



Oklahoma Heart Institute

WHEN TO REFER FOR ADVANCED HEART FAILURE THERAPIES



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OklahomaHeart.com

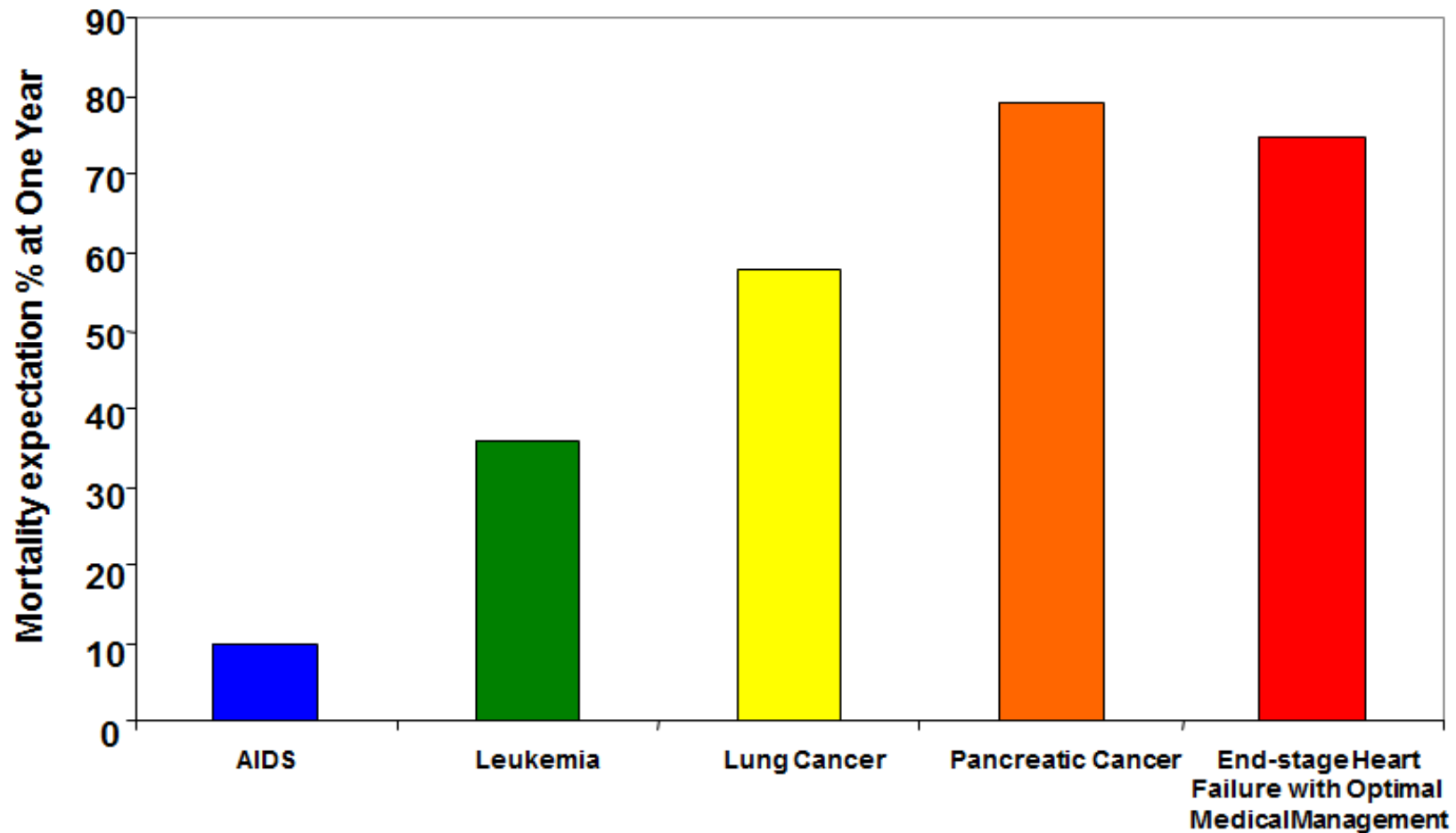
Heart Failure Prevalence

- Heart Failure affects 6.4 Million Americans
- 250, 000 patients die of heart failure each year

¹Rosamond, W, Flegal K, Furie K, et al. Heart Disease and Stroke Statistics—2008 Update: A Report From the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. *Circulation* 2008;117:e25-e146.

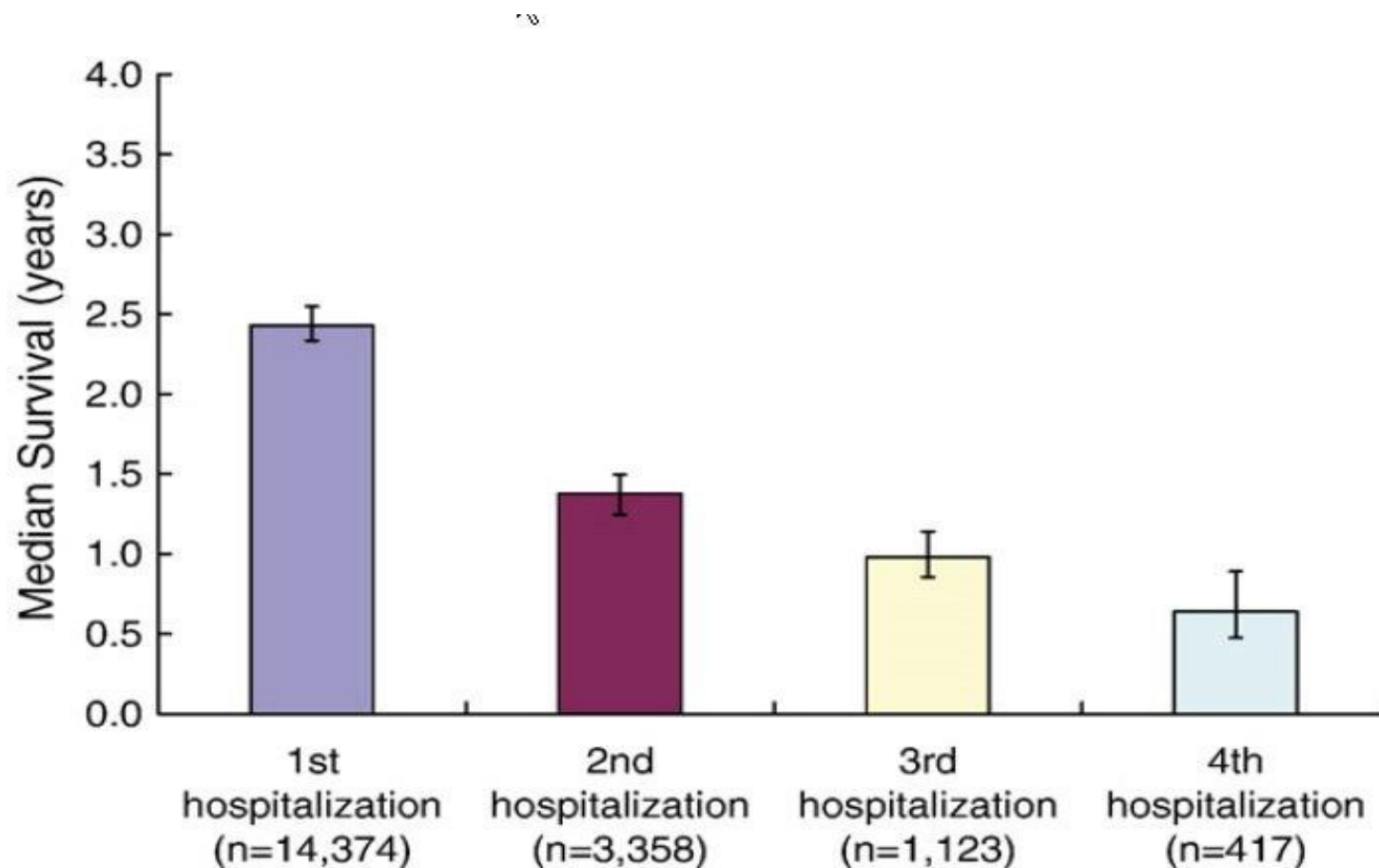
²Adams KF, Zannad F. Clinical definition and epidemiology of advanced heart failure. *Am Heart J* 1998;135:S204-S215. ³Russell, SD, Miller L, Pagani F. Advanced Heart Failure: A Call to Action. *Circulation* 2008. Publication Pending

Mortality of Heart Failure



Rose EA, et al. Long-term mechanical left ventricular assistance for end-stage heart failure. *N Engl J Med*. 2001 Nov 15;345(20):1435-43.

Survival after HF Hospitalization



Median survival (50% mortality) and 95% confidence limits in patients with HF after each HF hospitalization.

At Risk for Heart Failure

Stage A

At high risk for HF but without structural heart disease or symptoms of HF.

e.g.: Patients with:

- hypertension
- atherosclerotic disease
- diabetes
- metabolic syndrome

or

- Patients
- using cardiotoxins
 - with HFx CM

Therapy Goals

- Treat hypertension
- Encourage smoking cessation
- Treat lipid disorders
- Encourage regular exercise
- Discourage alcohol intake, illicit drug use
- Control metabolic syndrome

Drugs

- ACEI or ARB in appropriate patients (see text) for vascular disease or diabetes

Structural Heart Disease

Stage B

Structural heart disease but without symptoms of HF.

e.g.: Patients with:

- previous MI
- LV remodeling including LVH and low EF
- asymptomatic valvular disease

Therapy Goals

- All measures under stage A

Drugs

- ACEI or ARB in appropriate patients (see text)
- Beta-blockers in appropriate patients (see text)

Devices in Selected Patients

- Implantable defibrillators

Development of Symptoms of HF

Stage C

Structural heart disease with prior or current symptoms of HF.

e.g.: Patients with:

- known structural heart disease
- and
- shortness of breath and fatigue, reduced exercise tolerance

Therapy Goals

- All measures under stages A and B
- Dietary salt restriction
- Drugs for Routine Use
- Diuretic for fluid retention
- ACEI
- Beta-blockers

Drugs in Selected Patients

- Aldosterone antagonist
- ARBs
- Digitalis
- Hydralazine/nitrates

Devices in Selected Patients

- Biventricular pacing
- Implantable defibrillators

Refractory Symptoms of HF at Rest

Heart Failure

Stage D

Refractory HF requiring specialized interventions.

e.g.: Patients

who have marked symptoms at rest despite maximal medical therapy (e.g., those who are recurrently hospitalized or cannot be safely discharged from the hospital without specialized interventions)

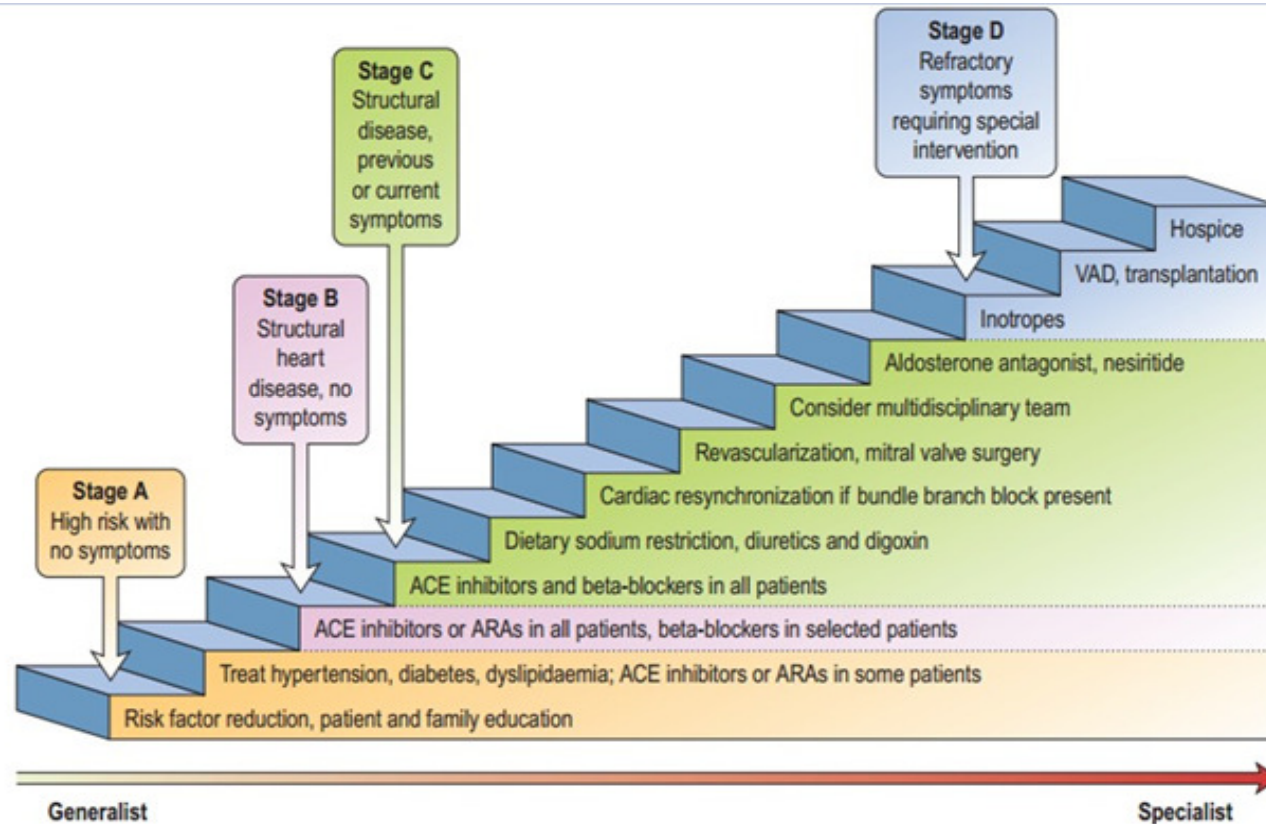
Therapy Goals

- Appropriate measures under stages A, B, C
- Decision re: appropriate level of care

Options

- Compassionate end-of-life care/hospice
- Extraordinary measures
 - heart transplant
 - chronic inotropes
 - permanent mechanical support
 - experimental surgery or drugs

Stages of heart Failure



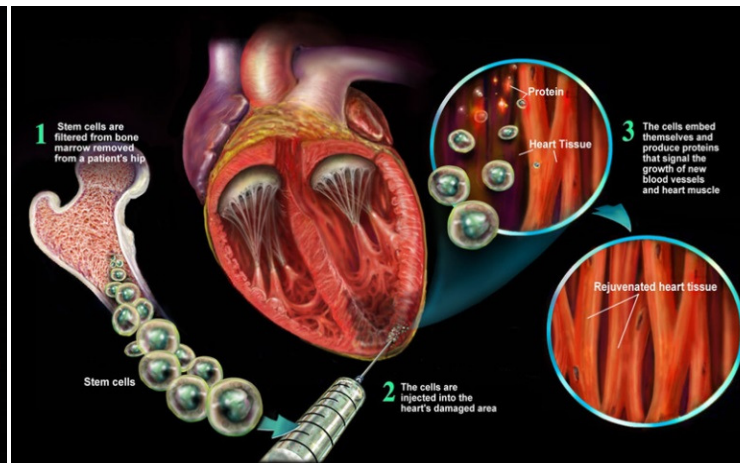
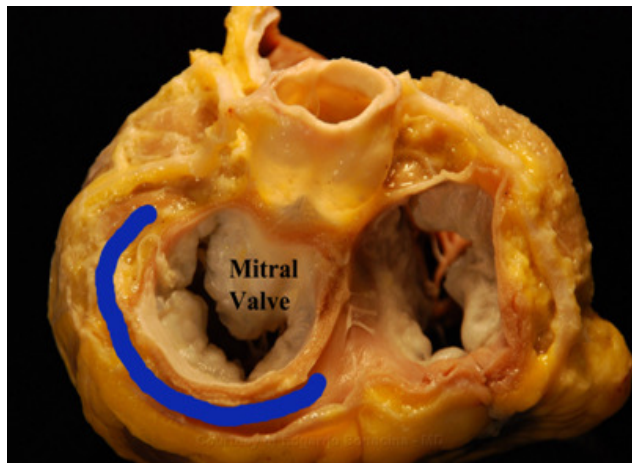
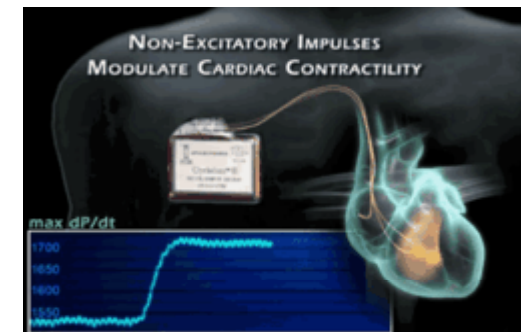
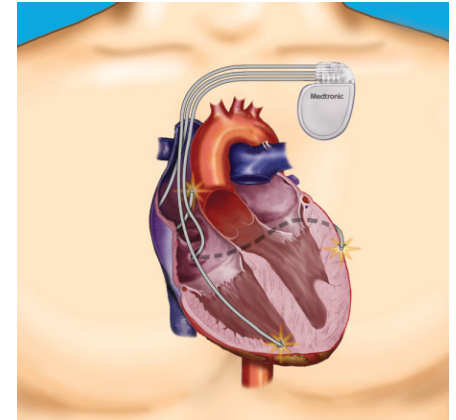
Jessup M, Brozena S. *N Engl J Med* 2003;348:2007-18.

Co-existing Comorbidities

- OSA
- Obesity
- Thyroid diseases
- Diabetes Mellitus
- Hypertension
- Anemia
- Vitamin deficiency

Stage C

- Revascularization
- ICD
- CRT-D
- Valvular heart disease



Advanced Heart Failure

- | |
|---|
| 1. Severe symptoms of HF with dyspnea and/or fatigue at rest or with minimal exertion (NYHA class III or IV) |
| 2. Episodes of fluid retention (pulmonary and/or systemic congestion, peripheral edema) and/or reduced cardiac output at rest (peripheral hypoperfusion) |
| 3. Objective evidence of severe cardiac dysfunction shown by at least 1 of the following: <ul style="list-style-type: none">a. LVEF <30%b. Pseudonormal or restrictive mitral inflow patternc. Mean PCWP >16 mm Hg and/or RAP >12 mm Hg by PA catheterizationd. High BNP or NT-proBNP plasma levels in the absence of noncardiac causes |
| 4. Severe impairment of functional capacity shown by 1 of the following: <ul style="list-style-type: none">a. Inability to exerciseb. 6-Minute walk distance \leq300 mc. Peak VO_2 <12 to 14 mL/kg/min |
| 5. History of \geq 1 HF hospitalization in past 6 mo |
| 6. Presence of all the previous features despite “attempts to optimize” therapy, including diuretics and GDMT, unless these are poorly tolerated or contraindicated, and CRT when indicated |

Refractory heart failure

- Vicious cycle
 - Progressive cardiac remodeling
 - Deterioration of renal function
 - End-organ compromise
- Progressive disease despite optimal medical therapy
- Recurrent hospitalizations
- Limit of neurohormonal and cytokine blockade may have been reached

When is it Refractory

- Recurrent hospitalizations
- Intolerance to previously tolerated medications
- Progressive decline in clinical symptoms
- Persistent hypotension
- End-organ dysfunction (cardio-renal syndrome, worsening LFTs or synthetic function of liver and tissue hypoxemia)
- Hyponatremia
- Persistent decline in functional status
- Resting symptoms

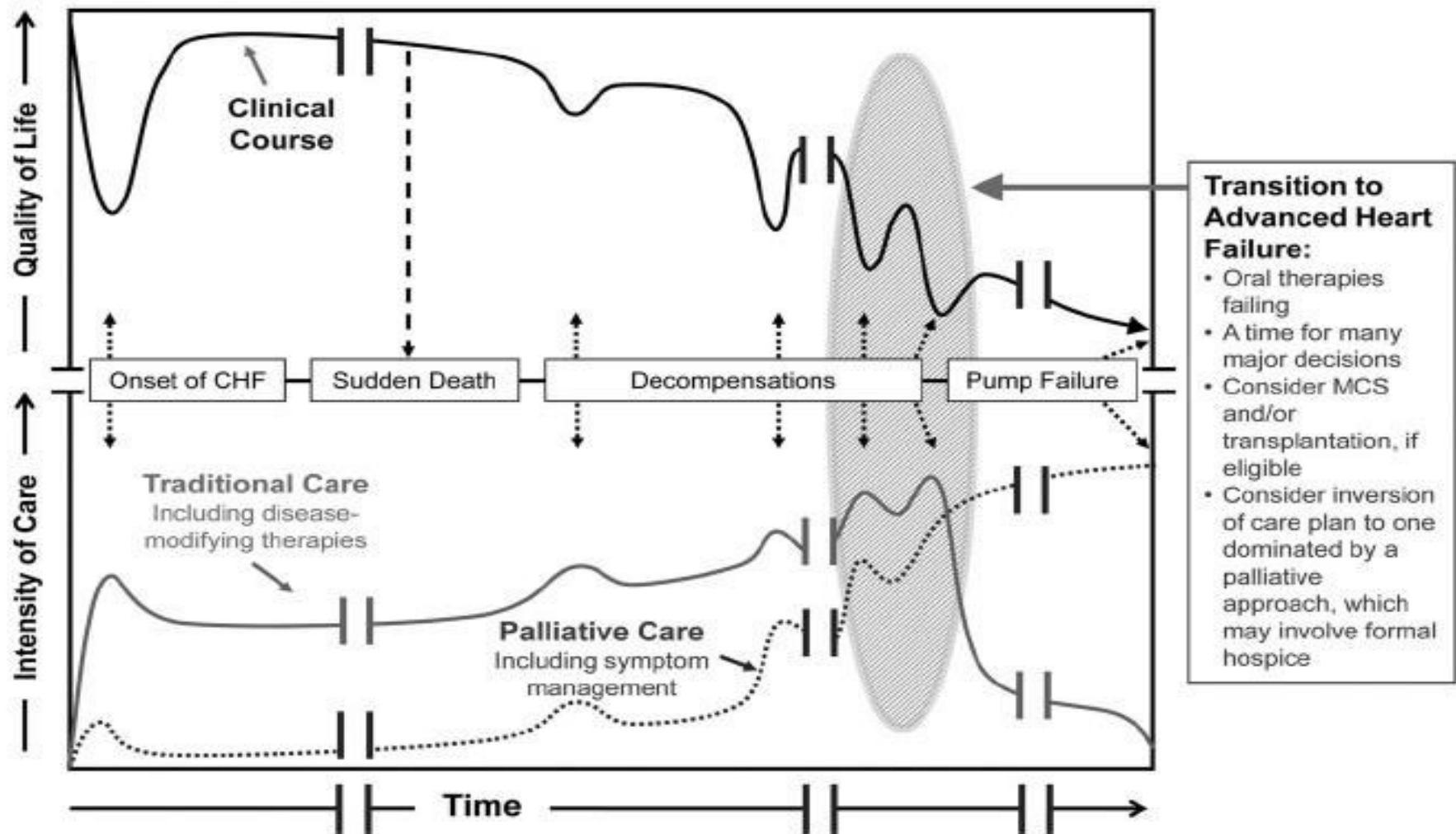
END STAGE HEART FAILURE

- Persistence of symptoms that limit daily life (NYHA class III or IV symptoms) despite receiving maximal tolerated guideline directed optimal medical therapy
- Corresponds to stage D heart failure
- Advanced heart failure therapy options

STAGE D HEART FAILURE – THERAPEUTIC OPTIONS

- Heart Transplant
 - Limited by donor hearts
- Mechanical Circulatory support
- Inotrope therapy
 - Bridge vs palliative
- Palliative care
- Hospice
- Interventional heart failure therapies
 - Mitra clip, TAVR & CCM
- Reconstructive surgeries
 - Batista, DOR & cardiac Sleeves

Clinical Course of Heart Failure



Risk Assessment

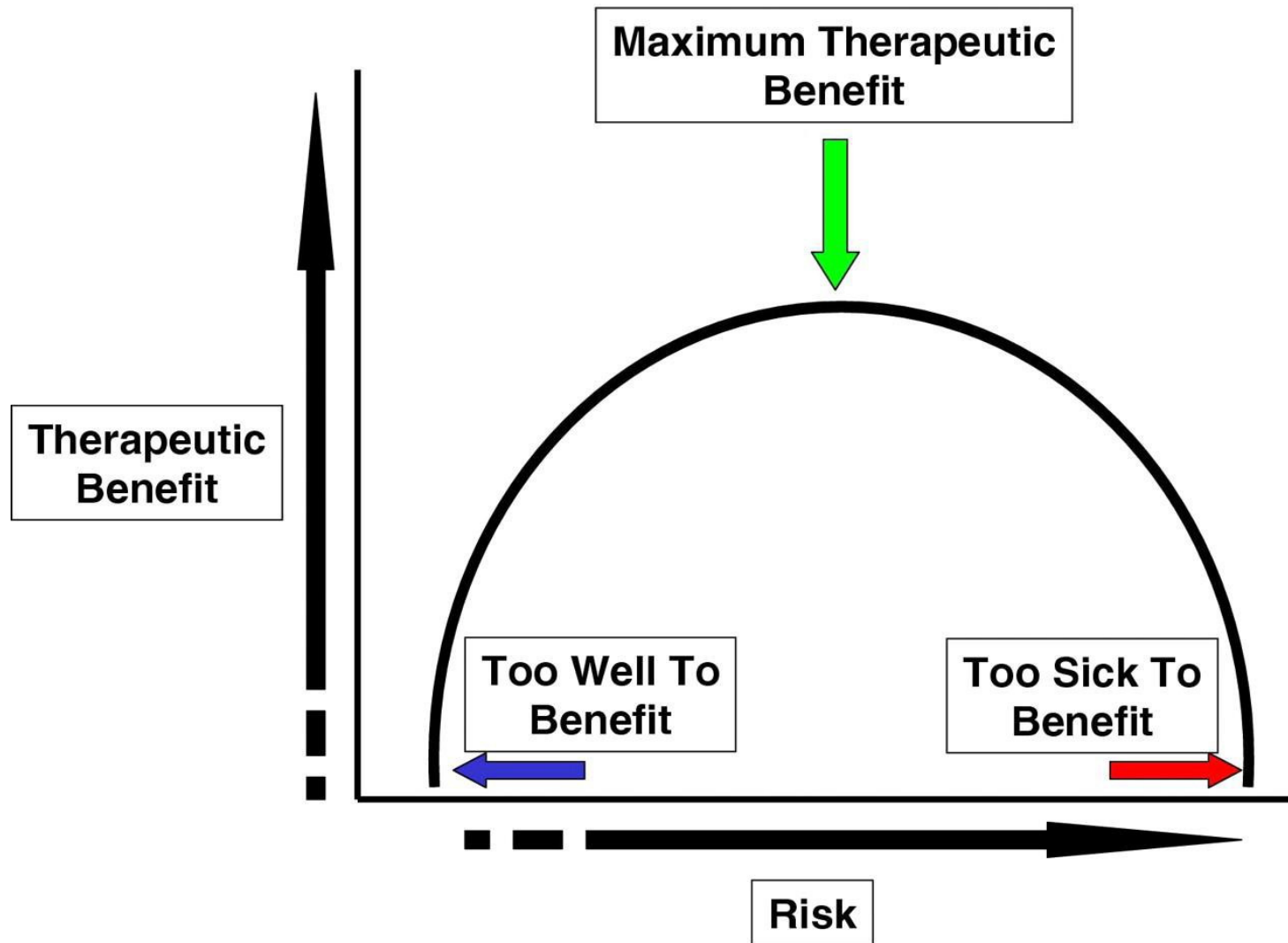
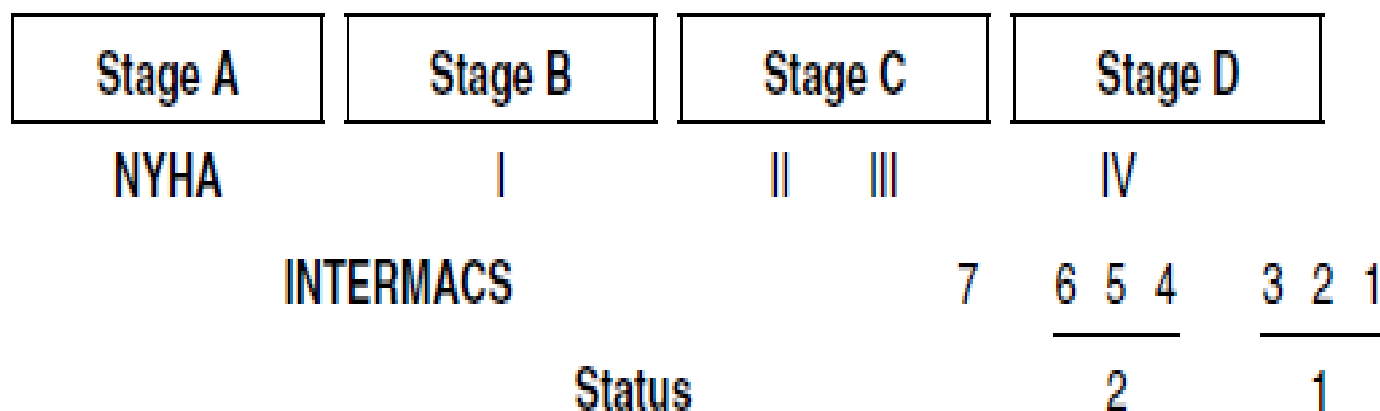

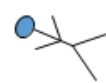







Table 2. INTERMACS Profiles

	Nickname	Time to VAD
1. Critical cardiogenic shock	Crash and burn	Hours
2. Progressive decline	Sliding fast	Days
3. Stable but inotrope-dependent	Dependent stability	Few weeks
4. Resting symptoms	Frequent flyer	Months
5. Exertion intolerant	House-bound	
6. Exertion limited	Walking wounded	
7. Advanced NYHA III		? (REVIVE-IT)

Modifiers for Profiles	Possible profiles to modify
Temporary circulatory support (TCS)	1, 2 & 3
A (arrhythmia)	Any profile
Frequent Flyer (FF)	3 (at home) 4, 5 & 6

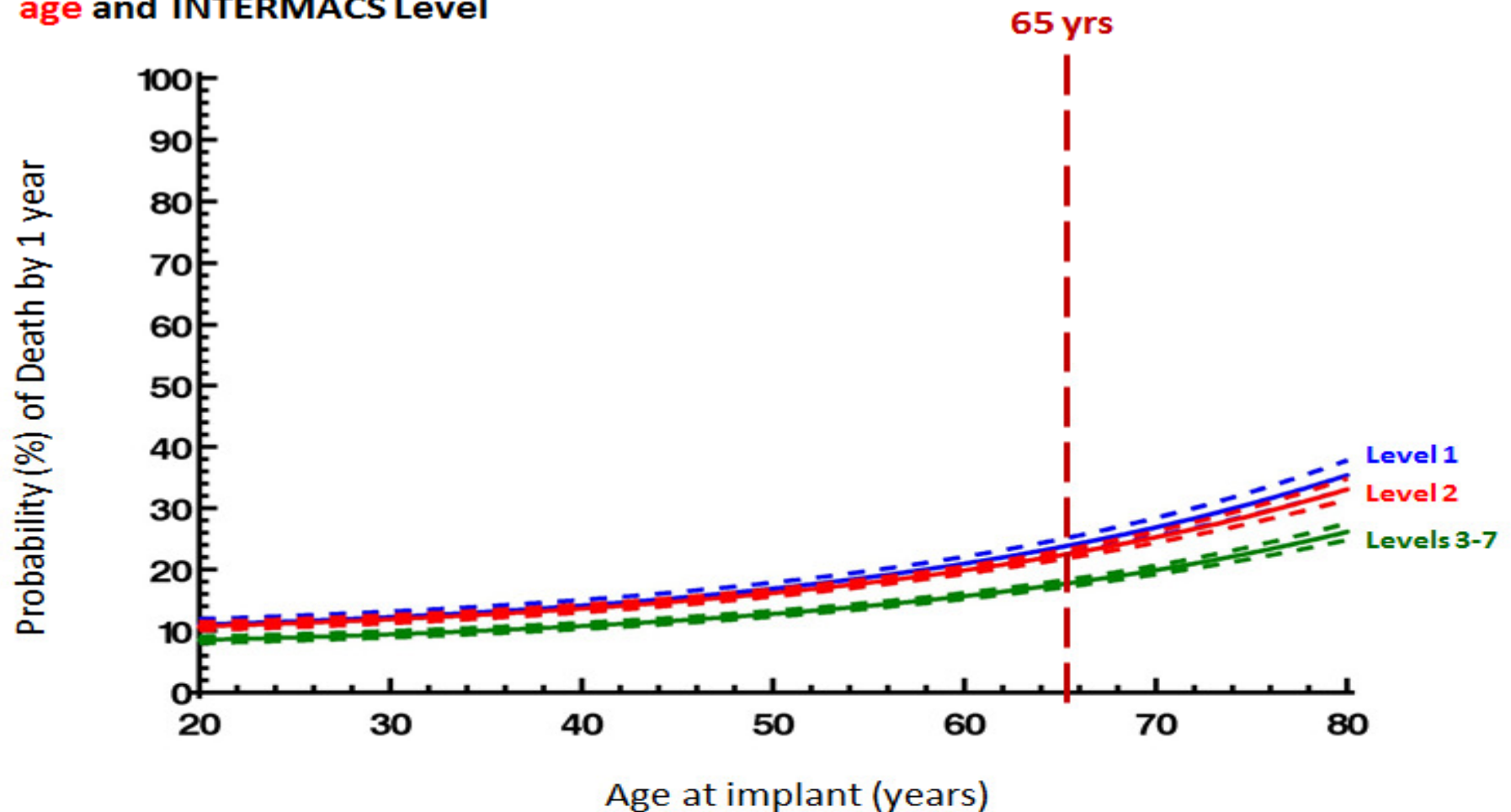


ADULT PROFILES	Current CMS - DT Functional Indication	IV INO*	Official Shorthand	NYHA CLASS Assumed	Modifier option
INTERMACS LEVEL 1	Met	X	"Crash and burn"	IV	TCS A
INTERMACS LEVEL 2	Met	X	"Sliding fast" on inot 	IV	TCS A
INTERMACS LEVEL 3	Met	X	"Stable" continuous inotropic dependent * Can be in hospital or at home 	IV	TCA if hosp FF if home A
INTERMACS LEVEL 4	+ Peak $VO_2 \leq 12$		<u>Resting symptoms</u> on oral at home 	AMB IV	FF A
INTERMACS LEVEL 5	+ Peak $VO_2 \leq 12$		"Housebound", Comfortable at rest, symptoms with minimum activity ADL 	AMB IV	FF A
INTERMACS LEVEL 6			"Walking wounded"-ADL possible but meaningful activity limited	IIIB 	FF A 
INTERMACS LEVEL 7			Advanced Class III	III	A only 

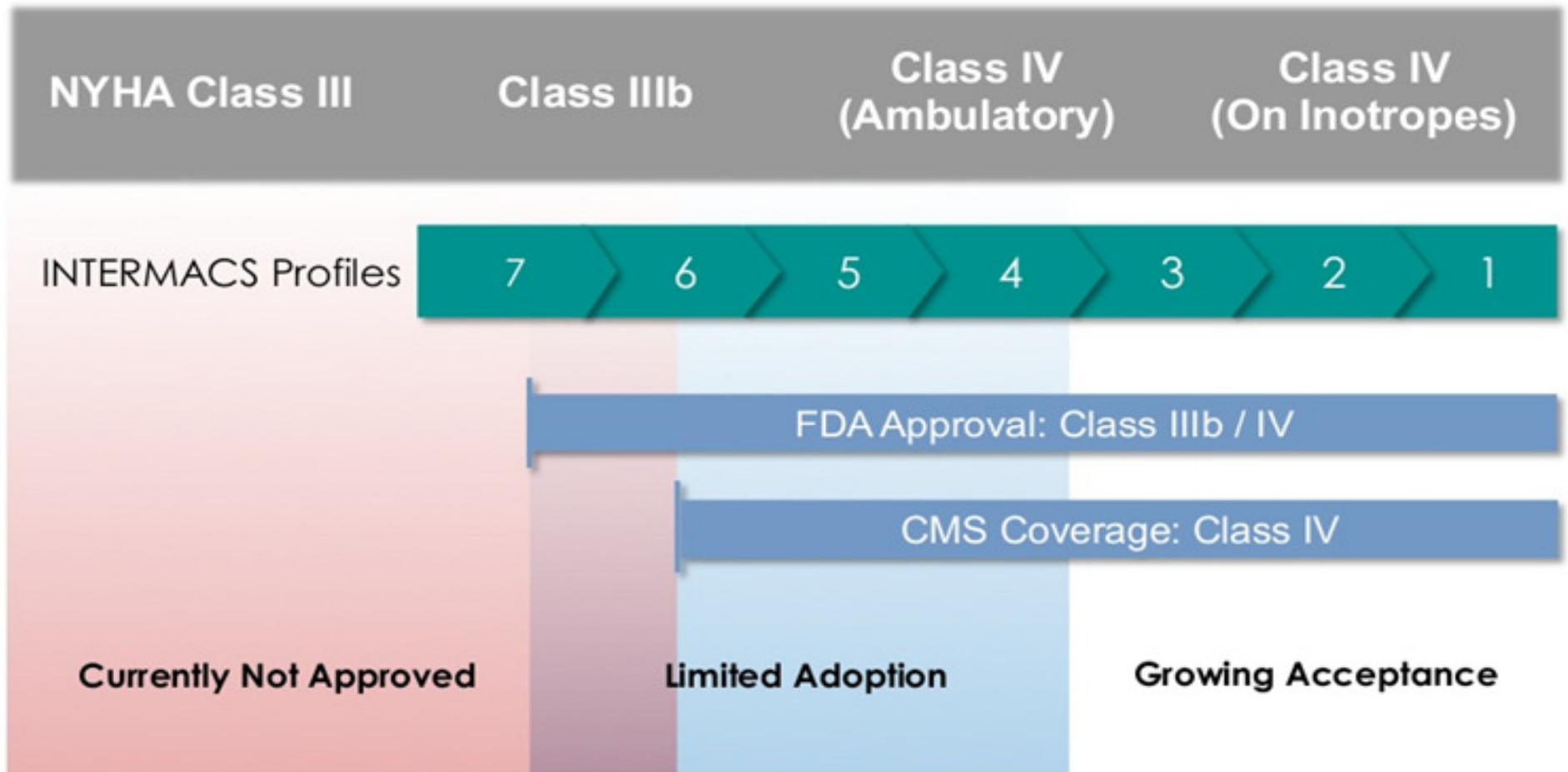
* Intravenous inotropic therapy only approved for refractory Class IV symptoms 

Outcomes based on INTERMACs profile

Predicted 1 year mortality according to **patient age** and INTERMACS Level



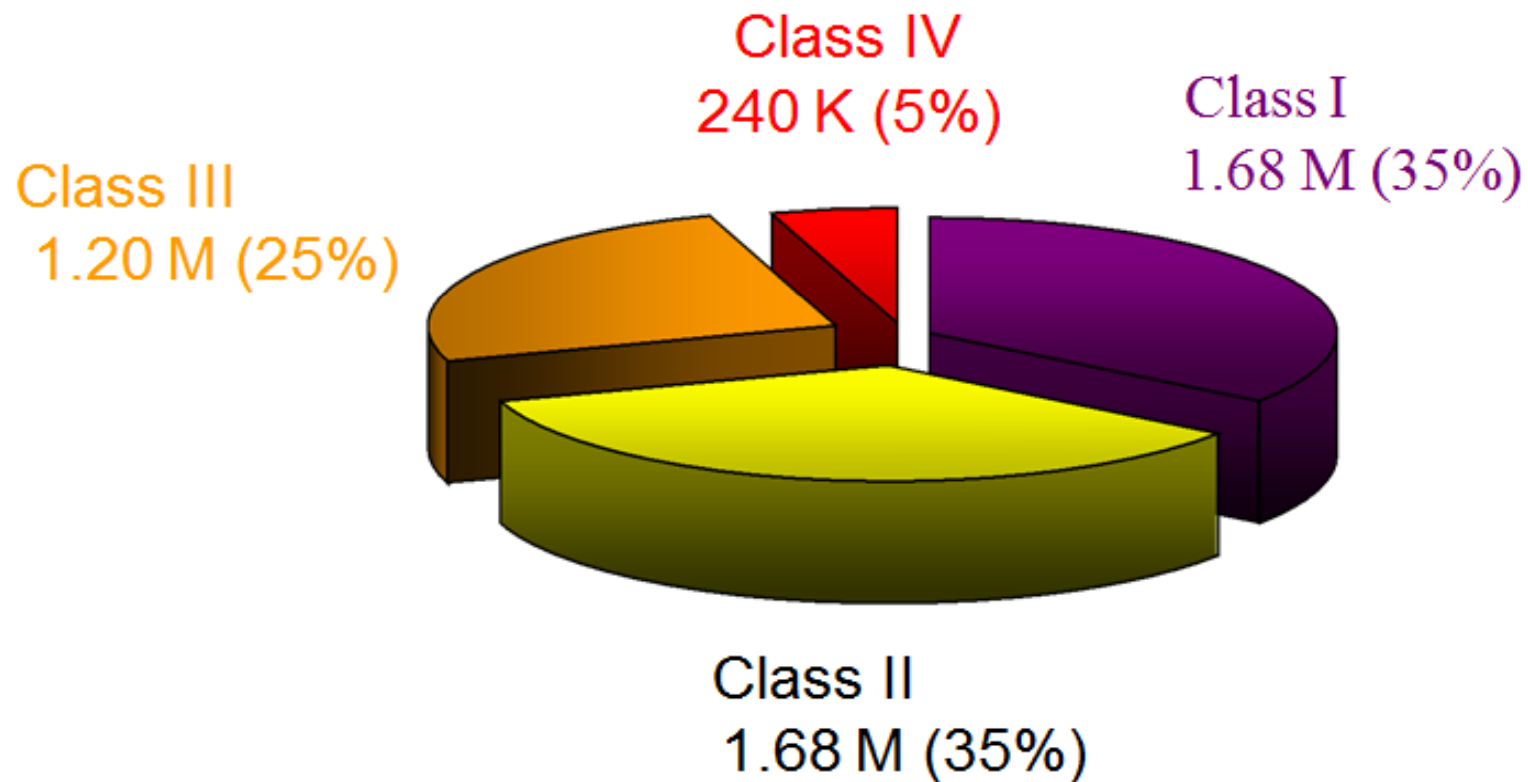
WHEN IS THE RIGHT TIME??



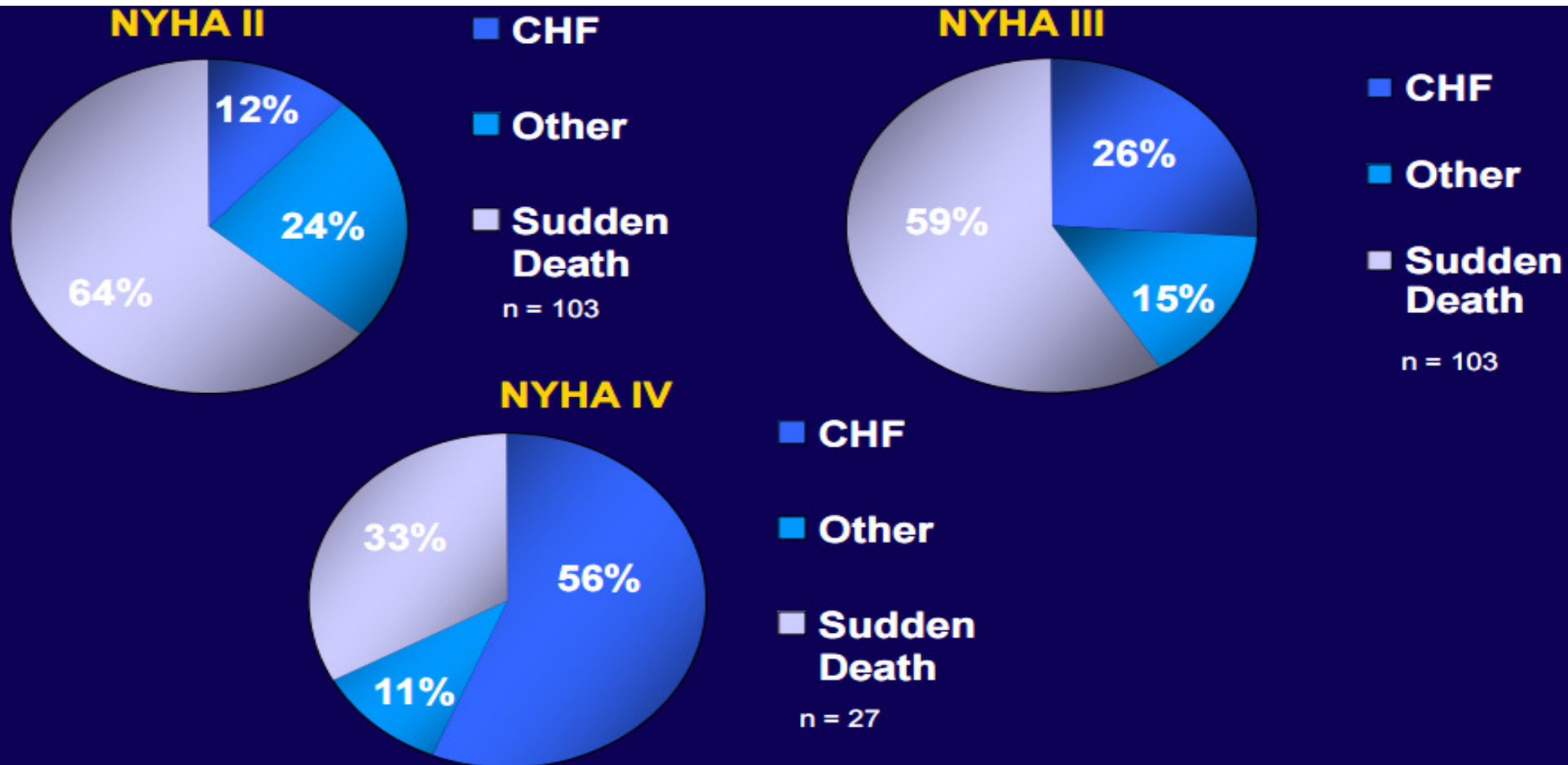
RE**IVEIT**

 **R O A D M A P**
Clinical Study

NYHA class distribution



Mortality in CHF



MERIT-HF Study Group. Effect of Metoprolol CR/XL in chronic heart failure: Metoprolol CR/XL randomized intervention trial in congestive heart failure (MERIT-HF). *LANCET*. 1999;353:2001-07.

Prognostication

NYHA Class	1 Year Mortality
I	5-10%
II-III	15-30%
IV	50-60%

Risk stratify

- INTERMACs
- Leitz-Miller score
- Columbia scoring
- Apache II
- Seattle Heart Failure Score

Predictors of poor operative outcome

- Age
- Female
- Prior CV surgery
- Pre existing RV failure
- Coagulopathy
- End organ failure
 - Renal
 - Liver
 - Respiratory

Multivariable Models: Seattle Model

University of Washington

SEATTLE HEART FAILURE MODEL

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* Please click here for technical details.

* If your browser is configured for Java, the SHFM calculator will appear below shortly. If not, please configure your browser to support Java applets.

	Baseline	1 year	2 year	5 year
Survival		70 %	49 %	17 %
Mortality		30 %	51 %	83 %
Mean life expectancy		2.7	years	

	Post-intervention	1 year	2 year	5 year
Survival		70 %	49 %	17 %
Mortality		30 %	51 %	83 %
Mean life expectancy		2.7	years	

100
0 1 2 3 4 5 Years

Baseline Characteristics

Clinical

Age

Gender

NYHA Class

Weight (kg)

EF

Syst BP

☒ Ischemic

Medications

☒ ACE-I

☐ Beta-blocker

☐ ARB

☐ Statin

☐ Allopurinol

☐ Aldosterone blocker

Diuretics

Furosemide

Bumetanide

Torsemide

Metolazone

HCTZ

Lab Data

Hgb

Lymphocyte%

Uric Acid

Total Chol

Sodium

☐ QRS > 120 msec

Devices

☒ None

☐ BiV Pacer

☐ ICD

☐ BiV ICD

[Defaults](#)

Interventions

☒ ACE-I ☐ ARB ☐ Beta-blocker

☐ Statin ☐ Aldosterone Blocker

Copyright 2004-2007 Wayne Levy & David Linker

[Click here to view the CMS criteria for devices.](#)

Devices

☒ None

☐ BiV Pacer ☐ BiV ICD

☐ ICD ☐ LVAD

Note: Some devices may be disabled if CMS clinical criteria are not met. See below.

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Table 4. Heart Failure Risk Scoring System*

Variable	No. of Points	
	30-Day Score†	1-Year Score‡
Age, y	+Age (in years)	+Age (in years)
Respiratory rate, min (minimal 20; maximum 45)§	+Rate (in breaths/min)	+Rate (in breaths/min)
Systolic blood pressure, mm Hg		
≥180	−60	−50
160-179	−55	−45
140-159	−50	−40
120-139	−45	−35
100-119	−40	−30
90-99	−35	−25
<90	−30	−20
Urea nitrogen (maximum, 60 mg/dL)§¶	+Level (in mg/dL)	+Level (in mg/dL)
Sodium concentration <136 mEq/L	+10	+10
Cerebrovascular disease	+10	+10
Dementia	+20	+15
Chronic obstructive pulmonary disease	+10	+10
Hepatic cirrhosis	+25	+35
Cancer	+15	+15
Hemoglobin <10.0 g/dL (<100 g/L)	NA	+10

Abbreviation: NA, not applicable to 30-day model.

*An electronic version of the risk scoring system is available at: <http://www.ccort.ca/CHFriskmodel.asp>.

†Calculated as age + respiratory rate + systolic blood pressure + urea nitrogen + sodium points + cerebrovascular disease points + dementia points + chronic obstructive pulmonary disease points + hepatic cirrhosis points + cancer points.

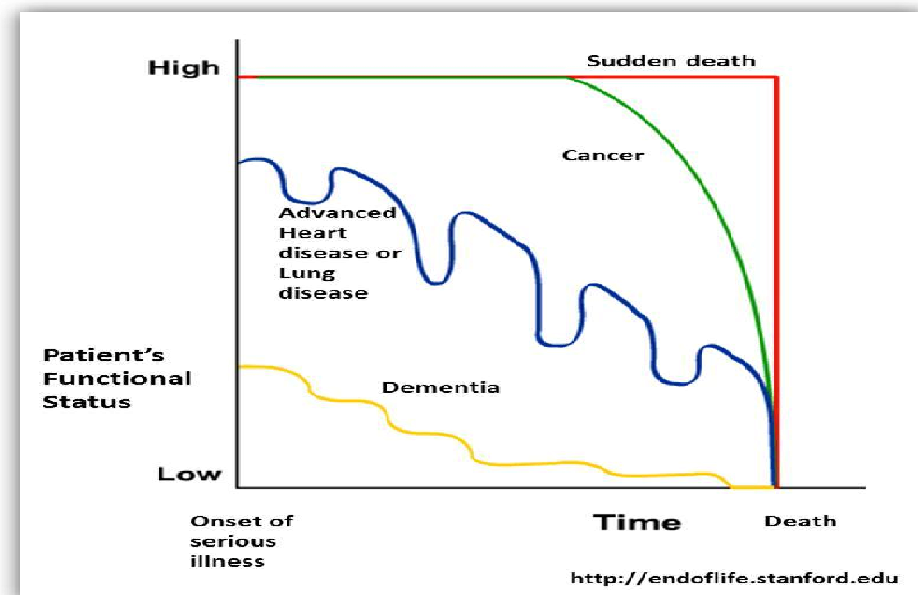
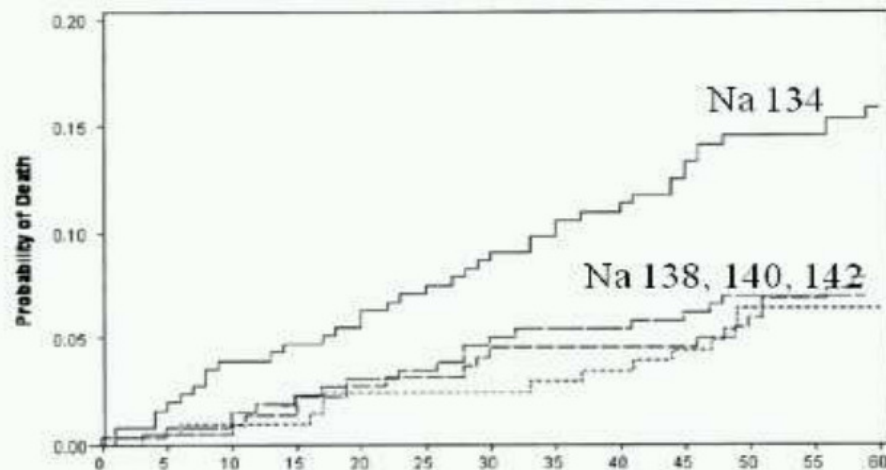
‡Calculated as age + respiratory rate + systolic blood pressure + urea nitrogen + sodium points + cerebrovascular disease points + dementia points + chronic obstructive pulmonary disease points + hepatic cirrhosis points + cancer points + hemoglobin points.

§Values higher than maximum or lower than minimum are assigned the listed maximum or minimum values.

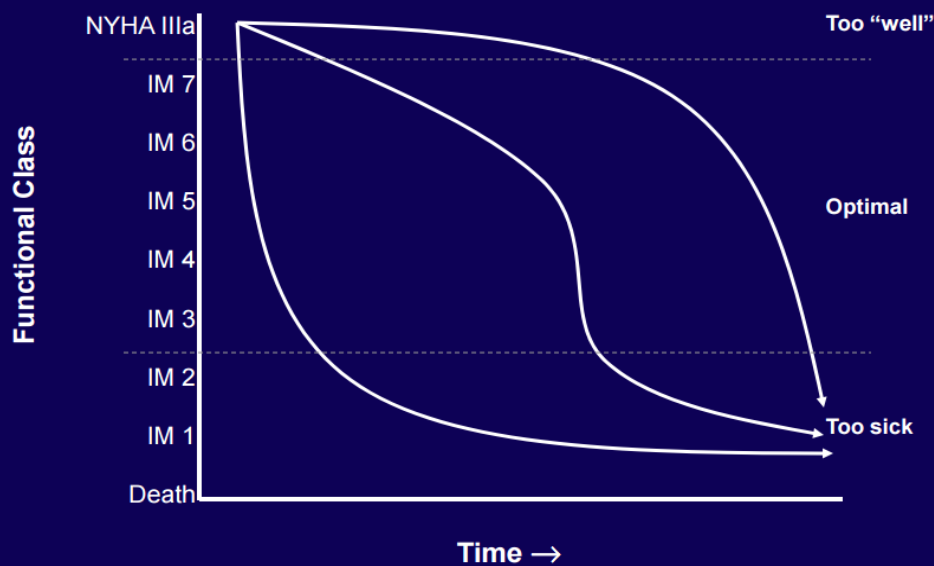
||Increases were protective in both mortality models. Points are subtracted for higher blood pressure measurements.

¶Maximum value is equivalent to 21 mmol/L. Score calculated using value in mg/dL.

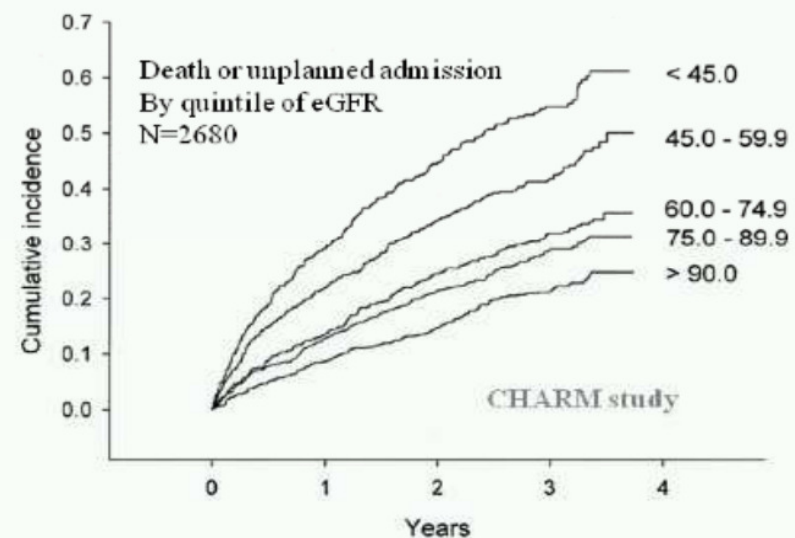
Kaplan-Meier survival curves to 60 days by serum sodium quartiles (unadjusted analysis) – OPTIME CHF



Timing of Mechanical Circulatory Support



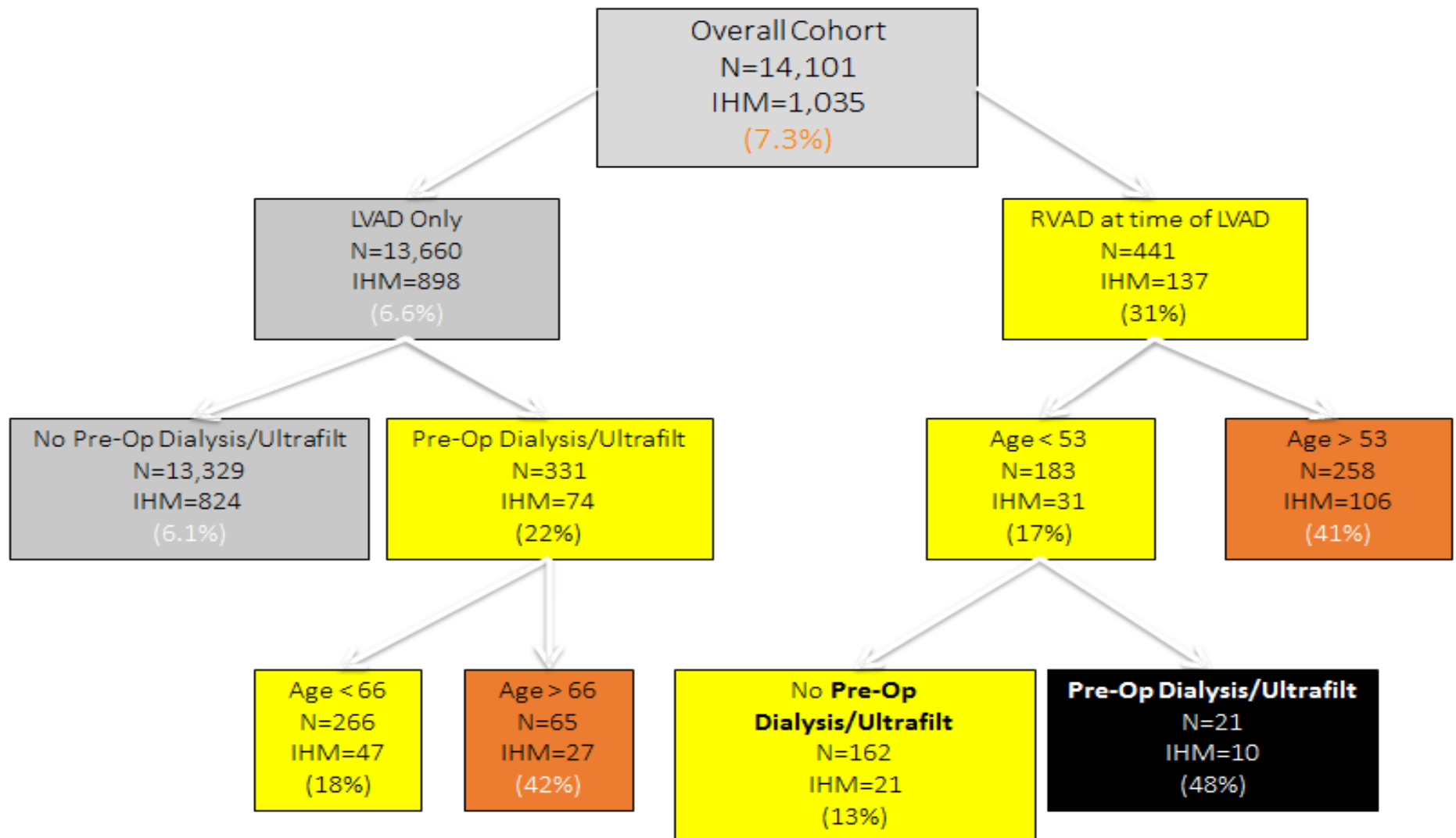
Renal Dysfunction and HF outcomes



Hege, H. L. et al. Circulation 2006; 113:671-678

Renal Dysfunction and HF outcomes

Profiles associated with high Mortality

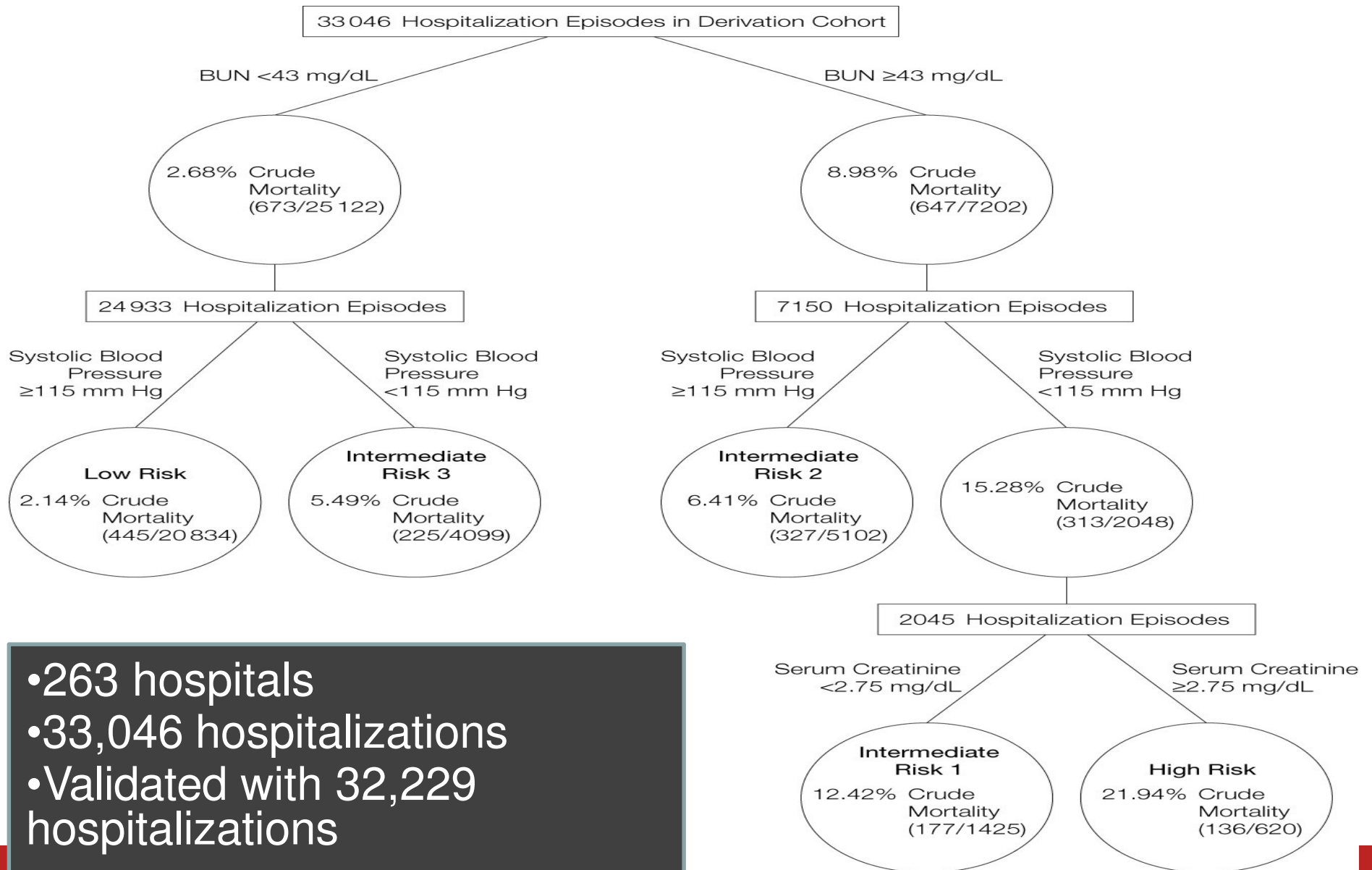


RL Kormos, AD Althouse et al., *Use of Classification & Regression Trees to Identify Patient Profiles Associated with High Risk of Implant Mortality* ISHLT 2016

What did we derive

- Patients with renal dysfunction
- Patients with RV dysfunction
- Patients with high CVP
- Older patients with significant co-morbidities
- Patients with persistent hyponatremia
- Recurrent hospitalizations

ADHERE CART ANALYSIS



- 263 hospitals
- 33,046 hospitalizations
- Validated with 32,229 hospitalizations

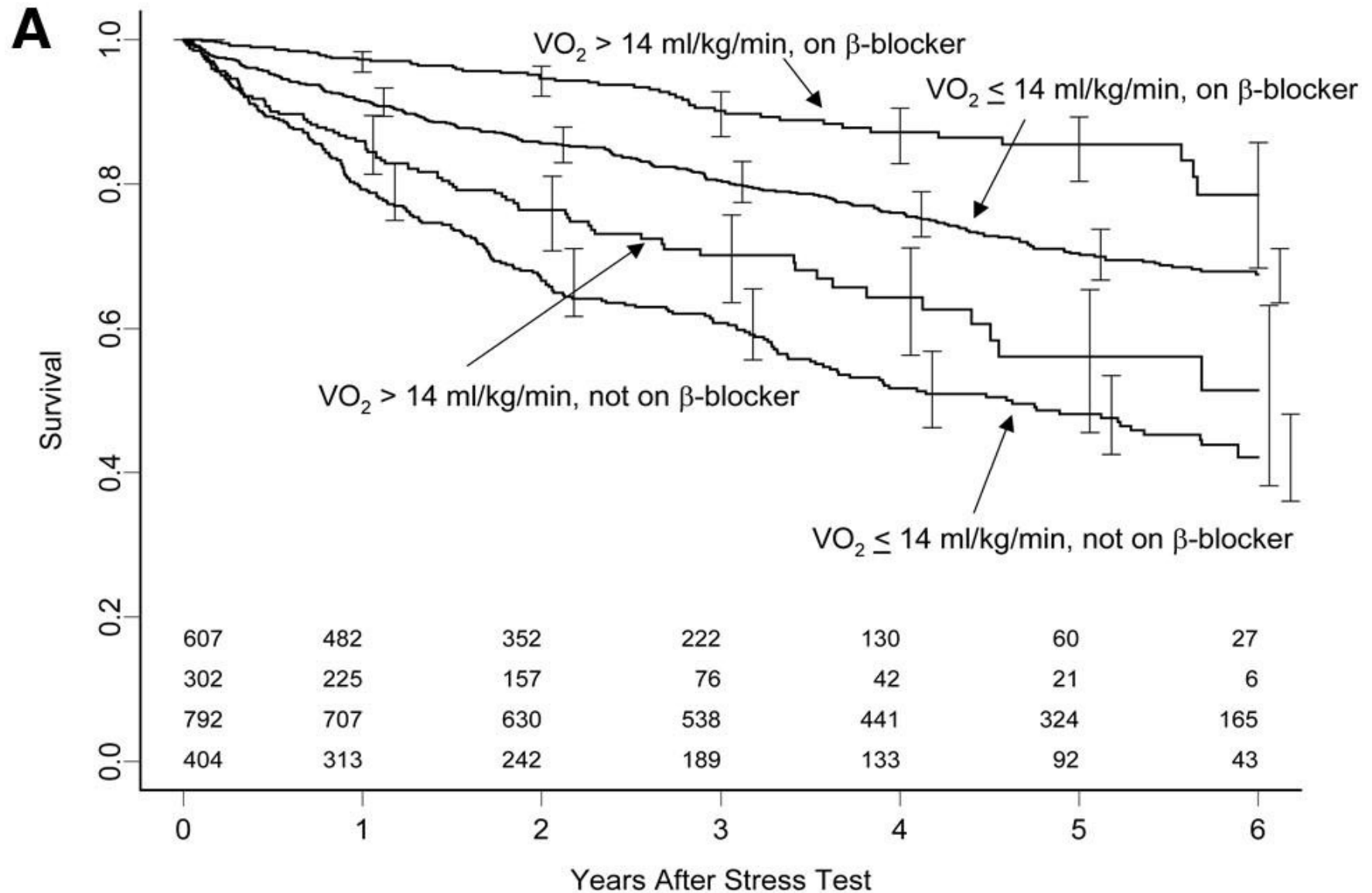
WHO GETS LVAD

- LVEF < 25%
- NYHA class IIIb to IV
- On maximal medical therapy (for 60days out of last 90 days)
- Inotrope dependent for > 2 weeks
- IABP dependent for > 7 days
- Peal VO2 < 14 ml/kg/mt
- Life expectancy < 2 years due to heart failure
- Refractory cardiogenic shock

Cardiopulmonary exercise testing

- Symptom limited exercise test
- Measures airflow, SpO₂, expired oxygen and CO₂
- Measures peak oxygen consumption
- Cardiac reserve

Peak VO₂: With / Without Beta Blockers



Mortality in CHF Patients

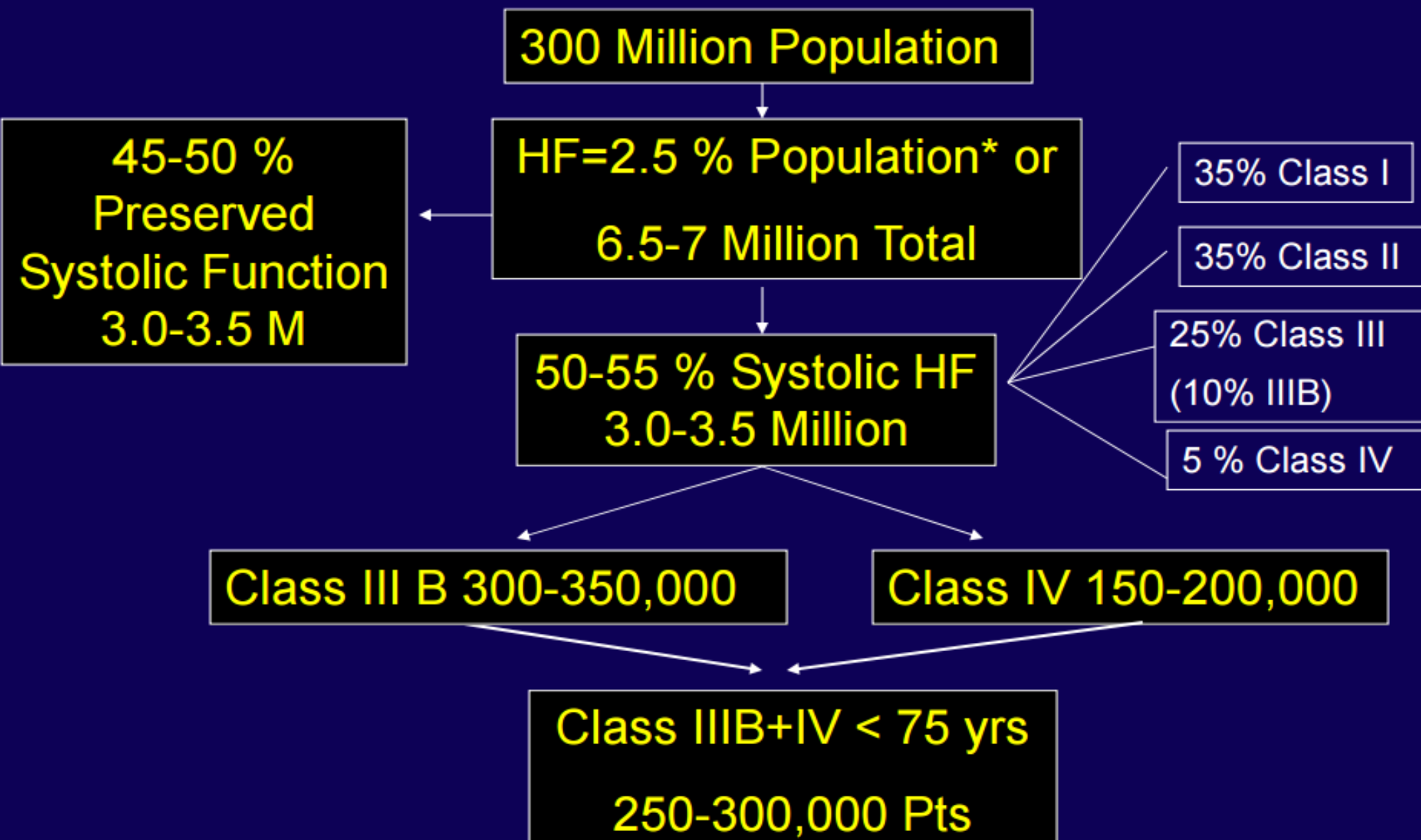
- Peak $\text{VO}_2 > 14 \text{ ml/kg/min}$:
 - 1-yr survival 94%
 - 2-yr survival 84%
- Peak $\text{VO}_2 \leq 14 \text{ ml/kg/min}$:
 - 1-yr survival 47%
 - 2-yr survival 32%

Mancini et al; Circulation 83: 778; 1991.

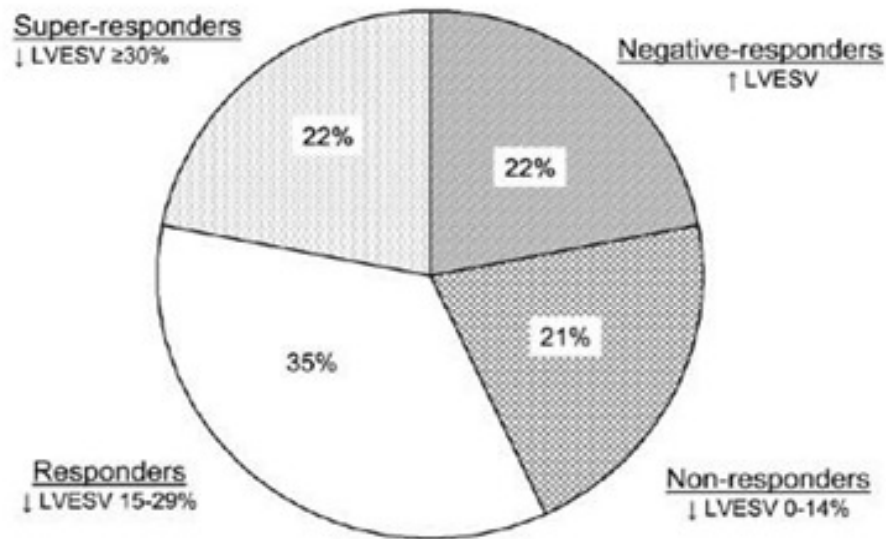
Parameters that can be used

- Functional
 - 6 minute walk distance
 - Cardiopulmonary exercise testing
- Imaging
 - LVEF (alone is not predictive)
 - End diastolic Volumes (LVEDV and LVESV)
 - LVEDD
 - TAPSE and TASV
 - Degree of regurgitations (MR and TR)
- Right heart catheterization
 - PA sat
 - CVP/PCWP

Estimated Number of Patients with Advanced HF

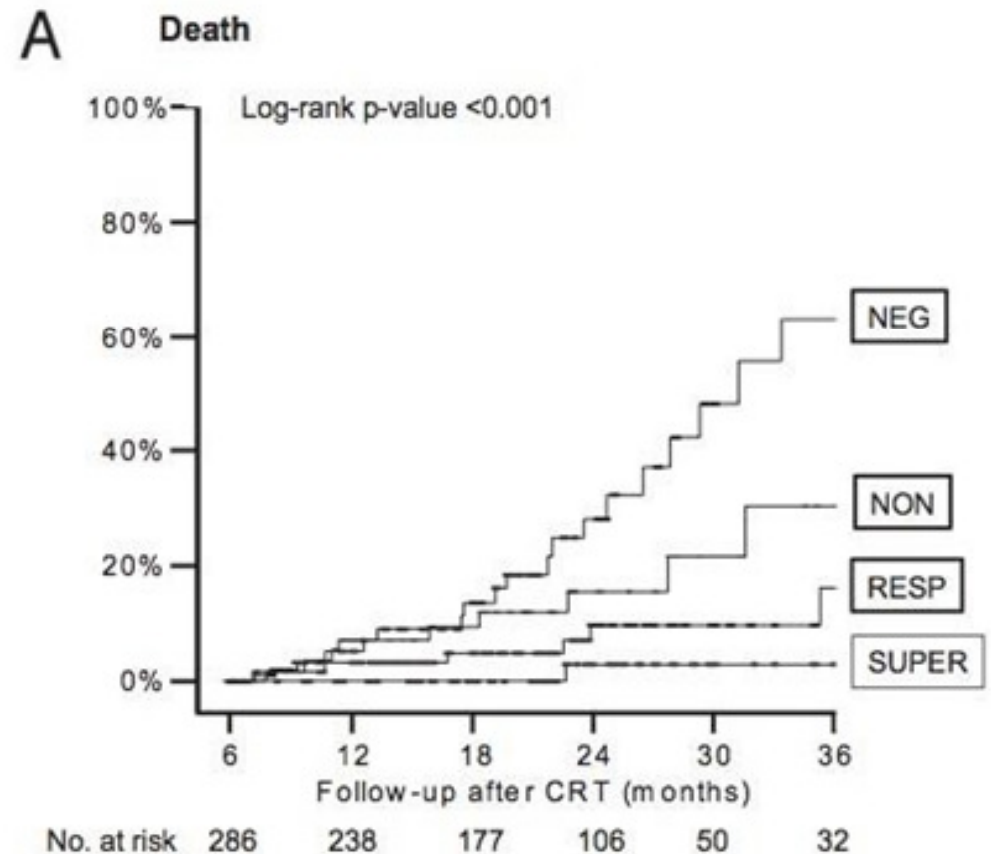


CRT – Negative and non responders



Extent of LV Reverse Remodeling After 6 Months of CRT

Distribution of patients according to extent of left ventricular (LV) reverse remodeling after 6 months of cardiac resynchronization therapy (CRT). LVESV = left ventricular end-systolic volume.

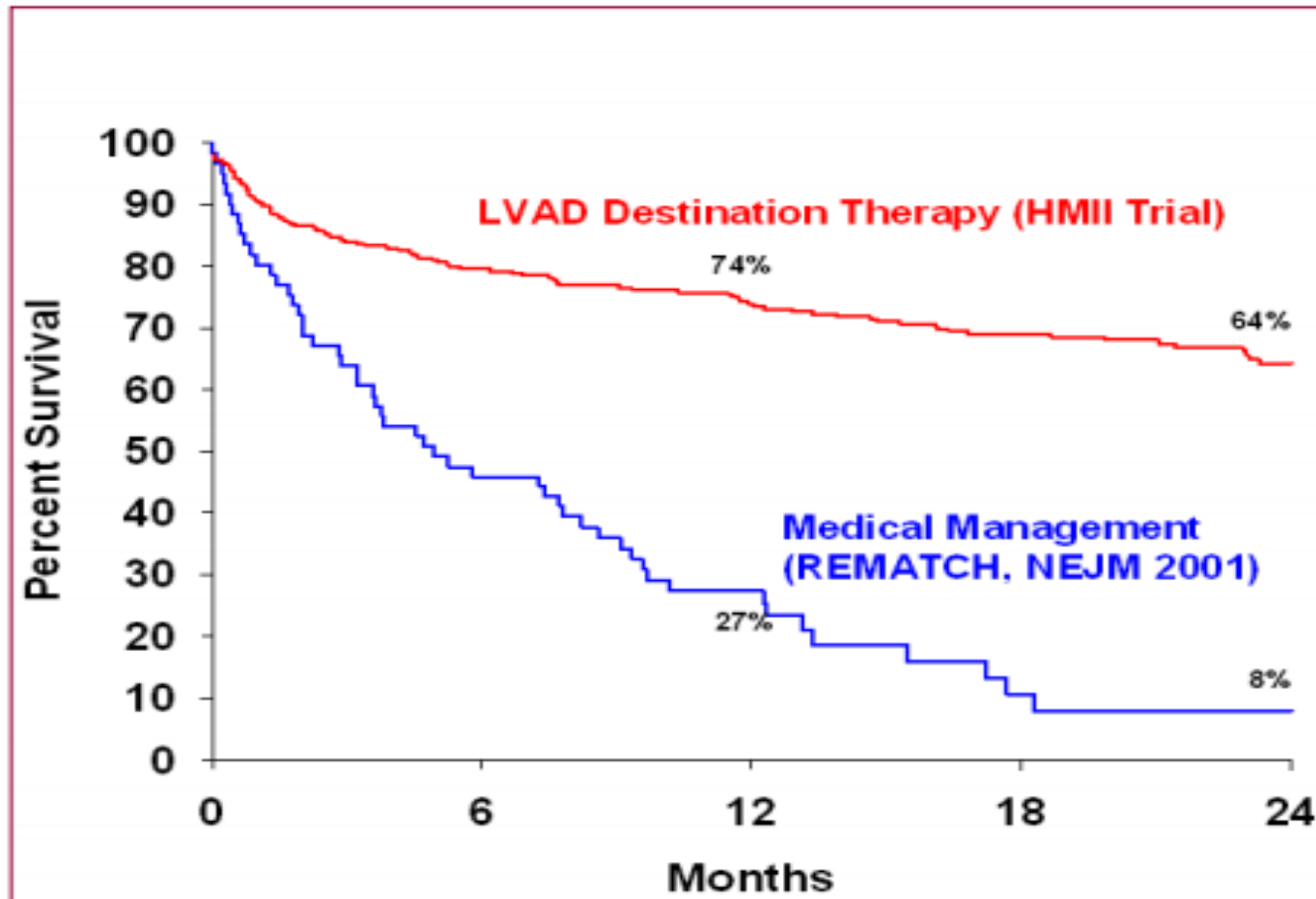


Do we need to wait until it is Refractory to refer???

- Recurrent hospitalizations
- Intolerance to previously tolerated medications
- Progressive decline in clinical symptoms
- Persistent hypotension
- End-organ dysfunction (cardio-renal syndrome, worsening LFTs or synthetic function of liver and tissue hypoxemia)
- Hyponatremia
- Persistent decline in functional status
- Resting symptoms



WHY IS THIS IMPORTANT??



NEJM 2009; 361(23): 2241-51

NEJM 2001; 345(20): 1435-43

Refer when...

- Higher doses of diuretics
- Hyponatremia
- Persistent elevation of BNP
- If you have to reduce doses of Beta blockers, ACEI, ARB or Entresto
- Persistent hyponatremia
- Hyperkalemia alternating with hypokalemia
- Elevated BUN and Cr ration
- Worsening renal function
- Any patient with persistent LV systolic dysfunction
LVEF < 30% (especially with dilated LVs)

Refer When....

- LVEDD > 6.5 cm
- Persistent hypotension (SBP ~ 90s)
- Recurrent hospitalizations
 - (≥ 2) hospitalizations or ED visits for HF in the past year
- Not able to walk < 1 block
- Difficulty in carrying out daily routine
- Any significant decline from previous functional status
- Recurrent ICD discharges
- Weight loss
 - cardiac cachexia

Table VI. Risk Scores Predicting Mortality After VAD Implantation

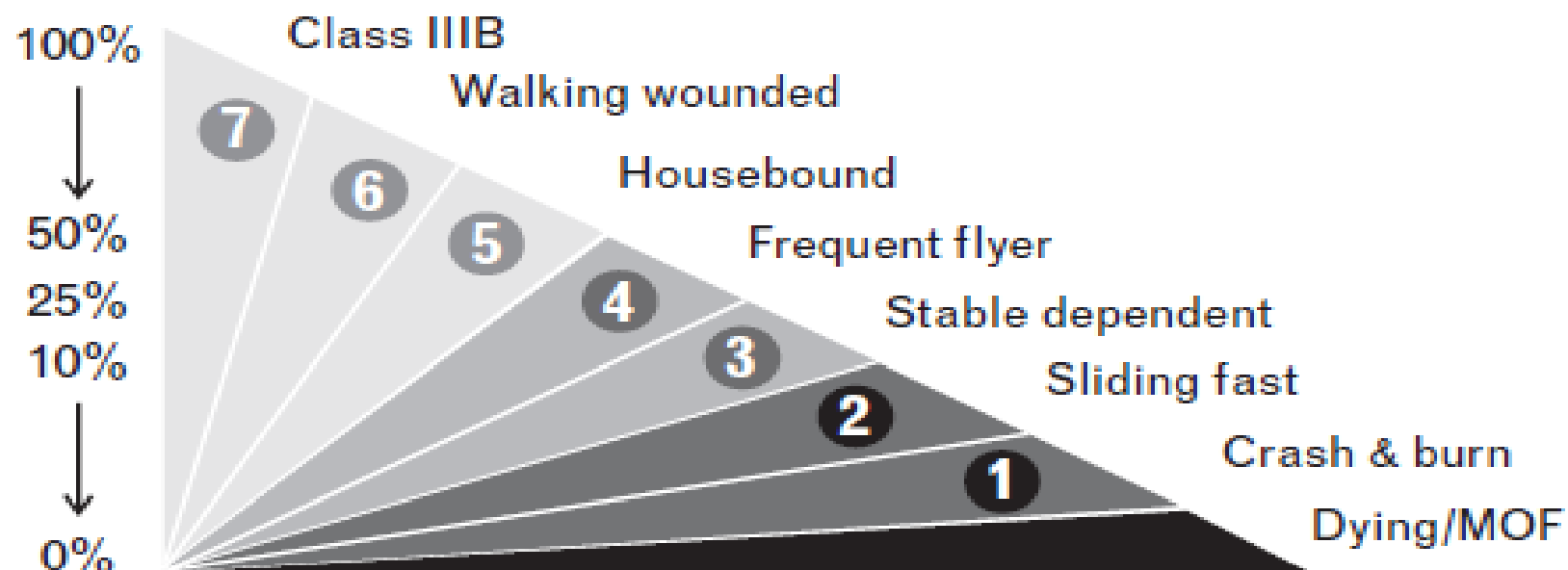
OZ ET AL ⁹		DENG ET AL ³⁵		LIETZ ET AL ²³ ("LIETZ-MILLER RISK SCORE")		KLOTZ ET AL ⁴⁶	
VARIABLE	RR/RISK SCORE	VARIABLE	OR/RISK SCORE	VARIABLE	OR/RISK SCORE	VARIABLE	OR/RISK SCORE
Urine output <30 mL/h	3.9/3	Respiratory failure and sepsis	11.2/1	Platelet count ≤148×10 ³ /μL	7.7/7	Transfusion ^a	16.1/6
CVP >16 mm Hg	3.1/2	Preexisting right heart failure	3.2/1	Serum albumin ≤3.3 g/dL	5.7/5	Inotropic support ^b	7.3/5
Mechanical ventilation	3.0/2	Age at implant >65 y	3.0/1	INR >1.1	5.4/4	Lactate >3 mg/dL	7.2/5
PT >16 s	2.4/2	Acute postcardiotomy	1.8/1	Vasodilator therapy	5.2/4	Heart values ^c	5.0/5
Reoperation	1.8/1	Acute infarction	1.7/1	Mean PAP ≤25 mm Hg	4.1/3	Infectious values ^d	4.6/4
WBC >15,000/mm ³	1.1/0	Maximum risk score	5	AST >45 U/mL	2.6/2	Resternotomy	4.2/4
Temperature >101.5°F	0/0			Hematocrit ≤34%	3.0/2	Mechanical support ^e	3.7/4
Maximum risk score	10	Risk score:		BUN >51 U/dL	2.9/2	Ventilation	3.7/3
		Low risk: 0 points		No intravenous inotropes	2.9/2	Renal impairment ^f	3.7/3
		High risk: ≥1 points		Maximum risk score	31	Emergency implant ^g	3.5/3
						Preoperative CPR	3.1/2
						ICM	2.4/2
						Heart rate >100/min	3.0/1
						Platelets <100×10 ³ /μL	2.8/1
						Blood values ^h	2.4/1
						Age >50 y	1.8/1
						Maximum risk score	50
						Risk score:	
						Low risk: 0–15 points	
						Medium risk: 16–30 points	
						High risk: 31–50 points	

Abbreviations: AST, aminotransferase; CPR, cardiopulmonary resuscitation; CVP, central venous pressure; ICM, ischemic cardiomyopathy; INR, international normalized ratio; OR, odds ratio; PAP, pulmonary artery pressure; PT, prothrombin time; RR, relative risk; VAD, ventricular assist device. ^aTransfusion: red blood cell count preoperatively >10 U and/or fresh frozen plasma preoperatively >10 U. ^bInotropic support: epinephrine and/or norepinephrine and/or dobutamine. ^cHeart values: lactic dehydrogenase >500 U/L and/or creatine kinase >200 U/L and/or troponin I >20 ng/mL. ^dInfectious values: C-reactive protein >8 mg/dL and/or white blood cell count (WBC) $13 \times 10^3/\mu\text{L}$. ^eExtracorporeal membrane oxygenation and/or intra-aortic balloon pump and/or previous cardiac surgery (<1 week). ^fRenal impairment: creatinine >1.5 mg/dL and/or serum urea nitrogen (BUN) >40 mg/dL and/or mechanical renal support (eg, continuous venovenous hemofiltration and dialysis). ^gEmergency implant: emergency implant and/or implant postcardiotomy. ^hBlood values: hemoglobin <12 g/dL and/or hematocrit <35%.

Risk – Benefit balance

- Infection
 - Nutritional status
 - Albumin and prealbumin
- Hemorrhage
 - Coagulopathy
- RV failure
 - RVSWI
 - CVP/PCWP ratio
 - LFTs and bilirubin
- Arrhythmias
- Renal failure

% 1-year survival



Intermacs level

5-7
3-4
1-2
MOF

Survival

Months to years
Weeks to months
Hours to weeks
Hours to days

VAD benefit

Not established
Yes
Yes
Bridge to decision in selected cases

Advanced Heart Failure

- Referral to specialized HF programs
- Mechanical circulatory support
- Cardiac transplant
- End-of-life planning
- Option to inactivate defibrillator

Thank
you!

