Séminaire
Winter Arrhythmia
School
Annual Cardiac Arrhythmia Meeting
Division of Cardiology, University of Toronto

Optimization of CRT in non-responders

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St. Michael's Hospital

14th Annual
Collingwood, Ontario,
February 10 -12, 2017

Disclosure

- I don’t like heart failure
- There was no CRT when I went into EP

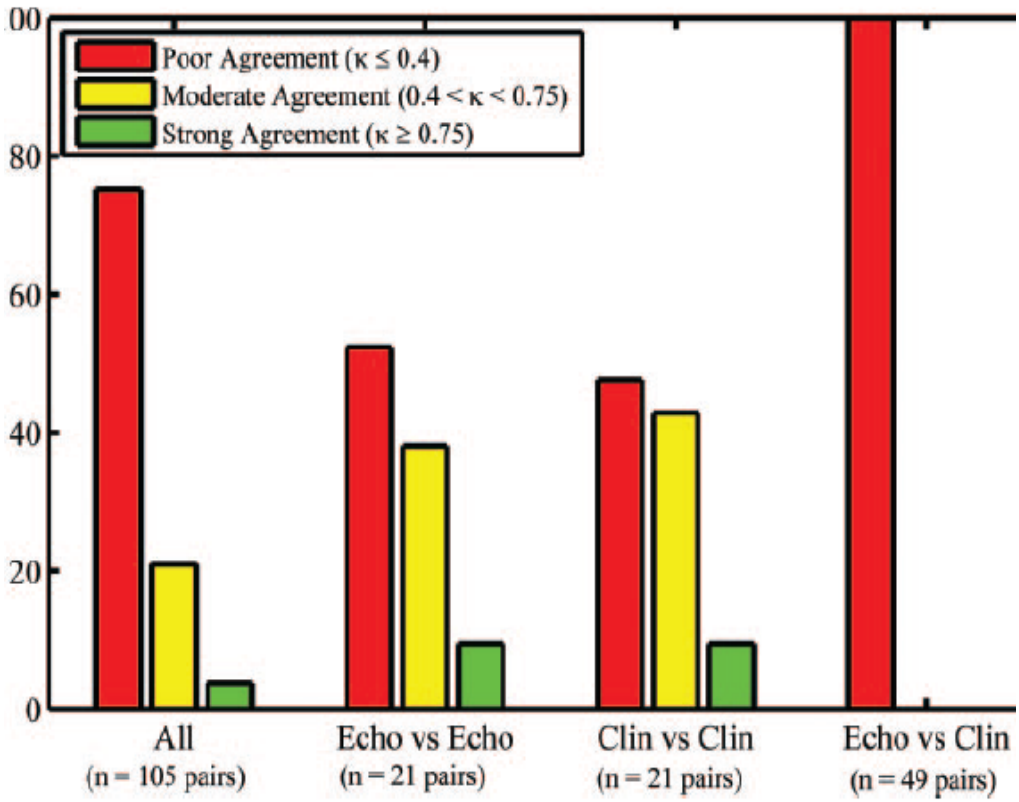
Definition of (non)-responder

Study	Definition of CRT response	Follow-up (months)	Predictors of CRT response
Lecoq et al.[68]	Alive, no HF readmission, > 1 NYHA class improvement (or > 10% increase in peak VO_2 and 6MW)	6	QRS shortening during CRT
Achilli et al.[69]	Improved clinical composite score and LVEF increase ≥ 5%	6	Smaller LVESD, longer interventricular mechanical delay
MIRACLE/ MIRACLE ICD[6,7]	Alive and > 1 NYHA class improvement	1, 3, and 6	None
Yeim et al.[70]	> 1 NYHA class improvement and no HF admission	6	Nonischemic etiology, wider baseline QRS width, QRS shortening during CRT
Mollema et al.[71]	≥ 1 NYHA class improvement or 10% decrease in LVESV	6	None
PROSPECT[72]	Improved clinical composite score and LVESV decrease ≥ 15%	6	None
Buck et al.[73]	LVESV decrease > 10%	6	Interlead distance > 127 mm, septal-lateral delay > 60 ms, nonischemic etiology, LV end-diastolic diameter < 67 mm, use of ACE inhibitor, absence of tricuspid regurgitation
Rickard et al.[74]	LVESV decrease ≥ 10%	> 2	Wider QRS
MADIT-CRT[75]	% decrease in LVEDV and response score	12	Female, nonischemic etiology, LBBB, QRS > 150 ms, previous HF hospitalization, LVEDV > 125 mL/m^2, left atrial volume < 40 mL/m^2
PROSPECT-ECG[57,76]	Improved clinical composite score, LVESV decrease ≥ 15%	6	LBBB morphology, LV paced QRS width and QRS shortening

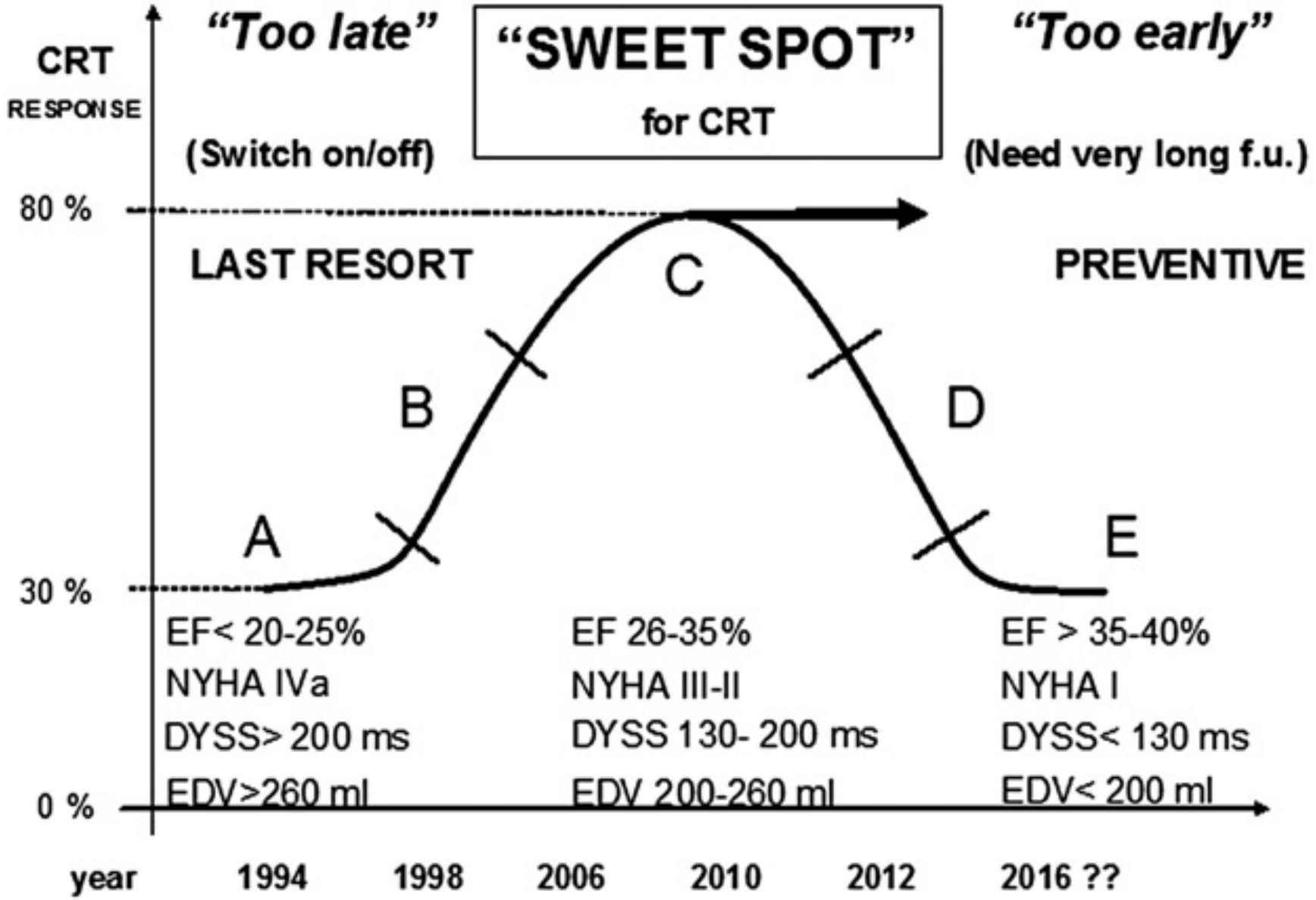
Parkash R et al. Can J Cardiol 29:1346-60

Responder? Non-responder? Responder?...

Response Criteria	Response Rate, %	No. Evaluable (% of Total)
Echocardiographic		
↑ LVEF >5 units	51	286 (67)
↑ LVEF >15% (relative)	54	286 (67)
↓ LVESV ≥10%, no HF death	62	291 (68)
↓ LVESV >15%	56	286 (67)
LVESV <115% of baseline	91	286 (67)
↓ LVEDV >15%	49	286 (67)
↑ Stroke volume ≥15%	34	286 (67)
Clinical		
↓ NYHA ≥1	71	385 (90)
↓ NYHA ≥1, no HF death	70	390 (92)
↓ NYHA ≥1 and ↑ 6MWD ≥25%	33	348 (82)
↓ NYHA ≥1 and ↑ 6MWD ≥25%, no HF death	32	353 (83)
↑ 6MWD ≥10%, no HF death, no transplant	61	353 (83)
Two of the following 3: ↓ NYHA ≥1, ↑ 6MWD ≥50 m, ↓ QOL ≥15	63	339 (80)
Clinical composite score improved	69	426 (100)
Combined		
↑ LVEF >5 units or ↑ 6MWD ≥50 m and ↓ NYHA ≥1 or ↓ QOL ≥10	71	250 (59)

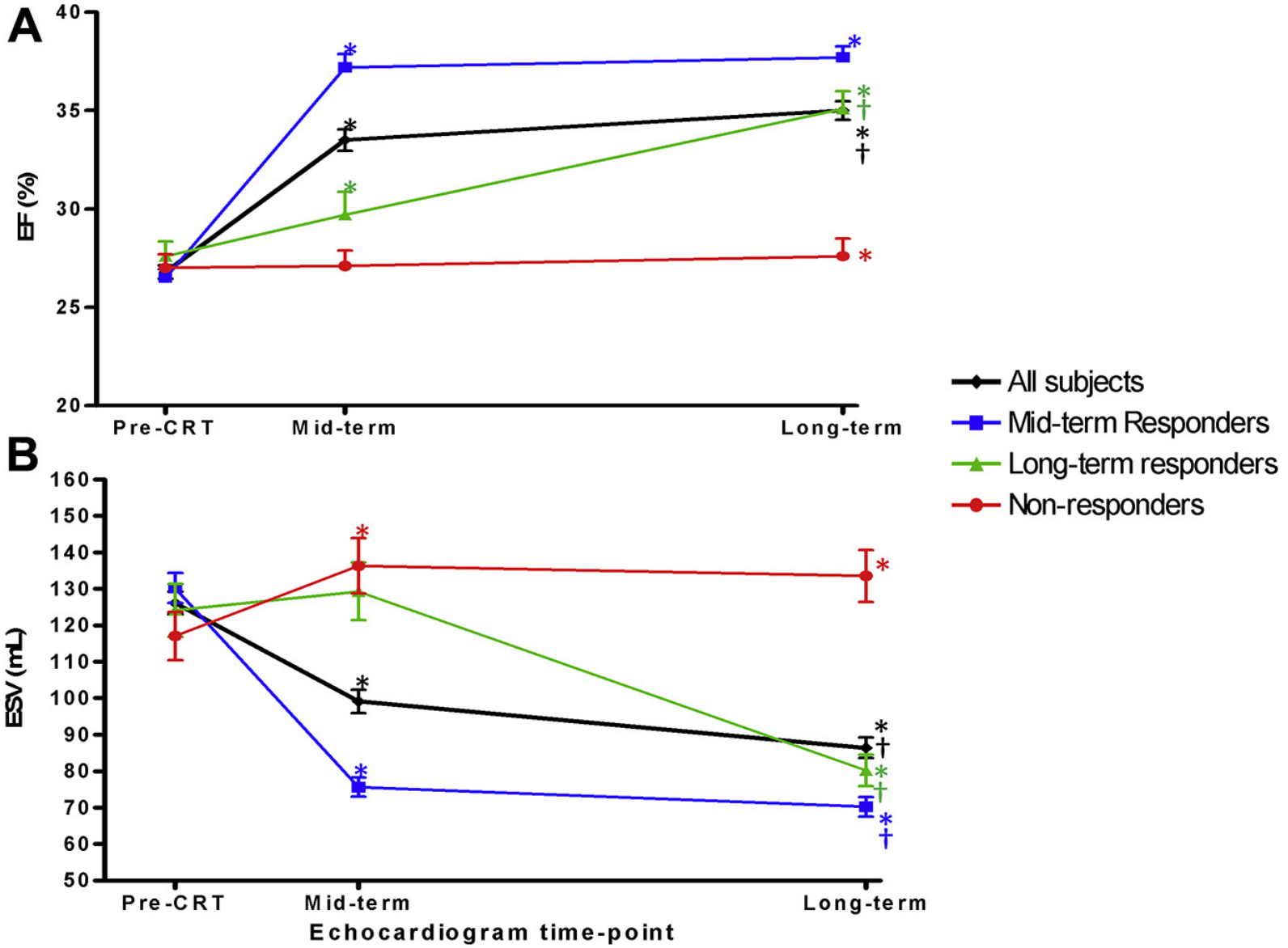


Fornwalt et al. Circulation 2010;121:1985-91



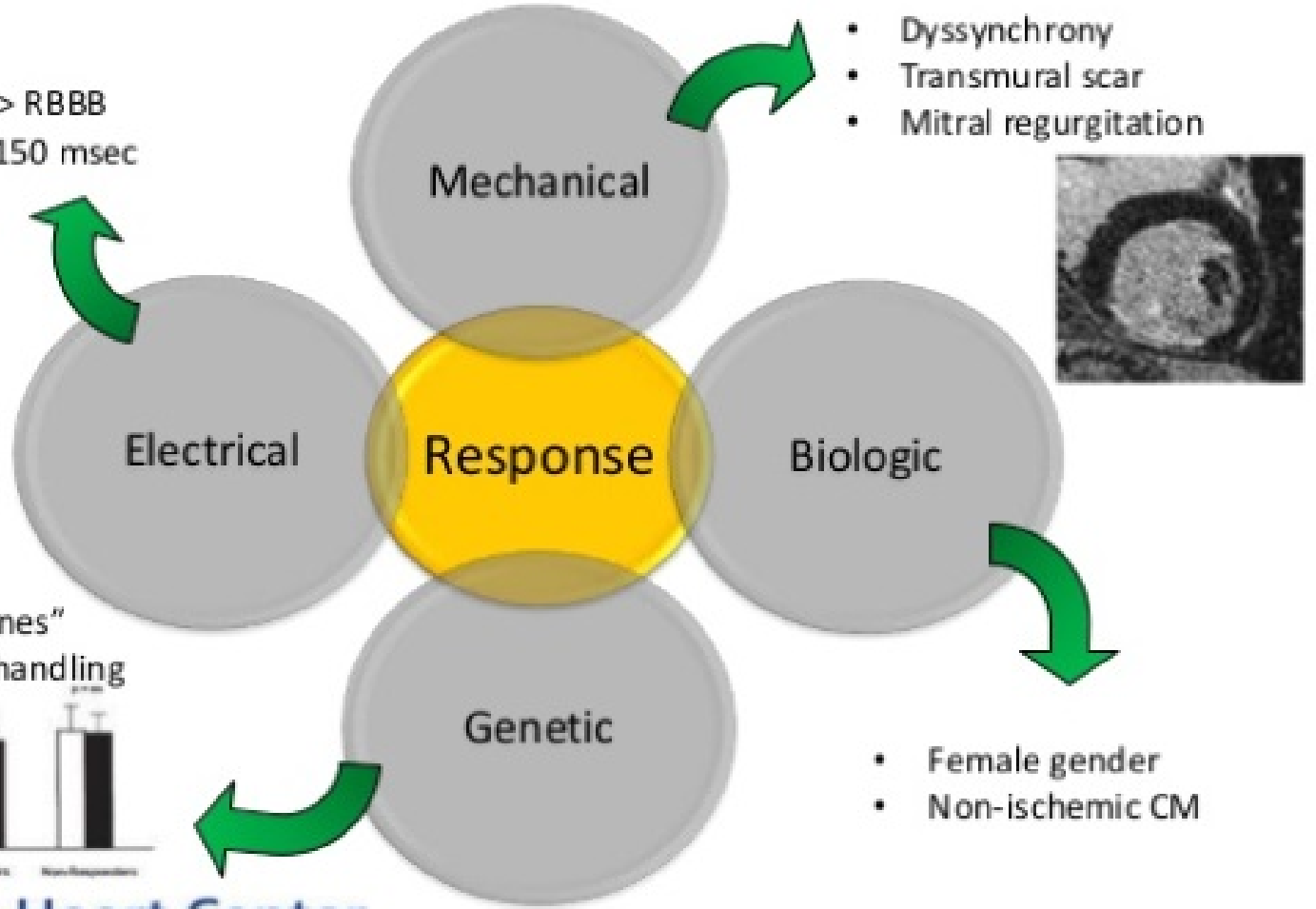
Gasparini M: JACC 2013;61:945-947

When to measure response?



Burns KV et al. JACC HF 2015;3:990-7

Response to CRT is Dependent Upon Multiple Factors



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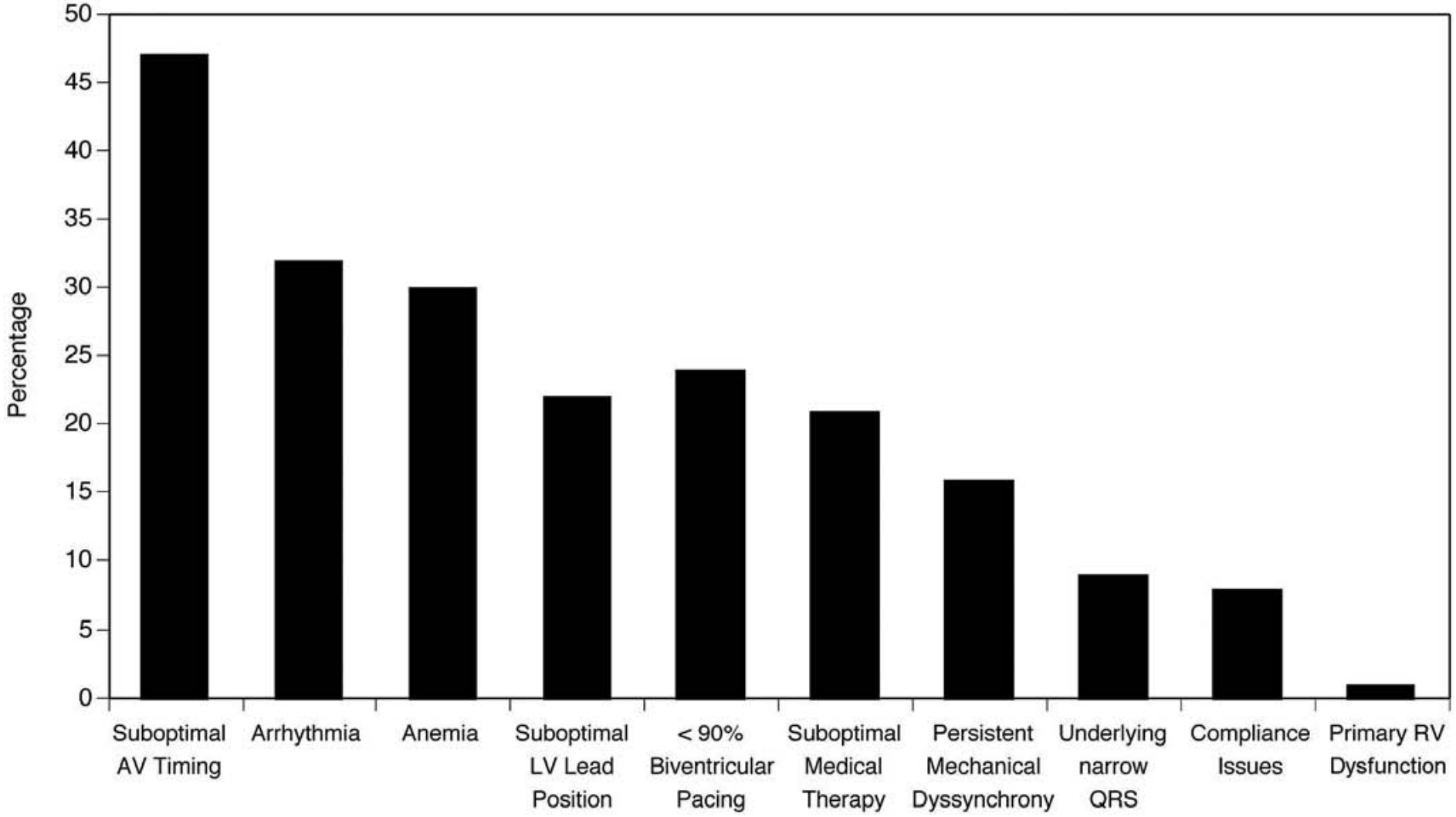
Vanderheyden M, et al. J Am Coll Cardiol 2008;51:129–36; Moss AJ et. al. N Engl J Med. 2009;361:1329–1338.

Potential reasons for non-response



Mullens W et al. JACC 2009;53:765-773

What to optimize?

- **Patient**
  - Medication optimization
    - Uptitration of neurohormonal blockers + dietary protocol[1]
  - Exercise training
    - 30 min supervised exercise x3/week[2]
  - **Atrial fibrillation**
  - **PVC**
- **Device**
- **Timing**

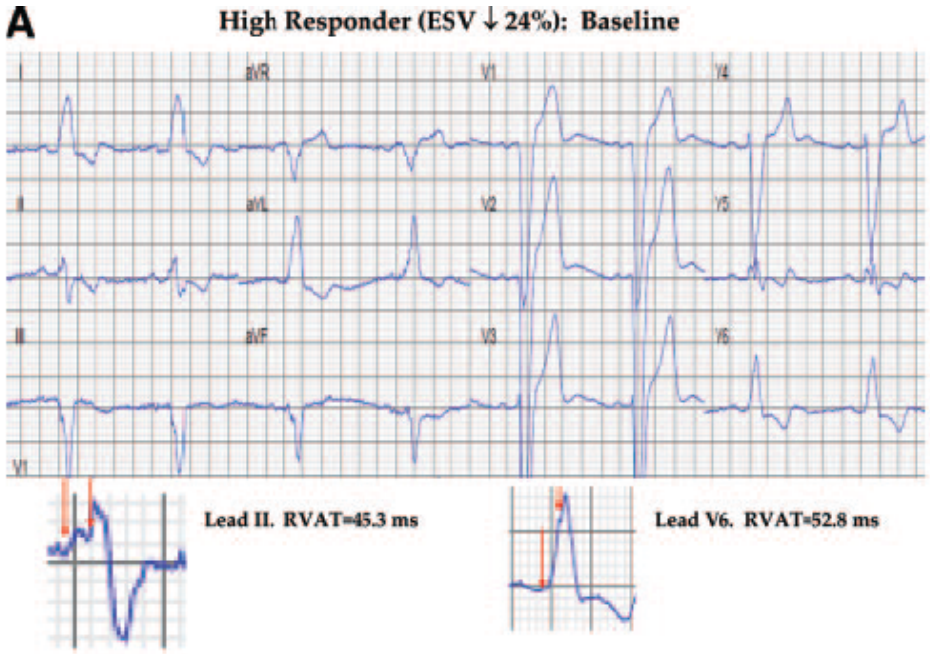
1. Mullens W et al. Am J Cardiol 2011;108:409
2. Patwala AY et al. JACC 2009;53:2332

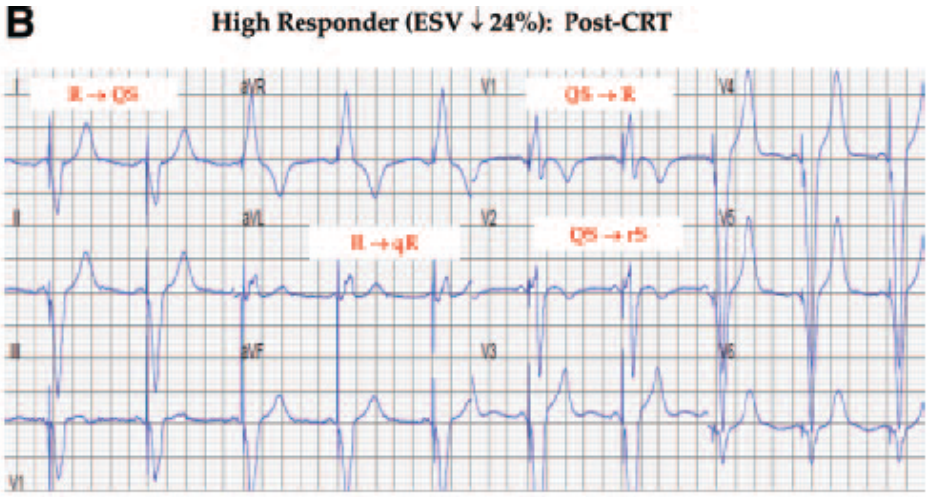
What to check on the ECG?

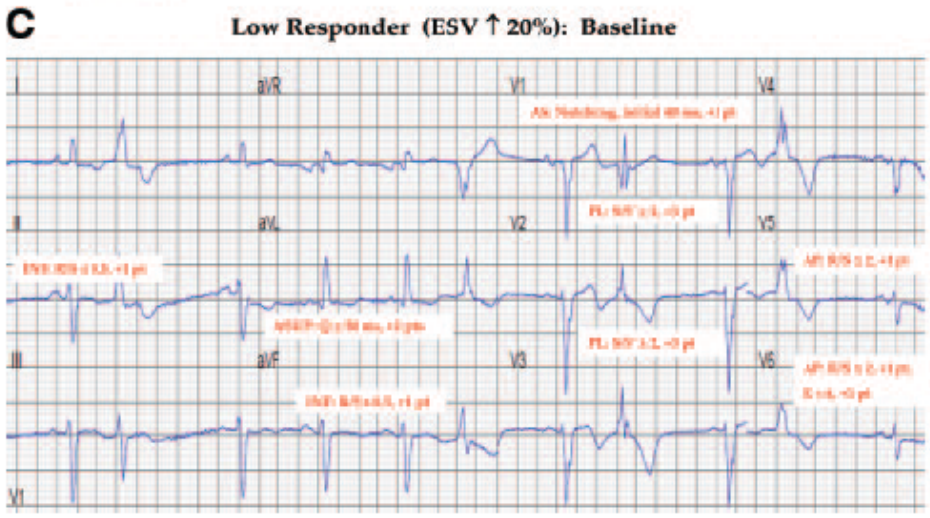
Atrial rhythm—NSR or atrial paced vs. atrial fibrillation
Evidence of appropriate atrial sensing or capture
Presence of ventricular pacing
Presence, frequency, and morphology of PVCs
Evidence of appropriate ventricular sensing or capture
Morphology of paced QRS—evidence of LV capture
Paced QRS width
Evidence of pacing fusion or pseudo-fusion in QRS

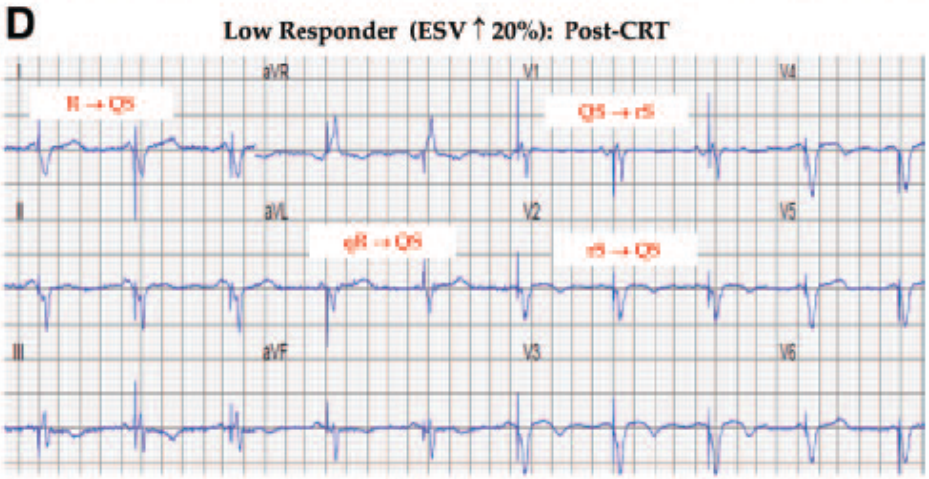
2012 EHRA/HRS Consensus

What is a promising QRS morphology?



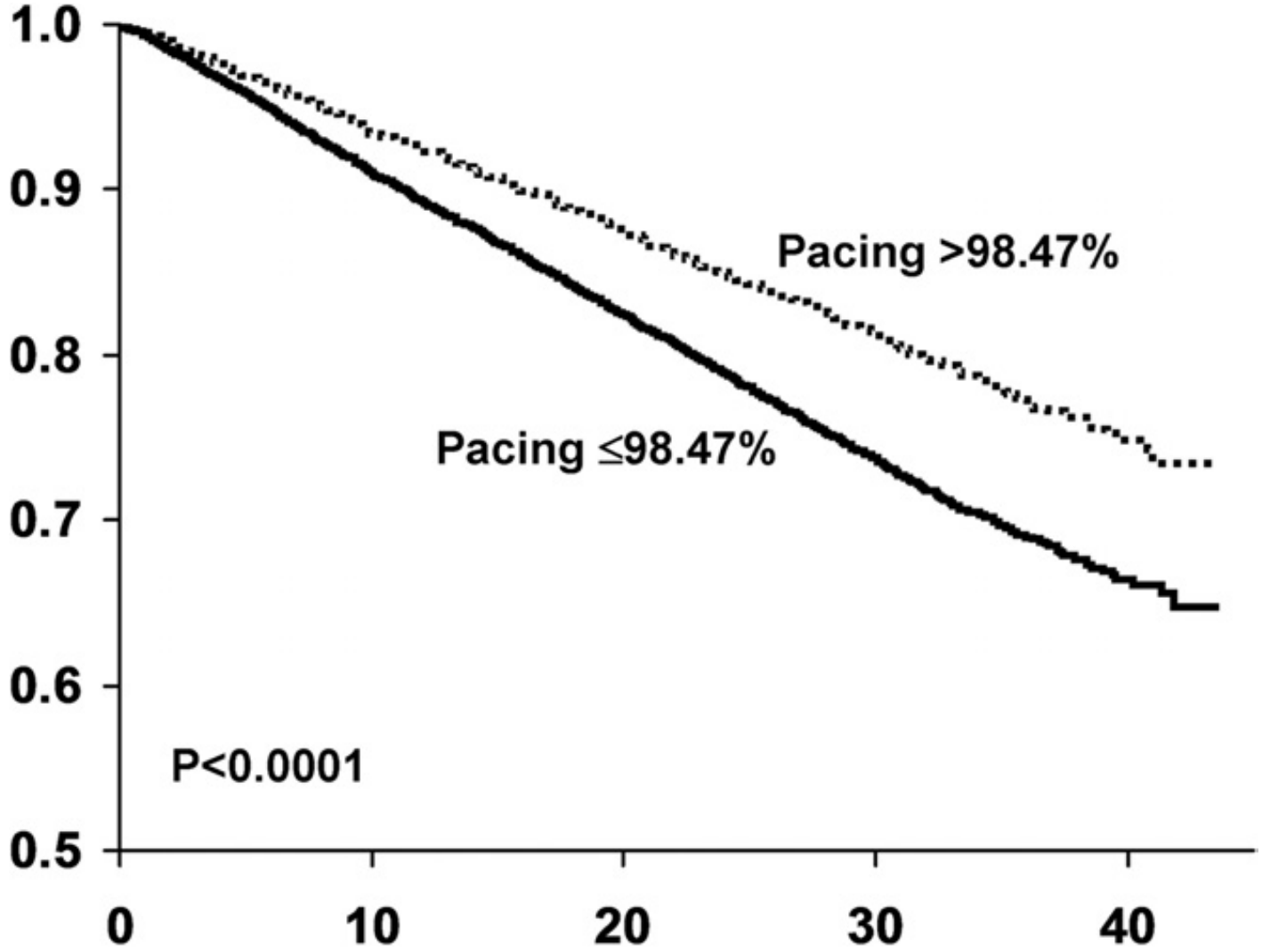






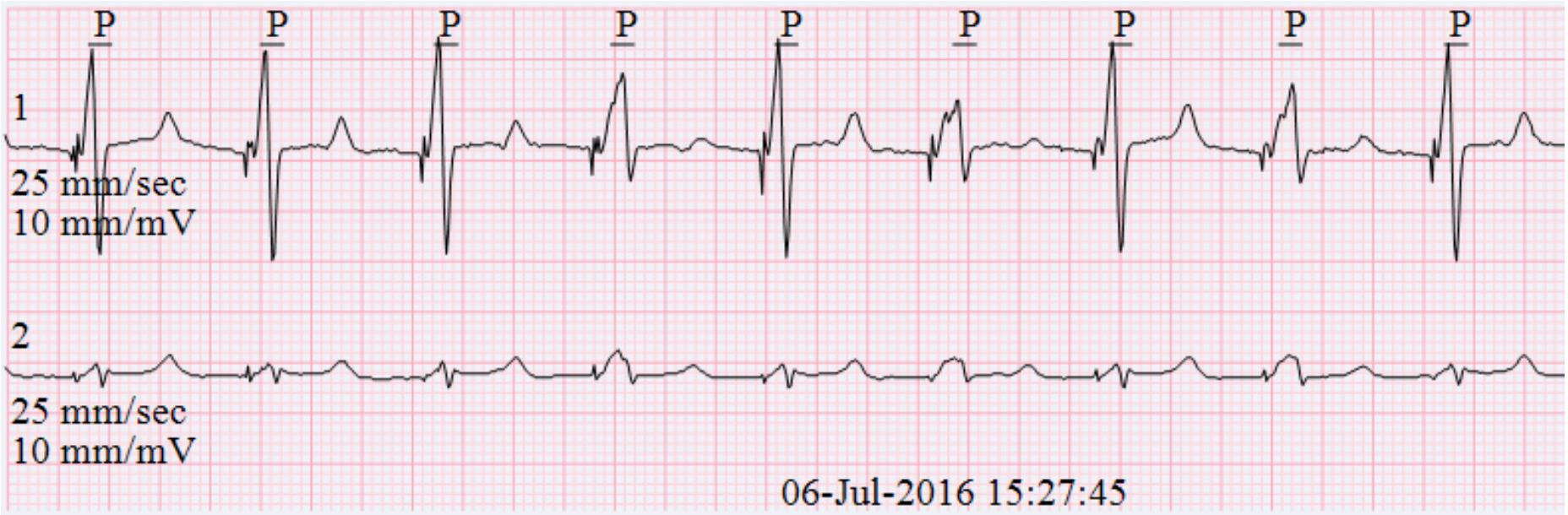
Sweeney MO, Circulation 2010; 121:626

BiV pacing % and survival

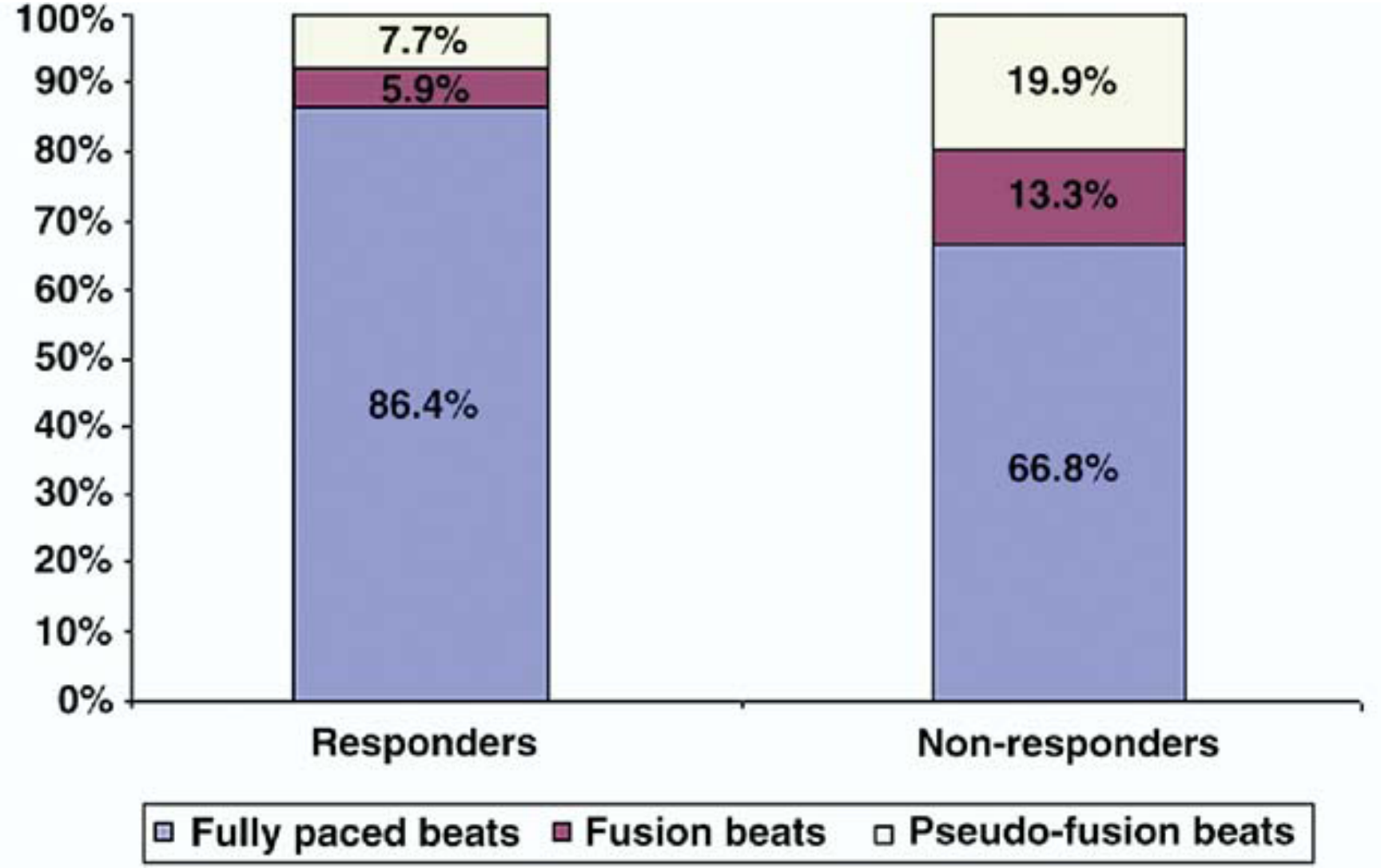


Hayes DL et al. Heart Rhythm 2011;8:1469-75

What does this Holter show?

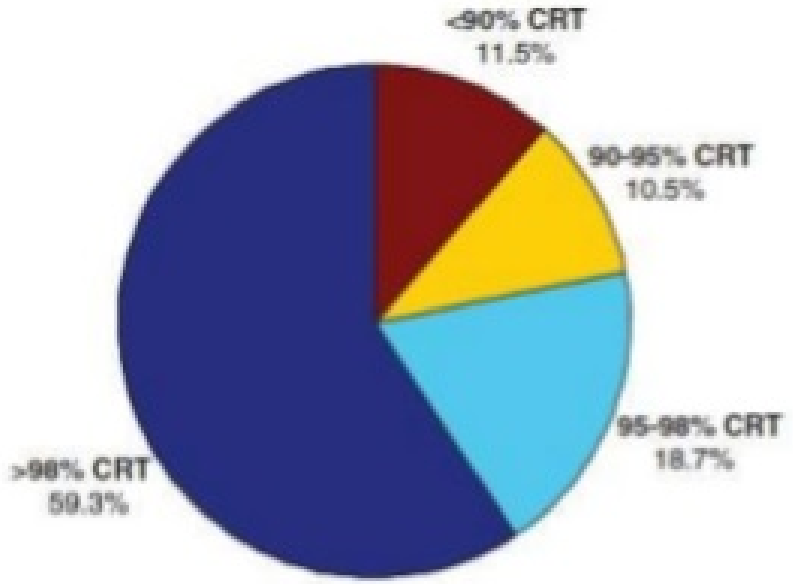


Devices overestimate effective biV pacing



Kamath GS et al. JACC 2009;53:1050-5

A Significant Percentage of Patients Do Not Achieve Optimal BiV Pacing %



Reasons for < 100% pacing

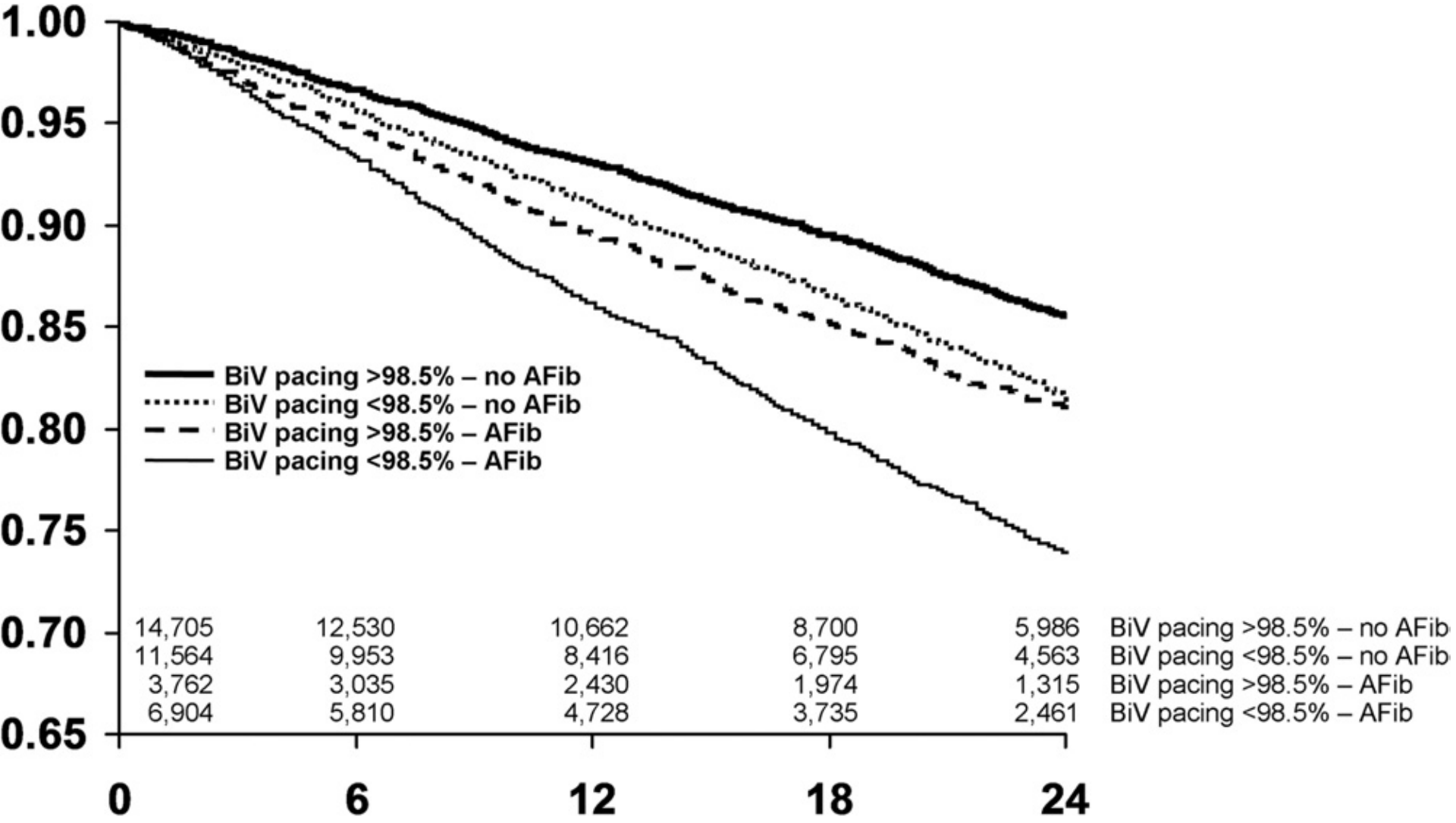
- Atrial fibrillation
- PVC's
- Competitive AV nodal conduction

In a cohort of > 80,000 patients, 40.7% exhibited less than 98% BiV pacing

Duke Heart Center

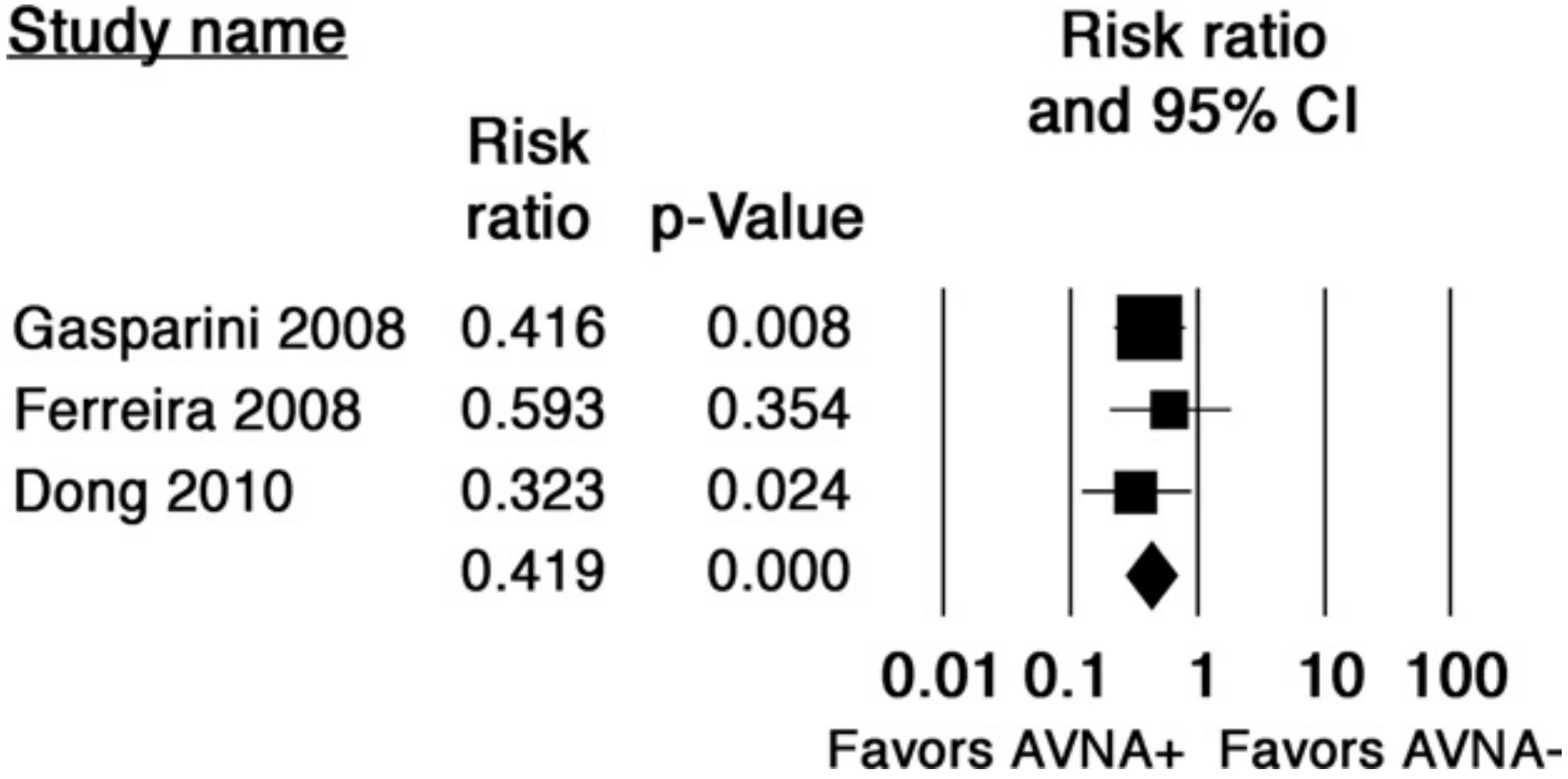
Cheng A, et al. Circ Arrhythm Electrophysiol. 2012;5:884-888k

If we can overcome RVR…



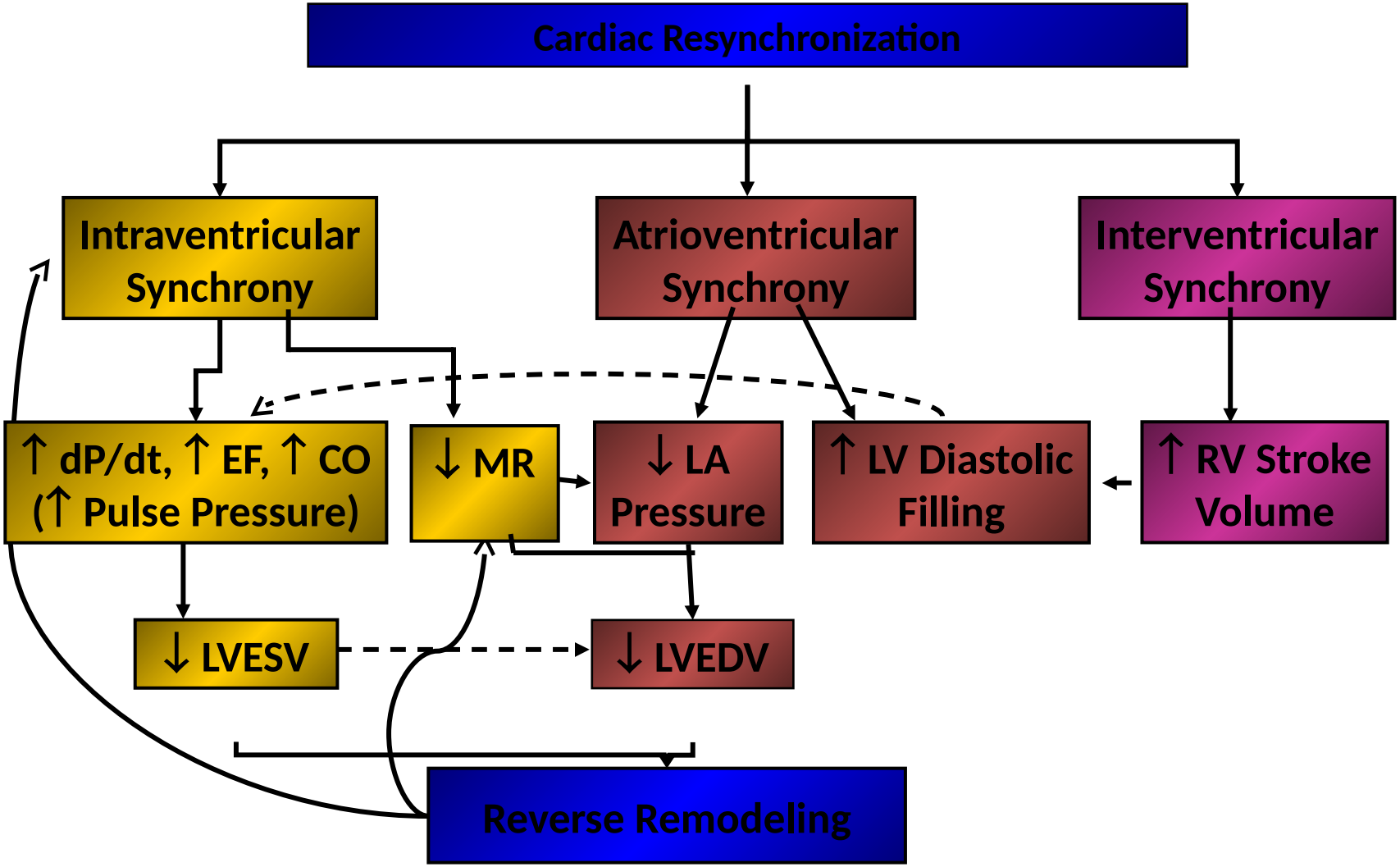
Hayes DL et al. Heart Rhythm 2011;8:1469-75

AVJ ablation vs medical rate control: Mortality in CRT patients with AF



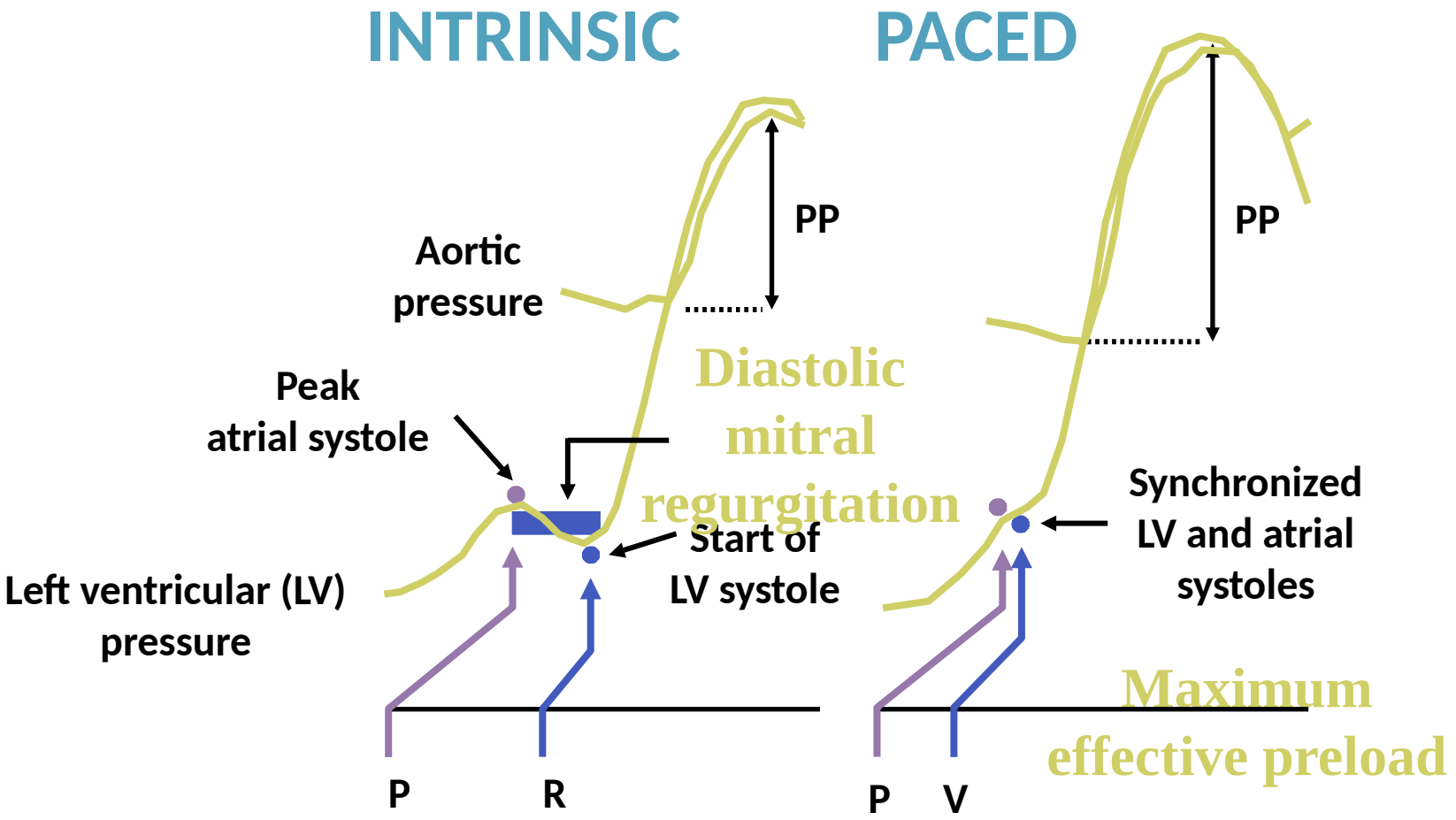
Ganesan AN et al. JACC 2012;59:719-26

What to re-synchronize?



Yu C-M, Chau E, Sanderson J, et al. *Circulation* 2002;105:438-445

Optimal AV Delay Improves hemodynamics

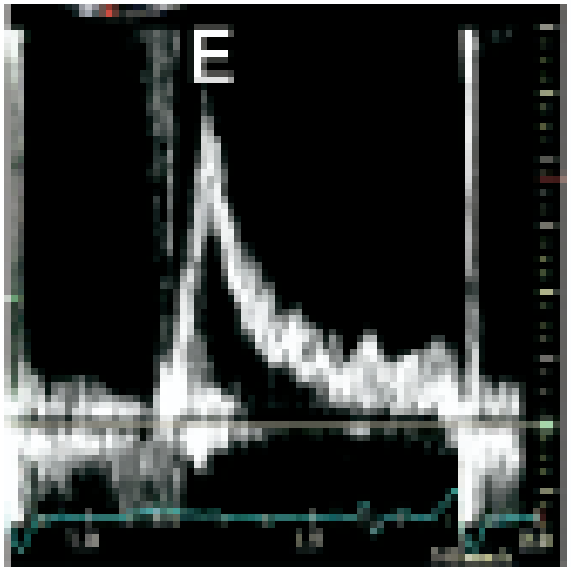


Auricchio A, et al. Association between preload and optimal pacing mode

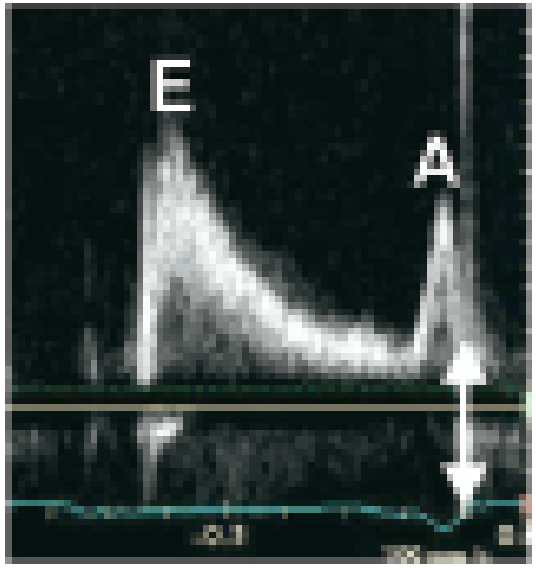
Heart Failure Society of America 1998.

The effect of AV delay on mitral inflow

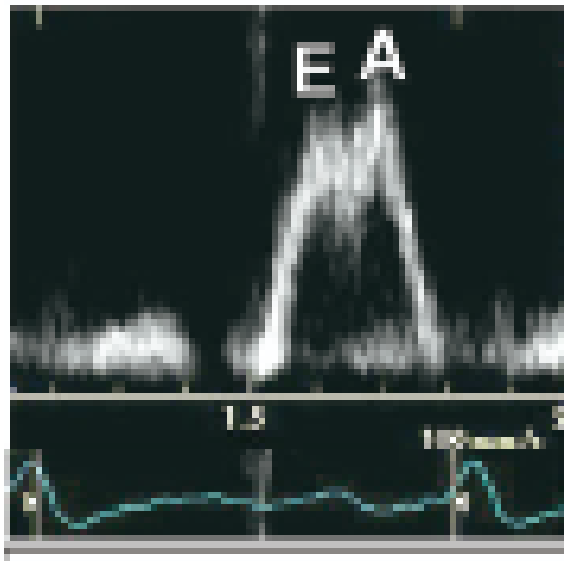
Too short

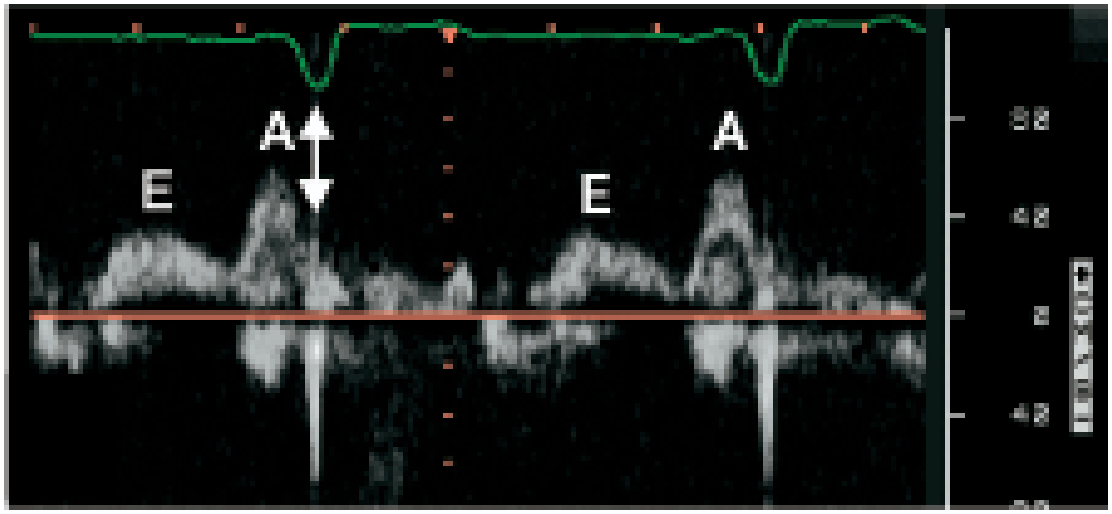


Just right



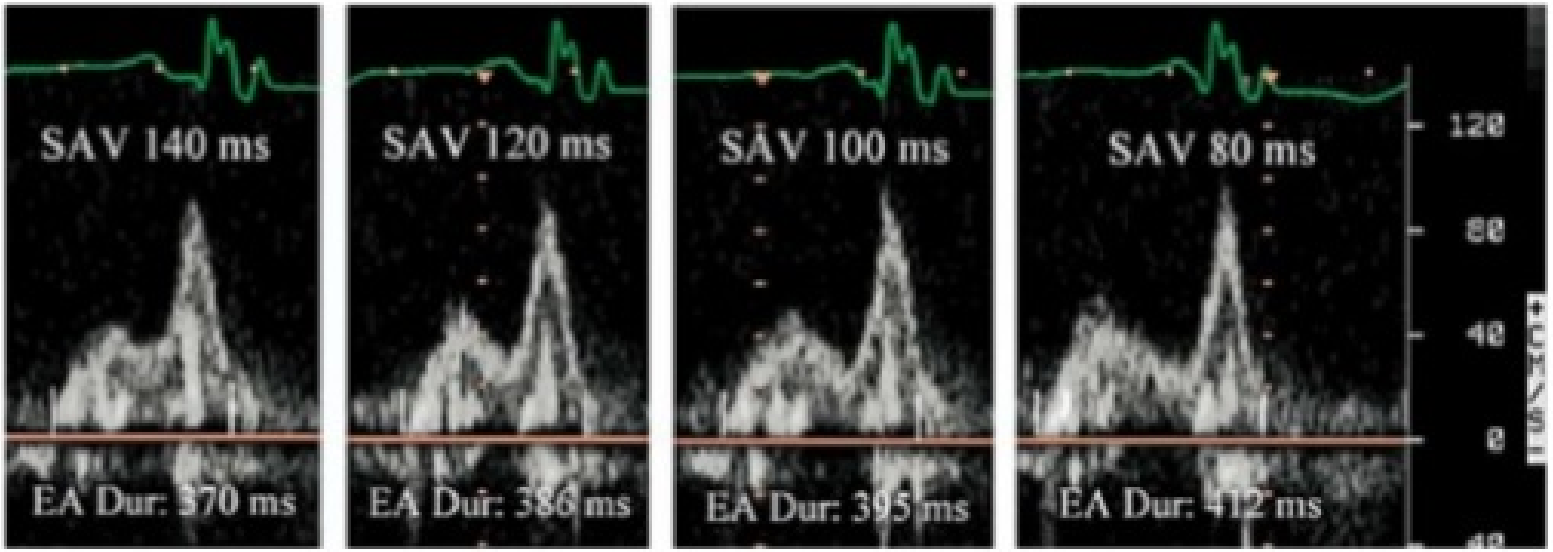
Too long



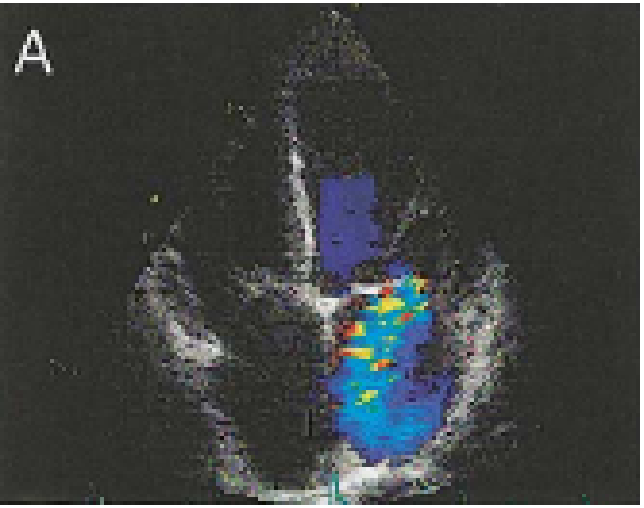


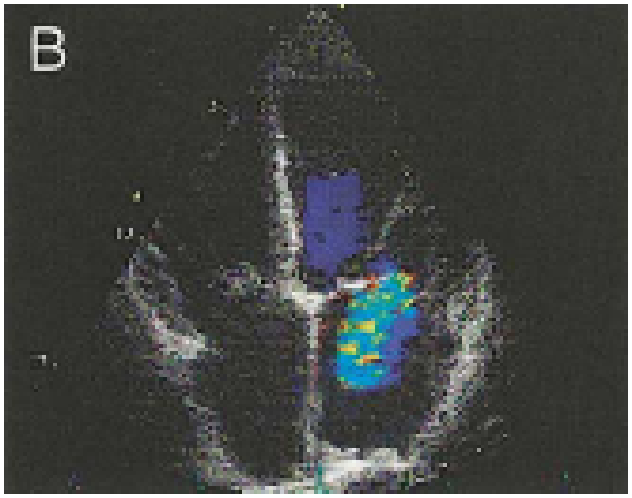
Gorcsan et al. J Am Soc Echocardiogr 21:191-213

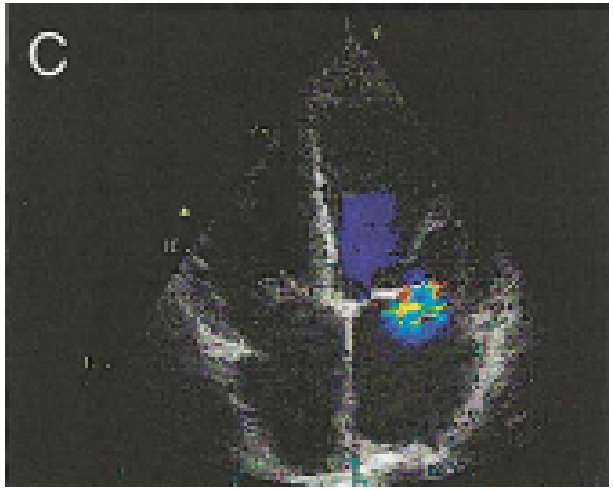
Iterative Method: Allowing Enough Time for Complete Filling of LV



Optimal AV delay reduces MR







intrinsic

VV = 0 ms

VV = -20 ms

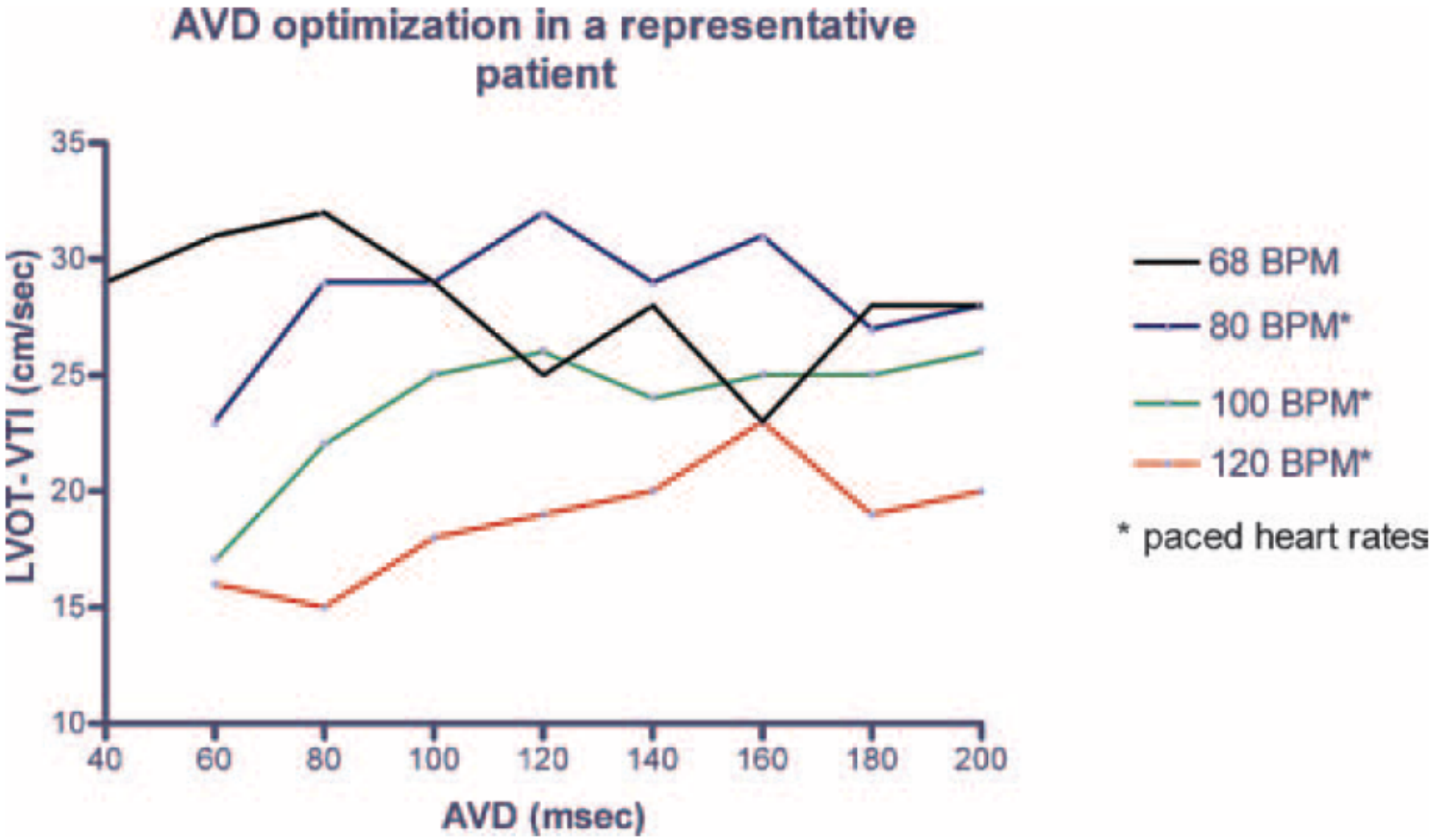
Bax et al. JACC 46:2168-82

Studies of systematic AV/VV timing optimization

Study	Comparison	Results
RHYTHM II[83]	Echo-optimized VV timing vs nominal VV settings	No difference in QOL, NYHA or 6MW
DECREASE-HF[85]	Simultaneous VV pacing vs EGM optimized VV timing	No difference in LV volumes or EF
FREEDOM[86]	Clinically optimized AV and VV timing vs serial EGM optimized AV and VV timing	No difference in clinical outcomes or functional measures
CLEAR[84]	Echo optimized AV and VV timing vs automatic adjustment of AV delays via contractility sensor	Improved clinical response with the contractility sensor
SMART AV[87]	Echo optimized AV and VV timing vs EGM optimized AV and VV timing vs fixed AV (120 ms) and VV (0 ms)	No difference in LV volumes, EF, or functional measures

Parkash R et al. Can J Cardiol 29:1346-60

Typical results of AV delay assessment



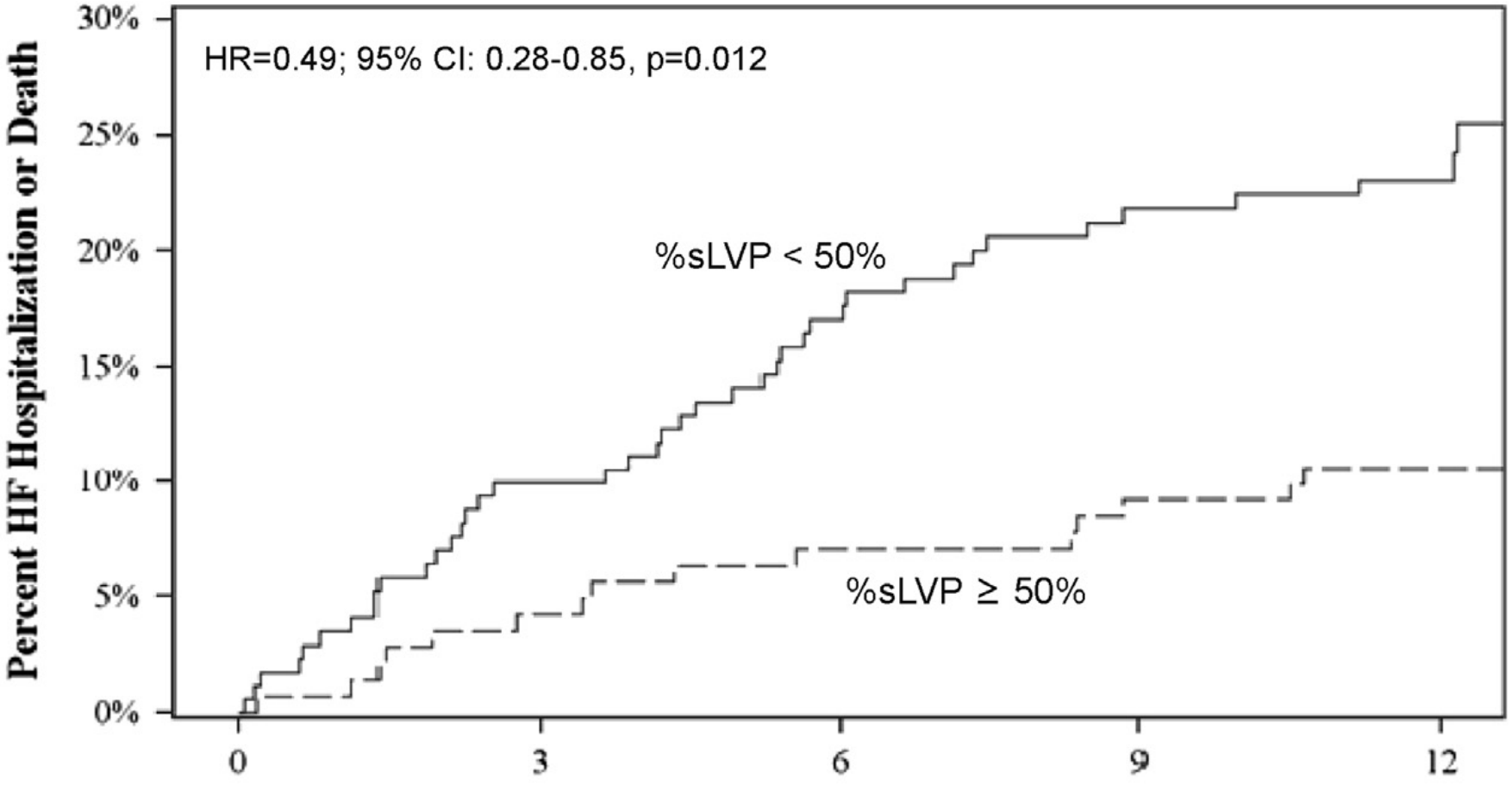
Scharf et al. PACE 28:279-84

Theoretical limitations to optimization

- Optimal AV and VV delay individually changes during exercise compared with rest[1]
- Most optimization methods are performed at rest
- Most patients have NYHA Class III
    - they have exertional symptoms, so they would symptomatically most benefit from exercise optimization
    - they spend most of their time resting, so resting optimization would have the biggest impact on reverse remodelling

1. Golovchiner G, Can J Cardiol

Synchronized LV pacing

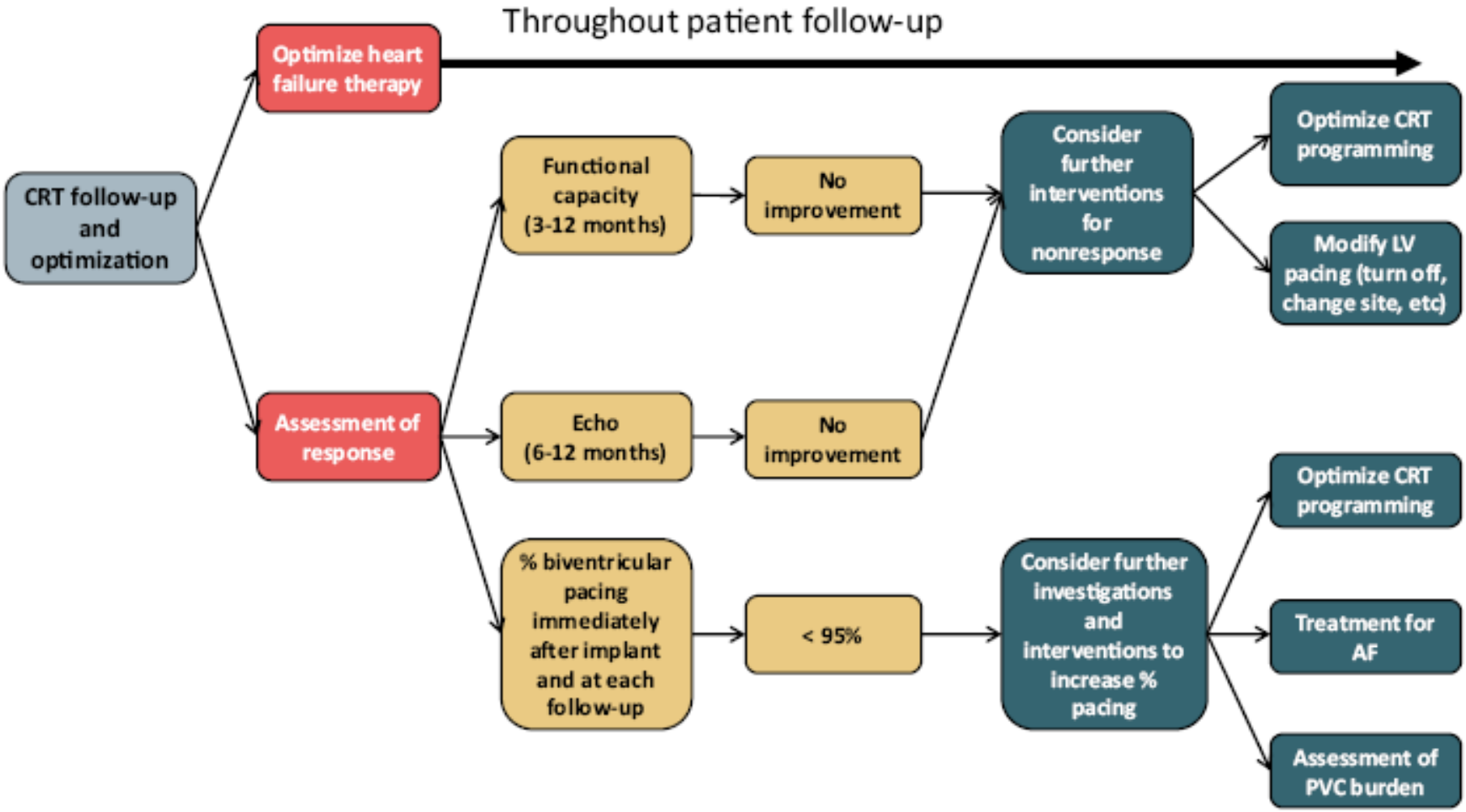


%sLVP < 50%	172	152	140	129	68
%sLVP ≥ 50%	142	136	131	128	76

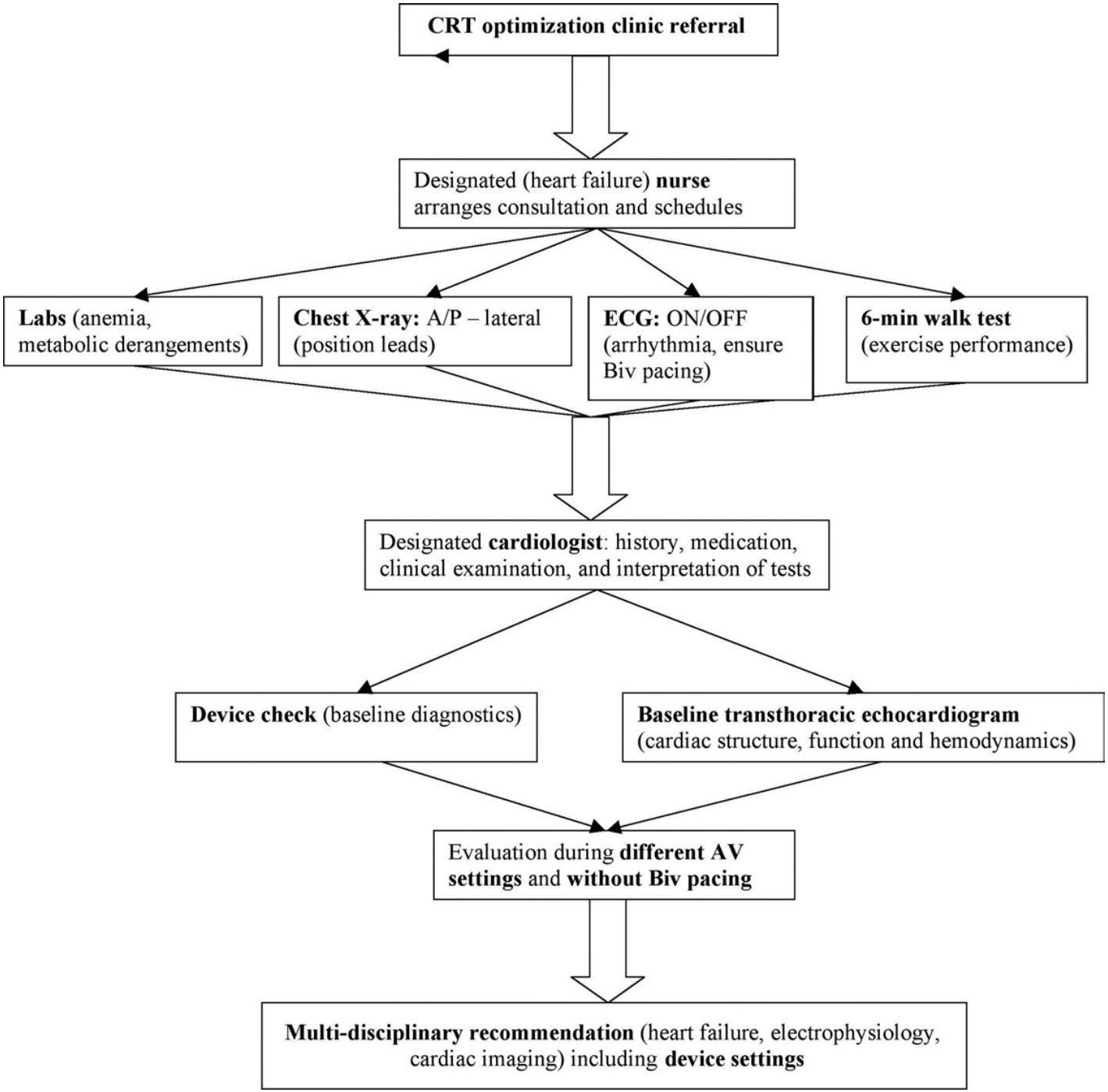
Birnie D et al. Heart Rhythm 2013;10:1368-74

Optimization methods

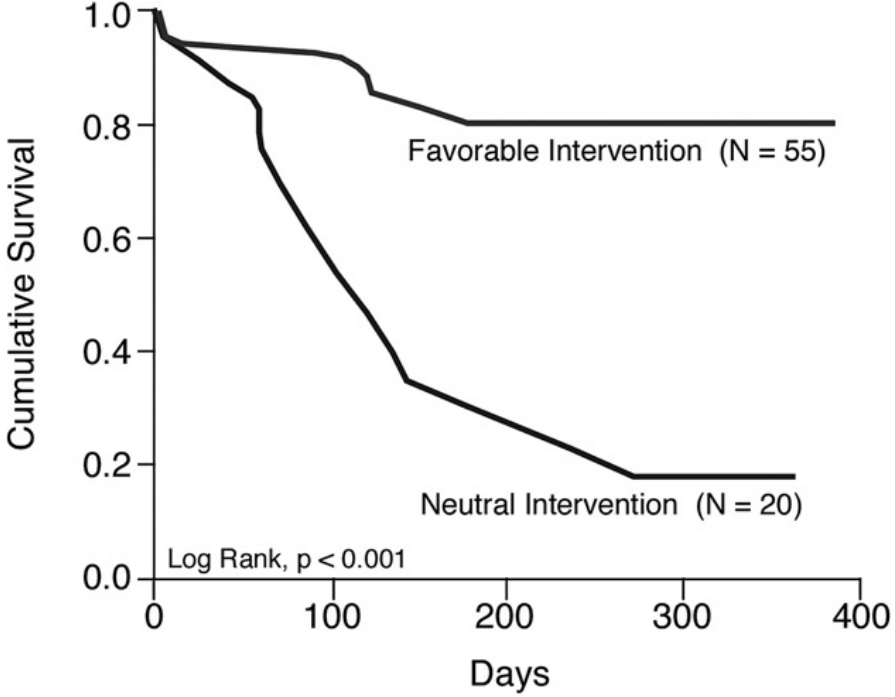
- Echo based
  - mitral inflow
  - aortic/LVOT VTI
  - Tissue Doppler
  - 3D
- EGM based
  - Quick Opt (SJM)
  - Expert Ease (Boston/Guidant)
- Hemodynamic methods
  - SonR (Sorin)
  - invasive (research)
- Other
  - Acoustic (Audiocor)
  - Impedance cardiography
  - Isotope methods
  - photopletizmography

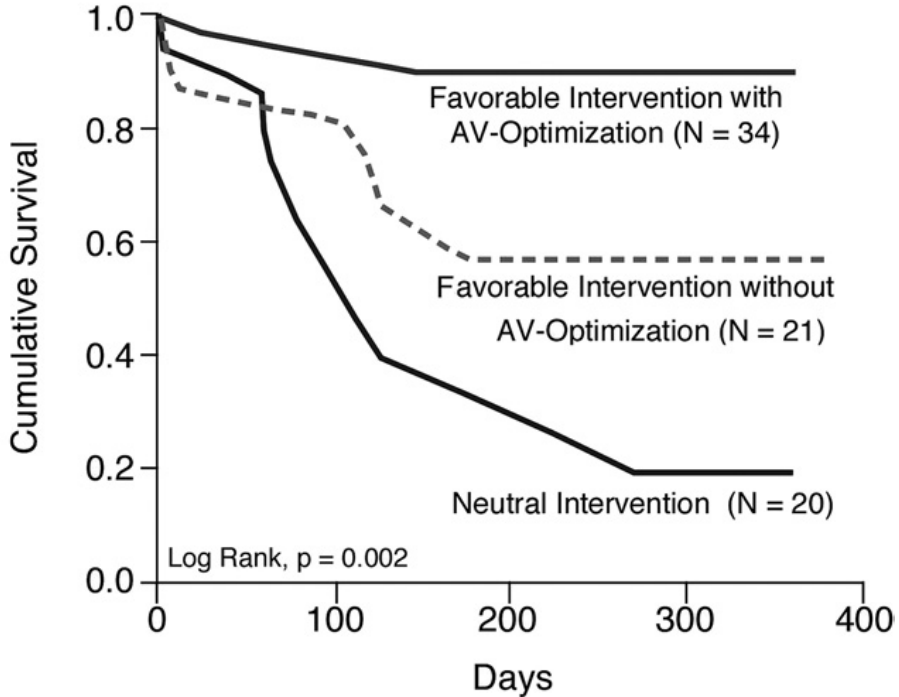


Parkash R et al. Can J Cardiol 29:1346-60



Mullens W et al. JACC 2009;53:765-773





Composite end-point after optimization visit

Mullens W et al. JACC 2009;53:765-773