# Indications and timing of MCS implant

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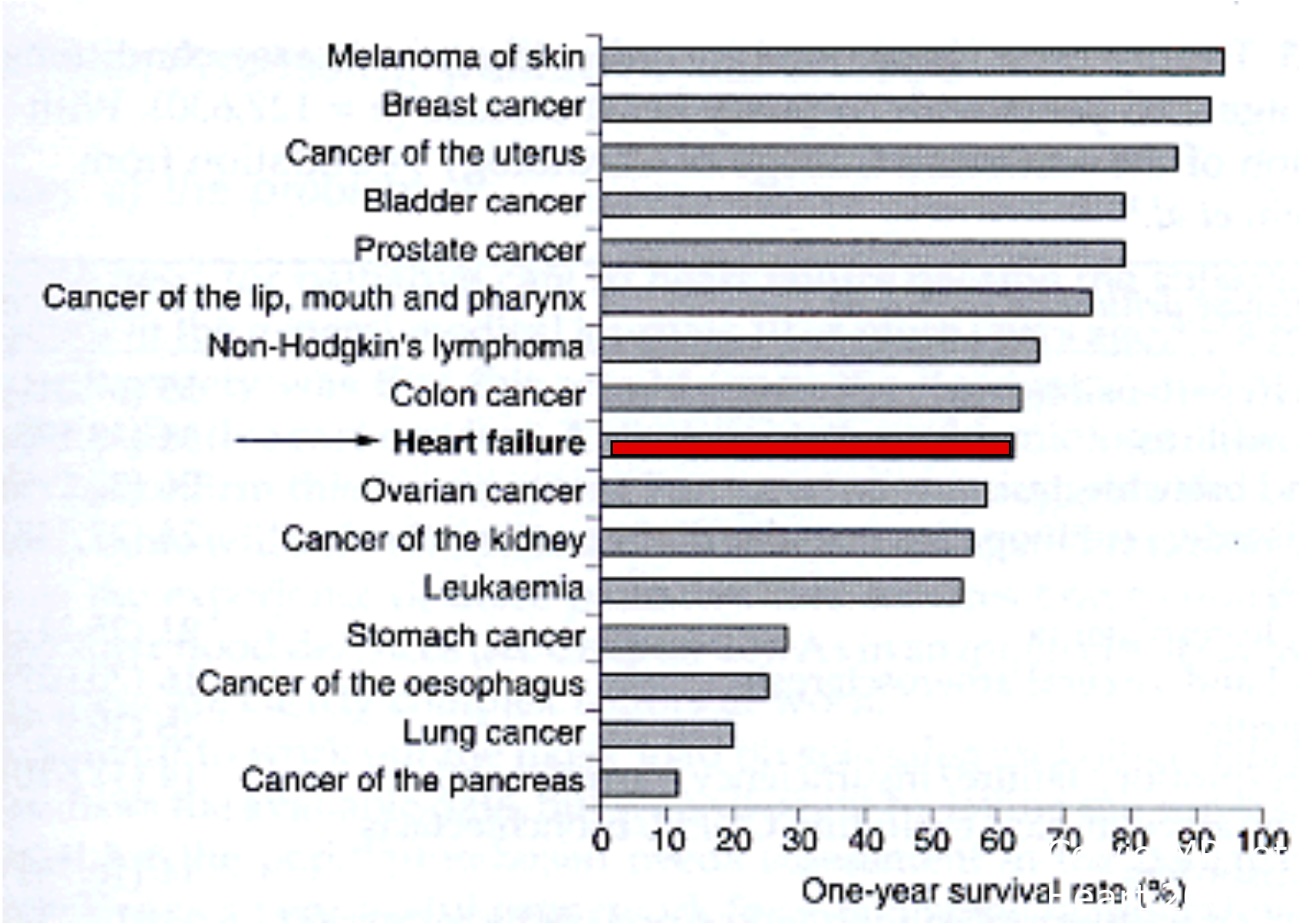
# Magnitude of HF Problem in Europe

- 637000 / year dead by HF
- 100-120/100000 die of HF (over last 40 years)
- DALY (disability adjusted life years) 360 Spain – 2600 Russia
- 880/100000 hospital discharges per year HF
- 2% of total European health care expenditures
- 24 Bill € health care costs (2006)
- 25 Bill € non-health care costs (productivity loss)
- 49 Bill € total costs per year

***EU cardiovascular disease statistics 2008 (Allender et al)***

# One year survival rates, heart failure and major cancers compared, mid-1990s, England and Wales



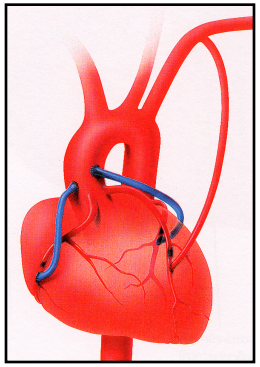
Life Style

Prophylaxis

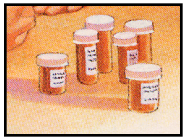
Palliation

CRT /ICD

Heart Failure Therapy

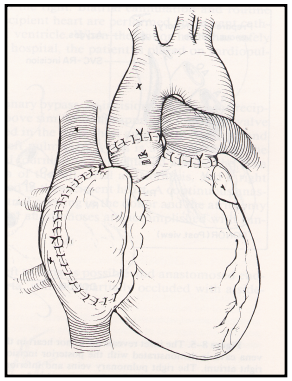


Drugs for CHF

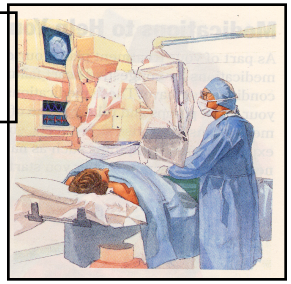


Surgery

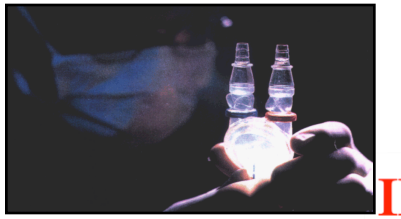
Transplantation



Cath Lab

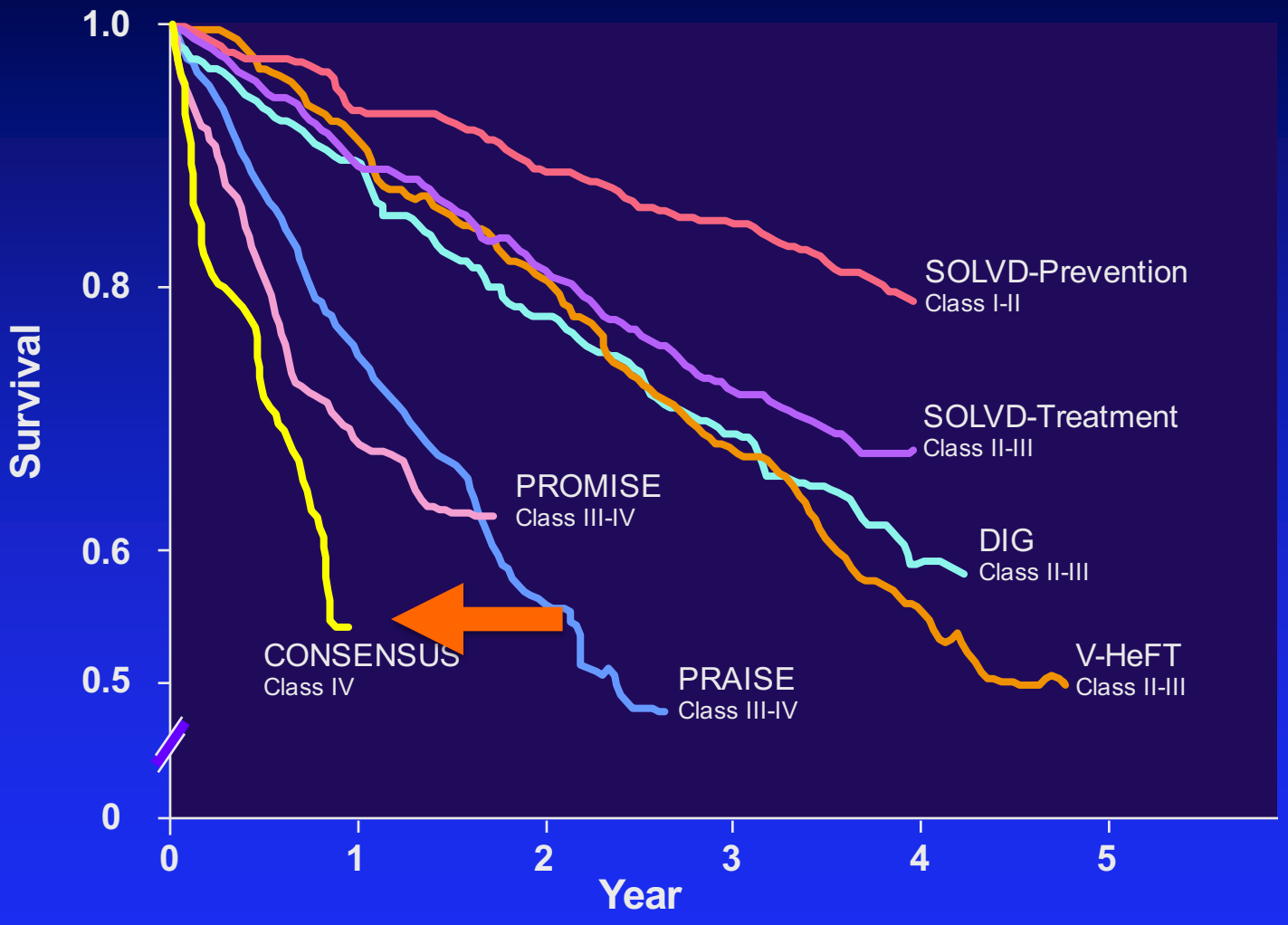


VADs



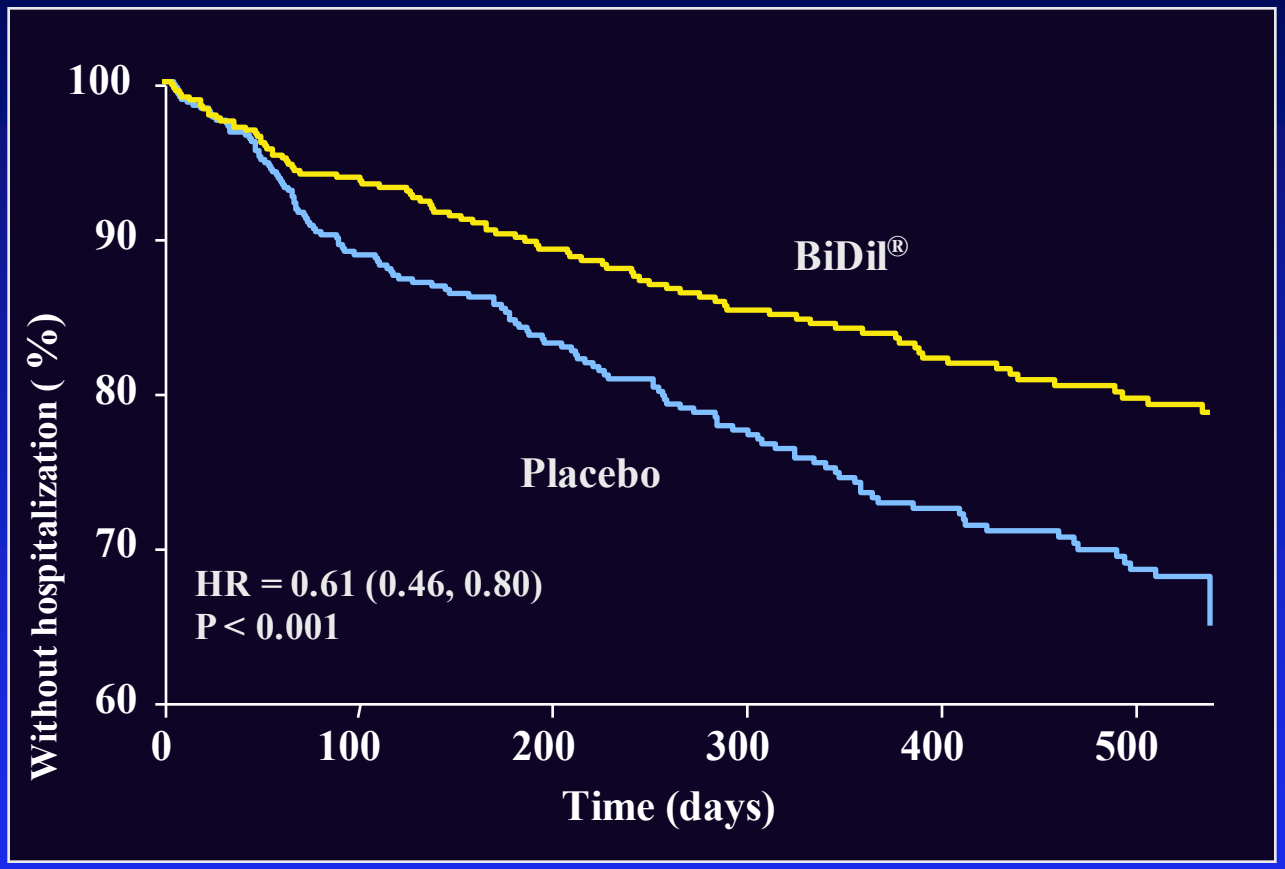
IK+E M

# Heart failure mortality



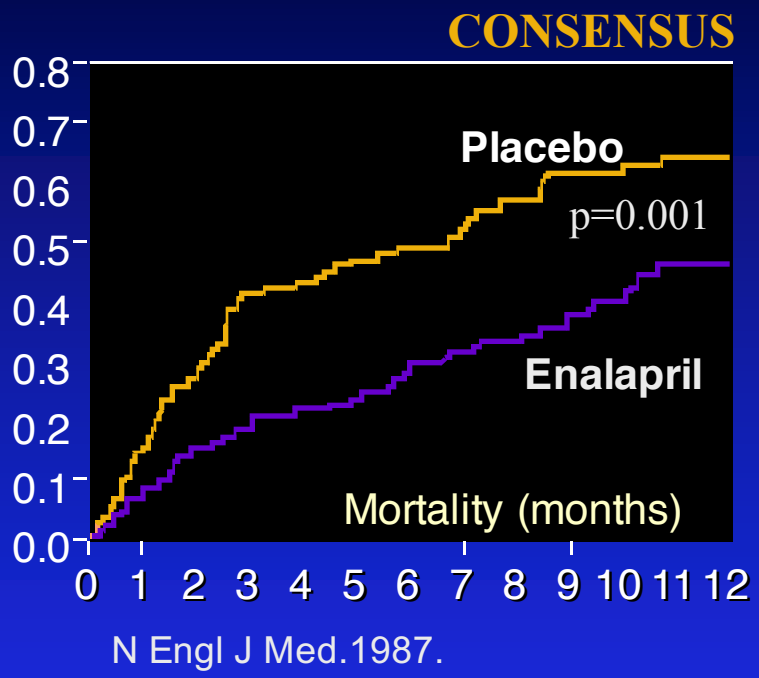
# Hydralazine & nitrates

**A-HeFT**



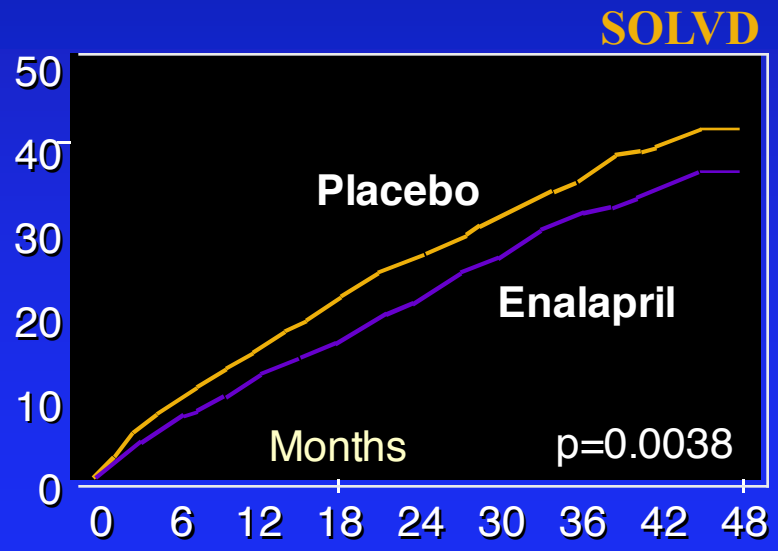

Taylor AL et al. NEJM, Nov 2004

# ACE-inhibitors



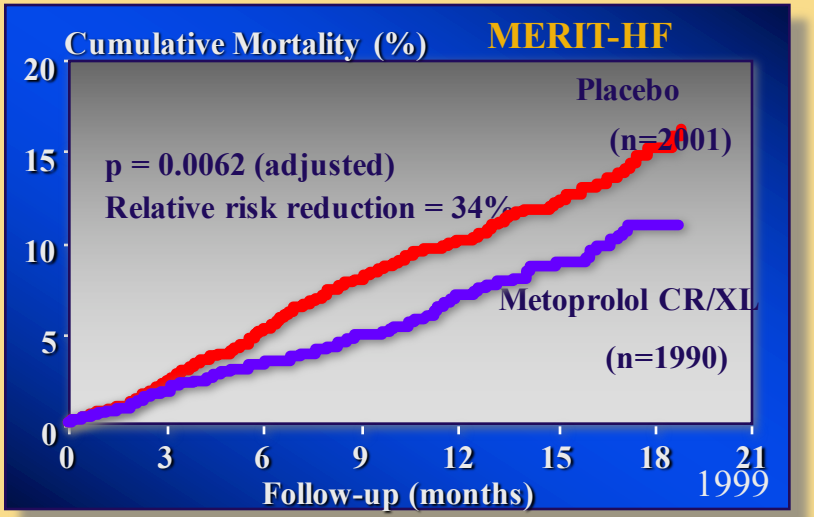

N Engl J Med.1987.

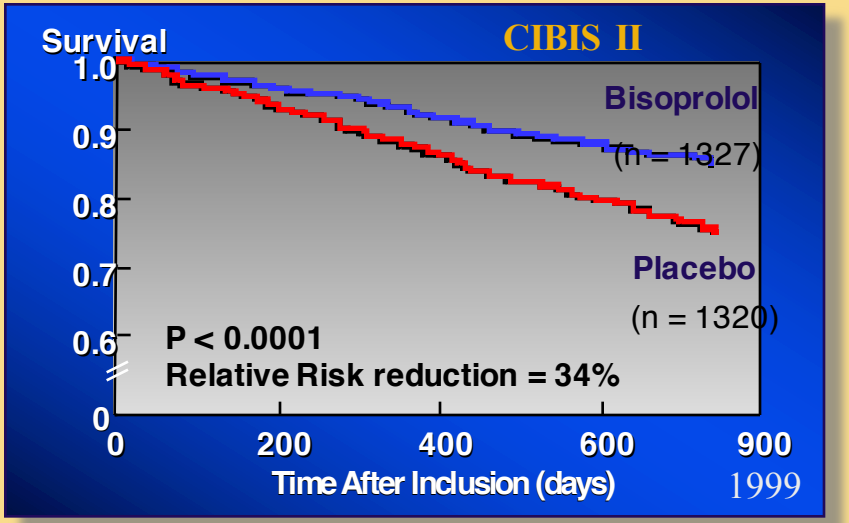
**CONSENSUS**
**V-HeFT-II**
**SOLVD-T**
**SOLVD-P**
**SAVE**
**AIRE**
**TRACE**
**ATLAS**

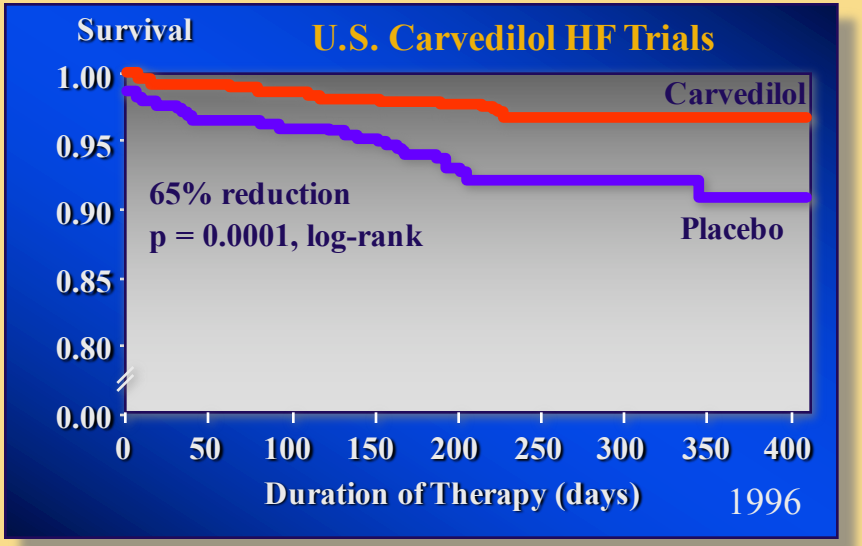


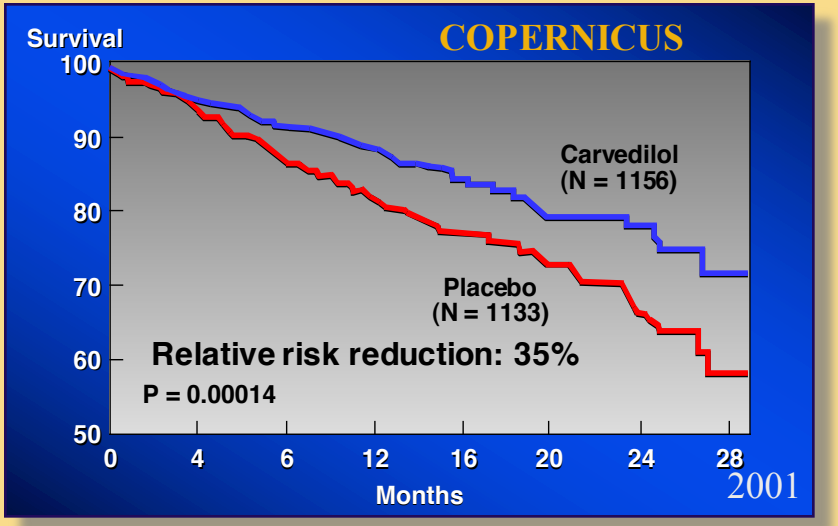

New Engl J Med.1992.

# Beta-blockers

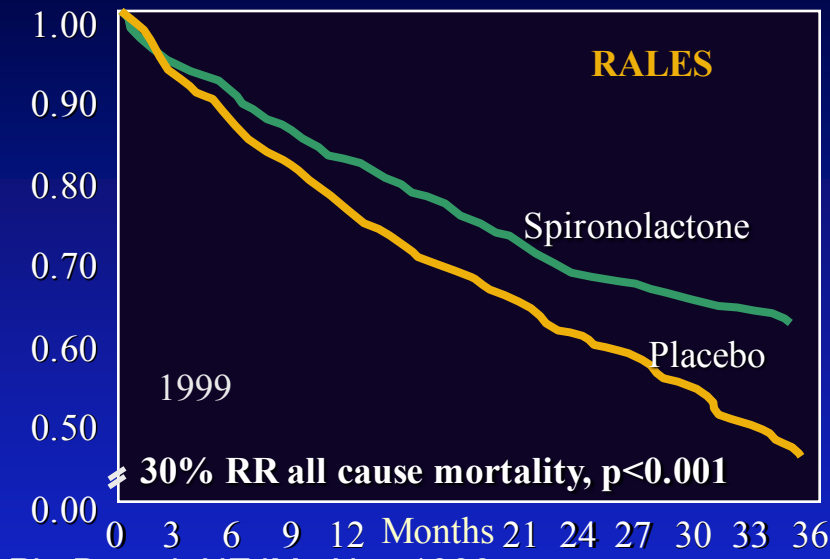


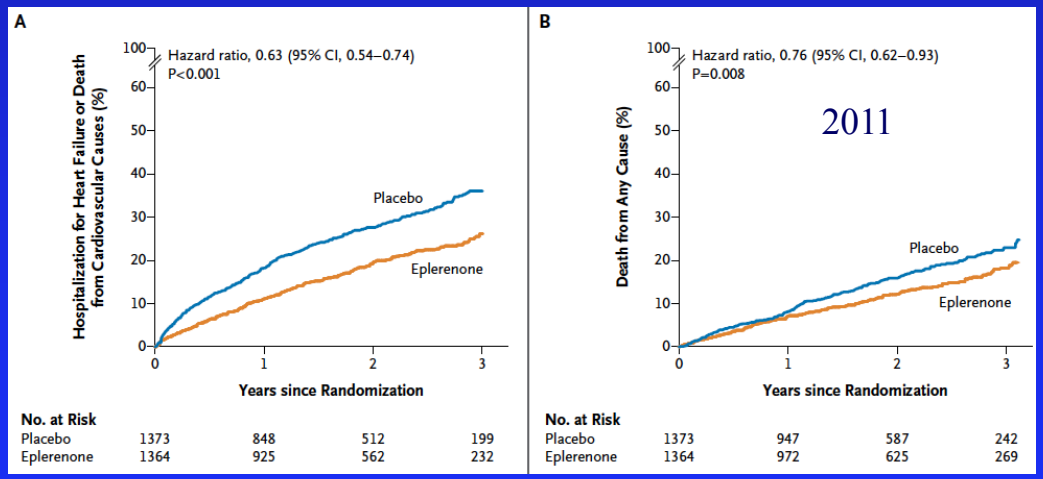
# Aldosterone blockers




Pitt B et al. NEJM, Nov 1999

Chronic Heart Failure
EF ≤ 35%, NYHA III-IV
Spironolactone 25 mg QD

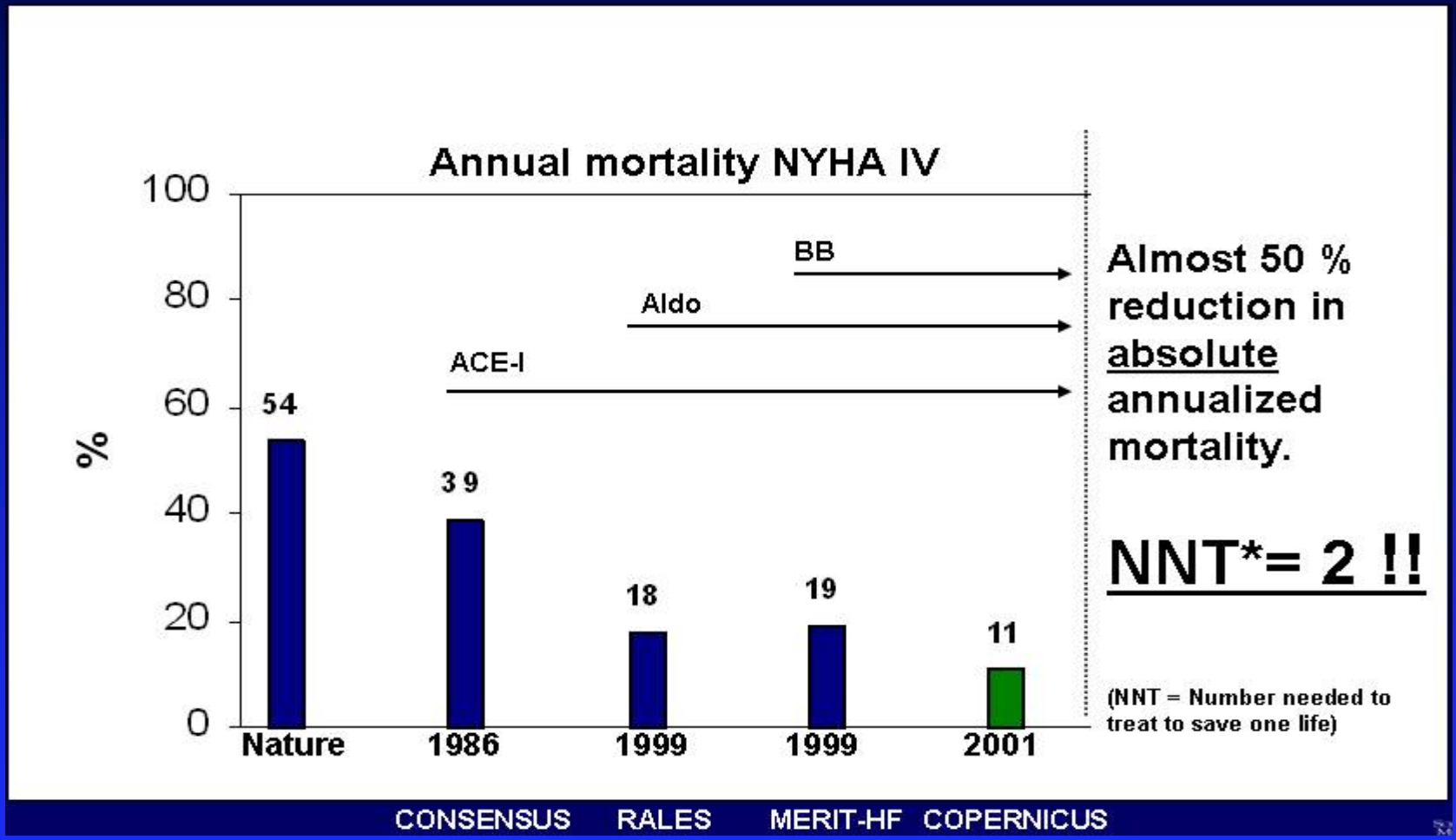
EMPHASIS-HF




Zannad F et al. NEJM, Nov 2011

Chronic Heart Failure
EF ≤ 30%
(or 30-35% with QRS >130ms)
NYHA II
Eplerenone 50 mg QD

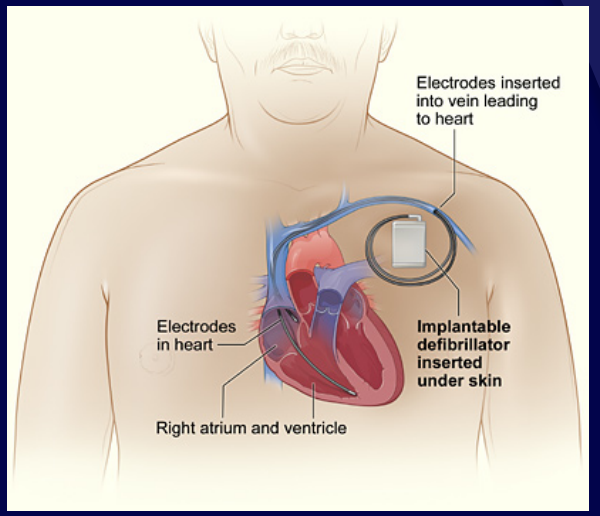
# Medical Rx has reduced 1-year mortality from 50 to 10% !



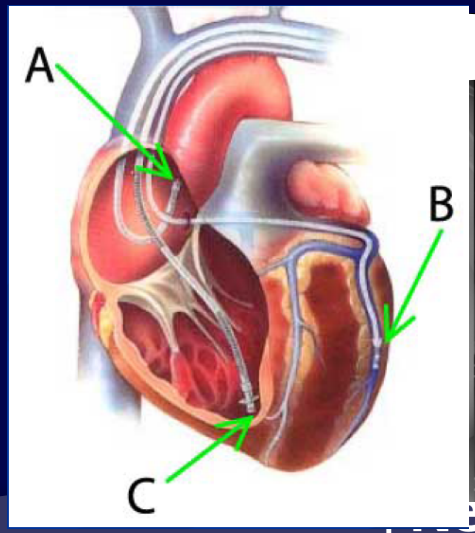

Jorde UP. Cardiol Rev. 2006 Mar-Apr;14(2):81-7.

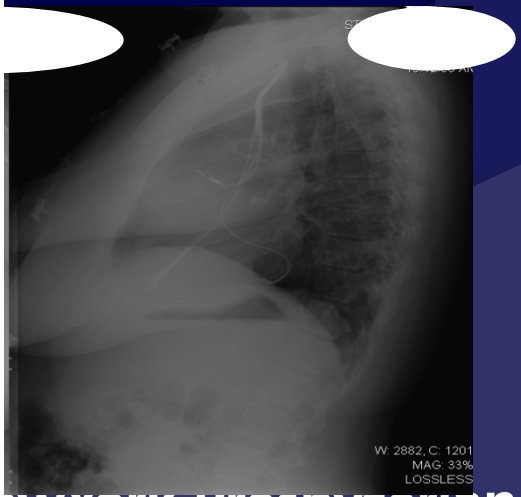
# ‘Device’ therapy

Implantable cardioverter-defibrillator (ICD)



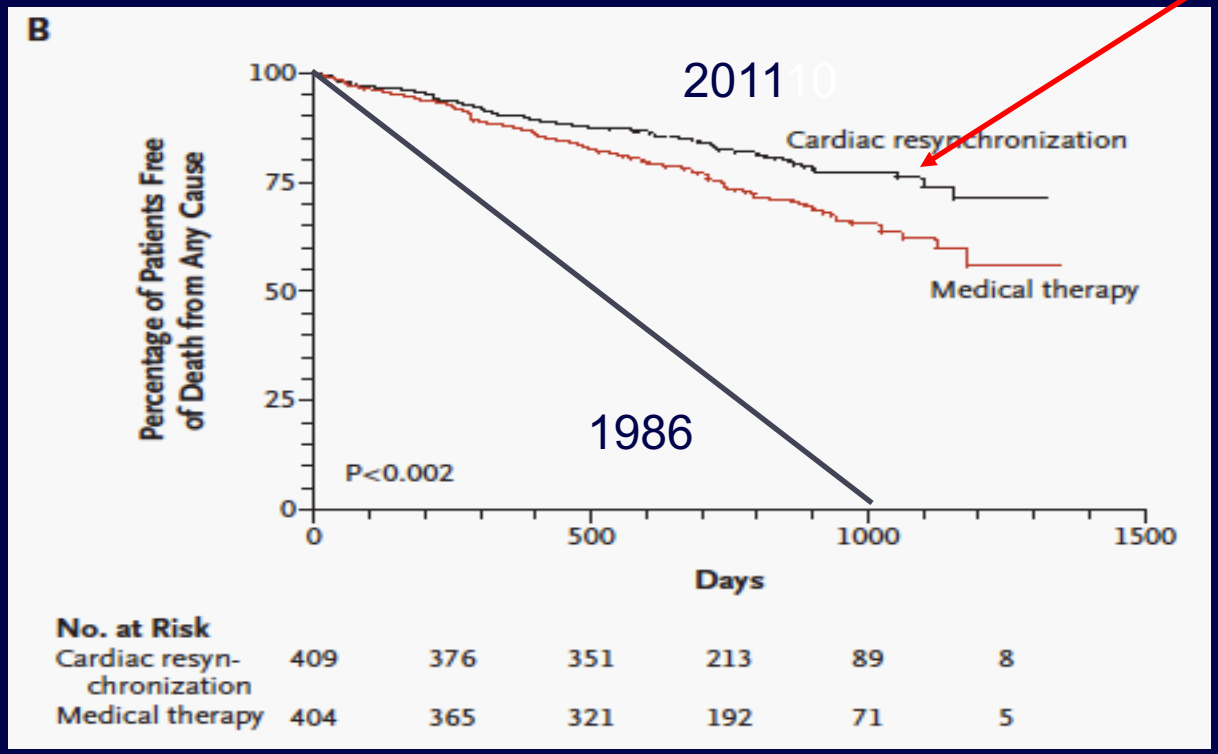

Cardiac resynchronzation therapy (CRT, CRT-D)



# OMM + CRT:

3 year mortality 25% !



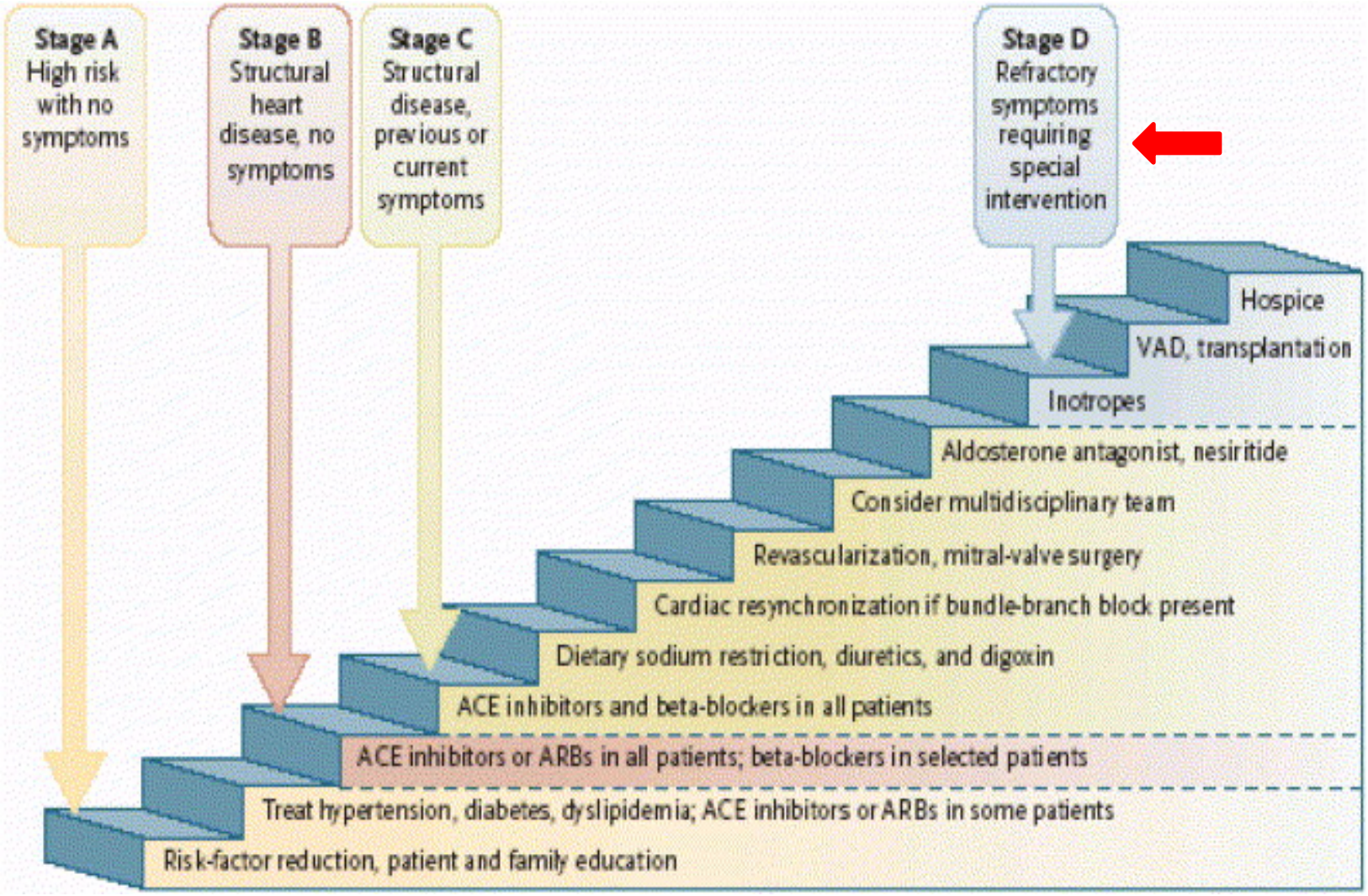

**Care-HF NEJM 2005**

Upon referral to quaternary care HF center:

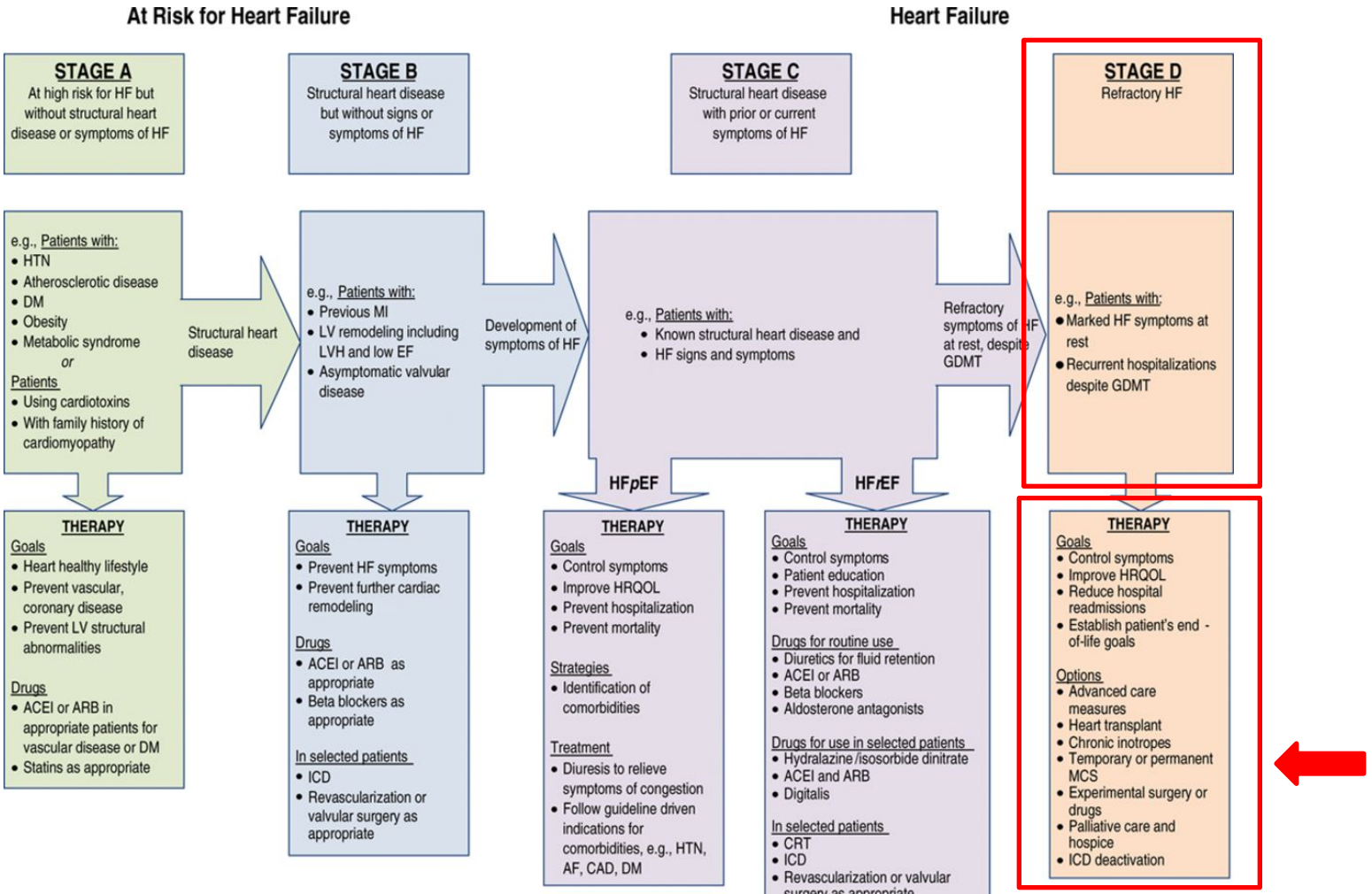
- 4/10 without CRT despite indication
- 7/10 women without ICD

**Sims D, ….Jorde, UP. Pace 2011**

# Progression of Heart failure



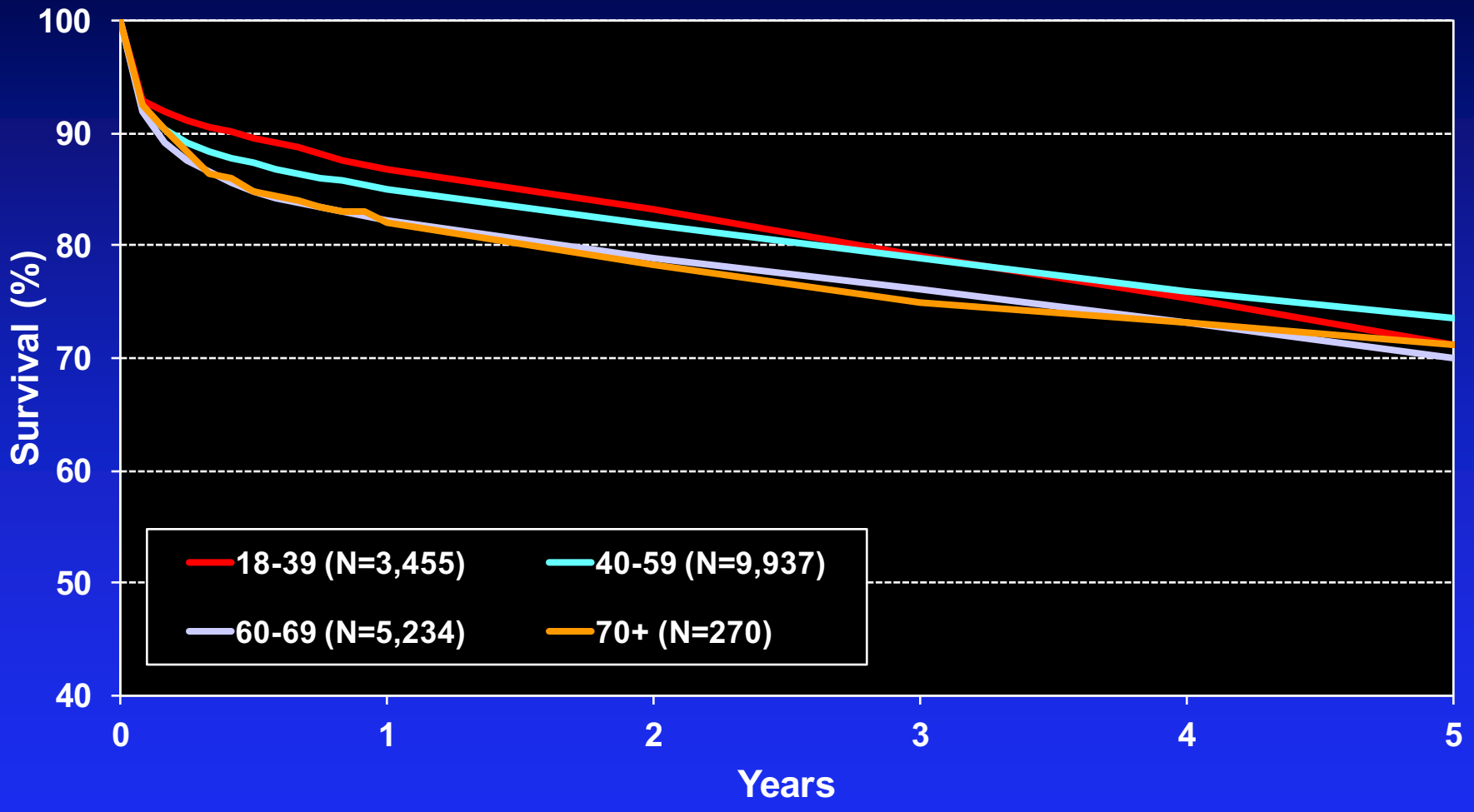
# MCS therapy Target



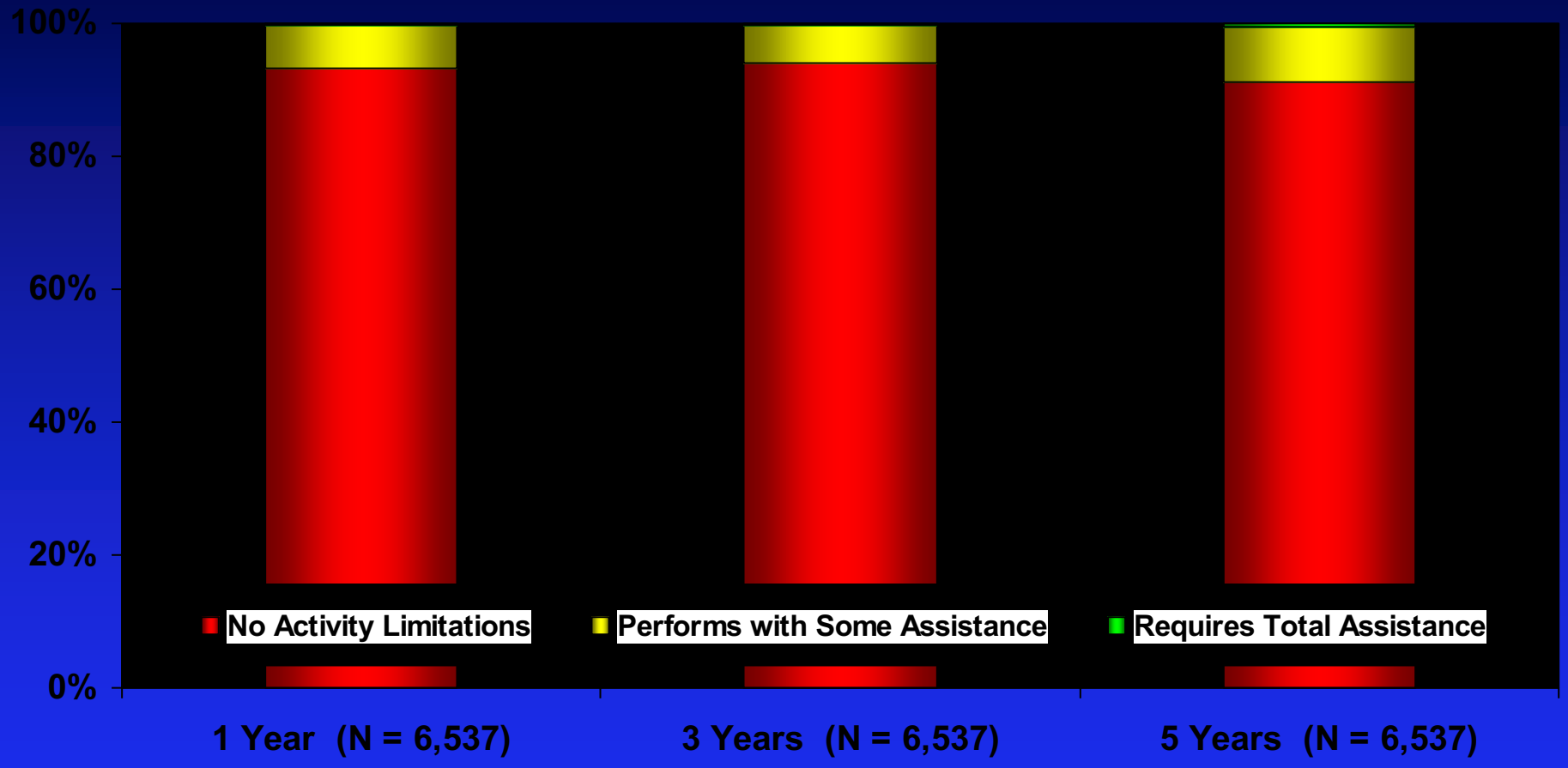

**Clyde W. Yancy et al. Circulation. 2013;128:e240-e327**

American Heart Association.

# Heart transplantation – survival by age

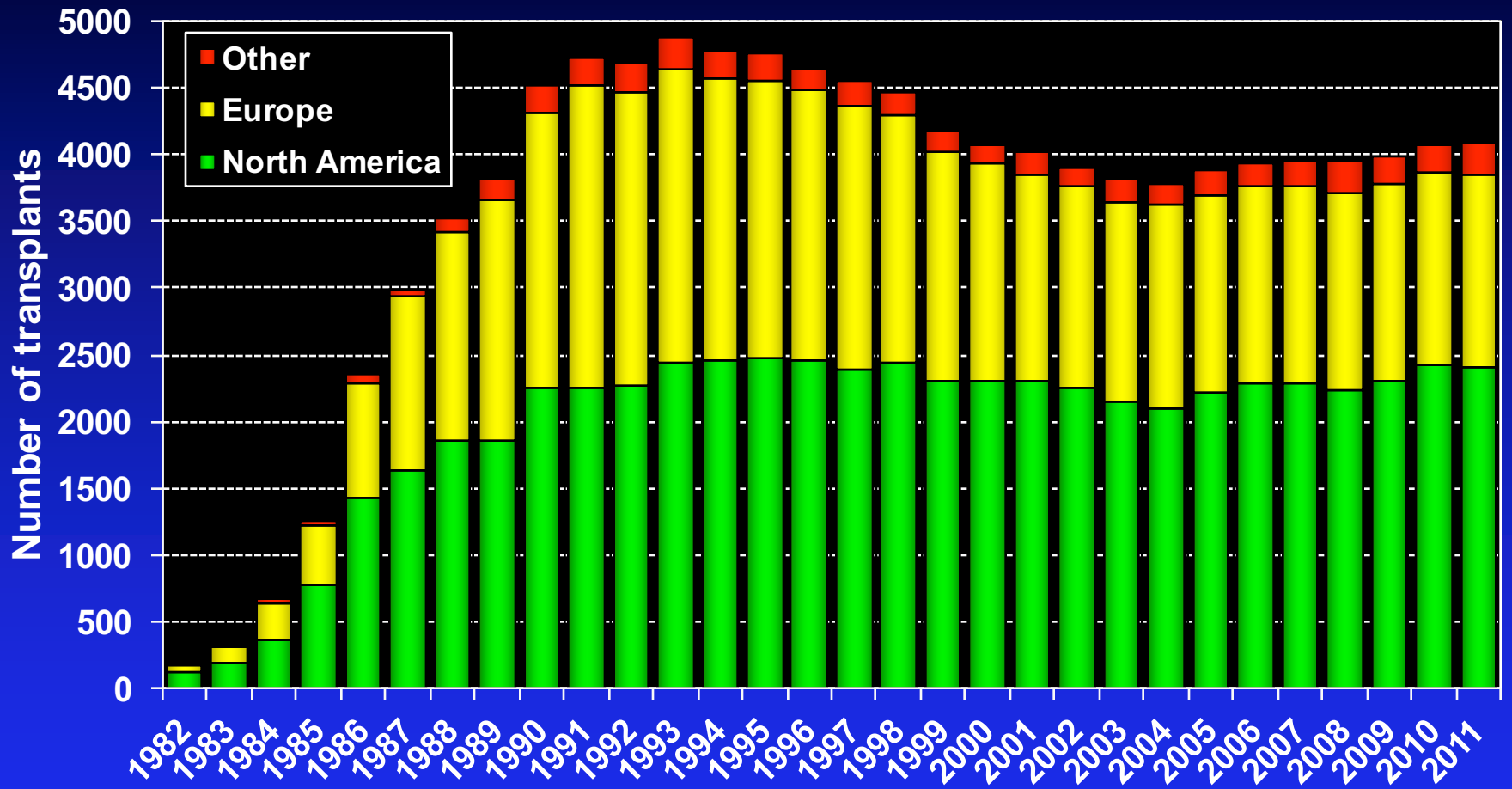


# Functional status after transplant




Stehlik J, et al. JHLT 2010 ; 29(10)

# Heart transplant volume



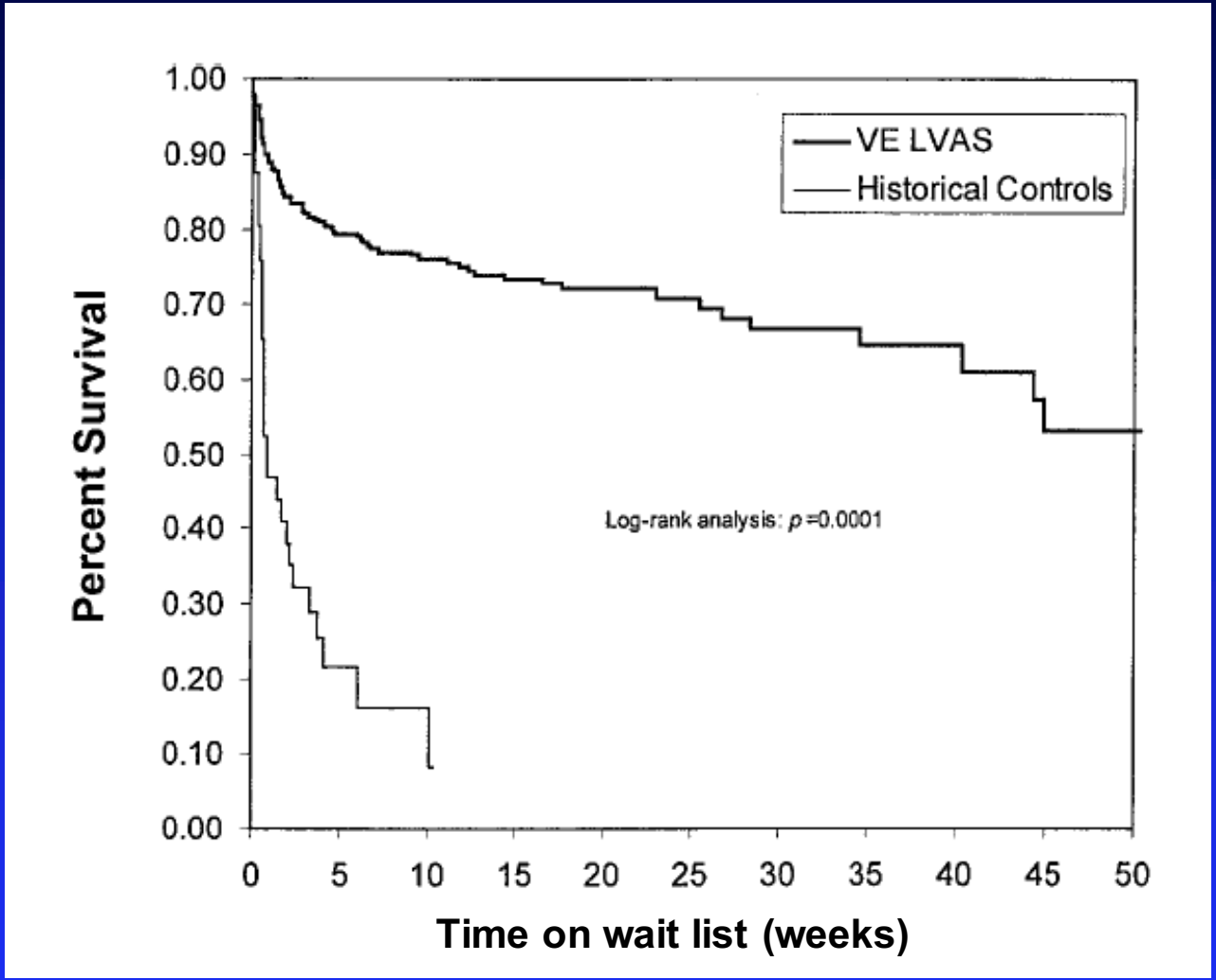

ISHLT • INTERNATIONAL SOCIETY FOR HEART AND LUNG TRANSPLANTATION

2013

30th Annual Report

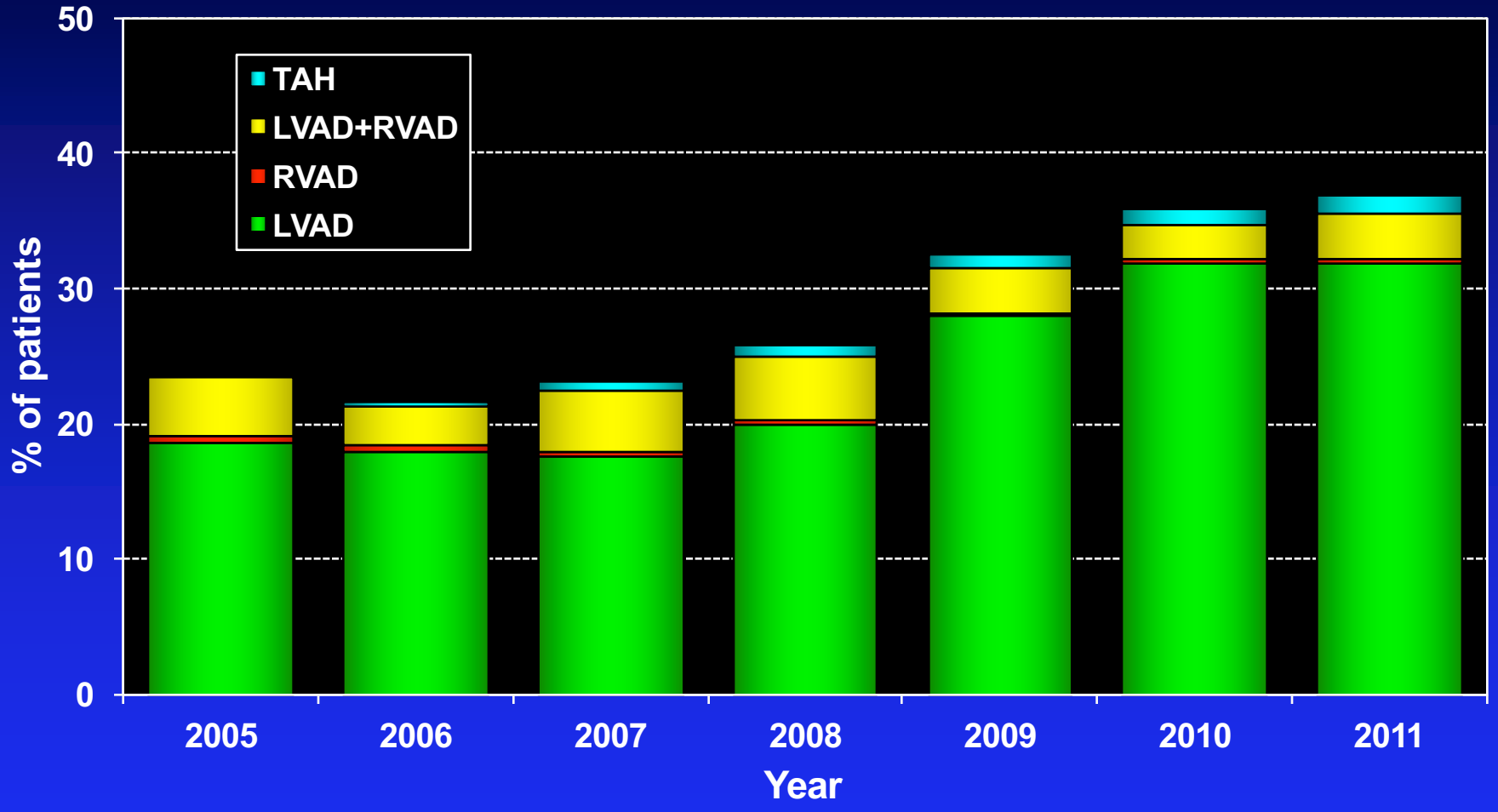
Stehlik J, ISHLT 2013

# VADs improve survival to transplant




Frazier OH et al. JTCS 2001;122(6)

# Mechanical assist before transplant

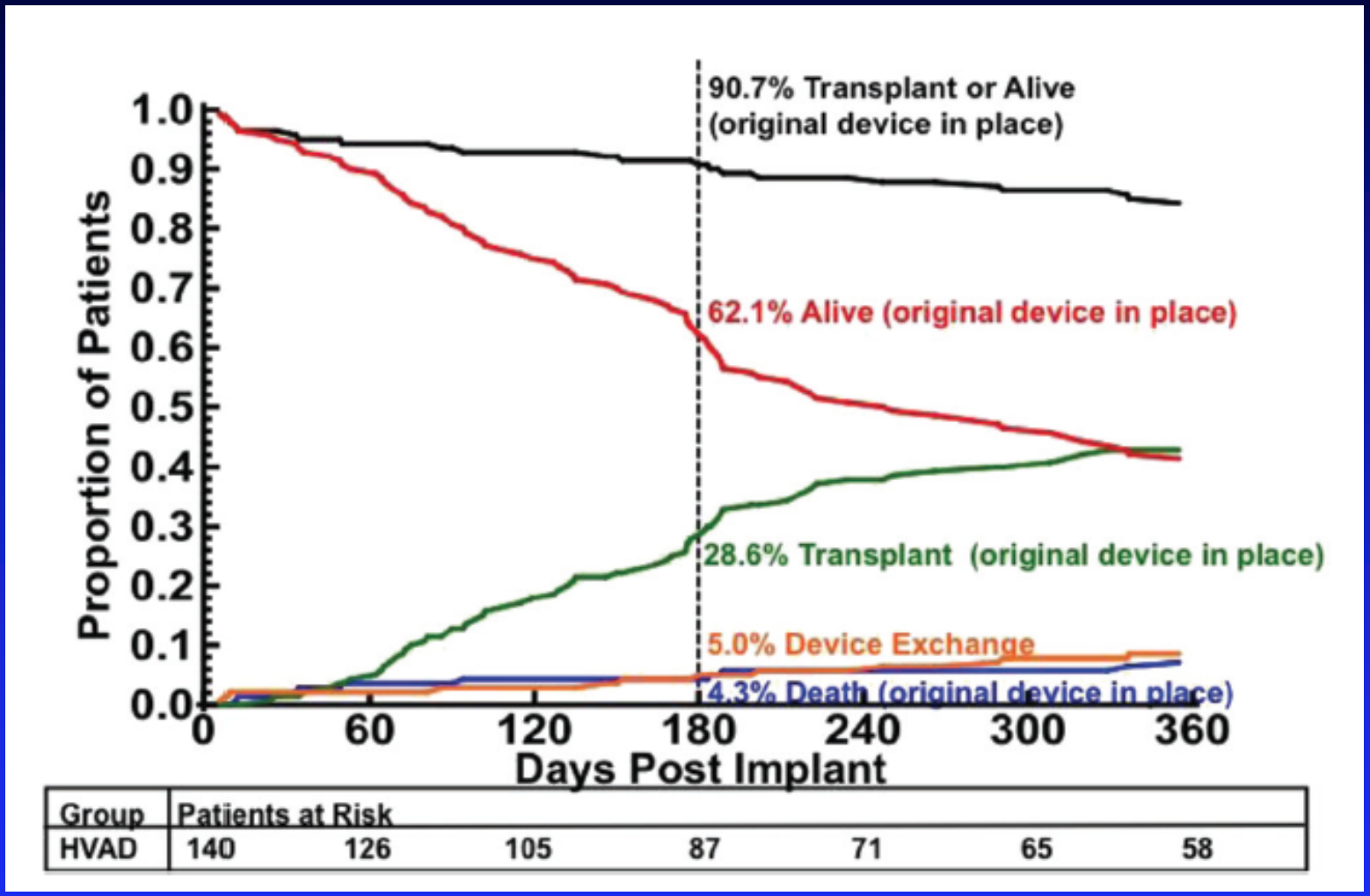



ECMO is excluded.

ISHLT • INTERNATIONAL SOCIETY FOR HEART AND LUNG TRANSPLANTATION
2013
30th Annual Report

Stehlik J, ISHLT 2013

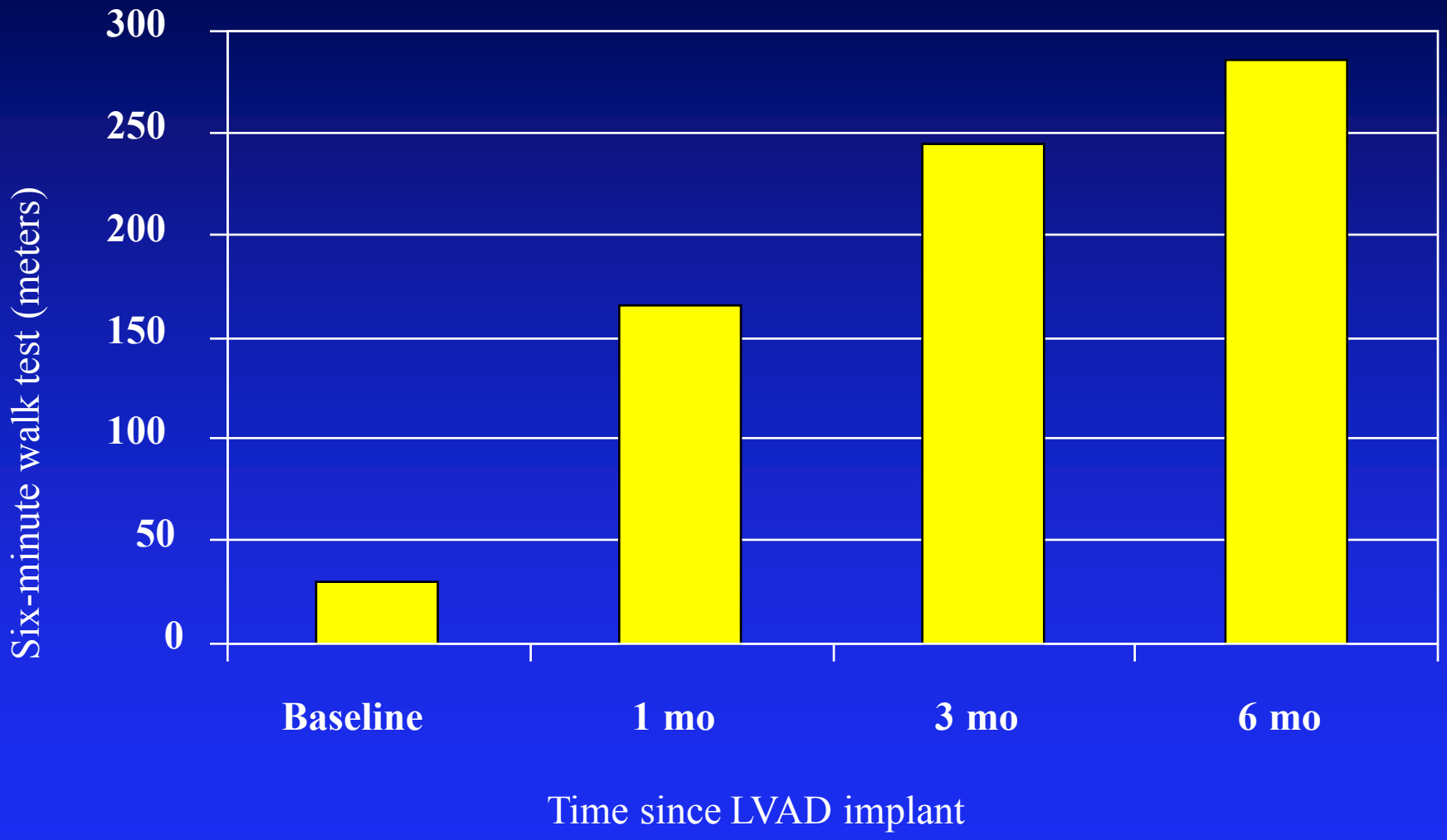
# BTT trial, primary outcome




| Group | Patients at Risk | | | | | | |
|---|---|---|---|---|---|---|---|
| HVAD | 140 | 126 | 105 | 87 | 71 | 65 | 58 |

Aaronson KD, Circulation, 2012

# Functional status after LVAD implant




Miller LW et al. NEJM, 2007 Aug 30;357(9)

## Recommendations for surgical implantation of LVADs in patients with systolic heart failure

| Recommendations | Class[a] | Level[b] | Ref[c] |
|---|---|---|---|
| An LVAD or BiVAD is recommended in selected patients[d] with end-stage HF despite optimal pharmacological and device treatment and who are otherwise suitable for heart transplantation, to improve symptoms and reduce the risk of HF hospitalization for worsening HF and to reduce the risk of premature death while awaiting transplantation. | I | B | 254, 255, 258 |
| An LVAD should be considered in highly selected patients[d] who have end-stage HF despite optimal pharmacological and device therapy and who are not suitable for heart transplantation, but are expected to survive >1 year with good functional status, to improve symptoms, and reduce the risk of HF hospitalization and of premature death. | IIa | B | 254 |

BiVAD = bi-ventricular assist device; HF = heart failure; LVAD = left ventricular assist device.
[a]Class of recommendation.
[b]Level of evidence.
[c]References.
[d]See text and *Table 25*.


References
254. Rose EA, et al, NEJM 2001
255. Slaughter MS et al, NEJM 2009
258. Pagani FD, et al, JACC 2009


## Table 25 Patients potentially eligible for implantation of a ventricular assist device

| Patients with >2 months of severe symptoms despite optimal medical and device therapy and more than one of the following: |
|---|
| • LVEF <25% and, if measured, peak $VO_2$ < 12 mL/kg/min |
| • ≥3 HF hospitalizations in previous 12 months without an obvious precipitating cause |
| • Dependence on i.v. inotropic therapy |
| • Progressive end-organ dysfunction (worsening renal and/or hepatic function) due to reduced perfusion and not to inadequate ventricular filling pressure (PCWP ≥20 mm Hg and SBP ≤80–90 mmHg or CI ≤2 L/min/m²) |
| • Deteriorating right ventricular function |

CI = cardiac index; HF = heart failure; i.v. = intravenous; LVEF = left ventricular ejection fraction; PCWP = pulmonary capillary wedge pressure; SBP = systolic blood pressure.

# Where is the Problem?

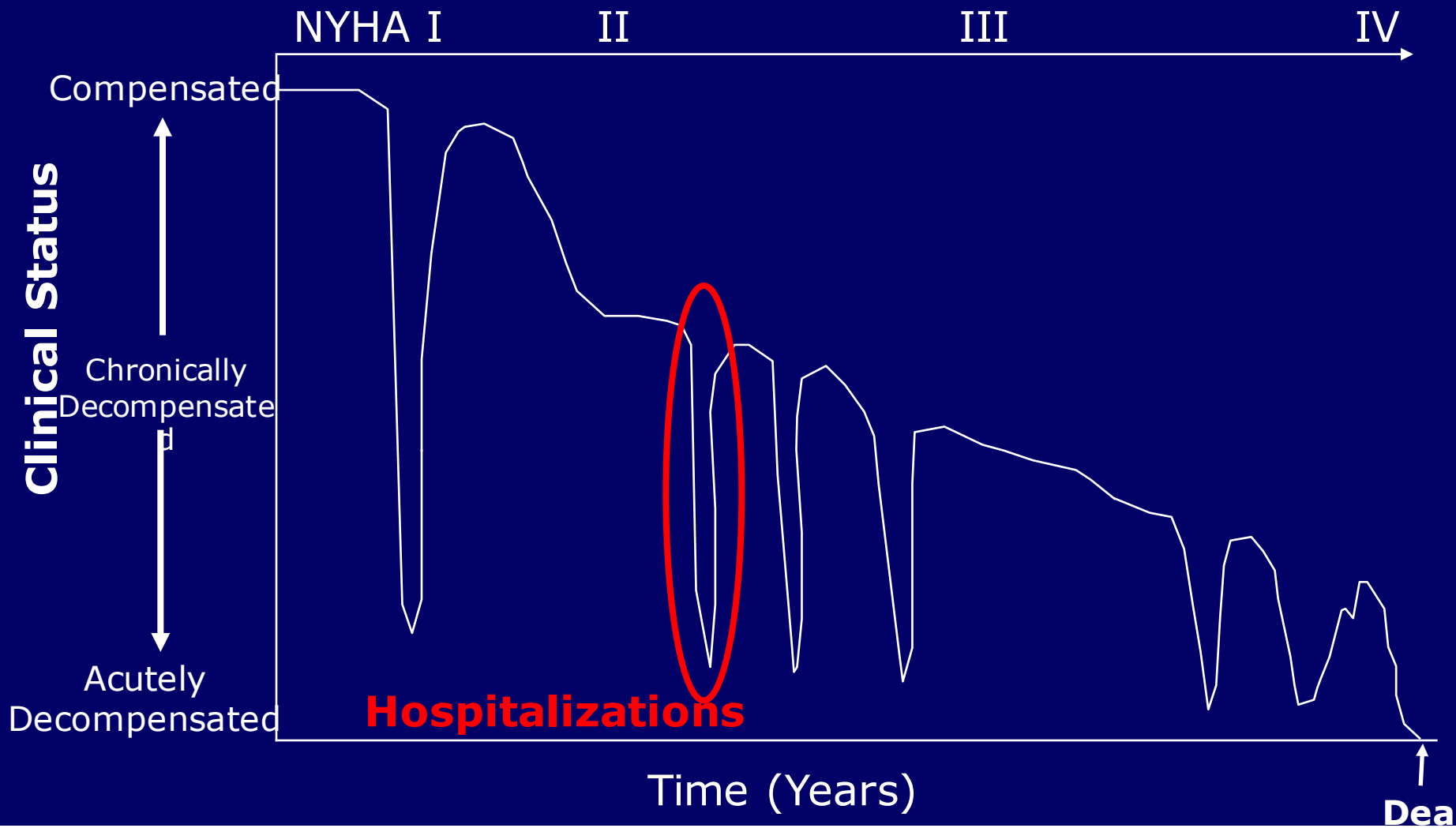
**TIMING = When to refer ?**

**PATIENT SELECTION**

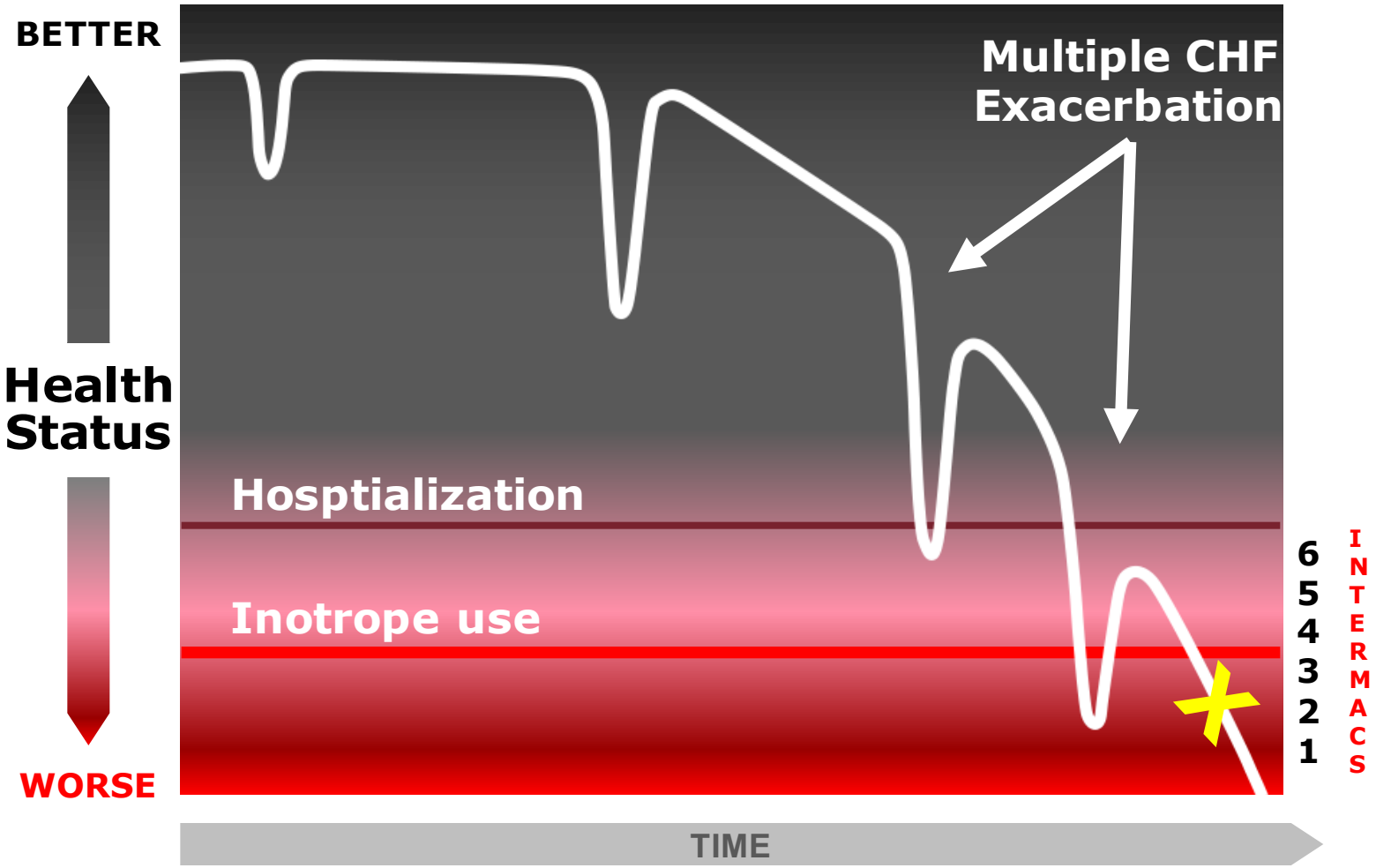
# Right Timing of VAD Therapy

1. Impaired renal function (CRS) (**to be avoided**)
2. Elevated pulmonary blood pressure (**to be avoided**)
3. Beginning cardiac cachexia (**too late**!)
4. Impairment of the clinical condition, according to the INTERMACS levels (**might be to late**!)
5. Deteriorating RV function (**might be to late**!)

# Clinical Course of Chronic Heart Failure – characterised by acute decompensations



# LVAD Use in the Perspective of CHF Disease Continuum



# Diagnosis and Treatment of ACUTE and chronic heart failure (2013 ACCF/AHA Guideline - Management of HF 2012 ESC Guidelines )

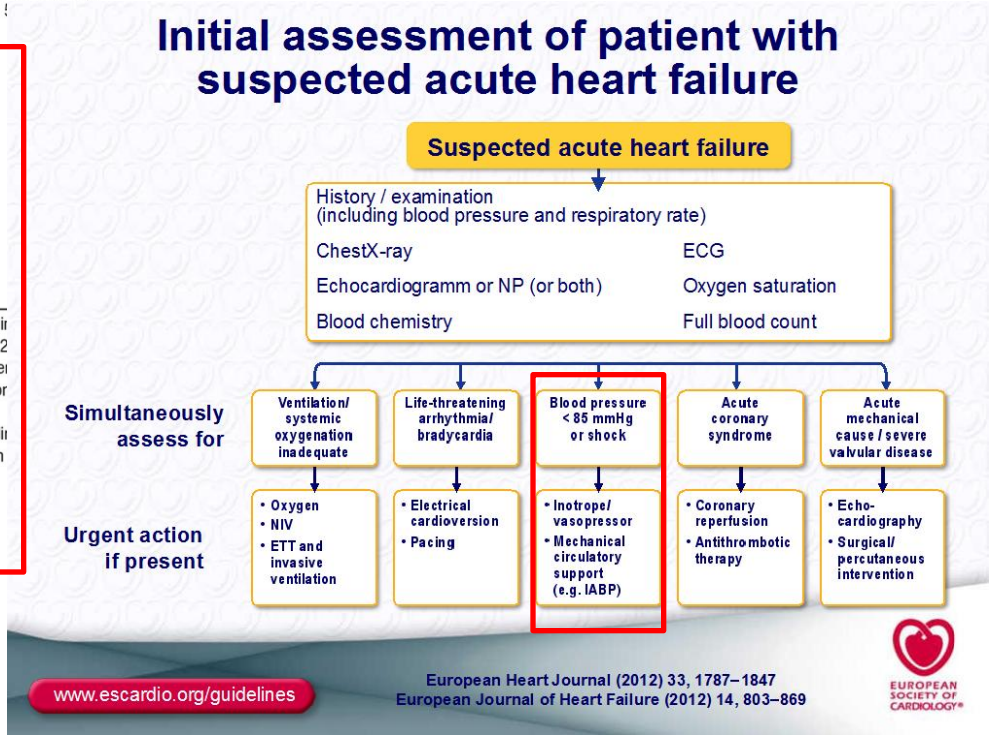
| Recommendations | COR | LOE | References |
|---|---|---|---|
| Inotropic support | | | |
| Cardiogenic shock pending definitive therapy or resolution | I | C | N/A |
| BTT or MCS in stage D refractory to GDMT | IIa | B | 647, 648 |
| Short-term support for threatened end-organ dysfunction in hospitalized patients with stage D and severe HF/EF | IIb | B | 592, 649, 650 |
| Long-term support with continuous infusion palliative therapy in select stage D HF | IIb | B | 651–653 |
| Routine intravenous use, either continuous or intermittent, is potentially harmful in stage D HF | III: Harm | B | 416, 654–659 |
| Short-term intravenous use in hospitalized patients without evidence of shock or threatened end-organ performance is potentially harmful | III: Harm | B | |
| MCS | | | |
| MCS is beneficial in carefully selected* patients with stage D HF in whom definitive management (eg, cardiac transplantation) is anticipated or planned | IIa | B | |
| Nondurable MCS is reasonable as a "bridge to recovery" or "bridge to decision" for carefully selected* patients with HF and acute profound disease | IIa | B | |
| Durable MCS is reasonable to prolong survival for carefully selected* patients with stage D HF/EF | IIa | B | |
| Cardiac transplantation | | | |
| Evaluation for cardiac transplantation is indicated for carefully selected patients with stage D HF despite GDMT, device, and surgical management | I | C | |

*Although optimal patient selection for MCS remains an active area of investigation, general indications for referral for MCS therapy i with LVEF <25% and NYHA class III–IV functional status despite GDMT, including, when indicated, CRT, with either high predicted 1- to 2 (eg, as suggested by markedly reduced peak oxygen consumption and clinical prognostic scores) or dependence on continuous parei support. Patient selection requires a multidisciplinary team of experienced advanced HF and transplantation cardiologists, cardiothor nurses and ideally, social workers and palliative care clinicians.

BTT indicates bridge to transplant; COR, Class of Recommendation; CRT, cardiac resynchronization therapy; GDMT, guideline-di therapy; HF, heart failure; HF/EF, heart failure with reduced ejection fraction; LOE, Level of Evidence; LVEF, left ventricular ejection mechanical circulatory support; N/A, not applicable; and NYHA, New York Heart Association.

Clyde W. Yancy et al. Circulation. 2013;128:e240-e327

American Heart Association.




"*So We **Should** Consider…*"

# Causes of Cardiogenic Shock

MI with Mechanical Complications

HOCM

Postcardiotomy

Acute Myocarditis

Peripartum cardiomyopathy

Takotsubo/Stress-induced CMP

**Acute Decompensation of Chronic HF**

**MI without Mechanical Complications**

Massive Pulmonary Embolism

Cardiac Tamponade

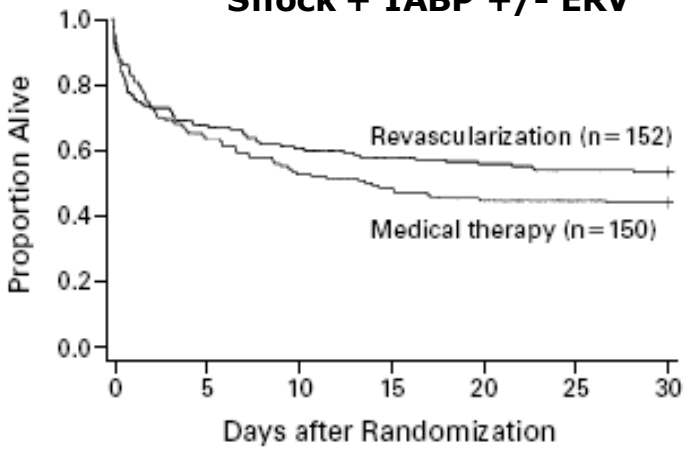
Refractory Arrhythmias

Acute Post Transplant Rejection

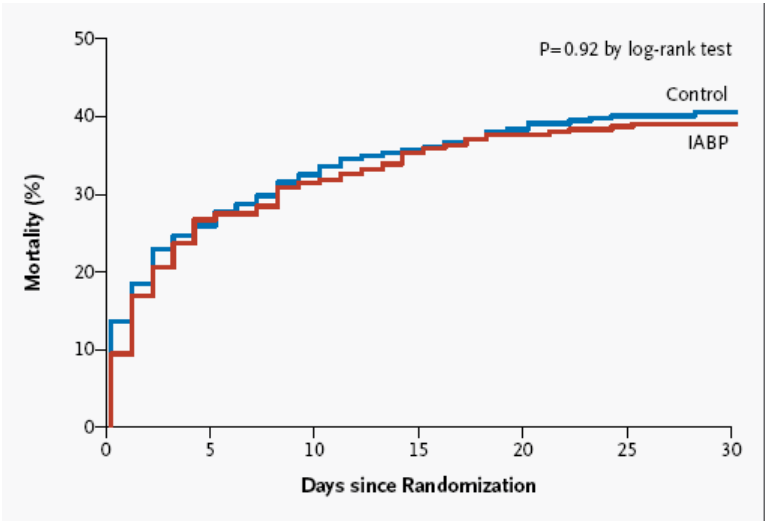
Aortic dissection – acute severe AI and/or MI

# Mortality in Shock Patients in Large RCT

**Shock + IABP +/- ERV**




**Shock + ERV +/- IABP (89% on catecholamine)**




**<u>SHOCK Trial</u>** (Hochman J, NEJM 1999 )

STEMI patients with IABP
***Randomized to emergency revasc (ERV):***
30-day mortality 53% vs 44% ; p NS
At 6 months significant: NNT 8
**Conclusion: ERV saves lives, but mortality is very high!**

**<u>SHOCK II Trial</u>** (Thiele, NEJM 2012)

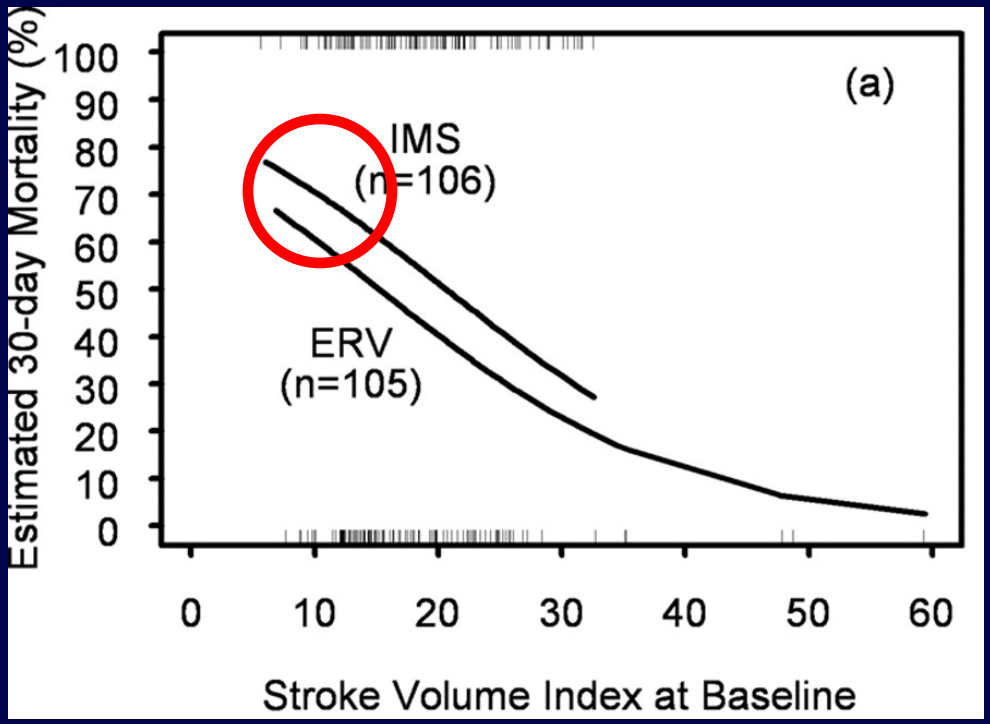
STEMI patients with ERV
***Randomized to IABP:***
30-day mortality 39.1% vs 41.3 % ; p NS
**Conclusion: IABP does not affect outcomes in shock pts already receiving catecholamines**

CHEST ONLINE

# Hemodynamic Parameters Are Prognostically Important in Cardiogenic Shock But Similar Following Early Revascularization or Initial Medical Stabilization*

Raban V. Jeger, April M. Lowe, Christopher E. Buller, Matthias E. Pfisterer, Vladimir Dzavik, John G. Webb, Judith S. Hochman and Ulrich P. Jorde

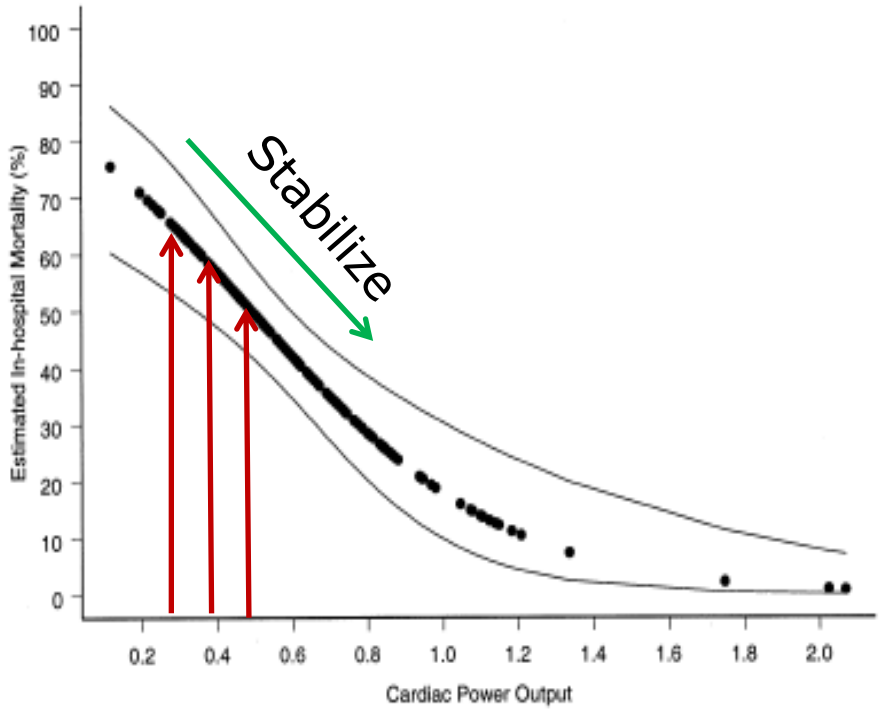
*Chest* 2007;132;1794-1803; Prepublished online October 20, 2007;




**Early Revascularization (ERV) confers consistent survival benefit.**

**30 day mortality in the sickest STEMI patients: 70-80% !**

# Estimated Mortality Target Population




## Assumptions:

| CI/CO (BSA 1.8) | MAP | CPO | Mortality |
|---|---|---|---|
| 1.8/3.4 | 65 | 0.49 | 50% |
| 1.6/2.9 | 60 | 0.38 | 60% |
| 1.5/2.7 | 55 | 0.32 | 70% |

Finke R et al. JACC 2004

# Refractory Shock - Therapeutic Gap……

- Advances have been made in the management of acute heart failure
- However, outcomes of refractory acute cardiogenic shock remain disproportionately poor
- Ideal support system and optimal therapeutic pattern **is not yet defined**

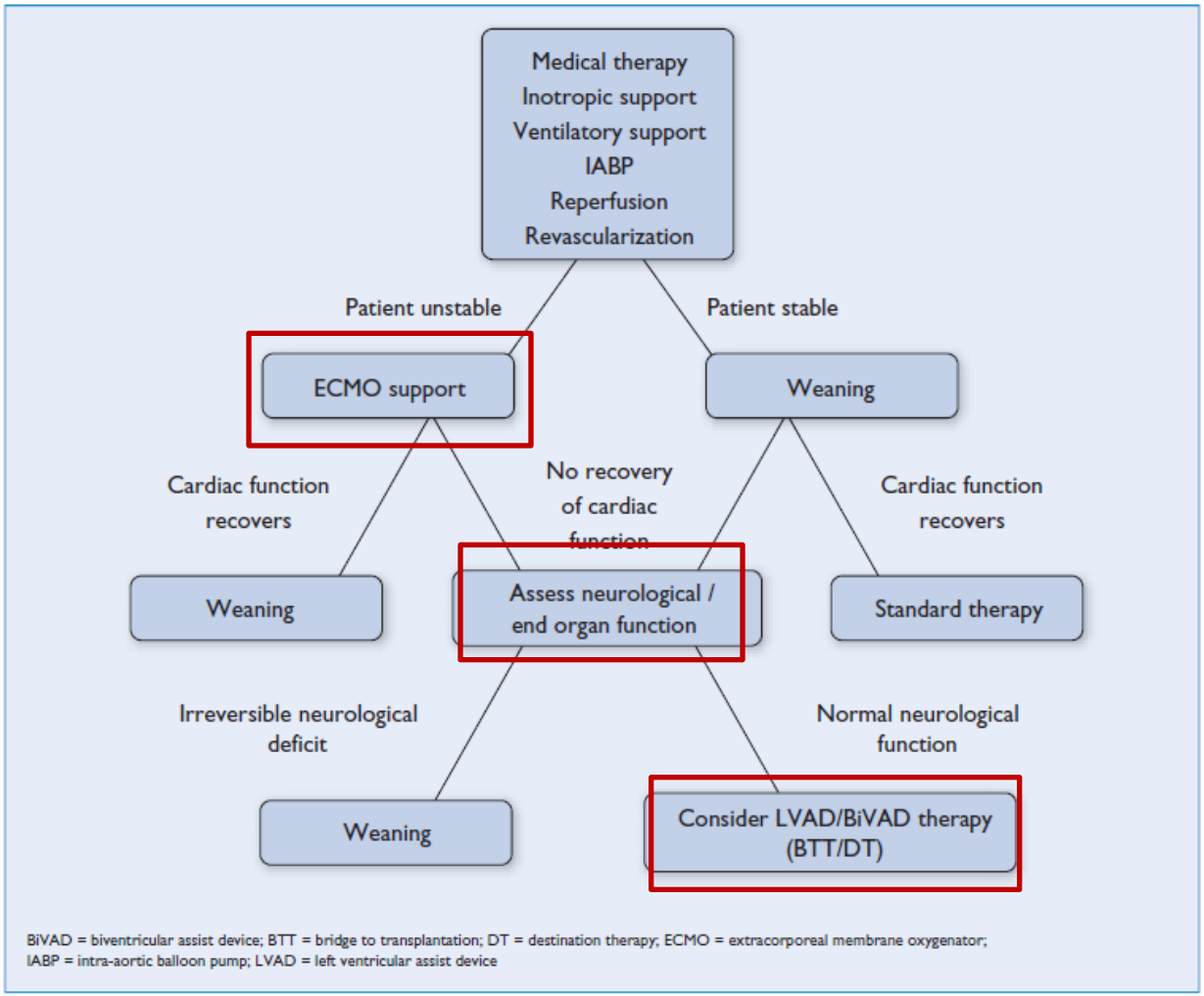
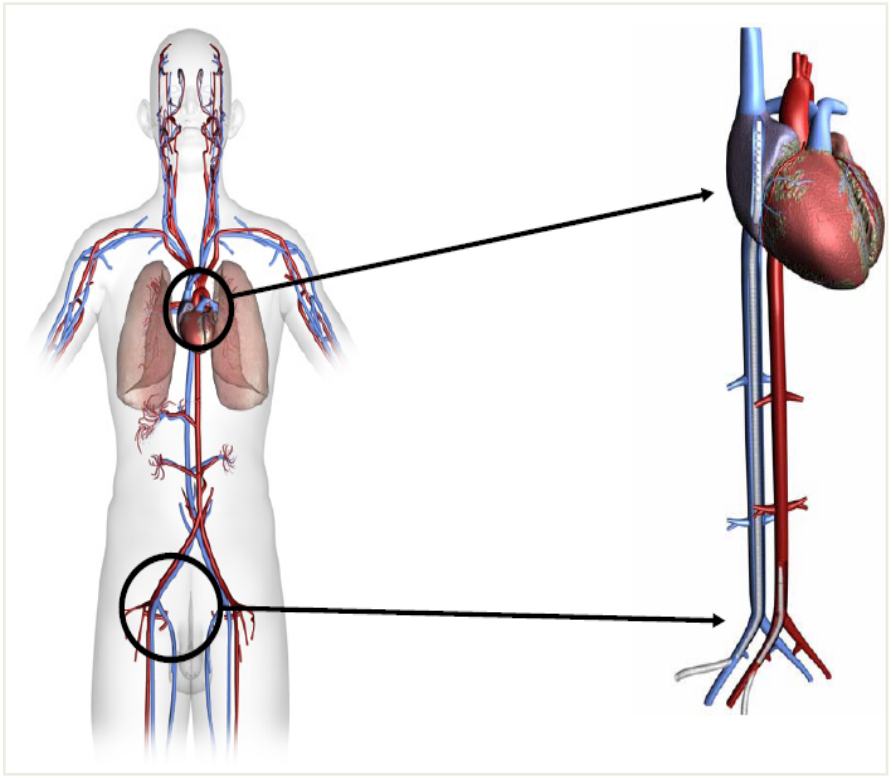
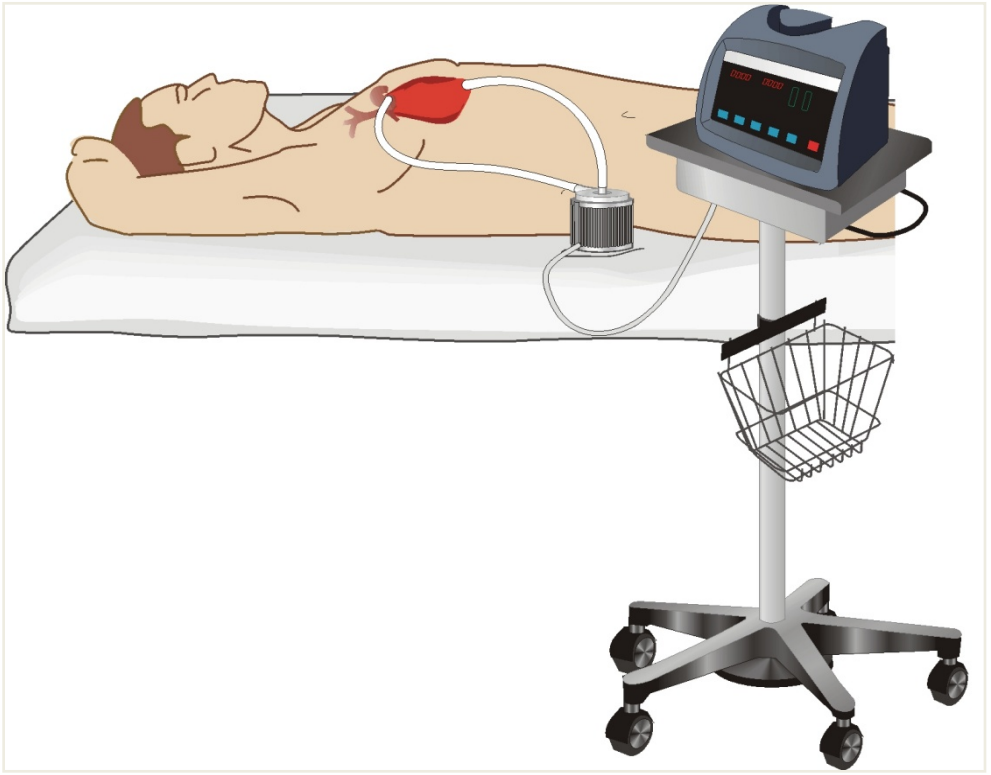



**Figure 2** Treatment algorithms for acute heart failure and cardiogenic shock. After failure of initial therapy including reperfusion and revascularization to stabilize haemodynamics, temporary mechanical support using an extracorporeal membrane oxygenator should be considered. If weaning from the extracorporeal membrane oxygenator fails or heart failure persists, left ventricular assist device/biventricular assist device therapy may be considered if neurological function is not permanently impaired.

# VA-ECMO x short-term VAD





# ECMO x short-term VAD

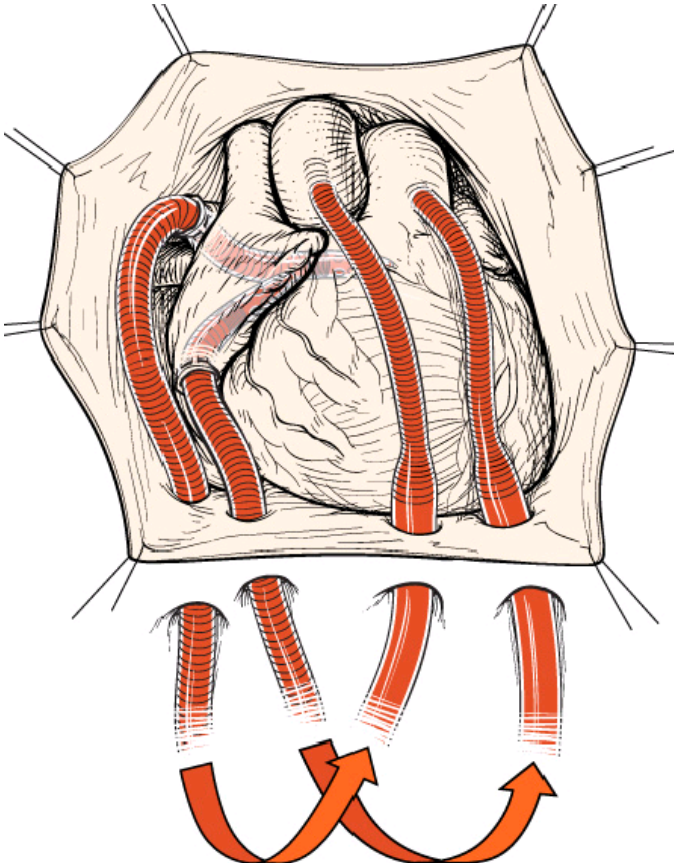
| | ECMO | VAD |
|---|---|---|
| **Blood elements destruction** | +++ | + |
| **Requirement for anticoagulation** | +++ | + |
| **LV unloading** | - | + |
| Physiological pulmonary circulation | - | + |
| Full flow support | +/+++ | +++ |
| Need for chest reexploration | -/+ | + |
| Peripheral vascular injury | +/- | - |
| Patients mobility | - | + |
| Cost effectivness | +++ | + |

# Surgical tool for refractory shock in IKEM



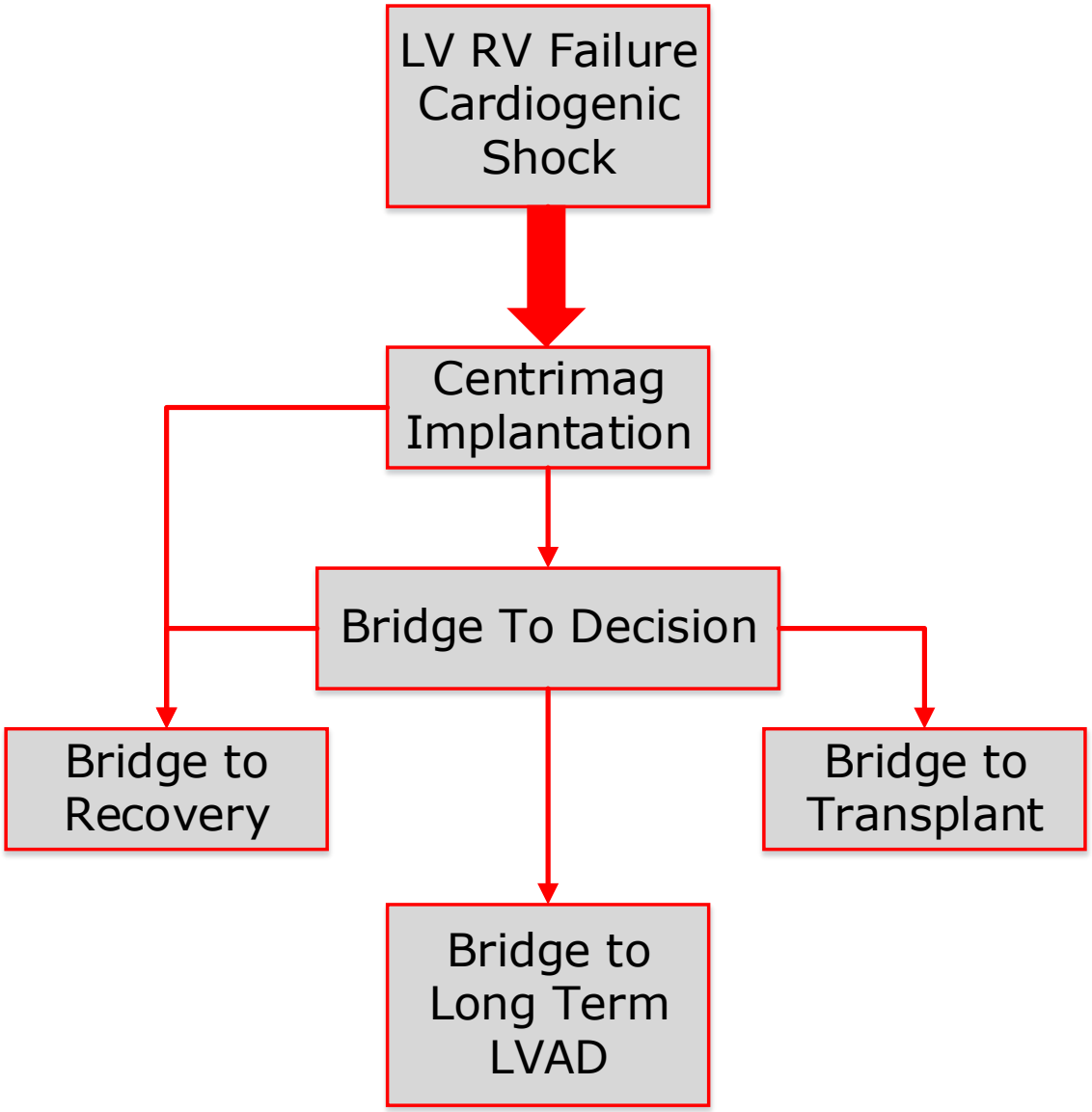

**CentriMag VAD**

# LVAD/RVAD/BiVAD



- pfenomenal versatility in various clinical scenarios
- max. flow - 9.9 lpm, **full flow device**
- **But still major surgery needed**

# Indications For Short-Term MCS



# Indications for CentriMag

- Cardiac Index <2.0L/min.$m^2$
- Systolic Blood Pressure <90 mm Hg
- Pulmonary Capillary Wedge Pressure >20 mm Hg
- Rising Creatinine and Liver Transaminases
- Patient oliguric, acidotic with cool extremities and worsening mental status

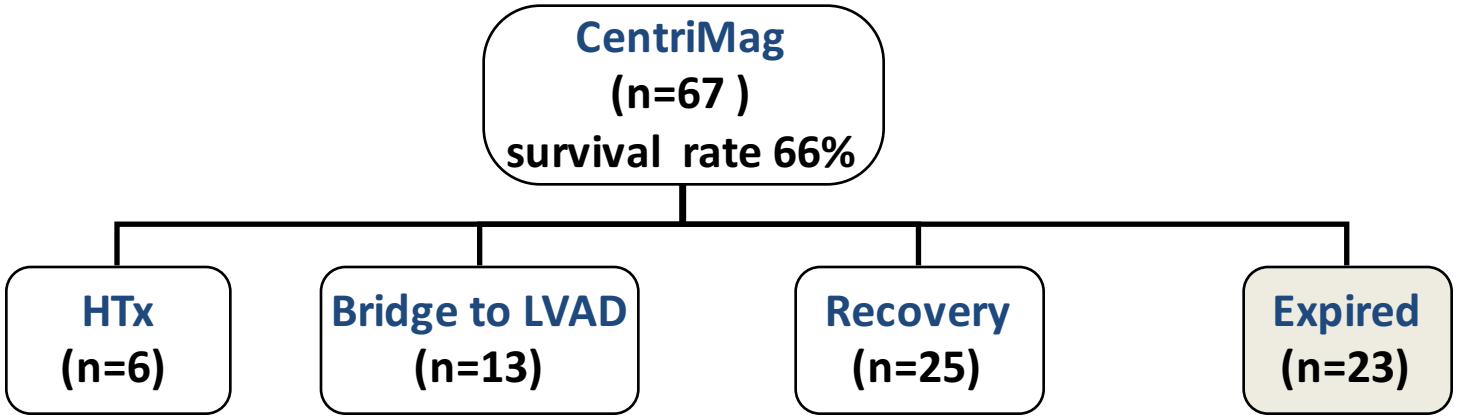
# CentriMag Overall Experience

## Institute for Clinical and Experimental Medicine, Prague

- 63 consecutive implants (11/2006 – 4/2012)

**Acceptable survival with low Adverse events**

- No thromboemolic events or pump failure



# Conclusion

## ECMO

- primarily failing ventricle not detectable
- compromised oxygenation
- **ICU crash situation**

## Short-term VAD

- primarily failing ventricle detectable
- bleeding complications
- compromised vascular access
- **longer –term support expected**


WHAT
NOW?

# So what are we looking for???

- Percutaneous VADs (PVADs) allow **emergent and effective ventricular unloading** while providing **sufficient systemic perfusion pressure to reverse end-organ dysfunction**

- For pre shock and mild shock pts the partial flow devices up to 2,5 lpm could be sufficient

- **BUT for profound and severe refractory shock we need full flow device!**

- **Ideal PVADs** should have the following characteristics:
  - Rapid and easy implantation via a percutaneous approach
  - Reliable full flow support to adequately unload the impaired ventricle(s) and to maintain systemic perfusion pressure to reverse end-organ dysfunction
  - Low complication rates

IK+E M

# Currently Available Percutaneous Ventricular Assist Devices

| | IABP | Tandemheart | Impella recover | ECMO |
|---|---|---|---|---|
| Pump mechanism | Pneumatic | Centrifugal | Axial | Centrifugal |
| Insertion | Retrograde 7-9F balloon catheter into descending aorta via femoral artery | 21F inflow cannula into left atrium via femoral vein and transeptal puncture and 15/17F outflow cannula into femoral artery | 12F catheter (13F sheath) retrograde across aortic valve via femoral artery | 18-31F inflow cannula into the right atrium via femoral vein and 15-22F outflow cannula into descending aorta via femoral artery |
| Difficult insertion | + | ++++ | +++ | ++ |
| Degree of circulatory support (with ideal SVR) | + (↑ CO by 0.5L/min) | +++ (↑ CO by 3.5-4.5 L/min) | ++ (↑ CO by 2.5 L/min) | ++++ (↑ CO to ≥ 4.5L/min) |
| Implantation time, min | 10 | 25-65 | 11-25 | 10-15 |
| Hemolysis | 0 | ++ | ++++ | +++ |
| Bleeding risk | + | +++ | ++ | ++++ |
| Evidence of Efficacy | ↑ CO and coronary and peripheral perfusion; ↓ afterload | ↑ CO, MAP, MVo2 and urine output; ↓ lactic acid, creatinine, PCWP | ↑ CO and MAP; ↓ lactic acid and PCWP | ↑ CO, MAP and oxygenation |

SVR=systemic vascular resistance; CO=Cardiac output; MAP=mean arterial pressure; MVo2=mixed venous oxygen saturation; PCWP=Pulmonary capillary wedge pressure

**Biswajit Kar *et al*. Circulation. 2012;125:1809-1817**

# TandemHeart

**From: The Percutaneous Ventricular Assist Device in Severe Refractory Cardiogenic Shock**

J Am Coll Cardiol. 2011;57(6):688-696. doi:10.1016/j.jacc.2010.08.613

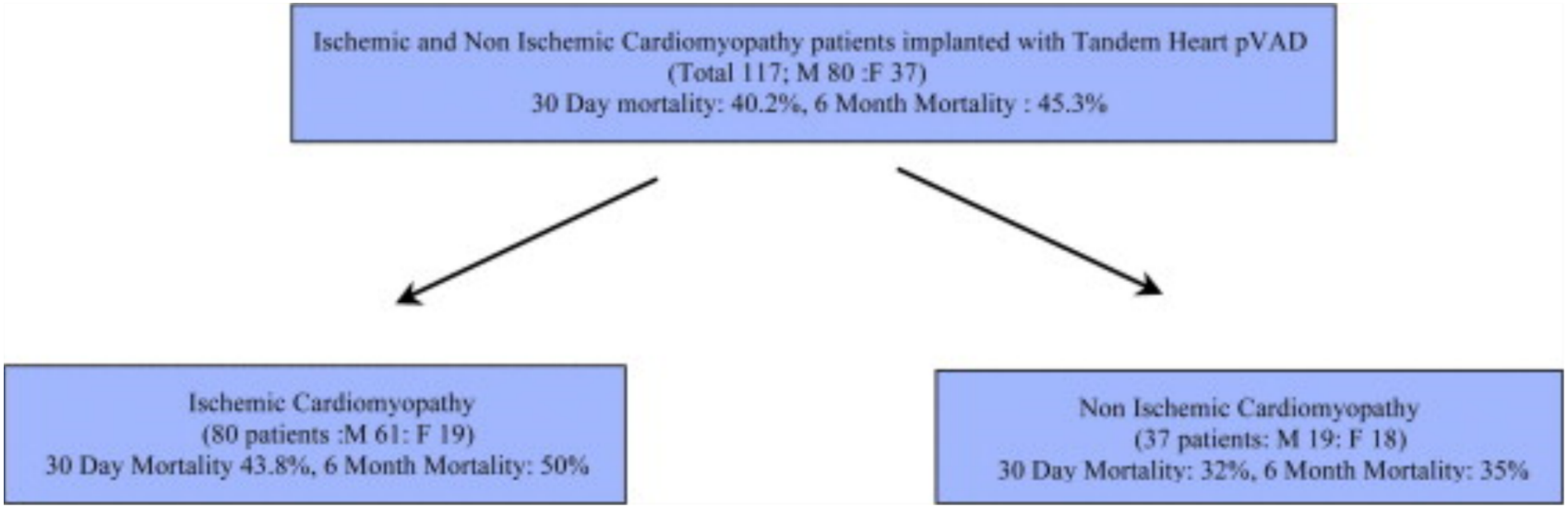



**Figure Legend:**

**Overall Study Design and Results**

**A total of 117 patients (80 with ischemic and 37 with nonischemic cardiomyopathy) with severe refractory cardiogenic shock were implanted with TandemHeart percutaneous ventricular assist device (pVAD).**

# TandemHeart

**From: The Percutaneous Ventricular Assist Device in Severe Refractory Cardiogenic Shock**

J Am Coll Cardiol. 2011;57(6):688-696. doi:10.1016/j.jacc.2010.08.613

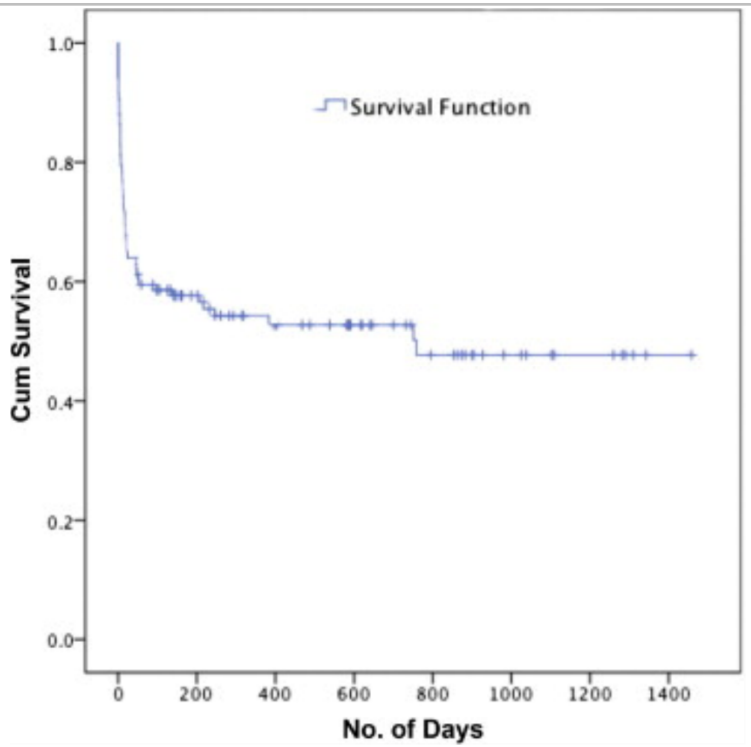



**Figure Legend:**

**Survival Analysis of All Patients**

**Kaplan-Meier survival curve of 117 patients showing survival at 30 days, 6 months, and last follow-up.**

# HeartMate PHP Cardiogenic Shock Study: Key Criteria

## Inclusion Criteria

- Patient has a cardiac index of < 2.2 L/min/$m^2$ and is being treated with at least one moderate dose inotrope or at least one moderate dose of vasopressor (e.g., milrinone ≥0.3 mcg/kg/min, dopamine > 5 mcg/kg/min, dobutamine > 5 mcg/kg/min) **AND:**
  - PWCP ≥ 20 mmHg, **AND**
  - Systolic blood pressure < 100 mmHg, **AND**
  - Decreased organ perfusion as evidenced by urine output of ≤50 mL/hr (average over 4 hours) **OR** increased creatinine of 0.3 mg/dl from baseline obtained within 2 weeks, **OR** cool extremities
- Written, signed, and dated informed consent

## Key Exclusion Criteria

- Right ventricular failure requiring mechanical circulatory support
- ST elevation myocardial infarction (STEMI) within 30d of procedure
- Cardiac arrest within 7 days of procedure requiring CPR
- Current treatment with mechanical circulatory device such as IABP, ECMO, centrifugal pump, etc.

IK+E M

HeartMate PHP™
Percutaneous Heart Pump™

# HeartMate PHP Cardiogenic Shock Study: Primary Performance and Safety Evaluation

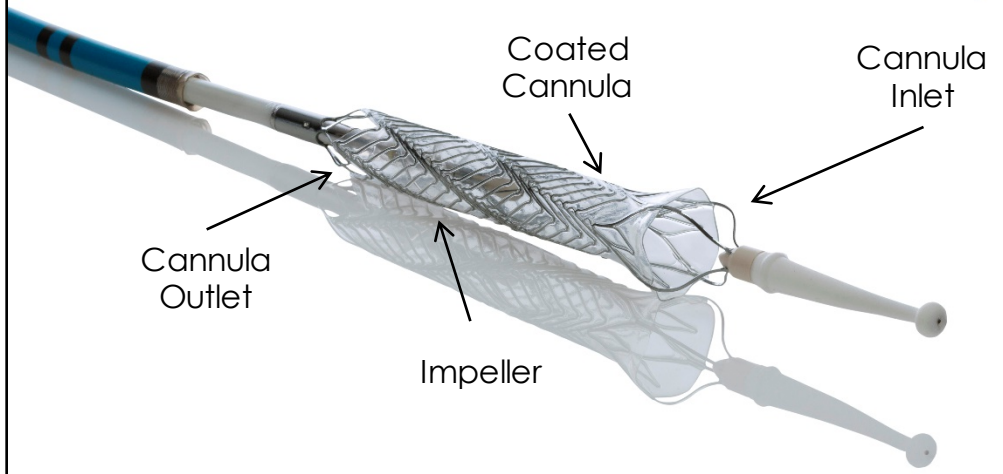
- **The primary performance evaluation will be clinical stabilization at 72 hours.** Clinical stabilization is defined as:
  - Improvement of CI to > 2.2 L/min/$m^2$ as determined by average Cardiac Index (CI) measurements (acquired every 4 hours for up to 72 hours) compared to baseline. CI will be measured using either the Fick or thermodilution methods.
- **Safety Evaluations will include:**
  - All Death
  - Debilitating stroke (an acute episode of a focal or global neurological deficit with at least one of the following: change in the level of consciousness, hemiplegia, hemiparesis, numbness, or sensory loss affecting one side of the body, dysphasia or aphasia, hemanopia, amaurosis fugax, or other neurological signs or symptoms consistent with stroke lasting ≥24 h and confirmed by neuroimaging [CT scan or brain MRI])
  - Device related serious adverse event requiring device removal
  - Bailout with an advanced mechanical circulatory support device other than HeartMate PHP (e.g., ECMO)
  - Addition of one or more inotrope(s) or vasopressor(s) above baseline OR a doubling of inotrope/vasopressor dosage over baseline within 72 hours

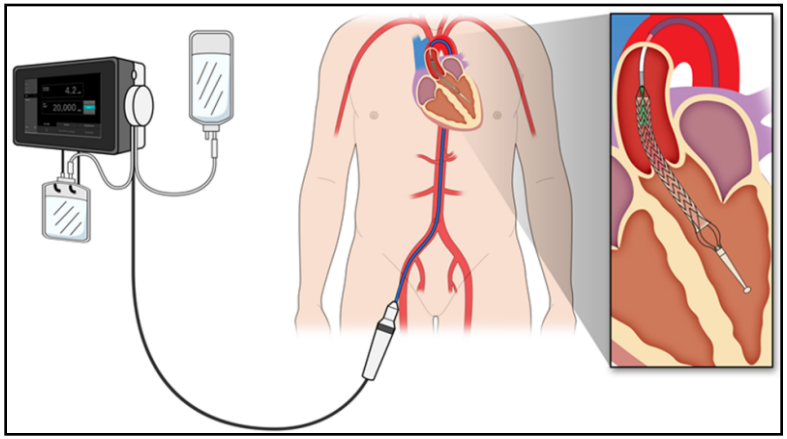
IK+E M

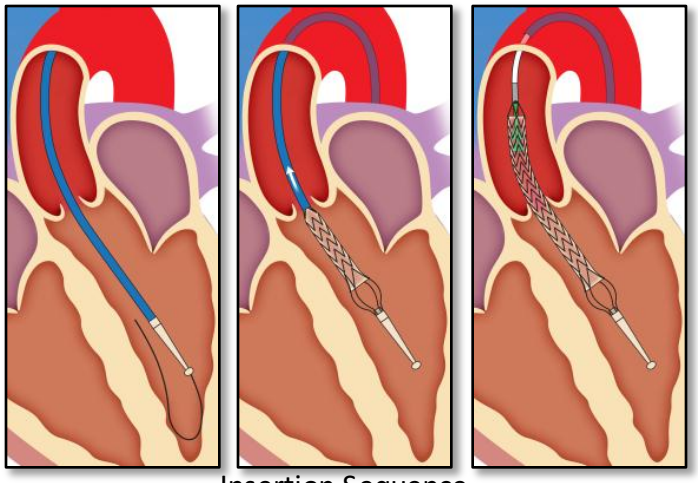
HeartMate PHP™ Percutaneous Heart Pump™

# HeartMate PHP™ (Percutaneous Heart Pump)

- Low-profile, rapid-insertion, catheter-based percutaneous heart pump
- Collapsible elastomeric impeller and nitinol cannula
- Designed to provide high forward flow to unload the LV and perfuse end organs
  - **Designed to deliver 4-5 lpm average flow**
- **Delivered through 14F sheath**
- **Distal cannula expands from 12F to 24F when unsheathed**



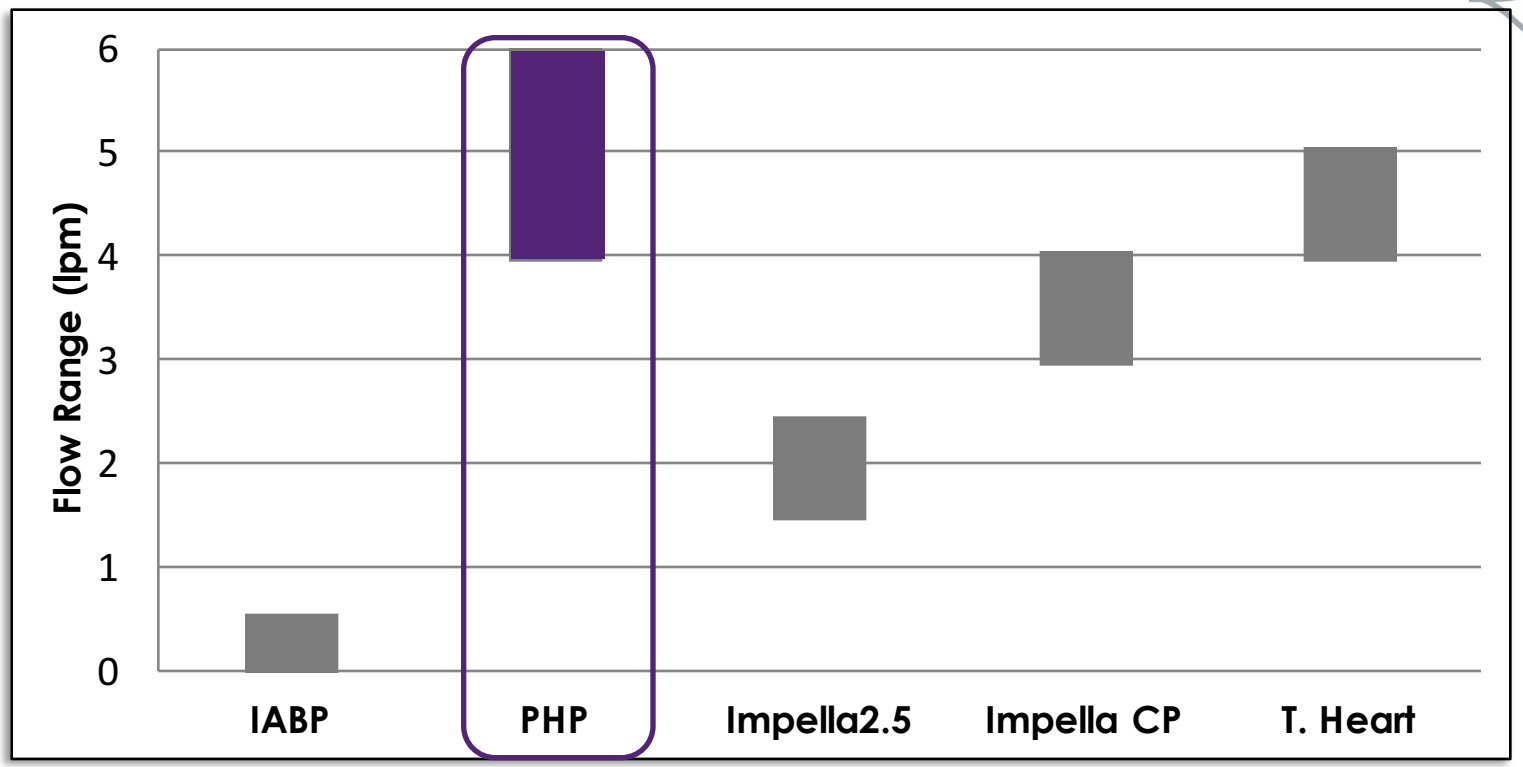


Insertion Sequence

In development. Not approved for commercial use

HeartMate PHP™
Percutaneous Heart Pump™

# HeartMate PHP Positioning – Profile & Flow

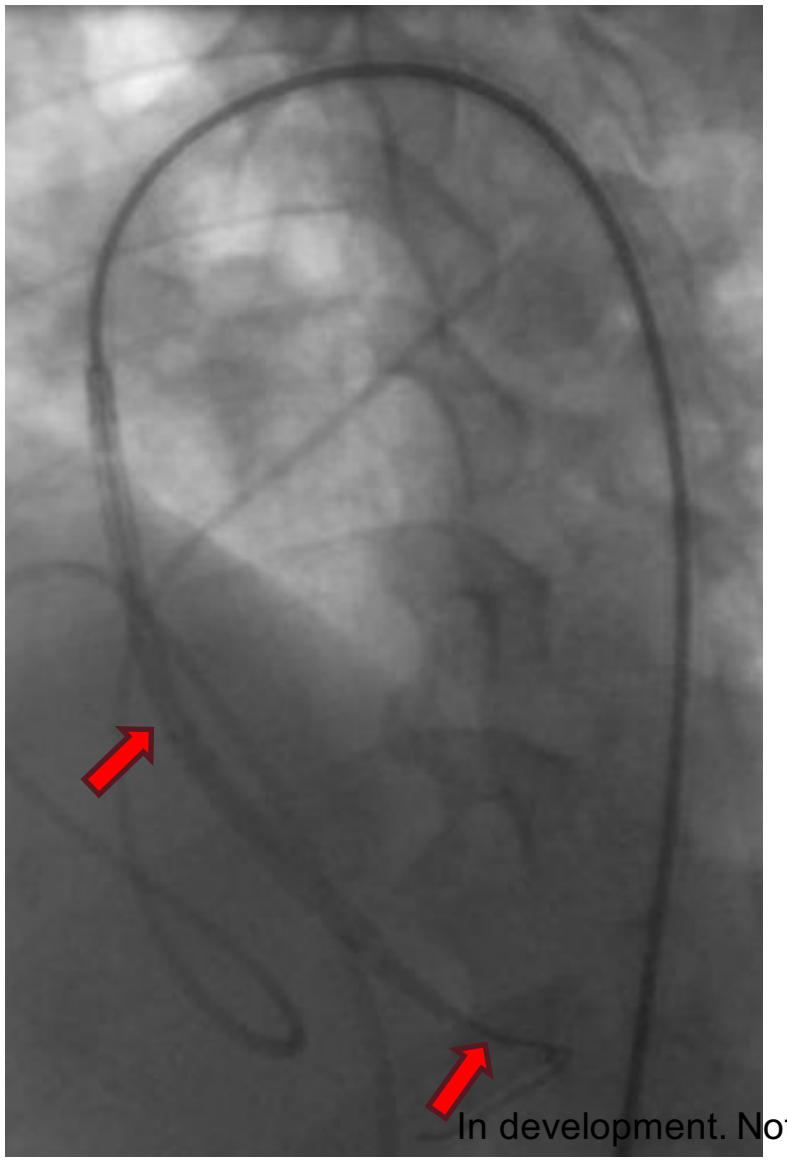


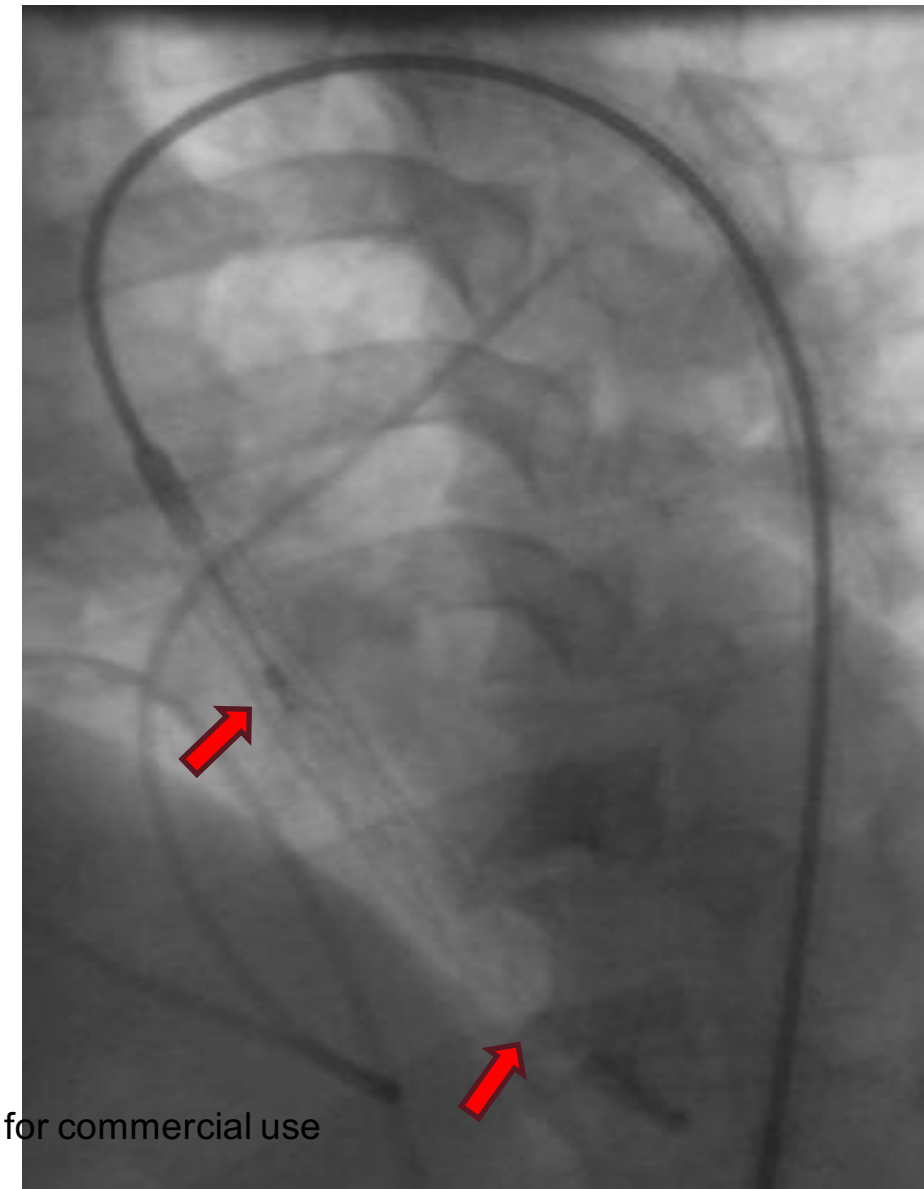

| French size | 7-8 | 13 | 13 | 14 | 15-17 |
|---|---|---|---|---|---|

**PHP expandable technology disrupts the traditional relationship between increased profile and flow**

HeartMate PHP™
Percutaneous Heart Pump™

# PHP Delivery & Deployment





# IKEM Patient 01-02 Baseline/History

**35 year old Caucasian male**

- Hx of supraventricular tachycardia, tobacco abuse, and bronchopneumonia
- Admitted with symptoms of heart failure and severe systolic dysfunction
- Treated with **dobutamine and levosimendan**
- Exacerbation of symptoms of heart failure; (**INTERMACS 2 sliding**)
- Baseline inotropic support at **6.5 mcg/kg/min dobutamine**

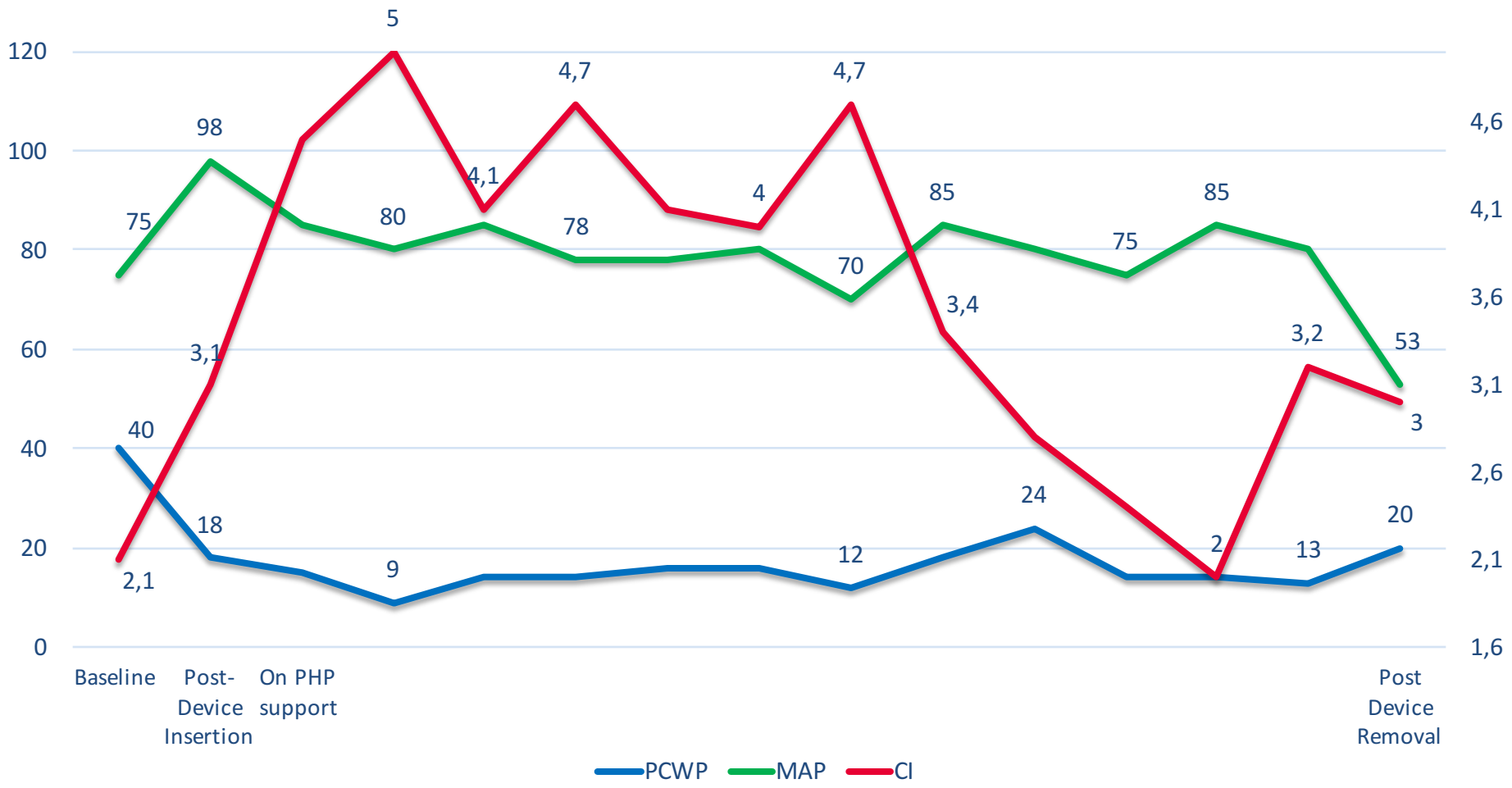
**Baseline ECHO**

- **LVEF 20 %**
- Severe dilatation and dysfunction of LV
- Mild to moderate RV dysfunction
- Aortic valve with no pathology
- MR 3/4, TR 3/4 , PR 1/4
- No thrombus present

**Baseline Hemodynamic Measurements**

- **CI 2.1**
- **PCWP 40**
- **MAP 75**

# IKEM Patient 01-02 Hemodynamics




**Total PHP run time:** 52 hours

# What we have now?

- **Ideal PVADs** should have the following characteristics:

  - rapidly and easy implant via a percutaneous approach

    **YES**

  - reliable full flow support to adequately unload the impaired ventricle(s) and to maintain systemic perfusion pressure to reverse end-organ dysfunction

    **YES**

  - complication rates

    ……?

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| Difficult insertion | + | ++++ | +++ | ++ | ++ |
| Degree of circulatory support (with ideal SVR) | + (↑ CO by 0.5L/min) | +++ (↑ CO by 3.5-4.5 L/min) | ++ (↑ CO by 2.5 L/min) | ++++ (↑ CO to ≥ 4.5L/min) | ++++ (↑ CO to ≥ 4.0 L/min) |
| Implantation time, min | 10 | 25-65 | 11-25 | 10-15 | 8-15 |
| Hemolysis | 0 | ++ | ++++ | +++ | ++ |
| Bleeding risk | + | +++ | ++ | ++++ | ++ |
| Evidence of Efficacy | ↑ CO and coronary and peripheral perfusion; ↓ afterload | ↑ CO, MAP, MVo2 and urine output; ↓ lactic acid, creatinine, PCWP | ↑ CO and MAP; ↓ lactic acid and PCWP | ↑ CO, MAP and oxygenation | ↑ CO and MAP ↓ PCWP |

SVR=systemic vascular resistance; CO=Cardiac output; MAP=mean arterial pressure; MVo2=mixed venous oxygen saturation; PCWP=Pulmonary capillary wedge pressure

**Biswajit Kar *et al*. Circulation. 2012;125:1809-1817**

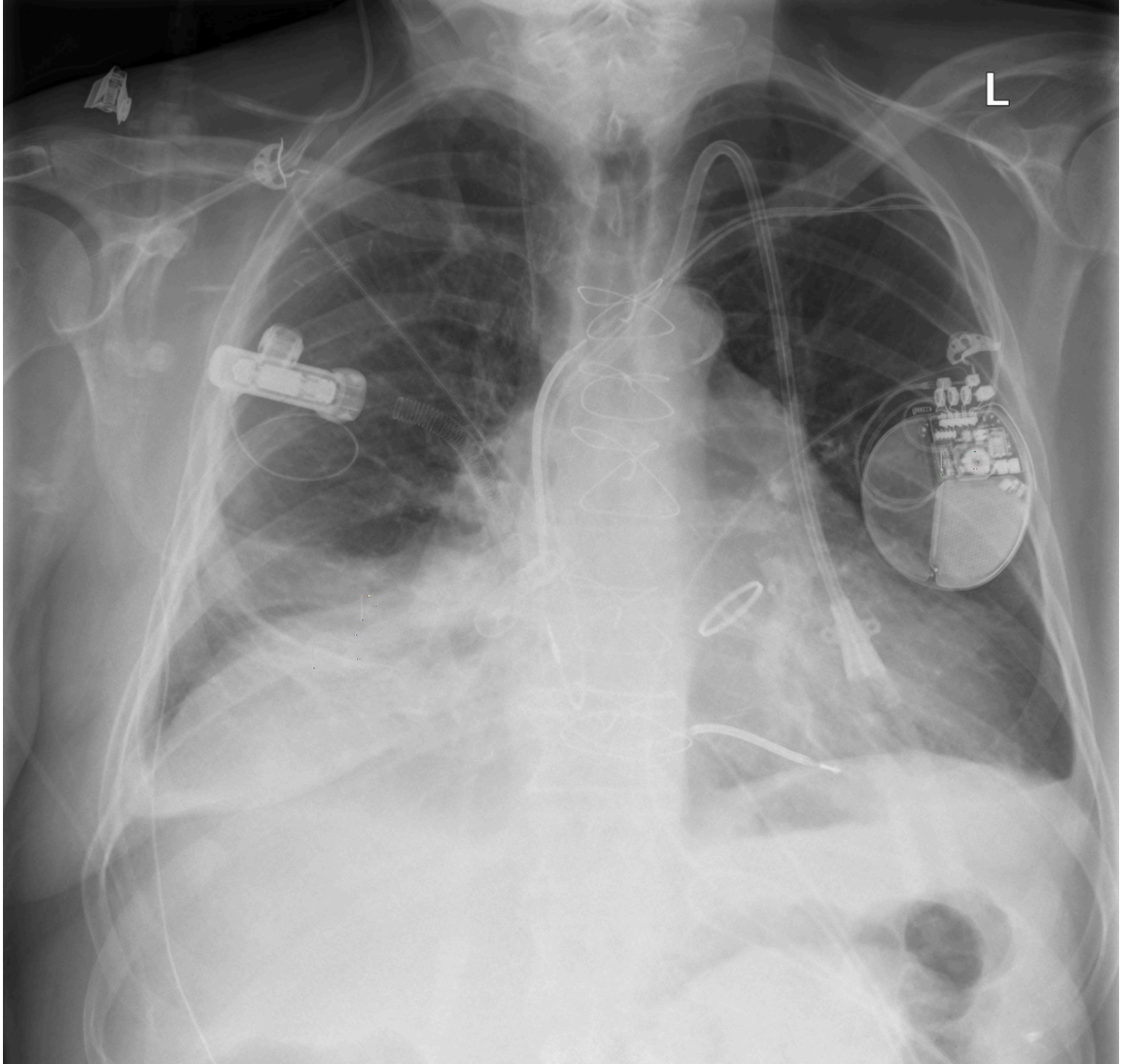
# Summary

- until randomized studies are performed, comparison among different therapeutic modalities/systems for acute cardiogenic shock will remain biased when based on a single center's experience

- early institution of mechanical circulatory assistance in cardiogenic shock remains a paradigm for satisfactory outcomes

# Final conclusion

- Evaluate the therapy in dedicated centers of excellence to obtain maximum understanding of the therapy and patient management
- Consider building site-specific Heart Team for best patient management
- Door-to-unload concept in SRCS pts to reduce infarct size!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