

CRT Super-Responders: Pre-OP Selection & Post-OP Rhythm Manage

Boyoung Joung

Professor of Internal Medicine

Director of Electrophysiology laboratory

Yonsei University Medical College, Seoul, Korea,



Case

M/70, Choi TY

CC: 2:1 AV block, Dyspnea

(He was managed with IV inotropics for 2 months)

PHx:

DCMP since 1999'

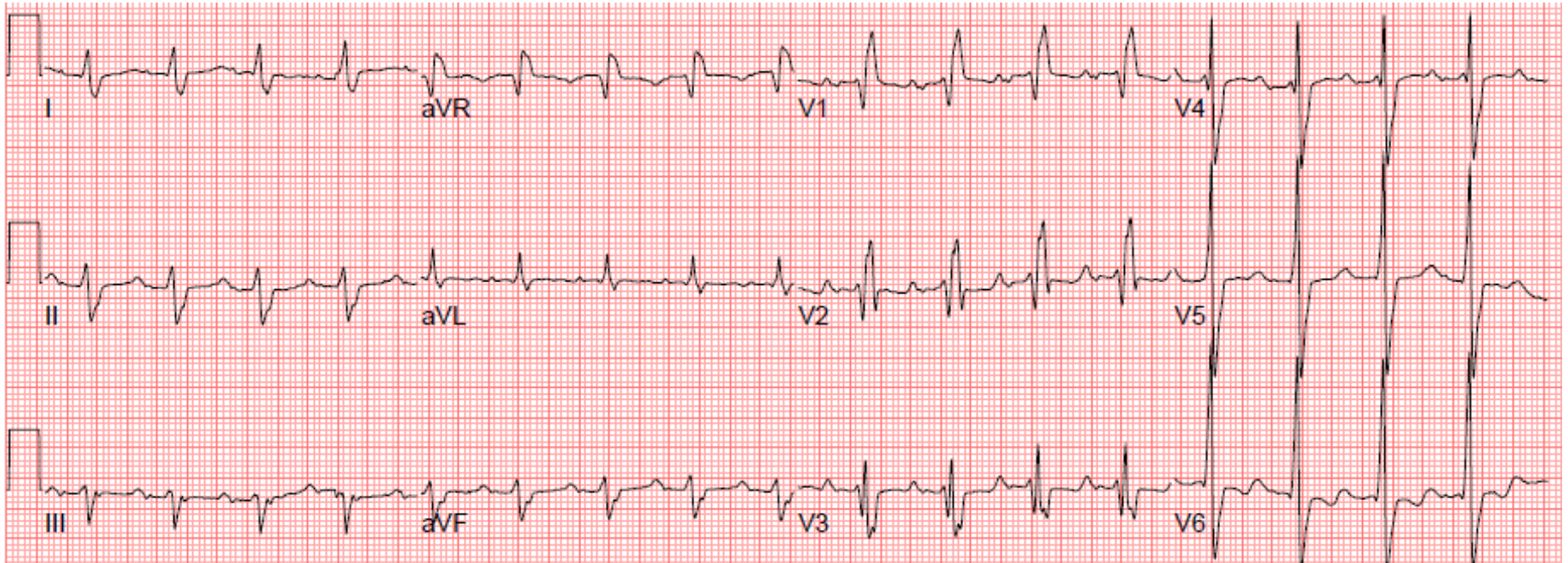
HTN, DM, CKD

Medication

ACEI, Diuretics, Beta blocker

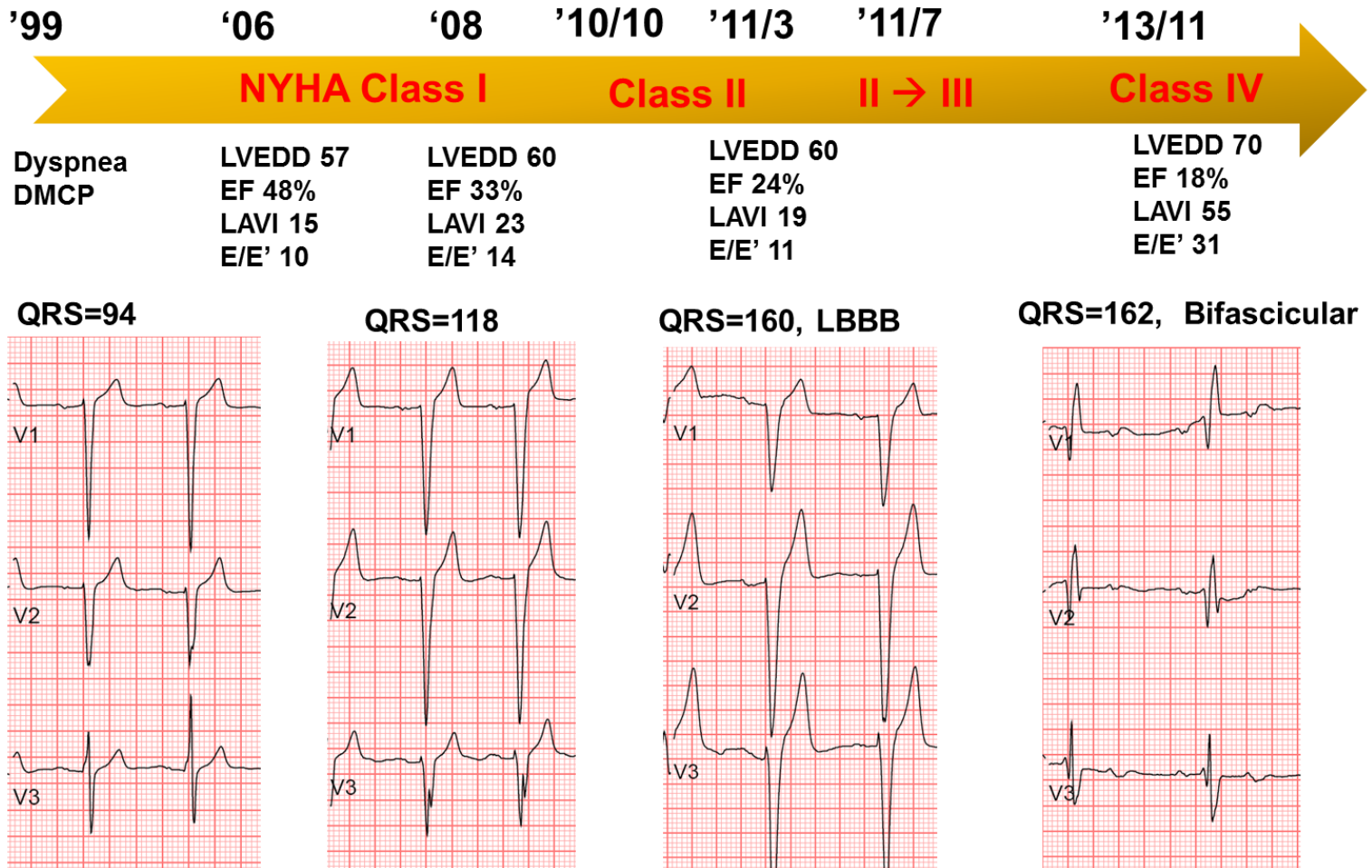
EKG

RBBB, QRS: 160 ms, PR 240ms, LV EF: 18%



Best Time and Candidate for CRT?

The Change of EKG and Clinical Course



CRT : ACC/AHA Guidelines 2013

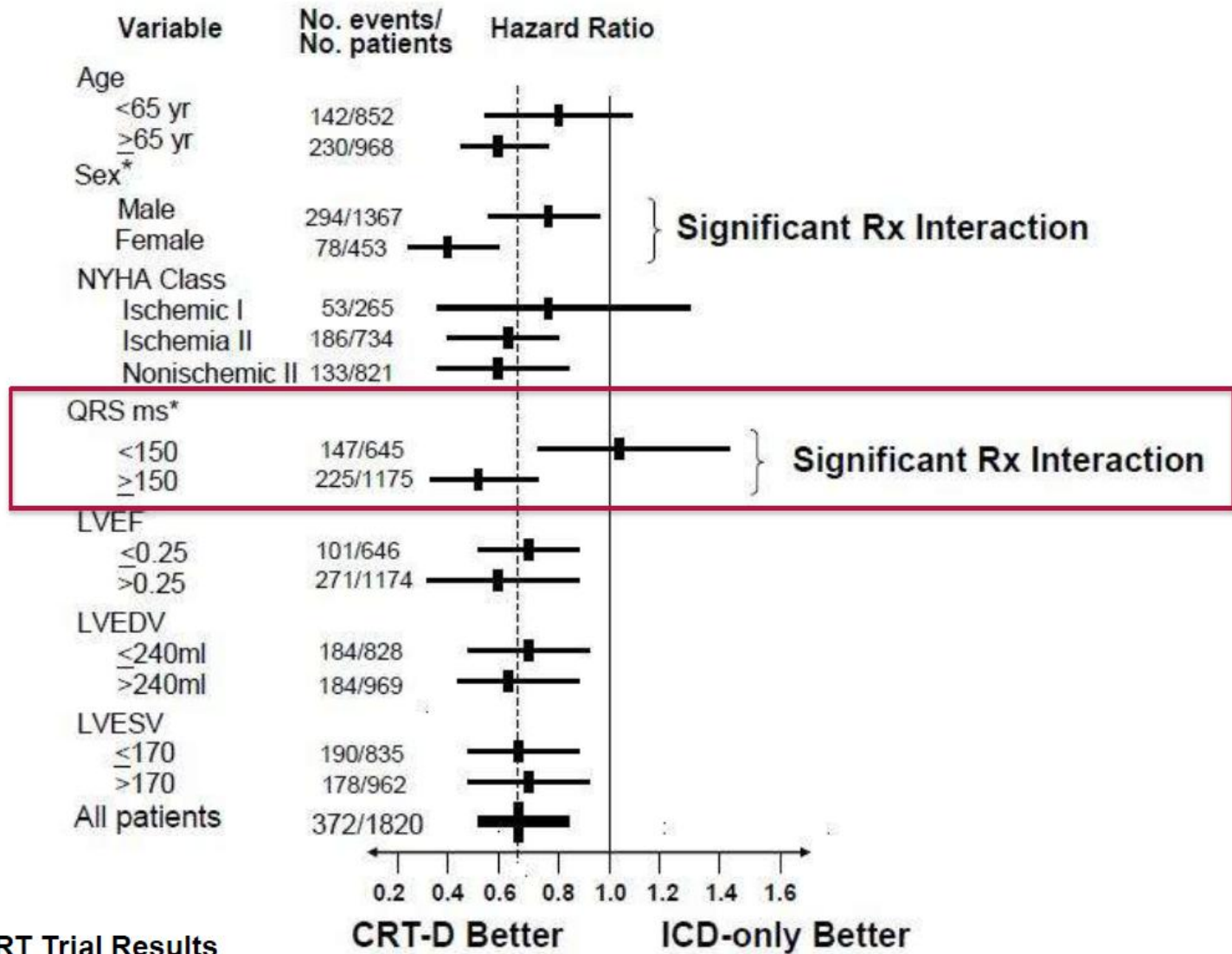
Class I

CRT is indicated for patients with LVEF \leq 35%, sinus rhythm, **LBBB with a QRS duration \geq 150 ms**, and NYHA class II, III, or ambulatory IV symptoms on GDMT

Class IIa

1. CRT can be useful for patients who have LVEF \leq 35%, sinus rhythm, LBBB with a QRS duration of 120–149 ms, and NYHA class II, III, or ambulatory IV symptoms on GDMT
2. CRT can be useful for patients who have LVEF \leq 35%, sinus rhythm, a non-LBBB pattern with a QRS duration \geq 150 ms, and NYHA class III/ambulatory class IV symptoms on GDMT
3. CRT can be useful in patients with atrial fibrillation and LVEF \leq 35% on GDMT if (1) the patient requires ventricular pacing or otherwise meets CRT criteria and (2) AV nodal ablation or pharmacological rate control will allow near 100% ventricular pacing with CRT
4. CRT can be useful for patients on GDMT who have LVEF \leq 35% and are undergoing new or replacement device placement with anticipated requirement for significant (>40%) ventricular pacing

CRT-D: ICD Hazard ratios for prespecified subgroups

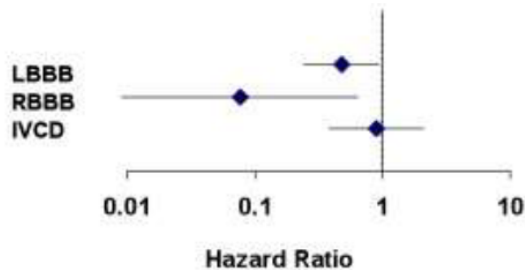


MADIT-CRT Trial Results

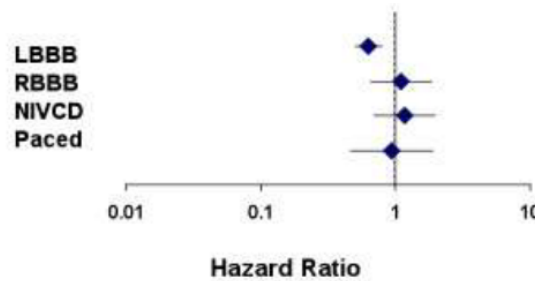


REVERSE, RAFT and MADIT-CRT: HF Hospitalization/Event or All-cause Death by QRS morphology

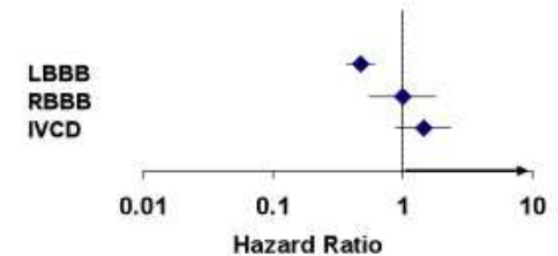
REVERSE – HF Hosp/Death



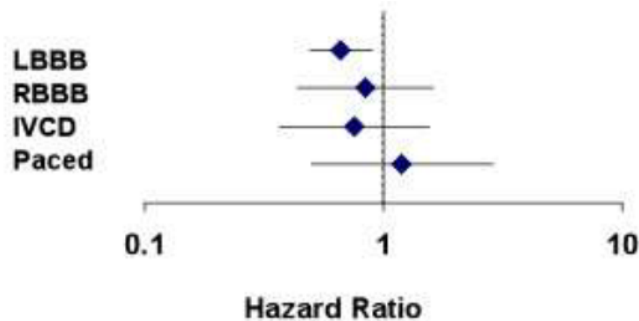
RAFT Class II – HF Hosp/Death



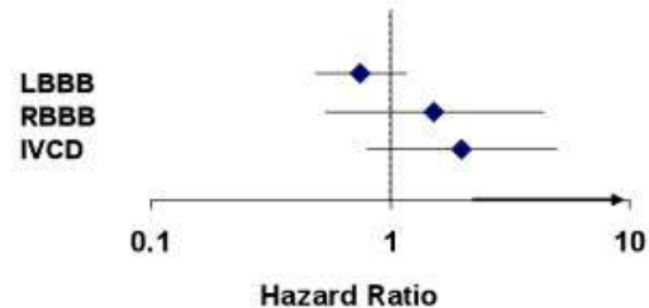
MADIT-CRT – HF Event/Death



RAFT Class II
Mortality



MADIT-CRT
Mortality



Definitions of Super-response to CRT

(1) a decrease in LV end-systolic volume of $\geq 30\%$.

Ypenburg C, et al. J Am Coll Cardiol 2009;53:483-90

Poller W, et al. Clin Res Cardiol 2014;103:457-66

(2) a decrease in LV end-diastolic volume of $\geq 10\sim 20\%$.

Yu C, et al. Circulation 2005;112:1580-6

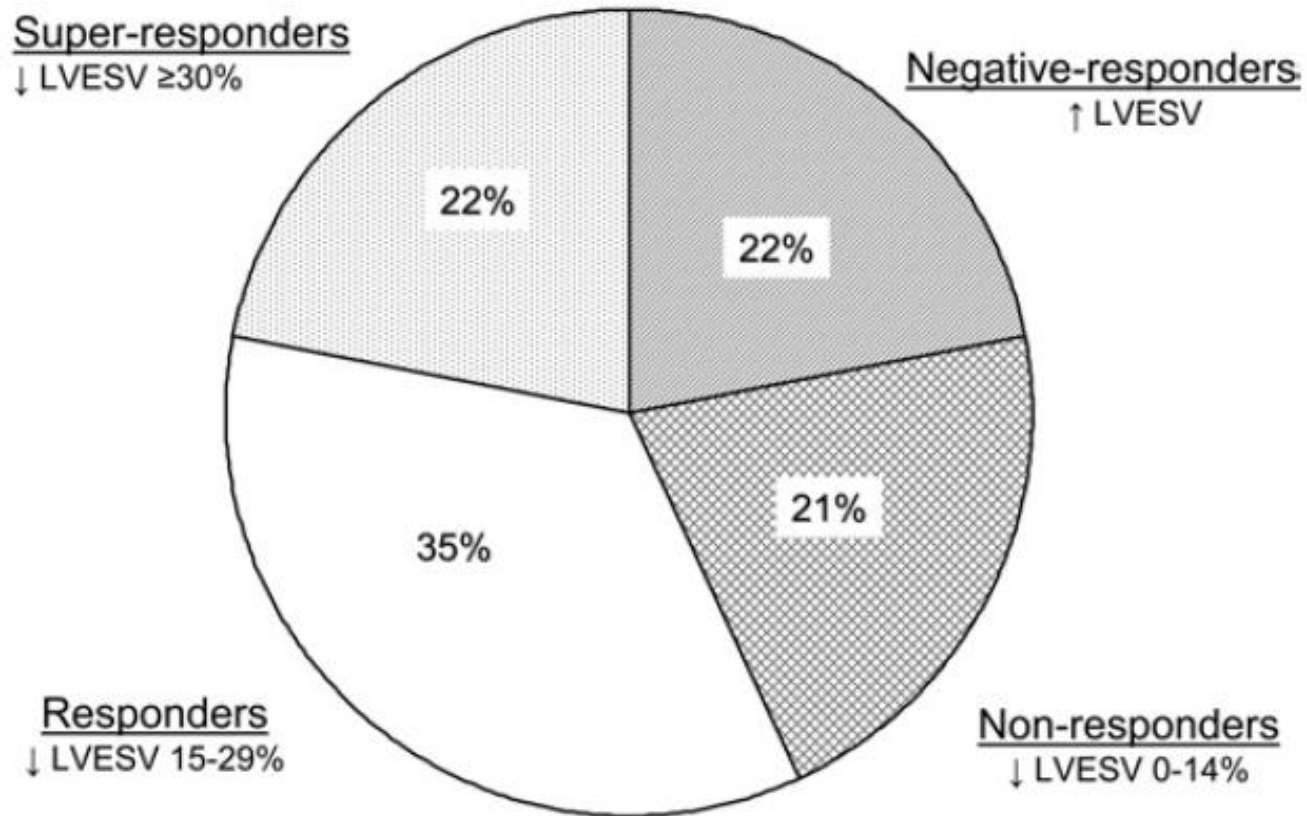
(3) an absolute increase in EF of $\geq 10\sim 15\%$.

Poller W, et al. Clin Res Cardiol 2014;103:457-66



CRT response

Extent of LV Reverse Remodeling After 6 Months of CRT

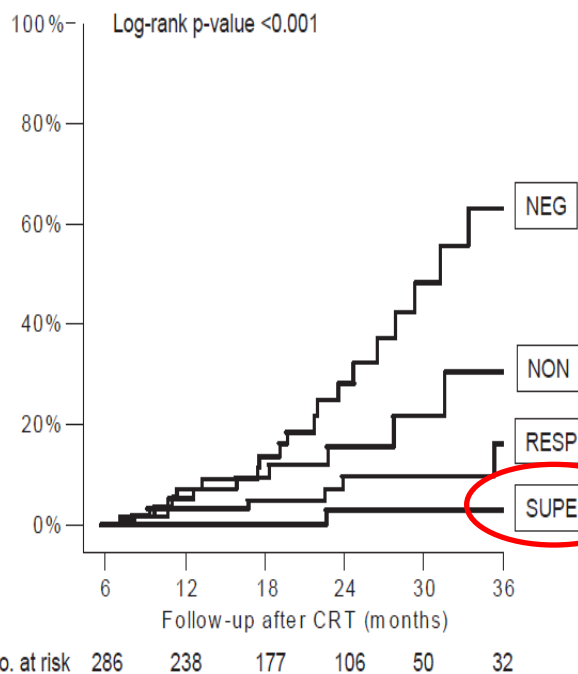


Ypenburg C, J Am Coll Cardiol 2009;53:483–90.

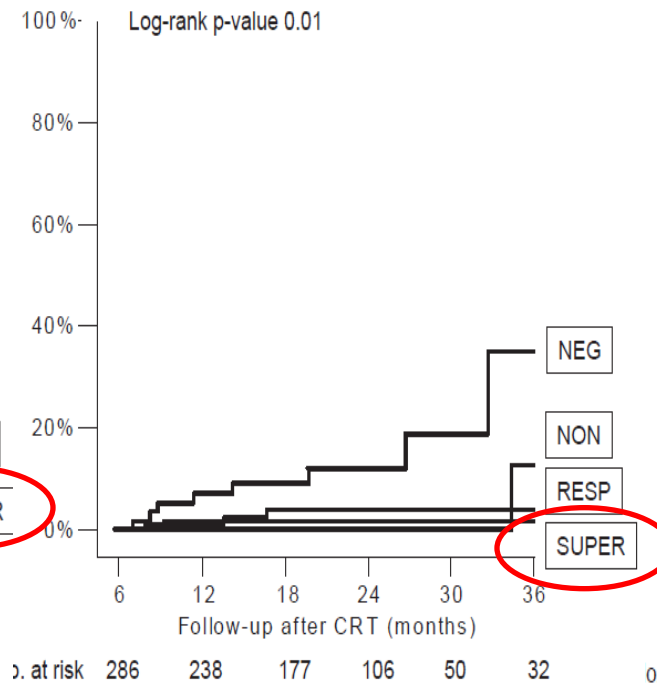


Long-Term Outcome After CRT According to the Extent in LV Reverse Remodeling

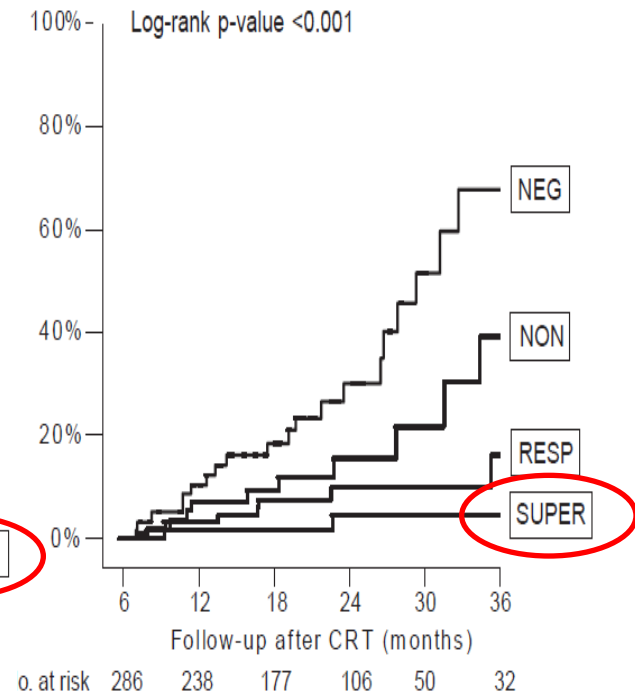
Death



Hospitalization for HF



Death, heart transplantation & hospitalization for HF



Ypenburg C, J Am Coll Cardiol 2009;53:483-90.



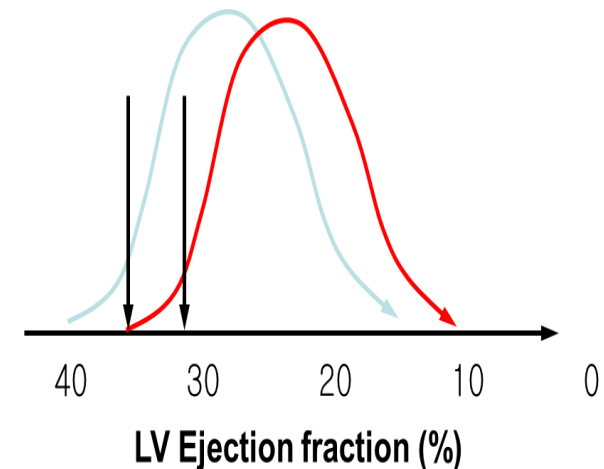
Predictors of Super-Response to Cardiac Resynchronization Therapy and Associated Improvement in Clinical Outcome

The MADIT-CRT (Multicenter Automatic Defibrillator Implantation Trial With Cardiac Resynchronization Therapy) Study

Table 3

Multivariate Analysis of Predictors of LVEF Super-Response

| Variable | Odds Ratio | 95% Confidence Interval | p Value |
|--|------------|-------------------------|-----------|
| Female | 1.96 | 1.32-2.90 | 0.001 |
| QRS duration ≥ 150 ms | 1.79 | 1.17-2.73 | 0.007 |
| LBBB | 2.05 | 1.24-3.40 | 0.006 |
| Body mass index < 30 kg/m ² | 1.51 | 1.03-2.20 | 0.035 |
| No prior myocardial infarction | 1.80 | 1.20-2.71 | 0.005 |
| Left atrial volume index, SD* | 1.47 | 1.21-1.79 | < 0.001 |



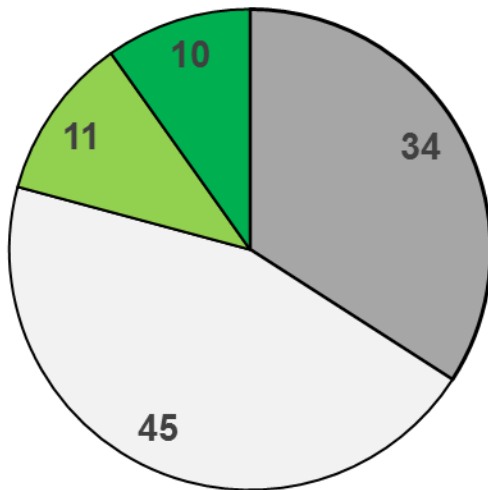
* Super-responder: LVEF $\geq 14.5\%$

Hsu J, J Am Coll Cardiol 2012;59:2366-73



Severance Hospital Experience

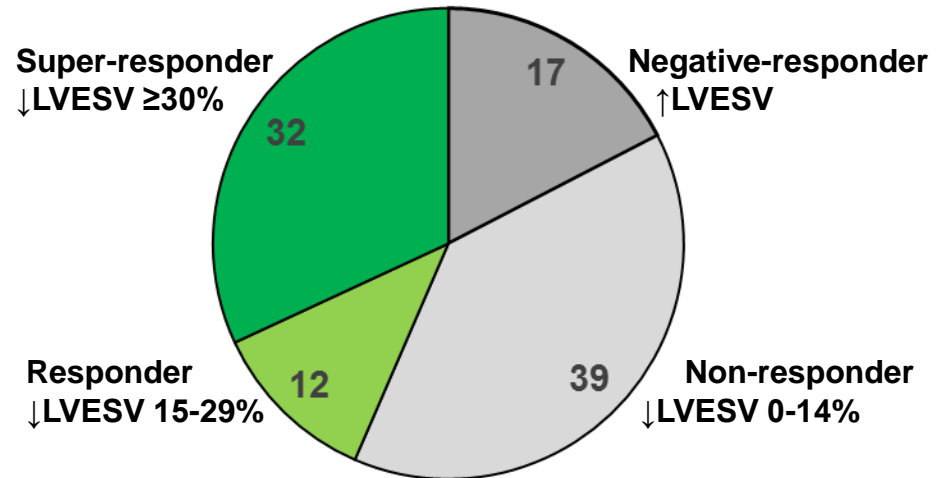
3 months (n=83)



Super-responder

- Smaller LVEDD (64 vs. 72mm)
- **Smaller LAVI (34 vs. 55ml/m²)**

> 6 months (n=71)



Responder

- Smaller LAVI (42 vs. 57ml/m²)
- LBBB (84.8% vs. 66.7%)
- **Lower RVSP (33 vs. 43mmHg)**

Postop Rhythm Management

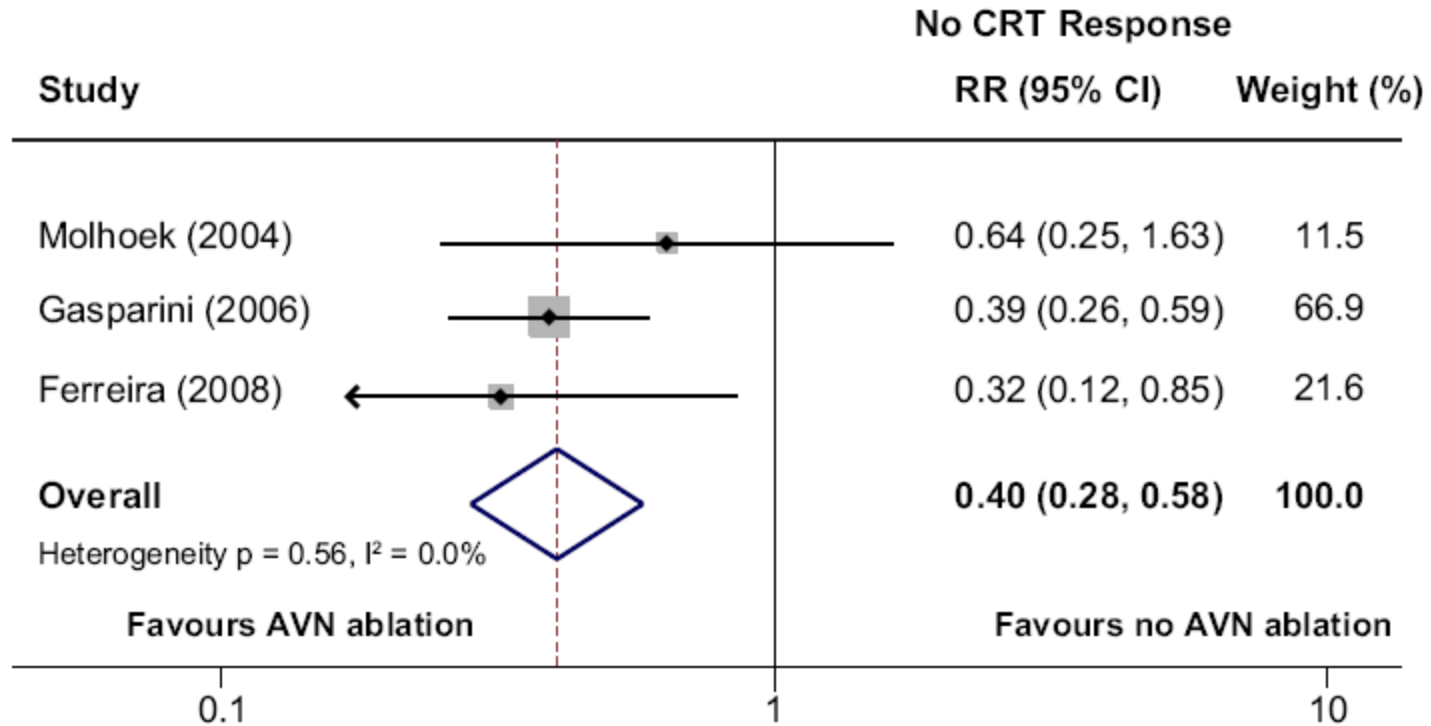
Favorable relationship; increased BVP

| | Pacing | Mortality | Patients |
|-------------------|-----------------|---|----------|
| Hayes et al (1) | 100% vs. < 95% | 27% reduction vs. 35% increase | >30,000 |
| Koplan et al (2) | ≥ 92% vs. < 92% | HR of HF or mortality; 0.44 | 1,812 |
| Santini et al (3) | AT/AF > 10 min | 2-fold increase in composite death/HF hospitalization | 1,193 |

1. Hayes DL. Heart Rhythm 2009;6:S134.
2. Koplan BA, J Am Coll Cardiol 2009;53:355–60.
3. Santini M, J Am Coll Cardiol 2011;57:167–72.



AF: AVN ablation

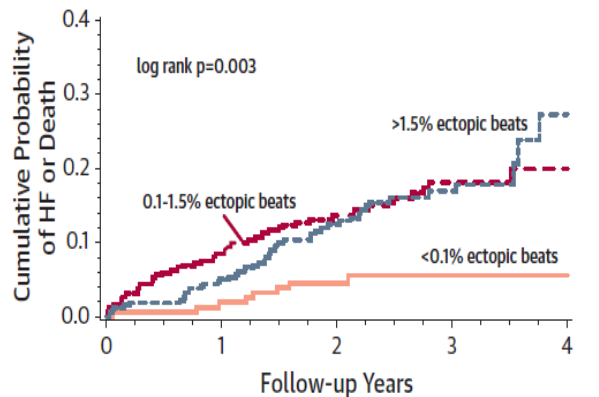


Wilton S, et al. Heart Rhythm 2011;8:1088–1094



Ectopic Burden at Pre-Implantation 24-h Holter : HF/death, VT/VT

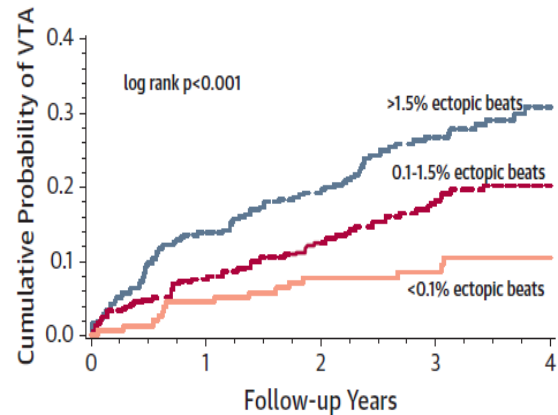
HF or Death



Patients at Risk

| | | | | |
|-----|------------|------------|-----------|-----------|
| 160 | 156 (0.02) | 106 (0.05) | 41 (0.05) | 12 (0.05) |
| 321 | 291 (0.08) | 202 (0.14) | 93 (0.18) | 24 (0.20) |
| 320 | 302 (0.05) | 192 (0.12) | 93 (0.17) | 16 (0.27) |

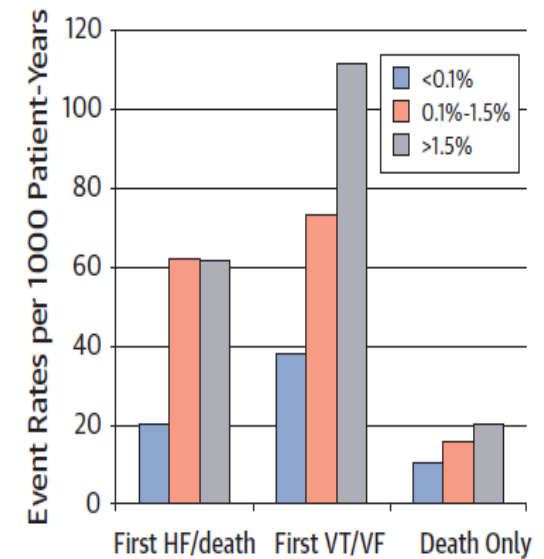
VTA



Patients at Risk

| | | | | |
|-----|------------|------------|------------|-----------|
| 160 | 151 (0.04) | 140 (0.08) | 96 (0.08) | 35 (0.10) |
| 321 | 288 (0.08) | 262 (0.12) | 178 (0.18) | 80 (0.20) |
| 320 | 273 (0.14) | 240 (0.19) | 147 (0.27) | 60 (0.31) |

C



* Ectopic burden at pre-implantation

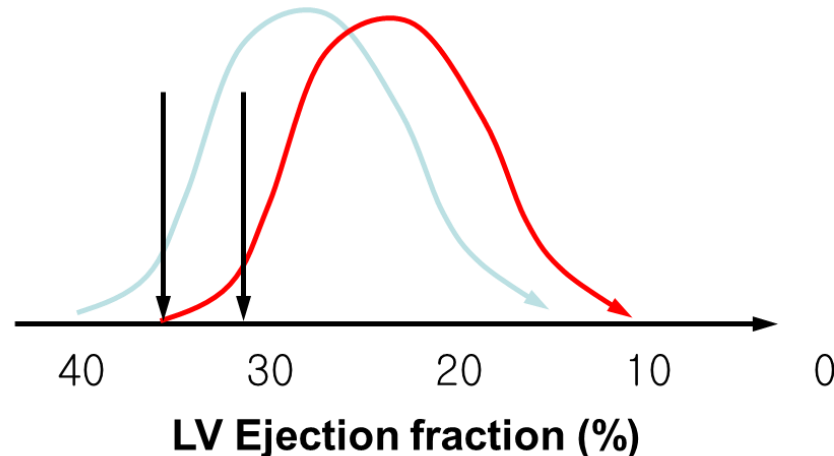
Ruwald M, J Am Coll Cardiol 2014;64:971–81



“Takehome message”

LVEF super-response to CRT-D therapy:

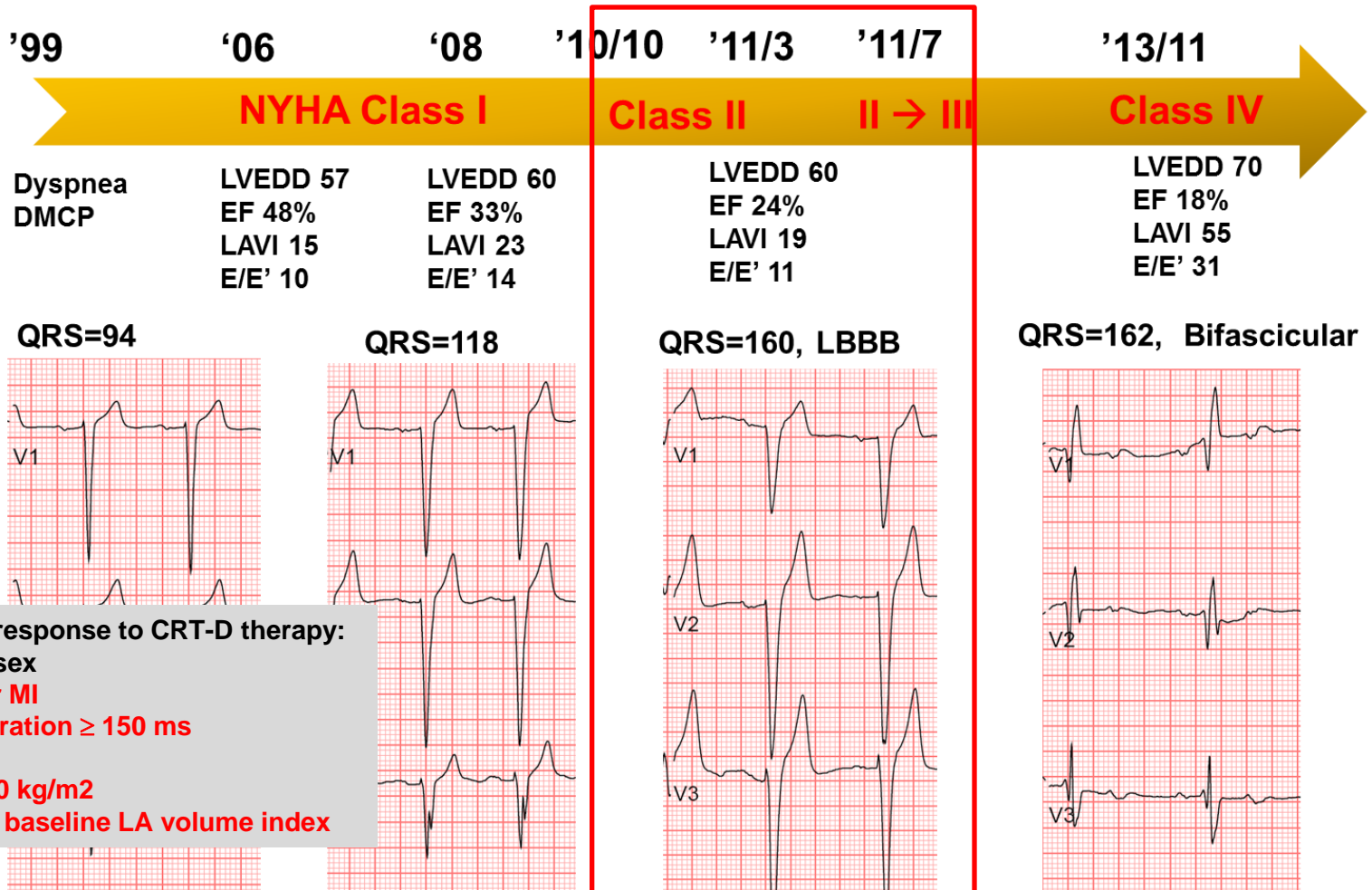
1. female sex (odds ratio [OR]: 1.96; $p=0.001$),
2. no prior MI (OR: 1.80; $p=0.005$),
3. QRS duration ≥ 150 ms (OR: 1.79; $p=0.007$),
4. LBBB (OR: 2.05; $p=0.006$),
5. BMI < 30 kg/m² (OR: 1.51; $p=0.035$),
6. smaller baseline LA volume index (OR: 1.47; $p=0.001$)



J Am Coll Cardiol 2012;59:2366-73

Best Time and Candidate for CRT?

The Change of EKG and Clinical Course



LVEF super-response to CRT-D therapy:

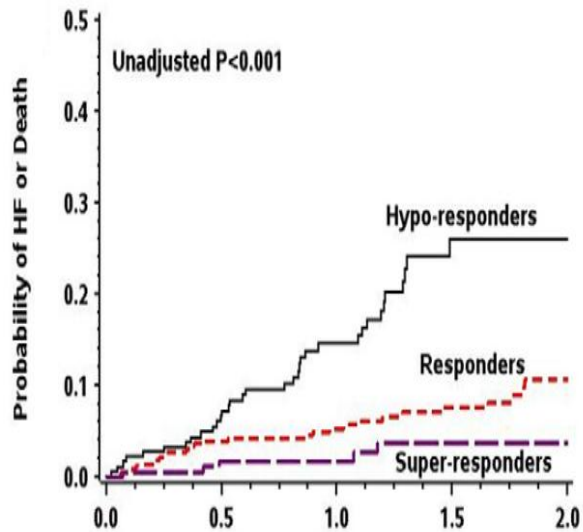
1. female sex
2. no prior MI
3. QRS duration ≥ 150 ms
4. LBBB
5. BMI < 30 kg/m²
6. Smaller baseline LA volume index

Thanks for your attention!



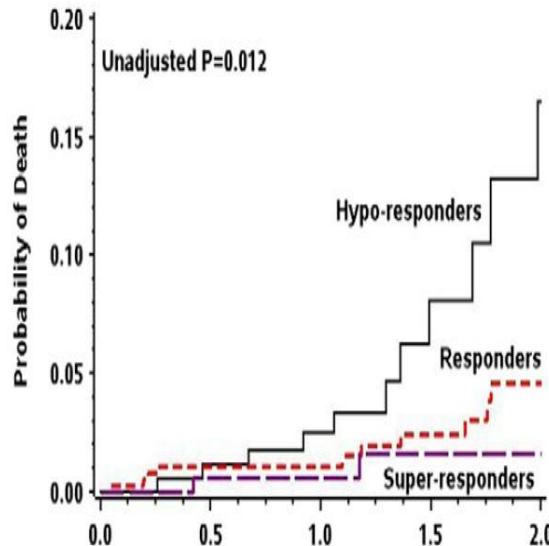
Kaplan-Meier Estimates of Cumulative Probability of Heart Failure or Death, Death Alone, and Death or ICD Therapy for VT or VF Stratified by Response Category

HF or Death



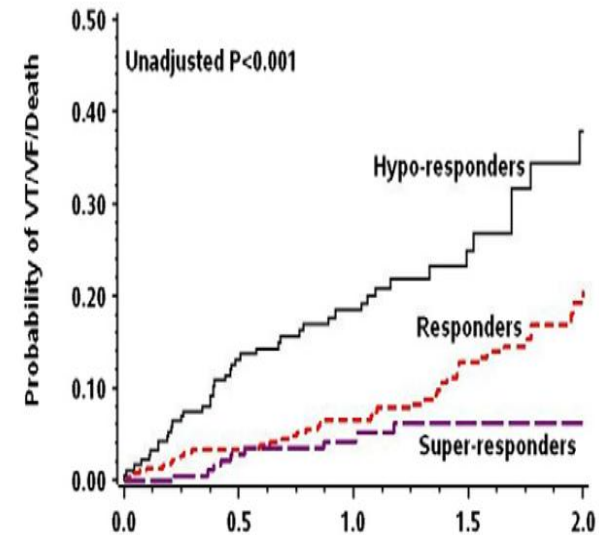
| Patients at Risk | Time(Years) after One Year Echo | | | |
|------------------|---------------------------------|------------|------------|-----------|
| | 0.0 | 0.5 | 1.0 | 1.5 |
| Hypo-resp 190 | 162 (0.07) | 105 (0.14) | 39 (0.26) | 23 (0.26) |
| Responders 371 | 320 (0.04) | 244 (0.05) | 173 (0.08) | 80 (0.11) |
| Super-resp 191 | 164 (0.02) | 111 (0.02) | 65 (0.04) | 26 (0.04) |

Death



| Patients at Risk | Time(Years) after One Year Echo | | | |
|------------------|---------------------------------|------------|------------|-----------|
| | 0.0 | 0.5 | 1.0 | 1.5 |
| Hypo-resp 190 | 171 (0.01) | 120 (0.02) | 49 (0.08) | 26 (0.16) |
| Responders 371 | 329 (0.01) | 254 (0.01) | 182 (0.02) | 84 (0.05) |
| Super-resp 191 | 166 (0.01) | 112 (0.01) | 67 (0.02) | 28 (0.02) |

VT/VF/Death



| Patients at Risk | Time(Years) after One Year Echo | | | |
|------------------|---------------------------------|------------|------------|-----------|
| | 0.0 | 0.5 | 1.0 | 1.5 |
| Hypo-resp 190 | 150 (0.13) | 102 (0.18) | 42 (0.25) | 18 (0.38) |
| Responders 371 | 321 (0.04) | 241 (0.07) | 163 (0.13) | 66 (0.20) |
| Super-resp 191 | 163 (0.03) | 108 (0.04) | 64 (0.06) | 25 (0.06) |

Super-response: top quartile of LVEF change

Hsu J, J Am Coll Cardiol 2012;59:2366-73

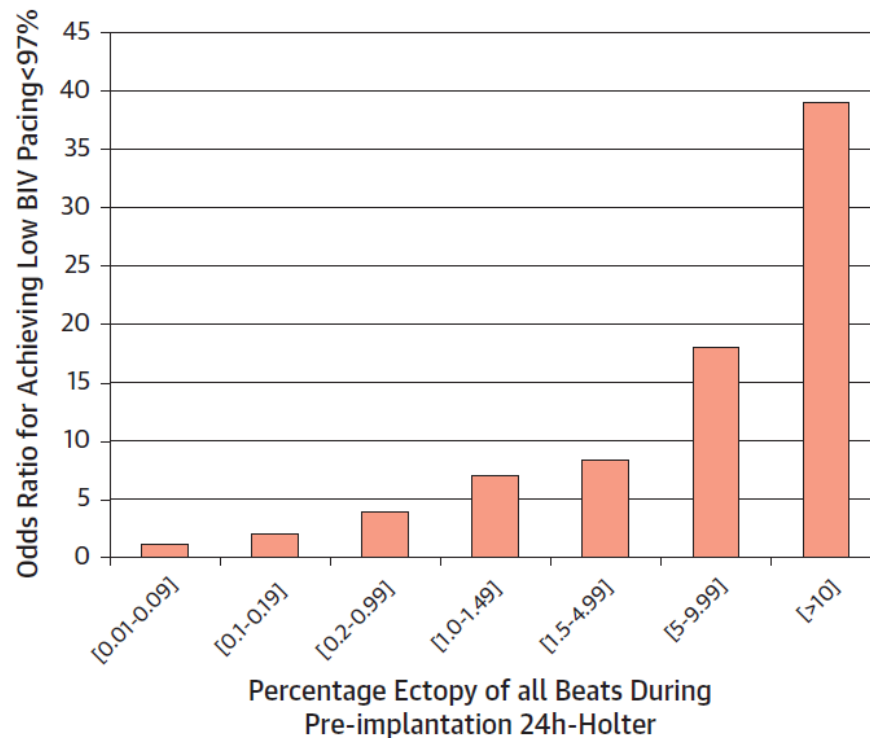


“Takehome message”

- 1) CRT has been shown to have significant benefit in terms of symptomatic relief and LV reverse remodeling and mortality in **HF patients with wide QRS complex.**
- 2) Echocardiography, CT and MRI might help to identify **non-responder to CRT.**



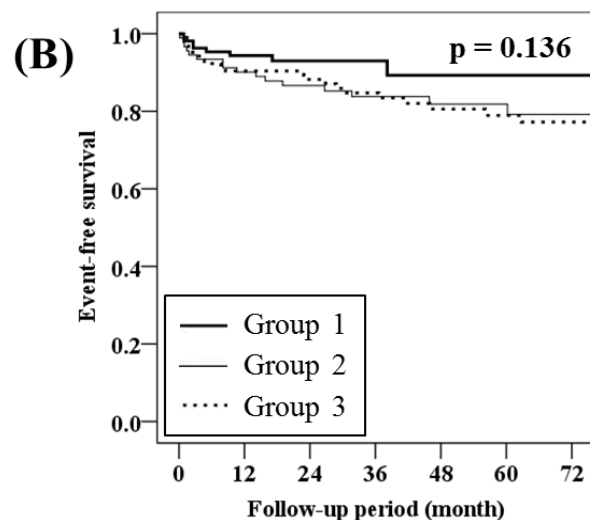
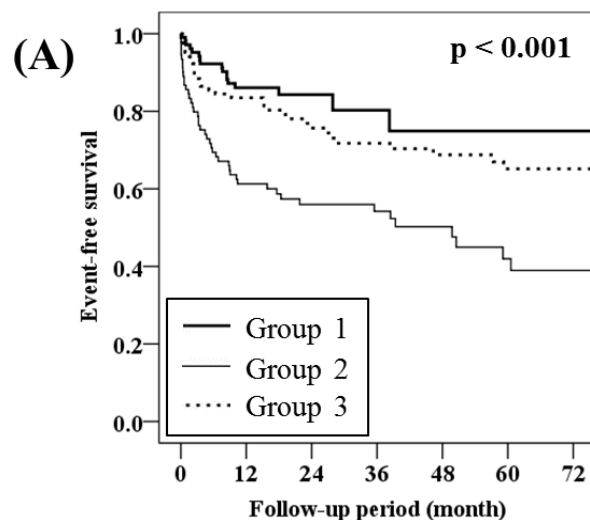
Association Between Frequency of Atrial and Ventricular Ectopic Beats and Biventricular Pacing Percentage and Outcomes in Patients With Cardiac Resynchronization Therapy



Ruwald M, J Am Coll Cardiol 2014;64:971–81



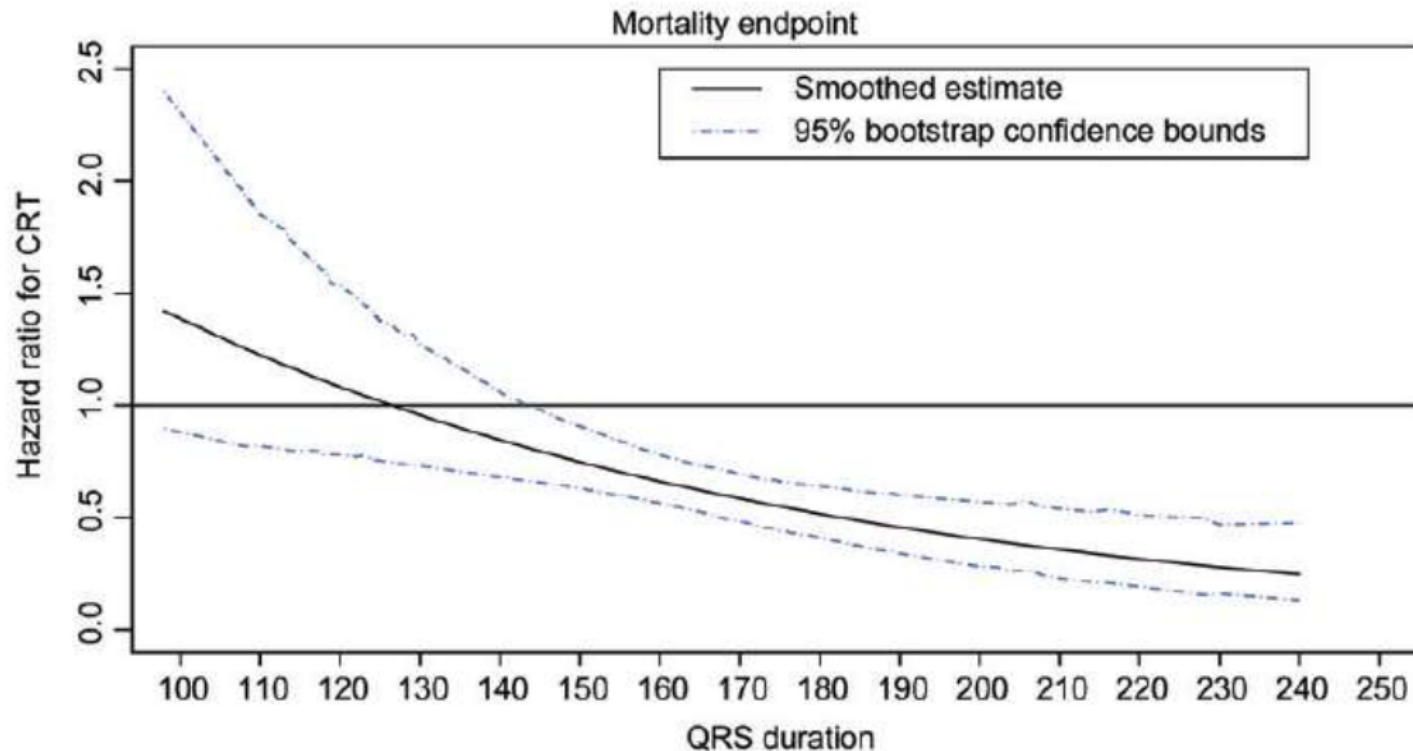
ICD therapy in 1HF, 2HF, IPAS



| | Group 1 (n = 118) | Group 2 (n = 93) | Group 3 (n = 106) | p-Value |
|---------------------------|----------------------|---------------------|----------------------|----------|
| Follow-up period (month) | 31.7 ± 33.5 | 61.8 ± 42.7 | 73.6 ± 53.4 | < 0.001* |
| ICD therapy | | | | |
| Appropriate, annual (%) | 6.1 | 10.4 | 5.7 | < 0.001† |
| Inappropriate, annual (%) | 3.2 | 4.2 | 3.5 | 0.054 |
| Annual mortality (%) | 3.2 | 5.2 | 0.5 | 0.963 |

Uhm JS, Korea Circ 2015

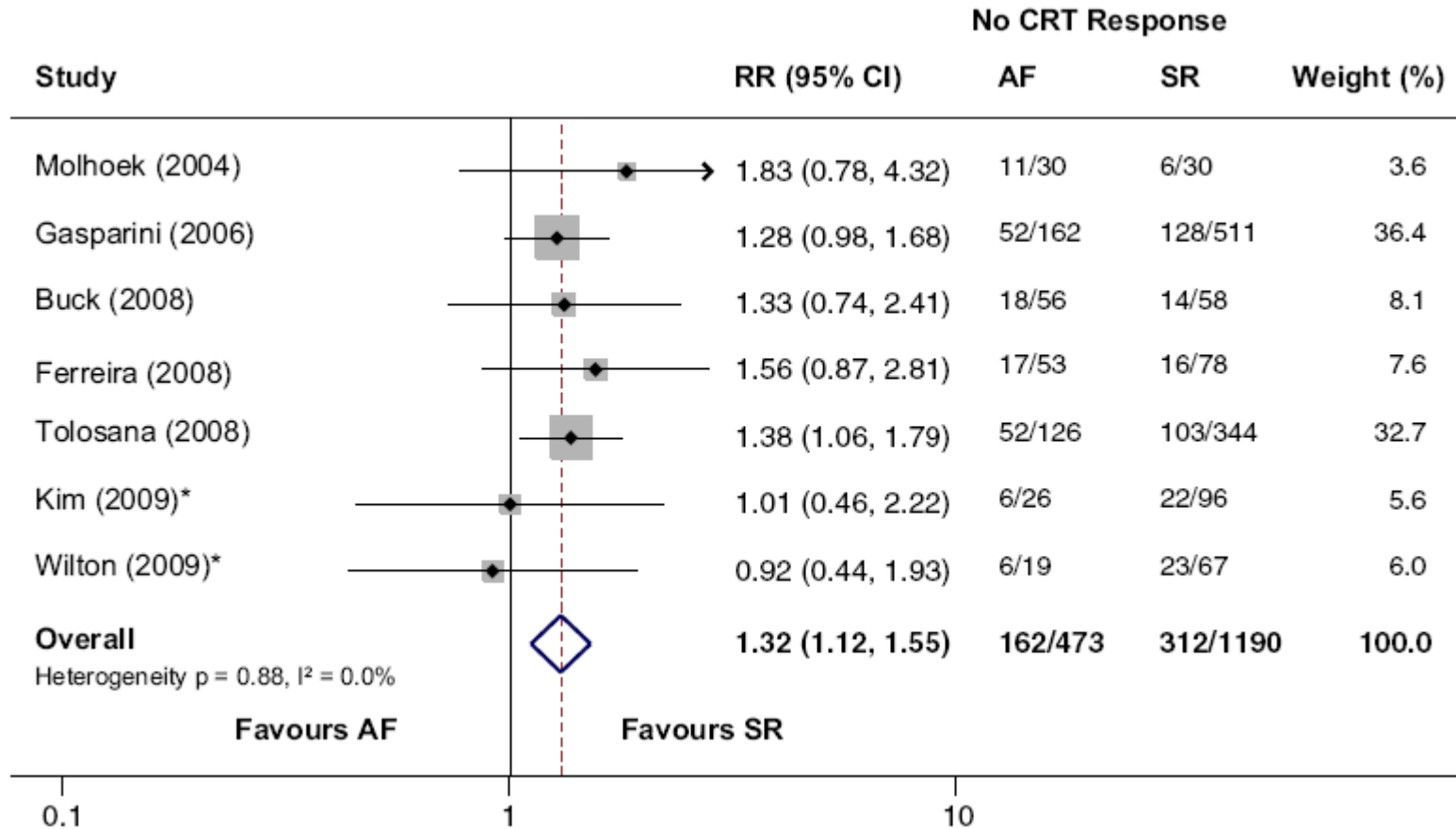
CRT across QRS duration: Effect on all-cause mortality



Cleland JG, et al. Eur Heart J 2013;34:3547–55.



AF: No CRT Response



Wilton S, et al. Heart Rhythm 2011;8:1088–1094

