DEUTSCHES HERZZENTRUM
DER CHARITÉ

Johannes Lucas

How We Came Here
Biventricular Pacing

CSP Summer Summit Berlin 2025

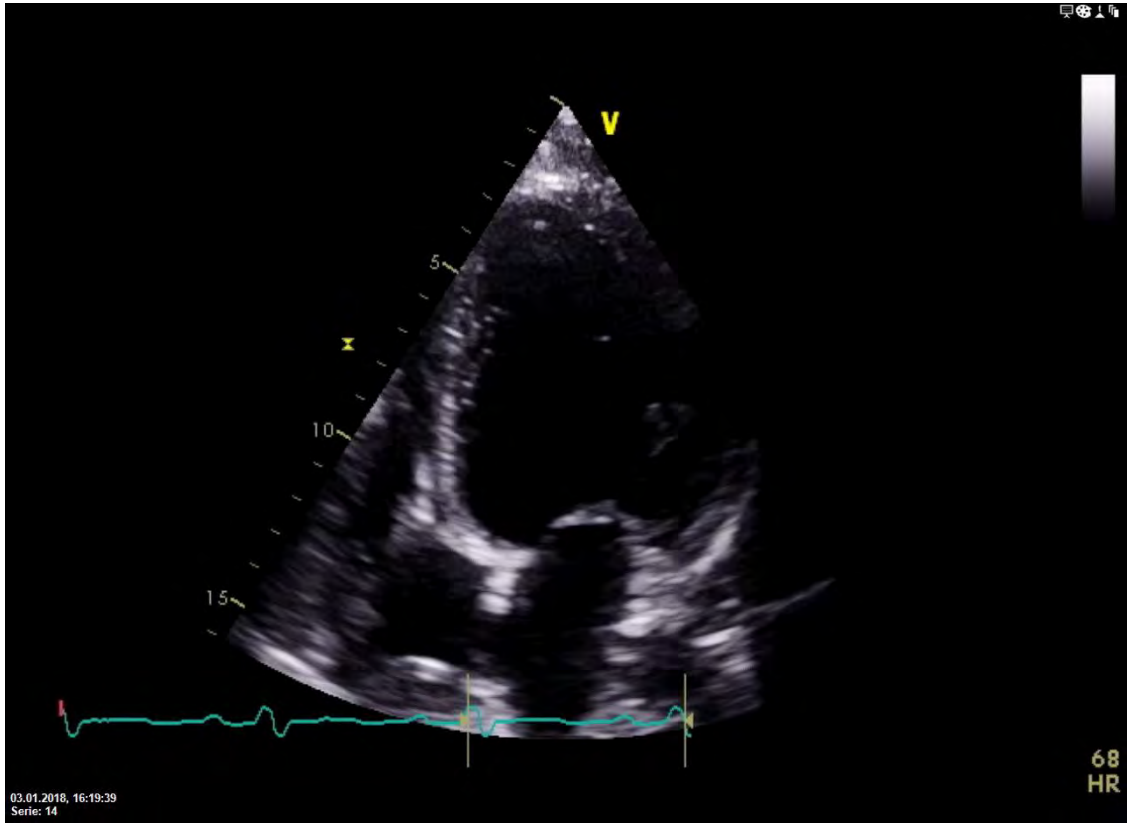
June 13, 2025

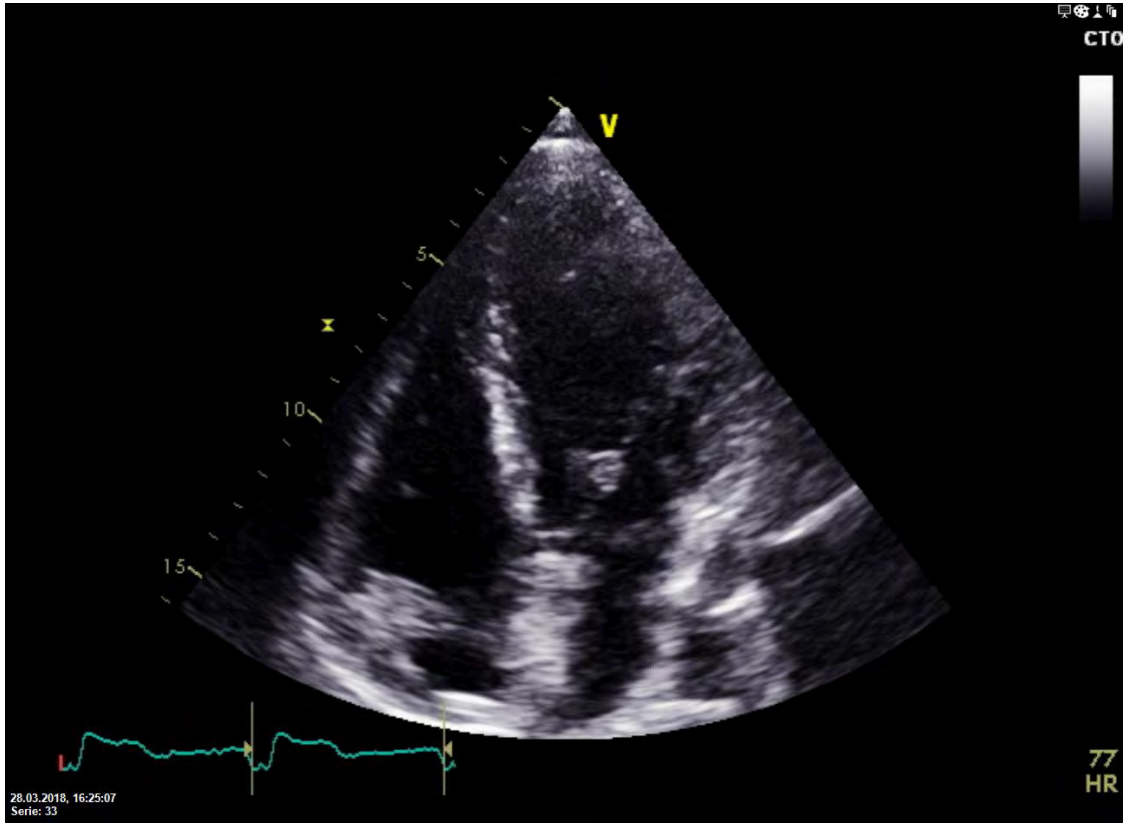
CHARITÉ

Disclosures

- Speaker‘s honoraria: Biotronik, Medtronic

Biventricular Pacing = Physiologic Pacing?





Biventricular Pacing → Physiologic Contraction!

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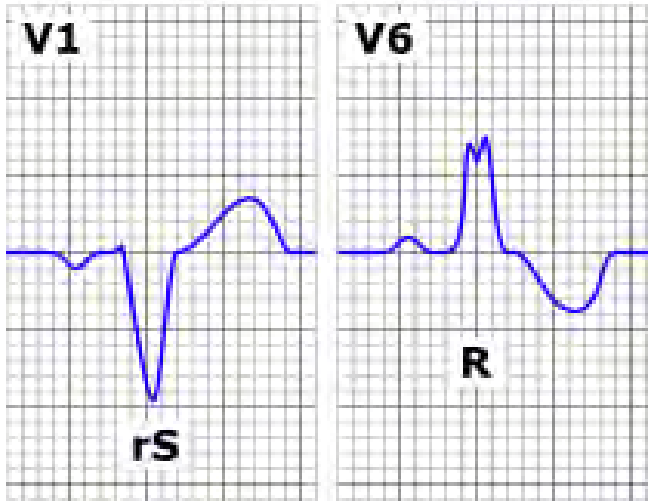
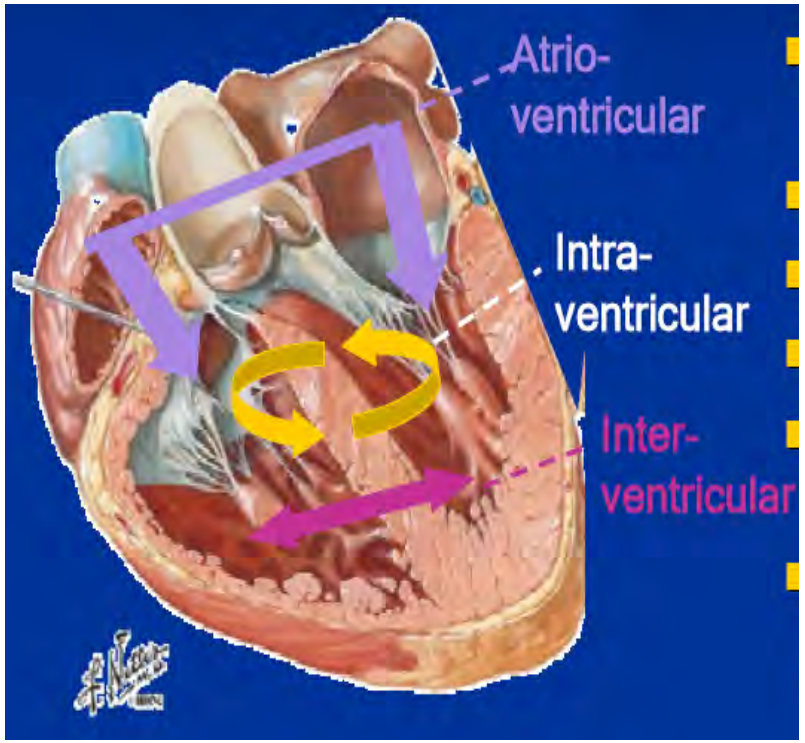
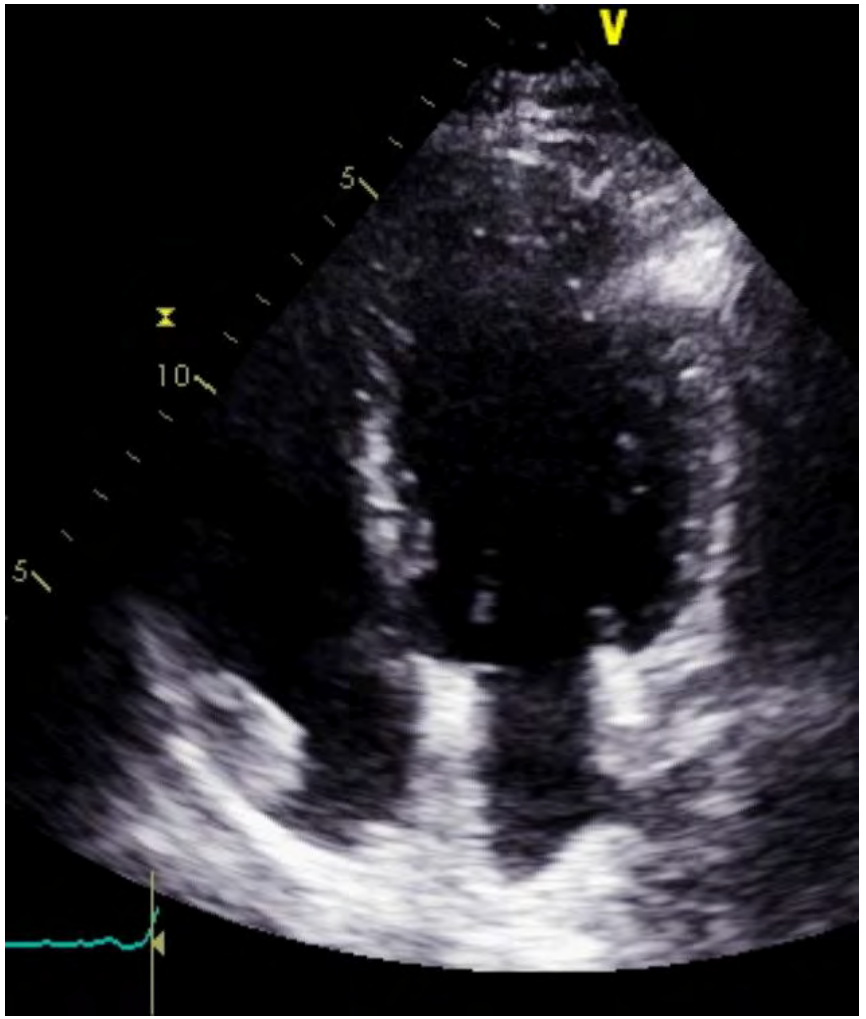


Left Bundle Branch Block leads to mechanical Dyssynchrony





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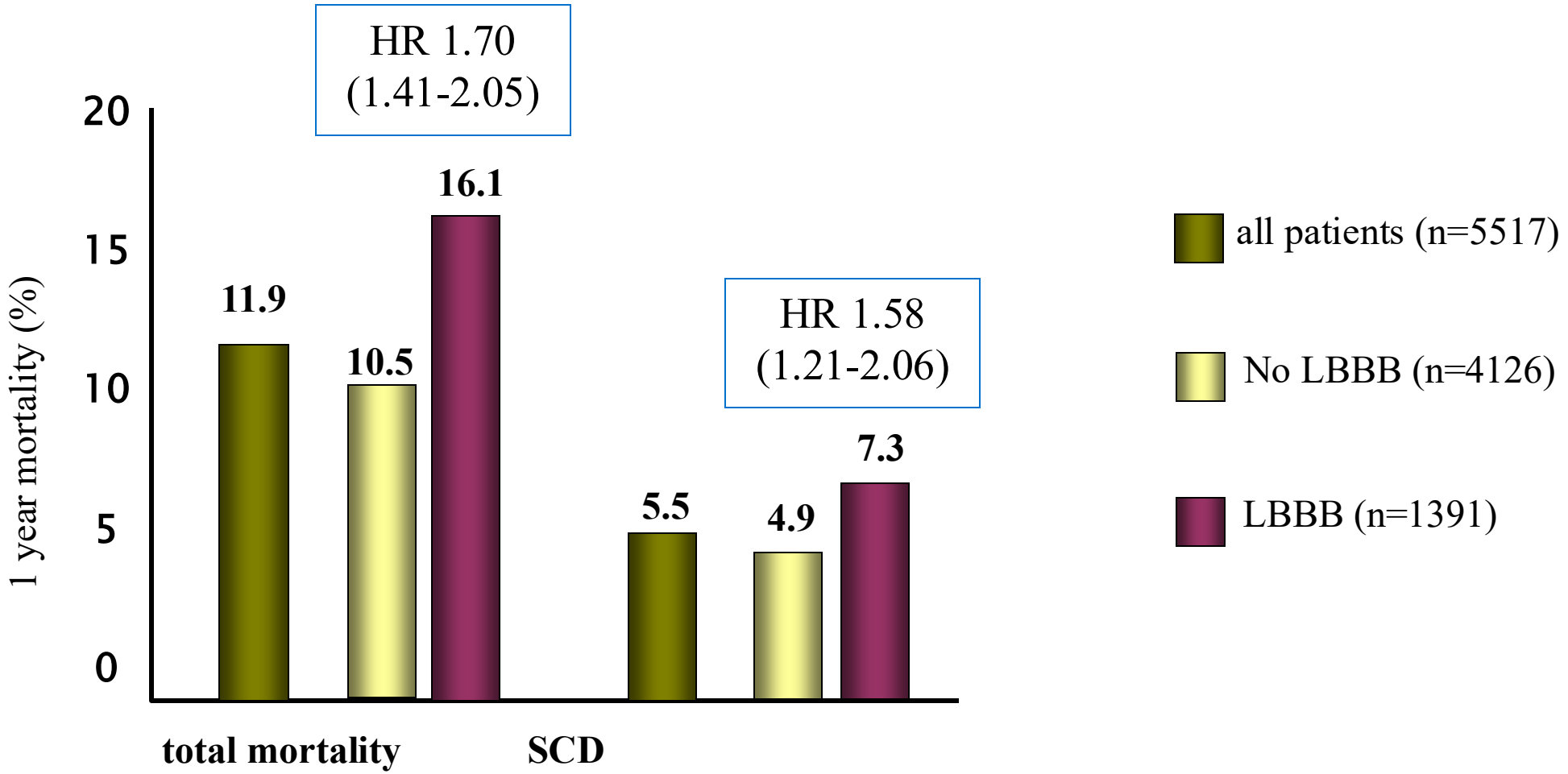
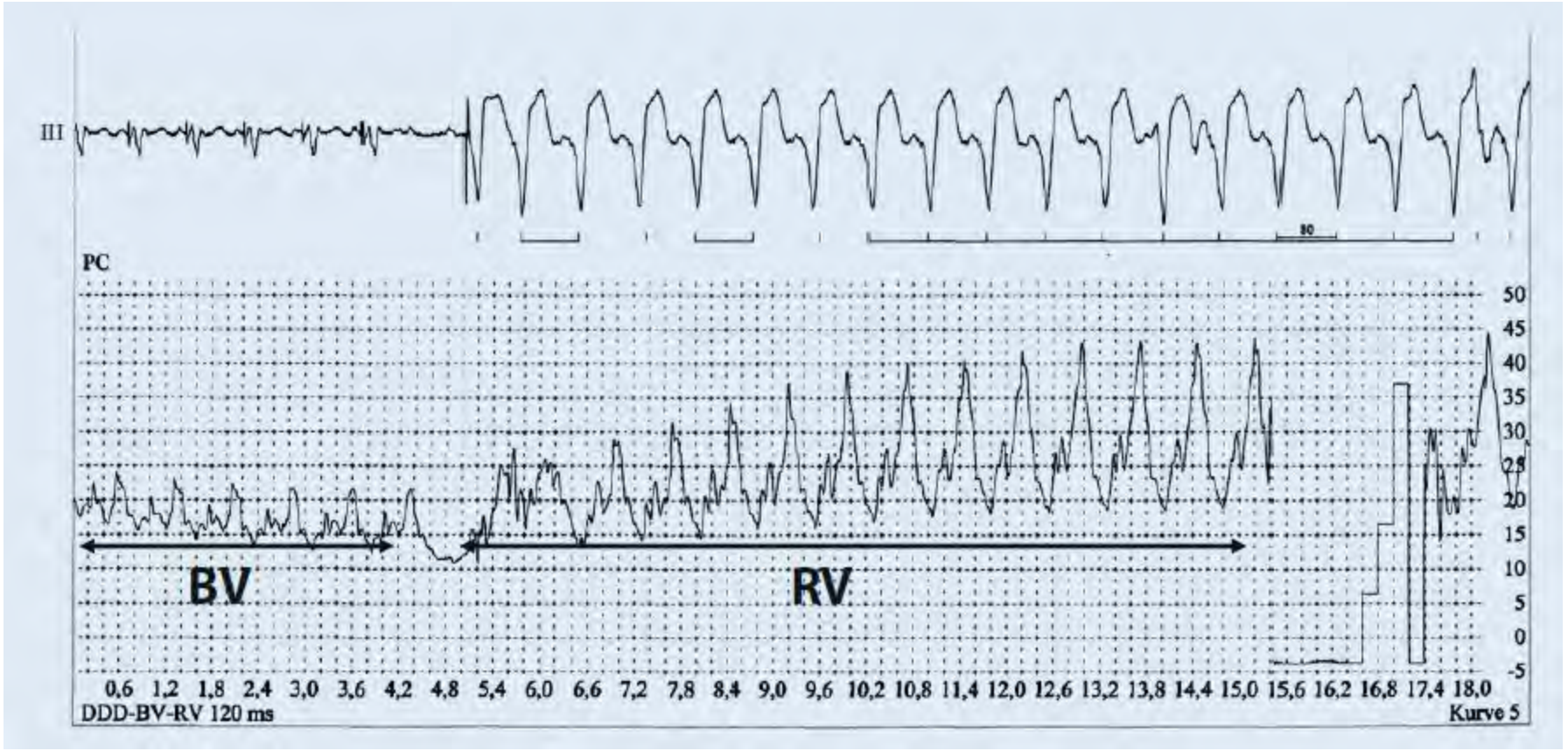
Left Bundle Branch Block Increases Mortality in Heart Failure



Baldasseroni et al., Am Heart J 2002

Biventricular Pacing improves hemodynamics compared to RV Pacing



Stellbrink; Herzschr Elektrophys 2024

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Biventricular Pacing – First Case Series in mid 1990s

Case Reports > Pacing Clin Electrophysiol. 1994 Nov;17(11 Pt 2):1974-9.
doi: 10.1111/j.1540-8159.1994.tb03783.x.

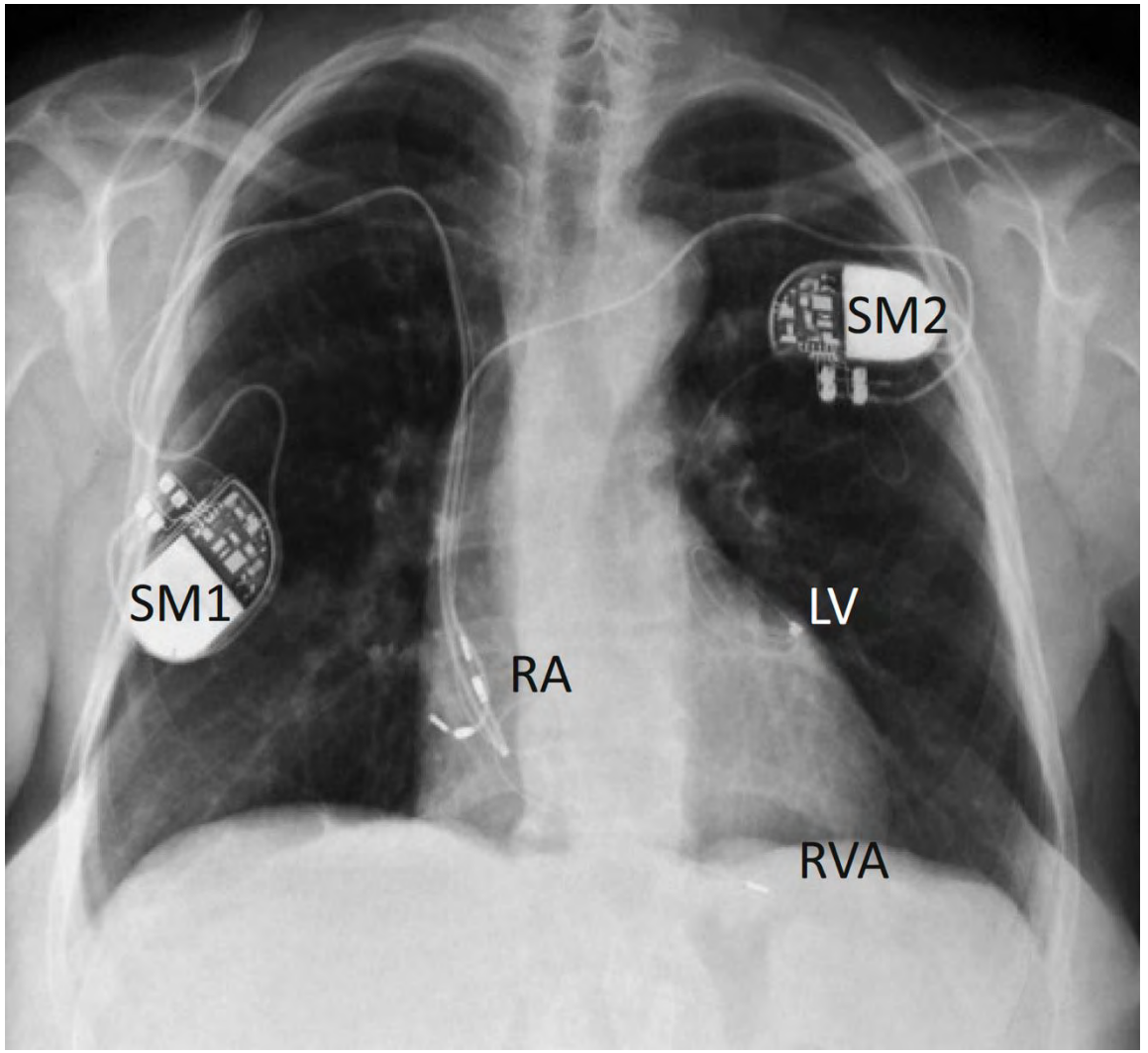
Four chamber pacing in dilated cardiomyopathy

S Cazeau [1], P Ritter, S Bakdach, A Lazarus, M Limousin, L Henao, O Mundler, J C Daubert, J Mugica

> J Interv Card Electrophysiol. 2000 Jun;4(2):395-404. doi: 10.1023/a:1009854417694.

Biventricular pacing in end-stage heart failure improves functional capacity and left ventricular function

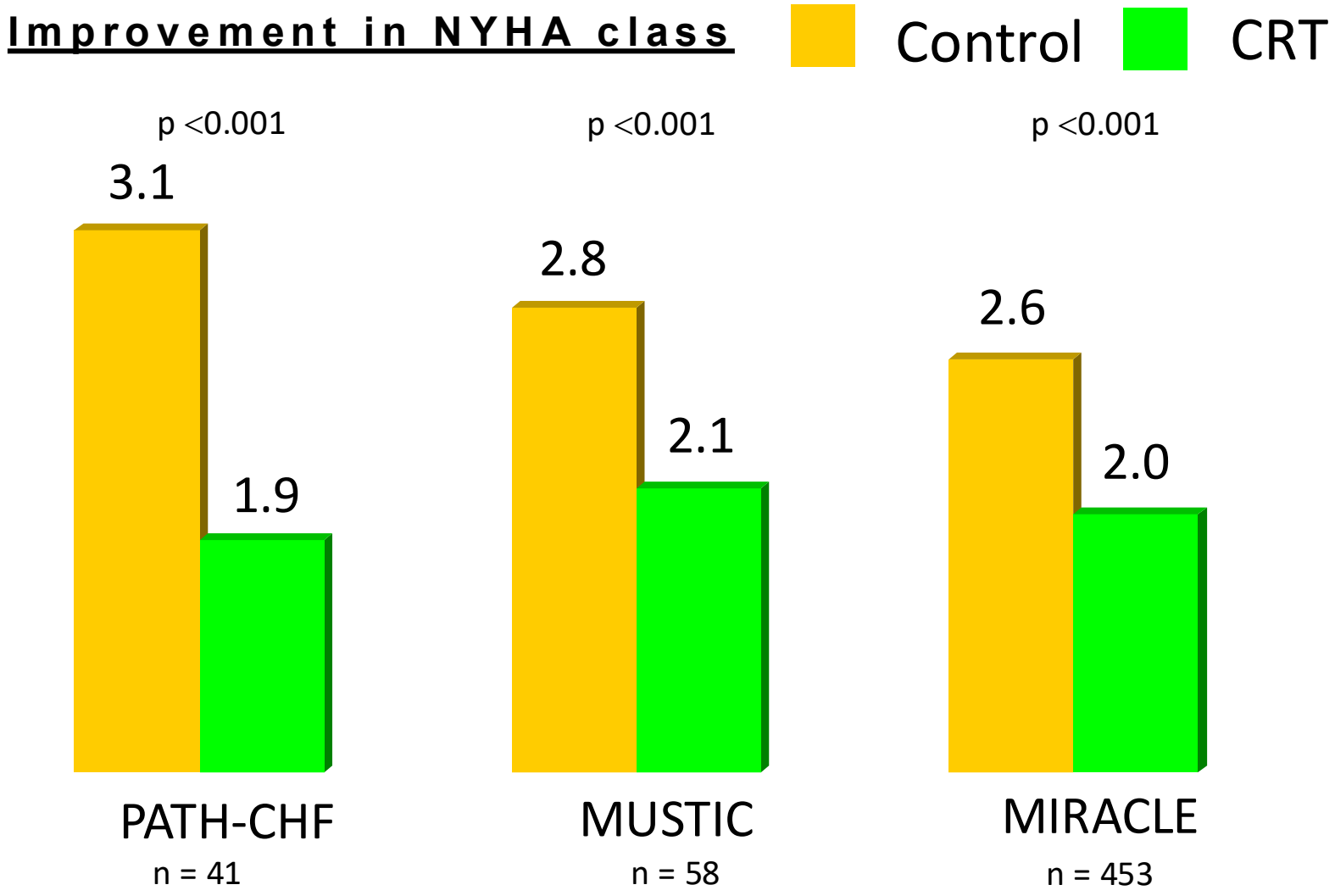
P F Bakker [1], H W Meijburg, J W de Vries, M M Mower, A C Thomas, M L Hull, E O Robles De Medina, J J Bredée



Stellbrink; Herzschr Elektrophys 2024

CRT for wide QRS: success story beginning in the early 2000s

- QRS-Width ↓
- dP/dT ↑
- CI ↑, PCWP ↓
- EF ↑; LVEDV & LVESV ↓
- MR ↓
- BNP levels ↓



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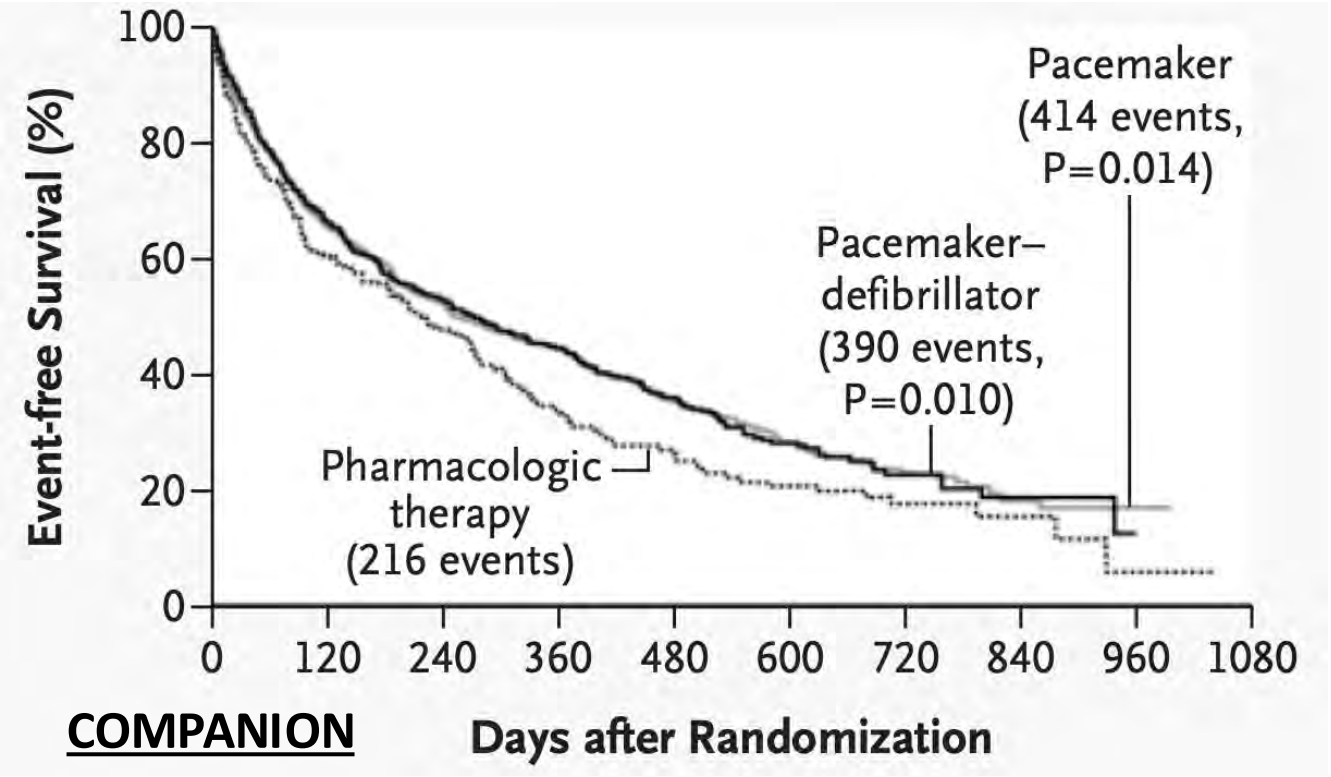
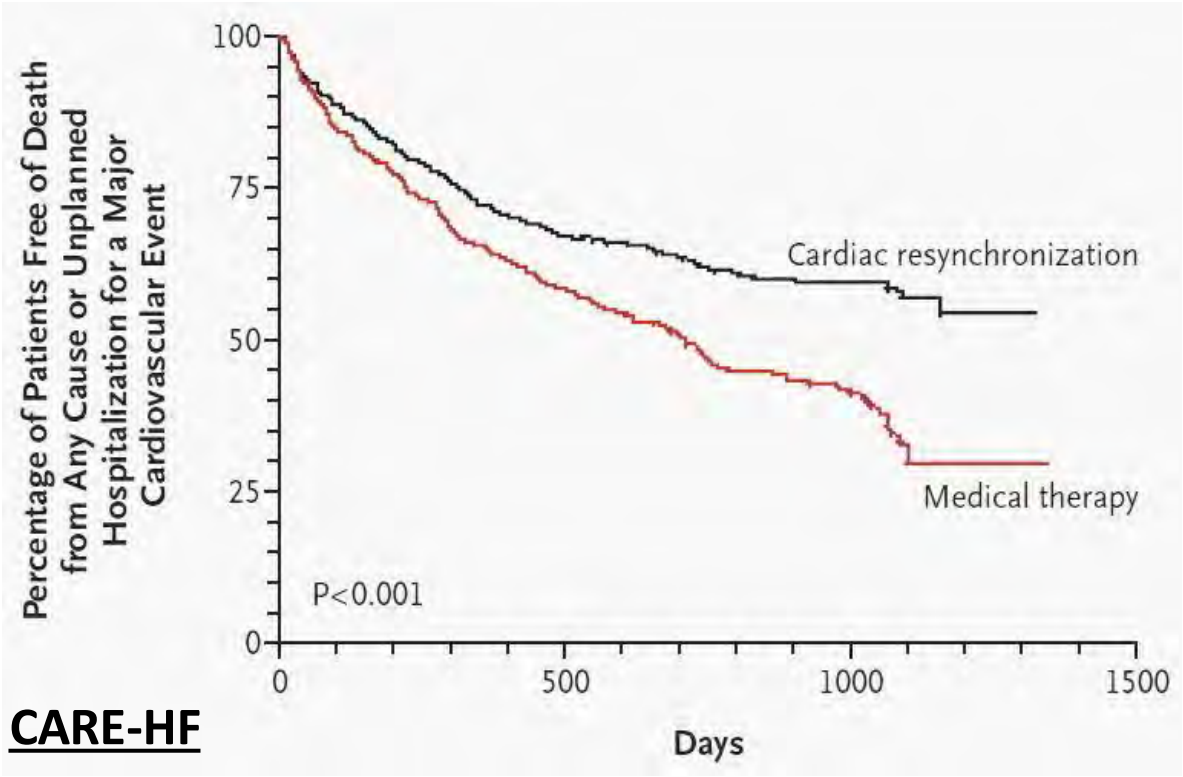
Breakthrough in mid 2000s: Reduction of Death and Hospitalizations in NYHA III/IV



COMPANION

Bristow et al.; N Engl J Med 2004



CARE-HF

Cleland et al.; N Engl J Med 2005

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5 years later: Benefit from CRT also for NYHA II patients

REVERSE 2009

MADIT-CRT 2009

RAFT 2010

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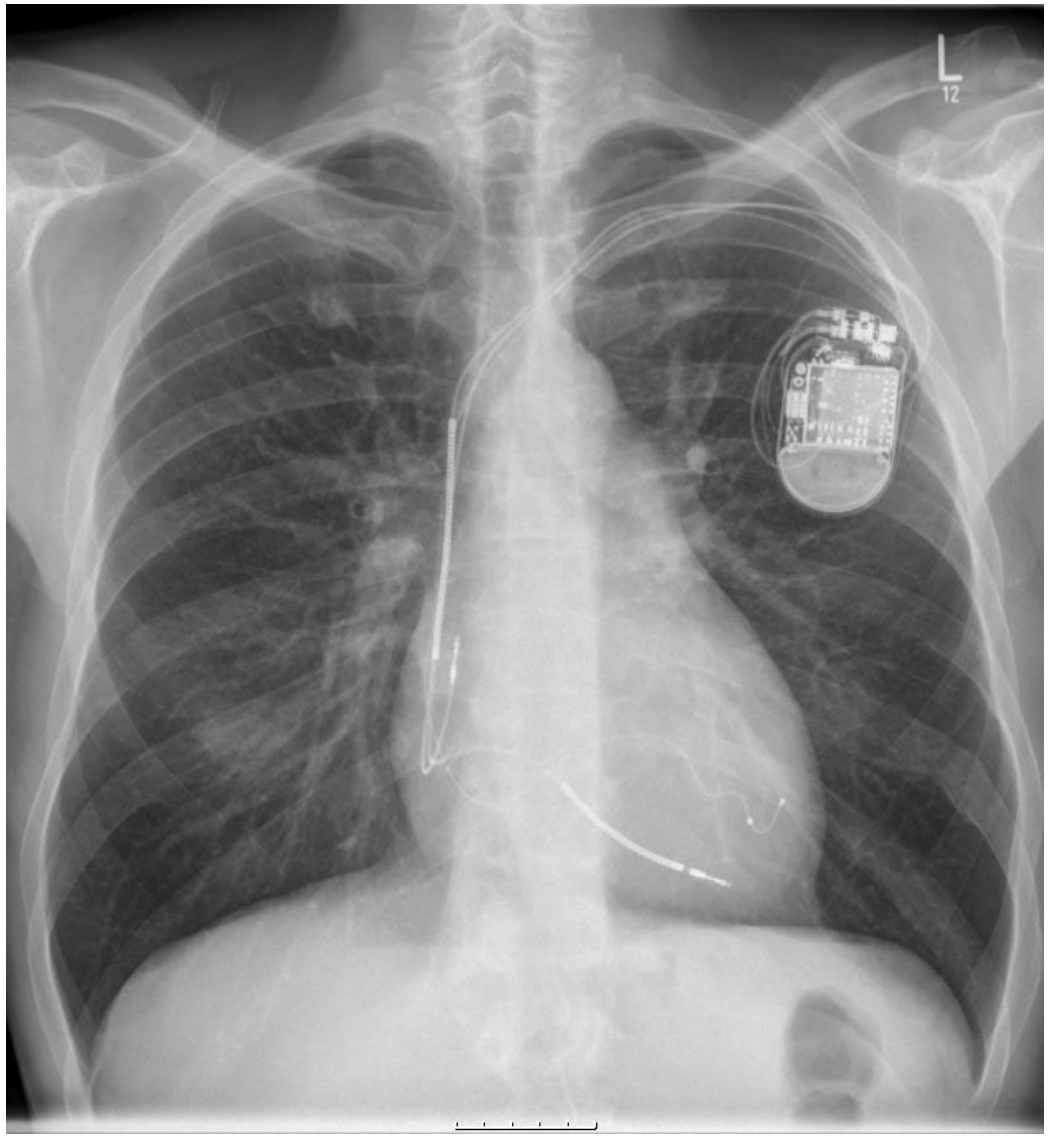

So, no questions to answer anymore, right?

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The issue of „CRT Non Responders“

- Individual response to CRT was investigated in different trials
- Different definitions: NYHA class, 6 min. walking distance, reduction of LVESV by ≥ 15% ….
- Rate of CRT Non Responders varies between different studies, but is around 30% +
- Is it a matter of programming or patient selection?
- Female sex, NICM and low scar burden seem to be associated with better response

- **But is it important to measure individual effects of a treatment that is proven to be beneficial in a certain population?**
- **e. g. „Non Responder Rate“ of Spironolactone with regard to improvement by ≥ 1 NYHA class is 59% (Pitt et al., NEJM 1999)**

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Prediction of Response by echocardiographic parameters?

Circulation
Volume 117, Issue 20, 20 May 2008; Pages 2608-2616
https://doi.org/10.1161/CIRCULATIONAHA.107.743120

HEART FAILURE

Results of the Predictors of Response to CRT (PROSPECT) Trial

Eugene S. Chung, MD, Angel R. Leon, MD, Luigi Tavazzi, MD, Jing-Ping Sun, MD, Petros Nihoyannopoulos, MD, John Merlino, MD, William T. Abraham, MD, Stefano Ghio, MD, Christophe Leclercq, MD, Jeroen J. Bax, MD, Cheuk-Man Yu, MD, FRCP, John Gorcsan, III, MD, Martin St John Sutton, FRCP, Johan De Sutter, MD, PhD, and Jaime Murillo, MD

Conclusion

— Given the modest sensitivity and specificity in this multicenter setting despite training and central analysis, no single echocardiographic measure of dyssynchrony may be recommended to improve patient selection for CRT beyond current guidelines. Efforts aimed at reducing variability arising from technical and interpretative factors may improve the predictive power of these echocardiographic parameters in a broad clinical setting.

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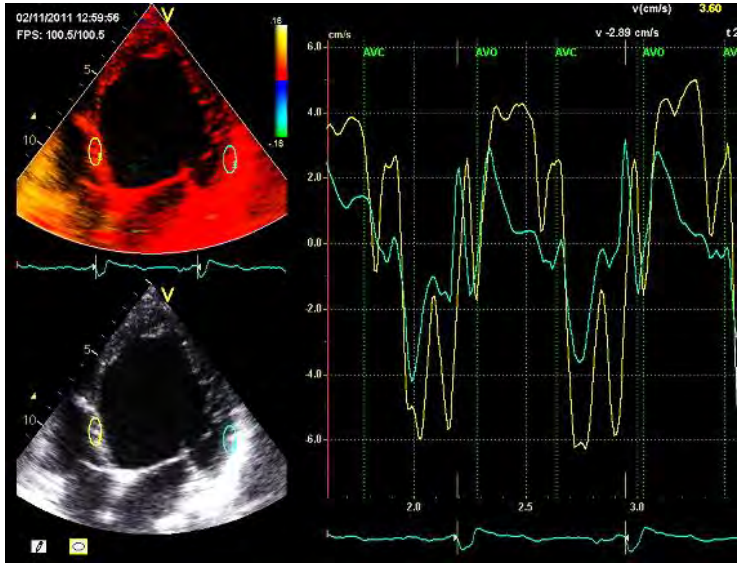
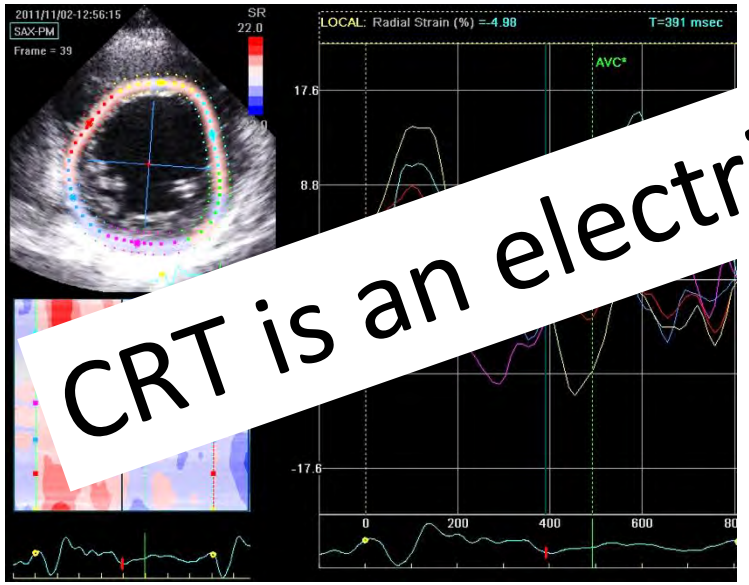
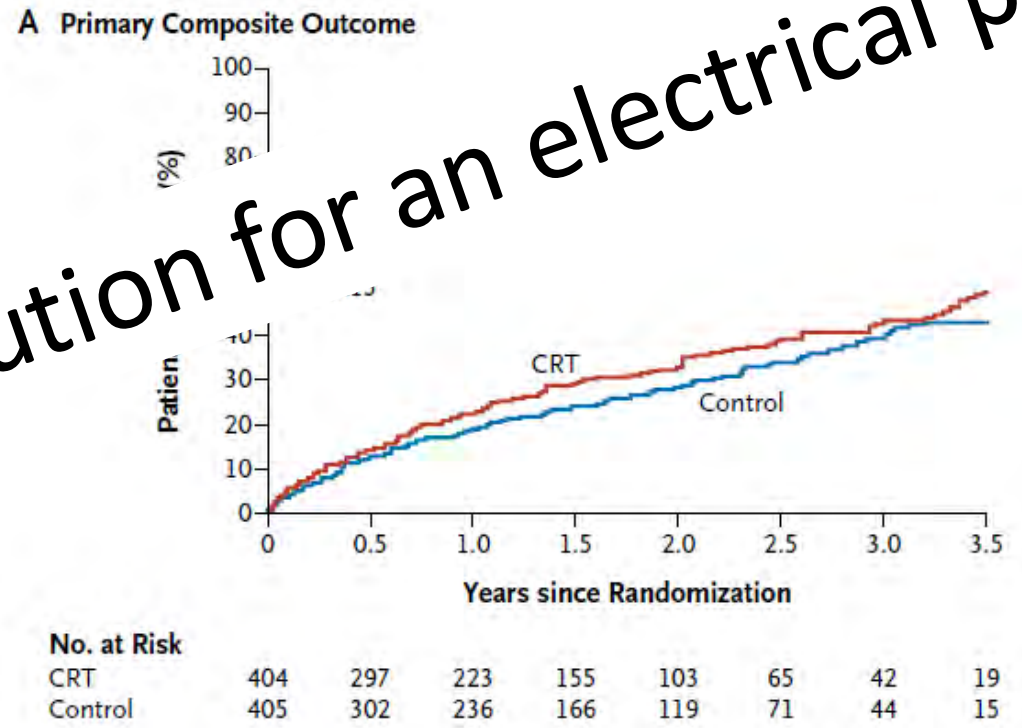
Mechanical dyssynchrony in narrow QRS





CRT is an electrical solution for an electrical problem

EchoCRT Trial



Ruschitzka et al.; N Engl J Med 2013

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QRS duration or type of block?

In most important trials QRS duration was the inclusion criterion, not type of block

Patients with QRS ≥ 150 ms seem to benefit most from CRT

Great overlap between QRS ≥ 150 ms and LBBB

Friedman et al; Circulation 2023

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ESC Guidelines

Recommendations	Class[a]	Level[b]
LBBB QRS morphology		
CRT is recommended for symptomatic patients with HF in SR with LVEF ≤35%, QRS duration ≥150 ms, and LBBB QRS morphology despite OMT, in order to improve symptoms and reduce morbidity and mortality.[37,39,40,254–266,283,284]	I	A
CRT should be considered for symptomatic patients with HF in SR with LVEF ≤35%, QRS duration 130–149 ms, and LBBB QRS morphology despite OMT, in order to improve symptoms and reduce morbidity and mortality.[37,39,40,254–266,283,284]	IIa	B
Non-LBBB QRS morphology		
CRT should be considered for symptomatic patients with HF in SR with LVEF ≤35%, QRS duration ≥150 ms, and non-LBBB QRS morphology despite OMT, in order to improve symptoms and reduce morbidity.[37,39,40,254–266,283,284]	IIa	B
CRT may be considered for symptomatic patients with HF in SR with LVEF ≤35%, QRS duration 130–149 ms, and non-LBBB QRS morphology despite OMT, in order to improve symptoms and reduce morbidity.[273–278,281]	IIb	B

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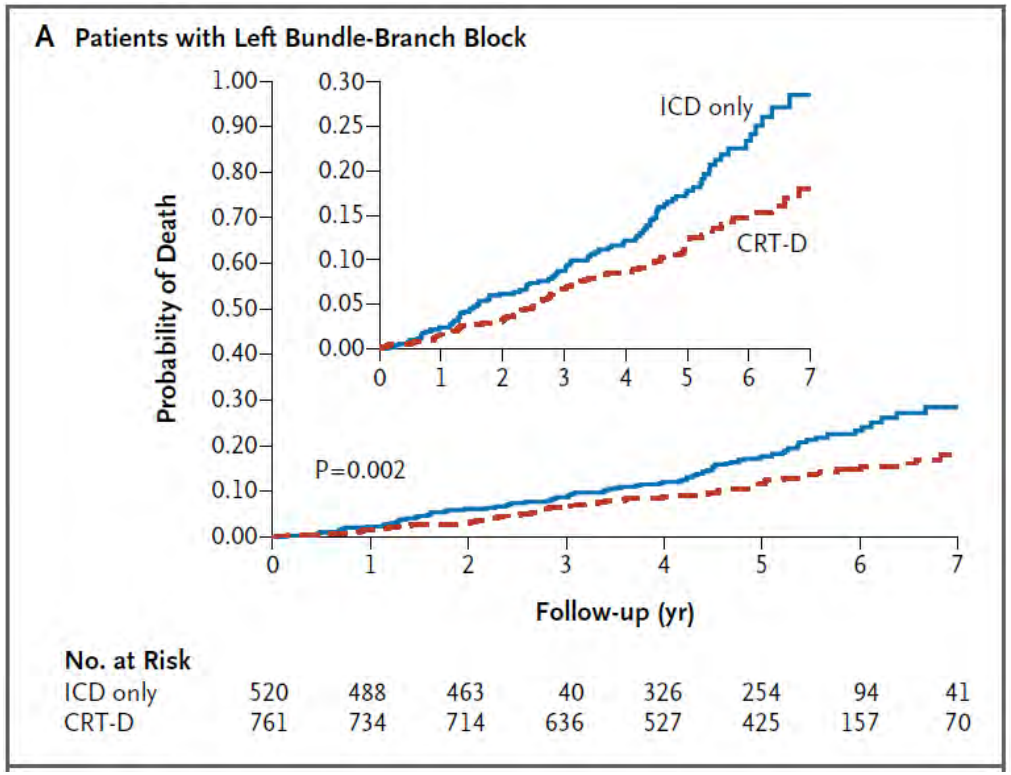
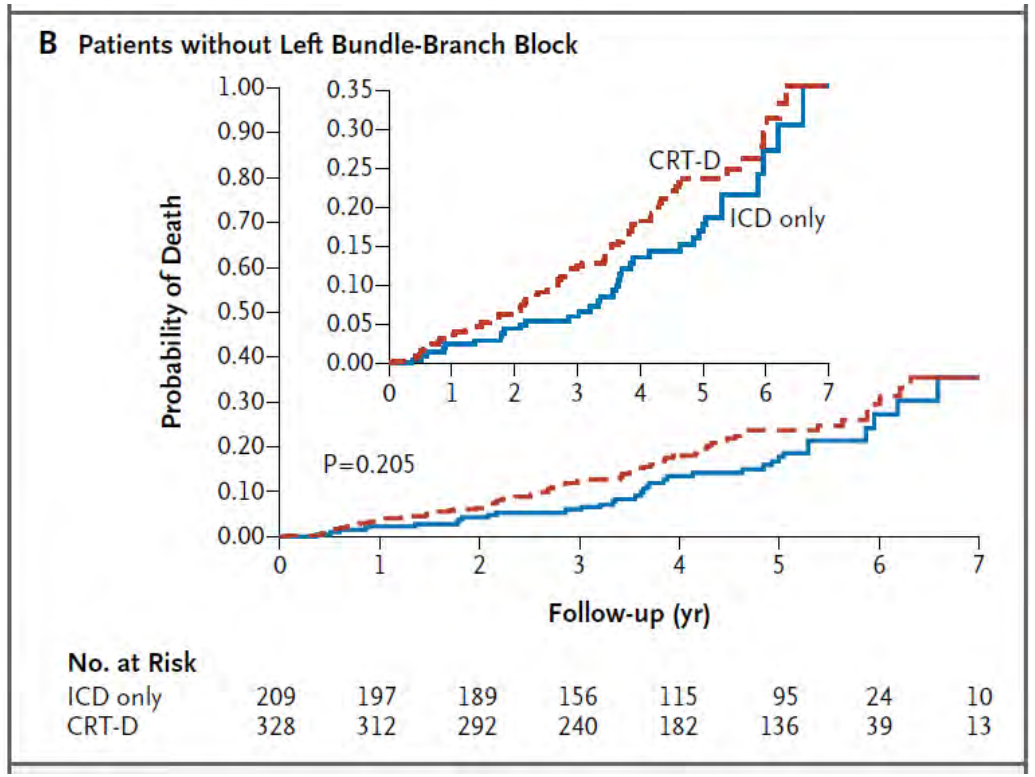
Post hoc analysis from MADIT-CRT:





Goldenberg et al; NEJM 2014

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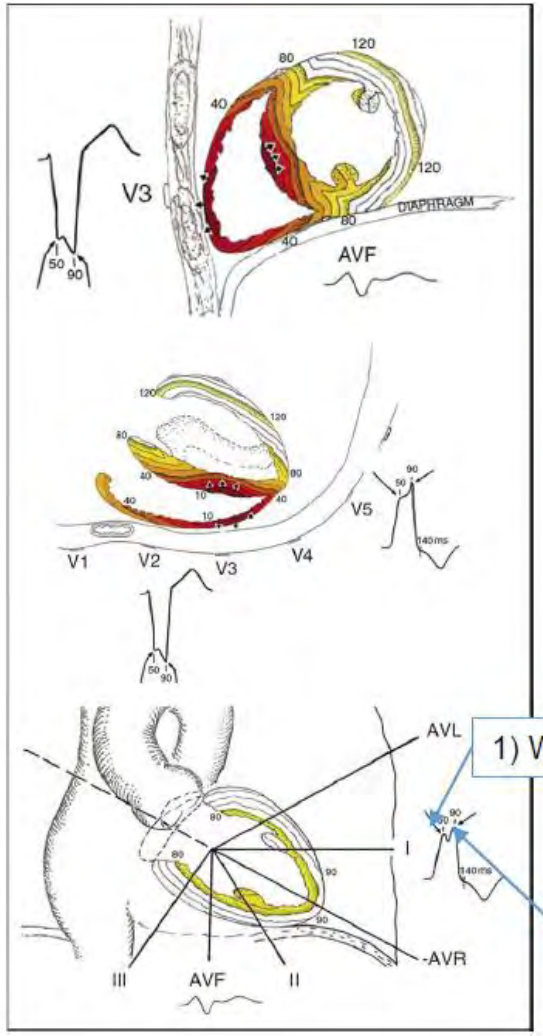
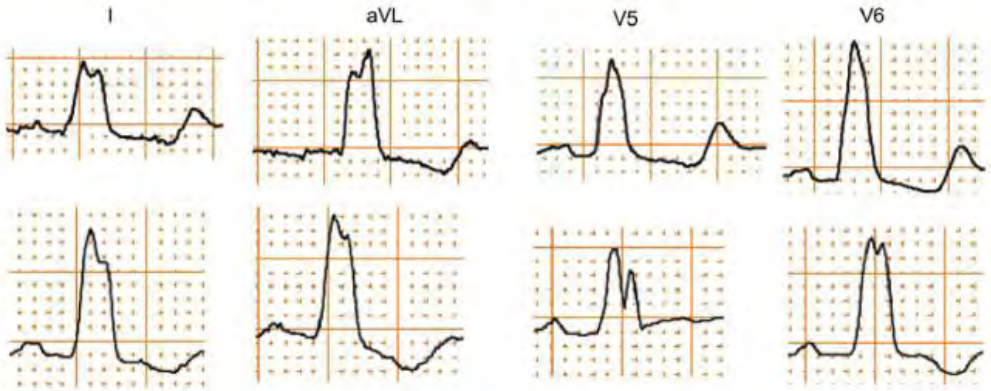
New Definition of LBBB in the era of CRT – „Strauss Criteria“



- **QRS ≥ 130 ms (♀) ≥140 ms (♂)**
- QS oder rS in V1 und V2
- Mid Notching oder slurring in ≥2 Ableitungen in I, aVL, V1, V2, V5, V6



1) Wellenfront erreicht LV-Endokard septal

2) Wellenfront erreicht LV-Epikard posterolateral

Strauss DG, Am J Cardiol, 2011

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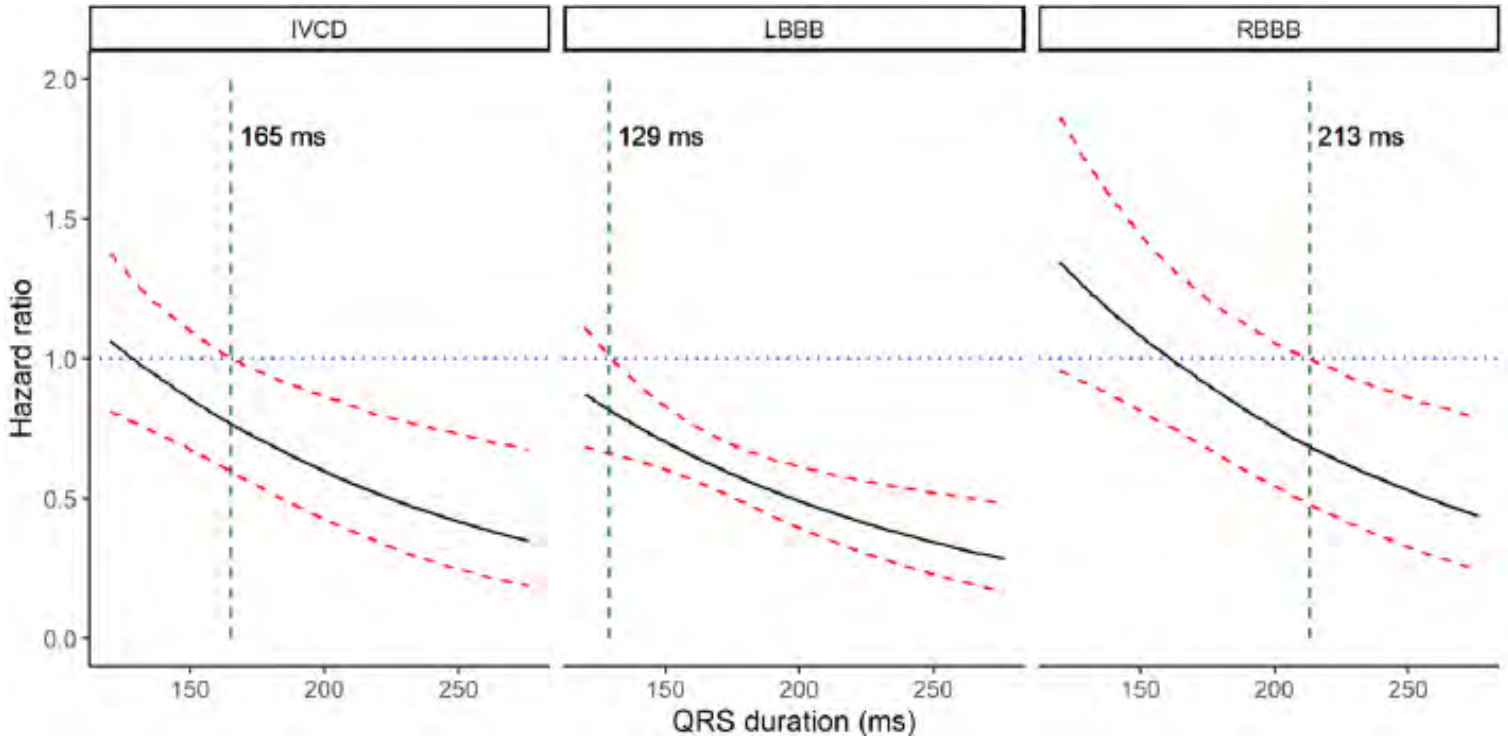
RESEARCH ARTICLE | Originally Published 26 January 2023 | Check for updates

Cardiac Resynchronization Therapy Improves Outcomes in Patients With Intraventricular Conduction Delay But Not Right Bundle Branch Block: A Patient-Level Meta-Analysis of Randomized Controlled Trials

Friedman et al; Circulation 2023

Meta-Analysis from 8 pivotal CRT trials



CONCLUSIONS: CRT is associated with reduced HFH or death in patients with QRS ≥150 ms and LBBB or IVCD, but not for those with RBBB. Aggregating RBBB and IVCD into a single "non-LBBB" category when selecting patients for CRT should be reconsidered.

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AdaptResponse Trial

- Intention of the trial was to test the „AdaptivCRT“ algorithm regarding clinical outcomes
- 3,617 pts. with LBBB according to Strauss Criteria randomized to „AdaptivCRT ON“ versus conventional CRT
- Although numerically present a significant benefit of the algorithm could not be statistically proven
- But: 92,6% of patients in the whole cohort improved or stabilized which is a higher number than in previous trials

Wilkoff et al; Lancet 2023

→ patient selection according to type of block seems to matter…

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What about indications for ventricular antibradycardia pacing?

Incidence of Pacing Induced Cardiomyopathy around 12% in RVP > 40%

Table 1 Definition and prevalence of pacing induced cardiomyopathy

No.	Study	Sample size	Study design	Definition	Prevalence	Follow-up (years)
1	Lee *et al*[21]	234	Retrospective	LVEF decrease >5% with symptoms of HF without other aetiology for HF	20.5%	15.6
2	Kaye *et al*[7]	118	Prospective	LVEF ≤40%, if baseline LVEF was ≥50%, or absolute reduction in LVEF ≥5% if baseline was<50%	9.3%	3.4±1.4
				LVEF ≤40%, if baseline LVEF was ≥50%, or absolute reduction in LVEF ≥10% if baseline was <50%	5.9%	
				Absolute reduction in LVEF ≥10%, regardless of baseline	39%	
3	Khurshid *et al*[50]	257	Retrospective	Drop in LVEF ≤10% and resulting in an LVEF <50%	19.5%	3.3
4	Kiehl *et al*[51]	823	Prospective	Drop in LVEF (to ≤40%) or need for upgrade to CRT	12.3%	4.3
5	Kim *et al*[52]	130	Retrospective	≥10% decrease in LVEF resulting in LVEF <50%	16.1%	4.5
6	Perla *et al*[53]	749	Retrospective	Fall in LVEF by 10 percentage points to a LVEF of <50.0% from baseline due to RV pacing in the absence of other known causes of cardiomyopathy	9.9%	2.2
7	Abdin *et al*[54]	173	Retrospective	LVEF ≥10%, resulting in LVEF <50%, which cannot be explained by other causes	16%	3.3±1.8
8	Cho *et al*[55]	618	Retrospective	Reduction in LVEF (<50%) along with either (1) ≥10% decrease in LVEF, or (2) new-onset regional wall motion abnormality unrelated to coronary artery disease	14.1%	4.7
9	Tayal *et al*[56]	27 704	Retrospective	HF symptoms including fatal HF	10.6%	2

CRT, cardiac resynchronisation therapy; HF, heart failure; LVEF, left ventricular ejection fraction; RV, right ventricle.

Ponnusamy SS et al. Pacing induced cardiomyopathy: recognition and management *Heart* 2022

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Treatment of pacing induced cardiomyopathy

Budapest CRT Upgrade — BP

International randomized controlled trial — CRT

Key inclusion criteria

- HFrEF patients with previously implanted pacemaker or ICD
- Right ventricular pacing ≥ 20%
- Paced QRS complex ≥ 150 ms

Enrollment	Randomization	Procedure
Intention-to-treat analysis **360** patients enroled	Randomly assigned to procedure in a **3:2** ratio	**215** assigned to **CRT-D** upgrade **145** assigned to **ICD** upgrade

Follow-up for 12 months

Endpoints

Primary endpoint: composite of all-cause mortality, HF hospitalization, or < 15% reduction of LVESV within 1 year

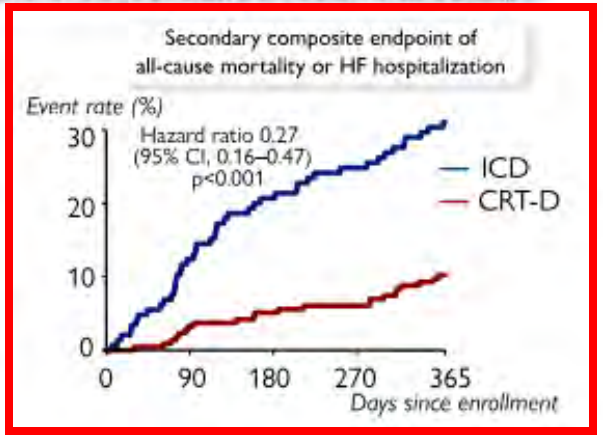
Secondary endpoints: composite of all-cause mortality or HF hospitalization, all-cause mortality alone, and LV reverse remodelling

Primary composite endpoint

CRT-D	ICD	
32.4% reached	78.9% reached	OR 0.11 [95% CI 0.06–0.19] p<0.001

Secondary composite endpoint

CRT-D	ICD	
10.2% reached	31.7% reached	HR 0.27 [95% CI 0.16–0.47] p<0.001

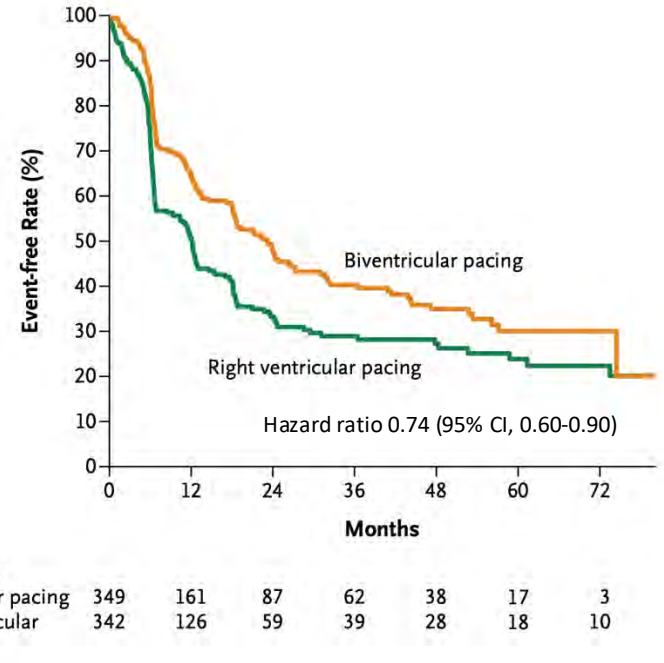


Merkely et al; EHJ 2023

Prevention of pacing induced cardiomyopathy?

BLOCK HF:

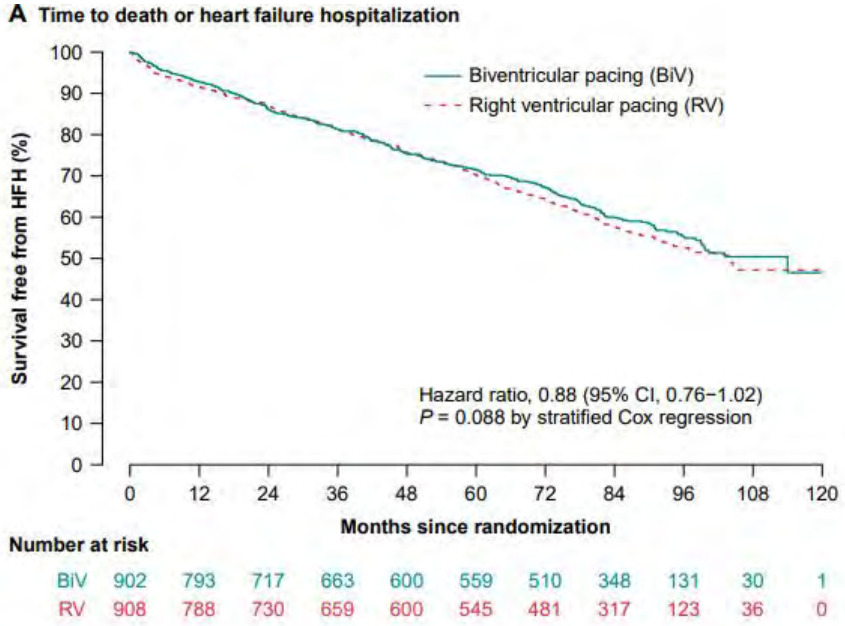
- EF < 50% inclusion criterion
- mean EF 40%



Curtis et al; NEJM 2013

BIOPACE:

- EF not a defined inclusion criterion
- mean EF 55%



Funck et al; Europace 2025

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Maybe CRT is not the optimal modality to prevent PICM?

Conclusions

- CRT for heart failure is a success story
- Best outcomes in patients with LBBB but not every aspect fully understood
- CRT effective in treating PICM
- Effect of CRT in prevention of PICM is less pronounced
- Maybe CSP is the better modality to prevent PICM?

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Thank you very much for your attention!

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