Cardiogenic Shock and Initiatives to Reduce Mortality

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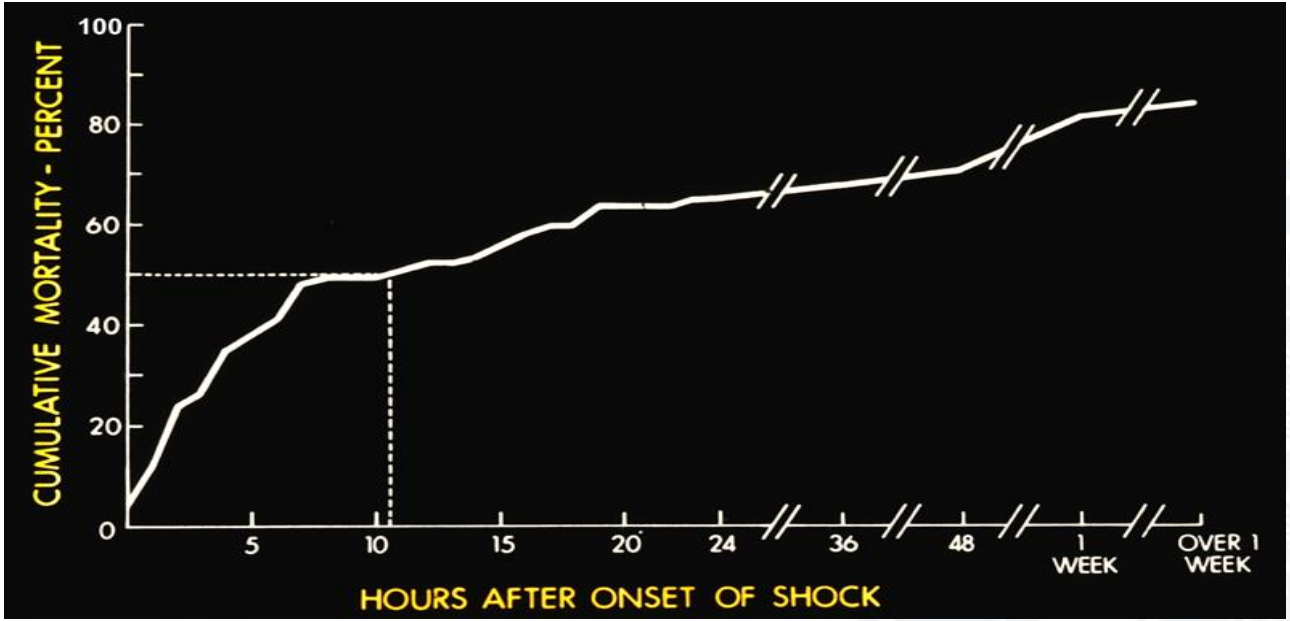
The Golden “Hours”?



- 50% dead within 10 hours
- Overall mortality 86%
- Need: right treatment, right place, right time

Killip et al Am J Cardiol 1967

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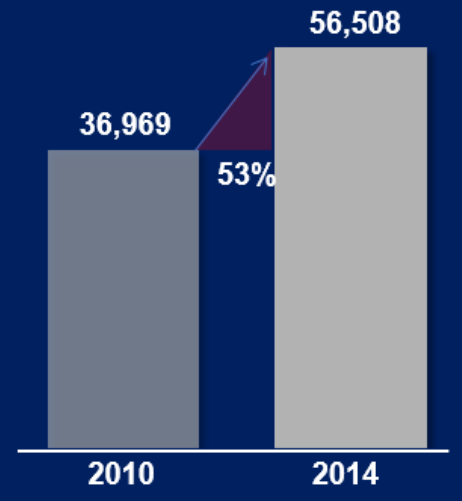
Incidence of Cardiogenic Shock Growing

Cardiogenic Shock in STEMI Increasing [1]

STEMI Cardiogenic Shock in Medicare Age Increasing [2]



Age ≥65 only, excludes non-Medicare population

1. Dhaval Kolte et al. J Am Heart Assoc 2014 NATIONWIDE INPATIENT SAMPLE
2. Centers for Medicare and Medicaid database, MEDPAR FY14

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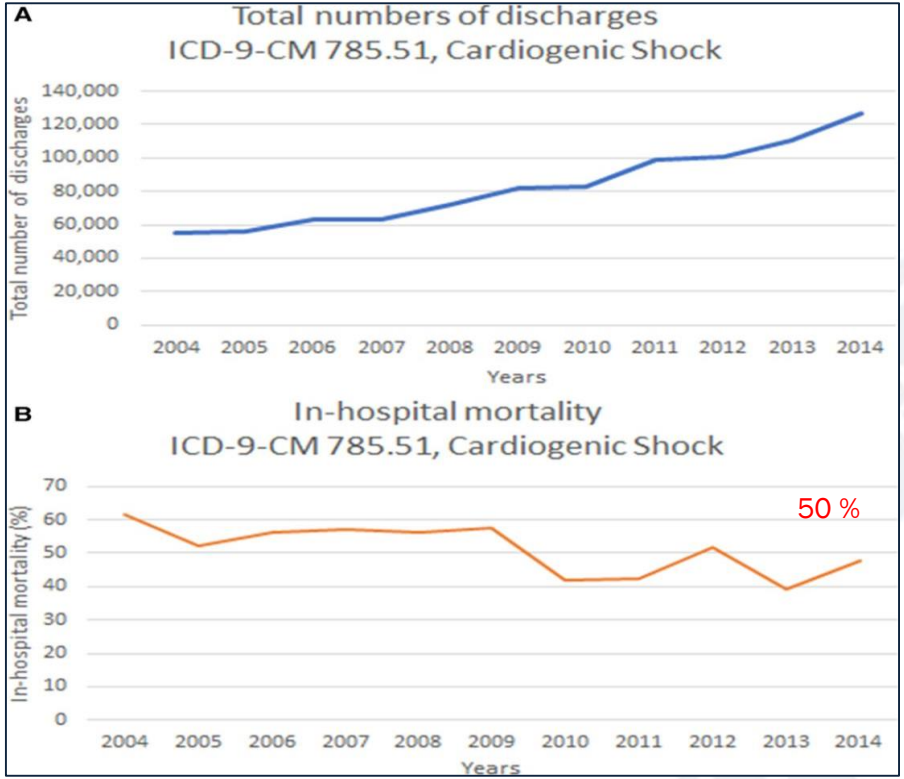
Nationwide Inpatient Sample Databases



Circ Cardiovasc Interv. 2017;10:e004337

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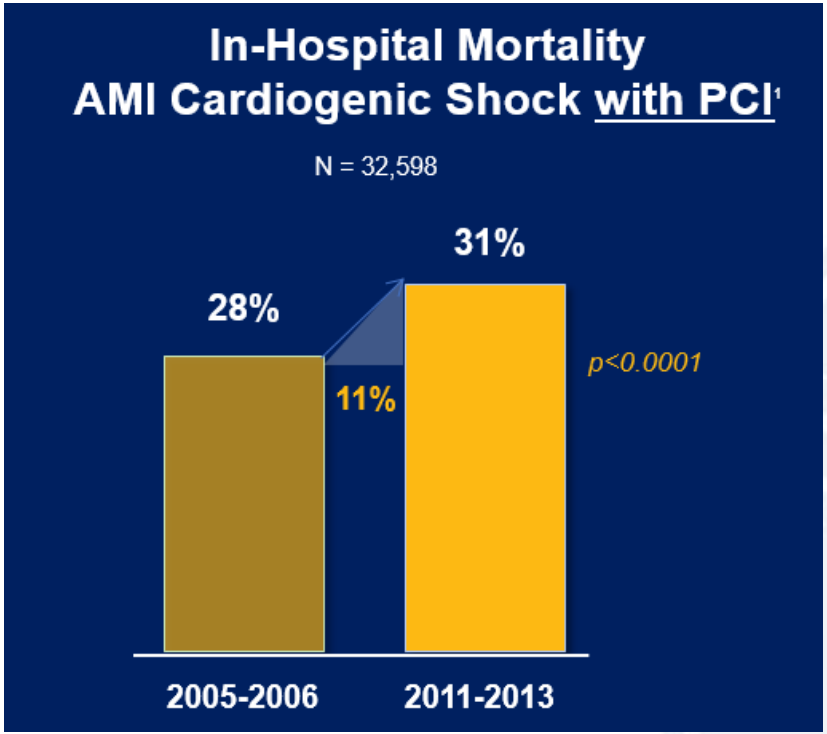
PCI Mortality with Cardiogenic Shock Remains a Clinical Challenge



AMI Cardiogenic Shock with PCI only; Overall mortality >50%

Wayangankar, et al. JACC Int 2016 CATH-PCI Registry

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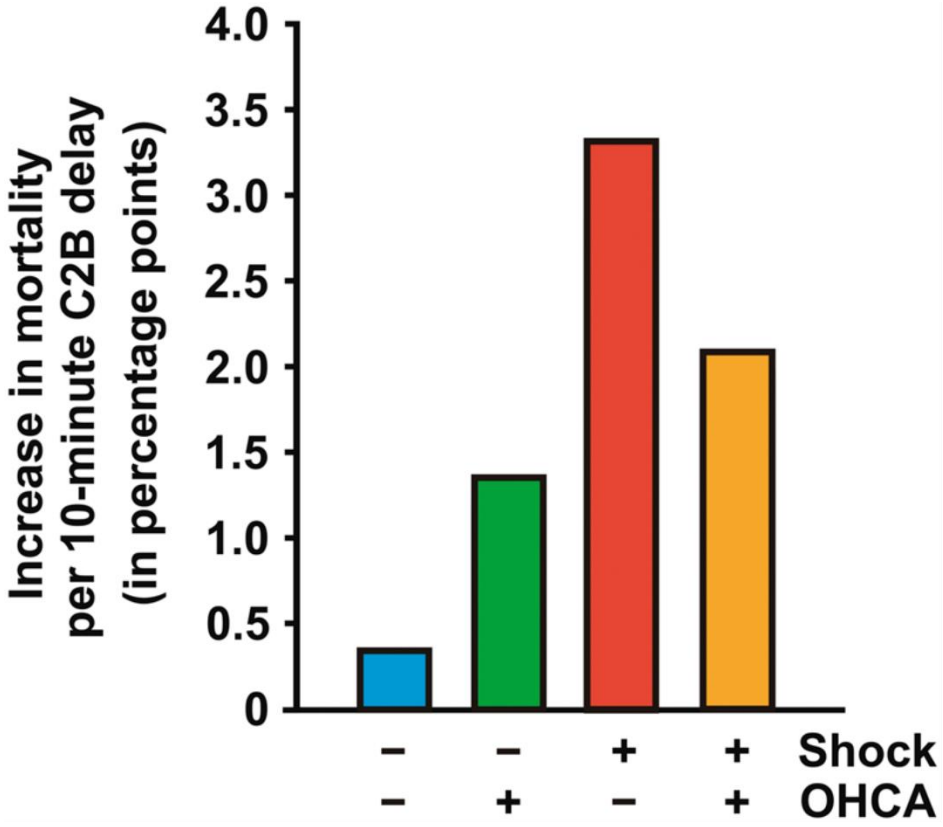
FITT-STEMI TRIAL



Q10min delay after 90 min → 3.31xdeath/100 PCI tx CS pts w/o OHCA

Scholz KH et al. EHJ 2018

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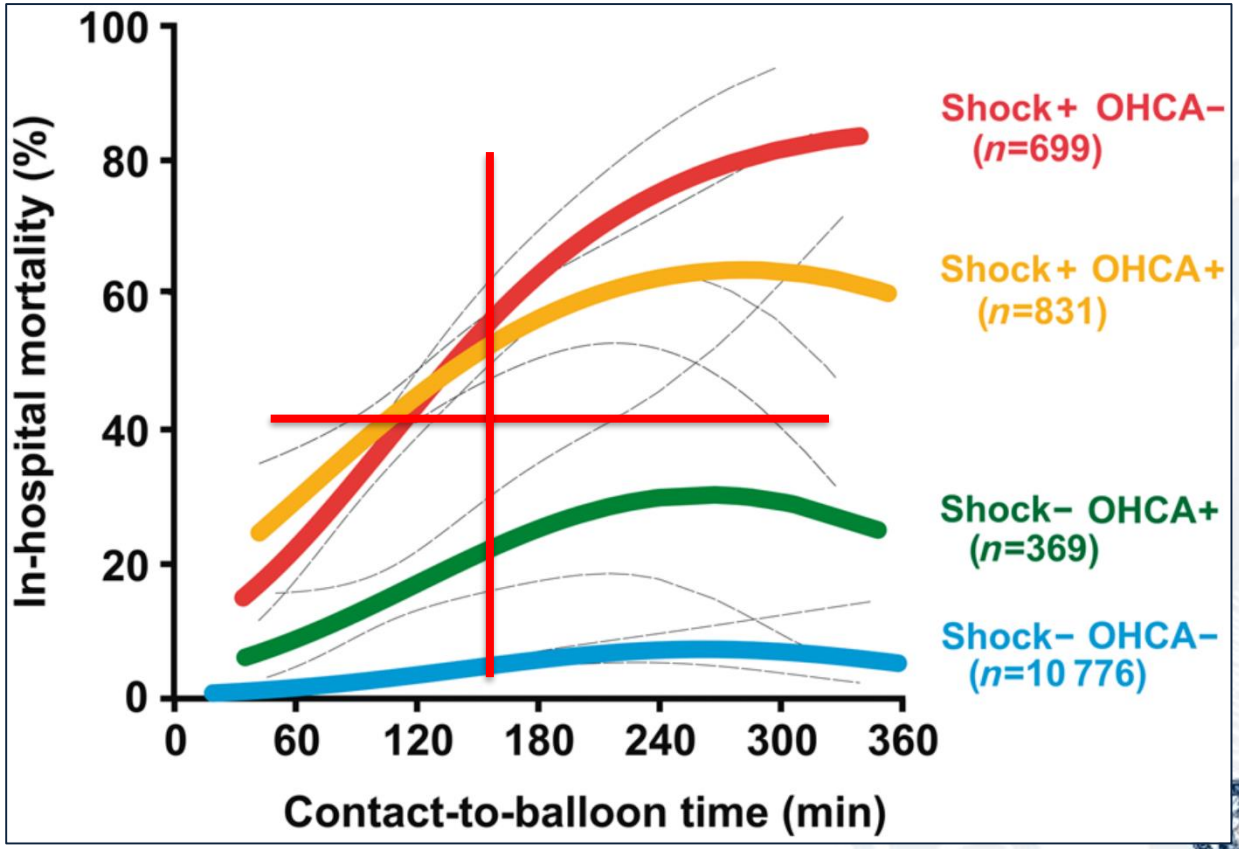
FITT-STEMI TRIAL



Scholz KH et al. EHJ 2018

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Deaths from Cardiogenic Shock Complicating STEMI are Increasing

EDITORIAL COMMENT

Disappointing Results, But We Must Carry On*

Tanveer Rab, MD

- Lack of early Mechanical Circulatory Support
- Use of IABP

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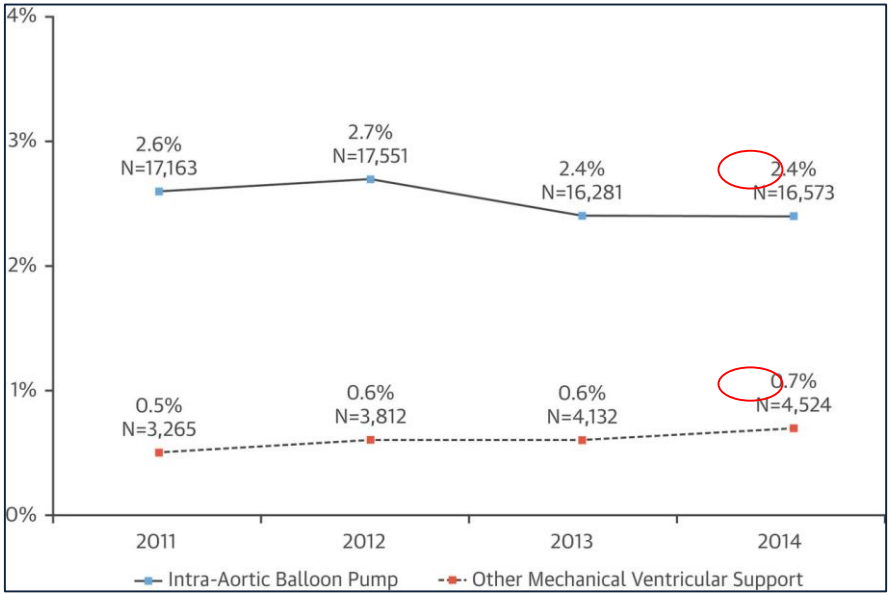
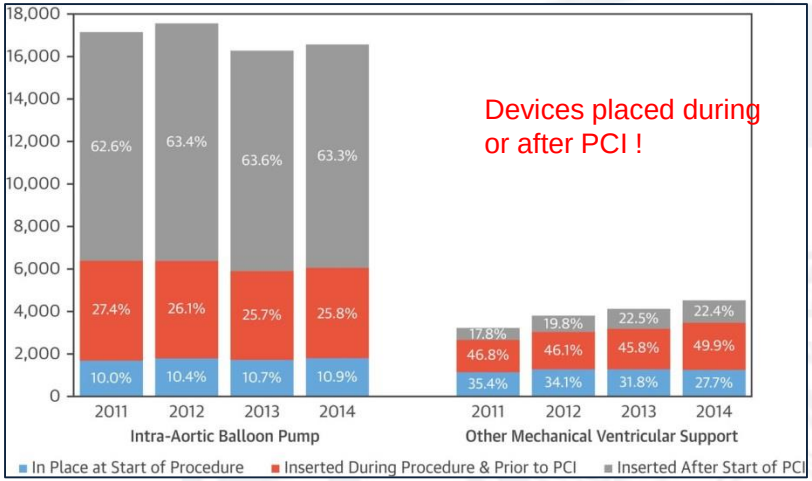
J Am Coll Cardiol Intv. 2016;9(4):341-351.

NCDR 2017: Low use of LV support (< 3 %)





Devices placed during or after PCI !

IABP used predominantly

Frederick A. Masoudi et al. JACC 2017;69:1427-1450

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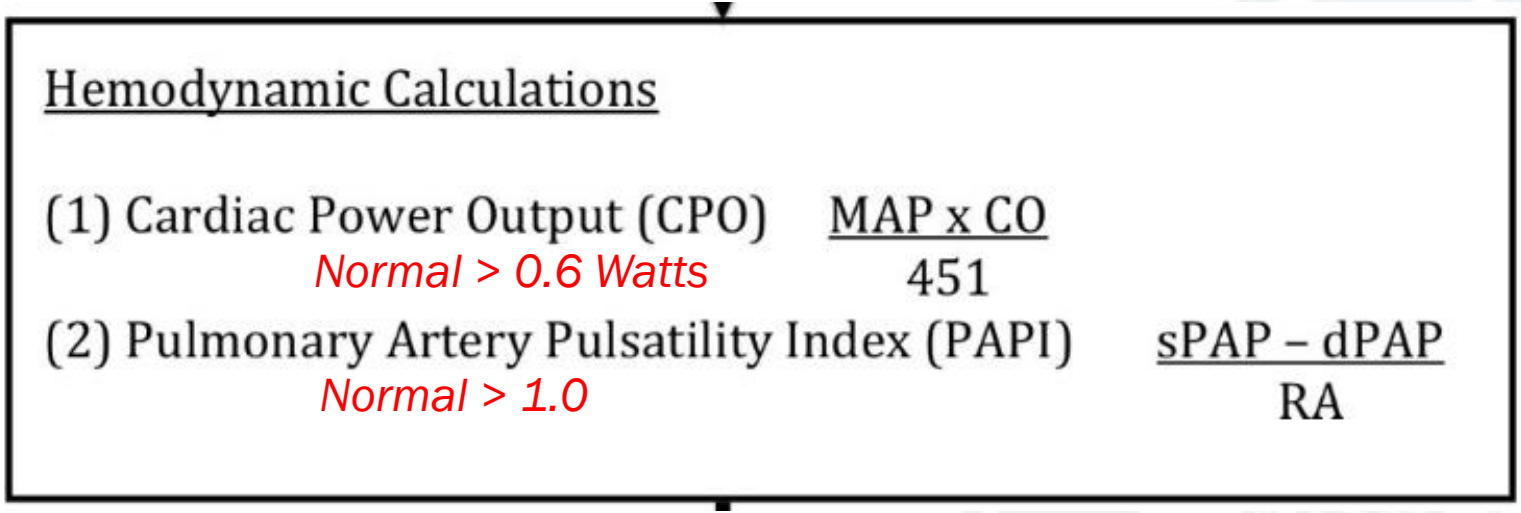
Right Heart Cath is important with two important derived hemodynamic calculations



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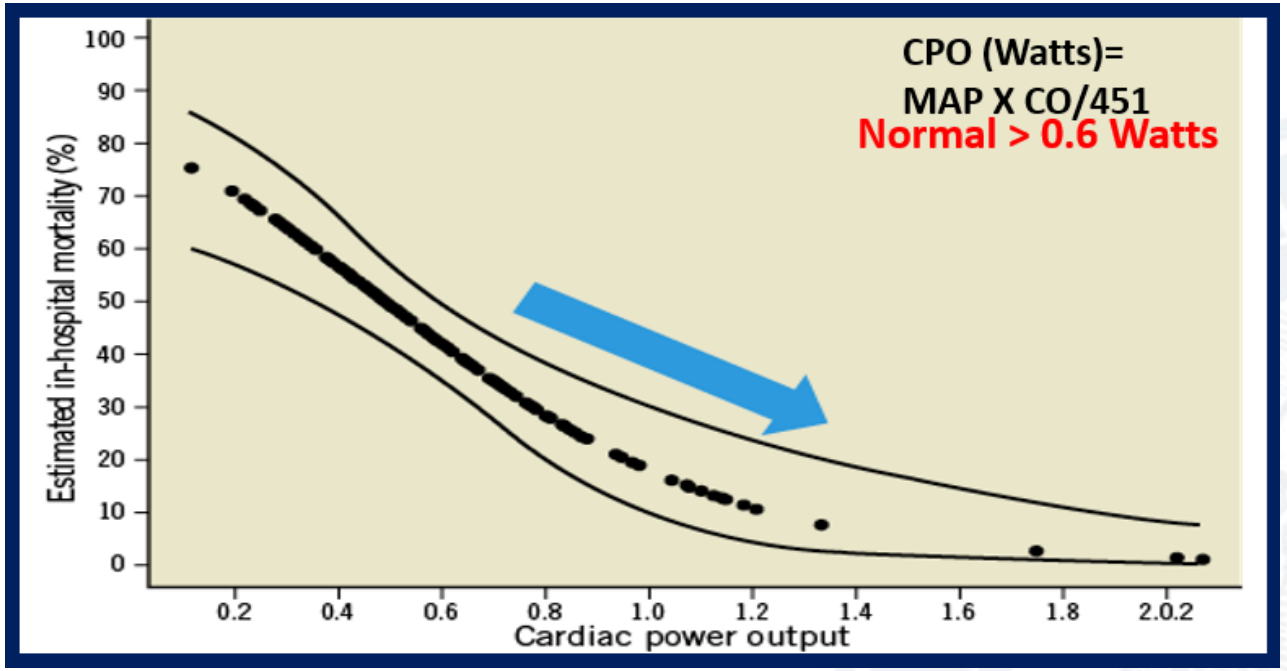
Cardiac power is the strongest hemodynamic correlate of mortality in cardiogenic shock SHOCK trial registry



Unadjusted estimated in-hospital mortality by cardiac power output (n = 189) with pointwise 95% confidence bands.

J Am Coll Cardiol. 2004;44(2):340-348

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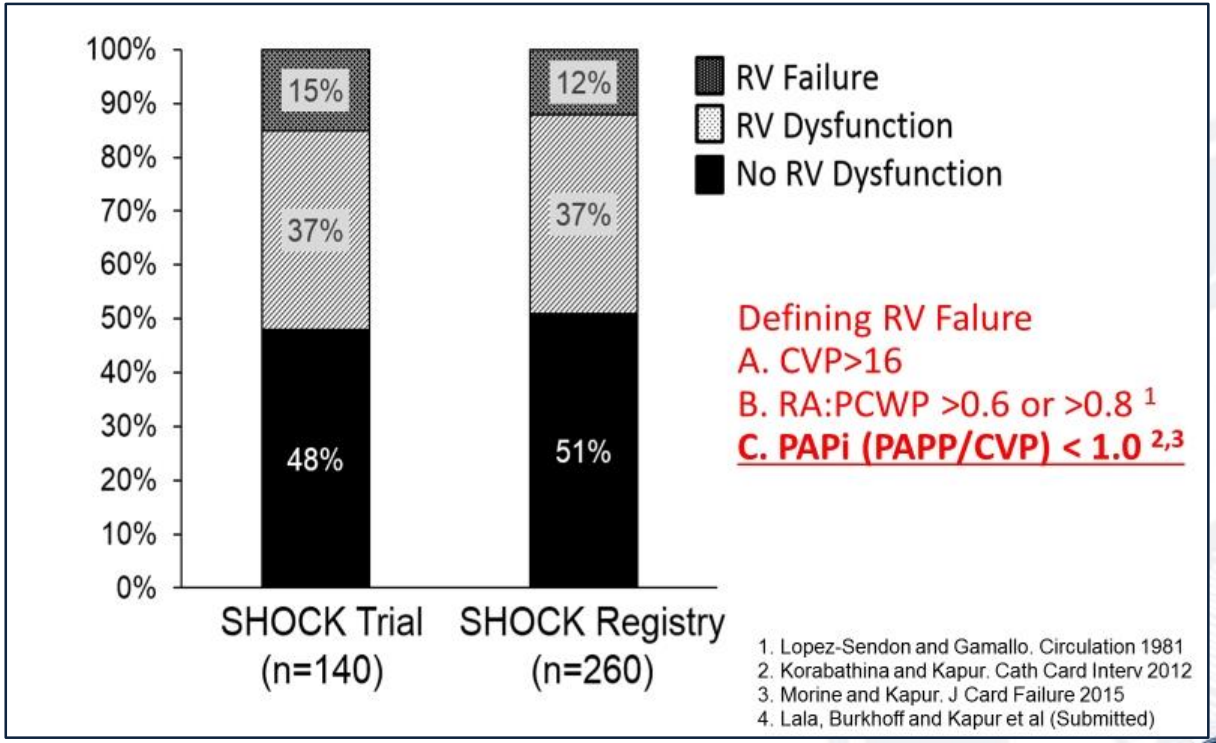
Right sided involvement in 50 % of shock patients



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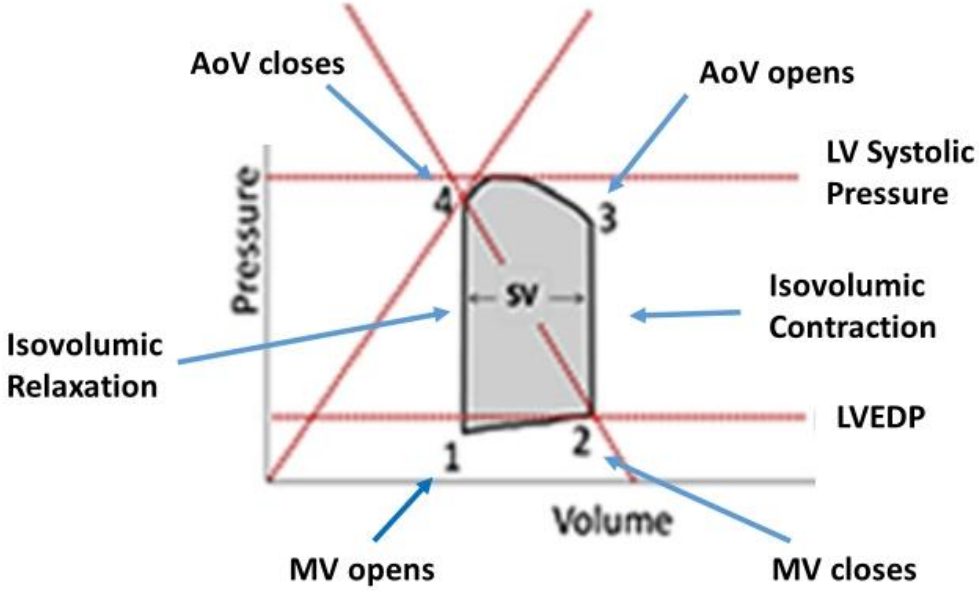
Haemodynamics

The Pressure-Volume Loop



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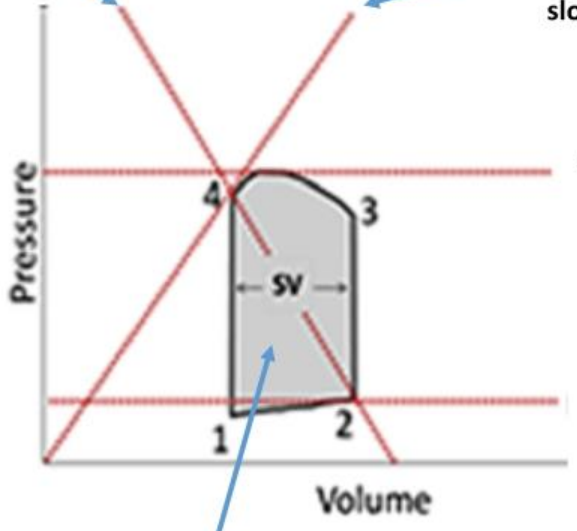
Haemodynamics

Ea - Effective Arterial Elastance – a component of afterload

Emax – load-independent LV contractility = maximal slope of ESPVR



LV Systolic Pressure

LVEDP

Stroke Work

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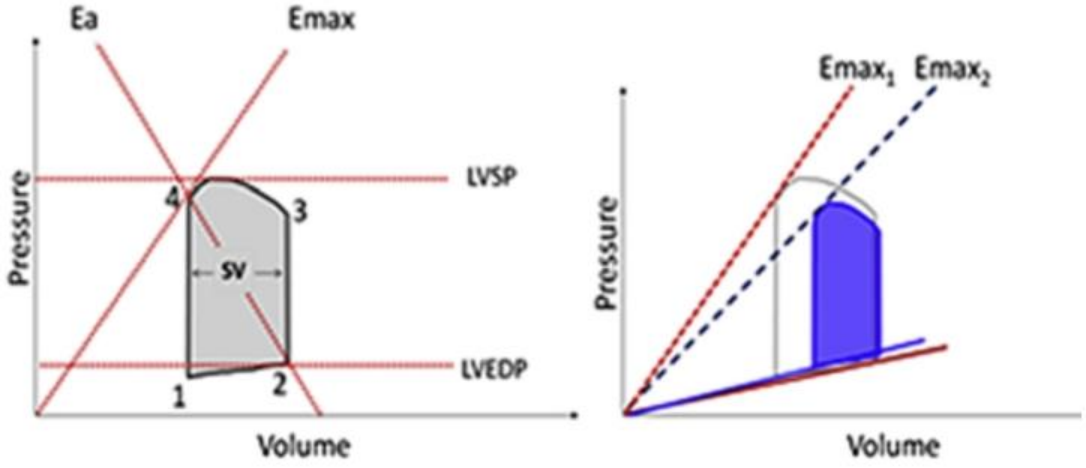
Myocardial Infarction



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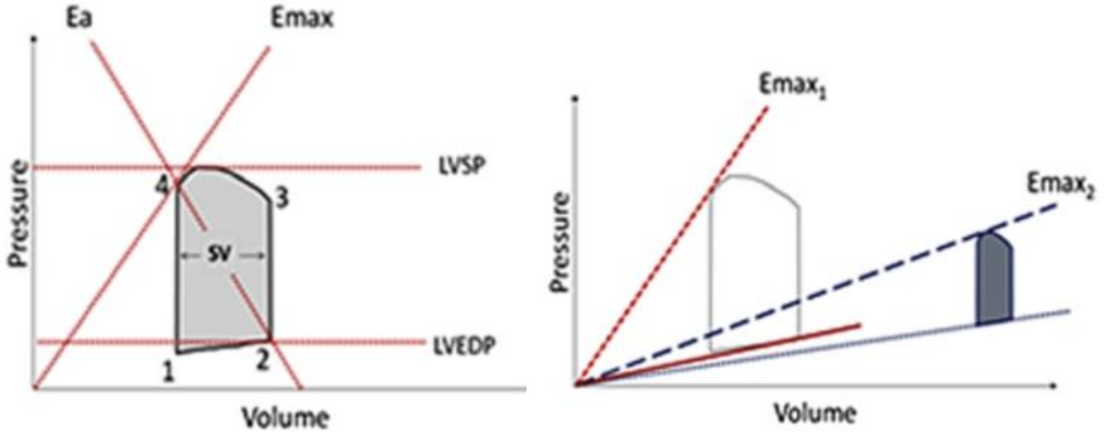
Cardiogenic Shock



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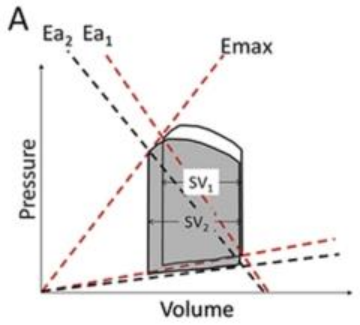
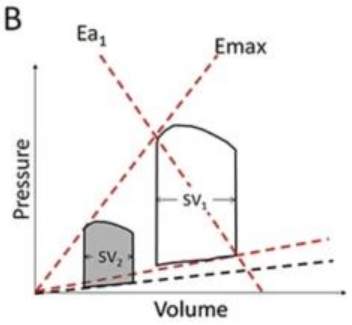
Effects of Mechanical Support



IABP

- Reduces peak systolic and diastolic pressures
- Increases LV stroke volume

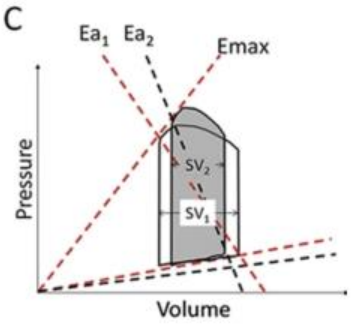
Reduced slope of arterial elastance (Ea_2)



pLVAD

- Reduces LV pressures, LV volumes and LV stroke volume

Reduced cardiac workload



V-A ECMO (no vent)

- Increases LV systolic and diastolic pressures
- Reduces LV stroke volume

Increased slope of arterial elastance (Ea_2)

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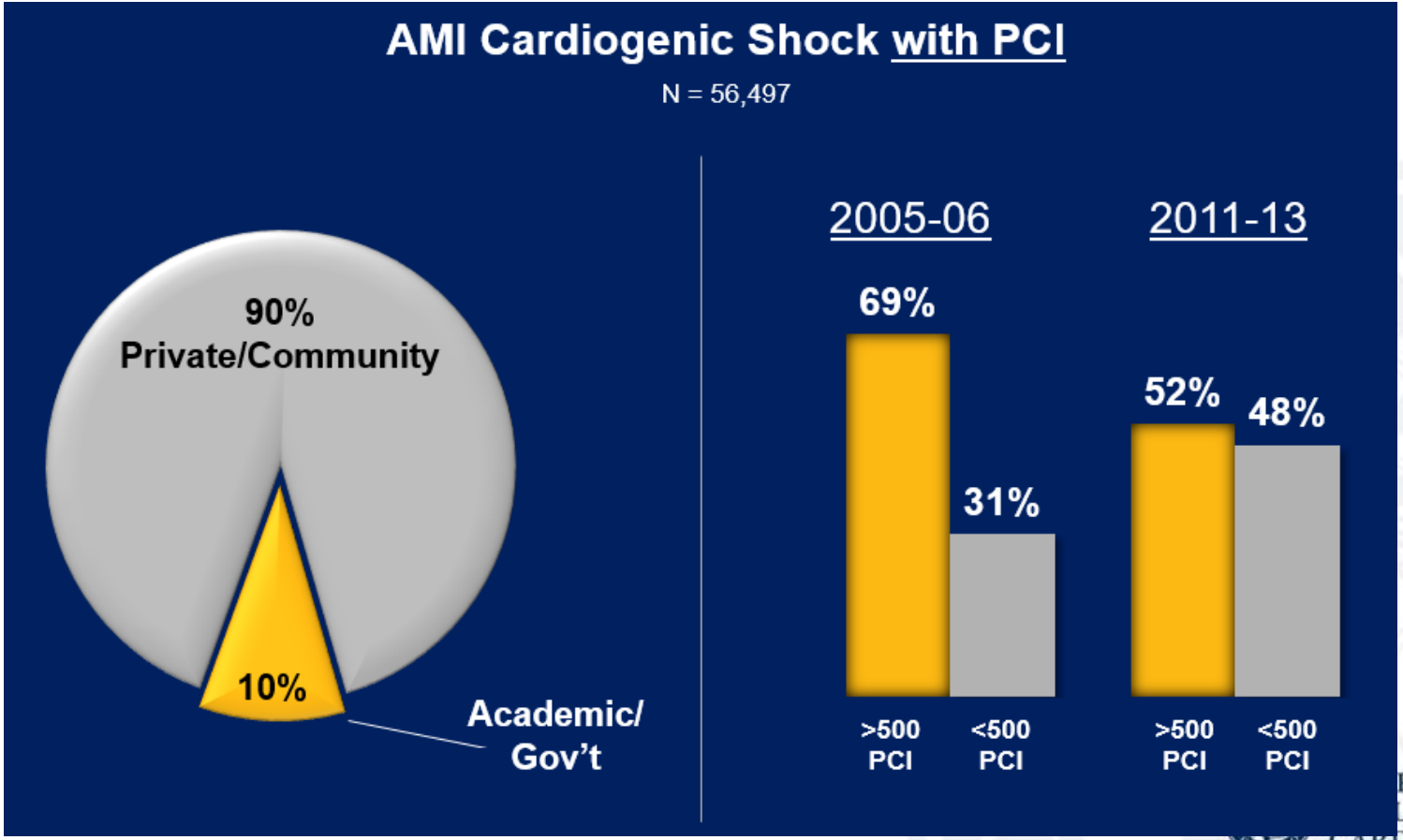
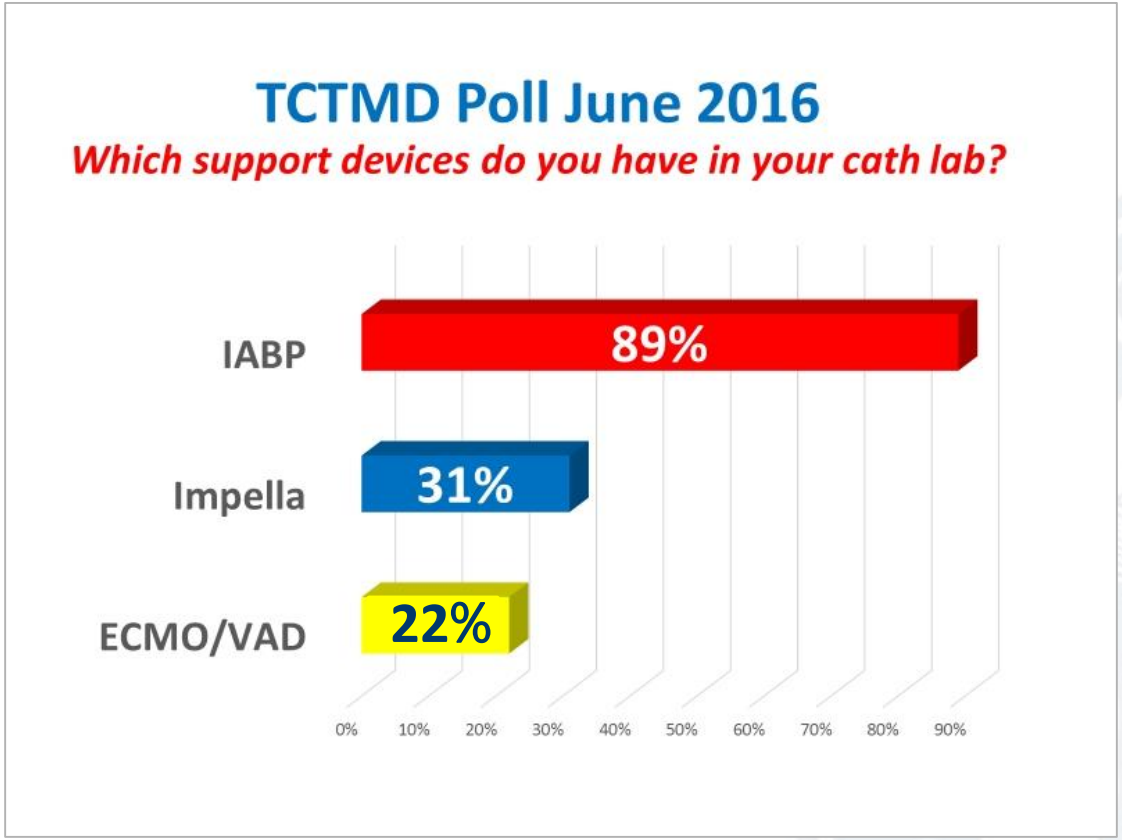
AMI Shock Often Treated in Community Hospitals



Wayangankar et al. JACC Interventions 2016 CATH-PCI REGISTRY

The arguments are:
I only have the balloon pump in my lab



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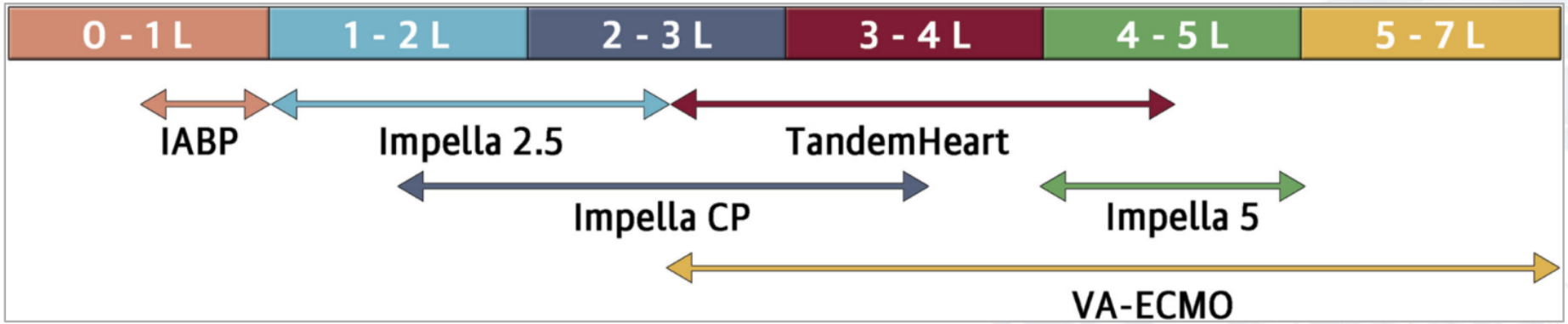


J Am Coll Cardiol Intv. 2016;9(9):871-883

ACC/AHA 2013 and ESC 2017 Guidelines for LV support in Cardiogenic Shock

- IABP

Disagreement:
Class IIb (ACC/AHA)
Class III (ESC)

- MCS

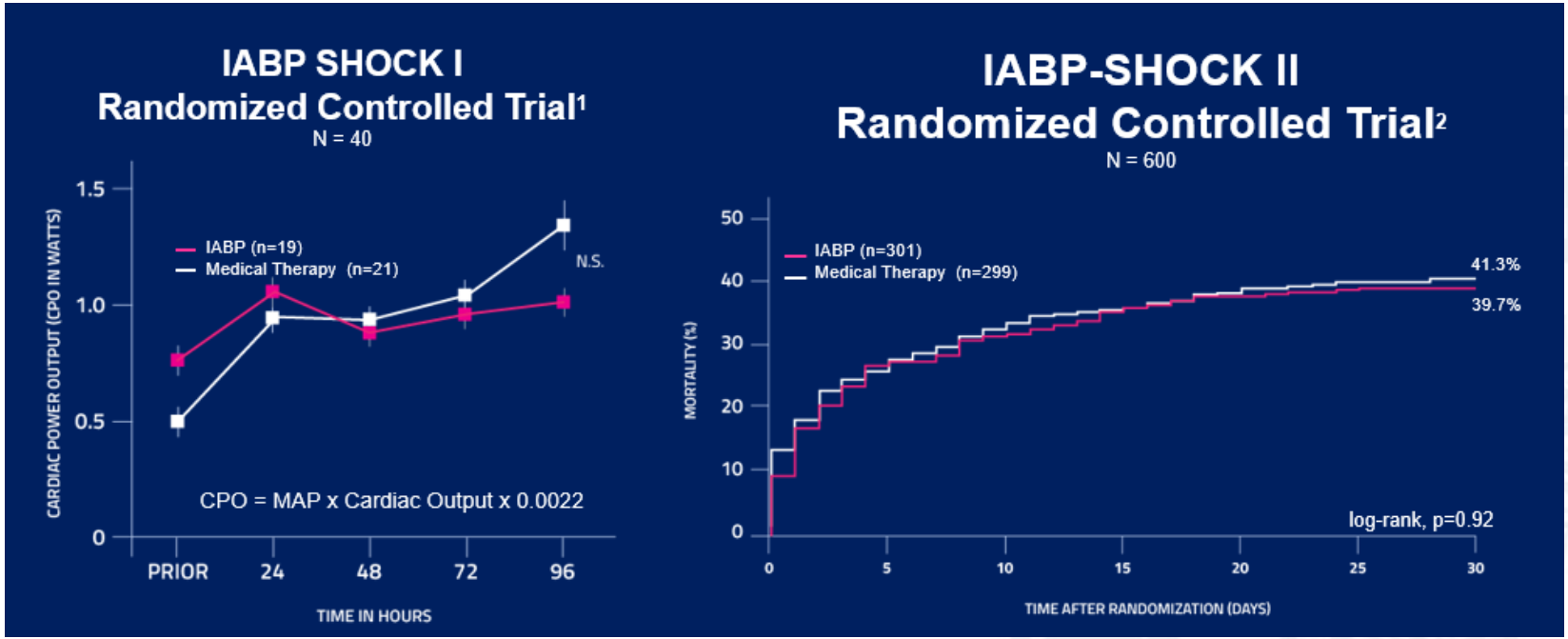
Agreement:
Class IIb in refractory cardiogenic shock

Mechanism	Pneumatic
Device Configuration	Descending aorta via femoral artery
Maximal Support	0.5 – 1 LPM
LV Unloading	+
Implant time, complexity	+
Management Complexity	+
Limb Ischemia Risk	+
Hemolysis Risk	0
Hemorrhage Risk	+
Contraindications	AI, severe PAD, Aortic disease

IABP

Modified from Atkinson TM et al, JACC Cardiovasc Interv 2016.

IABP in AMI Cardiogenic Shock: No Hemodynamic or Survival Benefit



IABP Increased hazard risk of stroke, downgraded to Class III (harm), Level of Evidence A, ESC STEMI Guidelines 2014

1- Prondzinsky R. et al. Jn Critical Care Medicine IABP SHOCK I 2010 – Clinicaltrial.gov # NCT00469248

2- Thiele H et al. NEJM 2012

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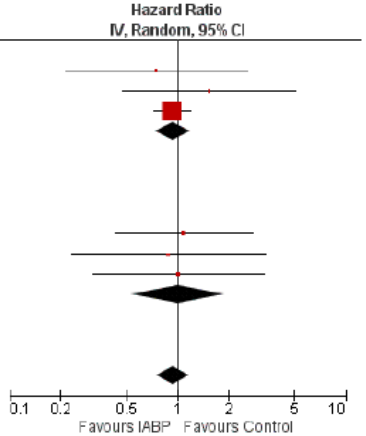
Cardiogenic Shock in Acute MI

Evidence: Intra-Aortic Balloon Pump

- 7 randomized trials, n 790 (75% from SHOCK II)
- 4 IABP vs no MCS
- 3 IABP vs other MCS
- No significant difference in survival

Figure 6. Forest plot of comparison: IABP versus control, outcome: all-cause 30-day mortality distribution.

Study or Subgroup	log[Hazard Ratio]	SE	IABP Total	Control Total	Weight	Hazard Ratio IV, Random, 95% CI
1.1.1 IABP versus non-IABP						
Ohman 2005	-0.28835	0.63385	12	10	3.3%	0.75 [0.22, 2.60]
Prondzinsky 2010	0.43586	0.60641	19	21	3.6%	1.55 [0.47, 5.08]
Thiele 2012	-0.0758	0.12808	301	299	80.7%	0.93 [0.72, 1.19]
Subtotal (95% CI)			332	330	87.6%	**0.94 [0.74, 1.20]**
Heterogeneity: Tau² = 0.00; Chi² = 0.81, df = 2 (P = 0.67); I² = 0%						
Test for overall effect: Z = 0.51 (P = 0.61)						
1.1.2 IABP versus other LVAD						
Thiele 2005	0.08595	0.47965	20	21	5.8%	1.09 [0.43, 2.79]
Burkhoff 2006	-0.12869	0.67585	10	11	2.9%	0.88 [0.23, 3.31]
Seyfarth 2008	0.01788	0.59305	13	13	3.8%	1.02 [0.32, 3.26]
Subtotal (95% CI)			43	45	12.4%	**1.02 [0.54, 1.93]**
Heterogeneity: Tau² = 0.00; Chi² = 0.07, df = 2 (P = 0.97); I² = 0%						
Test for overall effect: Z = 0.05 (P = 0.96)						
Total (95% CI)			375	375	100.0%	**0.95 [0.76, 1.19]**
Heterogeneity: Tau² = 0.00; Chi² = 0.93, df = 5 (P = 0.97); I² = 0%						
Test for overall effect: Z = 0.46 (P = 0.64)						
Test for subgroup differences: Chi² = 0.05, df = 1 (P = 0.82), I² = 0%						



Unverzagt et al.Cochrane Database Syst Rev. 2015 Mar 27;(3)

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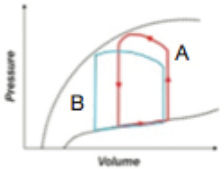
Conclusion: IABP and inotropes increase mortality in Cardiogenic Shock

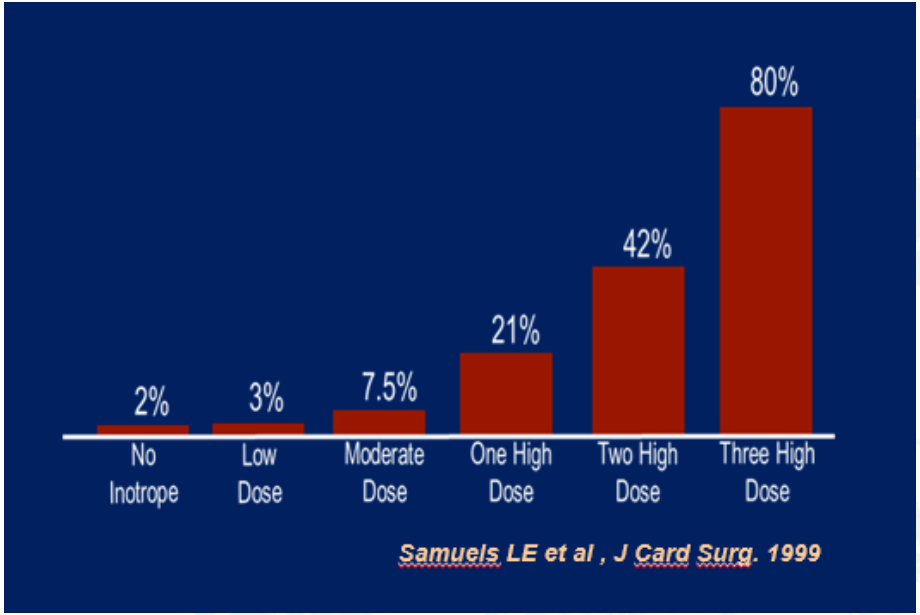
Balloon Pump

- Reduces systolic aortic pressure
- Increases Stroke volume



Effect on Cardiac Work

Stroke Volume increase offsets pressure reduction

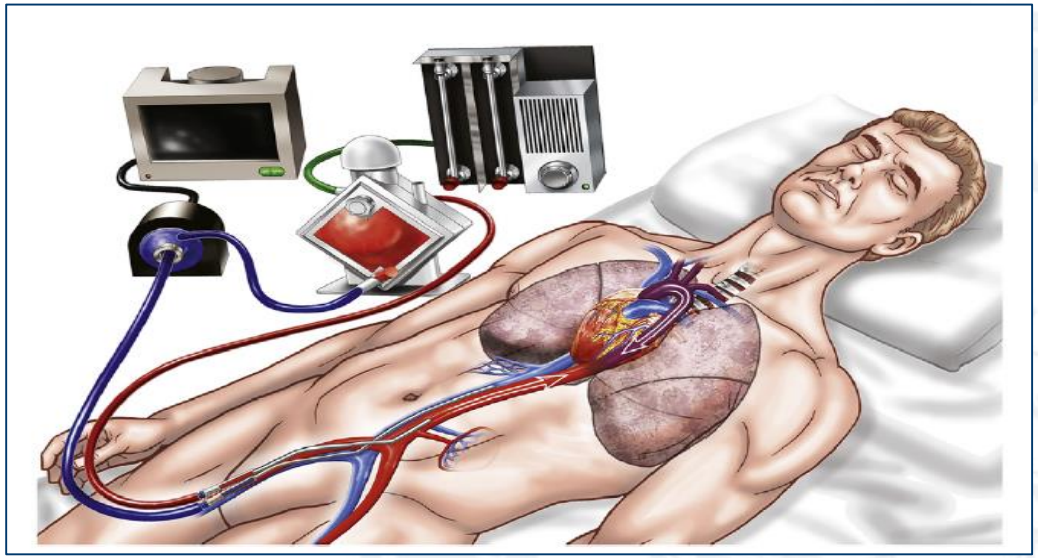


IABP increase cardiac work

Inotropes increase myocardial oxygen consumption and impair microcirculation

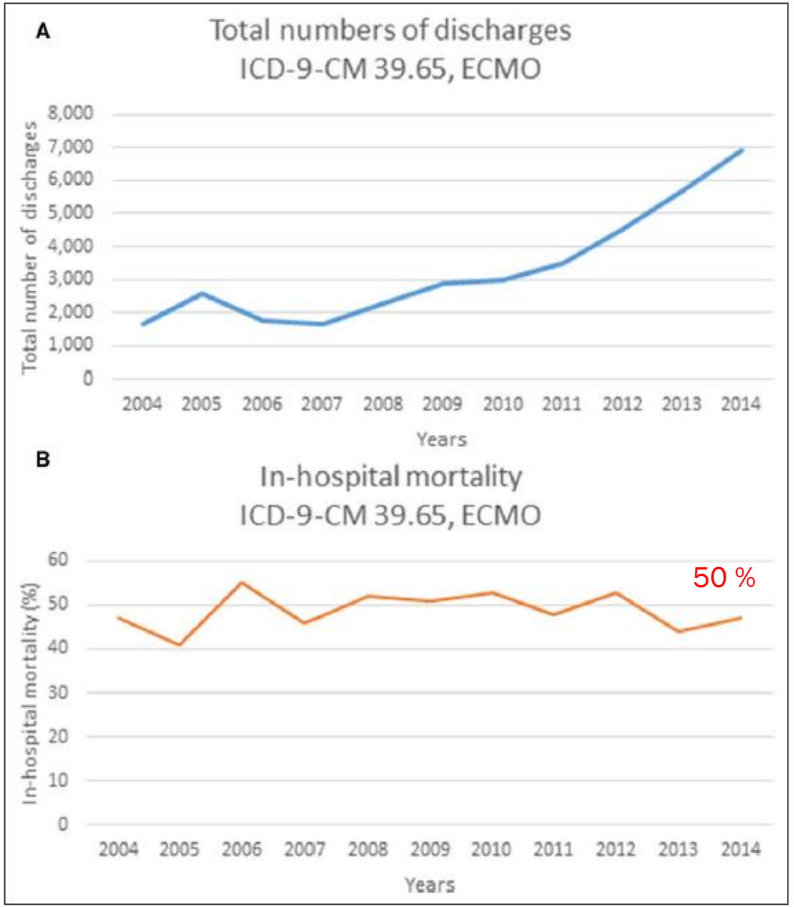
VA ECMO

Mechanism	Centrifugal
Device Configuration	Inflow: Femoral vein/IVC Outflow: Femoral artery Pump: Extracorporeal
Maximal Support	>5 LPM
LV Unloading	0
Implant time, complexity	++
Management Complexity	+++
Limb Ischemia Risk	+++
Hemolysis Risk	++
Hemorrhage Risk	++++
Contraindications	AI, severe PAD, contraindication to AC



Nationwide Inpatient Sample databases

VA- ECMO



4 fold increase in use

Mortality unchanged at 50 %

Circ Cardiovasc Interv. 2017;10:e004337

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Outcomes in Cardiac Arrest with VA ECMO

Nichol et al. (54)	CS and/or cardiac arrest		1,494 84 studies	VA-ECMO	50% survival to hospital discharge	Vascular injury, bleeding and stroke
ELSO registry (39)	Cardiac arrest	75% cardiac disease	2,633: 295 ECPR	VA-ECMO 91%	27% survival to hospital discharge	Neurologic complications 33%
Takyama et al. (53)	Refractory CS, 23% active CPR	SBP <90 mm Hg, CI <2.0 l/min/m^2, evidence of end-organ failure despite inotropes/vasopressors or IABP	90	VA-ECMO	49% survival to hospital discharge	Bleeding and stroke: 26% and 18% LV distention and pulmonary edema

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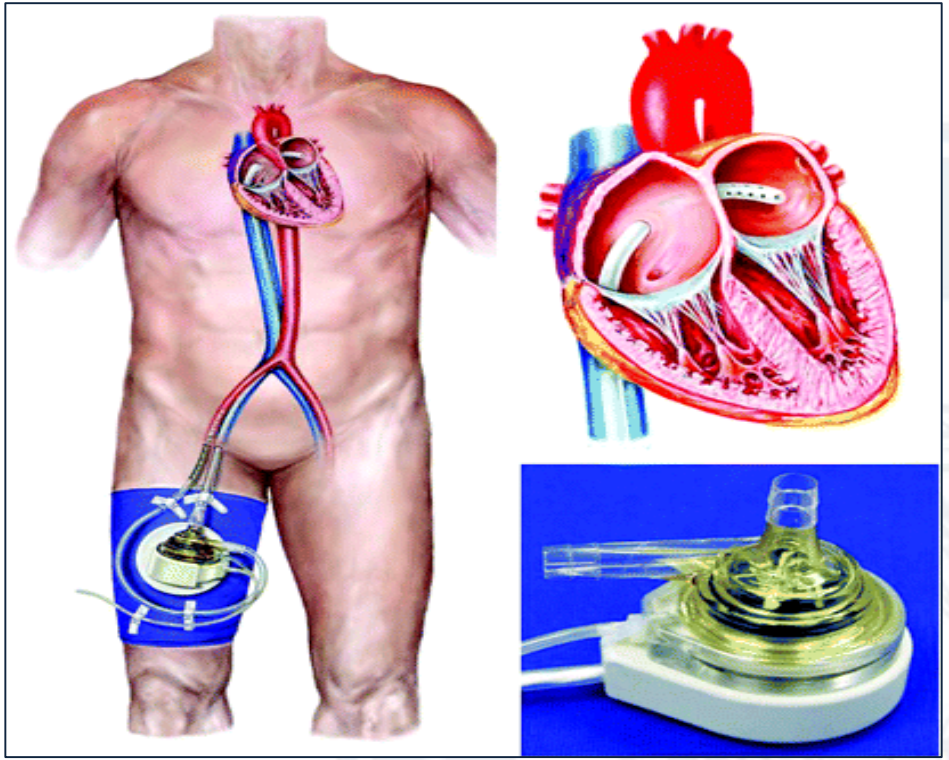
Tandem Heart

Mechanism	Centrifugal
Device Configuration	Inflow: LA via transeptal Outflow: Femoral artery Pump: Paracorporeal
Maximal Support	Up to 5 LPM
LV Unloading	++
Implant time, complexity	+++
Management Complexity	+++
Limb Ischemia Risk	+++
Hemolysis Risk	++
Hemorrhage Risk	+++
Contraindications	AI, severe PAD, contraindication to AC, LA thrombus



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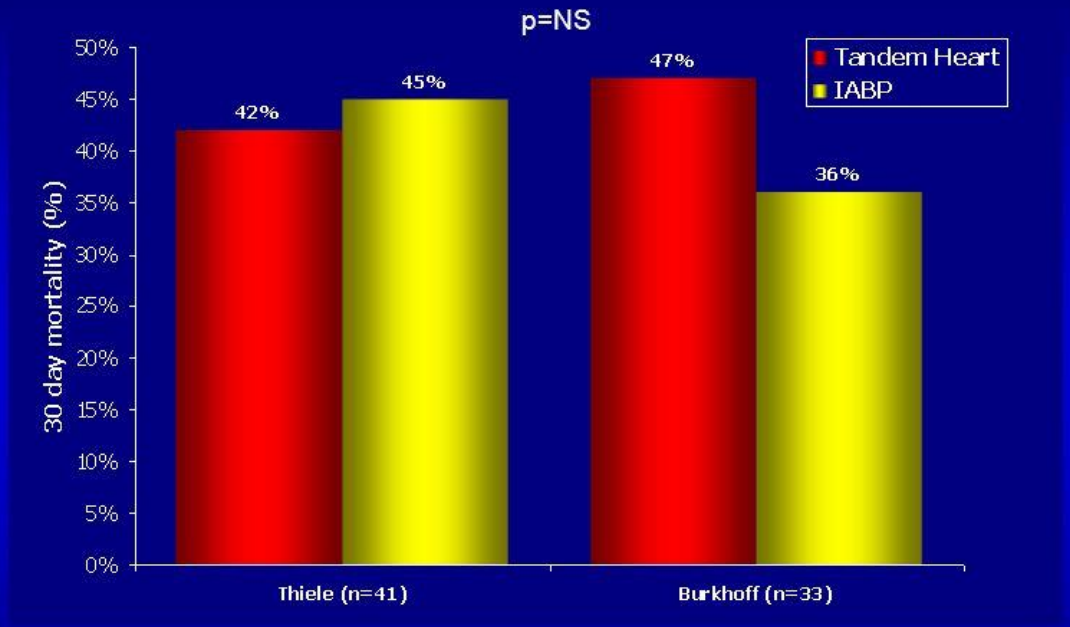
Tandem Heart Outcome Data



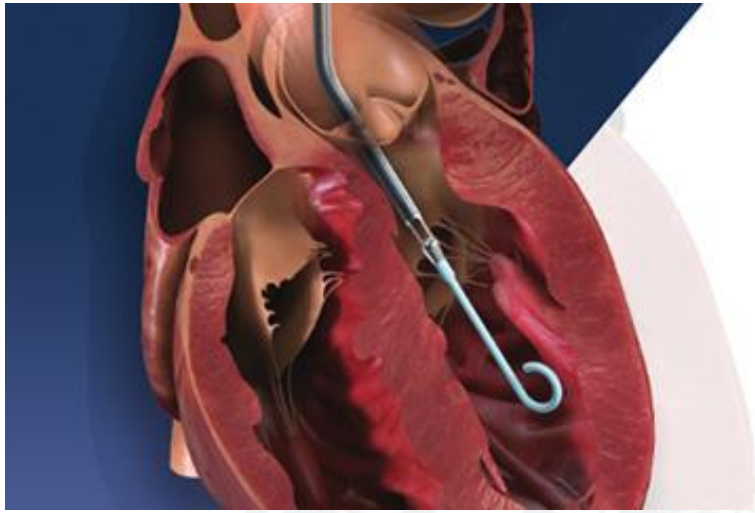
Improved haemodynamic parameters

Increase in bleeding, limb ischaemia, and sepsis

Thiele EHJ 2005;26:1276. Burkhoff AHJ 2006;152:e1

IMPELLA

Mechanism	Axial
Device Configuration	Inflow: LV Outflow: Aorta Pump: Transaortic
Maximal Support	1-5 LPM (Impella 2.5, Impella CP, Impella 5)
LV Unloading	++ - +++
Implant time, complexity	++ - +++
Management Complexity	++
Limb Ischemia Risk	++
Hemolysis Risk	++
Hemorrhage Risk	++
Contraindications	LV thrombus, mechanical aortic valve, severe AS/AI, contraindication to AC



Received FDA Approval for Cardiogenic Shock after MI or OHS due to LV failure -2016

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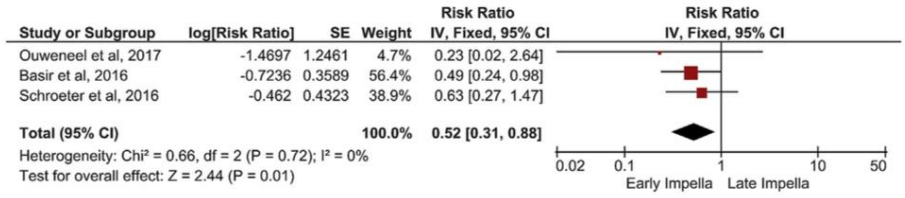
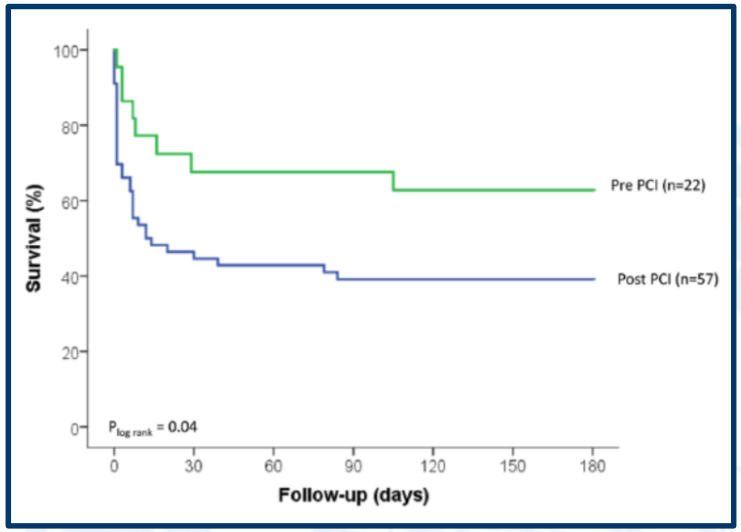
Door to "Unloading"?

FIGURE 1 Forest Plot Comparing In-Hospital/30-Day Mortality in "Early" vs. "Late" Impella



CI = confidence interval.



- ***Do as Surgeons do (bypass first [unload LV/RV], reperfuse last)***
- ***Increasing clinical evidence that implantation of an Impella device prior to PCI STEMI and shock may improve survival***

Lauten et al Circ Heart Fail 2013
Kapur et al Circulation 2013
O'Neill et al J Interv Cardiol 2014
Kapur et al JACC Heart Fail 2015
Thiele et al Eur Heart J2015

Basir et al Am J Cardiol 2016
Schroeter et al J Invasive Cardiol 2016
Flaherty et al JACC Interv 2017
Jensen et a; Eur Heart J Acute Cardiovasc Care 2018

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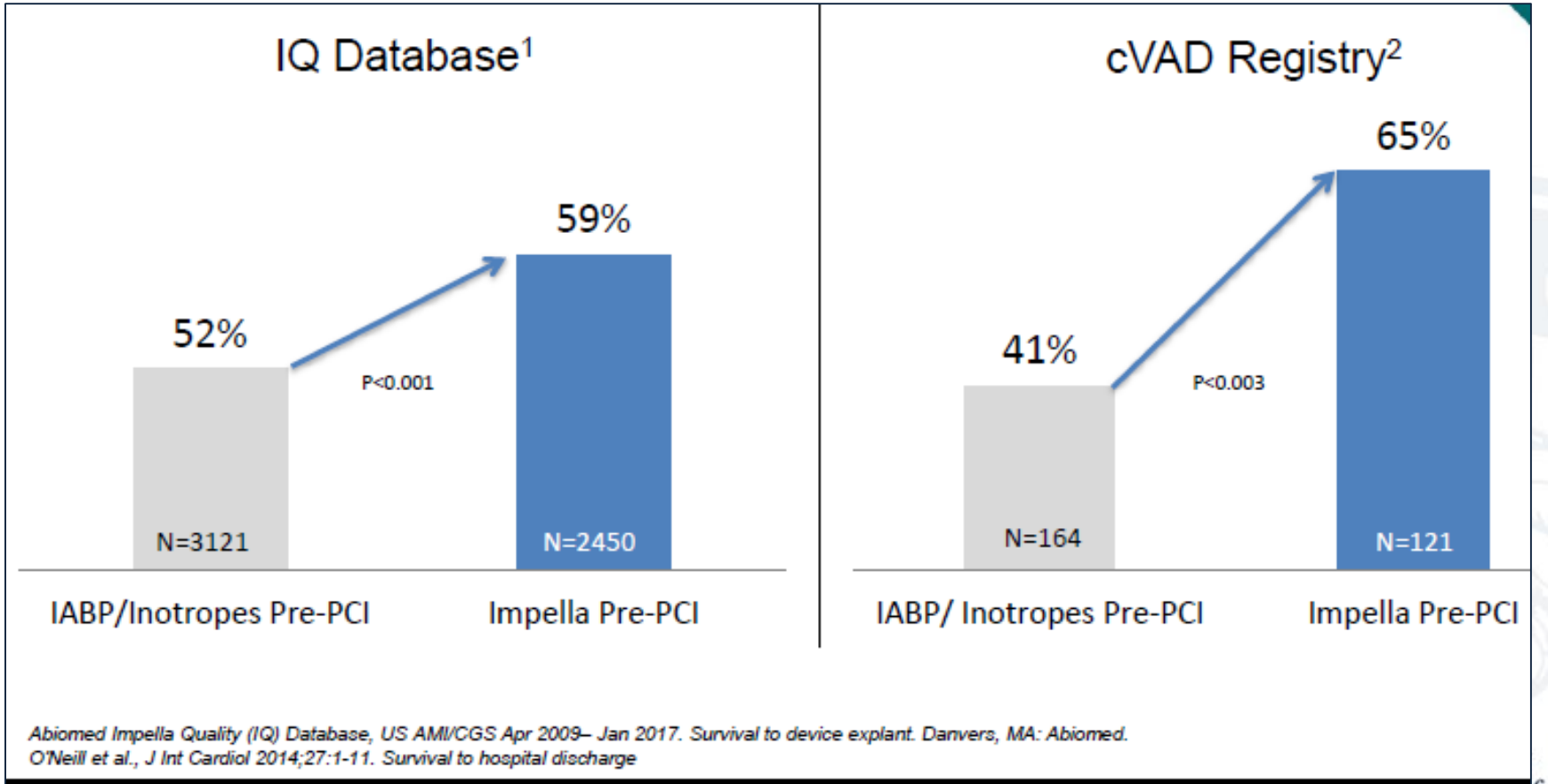
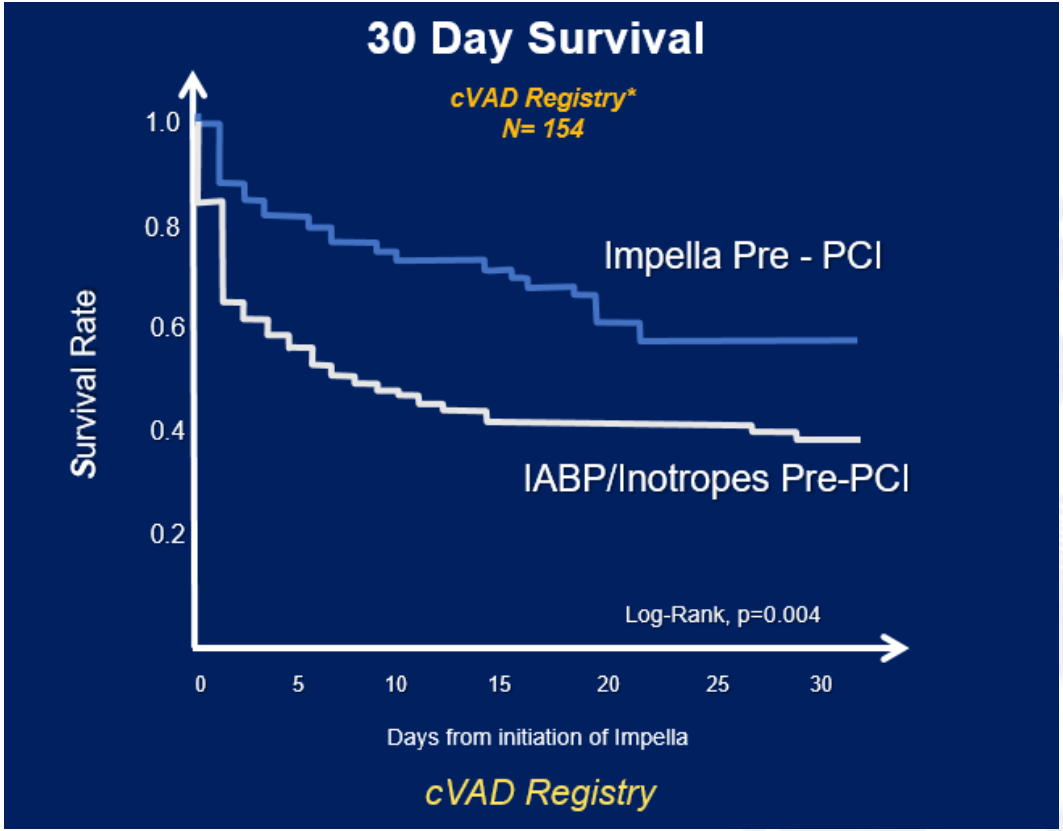


Abiomed Impella Quality (IQ) Database, US AMI/CGS Apr 2009– Jan 2017. Survival to device explant. Danvers, MA: Abiomed.
O'Neill et al., J Int Cardiol 2014;27:1-11. Survival to hospital discharge

Timing of Support Impacts Outcomes



O'Neill, et. al, J Interven Cardiol, 2014

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Randomization in AMI CS is Challenging

Prospective Impella Trials In Emergent Settings

Study	Trial ID	Condition	Pts Required (n)	Pts Enrolled (n)	Duration (months)	Status	Reason for Discontinuation
FRENCH TRIAL (2006)	NCT00314847	AMI CS	200	19	52	Discontinued	Low Enrollment
ISAR-SHOCK (2006)	NCT00417378	AMI CS	26	26	19	Completed	N/A
IMPRESS (2007)	NTR1079 trialregister.nl	STEMI Pre-CS	130	18	22	Discontinued	Low Enrollment
RECOVER I FDA (2008)	NCT00596726	PCCS	Up to 20	17	28	Completed	N/A
RECOVER II FDA (2009)	NCT00972270	AMI CS	384	1	18	Discontinued	Low Enrollment
RELIEF I (2010)	NCT01185691	ADHF	20	1	33	Discontinued	Low Enrollment
DANSHOCK (2012)	NCT01633502	AMI CS	360	~50	40	Enrolling	N/A

Problem: Low Enrollment

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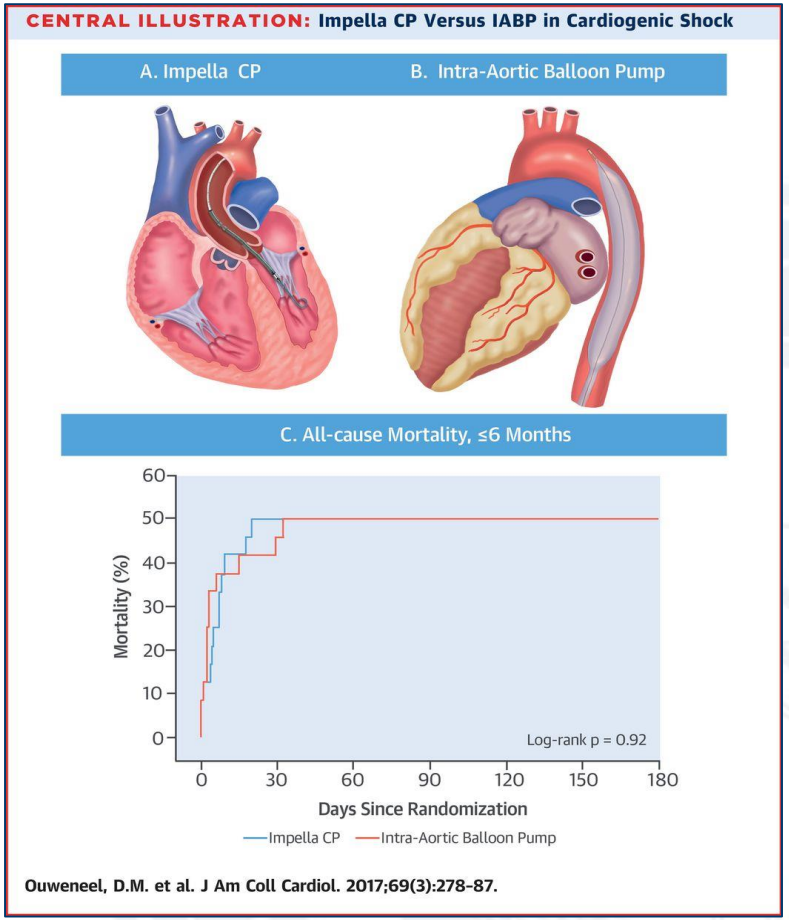
Impella vs Intra-Aortic Balloon Pump

IMPRESS TRIAL

- 48 patients (underpowered)
- Majority in cardiogenic shock after cardiac arrest
- 100% mechanical ventilation
- 35% not salvageable – anoxic brain injury and refractory CGS
- Enrollment not completed
- No difference in outcomes

Majority had device placement *AFTER* PCI



Initiatives to Reduce Mortality

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National Cardiogenic Shock Initiative Algorithm

INCLUSION CRITERIA

Acute Myocardial Infarction: STEMI or NSTEMI
- Ischemic Symptoms
- EKG and/or biomarker evidence of AMI (STEMI or NSTEMI)

Cardiogenic Shock
- Hypotension (<90/60) or the need for vasopressors or inotropes to maintain systolic blood pressure >90
- Evidence of end organ hypoperfusion (cool extremities, oliguria, lactic acidosis)

EXCLUSION CRITERIA
- Evidence of Anoxic Brain Injury
- Unwitnessed out of hospital cardiac arrest or any cardiac arrest in which ROSC is not achieved in 30 minutes
- IABP placed prior to Impella
- Septic, anaphylactic, hemorrhagic, and neurologic causes of shock
- Non-ischemic causes of shock/hypotension *(Pulmonary Embolism, Pneumothorax, Myocarditis, Tamponade, etc.)*
- Active Bleeding
- Recent major surgery
- Mechanical Complications of AMI
- Known left ventricular thrombus
- Patient who did not receive revascularization
- Contraindication to intravenous systemic anticoagulation
- Mechanical aortic valve

ACTIVATE CATH LAB

ACCESS & HEMODYNAMIC SUPPORT
- Obtain femoral arterial access (via direct visualization with use of ultrasound and fluoro)
- Obtain venous access (Femoral or Internal Jugular)
- Obtain either Fick calculated cardiac index or LVEDP

IF LVEDP >15 *or* Cardiac Index < 2.2 AND anatomy suitable, place IMPELLA

Coronary Angiography & PCI
- Attempt to provide TIMI III flow in all major epicardial vessels other than CTO
- If unable to obtain TIMI III flow, consider administration of intra-coronary vasodilators

Perform Post-PCI Hemodynamic Calculations

1. Cardiac Power Output (CPO): $\frac{MAP \times CO}{451}$

2. Pulmonary Artery Pulsatility Index (PAPI): $\frac{sPAP - dPAP}{RA}$

Wean OFF Vasopressors and Inotropes

If CPO is >0.6 and PAPI >0.9, operators should wean vasopressors and inotropes and determine if Impella can be weaned and removed in the Cath Lab or left in place with transfer to ICU.

Escalation of Support

If CPO remains <0.6 operators should consider the following options:
- PAPI is <0.9 consider right sided hemodynamic support
- PAPI >0.9 consideration for additional hemodynamic support

Local practice patterns should dictate the next steps:
- Placement of more robust MCS device(s)
- Transfer to LVAD/Transplant center

If CPO is >0.6 and PAPI <0.9 consider providing right sided hemodynamic support if clinical suspicion for RV dysfunction/failure

Vascular Assessment
- Prior to discharge from the Cath Lab, a detailed vascular exam should be performed including femoral angiogram and Doppler assessment of the affected limb.
- If indicated, external bypass should be performed.

ICU Care
- Daily hemodynamic assessments should be performed, including detailed vascular assessment
- Monitor for signs of hemolysis and adjust Impella position as indicated

Device Weaning

Impella should only be considered for explantation once the following criteria are met:
- Weaning off from all inotropes and vasopressors
- CPO >0.6, and PAPI > 0.9

Bridge to Decision

Patients who do not regain myocardial recovery within 3-5 days, as clinically indicated, should be transferred to an LVAD/Transplant center. If patients are not candidates, palliative care options should be considered.

**** QUALITY MEASURES ****
- Impella Pre-PCI
- Door to Support Time < 90 minutes
- Establish TIMI III Flow
- Right Heart Cath
- Wean off Vasopressors & Inotropes
- Maintain CPO >0.6 Watts
- Improve survival to discharge to >80%

NATIONAL CARDIOGENIC SHOCK INITIATIVE

NationalCSI@hfhs.org

www.henryford.com/cardiogenicshock

NationalCSI – Algorithm – v1.5 – 11/2017

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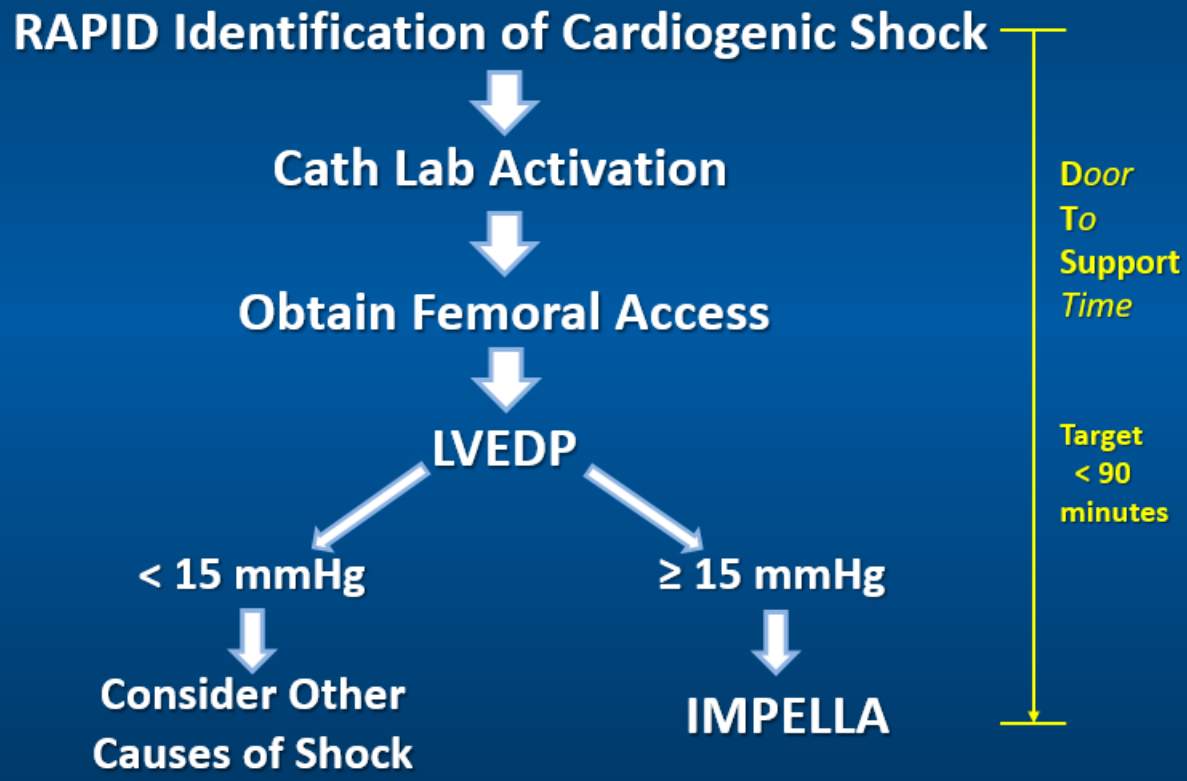
NATIONAL CSI ALGORITHM

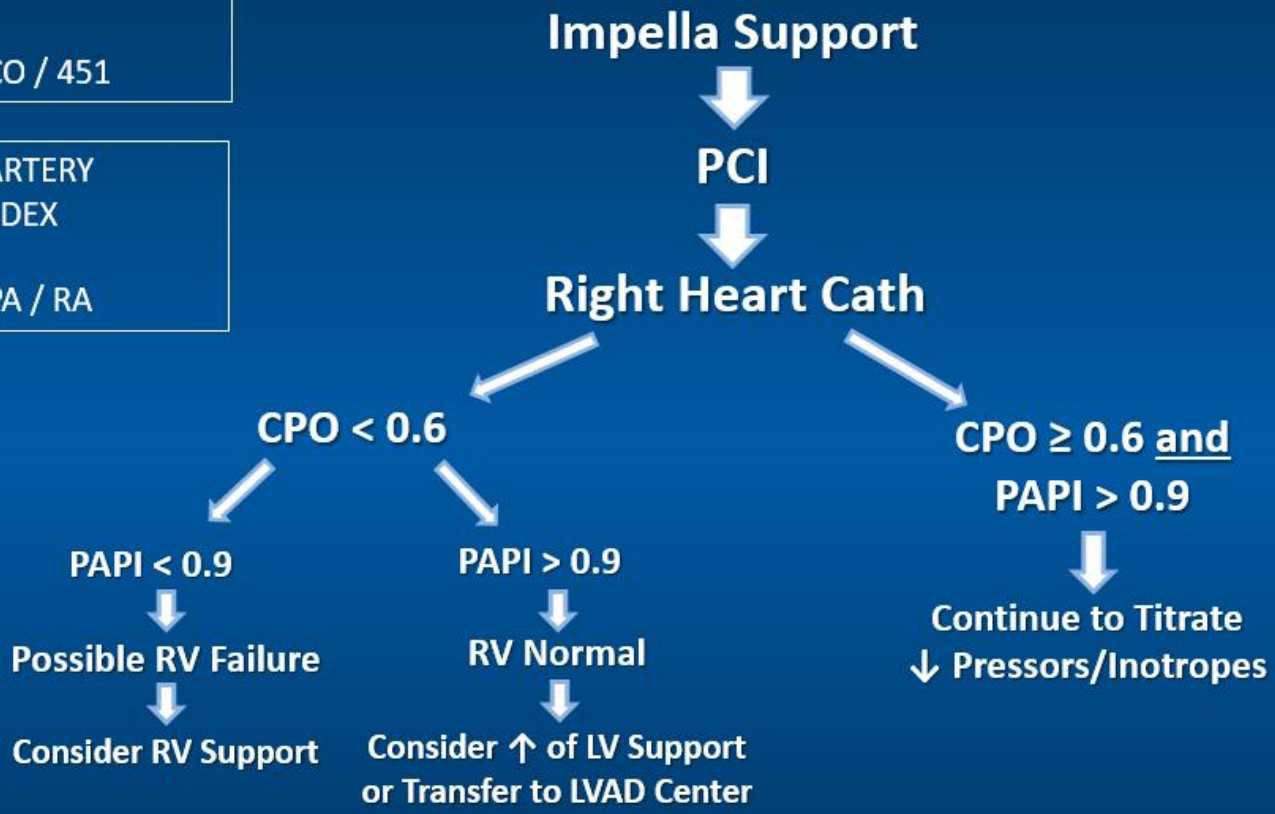


CARDIAC POWER OUTPUT

CPO = MAP x CO / 451

PULMONARY ARTERY PULSATILITY INDEX

PAPI = sPA – dPA / RA



The National Cardiogenic Shock Initiative

88 Patients

Excluded

23 patients
- 4 unwitnessed arrest w/ delay CPR
- 2 Septic Shock
- 1 Aortic Stenosis
- 1 massive PE
- 5 patients without evidence of shock
  - Procedural complication
  - Decompensated Heart Failure (2)
  - Hypertensive Emergency
- 9 patients with IABP prior to MCS

65 AMICS w/ Early MCS Support

Out of Hospital Cardiac Arrest – 10/65 (15%)
In Hospital Cardiac Arrest – 17/65 (31%

Pre-PCI Impella 48/65 (74%)
IP/Post Impella 17/65 (26%)

Door to Balloon (STEMI) 98.3 min
Door to Support 91.5 min

74% Survival (N=48/65)

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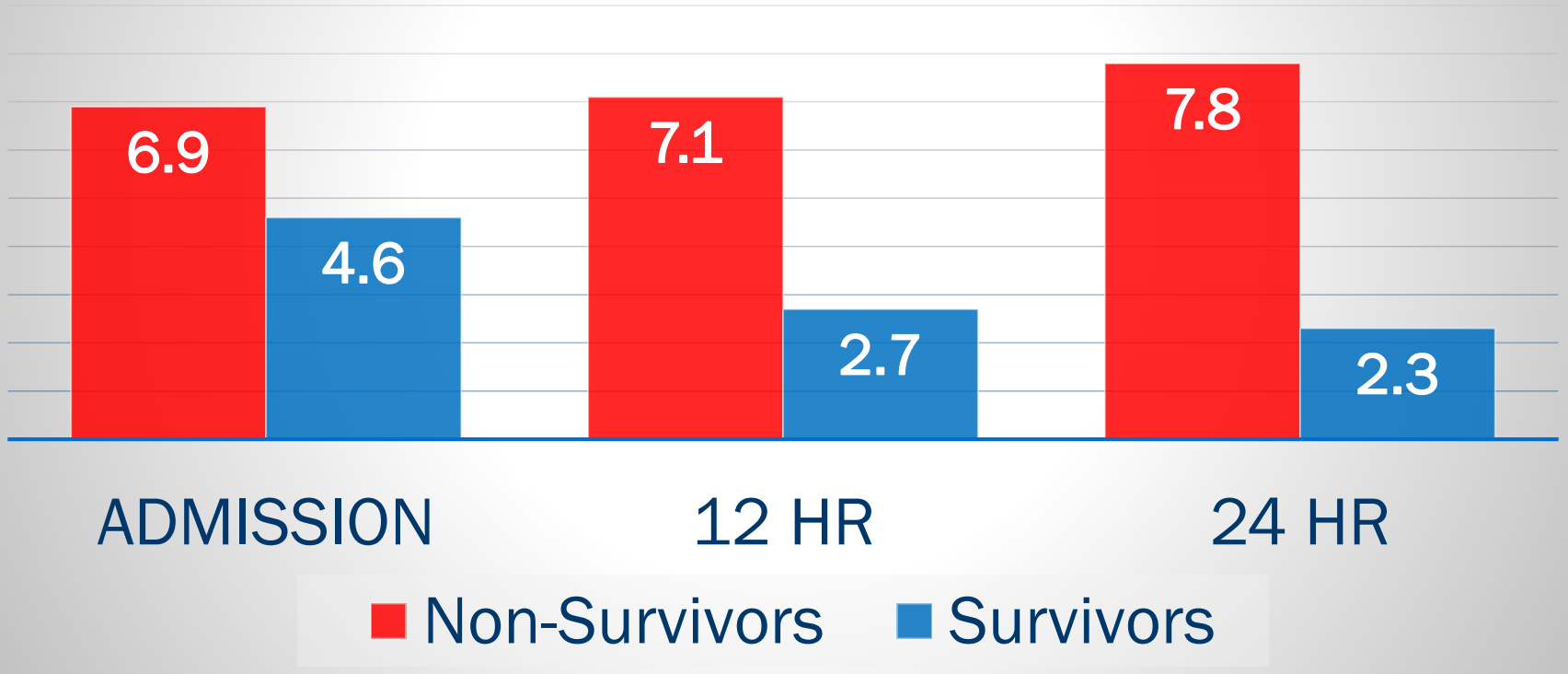
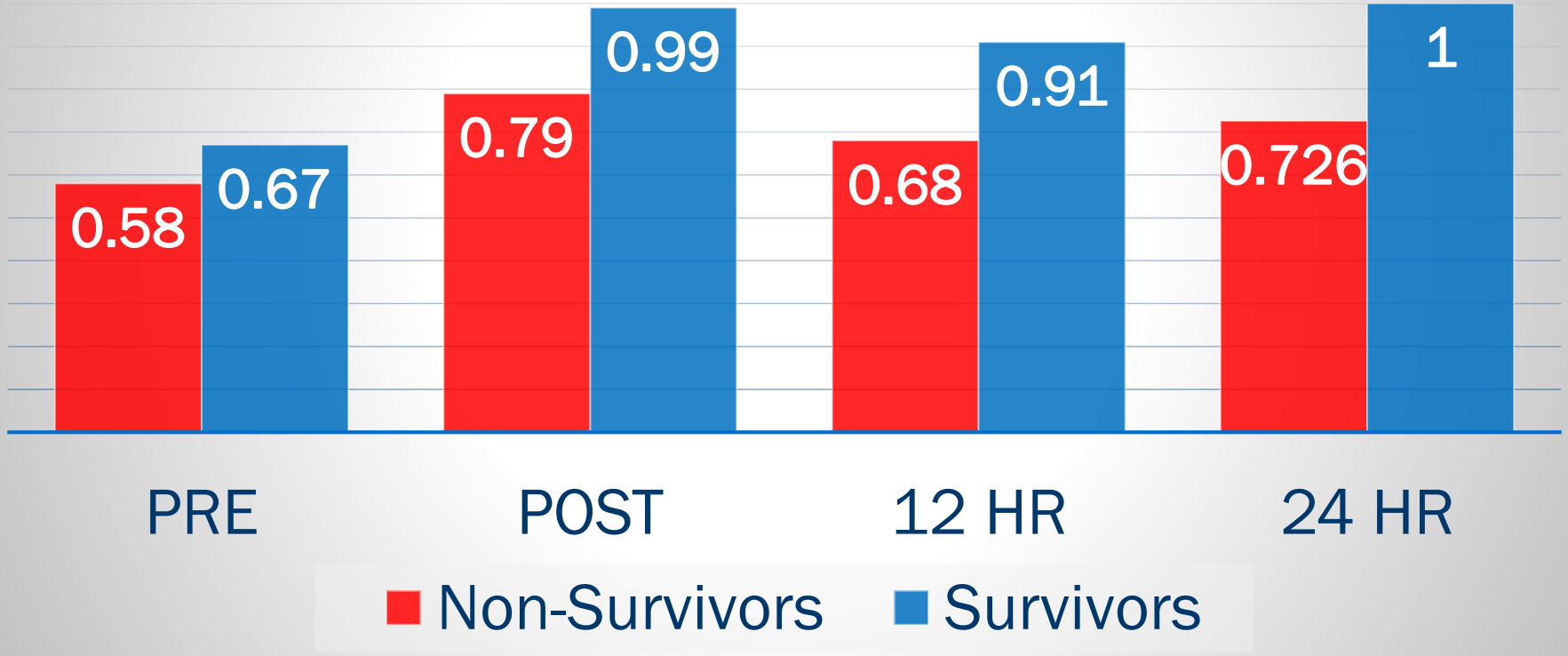
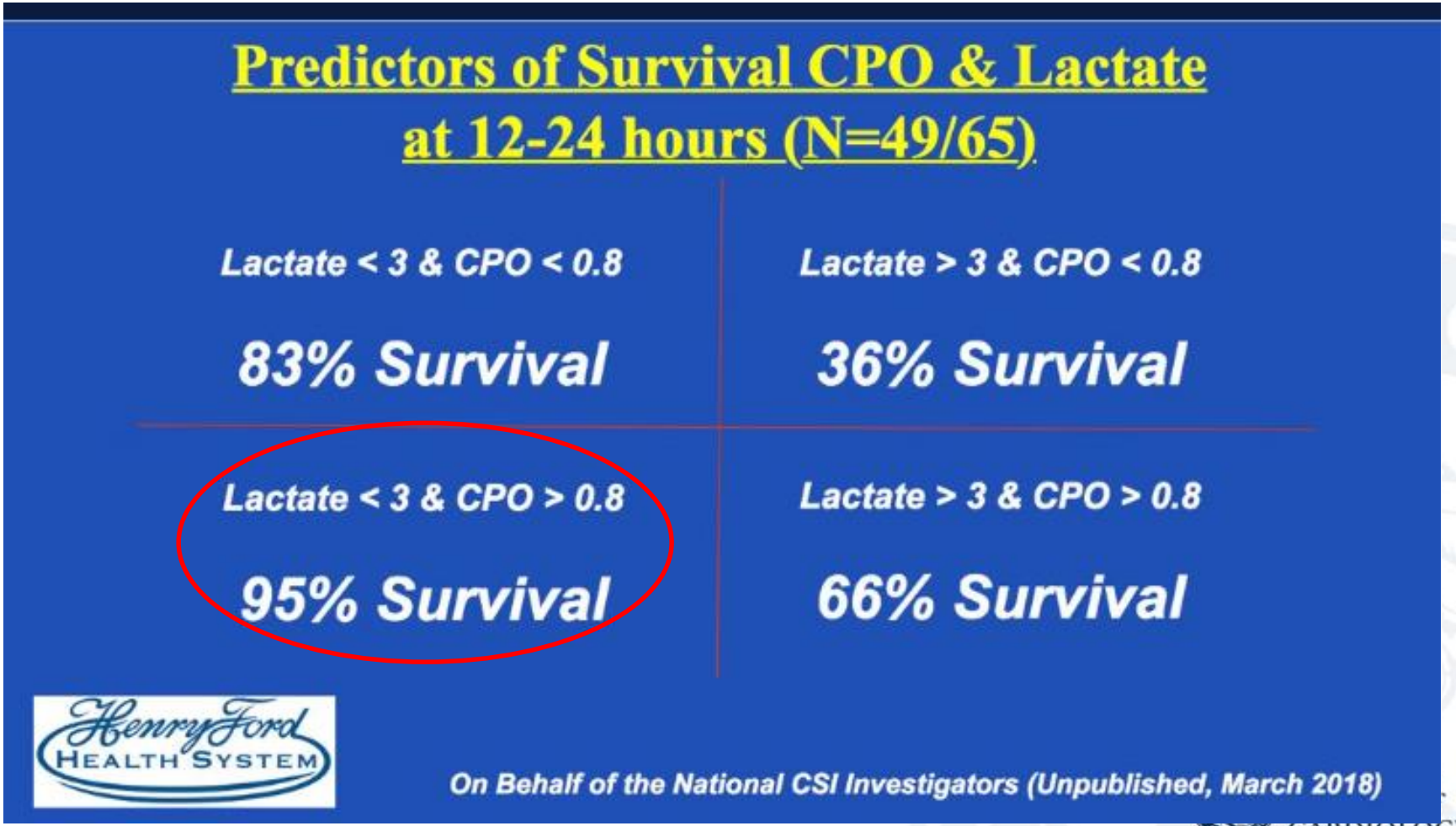
LACTATE LEVELS ACCORDING TO SURVIVAL

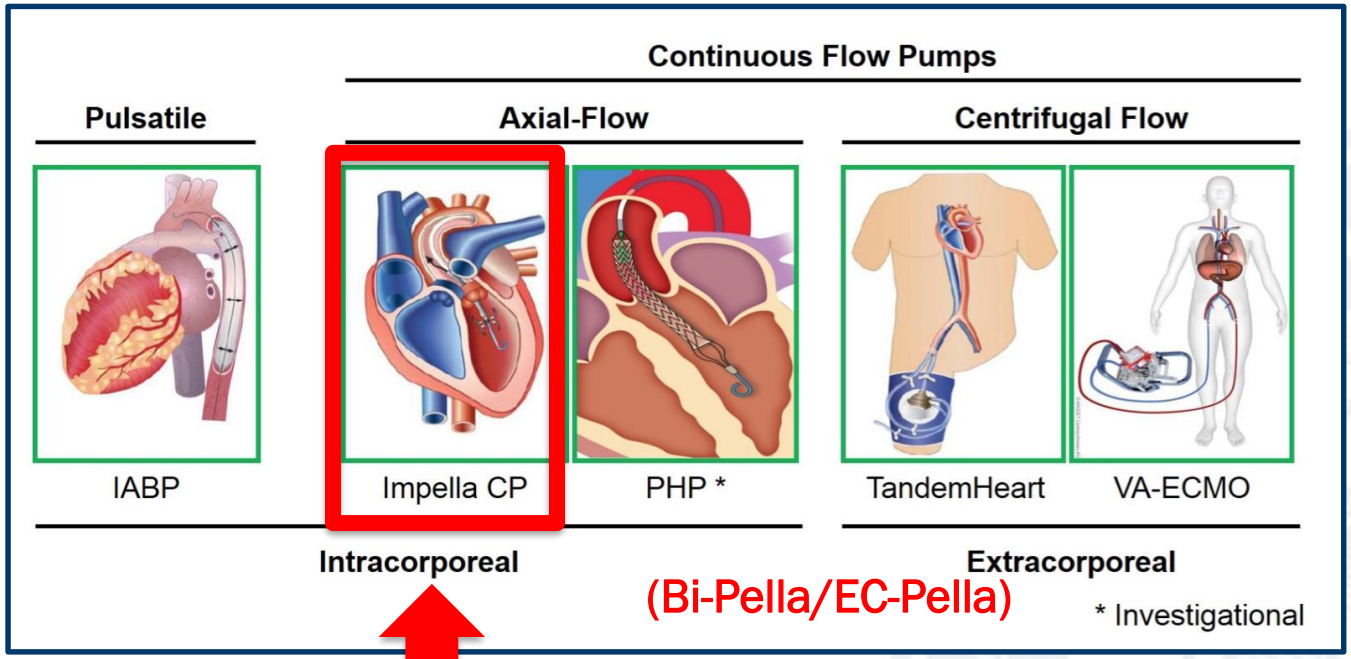


CARDIAC POWER OUTPUT ACCORDING TO SURVIVAL




Predictors of Survival CPO & Lactate at 12-24 hours (N=49/65)
Lactate < 3 & CPO < 0.8
83% Survival
Lactate > 3 & CPO < 0.8
36% Survival
Lactate < 3 & CPO > 0.8
95% Survival
Lactate > 3 & CPO > 0.8
66% Survival
Henry Ford Health System
On Behalf of the National CSI Investigators (Unpublished, March 2018)

MCS Options



Minimal benefit in clinical trials

Labor intensive

No LV unloading

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A Practical Approach to Mechanical Circulatory Support in Patients Undergoing Percutaneous Coronary Intervention

An Interventional Perspective

Tamara M. Atkinson, MD,[a] E. Magnus Ohman, MD,[b] William W. O'Neill, MD,[c] Tanveer Rab, MD,[d]
Joaquin E. Cigarroa, MD,[a] on behalf of the Interventional Scientific Council of the American College of Cardiology

(J Am Coll Cardiol Intv 2016;9:871–83)

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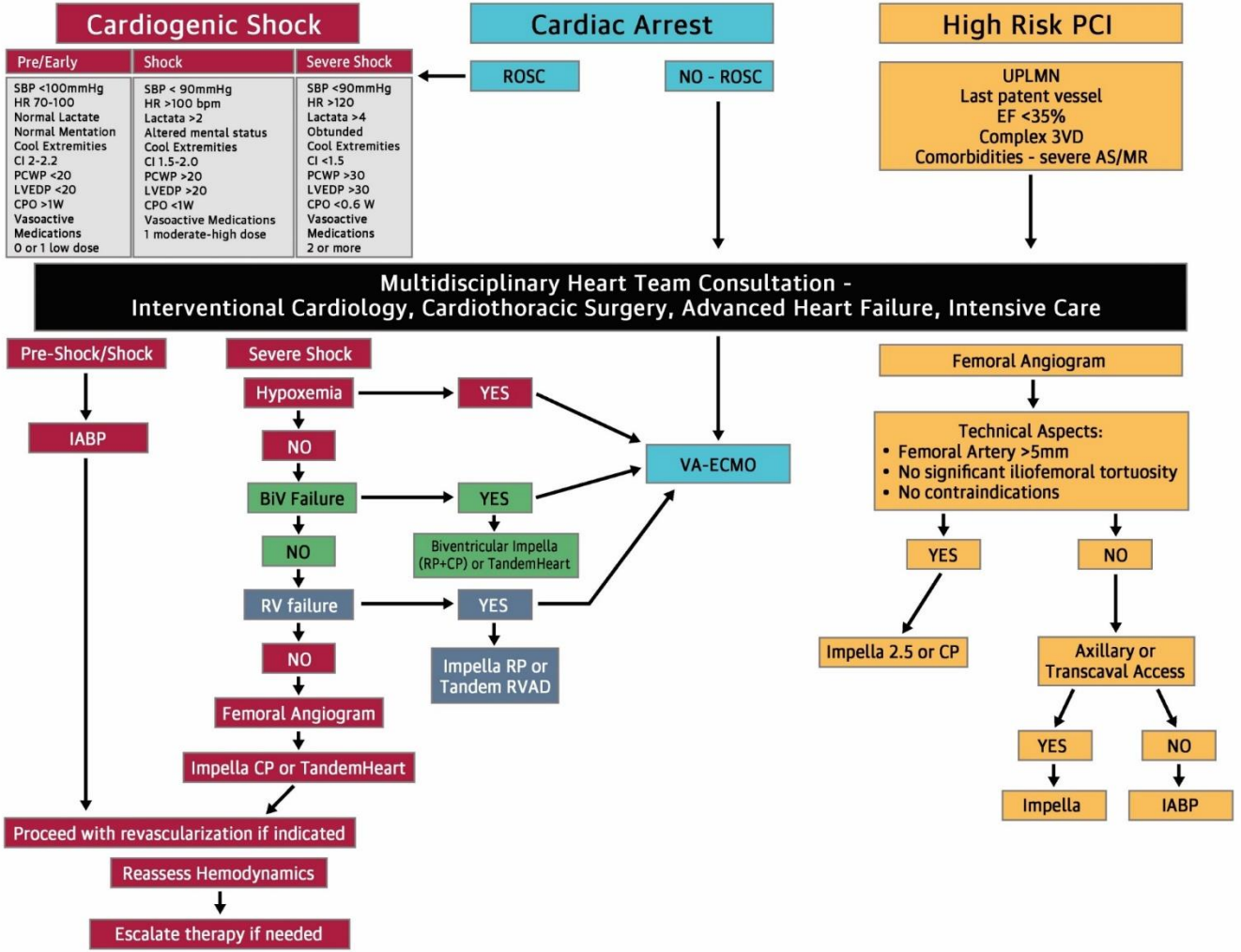
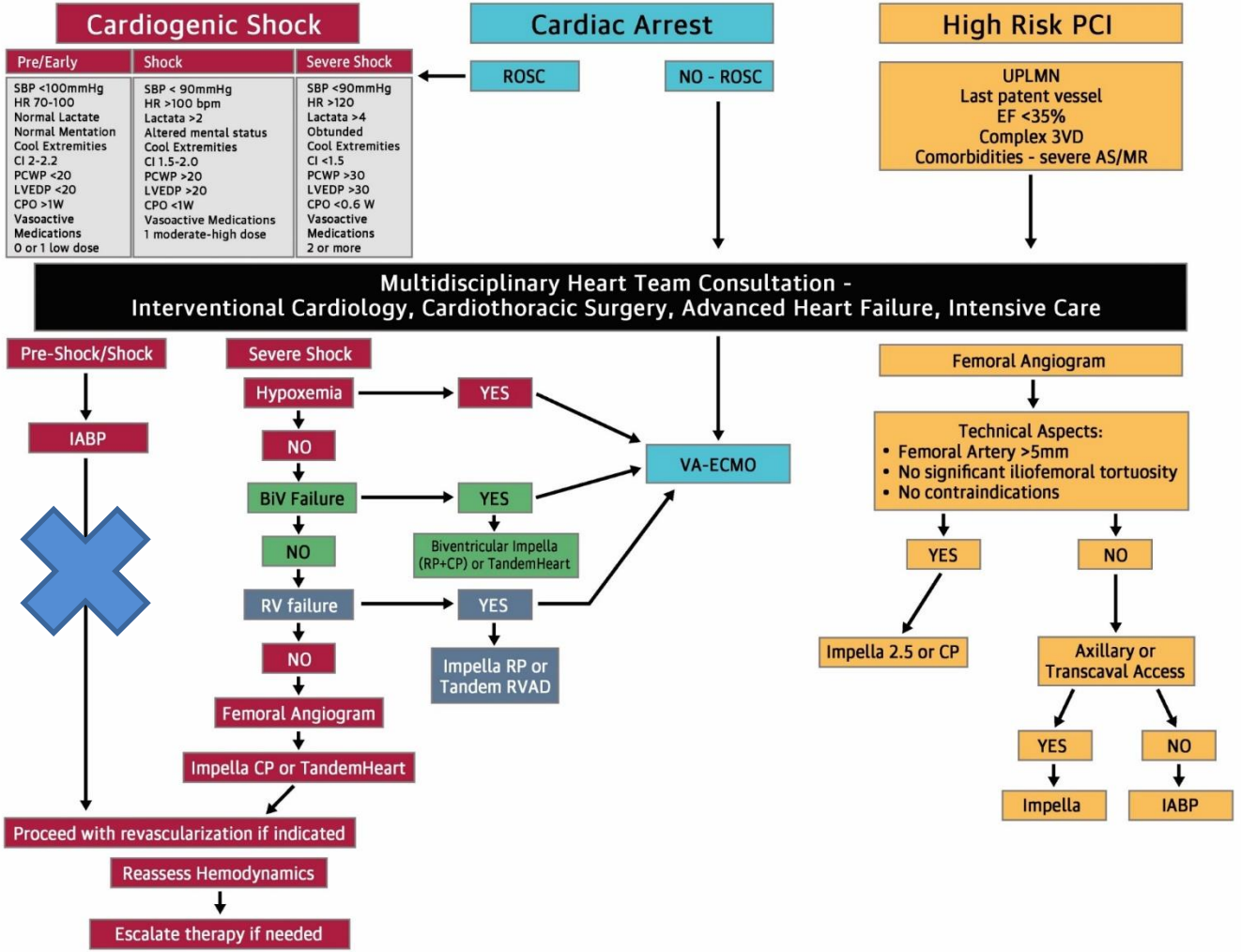
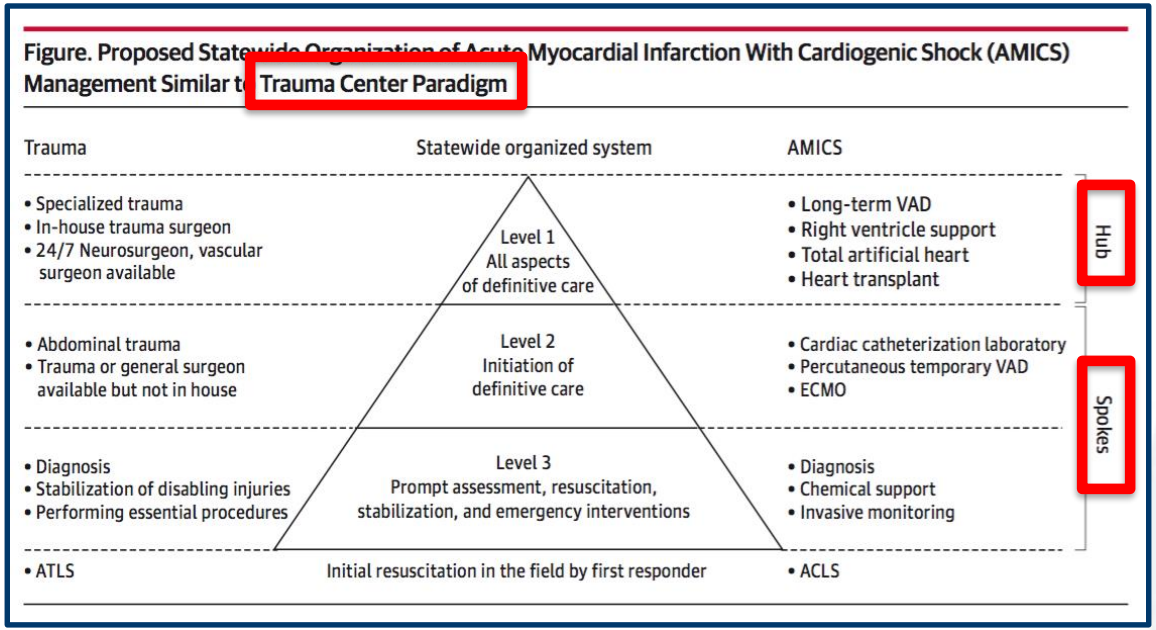




Call for Organized Statewide Networks for Management of Acute Myocardial Infarction–Related Cardiogenic Shock



- *Network of partners (spoke and hub)*
  - *EMS/ER (rapid triage/transport)*
    - *Access/communications*
      - *High-volume*
- *Specialty care (center of excellence)*
- *Advanced (and integrated) therapies*
  - *Common set of providers*
    - *Quality (ongoing QI)*
    - *Data management*
  - *Administration, oversight, leadership…*
    - *Research*

Nathens et al Lancet 2004
Ko et al www.acc.org 2015
Shaefi et al JAHA 2015
Tchantchaleishvili et al JAMA Surgery 2015
Engelman et al J Thorac Cardiovasc Surg 2017

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Shock Team Activation

- *"One-call" system*
- *CCU Critical Care, CCU Cardiology, Cardiac Surgery, Interventional Cardiology, Advanced Heart Failure*
- *Rapid, collaborative decision-making*
- *"Bedside" or "Virtual" consultation*
- *Consensus plan of care*
- *Early MCS (as appropriate)*
- *Hemodynamic-guidance*
- *Formalized process*

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Conclusions

- There is increasing mortality in cardiogenic shock complicating myocardial infarction
- There is very low use of LV support
- IABP and inotropes increase mortality
- *Mechanical Hemodynamic Support* in Cardiogenic Shock Should be Used in All Patients!

AND SHOULD BE PLACED BEFORE PCI

Questions?

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