient population**
- **Enrollment Goal**
  - **1800 patients @ 94 centers**
  - **Follow-up phase**
- **Evaluate whether patients with standard pacing indication (pacemaker or ICD)**
  - **any standard-indication for permanent ventricular pacing**
  - **LVEF without any limitation**
  - **any QRS-width**
  - **benefit from the prevention of ventricular remodeling (induced by RV pacing) with the implantation of a BiV pacing system**
- **A landmark study which results will impact the future of pacemaker therapy**

Biventricular pacing in patients with normal systolic function who should undergo conventional pacing (right ventricular apex) can prevent adverse left ventricular remodeling and reduction of left ventricular ejection fraction (PM-induced myopathy).

CRT: Open issues

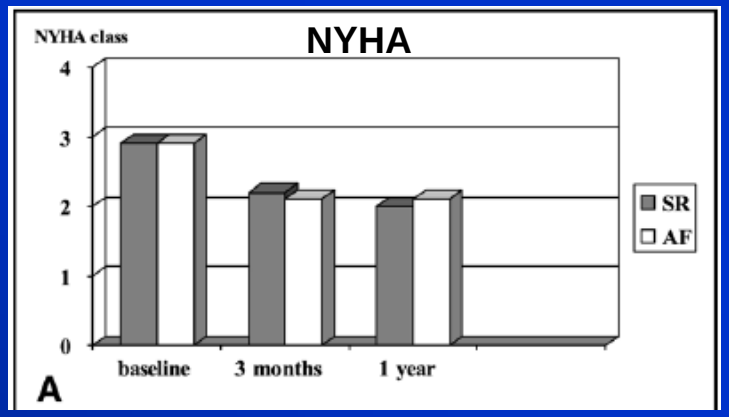
- ✓Patients in I/II NYHA functional class
- ✓Patients with indication to chronic right ventricular stimulation
- ✓Patients with **chronic atrial fibrillation**
- ✓Patients without electrical dyssynchrony

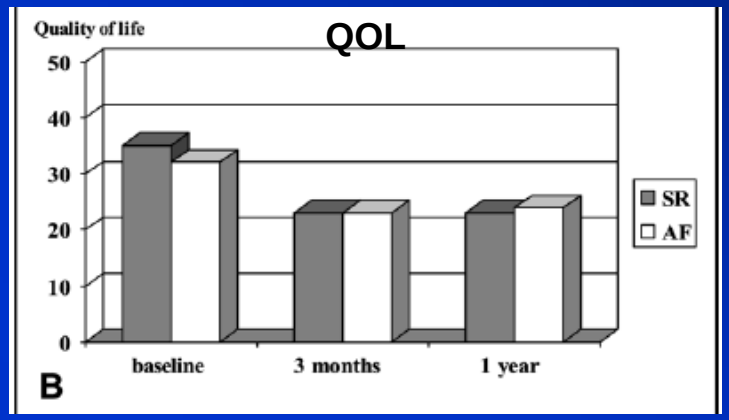
Comparison of Usefulness of Cardiac Resynchronization Therapy in Patients With Atrial Fibrillation and Heart Failure Versus Patients With Sinus Rhythm and Heart Failure

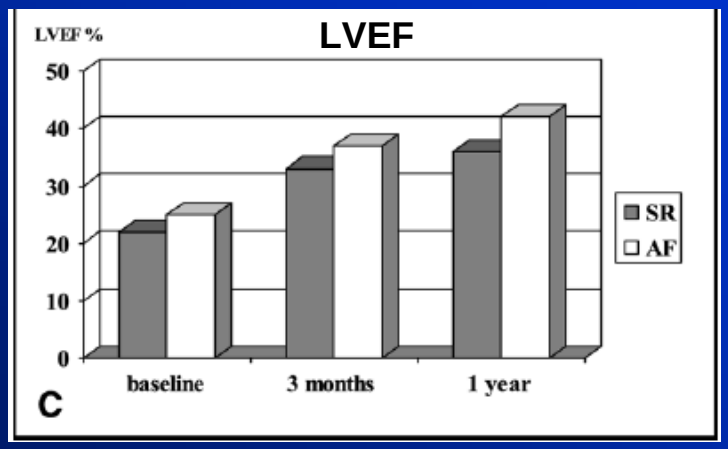
Peter Paul H.M. Delnoy, MD[a,*], Jan Paul Ottervanger, MD, PhD[a], Henk Oude Luttikhuis, MD[a], Arif Elvan, MD, PhD[a], Anand R. Ramdat Misier, MD, PhD[a], Willem P. Beukema, MD[a], and Norbert M. van Hemel, MD, PhD[b]

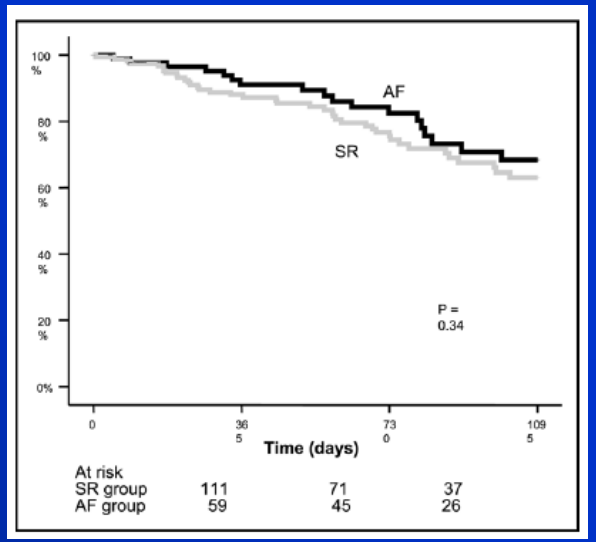
CRT and AF

Evaluation of CRT in 263 consecutive pts, 96 with chronic AF and 167 in sinus rhythm









Delnoy et al., Am J Cardiol 2007

Four-Year Efficacy of Cardiac Resynchronization Therapy on Exercise Tolerance and Disease Progression

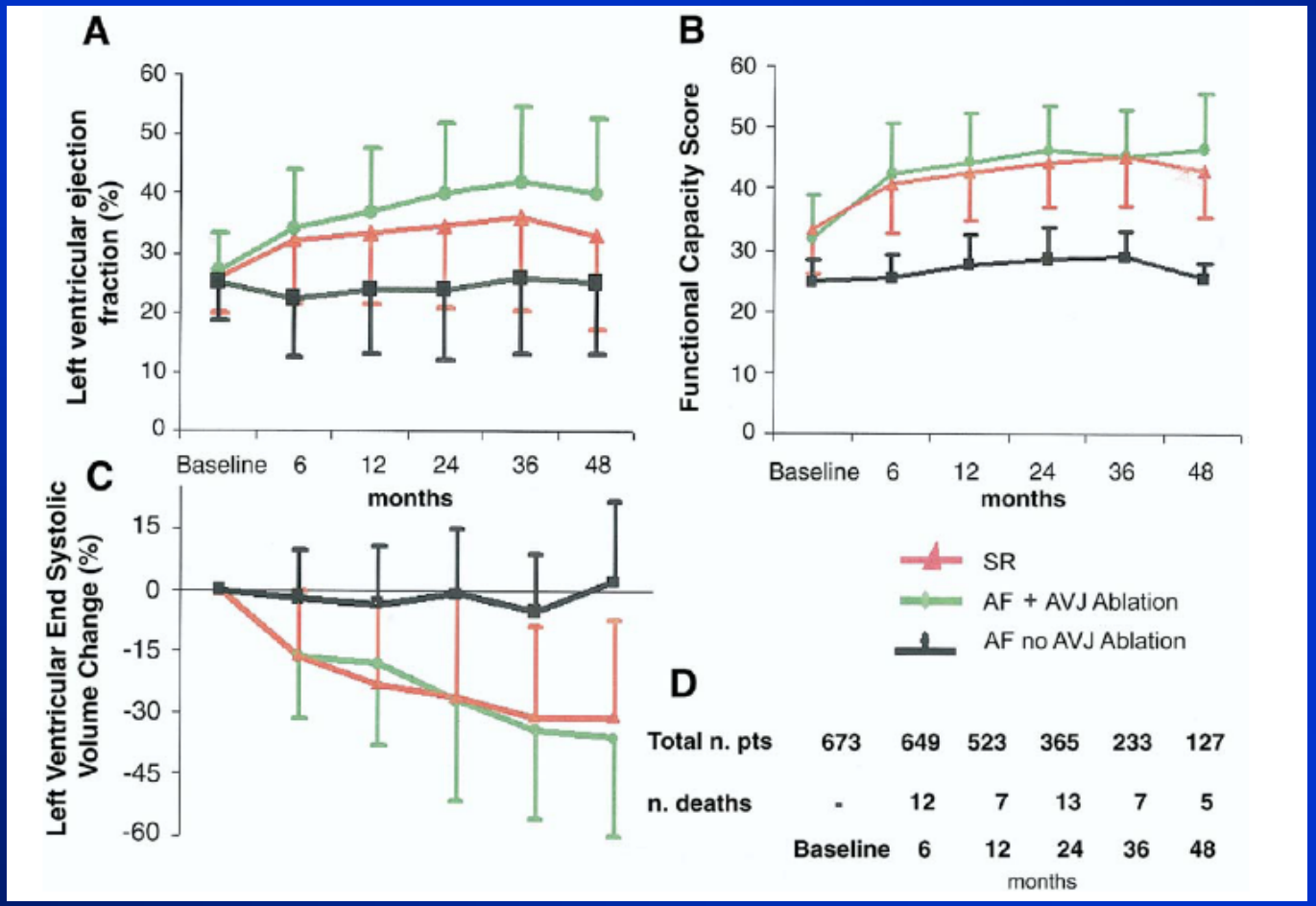
The Importance of Performing Atrioventricular Junction Ablation in Patients With Atrial Fibrillation

Maurizio Gasparini, MD,* Angelo Auricchio, MD, PHD,‡§ François Regoli, MD,* Cecilia Fantoni, MD,‡ Mihoko Kawabata, MD,‡ Paola Galimberti, MD,* Daniela Pini, MD,* Carlo Ceriotti, MD,* Edoardo Gronda, MD,* Catherine Klersy, MD, MSC,† Simona Fratini, MD,‡ Helmut H. Klein, MD‡

CRT and AF

In 162 pts with permanent AF vs 511 pts in SR

162 pts with permanent AF where: 48 pts with rhythm control by drugs; 114 pts with AVJ ablation



Gasparini et al., JACC 2006

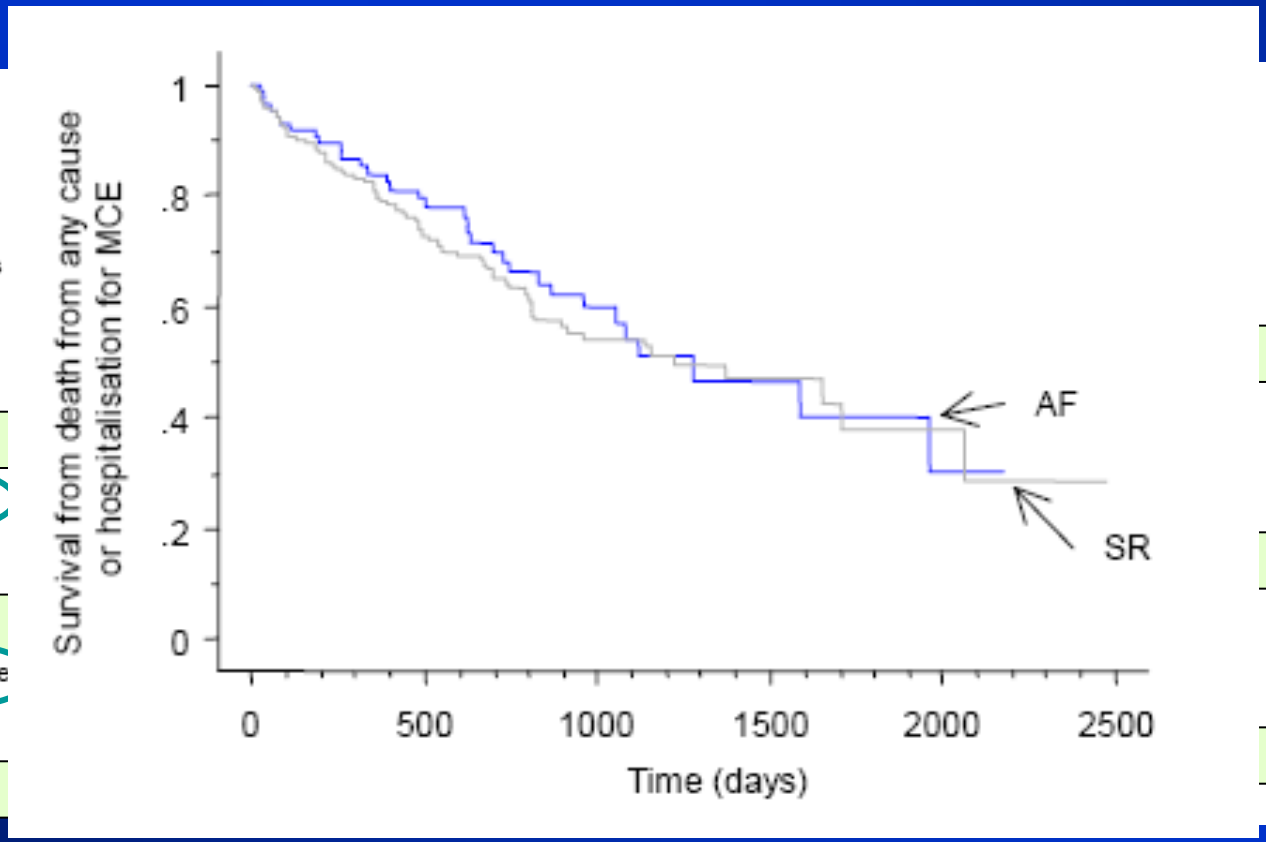
CRT and AF

Long-term effects of cardiac resynchronisation therapy in patients with atrial fibrillation

Kayvan Khadjooi, Paul Foley, Jeffrin Anthony, Shajil Chalil, Russell Smith, Michael Frenneaux and Francisco Leyva

In 86 pts with AF vs 209 pts in SR

86 pts with AF where: 66 permanent AF, 20 paroxismal AF



	Atrial fibrillation
N	
Follow-up, days	
Clinical variables	
NYHA class	
Baseline	224.1 (89.4)
Follow-up	203.3 (85.1) **
6-min walk test, m	
Baseline	169.7 (80.2)
Follow-up	140.1 (76.1) ***
Quality of life score	
Baseline	26.0 (11.8)
Follow-up	33.8 (11.0) ***

*, p<0.05; **, p<0.001, ***, p<0.0001

Khadjooi et al., Heart 2008

Biventricular pacing is as effective in patients with chronic atrial fibrillation as in patients in synus rhythm.

CRT: Open issues

- ✓Patients in I/II NYHA functional class
- ✓Patients with indication to chronic right ventricular stimulation
- ✓Patients with chronic atrial fibrillation
- ✓Patients without **electrical dyssynchrony**

Interventricular and intraventricular dyssynchrony are common in heart failure patients, regardless of QRS duration

Stefano Ghio[a,*], Cristina Constantin[a], Catherine Klersy[b], Alessandra Serio[a], Alessandra Fontana[a], Carlo Campana[a], Luigi Tavazzi[a]

[a] Division of Cardiology, IRCCS Policlinico San Matteo Hospital, V.le Golgi, 19 Pavia 27100, Italy
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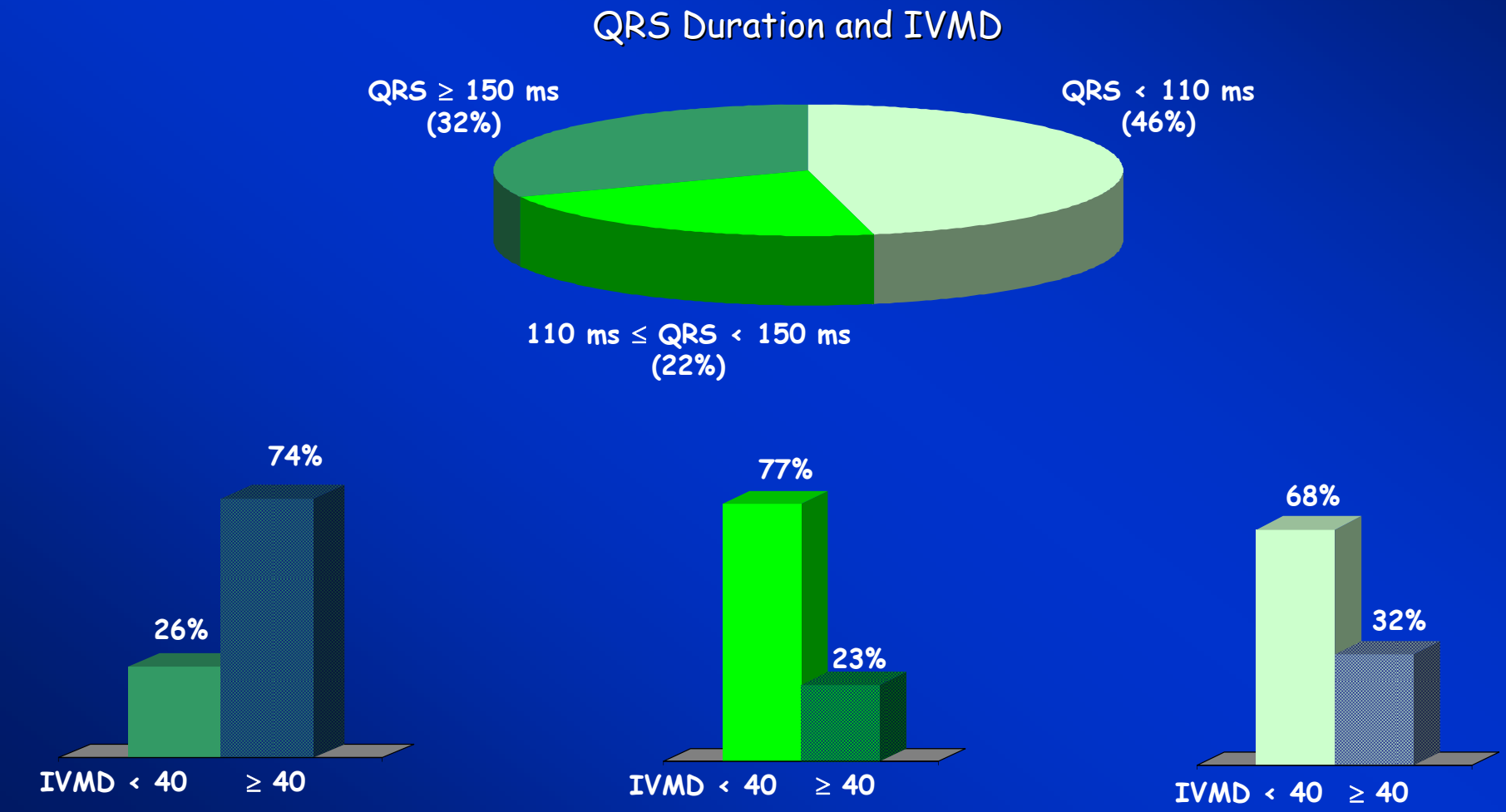
Received 11 April 2003; revised 3 September 2003; accepted 19 September 2003

QRS duration and dyssynchrony



Ghio et al EHJ 2004

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Long-Term Effectiveness of Cardiac Resynchronization Therapy in Patients With Refractory Heart Failure and "Narrow" QRS

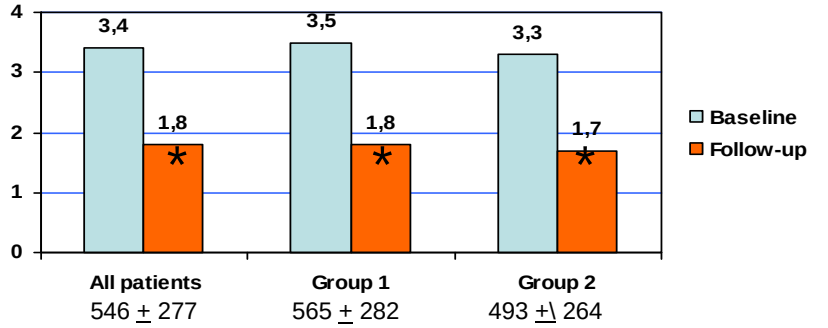
Augusto Achilli, MD,* Massimo Sassara, MD,* Sabina Ficili, MD,* Daniele Pontillo, MD,* Paola Achilli, MD,* Claudio Alessi, MD,* Stefano De Spirito, MD,* Roberto Guerra, MD,* Nicolino Patruno, MD,† Francesco Serra, MD*
Viterbo and Albano Laziale, Italy

CRT and narrow QRS

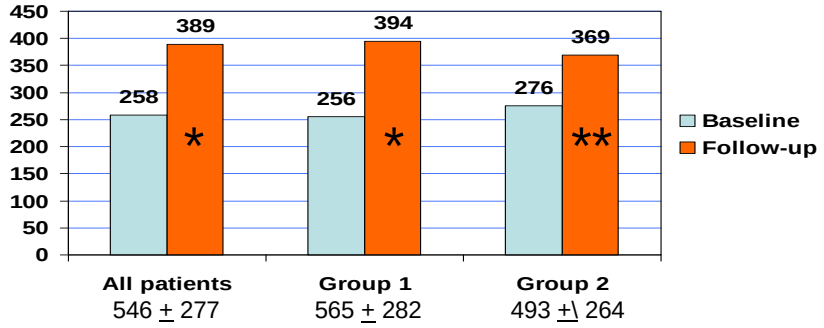
52 patients with severe HF and with echocardiographic evidence of interventricular and intraventricular asynchrony received biventricular pacing:

Group 1: QRS > 120 ms (38pts); Group 2: QRS ≤ 120 ms (14pts)

NYHA CLASS

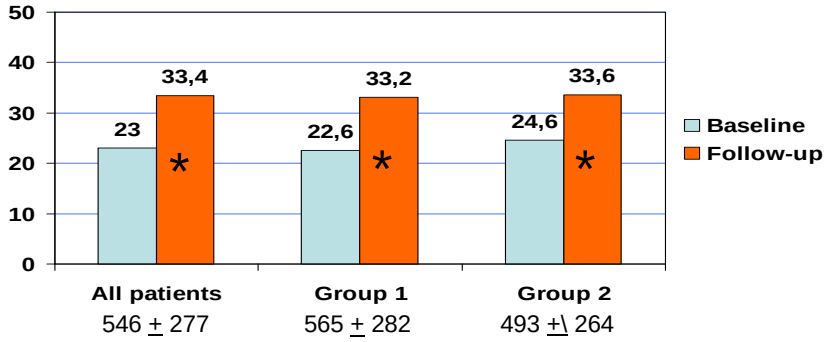


6 MINUTES WALKING TEST

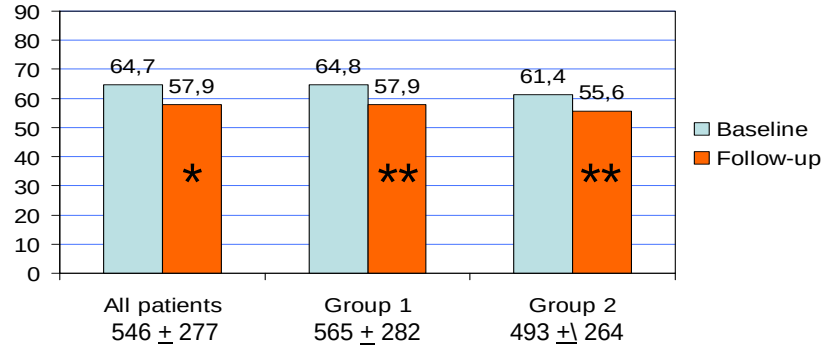


* p<0,001 vs baseline; ** p<0,01 vs baseline

EJECTION FRACTION



LVESD



Achilli et al. JACC 2003

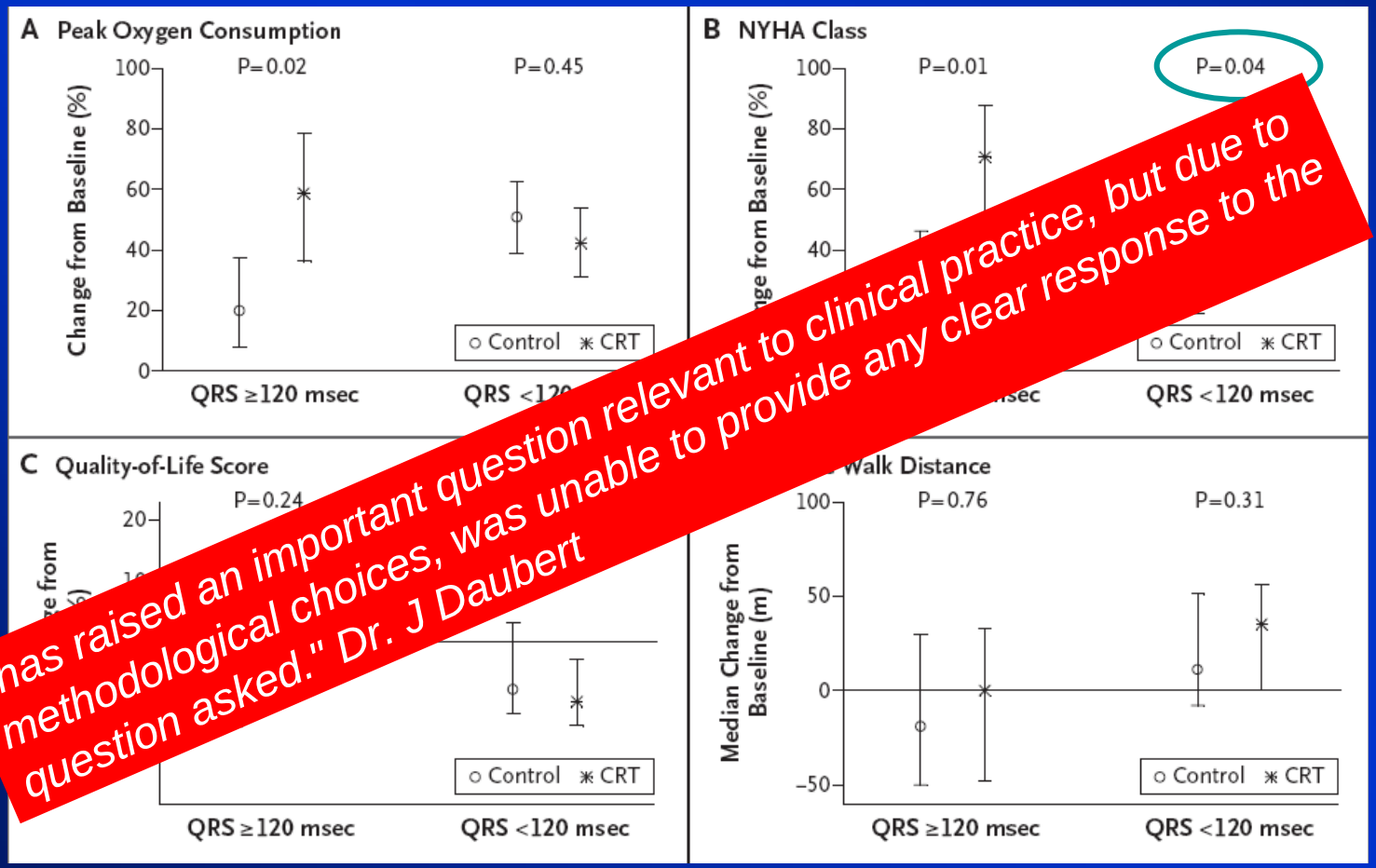
Cardiac-Resynchronization Therapy in Heart Failure with Narrow QRS Complexes

John F. Beshai, M.D., Richard A. Grimm, D.O., Sherif F. Nagueh, M.D., James H. Baker II, M.D., Scott L. Beau, M.D., Steven M. Greenberg, M.D., Luis A. Pires, M.D., and Patrick J. Tchou, M.D., for the RethinQ Study Investigators*

CRT and narrow QRS

172 pts with narrow QRS (<130ms), EF≤35% and NYHA III

Randomization 1:1 CRT ON vs CRT OFF



"has raised an important question relevant to clinical practice, but due to methodological choices, was unable to provide any clear response to the question asked." Dr. J Daubert

Beshai et al., RETHIN Q; NEJM 2007

We have no current guidance for doing something (CRT) in patients without wide QRS and dyssynchrony only.

The European cardiac resynchronization therapy survey

Kenneth Dickstein[1,2], Nigussie Bogale[1,2*], Silvia Priori[3], Angelo Auricchio[4], John G. Cleland[5], Anselm Gitt[6], Tobias Limbourg[6], Cecilia Linde[7], Dirk J. van Veldhuisen[8], and Josep Brugada[9] on behalf of the Scientific Committee and National Coordinators

The European cardiac resynchronization therapy (CRT) survey is a joint initiative taken by the Heart Failure Association and the European Heart Rhythm Association of the European Society of Cardiology. The primary aim of this survey is to describe current European practice associated with CRT implantations.

Table 1 Pre-implantation evaluation of the total cohort (n = 2438)

Demographics	
Age (years)[a]	70 (62–76)
Age ≥ 75 (%)	31
Females (%)	27
BMI (kg/m2)[a]	26 (24–29)
Heart failure aetiology (%)	
Ischaemic	51
Non-ischaemic	40
Other	9
Clinical evaluation (%)	
NYHA I	2
NYHA II	20
NYHA III	70
NYHA IV	8
Mean LV ejection fraction (%)	27 ± 8
<25%	37
25–35%	46
>35%	17
LV end-diastolic diameter (mm)	65 ± 10
LV end-systolic diameter (mm)	54 ± 11
ECG (%)	
Mean heart rate (b.p.m.)	72 ± 15
Sinus rhythm	73
Atrial fibrillation	23
QRS complex (%)	
LBBB	68
RBBB	6
Paced rhythm	19
Mean QRS duration (msec)	157 ± 32
QRS duration < 120 ms	9
QRS duration 120 - 129 ms	10
QRS duration 130 - 149 ms	20
QRS duration ≥ 150 ms	62

EHJ 2009

The European cardiac resynchronization therapy survey

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Table 6 Comparison between COMPANION, CARE-HF, REVERSE and CRT Survey cohorts

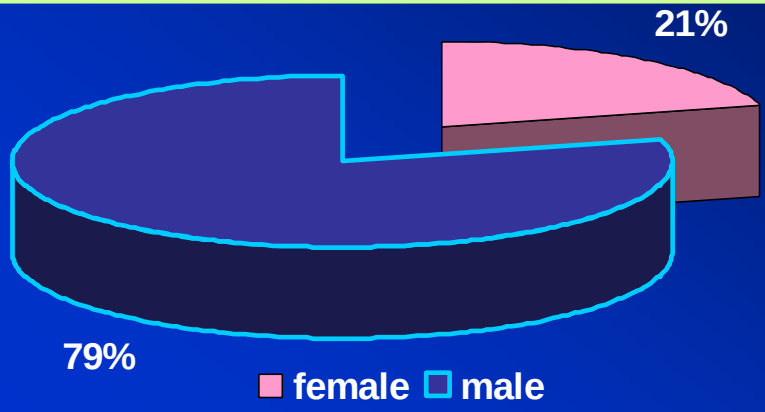
	COMPANION	CARE-HF	REVERSE	CRT Survey
Number of patients	1212	409	419	2438
Patients with a CRT-P (%)	51	100	18	27
Patients with a CRT-D (%)	49	NA	82	73
Previous device (PPM or ICD) (%)	0[a]	0[a]	0[a]	26
Mean age (years)	67	65	63	68
Women (%)	33	27	22	24
Ischaemic heart disease (%)	55	38	56	51
NYHA class III (%)	86	64	0[b]	70
LV ejection fraction (%)	22	26	27	26
LV diastolic diameter (mm)	67	72	69	66
QRS (ms)	160	165	153	160
Atrial fibrillation (%)	0[a]	0[a]	0[a]	23
Heart rate (b.p.m.)	72	70	67	70
Diuretics (%)	95	99	91	88
ARB/ACEI (%)	89	85	96	91
Betablockers (%)	68	72	96	85
Aldosterone antagonists (%)	54	56	NA	46

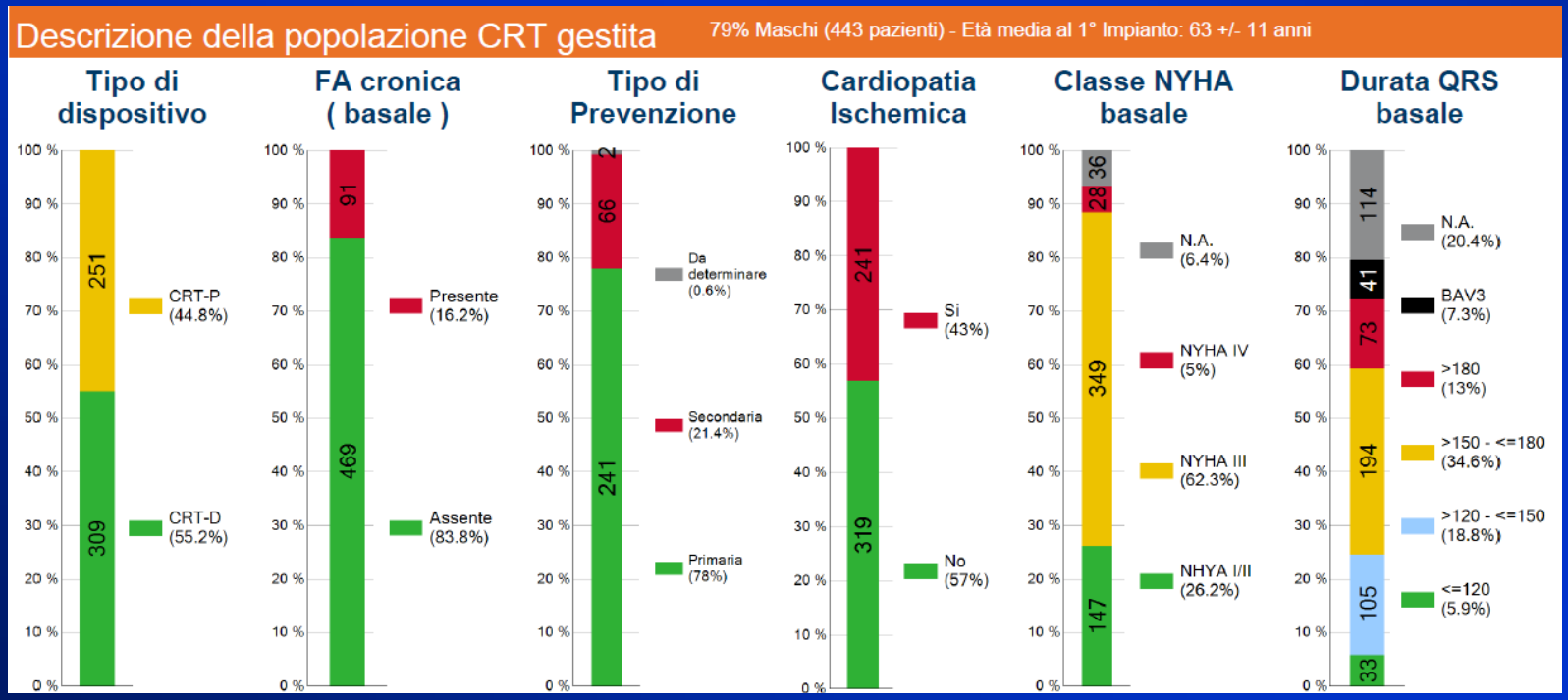
[a]Previous device implantation and atrial fibrillation were exclusion criteria. [b] NYHA class III/IV were exclusion criteria.

EHJ 2009

...our experience....

- ✓560 patients
- ✓Mean age: 63,7 ± 10,9 yrs





Clinical Service data

Conclusions

Cardiac Resynchronisation Therapy	
Class I Indication	**Synus Rhythm, Reduced EF (≤ 35%)** **Ventricular Dyssynchrony (QRS > 120ms)** **NYHA III-IV despite Optimal Medical Therapy**
Class II Indications	Synus Rhythm, Reduced EF (≤ 35%)
	Prevention ICD indication
	Chronic Right Ventricular Pacing, Reduced EF (< 35%)
	NYHA III-IV despite Optimal Medical Therapy
	Reduced EF (< 35%), **QRS < 120 ms**
	NYHA III-IV despite Optimal Medical Therapy

Strong evidence !!!

Convincing evidence !

Strong evidence !!

Need of other RCTs

The future...

Babec's Story

"On September 25th, 2004, the Birmingham Zoo successfully implanted the first cardiac resynchronization therapy device, or ***CRT, in a gorilla****. One year later* ***Babec is still alive****, an unlikely scenario without the device, and* ***his quality of life is significantly improved*** *from that prior to surgery."*

Babec died in 2009...

5 years later CRT!!!

http://www.birminghamzoo.com/babec%20story.asp