Σεμινάριο Ομάδων Εργασίας

ΟΜΑΔΑ ΕΡΓΑΣΙΑΣ ΚΑΡΔΙΟΧΕΙΡΟΥΡΓΙΚΗΣ

Μηχανική υποστήριξη της ανεπαρκούσης καρδιάς

ΕΠΙΛΟΓΗ ΑΡΡΩΣΤΩΝ ΓΙΑ ΜΗΧΑΝΙΚΗ ΥΠΟΣΤΗΡΙΞΗ

Ξυδώνας Σωτήριος

Καρδιολογική Μονάδα Εμφραγμάτων και Καρδιακής Ανεπάρκειας

Β' Καρδιολογικό Τμήμα, Π.Γ.Ν.Α. «Ο Ευαγγελισμός»

Heart Failure Statistics

- 4.900.000 pts with HF in USA
- 550.000 new cases every year
- 2.500 donor hearts every year

AHA. Heart Disease and Stroke Statistics 2008 Update.
Dallas, TX: American Heart Association; 2008.

- 60.000 NYHA IV in UK
- 12.000 under 65 yrs
- Ht TX: 130 in 2008
  128 in 2007
  156 in 2006

UK Transplant Org. Transplant Activity 2008-2009

Heart Failure Statistics

- End-stage refractory HF pts: 5-10% of all HF pts

a. Miller LW et al. The epidemic of heart failure. Cardiol Clin 2001;19:547–55.
b. Hunt SA, et al. American College of Cardiology. AHA Task Force on Practice Guidelines. JAMA 2005;46:e1–82.
c. Redfield MM. Heart failure: an epidemic of uncertain proportions. N Engl J Med 2002;347:1142–4.
d. Jessup M, Brozena S. Heart failure. N Engl J Med 2003;348:2007–18.
e. American Heart Association. Heart disease and strokestatistics—2005 update. Dallas, TX: AHA;2005.

- This group consumes 60% of health care expenditures for all pts with HF

a. O'Connell JB et al. Economic impact of HF in USA: time for a different approach. J Heart Lung Transplant 1994;13(suppl):S107–12.
b. Mackowiak J. Cost of heart failure to the healthcare system. Am J Manag Care 1998;4(suppl 6):S338–42.

VADs

- Have been used for 25 years in more than 10.000 pts
- Primarily as BTT
- 20-30% of pts with VAD as BTT will not survive to TX

a. Lietz K et al. LVAD: evolving devices and indications for use. Curr Opin Cardiol 2004;19:613–8.
b. Stevenson LW et al. VADs for durable support. Circulation 2005;112:111–5.
c. Stevenson LW et al. LVAD: bridges to transplantation, recovery, and destination for whom? Circulation 2003;103:3059–63.
d. Frazier OH et al. Mechanical circulatory support for advanced HF: where does it stand in 2003? Circulation 2003;108:3064–8.
e. Morgan JA et al. Bridging to transplant with the HeartMate LVAD: the Columbia Presbyterian 12-year experience. J Thorac Cardiovasc Surg 2004;127:1309–16.
f. DiBella I et al. Results with the Novacor assist system and evaluation of long-term assistance. Eur J Cardiothorac Surg 2000;18:112–6.
g. Deng MC et al. Mechanical circulatory support device database of the ISHLT: third annual report. J Heart Lung Transplant 2005;24:1182–7.

VADs

Advanced chronic heart failure: A position statement from the Study Group on Advanced Heart Failure of the Heart Failure Association of the European Society of Cardiology

Marco Metra [a,*], Piotr Ponikowski [b], Kenneth Dickstein [c], John J.V. McMurray [d], Antonello Gavazzi [e], Claes-Hakan Bergh [f], Alan G. Fraser [g], Tiny Jaarsma [h], Antonis Pitsis [i], Paul Mohacsi [j], Michael Böhm [k], Stefan Anker [l,m], Henry Dargie [n], Dirk Brutsaert [o], Michel Komajda [p]
on behalf of the Heart Failure Association of the European Society of Cardiology

Definition of ACHF

1. Severe symptoms of HF with dyspnoea and/or fatigue at rest or with minimal exertion (NYHA functional class III or IV)
2. Episodes of fluid retention (pulmonary and/or systemic congestion, peripheral oedema) and/or of reduced cardiac output at rest (peripheral hypoperfusion)
3. Objective evidence of severe cardiac dysfunction, shown by at least one of the following:
   a) A low LVEF (<30%),
   b) A severe abnormality of cardiac function on Doppler-echocardiography with a pseudonormal or restrictive mitral inflow pattern [5];
   c) High LV filling pressures (mean PCWP>16 mm Hg, and/or mean RAP>12 mm Hg by pulmonary artery catheterisation) [6],
   d) High BNP or NT-ProBNP plasma levels, in the absence of non-cardiac causes.
4. Severe impairment of functional capacity shown by one of the following:
   a) Inability to exercise,
   b) 6-MWT distance<300 m [7] or less in females and/or patients aged≥75 years [8]
   c) peak VO_2 <12 to 14 ml/kg/min [9,10]
5. History of ≥1 HF hospitalisation in the past 6 months
6. Presence of all the previous features despite "attempts to optimise" therapy including diuretics, inhibitors of the renin–angiotensin–aldosterone system, and beta-blockers, unless these are poorly tolerated or contraindicated, and CRT, when indicated.

European Journal of Heart Failure 2007;9:684–694

VADs

Advanced chronic heart failure: A position statement from the Study Group on Advanced Heart Failure of the Heart Failure Association of the European Society of Cardiology

Marco Metra [a,*], Piotr Ponikowski [b], Kenneth Dickstein [c], John J.V. McMurray [d], Antonello Gavazzi [e], Claes-Hakan Bergh [f], Alan G. Fraser [g], Tiny Jaarsma [h], Antonis Pitsis [i], Paul Mohacsi [j], Michael Böhm [k], Stefan Anker [l,m], Henry Dargie [n], Dirk Brutsaert [o], Michel Komajda [p]
on behalf of the Heart Failure Association of the European Society of Cardiology

LVAD should be used as:

- Bridge to Transplant (BTT)
- Bridge to Recovery (BTR)
- Destination Therapy (DT)

European Journal of Heart Failure 2007;9:684–694

VADs

European Heart Journal
doi:10.1093/eurheartj/ehn309

European Journal of Heart Failure
doi:10.1016/j.ejheart.2008.08.005

ESC GUIDELINES

ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure 2008

The Task Force for the Diagnosis and Treatment of Acute and Chronic Heart Failure 2008 of the European Society of Cardiology. Developed in collaboration with the Heart Failure Association of the ESC (HFA) and endorsed by the European Society of Intensive Care Medicine (ESICM)

- Current indications for LVADs and artificial hearts include **BTT** and managing pts with **acute, severe myocarditis**.

  Class of recommendation IIa, level of evidence C

- Although experience is limited, these devices may be considered for long-term (**DT**) use when no definitive procedure is planned.

  Class of recommendation IIb, level of evidence C

Stage D Therapy

Device Use

Consideration of an LVAD

as permanent or DT is reasonable in highly selected pts

with refractory end-stage HF

and an estimated 1-year mortality over 50% with medical therapy.

ACC/AHA IIa B

Surgical LVADs

Implantable LVADs have significantly improved survival in pts with refractory cardiogenic shock, effectively bridging them to orthotopic HT or, in non-HT candidates, treating their advanced congestive HF as DT

Frazier OH et al. Ann Thorac Surg 1994;57:1416–22.
Frazier OH et al. Ann Surg 1995;222:327–36.
Long JW et al. Congest Heart Fail 2005;11:133–8.
Oz MC et al. Circulation 1997;95:1844–52.
Park SJ et al. J Thorac Cardiovasc Surg 2005;129:9 –17.
Stevenson LW et al. Circulation 2004;110:975–81.

REMATCH Trial

- 129 pts
- NYHA IV
- Ineligible for HT
- Efficacy and safety of long term support
- mechanical support vs medical therapy
- 1 year survival: 52% vs 25%

  2 years survival: 23% vs 8%
- 48% reduction in the risk of death of any cause

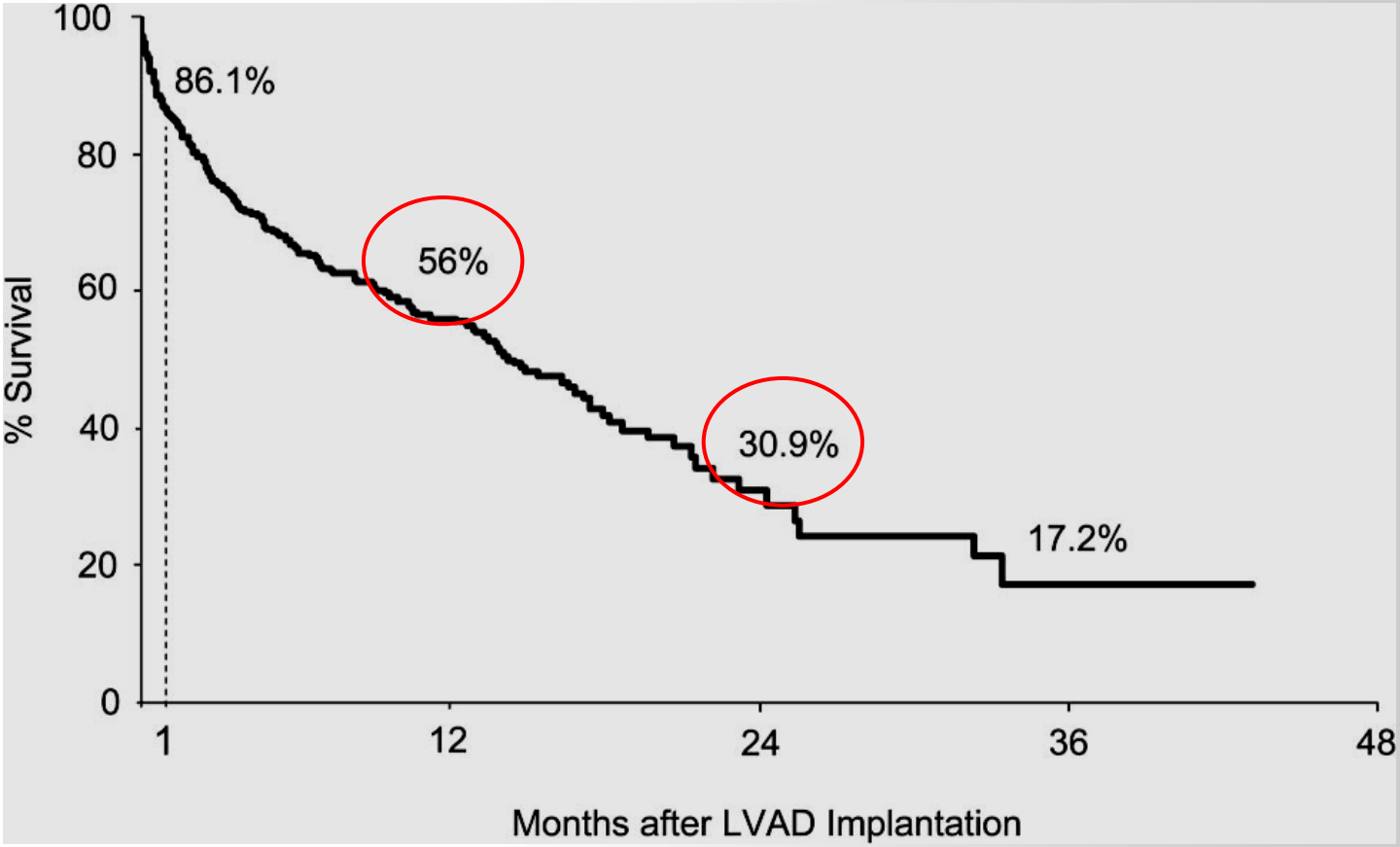
N Engl J Med 2001;345:1435-1443

LVAD as DT in the Post-Rematch Era

- 280pts
- 2001 – 2005
- HeartMate XVE LVAD (FDA approved as DT)
- investigate the impact of the modified HeartMate XVE LVAD on outcomes of DT
- identify preoperative predictors of in-hospital mortality

Circulation 2007;116:497-505

Post-Rematch Era



Survival after LVAD implantation as DT in the post-REMATCH era.

Circulation 2007;116:497-505

Causes of Death After LVAD Implantation as DT

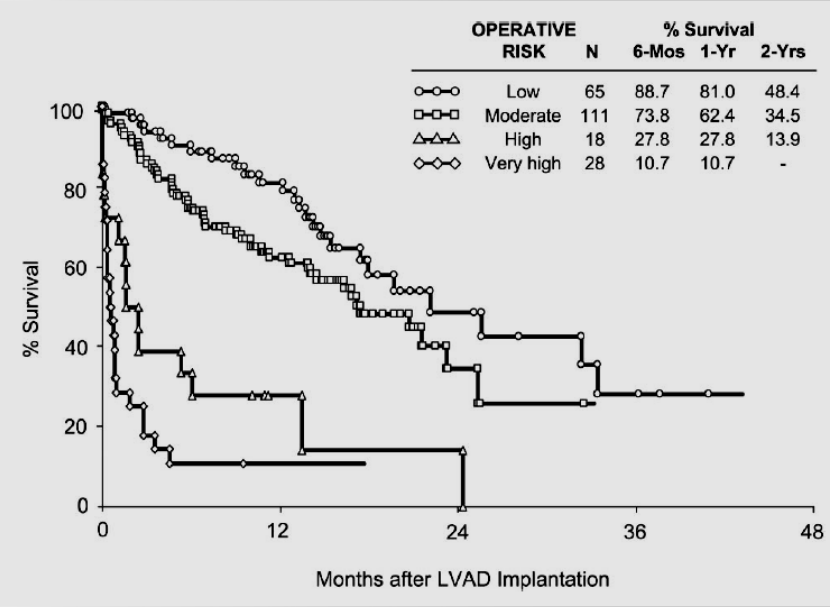
	Total Deaths (n=155)	In-Hospital Deaths (n=76)
Sepsis ★	46 (29.5)	25 (32.9)
Multiorgan failure ★	20 (12.8)	15 (19.7)
Stroke	14 (9.0)	2 (2.6)
Right heart failure ★	12 (8.4)	11 (14.5)
LVAD failure	10 (6.4)	4 (5.2)
Respiratory failure	7 (4.5)	5 (6.6)
Technical	5 (3.2)	4 (5.3)
Hemorrhage	5 (3.2)	2 (2.6)
Cancer	4 (2.6)	1 (1.3)
Arrhythmia	4 (2.6)	1 (1.3)
Accident	3 (1.9)	0
Pulmonary embolism	2 (1.3)	1 (1.3)
Sudden death	2 (1.3)	0
Left ventricular failure	2 (1.3)	0
Other causes	12 (7.7)	4 (5.2)
Not reported	7 (4.5)	1 (1.3)

Post-Rematch Era

Multivariable Analysis of Risk Factors In-Hospital Mortality After LVAD as DT Risk score

Patient Characteristics	Odds Ratio (CI)	*P*	Weighted Risk Score
Platelet count ≤148×10³/μL	7.7 (3.0 to 19.4)	<0.001	7
Serum albumin ≤3.3 g/dL	5.7 (1.7 to 13.1)	<0.001	5
International normalization ratio >1.1	5.4 (1.4 to 21.8)	0.01	4
Vasodilator therapy	5.2 (1.9 to 14.0)	0.008	4
Mean pulmonary artery pressures ≤25 mm Hg	4.1 (1.5 to 11.2)	0.009	3
Aspartate aminotransferase >45 U/mL	2.6 (1.0 to 6.9)	0.002	2
Hematocrit ≤34 %	3.0 (1.1 to 7.6)	0.02	2
Blood urea nitrogen >51 U/dL	2.9 (1.1 to 8.0)	0.03	2
No intravenous inotropes	2.9 (1.1 to 7.7)	0.03	2

Survival after LVAD implantation as DT by the candidate's operative risk



Circulation 2007;116:497-505.

LVAD as DT

Utah Artificial Heart Program

Inclusion Criteria

- NYHA IV for at least 3 m
- VO_2max < 12 ml/kg/min or iv inotropes dependence
- LVEF < 25%

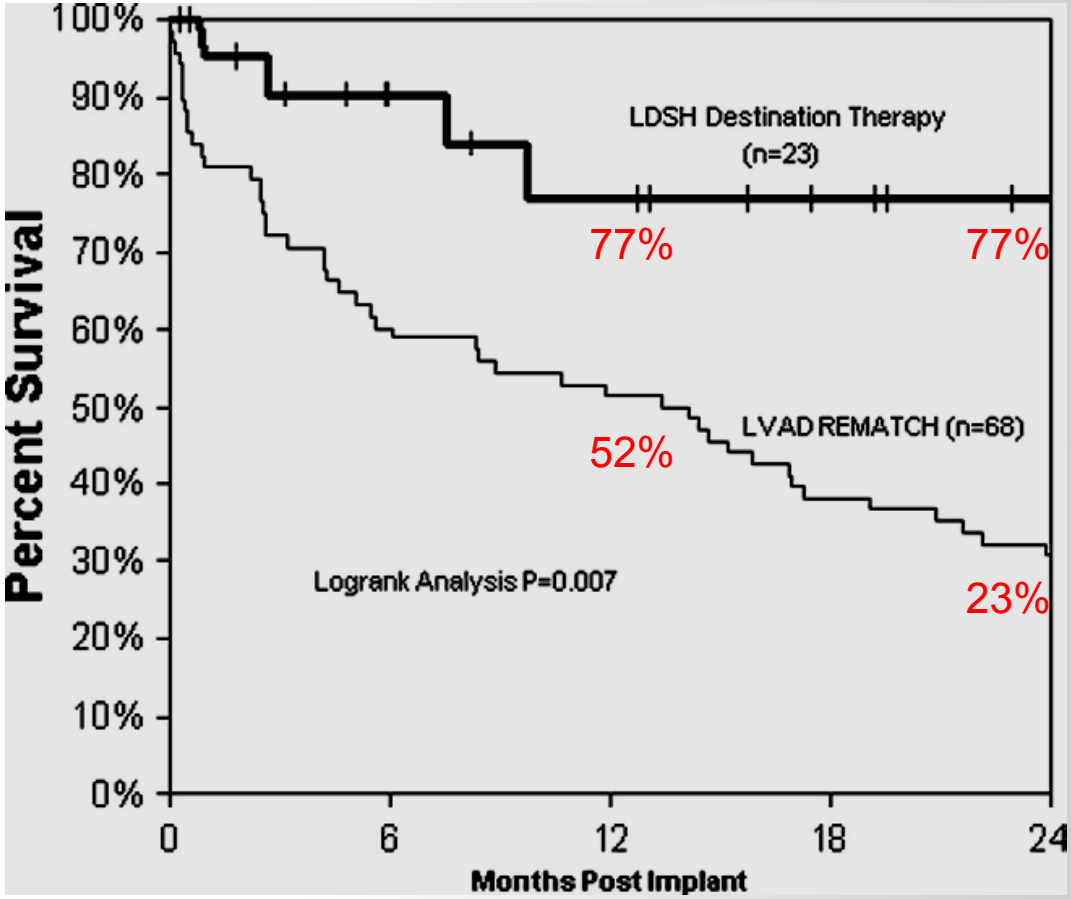
Exclusion Criteria

- Eligibility for HtTx
- Comorbid factors (< 2yrs survival)
- Small body size for HM VE or XVE (BSA<1,6m^2)

Long W et al. Improving outcomes with long-term “destination” therapy using left ventricular assist devices J Thorac Cardiovasc Surg 2008;135:1353-61.

LVAD as DT

Utah Artificial Heart Program



LDSH DT versus REMATCH LVAD.

One year post implant: REMATCH, 52% 6%; LDS DT, 77% 10%; *P .0355.*

Two years post-implant: REMATCH, 23% 6%; LDS DT, 77% 10%; *P < .0001.*

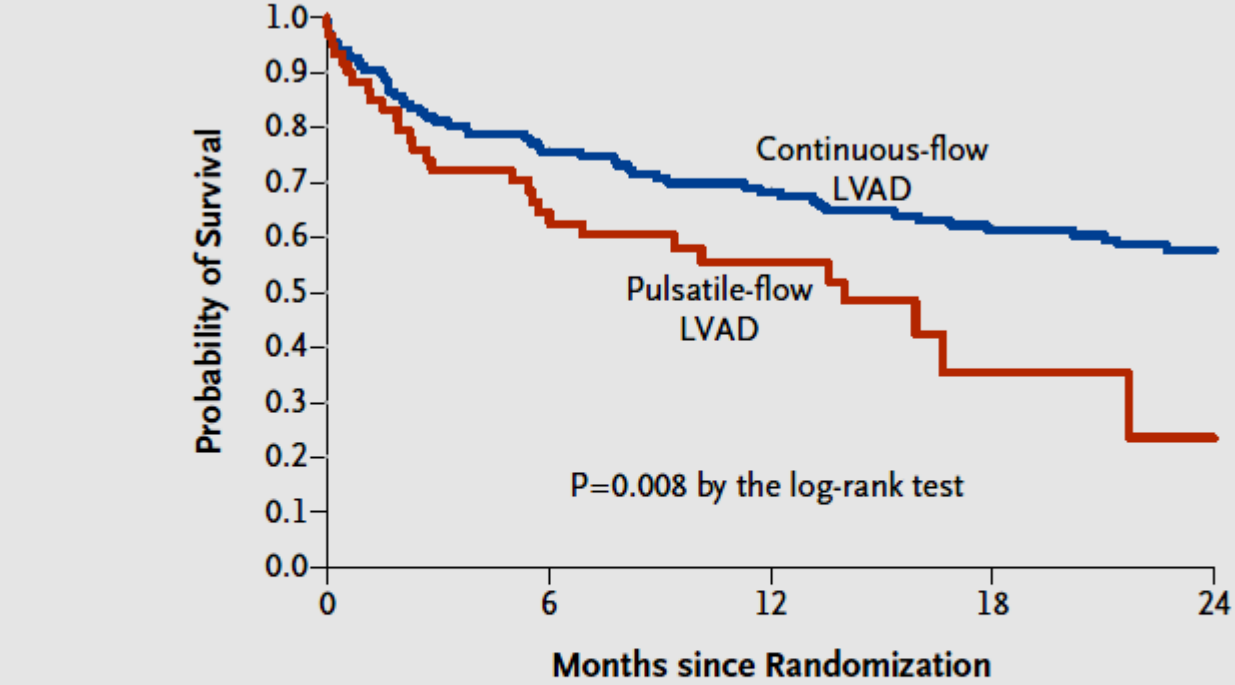
LVAD as DT

Utah Artificial Heart Program

	REMATCH (n = 68)	LDSH DT (n = 23)	*P* value
General			
Age (y)	66 ± 9.1	68 ± 8.7	.4360
Male sex (%)	78%	91%	.2204
Heart failure			
Ischemic cause (%)	78%	87%	.5456
NYHA class (IV/IIIb)	66/2	23/0	1.0000
★ VO_2 max (mL/kg/min), as obtainable	9.1 ± 2.0 (n = 37)	10.6 ± 1.4 (n = 13)	.0163*
LVEF (%EF)	17 ± 5.2	19 ± 4.4	.4102
Medications			
Digoxin (%)	87%	57%	.0056*
Loop diuretics (%)	96%	91%	.5972
Spironolactone (%)	34%	43%	.4566
ACE inhibitors (%)	62%	39%	.0881
A-II antagonists (%)	10%	22%	.1710
Amiodarone (%)	45%	30%	.2305
Beta-blockers (%)	24%	22%	1.0000
Organ function			
Serum creatinine (mmol/L)	1.7 ± 0.65	1.9 ± 1.2	.3153
★ Serum sodium (mmol/L)	135 ± 5.4	139 ± 5.8	.0079*
Hemodynamic status			
★ Systolic BP (mm Hg)	101 ± 15	108 ± 10	.0533
Diastolic BP (mm Hg)	61 ± 10	61 ± 9	1.0000
★ PCWP (mm Hg)	25 ± 9.9	20 ± 7.8	.0196*
CI (L*min^-1*m^-2)	1.9 ± 0.99	2.2 ± 0.51	.1684
Heart rate (beats/min)	84 ± 16	81 ± 13	.4170
PVR (Wood Units)	3.4 ± 1.8	3.2 ± 1.6	.6382
IABP (%)	10%	13%	1.0000
IV inotropes (%)	65%	61%	.8041

Small trend towards selecting slightly less compromised pts

LVAD as DT

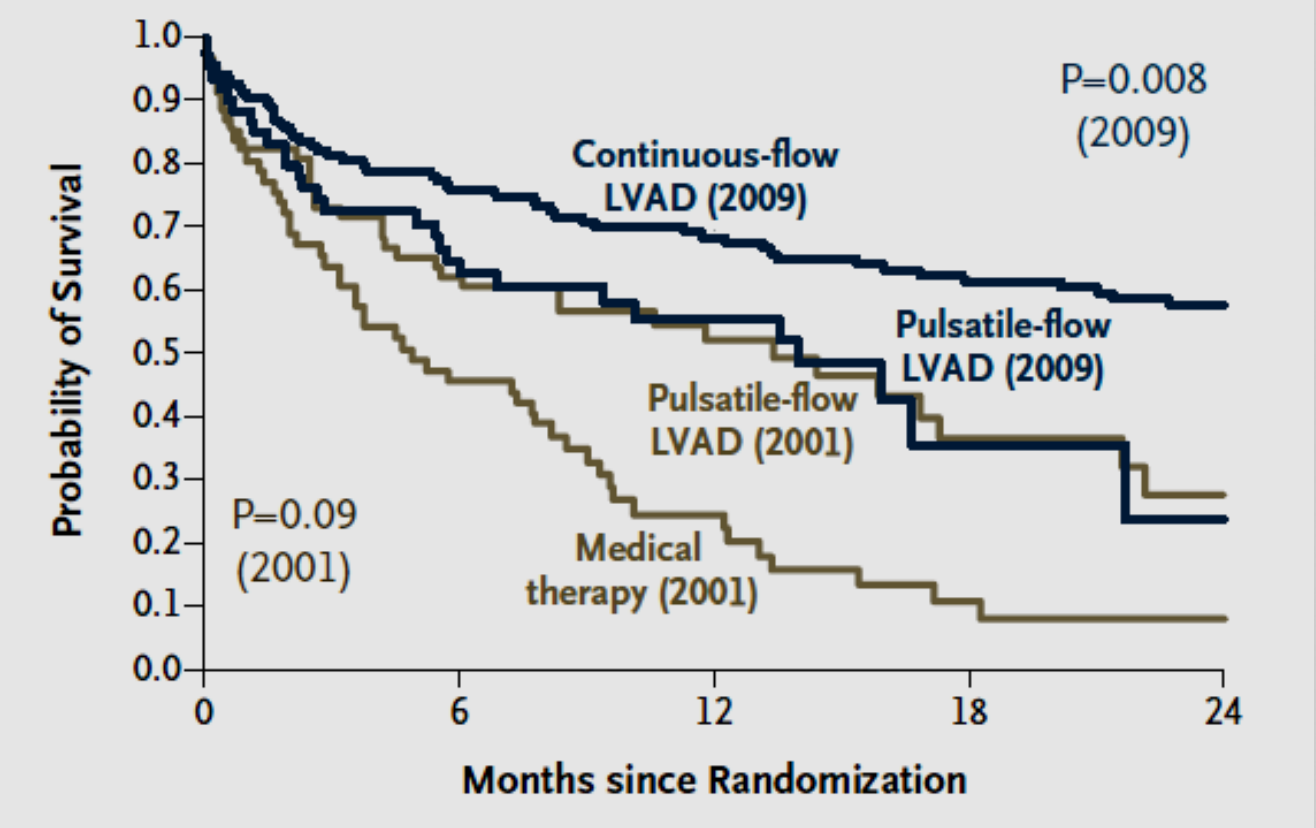


Kaplan–Meier Estimates of Survival from the As-Treated Analysis,According to Treatment Group.

Of the 59 patients who had a pulsatile-flow LVAD, 20 had the device replaced during the study period, with 18 (31%) receiving a continuous-flow LVAD instead of another pulsatile-flow LVAD. By 2 years, only 2 patients had a pulsatile-flow LVAD, both of whom had replacement devices.

Slaughter M et al. Advanced Heart Failure Treated with Continuous-Flow Left Ventricular Assist Device N Engl J Med 2009;361.

LVAD as DT

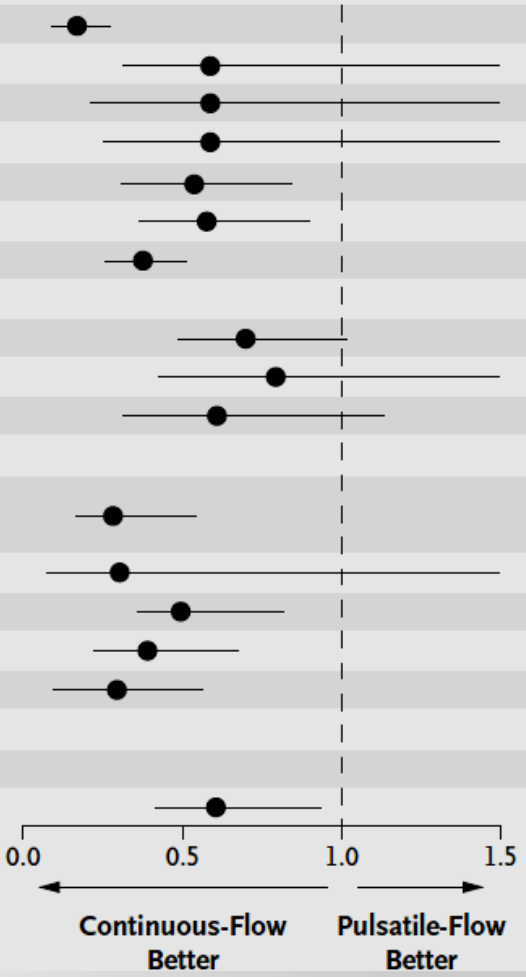


Survival Rates in Two Trials of Left Ventricular Assist Devices (LVADs) as Destination Therapy.

Fang J. Rise of the Machines - Left Ventricular Assist Devices as Permanent Therapy for Advanced Heart Failure NEJM 2009; 361:2282-2285.

LVAD as DT

Subgroup	Continuous-Flow LVAD (N=133) (211 patient-yr) no. (%)	no. of Events/ Patient-Yr	Pulsatile-Flow LVAD (N=59) (41 patient-yr) no. (%)	no. of Events/ Patient-Yr	P Value for Interaction
Pump replacement	12 (9)	0.06	20 (34)	0.51	<0.001
Stroke	24 (18)	0.13	8 (14)	0.22	0.21
Ischemic	11 (8)	0.06	4 (7)	0.10	0.38
Hemorrhagic	15 (11)	0.07	5 (8)	0.12	0.33
LVAD-related infection	47 (35)	0.48	21 (36)	0.90	0.01
Local non-LVAD infection	65 (49)	0.76	27 (46)	1.33	0.02
Sepsis	48 (36)	0.39	26 (44)	1.11	<0.001
Bleeding					
Bleeding requiring PRBC	108 (81)	1.66	45 (76)	2.45	0.06
Bleeding requiring surgery	40 (30)	0.23	9 (15)	0.29	0.57
Other neurologic event	29 (22)	0.17	10 (17)	0.29	0.14
Right heart failure					
Managed with extended use of inotropes	27 (20)	0.14	16 (27)	0.46	<0.001
Managed with RVAD	5 (4)	0.02	3 (5)	0.07	0.12
Cardiac arrhythmia	75 (56)	0.69	35 (59)	1.31	0.006
Respiratory failure	50 (38)	0.31	24 (41)	0.80	<0.001
Renal failure	21 (16)	0.10	14 (24)	0.34	<0.001
Hepatic dysfunction	3 (2)	0.01	0	0.00	
LVAD thrombosis	5 (4)	0.02	0	0.00	
Rehospitalization	107 (94)	2.64	42 (96)	4.25	0.02



Adverse Events and Associated Relative Risks from the As-Treated Analysis, According to Treatment Group.

Slaughter M et al. N Engl J Med 2009;361.

LVAD as Bridge to Recovery

- 1st reported case of BTR in a pt with idiopathic cardiomyopathy in 1996

  J Heart Lung Transplant 1996;15:840–2

- Several groups have reported their experience with variable success rates (5-36%)

Circulation 1998;98:2383–9.	Retrospective	5/111 explanted
J Heart Lung Transplant 2003;22:137–46.	Kahn et al	6/16 explanted (DCM 100%)
Ann Thorac Surg 2000;70:1255–8.	Helman et al	8/24 explanted (DCM 100%)
J Heart Lung Transplant 2001;20:209–10.	El Banayosy et al	1/13 explanted
J Heart Lung Transplant 2005;25:S107.	Berlin Heart Group	33% explanted (DCM 100%)
J Am Coll Cardiol 2005;41:165A.	Multicenter Study	6/61 explanted (DCM 55%, IHD 45%)
Circulation 2007;115:2497-2505	Multicenter Study LVAD Working Group	6/67 explanted

LVAD as Bridge to Recovery

- Harefield Experience:

  11 out 15pts (73%) with non-ishemic CM

  after receiving clenbuterol on top of classic therapy

  while being on LVAD support

  were weaned off the mechanical support

  N Engl J Med 2006;355:1873-84

- Harefield Recovery Protocol Study (HARPS)
- Safety Study of Clenbuterol in Combination With LVAD to Treat Chronic HF (HARPS)

Eligibility Criteria for LVAD

- No guidelines for patient selection
- No prospective randomized trials

  (aside REMATCH trial

  and FDA mandated Registry maintained by Thoratec)

- NYHA class III / IV,

  Stage C or D ACC/AHA
- LVEF < 25%
- Peak VO_2 < 12ml/kg/min
- Significant functional limitation > 3m

Rose EA et al. Randomized Evaluation of Mechanical Assistance for the Treatment of CHF (**REMATCH**) study group. Long-term mechanical left ventricular assistance for end-stage HF. N Engl J Med 2001;345:1435–43.

Eligibility Criteria for LVAD

- Percent predicted VO_2max: highest prognostic value
- <55% of the predicted for age, gender and BSA
- Anaerobic threshold should be reached
- RER > 1,1
- Without iv inotropes

Miller LW. Transplantation 1998;66:947–51.
Mancini D et al. Circulation 2000;101:1080–2.
Osada N et al. JAMA 1998;31577–82.
Stelken AM et al. J Am Coll Cardiol 1996;27:345–52

Eligibility Criteria for LVAD

- Pts considered for long-term iv inotropes should be assessed for LVAD therapy.

Hershberger REJ Cardiac Fail 2003;9:180 –7.

Stevenson LW Circulation 2003;108:492–7.

Jaski BE t al. J Heart Lung Transplant 2001;20:449–56.

Aaronson KD et al. JAMA 2002;39:1247–54.

- Inability to take neurohormonal antagonists (ACE inhibitors or ARBs)

Rose EA et al. N Engl J Med 2001;345:1435–43

Butler J et al. J Am Coll Cardiol 2005;45(suppl A):154.

- Development of significant renal impairment (cardiorenal syndrome)

Heywood JT et al. Heart Fail Rev 2004;9:195–201.

Butler J et al. Am Heart J 2004;147:331–8.

- BSA > 1,5m^2

Risk Factors with LVAD

Renal Function

- Cr, BUN, Urine Output/8h, Cl_{Cr}
- Cr < 3,5mg/dl (REMATCH)
- Renal dysfunction reversibility

(Cl_{Cr} measurement with CI>2,4 for 1-2days on iv inotropes support)

- Renal function assessment

24h Urine test for Cl_{Cr} , Inflammatory cells/Eosinophils

Albumin, Renal Biopsy, Abdominal Ultrasound

- Mandatory Urine Output > 1ml/kg/hour pre VAD implantation

Risk Factors with LVAD

Right Ventricular Failure

•Non-ischemic pts often have significant RV failure

(3-4-fold ↑ risk for bi-V support need)

Smith GL et al. J Cardiac Fail 2003;9:13–25.
Bart BA et al. J Am Coll Cardiol 2005;46:2043–6.

•↑ risk for RV failure post-LVAD with

a. temporary mechanical support preoperatively
b. female gender
c. non-ischemic origin
d. ↓ RV Stroke Work Index
e. $\downarrow PAP_{mean}$
f. RAP > PCWP
g. ↑ RVEDV

Ochiai Y et al. Circulation 2002;106(suppl):I-198 –I-202.

Risk Factors with LVAD

Right Ventricular Failure

- RV failure deteriorates renal dysfunction

(RAP > 20 mmHg reduces glomerular filtration)

Firth JD et al. Lancet 1988;1:1033–5.

- RAP > 15mmHg
- RV recovery delay post LV decompression

(interventricular dependence)

Risk Factors with LVAD

Hemodynamic Indices

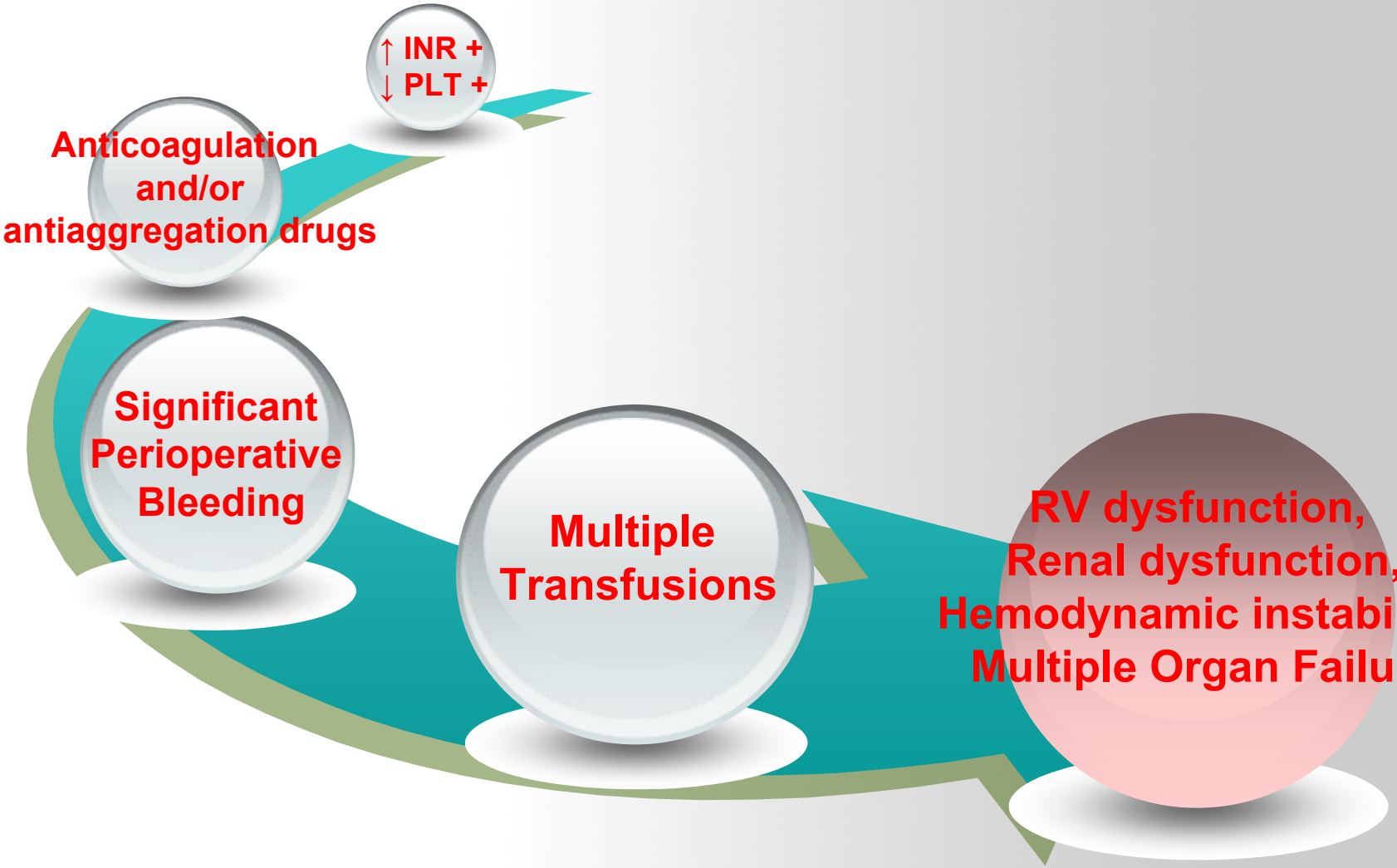
- SV rather than CO especially when ↑↑ HR

(CO overestimates ventricular function)

- CO should be measured by both Fick and thermodilution tecnique.
- Mixed Venous Saturation
- Pulmonary Artery Saturation
- RAP

Risk Factors with LVAD

Coagulation Factors



Goldstein DJ et al. Ann Thorac Surg 1995;59:1063–8.

Risk Factors with LVAD

Coagulation Factors

- Abnormal Coagulation (↑ INR)

(anti-coagulation drugs, chronically ↑ RAP and cardiac cirrhosis)

- Nutritional basis

(Factor VII depletion)

- Screening tests

PT, aPTT, INR, PLT, platelet aggregation studies, HIT assay

- Presence of HIT is associated with ↑↑ mortality rates perioperatively

Dewald O et al. Artif Organs 2005;29:292–9.

Risk Factors with LVAD

Liver Function

•3-fold increase of LFTs

(Total Bilirubin, ALT, AST)

is an independent risk factor for adverse outcome

(cardiac cirrhosis, drug-related, cholestatic jaundice, alcohol)

Stevenson LW et al. Ann Thorac Surg 1996;61:380–7.
Aaronson KD et al. Ann Thorac Surg 2003;75(suppl 6):S29 –35.

•Screening tests

a.Hepatitis A, B, C and other viruses tests

b.Abdominal Ultrasound

c.Liver Biopsy (Right Jugular approach)

Risk Factors with LVAD

Nutrition

- Serum Albumin lacks sensitivity and specificity
- Pre-Albumin: better indice of nutritional status
- Alb < 3,3gr/dl related to 6,6-fold ↑ mortality

Lietz K et al. N Engl J Med 2006

- Poor wound healing
- ↑ risk of infection
- T-lymphocyte malfunction

Risk Factors with LVAD

Nutrition

- 22 < Body Mass Index < 36
- BMI > 40: ↑ risk of infection
- Cachexia is worse risk factor than obesity

Filippatos GS, Anker SD, Kremastinos DT. Curr Opin Clin Nutr Metab Care 8:249 –54.

Reeves BC et al. J Am Coll Cardiol 2003;42:668–76.

- Poor Apetite, ↑ TNF, ↑ Cytokines, limited exertion, early satiety

Risk Factors with LVAD

Nutrition

- Feeding cessation for 24h results in 50% reduction in

a. acute phase proteins

b. critical proteins for wound healing

- Screening tests:

a. Serum Albumin

b. Prealbumin (transthyretin)

Risk Factors with LVAD

Pulmonary Function

- Implantable large pulsatile LVADs
- Impaired diaphragm motion
- Screening tests:

a.CXR (lung disease, diaphragms)

b.PFTs

c.FEV, FEV1, DLCO

Risk Factors with LVAD

Pulmonary Function

- PMH

a. COPD

b. Intrinsic lung disease

c. Smoking

- PFTs: <50% of pred values → HRCT
- O_2SAT < 92% → rule out:

a. R to L shunt

b. Thromboembolic disease

Risk Factors with LVAD

Malignancies

•Age and gender guided preoperative screening test for cancer

e.g. Colonoscopy for any candidate >55yrs

(American Medical Association, American Cancer Society)

Risk Factors with LVAD

Psychiatric Evaluation

- Psychiatric pathology
- Uknown chemical dependencies and social problems
- Network support
- Neurocognitive tests

(tests on VAD function prior to the implantation for pts and next of keen)