LVAD and Destination Therapy:
How much should I push on Technology ?

Antonio Loforte, MD, PhD

S. Orsola Hospital, Bologna University,
Dept Cardiothoracic, Transplantation and Vascular Surgery,
Bologna, Italy

No Disclosures

Antonio Loforte, MD, PhD

S. Orsola Hospital, Bologna University,
Dept Cardiothoracic, Transplantation and Vascular Surgery,
Bologna, Italy

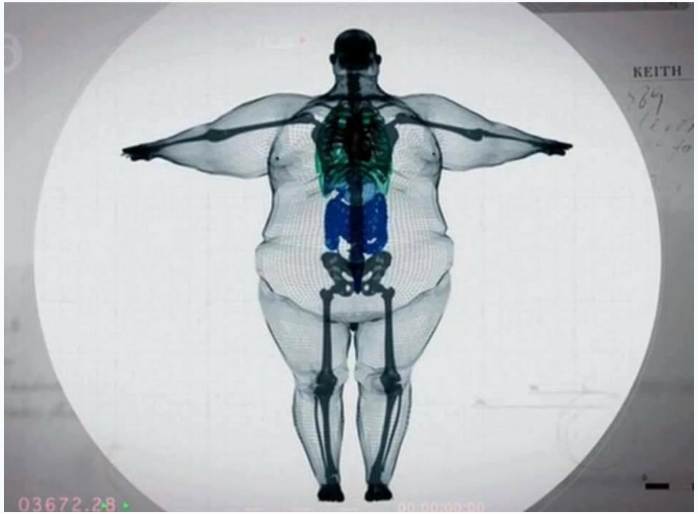
1974 – Workshop on Left Ventricular Assist

Transplantation has established that replacing the patient's own worn-out pump with a healthy one corrects the attendant circulatory ills. Hence, it can be expected that upon receipt of a well-functioning mechanical circulatory device, the patient will be restored to a healthy, productive life.

Theodore Cooper, M.D.
Director, NHLI, and
Chairman of the Workshop on
Left Ventricular Assist Pump

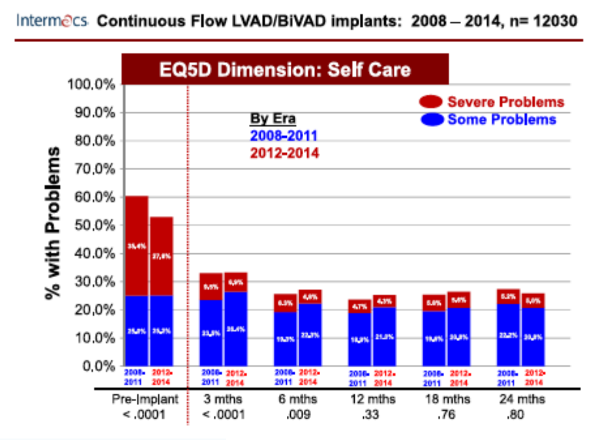
DT definition …

Vs.



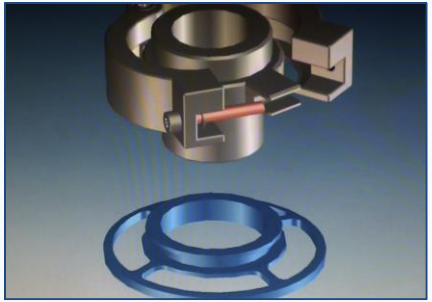
There will be no more DT category definition …

DT: it might be restriction or … pt choice

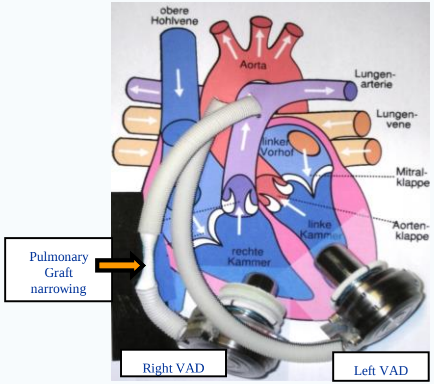


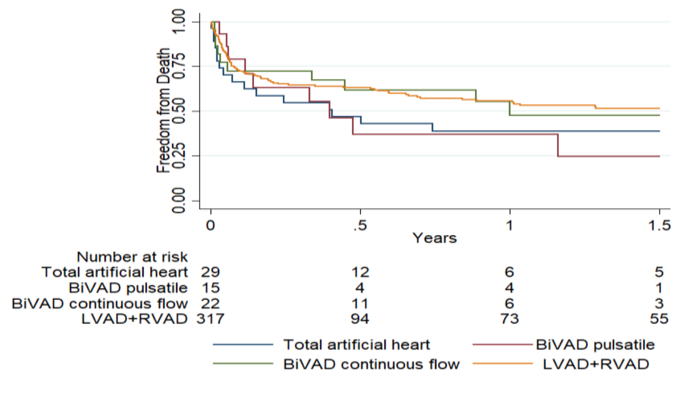
J Heart Lung Transplant 2015;34:1495–1504

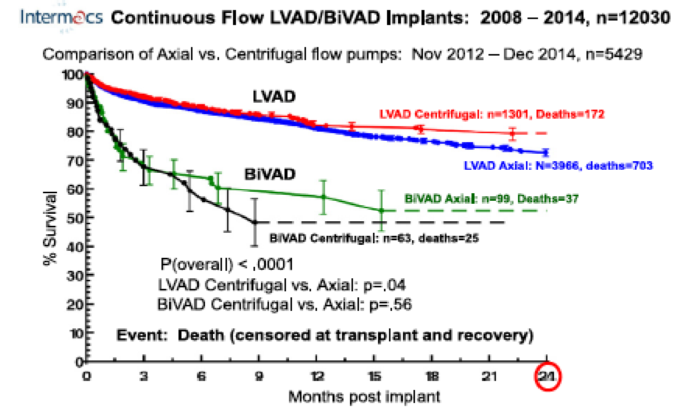
Durability



EUROMACS







J Heart Lung Transplant 2015;34:1495–1504

Am J Cardiol 2015;116:573–579

Comparison of 2-Year Outcomes of Extended Criteria Cardiac Transplantation Versus Destination Left Ventricular Assist Device Therapy Using Continuous Flow

Mani A. Daneshmand, MD[a], Arun Krishnamoorthy, MD[b,c,*], Marc D. Samsky, MD[b], G. Michael Felker, MD, MHS[b,c], John A. Pura, MPH[c], Yuliya Lokhnygina, PhD[c], Adrian F. Hernandez, MD, MHS[b,c], Paul B. Rosenberg, MD[b], Laura J. Blue, NP[b], Jacob N. Schroder, MD[a], Joseph G. Rogers, MD[b,c], Carmelo A. Milano, MD[a], and Chetan B. Patel, MD[b,c]

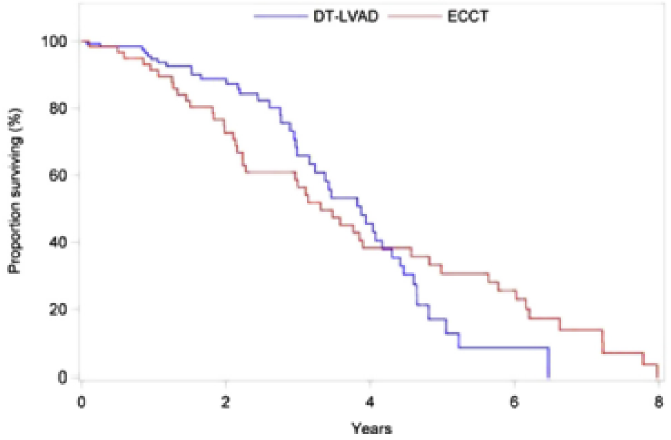


Figure 1. Kaplan–Meier estimates of survival for extended criteria cardiac transplantation versus continuous flow destination therapy left ventricular assist device recipients, in the overall unmatched cohort.

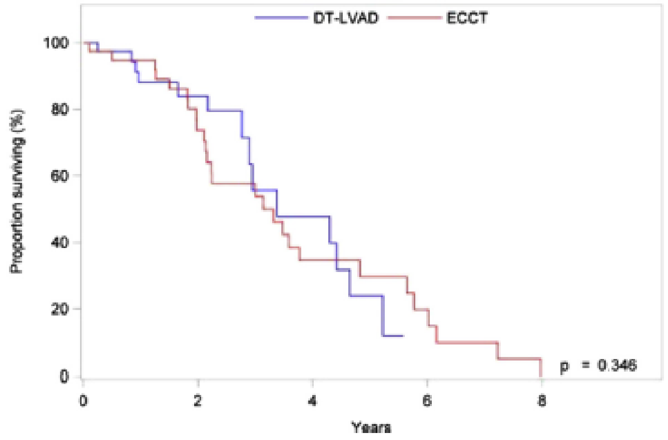
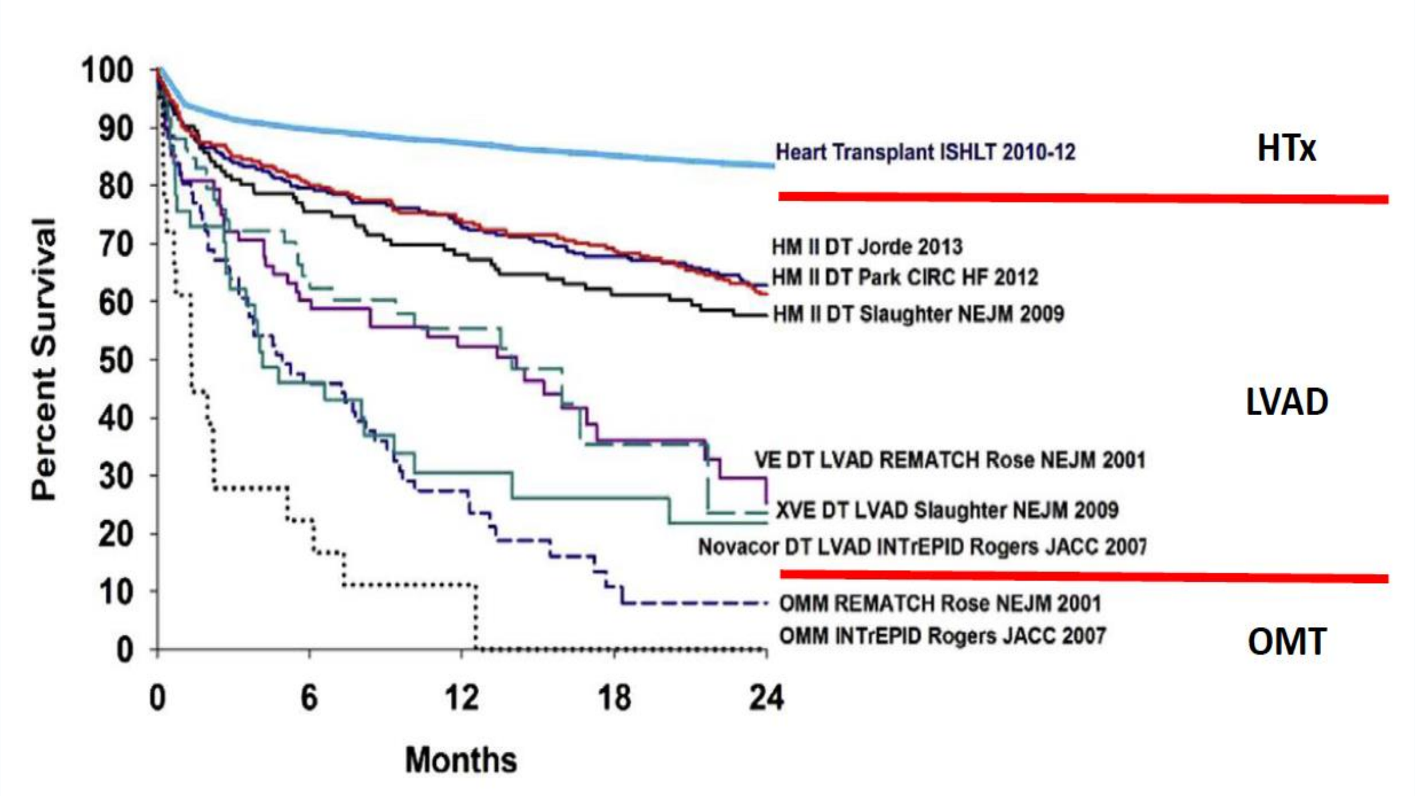


Figure 2. Kaplan–Meier estimates of survival for extended criteria cardiac transplantation versus continuous flow destination therapy left ventricular assist device recipients, after propensity score matching.


Percent Survival
100
90
80
70
60
50
40
30
20
10
0
0
6
12
18
24
Months
Heart Transplant ISHLT 2010-12
HM II DT Jorde 2013
HM II DT Park CIRC HF 2012
HM II DT Slaughter NEJM 2009
VE DT LVAD REMATCH Rose NEJM 2001
XVE DT LVAD Slaughter NEJM 2009
Novacor DT LVAD INTrEPID Rogers JACC 2007
OMM REMATCH Rose NEJM 2001
OMM INTrEPID Rogers JACC 2007
HTx
LVAD
OMT

Seventh INTERMACS annual report: 15,000 patients and counting

James K. Kirklin, MD,[a] David C. Naftel, PhD,[a] Francis D. Pagani, MD, PhD,[b] Robert L. Kormos, MD,[c] Lynne W. Stevenson, MD,[d] Elizabeth D. Blume, MD,[e] Susan L. Myers, BBA, QMIS,[a] Marissa A. Miller, DVM, MPH,[f] J. Timothy Baldwin, PhD,[f] and James B. Young, MD[g]

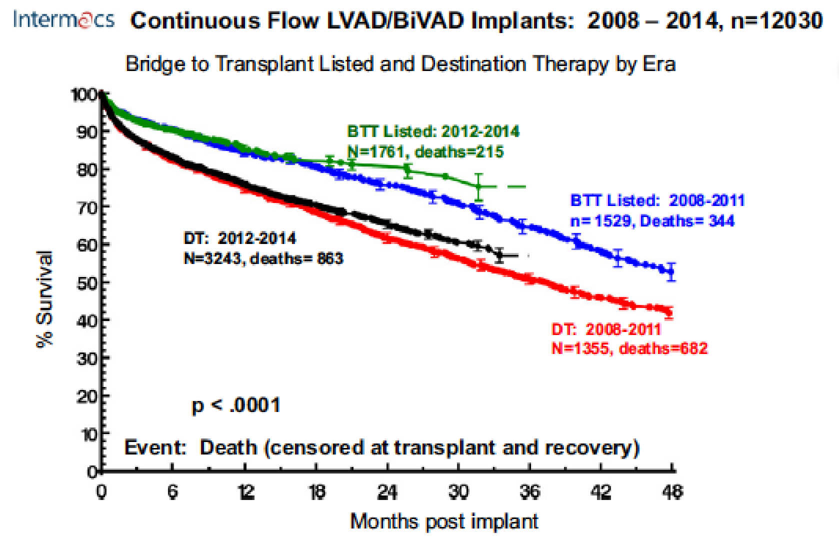


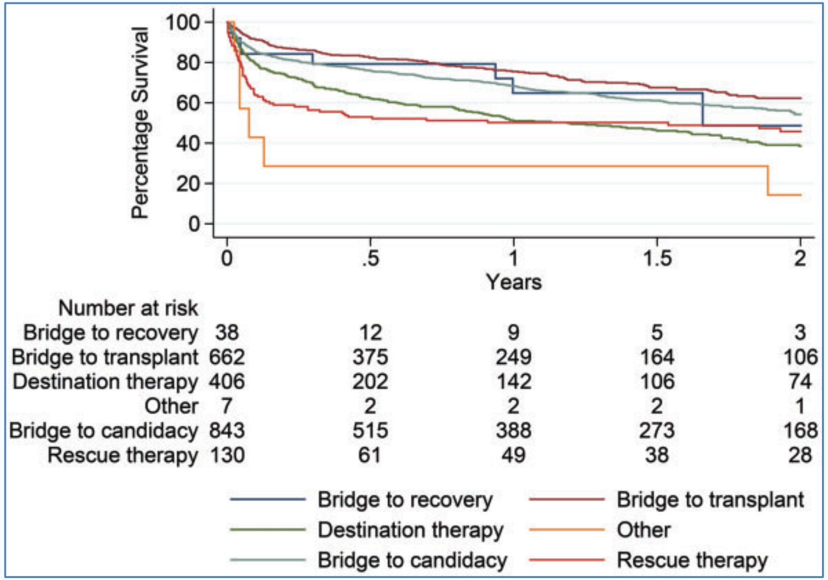
Table 2 CF and BiVAD Implants: April 2008 to December 2014 ($n = 12,030$)

Device strategy at time of implant	2008 to 2011 N	2008 to 2011 %	2012 N	2012 %	2013 N	2013 %	2014 N	2014 %	Total N	Total %
BTT listed	1,529	32.2%	404	18.2%	623	23.6%	734	30.3%	3,290	27.3%
BTT likely	1,163	24.5%	513	23.1%	511	19.3%	323	13.3%	2,510	20.9%
BTT moderate	480	10.1%	230	10.4%	273	10.3%	187	7.7%	1,170	9.7%
BTT unlikely	164	3.5%	73	3.3%	67	2.5%	54	2.2%	358	3.0%
DT	1,355	28.6%	983	44.2%	1,152	43.6%	1,108	45.7%	4,598	38.2%
BTR	29	0.6%	11	0.5%	10	0.4%	4	0.2%	54	0.5%
Rescue therapy	15	0.3%	7	0.3%	6	0.2%	10	0.4%	38	0.3%
Other	9	0.2%	0	0%	0	0%	3	0.1%	12	0.1%
Total	4,744	100%	2,221	100%	2,642	100%	2,423	100%	12,030	100%

Implant era (years): 2008 to 2011, 2012, 2013, 2014

J Heart Lung Transplant 2015;34:1495–1504

The European Registry for Patients with Mechanical Circulatory Support (EUROMACS) of the European Association for Cardio-Thoracic Surgery (EACTS): second report



Strategy	<50 years	50–64 years	65–70 years	>70 years	Total
Bridge to recovery	24 (2)	28 (2)	3 (1)	2 (1)	57 (2)
Bridge to candidacy	402 (42)	568 (39)	60 (18)	22 (12)	1052 (36)
Bridge to transplant	332 (34)	414 (28)	48 (14)	19 (10)	813 (28)
Destination therapy	22 (2)	170 (12)	157 (47)	109 (60)	458 (16)
Rescue therapy	68 (7)	105 (7)	19 (6)	18 (10)	210 (7)
Other	4 (0)	5 (0)	2 (1)	0 (0)	11 (0)
Unknown	112 (12)	176 (12)	45 (13)	13 (7)	346 (12)
Total	964	1466	334	183	2947

European Journal of Cardio-Thoracic Surgery 0 (2017) 1–8

But … still AEs

Table 3. Major Adverse Events in the Per-Protocol Population.*

Event	Centrifugal-Flow Pump Group (N = 151)		Axial-Flow Pump Group (N = 138)		Relative Risk (95% CI)	P Value
	no. of patients with events (%)	*no. of events*	*no. of patients with events (%)*	*no. of events*		
Suspected or confirmed pump thrombosis	0	0	14 (10.1)	18	NA	<0.001
Stroke						
Any stroke	12 (7.9)	12	15 (10.9)	17	0.73 (0.35–1.51)	0.39
Hemorrhagic stroke	4 (2.6)	4	8 (5.8)	8	0.46 (0.14–1.48)	0.18
Ischemic stroke	8 (5.3)	8	9 (6.5)	9	0.81 (0.32–2.05)	0.66
Disabling stroke	9 (6.0)	9	5 (3.6)	5	1.65 (0.57–4.79)	0.36
Other neurologic event†	9 (6.0)	9	8 (5.8)	8	1.03 (0.41–2.59)	0.95
Bleeding						
Any bleeding	50 (33.1)	100	54 (39.1)	98	0.85 (0.62–1.15)	0.29
Bleeding requiring surgery	15 (9.9)	15	19 (13.8)	21	0.72 (0.38–1.36)	0.31
Gastrointestinal bleeding	24 (15.9)	47	21 (15.2)	36	1.04 (0.61–1.79)	0.87
Sepsis	14 (9.3)	19	9 (6.5)	10	1.42 (0.64–3.18)	0.39
LVAS drive-line infection	18 (11.9)	21	9 (6.5)	11	1.83 (0.85–3.93)	0.12

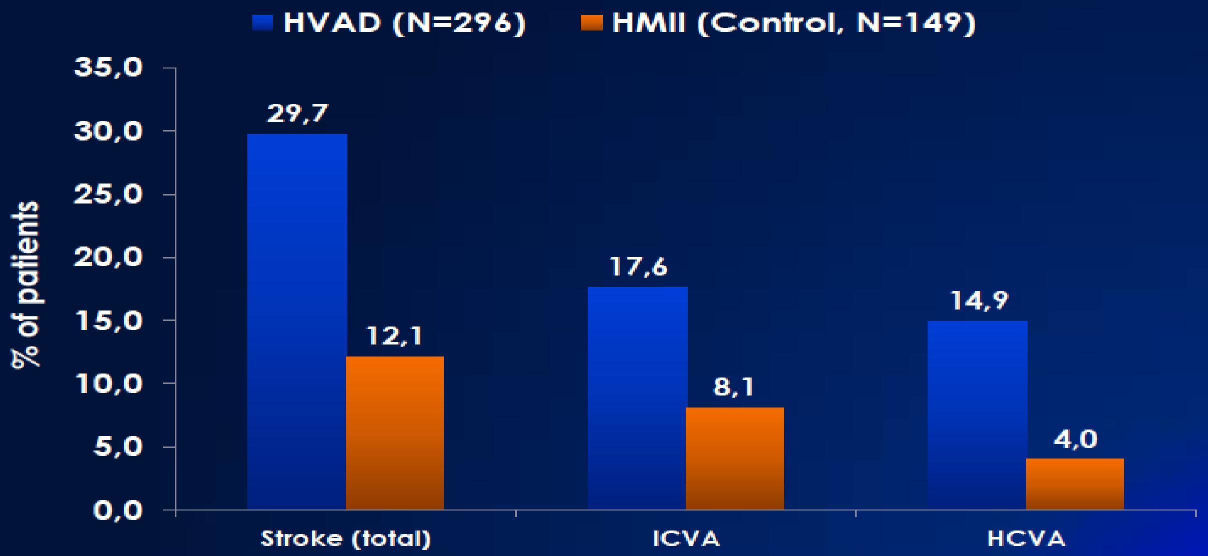
Mehra et al . A Fully Magnetically Levitated Circulatory Pump for Advanced Heart Failure NEJM 2017 Feb 2;376(5):440-450

Table 3. Major Adverse Events in the Per-Protocol Population.*

Event	Centrifugal-Flow Pump Group (N = 189)		Axial-Flow Pump Group (N = 172)		Hazard Ratio (95% CI)	P Value†
	no. of patients with event (%)	*no. of events*	*no. of patients with event (%)*	*no. of events*		
Suspected or confirmed pump thrombosis	2 (1.1)	2	27 (15.7)	33	0.06 (0.01–0.26)	<0.001
Pump thrombosis resulting in reoperation or removal of device	0	0	21 (12.2)	25	NA	<0.001
Stroke						
Any stroke	19 (10.1)	22	33 (19.2)	43	0.47 (0.27–0.84)	0.02
Hemorrhagic stroke	8 (4.2)	8	16 (9.3)	17	0.42 (0.18–0.98)	0.06
Ischemic stroke	12 (6.3)	14	23 (13.4)	26	0.44 (0.22–0.88)	0.03
Disabling stroke	13 (6.9)	15	9 (5.2)	11	1.25 (0.54–2.93)	0.66
Other neurologic event‡	22 (11.6)	25	15 (8.7)	16	1.27 (0.66–2.45)	0.39
Bleeding						
Any bleeding	81 (42.9)	187	90 (52.3)	206	0.71 (0.53–0.96)	0.07
Bleeding that led to surgery	23 (12.2)	29	30 (17.4)	34	0.66 (0.38–1.13)	0.18
Gastrointestinal bleeding	51 (27.0)	107	47 (27.3)	100	0.92 (0.62–1.37)	1.00
Sepsis	26 (13.8)	37	24 (14.0)	28	0.95 (0.55–1.66)	1.00
LVAS drive-line infection	45 (23.8)	68	34 (19.8)	59	1.15 (0.73–1.79)	0.37
Local infection not associated with LVAS	70 (37.0)	108	60 (34.9)	114	1.00 (0.71–1.42)	0.74
Right heart failure						
Any right heart failure	60 (31.7)	73	48 (27.9)	53	1.12 (0.77–1.64)	0.49
Right heart failure managed with RVAS	6 (3.2)	6	8 (4.7)	8	0.67 (0.23–1.94)	0.59
Cardiac arrhythmia						
Any cardiac arrhythmia	71 (37.6)	108	70 (40.7)	105	0.88 (0.63–1.23)	0.59
Ventricular arrhythmia	45 (23.8)	67	39 (22.7)	64	1.04 (0.67–1.59)	0.80
Supraventricular arrhythmia	33 (17.5)	40	36 (20.9)	37	0.79 (0.49–1.26)	0.42
Respiratory failure	45 (23.8)	61	39 (22.7)	46	1.04 (0.68–1.59)	0.80
Renal dysfunction	25 (13.2)	29	18 (10.5)	18	1.23 (0.67–2.25)	0.52
Hepatic dysfunction	8 (4.2)	8	7 (4.1)	7	0.98 (0.36–2.71)	1.00

2018, at NEJM.org.

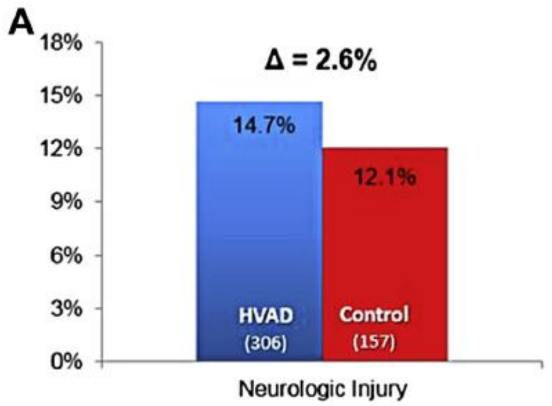
Background: Stroke Events in ENDURANCE at **2 Years** on the original device



ICVA: Ischemic cerebrovascular accident;
HCVA: Hemorrhagic Cerebrovascular accident
Rogers JG and Pagani FD et al. NEJM 2017; 376:451-460.

	HVAD ENDURANCE (n = 296)	HVAD ENDURANCE Supplemental (n = 308)	p Value
All stroke	22.3	16.9	0.10
Ischemic cerebrovascular event	13.9	13.0	0.81
Hemorrhagic cerebrovascular event	10.5	5.2	0.02
Disabling stroke	8.1	6.5	0.53
Transient ischemic attack	5.4	4.2	0.57

JACC: HEART FAILURE VOL. 6, NO. 9, 2018
SEPTEMBER 2018:792-802

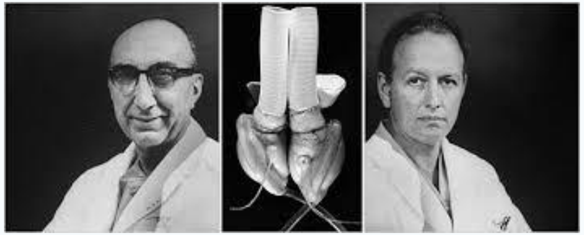


Neurologic injury was defined as any stroke with MRS > 0 at 24 weeks post-stroke, or a TIA, or spinal cord injury. *Note: this endpoint does not include device exchange*

	Study Device (n = 308)		Control Device (n = 157)		
	Patients With Events	Number of Events	Patients With Events	Number of Events	p Value
Major bleeding	159 (51.6)	310	89 (56.7)	196	0.33
Cardiac arrhythmia	105 (34.1)	151	49 (31.2)	56	0.60
Hepatic dysfunction	12 (3.9)	12	6 (3.8)	6	>0.99
Hypertension	40 (13.0)	54	20 (12.7)	21	>0.99
Major infection	166 (53.9)	300	93 (59.2)	181	0.28
Driveline exit site infection	50 (16.2)	59	19 (12.1)	22	0.27
Device malfunction/failure	74 (24.0)	107	38 (24.2)	47	>0.99
Hemolysis	4 (1.3)	5	9 (5.7)	9	0.01
Stroke	52 (16.9)	75	23 (14.6)	25	0.60
Ischemic cerebrovascular event	40 (13.0)	58	12 (7.6)	14	0.09
Hemorrhagic cerebrovascular event	16 (5.2)	17	11 (7.0)	11	0.53
TIA	13 (4.2)	13	1 (0.6)	1	0.04
Renal dysfunction	32 (10.4)	35	23 (14.6)	25	0.22
Respiratory failure	61 (19.8)	77	31 (19.7)	37	>0.99
Right heart failure	109 (35.4)	116	60 (38.2)	65	0.61
Pump replacement	16 (5.2)	NA	18 (11.5)	NA	0.02
Exchange for pump thrombosis	14 (4.5)	NA	16 (10.2)	NA	0.03


Why
How
When
What
Where
Who

Look at History to get the Present …

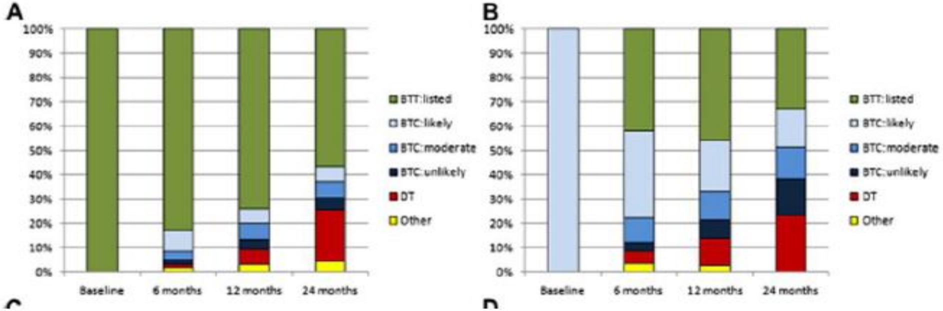


- 1909 Carrel, Htx in animals
- 1938 Demikhov - 1964 DeBakey, Liotta , TAH project in animals
- 1966 DeBakey, **Partial Artificial Heart** (LVAD) … due **lack of TAH and Htx**
- 1967 Barnard, Heart Transplantation
- 1969 Cooley, **two-stage Cardiac Replacement** concept (TAH) … due to **lack of donors (DCD)** … with 'Shumway Stanford Nightmare' concept
- March1971: 167 Htx in 20 countries with 143 deaths … **Htx abandon** for a decade … **Research funds** redirected **towards implantable LVAD as permanent support**
- 1985 Copeland, **TAH as successful BTT** … thx to Cyclosporine
- 1994, 1998 **FDA** approval for pulsatile LVAD as **BTT**
- 1998 Hetzer, DeBakey, first **CF LVAD** implanted
- 2002, **FDA** approval for **DT** treatment

2018, we do have again a lack of donors matter and Htx seems to be not enough …

What Happens To Transplant Eligibility After Prolonged VAD Support? 1/3 of Surviving Candidates No Longer Listed

Teuteberg. G. Stewart et al JACC 2013



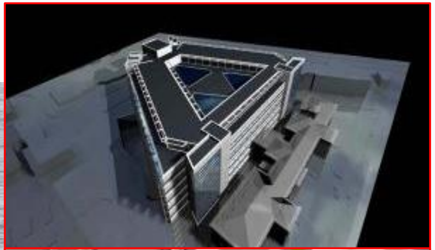
Listed at Implant | **Likely at Implant**

Worldwide 50,000 candidates are waiting for **heart transplantation**, yet only approximately **4000 heart transplants** are performed each year

Miller, L, et al. Is left ventricular assist device therapy underutilized in the treatment of heart failure? Circulation. 2011;123:1552-1558.
Peura, J, et al. AHA. Recommendations for the use of mechanical circulatory support: device strategies and patient selection.2012;126:2653-2667.
Ponikowski, P, et al. ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure. 2016 Eur Heart J. 2016;37:2129–2200.
Ambrosy, P, et al. The global health and economic burden of hospitalizations for heart failure. J Am Coll Cardiol. 2014;63:1123 -1133.

Thus … How ?

Weight your Army, Energy and Resources



ISHLT GUIDELINES

The 2013 International Society for Heart and Lung Transplantation Guidelines for mechanical circulatory support: Executive summary

Co-chairs: David Feldman, MD, PhD;* Salpy V. Pamboukian, MD, MSPH;*
Jeffrey J. Teuteberg, MD;*
Task Force Chairs (exclusive of co-authors): Emma Birks, MD; Katherine Lietz, MD;
Stephanie A. Moore, MD; Jeffrey A. Morgan, MD
Contributing Writers (exclusive of co-chairs or chairs): Francisco Arabia, MD; Mary E. Bauman, MScN, NP;
Hoger W. Buchholz, MD; Mario Deng, MD; Marc L. Dickstein, MD; Aly El-Banayosy, MD; Tonya Elliot, RN, MSN;
Daniel J. Goldstein, MD; Kathleen L. Grady, PhD, APN; Kylie Jones, RN; Katarzyna Hryniewicz, MD;
Ranjit John, MD; Annemarie Kaan, MCN, RN; Shimon Kusne, MD; Matthias Loebe, MD, PhD;
M. Patricia Massicotte, MHSc, MD; Nader Moazami, MD; Paul Mohacsi, MD; Martha Mooney, MD;
Thomas Nelson, MD; Francis Pagani, MD; William Perry, RN;
Evgenij V. Potapov, MD; J. Eduardo Rame, MD, MPhil; Stuart D. Russell, MD;
Erik N. Sorensen, PhD; Benjamin Sun, MD; and Martin Strueber, MD
Independent Reviewers: Abeel A. Mangi, MD; Michael G. Petty, PhD,RN; and Joseph Rogers, MD.

J Heart Lung Transplant 2013;32:157–187

Recommendations for the Use of Mechanical Circulatory Support: Ambulatory and Community Patient Care

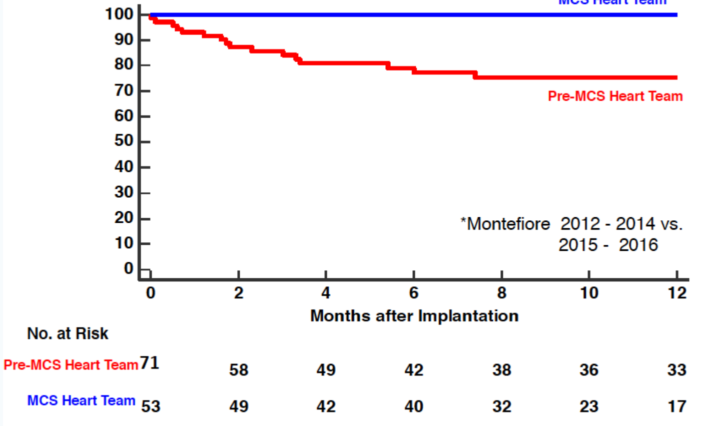
A Scientific Statement From the American Heart Association

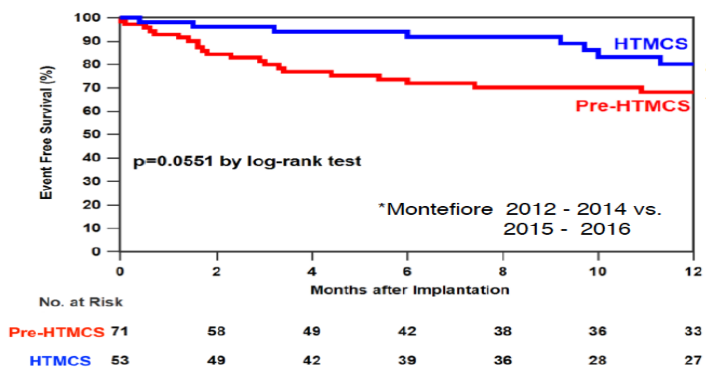
Circulation. 2017;135:00–00.

… speak same Language !

Trained Multisciplinary Team Work

The Journal of Heart and Lung Transplantation, Vol 37, No 4S, April 2018





Selection …

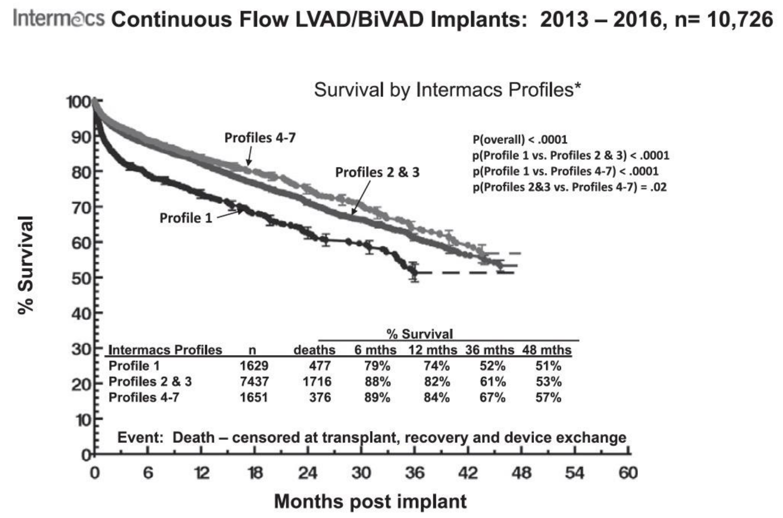


Table 1 Continuous Flow LVAD/BiVAD Implants: 2008 – 2016, n=17633

	Early hazard		Late hazard	
Pre-implant Risk Factors for Death	**Hazard Ratio**	***p*-value**	**Hazard Ratio**	***p*-value**
Demographics				
Age[2] (older)	1.41	<.0001	1.16	<.0001
Female	1.47	<.0001		
BMI (higher)	1.02	<.0001		
Blood Type Not O			0.88	.002
White race			1.20	.0003
Clinical Status				
ICD	1.34	.001	1.29	<.0001
INTERMACS Profile 1	1.98	<.0001		
INTERMACS Profile 2	1.59	<.0001		
Intervention within 48 hours IABP			1.19	.0004
Destination Therapy			1.22	<.0001
Non-Cardiac Systems				
Peripheral Vascular Disease			1.28	.004
Pre-COPD			1.27	.001
Albumin (lower)	0.80	<.0001		
Creatinine (higher)			1.12	<.0001
Dialysis	3.29	<.0001		
BUN (higher) (10 unit increase)	1.07	<.0001	1.05	<.0001
Right Heart Dysfunction				
RVAD in same operation	3.76	<.0001		
Bilirubin (higher) (5 unit increase)	1.28	<.0001		
Surgical Complexities				
History of cardiac surgery	1.31	.004		
History of CABG	1.38	.001		
Concommitant Cardiac Surgery	1.53	<.0001		
Quality of Life – Pre Implant				
Too Sick to complete EQ5D	1.65	<.0001		
Worse Self Care Score (pre-implant)			1.25	<.0001

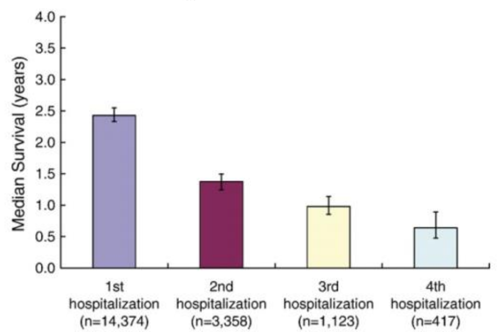
J Heart Lung Transplant 2017; 36:1080–1086

Table 1 "I Need Help"—Markers of Advanced Heart Failure

I	Inotropes	Previous or ongoing requirement for dobutamine, milrinone, dopamine or levosimendan
N	NYHA class/Natriuretic peptides	Persisting NYHA Class III or IV and/or persistently high BNP or NT-pro-BNP
E	End-Organ Dysfunction	Worsening renal or liver dysfunction in the setting of heart failure
E	Ejection Fraction	Very low ejection fraction < 20%
D	Defibrillator shocks	Recurrent appropriate defibrillator shocks
H	Hospitalizations	More than 1 hospitalization with heart failure in the last 12 months
E	Edema/Escalating diuretics	Persisting fluid overload and/or Increasing diuretic requirement
L	Low blood pressure	Consistently low BP with systolic < 90 to 100 mm Hg
P	Prognostic medication	Inability to up-titrate (or need to decrease/cease) ACEI, B-blockers, ARNIs or MRAs

ACEI, angiotensin-converting enzyme inhibitor; ARNI, angiotensin-receptor neprilysin inhibitor; BNP, B-type natriuretic peptide; BP, blood pressure; MRA, mineralocorticoid receptor antagonist; NT-ProBNP, N-terminal pro-b-type natriuretic peptide; NYHA New York Heart Association.

Baumwol J. JHLT 36(5): 593-4. May 2017



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

Setoguchi et al. Am Heart J 2007

What is the probability of achieving a good result?

- Assessment phase – "Evaluation"
- Team analysis to determine risk – benefit / QoL to help guide individual decisions
- Advice and education to the patient / family prior to moving forward

In Summary …

Technology ?

It’s a resource we should offer …

Dr. E. Potapov, EACTS 2017, Vienna, Austria

ISMCS

BOLOGNA ITALY

Royal Carlton Hotel

OCTOBER 21-23 2019

27th ANNUAL MEETING of International Society for Mechanical Circulatory Support

www.ismcs.org

FORMAT

- Interactive lectures
- Live-in-a-box cases
- Keynote presentations

TARGET AUDIENCE

- BioEngineers
- Heart Failure Cardiologists
- Cardiac Surgeons
- VAD coordinators
- Nurses
- Perfusion Technicians
- Anaesthesiologists
- Medical Industry (cardiac devices including ECMO development and production)

CONTENT

Focused robust sessions on Adult / Pediatric temporary (including ECMO) and long-term Mechanical Circulatory Support systems (bioengineering, biocompatibility, new technologies, MCS tools and peripherals, surgical strategies, clinical management, VAD coordinator programs) will take place with the presence of prestigious well- known speakers and discussants coming from all over the world.

Additionally, parallel sessions by the International Consortium of Circulatory Assist Clinicians (ICCAC) with an official proficiency verification course (MPV) will be scheduled and directed by worldwide VAD coordinators.

A complete and variegated scientific program, containing a full spectrum of exchange and learning opportunities will be offered.

Program Chair
Antonio Loforte, MD, PhD
S. Orsola Hospital
Department of Cardiothoracic, Transplantation and Vascular Surgery
University of Bologna, Italy

Program Co-Chair
Francesco Moscato, EngD, PhD
Center for Medical Physics and Biomedical Engineering
Medical University of Vienna, Austria

ORGANIZING SECRETARIAT
NOEMA
Via Orefici, 4 – 40124 Bologna (Italy)
ph. +39 051 230385
info@noemacongressi.it
www.noemacongressi.it

ISMCS
International Society for Mechanical Circulatory Support