CRT Fundamentals

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Learning Objectives

- Describe the basics of heart failure as a clinical syndrome and its various causes
- Identify landmark CRT Trials & history
- Describe how CRT benefits patients with heart failure
- Become familiar with the 2021 ESC guidelines on cardiac pacing and cardiac resynchronization therapy
- Discuss the 2023 HRS/APHRS/LAHRS guideline on cardiac physiologic pacing for the avoidance and mitigation of heart failure document

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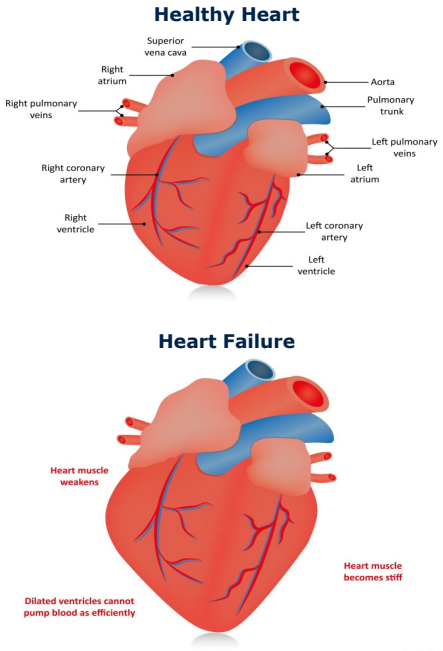
Heart Failure (HF)

Is a complex clinical syndrome

- May result from any functional/structural cardiac disorder
- Left ventricular ability to fill with and/or eject blood is impaired
- Patients should already be on optimized pharmacologic therapy prior to CRT implant

Different types of heart failure

- Ischemic vs. non-ischemic
- Systolic vs. diastolic
- HFrEF and HRpEF
- Left-sided vs. right-sided
- Acute vs. chronic



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Heart Failure is Progressive

NYHA Classification (New York Heart Association)

Class I

Asymptomatic
EF <40%

Class II

Mildly symptomatic with ordinary exertion

Class III

Moderately symptomatic with less than ordinary exertion

Class IV

Symptomatic at rest

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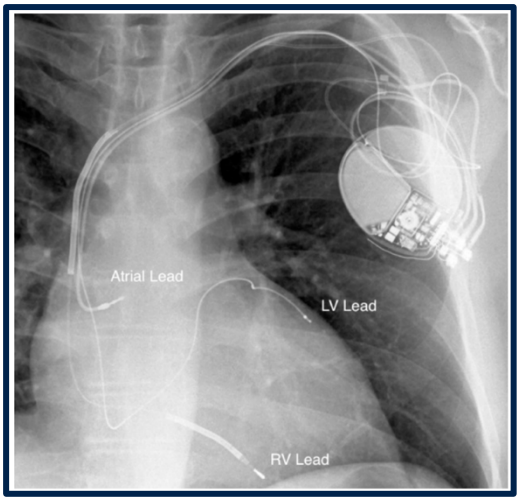
Benefits of CRT?

- Designed to treat ventricular dyssynchrony, which affects up to one-third of patients with symptomatic systolic heart failure
- Provides mechanical improvement of the heart to improve cardiac output
- Can improve HF symptoms, decrease hospitalizations and improve mortality
- May be considered as a means of preventing pacing-induced ventricular dysfunction in patients who require pacing for AV Block



Jaffe, L. M., & Morin, D. P. (2014). Cardiac resynchronization therapy: history, present status, and future directions. Ochsner journal, 14(4), 596–607.

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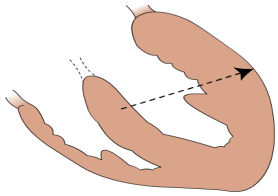
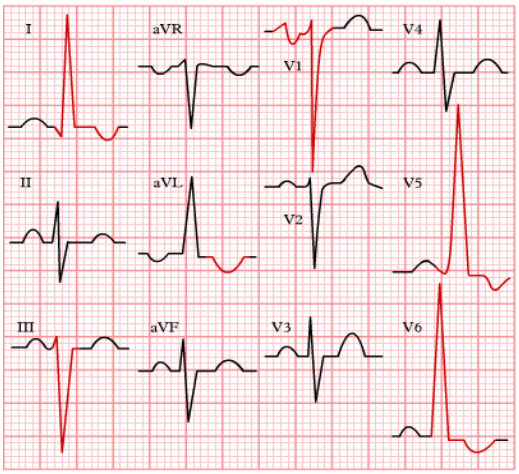
Determination of LV Hypertrophy via ECG

Does a wide QRS necessarily indicate dyssynchrony?

- If LBBB pattern: yes, particularly when >150ms[1]
- If RBBB pattern: no[2]





1. Glickson, et al. 2021 ESC Guidelines on cardiac pacing and cardiac resynchronization therapy. European Heart Journal 2021;42:3427-3520
2. Tedrow U, et al. Curr Cardiol Rep 2004; 6: 189-193

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Coronary Sinus Lead Placement

Anterior Placement Not Optimal

PATH-CHF[1]:

- Greater improvement in LV ejection fraction among the anterolateral and posterolateral locations than the anterior location
- Survival estimate at 4 years varied by location:
  - anterolateral, 72%
  - anterior, 48%
  - posterolateral, 62%
  - posterior, 72%

MADIT-CRT[2]

- CRT with posterior or lateral LV lead position associated with decreased risk of arrhythmic events in comparison to anterior lead location
- Apical lead position associated with an increased risk for death

1. Auricchio A, Stellbrink C, Sack S, Block M, Vogt J, Bakker P, Mortensen P, Klein H. The Pacing Therapies for Congestive Heart Failure (PATH-CHF) study: rationale, design, and endpoints of a prospective randomized multicenter study.Am J Cardiol 1999 Mar 11;83(5B):130D-135D.
2. Moss A, et al. N Engl J Med 2009;361:1329-1338

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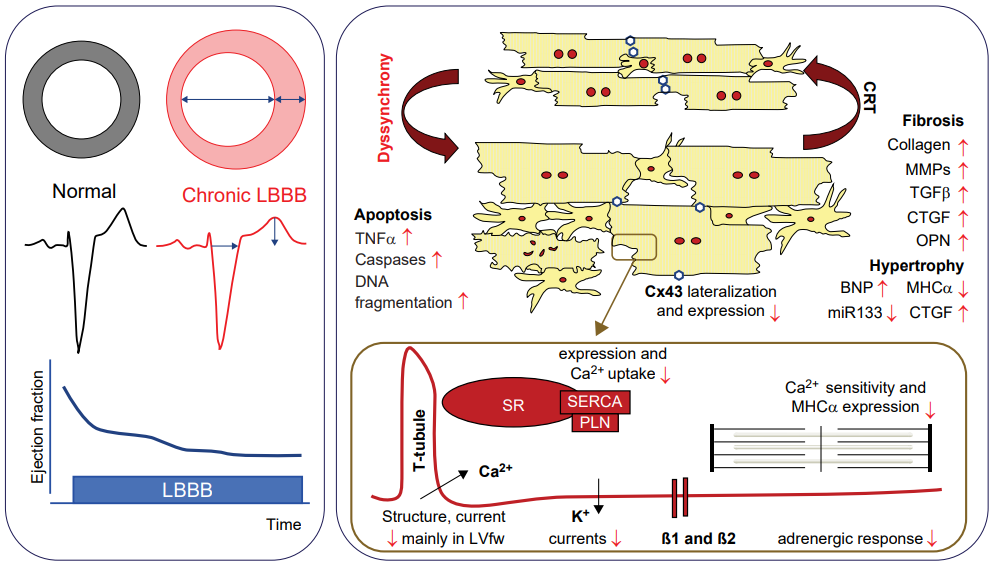

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CRT: A Brief History

1996
First CRT device implanted OUS

2001
FDA approval of CRT therapy

2005
CRT shown effective for severe HF (COMPANION[1] and CARE-HF)[2]

2009
MADIT-CRT[3] supported use of CRT in NYHA Class II CHF

2013
Focus on QRS duration; ECHO-CRT[4] demonstrating no benefit for QRS < 130ms

2013-2022
CRT improvements, e.g. adaptive algorithms, multi-point pacing, pacing polarities, etc.

2022-Present
CSP a 'bail-out' for failed CRT attempt vs. CSP instead of CRT

1996 | 2001 | 2005 | 2009 | 2013 | 2022 | Present

1. Bristow, et al. CRT with or without an ICD in advanced chronic heart failure NEJM 2004;350:2140-2150
2. Cleland, et al. The effect of CRT on morbidity and morality in heart failure NEJM 2005;352:1539-1549
3. Moss, et al. CRT for the prevention of heart-failure events NEJM 2009;361:1329-1338
4. Ruschitzka, et al. CRT in heart failure with a narrow QRS complex NEJM 2013;369:1395-1405

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Year	Study	Inclusion Criteria	Comparison	Effect of CRT
2001	MUSTIC-SR (n=67)	NYHA III, QRS ≥ 150 ms	CRT vs. VVI (no pacing indications)	CRT improved QoL, 6-min walk, peak VO_2; ↓ hospital
2002	MUSTIC-AF (n=43)	NYHA III, RV-paced QRS ≥ 200 ms	VVIR vs. BiV	CRT improved 6MWD, peak VO_2, QoL, and NYHA class; ↓ hospital (no Δ on intention-to-treat analysis)
	PATH-CHF (n=42)	NYHA II-IV, QRS > 120 ms	RV vs. LV vs. BiV	CRT improved NYHA class, QoL, walking distance
	MIRACLE (n=453)	NYHA III-IV, QRS ≥ 130 ms	CRT-on vs. CRT-off	CRT improved NYHA class, QoL, walking distance, LVEF, peak VO2, mitral regurgitation; ↓ hospital
2003	MIRACLE-ICD I (n=369)	NYHA III-IV, QRS ≥ 130 ms	CRT-D vs. ICD	CRT improved NYHA class, QoL, walking distance, and ↓ hospital
	CONTAK-CD (n=490)	NYHA II-IV, QRS ≥ 120 ms	CRT-on vs. CRT-off	CRT improved peak VO_2 and walking distance, not NYHA or QoL; ↓ LV volumes and ↑ LVEF; no effect on HF progression
	COMPANION (n=1520)	NYHA III-IV, QRS ≥ 120 ms	OMT vs. CRT-P or CRT-D	CRT-D and CRT-P ↓ composite of all-cause mortality and hospitalization
2004	MIRACLE-ICD II (n=186)	NYHA II, QRS ≥ 130 ms	CRT-on vs. CRT-off	CRT ↓ LV volumes, LVEF and improved composite score; no effect on QoL, walking distance, or peak VO_2
2005	CARE-HF (n=813)	NYHA III-IV, QRS > 120 ms	CRT-P vs. OPT	CRT ↓ total mortality and HF hospitalizations

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Year	Study	Inclusion Criteria	Comparison	Effect of CRT
2006	HOBIPACE (n=30)	LVEF < 40%	CRT-P vs. RV pacing	CRT ↓ LV volumes and improved QoL, LVEF, peak VO_2
2007	ReThinQ (n=172)	NYHA III, QRS < 130 ms	CRT-on vs. CRT-off in CRT-D recipients	CRT improved NYHA class, but not walking distance, LVEF, or QoL
2008	PROSPECT (n=498)	NYHA II-IV, QRS > 130 ms	Echo dyssynchrony measures as predictor of CCS and LVRR	Echo dyssynchrony measures did not predict outcome after CRT
	REVERSE (n=610)	NYHA I-II, LVEF < 40%, QRS > 120 ms	CRT-on vs. CRT-off (ICD on)	CRT ↓ HF hospitalization and improved LVEF and NYHA class; no effect on mortality
2009	MADIT-CRT (n=1820)	NYHA I-II, QRS > 130 ms	CRT-D vs. ICD	CRT ↓ HF events; no effect on mortality
2010	RAFT (n=1798)	NYHA II-III, QRS > 120 ms	CRT-D vs. ICD	CRT ↓ total mortality and HF hospitalization
2011	BLOCK-HF (n=691)	NYHA I-III, AV block, LVEF < 50%	CRT vs. RV pacing	CRT ↓ composite of total mortality, HF event, or 15% increase in LVESVi
2013	Echo-CRT (n=809)	NYHA III-IV, QRS < 130 ms	CRT-on vs. CRT-off	No effect on composite of total mortality or HF hospital; higher total mortality with CRT-on

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CRT Landmark Trials

COMPANION[1]

1520 patients, RCT

NYHA III-IV, EF<35%, QRS>120 ms

OMT vs CRT-P vs CRT-D

CRT-D and CRT-P reduces composite of all-cause mortality and hospitalization

CARE-HF[2]

813 patients, RCT

NYHA III-IV, EF<35%, QRS>120 ms

OMT vs CRT-P

CRT-P reduces total mortality and HF hospitalizations

MADIT-CRT[3]

1820 patients, RCT

NYHA **I-II**, **EF<30%**, **QRS>130** ms

CRT-D vs ICD

CRT-D reduces HF events, no effect on mortality

ECHO-CRT[4]

809 patients, RCT

NYHA III-IV, EF<35%, **QRS<130** ms

CRT ON vs CRT OFF

No effect; higher mortality with CRT ON

1. Bristow, et al. CRT with or without an ICD in advanced chronic heart failure NEJM 2004;350:2140-2150
2. Cleland, et al. The effect of CRT on morbidity and morality in heart failure NEJM 2005;352:1539-1549
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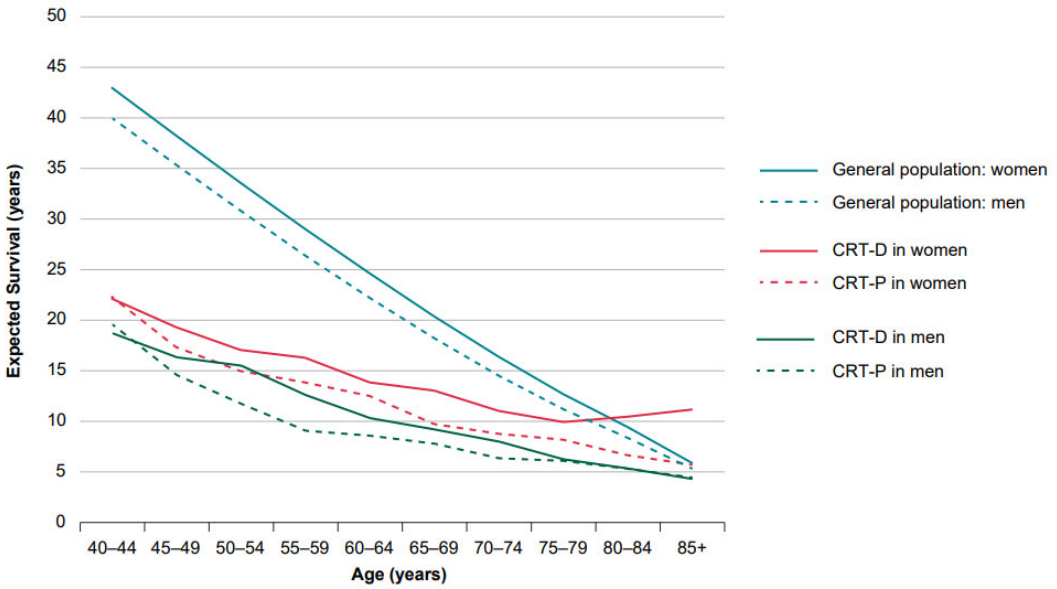

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CRT Response Criteria

Response	Criteria
Clinical response	1. Reduction in mortality 2. Reduction in HF hospitalization 3. Improvement in NYHA class 4. Improvement in quality of life, symptoms, or clinical composite scores 5. Increase in peak VO_2 (eg, >10%) 6. Improvement in 6-minute walk distance 7. Reduction in HF medications, such as diuretic therapy (note: continuation of GDMT is advised)
Echocardiographic response	1. Improvement or stability in LVEF (eg, ≥5% absolute increase or absence of worsening) 2. Reduction in LV size (eg, reduction in LV systolic or diastolic dimensions or volume indices) 3. Increase in LV stroke volume 4. Reduction in mitral regurgitation

CRT = cardiac resynchronization therapy; GDMT = guideline-directed medical therapy; HF = heart failure;
LV = left ventricle/ventricular;
LVEF = left ventricular ejection fraction;
NYHA = New York Heart Association;
VO_2 = oxygen uptake

Chung MK, et al.. 2023 HRS/APHRS/LAHRS guideline on cardiac physiologic pacing for the avoidance and mitigation of heart failure. Heart Rhythm. 2023 Sep;20(9):e17-e91.

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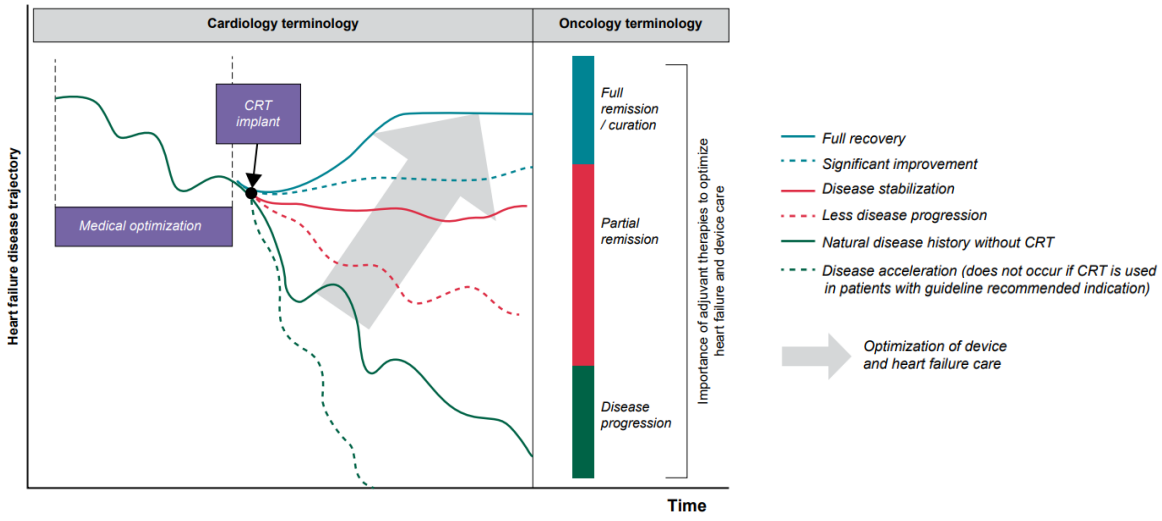
Expanded Concept of CRT Response



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2021 ESC Guideline Changes

		2013	2021
	Cardiac resynchronization therapy		
Indications for upgrade →	Patients who have received a conventional pacemaker or an ICD and who subsequently develop symptomatic HF with LVEF ≤35% despite OMT and who have a significant[b] proportion of RV pacing should be considered for upgrade to CRT.	I	IIa
Indications for patients requiring pacing or in AF →	CRT rather than RV pacing is recommended for patients with HFrEF (<40%) regardless of NYHA class who have an indication for ventricular pacing and high-degree AVB in order to reduce morbidity. This includes patients with AF.	IIa	I
Indications for patients in sinus rhythm →	CRT should be considered for symptomatic patients with HF in SR with LVEF ≤35%, a QRS duration of 130–149 ms, and LBBB QRS morphology despite OMT, to improve symptoms and reduce morbidity and mortality.	I	IIa
Indications for patients in AF →	In patients with symptomatic AF and uncontrolled heart rate who are candidates for AVJ ablation (irrespective of QRS duration), CRT is recommended in patients with HFrEF.	IIa	I

Glickson, et al. 2021 ESC Guidelines on cardiac pacing and cardiac resynchronization therapy. European Heart Journal 2021;42:3427-3520

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2021 ESC Guidelines: Relevant Points

Sinus rhythm:

- Confirm the importance of reduced EF **(<35%)** for CRT effectiveness;
- Increased the threshold for QRS duration from **120ms to 130ms**;
- Strengthen the importance of **LBBB morphology** to predict CRT response and effectiveness;
- Women confirmed to **respond better** than men especially in the QRS of 130-149 segment with LBBB;
- Present CRT recommendations are applicable to all patients in **NYHA functional class II – III – IV**

AF:

- AF ablation can improve LVEF end reduce HF thus CRT should be considered in those patients with persistent AF and reduced EF **when ablation cannot be performed**;
- In AF patients, a major determinant of success of CRT is the **delivery of BIV pacing**;
- CRT is good for patients with permanent AF and **NYHA class III or IV, provided** AVJ ablation is added in the case BIV pacing < than 90%-95%;

Glickson, et al. 2021 ESC Guidelines on cardiac pacing and cardiac resynchronization therapy. European Heart Journal 2021;42:3427-3520

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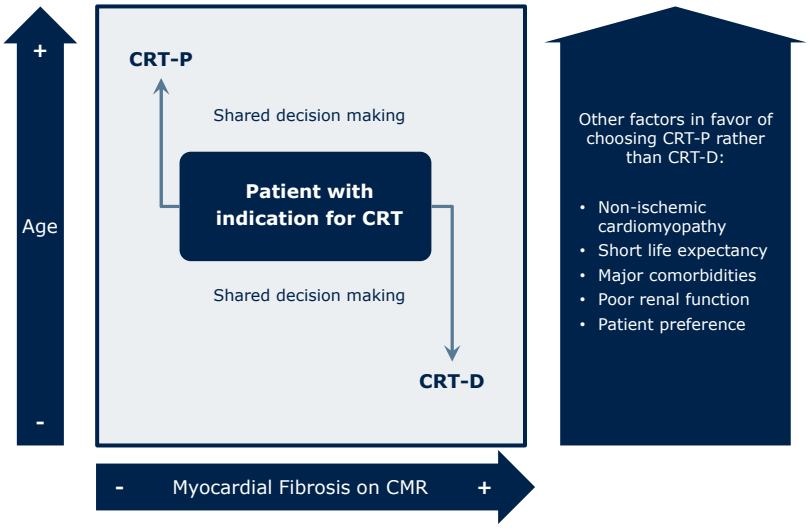
2021 ESC Guidelines: CRT-D vs CRT-P



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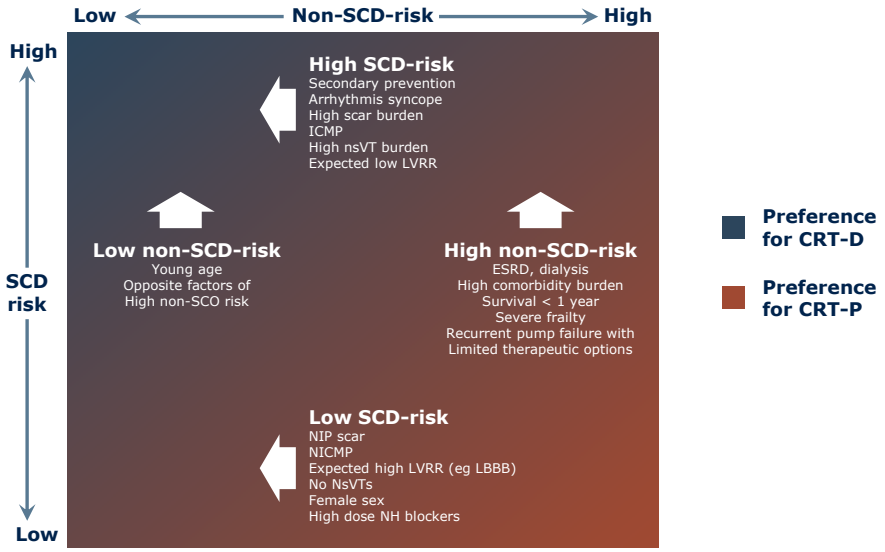

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2023 HRS/APHRS/LAHRS

Guideline on cardiac physiologic pacing for the avoidance and mitigation of heart failure

"Cardiac physiologic pacing (CPP), encompassing cardiac resynchronization therapy (CRT) and conduction system pacing (CSP), has emerged as a pacing therapy strategy that may mitigate or prevent the development of heart failure (HF) in patients with ventricular dyssynchrony or pacing-induced cardiomyopathy. This clinical practice guideline is intended to provide guidance on indications for CRT for HF therapy and CPP in patients with pacemaker indications or HF, patient selection, pre-procedure evaluation and preparation, implant procedure management, follow-up evaluation and optimization of CPP response, and use in pediatric populations."

Chung MK, et al. 2023 HRS/APHRS/LAHRS guideline on cardiac physiologic pacing for the avoidance and mitigation of heart failure. Heart Rhythm. 2023 Sep;20(9):e17-e91.

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CRT for Patients with Mild-Moderately Reduced LVEF and LBBB

LBCT HRS 2024; Professor YM Cha, Mayo Clinic

- CRT improves LVEF and ventricular remodeling in 6-month therapy in patients with HFmmrEF and LBBB
  - Mild-moderately reduced LVEF = 36-50%
- Despite CRT being turned off, the effects of CRT may persist beyond 6 months
- Further studies are needed to investigate the CRT long-term outcomes of heart failure progression and survival in this patient population

Cha, et al. Heart Rhythm Society Published online May 19, 2024: https://doi.org/10.1016/j.hrthm.2024.05.014

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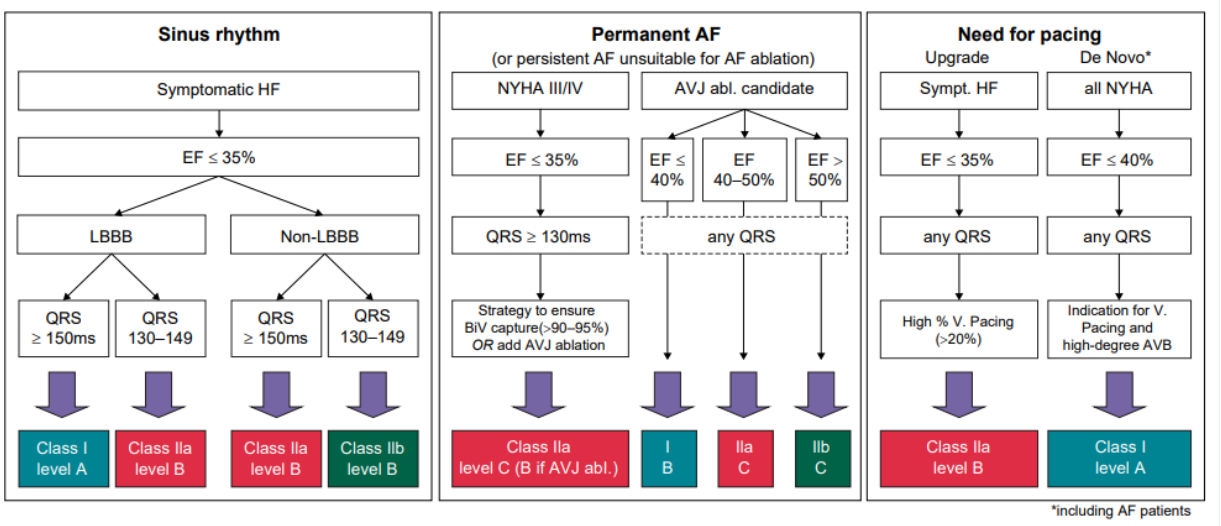

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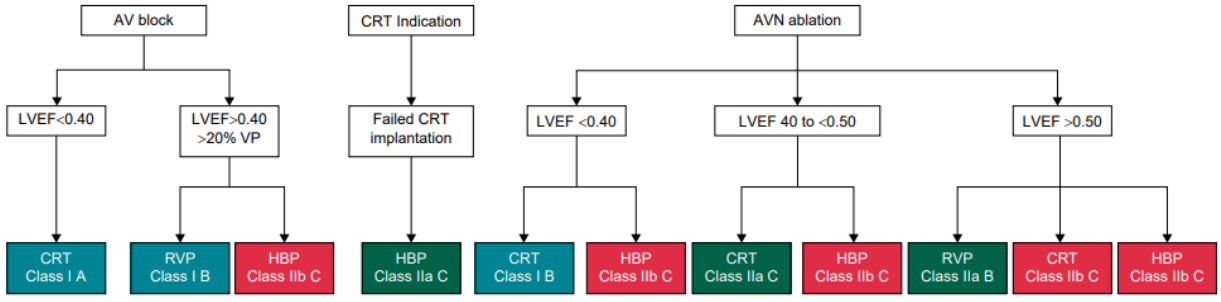

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CRT Fundamentals

- With 25 years of experience, CRT remains an important therapy for heart failure
- Historically it has been said that 60 to 70% of CRT recipients are responders
  - Definitions of a 'CRT responder' continue to evolve
  - Including those patients whose clinical symptoms stabilize with CRT, current response rate is thought to be 70 to75%
- Indications for CRT also continue to evolve
- Over time there has been a shift in the USA for greater use of CRT-P
  - Historically, CRT-P use in the USA was markedly less than other parts of the world and CRT-D utilization much greater in the USA
- Conduction system pacing is being called by many as a 'bail-out' for failed coronary sinus lead placement and others have adopted LBBAP over CRT
  - The first large randomized trial of CRT vs. CSP will likely not have results until 2028-2029
  - CSP has been incorporated into the guidelines
- The role of other therapeutic tools such as cardiac contractility modulation and cardiac neuromodulation continue to evolve

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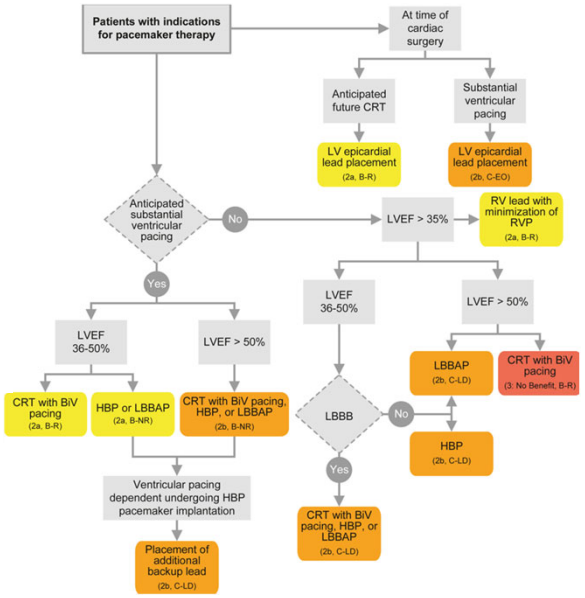
Pacing Strategy

Affected by anticipated amount of V-pacing and the pre-Pacing LVEF



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