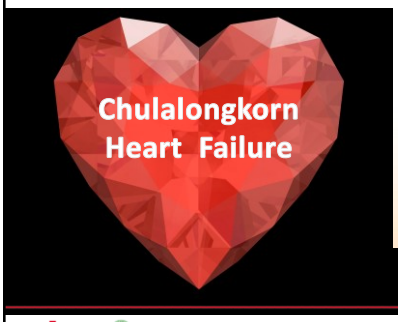
Mechanical circulatory support II : LVAD



เอกราช อริยะชัยพาณิชย์
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Heart Failure Essentials For Cardiology Fellows 2018
18.08.2018

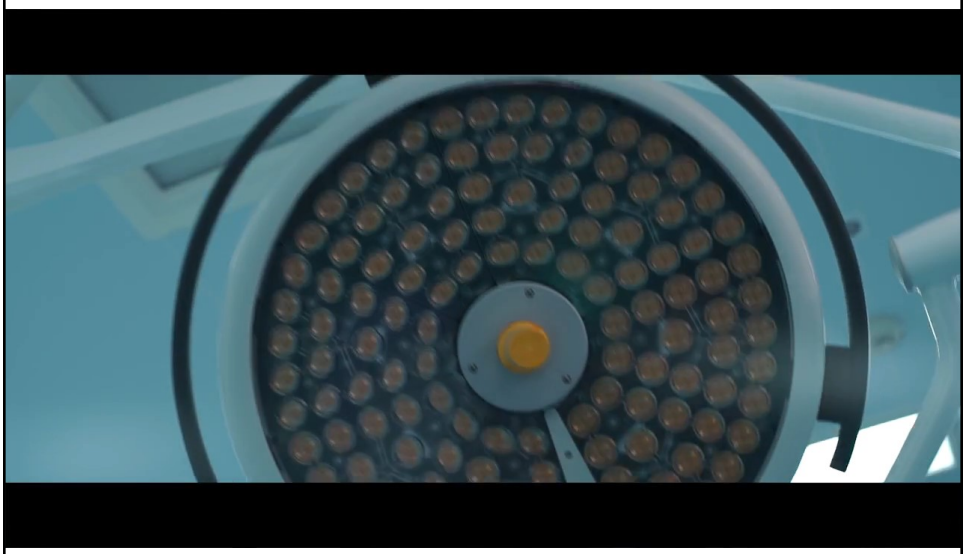
Disclosure

- There are no relevant financial relationships exist related to my role in this session.
- Speaker, CME service:
  Berlin, Merck, Novartis, Thai-Otsuka, Roche Diagnostics, Servier
- Consultant, non-CME service:
  Novartis

In 2013, the American Heart Association funded $32 million in research related to heart failure...

We found Wesley to be excellence candidate for a heart transplant but because of the shortage of the donor organ. We were concern that he may not survive until the donor heart is available.

5



6

7

Indications for MCS

- **Bridge to transplant (BTT)**
  - In a patient who is on waiting list
- **Destination therapy (DT)**
  - In a patient who is not a transplant candidate
- Bridge to …
  - To recovery:
    - Shock, post cardiac surgery, acute MI, myocarditis
  - **To decision:**
    - Evaluation for OHT candidacy status
  - Short term:
    - High risk PCI, valve intervention, ablation.

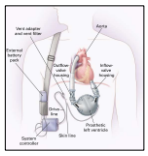
Table 13.3 Patients potentially eligible for implantation of a left ventricular assist device

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/m²).
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.

2016 ESC HF guideline

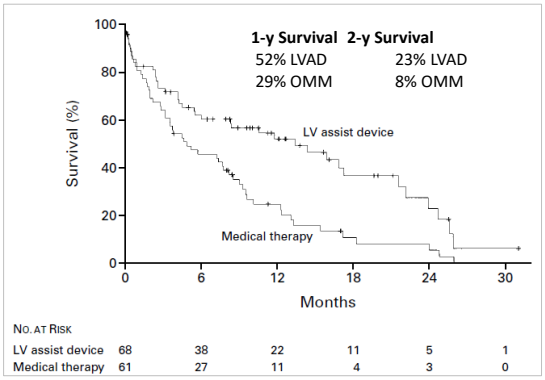
REMATCH study



- Pts w chronic stg D HF who is not a transplant candidates
- N = 129
- RCT to
  pulsatile flow LVAD vs. OMM

- LVAD resulted
  - ↑ Survival
  - ↑ QoL

- Established **destination therapy** as indication for MCS



NEJM 2001; 345:1435-43

HF (acute or chronic)

Rx

Non pharmacologic | Pharmacologic | CRT/ICD | Multidisciplinary

Inotrope

Heart transplant

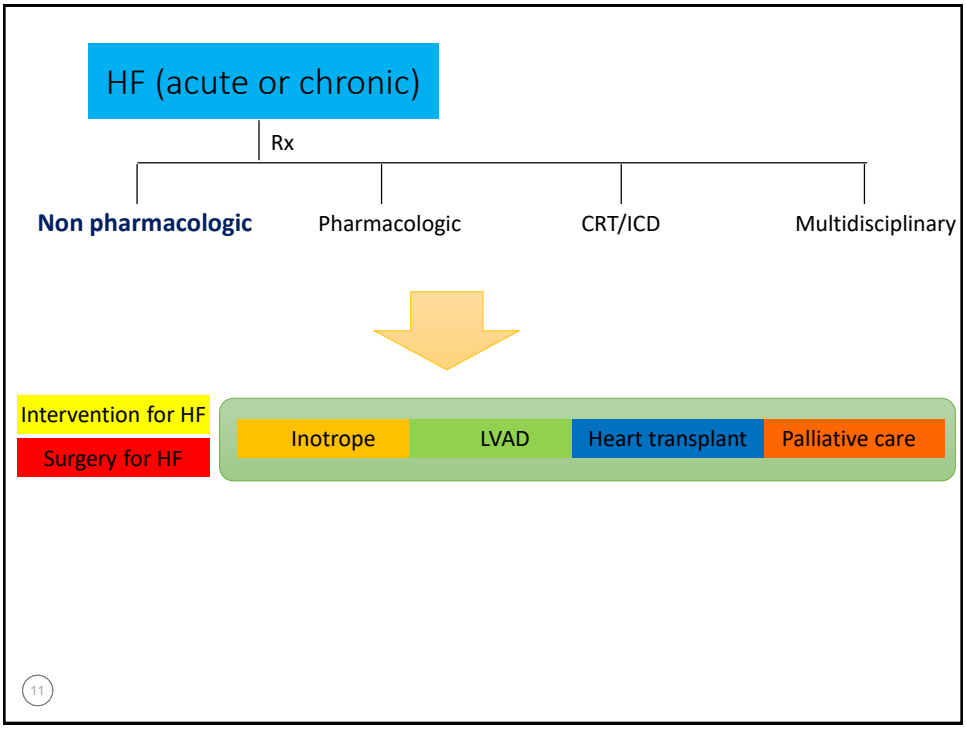
LVAD

Palliative care

Intervention for HF

Surgery for HF

10



Landmarks in MCS

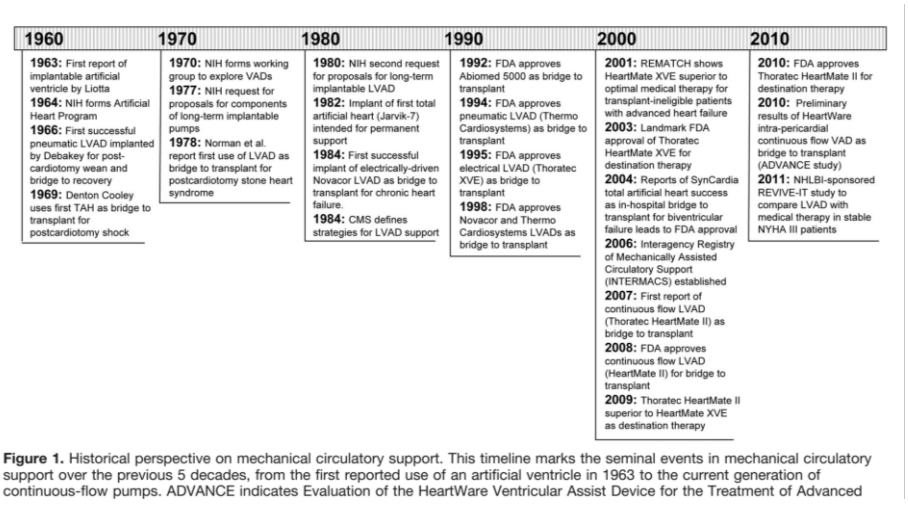


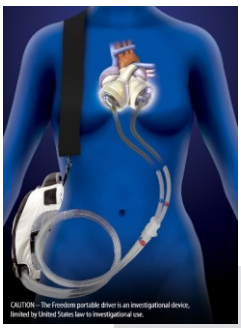
Figure 1. Historical perspective on mechanical circulatory support. This timeline marks the seminal events in mechanical circulatory support over the previous 5 decades, from the first reported use of an artificial ventricle in 1963 to the current generation of continuous-flow pumps. ADVANCE indicates Evaluation of the HeartWare Ventricular Assist Device for the Treatment of Advanced

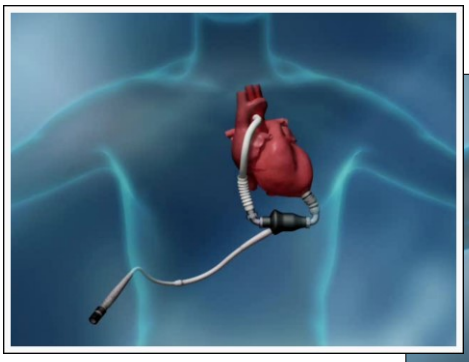
Stewart et al. *Circulation* 2012, 125:1304-1315

Type / terminology of MCS

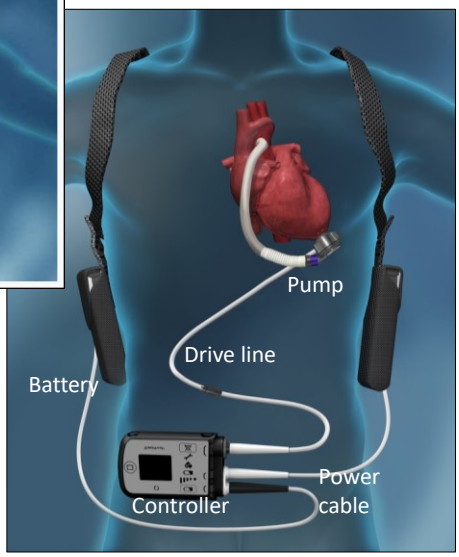
- **Duration of support:** Non-durable (short-term) vs nondurable (long-term)
- **Flow characteristic**: Pulsatile vs Continuous
- **Degree of support**: Partial support vs Full support
- **Implant approach**: Percutaneous vs Surgical
- **Pump location**: Intra vs Extracorporeal
- **Type:** LVAD, RVAD, ECMO, TAH
- **Generation:** 1. pulsatile flow
  2. Continuous flow – axial
  3. Continuous flow – centrifugal

Total Artificial Heart



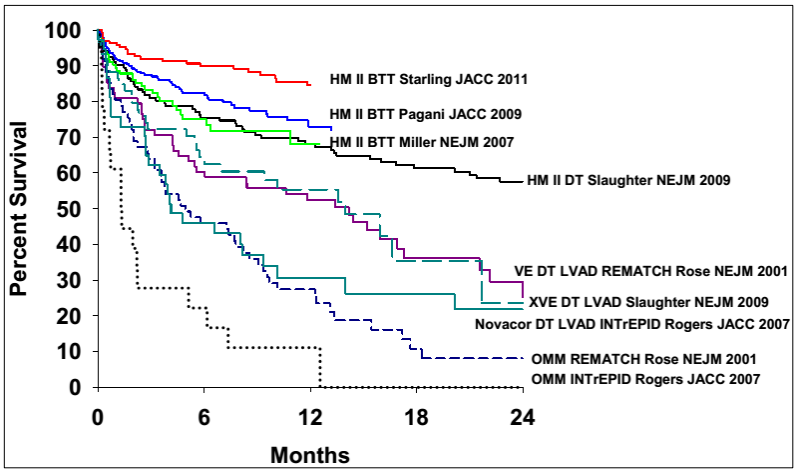


Heartmate II device



Heartmate III device

VAD survival outcome



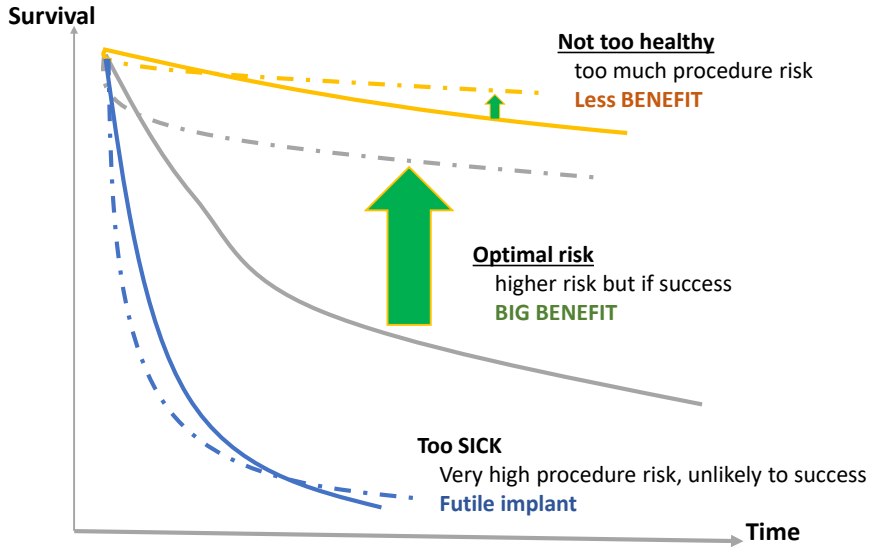
Outcome

- 1-year survival = 70-80%
  - Improve quality of life
- **High event rate** (1st year event)*
  - Infection 5-25%
  - RV failure 10%
  - Stroke 10%
  - GI Bleeding 5%
  - Pump thrombosis/malfunction rare
  - Aortic insufficiency

* Data from HM II device

JACC. 2009;54:312-21.

3 months too early is better than 5 mins too late



Adapt from circ 2011;123:1559.

INTERMACS profile

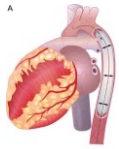
Level	INTERMACS Description	NYHA Class	Suggested timing for definite treatement
1	Critical cardiogenic shock "Crash and burn"	IV	Hours
2	Progressive decline despite inotropic support "Sliding fast on inotropes"	IV	Hours to days
3	Stable but inotrope dependent, can be in hospital or at home "Dependent stability"	IV	Week to months
4	Resting symptoms. Recurrent decompensatory. "Frequent flyer"	IV ambulatory	Variable
5	Exertion intolerant, comfort at rest, symptoms with minimal ADL. "Housebound"	IV ambulatory	Variable
6	Exertion limited, possible ADL but meaningful activity limit. "Walking wounded"	III	Variable
7	Advanced NYHA III "Placeholder"	III	Variable

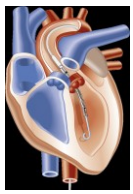
J Heart Lung Transplant 2009;28:535.

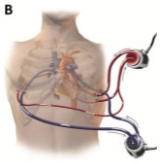
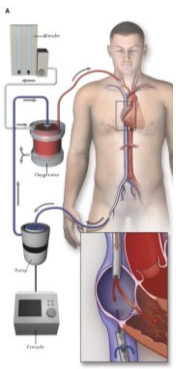
INTERMACS 1

- Critical cardiogenic shock - "Crash and burn"
  - Dying in front of you – hours
  - Even IABP is not enough
- Need to save end-organ, hemodynamics
- Bridge to
  - To long term LVAD (too sick now)
  - To transplant/ transplant evaluation
- Temporary MCS
  - Centrimag, ECMO, TandemHeart, Impella

Short-term MCS



IABP* **TandemHeart** **Impella** **CetriMag*** **ECMO***

Short-term MCS

Improve hemodynamics but not outcomes

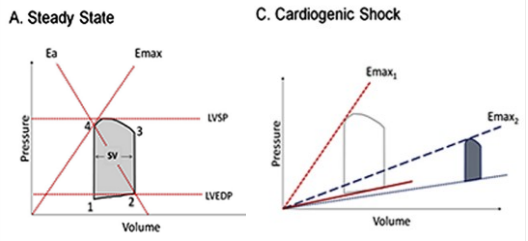
	IABP	ECMO	TandemHeart	Impella 2.5	Impella 5.0
Pump mechanism	Pneumatic	Centrifugal	Centrifugal	Axial flow	Axial flow
Cannula size	7.9 Fr	18–21 Fr inflow;15–22 Fr outflow	21 Fr inflow; 15–17 Fr outflow	13 Fr	22 Fr
Insertion technique	Descending aorta via the femoral artery	Inflow cannula into the right atrium via the femoral vein, outflow cannula into the descending aorta via the femoral artery	21 Fr inflow cannula into left atrium via femoral vein and transseptal puncture and 15–17 Fr outflow cannula into the femoral artery	12 Fr catheter placed retrogradely across the aortic valve via the femoral artery	21 Fr catheter placed retrogradely across the aortic valve via a surgical cutdown of the femoral artery
Haemodynamic support	0.5 – 1.0 L min^{-1}	>4.5 L min^{-1}	4 L min^{-1}	2.5 L min^{-1}	5.0 L min^{-1}
Implantation time	+	++	+++	++	++++
Risk of limb ischaemia	+	+++	+++	++	++
Anticoagulation	+	+++	+++	+	+
Haemolysis	+	++	++	++	++
Post-implantation management complexity	+	+++	++++	++	++
Optional active cooling in post-cardiopulmonary resuscitation patients	No	Yes	(Yes)	No	No

ECMO, extracorporeal membrane oxygenation; IABP, intra-aortic balloon pump; +, ++, +++, ++++, relative qualitative grading concerning time ('implantation time'), risk ('risk of limb ischaemia'), intensity ('anticoagulation', post-implantation management complexity'), and severity ('haemolysis'). Modified from Ouweneel and Henriques.[32]

Mechanical circulatory support in cardiogenic shock

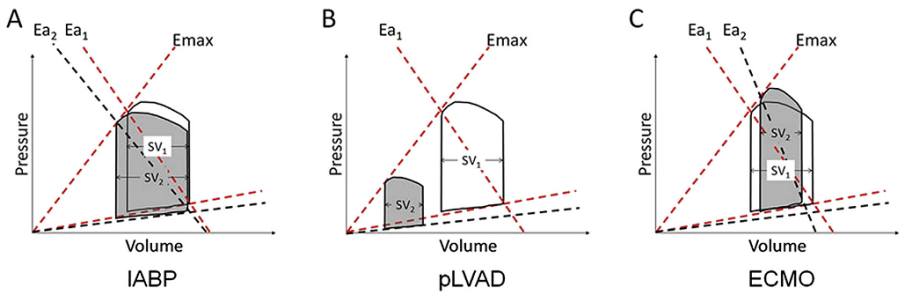
Karl Werdan[1]*, Stephan Gielen[1], Henning Ebelt[1], and Judith S. Hochman[2]

Eur Heart J 2014;35:156-167.

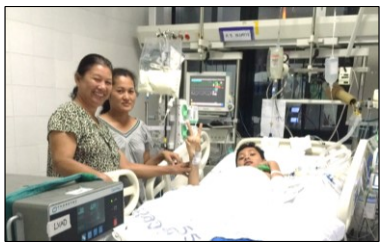


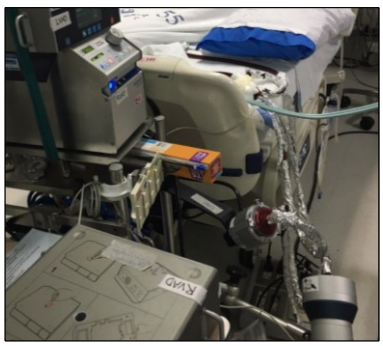
EXPERT CONSENSUS DOCUMENT

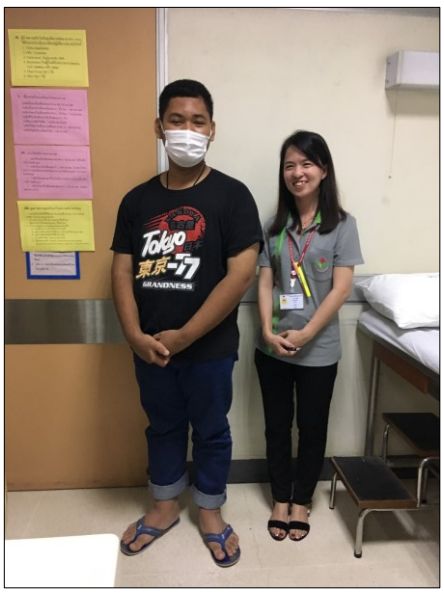
2015 SCAI/ACC/HFSA/STS Clinical Expert Consensus Statement on the Use of Percutaneous Mechanical Circulatory Support Devices in Cardiovascular Care



JACC 2015;65:e7-26







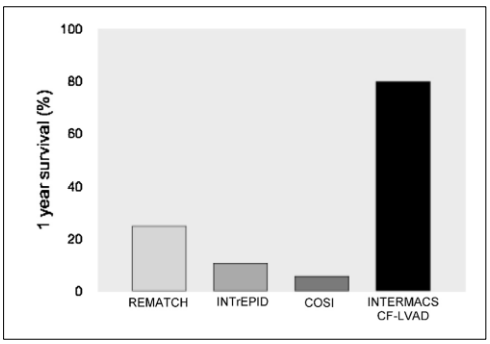
INTERMACS 2-3

INTERMACS 2
- Progressive decline despite inotropic support
- "Sliding fast on inotropes"
- Days to week

INTERMACS 3
- Stable but inotrope dependent, can be in hospital or at home
- "Dependent stability"
- Weeks to months

Most appropriate use of long term LVADs
Mean HTx waiting time in Thailand = 80 days

INTERMACS 2-3



- 1-year survival of patients on continuous inotropic support compared to those supported with a durable continuous flow left ventricular assist device.
  - REMATCH 25%
  - INTrEPID 11%
  - COSI 6%
  - LVAD 80%

indianheartjournal68(2016)s45–s51

INTERMACS 4-7

- NYHA IV, IIIb, III
- Uncertainty time frame
- Less sick patients

- ROADMAP study
- REVIVE study

Potential benefit in functional capacity and QoL
But risks of stroke, bleeding, infection.

ROADMAP study

- Prospective, non-randomized, **observational study**
- EF < 25%, INTERMACS 4-7
- **Significant different in primary endpoint.**
- HM II is related to
  - ↑ QoL
  - ↑ adverse events

REVIVE-IT - "clinical hold"

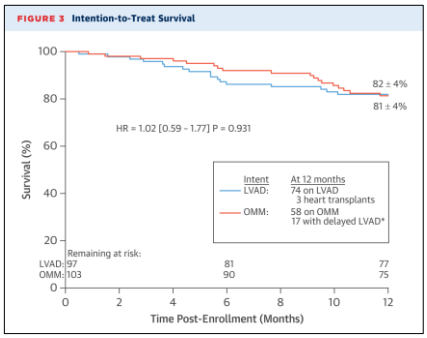


TABLE 4 Primary Endpoint and Components that Prevented Success

	OMM (n = 82)*	LVAD (n = 85)†	Odds Ratio (95% Confidence Interval)
Alive at 12 months on original therapy with increase in 6MWD by 75 m	17 (21)	33 (39)	2.4 (1.2-4.8) p = 0.012
First event that prevented success:	65 (79)	52 (61)	
Death within 1 yr	18 (22)	17 (20)	
Delayed LVAD	18 (22)‡	NA	
Delta 6MWD <75 m	29 (35)	33 (39)	
Urgent transplant	0	2 (2)	

JACC 2015;66:1747–61

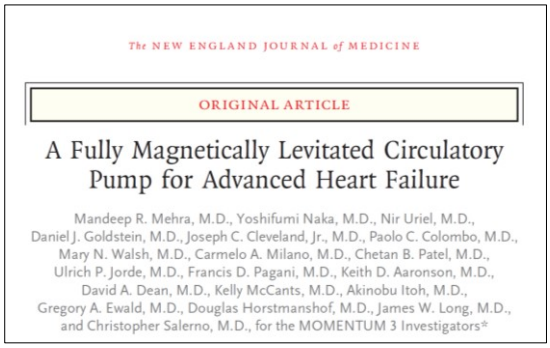
More than half of patient underwent LVAD placement are INTERMAC 2-3

Table 1 – Current distribution of durable mechanical circulatory support devices across INTERMACS levels.

INTERMACS Level	Definition	% Of durable MCS
1	Critical cardiogenic shock	14.3%
2	Progressive decline	36.0%
3	Stable but inotrope dependent	29.6%
4	Resting symptoms	14.5%
5	Exertion-intolerant	3.0%
6	Exertion-limited	1.2%
7	Advanced NYHA Class 3	0.7%

INTERMACS, Interagency Registry for Mechanically Assisted Circulatory Support; MCS, mechanical circulatory support; NYHA, New York Heart Association.

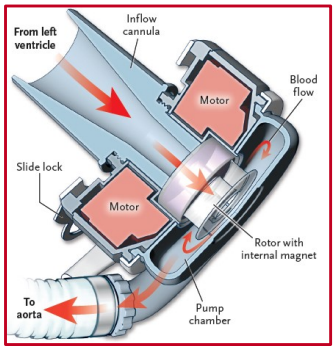
HeartMate 3™ LVAS


The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

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*



- **Wide** blood-flow passages to reduce shear stress
- **Frictionless** with absence of mechanical bearings
- **Intrinsic Pulse** designed to reduce stasis and avert thrombosis

Caution – HeartMate 3 LVAS is an investigational device. Limited by Federal (United States) law to investigational use

SJM-HM3-1116-0003 | Item approved for global use.

Baseline Characteristics - 2

Characteristic	HeartMate 3 (n=152)	HeartMate II (n=142)
Left ventricular ejection fraction - %	17.1 ± 5.0	17.3 ± 4.9
Arterial blood pressure - mmHg		
Systolic*	110 ± 16	106 ± 12
Diastolic	67 ± 10	66 ± 10
Mean arterial pressure* - mmHg	81 ± 10	79 ± 9
PCWP - mmHg	23 ± 9	22 ± 9
Cardiac index - liters/min/m^2 of body surface area	1.9 ± 0.5	2.0 ± 0.7
PVR - Wood Units	3.3 ± 1.7	3.0 ± 1.6
Right atrial pressure - mmHg	10 ± 6	11 ± 7
Serum sodium - mmol/liter	135.6 ± 3.9	134.9 ± 4.2
Serum creatinine - mg/ml	1.4 ± 0.4	1.4 ± 0.4
INTERMACS Profile** – no (%)		
1	1 (1)	4 (3)
2	50 (33)	44 (31)
3	76 (50)	69 (49)
4	22 (14)	23 (16)
5-7†	2 (1)	2 (1)
Intended Use of device at implant – no (%)		
Bridge to Transplant (BTT)	41 (27)	37 (26)
Bridge to Candidacy	27 (18)	27 (18)
Destination Therapy (DT)	84 (55)	78 (55)

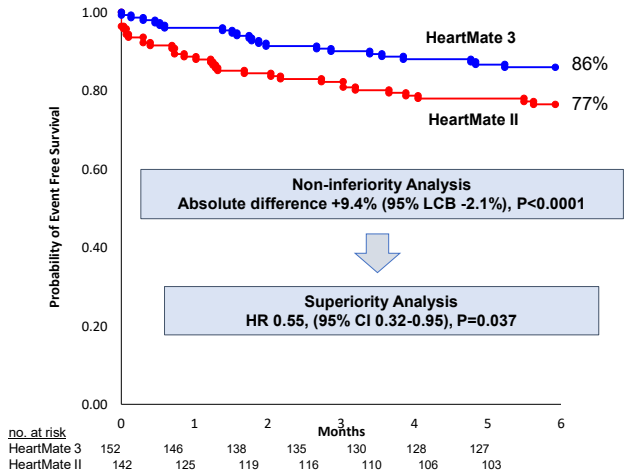
* Systolic blood pressure (P= 0.01) and Mean arterial pressure (P=0.04) were statistically significantly;
** one subject in HM3 group expired prior to INTERMACS Assessment;
† There were no subjects with INTERMACS 6 and 7 in either groups; PCWP denotes pulmonary capillary wedge pressure and PVR pulmonary vascular resistance

Caution – HeartMate 3 LVAS is an investigational device. Limited by Federal (United States) law to investigational use

SJM-HM3-1116-0003 | Item approved for global use.

Primary End Point Analysis (ITT)

Survival at 6 months free of disabling stroke or reoperation to replace or remove the pump



LCB, lower confidence boundary, HR, hazard ratio, and CI, confidence interval

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SJM-HM3-1116-0003 | Item approved for global use.

Key Adverse Events: Pump Thrombosis, Neurological Events, Bleeding

	HeartMate 3 (n=151)		HeartMate II (n=138)				
	n (%)	no. of Events	n (%)	no. of Events	RR	95% CI for RR	P Value
Suspected or Confirmed Pump Thrombosis	**0 (0)**	**0**	**14 (10)**	**18**	**N/A**	**N/A**	**< 0.0001**
All Stroke	12 (7)	12	15 (10)	17	0.73	0.35-1.51	0.39
Hemorrhagic Stroke	4 (2)	4	8 (5)	8	0.46	0.14-1.48	0.18
Ischemic Stroke	8 (5)	8	9 (6)	9	0.81	0.32-2.05	0.66
Disabling Stroke	9(6)	9	5(3)	5	1.65	0.57-4.79	0.36
Other Neurologic Events*	9 (6)	9	8 (5)	8	1.03	0.41-2.59	0.95
Bleeding	50 (33)	100	54 (39)	98	0.85	0.62-1.15	0.29
Bleeding Requiring Surgery	15 (9)	15	19 (13)	21	0.72	0.38-1.36	0.31
Gastrointestinal Bleeding	**24 (15)**	**47**	**21 (15)**	**36**	**1.04**	**0.61-1.79**	**0.87**

No Pump Thrombosis in the HeartMate 3 LVAS group

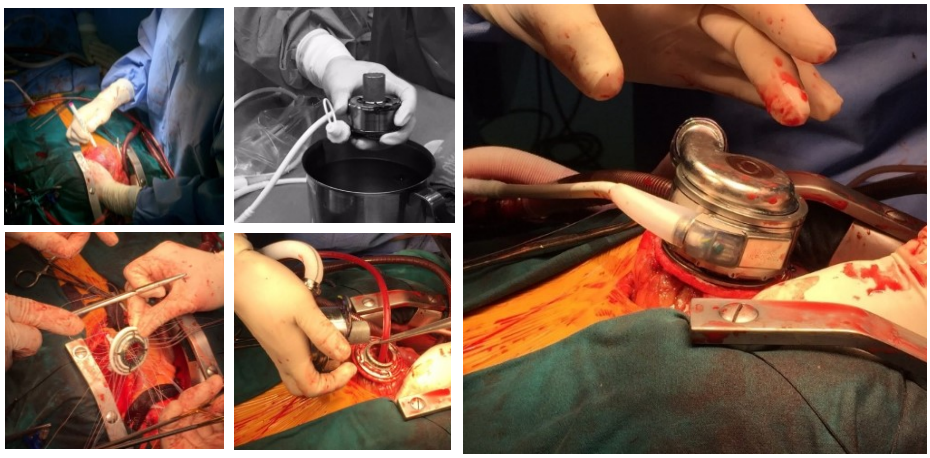
Similar Stroke and Bleeding rates in both groups

RR, denotes Relative Risk and CI, confidence interval
*Includes transient ischemic attacks and neurologic events other than stroke

Caution – HeartMate 3 LVAS is an investigational device. Limited by Federal (United States) law to investigational use

SIM-HM3-1116-0003 | Item approved for global use.

Surgical Implant



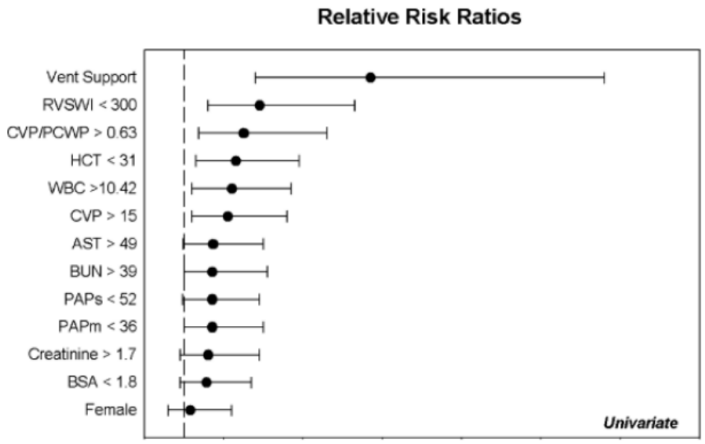
Experience of Durable LVAD in Thailand

- Since 2014
- ~ 10 pts
  - Heartmate II
  - Heartmate III

Evaluate patient <u>for LVAD</u>

- Relatively the same as HTx eval
  - Medical, surgical, psychosocial
  - Patient and care-giver
- Contraindication
  - Active infection
  - Cannot take coumadin
  - HFpEF
  - Severe RV failure
  - Irreversible end-organ dysfunction – dialysis, cirrhosis
- Earlier referral is better

Univariate Predictors of RV failure

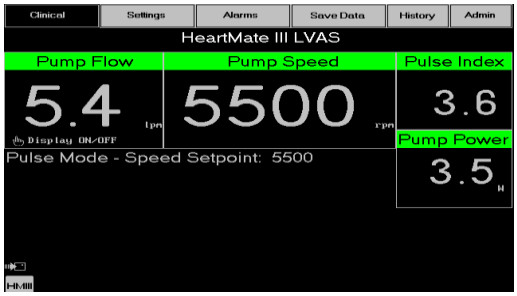


Thorac Cardiovasc Surg 2010;139:1316-24.

Evaluate patient with LVAD

- Always evaluate patient not the pump
- High suspicious for
  - Hemolysis, bleeding, infection, RV failure, stroke
  - HF, arrhythmia, ischemic, valve
- OPD
  - Continuous flow = No pulses
  - Doppler BP = 70-80 mmHg
  - Anticoagulation INR 2-2.5
  - Drive line dressing daily
  - HF meds

Basic VAD parameters



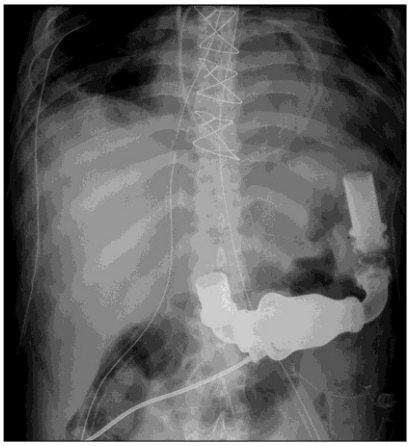
- Speed (rpm)
  - Fixed, set by the clinician
  - HMIII 5000 ± 1000
  - HMII 9000 ± 1000
- Power (watt)
  - Direct measurement of pump motor energy use in Watts
  - 4 ± 1.5
- Pump flow estimator (L/min)
  - Estimated CO thru pump
  - 4 ± 1.5
- Pulsatility Index (PI)
  - The magnitude of flow pulses
  - 4 ± 1.5

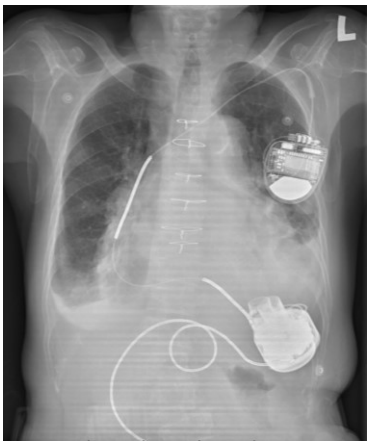
All parameters depend on patient condition and characteristics

HeartMate 3 System Overview

System Components

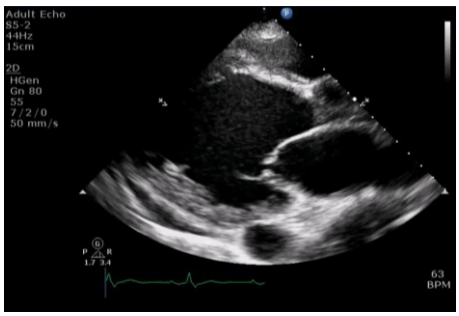
*New for HM 3



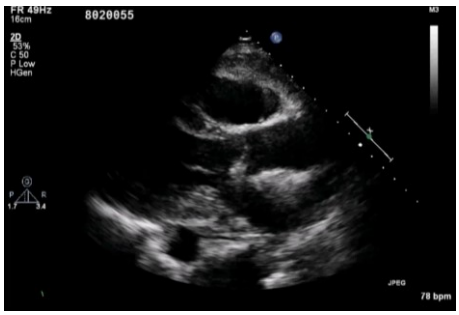


LVAD placement

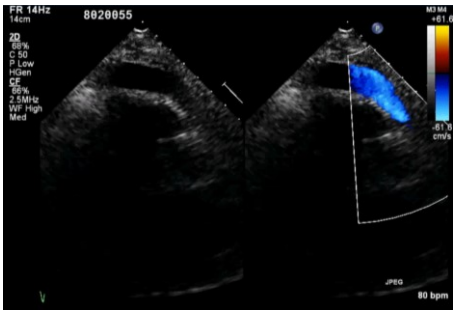
Pre VAD

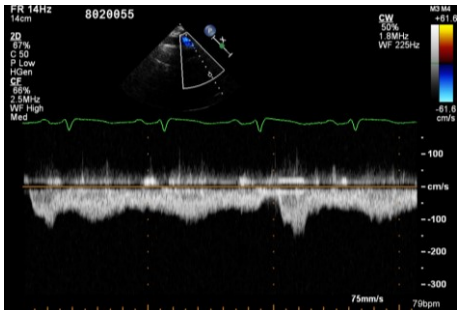


Post VAD



Outflow cannula





Dos and Donts in VAD

Do

- TTE (always helpful)
- ECG
- Xray, USG, CT
- Defibrillation
- Cardiac cath
- Ablation

- Discuss with patients
- Switch to battery
- Contact pt's VAD coordinator
- Call me 091-879-6108

Don't

- No CPR
- Pregnant
- Stop treating HF

Recommendations for implantation of mechanical circulatory support in patients with refractory heart failure

Recommendations	Class [a]	Level [b]	Ref [c]
An LVAD should be considered in patients who have end- stage HFrEF despite optimal medical and device therapy and who are eligible for heart transplantation in order to improve symptoms, reduce the risk of HF hospitalization and the risk of premature death (Bridge to transplant indication).	IIa	C	
An LVAD should be considered in patients who have end-stage HFrEF despite optimal medical and device therapy and who are not eligible for heart transplantation to, reduce the risk of premature death.	IIa	B	605, 612, 613

HF = heart failure; HFrEF = heart failure with reduced ejection fraction; LVAD = left ventricular assist device.
[a]Class of recommendation.
[b]Level of evidence.
[c]Reference(s) supporting levels of evidence.

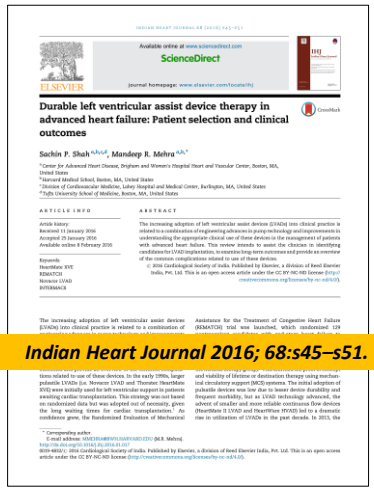
ESC 2016:
Class: IIa

AHA/ACC 2013:
Class IIa

MCS		
MCS is beneficial in carefully selected* patients with stage D HF in whom definitive management (eg, cardiac transplantation) is anticipated or planned	IIa	B
Nondurable MCS is reasonable as a "bridge to recovery" or "bridge to decision" for carefully selected* patients with HF and acute profound disease	IIa	B
Durable MCS is reasonable to prolong survival for carefully selected* patients with stage D HFrEF	IIa	B

End-Staged Heart Failure - Recommendation

Recommendation	COR	LOE
Heart transplant		
In carefully selected patients who are transplant candidates, heart transplants are recommended to improve survival, symptoms and quality of life.	I	C
Mechanical circulatory support (MCS) include LVAD		
In carefully selected patients, a short-term MCS should be considered in patients with severe cardiogenic shock to improve hemodynamic in between evaluation ("bridge to decision").	IIa	B
In carefully selected patients, a short-term or long-term MCS should be considered in patients with advanced HF who are transplant candidates to improve survival, symptoms and quality of life while awaiting suitable donors ("bridge to transplant")	IIa	B
In carefully selected patients, a long-term MCS should be considered in patients with advanced HF who are not transplant candidates to improve survival, symptoms and quality of life. ("destination therapy")	IIa	B
Palliative care		
Integration of palliative care as an adjunctive treatment in combination with other curative treatments is recommended for patients with advanced HF to improve quality of life.	I	B
In patients whose prognosis are weeks to months, an end-of-life or specialized hospice care service should be considered.	IIa	B



Durable left ventricular assist device therapy in advanced heart failure: Patient selection and clinical outcomes

Sachin P. Shah [a,b,c,d], Mandeep R. Mehra [a,b,*]

Indian Heart Journal 2016; 68:s45–s51.

CONTROVERSIES IN CARDIOVASCULAR MEDICINE

Is Left Ventricular Assist Device Therapy Underutilized in the Treatment of Heart Failure?

Left Ventricular Assist Devices Are Underutilized

Leslie W. Miller, MD

Circulation 2011;123:1552-1558

Thank you

จุฬาลงกรณ์
ภาวะหัวใจล้มเหลว
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Back up slide

Quality of life

TABLE 6 Adverse Events

	OMM (n = 103)	LVAD (n = 94)	DT Trial§ (EPPY)
Bleeding	1 (1) [0.02]	44 (47) [1.22]‡	1.13
GI bleeding	1 (1) [0.02]	29 (31) [0.76]‡‖	–
Driveline infection	–	9 (9.6) [0.14]‡	0.22
Pump thrombus	–	6 (6.4) [0.08]†	0.07¶
Within 90 days	–	1 (1.1)	–
Pump exchange yr 1	–	4 (4.3)	2.1%
Stroke	2 (2) [0.02]	8 (8.5) [0.09]*	0.08
Ischemic	1 (1) [0.01]	5 (5.3) [0.06]*	0.05
Hemorrhagic	1 (1) [0.01]	4 (4.3) [0.03] NS	0.03
Arrhythmias VT/VF	6 (5.8) [0.12]	17 (18.1) [0.23]*	0.46
Worsening HF#	36 (35) [0.68]	10 (10.6) [0.12]‡	–
Rehospitalizations	64 (62) [1.43]	75 (79.8) [2.49]‡	2.64**
Composite event rate††	39 (38) [0.83]	62 (66) [1.89]‡	2.09
Relative risk (95% CI)	OMM/LVAD: 0.44 (0.35–0.56)‡		–

No Chest Compression

- Ok to cardioversion/defib