Mechanical Circulatory Support & Heart Transplant

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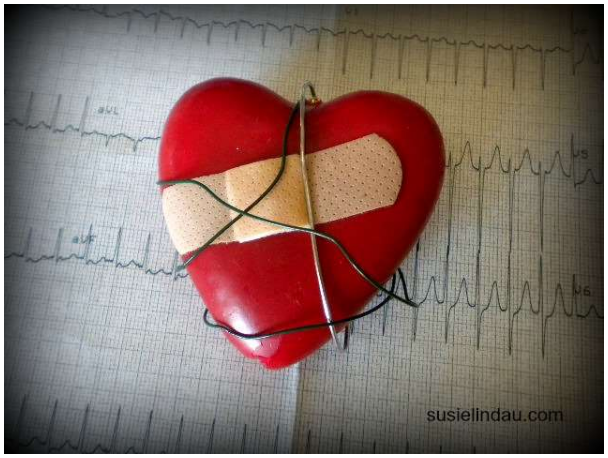
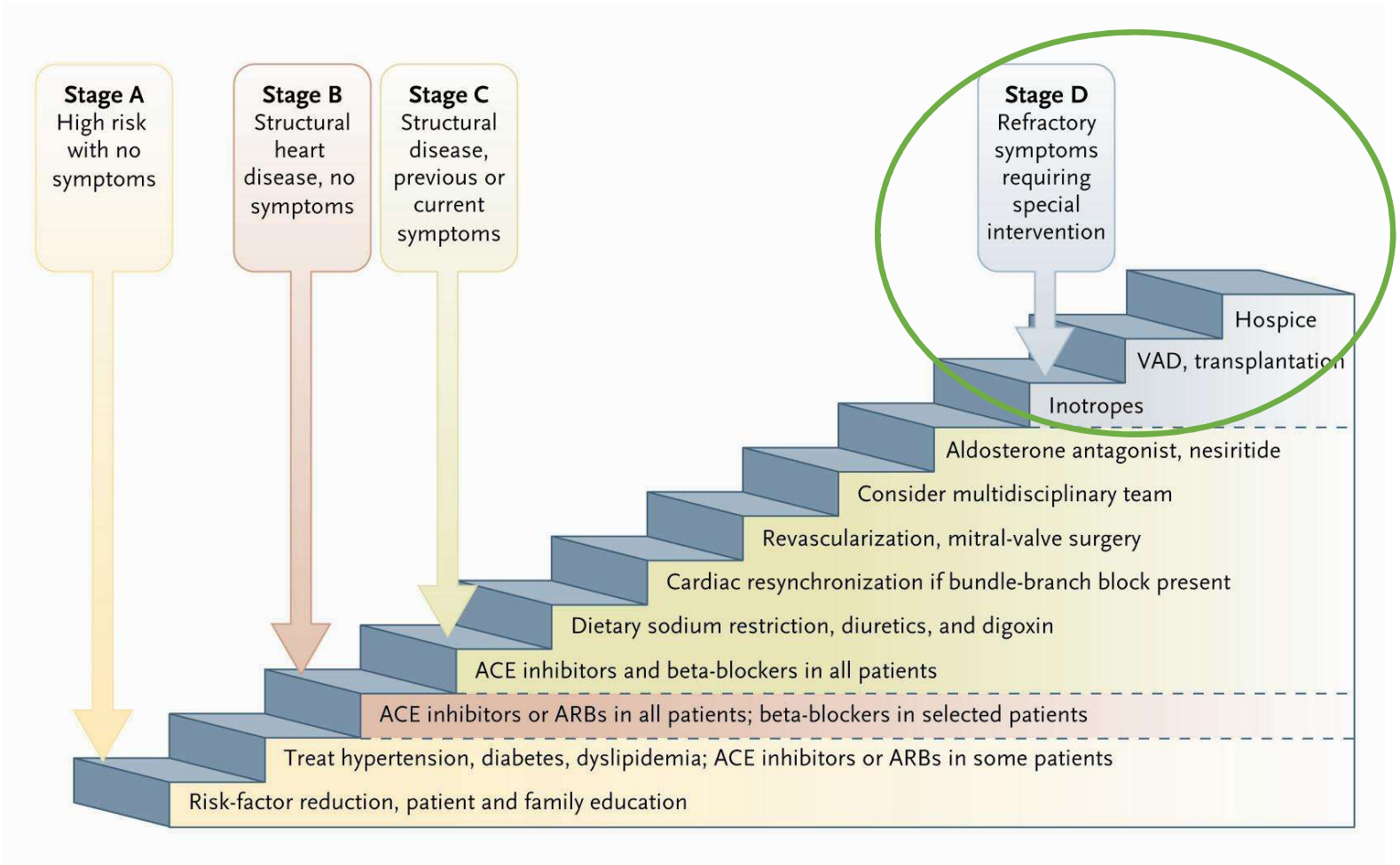
HKCC Core Cardiology Certificate Course

14th July 2019



* Heart Failure

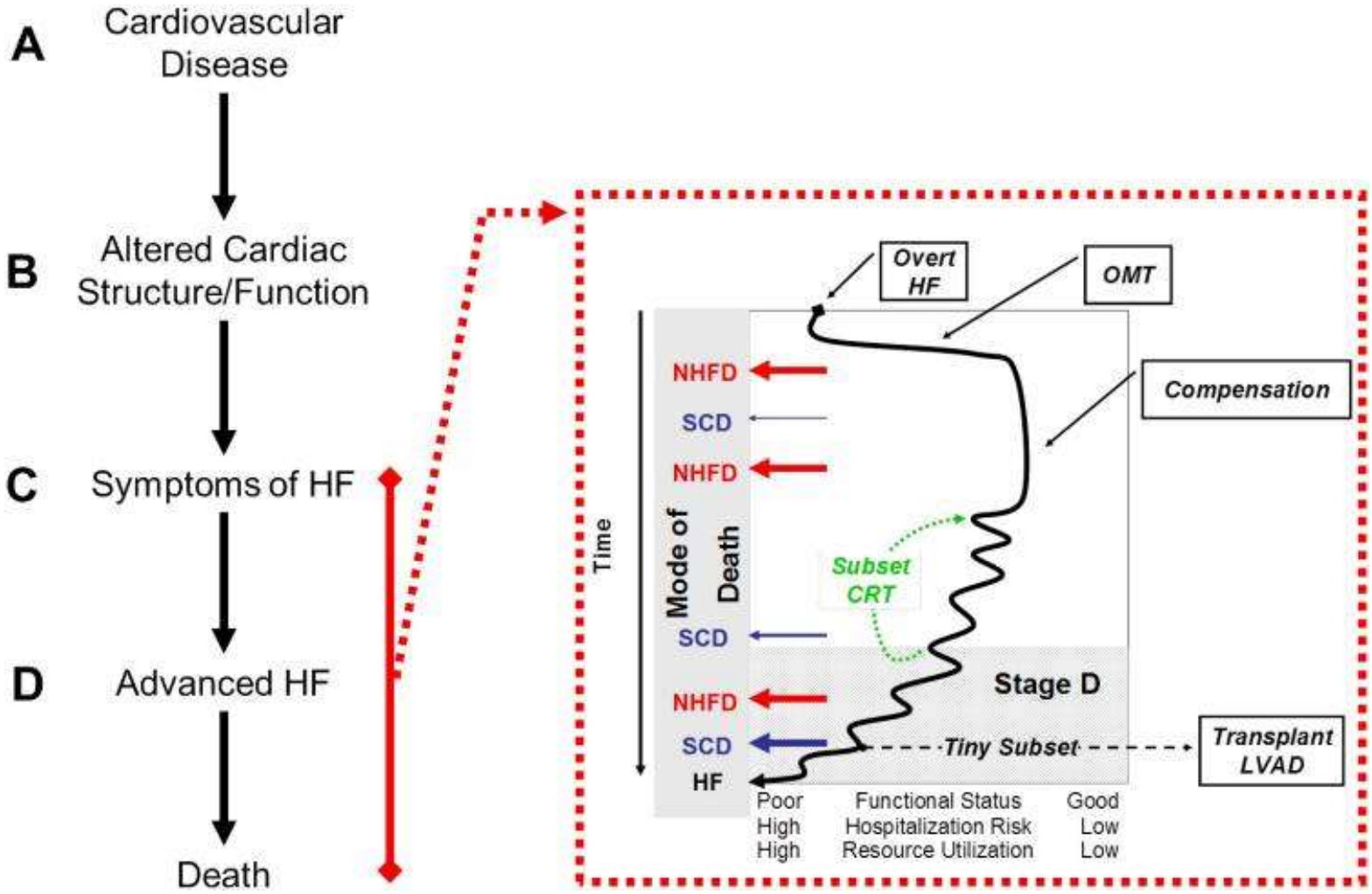
Treatment: Stepped approach to care



Who has advanced heart failure?

- Heart failure has been termed as an “epidemic”
- Complex epidemiology due to multiple factors which interact in a complex manner to impact the prevalence and incidence of HF
- Most **HF-related hospitalizations and deaths** are incurred to subgroup of patients that is **refractory to guideline-based medical management**, a group categorized as having “advanced HF”
- This cohort constitutes an important and rapidly expanding patient population that warrants special care and management

Natural history of HF defines advanced HF



ESC definition of Advanced HF

Metra M et al. A position statement from the Study Group on Advanced Heart Failure of the Heart Failure Association of ESC. Eur J Heart Failure 2007;9(6-7): 684-694
1. NYHA Class III-IV symptoms
2**. Episodes of volume overload and/or peripheral hypoperfusion**
3. **Objective evidence of severe cardiac dysfunction** -EF <30% -Doppler pseudonormal or restrictive filling patern -PCWP>16mmHG -RAP > 12mmHG
4**. Severely impaired functional capacity** -inability to exercise -6MWD <300m -Peak VO2 <12-14 ml/kg/min
5. **HF hospitalizations** ->1 in past 6 months
6. **Above occurring despite attempts to optimize diuretics, RAAS antagonists, BB,CRT or in setting ogf intolerance to OMT**

Acute Decompensated HF

- ADHF is NOT always Advanced HF
- Pt can present with NYHA class IV at their index HF presentation yet not considered advanced disease
- Respond to treatment of etiologic factors and optimization of medical therapy and improved to NYHA classes I-II

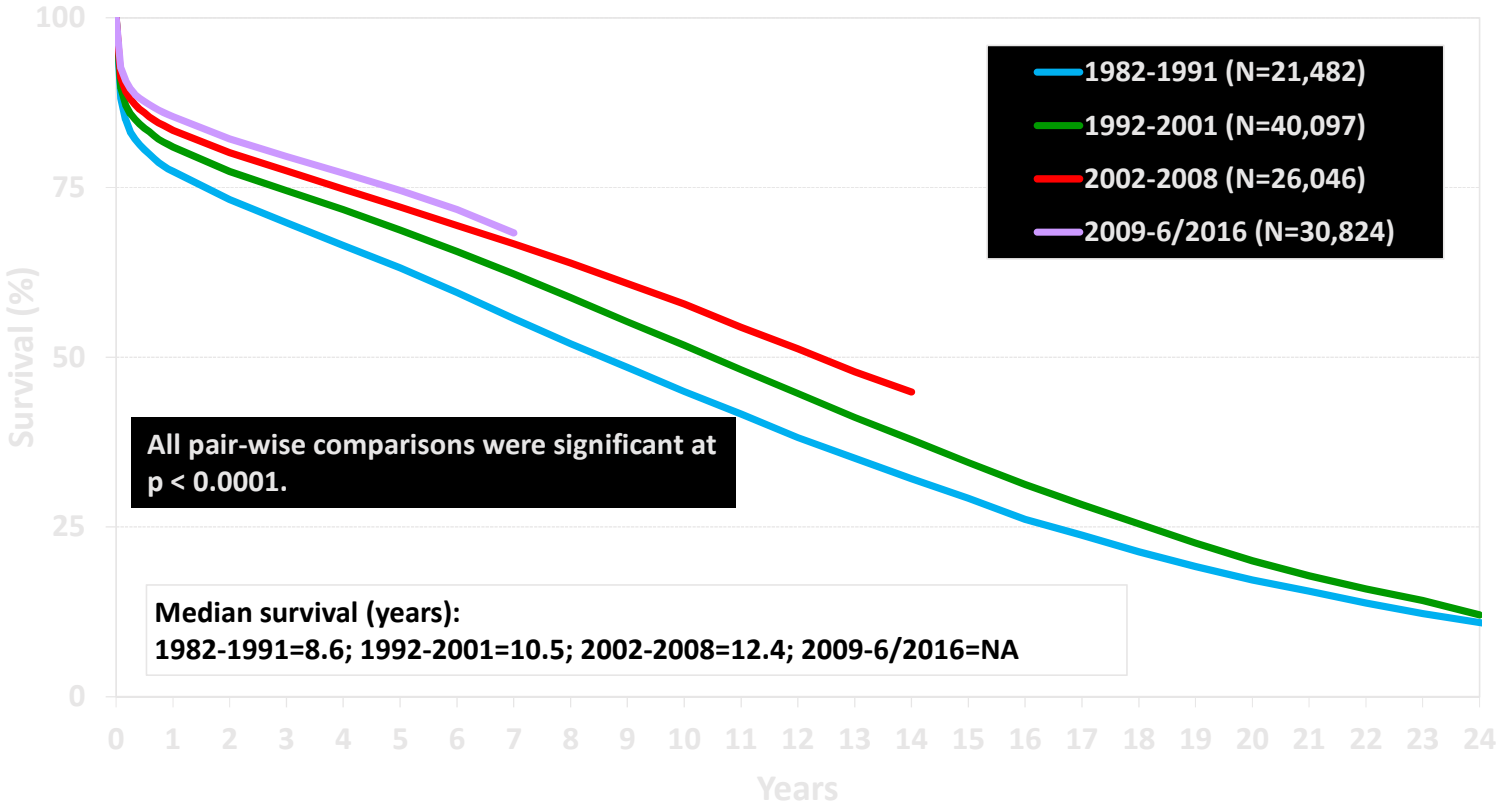
Recognizing the advanced HF patient

- No one single feature which identifies advanced HF
- Integration of clinical, imaging, hemodynamic, functional and biomarker data
- Symptoms
- Hospitalizations
- ECHO
- Hemodynamics
- Biomarkers: hyponatremia, BNP, uric acid, renal dysfunction

Heart Transplant

- Heart transplantation is the procedure by which the failing heart is replaced with another heart from a suitable donor
- Reserved for end-stage heart failure
- Estimated to have less than 1 year to live without the transplant
- Not candidate for or have not been helped by conventional medical therapy/ excluded from other surgical options because of poor condition of the heart

Adult Heart Transplants
Kaplan-Meier Survival by Era
(Transplants: January 1982 – June 2016)



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Selection Criteria for Cardiac Transplantation

Indications for Heart Transplant

- Cardiogenic shock requiring either continuous intravenous inotropic support or MCS with an intra-aortic balloon pump or MCS
- Persistent NYHA class IV congestive heart failure symptoms refractory to maximal medical therapy (LVEF <20%; peak VO2 <10-12ml.kg^{-1}. min^{-1})
- Intractable or severe anginal symptoms in patients with coronary artery disease not amendable to percutaneous or surgical revascularization
- Intractable life-threatening arrhythmias unresponsive to medical therapy, catheter ablation, and/or implantation of intra-cardiac defibrillator
- Congenital heart disease with severe ventricular dysfunction or which is unable to be corrected or palliated by either surgical or medical treatment
- Re-transplantation for graft dysfunction from severe allograft vasculopathy

Contra-indications to Cardiac Transplantation

- **Factors considered**:
- **Impact long-term survival**
  - Eg cancer
- **Increase post-operative risks**
  - Renal insufficiency
  - Active fulminant infection
  - Fixed pulmonary hypertension
- **Impair patient's ability to care for themselves**
  - Major psychiatric illness
  - Neurocognitive disorder
  - Recent substance abuse

Contraindications to Heart Transplant- Absolute

- Systemic illness with a life expectancy <2 years despite heart transplant, including
  - Active or recent solid organ or blood malignancy within 5 years
    - Eg leukemia, low grade neoplasms of prostate with persistently elevated PSA
  - AIDS with frequent opportunistic infections
  - Systemic lupus erythematosus, sarcoidosis or amyloidosis that has multi-system involvement and is still active
  - Irreversible renal or hepatic dysfunction in patients considered for only heart transplant
  - Significant obstructive pulmonary disease

Contraindications to Heart Transplant-Absolute

- **Fixed pulmonary hypertension**
  - PA systolic pressure >60mmHg
  - Mean transpulmonary gradient >15mmHg
  - Pulmonary vascular resistance >6 Wood units

Contraindications to Heart Transplant- Relative (I)

- Age >72 years in USA; >65 years in HK
- Any active infection (with exception of device related infection in VAD recipients)
- Active peptic ulcer disease
- Severe DM with end-organ damage (neuropathy, nephropathy or retinopathy)
- Severe peripheral vascular or cerebrovascular disease
  - Peripheral vascular disease not amenable to surgical or percutaneous therapy
  - Symptomatic carotid stenosis
  - Ankle brachial index <0.7
  - Uncorrected abdominal aortic aneurysm >6cm

Contraindications to Heart Transplant- Relative (II)

- Morbid obesity (body mass index >35kg/m^2) or cachexia (body mass index <18kg/m^2)
- Creatinine >2.5mg/dl or creatinine clearance <25 ml/min
- Bilirubin >2.5mg/dl, serum transaminases X 3x, INR >1.5 off warfarin
- Severe pulmonary dysfunction with FEV1 <40% normal
- Recent pulmonary infarction within 6-8 weeks
- Irreversible neurological or neuromuscular disease
- Active mental illness or psychosocial instability
- Drug, tobacco or alcohol abuse within 6 months

Heart Transplantation Indications

ESC Guidelines for acute and chronic HF 2012

- **Patients to consider:**
- End-stage heart failure with severe symptoms, poor prognosis and no remaining alternative treatment options
- Motivated, well informed, and emotionally stable
- Capable of complying with the intensive treatment required post-operatively

McMurray et al.Eur Heart J 2012;33(14):1787-1847

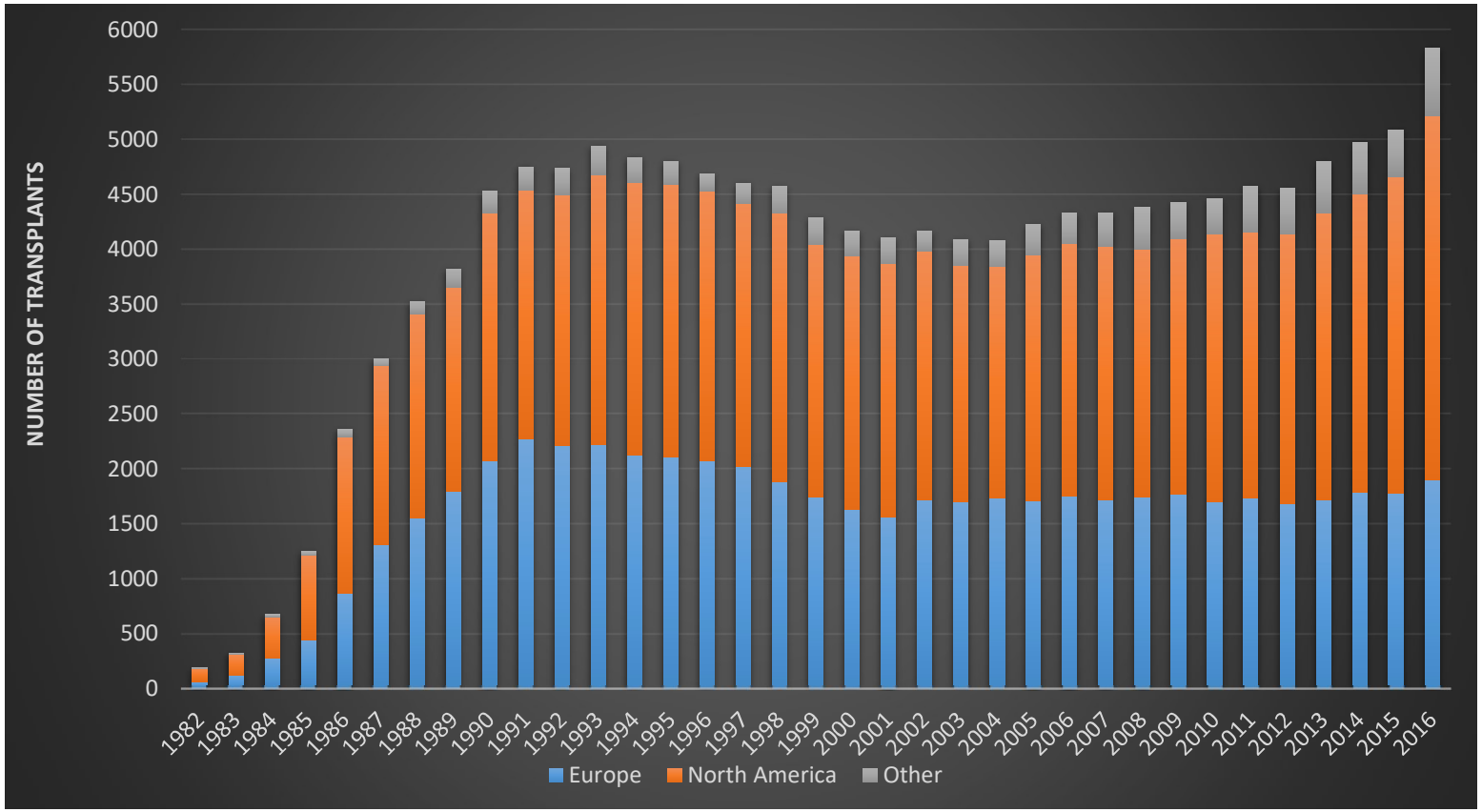
Heart Transplantation: Contra-Indications

ESC Guidelines for acute and chronic HF 2012

- Active infection
- Severe peripheral arterial or cerebrovascular disease
- Current alcohol or drug abuse
- Treated cancer in previous 5 years
- Unhealed peptic ulcer
- Recent thrombo-embolism
- Significant renal failure (eg Cr Cl <50ml/min)
- Significant liver disease
- Systemic disease with multi-organ involvement
- Other serious co-morbidity with poor prognosis
- Emotional instability or untreated mental illness
- High fixed pulmonary vascular resistance (>4-5 Wood units and mean transpulmonary gradient >15mmHg)

McMurray et al.Eur Heart J 2012;33(14):1787-1847

Adult and Pediatric Heart Transplants
Number of Transplants by Year and Location



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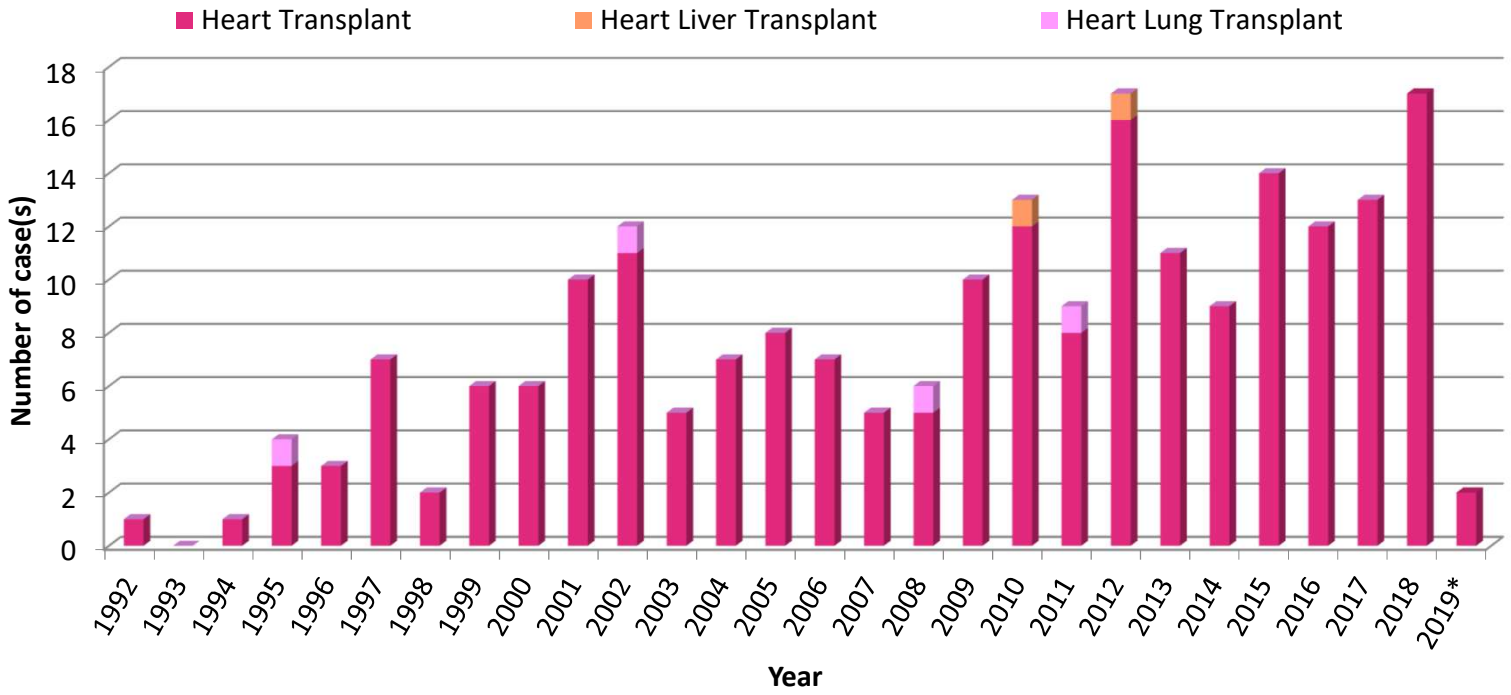
Numbers of Heart Transplants, Heart-Liver & Heart-Lung Transplants in HK

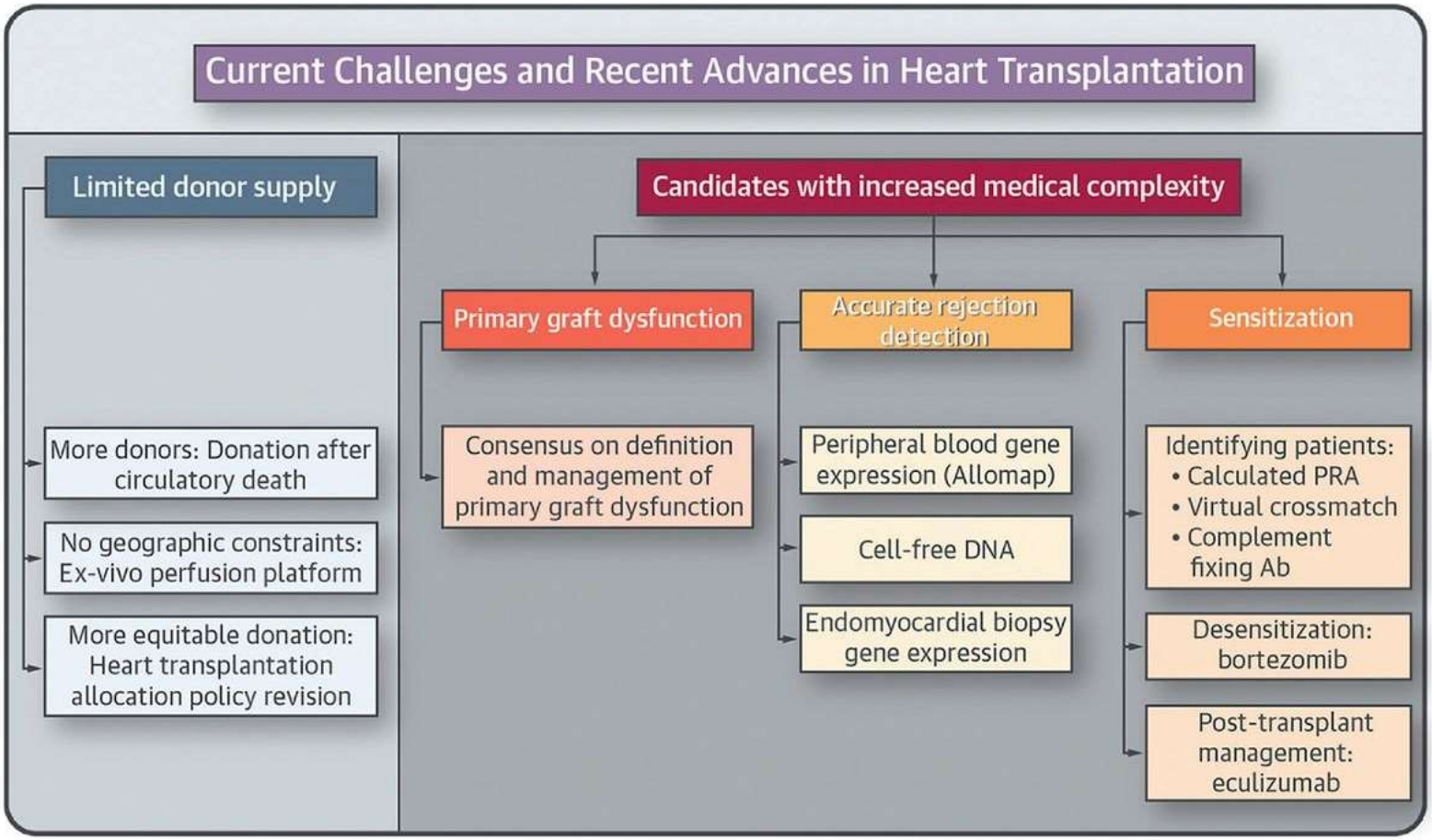


* Total numbers of Heart Transplants: 212 (include. 2 Heart-Liver), and 4 Heart-Lung as at 30 June 2019

Heart Transplant- Future and Controversies

- Ongoing shortage of donor organs
  - Ongoing search for alternative therapies eg:
  - Artificial assist devices, Pacing therapy, New pharmacological interventions and genetic therapy
- Prevention of allograft vascular disease
- Recipient selection and listing status
  - Continue to pose medical and ethical dilemmas

CENTRAL ILLUSTRATION: Overview of Challenges of Heart Transplantation in the Current Era and Potential Solutions



Kittleson, M.M. et al. J Am Coll Cardiol HF. 2017;5(12):857-68.

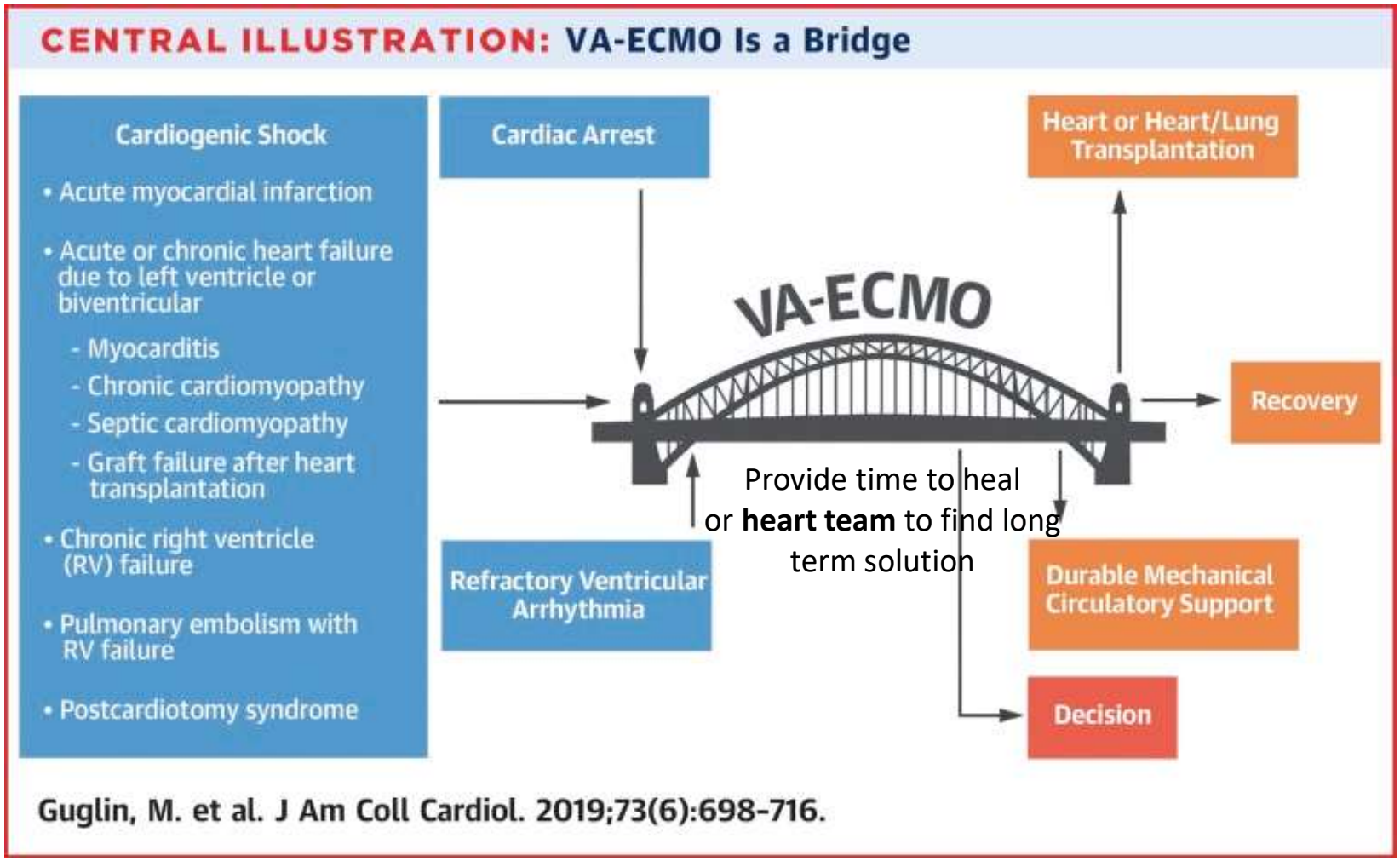
Heart Transplant New Allocation

TABLE 2 Proposed New Tiers for Heart Allocation Model

	Proposed New Tiers	Corresponding Current Tiers
1	i. VA ECMO	Status 1A
	ii. Non-dischargeable BiVAD	Status 1A or 1B
	iii. MCS with life-threatening ventricular arrhythmia	Status 1A
2	i. Non-dischargeable LVAD	Status 1A
	ii. TAH, BiVAD, or RVAD	Status 1A or 1B
	iii. MCS with device malfunction	Status 1A
	iv. Percutaneous endovascular MCS device	Status 1A
	v. IABP	Status 1A
	vi. VT or VF	Status 1A
3	i. Dischargeable LVAD for discretionary 30 days	Status 1A
	ii. Multiple inotropes or single inotrope with continuous hemodynamic monitoring	Status 1A
	iii. MCS with hemolysis	Status 1A
	iv. MCS with pump thrombosis	Status 1A
	v. MCS with right heart failure	Status 1A
	vi. MCS with device infection	Status 1A
	vii. MCS with mucosal bleeding	Status 1A
	viii. MCS with aortic insufficiency	Status 1A
	ix–xi. VA ECMO, percutaneous endovascular circulatory support devices, or IABP after 14 days	Status 1A
4	i. Dischargeable LVAD without discretionary 30 days	Status 1B
	ii. Inotropes without hemodynamic monitoring	Status 1B
	iii. Congenital heart disease	NA
	iv. Ischemic heart disease with intractable angina	NA
	v. Amyloidosis, hypertrophic, or restrictive cardiomyopathy	NA
	vi. Re-transplant	NA
5	Combined organ transplants	NA
6	All remaining candidates	Status 2
7	Inactive/not transplantable candidates	Status 7/inactive

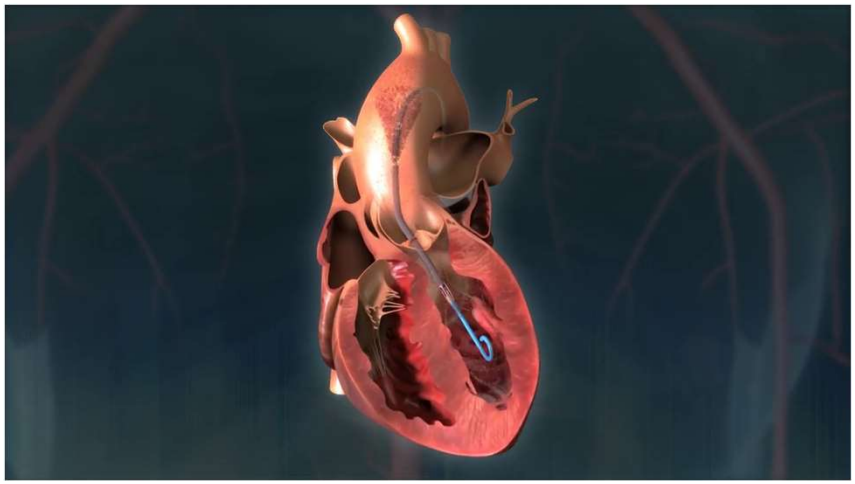
Mechanical Circulatory Support
“Bridge over trouble water?”

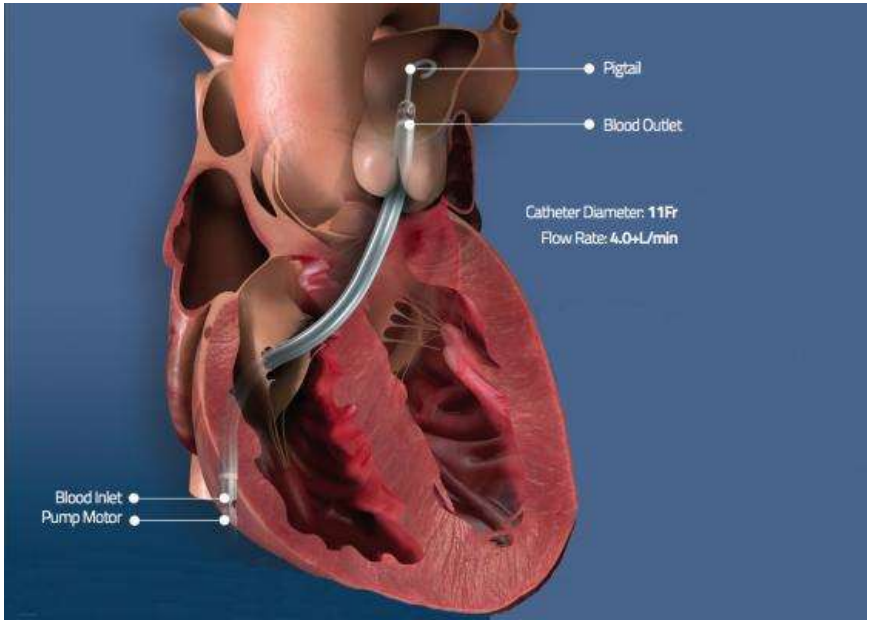
Principle thoughts for short term MCS in CS



Impella – a longer-term temporary support

- Miniature rotary pump
- Inserted retrograde across AV to provide short term ventricular support
- Very hemocompatible- minimal hemolysis
- Impella RP- tests RV tolerance
  - If RV doing well- predictive of tolerance of durable LVAD





Extracorporeal Circulatory Support

Levotronix (Centrimag) VAD

- Short term support (LVAD/ RVAD/ BiVAD)
- **Bridge-to decision (recovery vs definitive therapy such as transplant)**

New clinical algorithms proposed earlier timing of MCS in high urgency HTx candidate

THORATEC: CENTRIMAG BLOOD PUMP

- Single-use centrifugal pump, motor and a primary drive console
- Motor magnetically levitates the impeller
- Achieving rotation with no friction
- Rotates at 1500-5500 rpm
- Flows: up to 9.9L/min

心肝衰竭 好爸爸求心覓新生

育兩歲兒 身形高移植配對添難度

刻不容緩

■甘明光需要依賴機器維持心臟功能。（何天成攝）

瑪麗醫院一名「心肝俱衰竭」男病人急需換心。該名任職銀行投資顧問、現年四十六歲的爸爸甘明光，今年七月起被診斷為嚴重心臟衰竭，近月更曾出現肝功能問題，出現心和肝雙重衰竭的打擊，現在心臟功能低於百分之五，於同血型及體形病人中位列移植名單首位。甘明光昨堅持現身呼籲「有心人」捐心助重生，得以上班及與兩歲多兒子到迪士尼樂園遊玩。瑪麗醫院心胸外科顧問醫生何嘉麗表示，由於病人身高達一百八十三厘米，故增加尋找合適心臟的難度。

甘明光在十八歲負笈加拿大時接受身體檢查，被醫生告知有心肌肥大，但由於沒有徵狀，當時未影響健康。直至約六年前，他開始出現氣促及心房纖維性顫動證實有肥厚性心肌病，需接受藥物治療。

好景不常，甘在去年七月於街上暈倒，其後證實嚴重心臟衰竭，開始影響其他器官，導致雙腳水腫、排尿差。今年八月在瑪麗醫院接受連續性動靜脈血液透析過濾（俗稱洗血），以維持腎功能，期間出現血壓低，要強心藥支持。之後轉到葛量洪醫院作心臟移植評估，曾出現發燒、血壓低、心源性休克等情況，需要四種強心藥及主動脈內球囊反搏裝置（IABP）維持生命。

心功能急跌 靠儀器續命

兩個月後，甘的情況轉趨嚴重，再轉往瑪麗醫院心胸外科加裝人工心肺機（ECMO），作短暫性支援，心臟功能只有兩成，並已納入心臟移植名單。其後又安裝雙心室輔助裝置，作為代替心臟移植的過渡性治療。今年九至十一月期間，他的膽紅素曾一度升高，肝功能出現衰竭，人工心臟裝置出現血塊，已進行更換，以免相關併發症出現，惟換心才是最有效的「救命」措施。

曾因肝中毒 昏迷逾一周

何嘉麗表示，甘的情況曾不樂觀，肝中毒昏迷一個多星期，但現時精神狀況不錯，可以一般飲食及走動，並認為現時合適接受移植的時機。甘的血型為O+，體重只有六十二公斤，而身高約一米八，需要的心臟亦較一般需要器官移植人士更大，故增加尋找合適心臟的難度。

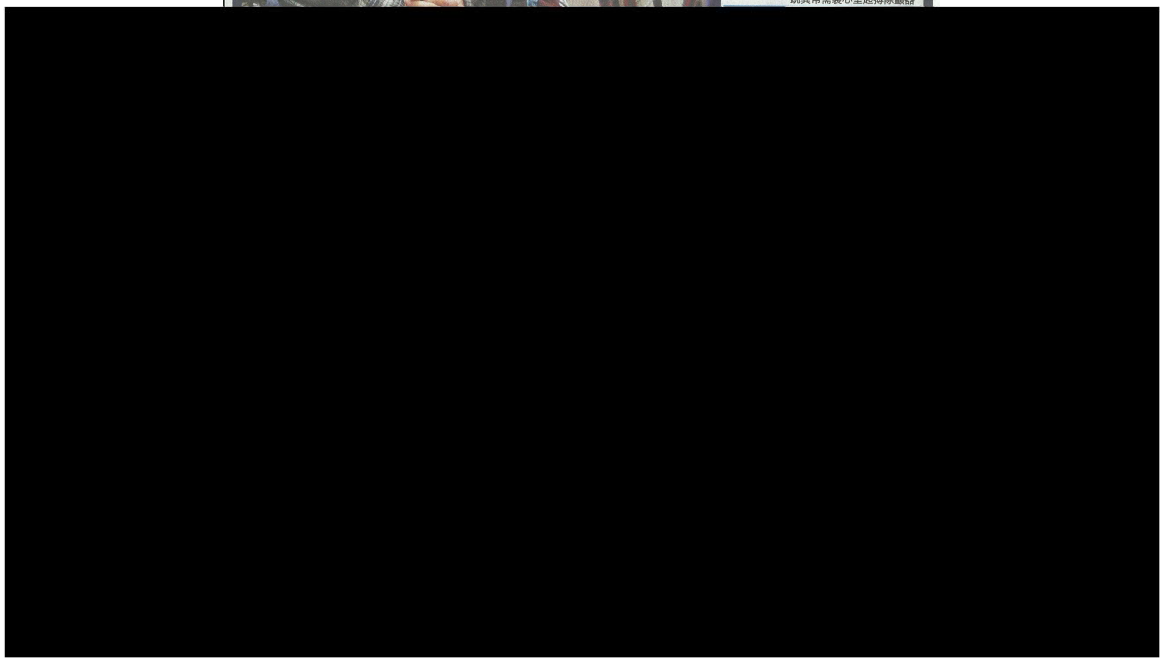
何嘉麗

遺傳心肌肥厚症 父母兄長離世

律師樓OL求心 想活下去

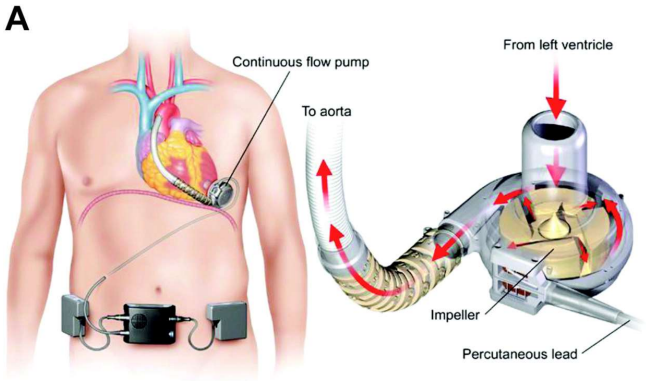
求心若嘉患病經過

約20多年前	讀中一的哥哥猝死，發現患心肌肥厚症，檢查後證實媽媽及當時6歲的若嘉亦患病
1995年	16歲的若嘉在街上暈倒，心跳異常需裝心室起搏除顫器



Durable Ventricular Assist Device (VAD)

- For the larger group of individuals who face a high risk of short-term mortality and little chance of receiving a transplant that the emergence of continuous flow LVAD holds the greatest promise
- Durable VADs devices are capable of augmenting the circulation to meet the body's physiological needs, both at rest and with exercise, extending survival and improving QoL



Centrifugal flow with levitating magnetic discs

Axial flow pump

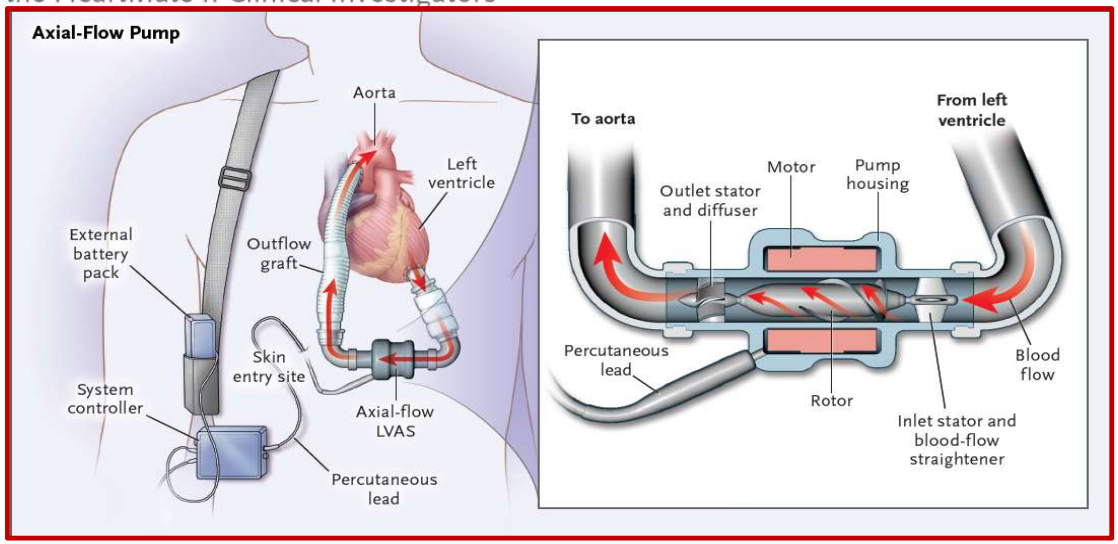
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Use of a Continuous-Flow Device in Patients Awaiting Heart Transplantation

Leslie W. Miller, M.D., Francis D. Pagani, M.D., Ph.D., Stuart D. Russell, M.D., Ranjit John, M.D., Andrew J. Boyle, M.D., Keith D. Aaronson, M.D., John V. Conte, M.D., Yoshifumi Naka, M.D., Donna Mancini, M.D., Reynolds M. Delgado, M.D., Thomas E. MacGillivray, M.D., David J. Farrar, Ph.D., and O.H. Frazier, M.D., for the HeartMate II Clinical Investigators*

NEJM 2007
FDA 2008



Terms describing various uses of mechanical circulatory support (MCS)

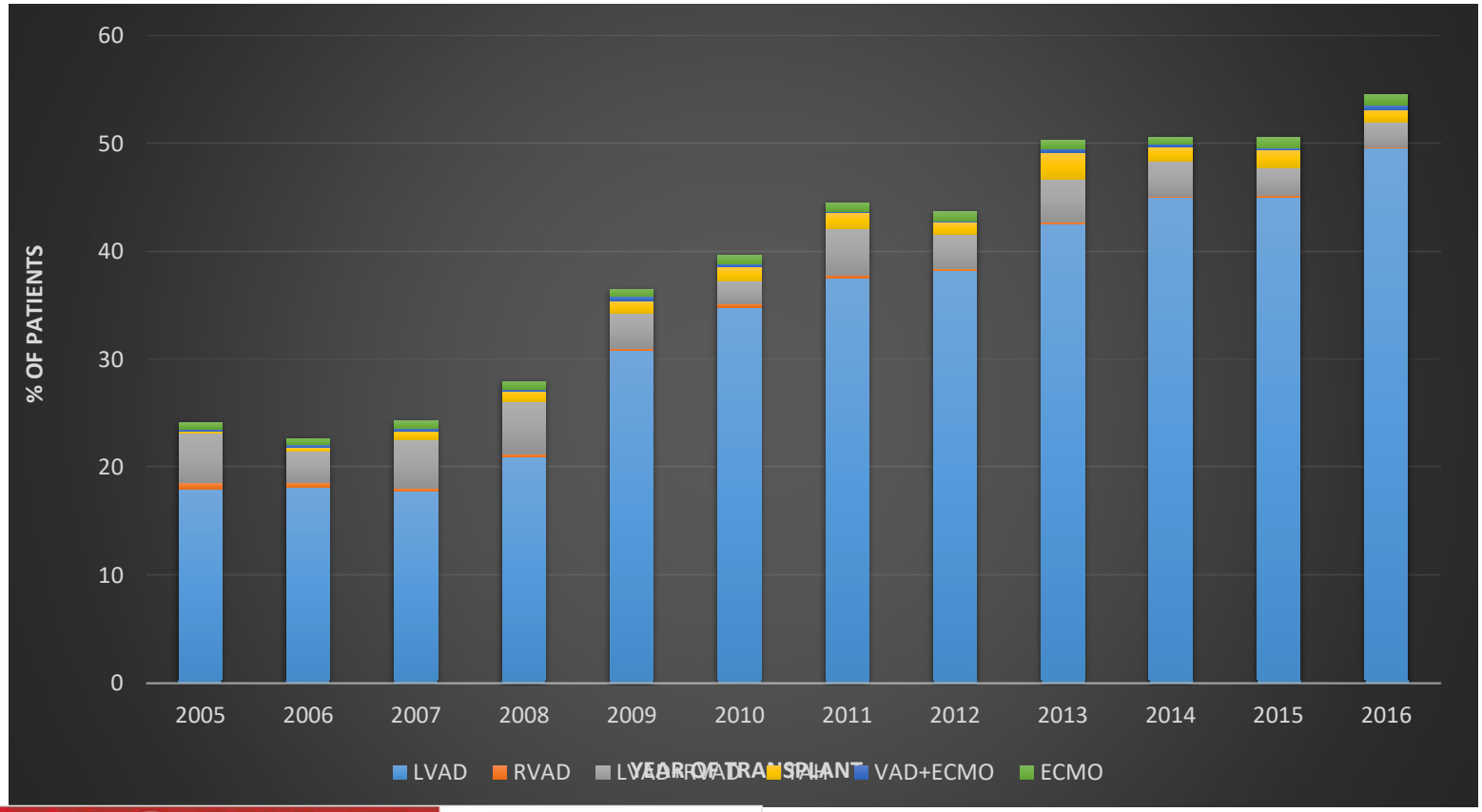
Terms	
Bridge to decision (BTD)	Use of MCS in patients with drug-refractory acute circulatory collapse and at immediate risk of death to sustain life until a full clinical evaluation can be completed and additional therapeutic options can be evaluated
Bridge to candidacy (BTC)	Use of MCS to improve end-organ function in order to make ineligible patient eligible for transplantation
Bridge to transplantation (BTT)	Use of MCS to keep a patient at high risk of death before transplantation alive until a donor organ becomes available
Bridge to recovery (BTR)	Use of MCS to keep patient alive until intrinsic cardiac function recovers sufficiently to remove MCS
Destination therapy	Longterm use of MCS as an alternative to transplantation in patients with end-stage heart failure ineligible for transplantation

Bridge to Transplant

- Patient approved and listed for transplant
- Patients who are unable to survive until transplantation without VAD
- Patient who might profit from VAD therapy (rehabilitation)
- Mostly INTERMACS 1,2,3

Adult Heart Transplants

% of Patients Bridged with Mechanical Circulatory Support* by Year and Device Type



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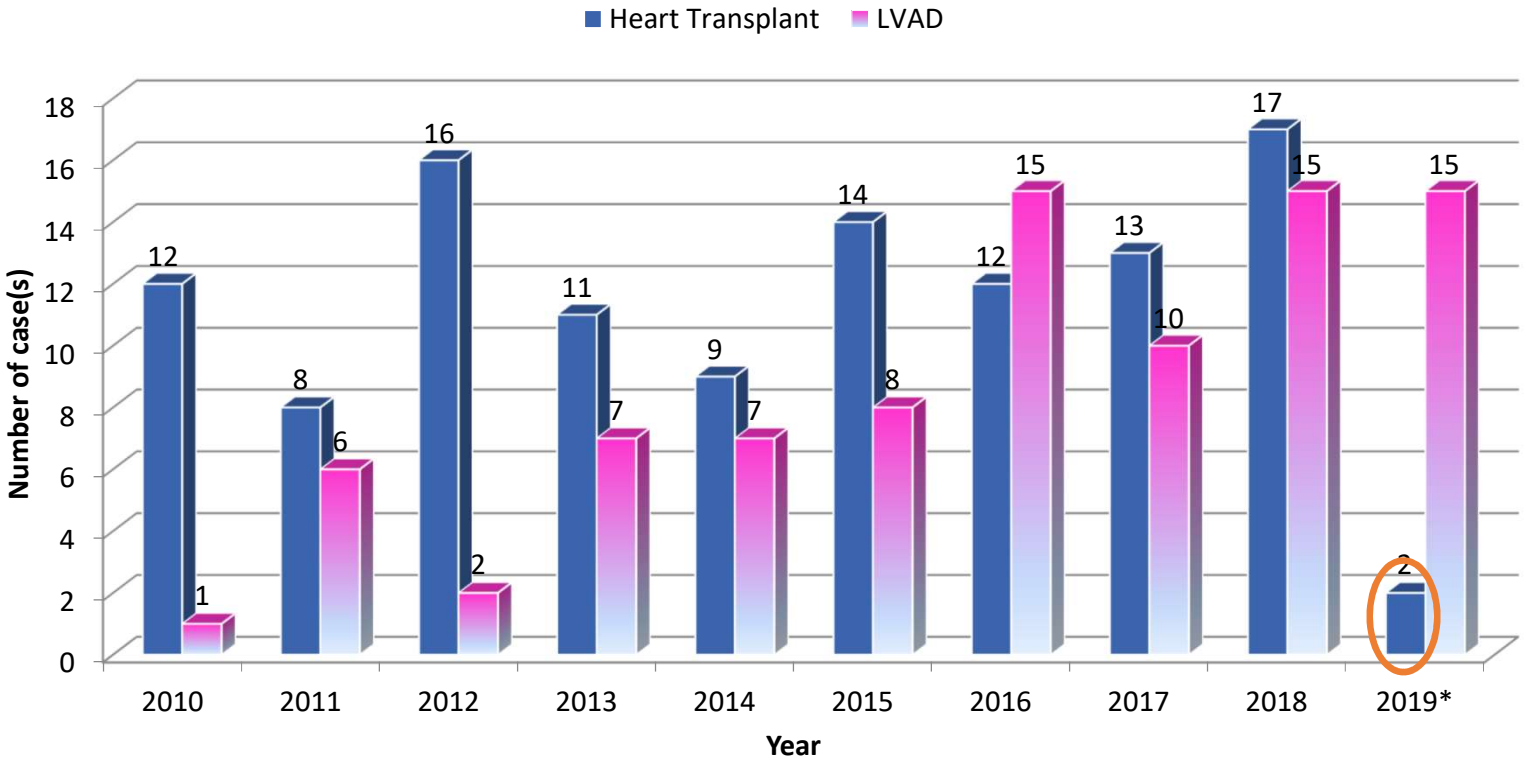
*** LVAD, RVAD, TAH, ECMO**

Numbers of Heart Transplant & LVAD in HK



* Total numbers of LVAD: 86 as at June 2019

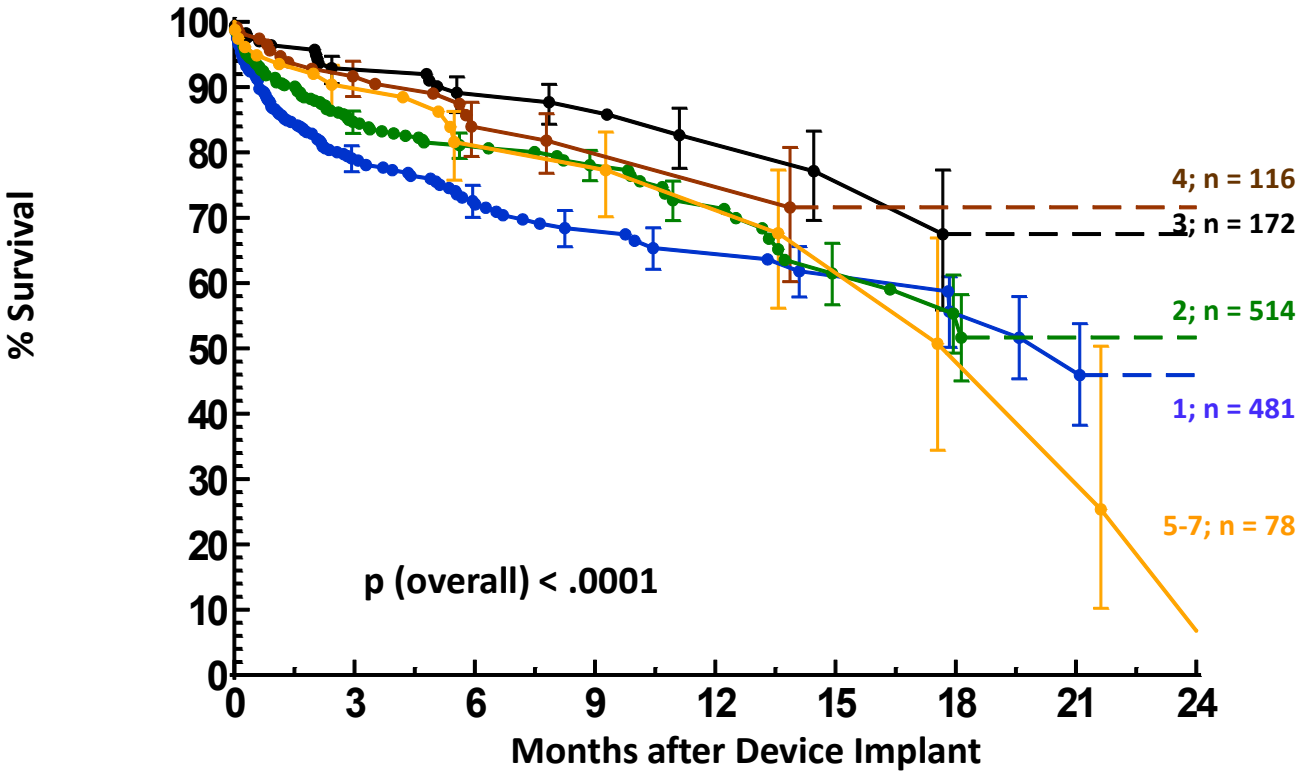
INTERMACS

Profile Level	Official Shorthand	NYHA Class	Modifier
INTERMACS Level 1	"Crash and burn"	IV	
INTERMECS Level 2	"sliding fast" on inotropes	IV	
INTERMECS Level 3	Stable but Inotropes-dependent /Can be hospital or home	IV ish	
INTERMECS Level 4	Resting symptoms on oral therapy at home	Ambul IV	FF++ A
INTERMECS Level 5	"Housebound", comfortable at rest, symptoms with minimal activity ADL	Ambul IV	FF++ A
INTERMECS Level 6	"Walking wounded"- ADL possible but meaningful activity limits	IIIB	FF++ A
INTERMECS Level 7	Advanced Class III	III	A

Current indications for HTx /VAD

FF= frequent flyer A= Arrhythmias

INTERMACS level and SURVIVAL



Implant Dates: June 23, 2006 – March 31, 2009

2016 ESC Heart Failure Guideline[1]

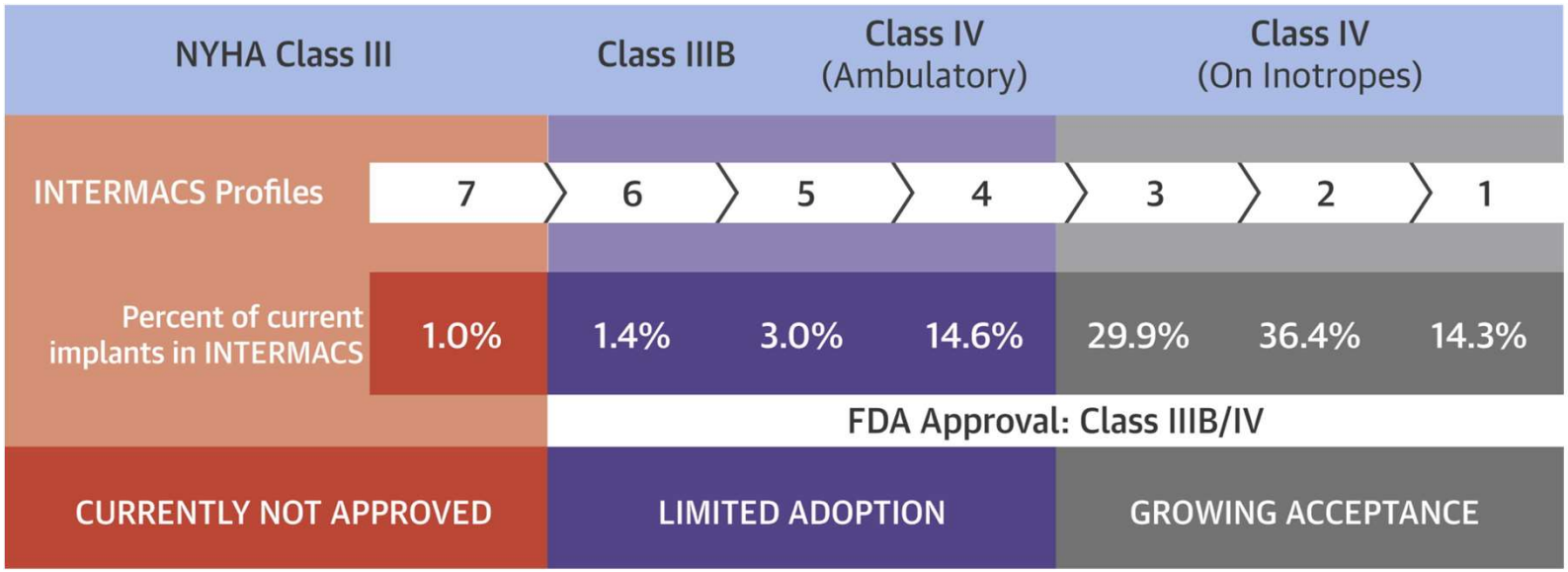
INTERMACS stages for classifying patients with advanced heart failure

INTERMACS Level	NYHA Class	Description	Devices	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"	III	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%
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	-

ECLS = extracorporeal life support; ECMO = extracorporeal membrane oxygenation; INTERMACS = Interagency Registry for Mechanically Assisted Circulatory Support; LVAD = left ventricular assist device; NYHA – New York Heart Association.
Kaplan-Meier estimates with standard error of the mean for 1 year survival with LVAD therapy. Patients were censored at time of last contact, recovery or heart transplantation. Due to small numbers outcomes for INTERMACS levels 5,6,7 were combined. [610]

1. Ponikowski, P, et al. 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure. Eur Heart J (2016) 37 (27): 2129-2200.

INTERMACS scale for classifying patients with advanced HF



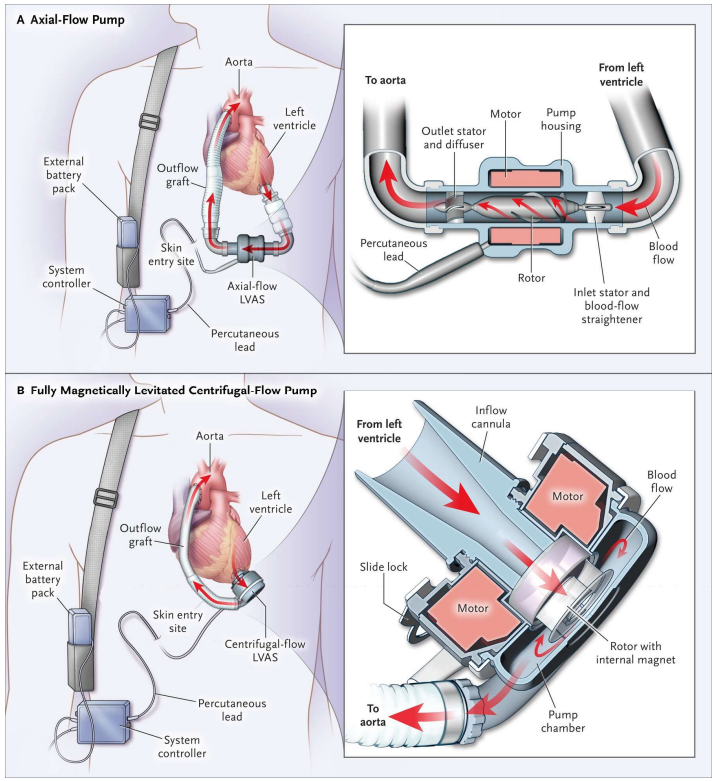
Mancini et al. JACC 2015;65(23):2542-2555

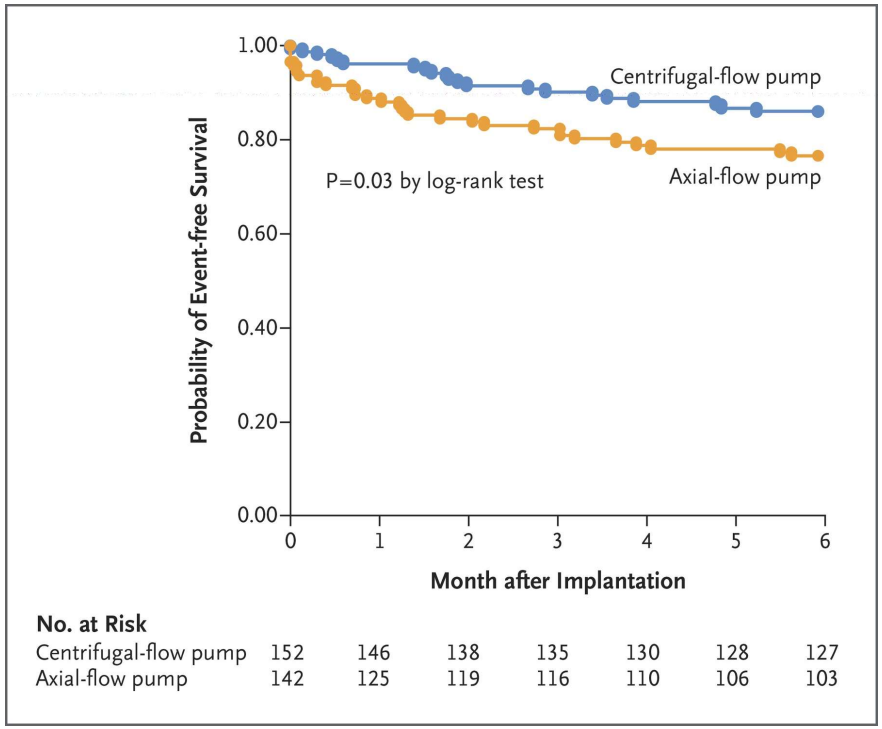
A Fully magnetically levitated circulatory pump for advanced heart failure

MOMENTUM 3

Mehra et al. NEJM 2017;376:440-450

- Primary end-point= composite of survival free of disabling stroke (modified Rankin score >3 or Survival free of reoperation to replace or remove the device at 6 mths after implant





The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

A Fully Magnetically Levitated Left Ventricular Assist Device — Final Report

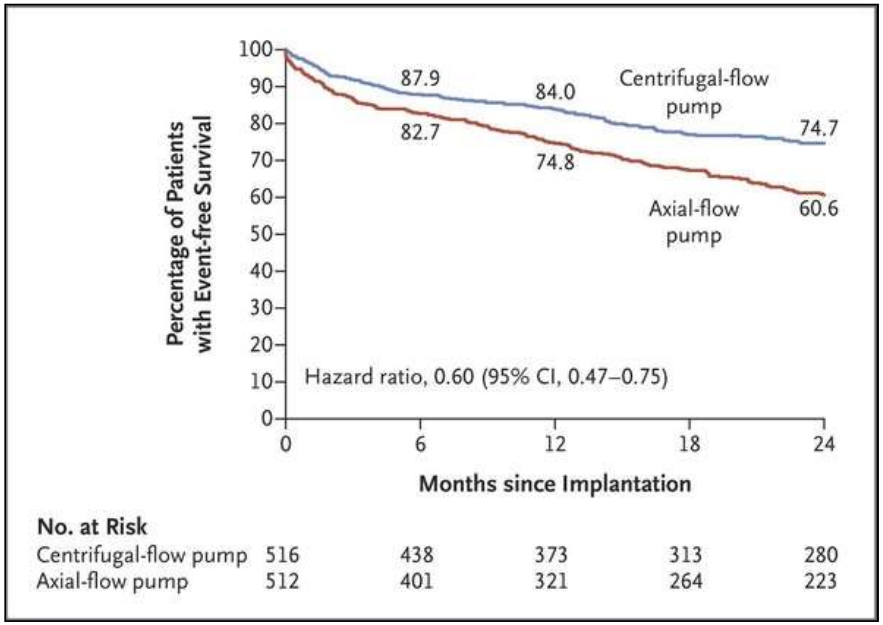
M.R. Mehra, N. Uriel, Y. Naka, J.C. Cleveland, Jr., M. Yuzefpolskaya, C.T. Salerno, M.N. Walsh, C.A. Milano, C.B. Patel, S.W. Hutchins, J. Ransom, G.A. Ewald, A. Itoh, N.Y. Raval, S.C. Silvestry, R. Cogswell, R. John, A. Bhimaraj, B.A. Bruckner, B.D. Lowes, J.Y. Um, V. Jeevanandam, G. Sayer, A.A. Mangi, E.J. Molina, F. Sheikh, K. Aaronson, F.D. Pagani, W.G. Cotts, A.J. Tatooles, A. Babu, D. Chomsky, J.N. Katz, P.B. Tessmann, D. Dean, A. Krishnamoorthy, J. Chuang, I. Topuria, P. Sood, and D.J. Goldstein, for the MOMENTUM 3 Investigators*

N Engl J Med 2019;380:1618-1627

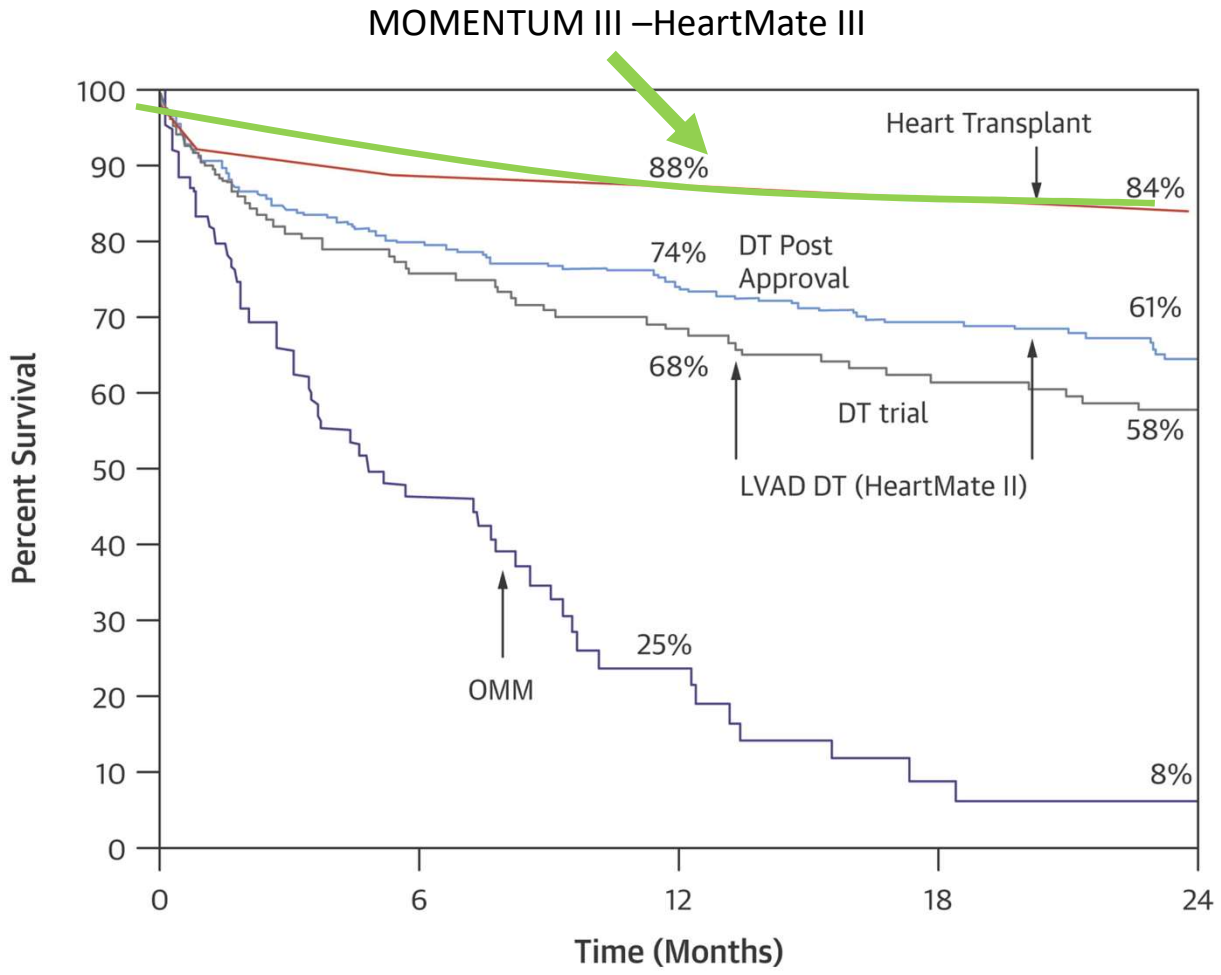
- Pts with advanced HF to receive either centrifugal flow pump or axial flow pump irrespective of intended goal of use
- Composite primary end point:
  - Survival at 2 years free of disabling stroke or reoperation to replace or remove malfunctioning device
- Secondary end point:
  - Pump replacement at 2 years

Improved event-free survival of Stroke or re-operation

- HM III fully magnetically centrifugal flow pump was superior to HM II axial-flow pump with respect to survival free of disabling stroke or reoperation to replace or remove malfunctioning device
- CF pump associated with lower incidence of either ischemic or hemorrhagic strokes

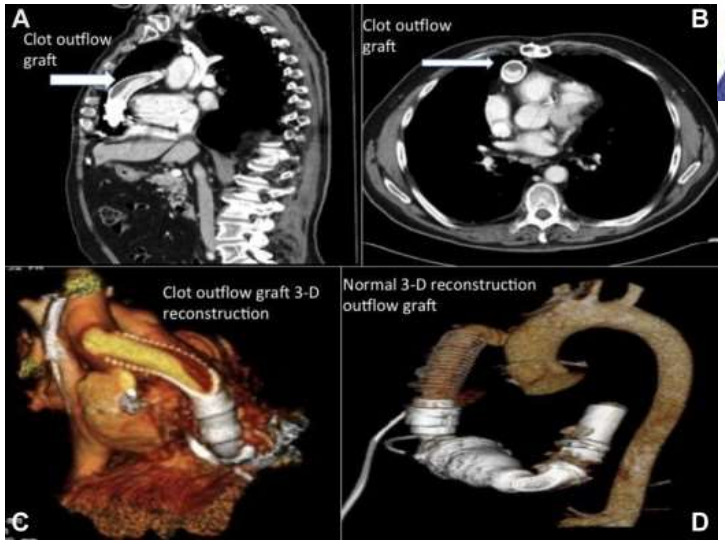


Survival in Stage D HF patients with different treatment modalities

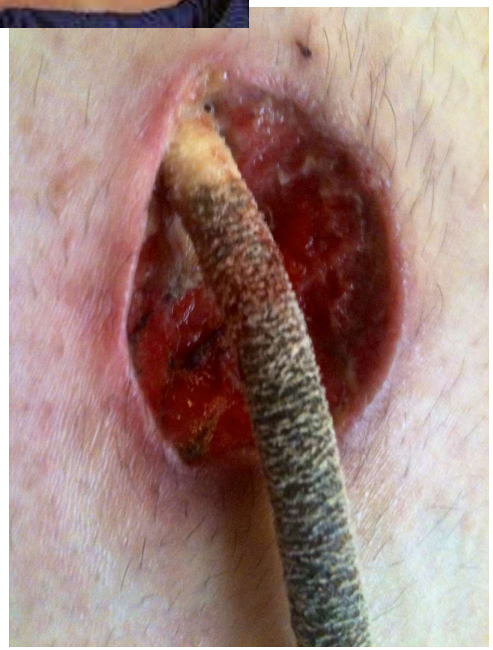


Complications

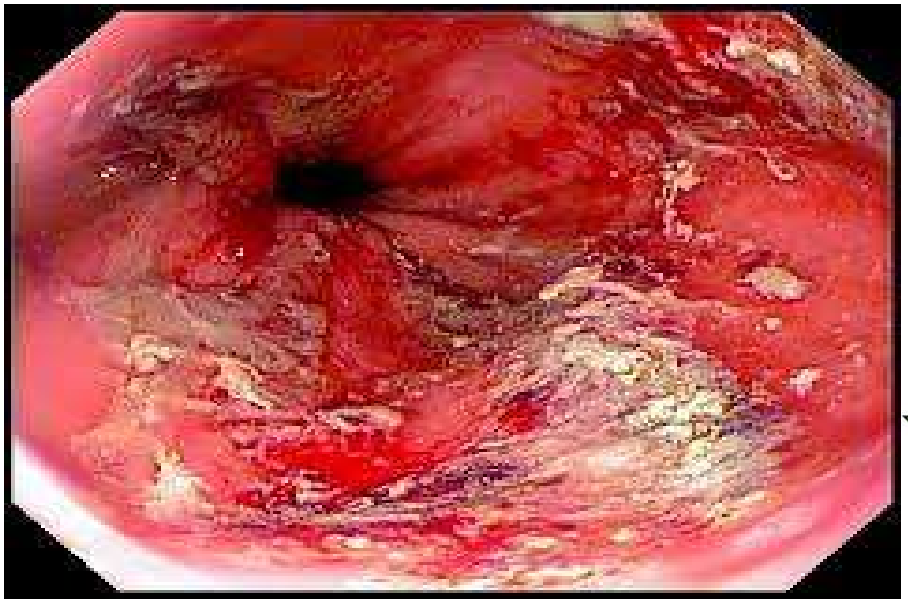
Thrombosis

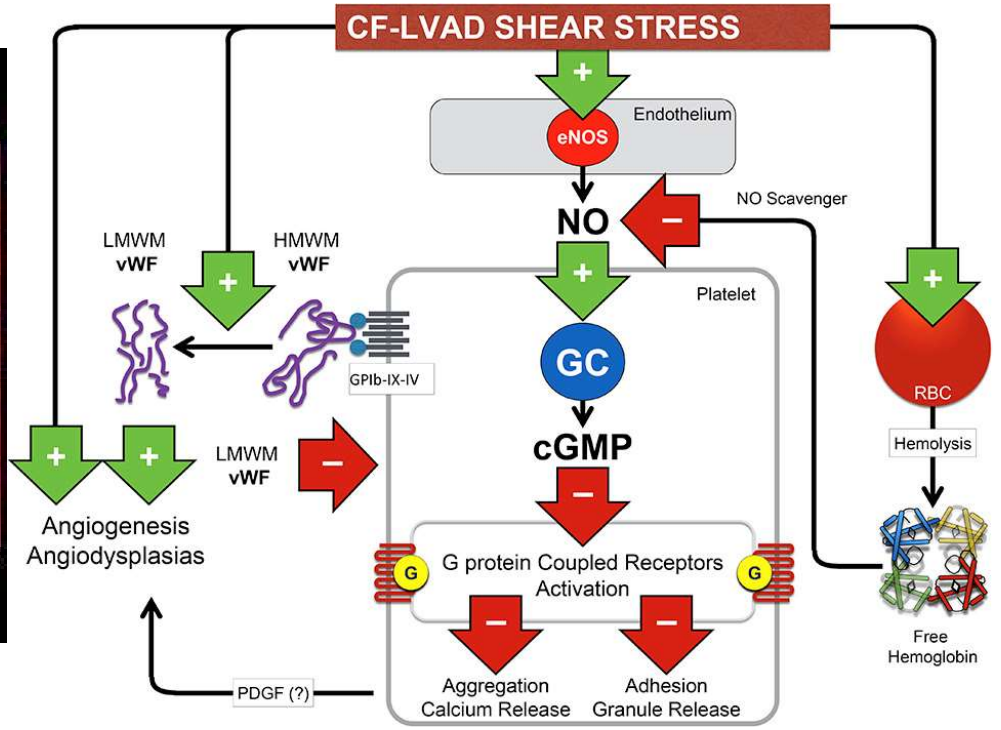


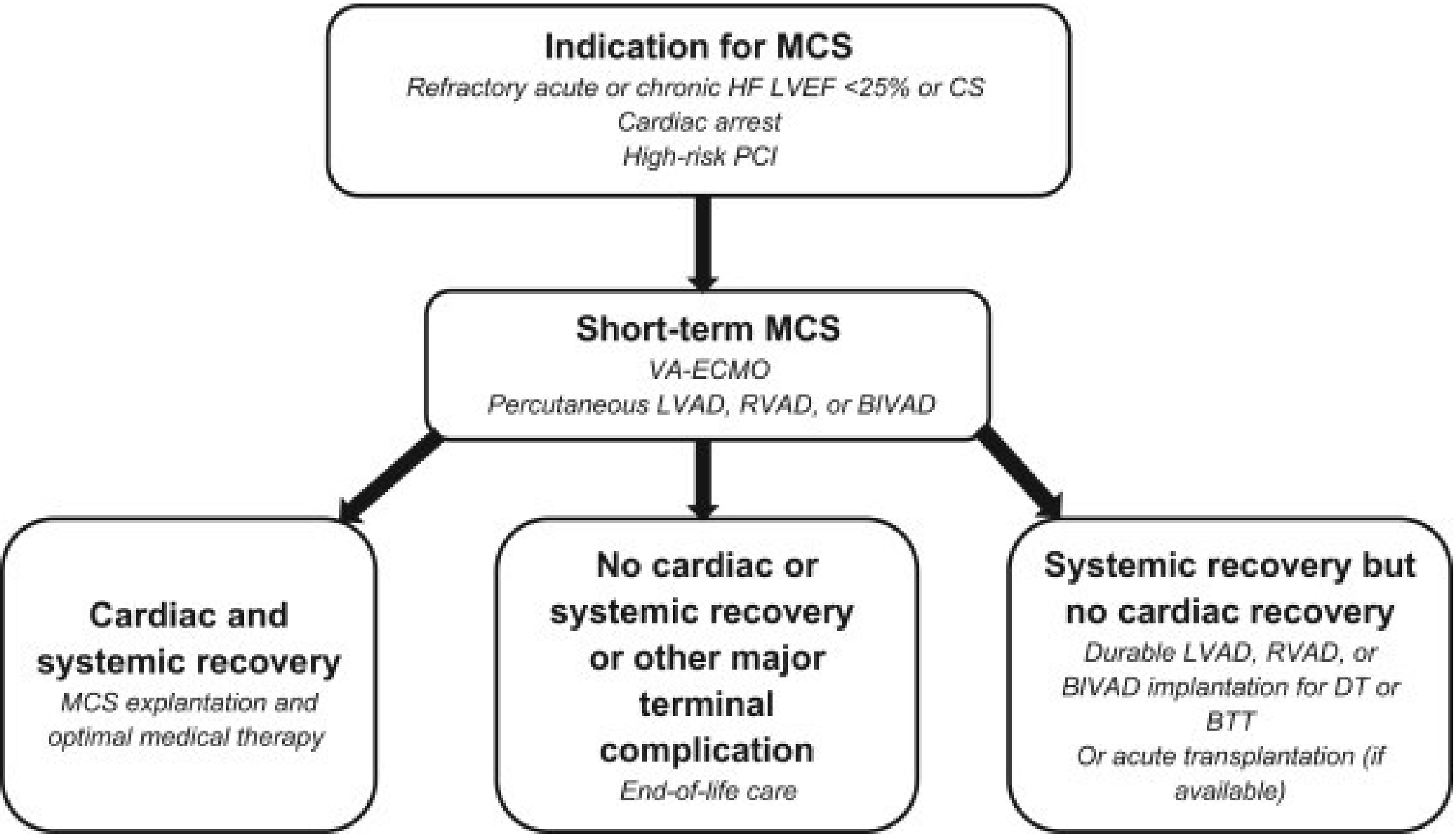
Driveline Infections



GI Bleeding- Angiodysplasia






Indication for MCS
Refractory acute or chronic HF LVEF <25% or CS
Cardiac arrest
High-risk PCI
Short-term MCS
VA-ECMO
Percutaneous LVAD, RVAD, or BIVAD
Cardiac and systemic recovery
MCS explantation and optimal medical therapy
No cardiac or systemic recovery or other major terminal complication
End-of-life care
Systemic recovery but no cardiac recovery
Durable LVAD, RVAD, or BIVAD implantation for DT or BTT
Or acute transplantation (if available)

Considerations before Finalized MCS strategy

- Guidelines strongly recommend consideration of use of temporary MCS in patients with multi-organ failure, sepsis or on mechanical ventilation to allow successful optimization of clinical status and neurologic assessment prior to placement of *a long term MCS device*
- **Considerations prior to finalizing an individualized MCS strategy**
  - Underlying cause of cardiac dysfunction and projected time course of recovery
  - Severity of pulmonary dysfunction and projected course of recovery
  - Functional reserve of each ventricle
  - Presence and severity of valvular pathology
  - Risk of arterial access and size of vessels
  - Severity of coagulopathy
  - Risk of sternotomy
  - Planned future surgery such as long-term VAD or transplant

Heart Team Discussions

Timing is Important: Early Referral

- Well recognized that function and outcomes on medical therapy benefit from ongoing heart failure management as offered at a transplant center
- Detailed evaluation necessary to determine eligibility for transplant is often incomplete or misleading in a patient in "critical condition"
  - Determination of "acceptability" for transplantation in a non-urgent candidate remains desirable
- All efforts should be made to foster this idea with primary care providers and community/ hospital specialists

Thank You!