# Cardiogenic shock, MCS and heart transplantation

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# Declaration of Interests

- Support for educational activities from Abbott (formally St Jude), Boston Scientific, Medtronic, Microport (formally Sorin), PharmaCosmos, Novartis and Servier
- Consultancy advice and speakers fees from Abbott, Novartis, Servier, Vifor,. PharmaCosmos and 3R
- Member of British Society of Heart Failure board
- Member of NHS Blood and Transplant Cardiothoracic Audit Group
- Member of iMACS Research Committee

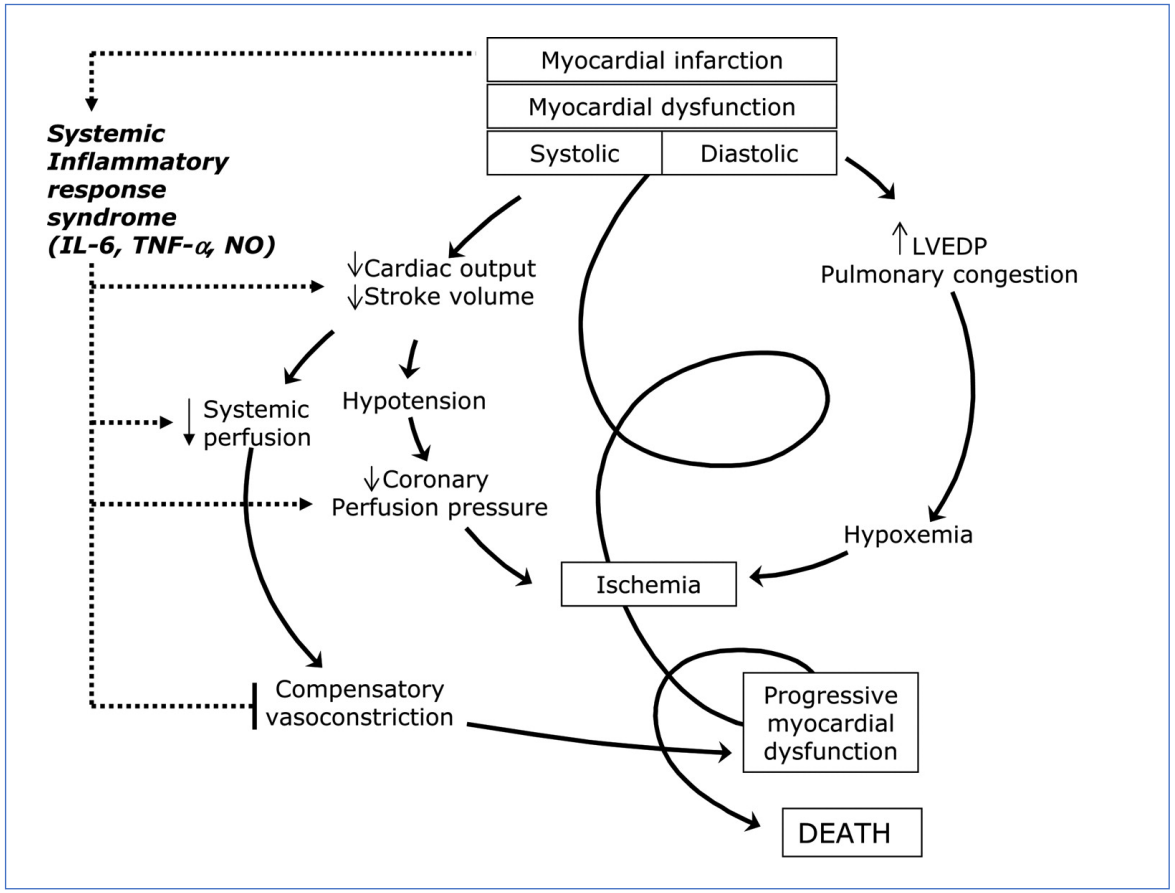
# Outline of talk

- Cardiogenic shock is dangerous with real-world mortality of 45-50%
  - Mortality is highest in those with worst haemodynamic status
  - Patients may be categorised using INTERMACS profiles
- Inotropes and vasoactive drugs should be used carefully
  - Use minimum dose of the most appropriate agent for the shortest length of time
  - PA catheter may help with choice of agent and determine if you're winning or losing
- Mechanical circulatory support may be used as bridge to heart transplantation
  - Options depend on many factors including LV/RV function, INTERMACS profile
  - Latest generation of implantable LVAD represent a major step forwards
- Phone for help if you have a patient in cardiogenic shock on your ICU and they may be a candidate for heart transplantation

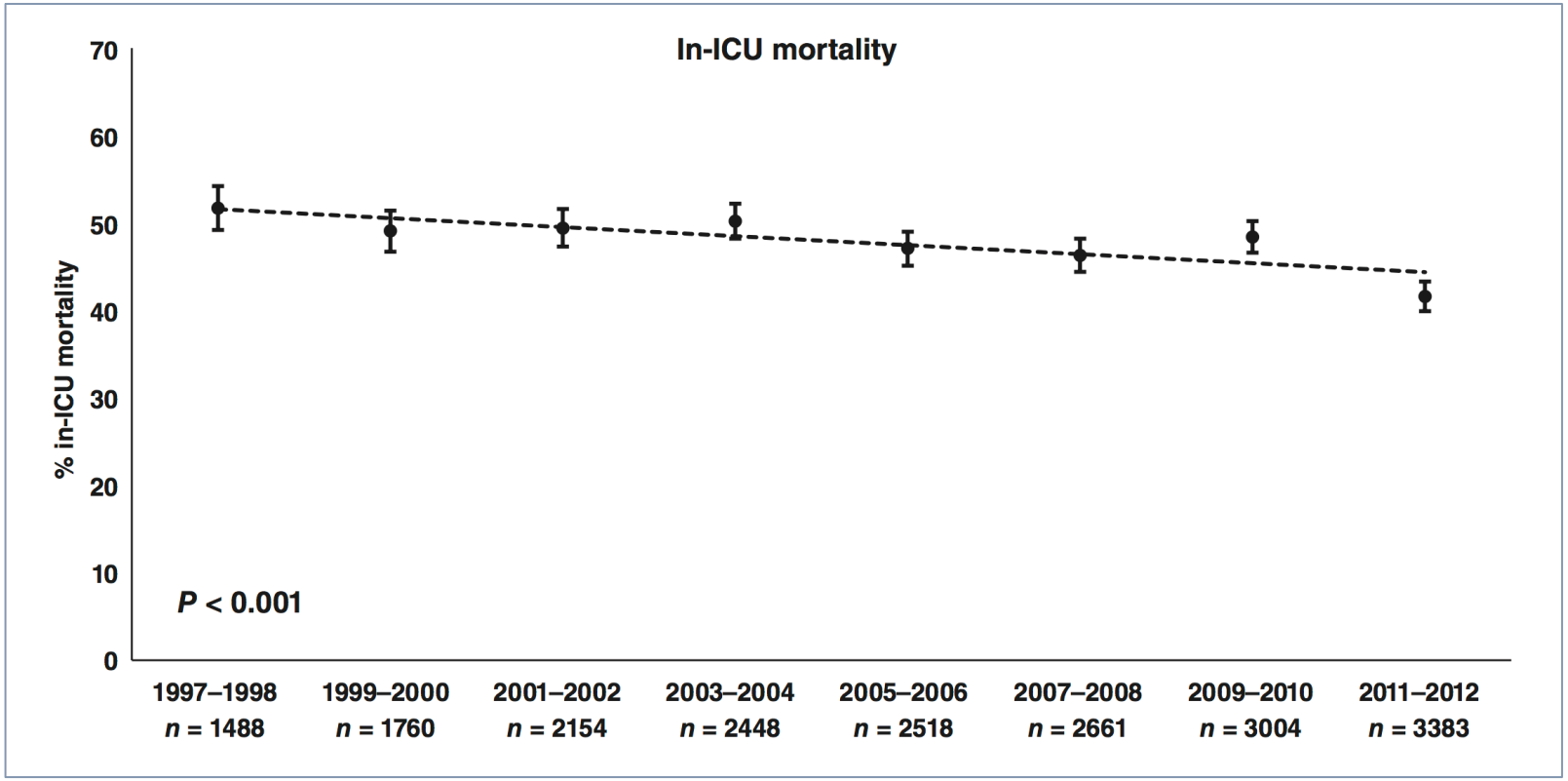
# Definition of cardiogenic shock

| | |
|---|---|
| Clinical criteria | Hypotension (systolic BP <90 mmHg for 30 minutes or need for support to maintain systolic BP of >90 mmHg)<br>AND<br>Heart rate of >60 bpm<br>AND<br>End-organ hypo-perfusion: cool extremities, urine output <0.5 ml/kg/hr, serum lactate >2 |
| Haemodynamic criteria | Cardiac index of <1.8 L/min/$m^2$<br>AND<br>Pulmonary-capillary wedge pressure of >20 mmHg |

# Cardiogenic shock leads to a spiral to death if untreated




# ICU mortality for cardiogenic shock not changed over last 15 years




Puymirat E et al. *Eur J Heart Fail* 2017;**19**:192-200

# Assessment of patient with cardiogenic shock on ICU

**BRAIN**
Level of consciousness

**KIDNEYS**
Urine output

**LIVER**
Jaundice
Coagulopathy

**CARDIOVASCULAR**
Rate and rhythm
Arterial pressure
Venous pressure
Cardiac output

**LUNGS**
Aa gradient
Need for PEEP

**METABOLIC**
Acid-base balance
Lactate

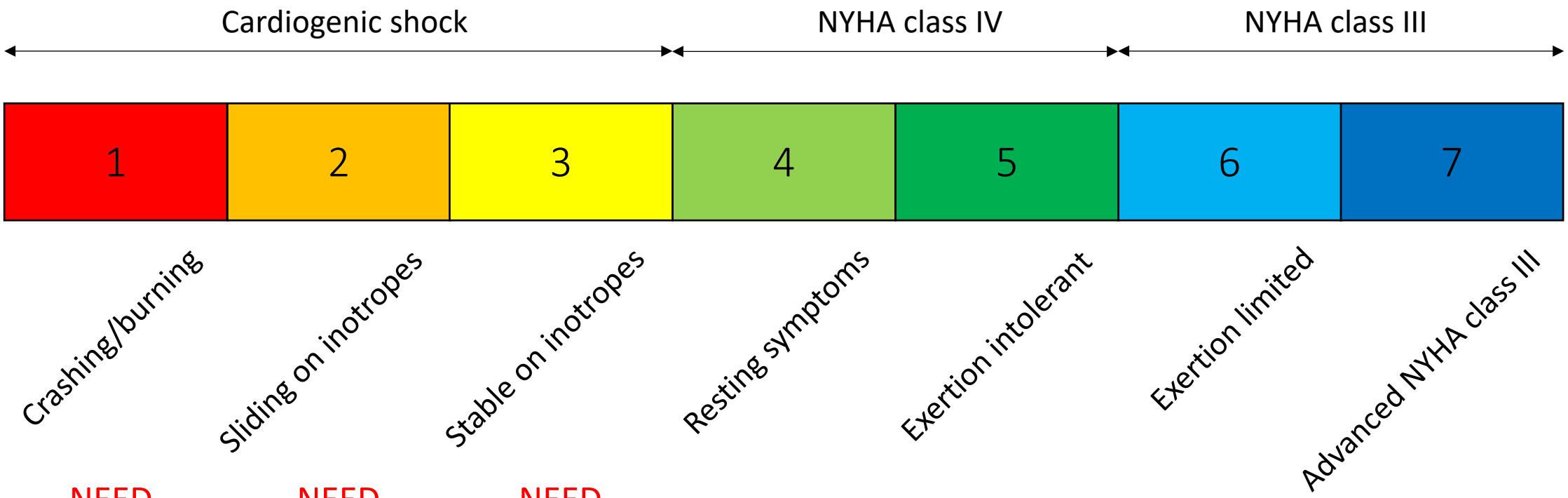
**TREATMENT**
Inotropes/dilators/pressors
IABP or peripheral MCS
CVVH, ET tube/ventilation

**BACKGROUND**
Past medical history
Height and weight
Smoking status
Alcohol and drug misuse
Social circumstances
Treatment eligibility
Next of kin

# Questions to ask with patients with cardiogenic shock

- Do they really have cardiogenic shock?
  - Need to know cardiac output and intra-cardiac filling pressures
- What is wrong with the heart?
  - ECG, CXR and echocardiogram, cardiac Troponin-I
- Why has the patient developed cardiogenic shock now?
  - New onset heart failure, arrhythmias, infection, pulmonary embolism?
- How sick is the patient?
  - Lactate >2 and/or MVO2 <50% are bad
  - End-organ dysfunction?
  - Amount of cardiovascular support required

# INTERMACS profiles



# Principles of management in cardiogenic shock

- Identify and treat any treatable pathology
  - Cardiac or non-cardiac
- Try to lower intra-cardiac filling pressures
  - RA pressure: diuretics, CVVH
  - LA pressure: systemic vasodilatation if possible, IABP counter-pulsation
- Careful use of inotropic support may be required
  - Watch cardiovascular status and end-organ function closely
- Start thinking about options in event of deterioration

# Inotropic and vasoactive drugs

| Drug | Mechanism | Effect on Mortality | Key Trials (Ref. #) |
|---|---|---|---|
| Digoxin | Na-K pump inhibitor, raises SR calcium | Neutral, increased mortality if long-term therapy discontinued | DIG (15,20) |
| Dopamine | Dose-dependent D1, α1-, and β1-adrendergic receptor agonist | Increased | (48) |
| Norepinephrine | β1- and α1-adrenergic receptor agonist | Increased | (48) |
| Dobutamine | β1- and β2-adrenergic receptor agonist | Increased | FIRST (47) |
| Milrinone | PDE inhibitor, raises SR calcium | Increased | OPTIME-CHF (5) |
| Levosimendan | Myofilament calcium sensitizer, PDE-3 inhibitor | Neutral | REVIVE-II (61), SURVIVE (7) |
| Omecamtiv mecarbil | Potentiates the effects of myosin on actin to prolong systole | Unknown | ATOMIC AHF (underway), (66,69) |
| Istaroxime | Na-K pump inhibitor, PDE inhibitor | Unknown | HORIZON-HF (75) |
| SERCA2a gene therapy | Restoration of SERCA2a to improve calcium release and reuptake from the SR | Unknown | CUPID (70) |

Francis GS *et al*. *J Am Coll Cardiol* 2014;**63**:2069–2078.

# No ‘best’ inotropic or vasodilator strategy in cardiogenic shock

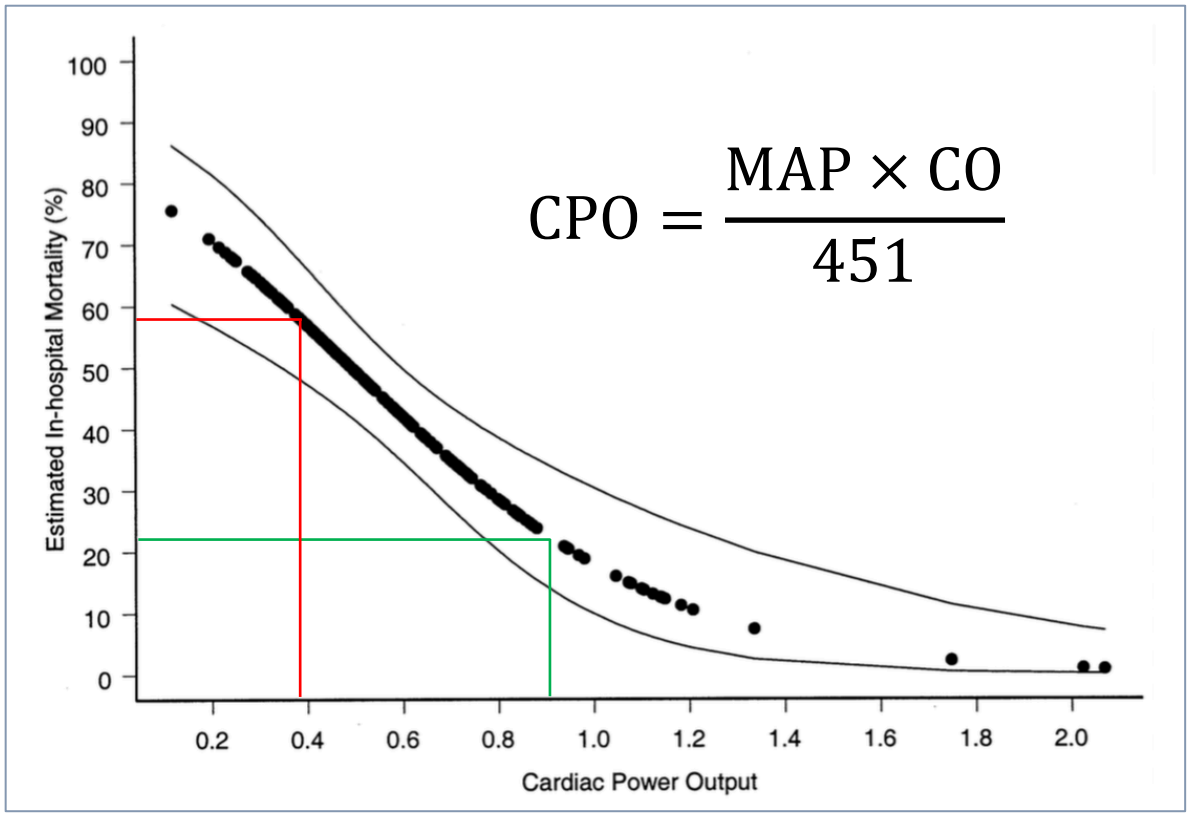
Cochrane

Trusted evidence.
Informed decisions.
Better health.

Apart from low quality of evidence data suggesting a short-term mortality benefit of levosimendan compared with dobutamine, at present there are no robust and convincing data to support a distinct inotropic or vasodilator drug-based therapy as a superior solution to reduce mortality in haemodynamically unstable people with cardiogenic shock or LCOS.

Schumann J *et al*. Cochrane Database of Systematic Reviews 2018, doi: 10.1002/14651858.CD009669.pub3

# PA catheters help you decide if you're winning or losing




$$\text{CPO} = \frac{\text{MAP} \times \text{CO}}{451}$$

Patient 1
MAP 80 mmHg and CO 5 L/min
CPO 0.89
Estimated mortality around 20%

Patient 2
MAP 60 mmHg and CO 3 L/min
CPO 0.39
Estimated mortality around 60%

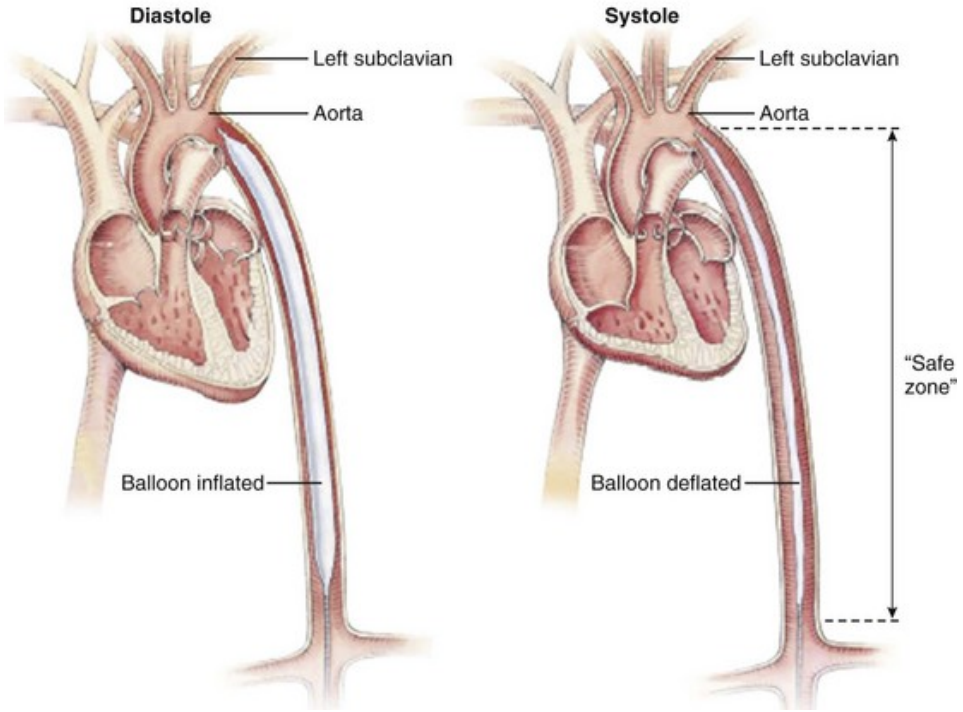
Fincke R *et al. J Am Coll Cardiol* 2004;**44**:340-8

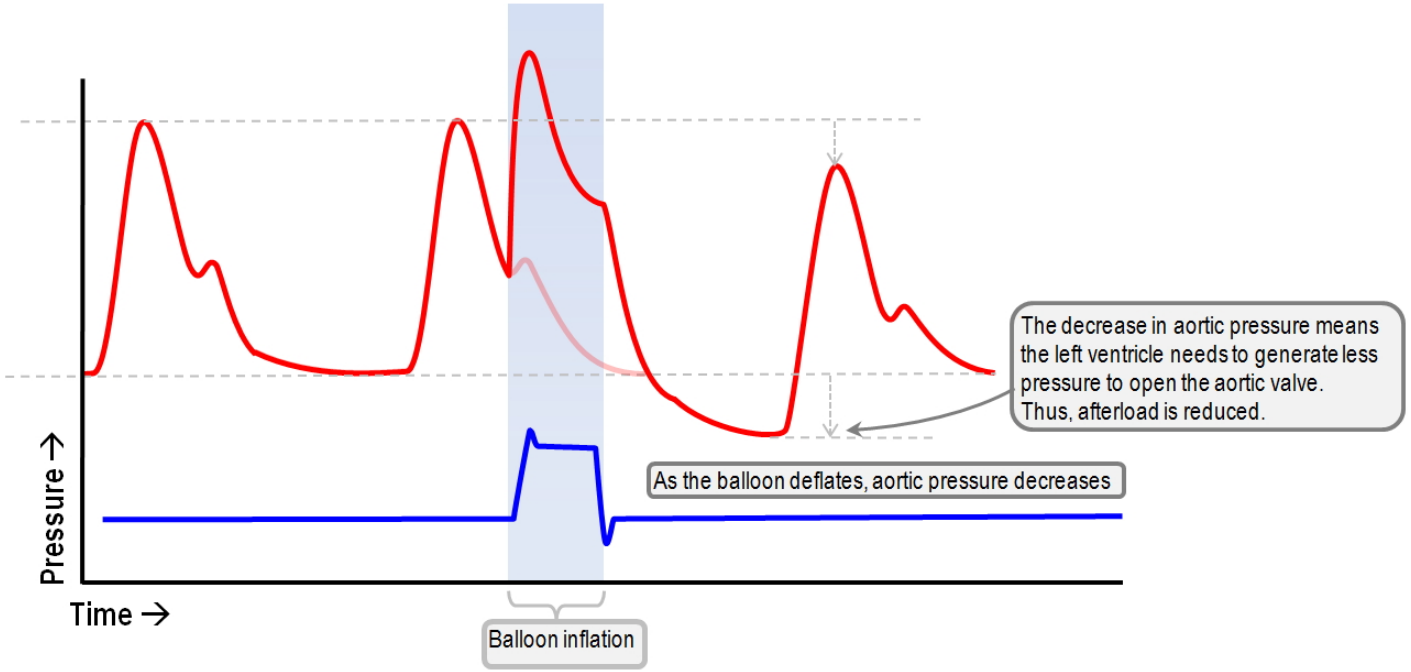
# Think about MCS in sick/deteriorating patients


# Purpose of MCS

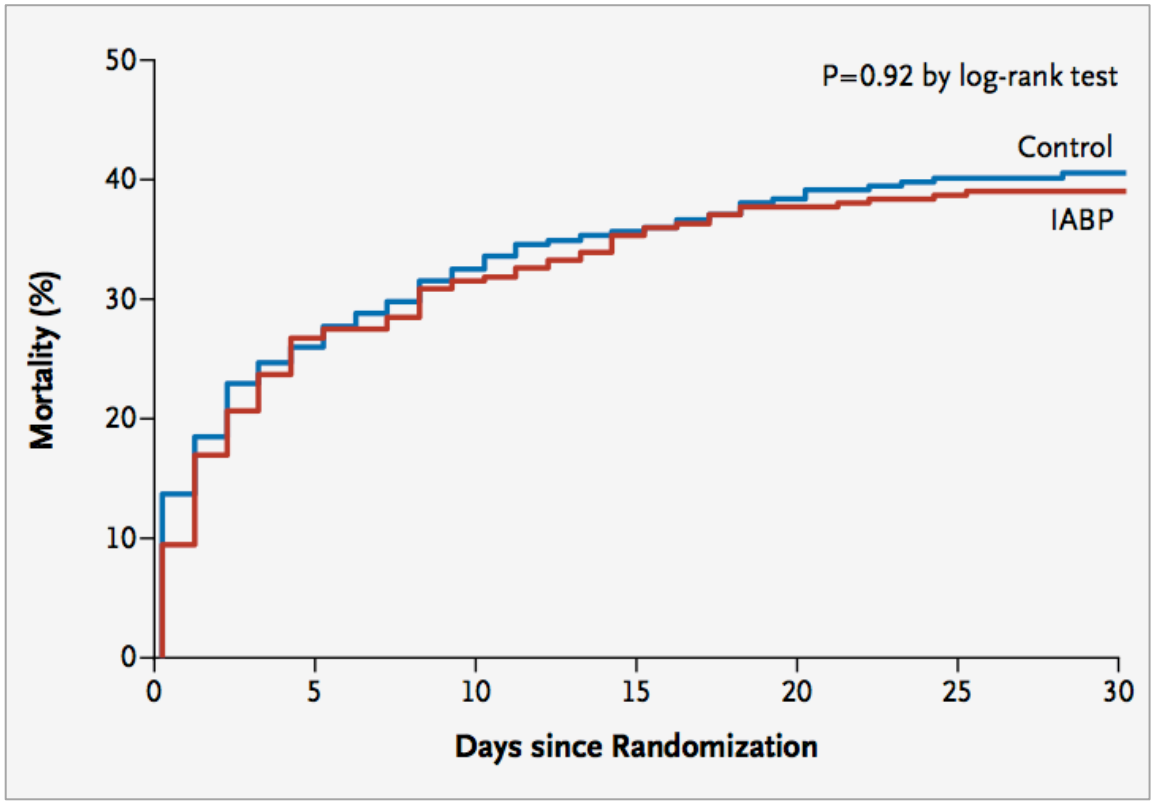
- Unload injured ventricles
- Improve end-organ perfusion
- Reduce levels of inotropes and vasopressors
- Allow cytokines to be metabolized and ATP stores to be replenished
- Allow myocardium to declare potential for recovery

# Intra-aortic balloon counterpulsation is physiologically attractive



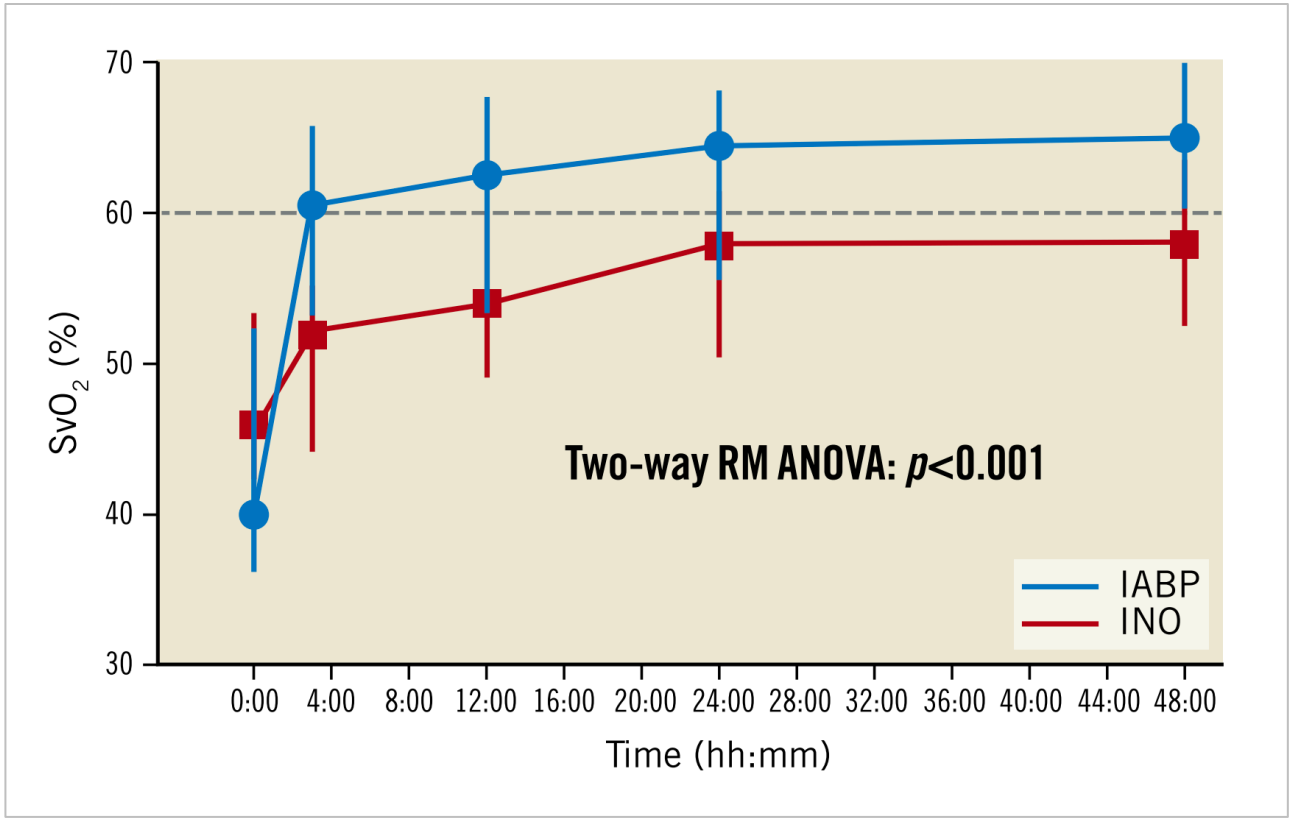



# IABP did not improve survival in IABP shock trial




Thiele H *et al. New Engl J Med* 2012;**367**:1287-1296

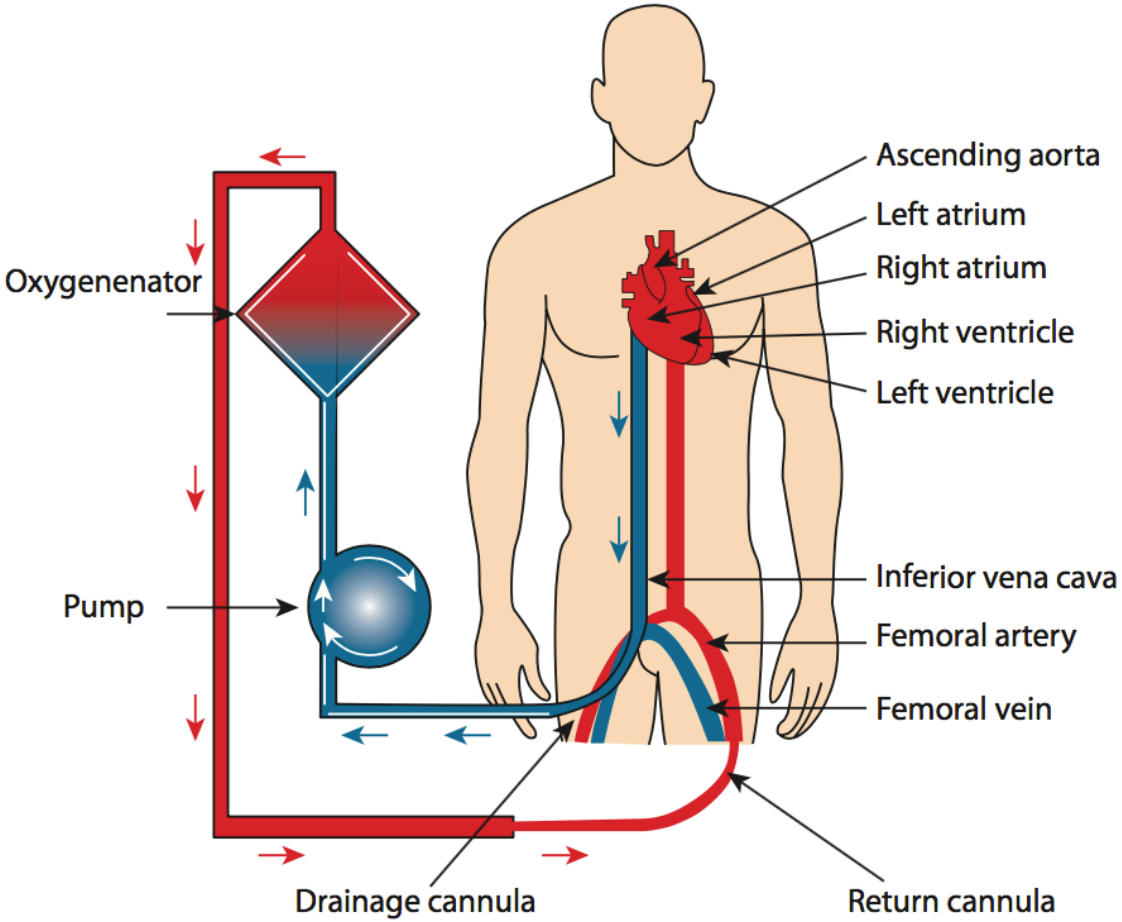
# But IABP superior to inotropes in many ‘surrogate’ measures



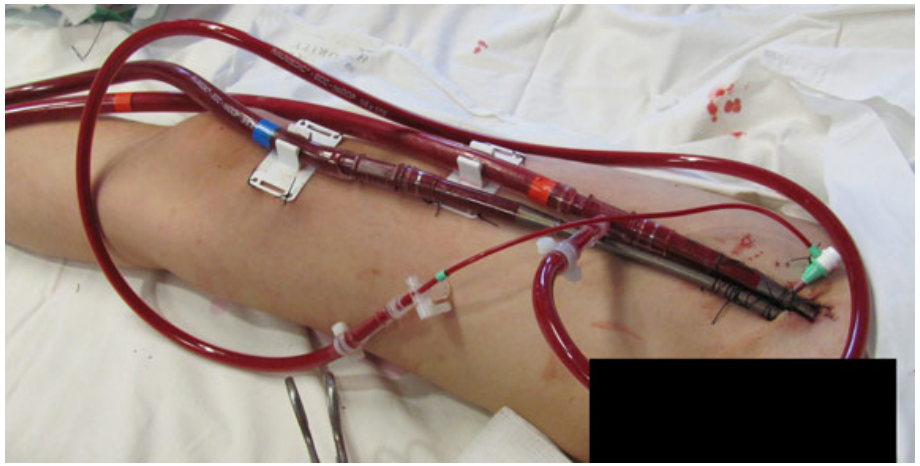

| Secondary endpoint | IABP | Inotrope | p value |
|---|---|---|---|
| Δ HR 48h | -14 bpm | -3 bpm | 0.15 |
| Δ MAP 48h | +16 mmHg | +1 mmHg | 0.002 |
| Δ CVP 48h | -9 mmHg | -6 mmHg | 0.64 |
| Δ Mean PA 48h | -9 mmHg | -5 mmHg | 0.03 |
| Δ Mean PCWP 48h | -10 mmHg | -2 mmHg | 0.002 |
| Δ CPO 48h | +0.27 | +0.09 | 0.004 |
| Δ Fluid balance 48h | -3.066 ml | -1.198ml | 0.006 |
| Δ NTproBNP 48h | -59.3% | -16% | <0.001 |

den Uil C *et al. EuroIntervention* 2019;**15**:586-593

# Peripheral veno-arterial ECMO



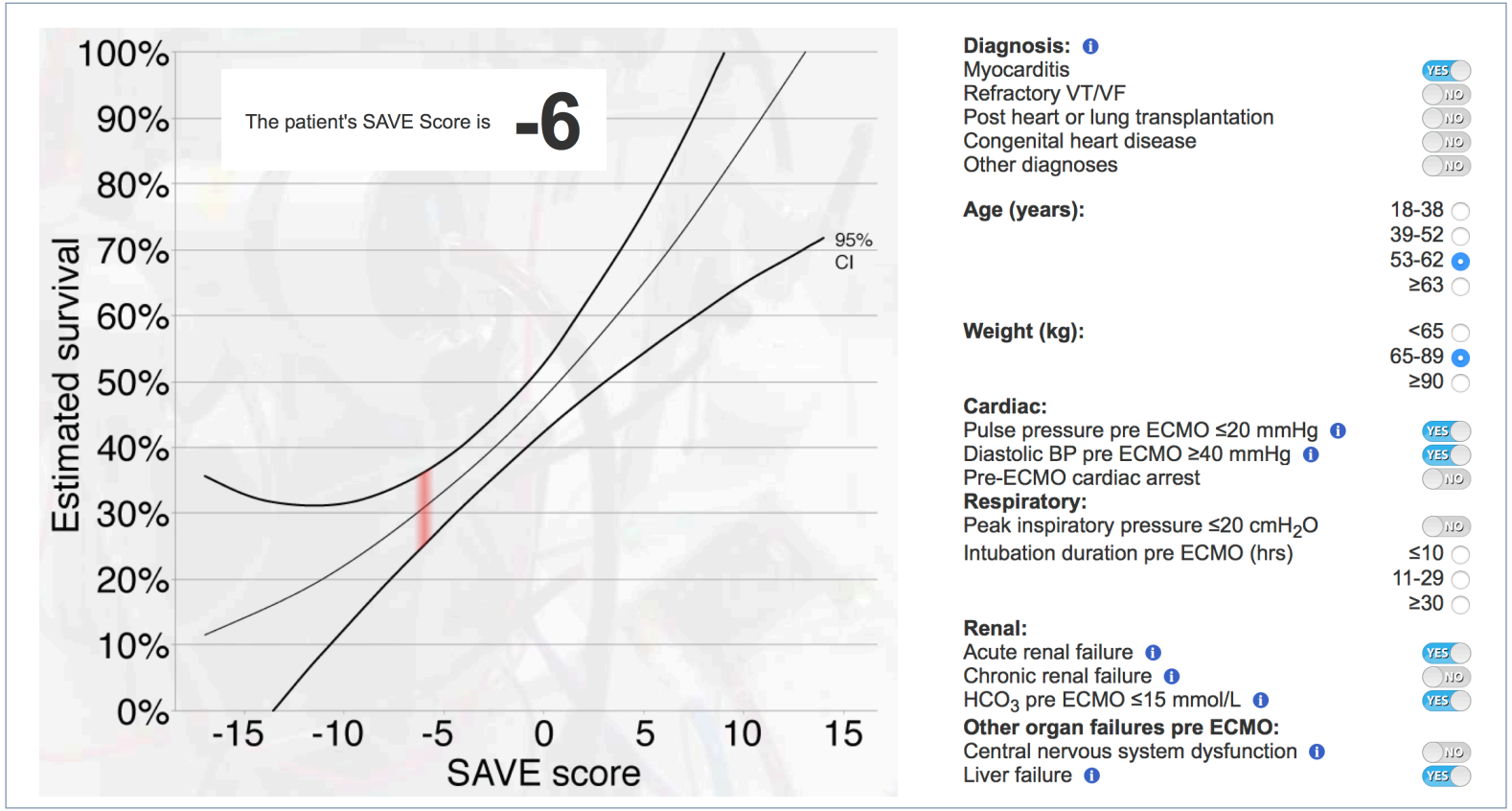




# Who should get peripheral veno-arterial ECMO?

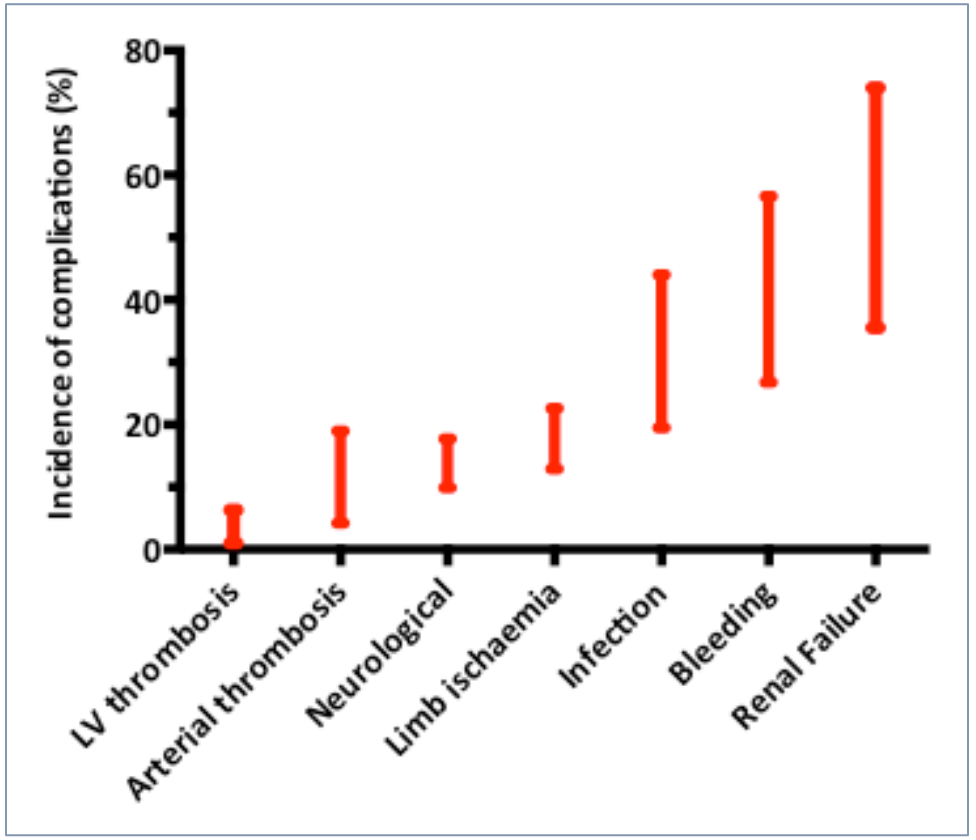
| May be appropriate | Likely to be inappropriate |
| --- | --- |
| Cardiogenic shock<br>• Severe (INTERMACS profile 1/2, SCAI category D/E)<br>• Worsening despite conventional treatment<br>• No immediate option for durable MCS | Unrecoverable heart function in non-transplant candidate<br>• Active malignancy<br>• Neurological or psychiatric disease<br>• Severe chronic organ dysfunction (lungs, kidneys, liver) |
| Failure to wean from cardiopulmonary bypass<br>• Routine cardiac surgery<br>• Heart or lung transplantation<br>• Pulmonary thromboendartectomy | Problem that makes VA ECMO ineffective or dangerous<br>• Moderate to severe aortic regurgitation<br>• Peripheral vascular disease<br>• Uncontrolled bleeding |
| Cardiac arrest (ECMO-assisted CPR) | Unwitnessed cardiac arrest or prolonged CPR |

# SAVE score predicts survival with ECMO but not treatment benefit




Schmidt M *et al. Eur Heart J* 2015;**36**:2246-56

# Adverse events during VA ECMO are common



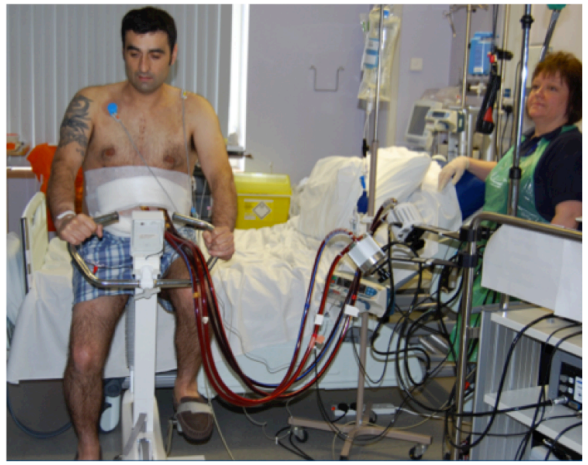


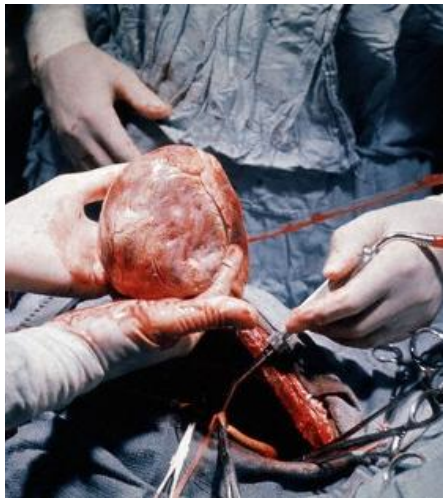
Adapted from Cheng R *et al*. *Ann Thorac Surg* 2014;**97**:610-6.

# Moving on from VA ECMO

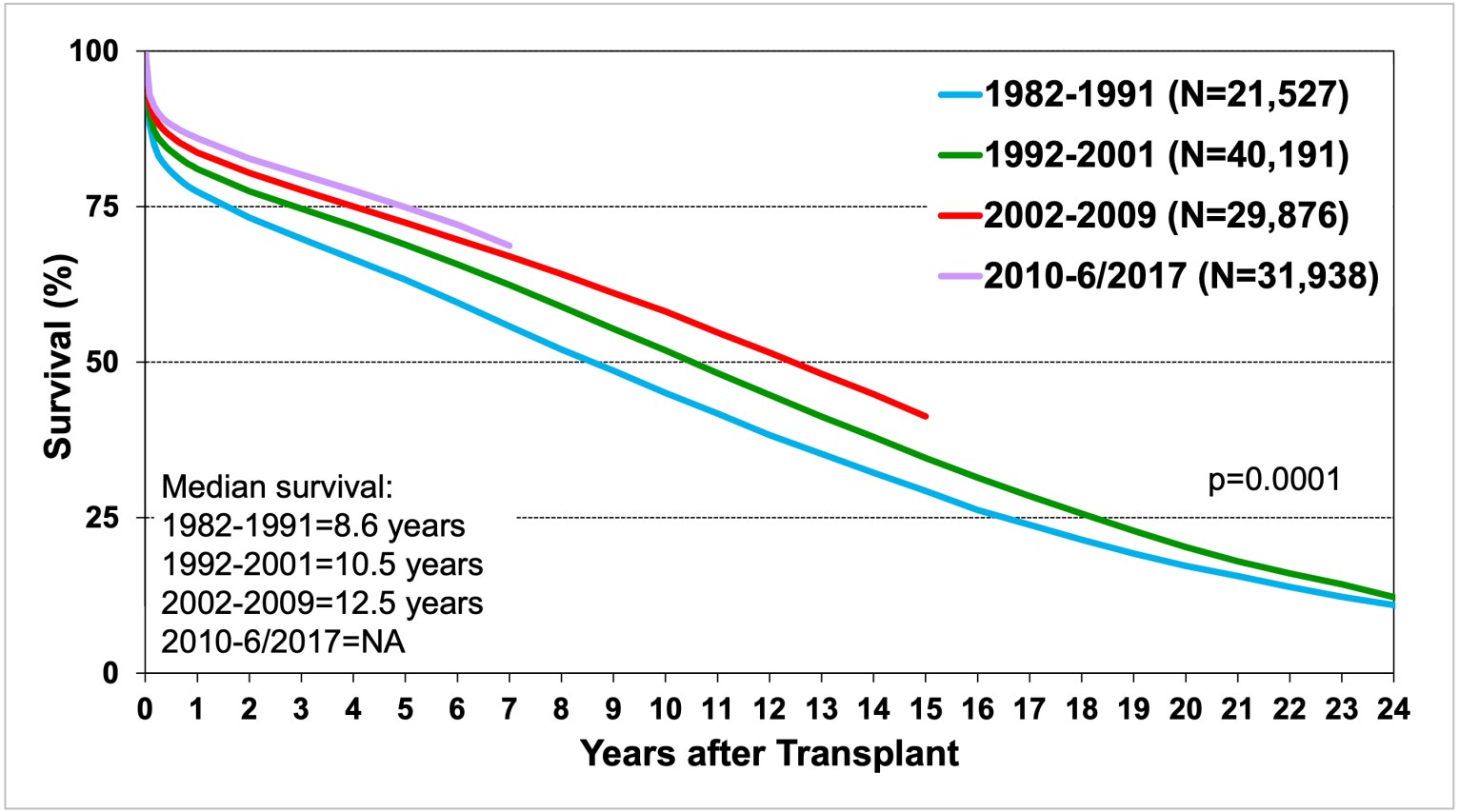
VA ECMO

- Palliation
- Recovery
- Temporary VAD
- Implantable LVAD
- Transplant

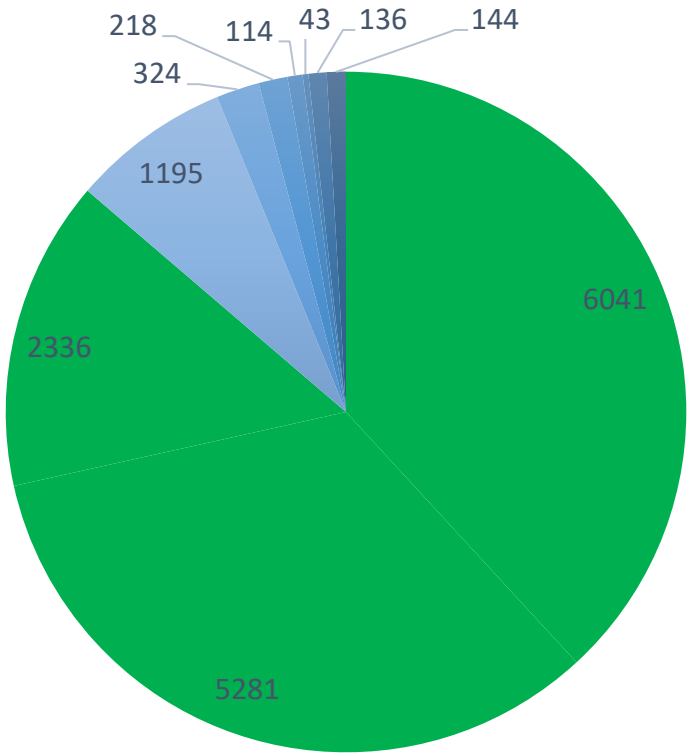


# Median survival after heart transplantation is 12.5 years




Khush K *et al*. *J Heart Lung Transplant* 2019; **38**:1056-66

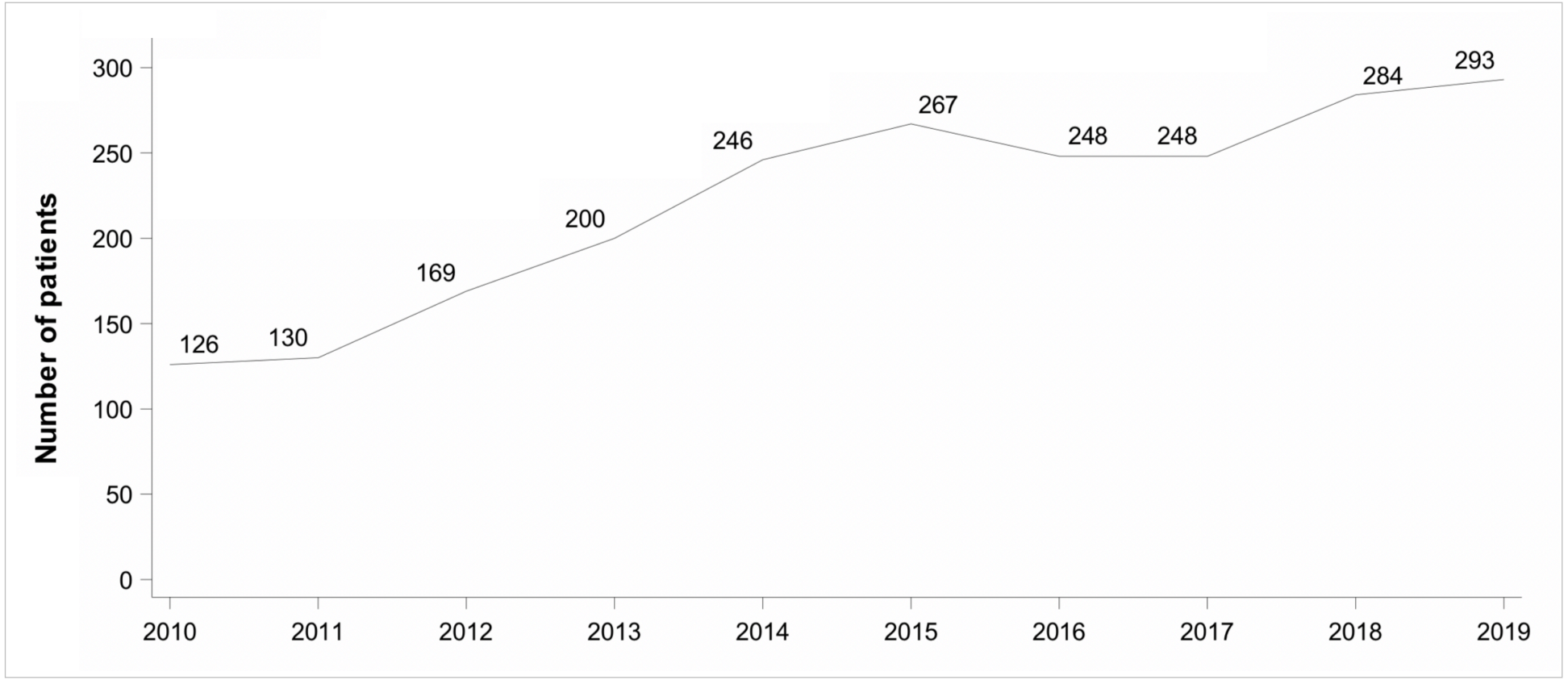
# Most have good quality of life after heart transplantation




| Karnofsky score | Description |
|---|---|
| 100 | Normal, no evidence of disease |
| 90 | Able to perform normal activities with only mild symptoms |
| 80 | Normal activity with effort, some symptoms |
| 70 | Able to care for self but unable to do normal activities |
| 60 | Requires occasional assistance; cares for most needs |
| 50 | Requires considerable assistance |
| 40 | Disabled; requires special assistance |
| 30 | Severely disabled |
| 20 | Very sick; requires active supportive treatment |
| 10 | Moribund |

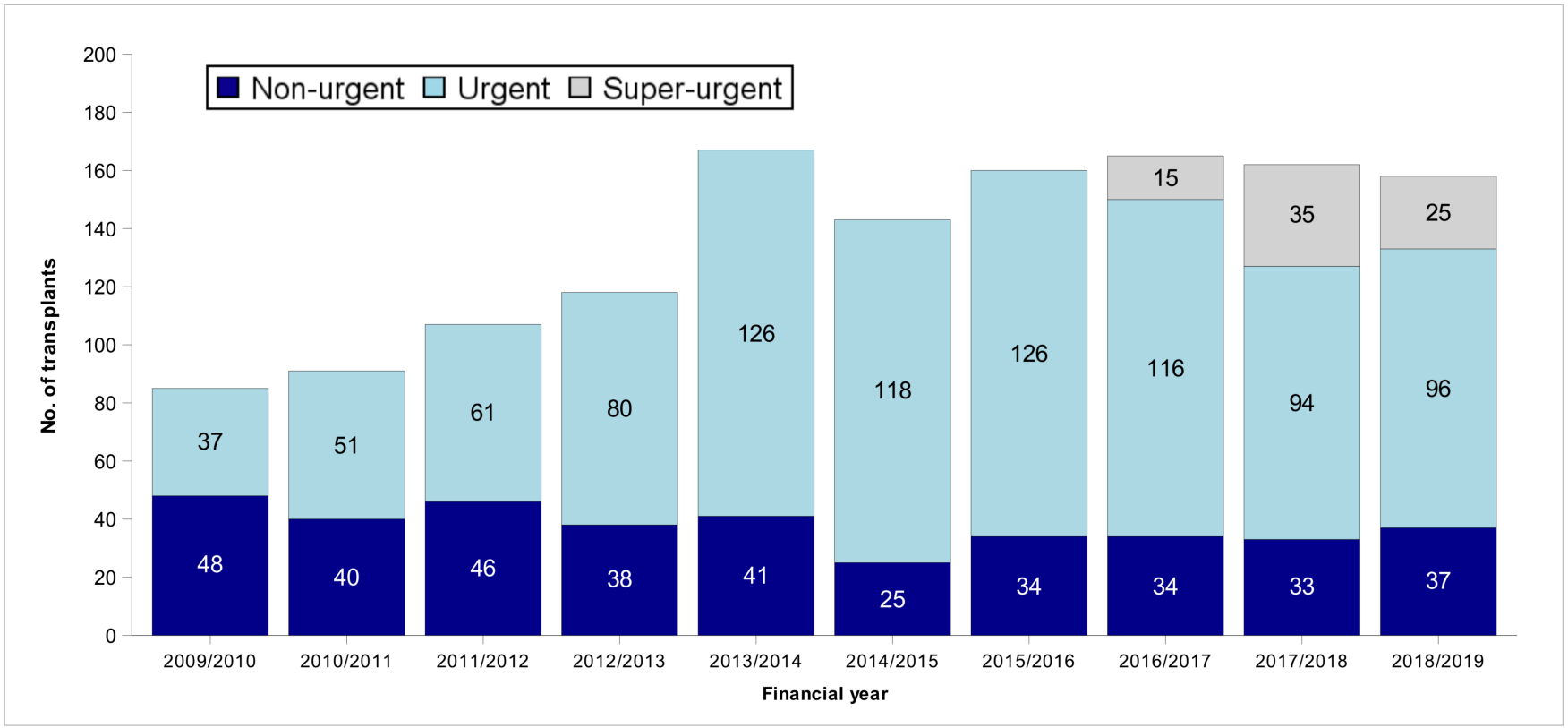
Adapted from ISHLT International Thoracic Organ Transplant Registry. Available at www.ishlt.org/registries/ttx-registry, accessed 29th April 2019

# Demand for heart transplantation in the UK is rising




NHS Blood and Transplant. Organ Donation and Transplantation: Activity Report 2018/2019

# Supply of donor hearts has plateaued in last five years



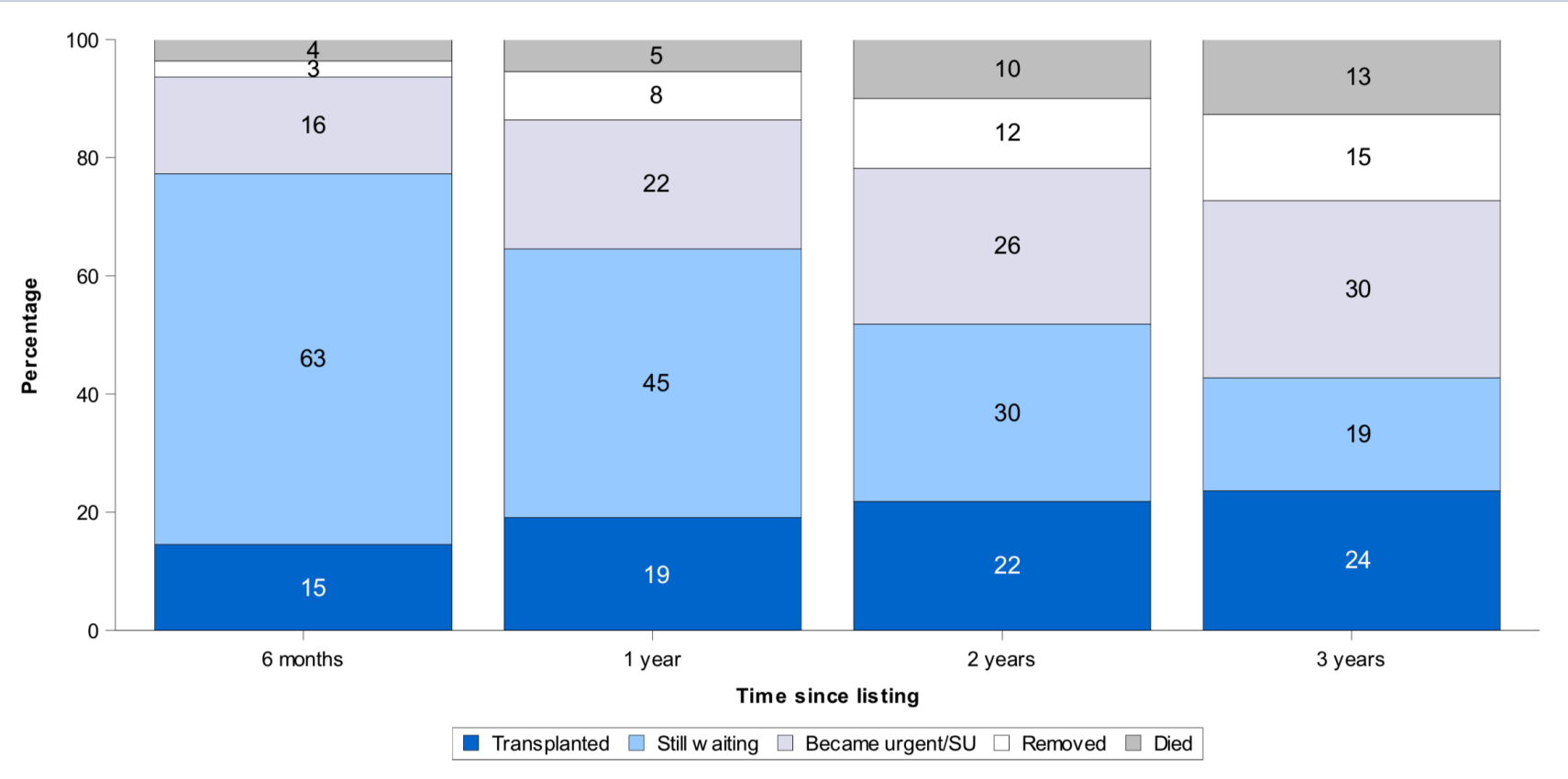

NHS Blood and Transplant. Organ Donation and Transplantation: Activity Report 2018/2019

# Long waiting times, particularly for blood group O patients

| Blood group | Number of patients registered | Waiting time (days) Median | 95% Confidence interval |
|---|---|---|---|
| **Non-urgent at initial registration** | | | |
| O | 178 | 861 | 714 - 1008 |
| A | 171 | 401 | 236 - 566 |
| B | 56 | 279 | 101 - 457 |
| AB | 13 | 276 | 0 - 1067 |
| **UK** | **418** | **559** | **407 - 711** |
| **Urgent at initial registration** | | | |
| O | 112 | 49 | 41 - 57 |
| A | 137 | 16 | 13 - 19 |
| B | 40 | 41 | 18 - 64 |
| AB | 19 | 20 | 8 - 32 |
| **UK** | **308** | **30** | **24 - 36** |

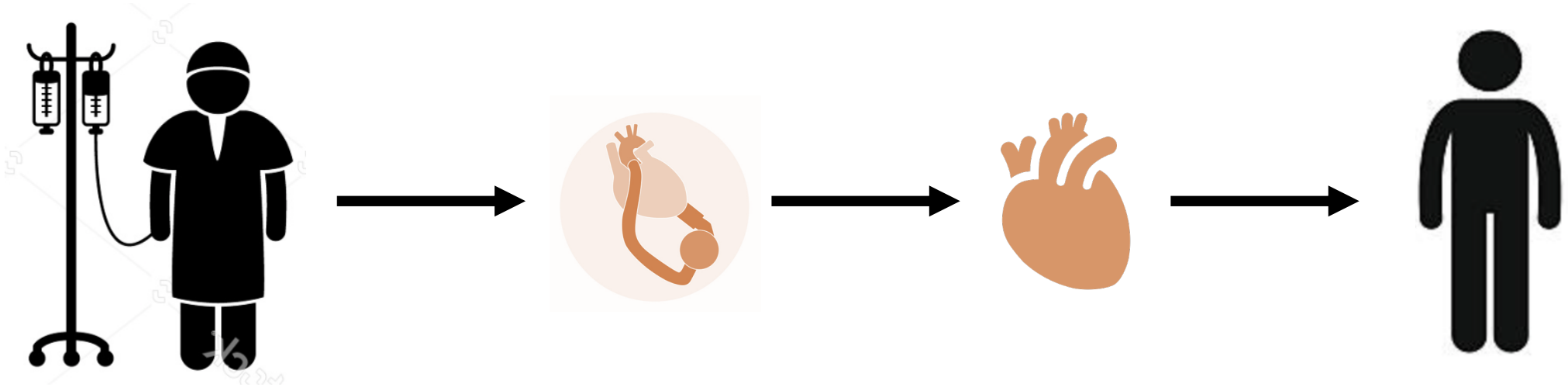
NHS Blood and Transplant. Organ Donation and Transplantation: Activity Report 2018/2019

# Many deteriorate, de-listed or die during wait for heart transplant

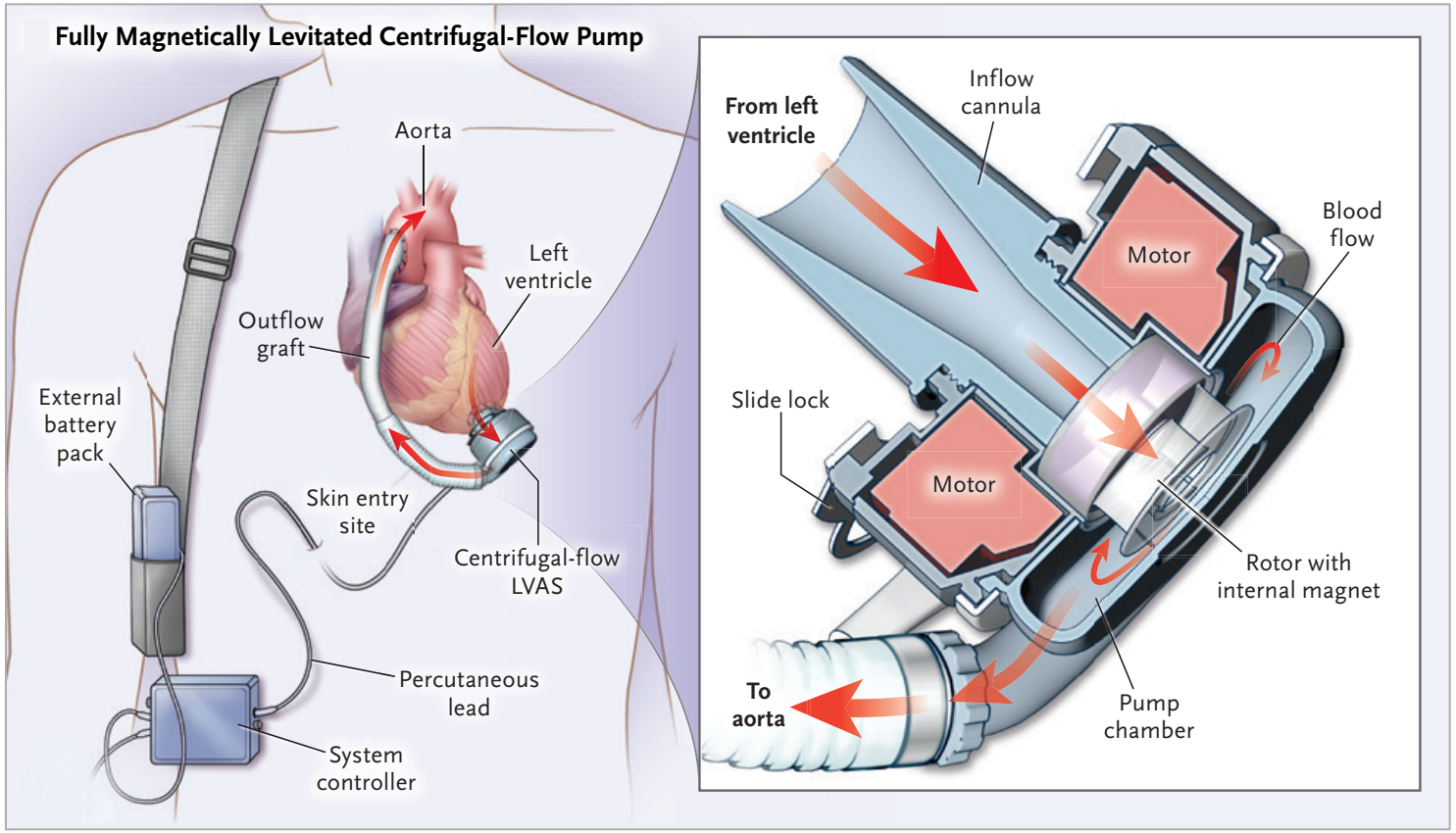



NHS Blood and Transplant. Organ Donation and Transplantation: Activity Report 2018/2019

# Implantable LVAD can be used as a bridge to heart transplantation



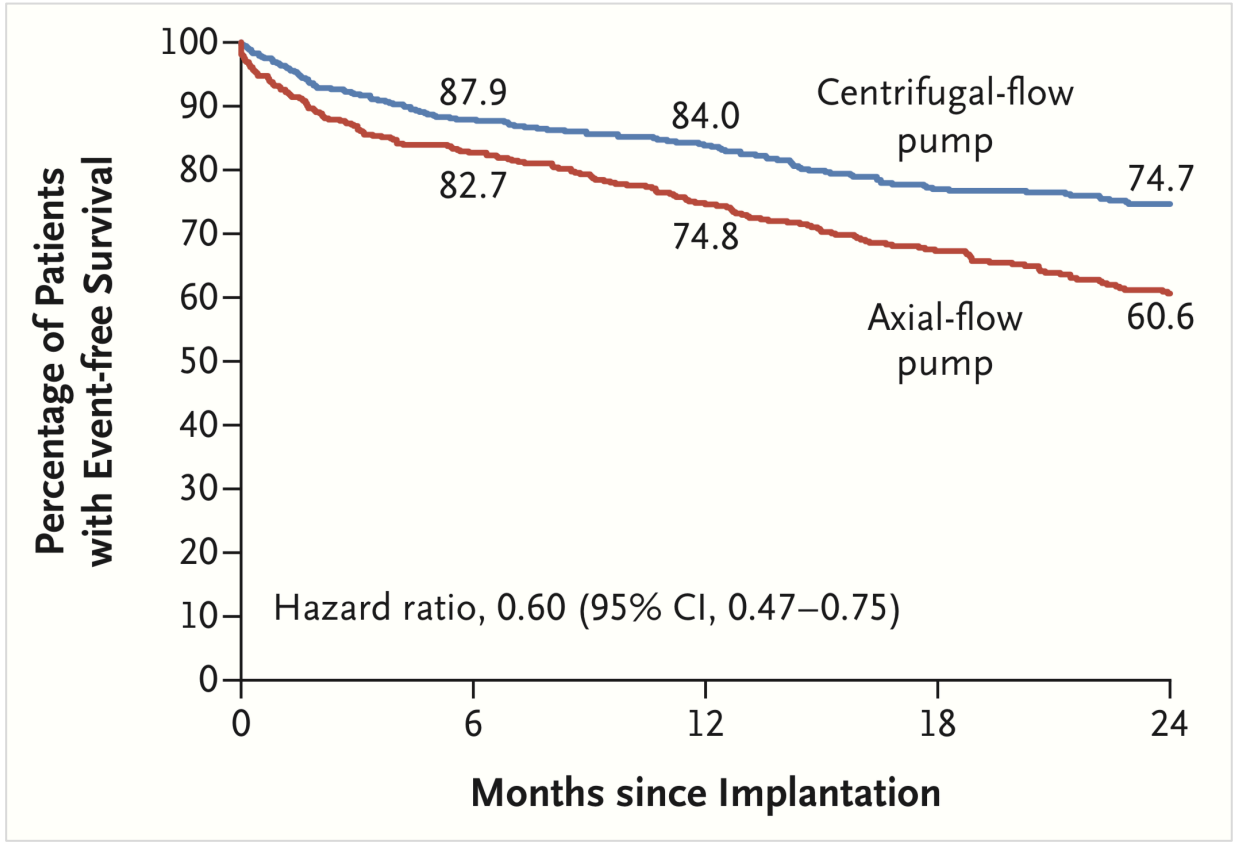
# HeartMate 3 is latest implantable LVAD




- Continuous flow, magnetically levitated pump
- Wide blood flow passages to reduce shear stress
- Frictionless; no mechanical or hydrodynamic bearings
- Intrinsic pulse; designed to reduce stasis and reduce risk of thrombosis

Mehra MR *et al*. *New Engl J Med* 2018;**378**:1386–1395

# HeartMate 3 delivered excellent outcomes in MOMENTUM3



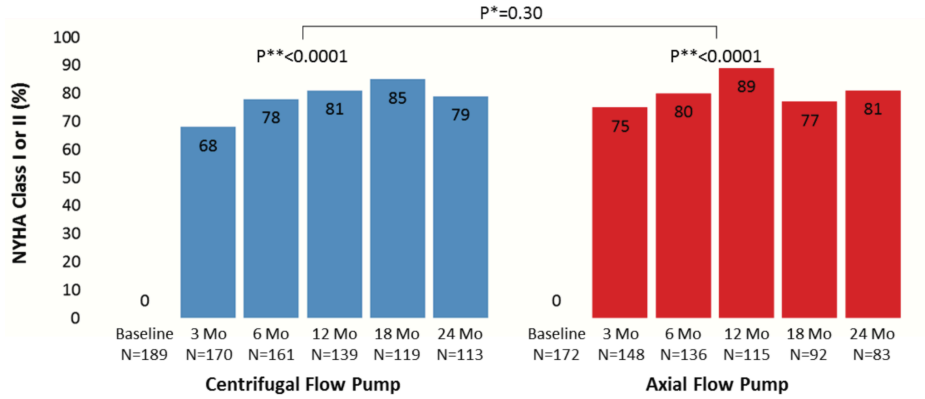

Largest LVAD trial ever conducted

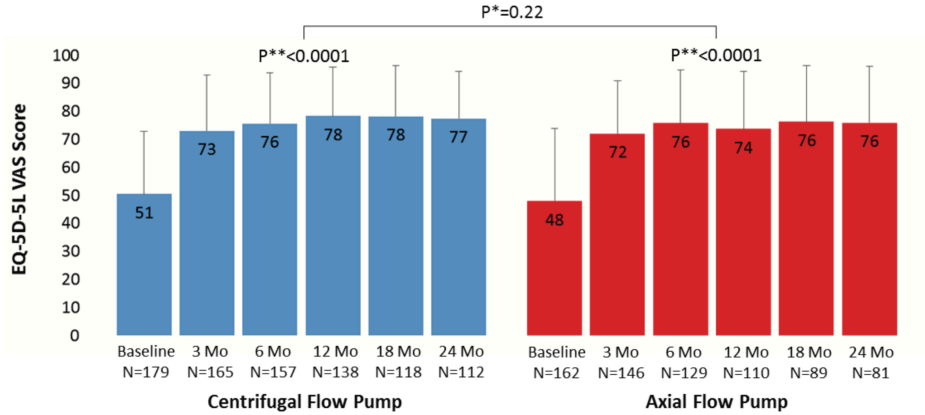
Best outcomes recorded with a continuous flow LVAD at 2 years

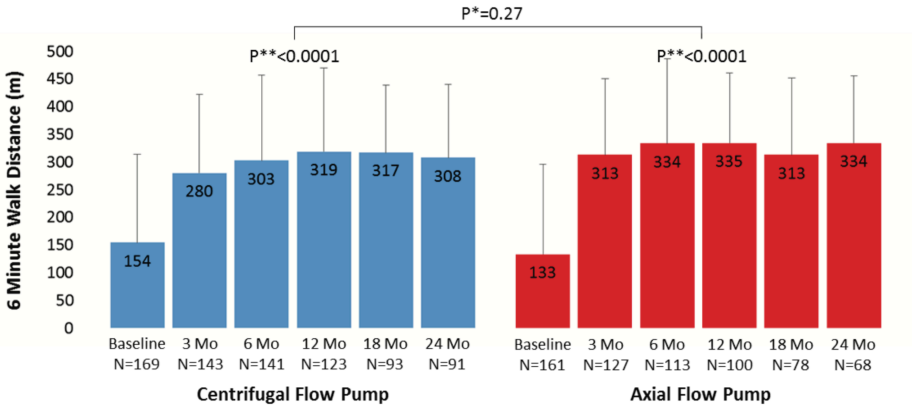
| 84% | 4% | 2% |
|---|---|---|
| Survival | Disabling Stroke | Pump Thrombosis |

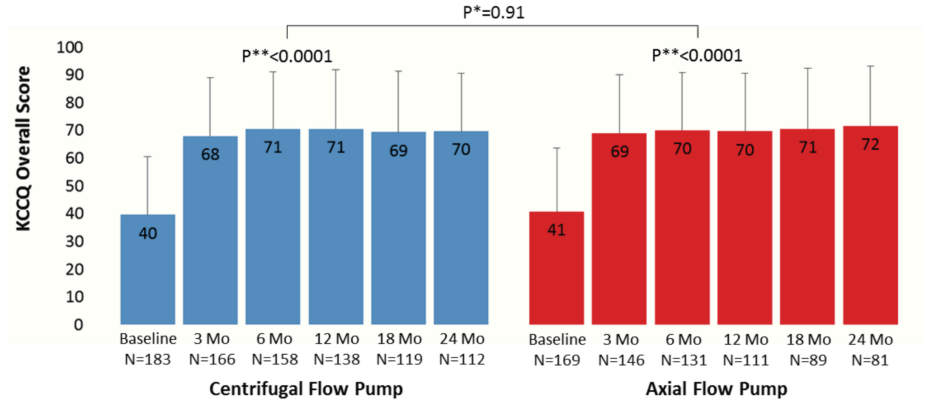
Mehra MR *et al*. *New Engl J Med* 2019;**380**:1618–1627

# Sustained improvement in NYHA class, 6MWD and QOL



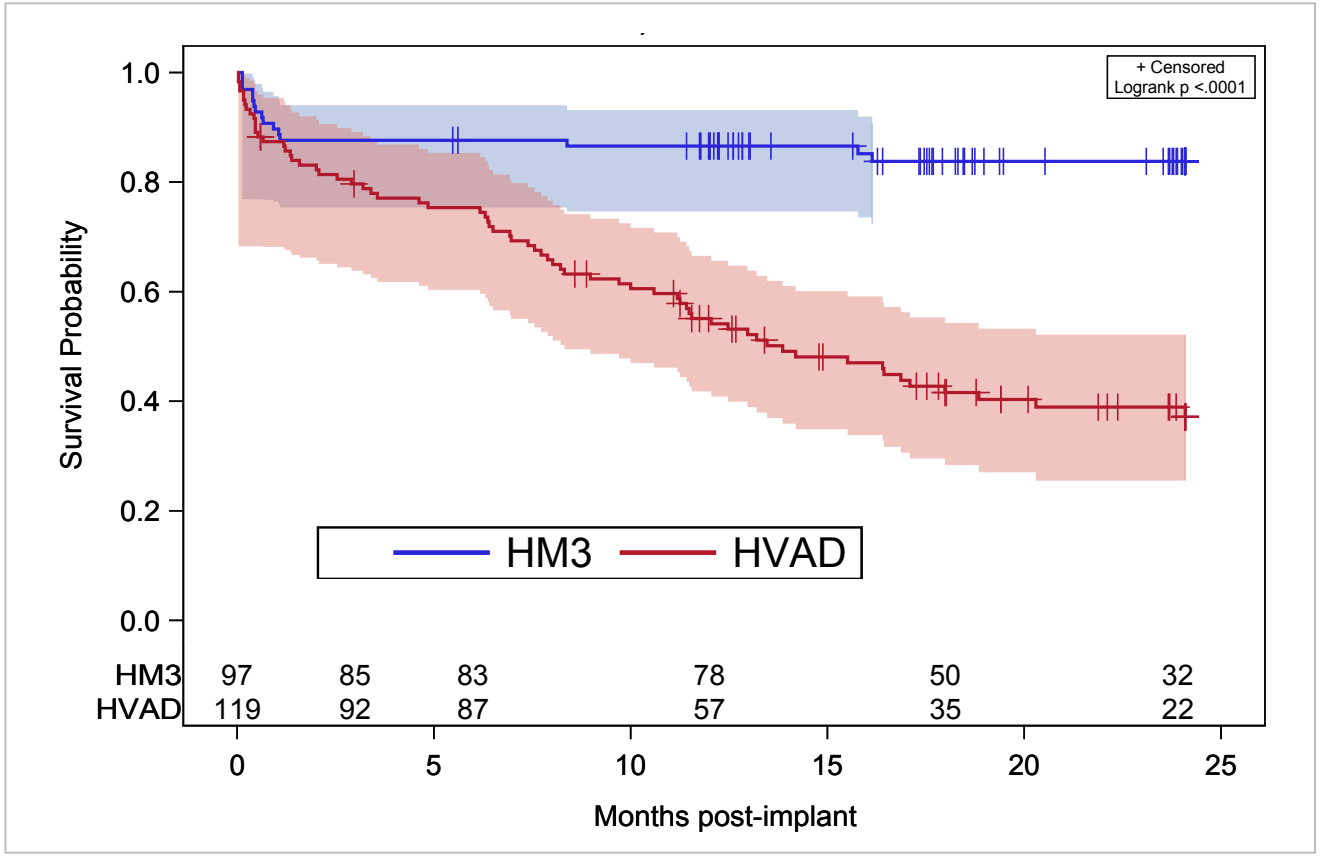




Mehra MR *et al*. *New Engl J Med* 2018;**378**:1386–1395.

# Excellent event-free survival with HeartMate 3 in UK




Data courtesy of NHS Blood and Transplant

# Take home messages

- Cardiogenic shock is dangerous with real-world mortality of 45-50%
  - Mortality is highest in those with worst haemodynamic status
  - Patients may be categorised using INTERMACS profiles
- Inotropes and vasoactive drugs should be used carefully
  - Use minimum dose of the most appropriate agent for the shortest length of time
  - PA catheter may help with choice of agent and determine if you're winning or losing
- Mechanical circulatory support may be used as bridge to heart transplantation
  - Options depend on many factors including LV/RV function, INTERMACS profile
  - Latest generation of implantable LVAD represent a major step forwards
- Phone for help if you have a patient in cardiogenic shock on your ICU and they may be a candidate for heart transplantation