

LVAD – A bridge to the future

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Disclosures

Research
NIH
Thoratec - consultant
Genentech
Scios

Cycling team
Cardiowest

Exercise Core Lab
Pfizer
Boston Scientific

Will discuss unapproved devices

Outline

An update on LVADs today
Interesting issues related to continuous flow VADs
Who to VAD

Heart Disease and Stroke Statistics

2006 Update – Heart Failure

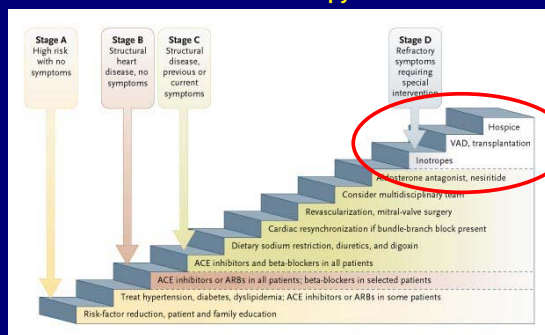
Prevalence	5,000,000
Incidence	550,000
Hospital d/c	1,093,000
Cost	\$29.6 billion

Deaths	57,218
Underlying or contributing cause	286,000

If < 65 years old, 80% of men and 70% of women will die within 8 years

Circulation 2006;113:e85-e151

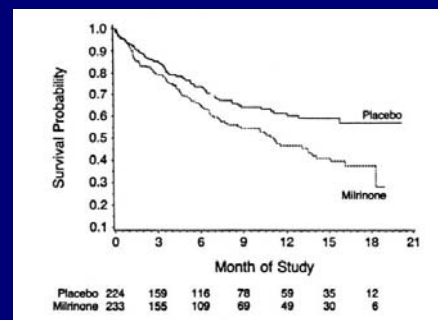
Heart Failure Therapy 2003



Jessup, M. et al. N Engl J Med 2003;348:2007-2018



Promise study



NEJM 1991;325:1468

Continuous outpatient inotropic support

Defined inotropic dependence as worsening of the patients clinical status with attempted inotrope withdrawal

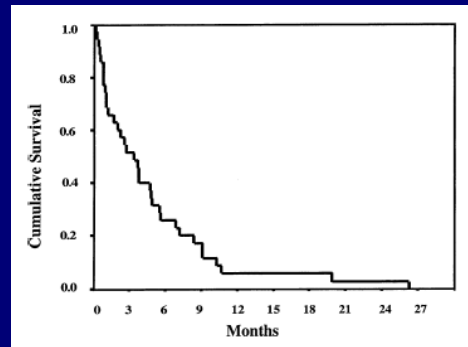
36 patients

Age (yrs)	55.4 ± 9.5
EF (%)	19.9 ± 8.5
LVEDD (mm)	70 ± 10
SBP (mm Hg)	97.4 ± 13.4
Na	131.7 ± 5.3
Creat	1.5 ± 0.6

1.9 + 1.8 hospitalizations in the previous 6 months

J Cardiac Failure 2003;9:180-187

Probability of survival with COSI

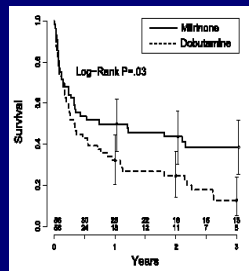


J Cardiac Failure 2003;9:180-187

Cleveland Clinic bridge to Tx with inotropes

112 non Tx pts felt to be inotrope dependent

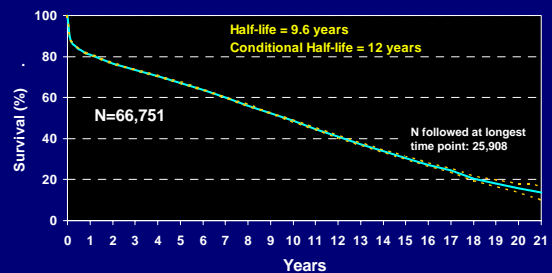
	mil	dobut
Na	133	133
Creat	1.7	1.7
BB	34%	5%
ACE/ARB	50%	46%
Lasix dose (mg)	103	149



Circ HF 2009;2:320-324

HEART TRANSPLANTATION

Kaplan-Meier Survival (1/1982-6/2003)



2005
J Heart Lung Transplant 2005;24: 945-982

HEART TRANSPLANTS IN THE US



UNOS.org

Ventricular Assist Devices

Current Uses

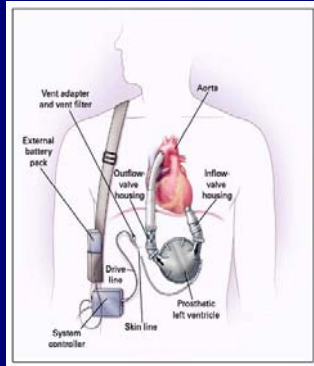
- Bridge to cardiac transplant
- Bridge to recovery after reversible insult (post-cardiotomy, acute MI, myocarditis)

Potential Uses

- Bridge to recovery in chronic heart failure
- Destination therapy

Reality – At least 50 % bridge to decision

Ventricular assist device therapy



NEJM 2001;345:1435-43

REMATCH inclusion criteria

Chronic heart failure, not transplant candidate
 NYHA class IV for at least 90 days
 EF < 25%
 Peak $\text{VO}_2 < 12 \text{ ml/kg/min}$ or continuous IV inotropes

Exclusion for transplant:

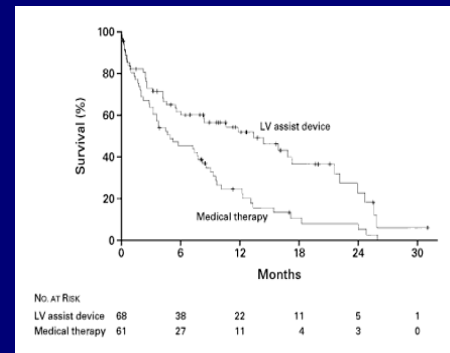
Age > 65
 Diabetes with end-organ damage
 Creatinine > 2.5 gm/dl

NEJM 2001;345:1435

Baseline characteristics

	REMATCH	Inotropes
N	61	91
Age (yr)	68	68
EF (%)	17	17
SBP (mmHg)	103	100
Na (mEq/l)	135	134
PCW (mmHg)	24	25
CI (l/min/m ²)	2.0	2.0
Creatinine (mg/dl)	1.8	1.8
Diuretics (%)	97	95
ACE inhibitors (%)	51	53
Beta blockers (%)	20	16

REMATCH trial



NEJM 2001;345:1435-43

REMATCH - Causes of death

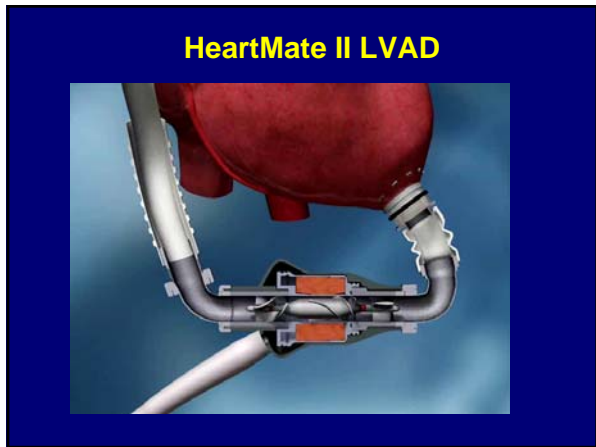
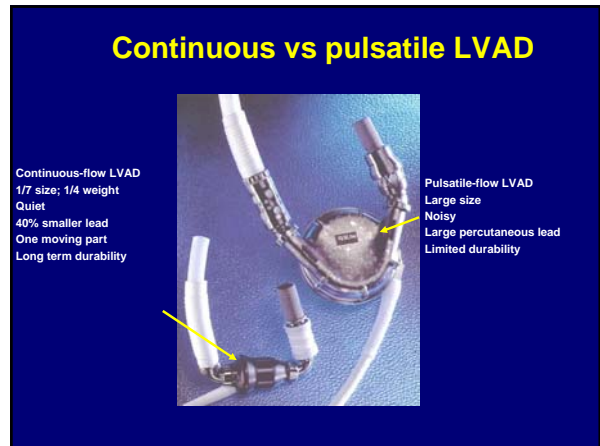
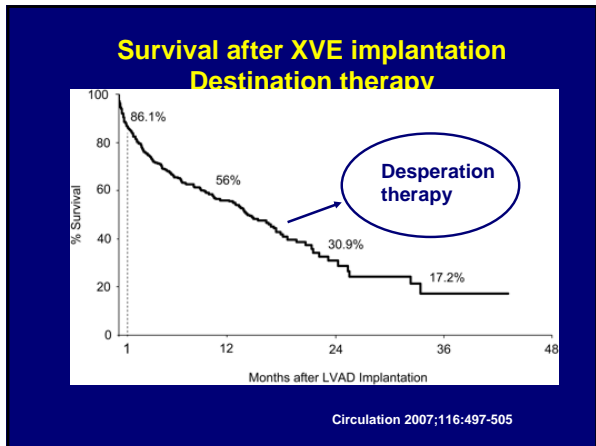
	Medical	LVAD
n	61	68
LV dysfunction	50	1
Sepsis	1	17
LVAD failure	0	7
CVA	0	4
Pulm embolism	0	2
Other	3	10
Total	54	41

NEJM 2001;345:1435-43

REMATCH - Hospitalizations

	Medical	LVAD
Days alive	150	408
Days out of hospital	106	340
Days in hospital	24	88
Initial days in hospital	5	29

NEJM 2001;345:1435-43



HeartMate II Clinical Trial

Primary endpoint
Survival to transplantation or 180 days of support remaining transplant eligible as status 1A or 1B

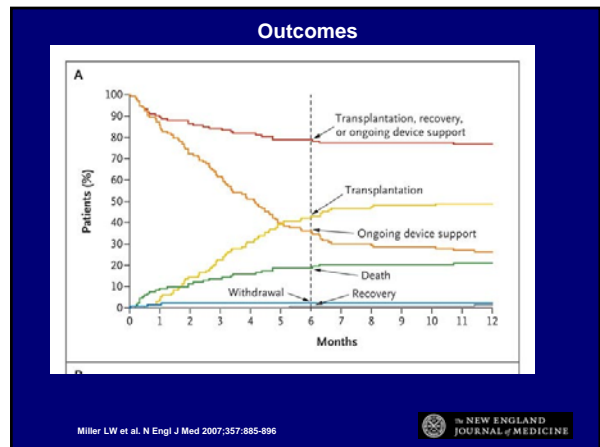
Secondary endpoints
Overall survival to transplantation
Survival at 30 days, and 1 yr post Tx
Frequency of adverse events
Functional Status (NYHA, 6 minute walk)
Quality of Life (MLWHF, KCCS)

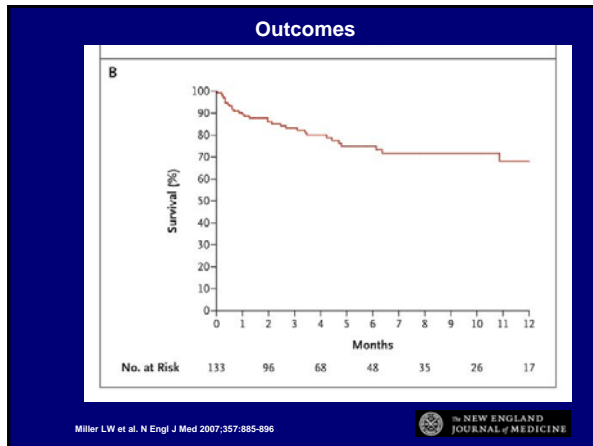
Miller LW et al. N Engl J Med 2007;357:885-896

Baseline characteristics – HM II

N	133	Na (mm/l)	132.9
Age (yr)	50.1	Chol (mg/dL)	126
Male (%)	79%	BUN (mg/dL)	31.4
Body mass index	26.8	Creat (mg/dL)	1.4
% ischemic	37		
EF	16.3		
NYHA class	IV		
SBP (mmHg)	95.8	Inotropes (%)	89
CVP (mmHg)	13.5	≥ 2 inotropes (%)	25
PA sys (mmHg)	53.0	Diuretic (%)	82
PA mean (mmHg)	36.5	ACE + ARB (%)	35
PCWP (mmHg)	26.1	Beta blocker (%)	38
CI (l/min/m ²)	2.0		
		CRT (%)	48
		ICD (%)	74
		IABP (%)	41

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





Adverse Events

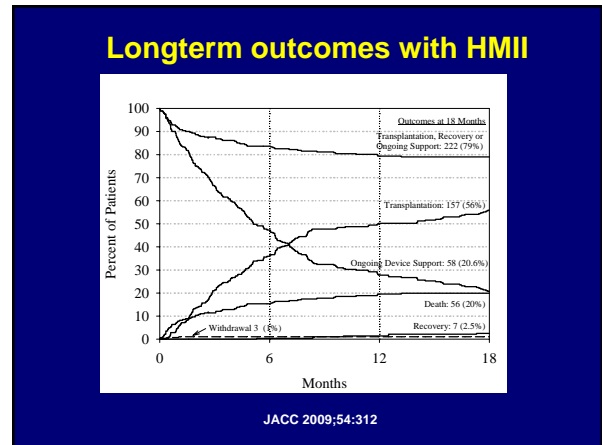
Event	Overall			0-30 Days			>30 Days		
	Patients with Event (%)	No. of Events	Event Rate per PY	Patients with Event	No. of Events	Event Rate per PY	Patients with Event	No. of Events	Event Rate per PY
Bleeding									
Requiring surgery	41 (31)	48	0.78	40	45	4.41	1	3	0.06
Requiring ≥2 units of packed red cells only	70 (53)	129	2.09	60	85	8.33	10	44	0.85
Ventricular arrhythmias	32 (24)	49	0.79	24	28	2.55	6	23	0.45
Infection									
Local, not related to device	37 (28)	70	1.13	28	37	3.63	9	33	0.64
Sepsis	27 (20)	38	0.62	18	18	1.77	9	20	0.39
Percutaneous lead	18 (14)	23	0.37	0	0	0.00	18	23	0.45
Pump pocket	0	0	0.00	0	0	0.00	0	0	0.00
Respiratory failure	34 (26)	43	0.70	30	33	3.14	4	11	0.21
Renal failure	18 (14)	19	0.31	15	15	1.47	3	4	0.08
Right heart failure									
Need for right ventricular assist device	5 (4)	5	0.08	4	4	0.39	1	1	0.02
Need for extended inotropic support	17 (13)	17	0.28	12	12	1.18	5	5	0.10

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

HeartMate II Clinical Study HeartMate I / II Comparison

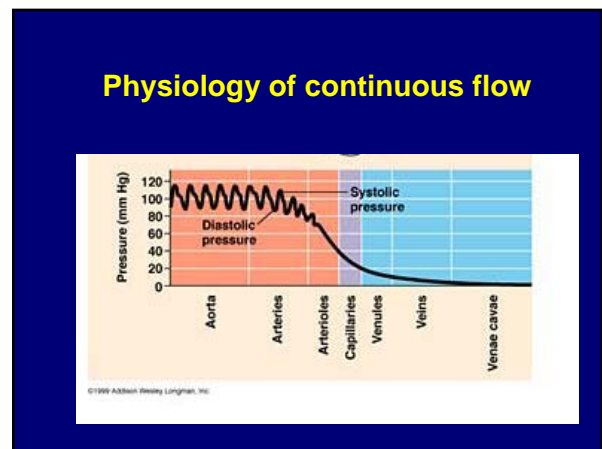
Event	HeartMate II BTT (181.0 pt yrs)		HeartMate VE BTT (86.2 pt yrs)		Risk Ratio (95% CI)
	# Events	Events/pt yr	# Events	Events/pt yr	
Stroke	25	0.14	38	0.44	0.34 (0.19 - 0.59)
Other non-stroke Neurologic Event	24	0.13	58	0.67	0.21 (0.12 - 0.35)
Bleeding requiring Surgery	82	0.45	127	1.47	0.31 (0.21 - 0.45)
Percutaneous Lead Infection	48	0.26	301	3.49	0.09 (0.06 - 0.13)
RHF requiring RVAD	17	0.09	26	0.30	0.31 (0.16 - 0.60)

*Frazier OH, Rose EA, Oz MC, et al. J Thorac Cardiovasc Surg 2001;122:1186-1195

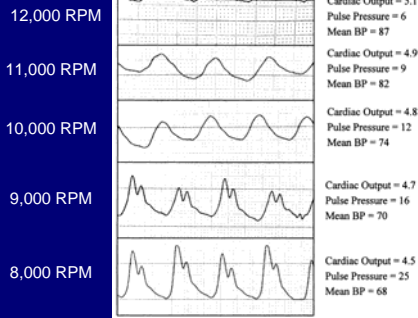


Concerns with continuous flow

Previous pumps associated with a high embolic and/or bleeding rate
 Unclear effects of no pulse longterm
 Require anticoagulation

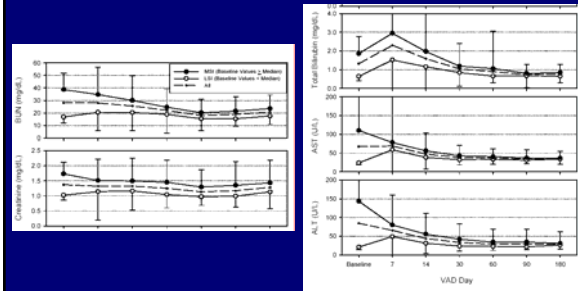


Pulsatility as a Function of Pump Speed



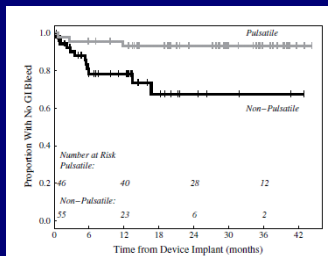
Frazier et al. Circulation 2002;105:2855

HM II and end organ function



In press Circulation

GI bleeds



7 of 12 documented or presumed AVM

JTCVS 2009;137:208

JHH bridge to transplant experience

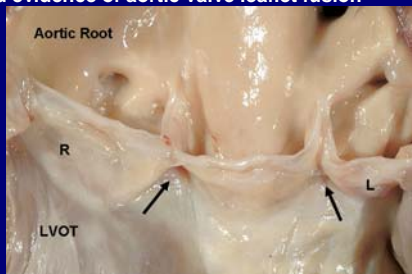
Only 17% of our patients had aortic valve opening on routine echo

Last 7 patients bridged to transplant with HM II
No evidence of thrombus formation in aortic v cusps

6/7 had evidence of aortic valve leaflet fusion with no valve thickening

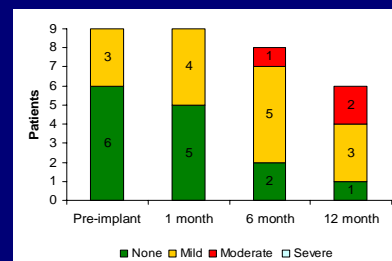
Gross Pathology

9 pts bridged to transplant with HM II
No evidence of thrombus formation in aortic v cusps
8/9 had evidence of aortic valve leaflet fusion



J Heart Lung Transplant. 2008;27:1269

Aortic Insufficiency



J Heart Lung Transplant. 2008;27:1269

Measuring blood pressure

41 patients post VAD with arterial line

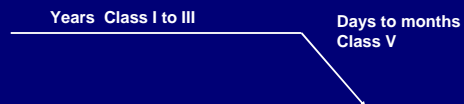
Measured bp by doppler, auto cuff, manual cuff, pulse

Doppler reliably measures systolic bp 88% of the time
Rest < 30%

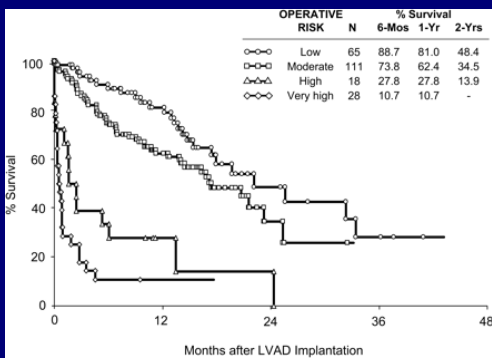
If on pressors, Doppler reliable 45%

HFSA 2008

When is someone sick enough and is anyone too sick?



Survival after LVAD by risk category



Characteristics of who dies with heart failure and a low EF

All patients seen in HF clinic between 1/1/2000 and 10/20/2003 who subsequently died

160 pts
80 died as outpatients
21% died suddenly

J Cardiac Failure 2006;12:47

Who dies – Baseline characteristics

	All	Outpt	Inpt
Time in clinic (months)	24.7	23.1	26.6
CHF duration (yr)	5.0	4.6	5.4
Age (yr)	59.5	57.9	61.1
% male	74	75	74
NYHA III (%)	14	13	14
NYHA IV (%)	79	74	83
% ICD	37	30	46
% CRT	5	7	5
EF (%)	20	22	19

J Cardiac Failure 2006;12:47

Who dies – baseline characteristics

	All	Outpt	Inpt
Medications			
ACE inhib (%)	55	58	53
ACE intol (%)	35	34	36
ARB (%)	7	5	9
Loop diuretic (%)	91	90	92
Spironolactone (%)	32	30	34
Beta blocker (%)	38	34	43
Labs			
Na (mmol/L)	135	135	134
BUN (mg/dL)	62	52	69
Cr (mg/dL)	2.2	2.1	2.4
Hosp in last 6 months (n)			
0	26	26	27
1	32	38	27
2+	42	37	46

J Cardiac Failure 2006;12:47

Inpatient risk studies

Author	n	Markers	1 year surv (%)
Chin	257	BP < 100, DM, non sinus rhythm	N/A
Alla	301	HR > 100, Na < 134, Creat > 2.0, Age > 70, prior hosp	57.6
Cowie	220	Age, crackles, low BP, high Creat	62
Jong	38,702	Male, age, malig, renal, dementia, cerebrovasc, rheum, periph vas, or pulm dis, ischemic etiology, DM	66.9
Bouvy	152	DM, high Creat, NYHA III/IV, low BMI, low BP, edema	N/A
Lee	4031	Age, low BP, high RR, high BUN, low Na	69.5
Kittleson	259	No ACE, low BP, low Na, high Creat	N/A
Felker	949	Age, low BP, NYHA IV, high BUN, low Na	N/A
Fonarow	37,772	BUN > 43, SBP < 115, Creat > 2.75	N/A
Rector	769	Age, low BP, low Hgb, low Na, high BUN	50% (high risk)
Rohde	779	Cancer, SBP < 124, Creat > 1.4, BUN > 37, Na < 136, age > 70	N/A

Outpatient risk studies

Author	n	Markers
Mahon	585	Low Creat cl, 6 MW < 262 m, low EF, recent hosp., diuretic
Eshaghian	1354	Low EF, low Na, low Hgb, high BUN, high Creat, diuretic dose
Greenberg	4280	NYHA III/IV, HF hosp, angina
Levy	1125	Diuretic dose, low BP, % lymph, Hgb < 16, ischemic etiol, EF, low chol, high uric acid/allopurinol, Na < 138, NYHA, age, male sex
Teuteberg	160	High BUN, Creat, low Na, low Hct, recent hosp, no ACE/BB

ESP trial Evaluation of Simplified Predictors study

EF < 35%, NYHA class III, IV

Walk < 1 block without SOB
Sodium < 136
BUN > 40 or Creatinine > 1.5
No ACE / ARB / BB
Diuretic > 1.5 mg/kg/d
1 HF admit past 6 months

Conclusions

Limited options for patients with end stage heart failure

New VADs appear to be quite durable, associated with improved clinical outcomes but still have unique side effects

New to think about endstage therapies earlier