Device Therapy in the Treatment of Heart Failure

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Disclosures

- NO disclosures

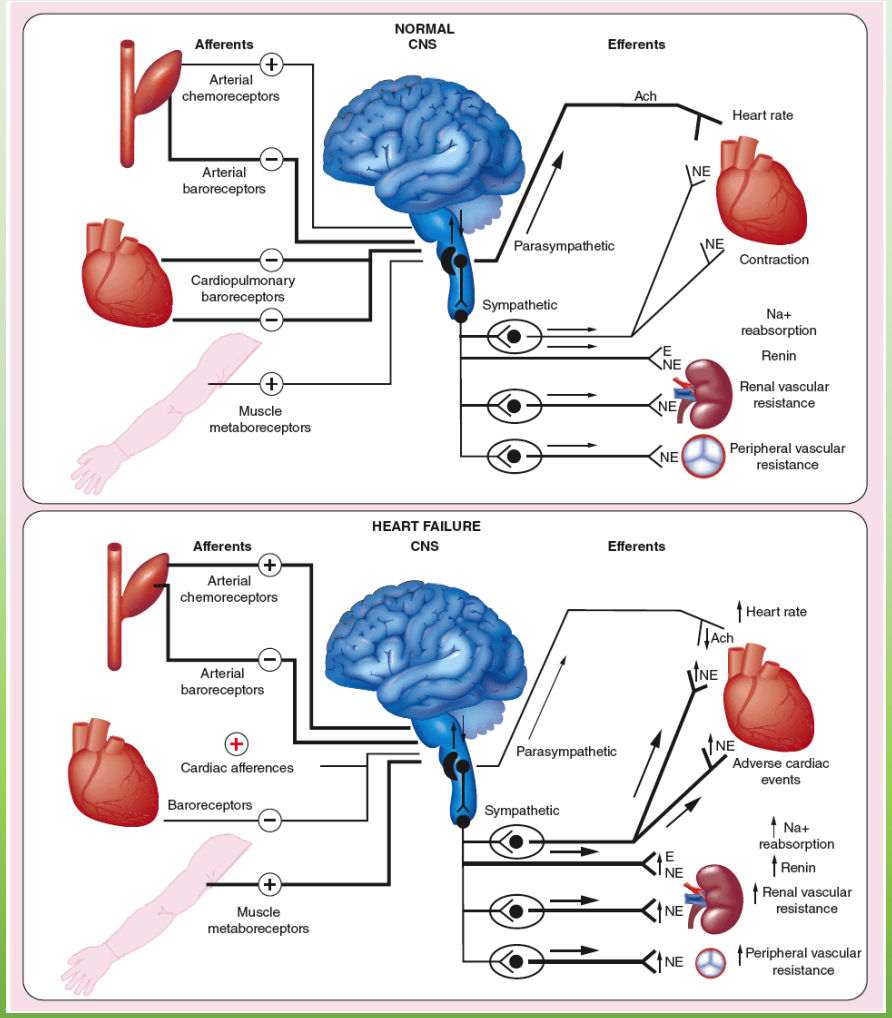
Objectives

- Review pathophysiology and autonomic nervous system (ANS) involvement in heart failure
- Review NYHA and Heart Failure stages functional classification
- I-NEED-HELP: clinical indicators of advanced stage heart failure
- FDA approved device therapies for symptomatic, Stage C and D heart failure, how they work, and who is a candidate
  - Heart failure monitoring technologies
  - Baroreflex Activation Therapy
  - Cardiac Contractility Modulation
  - Left Ventricular Assist Device (LVAD)

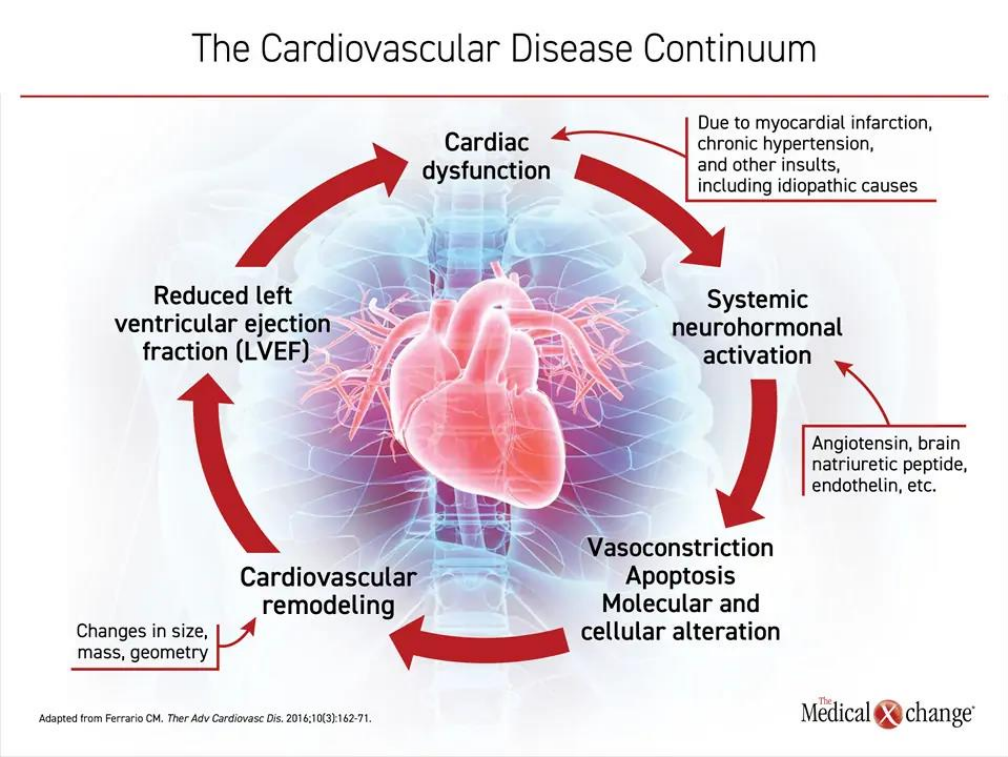
Introduction

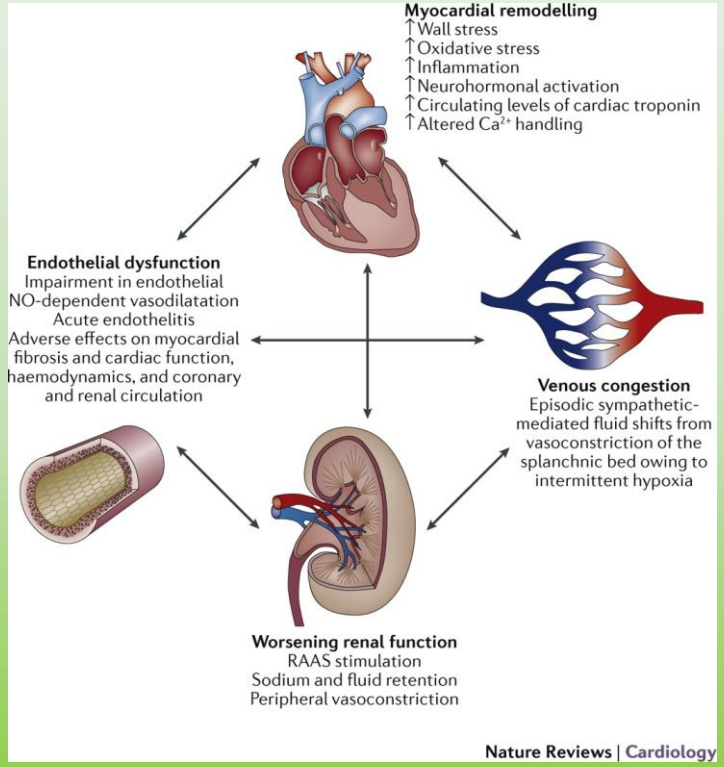
- 1-2% of all hospital admissions in Europe and North America
- 1-year mortality 15-30%
- HF hospitalization $10,000+, HF Rehospitalization $25,000 or higher
- Cost of care expected to rise to $53 billion in 2030
- Population is aging, have increased life expectancy, diagnosis of HF can be made earlier
- Side effects can limit best HF GDMT
- Only a fraction of eligible patients receive device therapy

Pathophysiology of Heart Failure: the Autonomic Nervous System

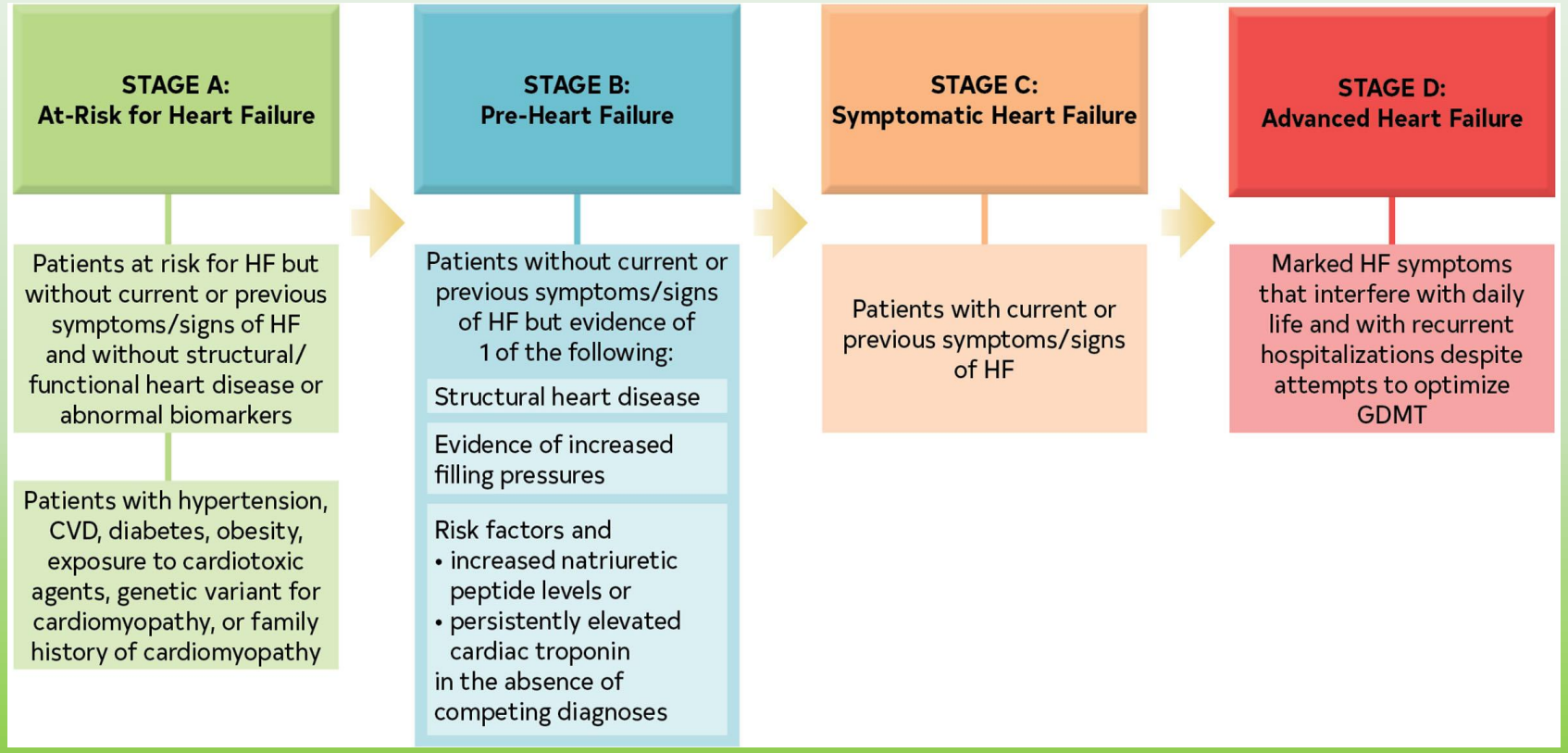


Pathophysiology of Heart Failure: the doom loop





Heart Failure Stages - Disease Progression

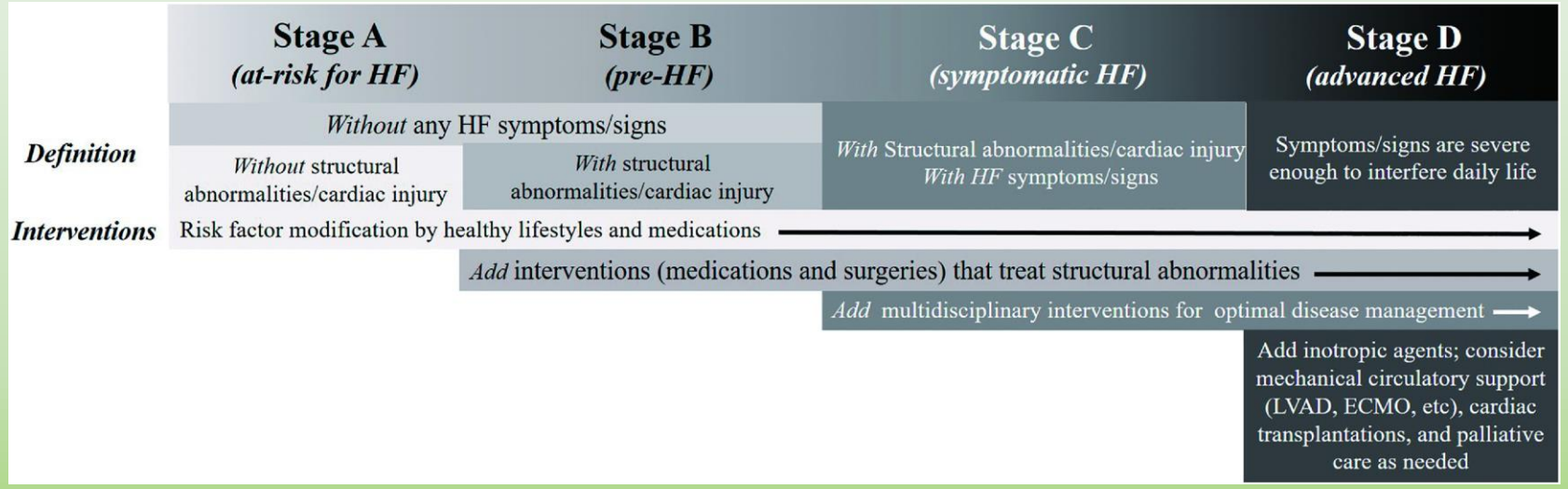


Paul A. Heidenreich. Circulation. 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines, Volume: 145, Issue: 18, Pages: e895-e1032, DOI: (10.1161/CIR.0000000000001063)

NYHA Functional Class

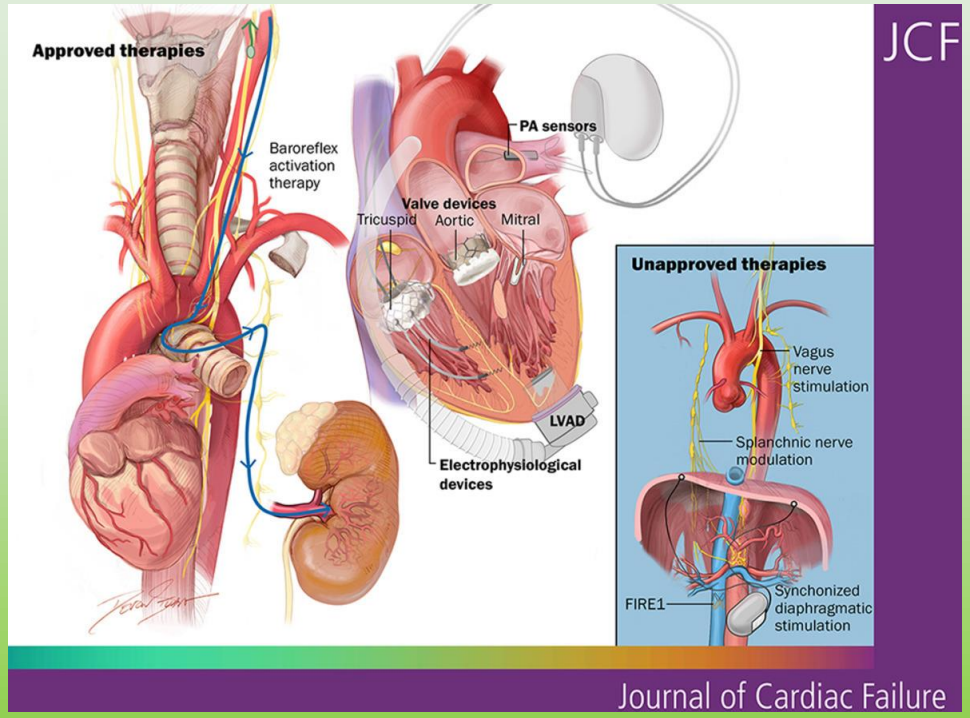
NYHA Class	Level of Clinical Impairment
I 	No limitation of physical activity. Ordinary physical activity does not cause undue breathlessness, fatigue, or palpitations.
II 	Slight limitation of physical activity. Comfortable at rest, but ordinary physical activity results in undue breathlessness, fatigue, or palpitations.
III 	Marked limitation of physical activity. Comfortable at rest, but less than ordinary physical activity results in undue breathlessness, fatigue, or palpitations.
IV 	Unable to carry on any physical activity without discomfort. Symptoms at rest can be present. If any physical activity is undertaken, discomfort is increased.

Lorenzini, Monica & Ricci, Caterina & Riccomi, Silvia & Abate, Federica & Casalgrandi, Barbara & Quattrini, Benedetta & Spagnoli, Gianbattista & Reggianini, Letizia & Capelli, Oreste. (2016). Integrated Care for Heart Failure in Primary Care. 10.5772/63946.


Stage A
(at-risk for HF)
Stage B
(pre-HF)
Stage C
(symptomatic HF)
Stage D
(advanced HF)
Definition
Without any HF symptoms/signs
Without structural abnormalities/cardiac injury
With structural abnormalities/cardiac injury
With Structural abnormalities/cardiac injury
With HF symptoms/signs
Symptoms/signs are severe enough to interfere daily life
Interventions
Risk factor modification by healthy lifestyles and medications
Add interventions (medications and surgeries) that treat structural abnormalities
Add multidisciplinary interventions for optimal disease management
Add inotropic agents; consider mechanical circulatory support (LVAD, ECMO, etc), cardiac transplantations, and palliative care as needed

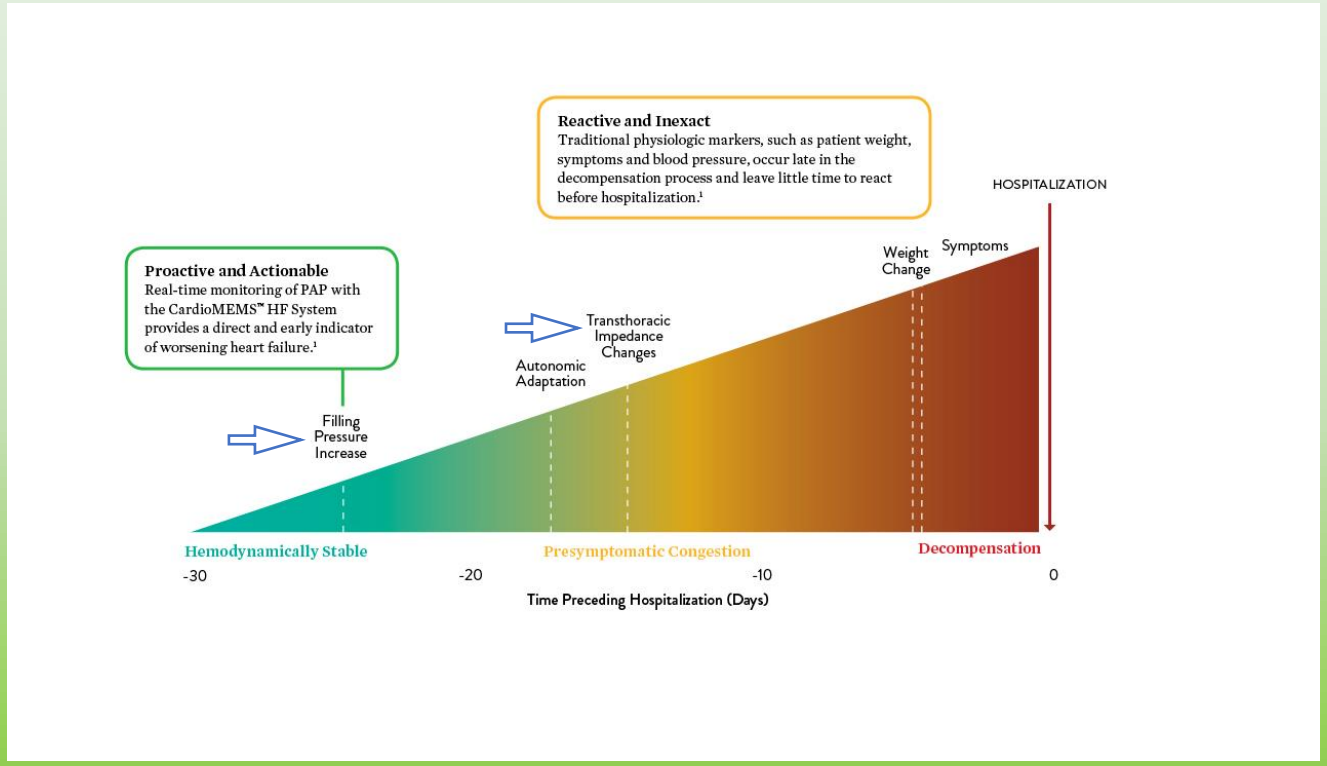
FDA-approved Device Therapies for Treatment of Heart Failure

- ICD/Cardiac Resynchronization Therapy (CRT)
- Structural Interventions
  - Transcatheter Valve repair or replacement (TAVR, TEER, TMVR, TVVR)
  - Interatrial shunt devices
- Heart Failure Monitoring Technologies
  - Chest impedance devices (ICD/CRT devices)
  - **Pulmonary artery pressure monitoring** (CardioMems, Cordella)
- Autonomic Modulation - **Baroreflex Activation Therapy** (BaroStim)
- Electrophysiological Modulation - **Cardiac Contractility Modulation** (CCM)
- Respiratory Modulation - Phrenic Nerve Stimulation (Remede)
- Cardiac Replacement Therapies
  - Temporary mechanical circulatory support (ECMO, temp RVAD, temp LVAD)
  - Durable MCS - **LVAD** (Heartmate 3)



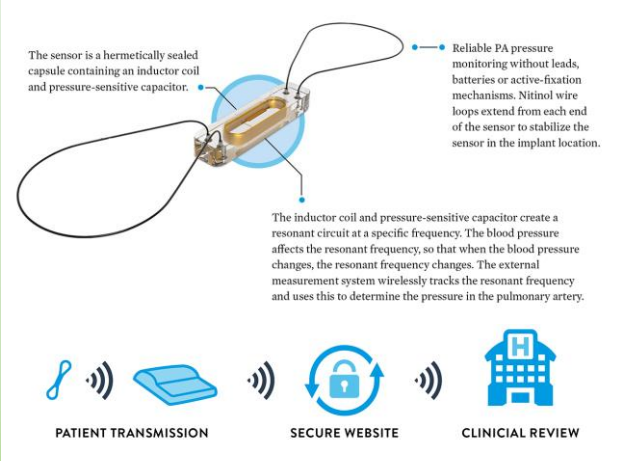
PA Pressure Monitoring

Prospective, Predictive, Preemptive, Proactive, Objective



PA Pressure Monitoring Systems

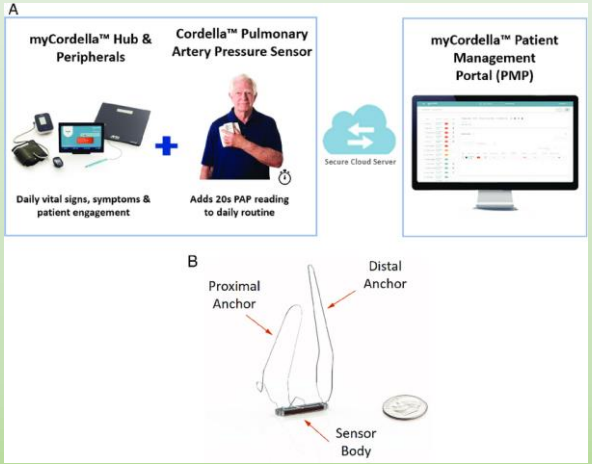
CardioMems (Abbott)



CHAMPION
GUIDE-HF
MONITOR-HF (EU)

Indications:
- NYHA 2/3
- HFrEF or HFpEF
- HF Hospitalization OR
- Elevated BNP

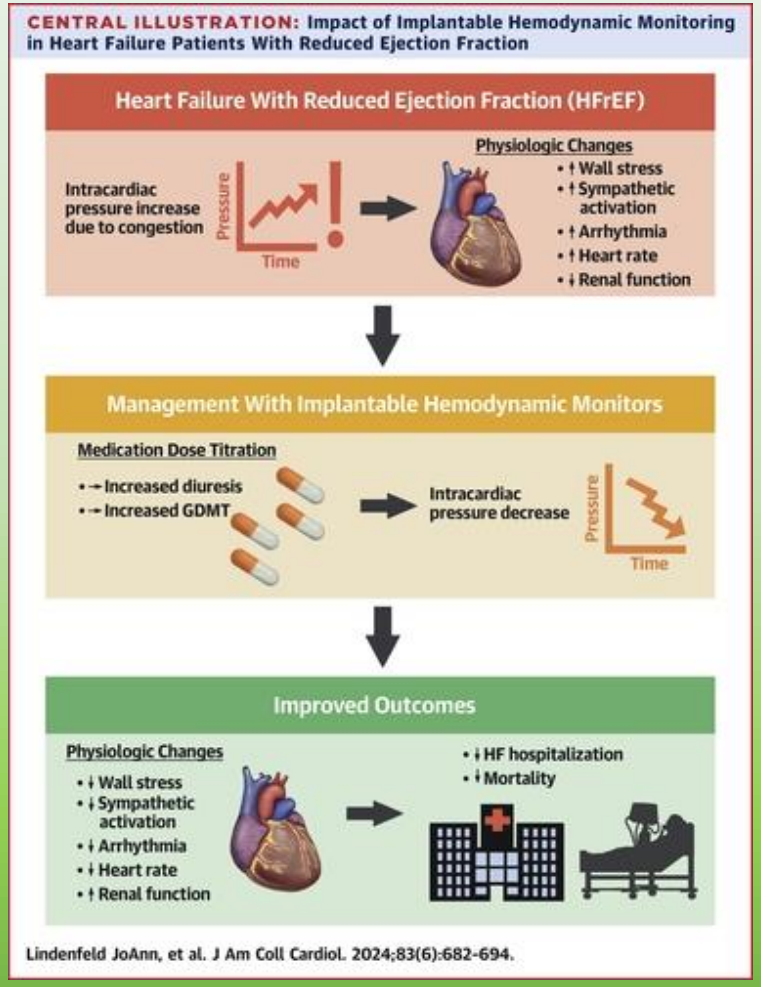
Cordella (Endotronix)



PROACTIVE-HF
PROACTIVE-HF 2 (ONGOING)
SIRONA (EU)

Benefits:
- Reduced HF hospitalizations
- Reduced HF events
- Improved QOL and functional status
- ?Reduced mortality

How does implantable hemodynamic monitoring work?

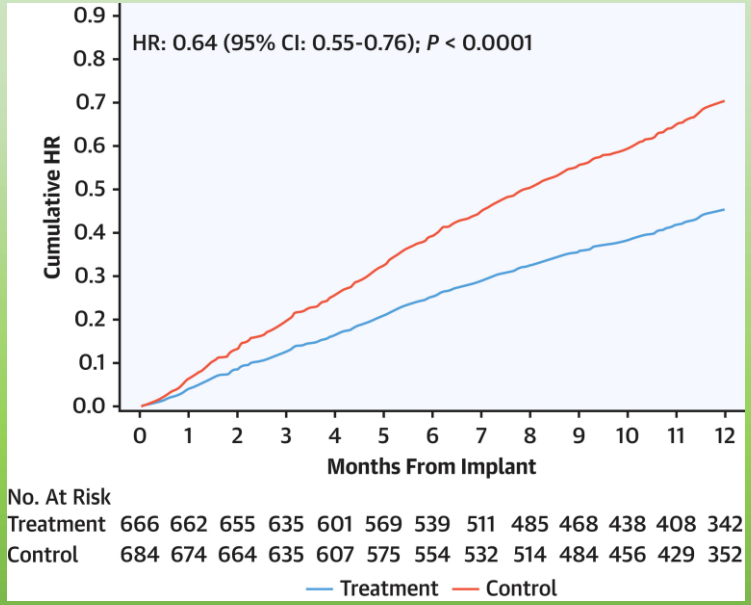


Lindenfeld et.al. JACC. 2024 Feb, 83 (6) 682–694

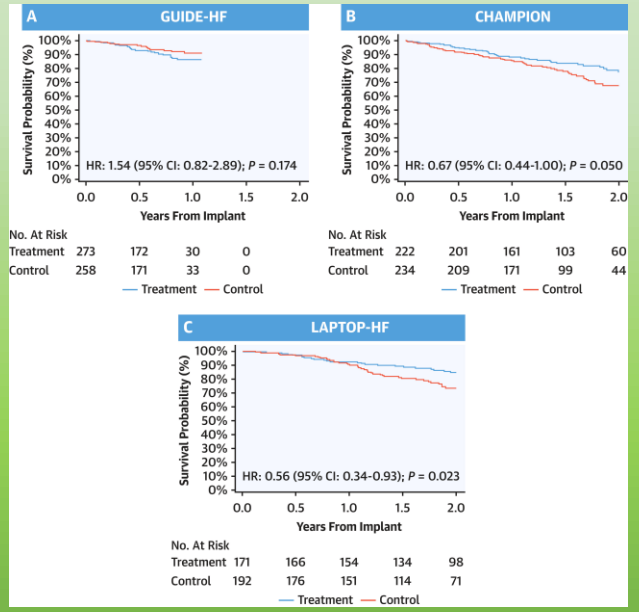
Meta-Analysis: Implantable Hemodynamic Monitors improve survival in HFrEF patients (probably)

- Pooled analysis of GUIDE-HF, CHAMPION, and LAPTOP-HF
- 1350 patients with HFrEF
- Hemodynamic-guided management:

36% reduction in HF Hospitalization



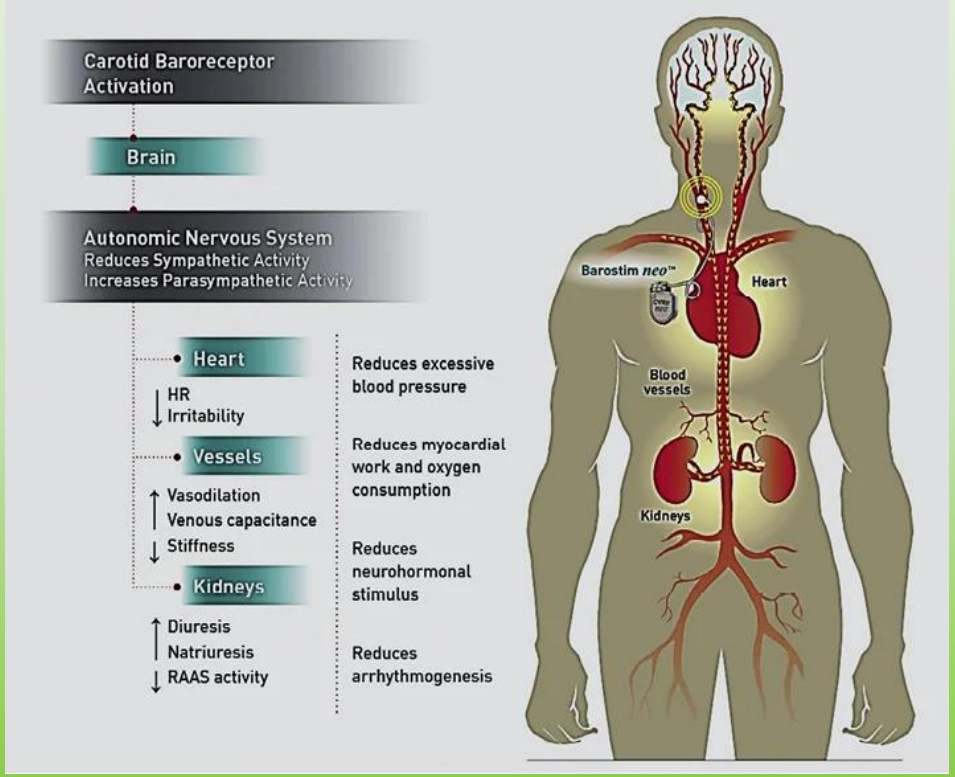
Pooled 25% reduction in mortality



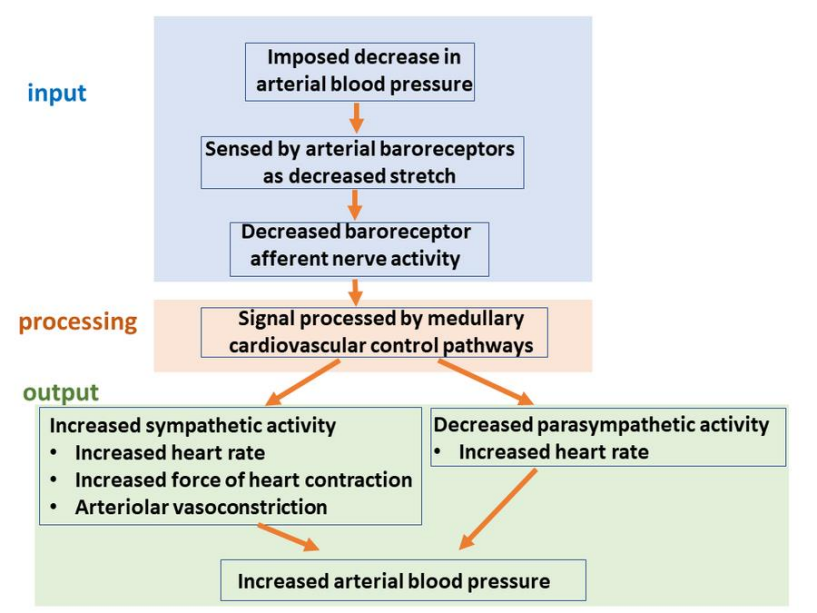
Lindenfeld et.al. JACC. 2024 Feb, 83 (6) 682–694

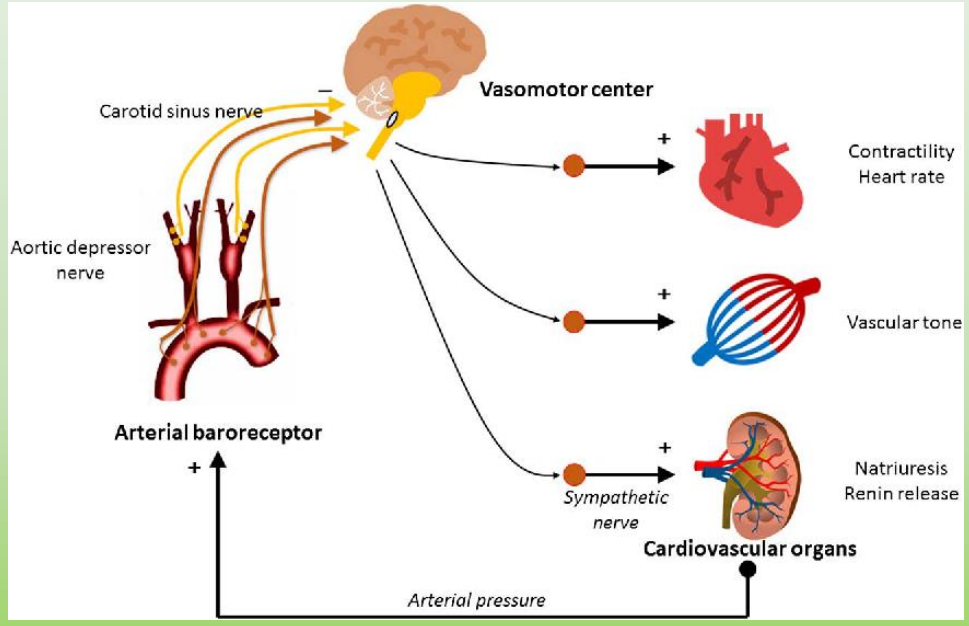
A Physiology Lesson: Baroreceptors

- Mechanoreceptors: maintain blood pressure at a constant level
  - High-pressure arterial baroreceptors
    - carotid sinus and aortic arch
    - prevent rapid changes in BP in the moment
  - Low-pressure cardiopulmonary receptors
    - atria, ventricles, and pulmonary vasculature
    - regulate blood volume via hormone secretion which influences intake and retention of salt and water
    - regulates mean pressure in the long-term
- Relay blood pressure information within the autonomic nervous system to change the peripheral resistance and cardiac output
- Reset over a period of days or weeks



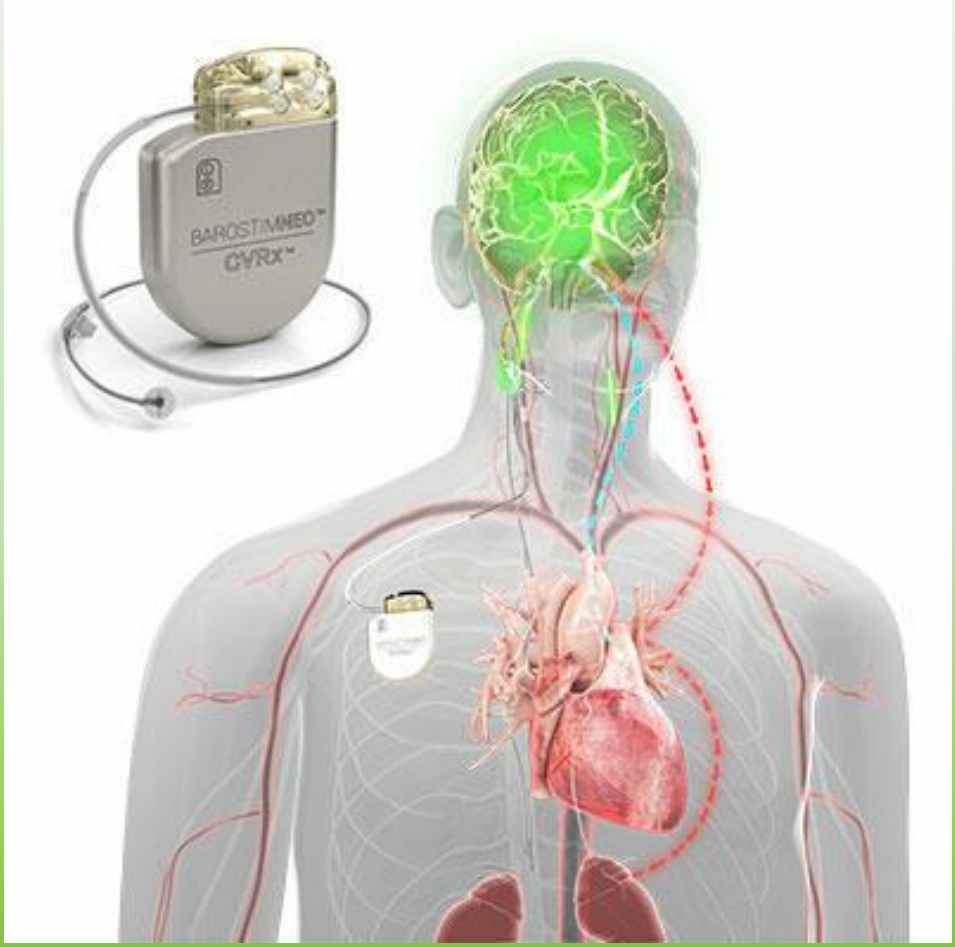
The Baroreceptor Reflex

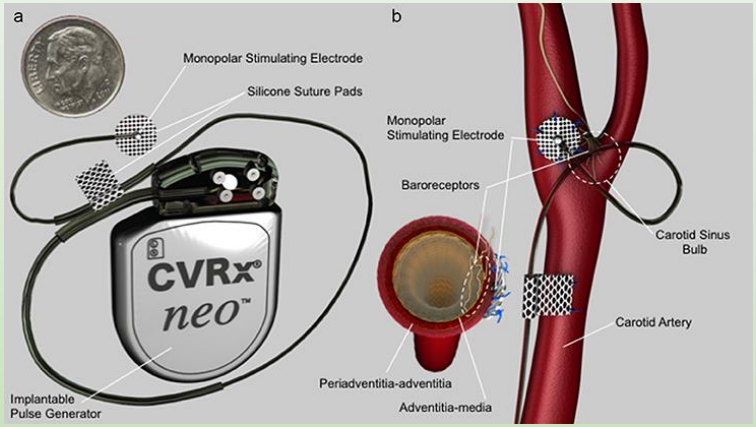




https://www.physio-pedia.com/Baroreceptors

BaroStim Neo (CVRx)



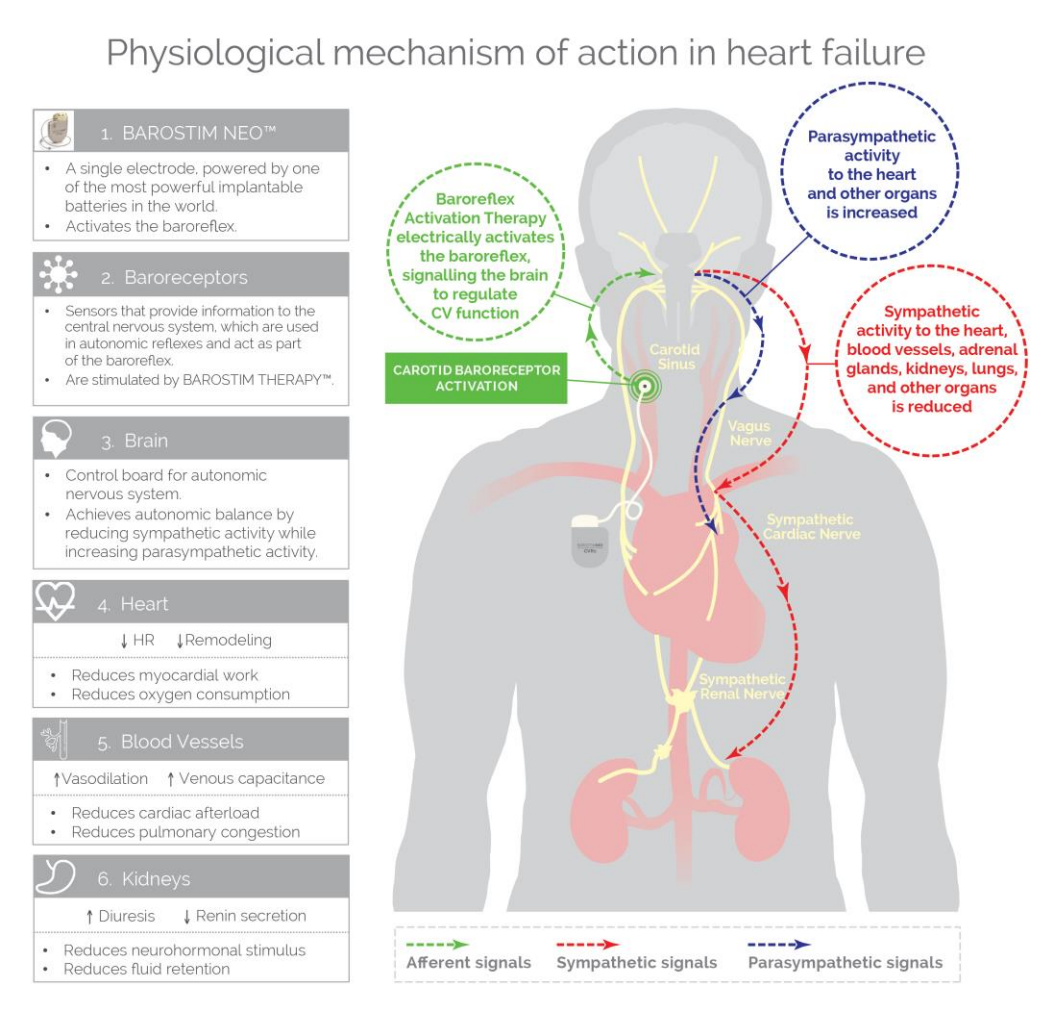


Indications

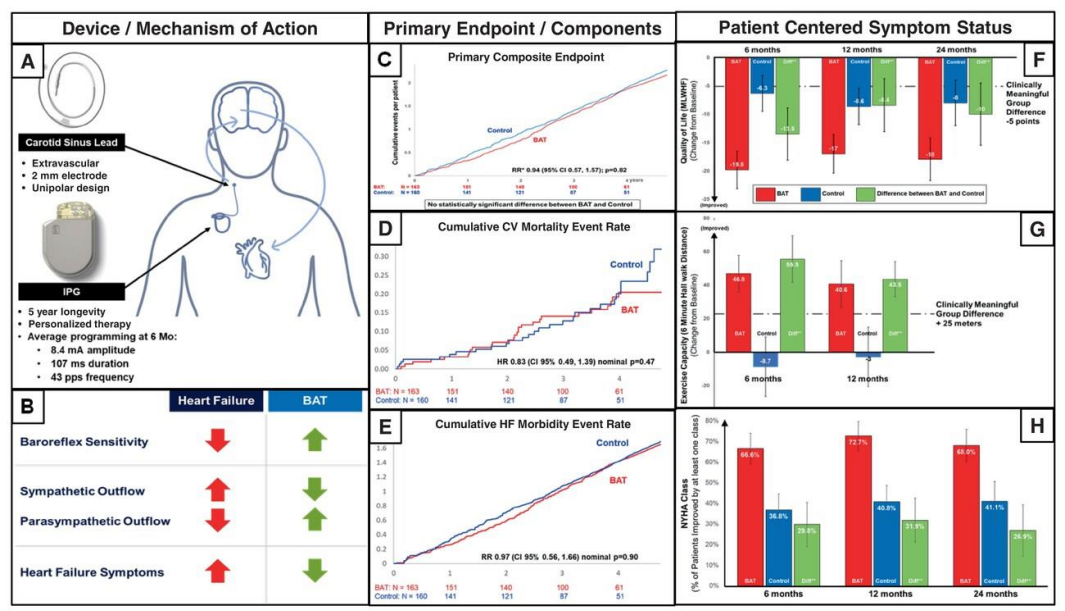
- NYHA Class III or Class II (who had a recent history of Class III)
- On guideline-directed medical therapies (medications and devices),
- LVEF ≤ 35%
- NT-proBNP <1600 pg/ml
- Not treated with CRT

Fudim et al. Device Therapy in Chronic Heart Failure: JACC State-of-the-Art Review. JACC. 2021 Aug, 78 (9) 931–956.

How does Baroreflex Activation Therapy work?



BEAT-HF

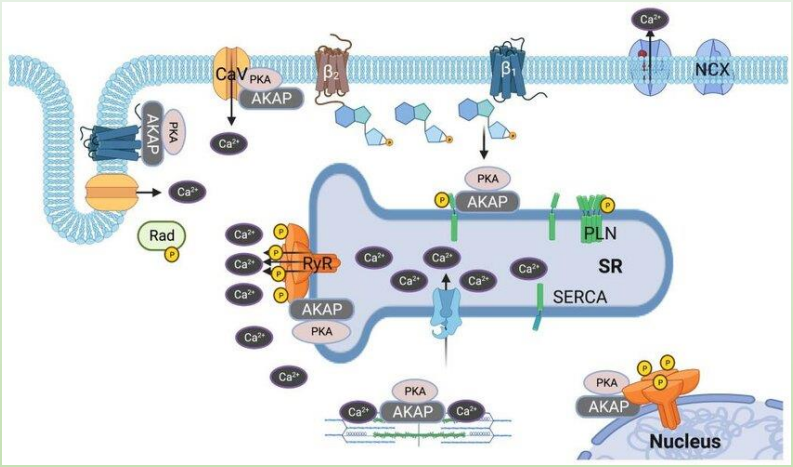


- Prospective, multicenter, randomized, two-arm, open-label, non-implanted control trial
- 323 patients (264 pre-market, 59 post-market)
  - NYHA 3
  - LVEF<35%
  - previous HF hospitalization OR NT-proBNP >400 pg/dl
  - no class I indication for CRT
  - NT-proBNP<1600 pg/dl
- Primary Endpoint: CV mortality and HF morbidity - neutral
- Additional Endpoints: **safety, QOL, exercise capacity, NYHA class**, freedom from death, LVAD implantation, heart transplant

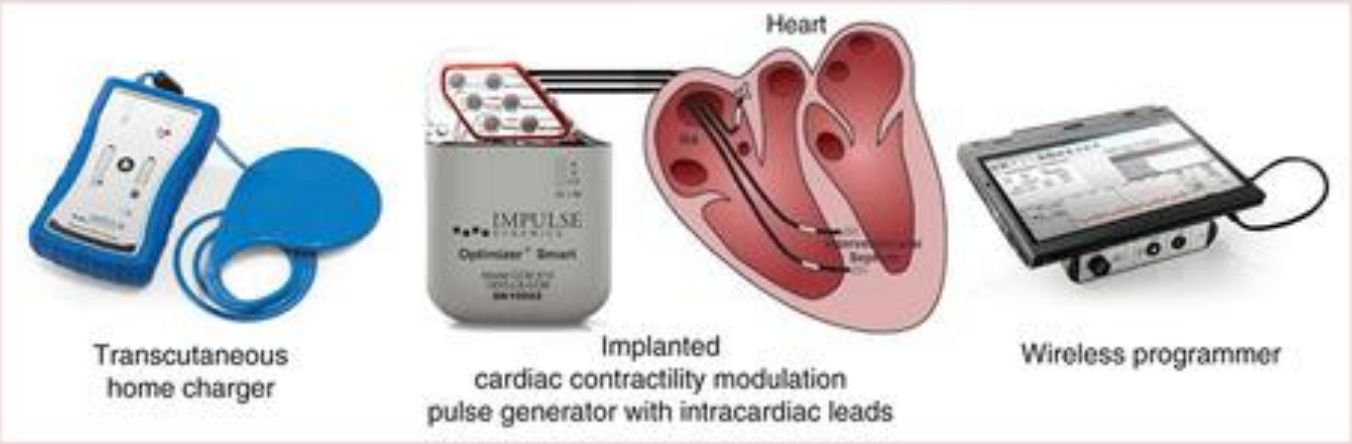
Zile et.al. Baroreflex activation therapy in patients with heart failure and a reduced ejection fraction: Long-term outcomes. European Journal of Heart FailureVolume 26, Issue

Abnormal calcium handling in HF

- Chronic over activation of the sympathetic nervous system leads to abnormalities of calcium regulatory proteins in the heart
  - reduced SERCA2 expression
  - leaky Ryanodine receptors (RyR2)
  - Phospholambin dysfunction
  - altered calcium channel function
- Disruptions in the normal calcium cycle
  - decreased contractility
  - impaired relaxation and impaired ventricular filling
  - arrhythmias



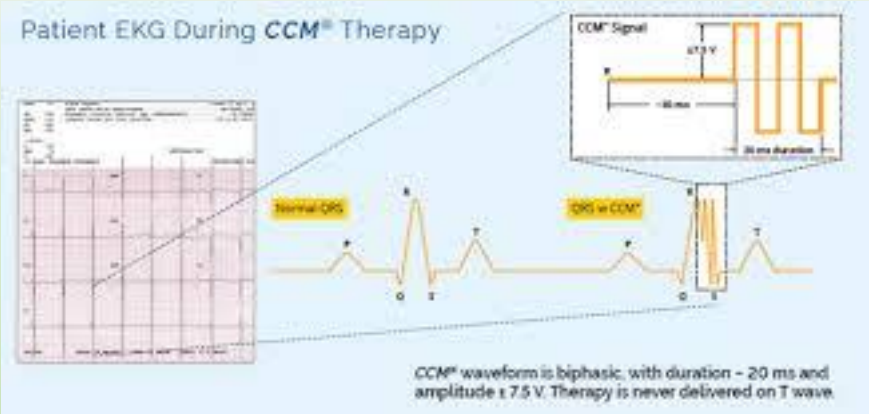
Cardiac Contractility Modulation (CCM Optimizer System - Impulse Dynamics)

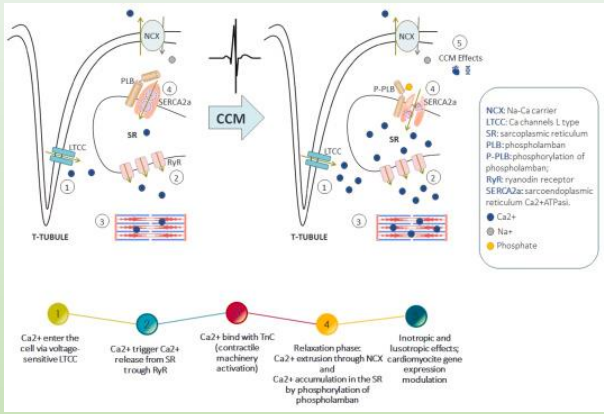


- Generator - rechargeable once weekly, battery lasts 20 years

Indications
- NYHA Class III or Class IV
- On guideline-directed medical therapies (medications and devices),
- LVEF 25-45%
- Not treated with CRT, or non-responder

How does CCM work?

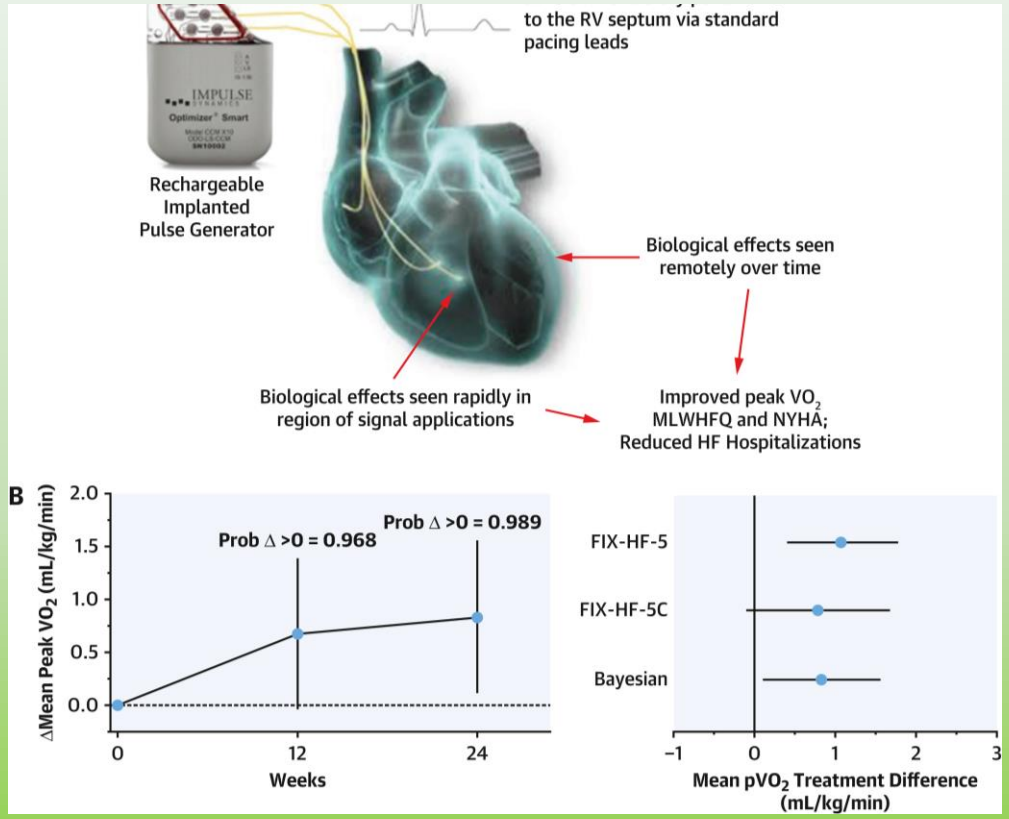




- Generator delivers nonexcitatory, high energy signals to the RV in the absolute refractory period
  - 1 hour stimulation cycles, 7 times/day, 2-3 hour breaks

- Improved calcium handling with enhanced systolic and diastolic function
- Gene expression changes related to proteins involved in calcium contraction and reuptake mechanisms
- Reduced cardiac fibrosis, reverse remodeling

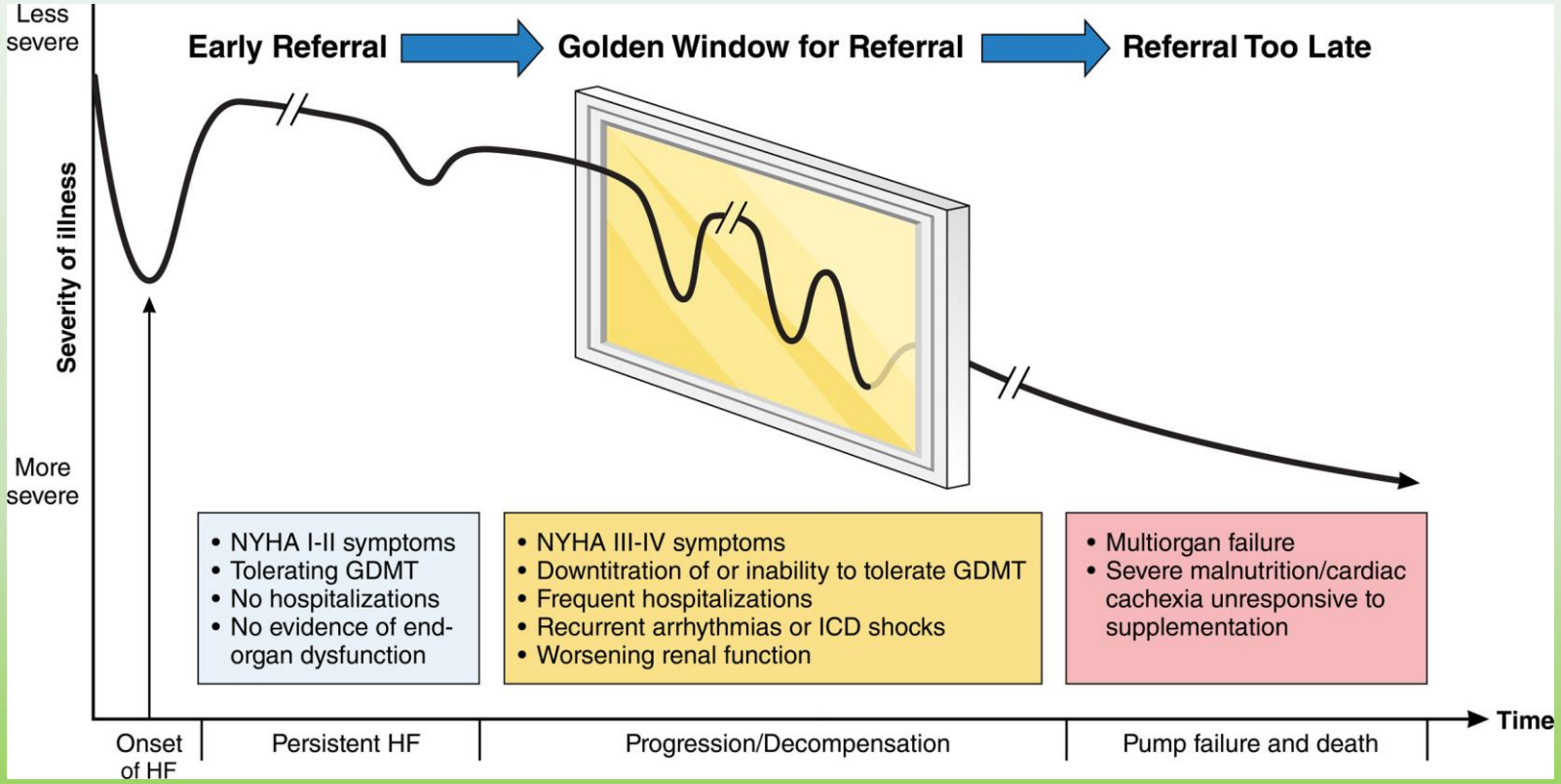
FIX-HF-5 Trials



- 2015:FIX-HF-5 428 patients NYHA 3 or 4, LVEF<35%
- 2018: FIX-HF-5C, 160 patients NYHA 3 or 4, LVEF 25-45%
- OMT vs. CCM
- Improved exercise tolerance
  - Improved peak VO2
  - Improved 6MWT
- Improved quality of life
- Reduced HF hospitalizations

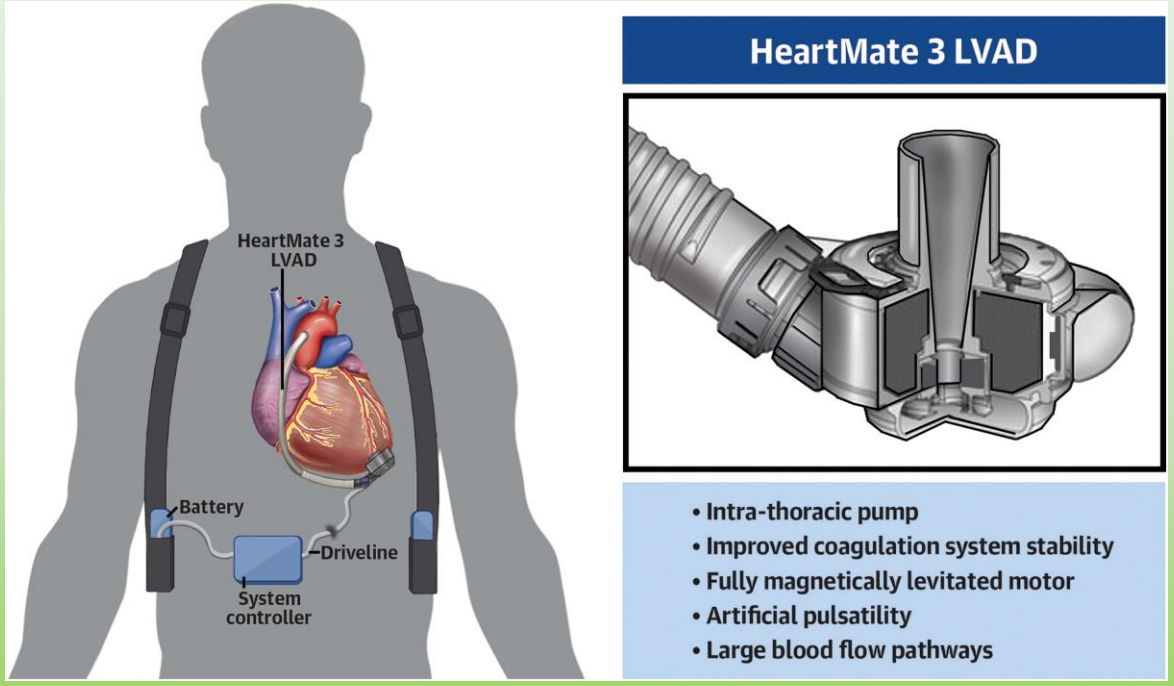
Fudim, M, Abraham, W, von Bardeleben, R. et al. Device Therapy in Chronic Heart Failure: JACC State-of-the-Art Review. JACC. 2021 Aug, 78 (9) 931–956. https://doi.org/10.1016/j.jacc.2021.06.040

Timely Referral for Heart Failure



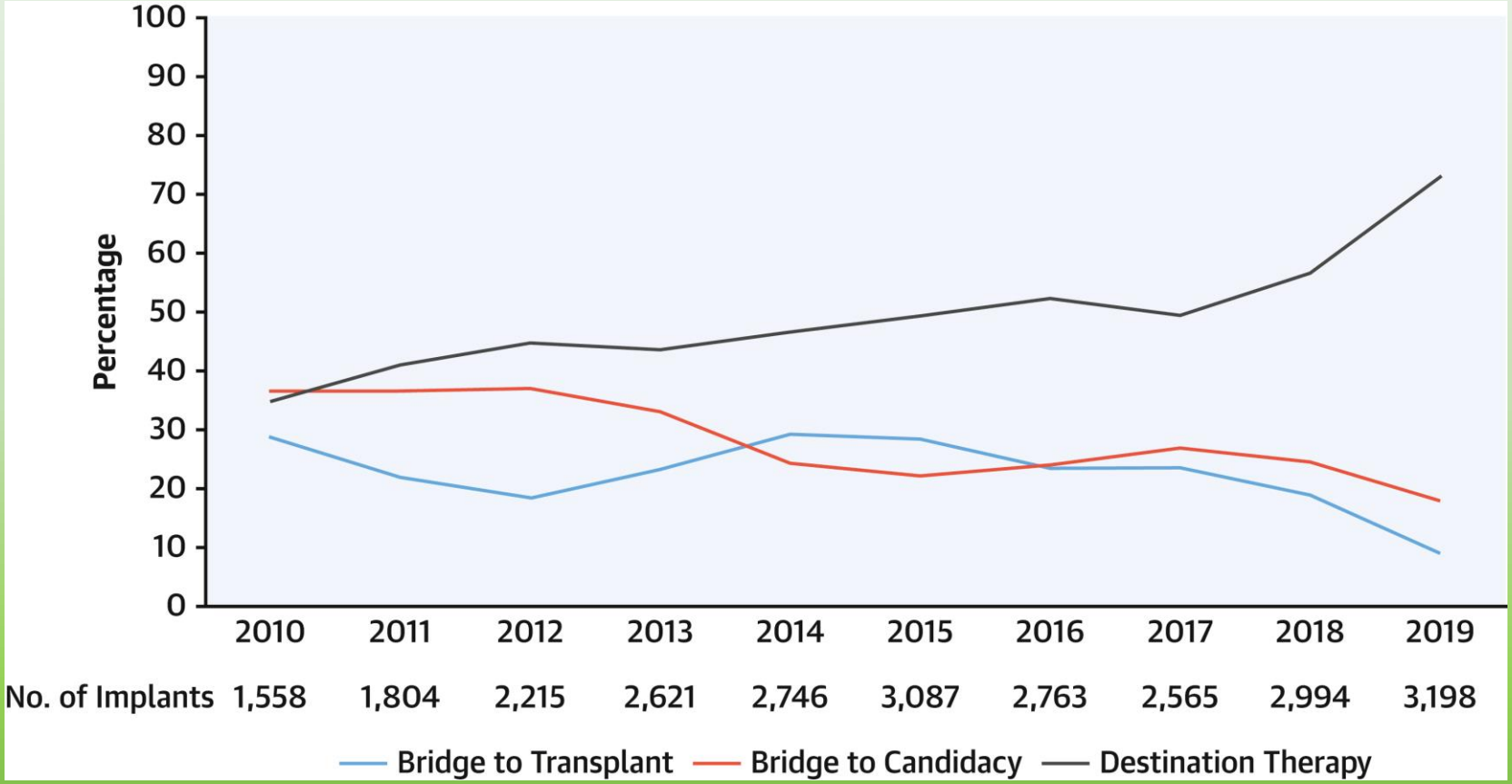
I	Need for **inotropes**
N	**New** York Heart Association Class IV
E	Worsening **end-organ** dysfunction
E	**Ejection fraction** <20%
D	**Defibrillator** shocks for ventricular arrhythmias
H	Recurrent **HF** hospitalizations
E	**Escalating** diuretic dose
L	**Low blood pressure**
P	**Progressive** intolerance of GDMT

Durable Left Ventricular Assist Device (LVAD) (Heartmate 3, Abbott) for Stage D Heart Failure

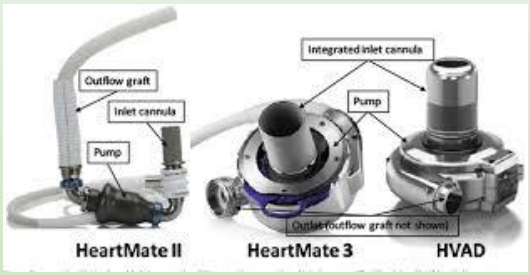


- Indications:
  - Stage D
  - NYHA 4 for 60-90 days
  - LVEF<25%
  - Max tolerated OMT
  - Inotrope dependence
- Contraindications
  - Severe/primary RV failure
  - Hypertrophic CM or uncorrectable septal defect
  - Neurologic compromise
  - Severe terminal comorbidity
  - Active bleeding
  - Psychosocial considerations

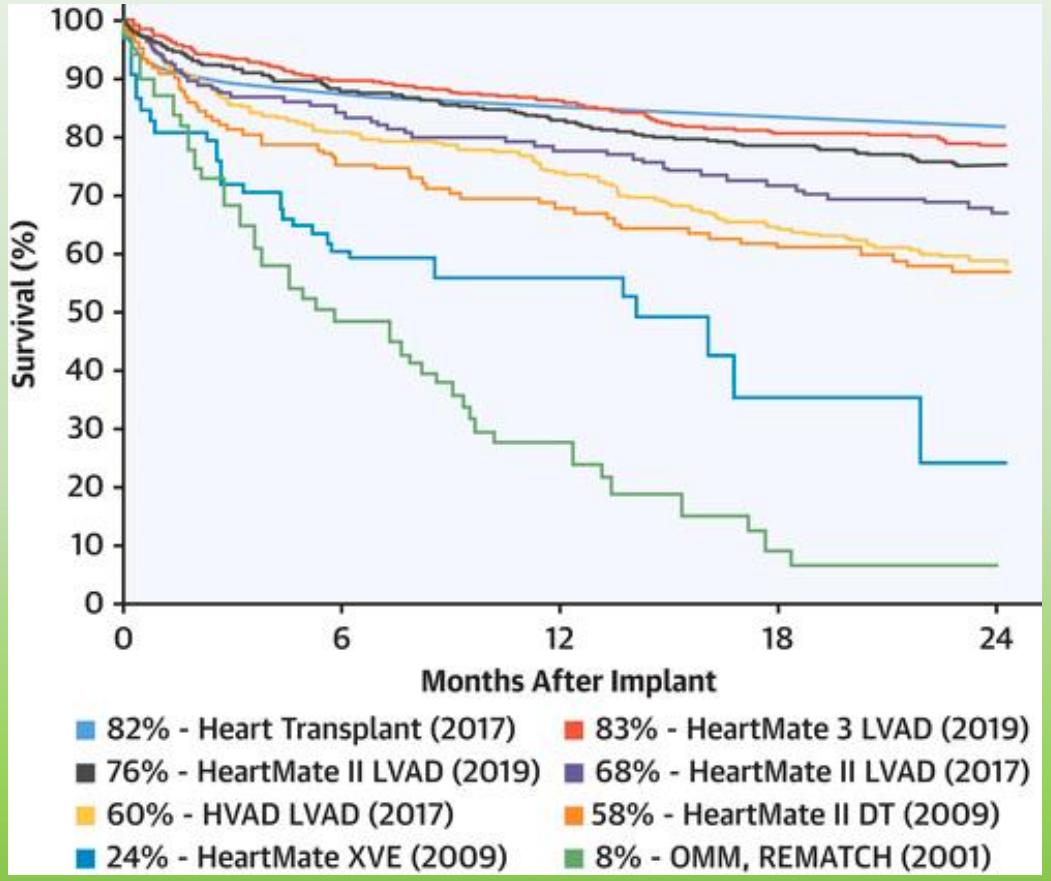
Indications for LVAD implant: BTT, DT



Improved Survival and symptoms on LVAD: Rematch, Heartmate 2 pivotal trial, Momentum



- Substantially improved survival
- Improved symptoms
  - 6MWT improved to >300m
  - >80% achieved NYHA I or II



CENTRAL ILLUSTRATION: Recent Trends in Left Ventricular Assist Device Implantation Strategies, Outcomes, and Management

Evolving Management Approaches

Surgical Approach
Thoracotomy-based implantation

Stroke
↓with HeartMate 3

Bleeding
Evaluation of ↓intensity antithrombotic therapy

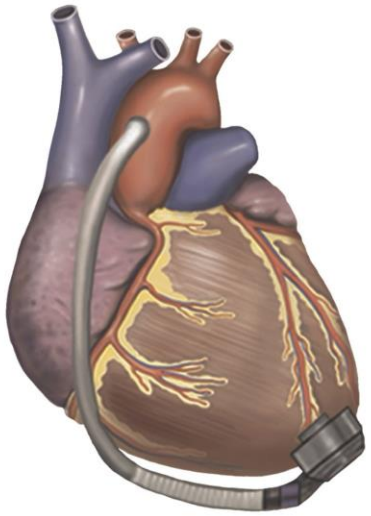
RV Failure
Assessment of RV reserve, evaluation of pulmonary vasodilators

Aortic Regurgitation
TAVR possible in select patients

Infection
Development of fully internalized devices

Myocardial Recovery
Possible with optimized mechanical unloading, pharmacotherapy, and serial functional assessment

Shared Decision Making
Implementation of decision aids



Recent Changes

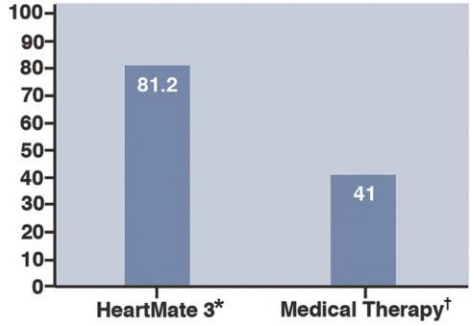
- HeartMate 3 LVAD FDA approved for DT
- UNOS donor heart allocation system revised
- Improved LVAD-related AE management

Contemporary Epidemiology

Recipient Phenotype
↑Comorbidities
↑Preoperative illness severity
> 50% in cardiogenic shock
> 1/3 on pre-implant TMCS

Implant Strategy
DT (73.1%) >> BTT (8.9%)
↓Durable LVAD at time of HT

2-Year Survival Rate of Advanced HF Patients Stratified by Treatment



Varshney AS, et al. J Am Coll Cardiol. 2022;79(11):1092-1107.

Conclusions

- The Autonomic nervous system is intimately linked to heart failure symptoms and progression.
- Device therapies for heart failure are are for people with symptomatic (Stage C or D) heart failure on optimal/best tolerated HF GDMT
- PA pressure sensors, Baroreflex Activation Therapy, and Cardiac Contractility Modulation are for symptomatic heart failure
  - Improve symptoms and functional status
  - Reduce HF hospitalizations
- LVAD is for advanced stage (stage D) HFrEF patients with LVEF<25%
  - Improve survival
  - Improve symptoms and functional status
  - Use I-NEED-HELP to identify advanced stage HF and refer to an advanced HF program