EHRA 2022: MELOS et RESET CRT

Dr Walid AMARA

Disclosures

- Consulting and Speaker’s fees from Bayer, BMS, Pfizer, Biotronik, Medtronic, Boston Scientific, Saint Jude Medical, Microport, Novartis.

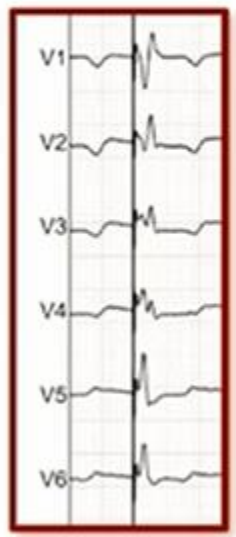
MELOS

Multicentre European Left Bundle Branch Area Pacing Outcomes Study

Marek Jastrzębski, Grzegorz Kiełbasa, Oscar Cano, Karol Curila, Luuk Heckman, Jan De Pooter, Milan Chovanec, Nard Rademakers, Wim Huybrechts, Domenico Grieco, Zachary I. Whinnett, Stefan A.J. Timmer, Arif Elvan, Petr Stros, Pawel Moskal, Haran Burri, Francesco Zanon, Kevin Vernooy.

JAGIELLONIAN UNIVERSITY MEDICAL COLLEGE

La Fe Hospital Universitari i Politècnic



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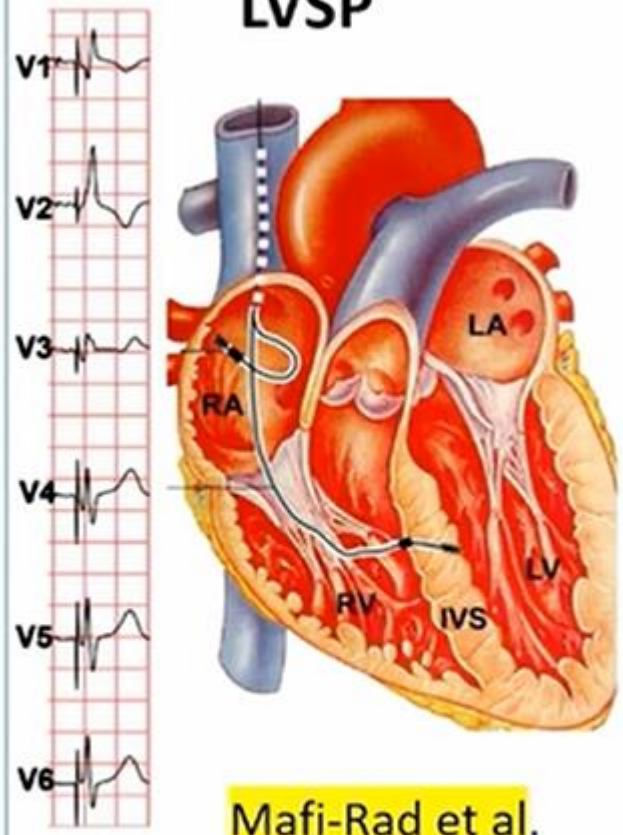
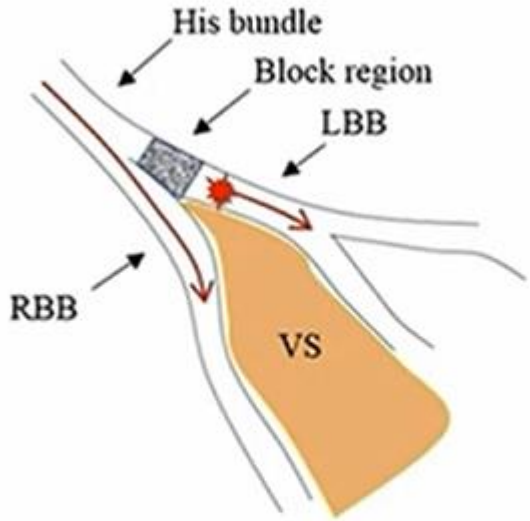
Background

LVSP



Mafi-Rad et al.
Circ AE 2016

LBBP



Huang et al.
Canadian JC 2017

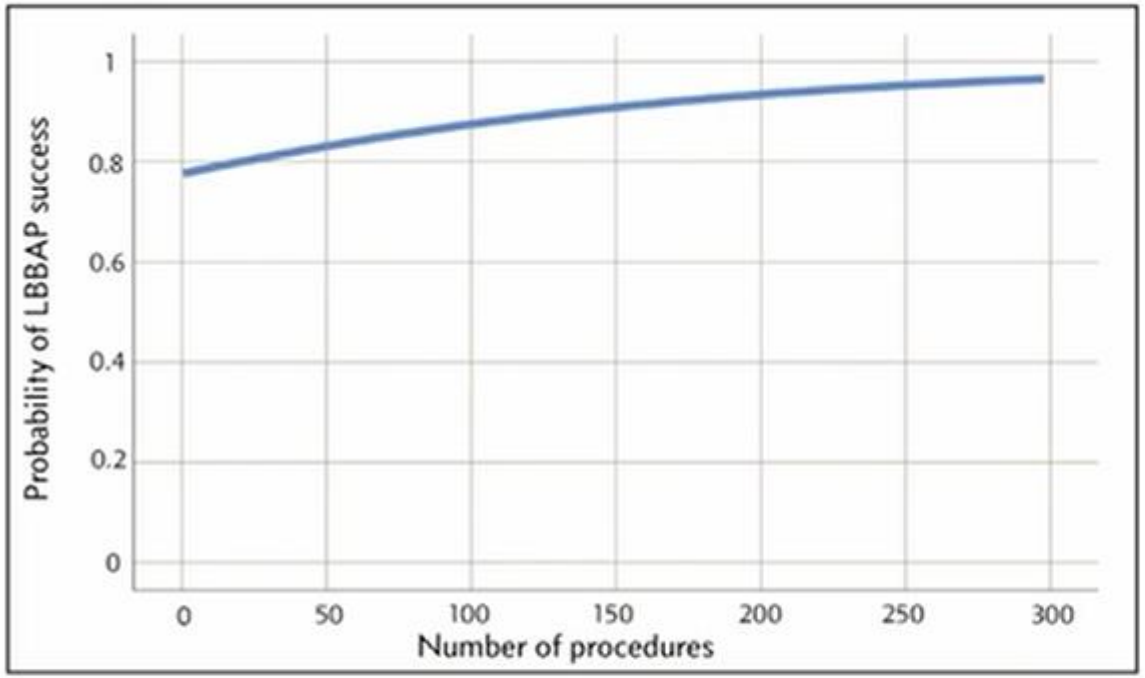
LBBAP

LBBP + LBFP + LVSP

CENTER	Country	First implant	N of patients	N of operators	Registry type
Amsterdam	Netherlands	02 Dec 2019	61	3	mixed
Antwerp	Belgium	04 Feb 2020	89	1	prospective
Eindhoven	Netherlands	08 Jan 2020	100	2	prospective
Geneva	Switzerland	25 Feb 2020	121	2	[illegible]ctive
Gent	Belgium	27 Nov 2019	150	[illegible]	[illegible]
Kraków	Poland	12 Jun 2018	607	[illegible]	[illegible]rospective
London	United Kingdom	23 Nov 2020	67	[illegible]	[illegible]ive
Maastricht	Netherlands	25 Nov 2019	120	2	mixed
Prague 1	Czechia	21 Nov 2019	358	2	prospective
Prague 2	Czechia	28 Apr 2020	114	1	mixed
Rome	Italy	15 Jan 2020	125	1	prospective
Rovigo	Italy	20 May 2019	202	4	mixed
Valencia	Spain	16 Jun 2019	292	1	prospective
Zwolle	Netherlands	12 Dec 2019	127	2	prospective
SUMMARY	14	12 Jun 2018	n = 2533	31	87% prospective

- Mean age: 73.9 y.
- Female: 57.6%
- Heart failure: 27.5%
- LBBB: 22.4%

Feasibility, Success Rate, Learning Curves



- Capture threshold (0.77 V)
- Sensing (10.6 mV)
- Paced QRS 137 - 145 ms
- Paced V_6 RWPT 77 – 83 ms

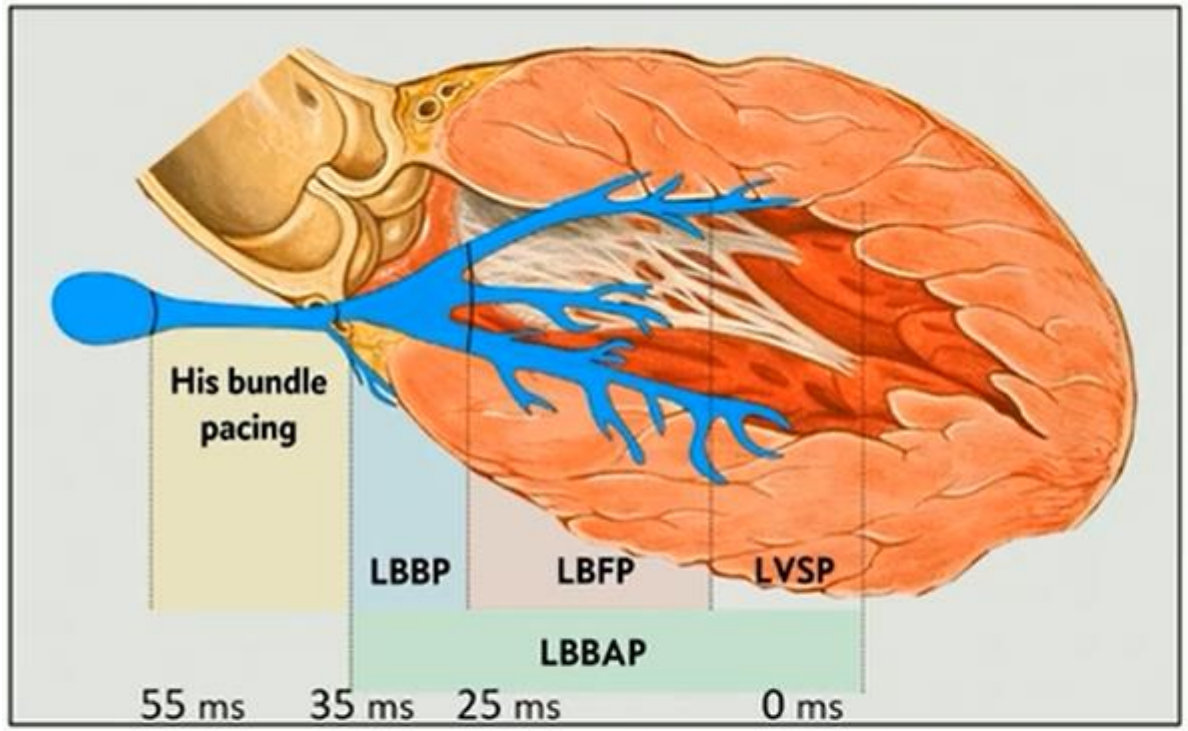
success rate:

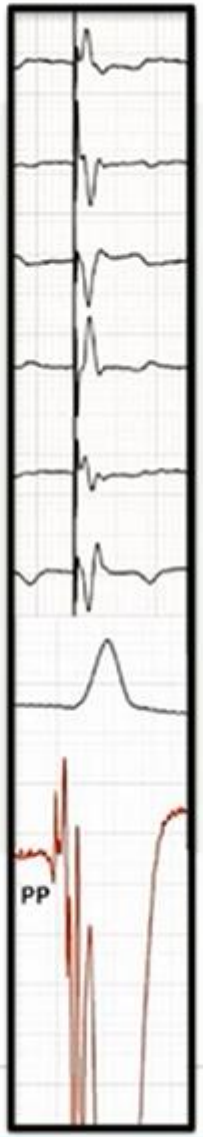
- bradyarrhythmia: **91.6%**
- for heart failure: **76.8%** (n = 383/499)

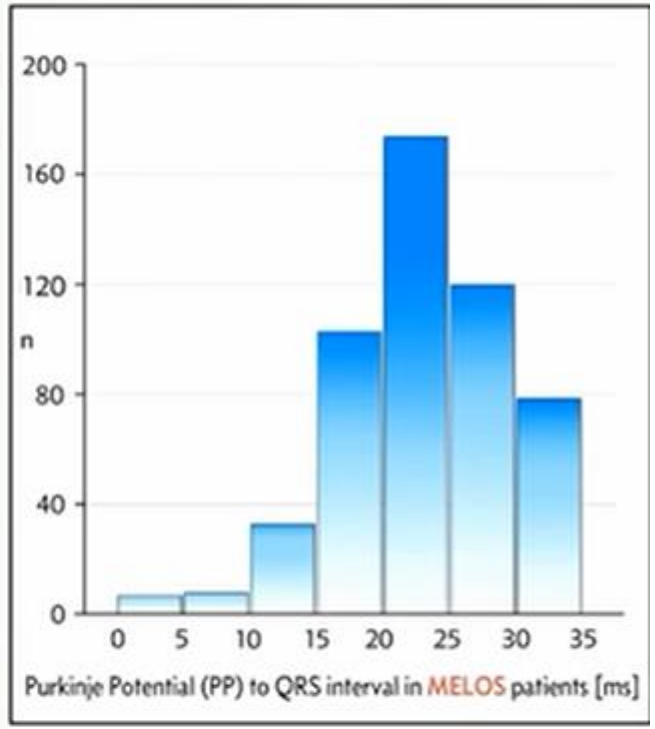
predictors of failure:

- broad baseline QRS
- depressed LVEF
- heart failure

Fascicular pacing is the dominant type







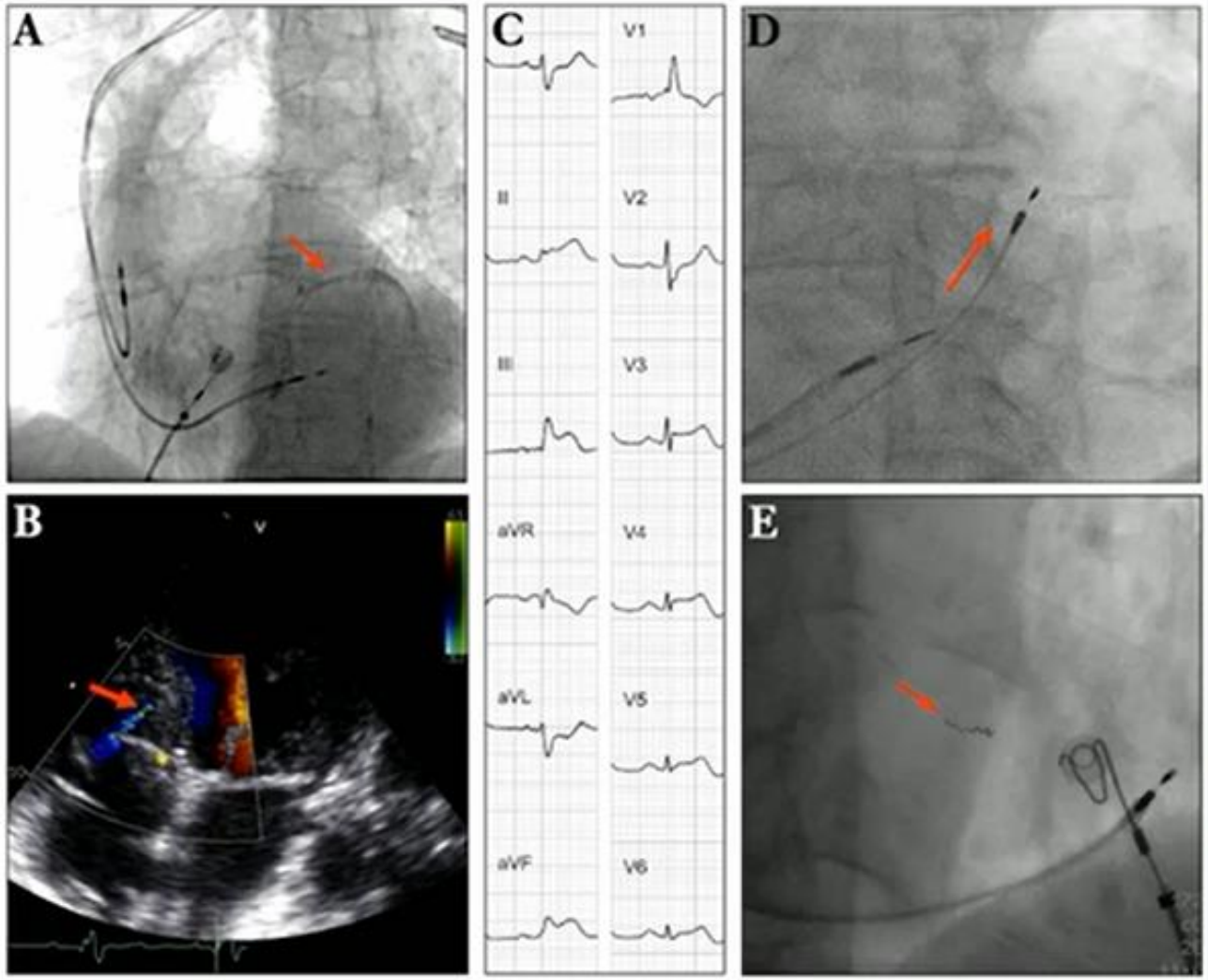
LBBAP capture types:

LBFP (69.5%), **LVSP** (25.1%) and **LBBP** (9%).

Complications

- Intraprocedural IVS perforation - 3.7%
- Delayed IVS perforation - 0.08%
- Acute chest pain - 1%
- ST elevation in multiple leads - 0.24%
- Acute coronary syndrome - 0.43%
- Coronary artery fistula - 0.28%
- LBBAP lead dislodgement - 1.5%
- Threshold > 2 V - 0.67%
- LBBAP lead non-screwable - 0.43%
- Stroke - 0%

TOTAL LBBAP lead related: 8.2%



In review

Majority of complications were resolved without sequelae

CONCLUSIONS

- This is the largest study to date reporting multicentre outcomes of LBBAP
- LBBAP is feasible as a primary pacing technique both for bradyarrhythmia and heart failure indications.
- Success rate in heart failure patients and safety need to be improved.
- This study redefines LBBAP technique from a proximal LBBP to a more straightforward distal left conduction system pacing technique that is to left bundle fascicular pacing and LVSP with fast secondary left conduction system activation.

Venus
of
MELOS

THANK YOU !

RESET CRT

Survival of cardiac resynchronization therapy patients with and without defibrillator
Real-world evidence from the observational part of the RESET-CRT project

Nikolaos Dagres, Moritz Hadwiger, Janina Haug, Michael Wolf, Ursula Marschall, Jan Tijssen, Alexander Katalinic, Fabian-Simon Frielitz, Gerhard Hindricks

Heart Center Leipzig, Germany

3 April 2022

EHRA 2022

Cardiac resynchronization therapy - Is the defibrillator needed?

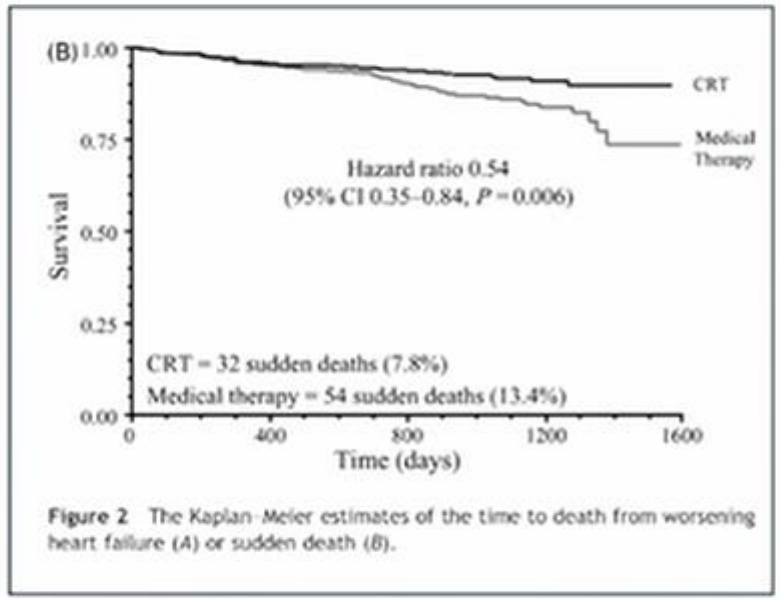
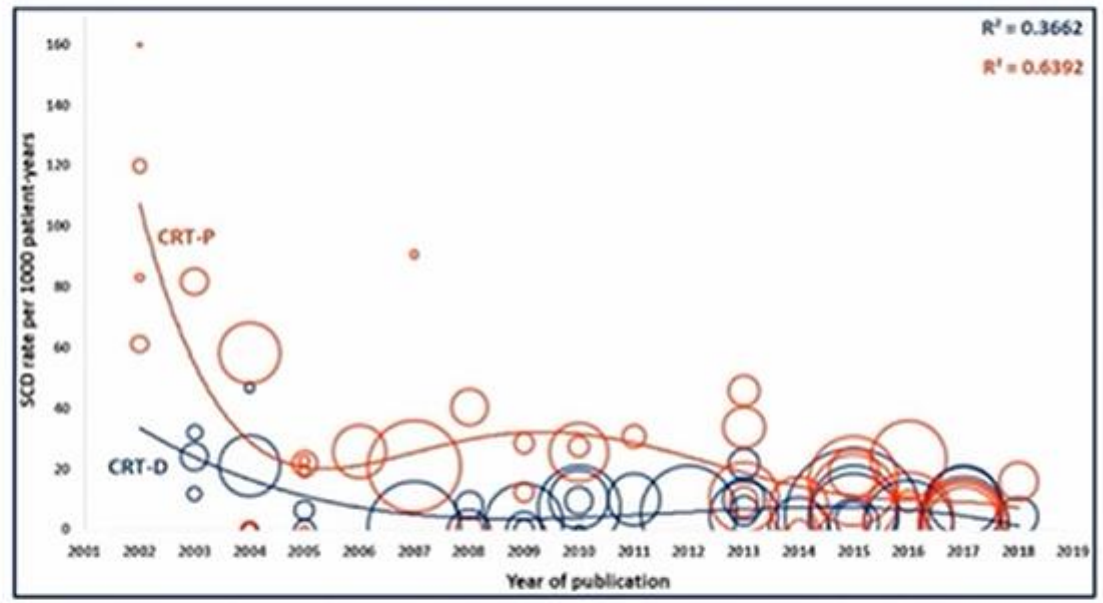


Figure 2 The Kaplan–Meier estimates of the time to death from worsening heart failure (*A*) or sudden death (*B*).

CARE-HF. Cleland et al. Eur Heart J 2006;27:1928-32

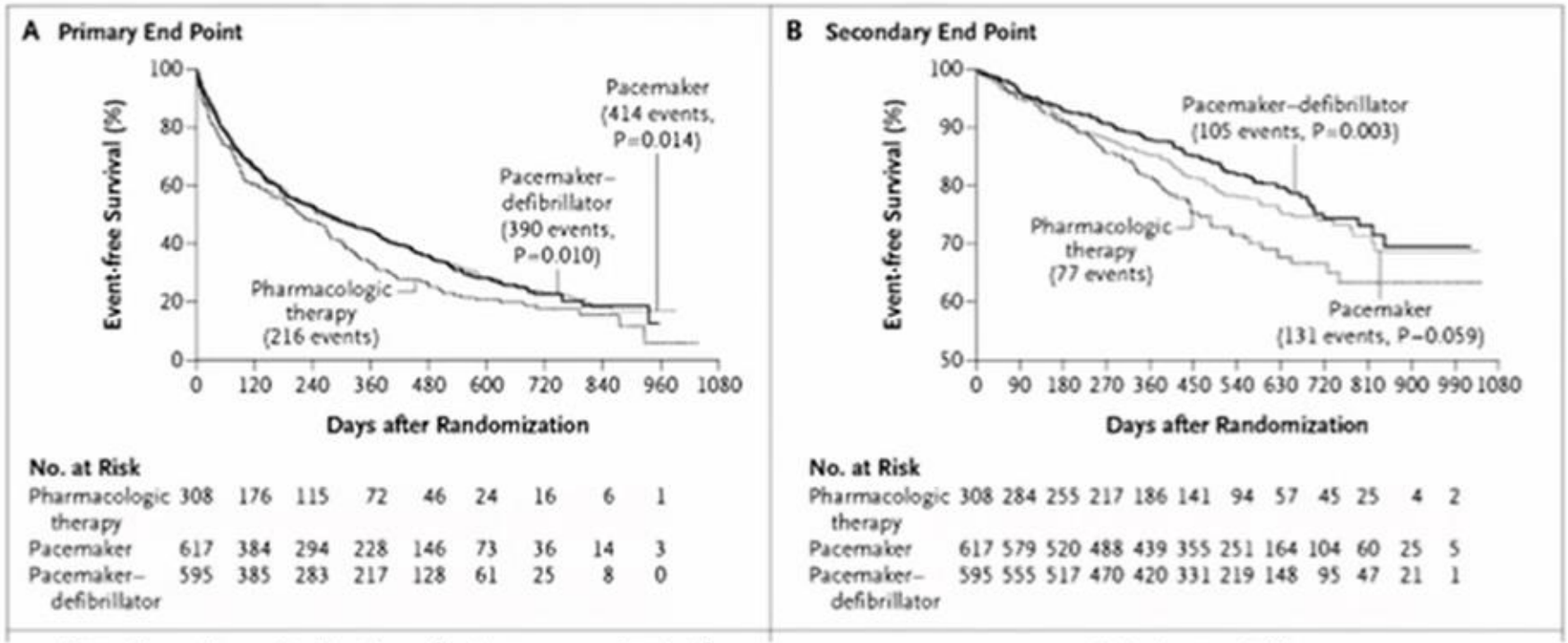


Barra S, et al. Eur Heart J 2020;41:1976-1986

COMPANION

RESET CRT

Conflicting observational data. Randomized evidence?

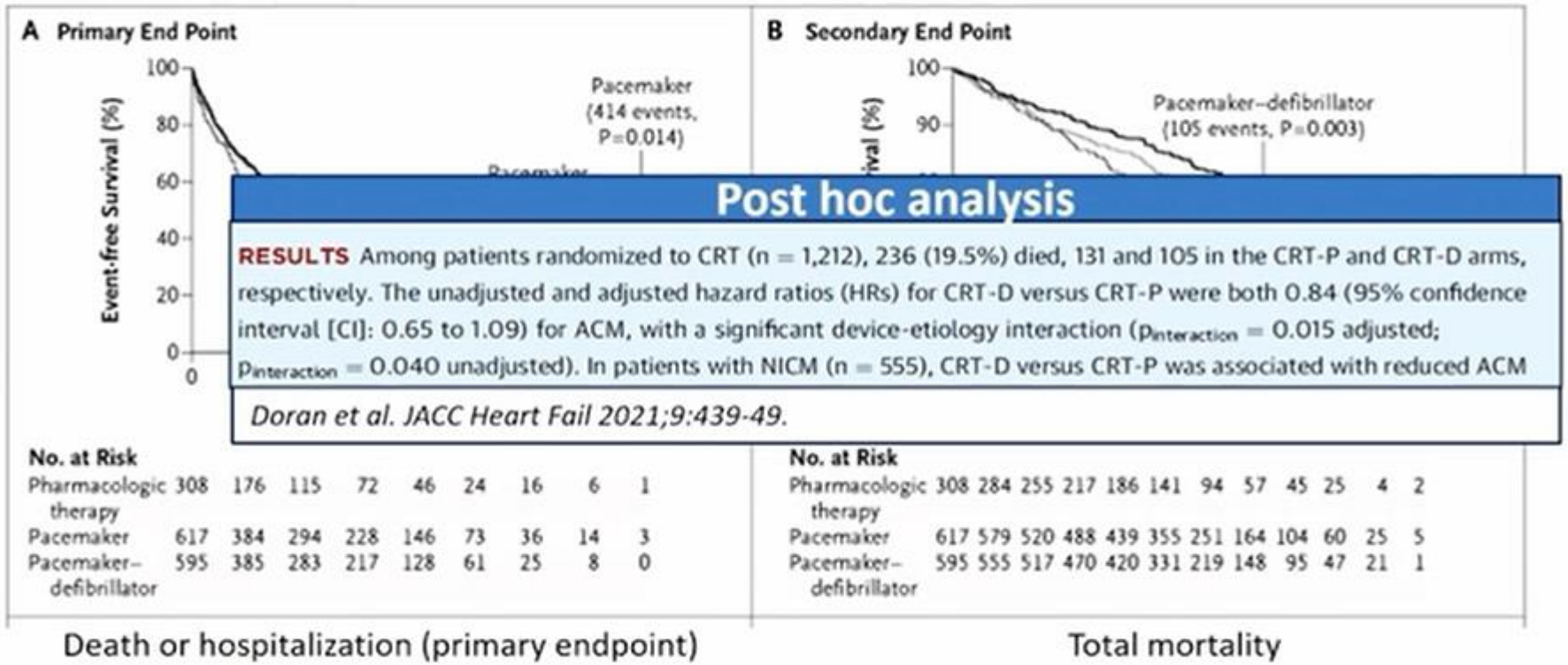


Death or hospitalization (primary endpoint)

Total mortality

Bristow MR et al. N Engl J Med 2004;350:2140-50.

Conflicting observational data. Randomized evidence?



Post hoc analysis

RESULTS Among patients randomized to CRT (n = 1,212), 236 (19.5%) died, 131 and 105 in the CRT-P and CRT-D arms, respectively. The unadjusted and adjusted hazard ratios (HRs) for CRT-D versus CRT-P were both 0.84 (95% confidence interval [CI]: 0.65 to 1.09) for ACM, with a significant device-etiology interaction ($p_{interaction}$ = 0.015 adjusted; $p_{interaction}$ = 0.040 unadjusted). In patients with NICM (n = 555), CRT-D versus CRT-P was associated with reduced ACM

Doran et al. JACC Heart Fail 2021;9:439-49.

Bristow MR et al. N Engl J Med 2004;350:2140-50.

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 SEPTEMBER 29, 2016 VOL. 375 NO. 13

Defibrillator Implantation in Patients with Nonischemic Systolic Heart Failure

Lars Køber, M.D., D.M.Sc., Jens J. Thune, M.D., Ph.D., Jens C. Nielsen, M.D., D.M.Sc., Jens Haarbo, M.D., D.M.Sc., Lars Videbæk, M.D., Ph.D., Eva Korup, M.D., Ph.D., Gunnar Jensen, M.D., Ph.D., Per Hildebrandt, M.D., D.M.Sc., Flemming H. Steffensen, M.D., Niels E. Bruun, M.D., D.M.Sc., Hans Eiskjær, M.D., D.M.Sc., Axel Brandes, M.D., Anna M. Thøgersen, M.D., Ph.D., Finn Gustafsson, M.D., D.M.Sc., Kenneth Egstrup, M.D., D.M.Sc., Regitze Videbæk, M.D., Christian Hassager, M.D., D.M.Sc., Jesper H. Svendsen, M.D., D.M.Sc., Dan E. Høfsten, M.D., Ph.D., Christian Torp-Pedersen, M.D., D.M.Sc., and Steen Pehrson, M.D., D.M.Sc., for the DANISH Investigators*

The DANISH Study – inclusion criteria

- Clinical heart failure
- Documented non-ischaemic aetiology
- Optimal medical treatment
- NYHA functional class II and III (class IV if planned CRT)
- Left ventricular ejection fraction ≤35%[1]
- NT-proBNP >200 pg/ml (23.6 pmol/l)[1]

[1]measured after maximum achievable drug target levels, which were the guideline-specified levels whenever possible

Køber L, et al. *N Engl J Med* 2016;375:1221-30

RESET CRT

Conflicting observational data. Randomized evidence?

CRT Subgroup of the DANISH trial

Subgroup	ICD Group	Control Group	Hazard Ratio (95% CI)	P Value	P Value for Interaction
	no. of events/total no.				
CRT					0.73
No	58/234	65/237	0.83 (0.58–1.19)	0.31	
Yes	62/322	66/323	0.91 (0.64–1.29)	0.59	

Kober L et al. N Engl J Med 2016;375:1221-30.

What do the guidelines say?

6.6 Benefit of adding implantable cardioverter defibrillator in patients with indications for cardiac resynchronization therapy

The mortality benefit of CRT-D over CRT-P is still unclear, mostly because no head to head RCTs have been designed to compare these two treatments. While CRT-D may further improve survival

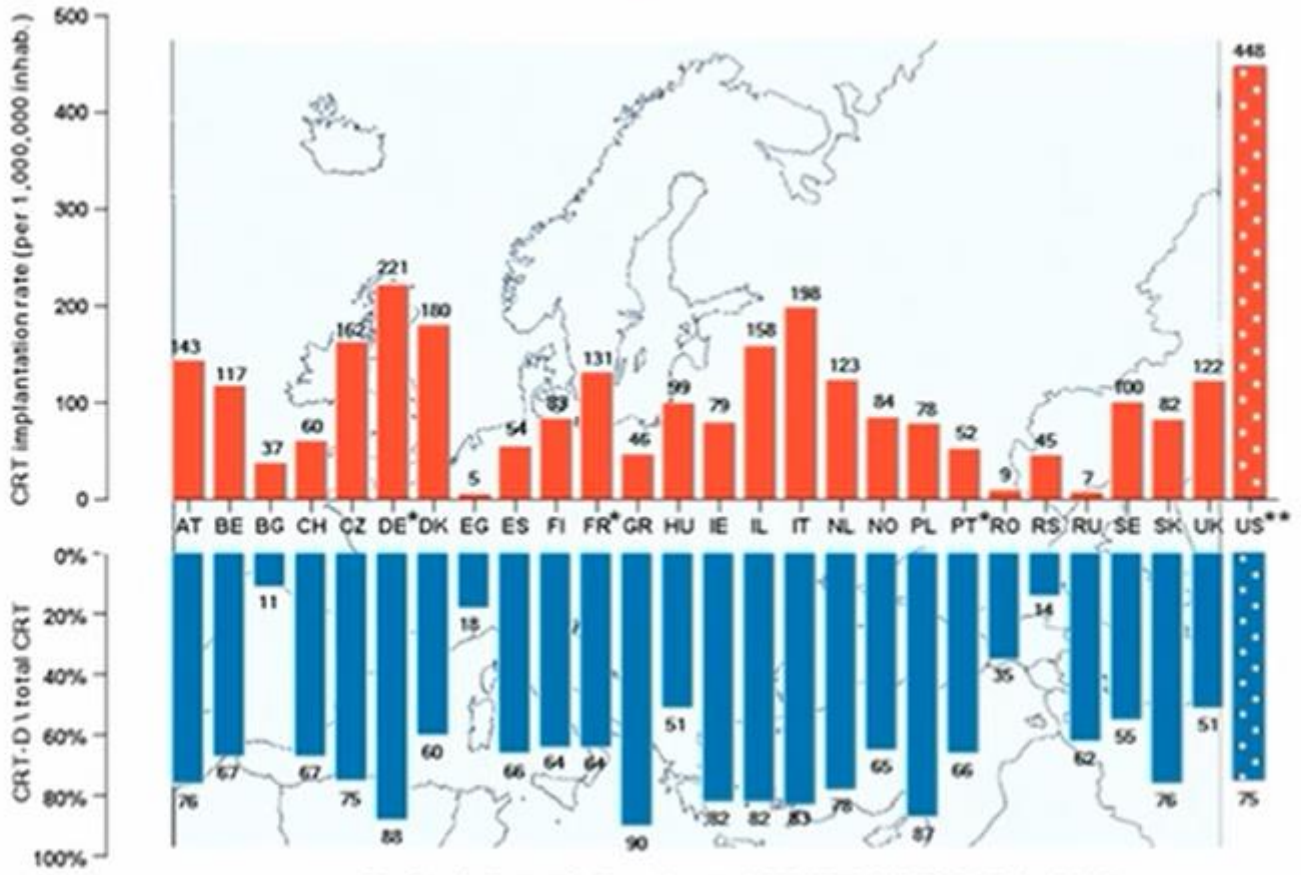
In conclusion, prospective randomized trials are lacking, and available data are insufficient to firmly prove a superiority of CRT-D over CRT-P. However, it is important to consider that CRT trials in mild

2021 ESC Pacing guidelines

and 149 ms and is recommended if QRS is ≥150 ms. However, clinical practice varies widely among countries and if the primary reason for implanting CRT is for the relief of symptoms, then the clinician should choose CRT-P or CRT-D, whichever they consider appropriate. The only randomized trial to compare CRT-P and CRT-D[210] did not demonstrate a difference in morbidity or mortality between these technologies (although the trial was not powered to show such a difference). Furthermore, in the DANISH study in patients with NICM where 58% of patients received CRT there was no suggestion from subgroup analysis that CRT-P was inferior to CRT-D.[166,167]

2021 ESC Heart failure guidelines

Clinical practice



Boriani G et al. Eur Heart J 2017;38(27):2129-2131

RESET CRT

RESET-CRT: Publicly funded head-to-head CRT-D / CRT-P comparison

Key question

- Is the defibrillator needed in patients receiving CRT?

Aim

- Compare survival between CRT-D and CRT-P in patients with CRT indication

Two parts

- Randomized clinical trial (NCT number 03494933)
- **Observational part**

Funded by the Innovation Committee of the Federal Joint Committee (G-BA) (highest decision-making body of the joint self-government of physicians, dentists, hospitals and health insurance funds in Germany). Funding code 01VSF17050.

RESET CRT

Observational part of the RESET-CRT project

- Conducted in parallel with the ongoing RESET-CRT randomized trial.

Aim

- Compare survival of patients receiving CRT-P or CRT-D in health claims data of the second largest German statutory health insurance (BARMER)

Study Design

- Mimicking the RESET-CRT randomized trial:
  application of the same inclusion-exclusion criteria
  entropy balancing to control for baseline imbalances
- Retrospective, non-experimental, population-based weighted cohort study design

RESET CRT

Observational part of the RESET-CRT project

Study Population

- Patients with de novo CRT implantation between 2014 and 2019
- ***Key Inclusion Criteria***

  Symptomatic chronic heart failure as indication for CRT
- ***Key Exclusion Criteria***

  Class I or IIa indication for ICD implantation for secondary prevention
  Previous pacemaker, defibrillator or CRT implantation

RESET CRT

Observational part of the RESET-CRT project

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  Symptomatic chronic heart failure as indication for CRT
- ***Key Exclusion Criteria***

  Class I or IIa indication for ICD implantation for secondary prevention
  Previous pacemaker, defibrillator or CRT implantation

Outcome

- All-cause death

RESET CRT

Observational part of the RESET-CRT project: Study Population

7110 patients recorded with CRT implantations between 2014-2019

7082 patients having information on demographics

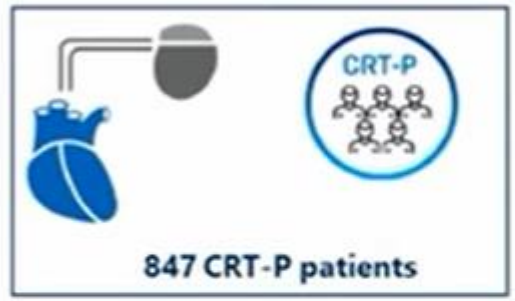
Violation of inclusion criteria
- I1) Age<18: 3
- I2) No ICD code for symptomatic heart failure: 612

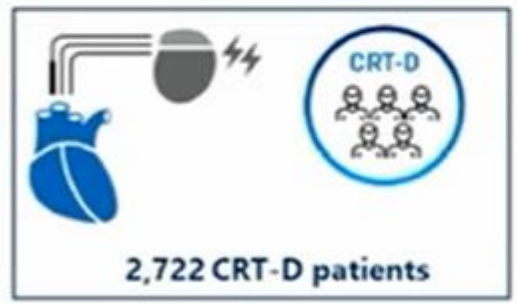
Satisfaction of the exclusion criteria
- E1) Class I or IIa indication for implantation of an ICD for secondary prevention:1144
- E2) No de novo implantation: 596
- E3) Unexplained syncope: 477
- E4) Hospitalized with unstable heart failure with NYHA class IV: 43
- E5) Acute coronary syndrome or cardiac revascularization therapy: 738
- E6) Cardiac valve surgery or percutaneous cardiac valvular intervention: 182
- E7) On the waiting list for heart transplant: 2
- E8) Severe chronic renal disease: 125
- E9) No information about NYHA class prior to implantation: 321
- E10) Less than three years continuous insurance before implantation: 104
- E11) Less than three months follow-up and not died: 56
- E12) Ambiguous information about NYHA class prior to implantation: 141

3569 eligible patients

2722 CRT-D
- 511 all cause death
- 2180 censored (end of follow-up)
- 31 censored (other reasons)

847 CRT-P
- 203 all cause death
- 639 censored (end of follow-up)
- 5 censored (other reasons)





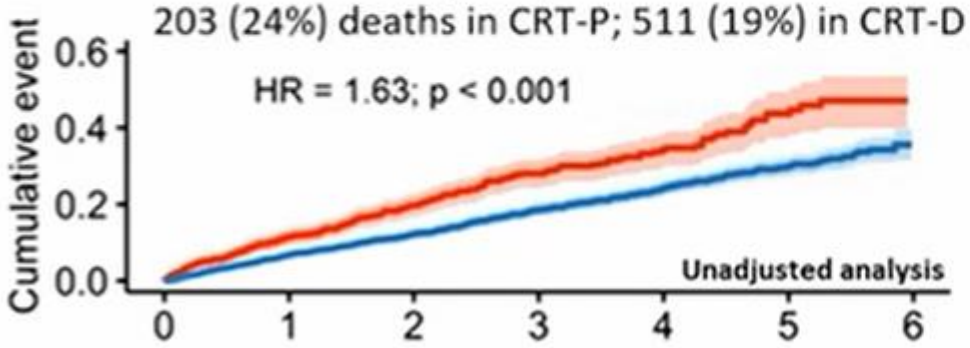
Baseline characteristics

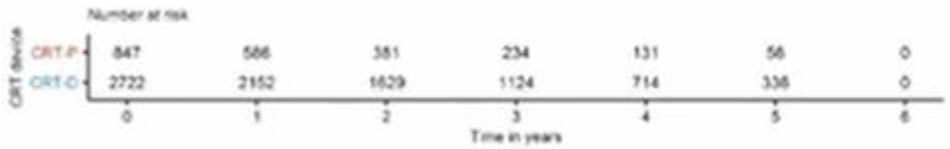
	CRT-P (n=847)	CRT-D (n=2,722)
Age (years), mean (SD)	**76.7 (8.9)**	**69.9 (9.6)**
Male sex, n (%)	440 (52)	1,768 (65)
Non-ischemic, n (%)	225 (27)	678 (25)
Number of hospitalisations one year prior to implantation, n (%)		
0	40 (5)	121 (4)
1	274 (32)	846 (31)
2	222 (26)	868 (32)
>2	311 (37)	887 (33)
NYHA class, n (%)		
II	131 (15)	420 (15)
III	548 (65)	1,712 (63)
IV	168 (20)	590 (22)
Heart failure specific comorbidities		
Diabetes, n (%)	272 (32)	982 (36)
Renal dysfunction III, n (%)	300 (35)	749 (28)
Renal dysfunction IV, n (%)	58 (7)	112 (4)
Atrial fibrillation, n (%)	497 (59)	1,105 (41)

RESET CRT

All-cause death

Median follow-up 2.4 years:
203 (24%) deaths in CRT-P; 511 (19%) in CRT-D





CRT device — CRT-P — CRT-D
HR = Hazard Ratio
CRT-P = Biventricular pacemaker
CRT-D = Biventricular defibrillator

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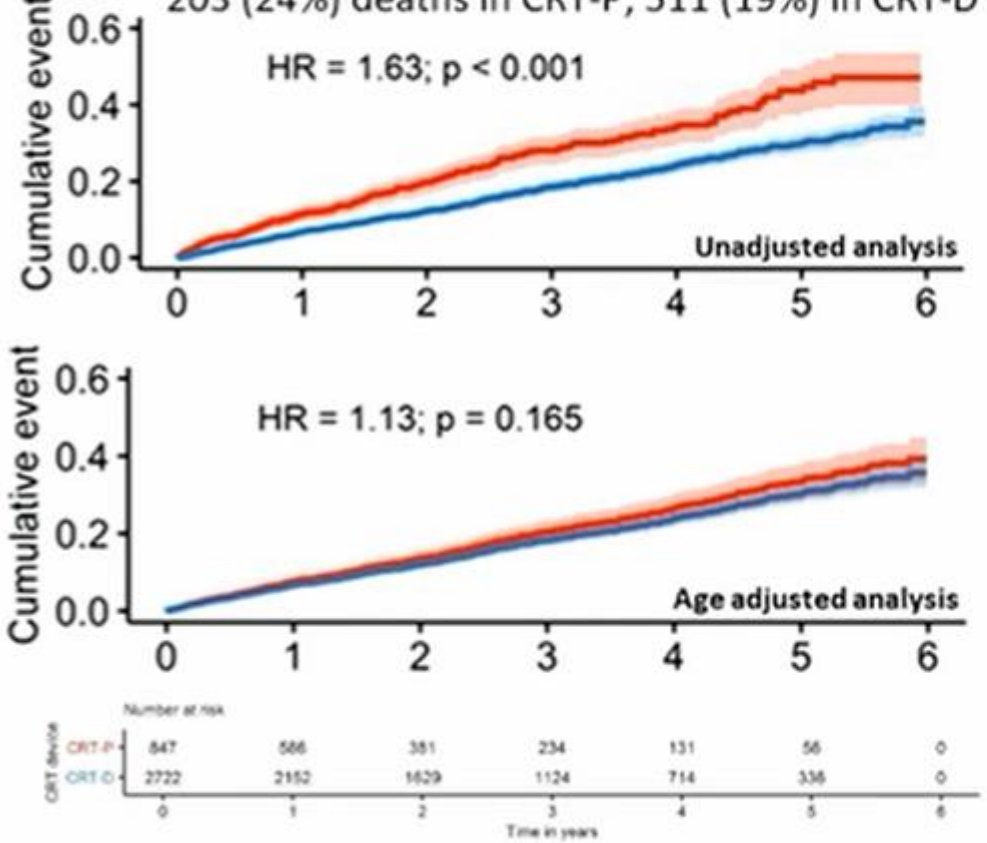

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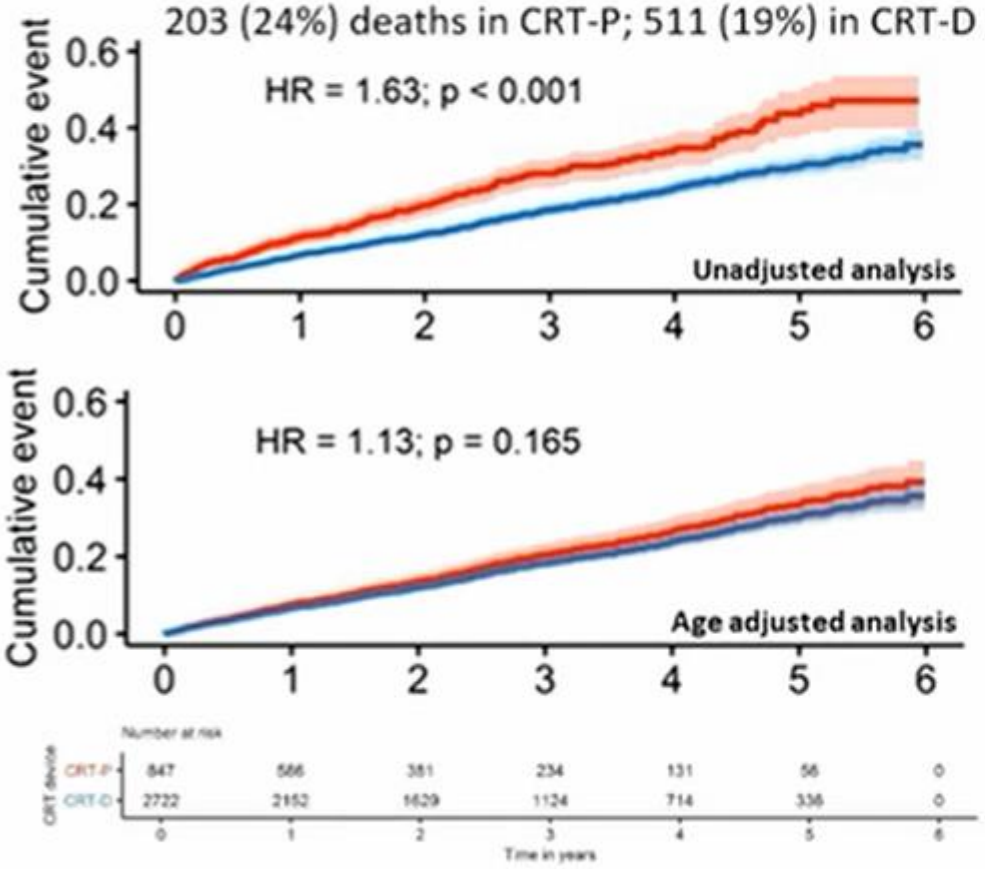
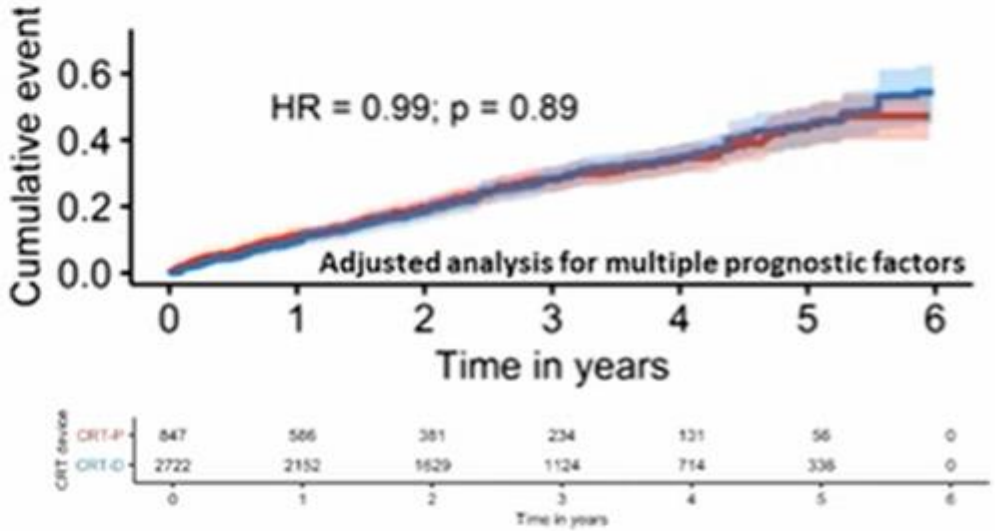


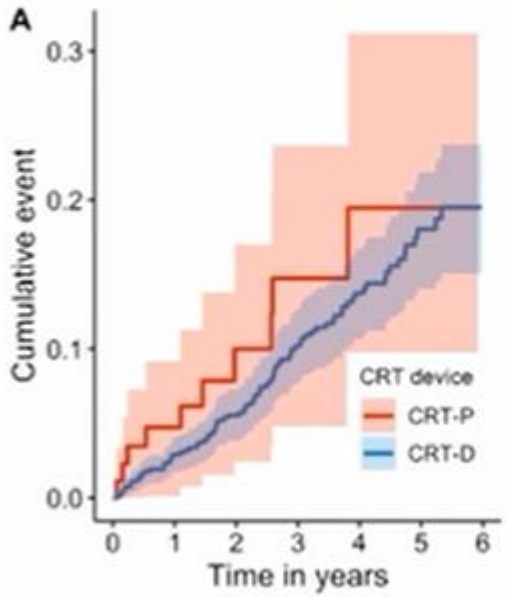


CRT device — CRT-P — CRT-D
HR = Hazard Ratio
CRT-P = Biventricular pacemaker
CRT-D = Biventricular defibrillator

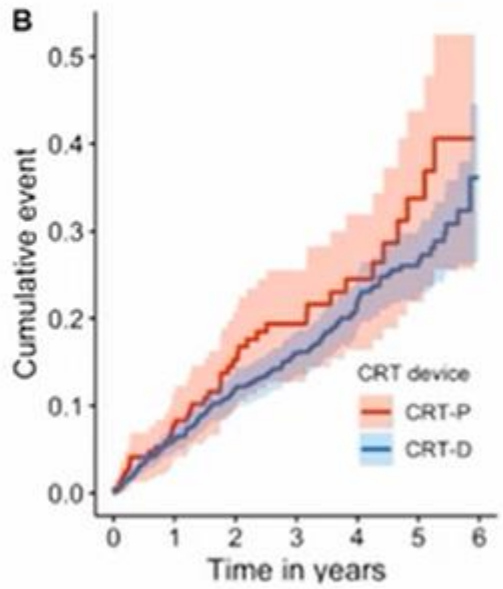
RESET CRT

Survival in age groups

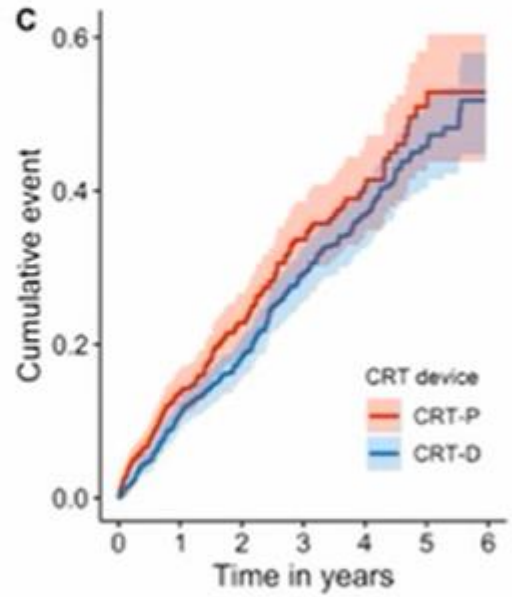
≤65 years



65-75 years



>75 years



Conclusions

- Age differences accounted for the greatest part of the observed survival difference
- After adjustment for age and entropy balancing **no survival difference between CRT-D and CRT-P**
- Results corroborate the hypothesis of the RESET-CRT randomized clinical trial that will provide randomized head-to-head comparison

Published today online at the European Heart Journal