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

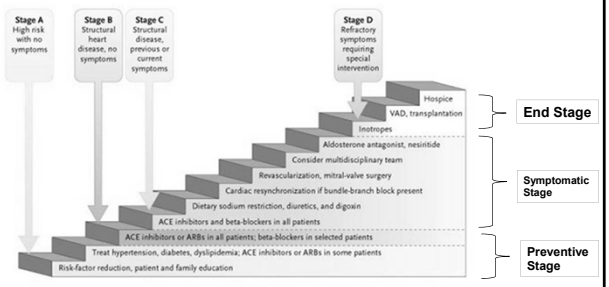
- Guidelines Directed Medical Therapy (GDMT)- represents the optimal medical therapy recommended with a class 1 indication
- Heart Failure with reduce Ejection Fraction (HFrEF). LVEF ≤ 40 %
- Heart failure with preserved Ejection Fraction (HFpEF). LVEF ≥ 50 %
  - HFpEF, borderline (LVEF 41-49 %)
  -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

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

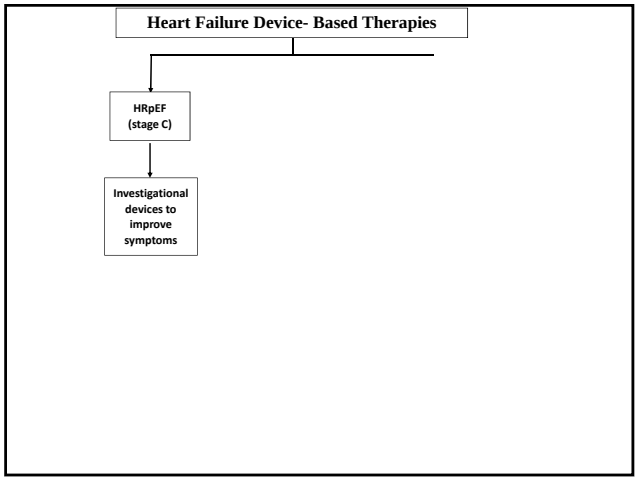
ACC/AHA HF Stage[1]	NYHA Functional Class
A At high risk for heart failure but without structural heart disease or symptoms of heart failure (eg, patients with hypertension or coronary artery disease)	None
B Structural heart disease but without symptoms of heart failure	I Asymptomatic
C Structural heart 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

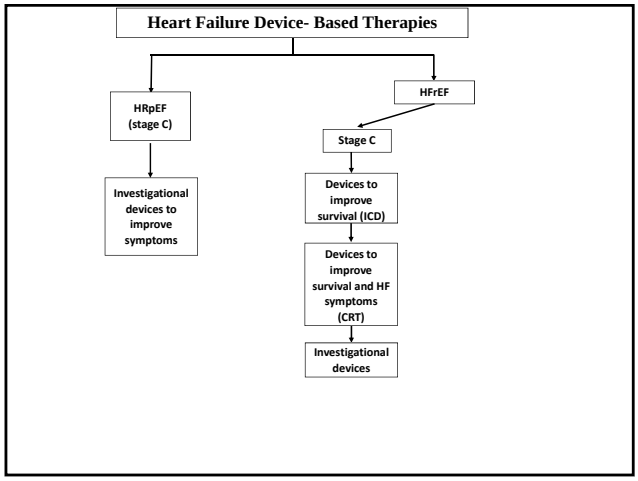
[1]Hunt SA et al. *J Am Coll Cardiol.* 2001;38:2101–2113.

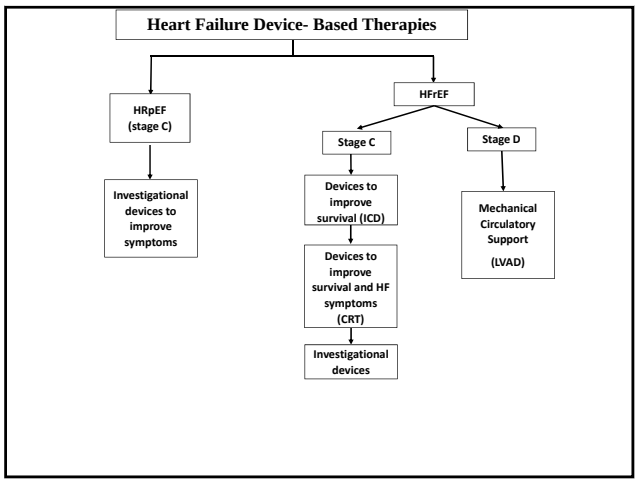
Therapeutic Options for Heart Failure Stages

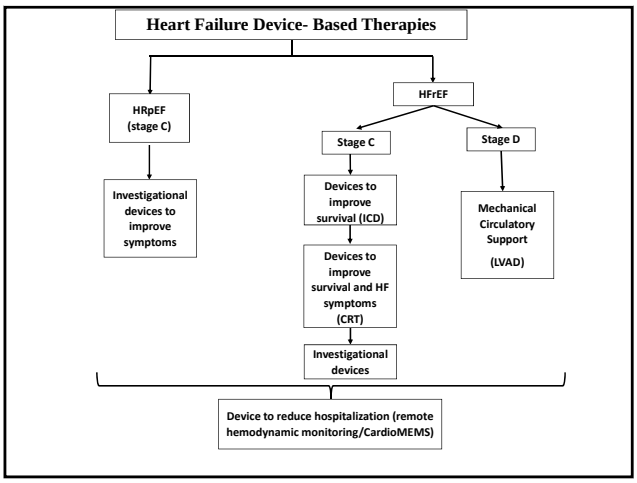


Hunt SA et al. *J Am Coll Cardiol.* 2001;38:2101–2113.

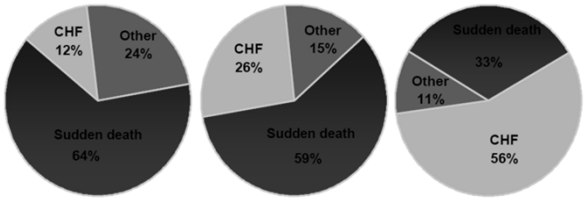








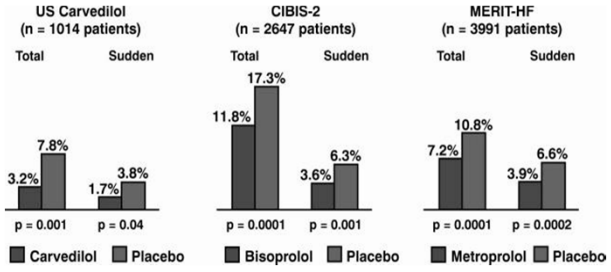
Mode of Death in Heart Failure



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

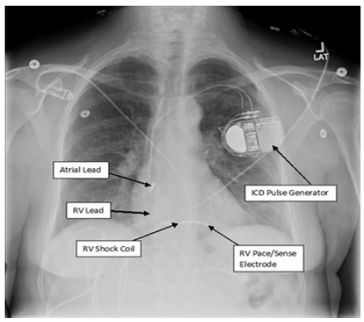


Heart 2001;85:97–103

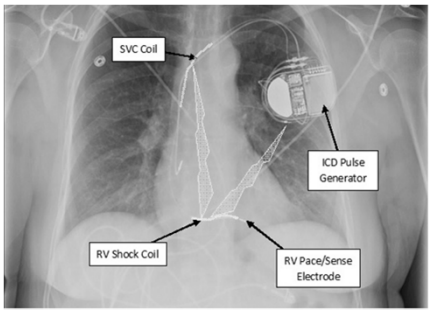
Implantable Cardioverter-Defibrillator (ICD) Basics

- 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

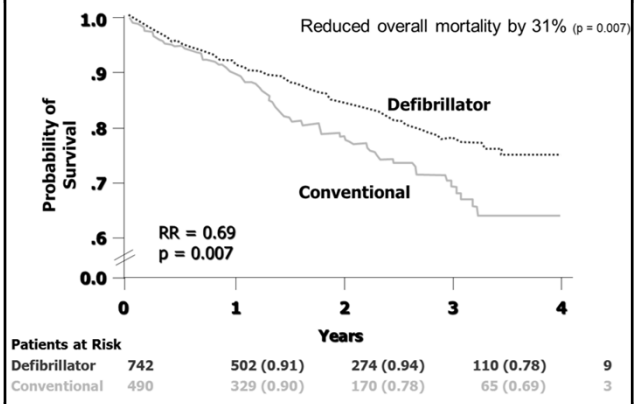
MADIT-II

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



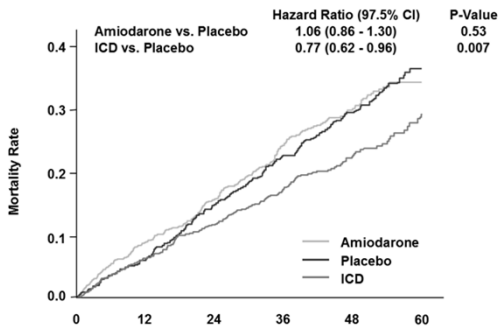
Patients at Risk					
Defibrillator	742	502 (0.91)	274 (0.94)	110 (0.78)	9
Conventional	490	329 (0.90)	170 (0.78)	65 (0.69)	3

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



No. at Risk						
Amiodarone	845	772	715	484	280	97
Placebo	847	797	724	505	304	89
ICD	829	778	733	501	304	103

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

Who should get an ICD?

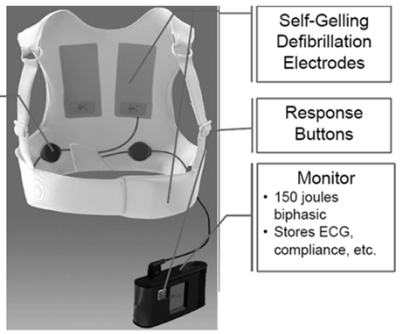
- Ischemic CM, LVEF <0.30 (MADIT II)
- Ischemic and nonischemic dilated cardiomyopathy, NYHA class II/III CHF, LVEF < 35%. (SCD-HeFT).

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

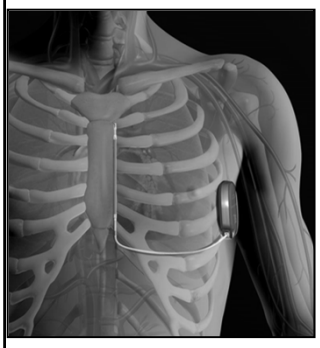
- End-of-life care
- Recurrent inappropriate shocks due to lead failure or SVT/ AF with rapid ventricular response
- During surgical procedures requiring the use to electrocautery in close proximity to the pulse generator

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

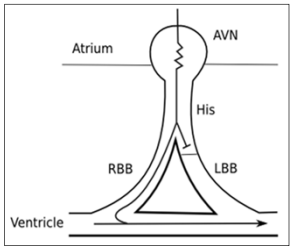


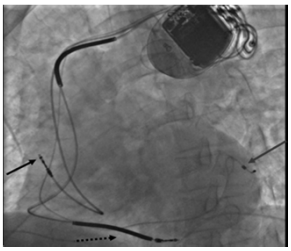
- 80 joules (delivered)
- 69cc, 145 grams
- Active generator
- 5 year longevity
- Post-shock pacing
- Single lead connection
- Full featured episode storage
- No Brady pacing or ATP

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)

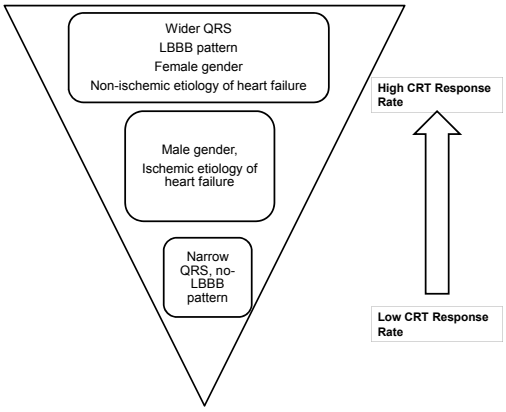




LBBB **CRT**

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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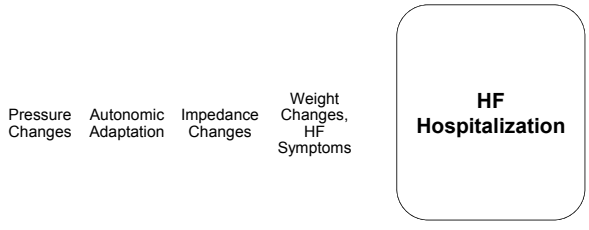
Burden of Heart Failure

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^{TM})
- 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

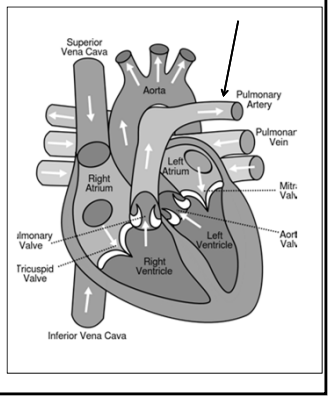
Hemodynamic Monitoring: The Secret Sauce

- **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

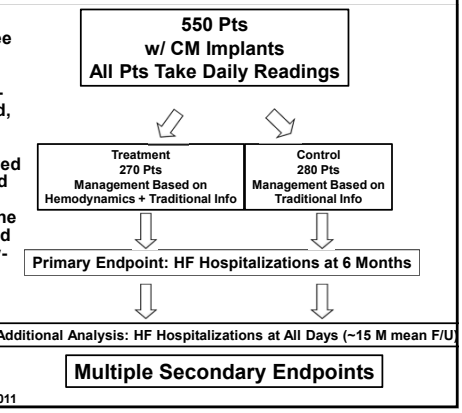
- Implanted via right heart cath technique
- Typically placed in branch of left PA
- Provide PA systolic, diastolic, and mean pressures
- PA diastolic pressures typically mirror PCWP/LA pressures



www.wikipedia.org

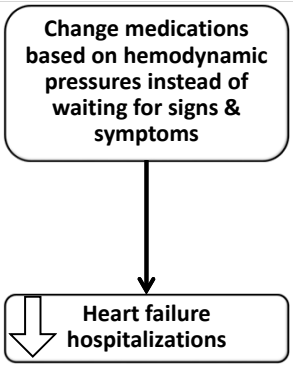
CHAMPION: CardioMEMS Heart Sensor Allows Monitoring of Pressure to Improve Outcomes in NYHA Class III Heart Failure Patients

- 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

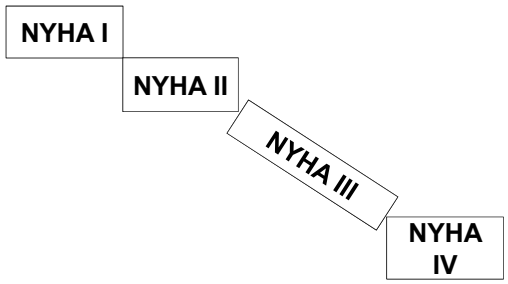
- **Implantable hemodynamic monitors provide direct and actionable measurements of intra-cardiac and pulmonary artery pressures**
- **Management guided by such monitors reduces the risk of heart failure hospitalizations**
- **This approach promises to revolutionize the management of heart failure patients**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

CardioMEMS™: Current Status

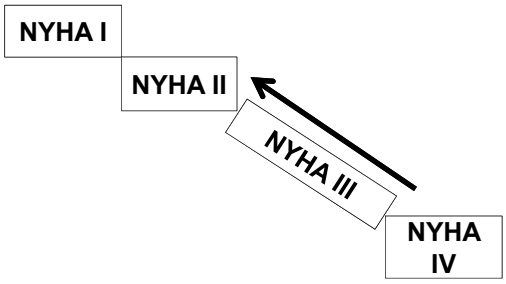
- **Only approved PA pressure monitoring system at present**
- **Approved for use in NYHA III HF patients**
- **Intended to:**
  - **Reduced HF hospitalizations**
  - **Improved QoL**
  - **No indication to improve survival**

Mechanical Circulatory Support Devices

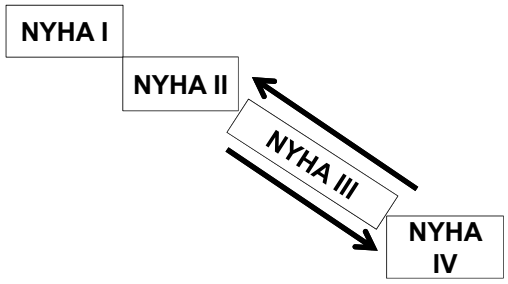
HF Topography



HF Topography



HF Topography



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

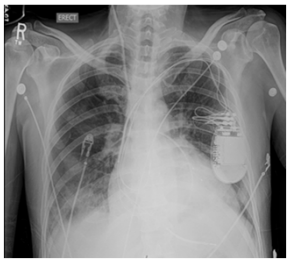
- Quality of life > survival

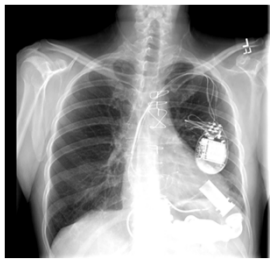
VAD Criteria

- 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
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