เอกราช อริยะชัยพาณิชย์

Heart Failure and Transplant Cardiology

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Chulalongkorn HEART FAILURE & TRANSPLANT CARDIOLOGY

Disclosure

- Speaker, CME service:
  Merck, Otsuka, Servier
- Consultant, non-CME service:
  Novartis, Menarini

5 Rx options for stage D HF

1. Heart transplant
2. MCS/VAD
3. Chronic home inotrope
4. Palliative care
5. Experimental surgery or meds

DEPEND ON

1. Patient's goal of care
2. Transplant candidacy
3. Available time (prognosis)

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/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.

2016 ESC guideline

Terminology/ type 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

Types of MCS

	Temporary MCS	Long-term MCS
Pulsatile flow	IABP* INCOR/EXCOR BerlinHeart*	HeartMate XVE LVAD Thoratec VAD Total Artificial Heart
Continuous flow	CentriMag* ECMO* Impella Recover TandemHeart	HeartMate II* HeartMate III* HVAD

	Heart Transplant	LVAD
Indication	Gold standard - In a very selected patient - Candidacy	Improve survival + QoL - Bridge to transplant - Destination therapy - Bridge to decision
1-yr survival	85 - 90%	70-80%
Limitation	Limited donors Cultural and believe	Many devices Financially restrict
Experiences **- Worldwide** **- Thailand**	 4000 / year 20 /year	 >5,000 / year 5 patients
Self-care	Immunosuppressant Endomyocardial biopsy “transplant” patient	Anticoagulation Wound dressing “VAD” patient

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Short-term MCS

12 yo with DCM
On dob
On list April 2016
Tranaplant July 2016

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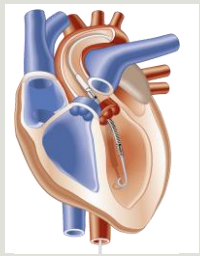
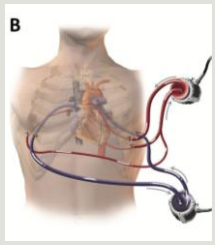
IABP*

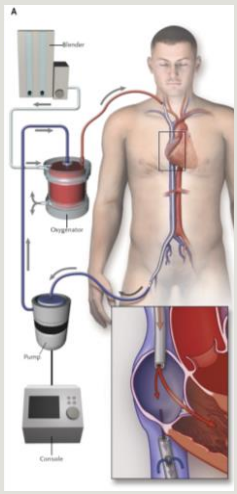

TandemHeart

Impella

CetriMag*



ECMO*

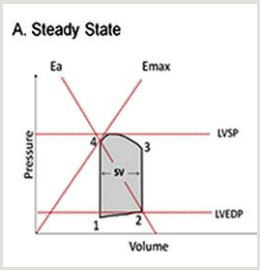
Short-term MCS

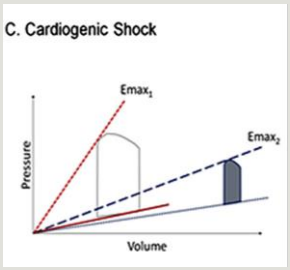
Improve hemodynamics but not outcomes

	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]

Eur Heart J 2014;35:156-167.

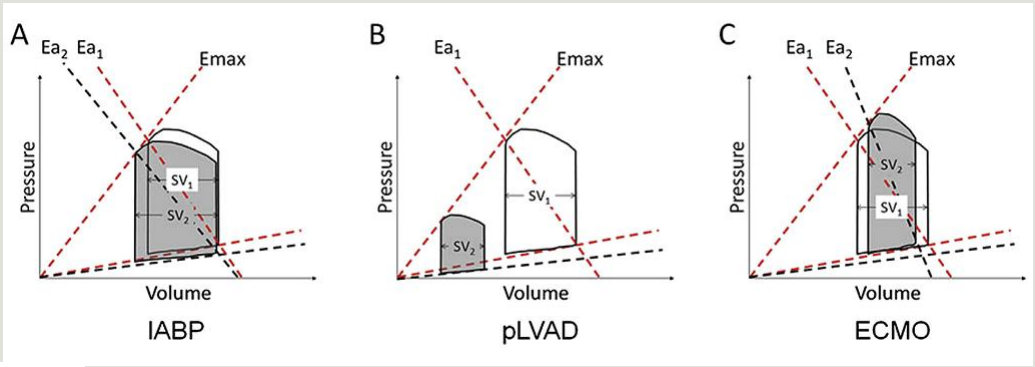




EXPERT CONSENSUS DOCUMENT

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



Chulalongkorn HEART FAILURE & TRANSPLANT CARDIOLOGY

Durable (Long-term) VAD

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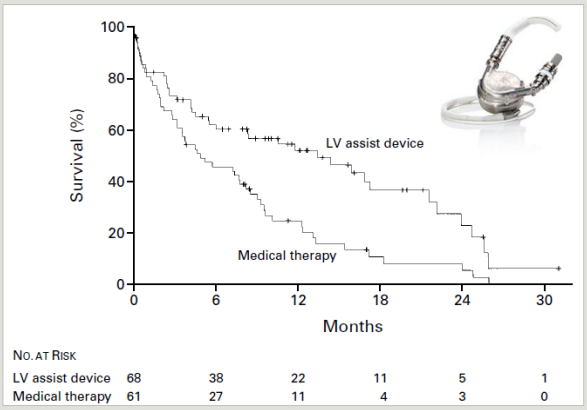
REMATCH study


The New England Journal of Medicine

LONG-TERM USE OF A LEFT VENTRICULAR ASSIST DEVICE FOR END-STAGE HEART FAILURE

- Pts w chronic stg D HF who is not a transplant candidates
- N = 129
- RCT to
  - pulsatile flow LVAD
  - OMM
- LVAD resulted in a survival benefit
  - ↑ QoL
- Established DT as indication for MCS



1-y Survival	2-y Survival
52% LVAD	23% LVAD
29% OMM	8% OMM

NEJM 2001; 345:1435-43

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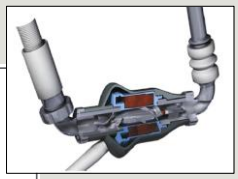
Improving survival with continuous-flow LVAD



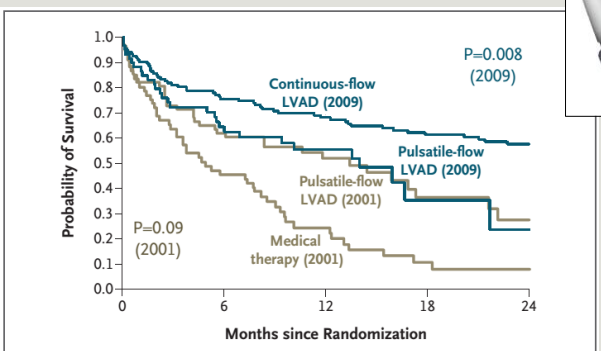


Figure 1. Survival Rates in Two Trials of Left Ventricular Assist Devices (LVADs) as Destination Therapy.

The curves labeled 2009 are those reported by Slaughter and colleagues in this issue of the *Journal*[2]; those labeled 2001 were reported for the REMATCH trial.[1]

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Fang JC, NEJM 2009;361:2282

VAD trials

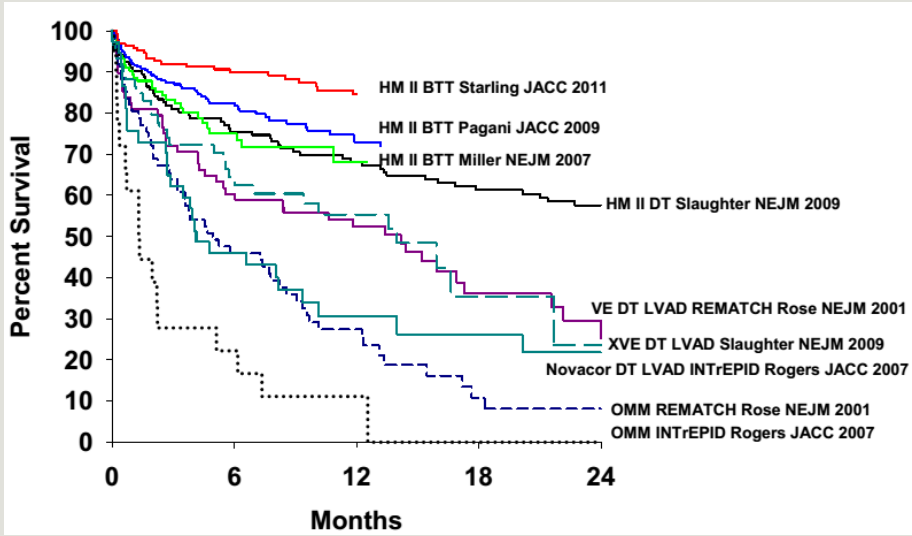
TABLE 2 Published LVAD Clinical Trials

Study, Year (Ref. #)	n	Device Tested	Indication	Design	Patient Population	Outcome
REMATCH, 2001 (19)	129	HeartMate XVE	DT	Prospective 1:1 HeartMate XVE vs. medical therapy	New York Heart Association functional class IV for 60 days, LVEF <25%, and peak oxygen consumption <14 ml/min/kg (unless on balloon pump, intravenous inotropes, or physically unable to perform exercise test), or intra-aortic balloon pump or IV inotrope dependent for 14 days	1- and 2-yr HeartMate XVE survival of 52% and 23% vs. 25% and 8% on medical therapy
INTREPID, 2007 (43)	55	Novacor	DT	Prospective nonrandomized	Inotrope-dependent patients	1-yr Novacor survival of 27% vs. 11% on medical therapy
HeartMate II, 2009 (7)	192	HeartMate II	DT	Prospective randomized 2:1 HeartMate II vs. HeartMate XVE	New York Heart Association functional class IIIB or IV symptoms for >45 of the last 60 days, LVEF <25%, and peak oxygen consumption <14 ml/min/kg (unless on balloon pump, intravenous inotropes, or physically unable to perform exercise test), or intra-aortic balloon pump dependent for 7 days or IV inotrope dependent for 14 days	1- and 2-yr HeartMate II survival of 68% and 58% vs. 55% and 24% with HeartMate XVE
HeartMate II post-approval, 2014 (45)	247	HeartMate II	DT	Prospective nonrandomized	Consecutive patients eligible for destination DT in INTERMACS	1- and 2-yr survival of 74% and 61%
HeartMate II, 2007 (8)	133	HeartMate II	BTT	Prospective nonrandomized	Transplant candidates	75% survival to transplant, recovery, or ongoing support although remaining eligible for transplant at 6 months
HeartMate II post-approval, 2011 (44)	169	HeartMate II	BTT	Prospective nonrandomized	Consecutive patients eligible for transplant in INTERMACS	90% survival to transplant, recovery, or ongoing support at 6 months
ADVANCE, 2012 (9)	137	HVAD	BTT	Prospective nonrandomized. HVAD compared with 499 patients who received FDA-approved LVADs in INTERMACS	Transplant candidates	90.7% survival to transplant, recovery, or ongoing support on the original device vs. 90.1% in control group at 6 months

ADVANCE = Evaluation of HeartWare ventricular Assist Device for the Treatment of Advanced Heart Failure; BTT = bridge to transplant; DT = destination therapy; FDA = Food and Drug Administration; HVAD = HeartWare Ventricular Assist Device; INTERMACS = Interagency Registry for Mechanical Assisted Circulatory Support; INTREPID = Investigation of Non Transplant Eligible Patients Who Are Inotrope Dependent; LVAD = left ventricular assist device; REMATCH = Randomized Evaluation of Mechanical Assistance for Treatment of Heart Failure.

JACC 2015;65:2542–55

VAD survival outcome



Thailand experience

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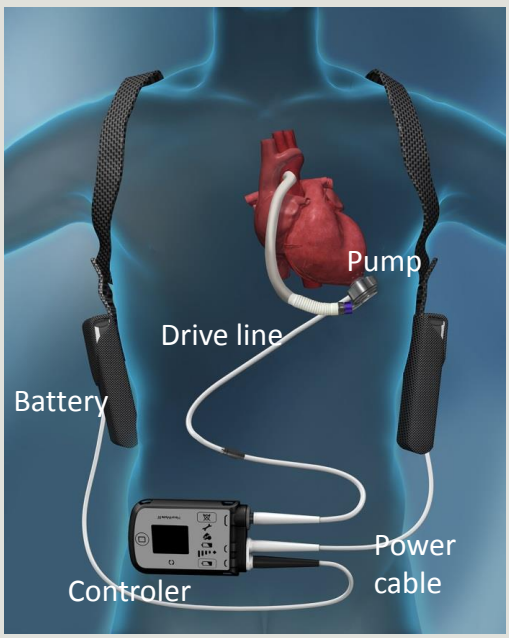
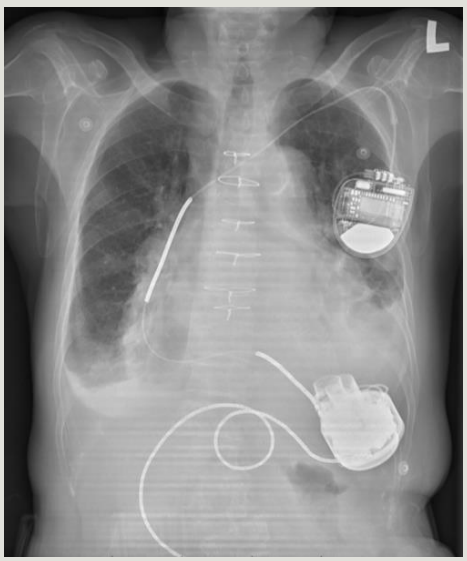
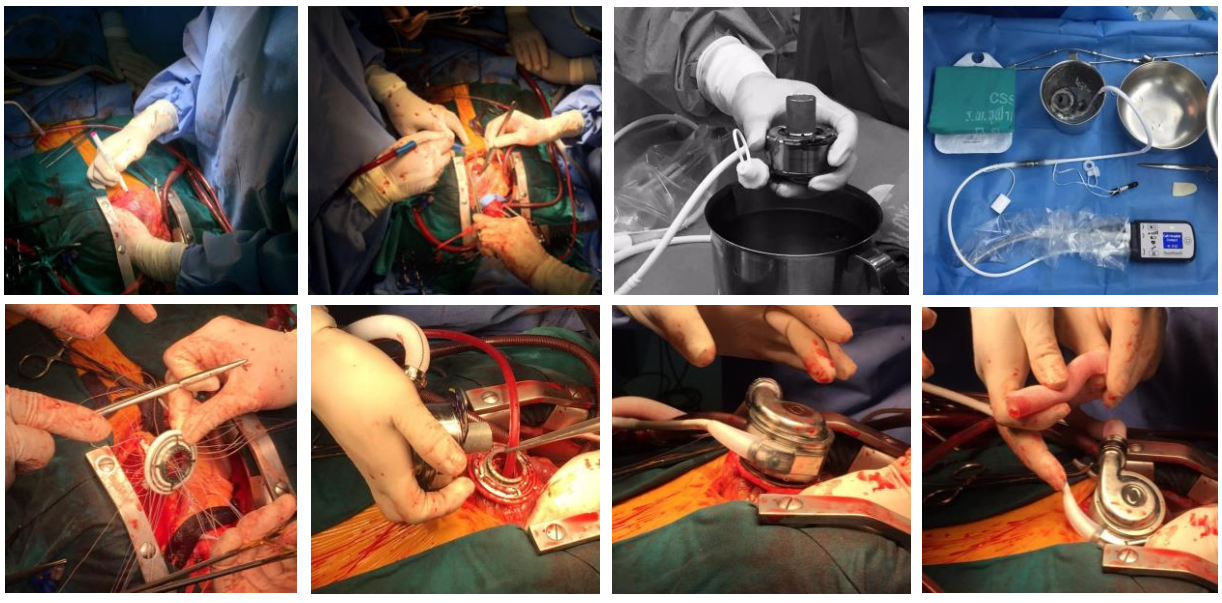


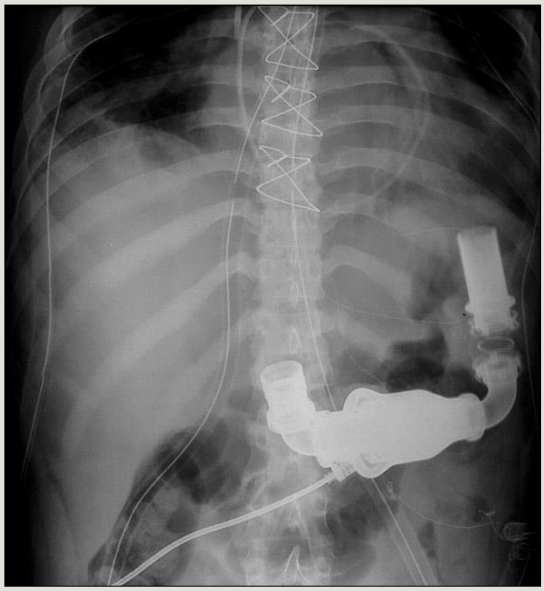


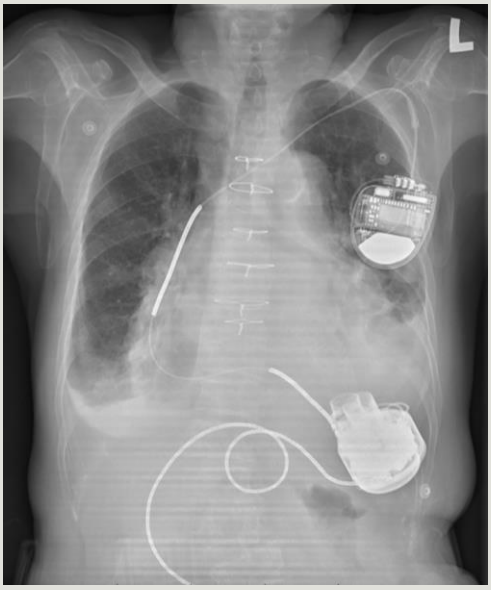
HeartMate 3 System Overview
System Components

*New for HM 3

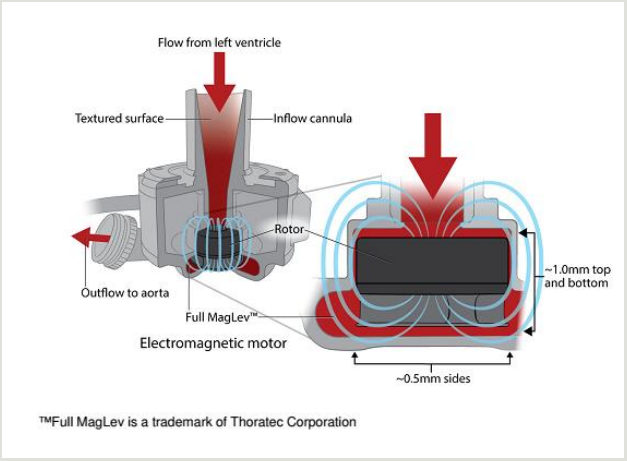


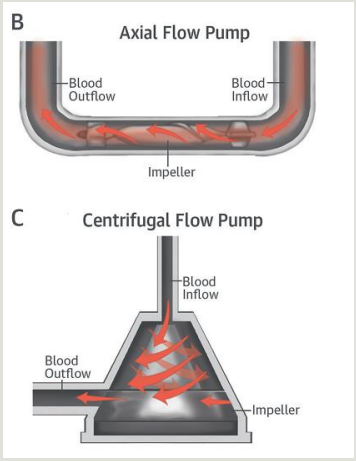
Implant operation





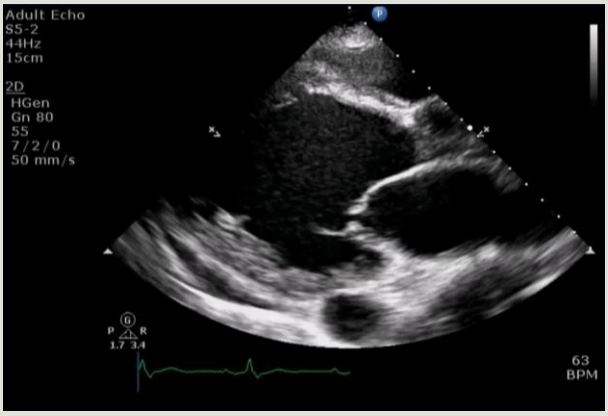
MagLev Centrifugal Pump



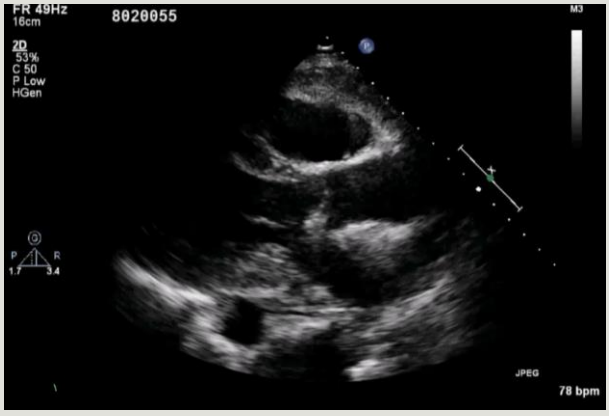


LVAD placement

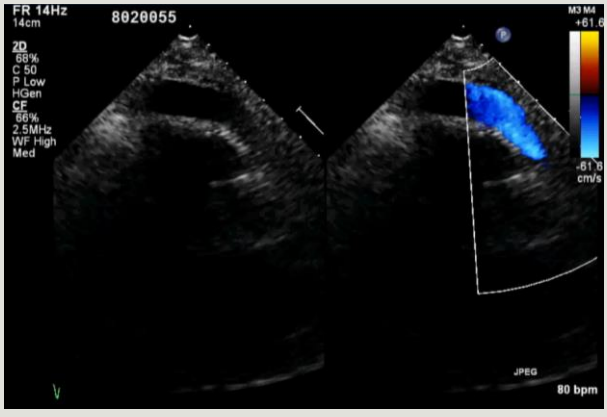
Pre VAD

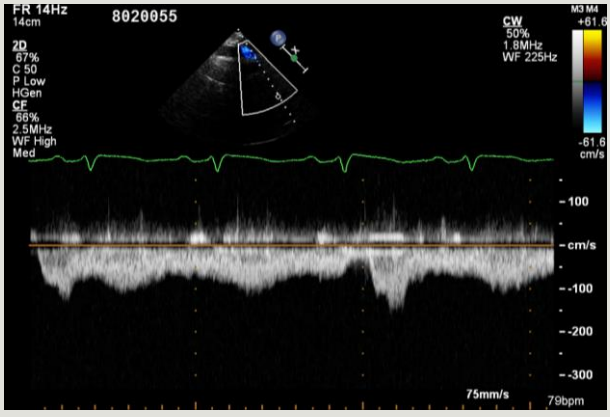


Post VAD



Outflow cannula





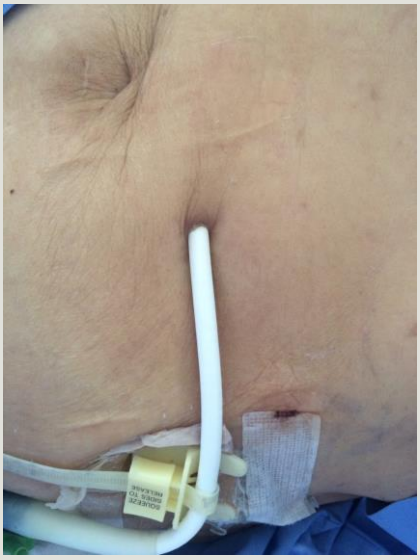
Outcome

- Improve survival
  - 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

JACC. 2009;54:312-21.

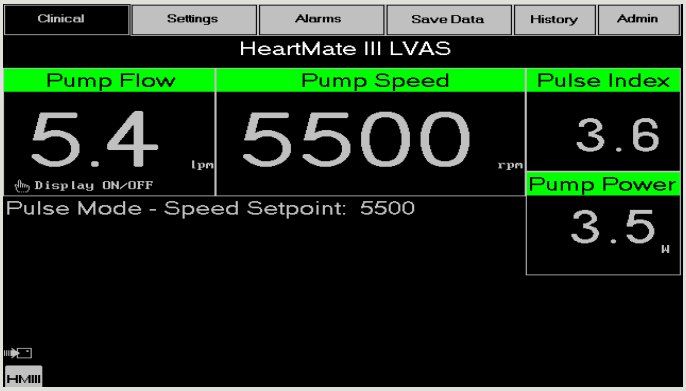
Patient care

- Continuous flow = No pulses
  - HR (listen only)
  - Doppler BP = 70-90 mmHg
- Never CPR
- Anticoagulation
- Drive line care (dressing)
- Hemolysis/bleeding
- Basic VAD parameters



[1]JHLT Apr 2010; Slaughter et al; Vol 29; No 4S.
"Clinical Management of continuous-flow Left Ventricular Assist Devices in Advanced Heart Failure"

SYSTEM MONITOR
CLINICAL SCREEN



DISPLAYS:

- Pump parameters
- Mode
- Monitor/Controller Communication
- 2 highest priority alarm messages

We set the SPEED

Optimum Speed Setting (RPM)

- Normal Cardiac Index
- Normal LV Size
- No Septal Shift
- Intermittent Aortic valve Opening

VAD parameter

Value	Normal
Speed (RPM)	4800 – 6500 RPM
FLOW (LPM)	3-6 LPM
Pulsatility Index (PI)	2-6
Power (Watts)	3-6 Watts

- Speed:
  - Fixed speed is set by the clinician
- Power
  - Direct measurement of pump motor energy use in Watts
- Pum flow estimator
  - Estimated based on power and speed
- Pulsatility Index (PI)
  - The magnitude of flow pulses through the pump. Averaged over 15-second intervals

All parameters depend on patient condition and characteristics

What should I do if ?

- What do you do if your pt with IABP has …..

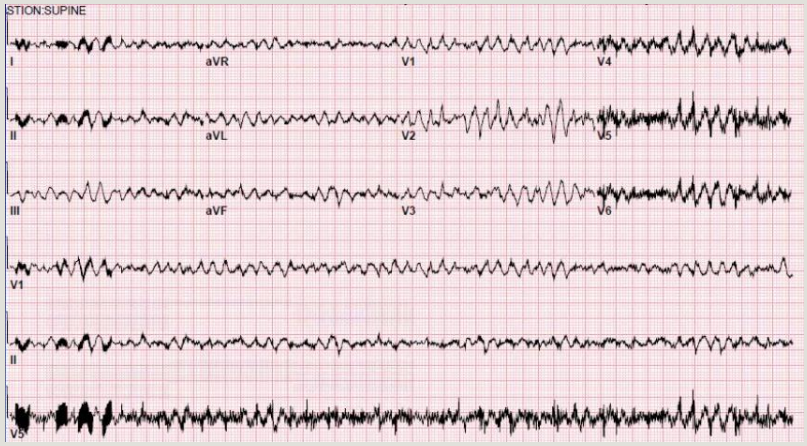
  A massive GI bleed, hypoxia, hypotension

  IABP poor augmentation, balloon rupture

ALWAYS EVALUATING PATIENT, NOT THE PUMP

No Chest Compression

- Ok to cardioversion/defib



When to put an LVAD

- A 71 yo female with HFrEF (EF 18%, LV 8.1 cm)
  - Admitted at other hospital for 2 months for cardiogenic shock
  - Cannot wean off Dobutamine (after multiple attempts)
  - Cr 0.5, INR 1.3, Alb 3.0
  - RA3, RV 45/16, PCWP 14

When to implant a VAD

Profile	Description	Time to MCS
1	"Crashing and burning" - critical cardiogenic shock.	Within hours
2	"Progressive decline" – inotrope dependence with continuing deterioration.	Within a few days
3	"Stable but inotrope dependent" - describes clinical stability on mild-moderate doses of intravenous inotropes. (Patients stable on temporary circulatory support without inotropes are within this profile).	Within a few weeks
4	"Recurrent advanced heart failure" - "recurrent" rather than "refractory" decompensation. "Resting symptoms"	Within weeks to months
5	"Exertion intolerant" - describes patients who are comfortable at rest but are exercise intolerant.	Variable
6	"Exertion limited" – a patient who is able to do some mild activity but fatigue results within a few minutes or any meaningful physical exertion.	Variable
7	"Advanced" - describes patients who are clinically stable with a reasonable level of comfortable activity, despite history of previous decompensation that is not recent.	Not a candidate for MCS

Good timing

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INTERMACS Levels per Era & VAD

Year/Level	2006-2007	2008-2009	2010-2011	2012	± 06-11
1	43%	25.3%	14.8%	15.3%	-27.7%
2	37.1%	44.6%	39.6%	37.6%	+0.5%
3	8.7%	16.2%	26.4%	28.4%	+19.7%
4	6.6%	9.5%	13.3%	13.5%	+6.9%
5	0.9%	1.8%	3.1%	3.0%	+2.1%
6	1.3%	1.4%	1.8%	1.2%	-0.1%
7	2.4%	1.2%	0.6%	0.7%	-1.7%

≥30% ≥15%

Kirklin, JHLTX 12; 31: 117

Intermacs quarterly statistical report, 4th Quarter 2012

REVIVE-HF ROAD MAP

ROADMAP trial (JACC 2015;66:1747–61)

- Prospective, multi-center, non-randomized, controlled, observational study
- HF stg D, NYHA III-IV, EF < 25%), INTERMACS 4-7
- HM II resulted in ↑ survival (80 vs 64%)
- ↑ QoL, ↑ adverse events

REVIVE-IT trial

- Prospective, RCT in HF NYHA III
- Sponsor by NHLBI
- "clinical hold"

J Heart Lung Transplant 2015;34:S80.

Case

- A 71 yo female with HFrEF (EF 18%, LV 8.1 cm)
  - Admitted at other hospital for 2 months for cardiogenic shock
  - Cannot wean off Dob
  - Alb 3.0
  - Cr 0.5
  - INR 1.3
  - RA3, RV 45/16, PCWP 14

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:
AHA/ACC 2013:

Rec. Class IIa
(BTT and DT)

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 HF/EF	IIa	B

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Guideline and further reading

ELSEVIER

The Journal of Heart and Lung Transplantation
http://www.jhltonline.org

The 2013 International Society for Heart and Lung Transplantation Guidelines for Mechanical Circulatory

EXPERT CONSENSUS DOCUMENT

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

Circulation
JOURNAL OF THE AMERICAN HEART ASSOCIATION

American Heart Association.

Recommendations for the Use of Mechanical Circulatory Support: Device Strategies and Patient Selection: A Scientific Statement From the American Heart Association

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Conclusion

- Search for alternative approach for transplantation are inevitable.
  - MCS, VAD, stem cell, etc.
- There are many types of VADs and MCS
  - For many indications
- LVAD is available with acceptable outcome
  - It is far from perfect (RV failure, infection, clot/bleed)
- Early referral is a key to preserved treatment options in patient with terminal HF.

Thank you

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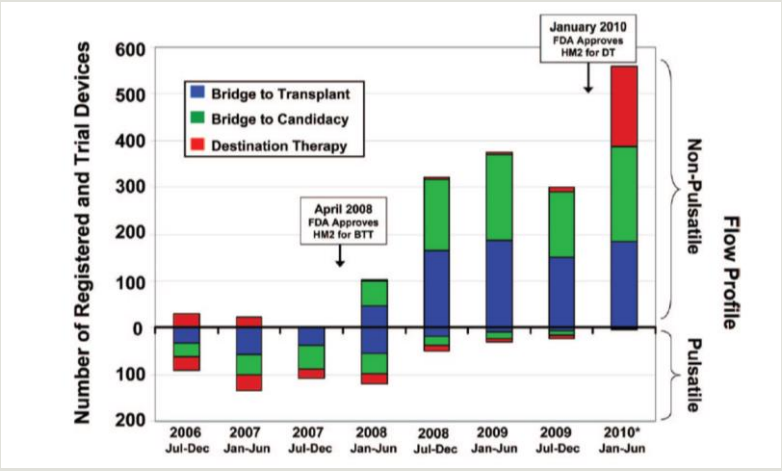
Back up slide

Implant strategies- real world



Circulation2011;123:1559-68.

Future

- Better clinical understanding (for less S/E)
  - Longer support
  - Surg: Implantation techniques, complex anatomy
- Need better technology
  - Smaller
  - Full implant – No driveline
- Need better patient selection
  - Less sick patient ?
- Advancing the field
  - Recovery
  - Pediatric
  - Compete with OHT (survival 4 vs 10 yr)

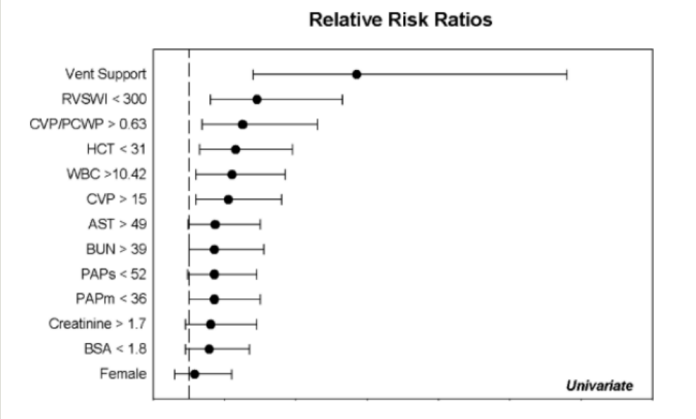
Total Artificial Heart

ROADMAP

Adverse Events at 12 Months

Adverse event	Optimal medical therapy, n=103 (%)	LVAD, n=97 (%)	*P*
Bleeding	1	47	<0.001
Gastrointestinal bleeding	1	31	<0.001
Driveline infection	NA	9.6	<0.001
Pump thrombus	NA	6.4	<0.01
Stroke	2	9.6	<0.05
Ischemic	1	5.3	<0.05
Ventricular tachycardia or ventricular fibrillation	5.8	18.1	<0.001
Worsening HF	35	10.6	<0.05
Rehospitalization	62	79.8	<0.001
"Composite" adverse events*	38	66	<0.001

Univariate Predictors of RV failure



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Heart Transplant in Asia

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KEYWORDS

• Heart transplant • Asia • Heart failure

KEY POINTS

- In Asia the heart transplant program began in Taiwan and Thailand
- least 10 Asian countries that have experience in heart transplant
- Data from registries in each Asian country have shown a trend tow
- heart transplants, mainly due to the implementation of legislation
- The underlying heart disease for heart transplant recipients wa
- followed by ischemic cardiomyopathy, similar to reports from West
- heart disease was more common in Asia.
- Survival at 1, 5, and 10 years after heart transplant in Asia was sim

INTRODUCTION

The history of heart transplant began with Alexis Carrel who conducted experiments on heterotopic heart transplant in animals.[1] For this work, he received the Nobel Prize in medicine and physiology in 1912. It took a long time before the first successful attempt in humans on 3 December, 1967, by Christiaan Bernard at the Groote Schuur Hospital in South Africa.[2] Since then, heart transplant has become the treatment of choice for help-

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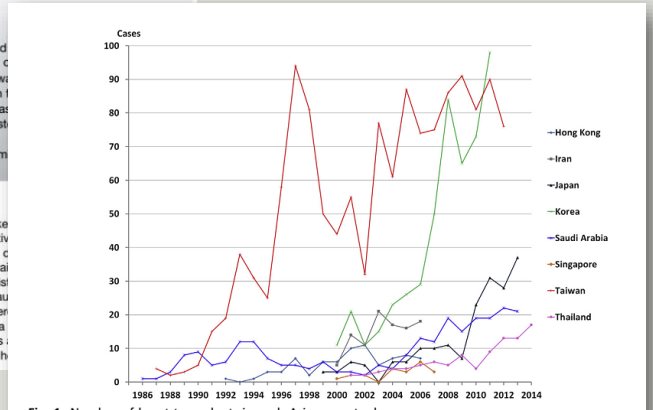

Fig. 1. Number of heart transplants in each Asian country by year.

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