Ventricular Assist Devices

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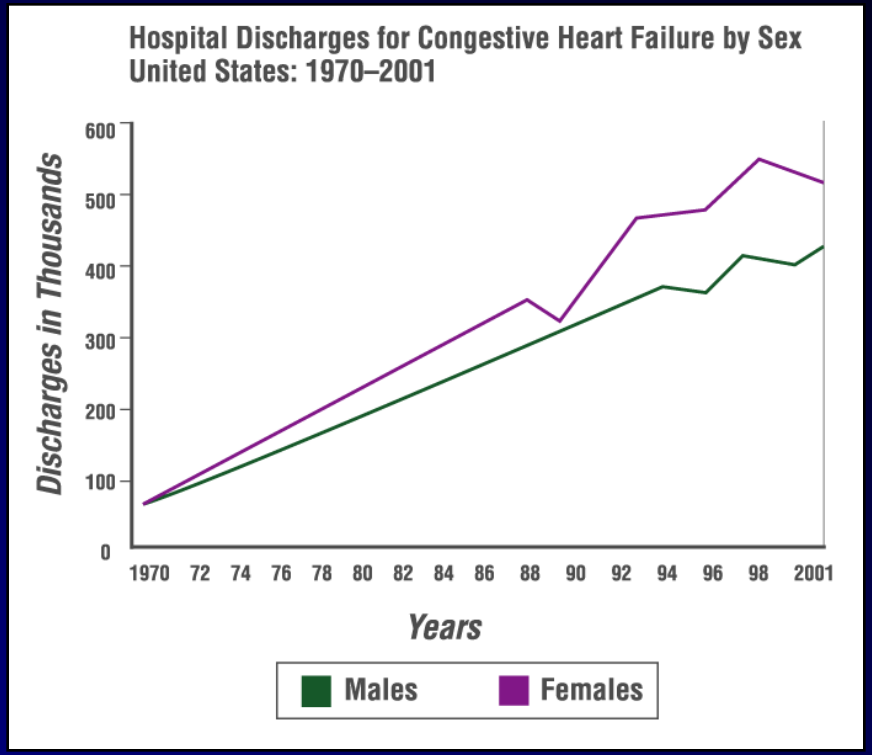
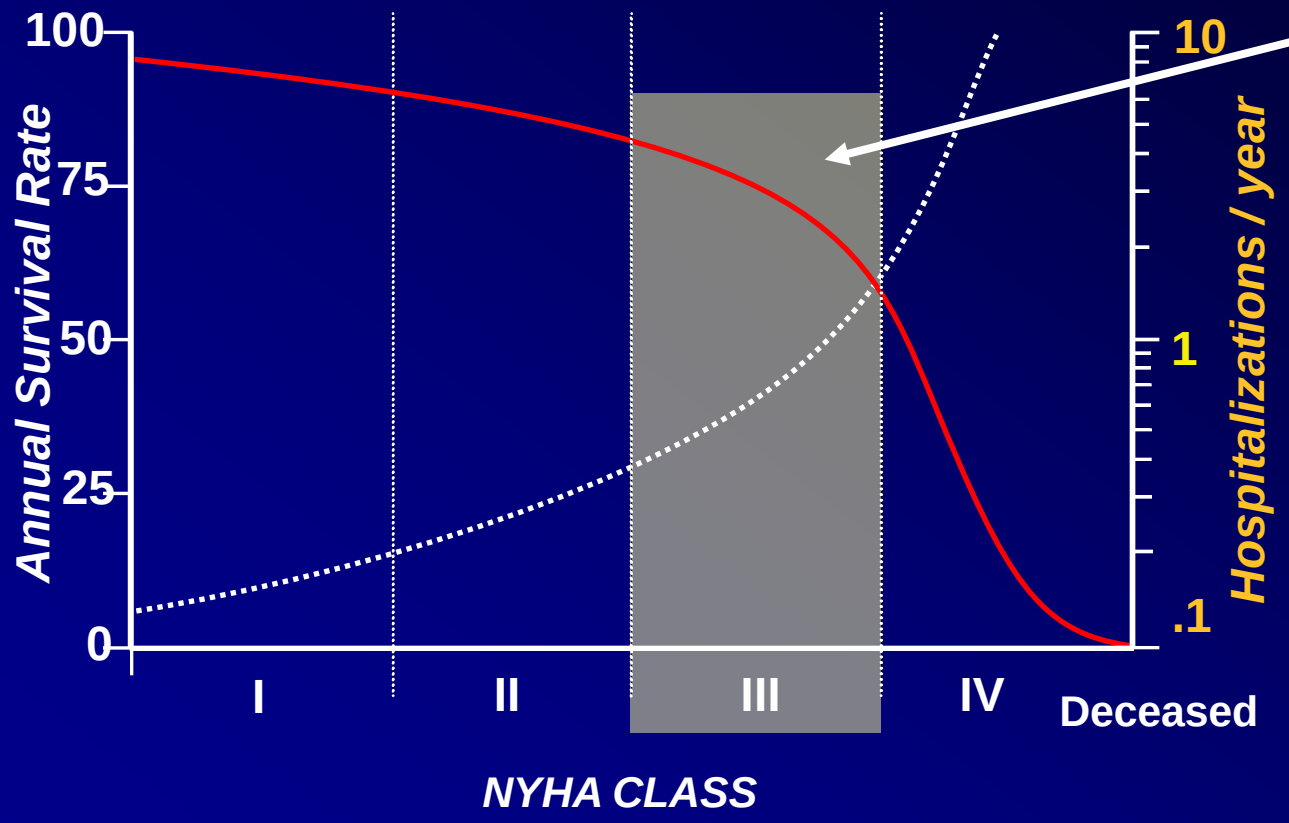
Prevalence of Heart Failure

- In 2004, 5 million Americans affected (2.2%)
- 550,000 new cases annually
- HF afflicts 10 out of every 1,000 over age 65 in the U.S.*
- By year 2030, estimated 10 million Americans will be affected



American Heart Association. Heart Disease and Stroke Statistics – 2004 Update.

Natural History of Heart Failure



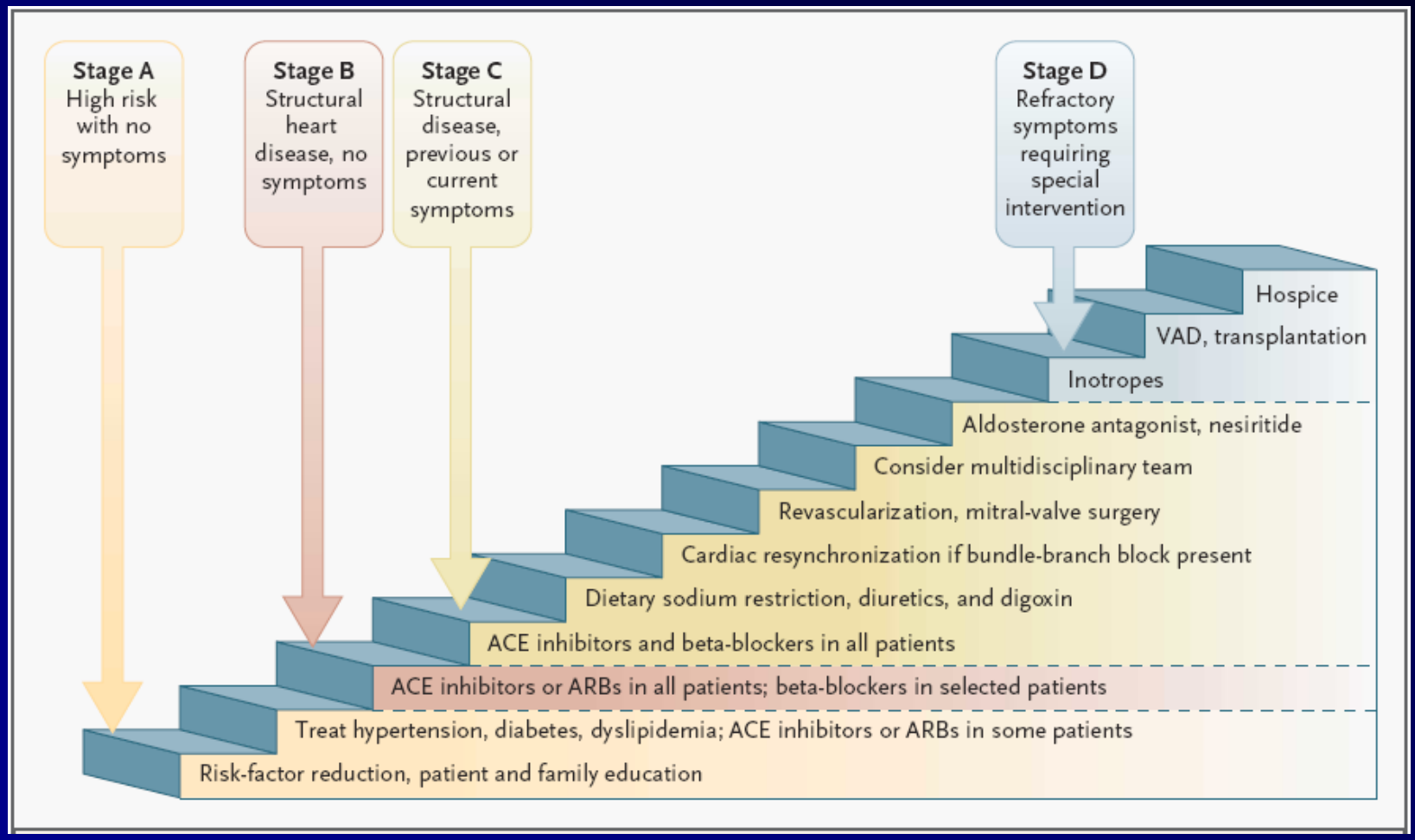
Class III

- 25% of HF Patients
- Frequent hospitalizations
- Worsening symptoms despite drug therapy
- Significant opportunity for new therapies

Survival Rate
Hospitalizations

Adapted from Bristow, MR Management of Heart Failure, Heart Disease: A Textbook of Cardiovascular Medicine, 6th edition, ed. Braunwald et al.

Heart Failure – Therapeutic Options



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

Ventricular Assist Device

- AKA – artificial heart
- Mechanical support for a failing heart
- Applications:
  - Acute Heart Failure
  - Chronic Heart Failure
- Duration of Support
  - Hours to years
- In-patient or out-patient

Hemodynamic Restoration Therapy (HdRT)

- **HdRT features VAD implantation as a means to partially or fully support the natural ventricle in circulating oxygenated blood throughout the body**
- **With timely intervention, most NYHA Class IV patients treated with HdRT improve to Class I or II***
- **HdRT can be utilized as a method of bridging a patient to recovery, transplant, or as destination therapy**

** Delgado RM III, Smart F, Gregoric I, et al: Quality of Life in Patients Implanted with the HeartMate II Left Ventricular Assist Device for Severe Heart Failure. Heart Failure Society of America, Boca Raton, Sep 18-21, 2005.c*

Transplant Alternative -- Continuous Inotropes

Table 1. "Severe" Heart Failure Populations With ACEI Rx

	CONSENSUS (ACEI)	VMAC (BNP)	OPTIME (Milrinone)	PROMISE (Oral Milrinone)	COPERNICUS (Carvedilol)	Wet/ Warm*	Wet/ Cold*	REMATCH (No Inotropes)	REMATCH (On IV Inotropes)	Oregon COSI
SBP	119	121	120	115	125	114	103	105	97	97
LVEF		26	24	21	20	26	21	17	17	20
Na	138		138	139	137	137	136	137	134	132
6-month mortality	24%	23%	10% 2 mos	32%inIV 18% in III	10%	20%	34%	39%	61%	75%

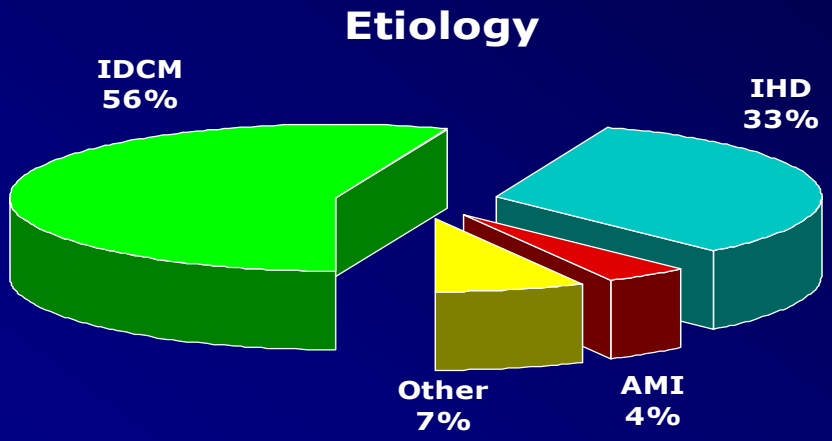
ACEI, angiotensin-converting enzyme inhibitor; Rx, treatment; VMAC, vasodilation in management of acute congestive heart failure (see reference 1); BNP, B-type natriuretic peptide; IV, intravenous; SBP, systolic blood pressure; LVEF, left ventricular ejection fraction.
See reference 3.

Hemodynamic Restoration Therapy (HdRT)

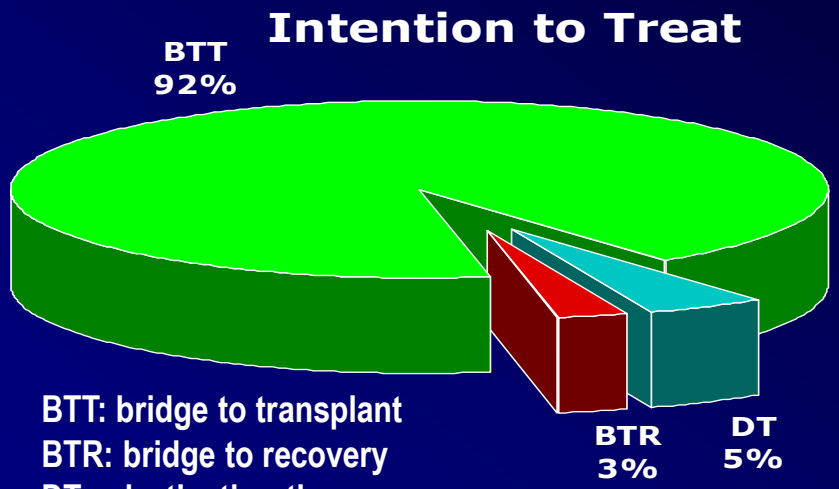
Study (therapy)	1 year Survival (%) (Tx vs. Control)	1 yr Relative Benefit of Treatment	Absolute Benefit = # patients/100
SOLVD (ACE inhibitor)	**89 vs. 86**	**3% ↑ survival**	**3**
CONSENSUS (ACE inhibitor)	**55 vs. 38**	**45% ↑ survival**	**17**
COPERNICUS (beta-blocker)	**89 vs. 81.5**	**10% ↑ survival**	**7.5**
RALES (spironolactone)	**83 vs. 75**	**11% ↑ survival**	**8**
SCD-HeFT (ICD)	**93.8 vs. 94.1**	**No effect**	**0 in Yr 1, 3 by Yr 2, 7 by Yr 5**
COMPANION (CRT+ICD)	**71 vs. 60**	**18% ↑ survival**	**11**
REMATCH (LVAD)	**52 vs. 25**	**108% ↑ survival**	**27**

Source: Lynne Warner Stevenson, MD 6/04

Etiology and Intention to Treat



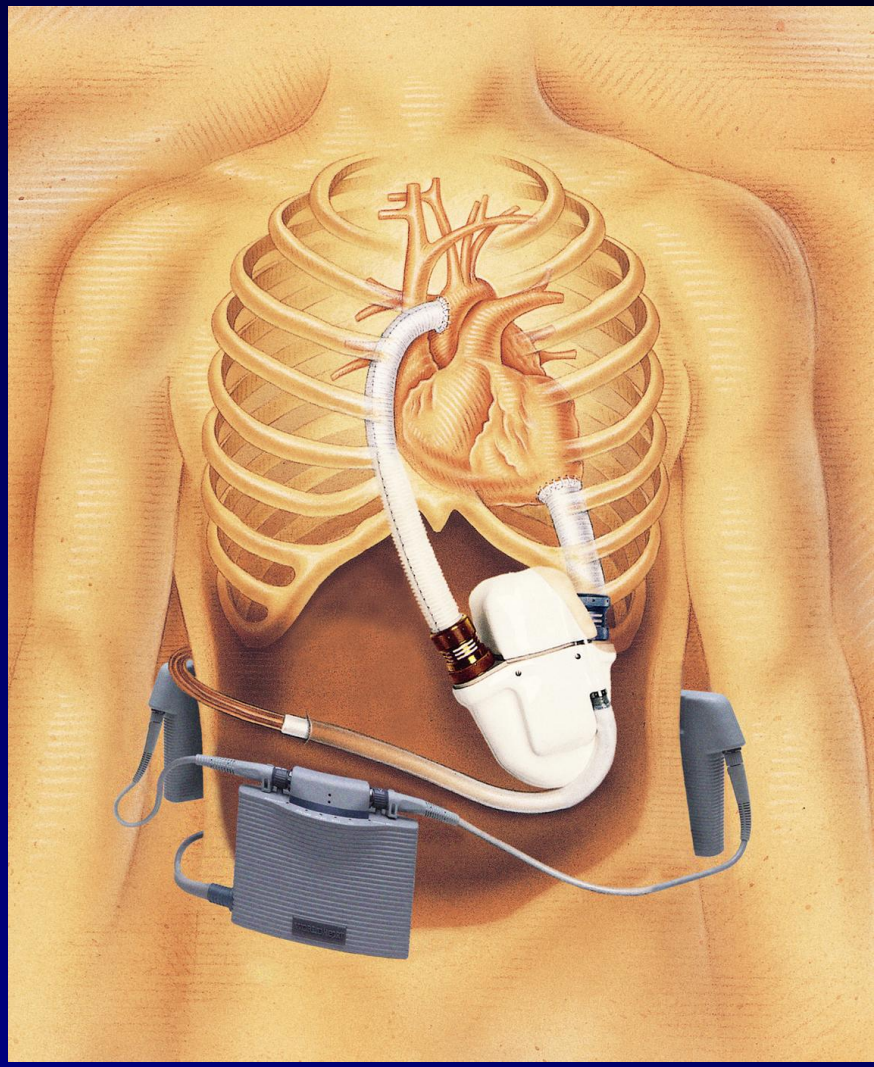
IDCM: idiopathic dilatated cardiomyopathy
IHD: ishemic heart diesase
AMI: acute myocardial infarction



BTT: bridge to transplant
BTR: bridge to recovery
DT: destination therapy

VAD Physiology

- Pump assumes the workload of the native ventricle
- Native ventricle acts as an atrium
- Outflow conduit to aorta or pulmonary artery
- Flexible percutaneous lead provides connection to controller & battery packs



Indications for VAD Support

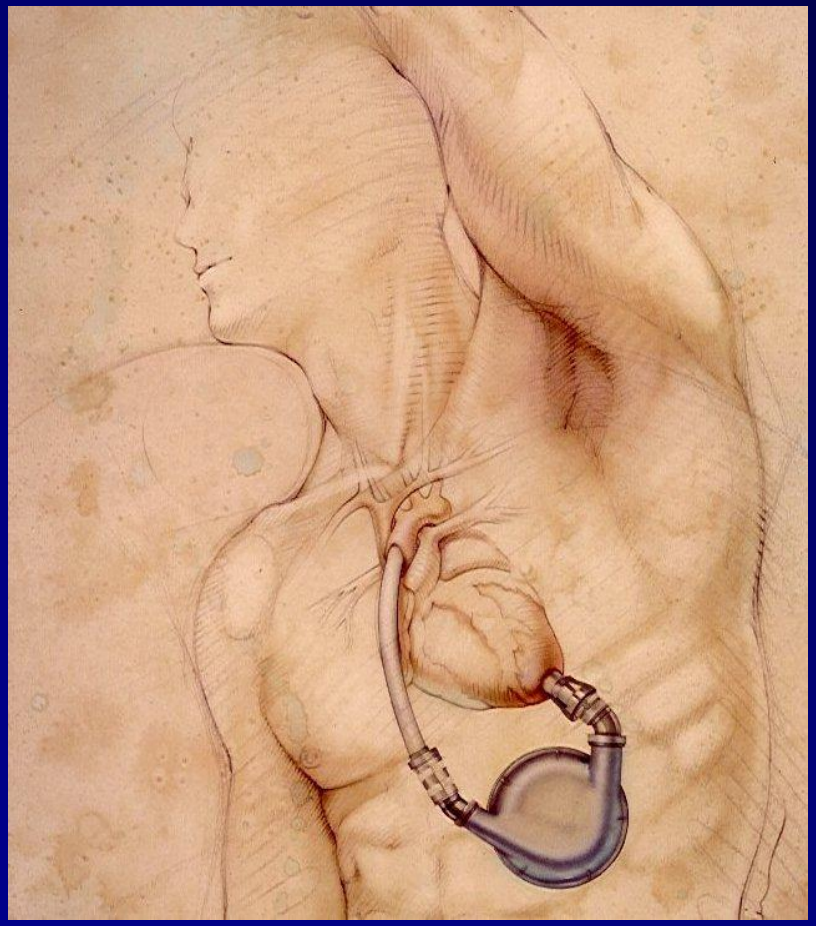
- **Instability despite OMM**
  - **Cardiac Index < 2.0 L/min/m2**
  - **PCWP > 20 mmHg**
  - **SVR > 2,100 dynes/s/cm3**
  - **UOP < 20 ml/hr**
  - **SBP < 80 mmHg**
  - **MAP< 65 mmHg**
- **Failure to wean inotropes**
- **End-organ damage**
  - **Nausea**
  - **Decreased mental status**
  - **Progressive renal or hepatic failure**
  - **Worsening arrhythmias**

J Thorac Cardiovasc Surg

Contraindications for VAD Support

- Absolute
  - Major irreversible neurologic deficits
  - Hepatic fibrosis or cirrhosis
  - Non-correctable intra-cardiac shunts
- Relative
  - Active infection
  - Nonreversible end-organ dysfunction

Ventricular Assist Devices



- Bridge to re-evaluation
- Bridge to recovery
- Bridge to transplant
- Destination therapy

Bridge to Re-evaluation

- New Concept
- Device placement prior to complete evaluation
- Goal: sustain life to determine ultimate therapy
- Not a true approved indication for mechanical support

Bridge to Recovery

- Mechanical support to facilitate myocardial healing
- Goal: sustain life and end-organ function during a period of reversible myocardial dysfunction

Bridge to Recovery

- **Recoverable**
  - **Acute Myocarditis**
  - **Sub acute (< 6 mos) cardiomyopathy**
  - **Post-cardiotomy**
  - **Post-transplant**
  - **Acute MI**
  - **Postpartum cardiomyopathy**
- **Non-recoverable**
  - **Giant cell myocarditis**
  - **Ischemic cardiomyopathy**
  - **Sarcoidosis**
  - **Amyloidosis**
  - **Toxic – ETOH**
  - **Restrictive cardiomyopathy**
  - **Acquired hypertrophic cardiomyopathy**

What Recovers?

- LV contractility
- Regression of fibrosis
- Improvement in myocyte architecture
- Decreased neurohormones

Bridge to Recovery

- German Heart Institute Berlin
  - 95 pts with IDC
    - 28 (29%) weaned and explanted
    - 18 with ideal hemodynamics
    - 10 urgent removal
    - 9 developed recurrent heart failure requiring additional support

Bridge to Myocardial Recovery

Left Ventricular Assist System as a Bridge to Myocardial Recovery
Frazier OH, Meyers TJ
***Annals of Thoracic Surgery* 1999 68:734-41**

5 patients with LVAS due to CHF

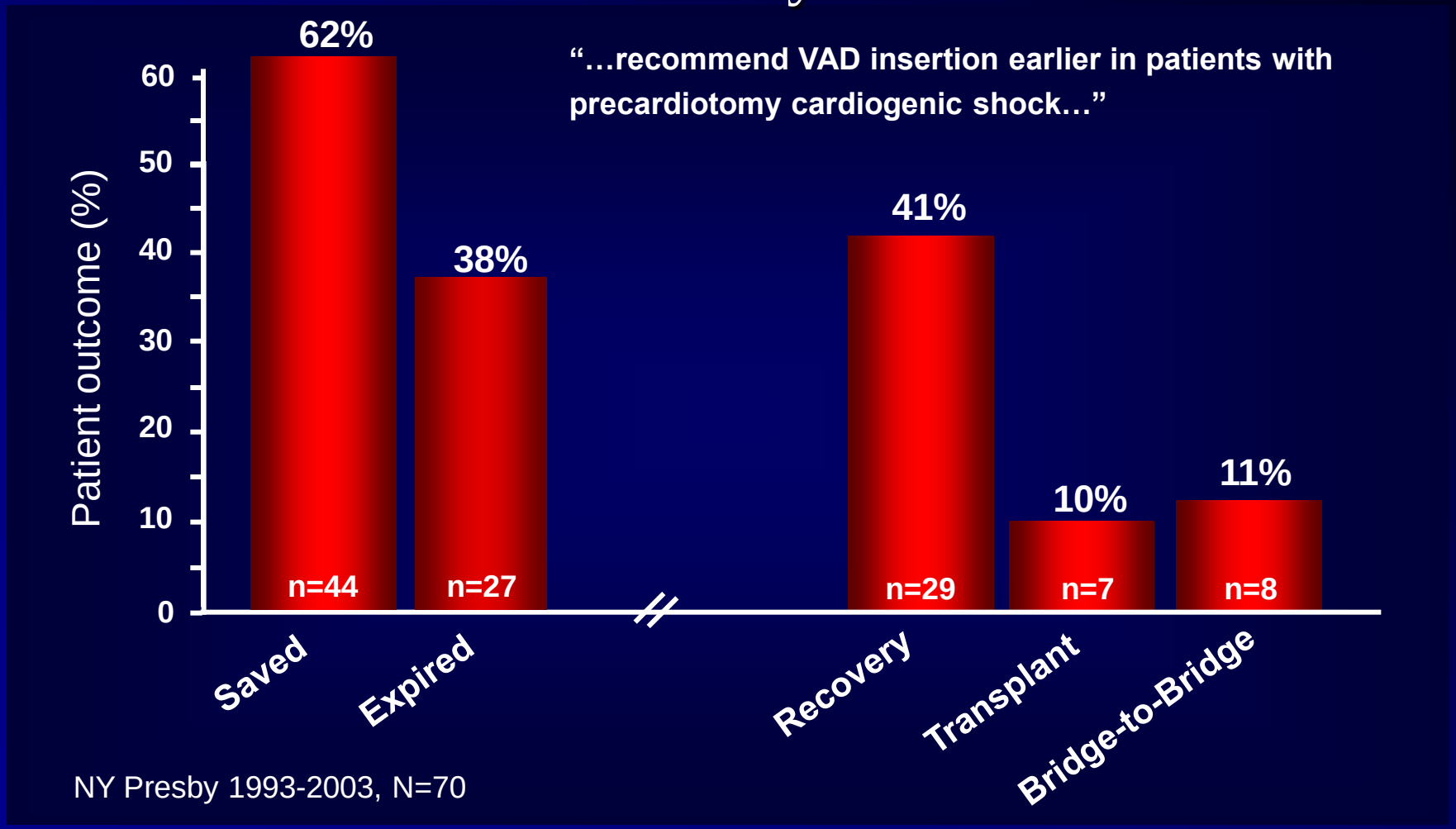
- Duration of support 229 days (range, 46-447)
- 3 removed electively
- 2 removed due to malfunction

Results: Significantly improved hemodynamics

- Increased CI (1.45 to 2.69 L/min/m^2)
- Increased LVEF (0.144 to 0.288)
- Improved functional status (NYHA class IV to I)
- Survival up to 35 months

Bridge to Recovery on Abiomed BVS

41 % Recovery on BVS



J Morgan et al. ASAIO J. 2004, Jul/Aug 50(4):360-3

Bridge to Transplant

- Most common indication for VAD therapy
- Goal: sustain life and end-organ function until a donor heart is available

Bridge to Transplant

- **Frazier OH et al. 1995 *Ann Surg.***
  - **75 LVAD pts (Heartmate IP) compared to 33 matched controls**
  - **PCWP>20, SBP<80, CI<2.0**
  - **Survival to transplant**
    - **LVAD 53/75 (71%):Controls 12/33 (36%) p=0.001**
  - **Time to transplant – mean**
    - **LVAD 76d (1-344):Controls 12d (1-72)**
  - **Survival with renal dysfunction**
    - **LVAD 58%: Controls 16%**
  - **Mean "pump index"**
    - **LVAD 2.77:Controls 1.86**

Bridge to Transplant

Device	No. of Patients	Survival to Transplant (%)		
		1992	1995	2002
Thoratec PVAD	1,333	65	63	67
IP	1,301	64	66	63
VE	1,905	—	—	65
Novacor	1,600	63	65	—

IP = pneumatic, implantable; PVAD = paracorporeal ventricular assist device; VE = vented electric.

Ann Thor Surg 2003; 75: S66-71

What is Destination Therapy?

- **Destination Therapy refers to the implantation of a ventricular assist device (VAD) for long-term use, rather than as a bridge-to-transplantation or recovery**

REMATCH – Destination Therapy

The New England Journal of Medicine

Long-Term Use of a Left Ventricular Assist Device for End-Stage Heart Failure

N Engl J Med 2001; 345:1435-1443, Nov 15, 2001

Study Overview

- Cooperative agreement among Thoratec, NIH and Columbia University
- 21 Centers
- 129 pts – non-transplant candidates
- 68 pts randomized to HeartMate VE LVAD
- 61 pts randomized to Optimal Medical Management (OMM)

REMATCH Eligibility Criteria

- NYHA Class IV for at least 60 of 90 days despite maximal medical therapy
- LVEF ≤ 25%
- Peak VO2 ≤ 14 ml/kg/min or IV inotrope dependent
- IV inotrope dependent with failed weaning
- Ineligible for cardiac transplantation

Baseline Characteristics*

n=129

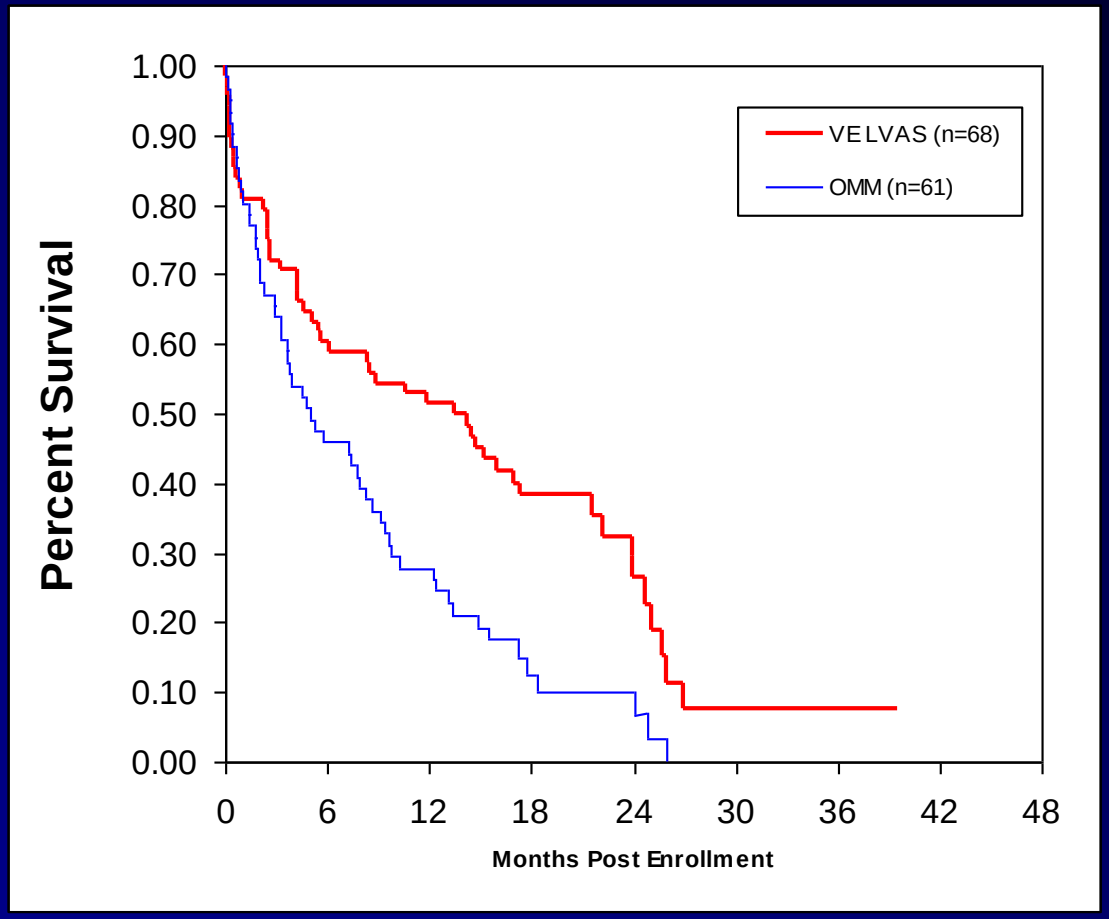
- **Median Age** — **69 years (range 34-84 yrs)**
- **Males** — **80%**
- **Ischemic Etiology** — **74%**
- **NYHA Class IV** — **98%**
- **LVEF** — **18% (range 4-25%)**
- **Cardiac Index** — **1.9 L/min/m^2**
- **VO_2max** — **9.5 ml/kg/min (3.9 to 13.9)**

* No statistical differences between LVAD and OMM groups

Control: Optimal Medical Management

- Guided and monitored by medical management committee
- Digoxin, diuretics, ACEI unless contraindicated
- Beta-blockers, spironolactone at investigator discretion
- Routinized intravenous inotropic drug weaning efforts

Kaplan-Meier Survival of LVAS versus OMM Patients



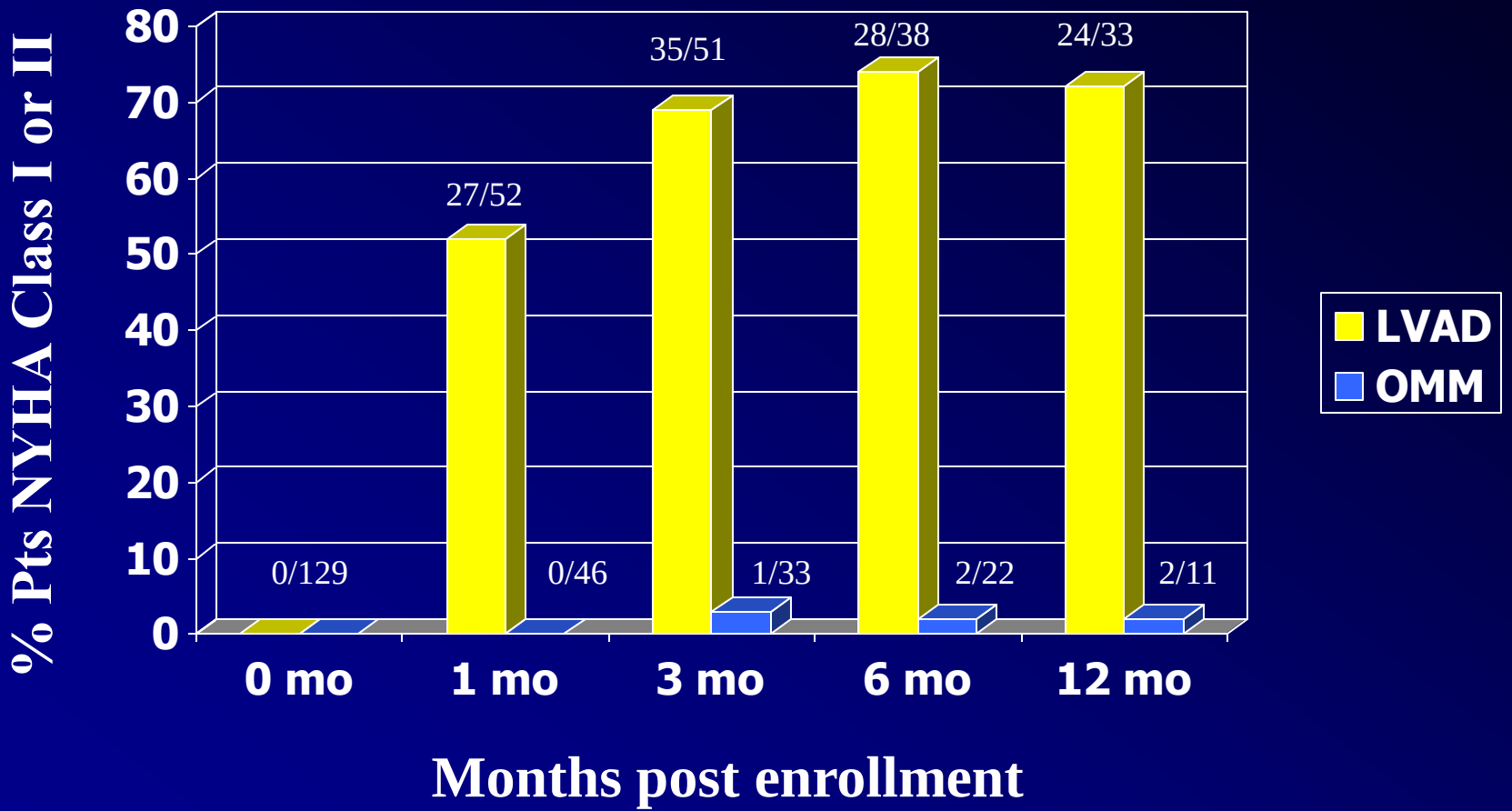
As of 4/02

Survival

- 1 yr survival = 51% LVAD vs. 28% OMM
  - One year survival for patients < 60 yrs (74%) approaches transplantation success rates
- 2 yr survival = 27% LVAD vs. 10% OMM
- Median survival was 408 days for LVAD patients compared to 150 days for medical therapy patients

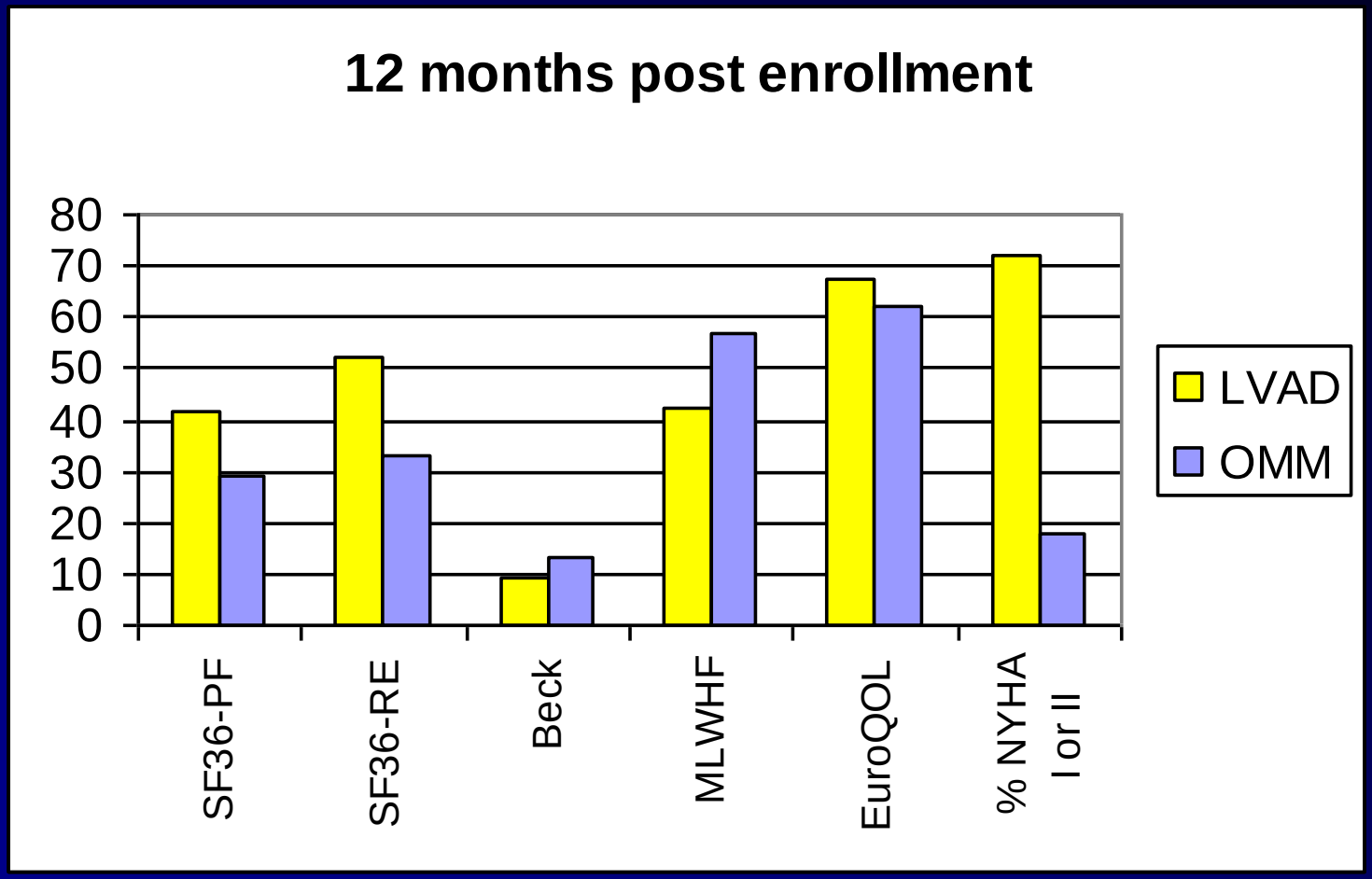
As of 4/02

SNAP-VE LVAS Improves NYHA Functional Class



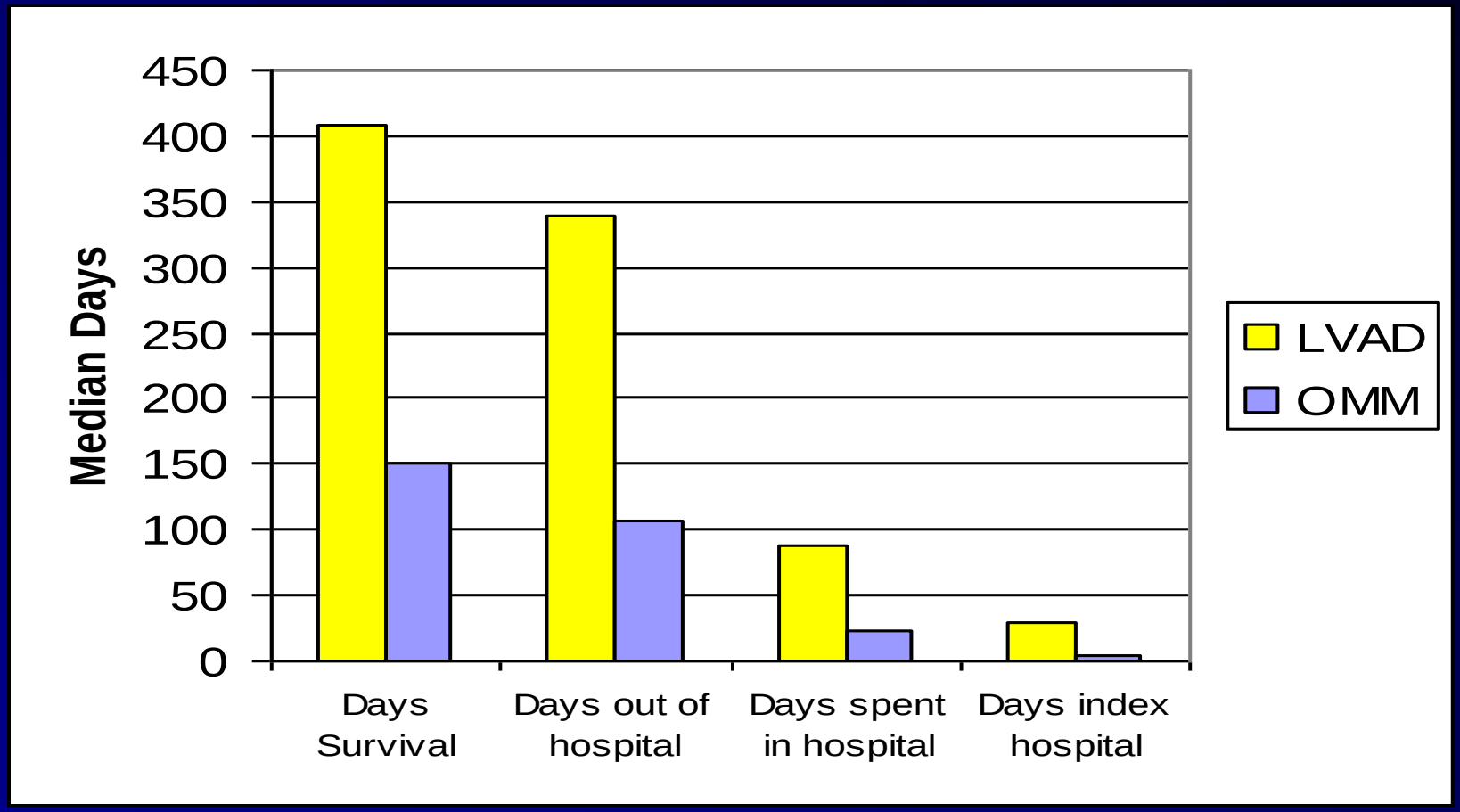
As of 4/02

Quality of Life



As of 4/02

Median Time Spent In and Out of Hospital

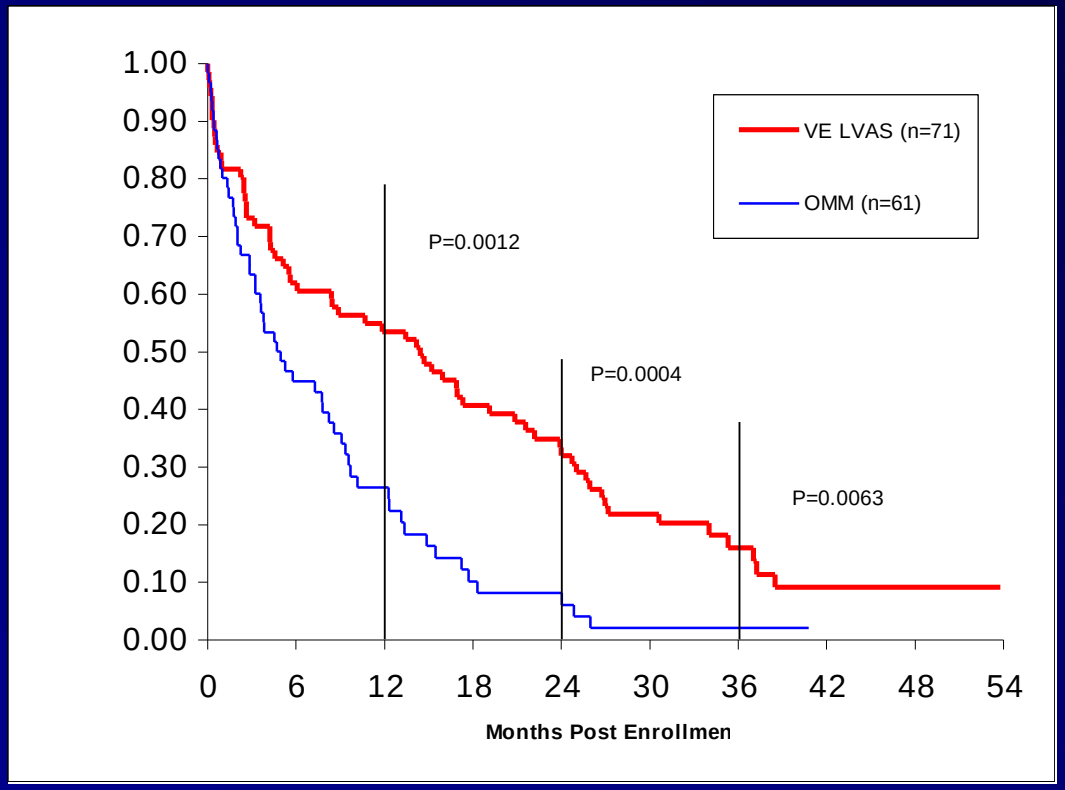


As of 4/02

Conclusions

Man-made circulatory support devices can provide clinically meaningful survival and quality of life benefit in non-transplantable ESHF patients.

LVADs as Destination Therapy - REMATCH Update



- 1 year LVAD vs. OMM survival = 53.5% vs. 26.5%
- 2 year LVAD vs. OMM survival = 32% vs. 8.2%
- 3 year LVAD vs. OMM survival = 15.9% vs. 2% (NS)

REMATCH Update (as of April 2004) – Source Thoratec Registry

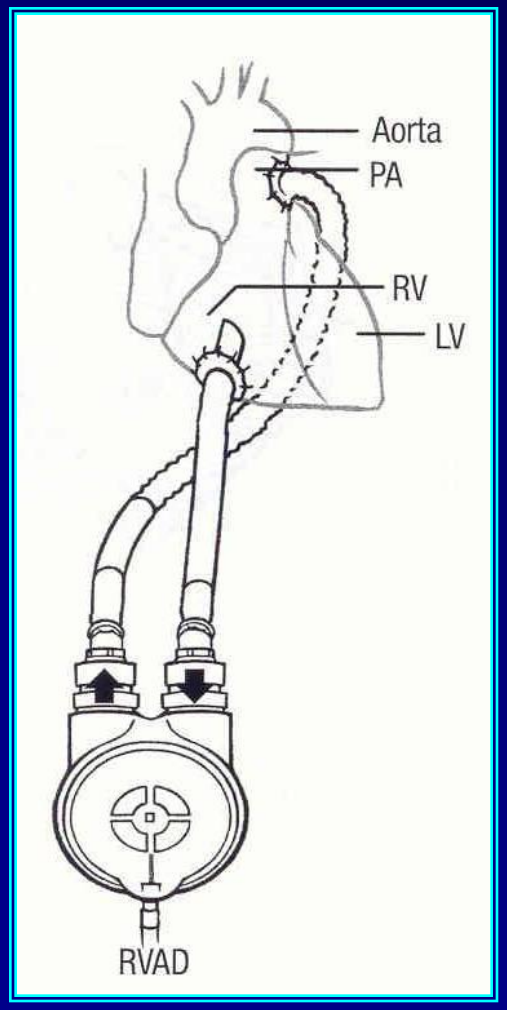
FDA/CMS Criteria for Destination Therapy

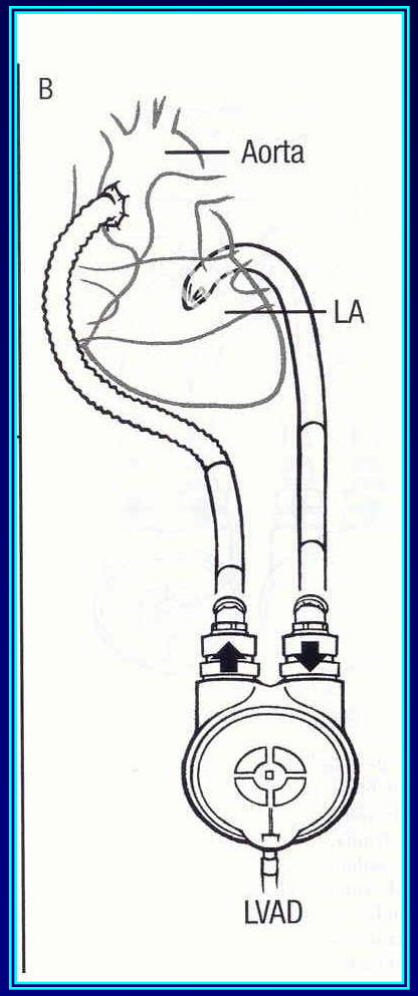
- Not a candidate for heart transplant
- NYHA class IV end-stage LV failure
- Life expectancy < 2 years
- Symptoms failed to respond despite optimal medical management for ≥ 60 of past 90 days
- LVEF < 25%
- Peak VO_2 < 12 ml/kg/min or inotrope dependence
- BSA ≥ 1.5 m^2

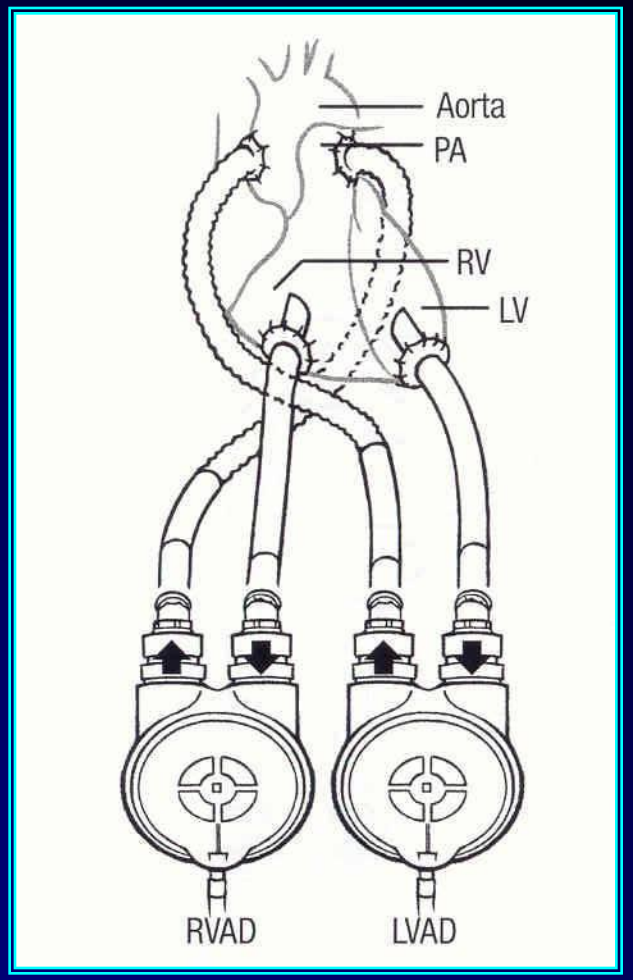
Current Mechanical Cardiac Support Options

- Partial Ventricular Support (IABP)
- Percutaneous VADs
- Implantable VADs
  - Combined support (BiVAD)
  - Individual support (LVAD, RVAD)
- Total Artificial Heart (TAH)

VAD Configuration

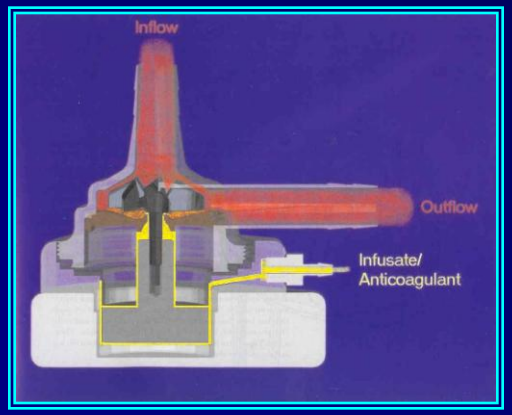


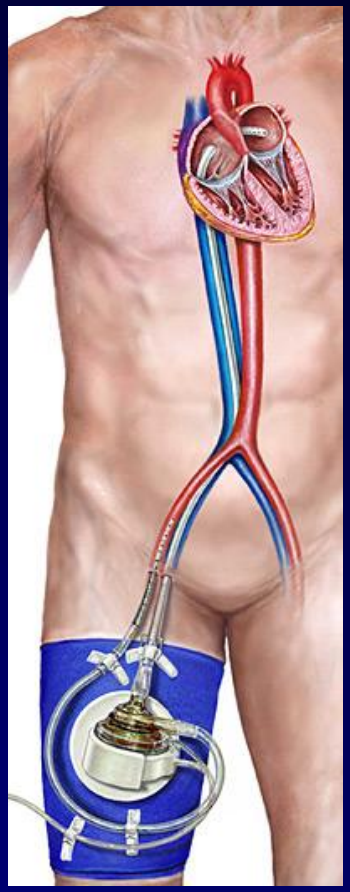




TandemHeart

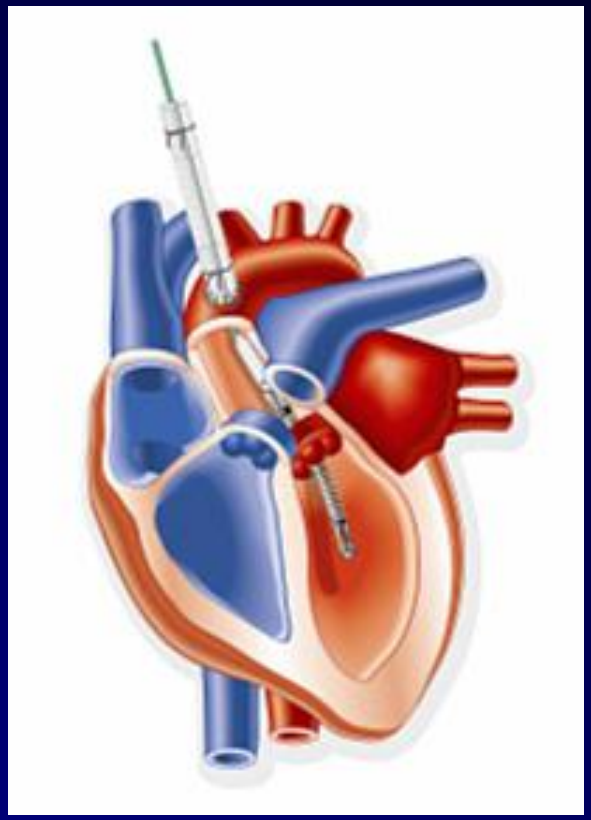
- Percutaneous/ femoral cut-down
- 4L/min flow
- RVAD or LVAD
- Days to weeks



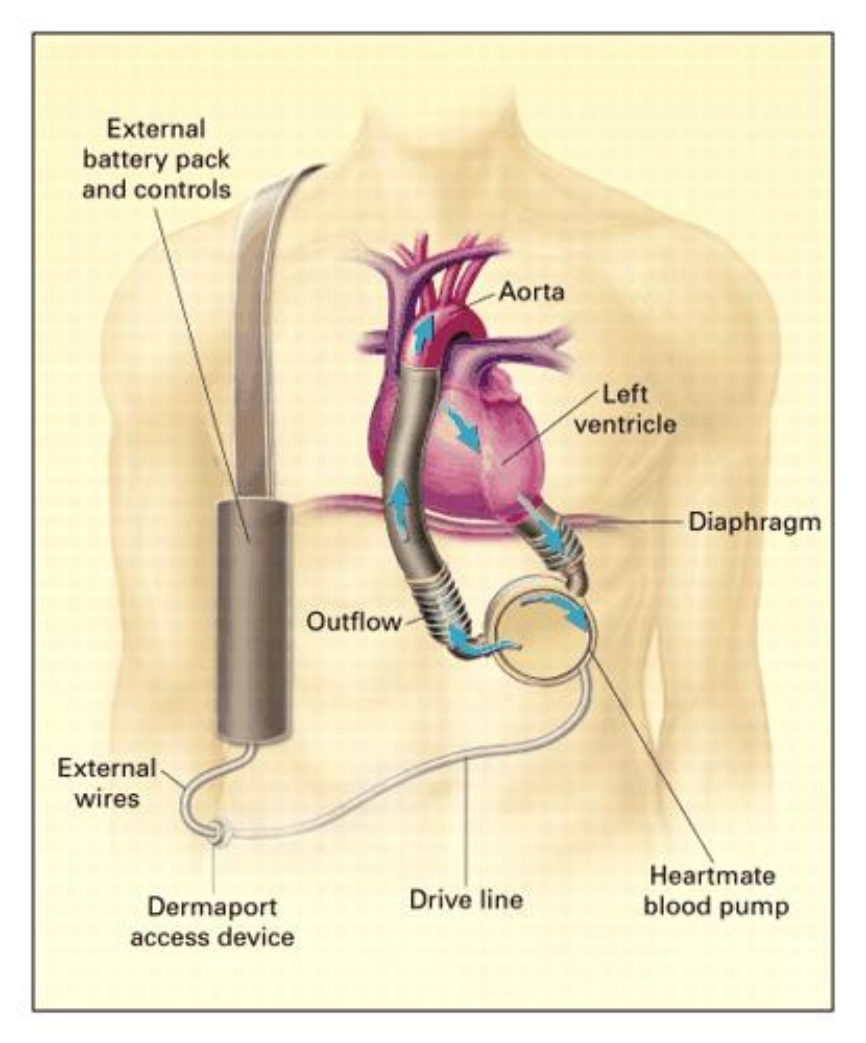


Impella

- Percutaneous/ femoral cut-down
- Directly unload the left ventricle
- Reduce myocardial workload and oxygen consumption
- Increase cardiac output and coronary and end-organ perfusion
- Flows 2.5L or 5L min

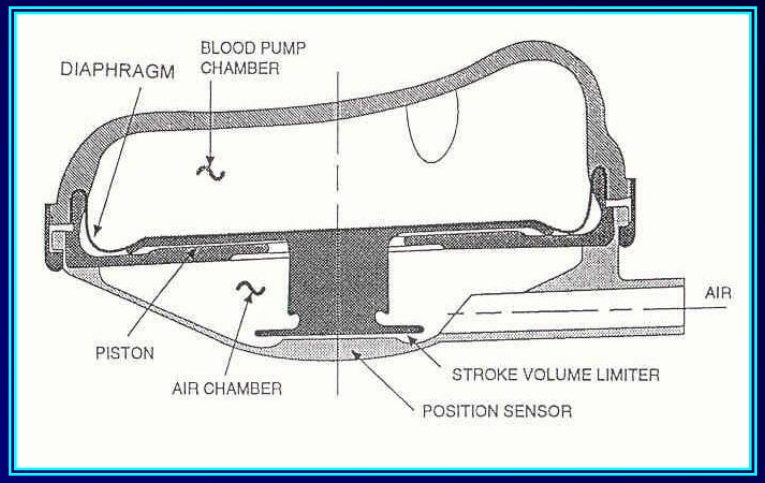


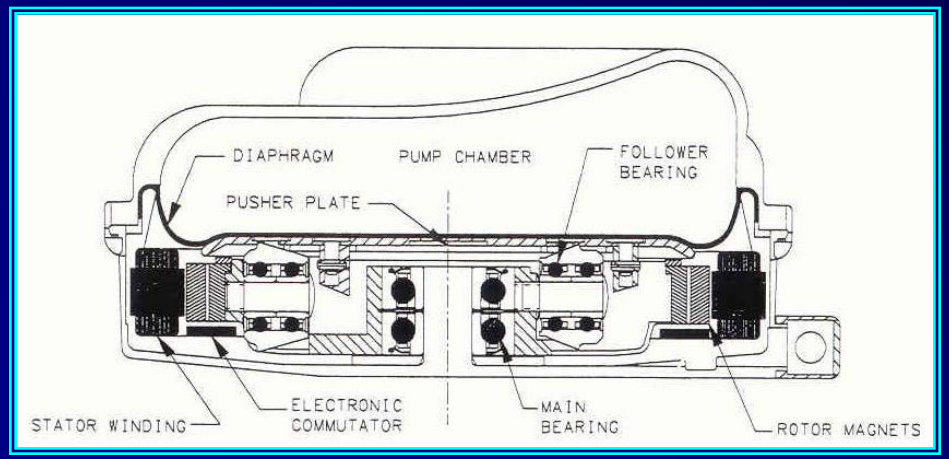
Heartmate VAD



- Implanted pump replaces LV
- External control system
- Textured surfaces minimize thromboembolic events and anti-coagulation therapy
- Able to supply up to 10 liters per minute
- Xenograft tissue valves
- Requires BSA > 1.5 m^2

HeartMate VAD





Heartmate Reliability

frequency of bleeding was 42 percent. No system had failed by 12 months, but the probability of device failure was 35 percent at 24 months. The device was replaced in 10 patients.

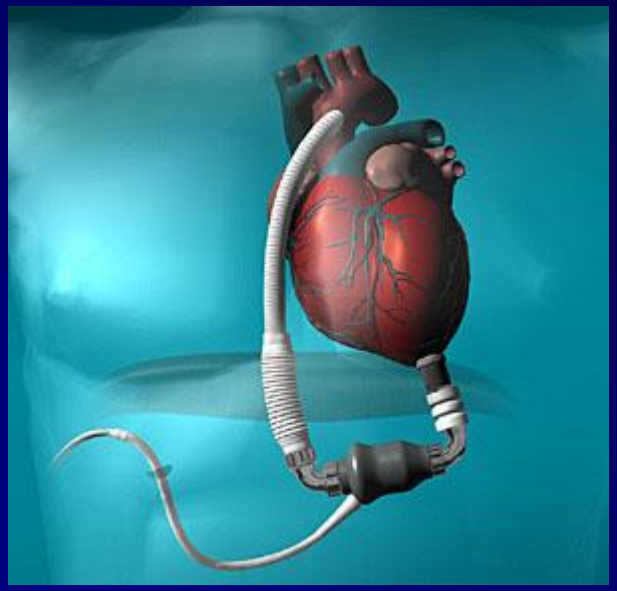
TABLE 2. CAUSES OF DEATH.*

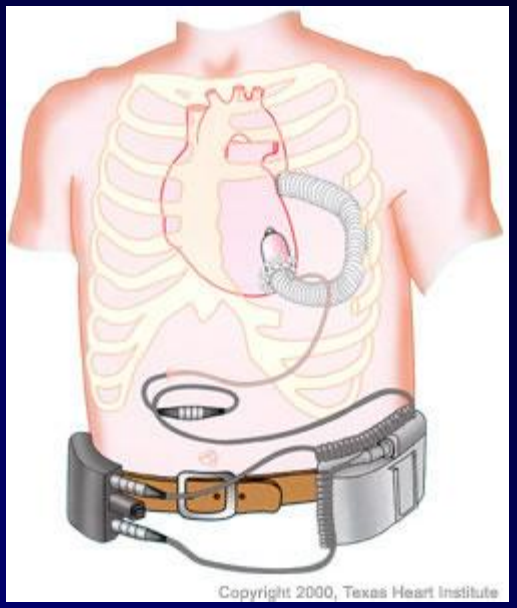
CAUSE OF DEATH	MEDICAL-THERAPY GROUP	LVAD GROUP	TOTAL
	no. of patients		
Left ventricular dysfunction	50	1	51
Sepsis	1	17	18
Failure of LVAD	0	7	7
Miscellaneous noncardiovascular causes	0	5	5
Cerebrovascular disease	0	4	4
Miscellaneous cardiovascular causes	1	2	3
Pulmonary embolism	0	2	2
Acute myocardial infarction	1	0	1
Cardiac procedure	1	0	1
Perioperative bleeding	0	1	1
Unknown	0	2	2
Total	54	41	95

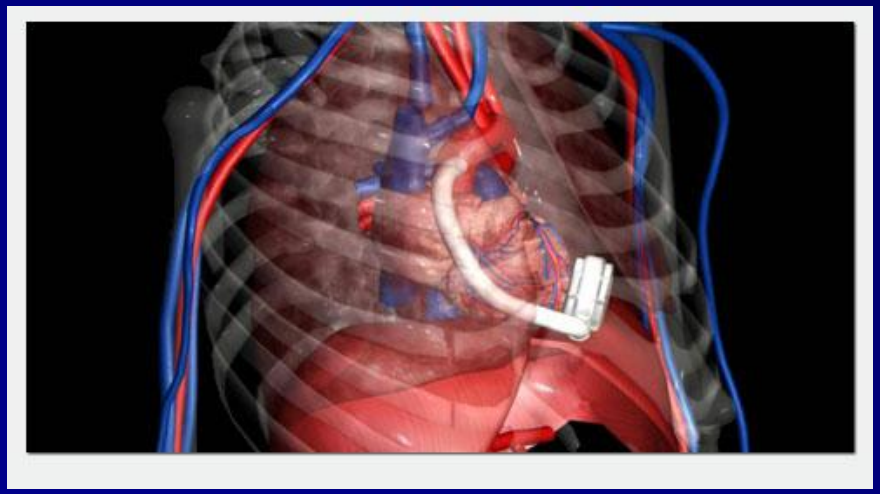
*LVAD denotes left ventricular assist device.

Source: Rose EA, et al. Long-term use of a left ventricular assist device for end-stage heart failure. N Eng J Med 2001; 345:1435-1343.

Continuous Flow Support



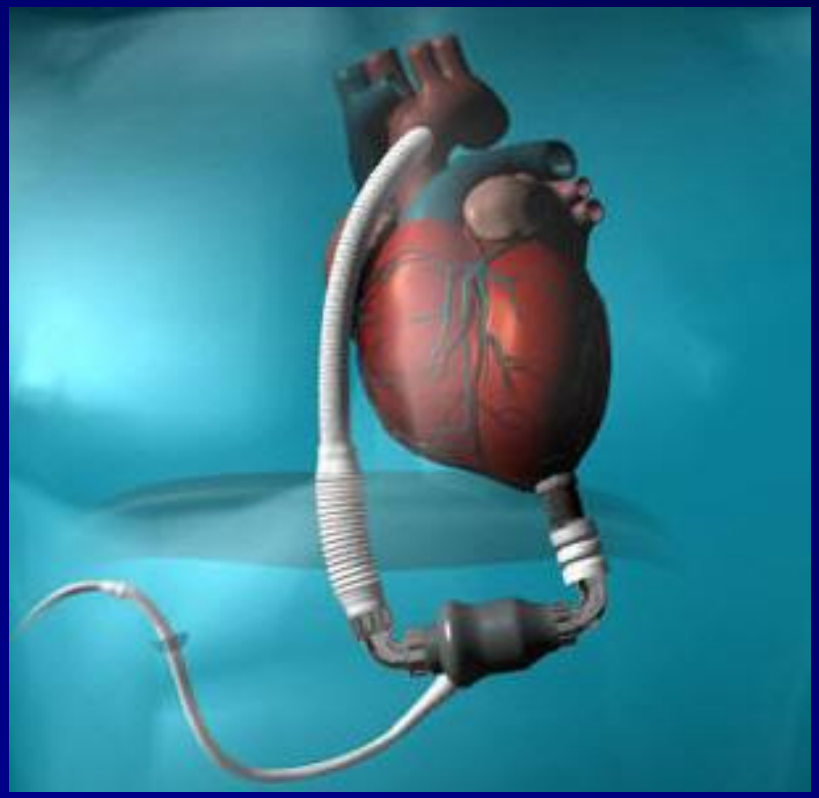




Continuous Flow Support

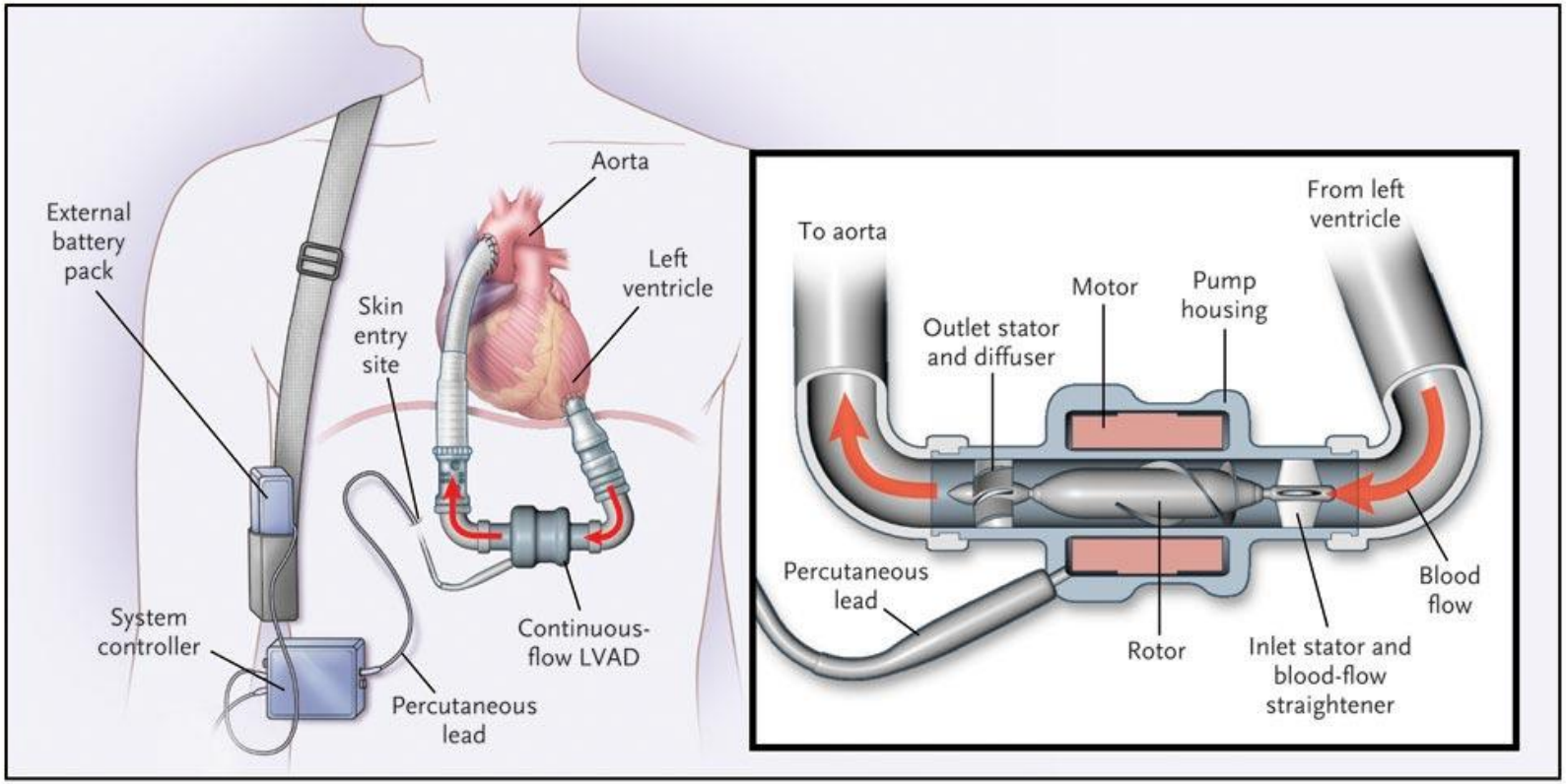
- Advantages
  - Minimize size
  - Improved reliability
  - Minimize pulse related trauma – infection
  - Unload LV in systole and diastole – accelerated ventricular remodeling
- Disadvantages
  - Arterial stasis
  - GI bleeding from AV malformations
  - Ineffective with severe hypertension
  - No heartbeat – difficult to measure BP
  - LV Thrombus

Heartmate 2



- Axial flow up to 10L/min
- Triple anticoagulation
- FDA approved for BTT

Components of the Continuous-Flow Left Ventricular Assist Device (LVAD)



Miller LW et al. N Engl J Med 2007;357:885-896

Original Article

Use of a Continuous-Flow Device in Patients Awaiting Heart Transplantation

Leslie W. Miller, M.D., Francis D. Pagani, M.D., Ph.D., Stuart D. Russell, M.D., Ranjit John, M.D., Andrew J. Boyle, M.D., Keith D. Aaronson, M.D., John V. Conte, M.D., Yoshifumi Naka, M.D., Donna Mancini, M.D., Reynolds M. Delgado, M.D., Thomas E. MacGillivray, M.D., David J. Farrar, Ph.D., O.H. Frazier, M.D., for the HeartMate II Clinical Investigators

N Engl J Med
Volume 357(9):885-896
August 30, 2007

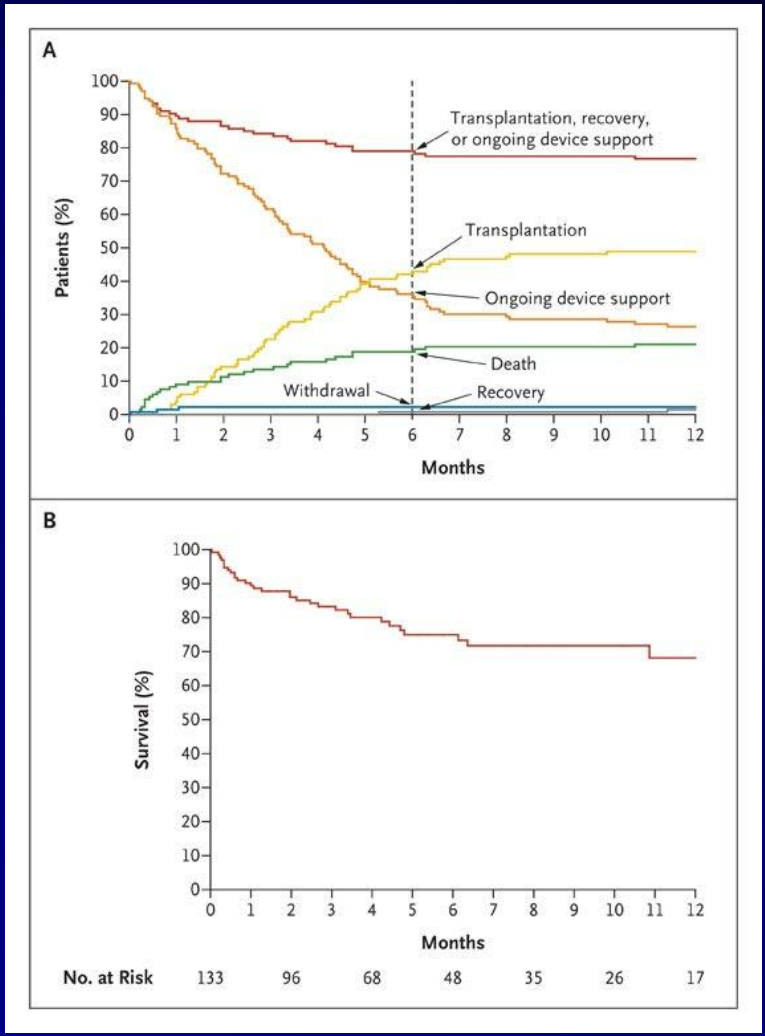
The NEW ENGLAND JOURNAL of MEDICINE

Study Overview

- 133 patients with severe heart failure implanted with of a continuous-flow left ventricular assist device
- At 6 months, 75% of the patients had undergone heart transplantation, had cardiac recovery with device explantation, or continued to receive device support without any contraindication to subsequent transplantation
- Minimal adverse events: bleeding, stroke, heart failure, and infection

The NEW ENGLAND JOURNAL of MEDICINE

Outcomes for 133 Patients after Implantation of the Continuous-Flow Left Ventricular Assist Device



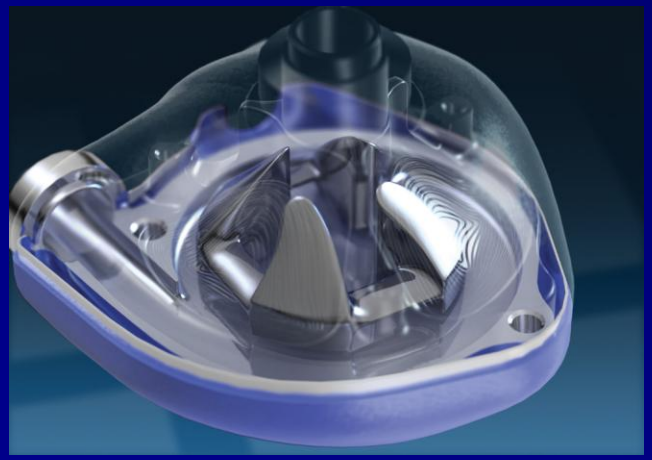
Miller LW et al. N Engl J Med 2007;357:885-896

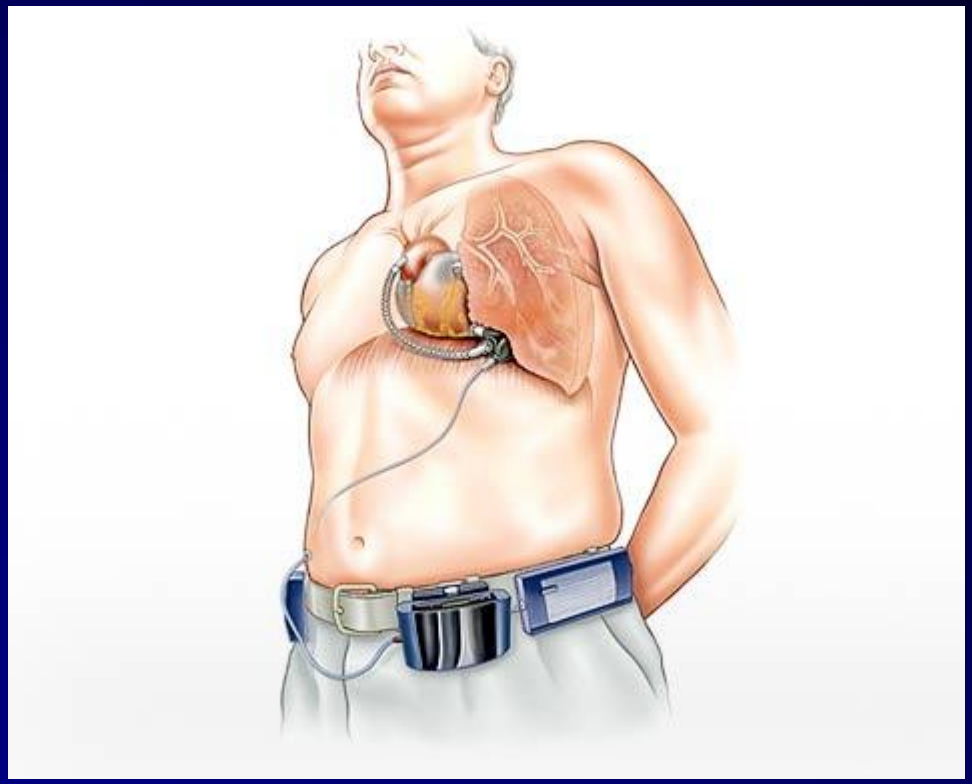
The NEW ENGLAND JOURNAL of MEDICINE

Conclusion

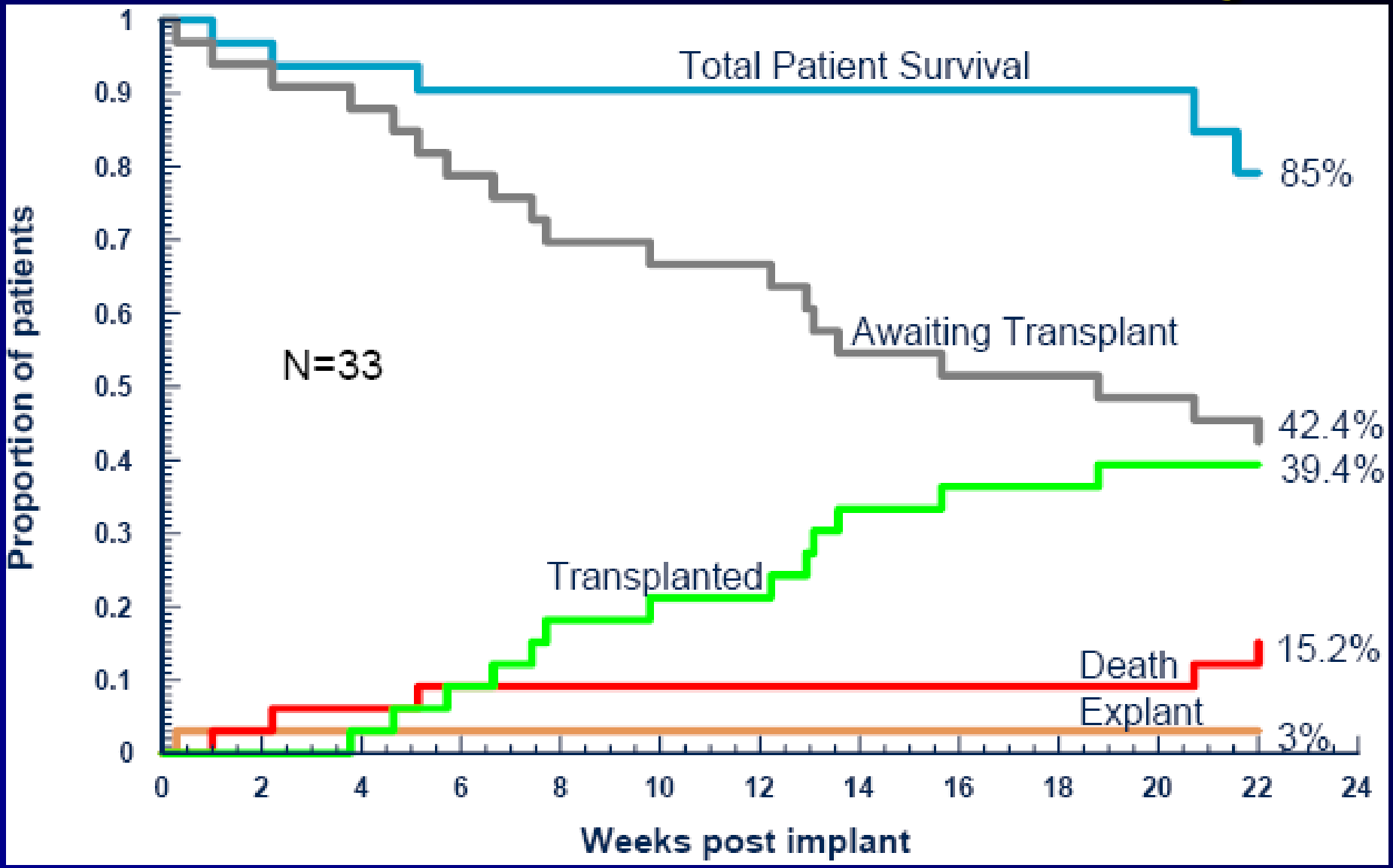
- A continuous-flow left ventricular assist device can provide effective hemodynamic support for a period of at least 6 months in patients awaiting heart transplantation, with improved functional status and quality of life

VentrAssist





CE Mark BTT - Efficacy



Esmore D et al. ISHLT presentation 4/2007.

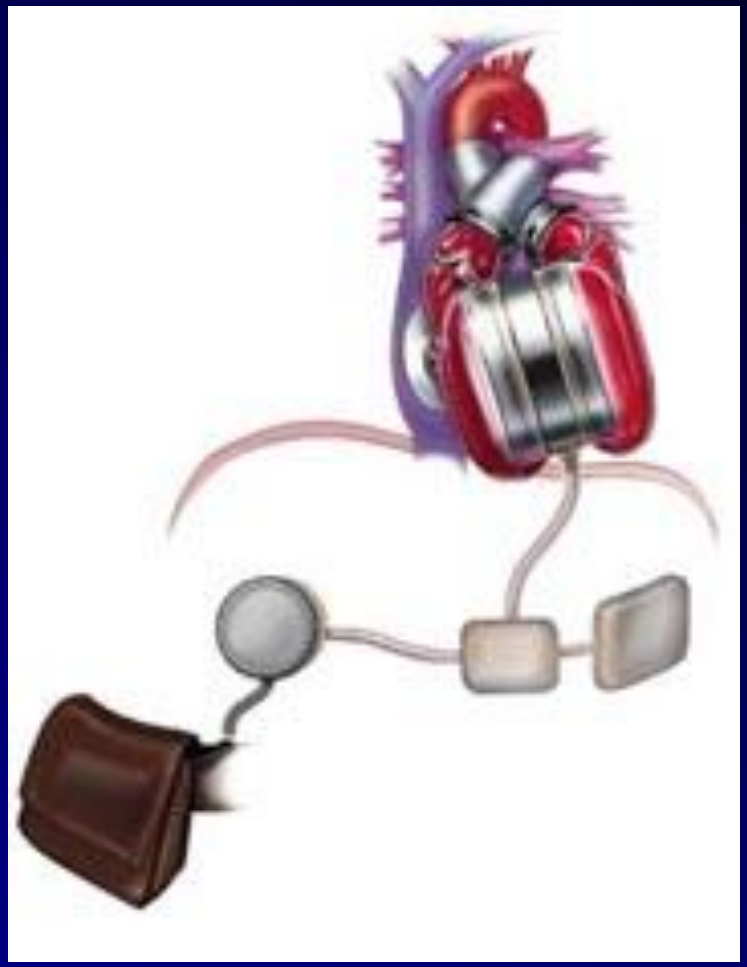
Overall VentrAssist Experience

Summary	
Total number of patients implanted	100
Longest support duration (d)	977
Mean support duration (d)	179
Number of patients currently supported	36
VentrAssist Support Duration	
> 6 months	32
> 12 months	16
> 24 months	2

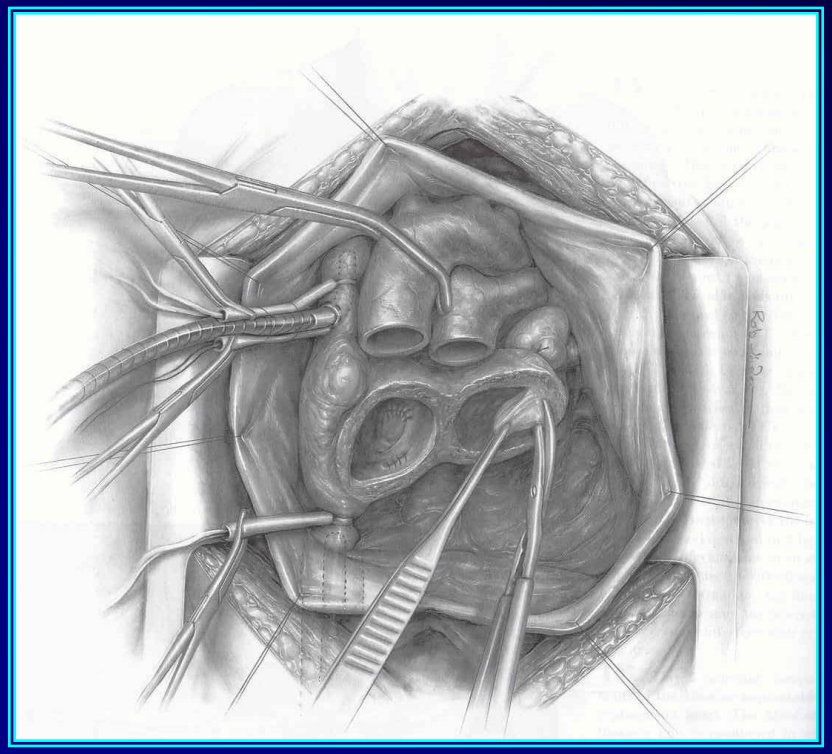
*1 April 07

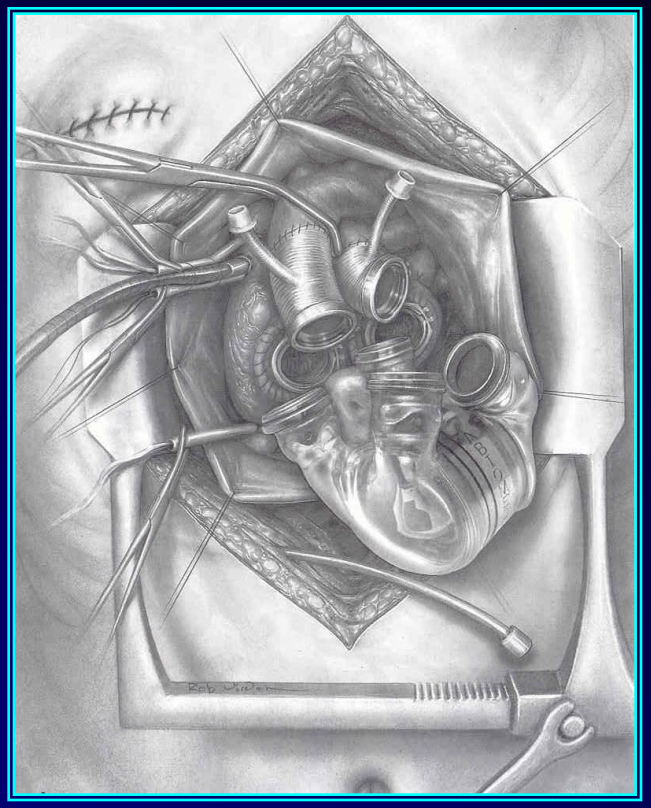
Esmore D et al. ISHLT presentation 4/2007.

Abiomed Total Artificial Heart



AbioCor TAH



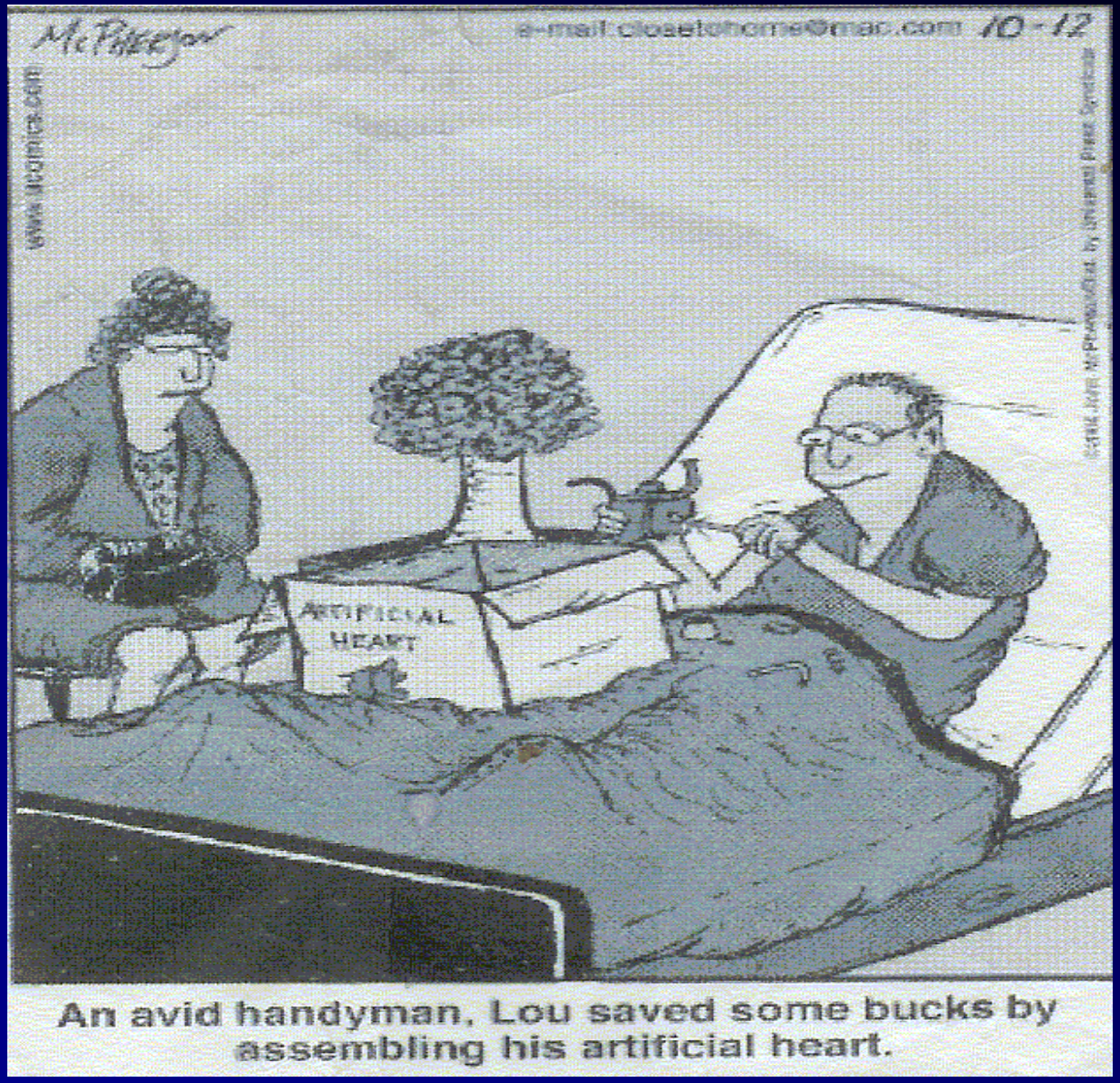


AbioCor

- Totally implantable, large
- Destination therapy
- 11 implants
  - Candidates had expected 30d mortality > 70%
- Longest survival 466 days
  - 2 intra-operative deaths
  - 3 CVAs
  - 2 patients discharged
- Variable anti-coagulation
- FDA Humanitarian Device Exemption

Summary

- VADs are proven therapy for end-stage heart failure
- Four potential uses:
  - Bridge to evaluation
  - Bridge to recovery
  - Bridge to transplant
  - Destination therapy



An avid handyman, Lou saved some bucks by assembling his artificial heart.