# Patient selection for ICD and CRT

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Stockholm

Sweden

**11 mill inhabitants**
**Public health care**
**7 university hospitals**


Cecilia Linde  Karolinska Institutet  Karolinska University Hospital

# Disclosure Cecilia Linde

Nothing to declare

# CRT in patients with HFrEF and wide QRS /LBBB

**Disease modifying and life-saving**

- Improves survival
- Reduces heart failure hospitalisations
- Through reverse remodelling

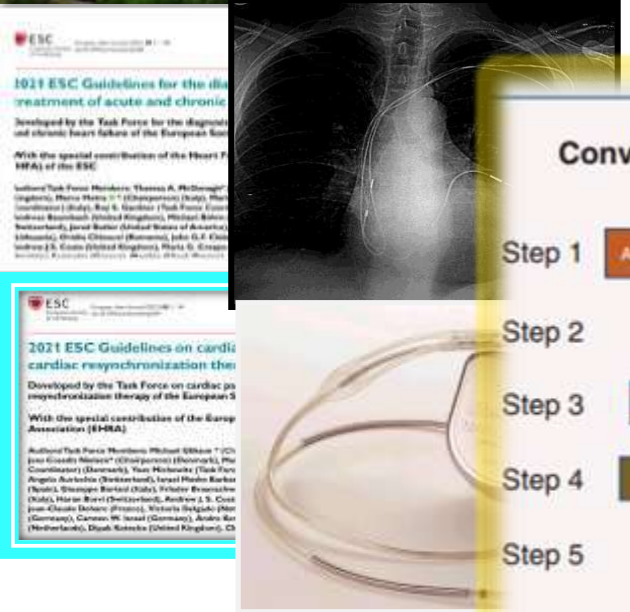
**Improves symptoms**

- And exercise tolerance, quality of life

*Applicable in 20% of HFrEF-patients in NYHA II-IV*

***but only about 1 in 5 gets therapy***

# What do the 2021 ESC HF guidelines say?



Management of patients with HFrEF

- ACE-I/ARNI
- Beta-blocker
- MRA
- Dapagliflozin/Empagliflozin

**Conventional Sequencing**

Step 1 — ACE inhibitor or angiotensin receptor blocker

Step 2 — Beta-blocker

Step 3 — Mineralocorticoid receptor antagonist

Step 4 — Angiotensin receptor neprilysin inhibitor

Step 5 — SGLT2 inhibitor

*Uptitration to target doses at each step*
*Typically requires 6 months or more*

**Rapid Sequencing**

Step 1 — Beta-blocker + SGLT2 inhibitor

Step 2 — Angiotensin receptor neprilysin inhibitor

Step 3 — Mineralocorticoid receptor antagonist

*All 3 steps achieved within 4 weeks*
*Uptitration to target doses thereafter*

SR and LVEF ≤35% and QRS ≥130 ms

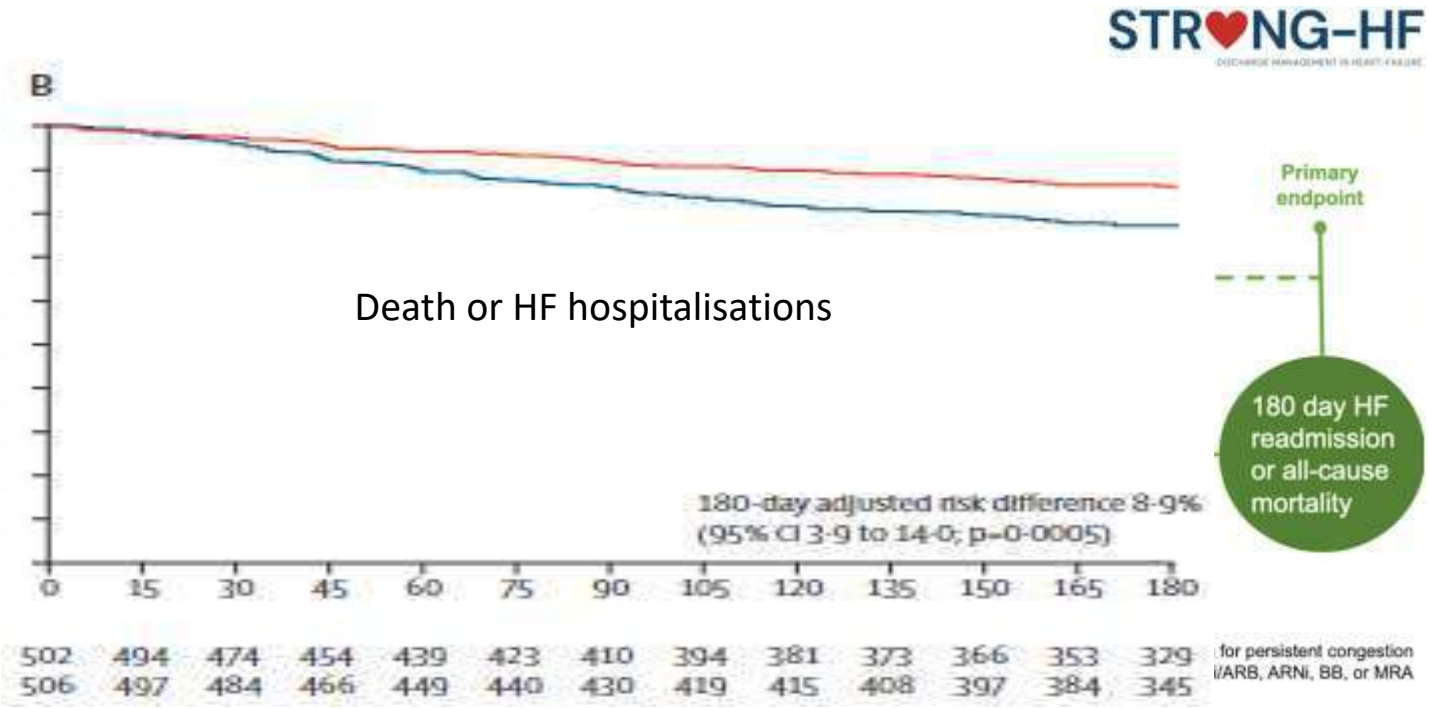
CRT-D[b]/-P

130-149 ms QRS ≥150 ms
(Class IIa) (Class I)

ESC

***All* disease modifying therapies need to be introduced rapidly to obtain the best results and modify heart failure**

# Heart failure medication needs to be introduced rapidly




https://www.cfrjournal.com/video-index/aha-22-late-breaker-discussion-strong-hf-trial

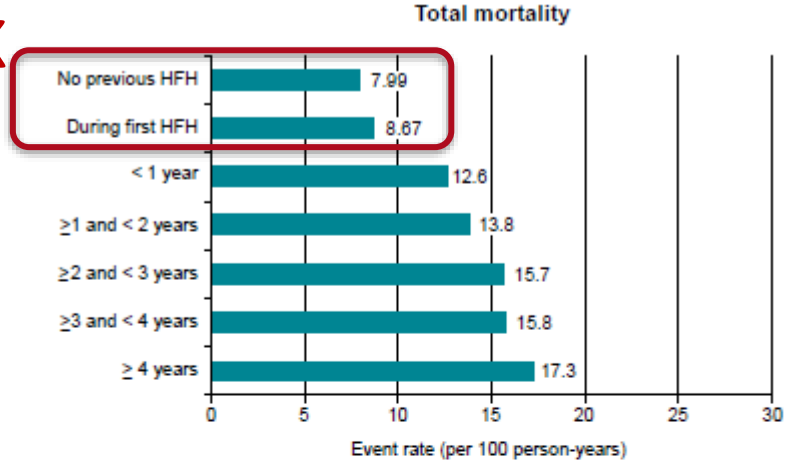
# Timing of CRT implantation in UK

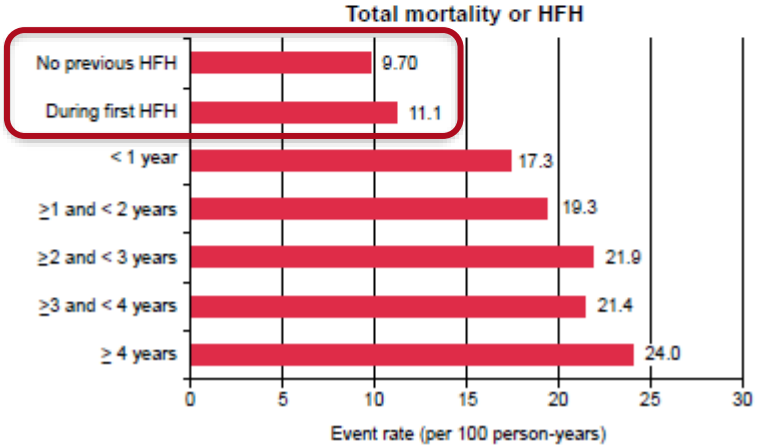
ESC European Society of Cardiology
Europace (2023) 00, 1–10
https://doi.org/10.1093/europace/euad059
CLINICAL RESEARCH

## Timing of cardiac resynchronization therapy implantation

Francisco Leyva [1]*, Abbasin Zegard [1,2], Peysh Patel [2], Berthold Stegemann [1,2], Howard Marshall [2], Peter Ludman [2], Jamie Walton [2], Joseph de Bono [2], Giuseppe Boriani [3], and Tian Qiu [2]

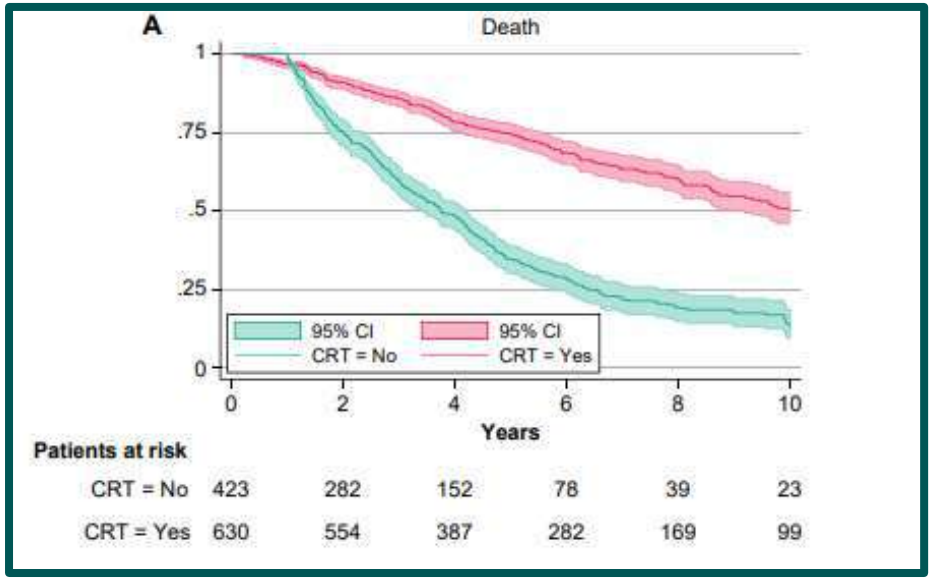


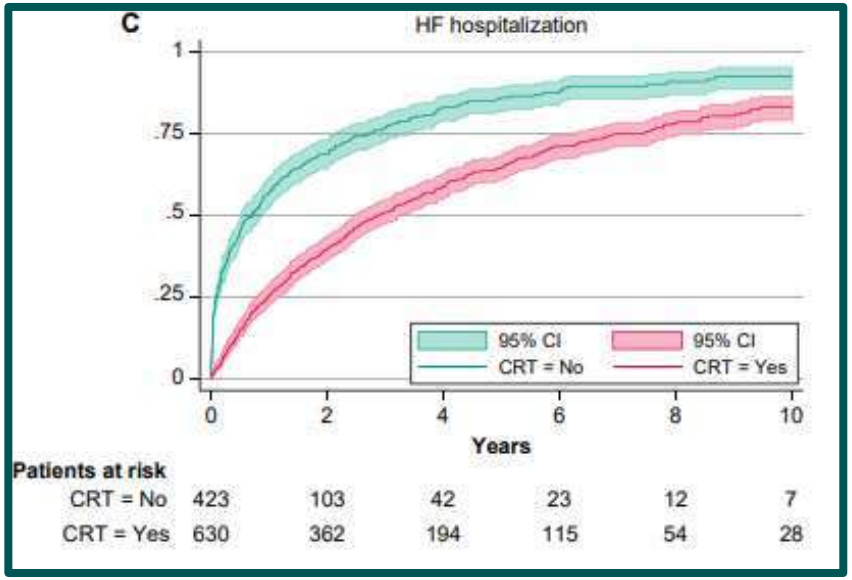



***Best outcome if CRT was implanted early in a British nationwide registry***

# The outcome of LBBB patients with HF in Stockholm who received CRT vs those who did not




*Delay time* ***from CRT*** *implantation from indication* (**LBBB on ECG** ) was 137 (35–378) days or **4.5 months**.

*Delay was associated with higher mortality and more HF hospitalizations*



*Gatti P et al Europace (2023) 25, 1–12*

# Patient selection for CRT

# Recommendations for cardiac resynchronization therapy in patients in sinus rhythm (1)

And left bundle branch block LBBB

| Recommendations | Class | Level |
|---|---|---|
| **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. | 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. | IIa | B |

CRT = cardiac resynchronization therapy; HF = heart failure; LBBB = left bundle branch block; LVEF = left ventricular ejection fraction; OMT = optimal medical therapy; SR = sinus rhythm.





2021 ESC Guidelines on cardiac pacing and cardiac resynchronization therapy
(European Heart Journal 2021 – doi:10.1093/eurheartj/ehab364)

# QRS Width and Bundle branch block morphology

- QRS width was the inclusion criteria in RCT
- 65% in RCT had LBBB!
- 10% had RBBB meaning little evidence in RCTs
- 25% intraventricular conduction disturbance

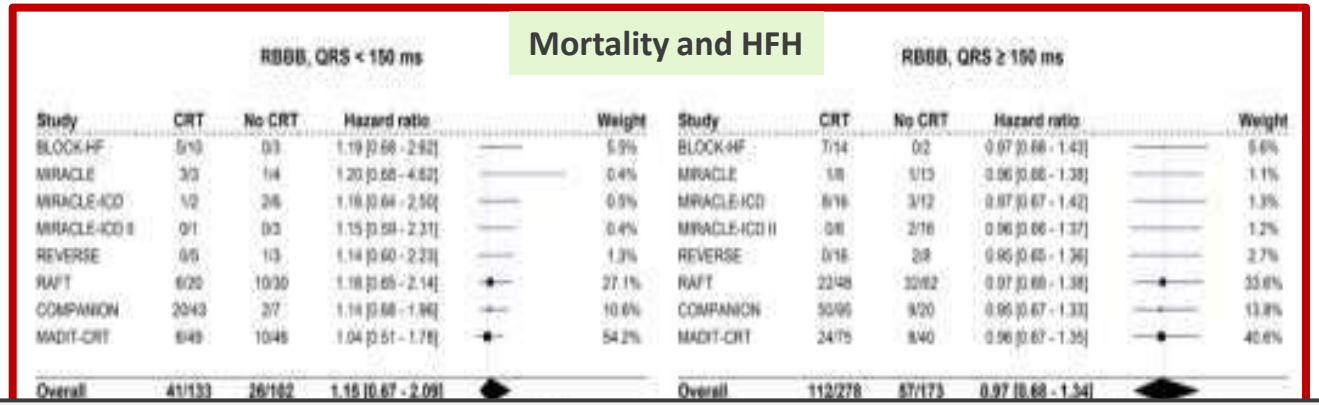
- Only 20-25% in trials were women

***When there are few patients in each randomised trials***

***- look for meta-analysis***

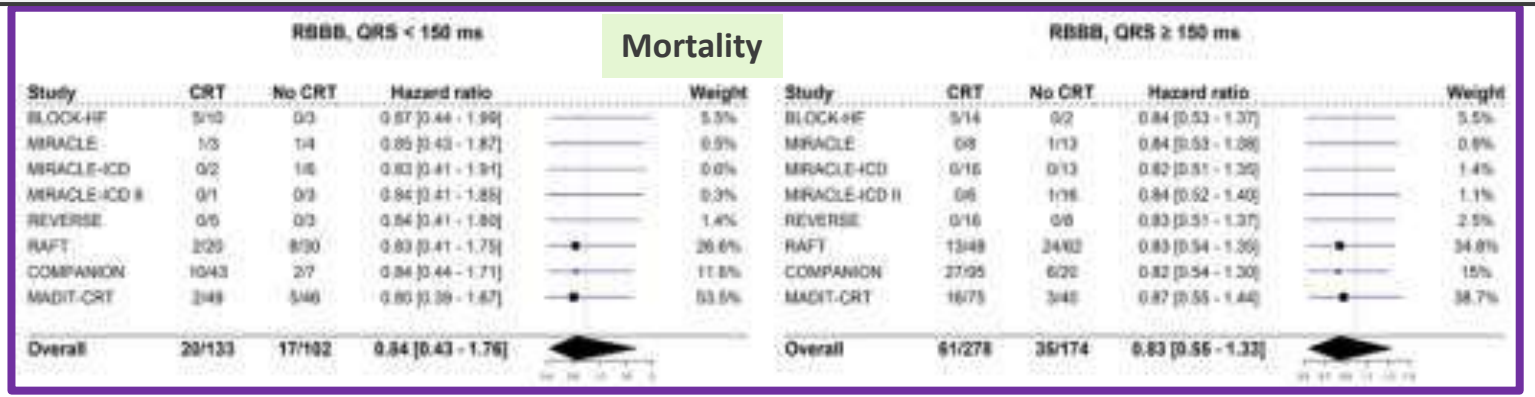
# Is CRT beneficial in RBBB -Individual patient based meta-analysis of 8 randomized trials

*Friedman D et al Circulation. 2023;147:812–823.*




LBBB n=4549
IVCD n=1024
RBBB n=691

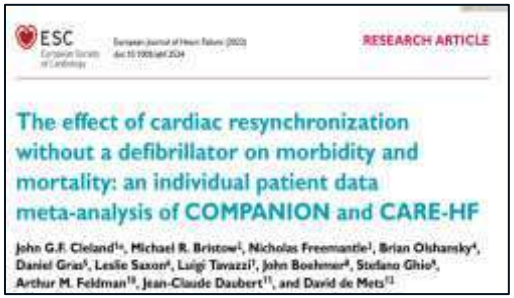
## *Meta-analysis shows no benefit of CRT in RBBB*



# Women and CRT

Do women respond better to CRT?

Why? female sex or the smaller body size?



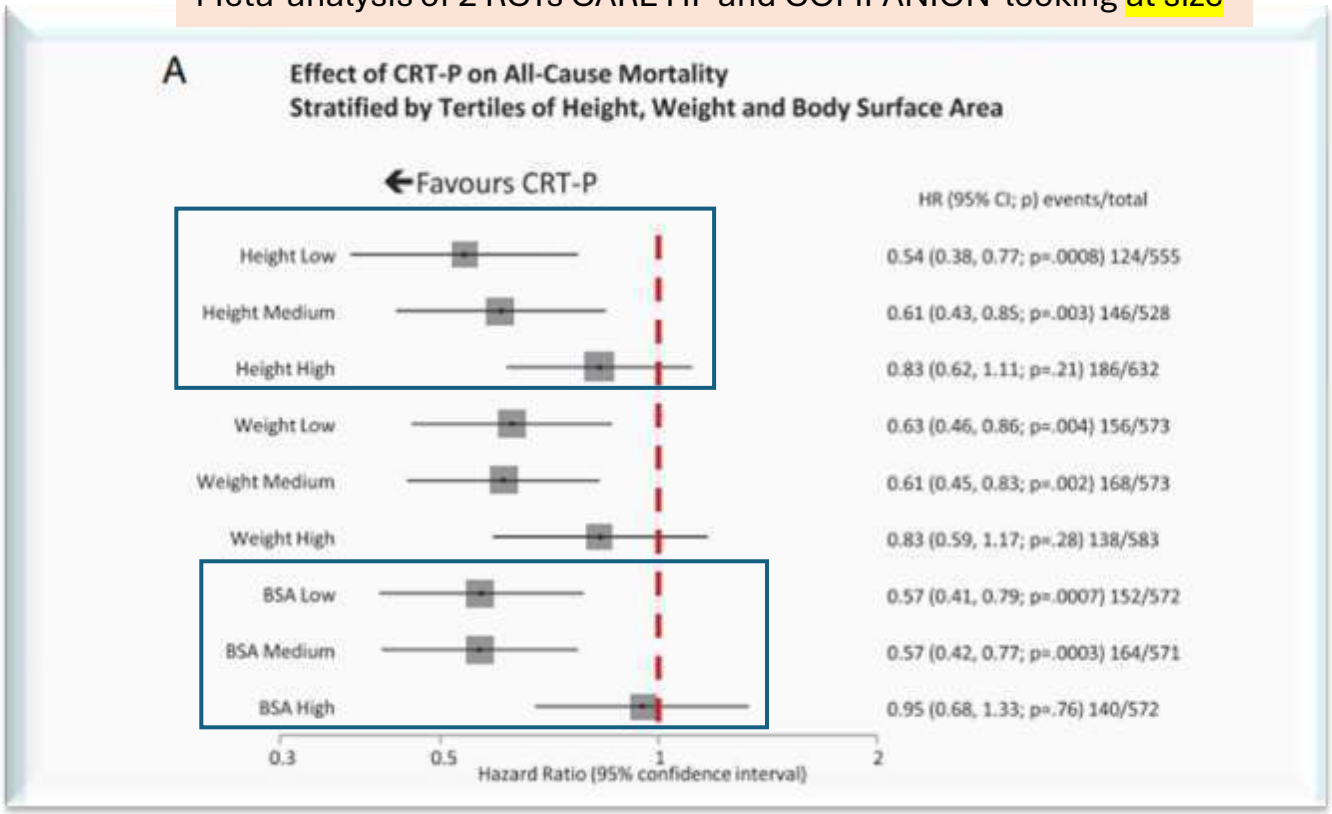
ESC

RESEARCH ARTICLE

The effect of cardiac resynchronization without a defibrillator on morbidity and mortality: an individual patient data meta-analysis of COMPANION and CARE-HF

John G.F. Cleland[1*], Michael R. Bristow[2], Nicholas Freemantle[3], Brian Olshansky[4], Daniel Gras[5], Leslie Saxon[6], Luigi Tavazzi[7], John Boehmer[8], Stefano Ghio[9], Arthur M. Feldman[10], Jean-Claude Daubert[11], and David de Mets[12]

Meta-analysis of 2 RCTs CARE HF and COMPANION looking at size




**In COMPANION and CARE HF smaller people (who are often women) derived greater CRT benefit**

Results of individual patient based Meta-analysis of 7 RCTs comparing CRT to no CRT

MIRACLE, MIRACLE-ICD, MIRACLE-ICD II, REVERSE, RAFT, COMPANION, and MADIT-CRT

Looking at size and sex

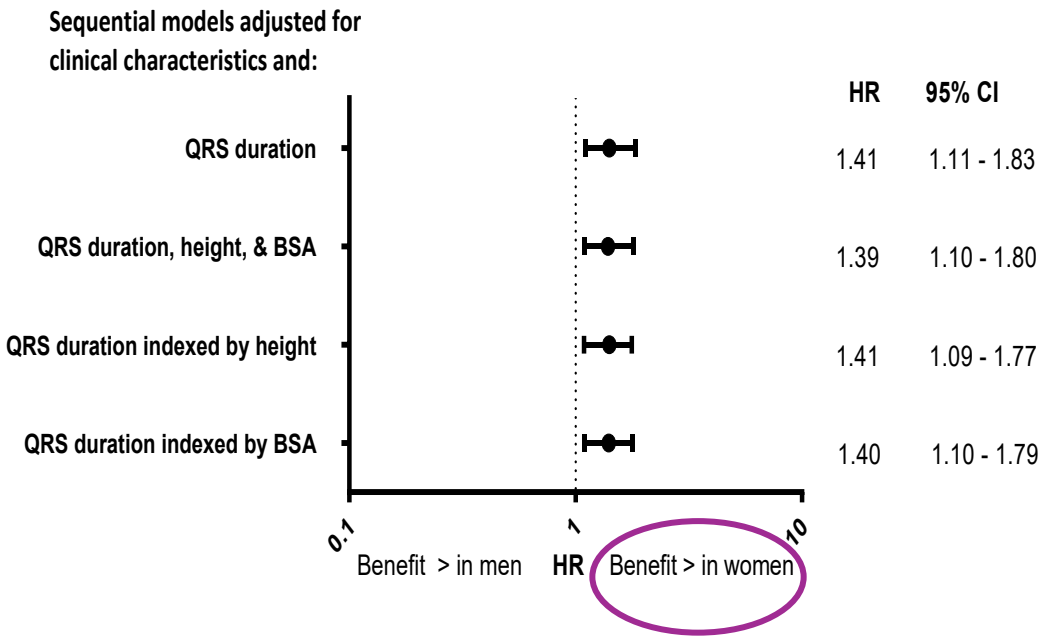
. 2024 Jun;21(6):845-854

# Women have similar QRS durations compared with men despite smaller bodies

| | Women (N=1,439) | Men (N=4,189) |
|---|---|---|
| QRS, ms | 160 (146, 172) | 160 (140, 175) |
| BSA, $m^2$ | 1.76 (1.62, 1.90) | 2.02 (1.89, 2.16) |
| Height, m | 1.62 (1.57, 1.65) | 1.75 (1.70, 1.80) |

Friedman DJ et al Heart Rhythm 2024

# *Greater CRT benefit in women than men independent of body size*




Friedman DJ et al Heart Rhythm 2024

# Response rates and CRT

**30-40% said not to respond to CRT**

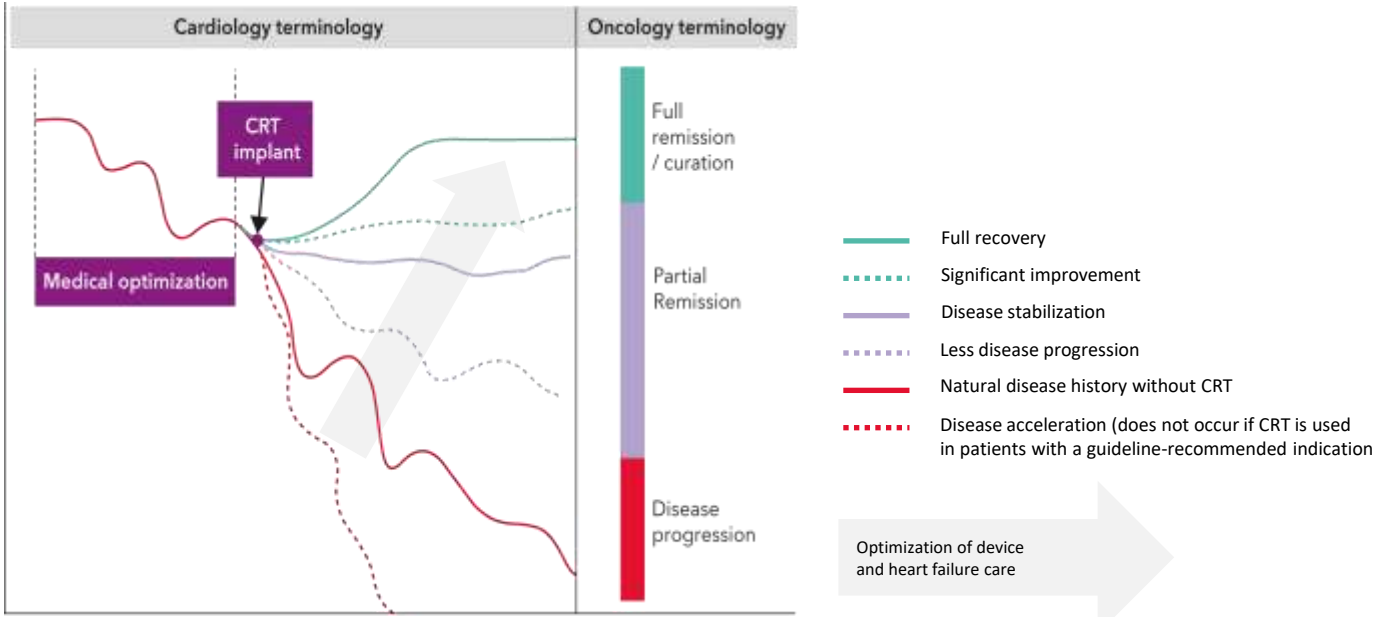
**What does respond mean?**

***Improved, stabilised or worsened***

**based on**

- **NYHA class, reverse left ventricular remodeling,**
- **Quality of life**
- **HF hospitalisation, mortality**


# Response, stabilization , disease progression=worsened Cardiology compared to oncology




**CRT should be classified as a treatment for 'disease stablisation'.**

As slowing of a progressive disease is a positive outcome.

Mullens W et al. *Eur J Heart Fail.* 2020;22:2349-69; Mullens W et al. *Europace.* 2021;23:1324-42

# 5-year analysis of the REVERSE trial

JACC: CLINICAL ELECTROPHYSIOLOGY VOL. ■, NO. ■, 2021

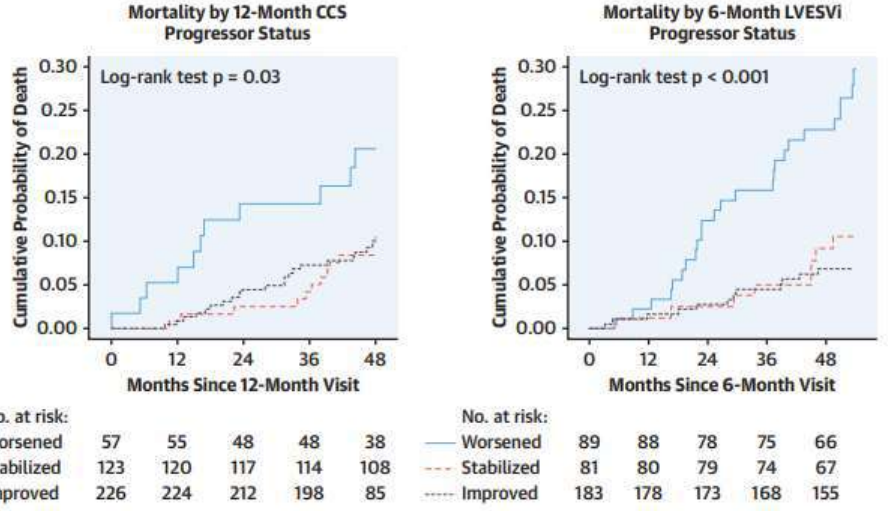

## Redefining the Classifications of Response to Cardiac Resynchronization Therapy

### Results From the REVERSE Study

Michael R. Gold, MD, PhD,[a] John Rickard, MD, MPH,[b] J. Claude Daubert, MD,[c] Patrick Zimmerman, PhD,[d] Cecilia Linde, MD, PhD[e]

**CENTRAL ILLUSTRATION** Responder Classification and Mortality by Progressor Status

| 12-Month CCS Responder Classification | 6-Month LVESVi Responder Classification |
|---|---|
| *56% Improved* | *52% Improved* |
| *30% Stabilized* | *23% Stabilized* |
| *14% Worsened* | *25% Worsened* |




Gold, M.R. et al. J Am Coll Cardiol EP. 2021;■(■):■-■.

Patients who worsened within 1st year of CRT had high mortality
Those stabilized (unchanged) had comparable 5-year survival as those who improved
Indicating that “non-responder” classification should be modified

- *1 million PMs or ICDs are implanted/ year worldwide.*

***Nearly 30% develop LV systolic dysfunction due to by RV pacing***

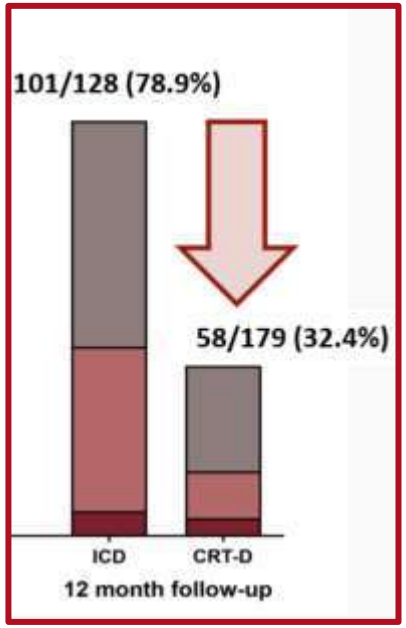
- ***which may lead to heart failure and hospitalisations***

- *But upgrading to CRT or CSP had poor evidence*

# Results of BUDAPEST-CRT Upgrade study randomised

Patients witn Pacing induced cardiomyopathy to upgrade to ICD or CRTD

## Primary endpoint

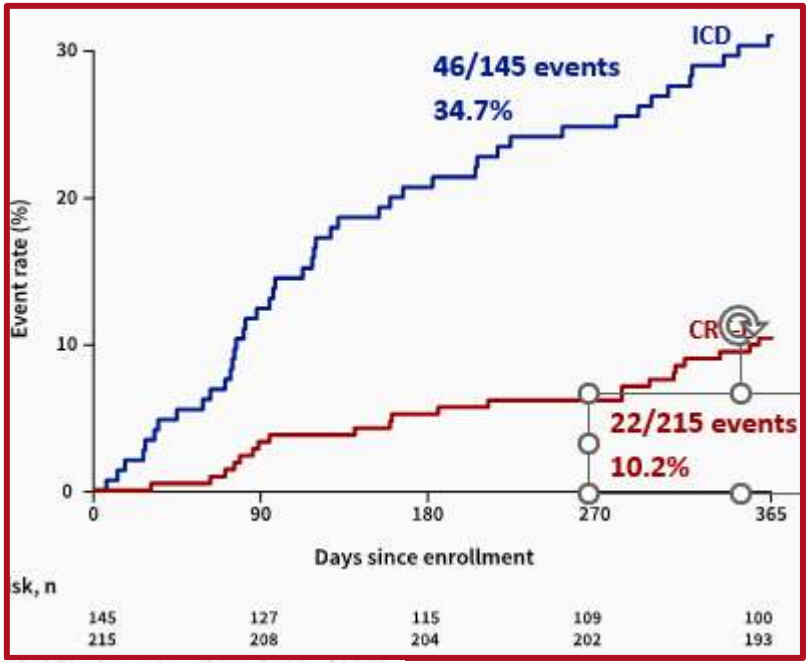



*OR 0.13
(95% CI 0.08-0.22);
p<0.001

Adjusted OR 0.11
(95% CI 0.06-0.19);
p<0.001

**NNT= 2.2**

## Secondary of HFH/total mortality




HR 0.28, 95%CI
0.17-0.46; p<0.001

Adjusted HR 0.27,
95%CI 0.16-0.47;
p<0.001

**NNT= 4.7**

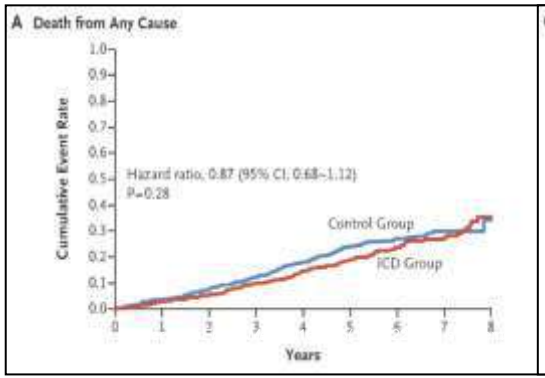
All-cause mortality  HF hospitalization  <15% reduction of LVESV

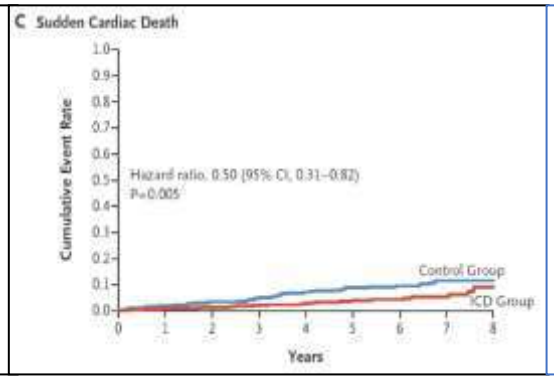
*Merkely B et al Eur Heart J. 2023 Oct 21;44(40):4259-4269*

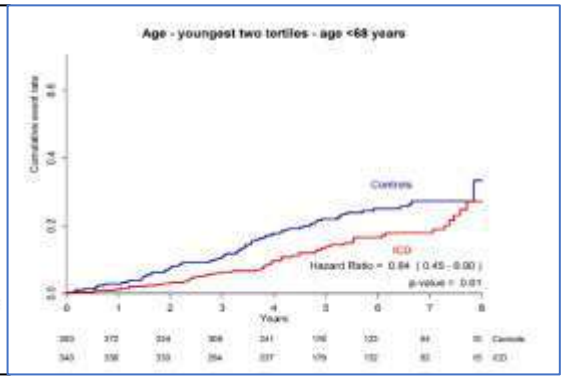
# Patient selection for CRT pacemaker or CRT defibrillator

# DANISH an RCT of ICD in non-ischemic HF

- 60% were on CRT therapy and with optimal heart failure medication
- No mortality benefit of ICD therapy on top of OMT (CRT in 58% )
- but with a 50% reduction in SCD
- 36% mortality benefit of ICD in pts. <68 years

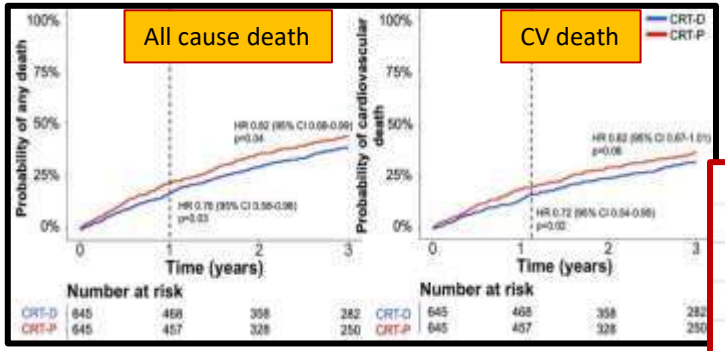


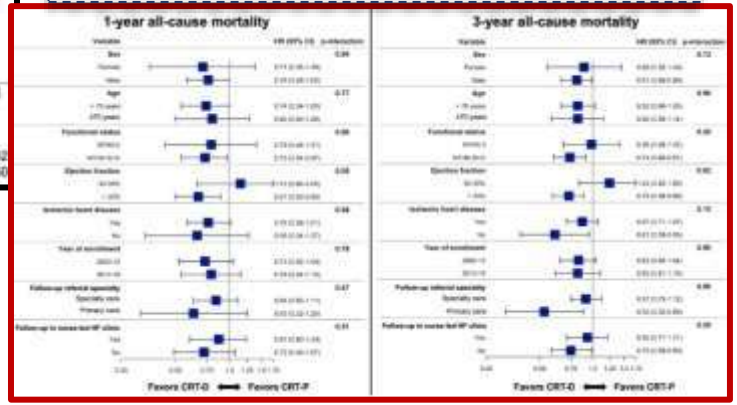

*Köber L et al New Engl J Med 2016*

# CRTP vs CRTD in the Swede-HF registry




Of 1,988 eligible for primary preventive ICDs,
1,108 (**56%) CRT-D** 880 (**44%) CRT-P.**

645 CRT-D were compared to 645 CRT-P patients




Over entire Follow up CRTD vs CRTP associated with
18% lower risk for all cause death p=0.04
18% lower risk for CV death p=0.06

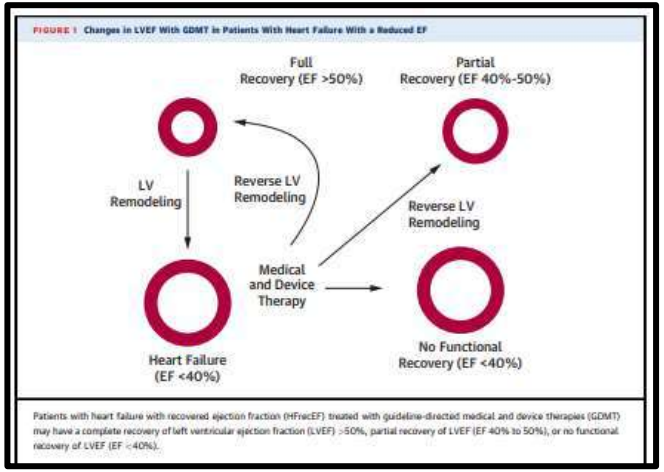
*Schrage B et al Europace 2022; Jan 4;24(1):48-57*

# Key question

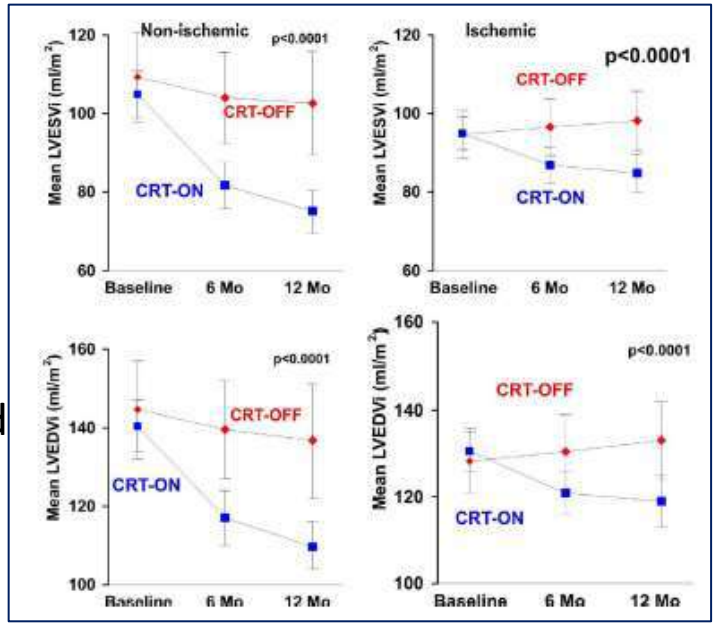
How rapidly does LV reverse remodeling evolve?

Is time course similar for RR by CRT + HF meds or HF meds?

When to determine LVEF after drugs to determine ICD need




*Wilcox J et al JACC 2020; 719*




*Linde C et al J Am Coll Cardiol. 2010 Nov 23;56(22):1826*

*When selecting between CRT-P and CRT-D get help from this position statement*

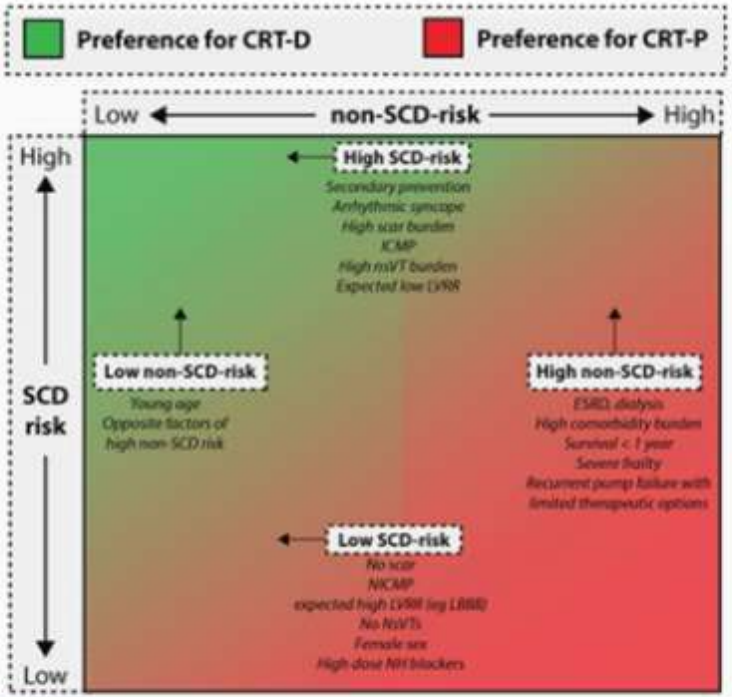
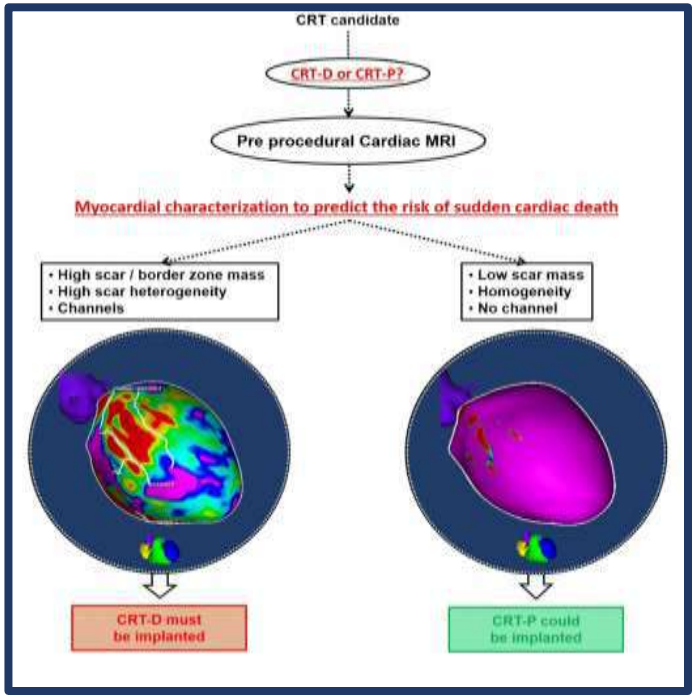



**Figure 3** Conceptual framework for individualizing of prescription of cardiac resynchronization therapy pacemaker (CRT-P) vs. cardiac resynchronization therapy defibrillator (CRT-D). Framework for individualizing CRT-P vs. CRT-D to help patients who have not opted to avoid an implantable cardioverter-defibrillator. Red indicates preference for CRT-P and green indicates preference for CRT-D. Balancing of choice is made by evaluating risk for sudden cardiac death (SCD) (yellow factors, with dark yellow indicating high SCD risk and light yellow indicating SCD risk) and the risk for non-SCD depicted in blue (dark blue indicates high risk for non-SCD and light blue indicates low risk for non-SCD). ESRD, end-stage renal disease; ICMP, ischaemic cardiomyopathy; LBBB, left bundle branch block; LVRR, left ventricular reverse remodelling; NH, neurohormonal; NICMP, non-ischaemic cardiomyopathy; nsVT, non-sustained ventricular tachycardia

# Imaging can help in decision making




Galand V et al
Curr Heart Fail reports 2020;17:116

# Take home message

- CRT saves lives and reduced HF hospitalisationsin Sinus rhythm and wide QRS *but not in RBBB*
- Upgrade to CRT/D if paced patients develop HF
- Women respond well to CRT
- Body size should be considered in decision making
- Responder term should be replaced by stabilization/improvement
- Worsening during CRT calls for other therapies
- Combine with ICD in pts with high risk of SCD and who are younger

# *The Pacemaker- a Swedish invention*

| The engineer | The Surgeon | The Patient |
|---|---|---|
| Rune Elmqvist<br>1906 - 1997 | Åke Senning<br>1915 - 2000 | Arne Larsson<br>1915 - **2001** |

## 1958

Thick, simple, short life

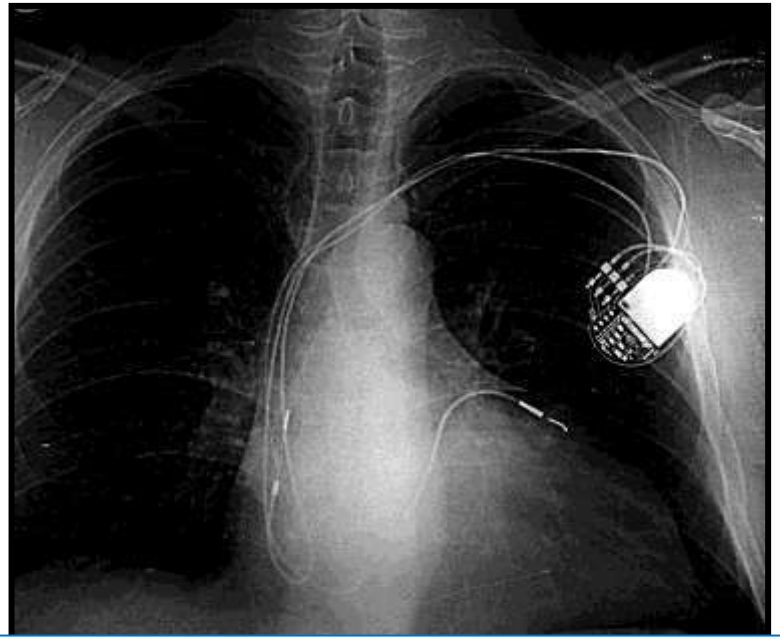
## Now

Leadless pacemaker small

# Thank you!


Cecilia Linde Karolinska Institutet Karolinska University Hospital

# Biventricular or left bundle LBB area pacing

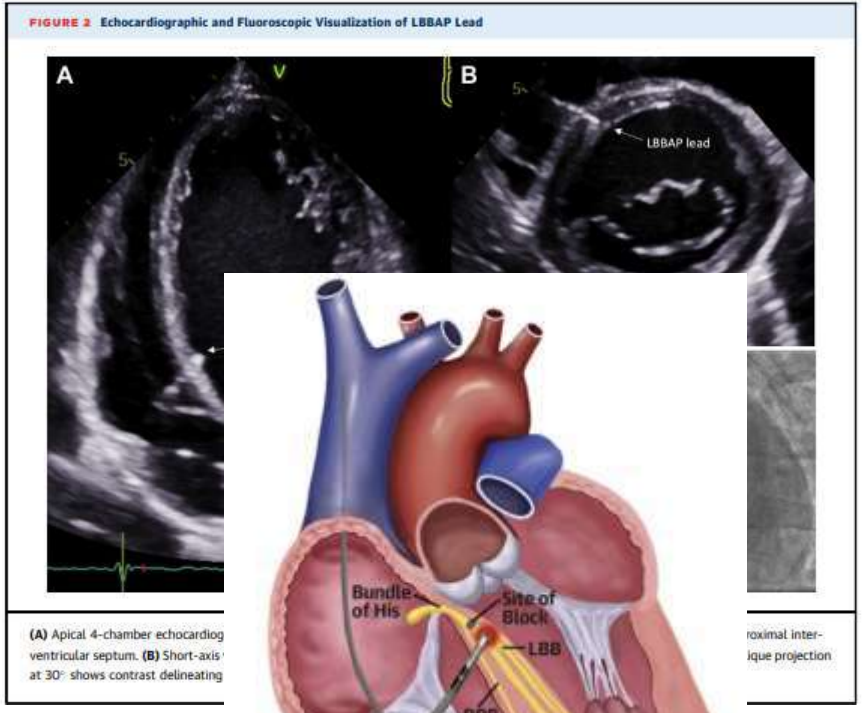


**Permanent Left Ventricular Pacing With Transvenous Leads Inserted Into The Coronary Veins**

J. CLAUDE DAUBERT[1], PHILIPPE RITTER[2], HERVÉ LE BRETON[1], DANIEL GRAS[1,2], CHRISTOPHE LECLERCQ[1], ARNAUD LAZARUS[2], JACQUES MUGICA[2], PHILIPPE MABO[1] and SERGE CAZEAU[2]

From the [1]Service de Cardiologie A, Hotel Dieu/CHRU 35033 Rennes Cedex, [2]Département de Stimulation Cardiaque, Centre Chirurgical du Val d'Or, Saint-Cloud France

PACE 1998;21:239-245

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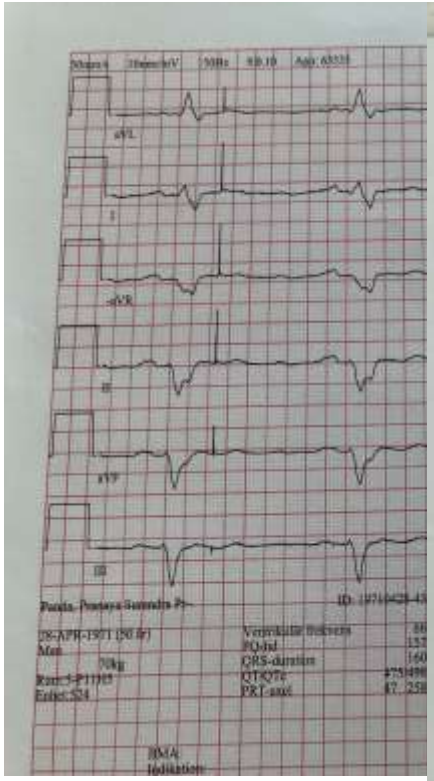
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Ventrikulär frekvens
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QRS-duration
QT/QTc
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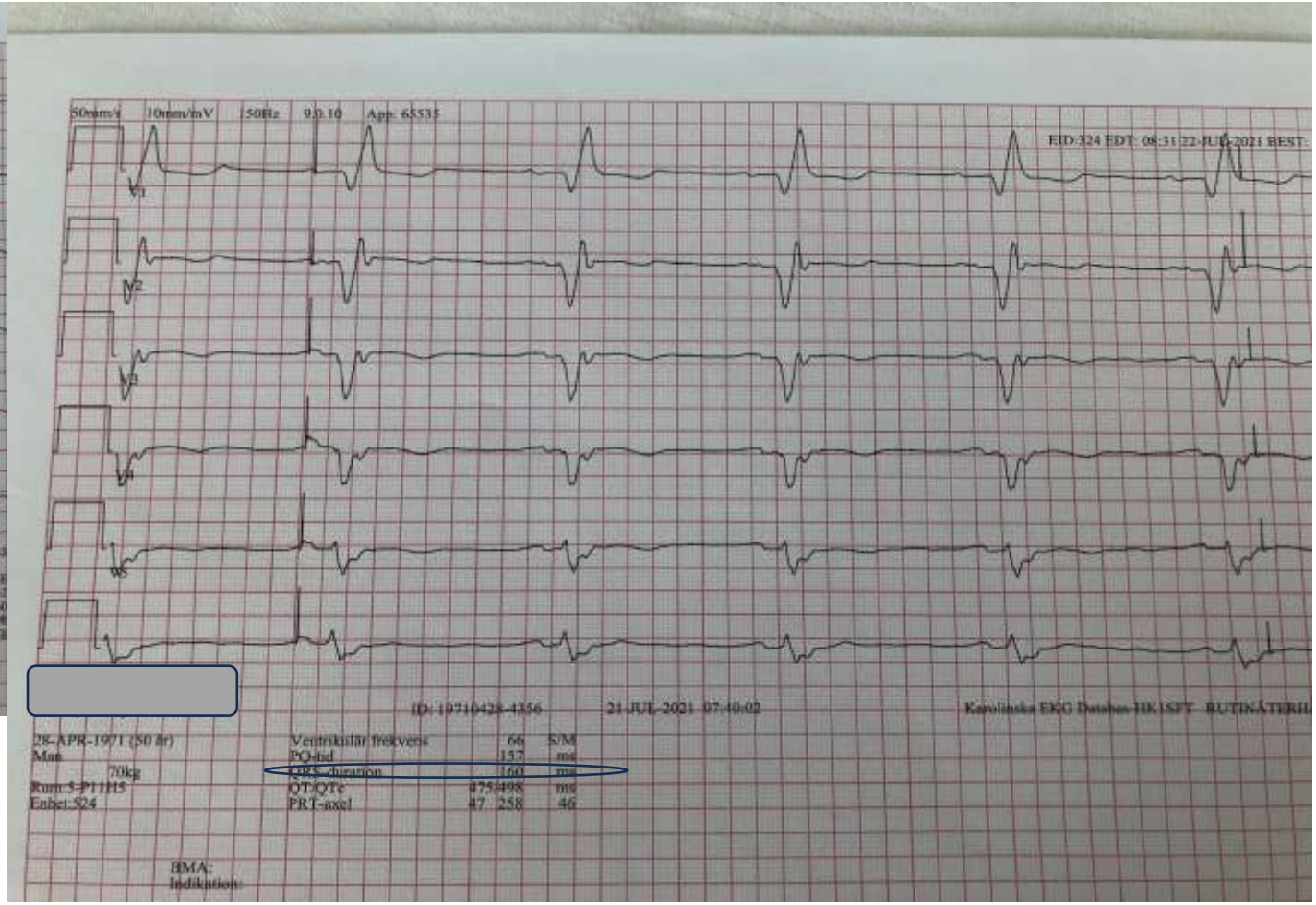
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Enhet:524
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QRS-duration 160 ms
QT/QTc 475/498 ms
PRT-axel 47 258 46
BMA:
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