Device Therapy for Heart Failure

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Learning Objectives

- **Overview of Heart failure stages and role of device-based therapies**
- **Implantable Cardioverter Defibrillator (ICDs) in primary prevention of SCD**
- **New defibrillation strategies (wearable ICD and subcutaneous ICD)**
- **Cardiac Resynchronization Therapy(CRT)**

Background

- In 2013, the ACC/AHA published an updated Guideline for the Management of Heart Failure
- New terminologies, concepts and recommendations were introduced
- An attempt was made to harmonize the guideline with other guidelines, consensus documents and position papers which are cross- referenced

Yancy CW, et all. Circulation 2013

Terminology

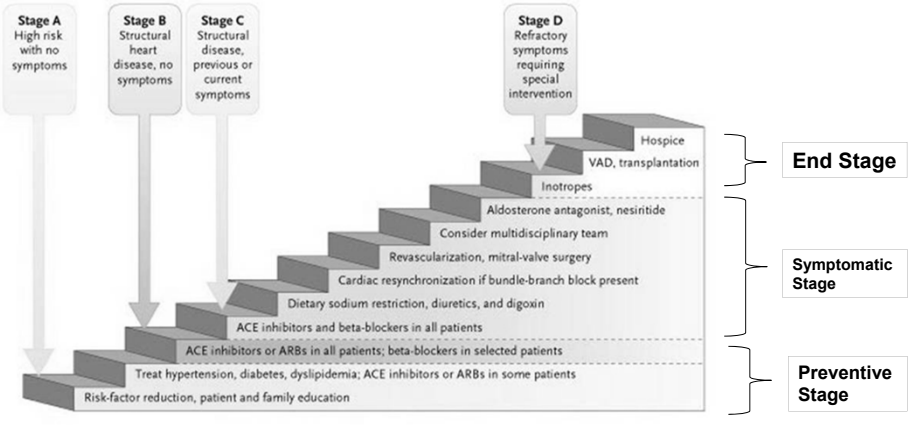
- Guidelines Directed Medical Therapy (GDMT)- represents the optimal medical therapy recommended with a class 1 indication
- Heart Failure with reduce Ejection Fraction (HFrEF). LVEF ≤ 40 %
- Heart failure with preserved Ejection Fraction (HFpEF). LVEF ≥ 50 %
  - HFpEF, borderline (LVEF 41-49 %)
  - HFpEF, improved (LVEF >40 %)
- Maintained the concept of "stages"

Classification of HF: Comparison Between ACC/AHA HF Stage and NYHA Functional Class

ACC/AHA HF Stage[1]	NYHA Functional Class
A At high risk for heart failure but without structural heart disease or symptoms of heart failure (eg, patients with hypertension or coronary artery disease)	None
B Structural heart disease but without symptoms of heart failure	I Asymptomatic
C Structural heart disease with prior or current symptoms of heart failure	II Symptomatic with moderate exertion
	III Symptomatic with minimal exertion
D Refractory heart failure requiring specialized interventions	IV Symptomatic at rest

[1]Hunt SA et al. *J Am Coll Cardiol.* 2001;38:2101–2113.

Therapeutic Options for Heart Failure Stages



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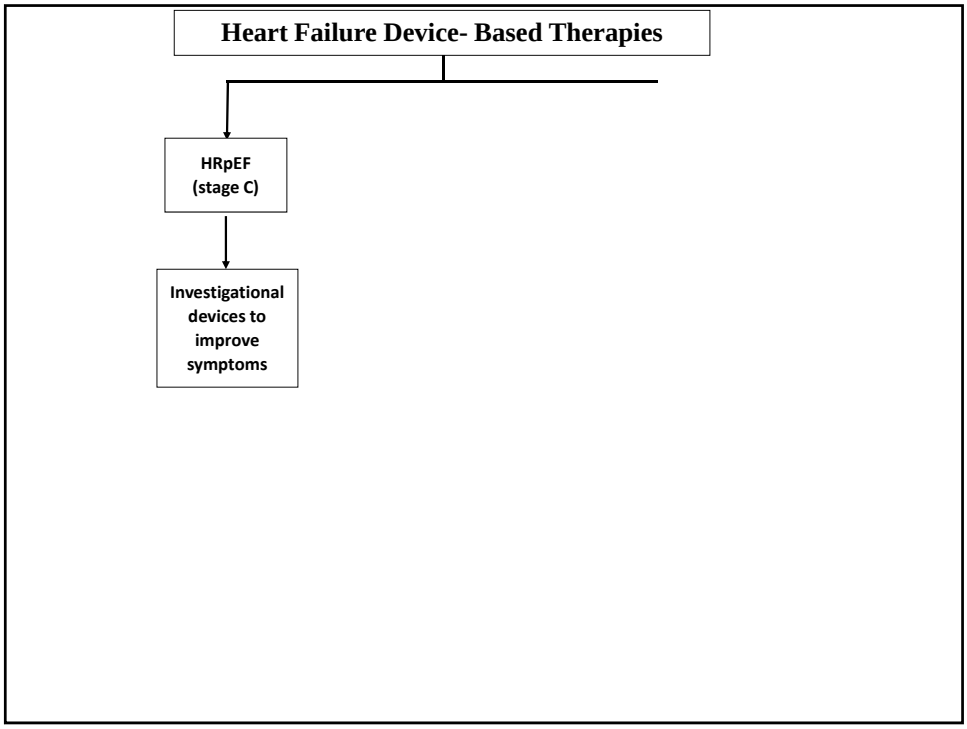
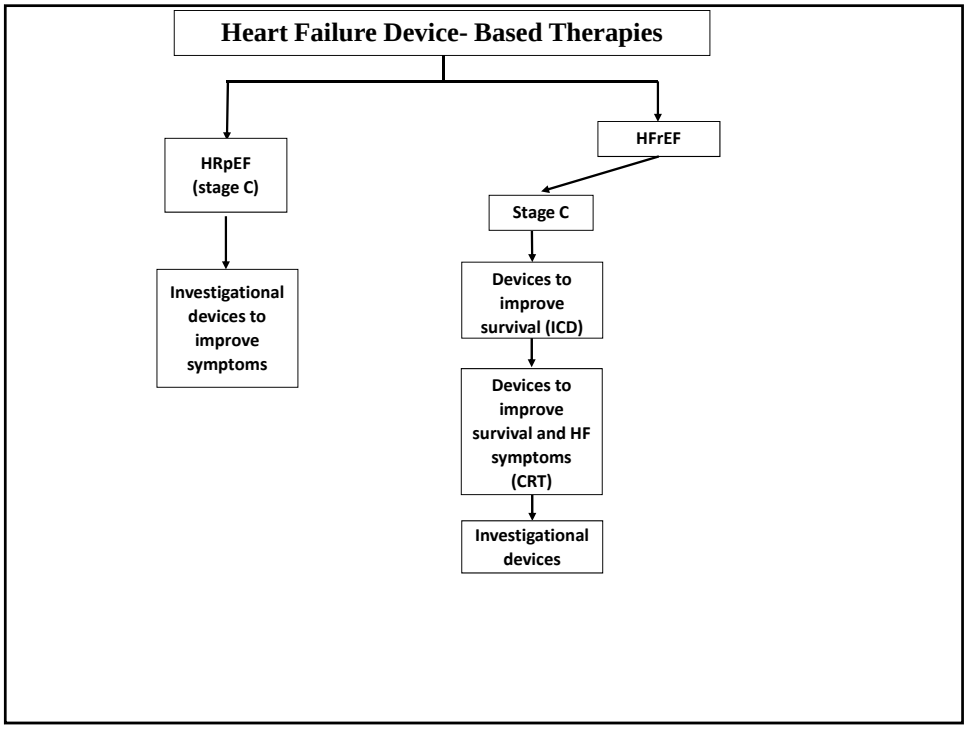

Heart Failure Device- Based Therapies
HRpEF (stage C)
Investigational devices to improve symptoms


Heart Failure Device- Based Therapies
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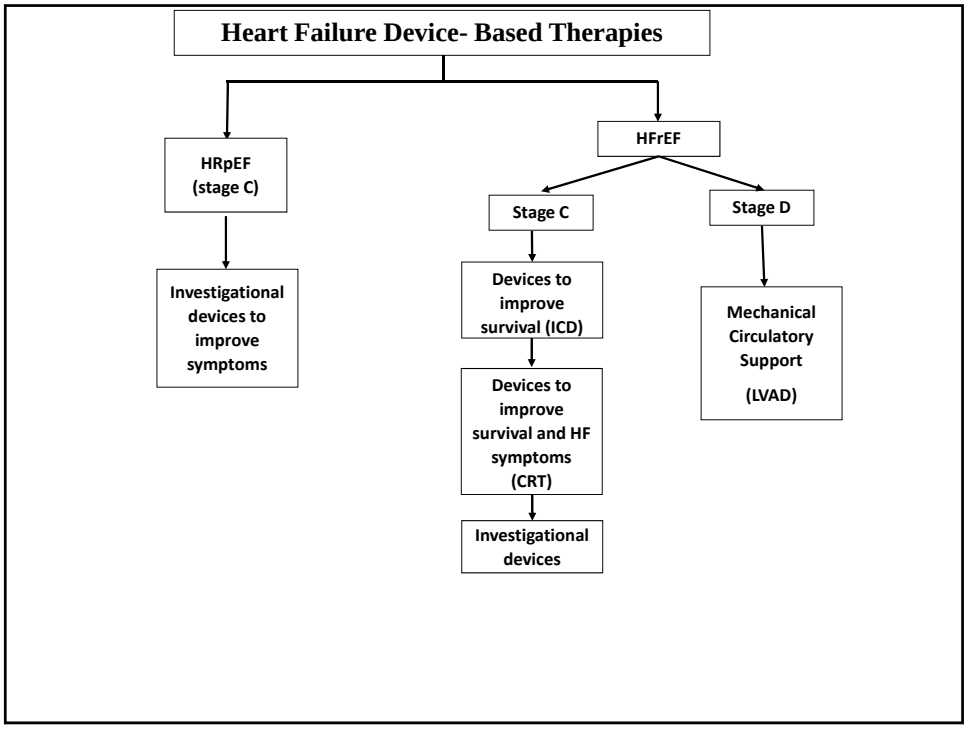
HFrEF
Stage C
Devices to improve survival (ICD)
Devices to improve survival and HF symptoms (CRT)
Investigational devices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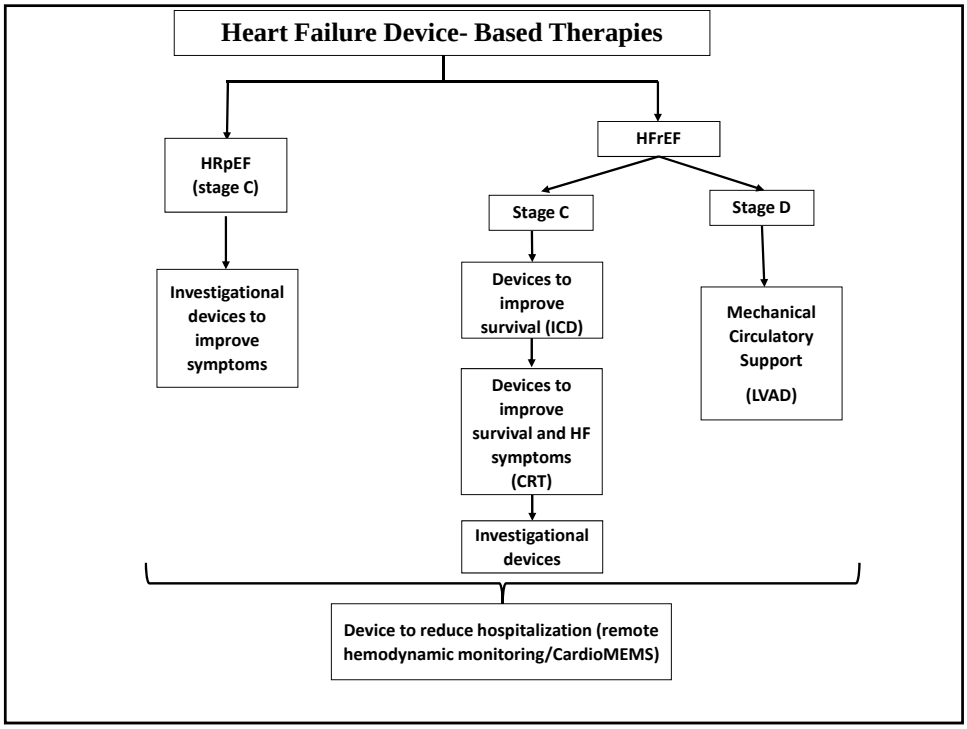
Investigational devices
Stage D
Mechanical Circulatory Support
(LVAD)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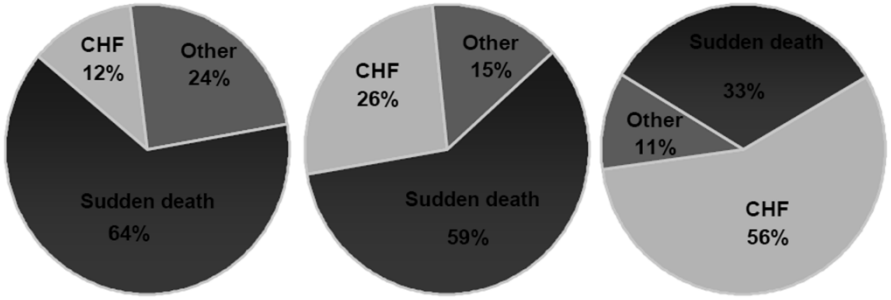
Devices to improve survival (ICD)
Devices to improve survival and HF symptoms (CRT)
Investigational devices
Stage D
Mechanical Circulatory Support
(LVAD)
Device to reduce hospitalization (remote hemodynamic monitoring/CardioMEMS)

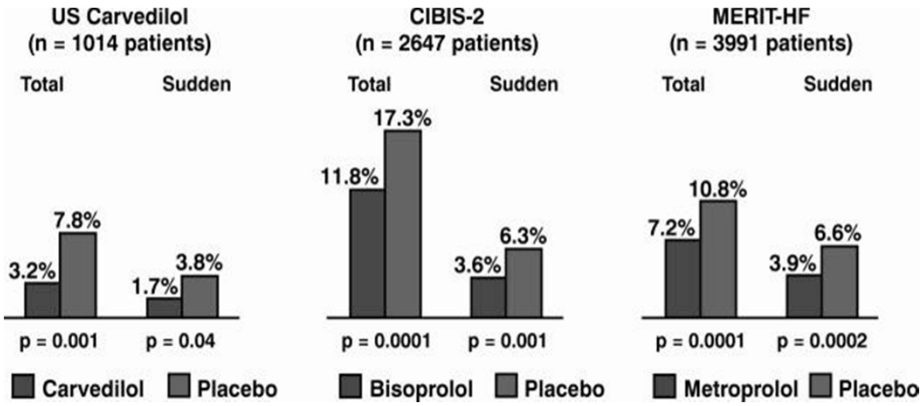
Mode of Death in Heart Failure



NYHA Class 2 **NYHA Class 3** **NYHA Class 4**

MERIT-HF Lancet 1999

Beta Blockers' Effects on total Mortality and Sudden Death in Patients with HF

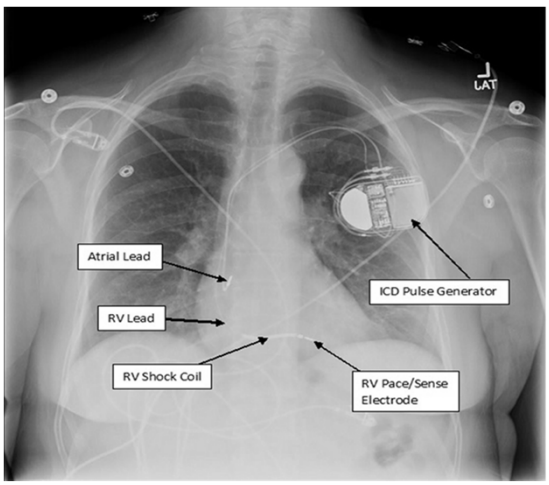


Heart 2001;85:97–103

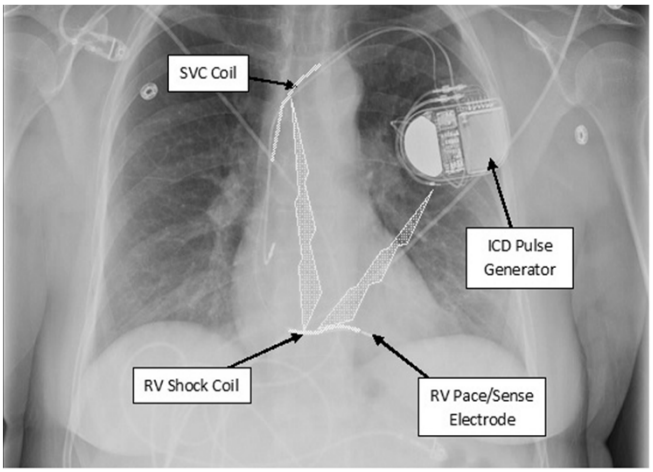
Implantable Cardioverter-Defibrillator (ICD) Basics

- Designed to treat a cardiac tachydysrythmia
- Performs cardioversion/defibrillation
  - Ventricular rate exceeds programmed cut-off rate
- ATP (antitachycardia pacing)
  - Overdrive pacing in an attempt to terminate ventricular tachycardias
- All have pacemaker function (combo devices)

Major Components of the ICD system



Schematic View of the Defibrillation Shock Generated by the ICD



SCD Primary Prevention Trials (ICD Vs. Conventional Therapy)

- MADIT II
- SCD-HeFT

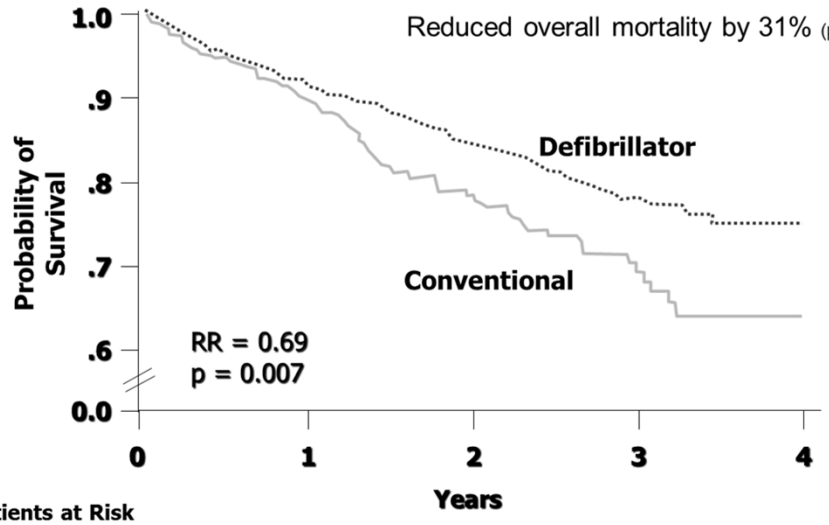
MADIT-II

Objective:

- Evaluate the effectiveness of ICD therapy (n = 742) compared to conventional therapy (n = 490) in high-risk post-MI patients
- Post-MI ≥ 4 weeks, and
- LVEF ≤ 30%

Moss AJ. *N Engl J Med*. 2002;346:877-883

MADIT-II Survival Results



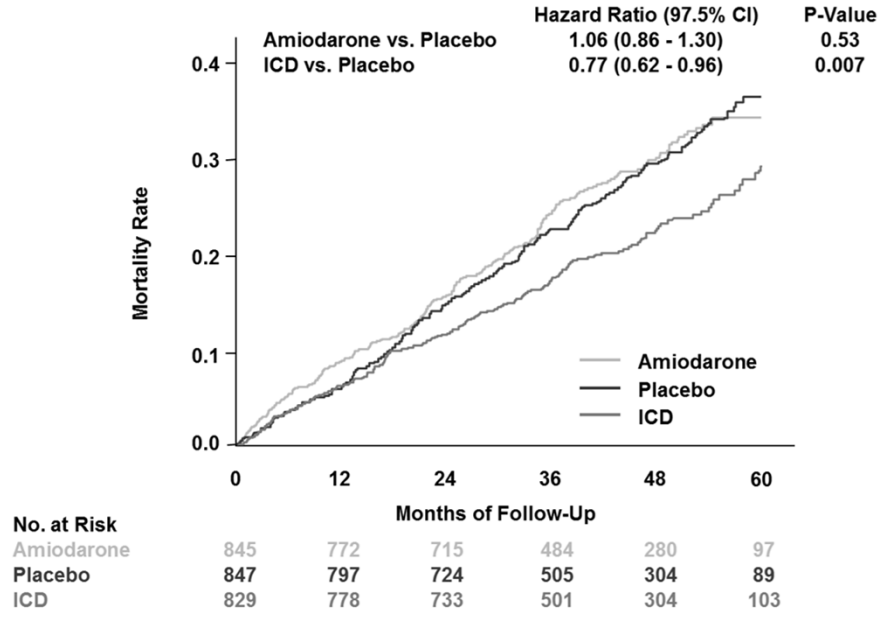
Patients at Risk					
Defibrillator	742	502 (0.91)	274 (0.94)	110 (0.78)	9
Conventional	490	329 (0.90)	170 (0.78)	65 (0.69)	3

Moss AJ. *N Engl J Med*. 2002;346:877-883.

SCD-HeFT
Sudden Cardiac Death in Heart Failure Trial

- Determine if amiodarone or ICD will decrease the risk of death from any cause in patients with mild-to-moderate heart failure (Class II and III).
- Maximally treated CHF for ≥ 3 months with a LVEF of ≥ .35

SCD-HeFT Mortality Rate Overall Results



Bardy GH. *N Engl J Med.* 2005;352:225-237.

Who should get an ICD?

- Ischemic CM, LVEF <0.30 (MADIT II)
- Ischemic and nonischemic dilated cardiomyopathy, NYHA class II/III CHF, LVEF < 35%. (SCD-HeFT).

Who should NOT get an ICD?

- CABG or PCI within the past 3 months-CABG-Patch [1]
- Acute MI within the past 40 days-DINAMIT [2]
- Concomitant disease with less than 1 year likelihood of survival.

1) Bigger et al. N Engl J Med 1997;337:1569-74
2) Hohnloser S et al. N Engl J Med 2004;351:2481-2488

Wearable ICD System

ICDs and MRI

- **It is becoming feasible to use MRI for certain ICD and lead models that are MRI compatible if done according to certain protocols**
- **Consulting with specialists is necessary before ordering MRIs in patients with ICDs**

Indications for ICD Deactivation

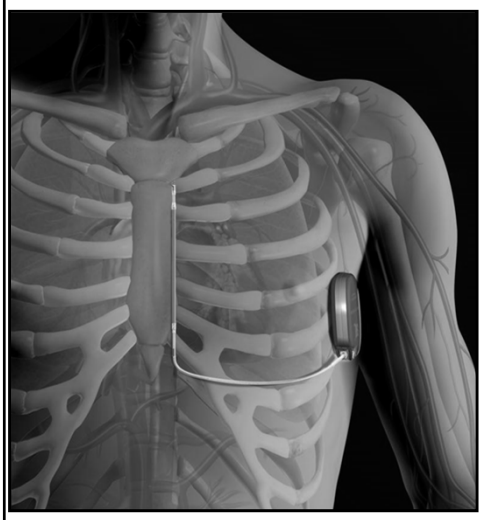
- **End-of-life care**
- **Recurrent inappropriate shocks due to lead failure or SVT/ AF with rapid ventricular response**
- **During surgical procedures requiring the use to electrocautery in close proximity to the pulse generator**

Case Presentation

- **A 45 year-old female with history of breast cancer, s/p bilateral mastectomy and chemotherapy (2 years ago). Her cancer is currently in remission with favorable prognosis. She developed Adriamycin induced cardiomyopathy and despite >9 months of guideline directed medical therapy for heart failure, her LVEF remains 30%. She belongs to NYHA FC II. Her ECG shows NSR, normal intervals, QRS 90 ms, nonspecific T-wave abnormalities. Her L subclavian vein is occluded and she has a history of DVT in the R subclavian vein as a complication of prior Port-a-cath.**
- **Intravenous ICD implant is recommended?**

A. True
B. False

Subcutaneous ICD

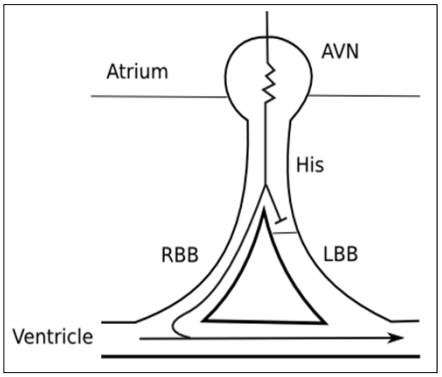


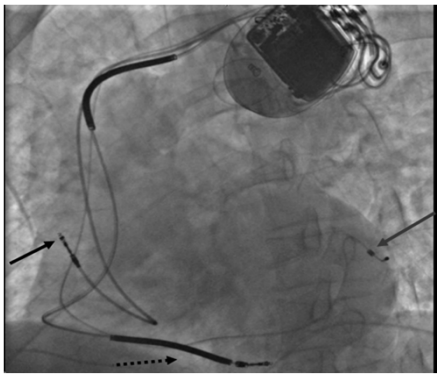
- 80 joules (delivered)
- 69cc, 145 grams
- Active generator
- 5 year longevity
- Post-shock pacing
- Single lead connection
- Full featured episode storage
- No Brady pacing or ATP

Subcutaneous ICD VS. Transvenous ICD

Factors Favor S-ICD	Factors Favor TV- ICD
➢ Young and active (less lead failure) ➢ CHD that limits lead placement, valve surgery ➢ Indwelling catheters ➢ Immunocompromised ➢ Inherited channelopathies (low VT risks).	➢ Recurrent monomorphic VT (role of ATP) ➢ Bradycardia requiring pacing ➢ Indication for CRT ➢ High risk for VT (e.g. sarcoidosis, ARVD). ➢ Preference for remote monitoring

Cardiac Resynchronization Therapy (CRT)

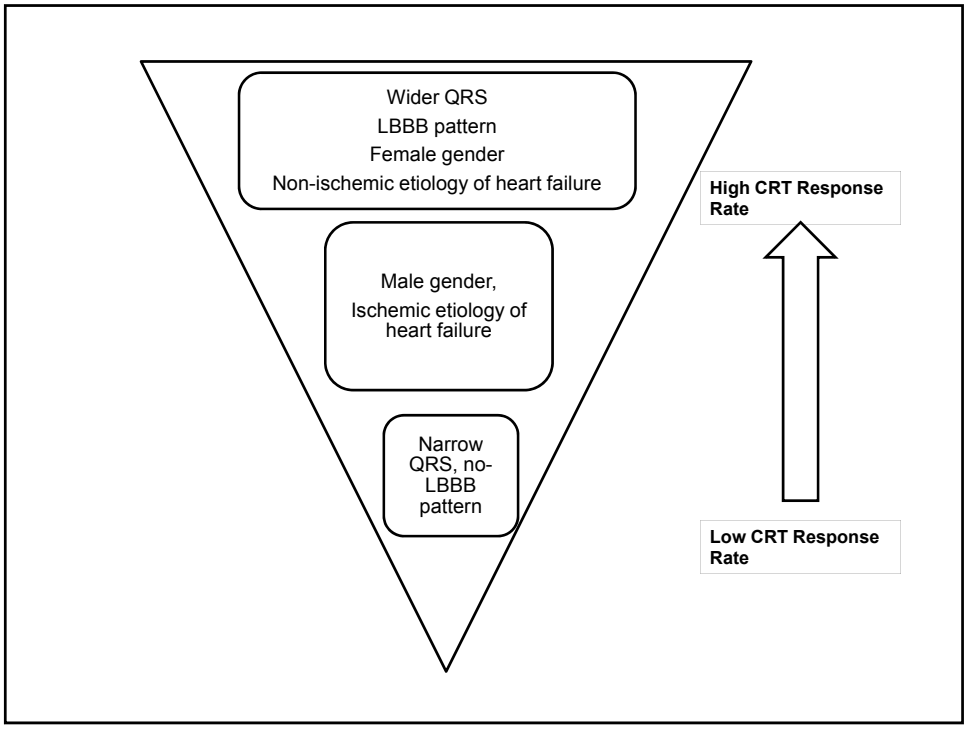




LBBB **CRT**

Major CRT Trials

Trial	Design	Patients	Mean follow-up	NYHA	LVEF Inclusion criteria	QRS Inclusion criteria	Primary end point	Results significantly favoring intervention group
COMPANION (2004)	• CRT-D • CRT-P • ICD	• 617 • 595 • 308	15	III, IV	≤35%	≥ 120 ms	All-cause mortality or hosp	+ / +
CARE-HF (2005)	• CRT-P • Med	• 409 • 404	29	III, IV	≤35%	≥ 120 ms	All-cause mortality or cardiovascular hospitalization	+
MADIT-CRT (2009)	• CRT-D • ICD	• 1089 • 739	29	I, II	≤30%	≥ 130 ms	All-cause mortality or HF hosp	+



Indications for CRT

	NYHA Class I	NYHA Class II	NYHA Class III & Ambulatory Class IV
Class I Indications		• LVEF ≤ 35% • QRS ≥ 150ms • LBBB pattern • Sinus rhythm	• LVEF ≤ 30% • QRS ≥ 150ms • LBBB pattern • Sinus Rhythm
Class IIa Indications		• LVEF ≤ 35% • QRS 120-149 ms • LBBB pattern • Sinus rhythm	• LVEF ≤ 35% • QRS 120-149 ms • LBBB pattern • Sinus rhythm
			• LVEF ≤ 35% • QRS ≥ 150ms • Non-LBBB pattern • Sinus rhythm
Class IIb Indications	• LVEF ≤ 30% • QRS ≥ 150ms • LBBB pattern • Ischemic cardiomyopathy	• LVEF ≤ 35% • QRS ≥ 150ms • Non-LBBB pattern • Sinus rhythm	• LVEF ≤ 35% • QRS 120-149 ms • Non-LBBB pattern • Sinus rhythm

Devices to Reduce Readmissions

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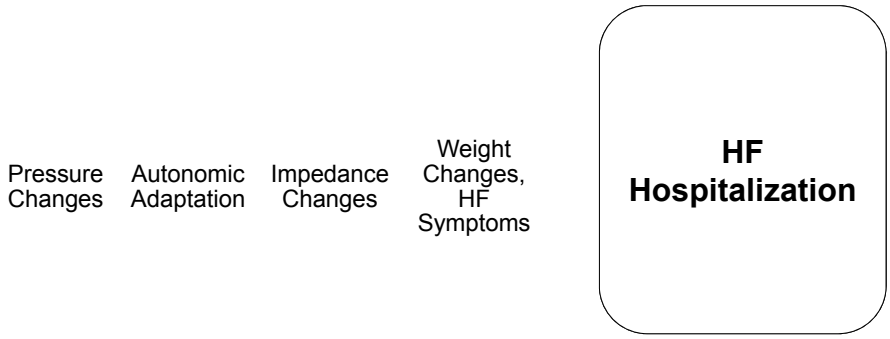
Burden of Heart Failure

Heart failure is a big problem …

- **HF affects 5.5-7 million Americans**
- **$31 Billion on HF hospitalizations**
- **Most frequent cause of rehospitalization in the US**
- **Importantly, *repeat HF admissions lead to worsening mortality!***

Heidenriech PA, et al, *Circ Heart Fail* 2013
Jencks SF, et al, *NEJM* 2009
Setoguchi S, et al, *Am Heart J* 2007

Evolution of Acute Heart Failure



Adamson P, et al, *Curr Heart Fail Report*, 2009

Traditional Methods: Weights & Symptoms

Benefits

- Easy to understand
- Minimal equipment
- Low costs

Drawbacks

- Low compliance rates
- Variability in implementation
- Sensitivity <25%

Moser DK, *Am Heart J* 2005
van der Wal MH, *Eur Heart J* 2006
Abraham WT, *Congest Heart Fail* 2011

Telemedicine Trials to Reduce Readmissions

TELE-HF	TIM-HF	BEAT-HF
NIH sponsored	710 patients	1400+ patients
1600+ patients	Telemonitoring of weight & symptoms	Electronic telemonitoring
Frequent phone interactions	**Not effective**	**Not effective**
Not effective		

Bioimpedance

Benefits

- Can be obtained from devices already implanted
- Correlate well to invasive measures

Drawbacks

- Not a primary indication for device implant
- Unlikely to be an option for HFpEF
- Low positive predictive value

Yu CM, *Circ* 2005
Conraads VM, *Eur Heart J* 2011

Bioimpedance Trials

FAST	DOT-HF	OptiLink-HF
☐ Good sensitivity	☐ **No reduction in hospitalizations**	☐ Recently conducted
☐ Good compliance	☐ Increased hospitalizations	☐ **No hospitalization reduction**
☐ Exploratory only		☐ Data did not induce clinical actions

Autonomic Adaptation: Biomarkers

Benefits

- Both HFpEF & HFrEF
- Repeatable and widely available

Drawbacks

- Requires phlebotomy (lab visit)
- Costs
- Confounding variables (*e.g.* obesity)
- Unclear what constitutes improvement

Yu CM, *Circ* 2005
Conraads VM, *Eur Heart J* 2011

Biomarker Trials for Rehospitalization

Trial	Biomarker	Size	Outcome
Troughton, et al	BNP	69	Positive
STARS-BNP	BNP	220	Positive
Berger R, et al	NT-proBNP	278	Positive
PROTECT	NT-ProBNP	151	Positive
PRIMA	NT-ProBNP	345	Negative
BATTLE-SCARRED	NT-proBNP	364	Negative
TIME-CHF	BNP	499	Negative
GUIDE-IT	NT-proBNP	1100 (planned)	Stopped Early (ineffective)

Hemodynamic Monitoring

Benefits

- Both HFpEF & HFrEF (CardioMEMS™)
- Hemodynamics correlate well to HF events
- Occurs early in the decompensation process
- Known targets (PAD < 18 mmHg)

Drawbacks

- Invasive procedure
- Additional device (CardioMEMS)
- Monitoring by staff required

Stevenson LW, *Am J Cardiol* 1990
Morley D, *Am J Cardiol* 1994
Stevenson LW, *Circ Heart Fail* 2010

Hemodynamic Monitoring: Sensor Choice

RV Lead	• Good for patients who need devices • Unavailable to patients without device • Worsening battery life
LA lead	• LA pressure better than PAD? • An additional device implant • Transseptal implant associated with increased complications
PA Sensor	• No battery • Low implant complication rate • Limited by body habitus • Cost & reimbursement factors

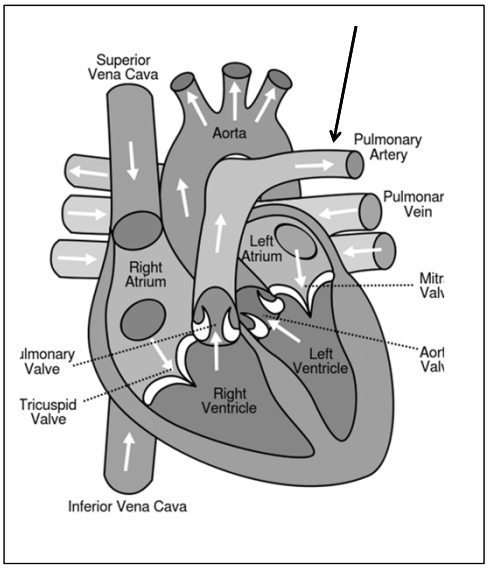
Hemodynamic Monitoring: The Secret Sauce

- **Early trials with hemodynamic monitoring did not improve outcomes. Why?**
- **Successful use of hemodynamics requires treatment to a numeric goal**
- **This must happen independent of symptoms**
  - **Physiologic changes will occur before symptoms**

Bourge RC, *JACC* 2008

PA Sensors

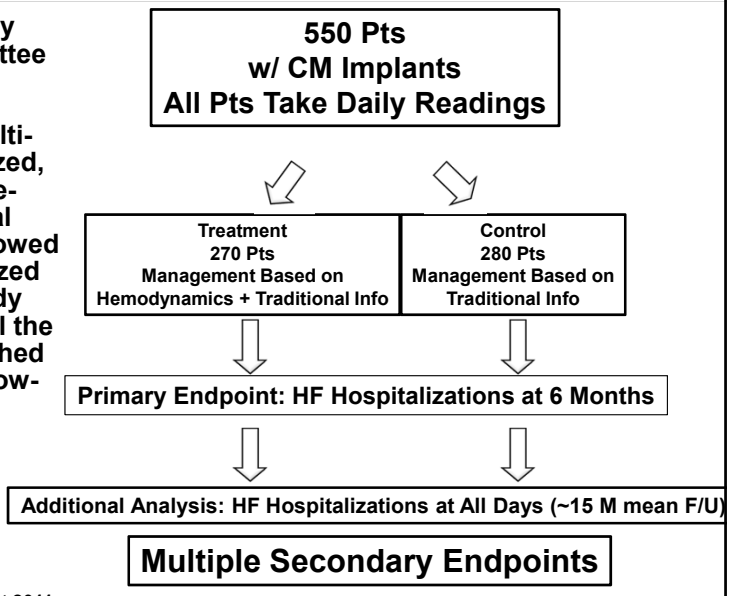
- Implanted via right heart cath technique
- Typically placed in branch of left PA
- Provide PA systolic, diastolic, and mean pressures
- PA diastolic pressures typically mirror PCWP/LA pressures



www.wikipedia.org

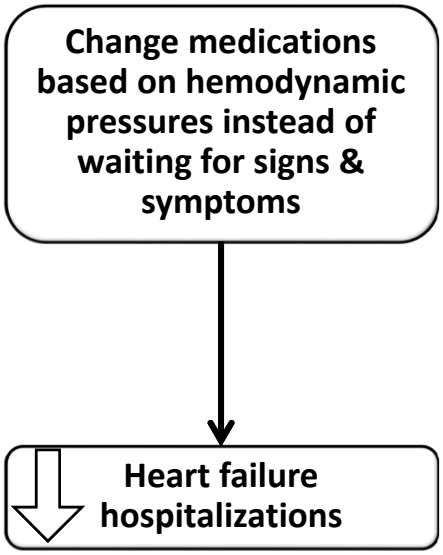
CHAMPION: CardioMEMS Heart Sensor Allows Monitoring of Pressure to Improve Outcomes in NYHA Class III Heart Failure Patients

- Trial Designed by Steering Committee with active FDA input
- Prospective, multi-center, randomized, controlled single-blind clinical trial
- All subjects followed in their randomized single-blind study assignment until the last patient reached 6 months of follow-up
- 64 US Centers
- PIs: William Abraham, Phil Adamson



Abraham WT, et al. Lancet 2011

Hypothesis of the CHAMPION Trial



Protocol Guidelines: PA Pressure Management

Treatment Recommendations for Elevated PA Pressures
• Add or increase diuretic – increase/add loop diuretic – change loop diuretic – add thiazide diuretic – IV loop diuretic
• Add or increase vasodilator – add or increase nitrate

Primary Efficacy Endpoint

	Treatment (n=270)	Control (n=280)	Relative Risk Reduction	p-value[1]	NNT
Primary Efficacy Endpoint: HF Related Hospitalizations (Rate for 6 months)	84 (0.32)	120 (0.44)	28%	0.0002	8
Supplementary Analysis: HF Related Hospitalizations (Full Duration - Annualized Rate)	158 (0.46)	254 (0.73)	37%	<0.0001	4

[1]p-value from negative binomial regression
NNT = Number Needed to Treat

Abraham WT, et al. Lancet 2011

PA Monitoring Benefits Are Additive

GDMT Class	HF Hospitalization		Mortality	
	Hazard Ratio	NNT	Hazard Ratio	NNT
ACEi/ARB	0.59	4	0.48	7
Beta-blocker	0.66	5	0.59	11
ACEi/ARB & Beta-blocker	0.57	3	0.43	7

Abraham WT, *JACC* 2015

Hemodynamic Monitoring Summary

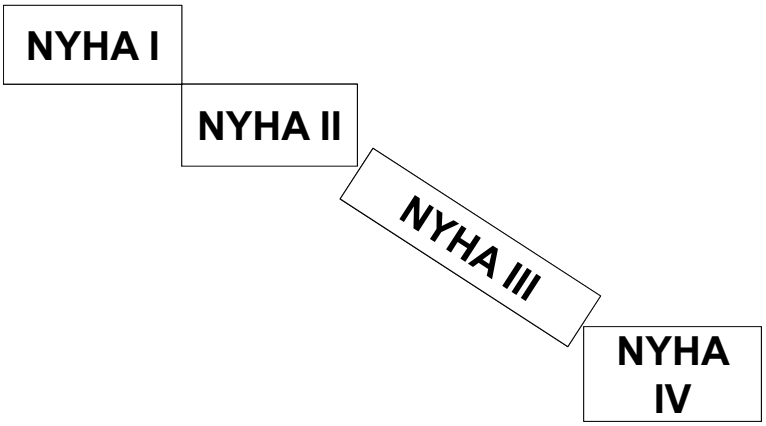
- Implantable hemodynamic monitors provide direct and actionable measurements of intra-cardiac and pulmonary artery pressures
- Management guided by such monitors reduces the risk of heart failure hospitalizations
- This approach promises to revolutionize the management of heart failure patients
  - Crisis management ➔ Stability management

CardioMEMS™: Current Status

- Only approved PA pressure monitoring system at present
- Approved for use in NYHA III HF patients
- Intended to:
  - Reduced HF hospitalizations
  - Improved QoL
  - No indication to improve survival

Mechanical Circulatory Support Devices

HF Topography



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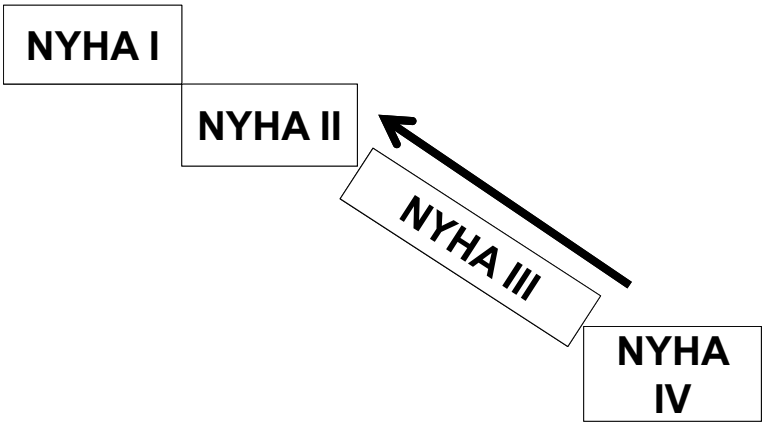

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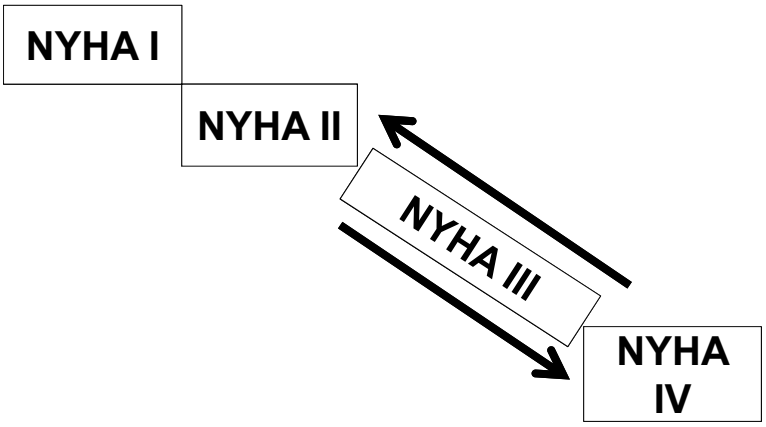


NYHA Classification

1 year mortality of NYHA III HF is 10-15%

Scrutenid *et al*, *EHJ* 1994
Gheorghiade *et al*, *JACC* 2013

NYHA Classification

1 year mortality of NYHA III HF is 10-15%

A HF hospitalization is a strong predictor of mortality (NYHA IIIb-IV)

Scrutenid *et al*, *EHJ* 1994
Gheorghiade *et al*, *JACC* 2013

NYHA Reproducibility

Inter-observer evaluation

- **Exact reproducibility: 56%**
- **Within 1 functional class: 93%**

Goldman *et al*, *Circ* 1981
Franciosa *et al*, *Am J Med* 1979
Bennett *et al*, *JHLT* 2002

NYHA Reproducibility

Inter-observer evaluation

- **Exact reproducibility: 56%**
- **Within 1 functional class: 93%**

NYHA III best correlated with exercise testing (75% of patients)

Goldman *et al*, *Circ* 1981
Franciosa *et al*, *Am J Med* 1979
Bennett *et al*, *JHLT* 2002

Cardiopulmonary Exercise Testing

- Also known as metabolic stress test, VO2 test
- Peak VO_2 performance <14 ml/kg/min is associated increased risk of death within 24 months in HF patients

Mancini D, et al, *Circ* 1991

No VO_2 testing? Try a 6-minute walk

- Distance ≤ 468 m (1535 ft) predicts higher mortality and hospitalization risk
- 6MWT is a good screening tool
- However, not as strongly correlated as VO_2 data

Wegrzynowska-Teodorczyk K, *et al*, *J Physiotherapy* 2013

The High-Risk HF Patient

1 or more of the following:

- **HF Sx that fail to respond to medical therapy (persistent NYHA III or worse symptoms)**
- **Peak VO_2 <14 ml/kg/min**
- **Intolerance to HF meds (esp new intolerance)**
  - **Hypotension**
  - **Renal dysfunction**
  - **Bradycardia**
- **Frequent hospitalizations**
  - **2 in 3 months**
  - **3 in 6 months**
  - **Need for inotropes during hospital stay**

Treatment Options for High-Risk HF Patients

Transplant

- Good long term survival
- Strict selection criteria
- Limited supply of donor hearts
- Complex post-transplant medical regimen

Ventricular Assist Devices

- Improving long term survival (>70% at 2 years)
- Non-limited resource
- Can be bridge-to-transplant (BTT) or destination therapy (DT)
- Requires anti-coagulation
- Complex post-implant medical regimen

Palliative Care/Hospice

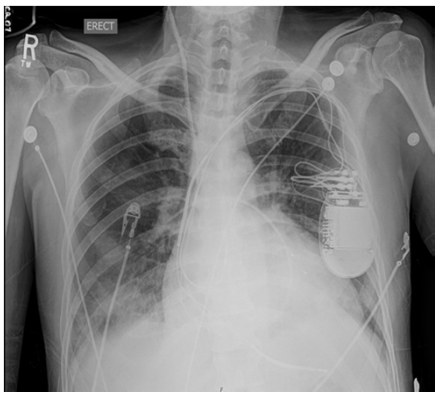
- Quality of life > survival

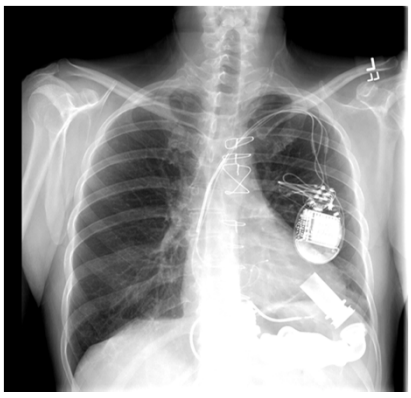
VAD Criteria

- **Used as either Bridge to Transplant (BTT) or Destination Therapy (DT)**
- **EF≤ 25%**
- **For BTT – must be listed for transplant**
- **For DT:**
  - **Failed optimal therapy for 45 of last 60 days**
    - **Or inotrope dependent (minimum 14 days)**
    - **Or IABP x 7 days**
  - **Peak VO_2 ≤ 14**

www.cms.gov

Ventricular Assist Devices





Summary of VAD Therapy for HF

- Improves survival
- Improves functional status
- Improves quality of life
- Improving technology to reduce complications
- Part of guideline recommendations for treatment of HF

Jorde U, et al, *JACC* 2014
Rogers J, et al, *JACC* 2010
Yancy CW, et al, *JACC* 2013