EVOLVING MCS THAT ARE RESHAPING OUTCOMES IN ADVANCED HEART FAILURE

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PreHospital ECMO on the Streets of Paris
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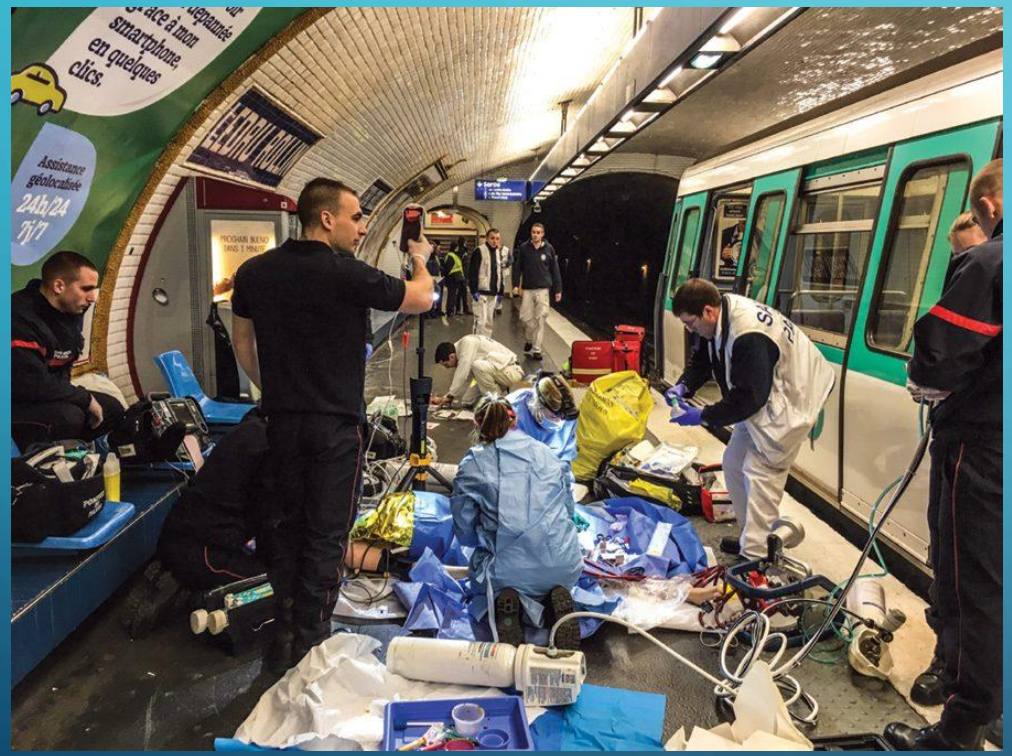


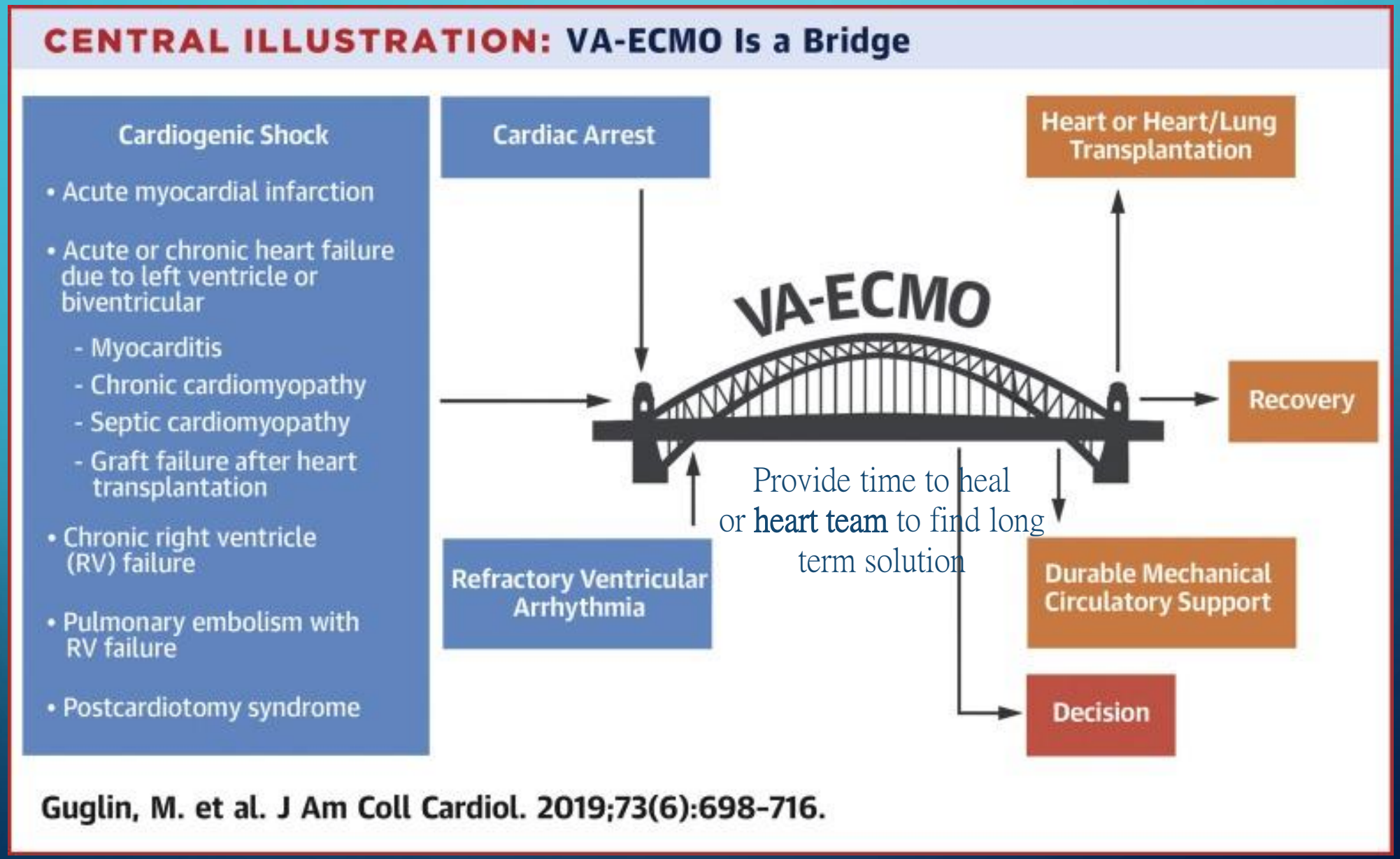
LAMHAUT JEMS 2017

IMPLEMENTING ON-SCENE ECMO

- ECPR is now Recommended by international guidelines in the management of refractory OHCA of suspected reversible cause, such as AMI, pulmonary embolism and intoxication [1]
- ECPR Team was sent out in absence of ROSC after 10 mins of ALS and by 2015, dispatched at the same time of MoICU
- Opposite of "scoop and run" concept, this system can do everything from "stay and treat" such as prehospital ECPR or "run and treat" in case of penetrating trauma for a damage control situation
- Results from implementing on-scene ECMO show an increase in survival rate from 8 to 29% with acceptable neurological status [2]

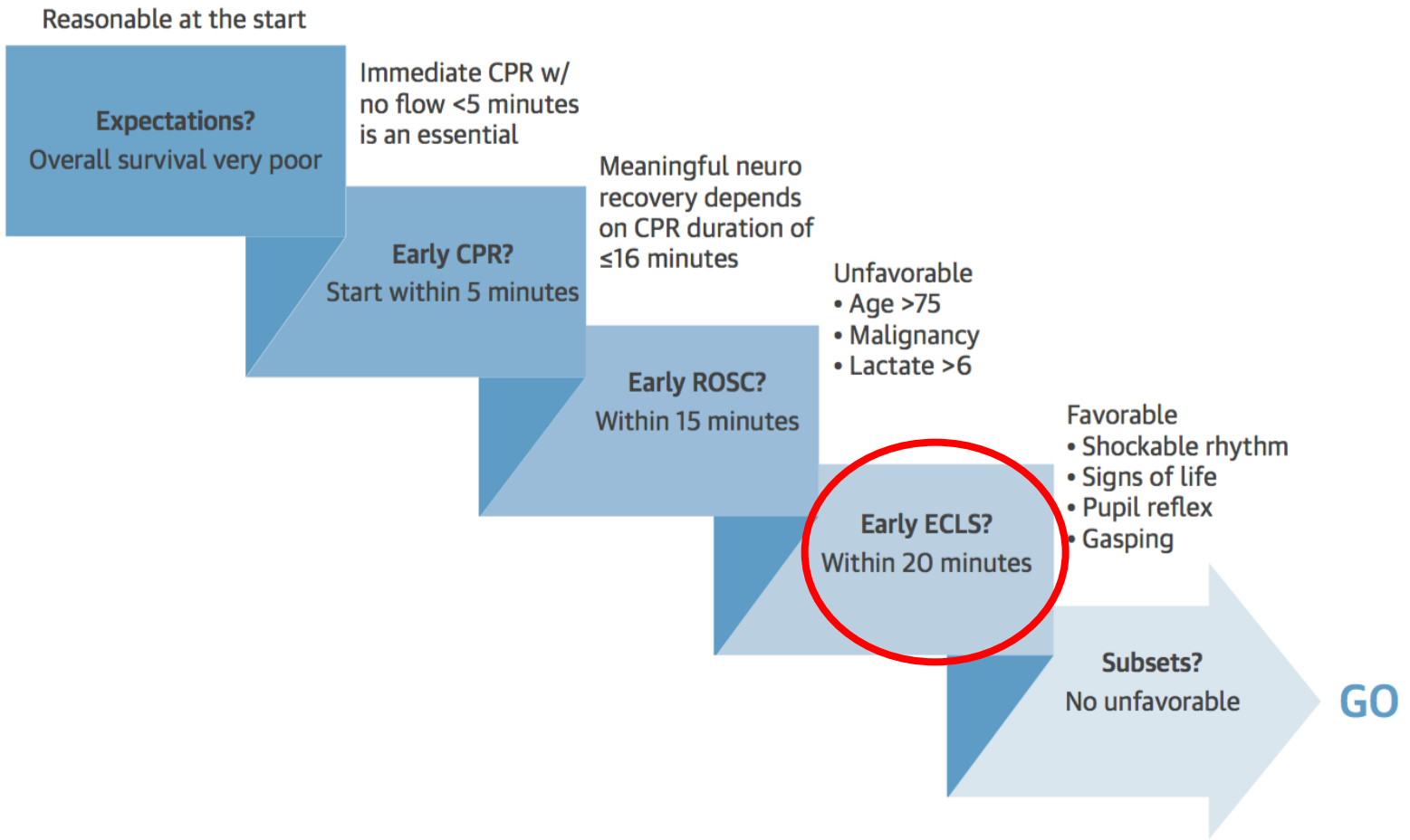
1. LINK ET AL. CIRCULATION 2015;132 (18 SUPPL 2): S444-S464
2. LAMHAUT ET AL. RESUSCITATION 2017;117:109-117

PRINCIPLE THOUGHTS FOR SHORT TERM MCS IN CS



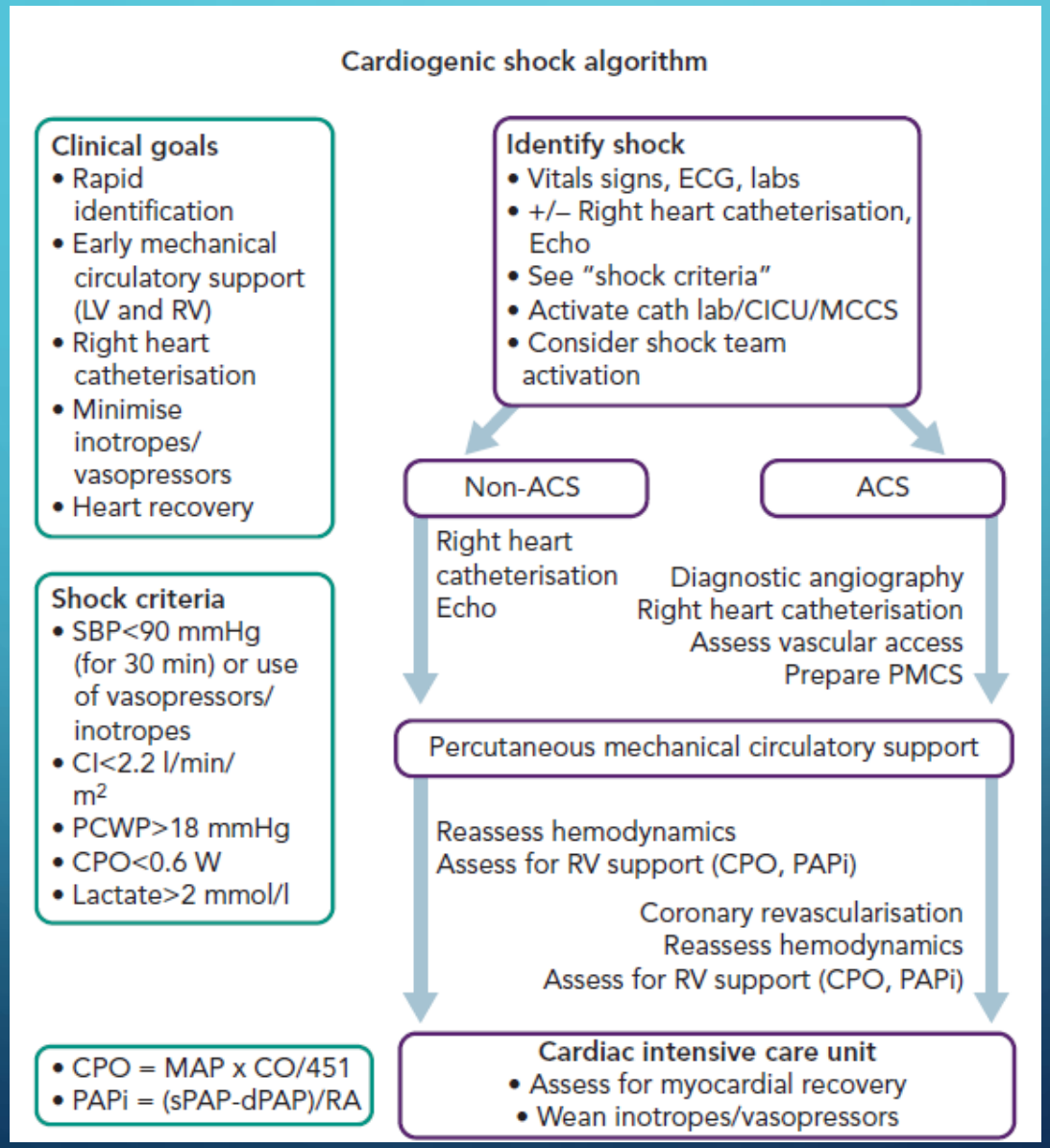
INITIATING ECPR- IMPORTANCE OF TIMING

FIGURE 6 **Decision-Making Algorithm on Initiation of ECPR**



Possible outcomes after initiating CPR within 5 min **(far left)** leading to either favorable or unfavorable outcomes based on timeline decisions to start return of spontaneous circulation (ROSC) or ECLS. Abbreviations as in Figure 5.

CARDIOGENIC SHOCK DIAGNOSIS, *TEAM ACTIVATION* AND TREATMENT ALGORITHM PROTOCOL



Activate multidisciplinary approaches:

1. Interventional cardiologists
2 Cardiac surgical team
3. Advanced Heart failure physicians
4. Critical care team

STANDARDIZED TEAM-BASED CARE FOR CARDIOGENIC SHOCK

TEHRANI ET AL. JACC 2019;73:1659-1669

CENTRAL ILLUSTRATION: Cardiogenic Shock Algorithm

Patient with suspected cardiogenic shock (CS)

Clinical criteria to rapidly identify shock state:

Systolic blood pressure (SBP) <90 mm Hg for >30 minutes (or use of inotropes/vasopressors to maintain SBP)

Evidence of end-organ hypoperfusion

Lactate level >2 mmol/l

Activate Shock Team through a one-call line for multidisciplinary discussion: Interventional Cardiology; Cardiac Surgery; Advanced Heart Failure; Critical Care

Transfer patient to cardiac catheterization lab or cardiac intensive care unit (CICU) for evaluation

If acute decompensated heart failure cardiogenic shock (ADHF-CS) suspected:

Right heart catheterization

Echo

If acute myocardial infarction cardiogenic shock (AMI-CS) suspected:

Right heart catheterization

Coronary angiography + revascularization

Assessment of peripheral vascular anatomy

Hemodynamic Criteria for Cardiogenic Shock:

Fick cardiac index <1.8 l/min/m² without inotropes/vasopressors (or <2.2 l/min/m² with inotropes/vasopressors)

Pulmonary capillary wedge pressure >15 mm Hg

Cardiac power output (CPO) <0.6 W

PAPi <1.0

If Hemodynamic Criteria are met, consider Percutaneous Mechanical Circulatory Support (PMCS)

Admit Patient to CICU

Daily bedside echocardiograms for patients with PMCS

Frequent neurovascular assessments for patients with PMCS

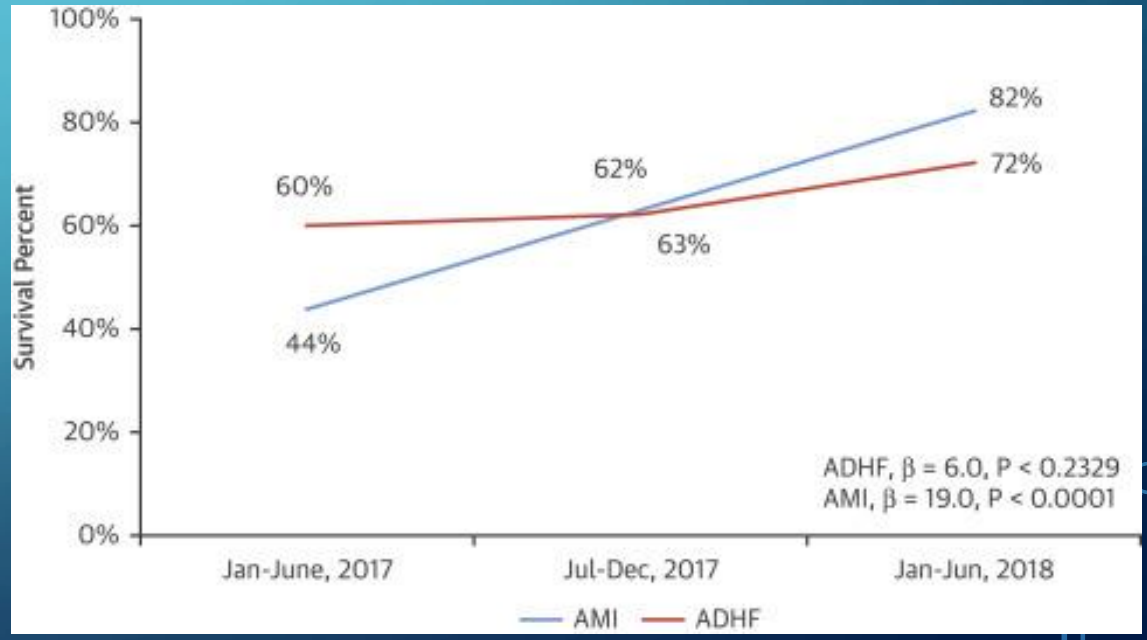
Serial assessment of end-organ perfusion and hemodynamics: CPO, PAPi and lactate

Evaluation for weaning vs. escalation of support

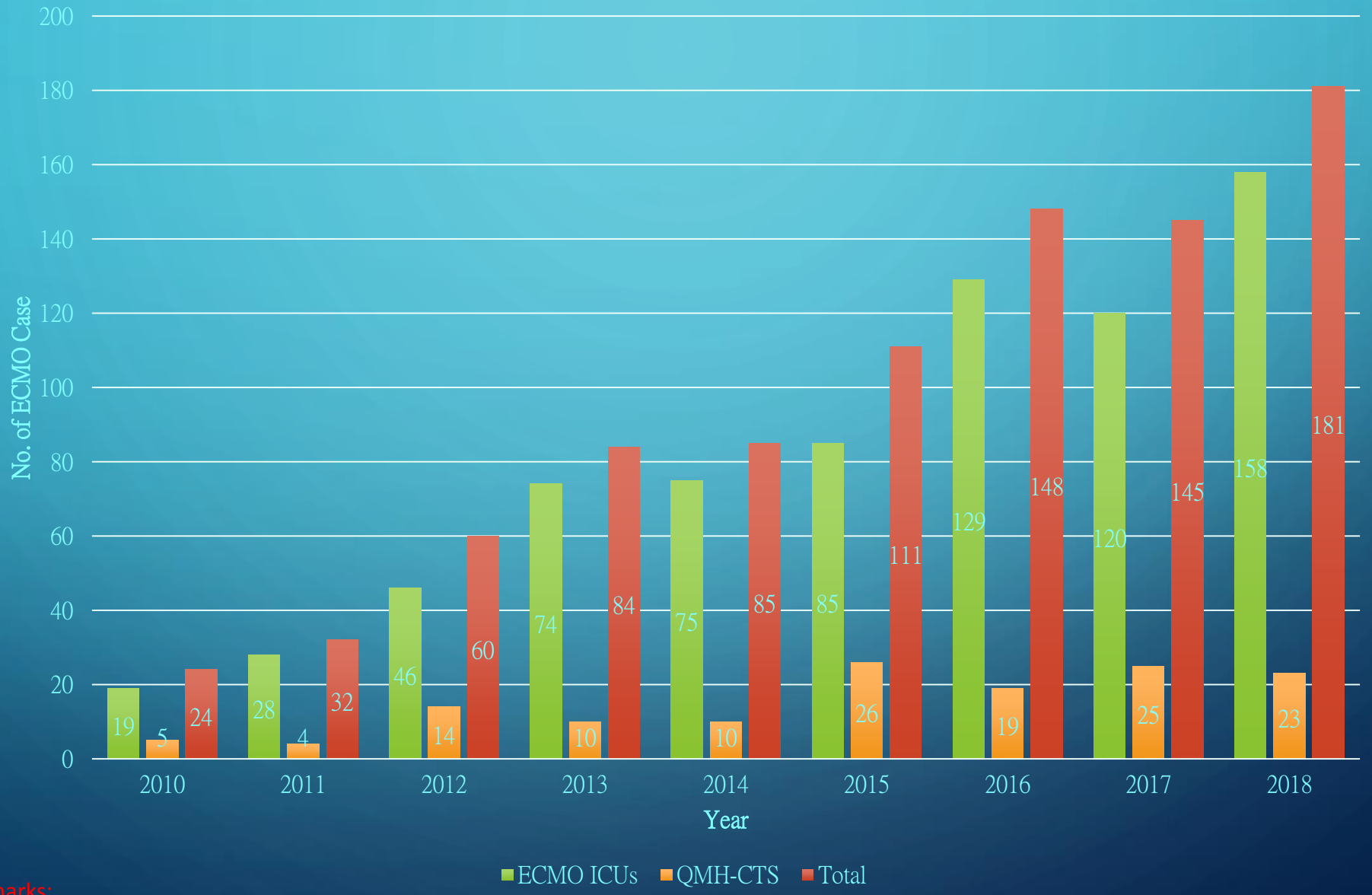
Tehrani, B.N. et al. J Am Coll Cardiol. 2019;73(13):1659-69.

	2016 (baseline)	2017	2018
30 days survival	47%	57.9%*	76.6% *

P <0.01*



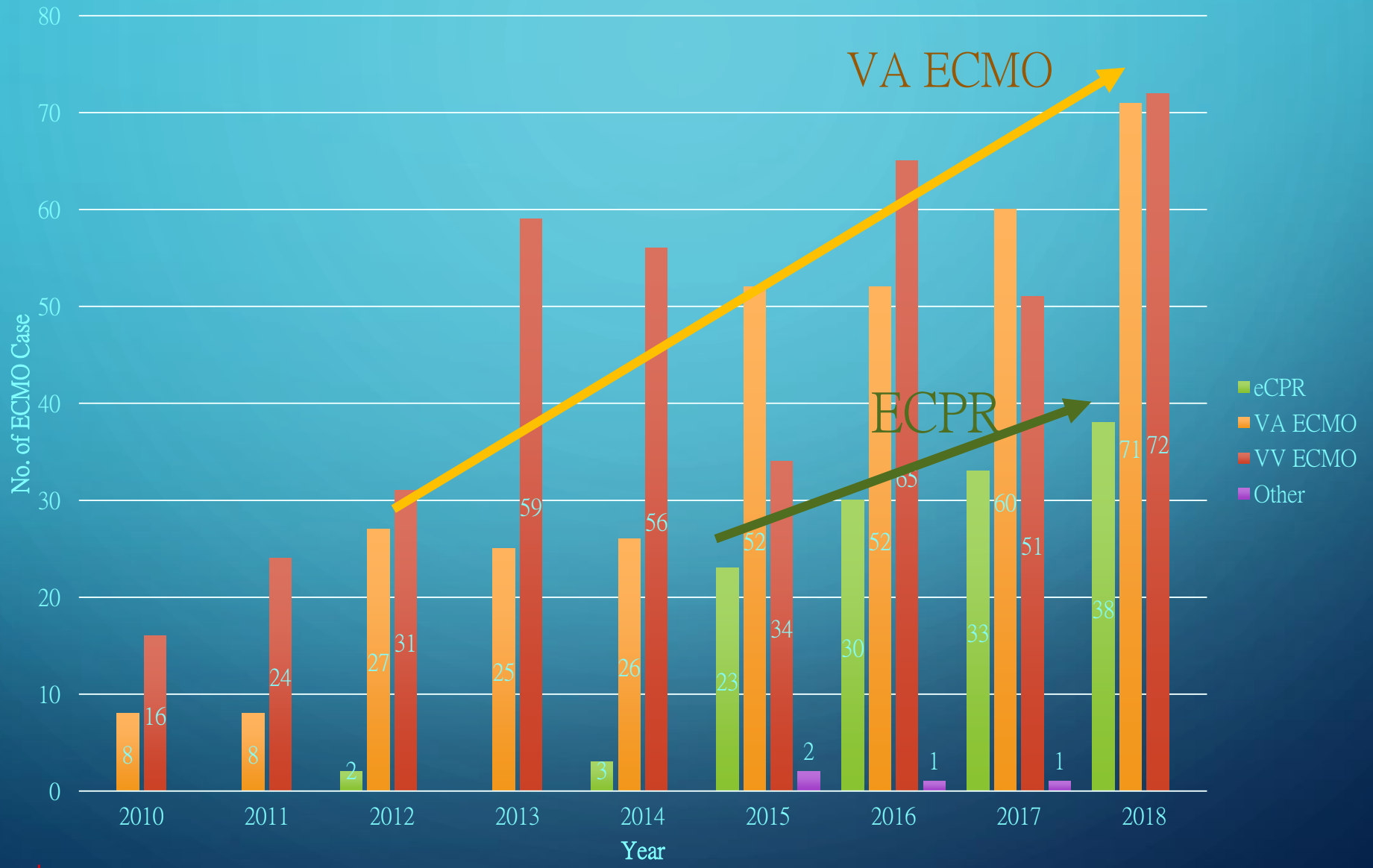
Total no. of ECMO Case in Hong Kong
(2010 - 2018)



Remarks:

- Total no. of ECMO case = 912, Total no. of ECMO patient = 870

Total no. of ECMO Case (By Type) (2010 - 2018)

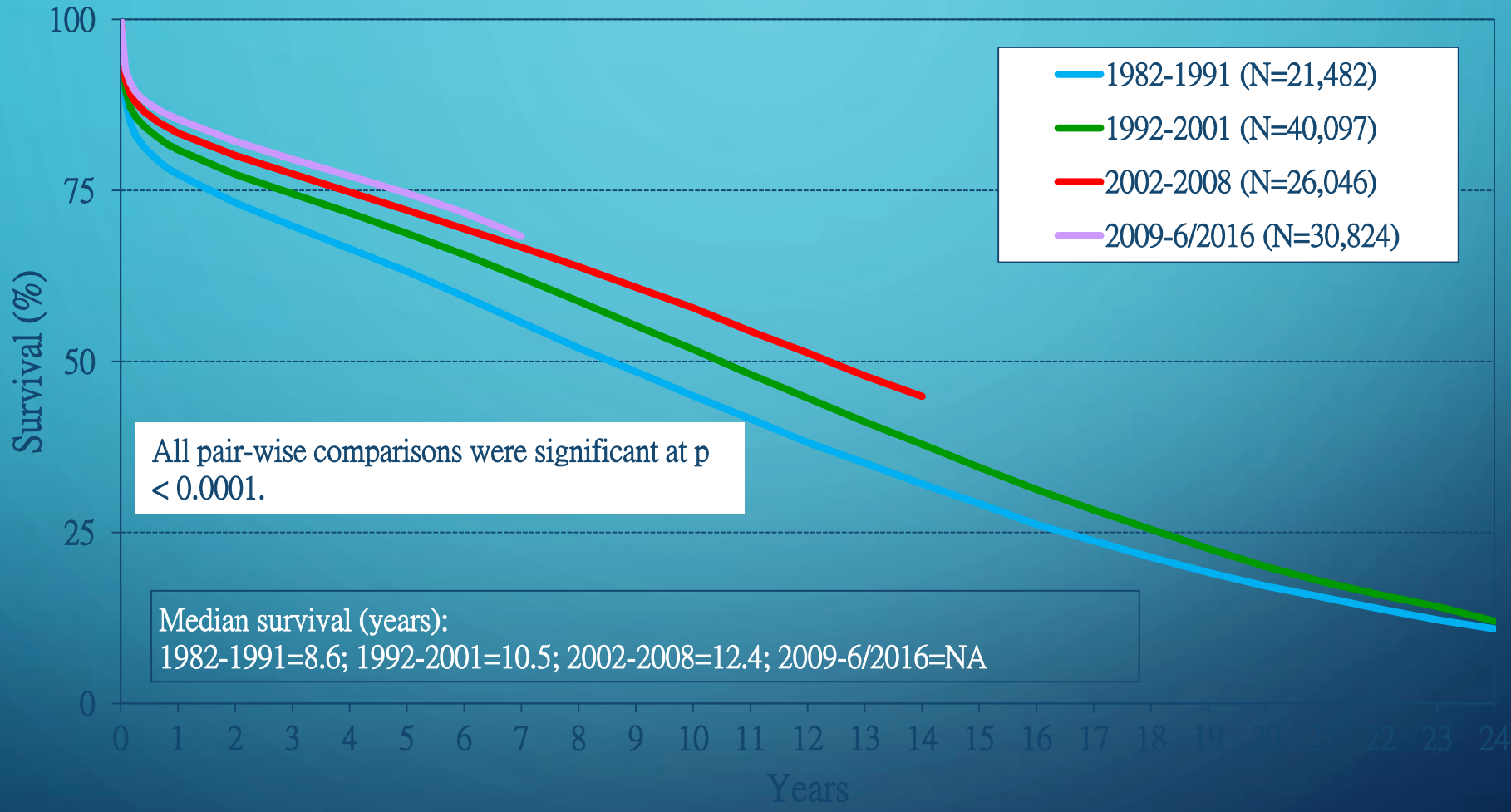


Remarks:

- Total no. of ECMO case = 912, Total no. of ECMO patient = 870

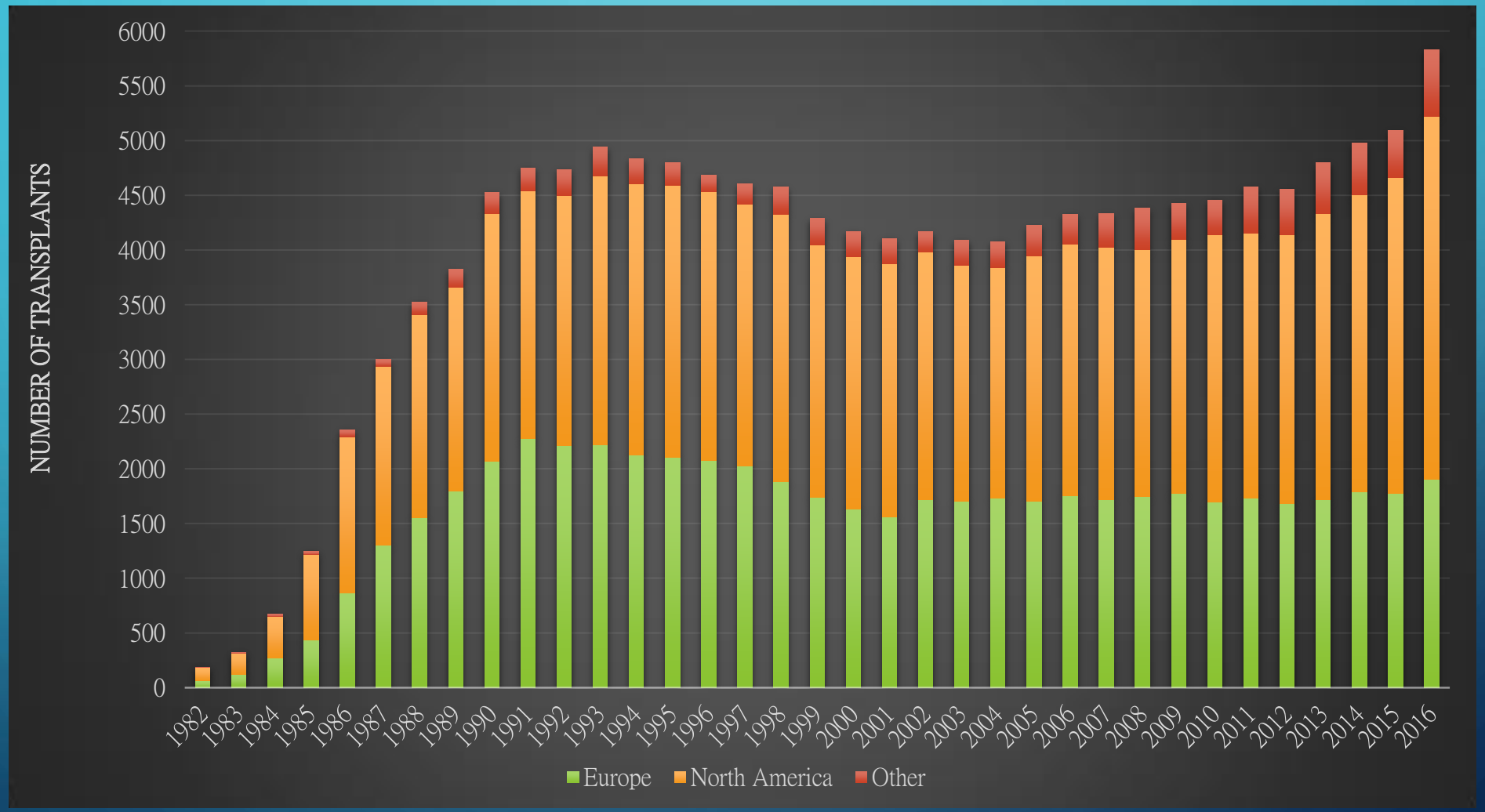
SO WHAT' S NEXT?

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



ISHLT • INTERNATIONAL SOCIETY FOR HEART AND LUNG TRANSPLANTATION
2018
JHLT. 2018 Oct; 37(10): 1155-1206

ADULT AND PEDIATRIC HEART TRANSPLANTS
NUMBER OF TRANSPLANTS BY YEAR AND LOCATION



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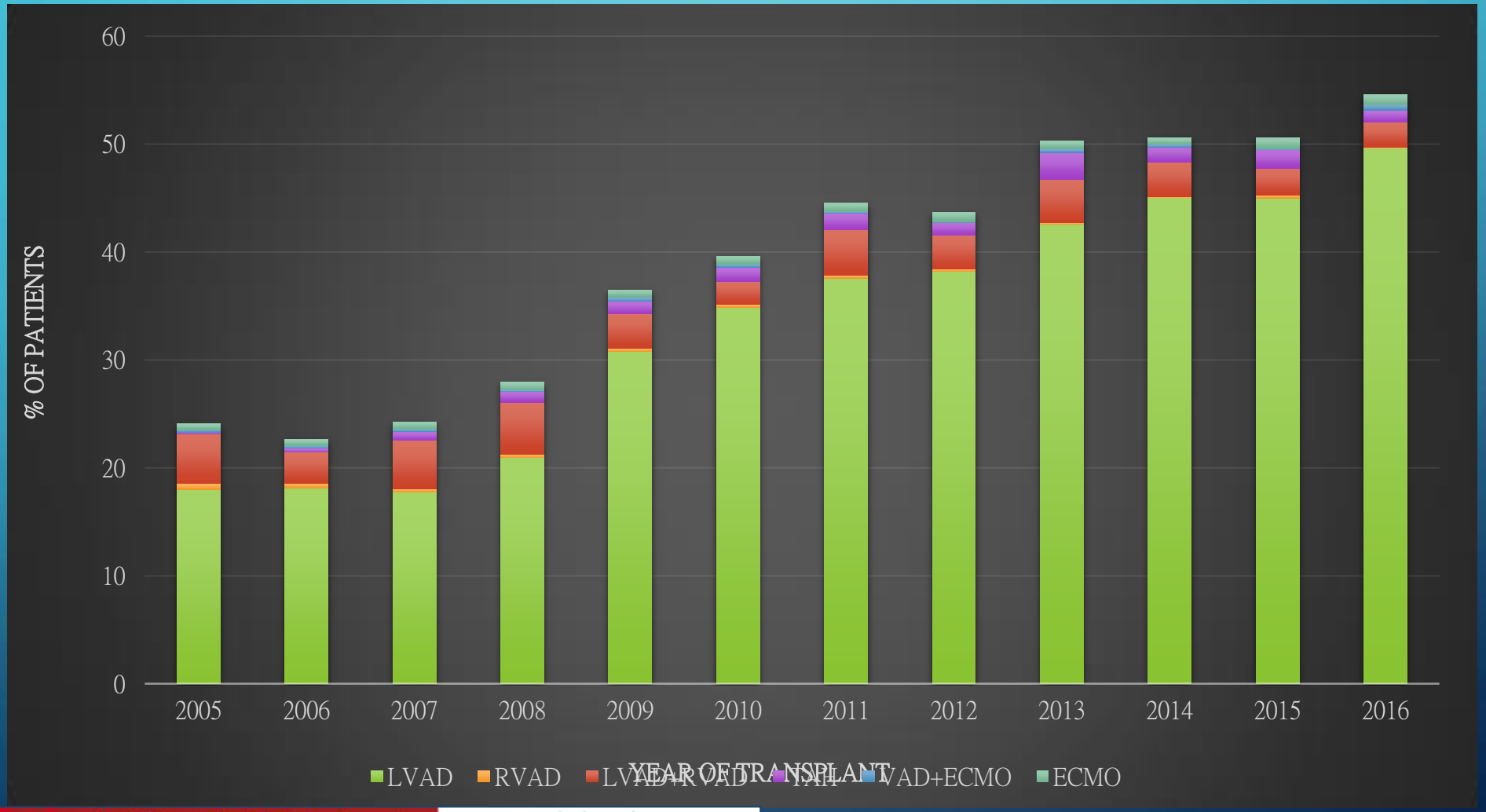
ADULT HEART TRANSPLANTS

% OF PATIENTS BRIDGED WITH MECHANICAL CIRCULATORY SUPPORT* BY YEAR AND DEVICE TYPE



* LVAD, RVAD, TAH, ECMO

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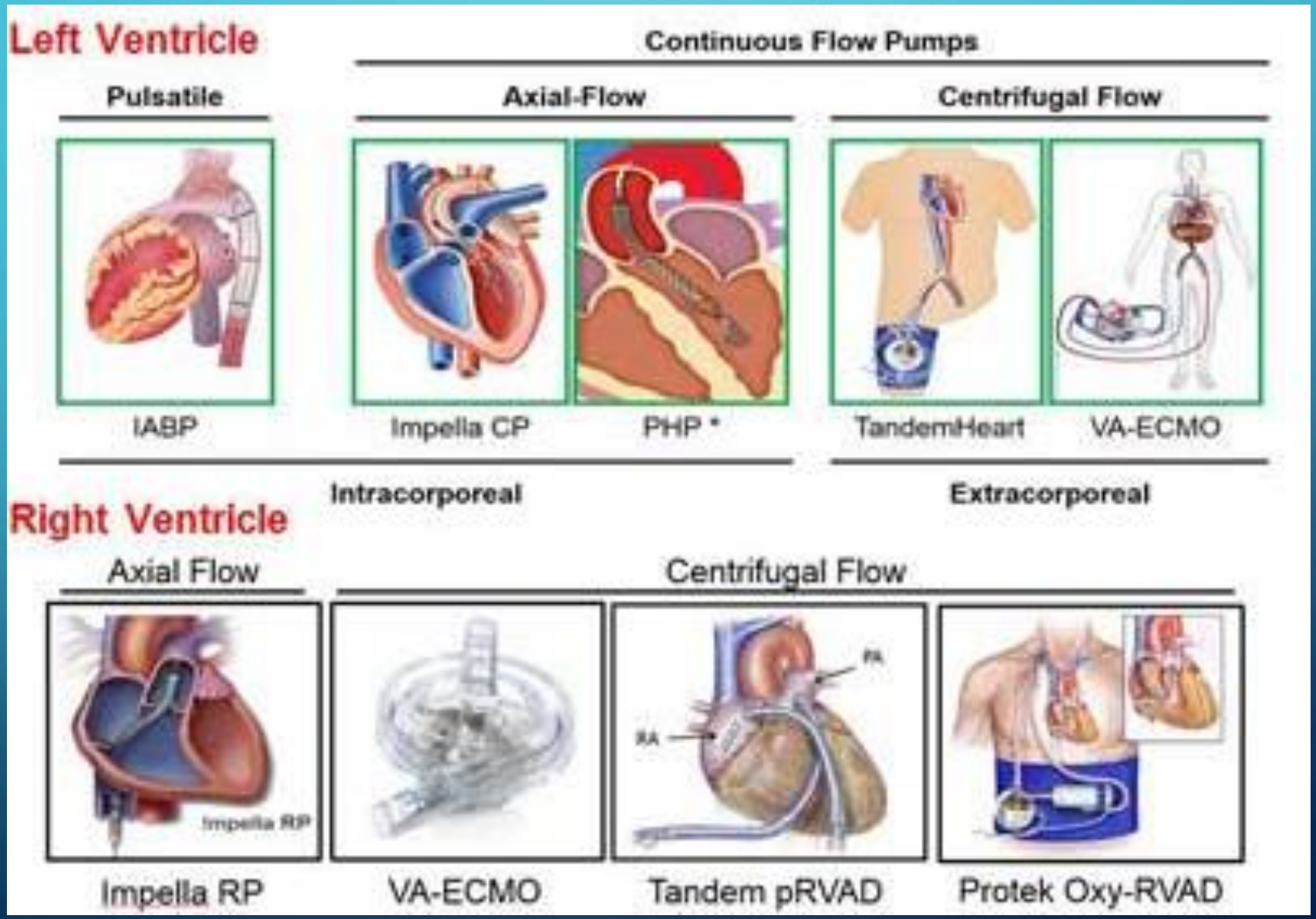
JHLT. 2018 Oct; 37(10): 1155-1206

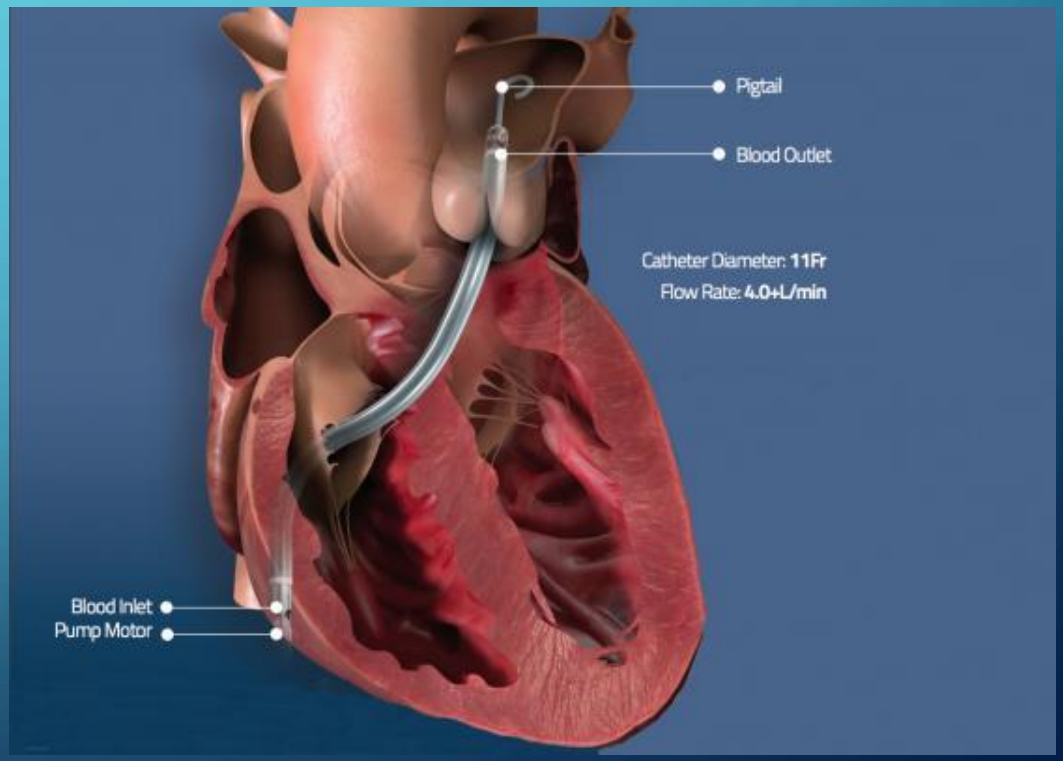
INCREASING ROLE OF TEMPORARY MCS MODALITIES

STABILIZE PATIENT IN HEMODYNAMIC EXTREMIS



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



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

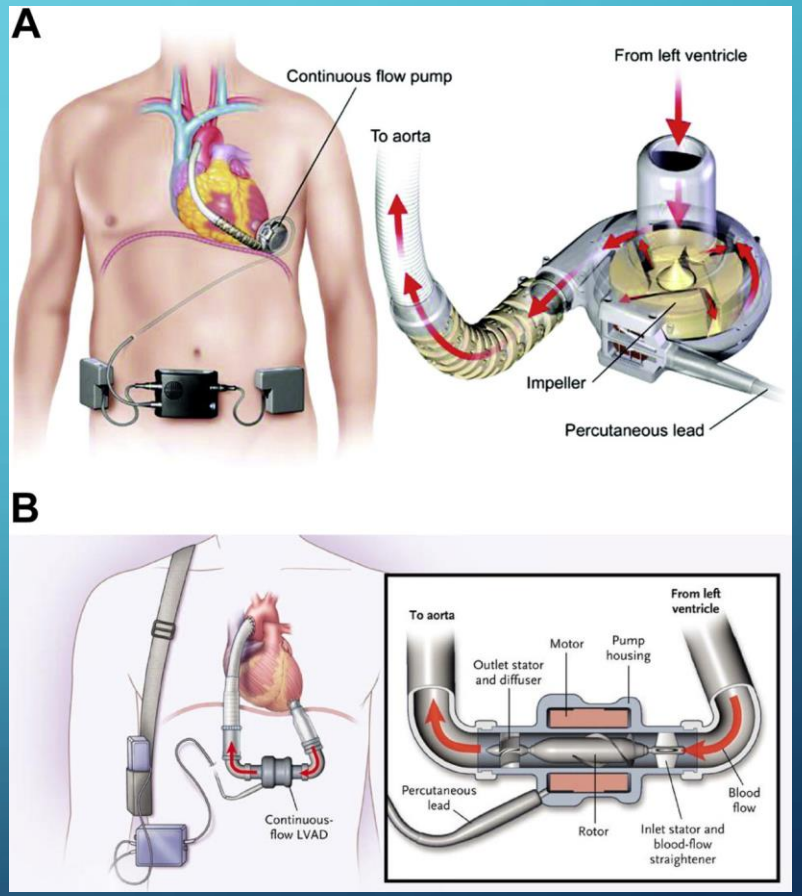
CONSIDERATIONS BEFORE FINALIZED MCS STRATEGY

- 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

DURABLE VENTRICULAR ASSISTS DEVICE (VAD)

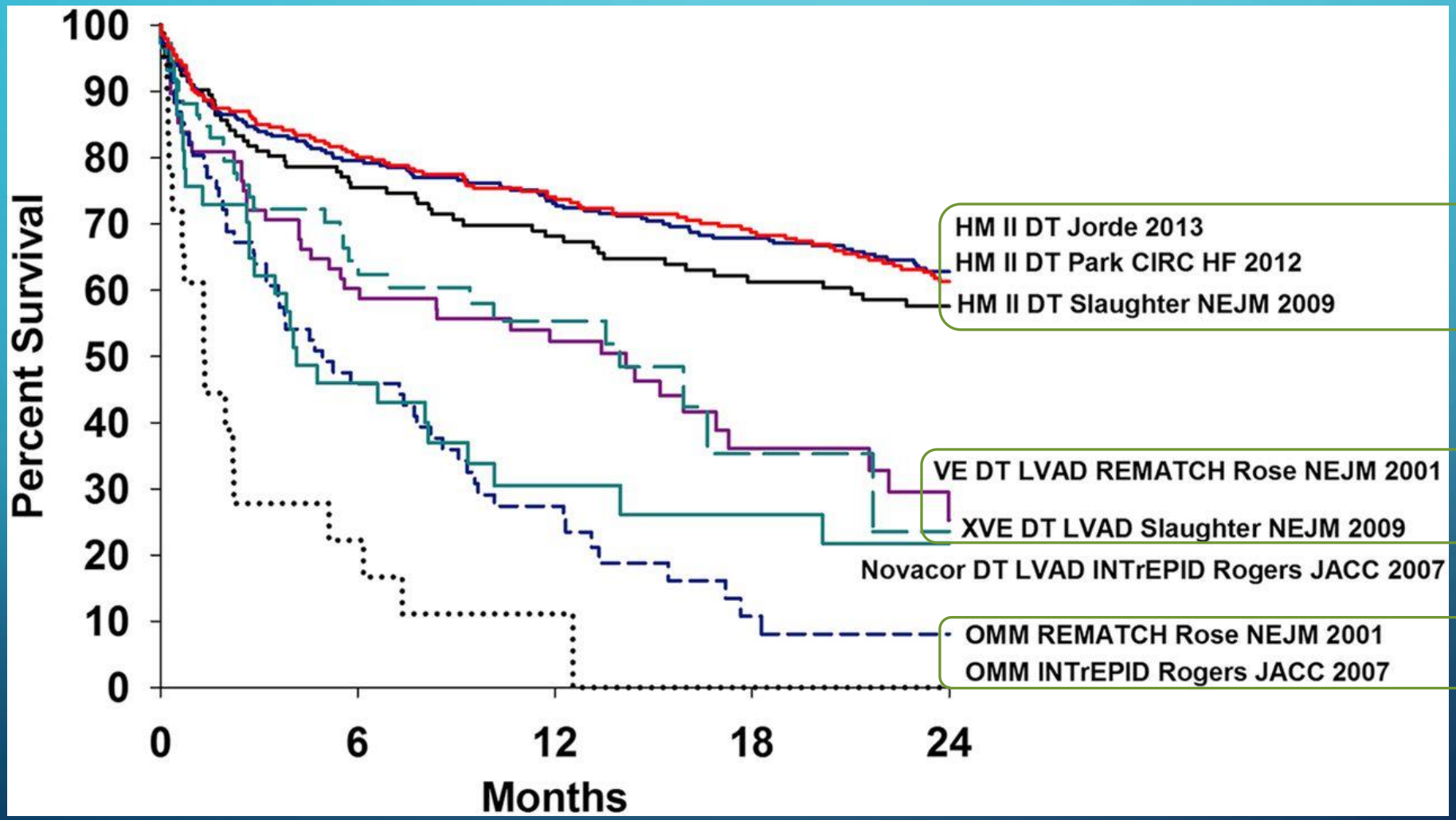
- For the larger group of individuals who face a high risk of short-term mortality and little chance of receiving a transplant that the emergence of continuous flow LVAD holds the greatest promise
- Durable VADs devices are capable of augmenting the circulation to meet the body’ s physiological needs,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



Centrifugal flow with levitating magnetic discs

Axial flow pump

SURVIVAL IMPROVEMENT OVER TIME



CURRENT CONSIDERATIONS IN LVADS: WHERE ARE WE NOW?

- New pump design changes
- Outcome benefits

OVERCOMING THE CHALLENGE OF ADVERSE EVENTS

Table 2 Most frequent adverse events during HeartMate II support as BTT

Adverse events	Author (Ref.), study period				
	Miller (8), 03/2005-05/2006	Pagani (9), 03/2005-04/2008	Starling (10), 04/2008-08/2008	John (11), 06/2005-06/2010	Lok (12), 03/2006-12/2011
Bleeding					
Re-exploration	31%	26%	NR	16%	NR
Gastrointestinal	NR	NR	NR	17%	4%
CVA				8%	20%
Stroke	8%	8%	6%	NR	NR
TIA	4%	2%	NR	NR	NR
RV failure			14%		31%
Inotropic	13%	13%	NR	NR	27%
MCS	4%	6%	NR	4%	4%
Driveline infection	14%	14%	17%	21%	14%
Pump thrombosis (replacement)	2%	1%	NR	0.98%	4%

BTT, bridge-to-transplantation; NR, not reported; CVA, cerebrovascular accidents; TIA, transient ischemic attack; RV, right ventricle; MCS, mechanical circulatory support.

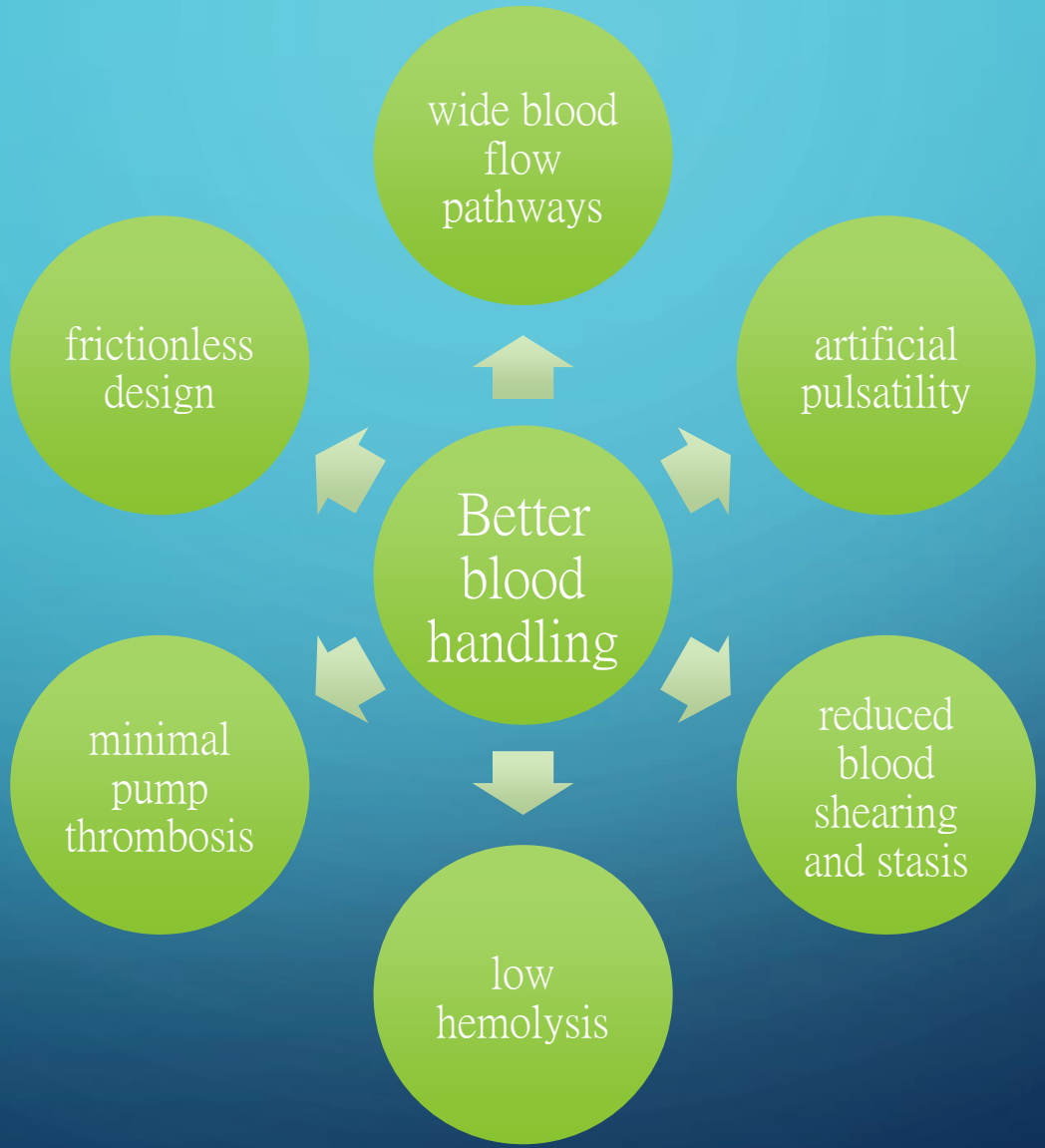
- Conceptually 3 categories AEs
- Intrinsic to the pump and its constituents
  - Pump malfunction
  - Controller faults
  - Driveline faults
  - Short-to-shield malfunctions
- Patient-related- liability of native heart
  - Arrhythmias
  - Valvular insufficiency
  - RV failure
- Pump-patient interface
  - Acquired von Willebrand disease
  - Infection
  - Stroke
  - Pump thrombosis

Major focus of pump redesign- Making a more "biocompatinle device"
Object of pt management decisions

PROGRESS TOWARDS "BIOCOMPATIBILTY"

- Biocompatibility refers to the ability of an implantable device to function without perturbing the body's homeostatic systems
- In theory, a fully compatible device would neither activate nor suppress the immune system and would not have any disruptive effect on blood elements, the coagulation system or thrombus formation
- Thrombus formation = "Hemocompatibility" – a complex interaction between pump-patient interface and is influenced at micro level by the blood-contacting surfaces and at a macro level by pump design and flow dynamics
- Inadequate hemocompatibility- Gastrointestinal bleeding, stroke (both hemorrhagic and ischemic), hemolysis and pump thrombosis

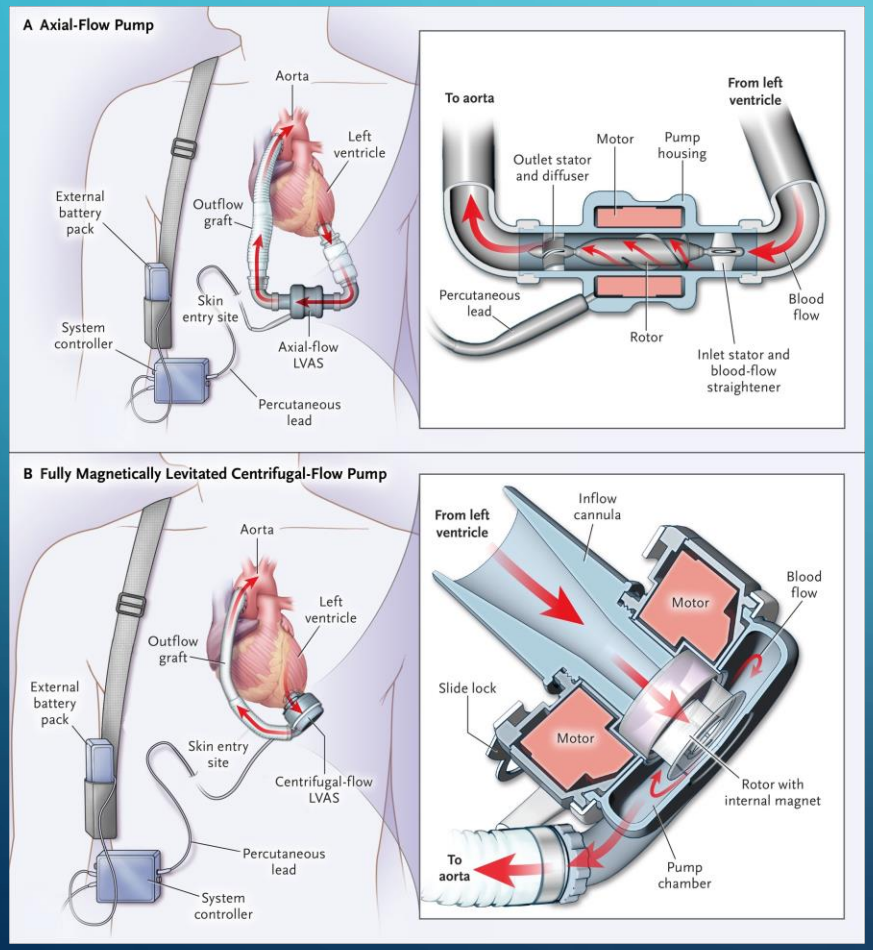
HEMOCOMPATIBILITY
DESIGNED FOR BETTER BLOOD HANDLING

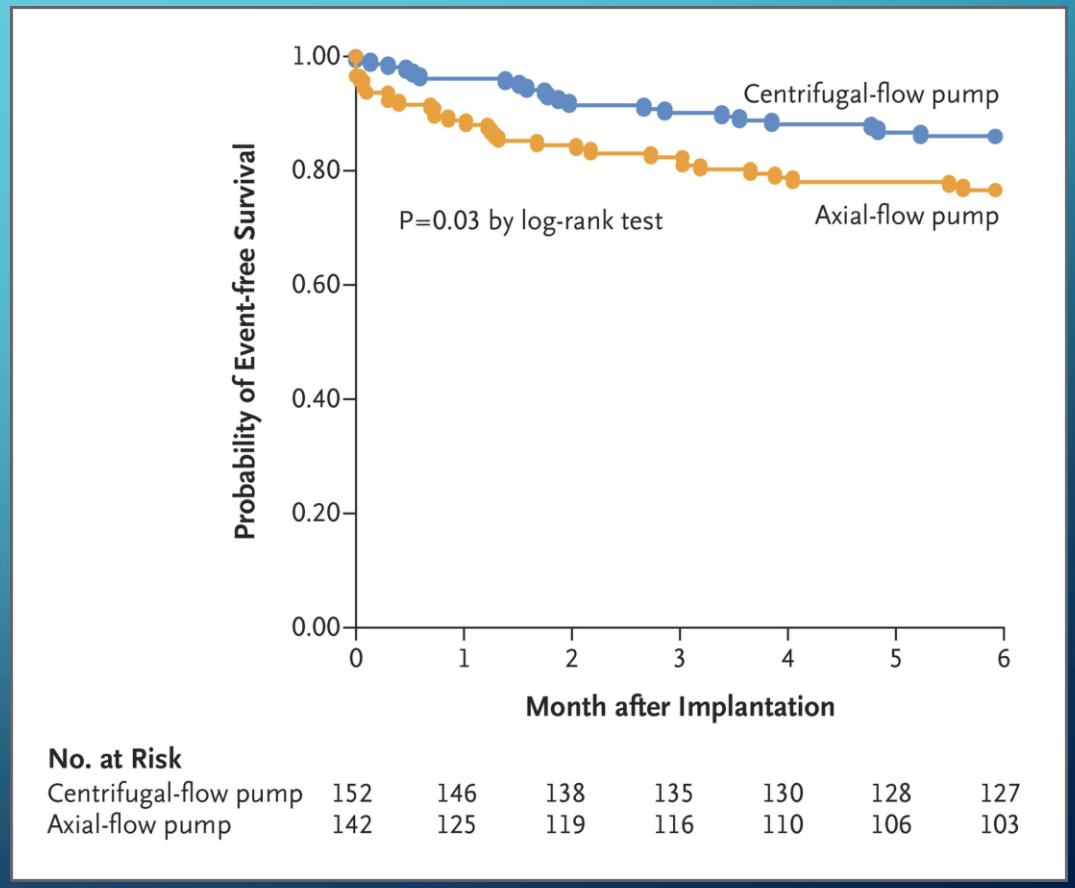


A FULLY MAGNETICALLY LEVITATED CIRCULATORY PUMP FOR ADVANCED HEART FAILURE MOMENTUM 3

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*

- 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

N Engl J Med 2019;380:1618-1627

METHODS & DEMOGRAPHICS

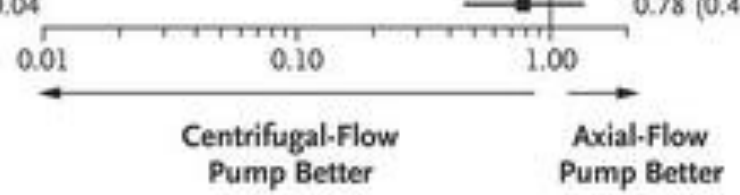
- From Sept 2014 to Aug 2016
- Total 1028 pts underwent randomization: CF pump 516 pts vs axial flow pump 512 pts (8 pts did not have LVADs implantation)
- A total of 126 surgeons performed 1020 implantations at 69 sites
- Discharge from hospitals:
  - CF flow VADS- 94.2% (mean LOS 19 days)
  - Axial flow VADs- 93.3% (mean LOS 17 days)

Table 1. Baseline Characteristics of Patients in the Intention-to-Treat Population.*

Characteristic	Centrifugal-Flow Pump Group (N=516)	Axial-Flow Pump Group (N=512)
Age — yr		
Mean	59±12	60±12
Median (range)	62 (18–83)	63 (21–84)
Male sex — no. (%)	411 (79.7)	419 (81.8)
Race or ethnic group — no. (%)†		
White	342 (66.3)	367 (71.7)
Black	145 (28.1)	120 (23.4)
Asian	8 (1.6)	3 (0.6)
Native Hawaiian or Pacific Islander	0	4 (0.8)
Other	21 (4.1)	18 (3.5)
Body-surface area — m^2	2.1±0.3	2.1±0.3
Ischemic cause of heart failure — no. (%)	216 (41.9)	240 (46.9)
History of atrial fibrillation — no. (%)	215 (41.7)	238 (46.5)
History of stroke — no. (%)	50 (9.7)	56 (10.9)
Previous cardiac surgical procedures — no. (%)		
Coronary-artery bypass	102 (19.8)	114 (22.3)
Valve replacement or repair	36 (7.0)	31 (6.1)
Left ventricular ejection fraction — %	17.3±5.1	17.2±5.0
Arterial blood pressure — mm Hg		
Systolic	108.4±14.7	106.5±14.5
Diastolic	66.8±10.6	65.7±10.2
Mean arterial pressure — mm Hg	79.2±10.4	79.2±10.1
Pulmonary-capillary wedge pressure — mm Hg	23.1±8.6	22.9±9.2
Cardiac index — liters/min/m^2	2.0±0.5	2.0±0.6
Pulmonary vascular resistance — Wood units	3.1±1.7	3.0±1.7
Right atrial pressure — mm Hg	10.8±6.5	10.7±6.8
Serum sodium level — mmol/liter	135.4±4.1	135.5±4.2
Serum creatinine level — mg/dl	1.4±0.4	1.4±0.4
Estimated glomerular filtration rate — ml/min/1.73 m^2	61.3±23.7	59.5±22.0
Intended goal of pump support — no. (%)		
Bridge to transplantation	113 (21.9)	121 (23.6)
Bridge to candidacy for transplantation	86 (16.7)	81 (15.8)
Destination therapy	317 (61.4)	310 (60.5)

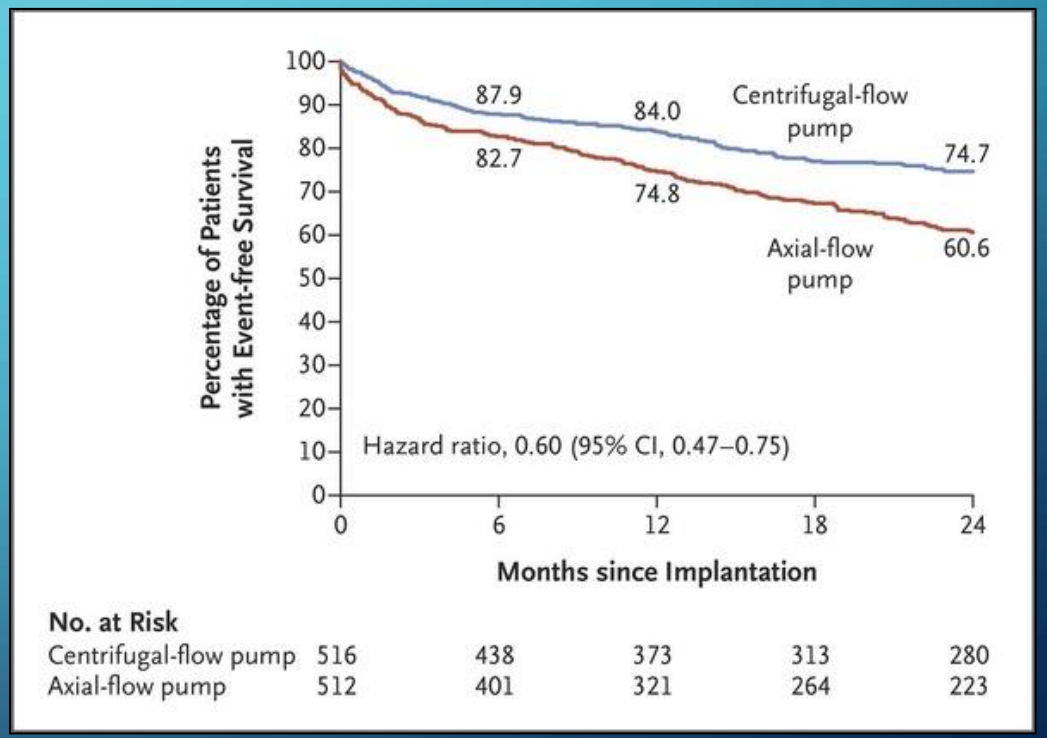
PRINCIPAL SAFETY OUTCOMES IN PER-PROTOCOL POPULATION

Adverse Event	Centrifugal-Flow Pump	Axial-Flow Pump	Centrifugal-Flow Pump	Axial-Flow Pump	Relative Risk (95% CI)	P Value
	no. of patients with events (%)		*events per patient-yr*			
Suspected or confirmed pump thrombosis	7 (1.4)	70 (13.9)	0.01	0.12	0.08 (0.04–0.16)	<0.001
Any stroke	51 (9.9)	98 (19.4)	0.08	0.18	0.42 (0.30–0.57)	<0.001
Disabling stroke	26 (5.0)	38 (7.5)	0.04	0.07	0.54 (0.34–0.85)	0.008
Any bleeding	225 (43.7)	278 (55.0)	0.61	0.95	0.64 (0.57–0.72)	<0.001
Gastrointestinal bleeding	126 (24.5)	156 (30.9)	0.31	0.49	0.64 (0.54–0.75)	<0.001
Other neurologic event	59 (11.5)	47 (9.3)	0.09	0.08	1.25 (0.88–1.79)	0.21
Any major infection	300 (58.3)	285 (56.4)	0.82	0.82	1.00 (0.89–1.12)	0.96
Right heart failure	176 (34.2)	143 (28.3)	0.27	0.23	1.15 (0.94–1.42)	0.18
Cardiac arrhythmia	185 (35.9)	207 (41.0)	0.37	0.45	0.82 (0.70–0.97)	0.02
Respiratory failure	111 (21.6)	98 (19.4)	0.19	0.17	1.10 (0.86–1.40)	0.44
Renal dysfunction	73 (14.2)	56 (11.1)	0.11	0.08	1.36 (0.98–1.89)	0.07
Hepatic dysfunction	25 (4.9)	27 (5.3)	0.03	0.04	0.78 (0.46–1.34)	0.38

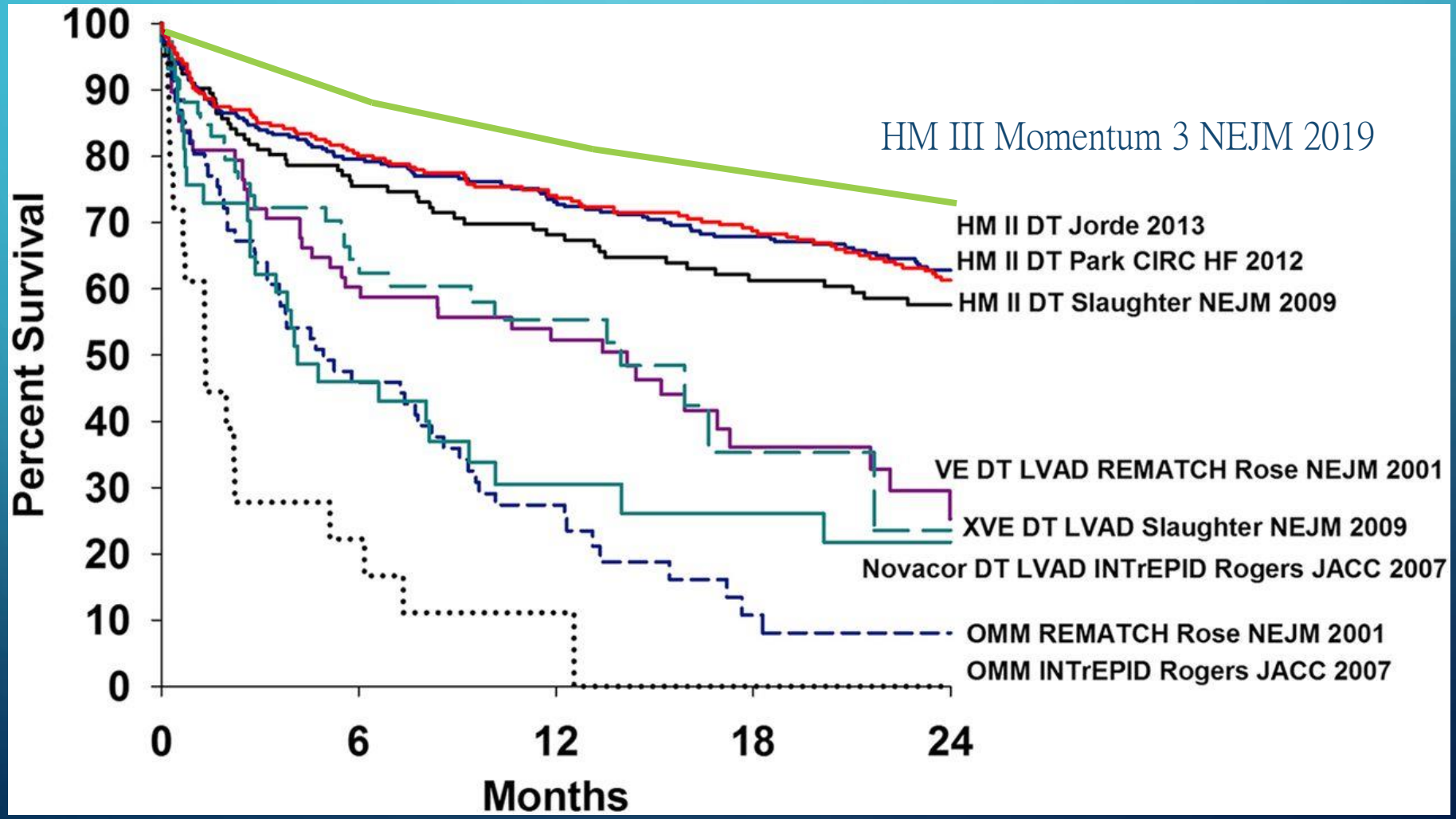


IMPROVED EVENT-FREE SURVIVAL OF STROKE OR RE-OPERATION

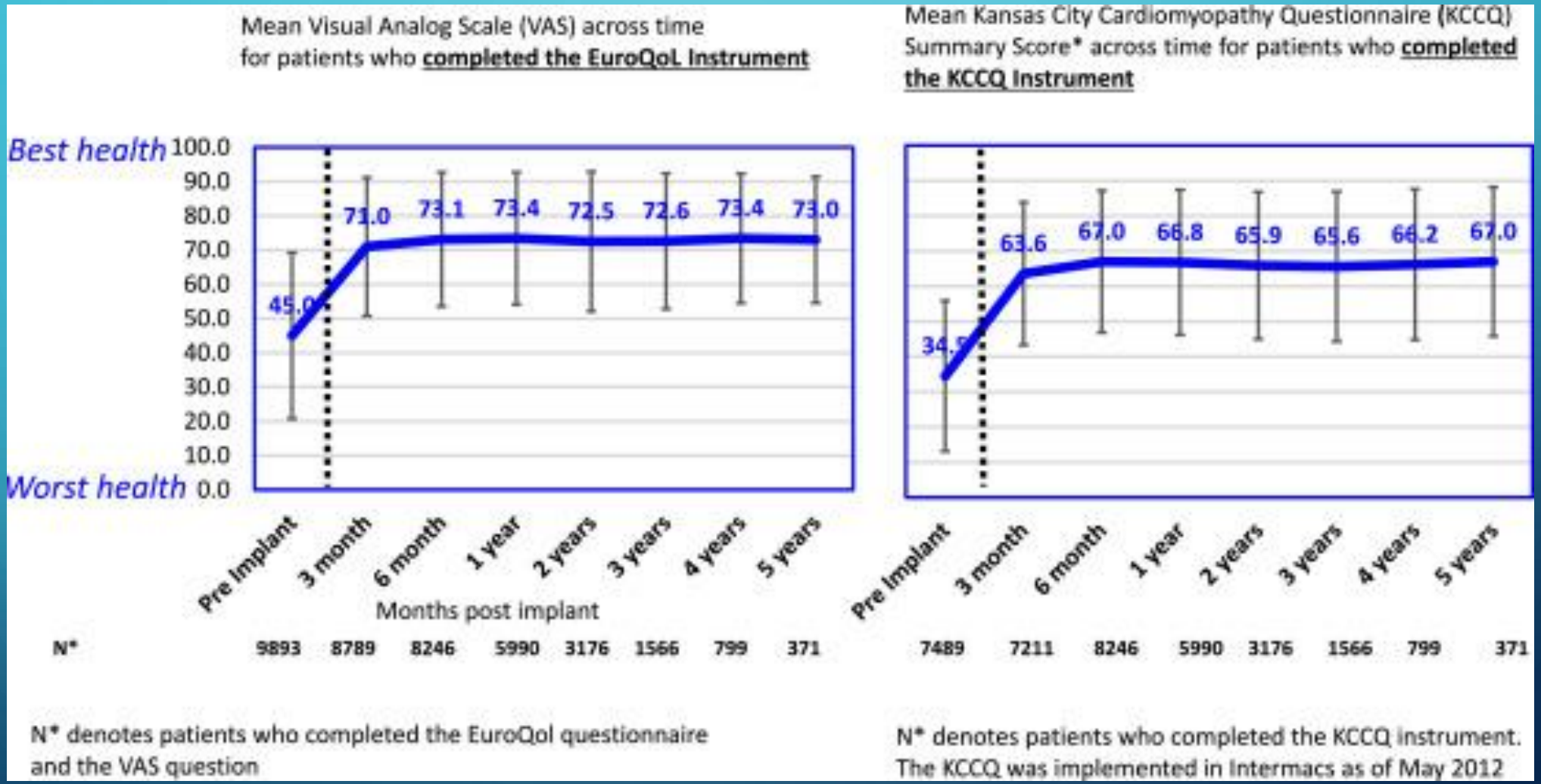
- HM III fully magnetically centrifugal flow pump was superior to HM II axial-flow pump with respect to survival free of disabling stroke or reoperation to replace or remove malfunctioning device
- CF pump associated with lower incidence of either ischemic or hemorrhagic strokes



PUTTING INTO PERSPECTIVES…

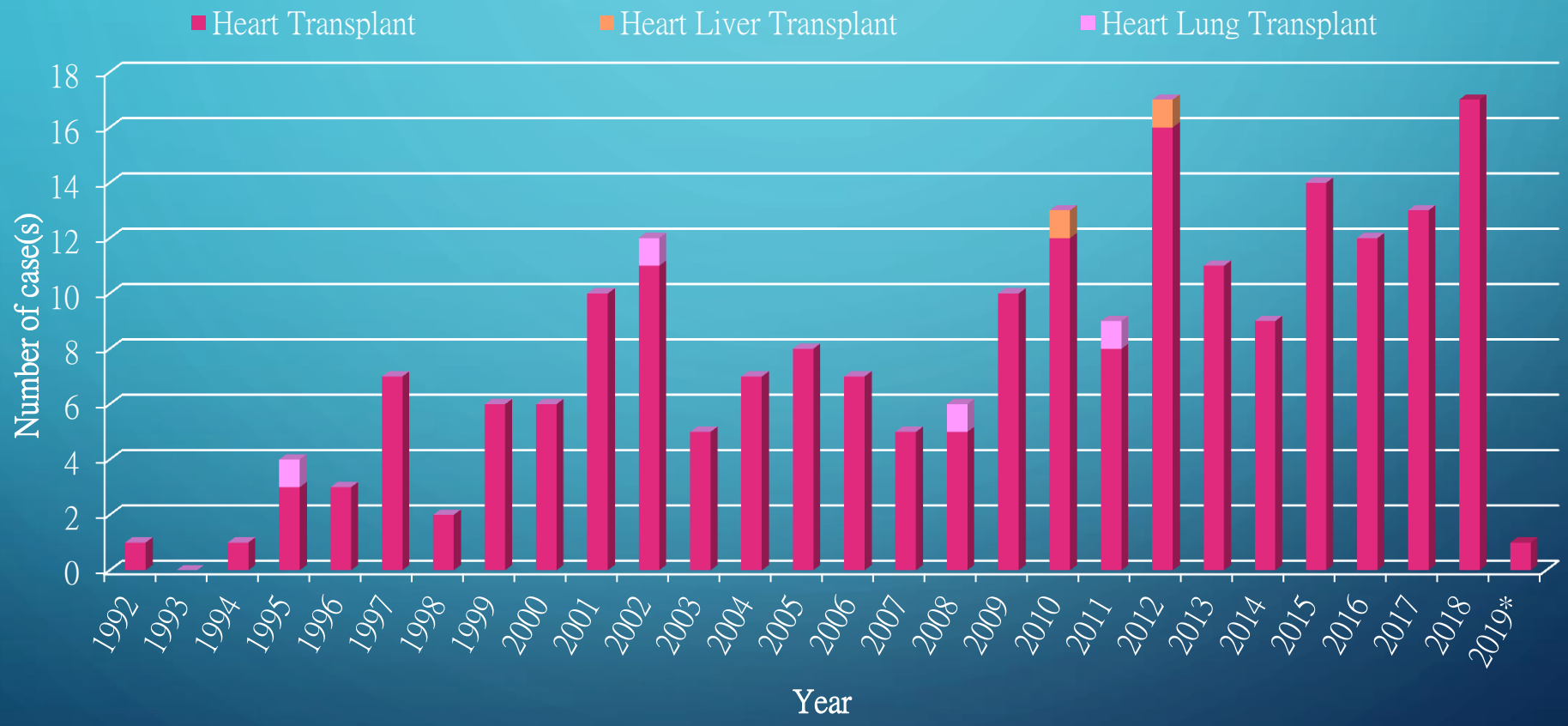


VAD QUALITY OF LIFE



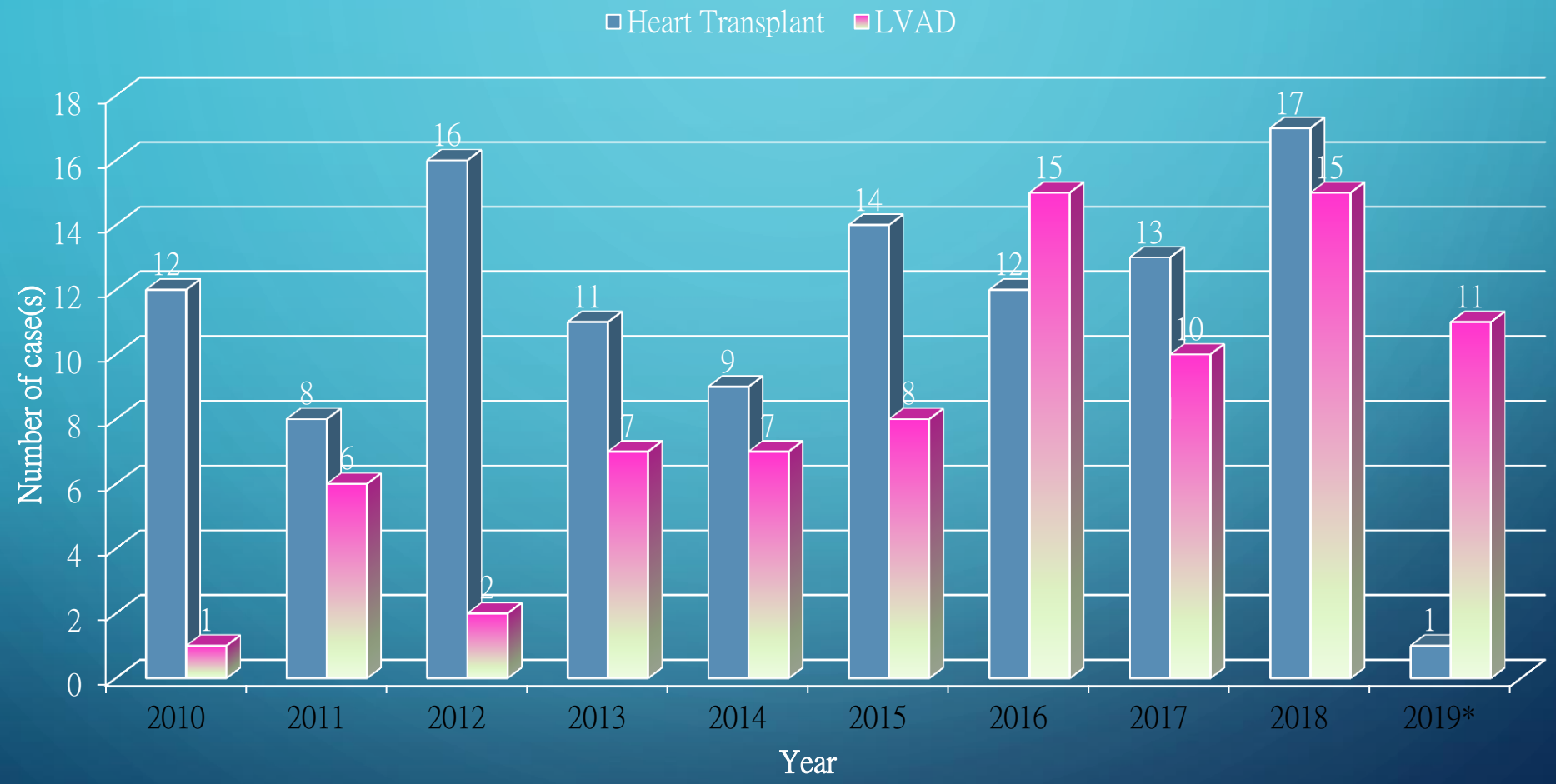
INTERMACS report ISHLT 2019

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 31 May 2019

NUMBERS OF HEART TRANSPLANT & LVAD IN HK



* Total numbers of LVAD: 82 as at 31 May 2019

ECMO AS BRIDGE IN ADVANCED HEART FAILURE PRELIMINARY HK DATA

	Number	Bridge from VA-ECMO	1 year/ current Survival
Durable LVAD	82	12 (14%)	9 (82.5%)
CentriMag L/RVAD or BiVAD	52	32 (61.5%)	16 (50%)

Only 1 pt directly bridge from VA-ECMO to Heart Transplantation

5 patients severe PAH received VA-ECMO
1 bridge to Lung Transplant
1 bridge to salvage triple PAH therapy
3 died on VA-ECMO support

CASE – MR L

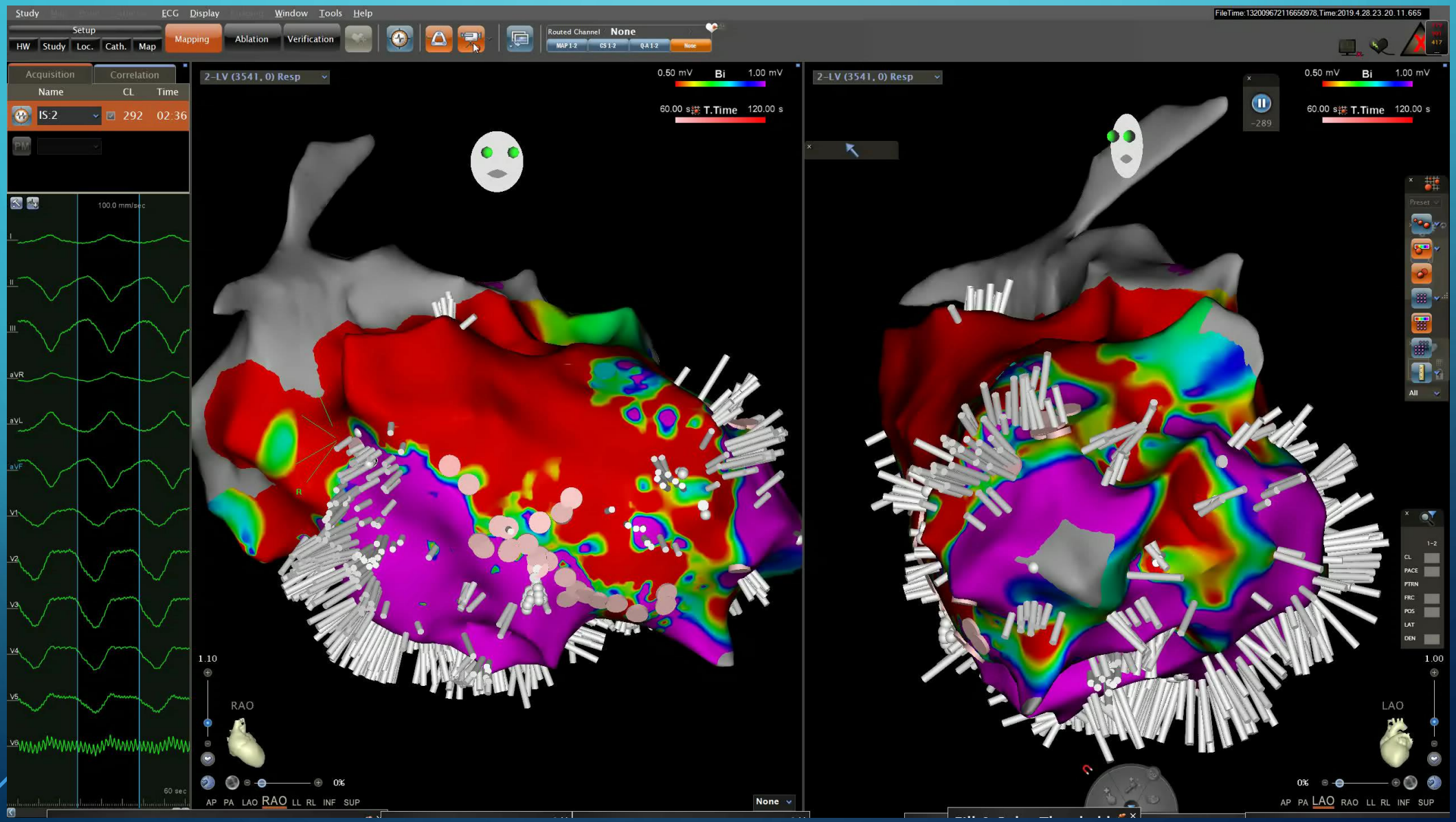
- M/59
- History of R MCA infarct due to thromboembolism
- AF on NOAC
- Presented with extensive anterolateral STEMI on 25th March 2019
- Primary PCI to Left main and LAD- TIMI III
- Post procedure: Cardiogenic shock/ APO/ VT
- IABP 26th March – removed soon due to lower limb ischemia
- ECMO 26th March

VENTRICULAR ARRHYTHMIAS BEFORE AND POST-LVAD PEROID

- Recurrent VTs requiring repeated DC shocks
- Amiodarone/ mexiletine/ metoprolol
- ECHO: EF 19% apical/ anteroseptal hypokinesia
- *LVAD 18/4/2019*

- Post op incessant VT- failed to be controlled despite iv amiodarone/ lignocaine/ mexiletine/ overdrive pacing
- RV failure- RVAD inserted

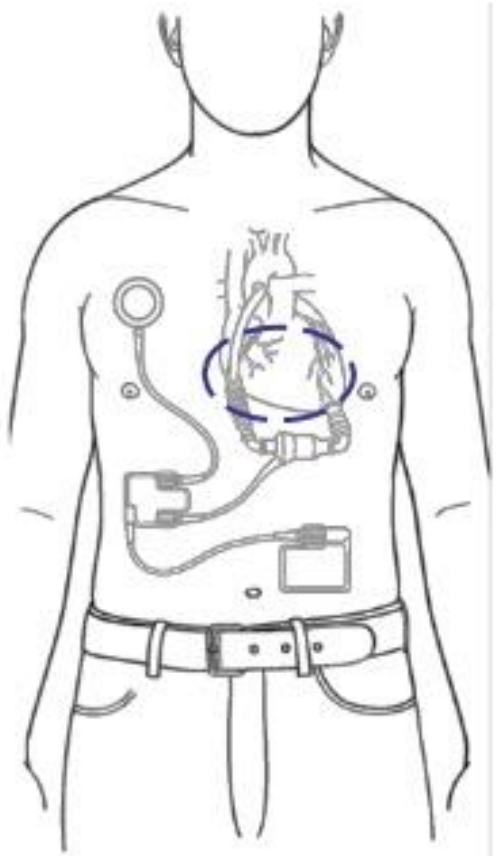
VT ABLATION


Study
ECG
Display
Window
Tools
Help
Setup
HW
Study
Loc.
Cath.
Map
Mapping
Ablation
Verification
Routed Channel
None
Acquisition
Correlation
Name
CL
Time
IS:2
292
02:36
100.0 mm/sec
I
II
III
aVR
aVL
aVF
V1
V2
V3
V4
V5
V6
60 sec
2-LV (3541, 0) Resp
0.50 mV
Bi
1.00 mV
60.00 s
T.Time
120.00 s
1.10
RAO
AP PA LAO RAO LL RL INF SUP
None
2-LV (3541, 0) Resp
0.50 mV
Bi
1.00 mV
60.00 s
T.Time
120.00 s
1.00
LAO
AP PA LAO RAO LL RL INF SUP

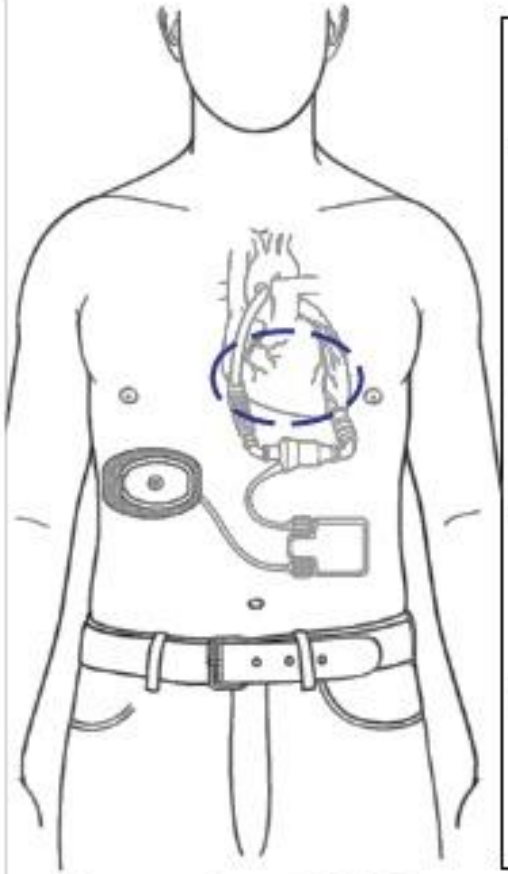
FUTURE OF THE FIELD

- Promise offered by LVADs = a viable alternative to heart transplantation
- Newer generation of LVAD capable of providing long-term support free of major disabling AEs
- Patient not in cardiogenic shock at time of LVAD implant can enjoy survival that is compatible with heart transplantation to approx 2 years
- More biocompatible device- meaningful clinical benefit with improved durability and fewer AEs.
- Future advances in QoL will come with a fully implantable device without need for an external driveline which will reduce infection risks and allow patients to swim and bathe.

Fully-Implantable LVAS (FILVAS)



Conventional FILVAS



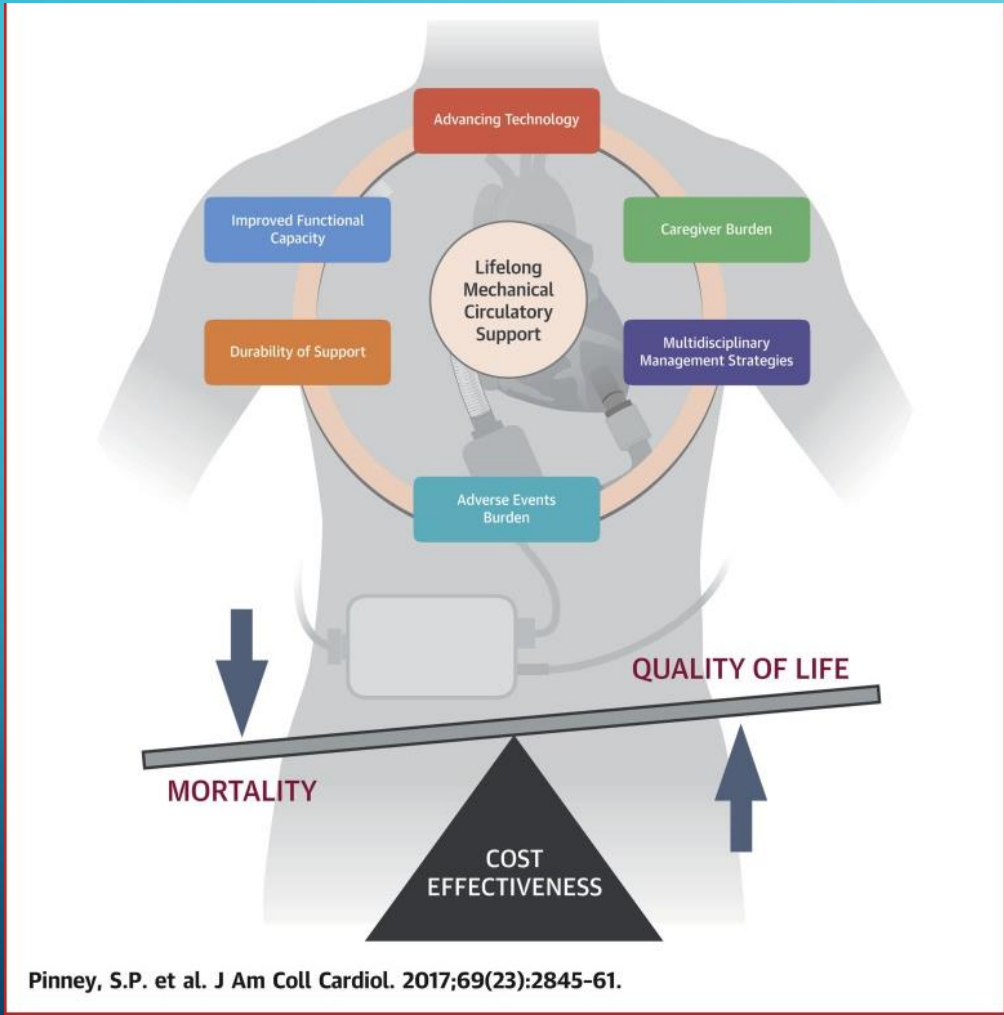
Alternative FILVAS

Project Objectives

- Develop a left ventricular assist system incorporating an implantable battery and control system enabling patients to have some duration of **"un-tethered time" without external components.**
- Mitigate the need for a standard **percutaneous lead**, reducing the incidence of infection.
- Minimize the need for external components, reducing the burden for patients and enhancing quality of life.

With permission of Thoratec

SUMMARY



Pinney, S.P. et al. J Am Coll Cardiol. 2017;69(23):2845-61.

- Technology advances in MCS have improved survival and clinical outcome
- Team based approach important for rapid response as well as long term strategy planning
- Clinical outcome of newer generation of LVAD is equal to and even better than heart transplant

BENEFITS OF HEART TEAM APPROACH

- Utilizing a multidisciplinary Heart Team for complex patients with severe advanced heart failure leads to improved outcomes for patients, clinicians and health systems
- Patients:
  - Improved patient knowledge and satisfaction
  - Incorporation of patient preferences through shared decision making
  - Increased QoL and improved survival
- Improved clinician outcomes
  - Improved skill sets
  - Increased job satisfaction
- Improved health system outcomes
  - More effective utilization of health care resources, leading to increased vaue

Thank You!