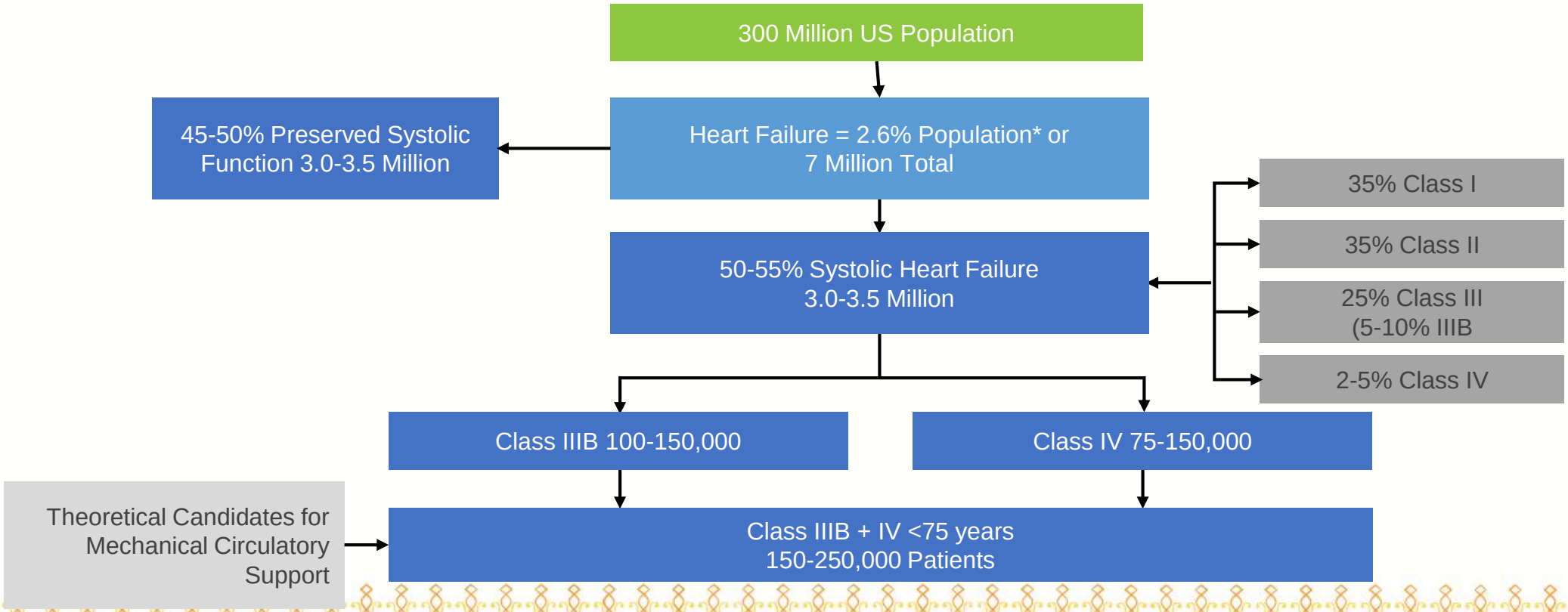
Mechanical Circulatory Support in the Management of Heart Failure

Feras Bader, MD, MS, FACC
Associate Professor of Medicine
Director, Heart Failure and Transplant
Cleveland Clinic Abu Dhabi
Chairman, Heart Failure Working Group of the Emirates Cardiac Society

ACC Middle East Conference 2017

Current Estimate of the Number of Advanced Heart Failure Patients

This represents approximate number of potential VAD candidates. Data from Miller (2).



[1] Miller L, Guglin M. Patient selection for ventricular assist devices: A moving target. J Am Coll Cardiol. 2013; 61:1209-21
[2] Miller, L. Is left ventricular assist device therapy underutizlied in the treatment of heart failure? Circulation. 2011;123:1552-1558

- The Gulf Region

(a

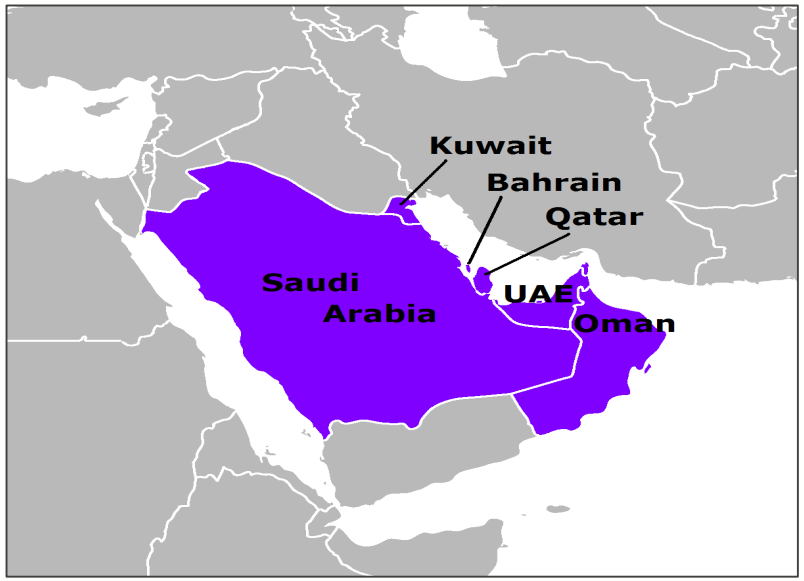
re

- W

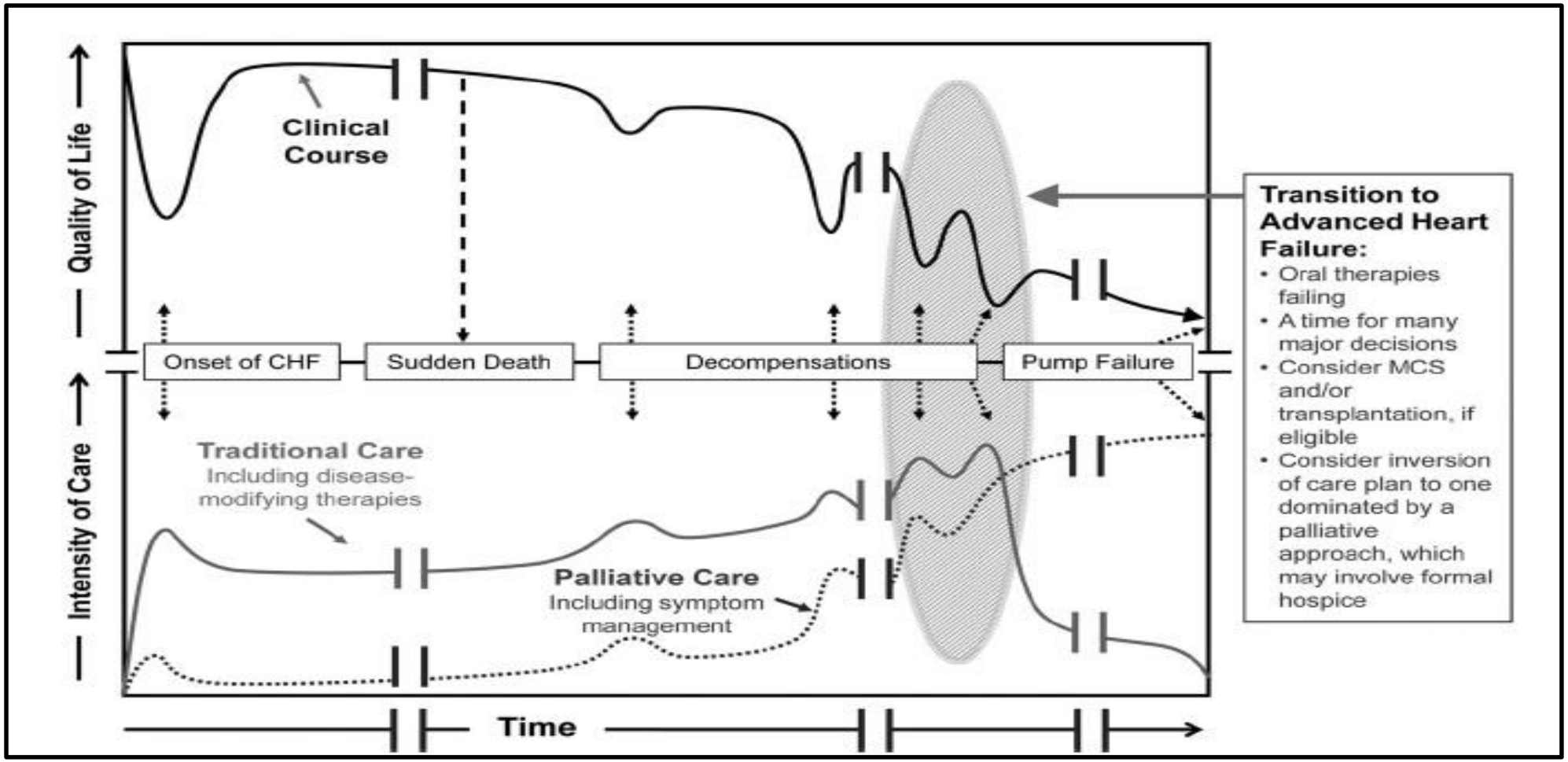
pl

The Gulf Region

- Population: Estimated around 50 million.
- Heart failure population: At 2.5%, estimated to be around 1.25 million.
- Advanced HF population (systolic HF, NYHA class IIIB and IV): At 5-10% of all HFrEF, estimated to be 40,000- 60,000.
- Advanced HF patients that should be transplanted: At least 400- 600 (1% of advanced HF).



Clinical Course of HF



Circulation 2012, 125:1928-1952

The NEW ENGLAND JOURNAL of MEDICINE

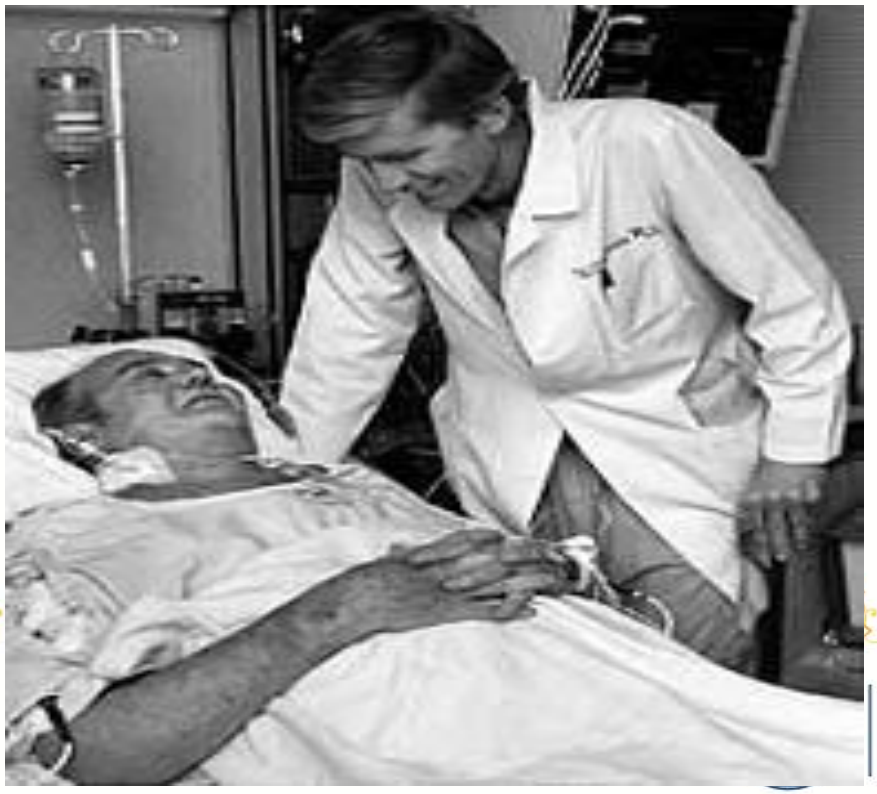
ORIGINAL ARTICLE

Volume 310:273-278 February 2, 1984 Number 5

Clinical use of the total artificial heart

WC DeVries, JL Anderson, LD Joyce, FL Anderson, EH Hammond, RK Jarvik, and WJ Kolff

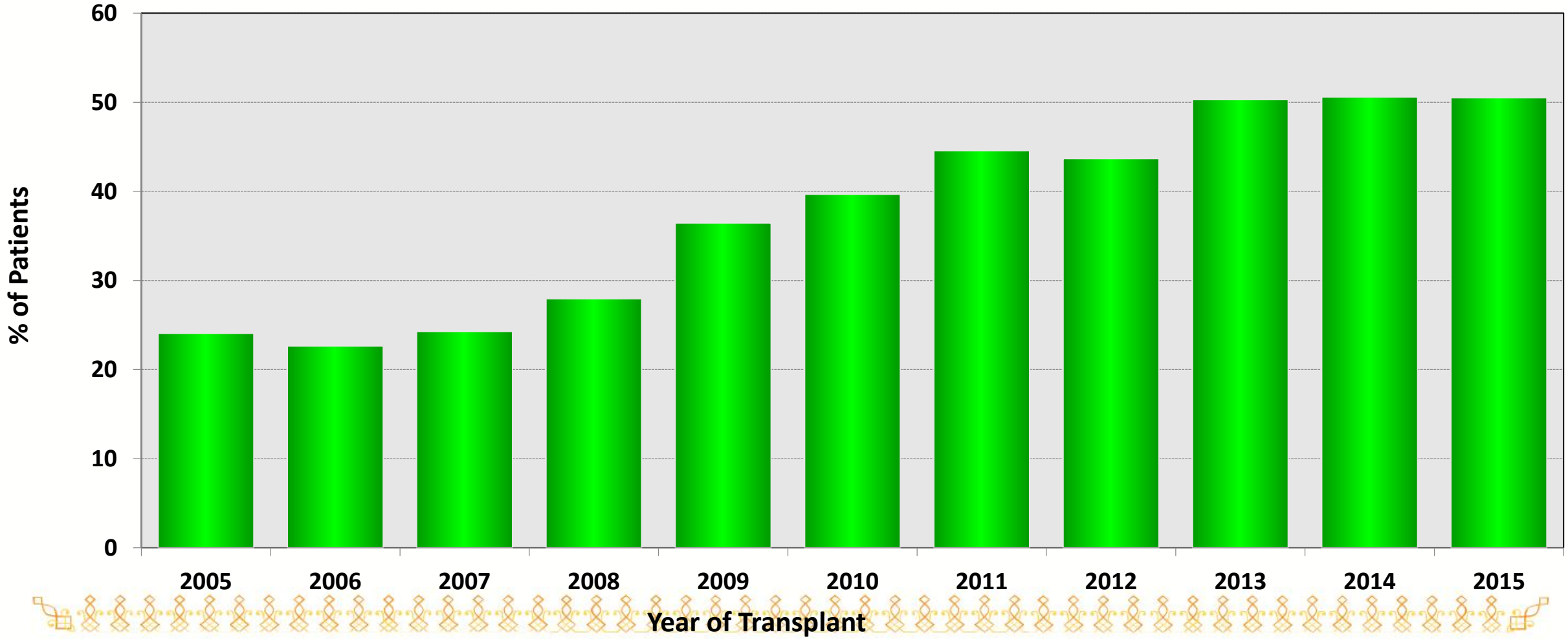
De Vries, Anderson, ….., Jarvik, Kolff. ***Departments of Artificial Organs, Cardiology & Cardiac Surgery***
University of Utah



Adult Heart Transplants

% of Patients Bridged with Mechanical Circulatory Support*

(Transplants: January 2005 – December 2015)



* LVAD, RVAD, TAH, ECMO

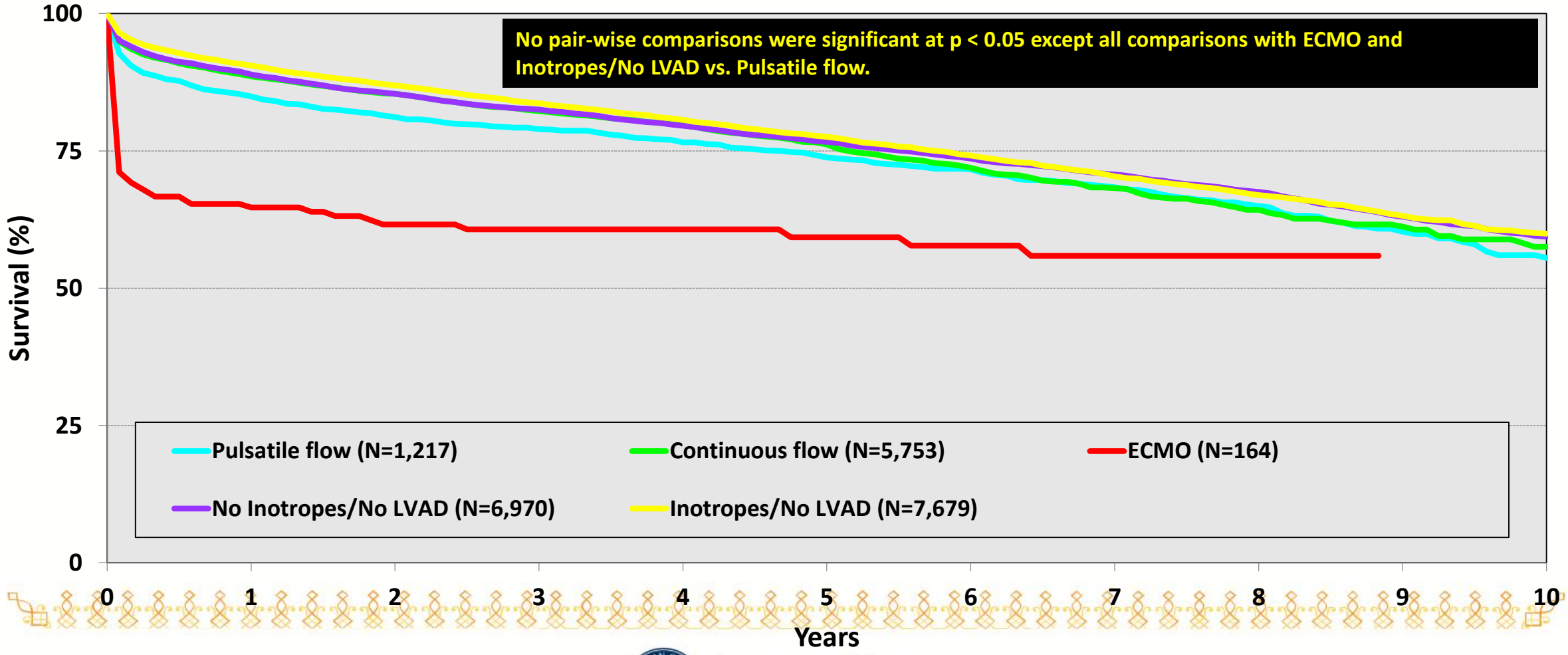
ISHLT • INTERNATIONAL SOCIETY FOR HEART AND LUNG TRANSPLANTATION

Middle East ence 2017

JHLT. 2017 Oct; 36(10): 1037-1079

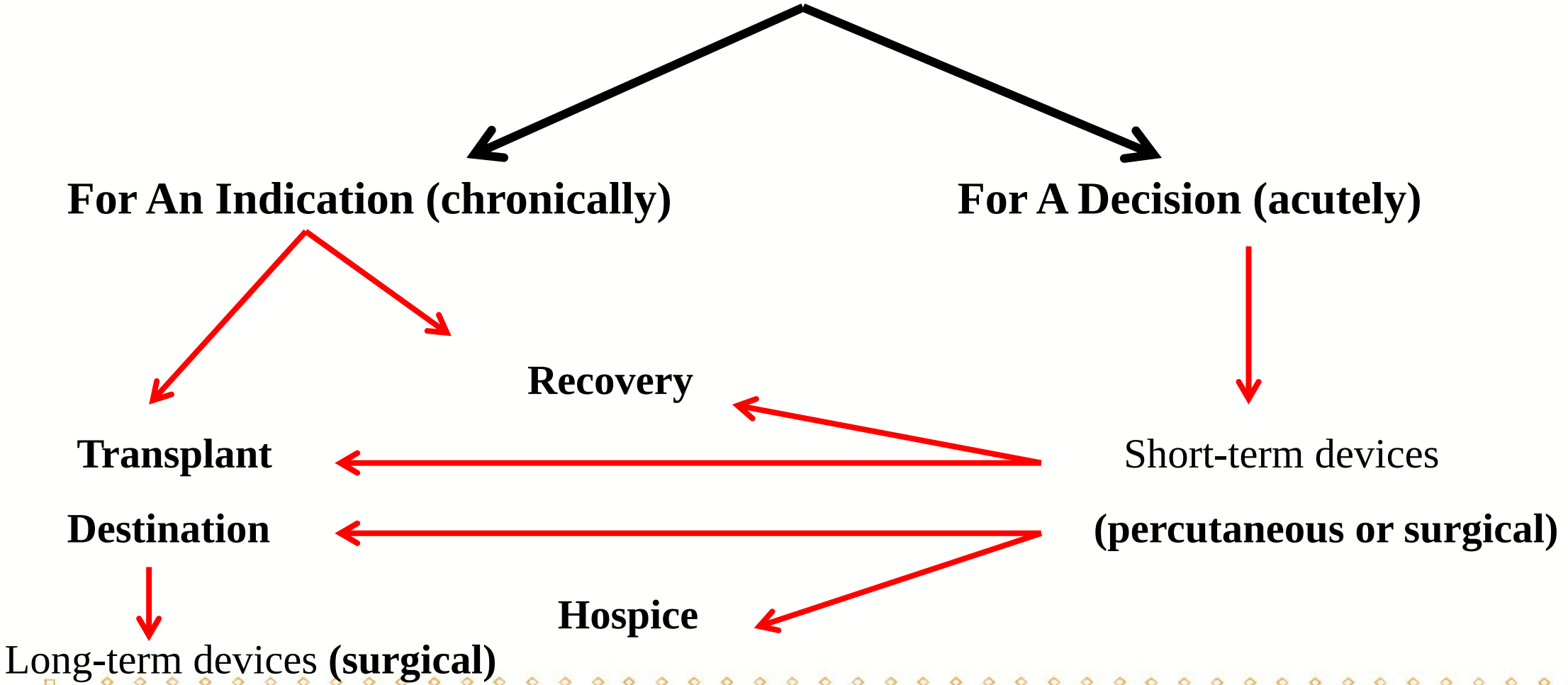
Adult Heart Transplant Kaplan-Meier Survival by Pre-Transplant Mechanical Circulatory Support Use

(Transplants: January 2005 – June 2015)



JHLT. 2017 Oct; 36(10): 1037-1079

Ventricular Assist Devices



2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure

The Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC)

European Heart Journal (2016) **37**, 2129–2200

The **INTERMACS** profile
(Interagency Registry for Mechanically Assisted Circulatory Support)

Table 13.2 INTERMACS (Interagency Registry for Mechanically Assisted Circulatory Support) stages for classifying patients with advanced heart failure

INTERMACS level	NYHA Class	Description	Device	1y survival with LVAD therapy
1. Cardiogenic shock "Crash and burn"	IV	Haemodynamic instability in spite of increasing doses of catecholamines and/or mechanical circulatory support with critical hypoperfusion of target organs (severe cardiogenic shock).	ECLS, ECMO, percutaneous support devices	52.6±5.6%
2. Progressive decline despite inotropic support "Sliding on inotropes"	IV	Intravenous inotropic support with acceptable blood pressure but rapid deterioration of renal function, nutritional state, or signs of congestion.	ECLS, ECMO, LVAD	63.1±3.1%
3. Stable but inotrope dependent "Dependent stability"	IV	Haemodynamic stability with low or intermediate doses of inotropics, but necessary due to hypotension, worsening of symptoms, or progressive renal failure.	LVAD	78.4±2.5%
4. Resting symptoms "Frequent flyer"	IV ambulatory	Temporary cessation of inotropic treatment is possible, but patient presents with frequent symptom recurrences and typically with fluid overload.	LVAD	78.7±3.0%
5. Exertion intolerant "Housebound"	IV ambulatory	Complete cessation of physical activity, stable at rest, but frequently with moderate fluid retention and some level of renal dysfunction.	LVAD	93.0±3.9%[a]
6. Exertion limited "Walking wounded"	III	Minor limitation on physical activity and absence of congestion while at rest. Easily fatigued by light activity.	LVAD / Discuss LVAD as option	-
7. "Placeholder"	III	Patient in NYHA Class III with no current or recent unstable fluid balance.	Discuss LVAD as option	-

European Heart Journal (2016) **37**, 2129–2200

Table 13.3 Patients potentially eligible for implantation of a left 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 mmHg and SBP ≤80–90 mmHg or CI ≤2 L/min/m^2).
Absence of severe right ventricular dysfunction together with severe tricuspid regurgitation.

CI = cardiac index; HF = heart failure; i.v. = intravenous; LVEF = left ventricular ejection fraction; PCWP = pulmonary capillary wedge pressure; SBP = systolic blood pressure; VO_2 = oxygen consumption.

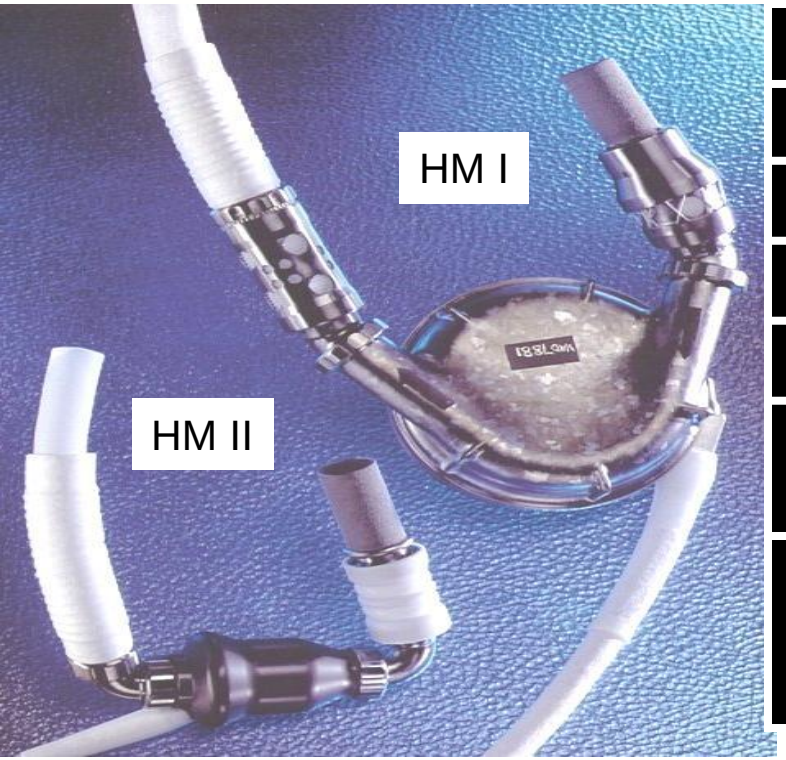
European Heart Journal (2016) **37**, 2129–2200

Types of LVAD Indications

Bridge to candidacy (BTC)	Use of MCS (usually LVAD) to improve end-organ function in order to make an ineligible patient eligible for heart transplantation.
Bridge to transplantation (BTT)	Use of MCS (LVAD or BiVAD) to keep patient alive who is otherwise at high risk of death before transplantation until a donor organ becomes available.
Bridge to recovery (BTR)	Use of MCS (typically LVAD) to keep patient alive until cardiac function recovers sufficiently to remove MCS.
Destination therapy (DT)	Long-term use of MCS (LVAD) as an alternative to transplantation in patients with end-stage HF ineligible for transplantation or long-term waiting for heart transplantation.

European Heart Journal (2016) **37**, 2129–2200

Comparison of HM I (XVE) and HM II



	HM I	HM II
Weight (gm)	1250	280
Volume (ml)	450	63
Noise	Audible	Silent
Moving parts	Many	One
Maximal flow (l/min)*	10	10
Clinical Durability (yr)	1.5	Est. > 5

* at mean pressure=100 mm Hg

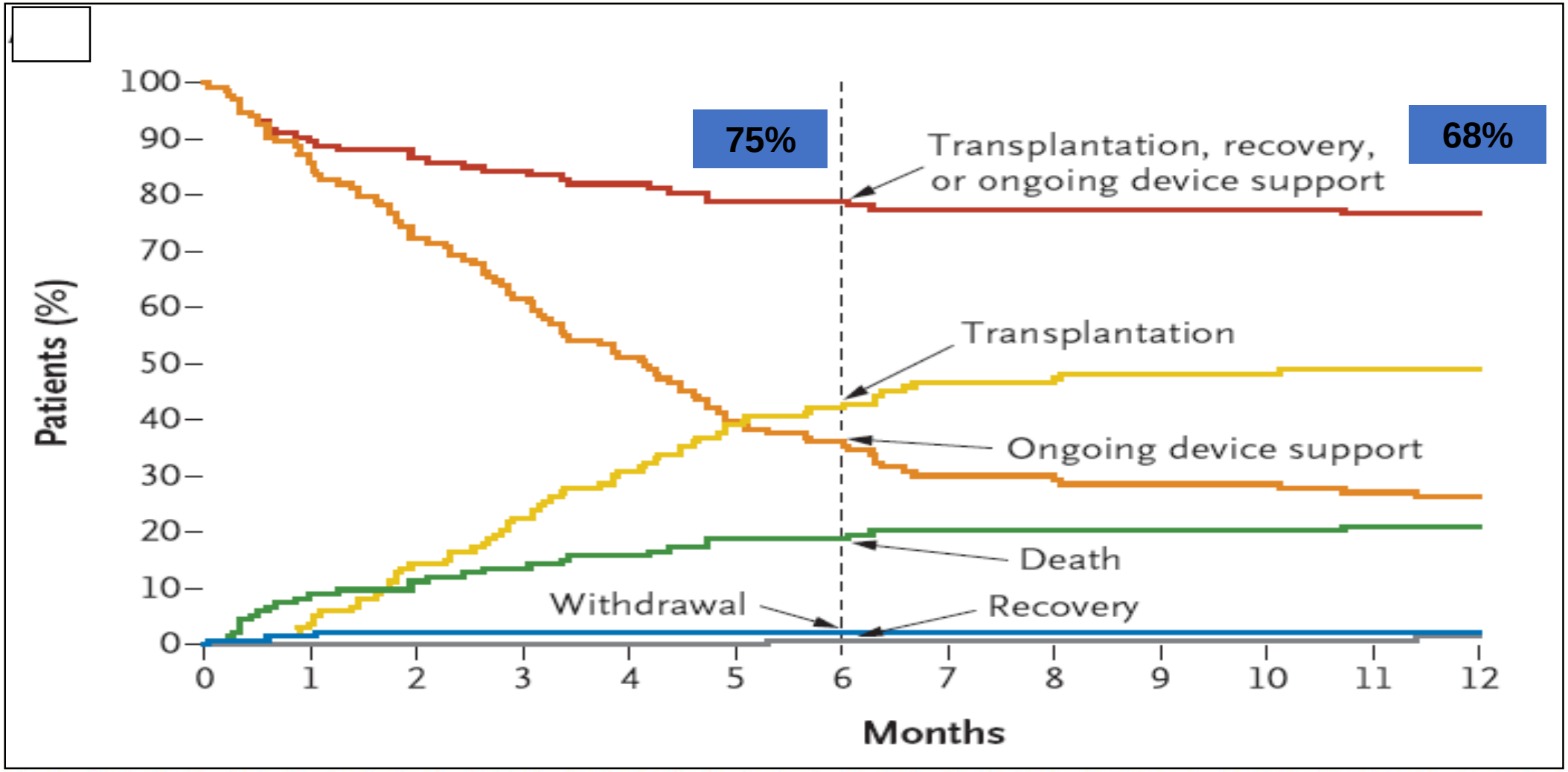
HeartMate II – BTT trial

- HeartMate II
- 133 patients
- no control group

- Primary outcome:
  transplantation, recovery or ongoing mechanical support while remaining eligible for transplantation, at 180 days.

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

HeartMate II BTT trial, primary outcome



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

HM II destination therapy

Advanced Heart Failure Treated with Continuous-Flow Left Ventricular Assist Device

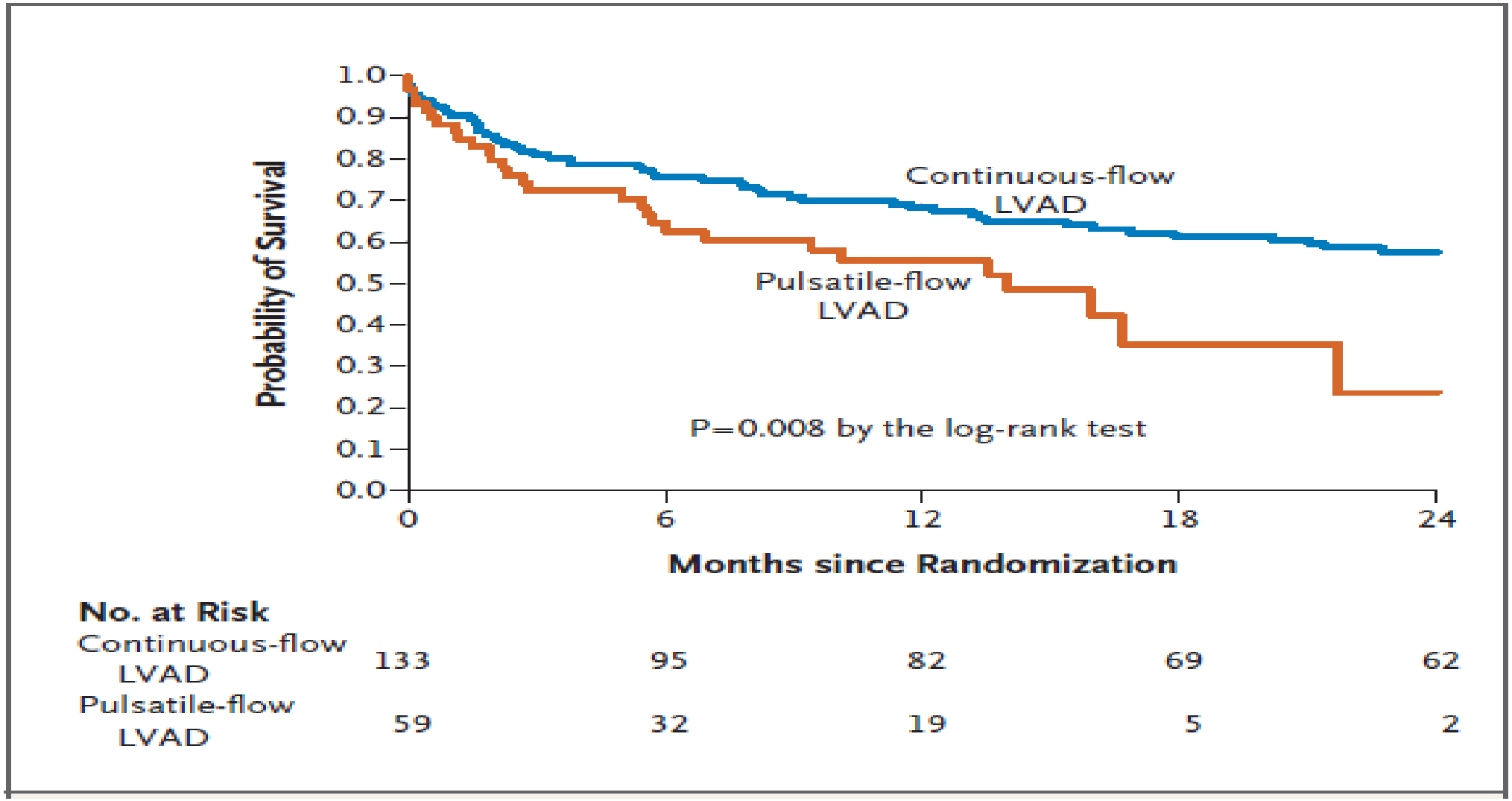
Mark S. Slaughter, M.D., Joseph G. Rogers, M.D., Carmelo A. Milano, M.D., Stuart D. Russell, M.D., John V. Conte, M.D., David Feldman, M.D., Ph.D., Benjamin Sun, M.D., Antone J. Tatooles, M.D., Reynolds M. Delgado, III, M.D., James W. Long, M.D., Ph.D., Thomas C. Wozniak, M.D., Waqas Ghumman, M.D., David J. Farrar, Ph.D., and O. Howard Frazier, M.D., for the HeartMate II Investigators*

- 200 patients, 38 centers (USA)
- 134 patients (CF-LVAD), 66 patient (Pulsatile LVAD)

✓**Primary endpoints :** 2 years survival free from stroke and reoperation to repair or replace the device.

✓**Secondary endpoints**: survival, frequency of adverse events, quality of life, and functional capacity.

NEJM 2009; 361: 2241-

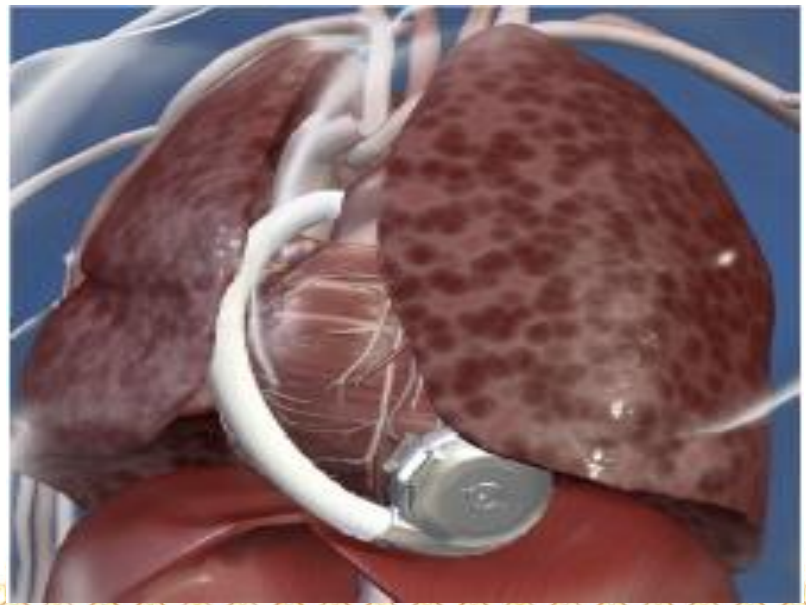


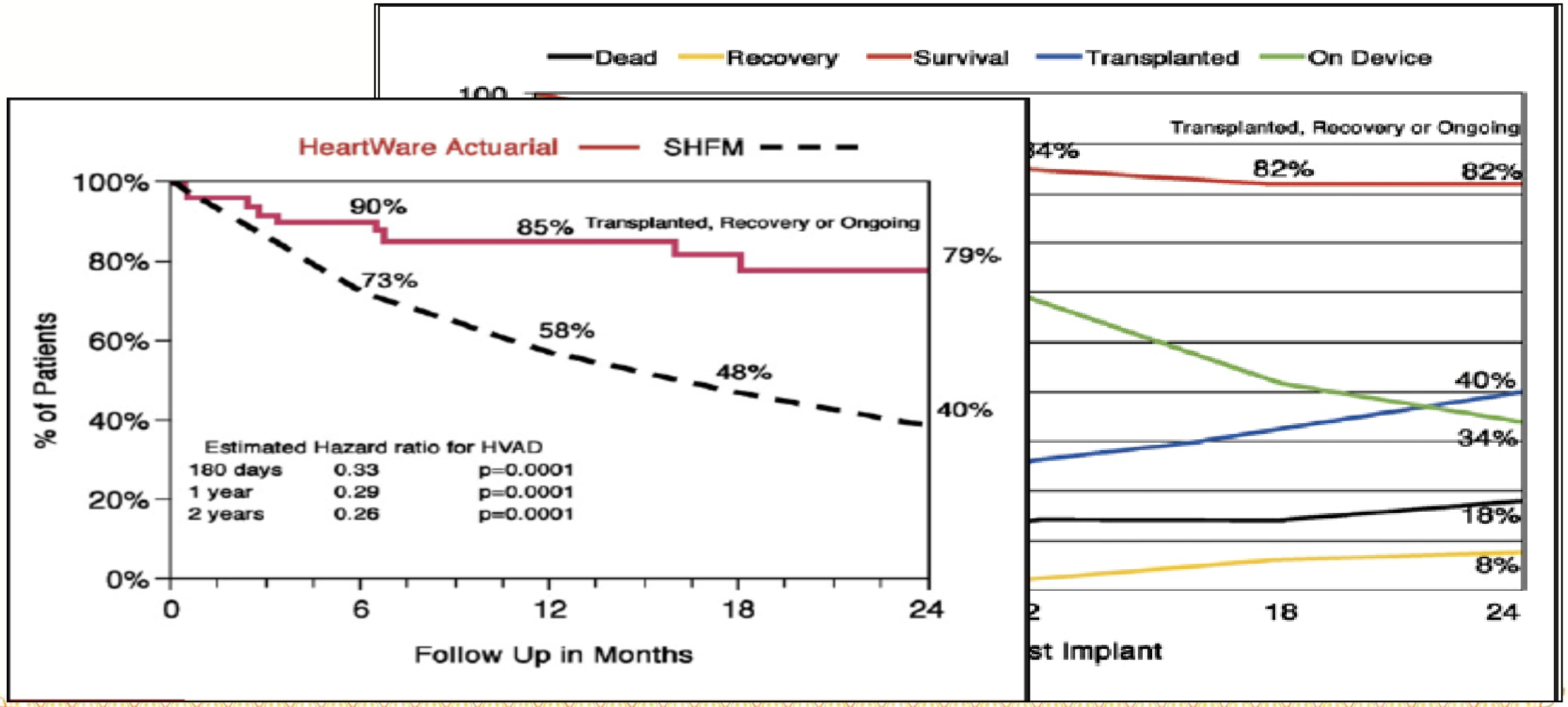
NEJM 2009; 361: 2241-51

Multicenter Evaluation of an Intrapericardial Left Ventricular Assist System

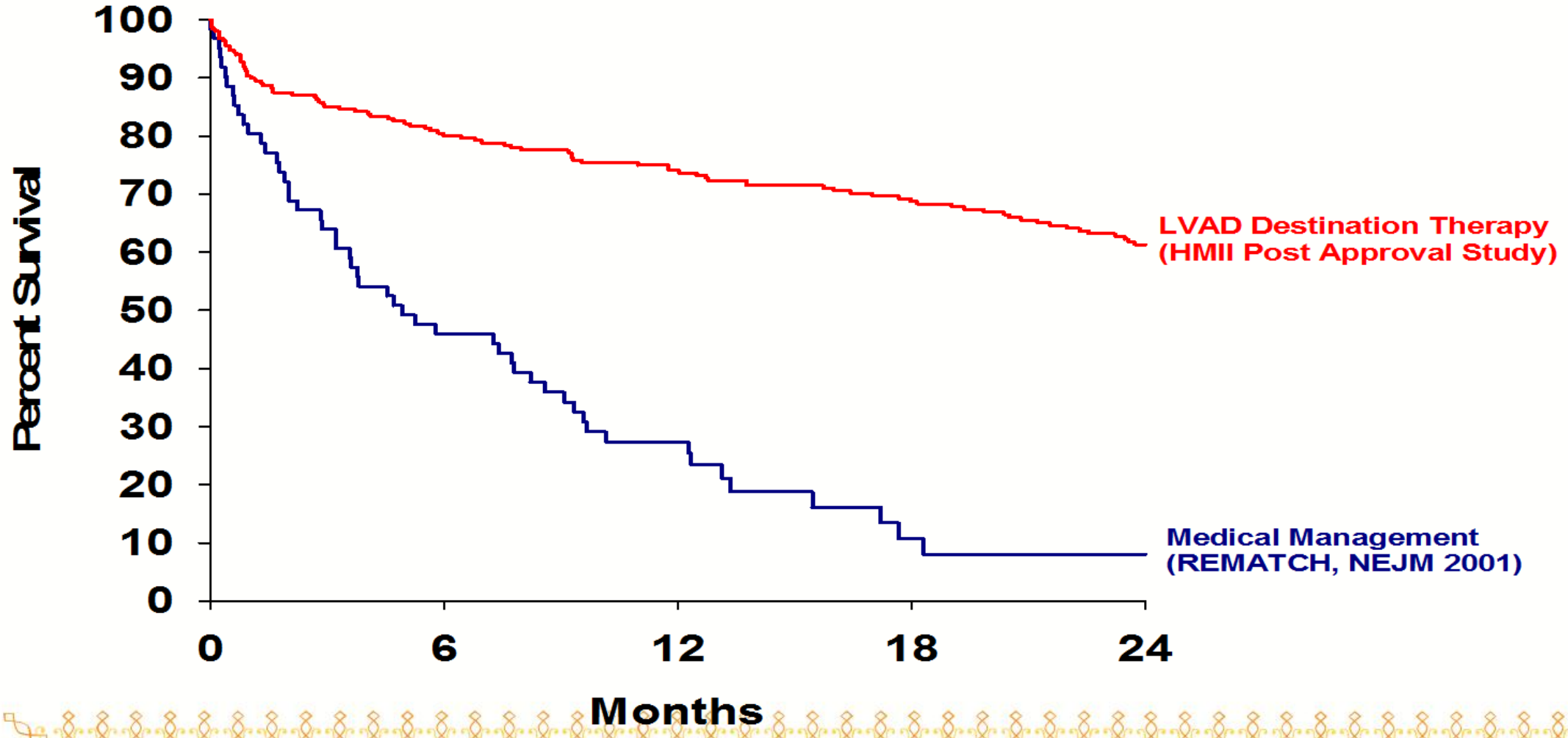
Martin Strueber, Gerry O'Driscoll, Paul Jansz, Asghar Khaghani, Wayne C. Levy, George M. Wieselthaler, and HeartWare Investigators

J. Am. Coll. Cardiol. 2011;57;1375-1382
doi:10.1016/j.jacc.2010.10.040




Dead
Recovery
Survival
Transplanted
On Device
Transplanted, Recovery or Ongoing
82%
82%
40%
34%
18%
8%
18
24
st Implant
HeartWare Actuarial
SHFM
100%
80%
60%
40%
20%
0%
% of Patients
90%
85%
Transplanted, Recovery or Ongoing
79%
73%
58%
48%
40%
Estimated Hazard ratio for HVAD
180 days 0.33 p=0.0001
1 year 0.29 p=0.0001
2 years 0.26 p=0.0001
0
6
12
18
24
Follow Up in Months

Destination Therapy Survival Benefit vs Medical Management



ACC Middle East Conference 2017

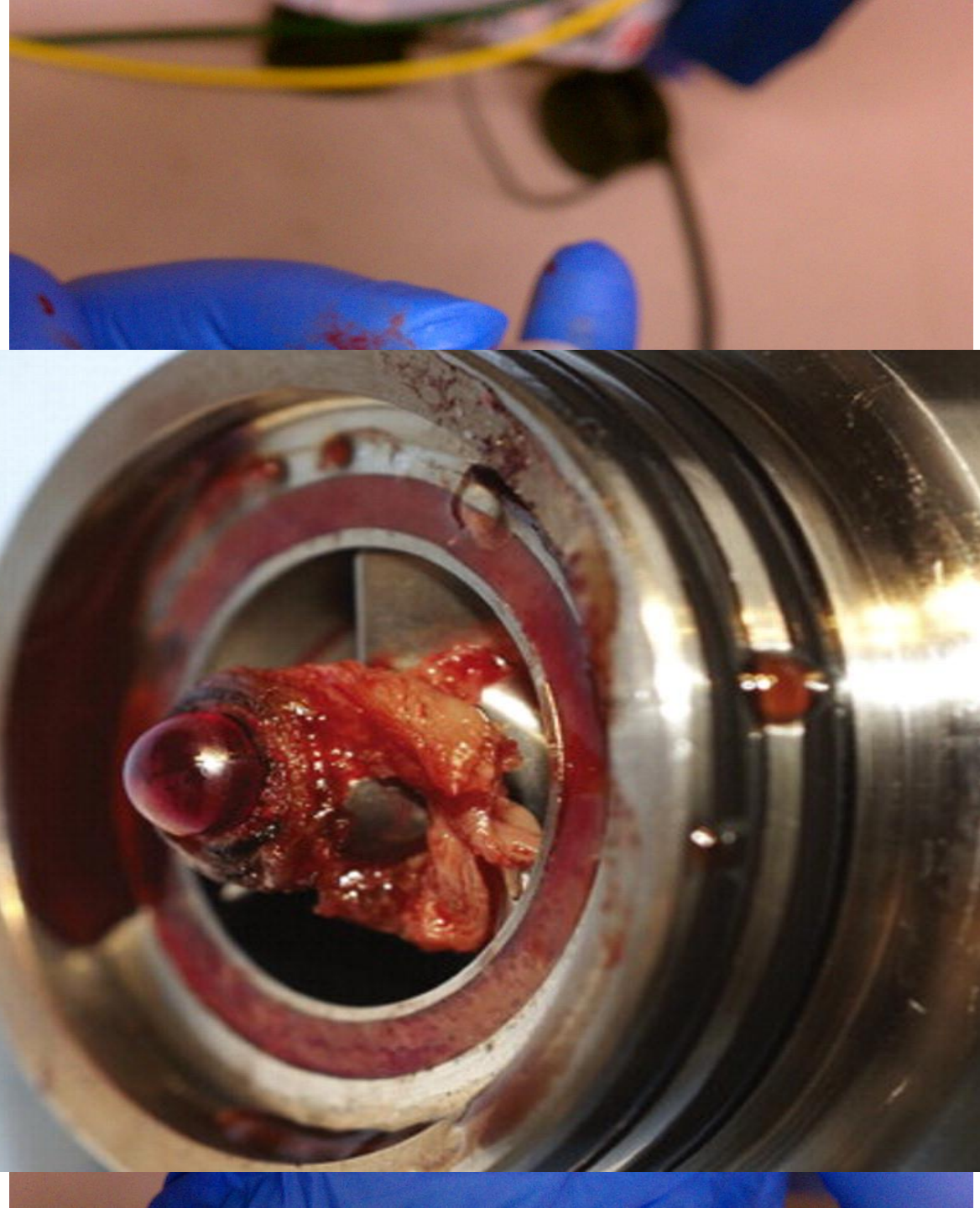
Two-Year Outcomes in the Destination Therapy Post-FDA-Approval Study with a Continuous Flow Left Ventricular Assist Device: A Prospective Study Using the INTERMACS Registry. U.P. Jorde, S.S. Khushwaha, A.J. Tatooles, et al. Presented at the ISHLT annual meeting, April 25, 2013.

Absolute Contraindications to LVAD therapy

- Untreated active systemic infection.
- Active or untreatable malignancy.
- Irreversible severe pulmonary hypertension.
- Symptomatic cerebrovascular disease not amenable to surgical correction.
- Severe peripheral vascular disease not amenable to surgical correction and precluding effective rehabilitation.
- History of medical non-compliance or lack of psycho-social support.

Important Potential Complications with LVAD therapy

- Cerebrovascular accidents.
- Pump malfunction or thrombosis.
- Systemic bleeding, especially GI tract.
- Driveline infections.
- RV dysfunction.
- Arrhythmias.



Mechanisms of pump thrombosis

- LVAD biomaterials in direct contact with blood/ coagulation system activation.
- End-stage HF patients (ICM) / LV thrombus.
- Blood stasis / no regular opening of AV.

Bleeding

- Major source of morbidity after LVAD implantation.
- Range 20%– 65%.
- Mainly GI bleed and epistaxis.
- Anticoagulation challenged.

(Boyle et al, 2009 JHLT)
(Crow et al, 2009 J Thoracic cardiovascular surg)

Mechanisms of bleeding

- Acquired von Willebrand syndrome (AVWS)
- GI tract Angiodysplagia
- Impaired platelet aggregation.
- Use of anticoagulation therapy.

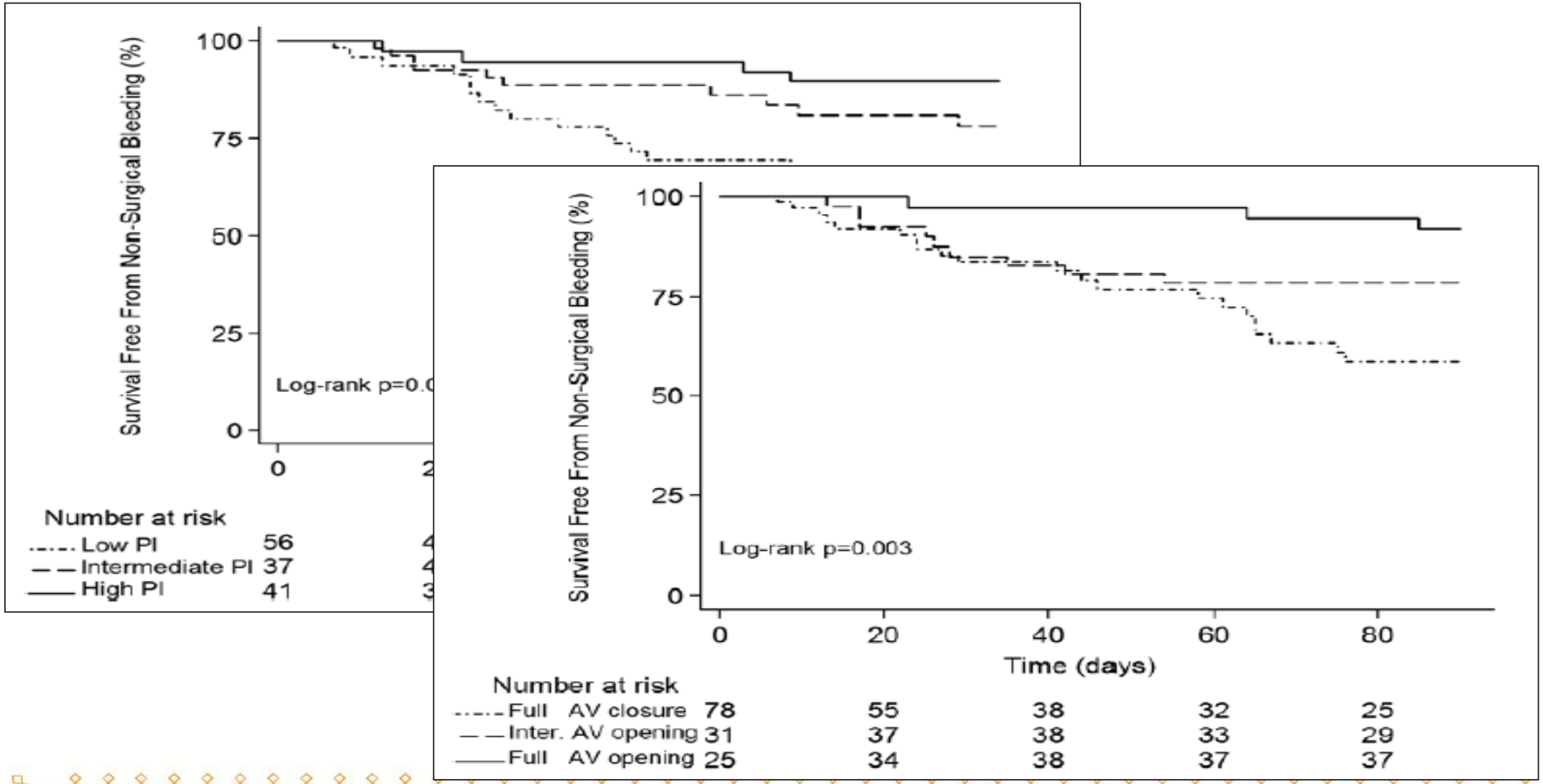
Circulation
Heart Failure
JOURNAL OF THE AMERICAN HEART ASSOCIATION

American Heart Association
Learn and Live

Pulsatility and the Risk of Nonsurgical Bleeding in Patients Supported With the Continuous-Flow Left Ventricular Assist Device HeartMate II

Omar Wever-Pinzon, MD; Craig H. Selzman, MD; Stavros G. Drakos, MD, PhD; Abdulfattah Saidi, MD; Gregory J. Stoddard, MPH; Edward M. Gilbert, MD; Mohamed Labedi, MD; Bruce B. Reid, MD; Erin S. Davis, RN, BSN; Abdallah G. Kfoury, MD; Dean Y. Li, MD, PhD; Josef Stehlik, MD, MPH; Feras Bader, MD, MS

Circ Heart Fail. 2013;6:517-526



Circ Heart Fail. 2013;6:517-526

Original Article

Clinical Outcomes After Continuous-Flow Left Ventricular Assist Device

A Systematic Review

Colleen K. McIlvennan, DNP, ANP; Kate H. Magid; Amrut V. Ambardekar, MD; Jocelyn S. Thompson, MA; Daniel D. Matlock, MD, MPH; Larry A. Allen, MD, MHS

52 articles analyzed in systemic review

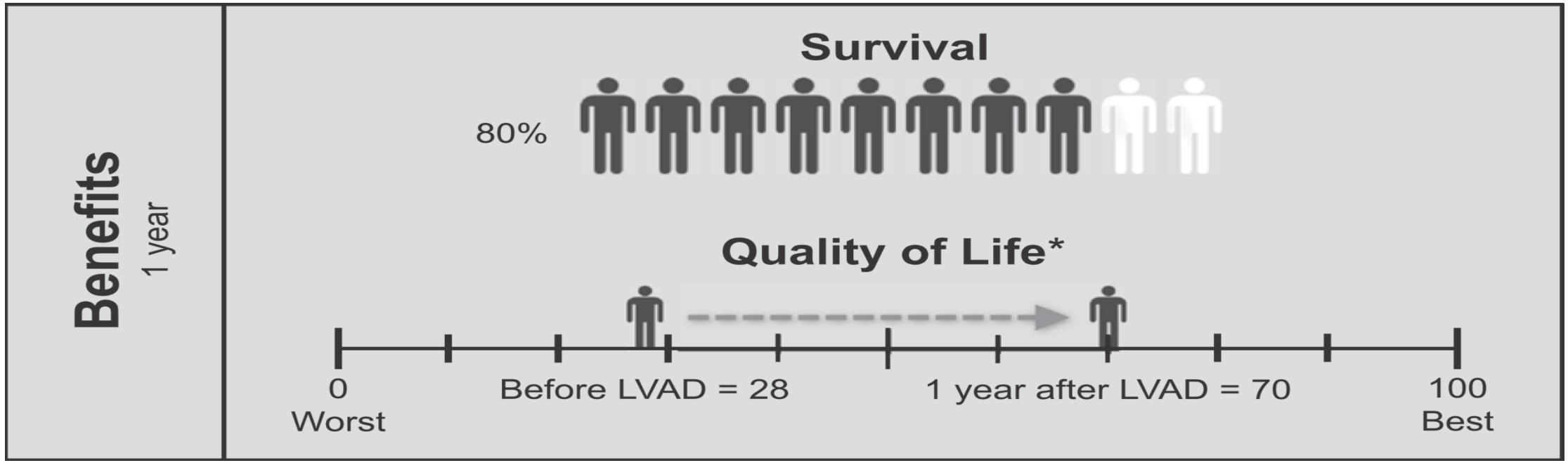
Industry-funded trials and related registries = 10

Multicenter registries = 10

Single center reports and case series = 32

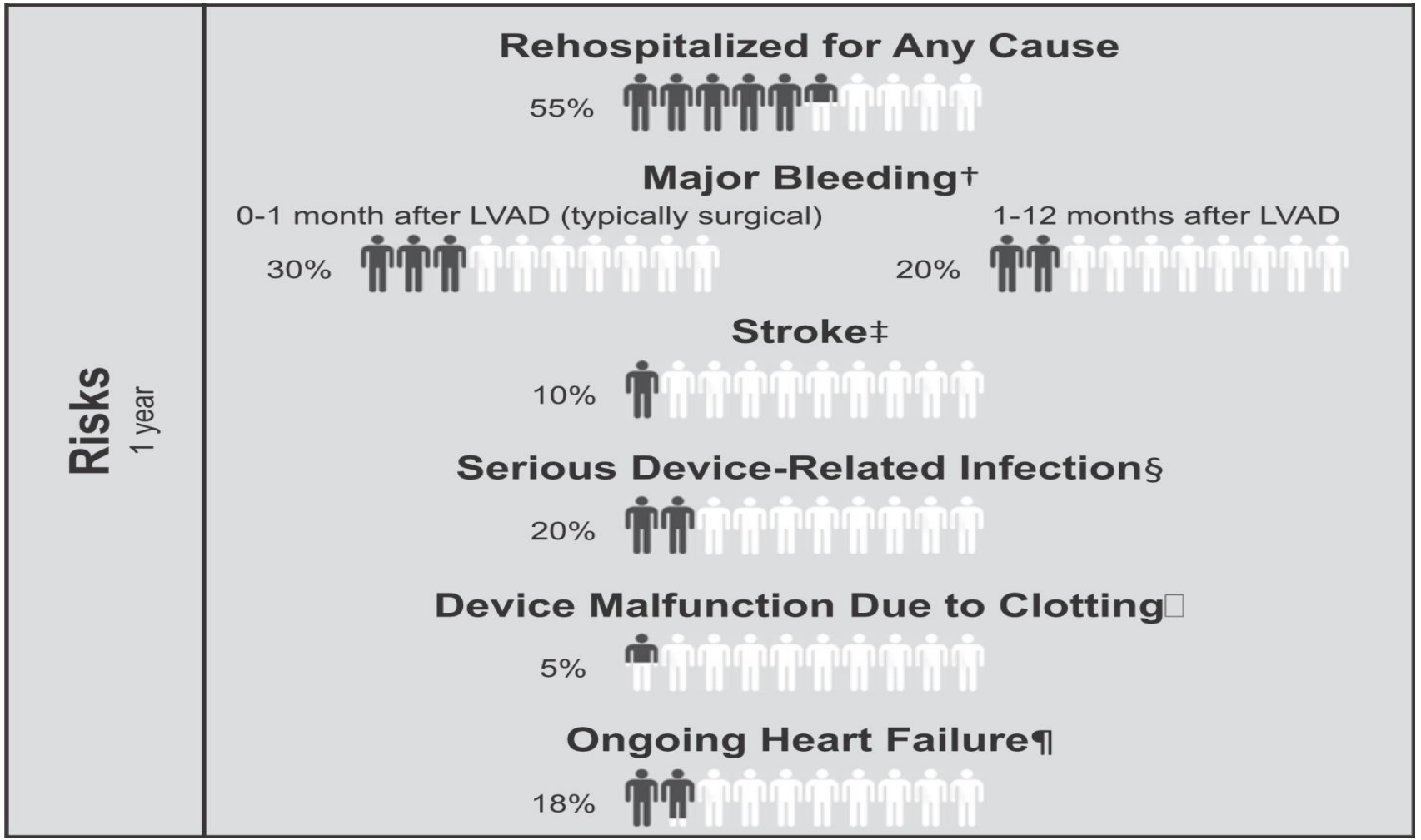
Circ Heart Fail 2014;7:1003-1013

Clinical benefits of CF-LVAD



Circ Heart Fail 2014;7:1003-1013

Risks of CF-LVAD



Circ Heart Fail 2014;7:1003-1013

Risk Assessment and Comparative Effectiveness of Left Ventricular Assist Device and Medical Management in Ambulatory Heart Failure Patients

Results From the ROADMAP Study

Jerry D. Estep, MD,* Randall C. Starling, MD, MPH,† Douglas A. Horstmanshof, MD,‡ Carmelo A. Milano, MD
Craig H. Selzman, MD,‖ Keyur B. Shah, MD,¶ Matthias Loebe, MD, PHD,* Nader Moazami, MD,†
James W. Long, MD, PHD,‡ Josef Stehlik, MD, MPH,‖ Vigneshwar Kasirajan, MD,¶ Donald C. Haas, MD,#
John B. O'Connell, MD,** Andrew J. Boyle, MD,†† David J. Farrar, PHD,** Joseph G. Rogers, MD,§
for the ROADMAP Study Investigators

(J Am Coll Cardiol 2015;66:1747–61)

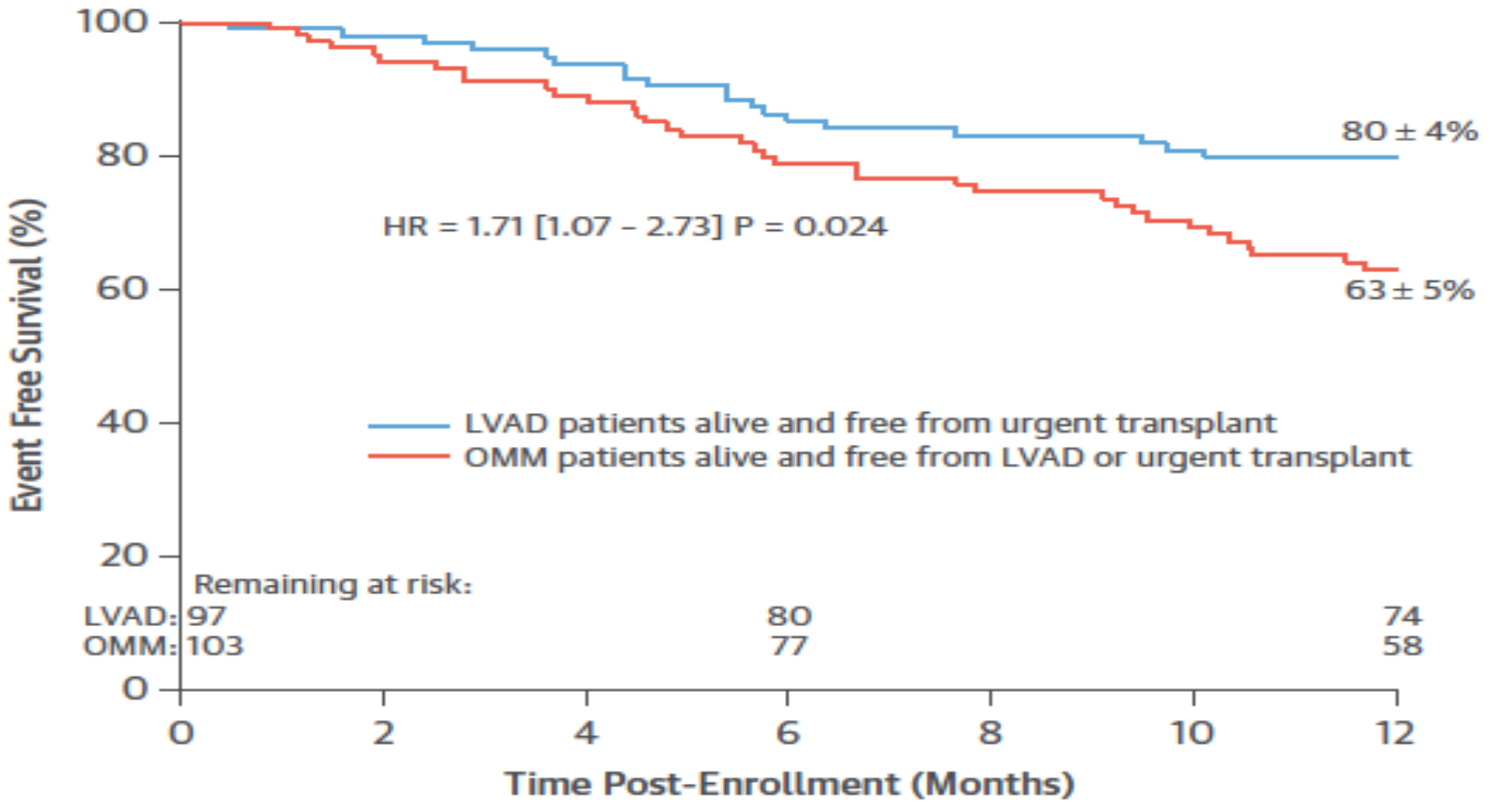
- A prospective study of 200 patients, NYHA class IIIb- IV, but not inotrope-dependent.
- Randomized to HM II versus OMT
- Composite endpoint of survival and improvement of 6-minute walk test of ≥75 m at 12 months.

	OMM (n = 103)	LVAD (n = 97)	p Value
Diuretic dose furosemide-equivalent, mg/day	93 (40–200)	133 (40–240)	0.127
ACE inhibitors or ARBs	79 (77)	66 (68)	0.205
Beta-blockers	99 (96)	84 (87)	0.021
BMI, kg/m^2	28 (23–37)	29 (25–33)	0.663
Creatinine, mg/dl	1.3 (1.0–1.8) (n = 103)	1.3 (1.0–1.6) (n = 97)	0.507
Cardiac index, l/min/m^2	1.9 (1.6–2.3) (n = 50)	1.9 (1.6–2.3) (n = 65)	0.921
PCWP, mm Hg	22 (17–30) (n = 50)	22 (17–27) (n = 61)	0.425
VO_2 max RER ≥ 1.1, ml/kg/min	10.9 (9.6–12.7) (n = 23)	10.2 (8.8–11.3) (n = 27)	0.131
VE/VCO_2	37.4 (34.0–49.0) (n = 51)	44.0 (36.9–49.0) (n = 58)	0.090
NYHA functional class			<0.001
IIIB	77 (75)	47 (48)	
IV	26 (25)	50 (52)	
INTERMACS profile			<0.001
Profile 4	35 (34)	63 (65)	
Profile 5	29 (28)	21 (22)	
Profile 6	35 (34)	10 (10)	
Profile 7	2 (2)	0	

TABLE 4 Primary Endpoint and Components that Prevented Success

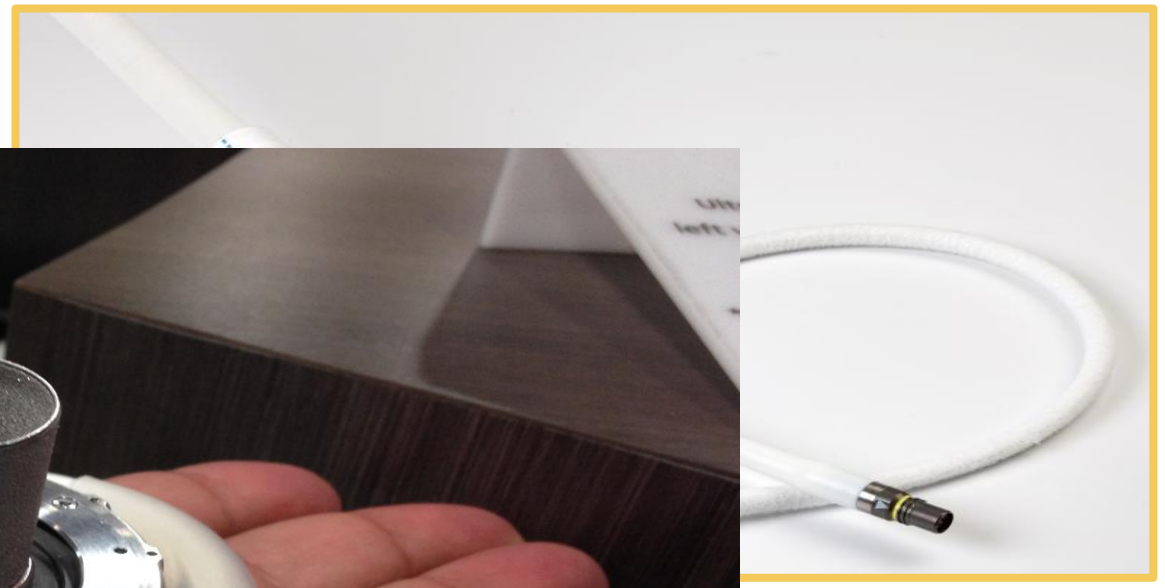
	OMM (n = 82)*	LVAD (n = 85)†	Odds Ratio (95% Confidence Interval)
Ali			

FIGURE 2 Survival As-Treated



HeartMate III: Features

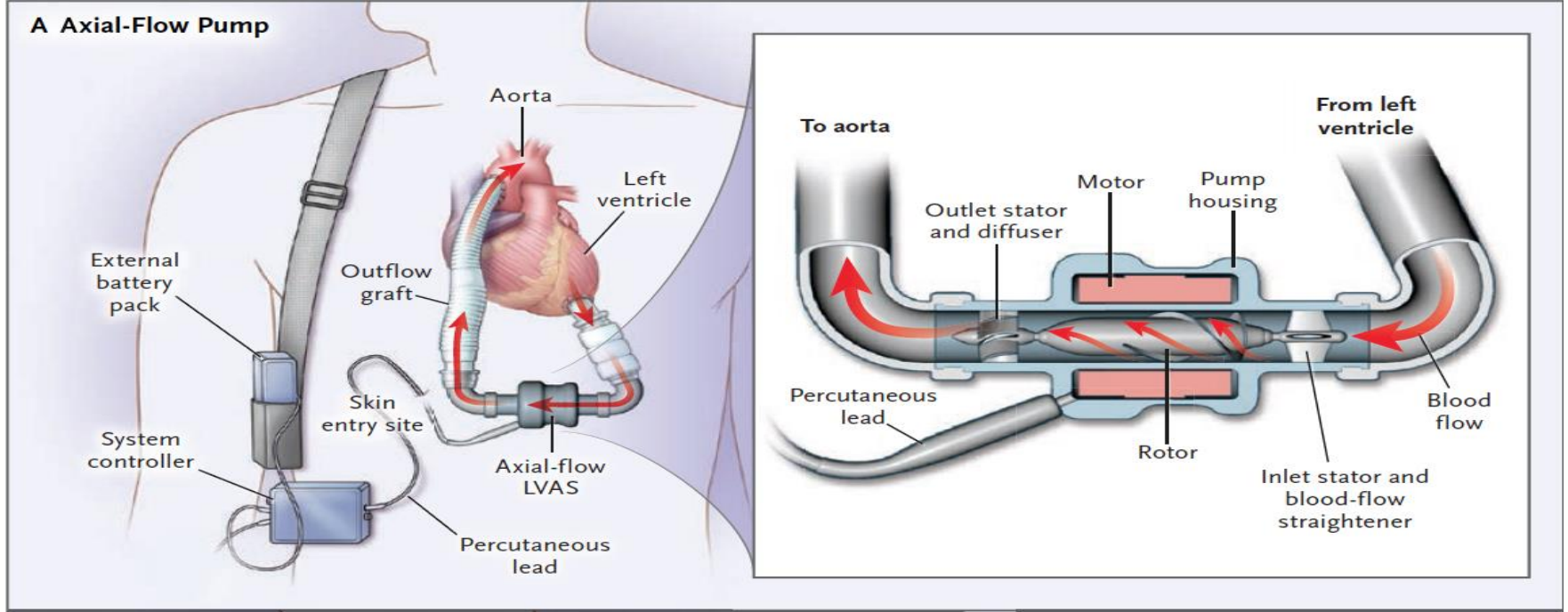
- Fully magnetically levitated
- Designed for hemocompatibility:
  - Large pu
    trauma
  - Texture
  - Artificia
- Wide range o
  - Full sup
- Surgically int
  - Enginee
  - Modula



A Fully Magnetically Levitated Circulatory Pump for Advanced Heart Failure

Mandeep R. Mehra, M.D., Yoshifumi Naka, M.D., Nir Uriel, M.D., Daniel J. Goldstein, M.D., Joseph C. Cleveland, Jr., M.D., Paolo C. Colombo, M.D., Mary N. Walsh, M.D., Carmelo A. Milano, M.D., Chetan B. Patel, M.D., Ulrich P. Jorde, M.D., Francis D. Pagani, M.D., Keith D. Aaronson, M.D., David A. Dean, M.D., Kelly McCants, M.D., Akinobu Itoh, M.D., Gregory A. Ewald, M.D., Douglas Horstmanshof, M.D., James W. Long, M.D., and Christopher Salerno, M.D., for the MOMENTUM 3 Investigators*

N Engl J Med 2017;376:440-50.


A Axial-Flow Pump
Aorta
Left ventricle
External battery pack
Outflow graft
Skin entry site
System controller
Axial-flow LVAS
Percutaneous lead
To aorta
From left ventricle
Motor
Pump housing
Outlet stator and diffuser
Percutaneous lead
Rotor
Blood flow
Inlet stator and blood-flow straightener

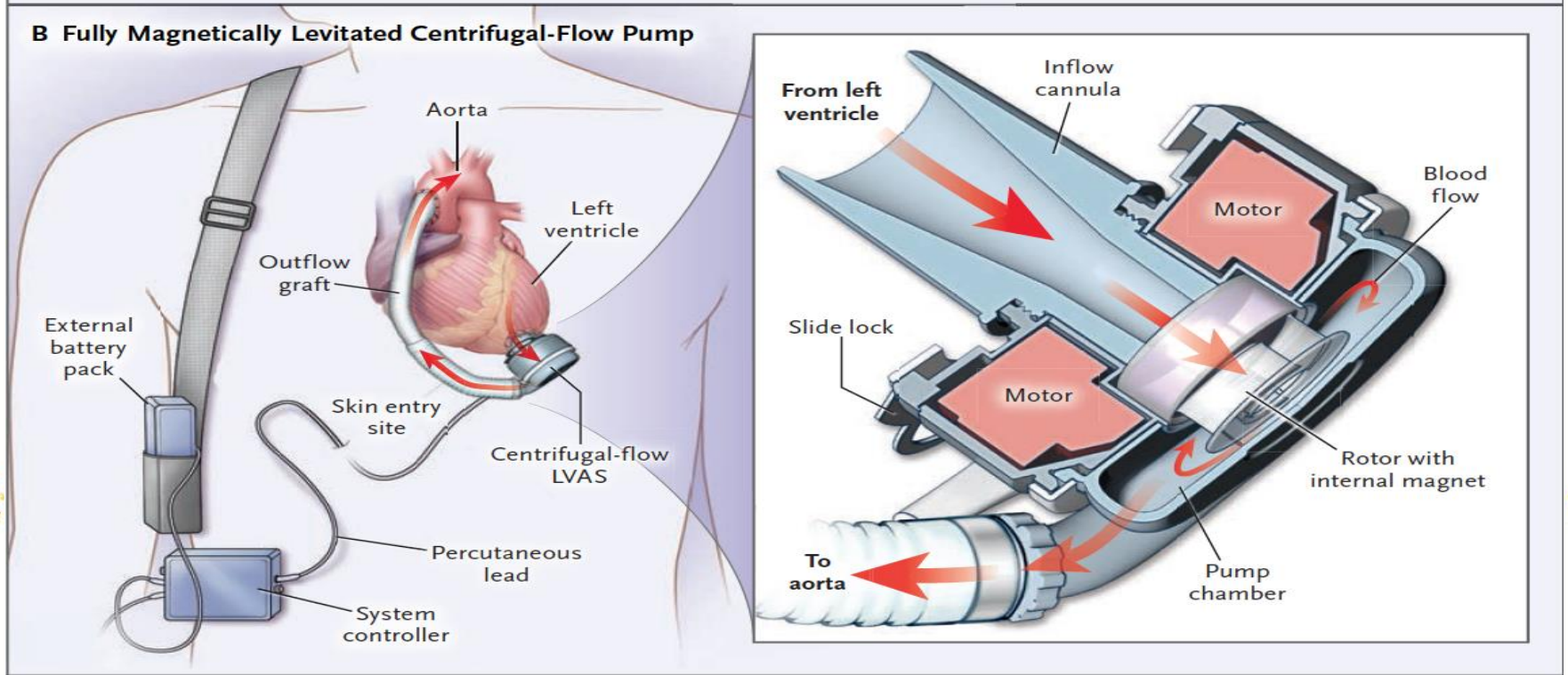
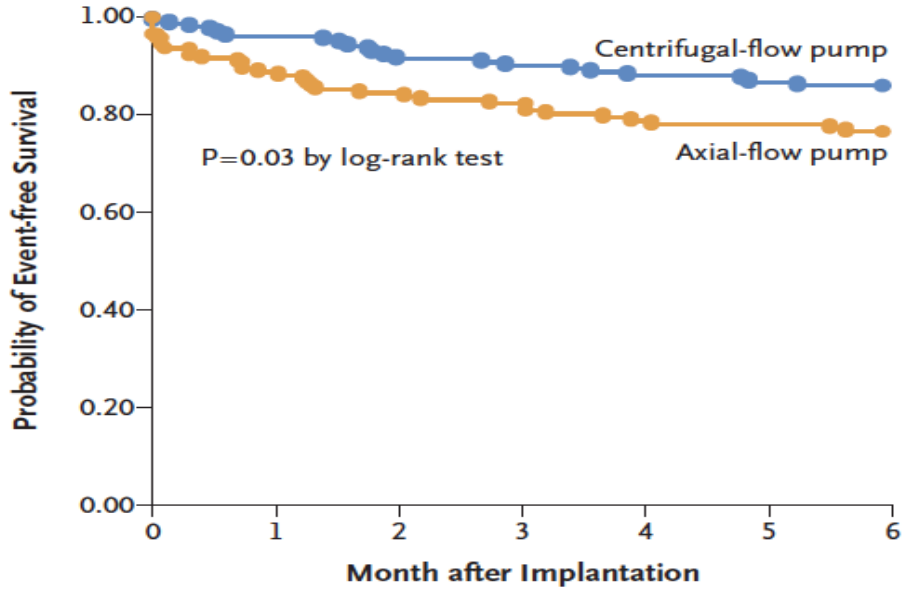

B Fully Magnetically Levitated Centrifugal-Flow Pump
Aorta
Left ventricle
Outflow graft
External battery pack
Skin entry site
Centrifugal-flow LVAS
Percutaneous lead
System controller
From left ventricle
Inflow cannula
Blood flow
Motor
Slide lock
Motor
Rotor with internal magnet
To aorta
Pump chamber

Table 2. Noninferiority and Superiority Analyses in the Intention-to-Treat Population.*

Variable	Centrifugal-Flow Pump Group (N=152)		Axial-Flow Pump Group (N=142)		Absolute Difference	Hazard Ratio (95% CI)	P Value†
	no. of patients	*% (95% CI)*	*no. of patients*	*% (95% CI)*	*percentage points (95% LCB)*		
Noninferiority analysis							
Primary end point	131	86.2 (79.7–91.2)	109	76.8 (68.9–83.4)	9.4 (–2.1)		<0.001
Superiority analyses							
Primary end point	131	86.2 (79.7–91.2)	109	76.8 (68.9–83.4)		0.55 (0.32–0.95)	0.04
First event that resulted in failure to reach the primary end point							
Did not receive the assigned implant	1	0.7 (0–3.6)	4	2.8 (0.8–7.1)		0.23 (0.03–2.09)	0.15
Had disabling stroke	6	3.9 (1.5–8.4)	4	2.8 (0.8–7.1)		1.31 (0.37–4.64)	0.59
Underwent reoperation to replace or remove pump‡	1	0.7 (0–3.6)	11	7.7 (3.9–13.4)		0.08 (0.01–0.60)	0.002
Died within 6 months after implantation	13	8.6 (4.6–14.2)	14	9.9 (5.5–16.0)		0.82 (0.38–1.73)	0.70



No. at Risk

Centrifugal-flow pump	152	146	138	135	130	128	127
Axial-flow pump	142	125	119	116	110	106	103

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
Local infection not associated with LVAS	46 (30.5)	57	36 (26.1)	58	1.17 (0.81–1.69)	0.41
Right heart failure						
Any right heart failure	45 (29.8)	49	34 (24.6)	36	1.21 (0.83–1.77)	0.33
Right heart failure managed with RVAS	4 (2.6)	4	8 (5.8)	8	0.46 (0.14–1.48)	0.18
Cardiac arrhythmia						
Any cardiac arrhythmia	47 (31.1)	61	52 (37.7)	68	0.83 (0.60–1.14)	0.24
Ventricular arrhythmia	27 (17.9)	33	27 (19.6)	37	0.91 (0.57–1.48)	0.71
Supraventricular arrhythmia	23 (15.2)	27	30 (21.7)	31	0.70 (0.43–1.15)	0.15
Respiratory failure	33 (21.9)	44	24 (17.4)	27	1.26 (0.78–2.02)	0.34
Renal dysfunction	17 (11.3)	18	12 (8.7)	12	1.29 (0.64–2.61)	0.47
Hepatic dysfunction	7 (4.6)	7	3 (2.2)	3	2.13 (0.56–8.08)	0.34
Hemolysis not associated with pump thrombosis	1 (0.7)	1	2 (1.4)	2	0.46 (0.04–4.98)	0.61

Summary

- *End stage CHF is associated with significant mortality and limited therapeutic options.*
- *Medical therapy ultimately becomes insufficient. Advanced therapies are still underutilized.*
- *The goal from referral to MCS is to significantly impact survival and quality of life.*
- *MCS should be individualized based on patient characteristics and excluded when prognosis is more influenced by conditions other than HF.*
- *Device technology is advancing rapidly to match prognosis with heart transplant.*

Thank you