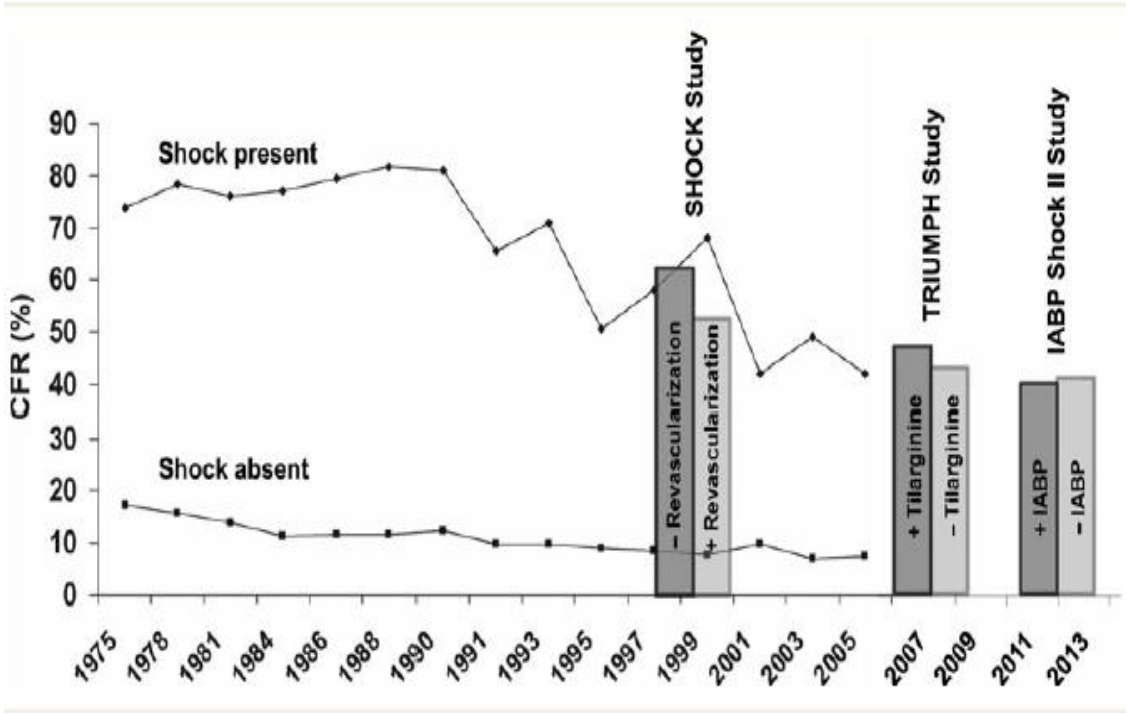
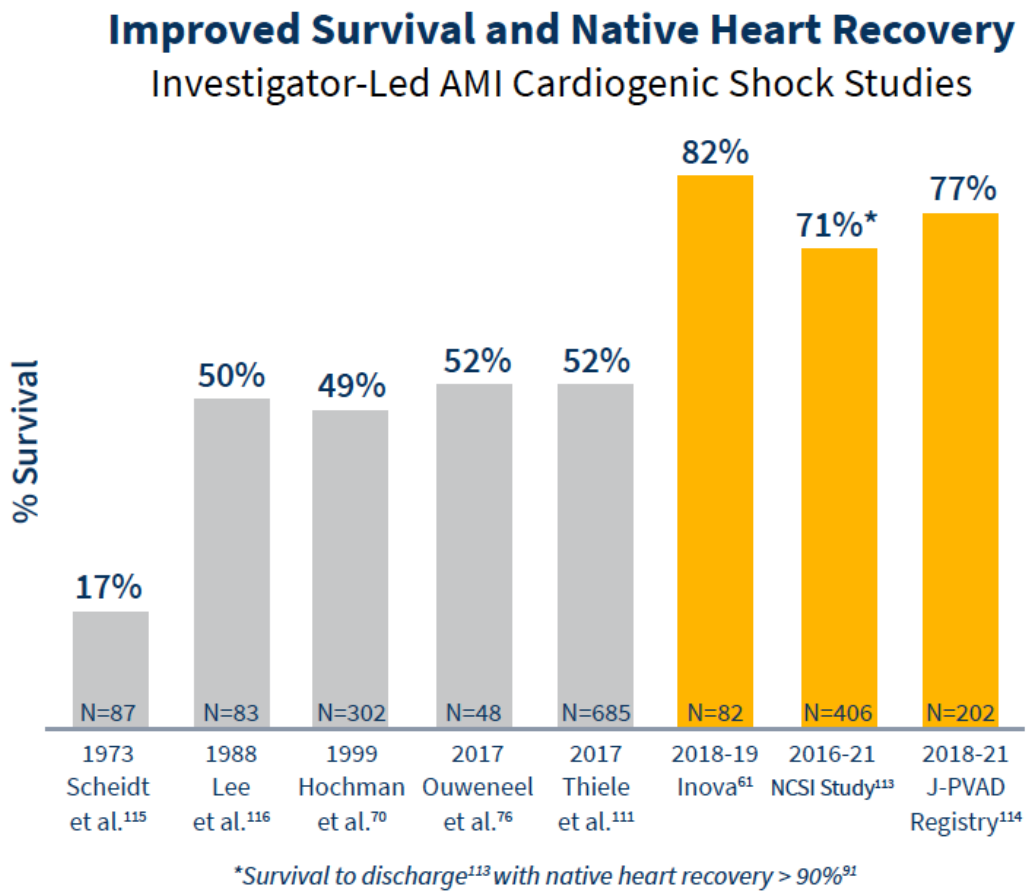
תמיכה מלעורית באי ספיקת לב אקוטית

ד"ר קלמנוביץ ערן
טיפול נמרץ לב, מרכז רפואי שמיר

Introduction

Despite advances in coronary revascularization and widespread use of primary percutaneous interventions, cardiogenic shock complicating an AMI- CS remains a clinical challenge with high mortality rates.

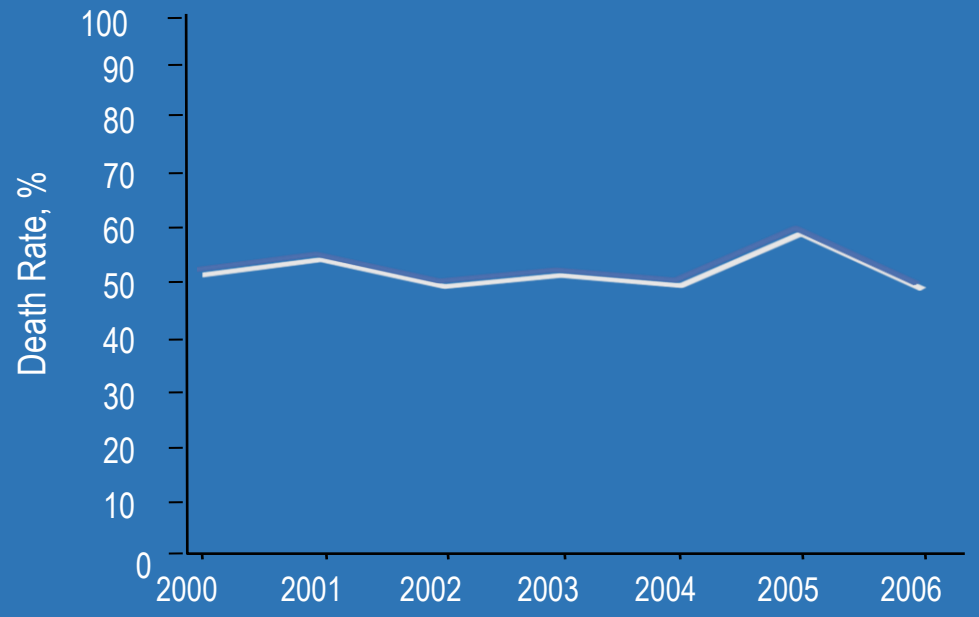




Cardiogenic Shock Remains Leading Cause of Mortality in Acute Myocardial Infarction

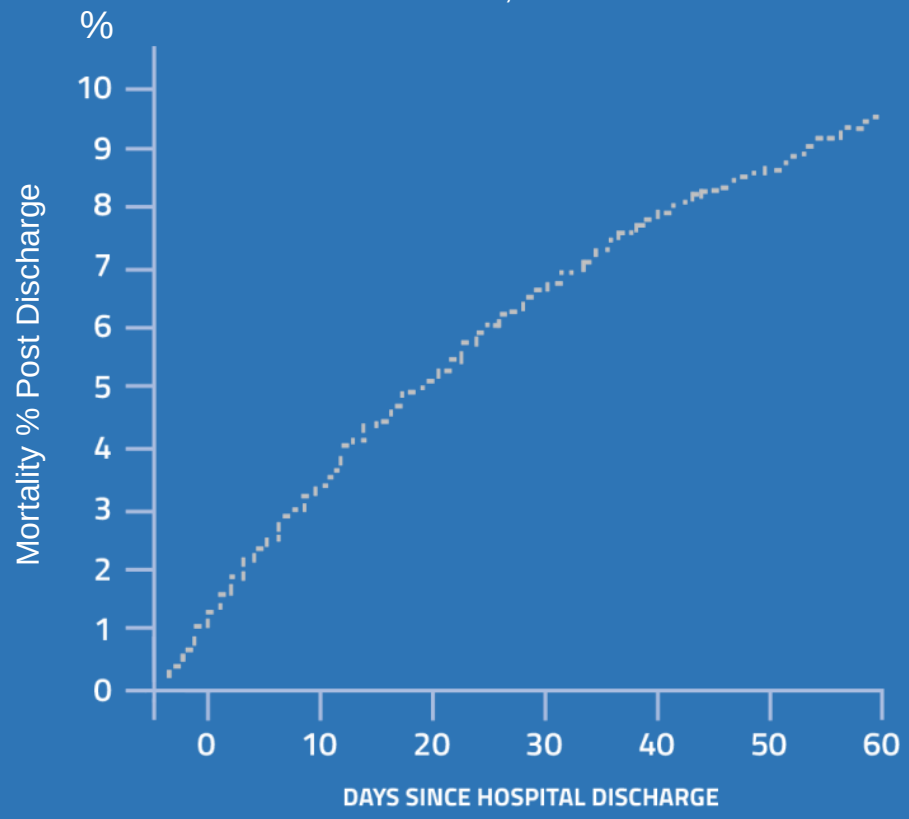
High In-Hospital Mortality During AMI Cardiogenic Shock[1]

N = 23,696



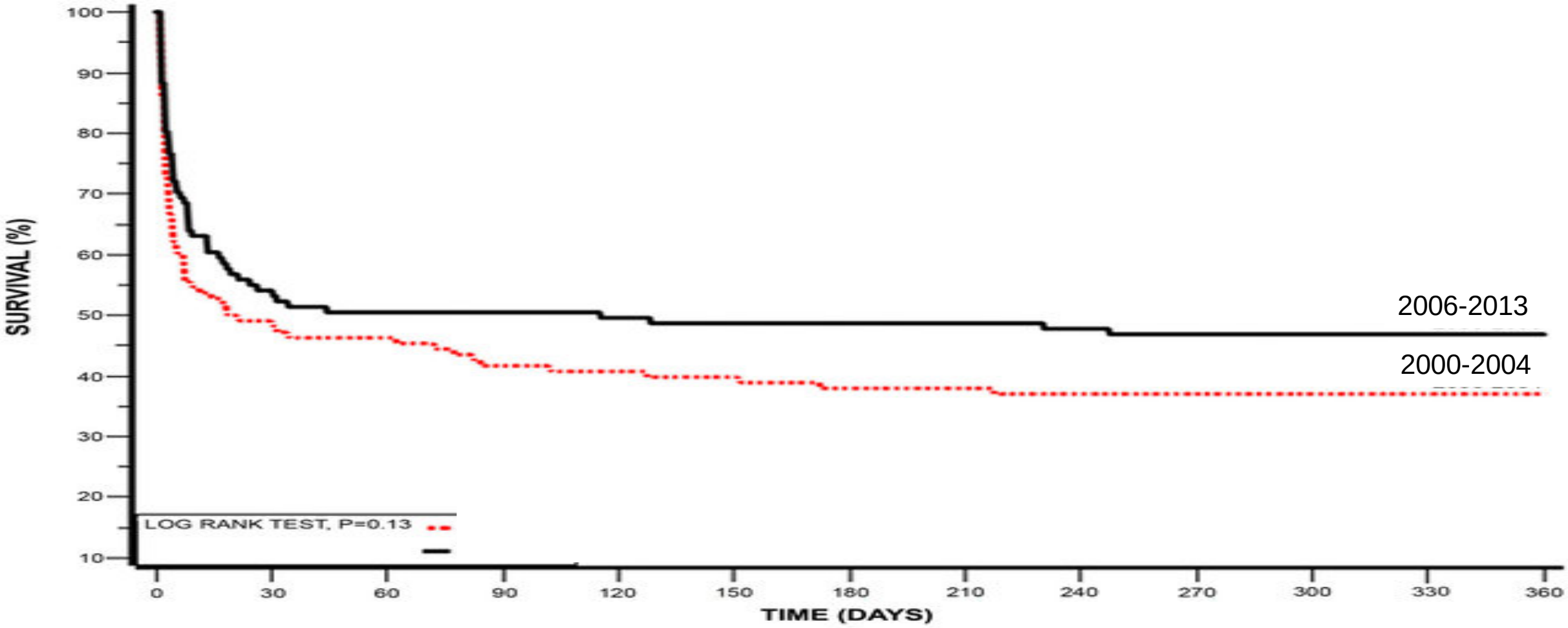
… and Ongoing Hazard Post Discharge After AMI Cardiogenic Shock[2]

N = 112,668



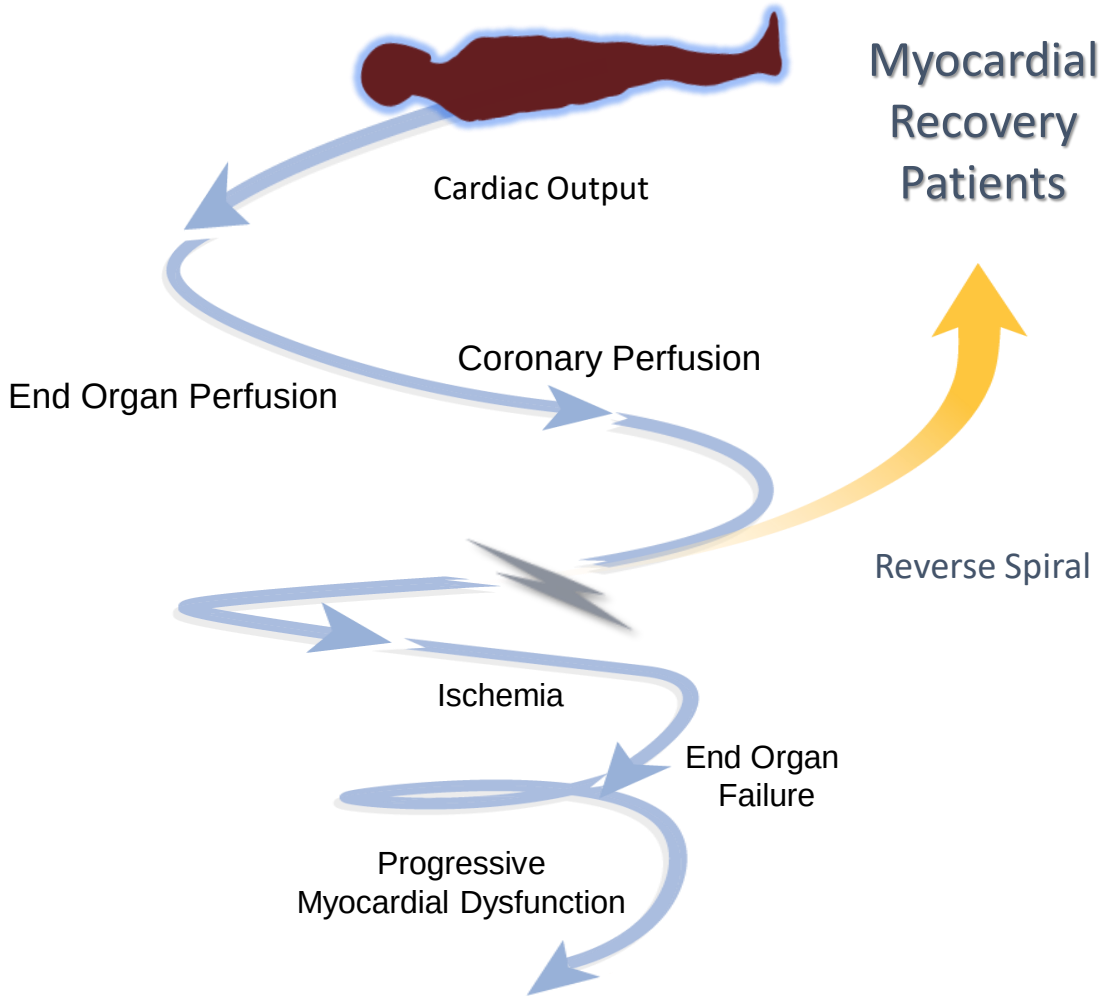
1. Jeger et al. *Ann Intern Med.* 2008
2. Patel et al. *JACC* 2016 NCDR Registry

Trends in ACS complicated by cardiogenic shock over the past decade (data from ACSIS)



Reverse the Cardiogenic Shock Spiral

Cardiogenic Shock Identifiers (Protocol elements)
- SBP <90 mmHg or on Inotropes/Pressors
- Cold, clammy, tachycardia
- Lactate elevated >2 mmol/L



IMP-1227 EU-EN v3

How to define Cardiogenic shock

Clinical definition	SHOCK Trial[2]	IABP-SHOCK II[1]	ESC heart failure guidelines[6]
Cardiac disorder that results in both clinical and biochemical evidence of tissue hypoperfusion	Clinical criteria: MI complicated by left ventricular dysfunction SBP <90 mm Hg for ≥30 min or support to maintain SBP ≥90 mm Hg and end-organ hypoperfusion (urine output <30 mL/hour or cool extremities) Haemodynamic criteria: Cardiac Index ≤2.2 L/min/m^2 and PCWP ≥15 mm Hg	Clinical criteria: Acute MI SBP <90 mm Hg or ≥30 min or catecholamines to maintain SBP >90 mm Hg and clinical pulmonary congestion and impaired end-organ perfusion (altered mental status, cold/clammy skin and extremities, urine output <30 mL/hour, or lactate >2.0 mmol/L)	Clinical criteria: SBP <90 mm Hg with adequate volume and clinical or laboratory signs of hypoperfusion Clinical hypoperfusion: Cold extremities, oliguria, mental confusion, dizziness, narrow pulse pressure Laboratory hypoperfusion: Metabolic acidosis, elevated serum lactate, elevated serum creatine

ESC, European Society of Cardiology; IABP, intra-aortic balloon pump; MI, myocardial infarction; PCWP, pulmonary capillary wedge pressure; SBP, systolic blood pressure; SHOCK, SHould we emergently revascularise Occluded Coronaries for cardiogenic shocK.

Shock is Variable ?

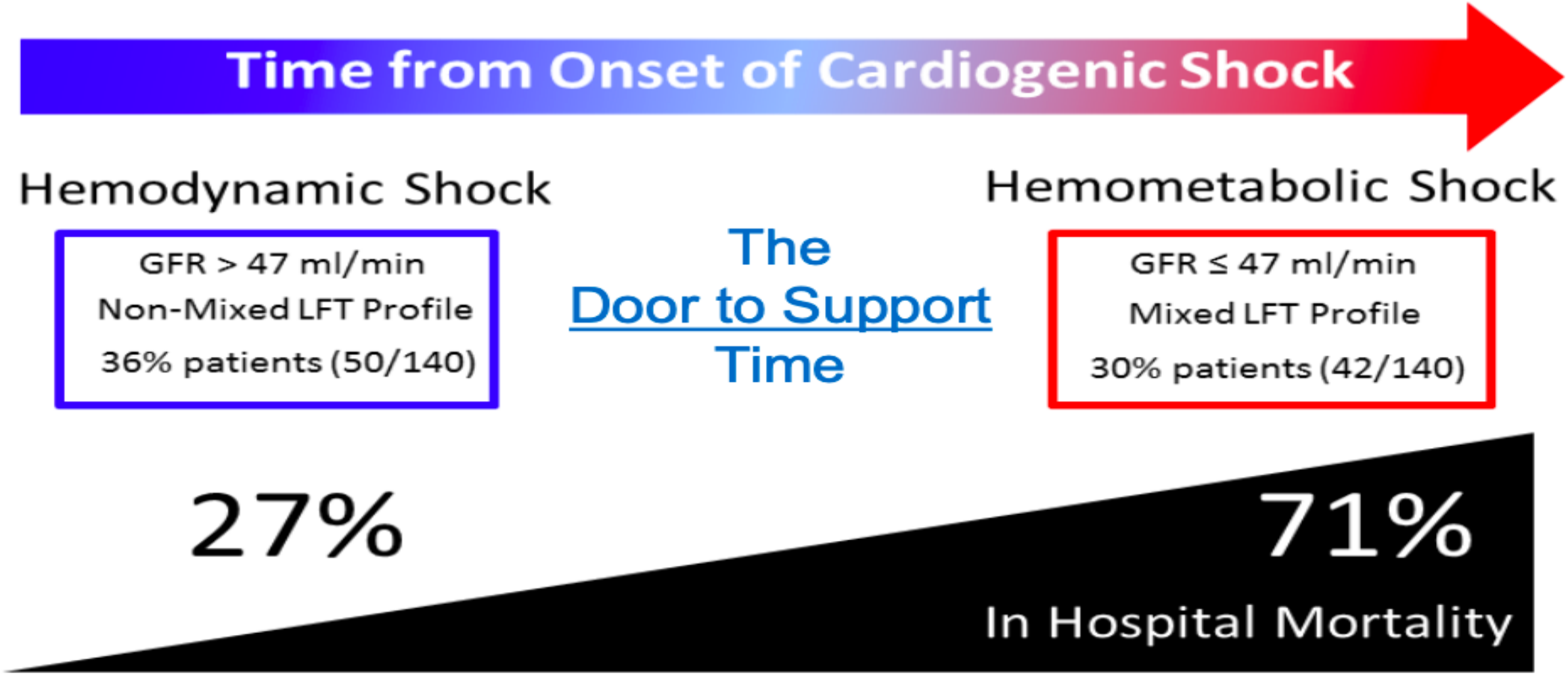
IMPRESS Trial

- SBP < 90 for 30 minutes
- Pressors to SBP > 90
- All pts intubated
- 90% cardiac arrest
- 20 minutes to ROSC
- 70-80% induced hypothermia
- Signs of Hypoperfusion
- (Lactate > 7-8, pH 7.1-7.2)

IABP SHOCK II Trial

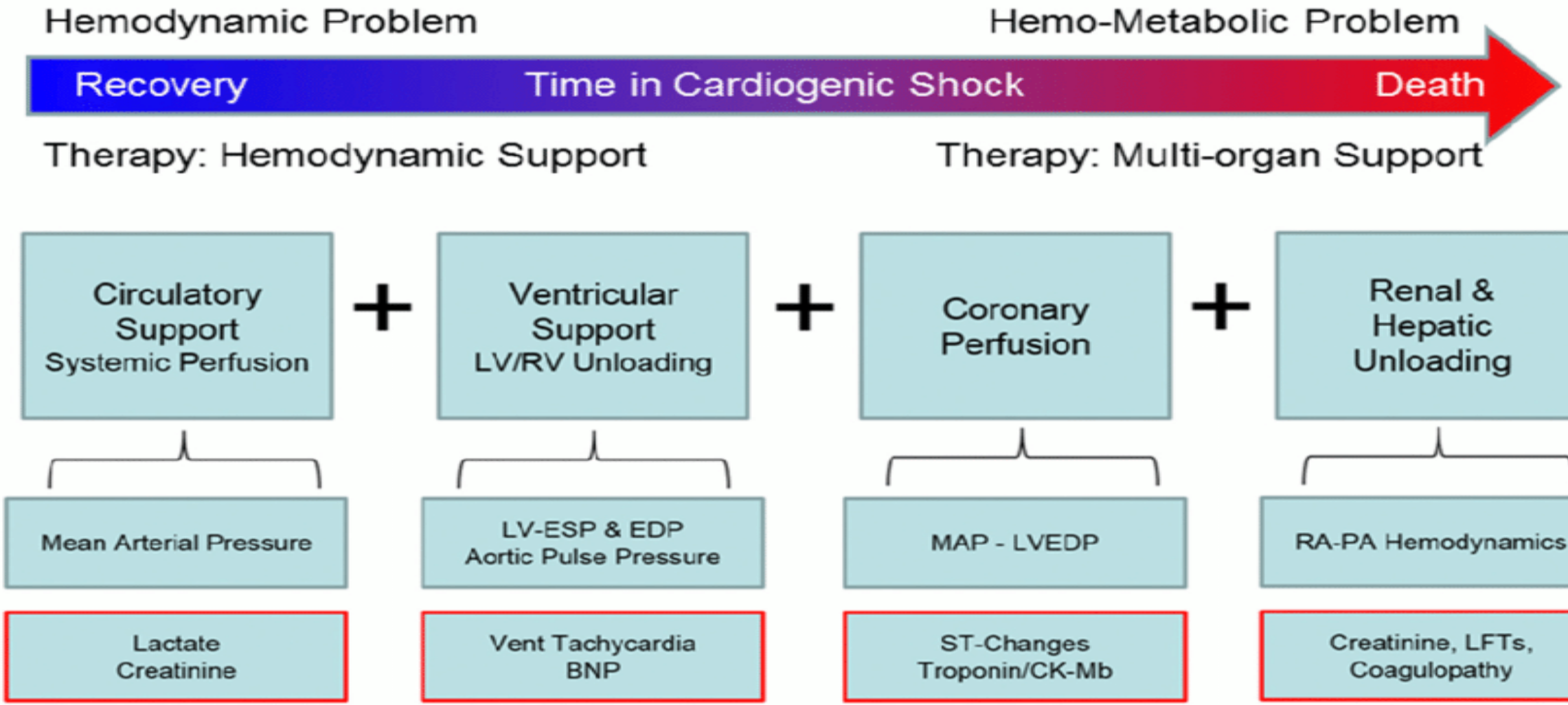
- SBP < 90 for 30 minutes
- Pressors to SBP > 90
- Pulmonary Congestion
- Signs of Hypoperfusion
- Lactate > 2, Alt mental status or Urine Output < 30/hour

One size does not fit all**: Lack of common language** has impeded the advancement of research on optimal diagnosis & management of these patients

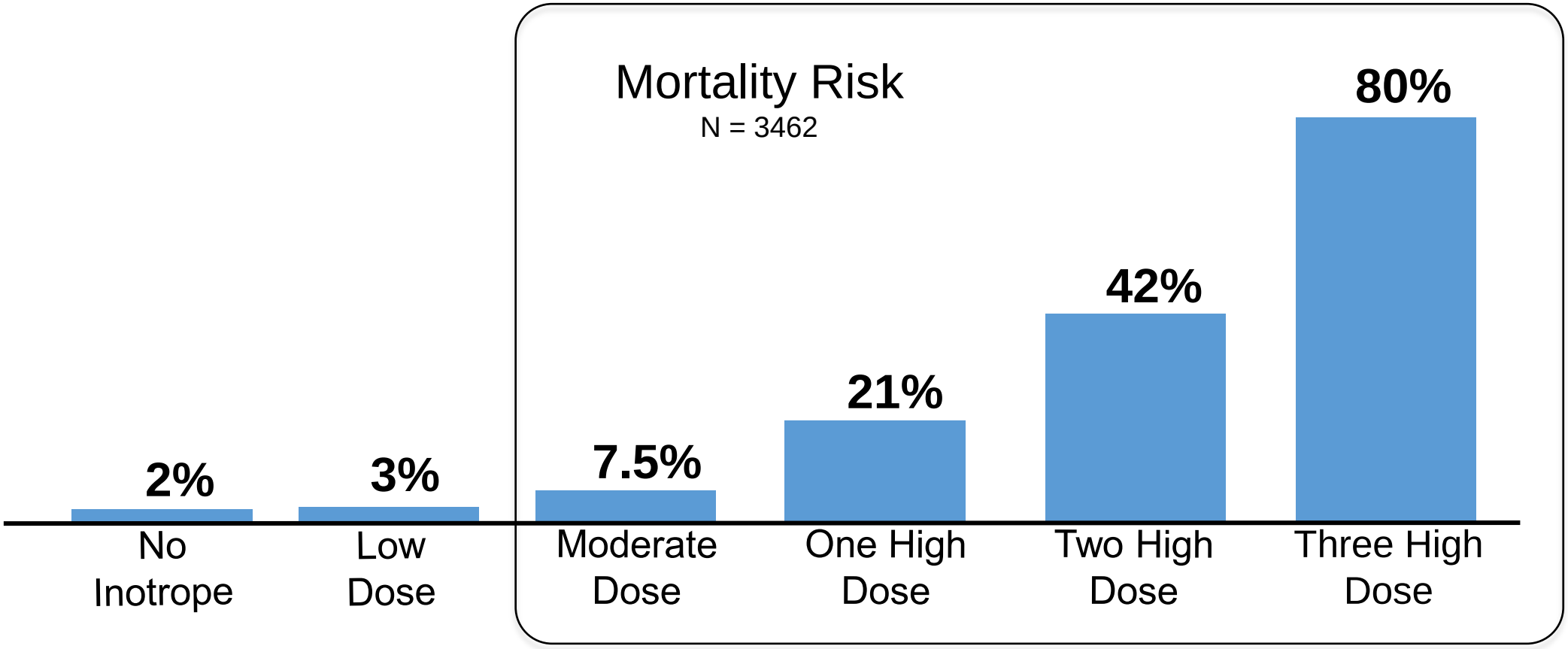


Morine & Kapur et al. Cardiogenic Shock Working Group

Treatment's Goals



High dose Vasopressors/inotropes Associated With Increased In-Hospital mortality

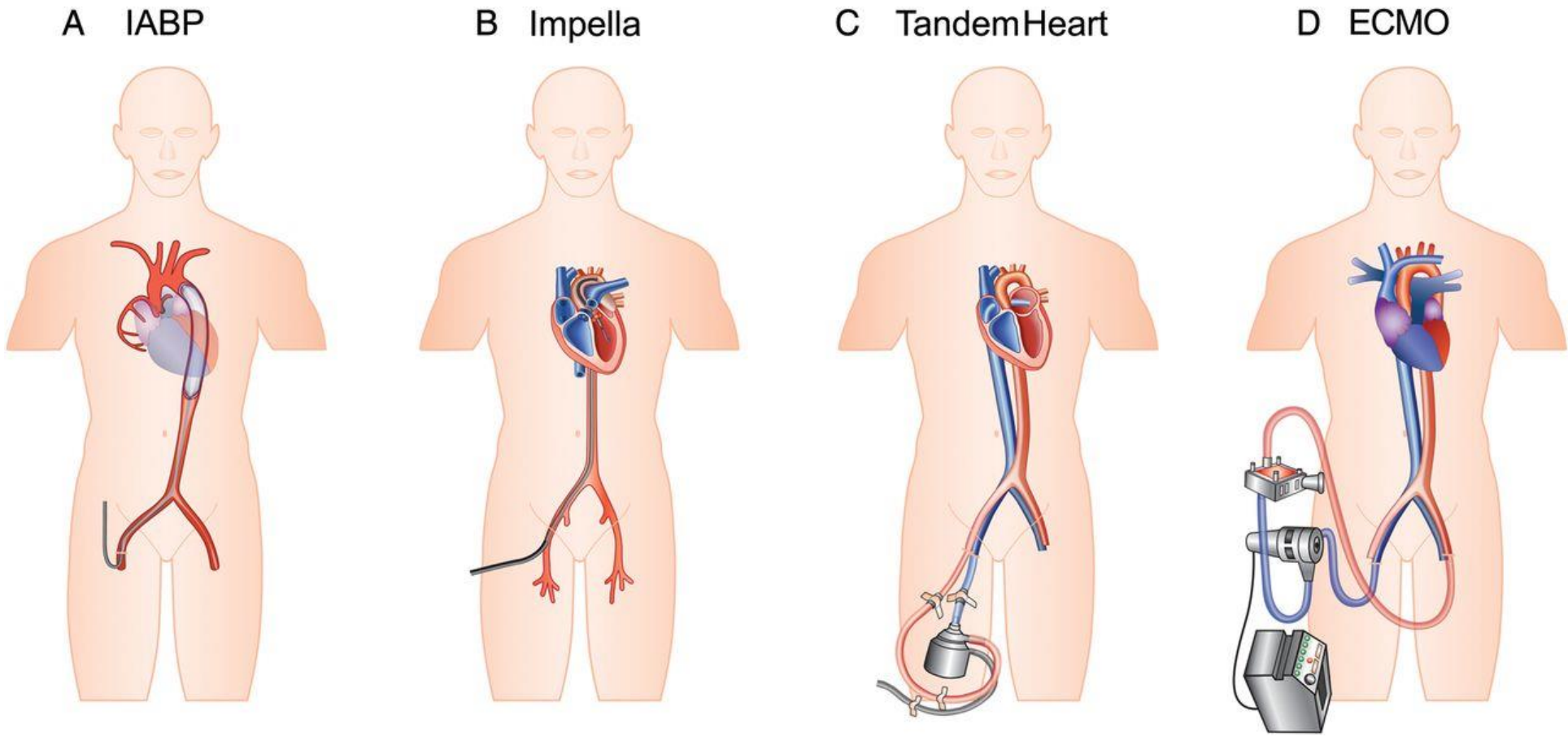


Samuels LE et al , J Card Surg. 1999

What is Mechanical circulatory support ?

- What is the ideal device ?
  - Enable both hemodynamic support and myocardial protection.
  - A percutaneous approach is preferable to provide for a quick and easy deployment.
  - Associated with a low complication rate (limb ischemia, embolization of atherosclerotic and/or thrombotic material, stroke, infection and hemolysis)
- Different technical strategies:
  - Improve cardiac output
  - Unload the critically damaged left ventricle by either afterload or pre-load reduction (i.e. pressure or volume unloading)
  - LV, RV or Both

Percutaneous Mechanical Support Options

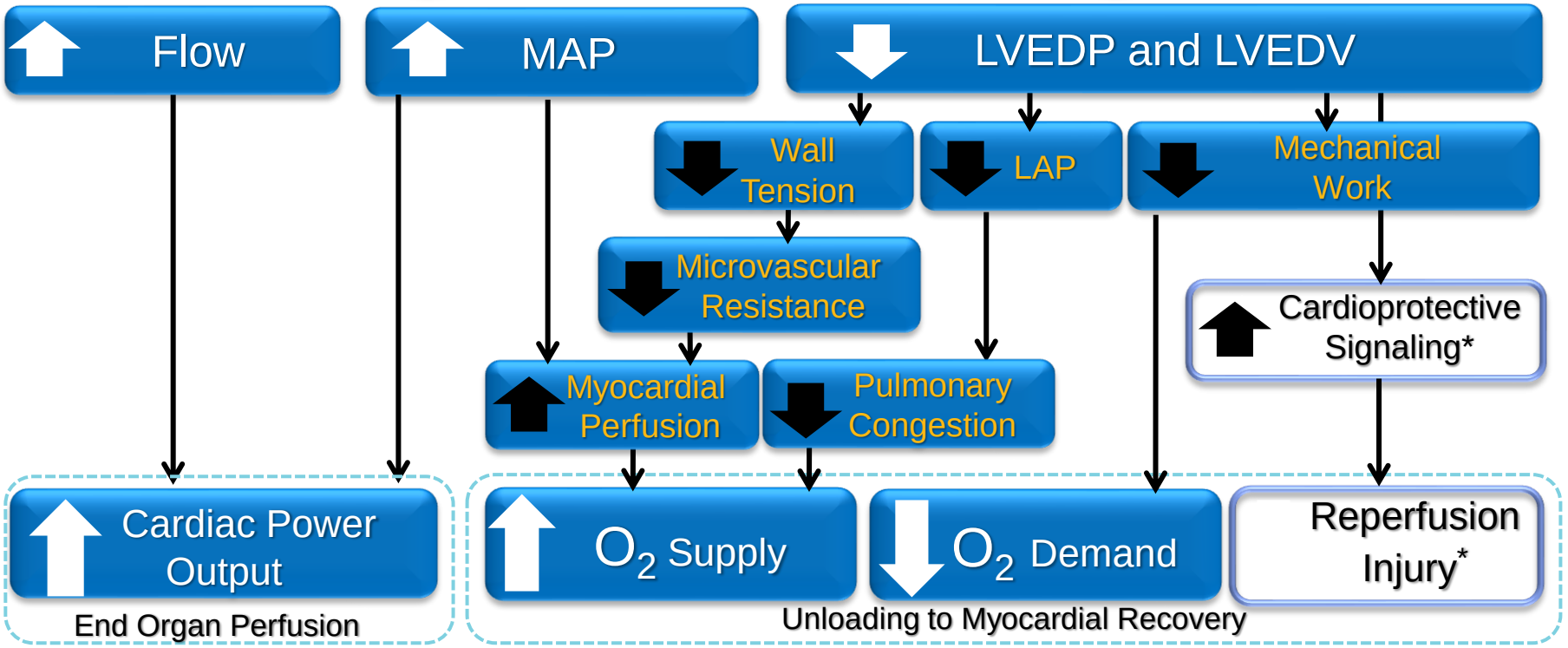


Temporary Circulatory Support (TCS) includes IABP, Impella Family, Tandem Heart, and ECMO

IMPELLA® HEART PUMP – QUICK GLANCE

	Impella 5.5® with SmartAssist®	Impella 5.0®	Impella LD®	Impella 2.5®	Impella CP®	Impella CP® with SmartAssist®
Catheter size	9 Fr (same size for all left-sided Impella heart pumps)					
Circulatory support	High-flow			Partial		
Placement measurement	Fiber optic sensor	Differential pressure sensor		Fluid-filled pressure lumen		Fiber optic sensor
Flow rate	Peak Flow Up to 5.5 L/min	Up to 5.0 L/min		Up to 2.5 L/min	Peak Flow Up to 4.3 L/min	
Pump size	18 Fr	21 Fr		12 Fr	14 Fr	
Cannula geometry	Curved	Curved, pigtail	Straight	Curved, pigtail		
Insertion method	Axillary or direct, surgical insertion	Arterial cut-down	Direct, surgical insertion	Percutaneous via introducer sheath		
Guidewire thickness	0.018”		N/A	0.018”		

Hemodynamic Effects of Impella® Devices



* Under study

Fincke R, et al. J Am Coll Cardiol 2004
den Uil CA, et al. Eur Heart J 2010
Mendoza DD, et al. Am Heart J 2007
Torgersen C, et al. Crit Care 2009
Torre-Amione G, et al. J Card Fail 2009

Suga H. Am J Physiol 1979
Suga H, et al. Am J Physiol 1981
Burkhoff D, et al. Am J Physiol Heart Circ Physiol 2005
Burkhoff D. Mechanical Properties Of The Heart And Its Interaction With The Vascular System. (White Paper) 2011

Sauren LDC, et al. Artif Organs 2007
Meyns B, et al. J Am Coll Cardiol 2003
Remmelink M, et al. Catheter Cardiovasc Interv 2007
Aqel RA, et al. J Nucl Cardiol 2009
Lam K, et al. Clin Res Cardiol 2009

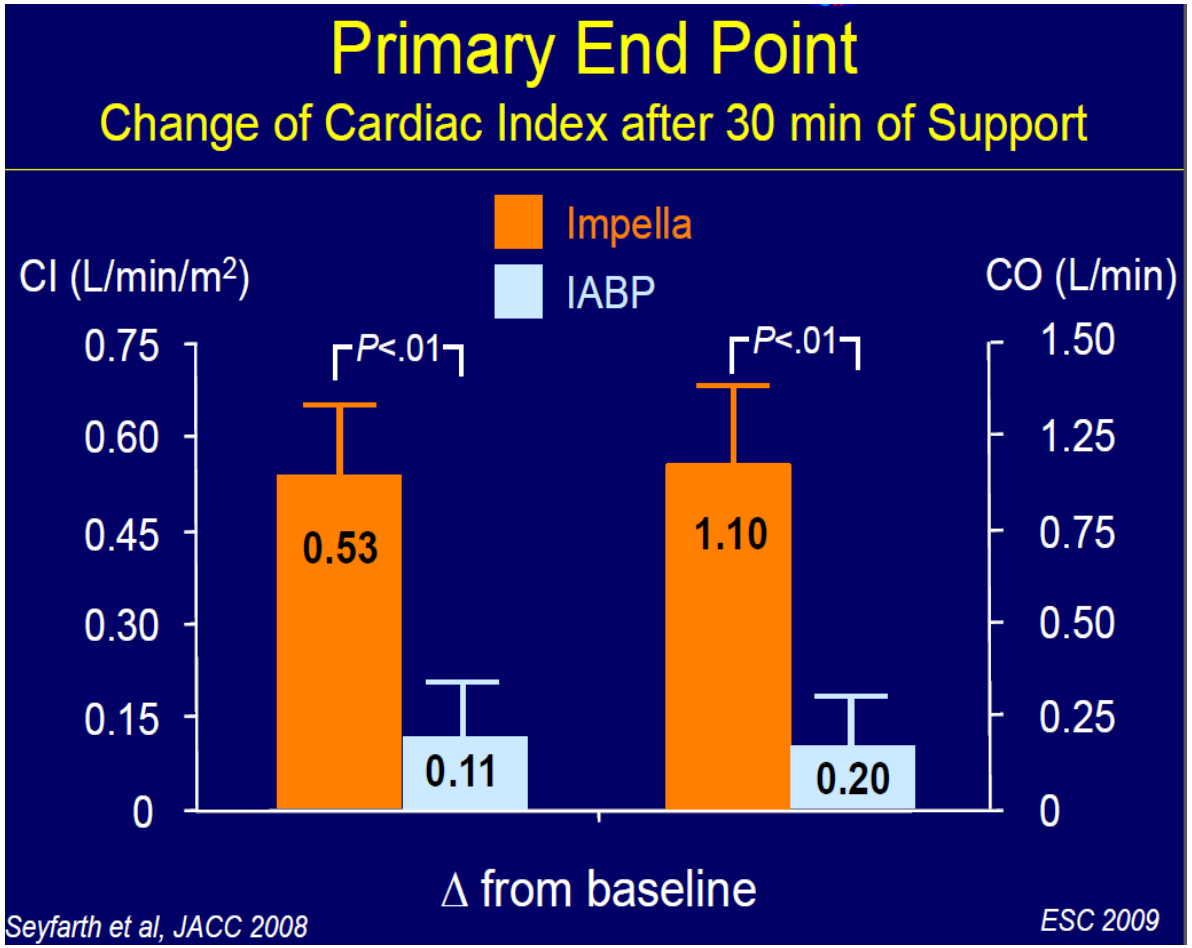
Reesink KD, et al. Chest 2004
Esposito M, et al. J Am Coll Cardiol 2018
Remmelink M, et al. Catheter Cardiovasc Interv 2010
Naidu SS. Circulation 2011
Weber DM, et al. Cardiac Interventions Today Supplement Aug/Sep 2009

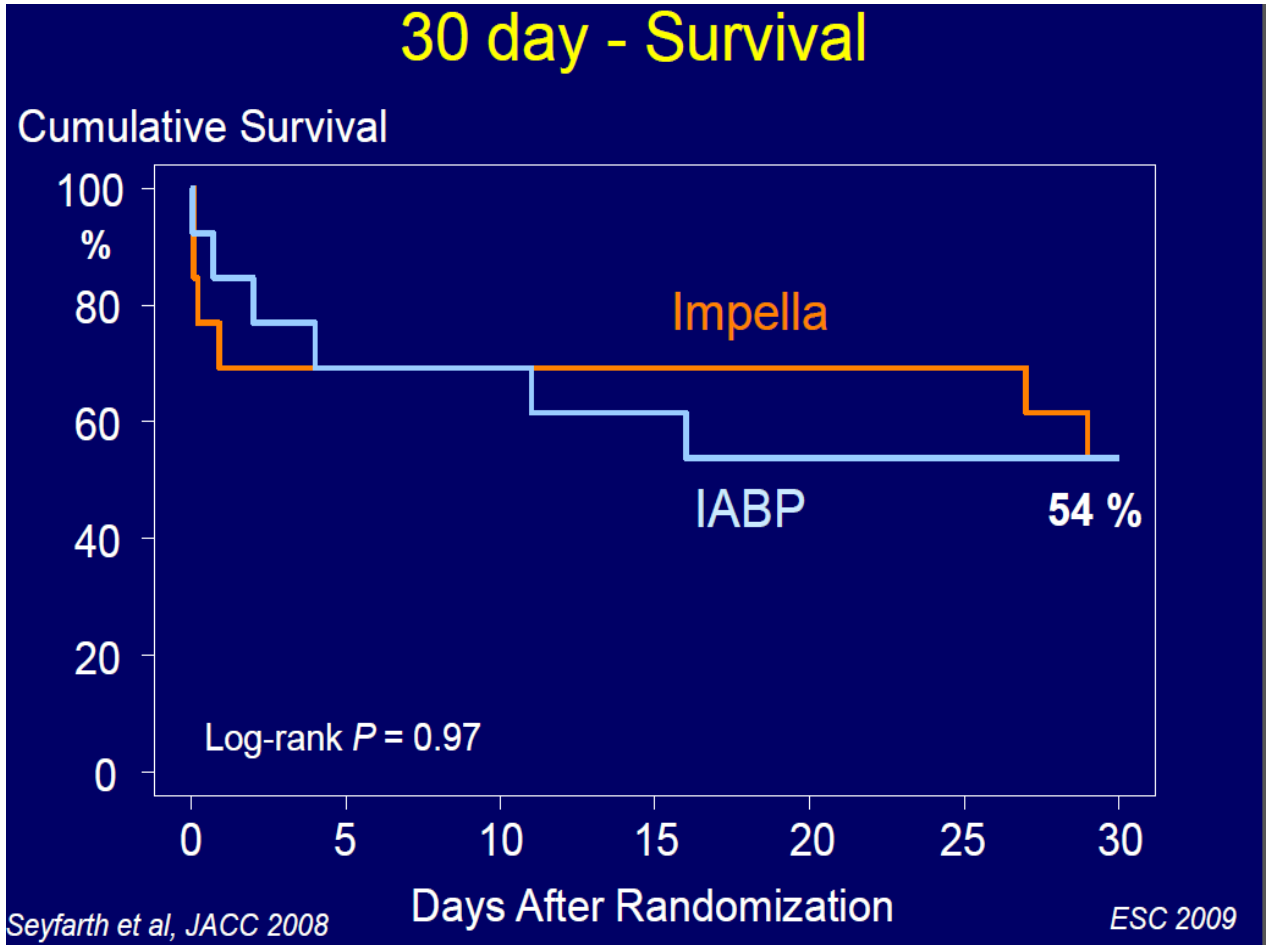
Randomization in Cardiogenic Shock is Challenging

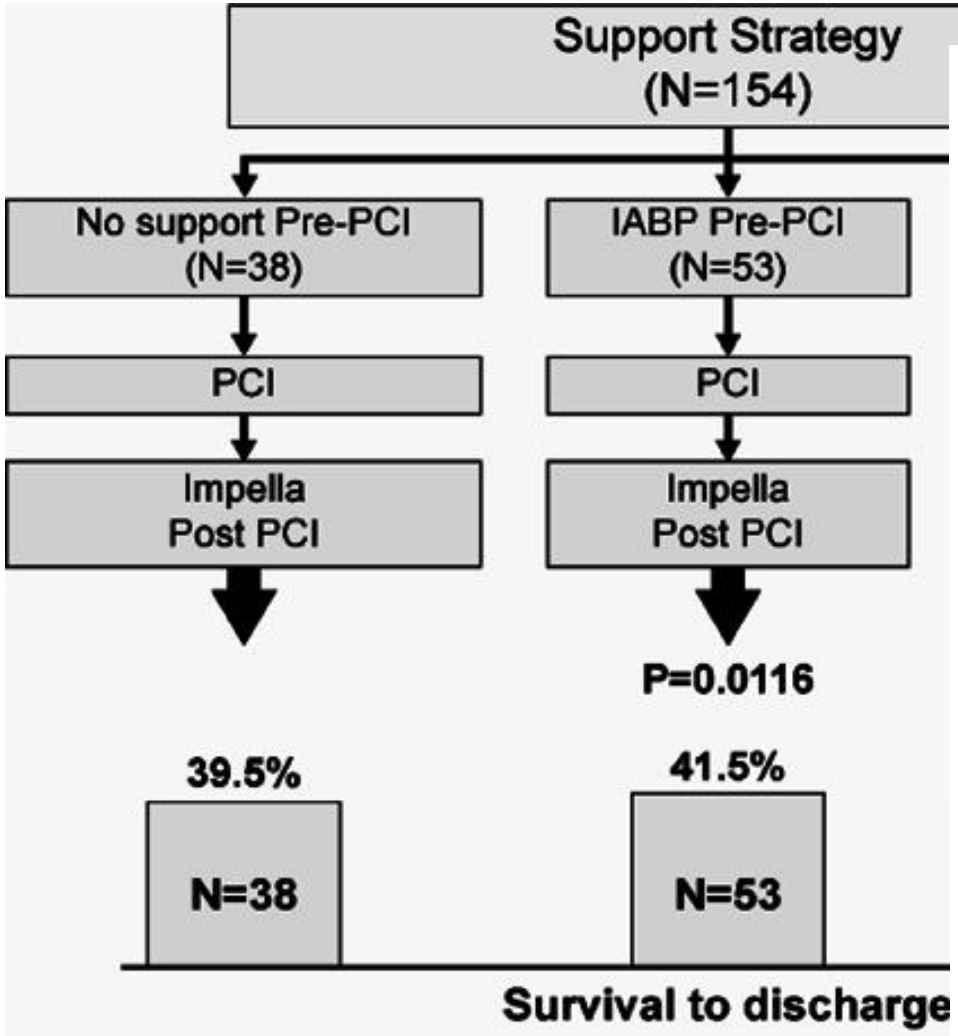
Attempted Randomized Impella® Trials In Emergent Settings

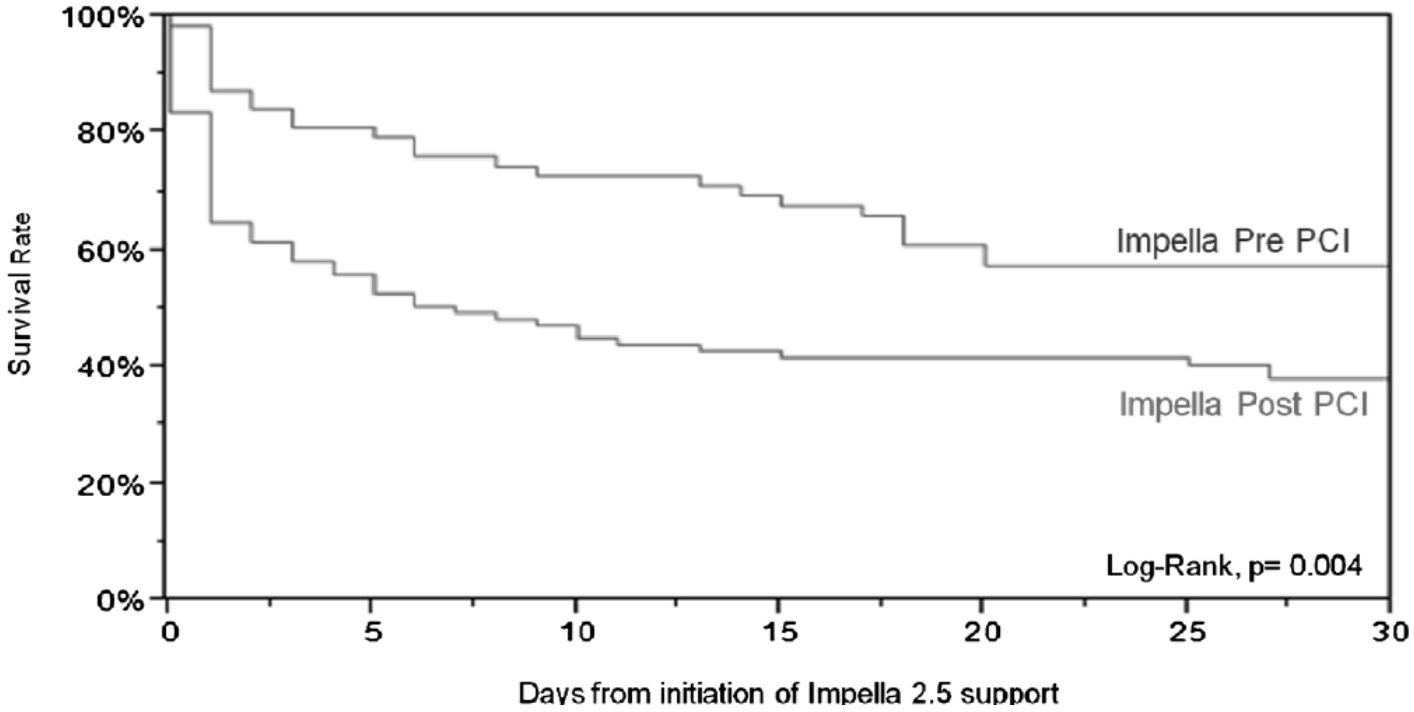
Study	Trial ID	Condition	Pts Required (n)	Pts Enrolled (n)	Duration (months)	Status	Discontinuation Reason/ comment
FRENCH TRIAL (2006)	NCT00314847	AMI CS	200	19	52	Discontinued	Low Enrollment
ISAR-SHOCK (2006)	NCT00417378	AMI CS	26	26	19	Completed	Non-Randomized Execution; Cardiac Output Study
IMPRESS in STEMI (2007)	NTR1079 trialregister.nl	STEMI Pre-CS	130	21	42	Discontinued	Low Enrollment
RECOVER I FDA (2008)	NCT00596726	PCCS	Up to 20	17	28	Completed	Feasibility Study
RECOVER II FDA (2009)	NCT00972270	AMI CS	384	1	18	Discontinued	Low Enrollment; 50 IRBs approved
RELIEF I (2010)	NCT01185691	ADHF	20	1	33	Discontinued	Low Enrollment
IMPRESS in CA (2016)	NTR3450	Cardiac Arrest Mechanical Ventilation	>100	48	52	Discontinued	Low Enrollment; Non-Randomized Execution
DanGer SHOCK (2012)	NCT01633502	AMI CS	360	>150	>84	Enrolling	ABMD funded, ongoing

Study Design of ISAR-SHOCK







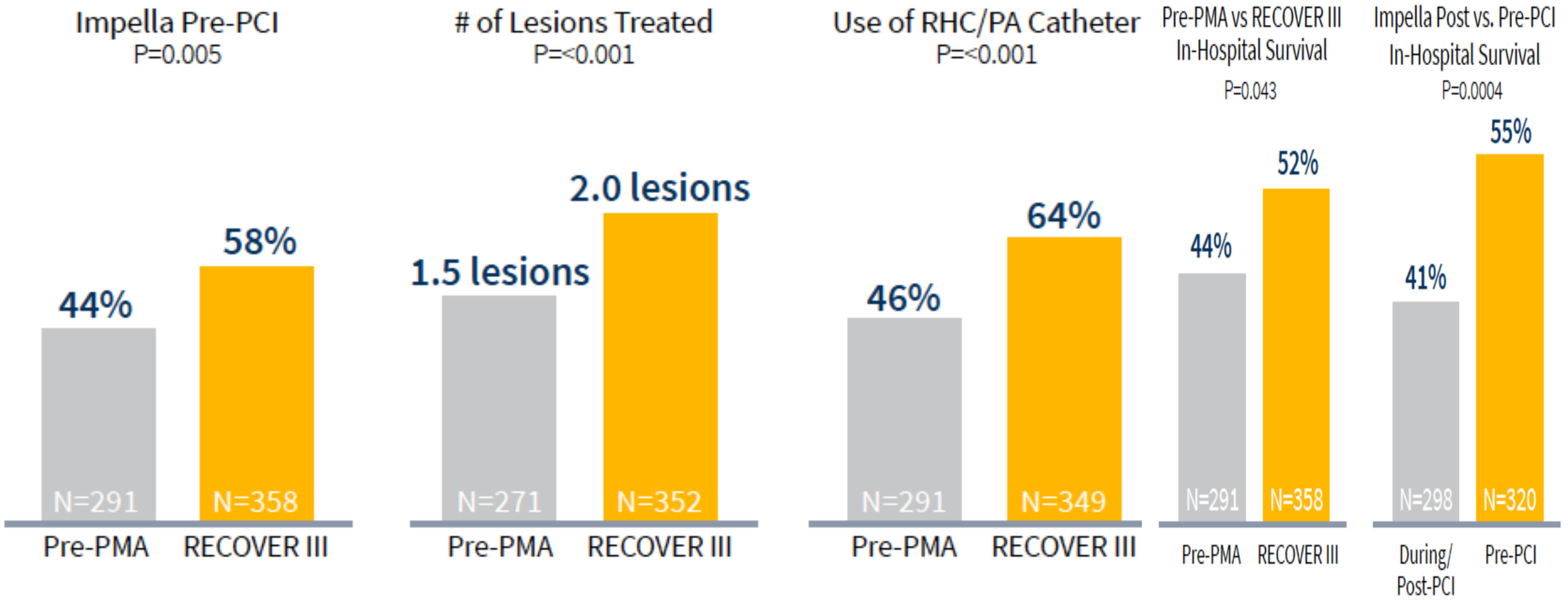


- The overall survival rate to discharge was 50.7%.
- A higher survival rate was observed in the pre-PCI group as compared with post-PCI group (65.1% vs. 40.7%, P=0.003).
- The odds ratio of discharge survival for Impella post-PCI versus pre-PCI was 0.37 (95% CI: 0.19–0.72), again indicating lower survival for Impella post-PCI vs. pre-PCI.

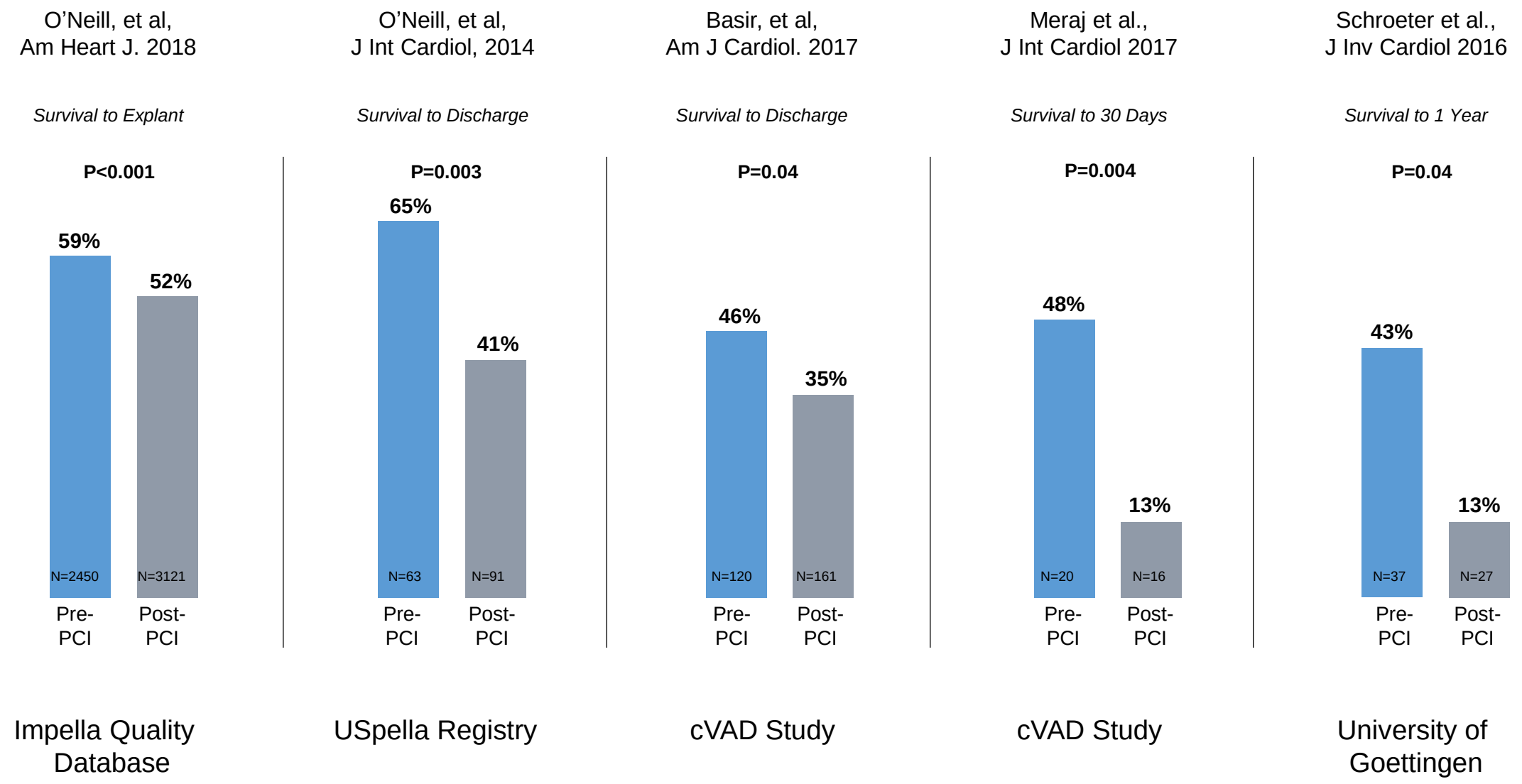
Mayo Clinic, Rochester, Minnesota; Winthrop Univer
Hospital, Royal Oak, Michigan; [8]Harvard Research In
Pennsylvania; and [10]Duke University Medical Center,

More Impella Pre-PCI and RHC to Optimize Therapy in RECOVER III Cohort

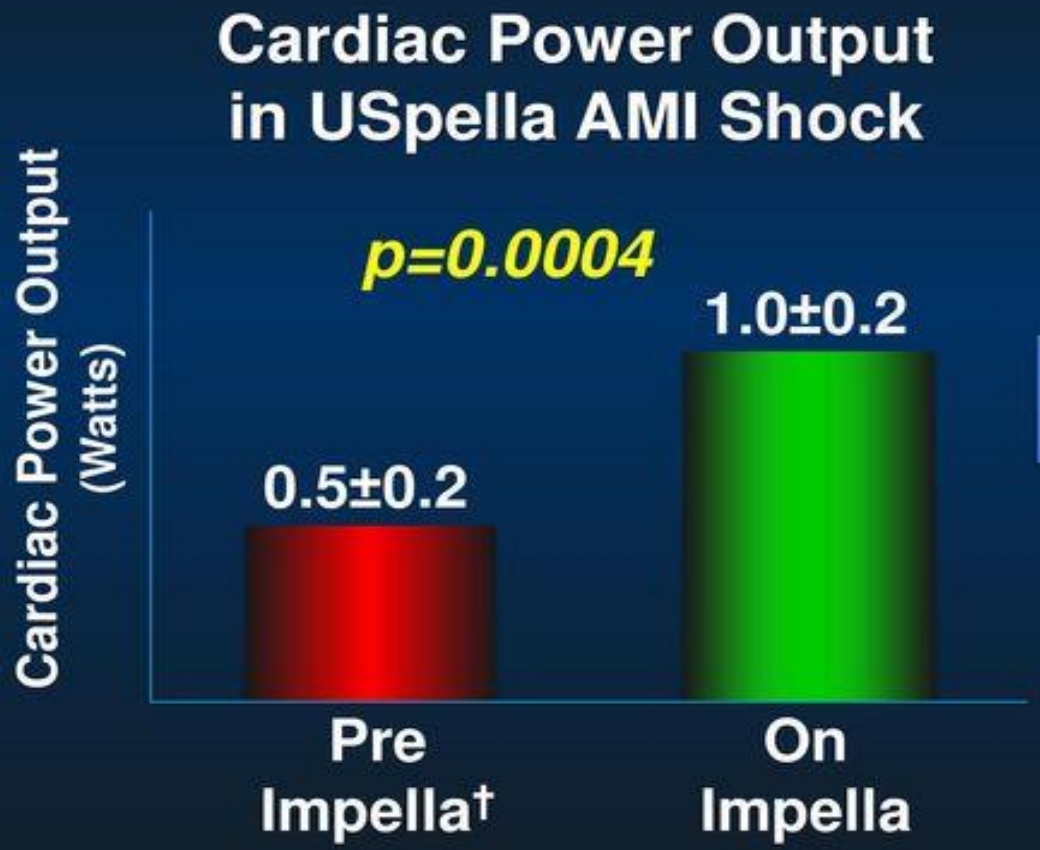
More Impella Pre-PCI and more lesions treated
More use of RHC/PA catheter to guide therapy and longer duration of Impella support

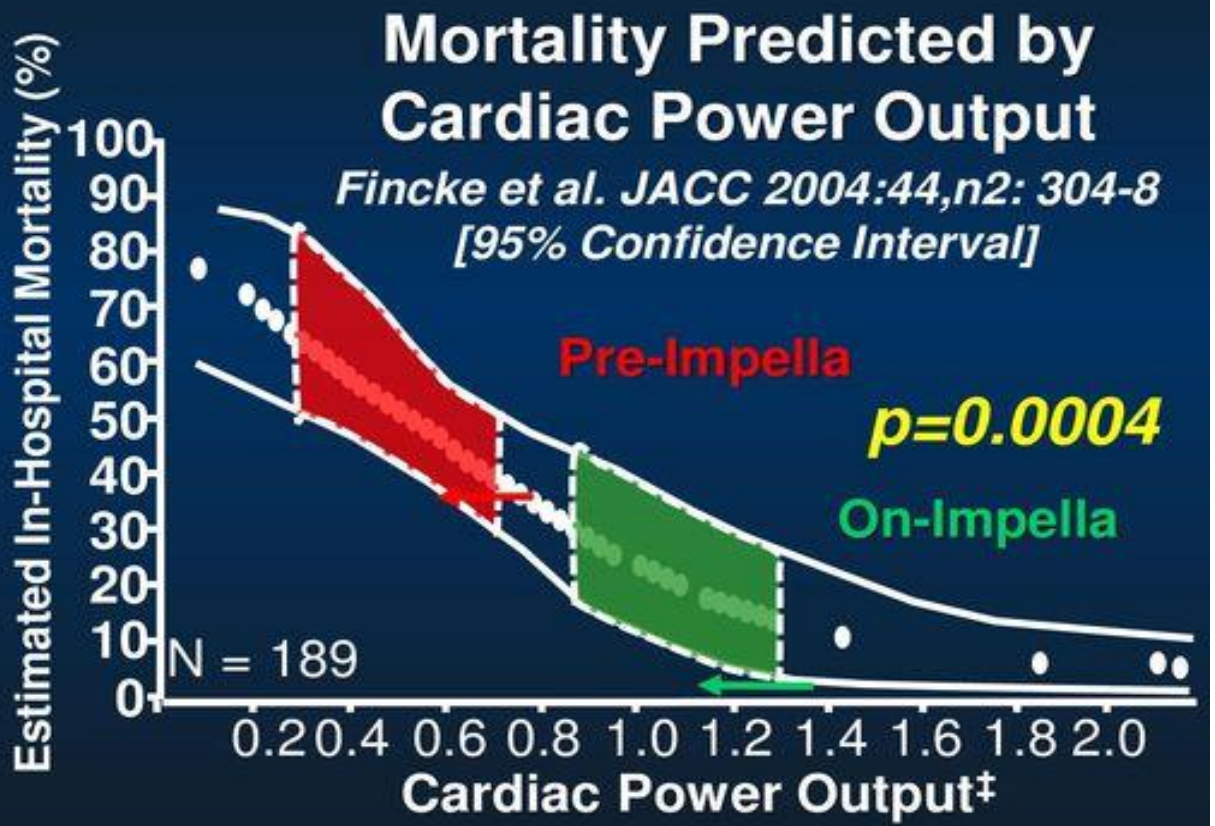


UNLOADING PRE-PCI ASSOCIATED WITH IMPROVED AMI-CGS OUTCOME



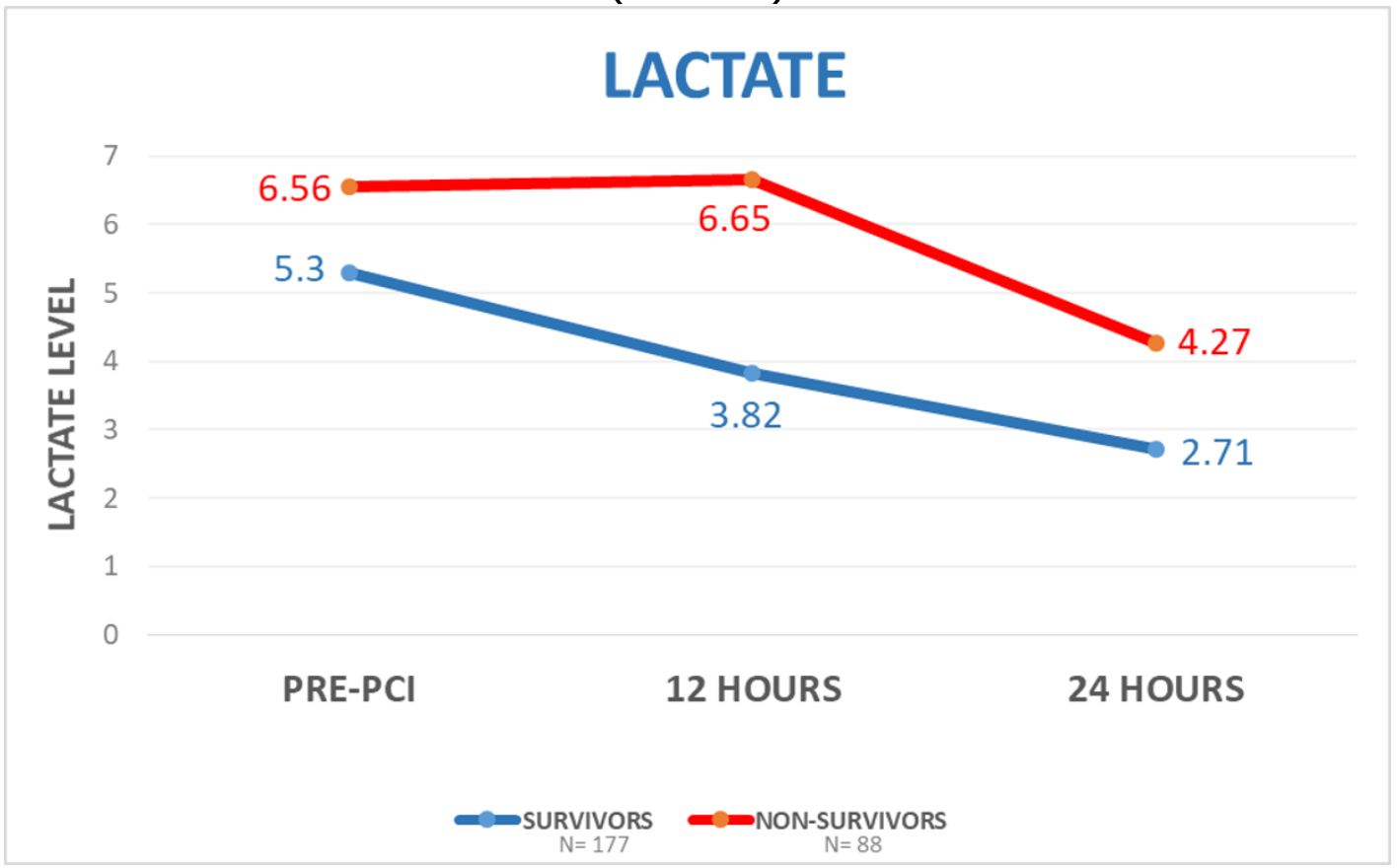
Impella Improves Cardiac Power Output, the Strongest Correlate of in-hospital Mortality



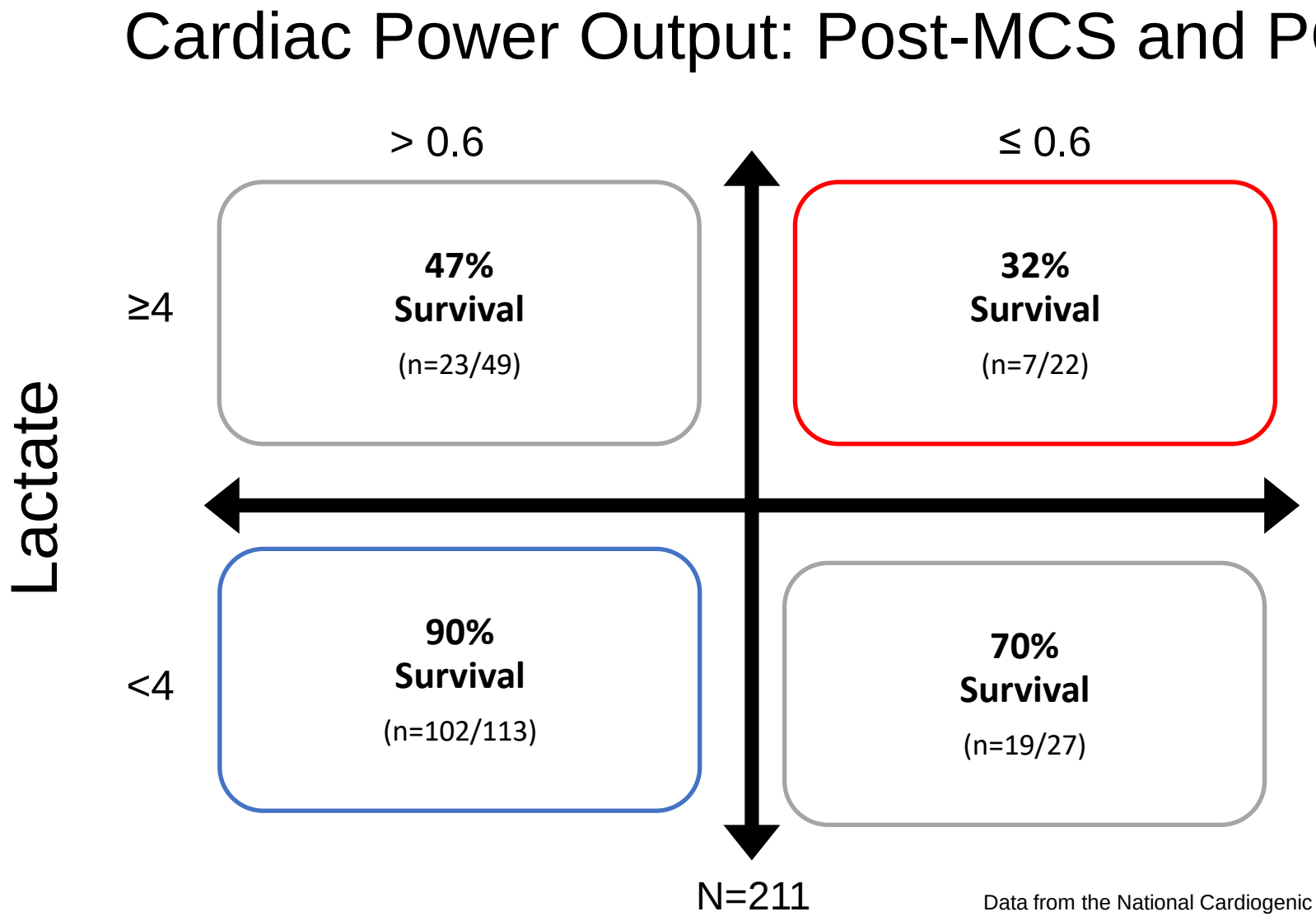


Lactate within the First 24 Hours, the Greatest Predictor

PREDICTORS OF SURVIVAL AT 12-24 HOURS
(N=265)



Predictors of Survival at 12-24 Hours on Impella®[1]

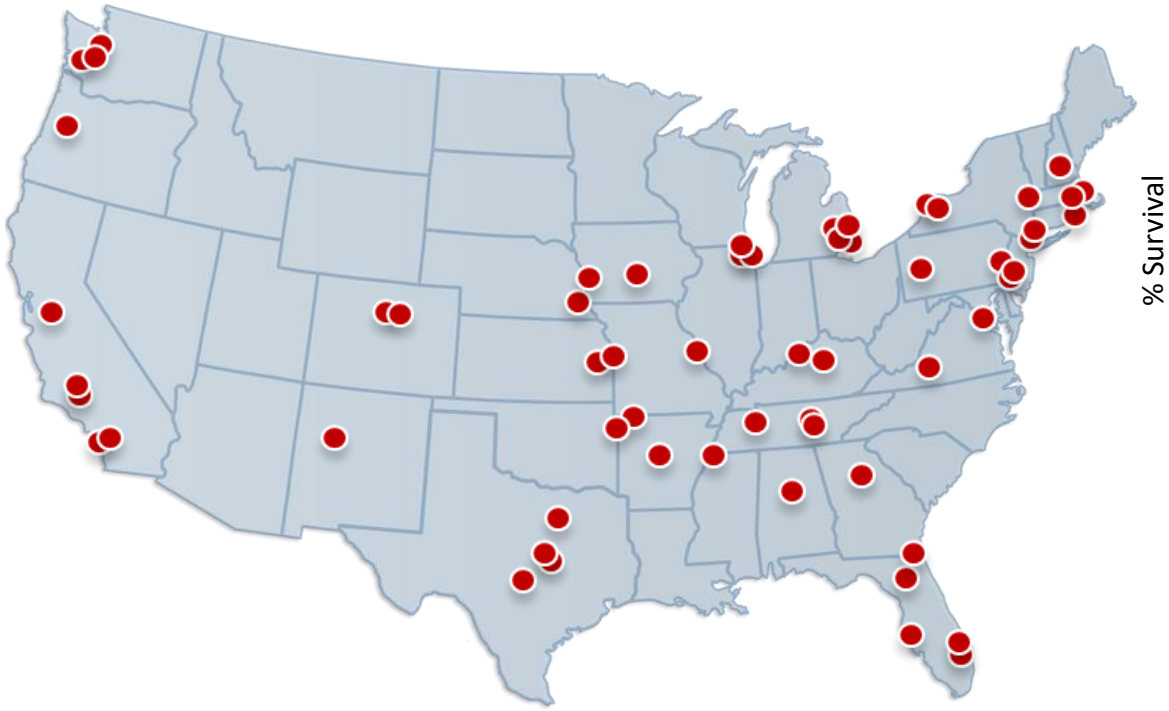


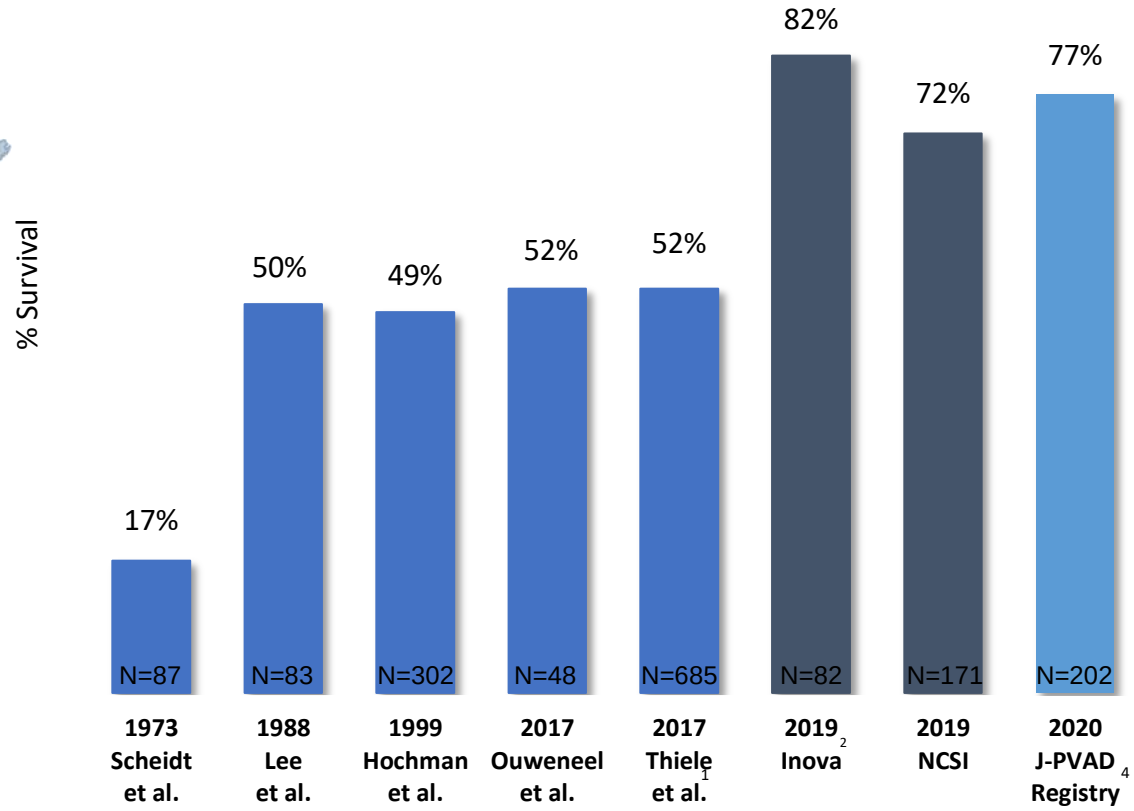
Data from the National Cardiogenic Shock Initiative (NCSI) AMI/CS Study

Presented by William O'Neill, MD and Babar Basir, DO at the NCSI Investigator Meeting, June 2020

National Cardiogenic Shock Initiative Study

70 sites in National CSI Study
(Sept 2020)





NCSI Study Native Heart Recovery = >90%[3]

* Basir, M. B., et al. (2019). Catheterization and Cardiovascular Interventions, 93(7), 1173–1183
1. Thiele, H., et al. (2017). New England Journal Of Medicine, 377(25), 2419-2432
2. Tehrani, B. N., et al. (2019). Journal of the American College of Cardiology, 73(13), 1659–1669
3. O'Neill, W. (2020). Achieving >70% AMI-CS Survival: Insights from National Cardiogenic Shock Initiative Presentation, TCT.
4. Kawai, T. (2020). Japanese Circulation Society, Kyoto

Detroit➡National CSI: Improved Protocol Adherence & Outcomes

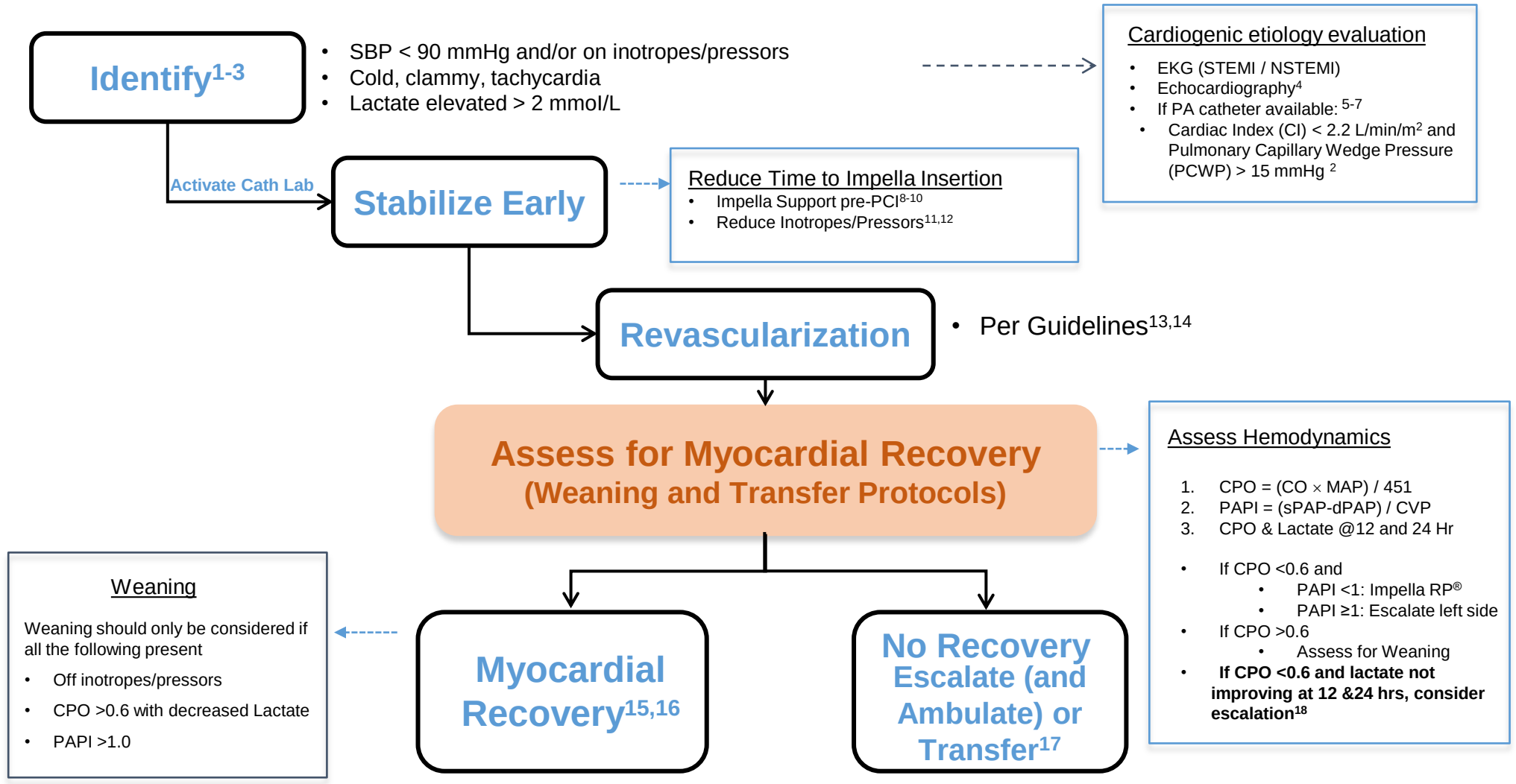
- **Impella® Use**
  - **Pre-PCI** **65%**
  - **Post-PCI** **23%**
  - **Intra-procedure** **12%**
- **RHC**
  - **Performed** **80%**
  - **Not Performed** **20%**
- **Survival** **72%**

Detroit CSI:
First 25 patients

- **Impella Use**
  - **Pre-PCI** **84%**
  - **Post-PCI** **12%**
  - **Intra-procedure** **4%**
- **RHC**
  - **Performed** **96%**
  - **Not Performed** **4%**
- **Survival** **88%**

National CSI:
First 25 patients
(all outside Detroit)

IMPELLA® BEST PRACTICES IN AMI CARDIOGENIC SHOCK



1. Reyentovich A, et al. Nat Rev Cardiol. 2016;13(8):481-492.
2. Hochman JS, et al. N Engl J Med. 1999;341(9):625-634.
3. Rihal CS, et al. J Am Coll Cardiol. 2015;65(19):e7-e26.
4. Picard MH, et al. Circulation. 2003;107(2):279-284.
5. Dhakal BP, et al. Am J Med. 2005;118(5):482-488.
6. Kahwash R, et al. Cardiol Clin. 2011;29(2):281-288.
7. Chatterjee K. Circulation. 2009;119(1):147-152.
8. O'Neill WW, et al. J Interv Cardiol. 2014;27(1):1-11.
9. Joseph SM, et al. J Interv Cardiol. 2016 Jun;29(3):248-56.
10. Schroeter MR, et al. J Invasive Cardiol. 2016 Aug 15. [Epub ahead of print]
11. Samuels LE, et al. J Card Surg. 1999;14(4):288-293.
12. De Backer D, et al. N Engl J Med. 2010;362(9):779-789.
13. O'Gara PT, et al. J Am Coll Cardiol. 2013;61(4):e78-e140.
14. Steg PG, et al. Eur Heart J. 2012;33(20):2569-2619.
15. Casassus F, et al. J Interv Cardiol. 2015;28(1):41-50.
16. Lemaire A, et al. Ann Thorac Surg. 2014;97(1):133-138.
17. Anderson MB, et al. J Heart Lung Transplant. 2015;34(12):1549-1560
18. Basir B, et al. Lactate and CPO reliably Predict. TCT 2018

CARDIOGENIC SHOCK ALGORITHM

INOVA HEART AND VASCULAR INSTITUTE

Cardiogenic Shock Algorithm

(Call 703-776-5905 to activate)

Clinical Goals

- Rapid identification
- Early mechanical circulatory support (LV and RV)
- Right heart catheterization
- Minimize inotropes/ vasopressors
- Heart recovery

Shock Criteria

- SBP < 90 mmHg (for 30 min) or use of vasopressors/ inotropes
- CI < 2.2 L/min/m^2
- PCWP > 18 mmHg
- CPO < 0.6 W
- Lactate > 2 mmol/L

- CPO = MAP x CO/451
- PAPi = (sPAP-dPAP)/RA

Identify Shock

- Vitals Signs, ECG, Labs
- +/- Right heart catheterization, Echo
- See "Shock Criteria"
- Activate Cath Lab/CCU/MCCS
- Consider Shock Team activation

Non-ACS

Right heart catheterization
Echo

ACS

Diagnostic angiography
Right heart catheterization
Assess vascular access
Prepare PMCS

Percutaneous Mechanical Circulatory Support (PMCS)

Reassess hemodynamics
Assess for RV support (CPO, PAPi)

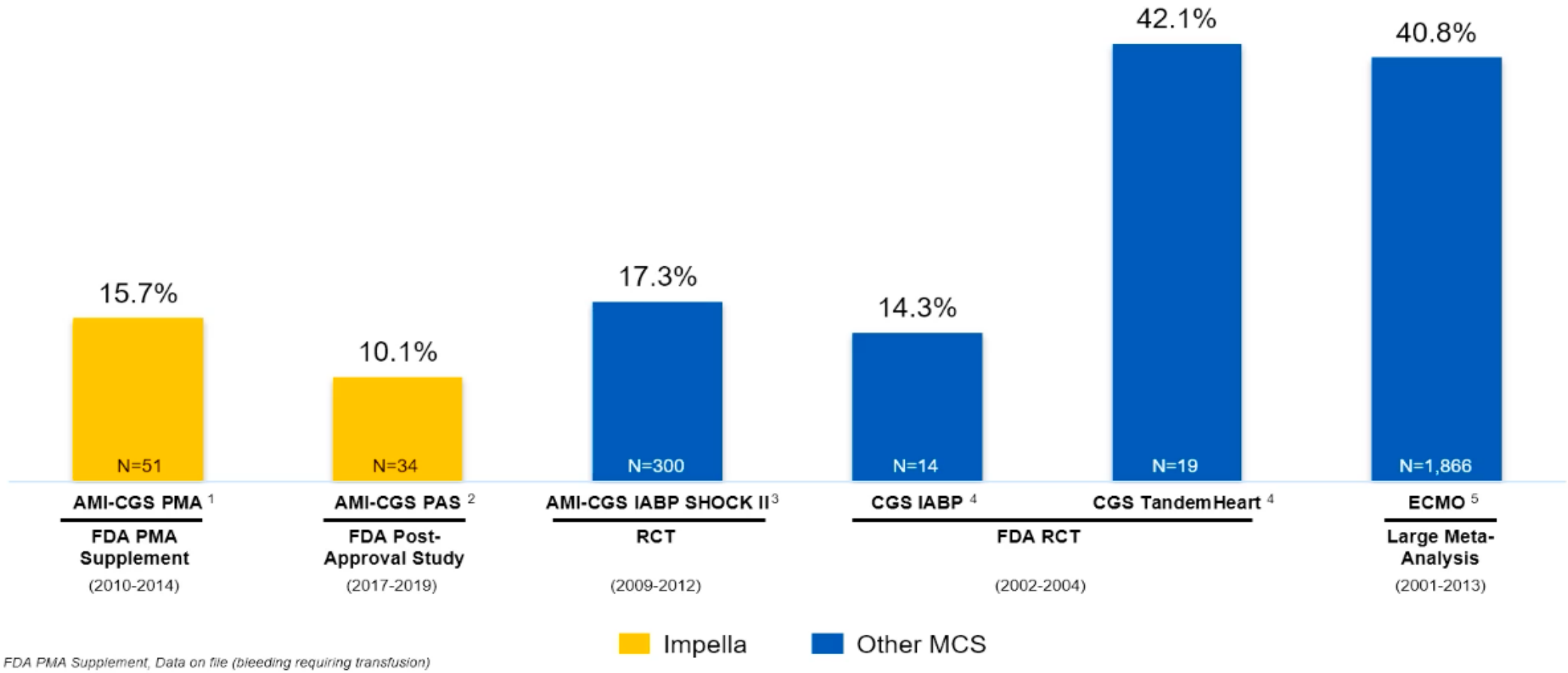
Coronary revascularization
Reassess hemodynamics
Assess for RV support (CPO, PAPi)

Coronary Care Unit

- Assess for myocardial recovery
- Wean inotropes/vasopressors

BLEEDING RATES REPORTED IN FDA AND LARGE STUDIES

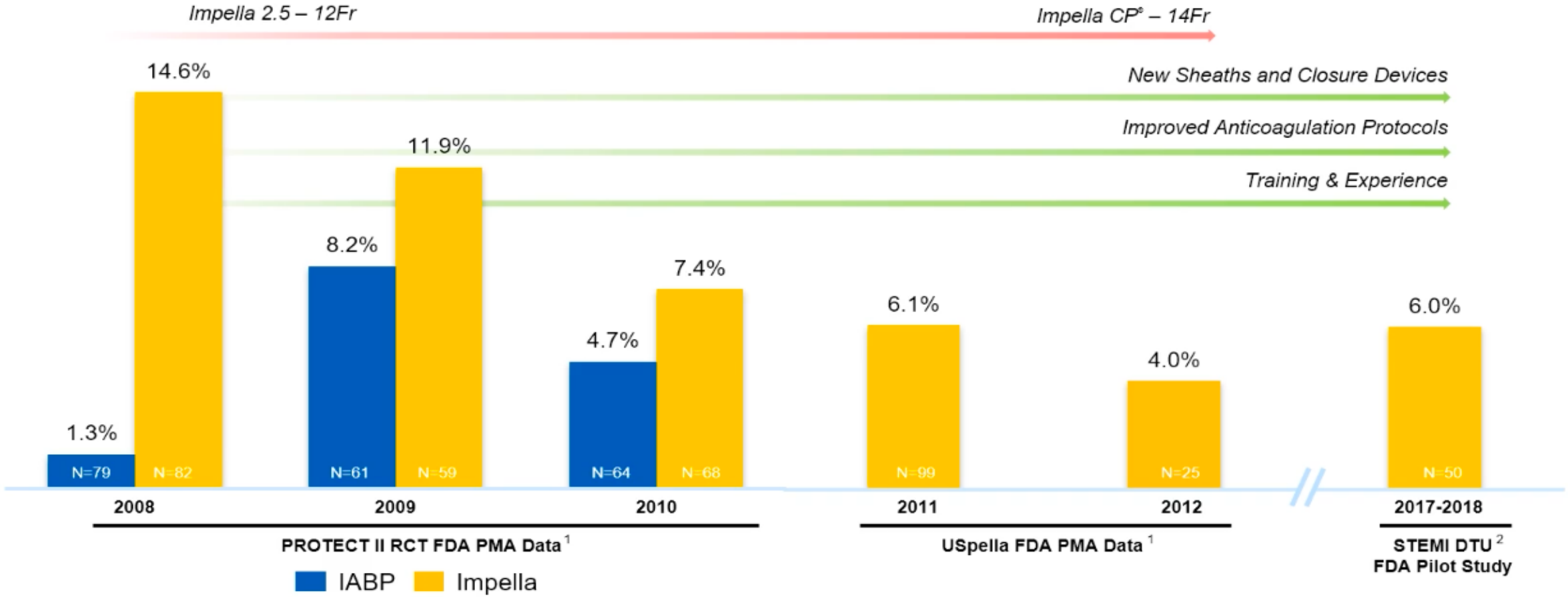
Cardiogenic Shock
Major or Significant Bleeding or Requiring Transfusion (if reported)



1. *FDA PMA Supplement, Data on file (bleeding requiring transfusion)*
2. *FDA Post-Approval Study, Data on file (bleeding requiring transfusion)*
3. *Thiele H et al., NEJM 2012; 367:1287-129 (bleeding requiring transfusion)*
4. *Burkhoff D et al., Am Heart J 2006;152:469.e12469.e8 (Major or significant bleeding)*
5. *Cheng R et al., Annals Thoracic Surgery 2014; 97: 610-6 (Major or significant bleeding)*

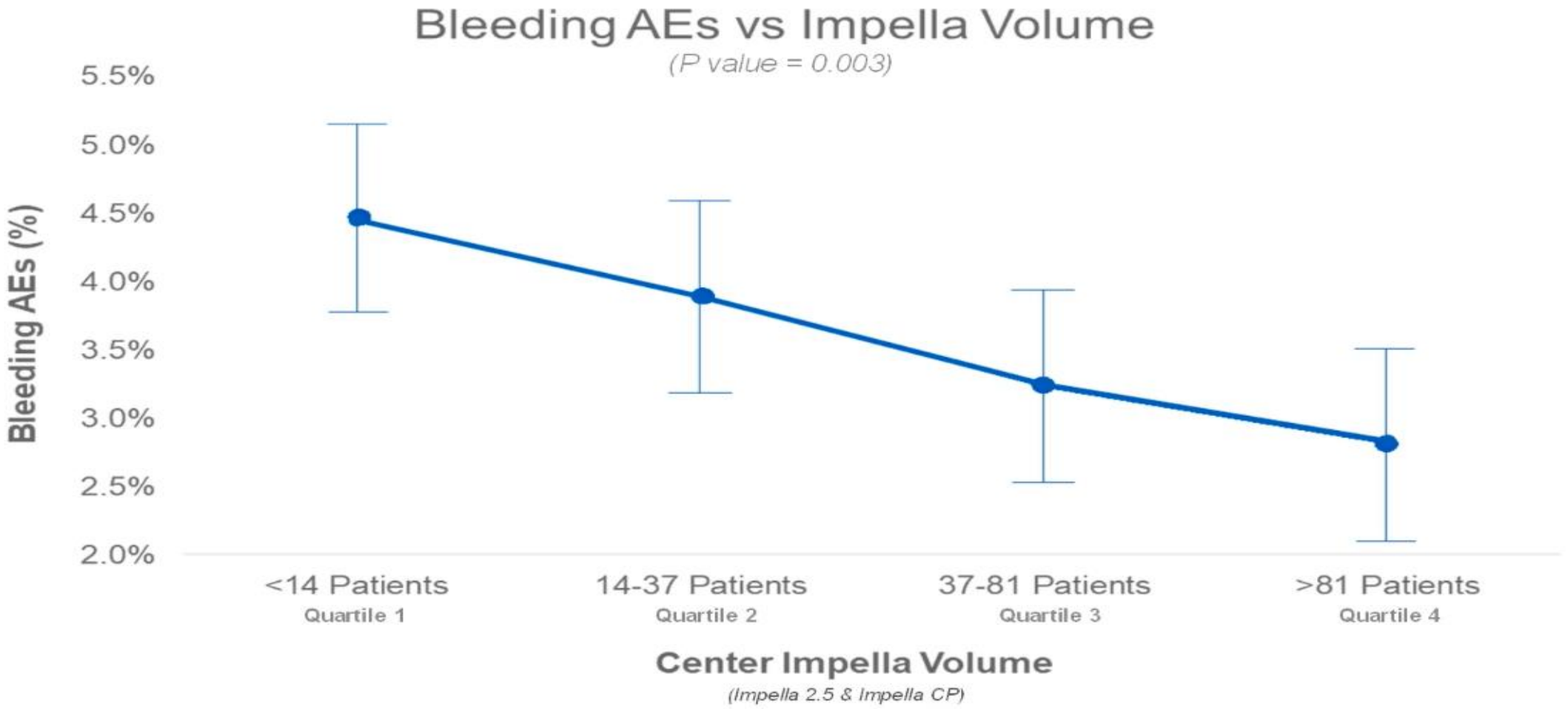
Impella Bleeding Rates Over Time Reported in FDA Studies

HRPCI / STEMI Bleeding Requiring Transfusion



1. *FDA PMA Submission, Data on file (bleeding requiring transfusion)*
2. *Kapur N et al., Circulation. 2019 Jan 15;139(3):337-346 (bleeding requiring transfusion)*

IMPELLA EXPERIENCE YIELDS LOWER BLEEDING RATES



1. *1420 sites supporting 96,265 patients. Data on file. Abiomed Impella Quality(IQ)Data, Jan 1 2016 – Sept 2019 to Date. Danvers, MA: Abiomed..*
2. *Mean patients treated by Impella Centers: Mean:61; Median: 37*

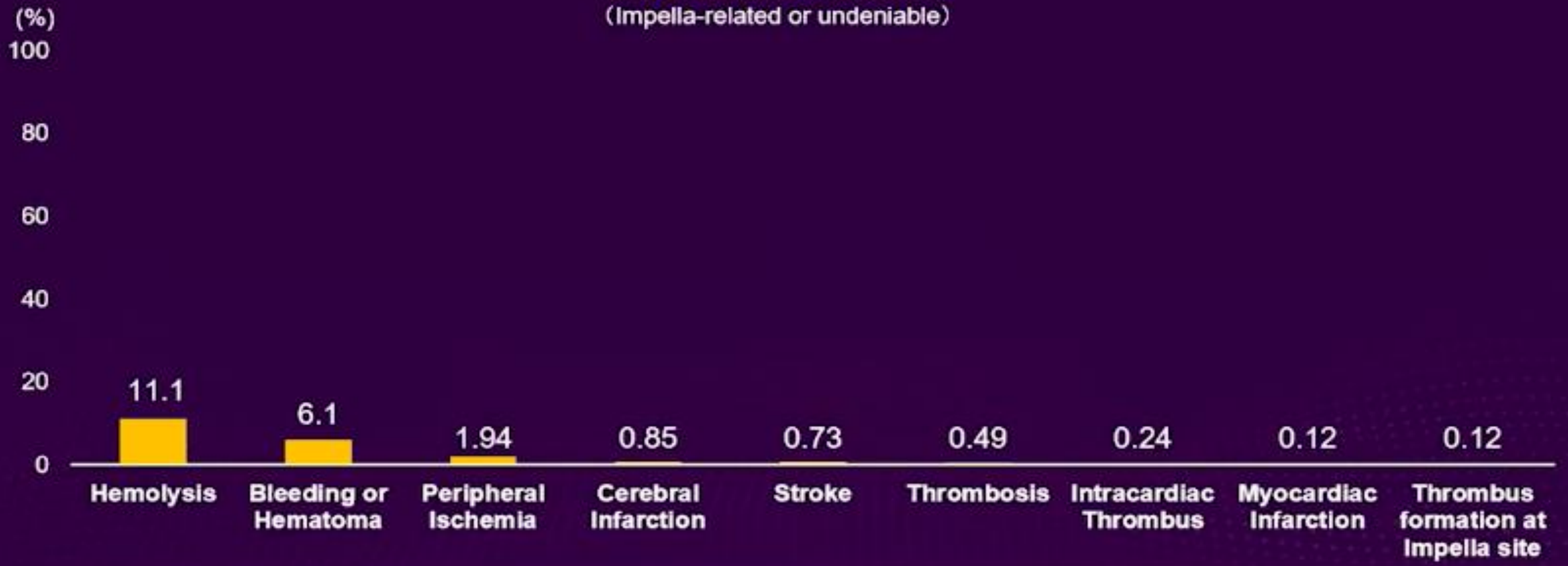
J-PVAD Registry

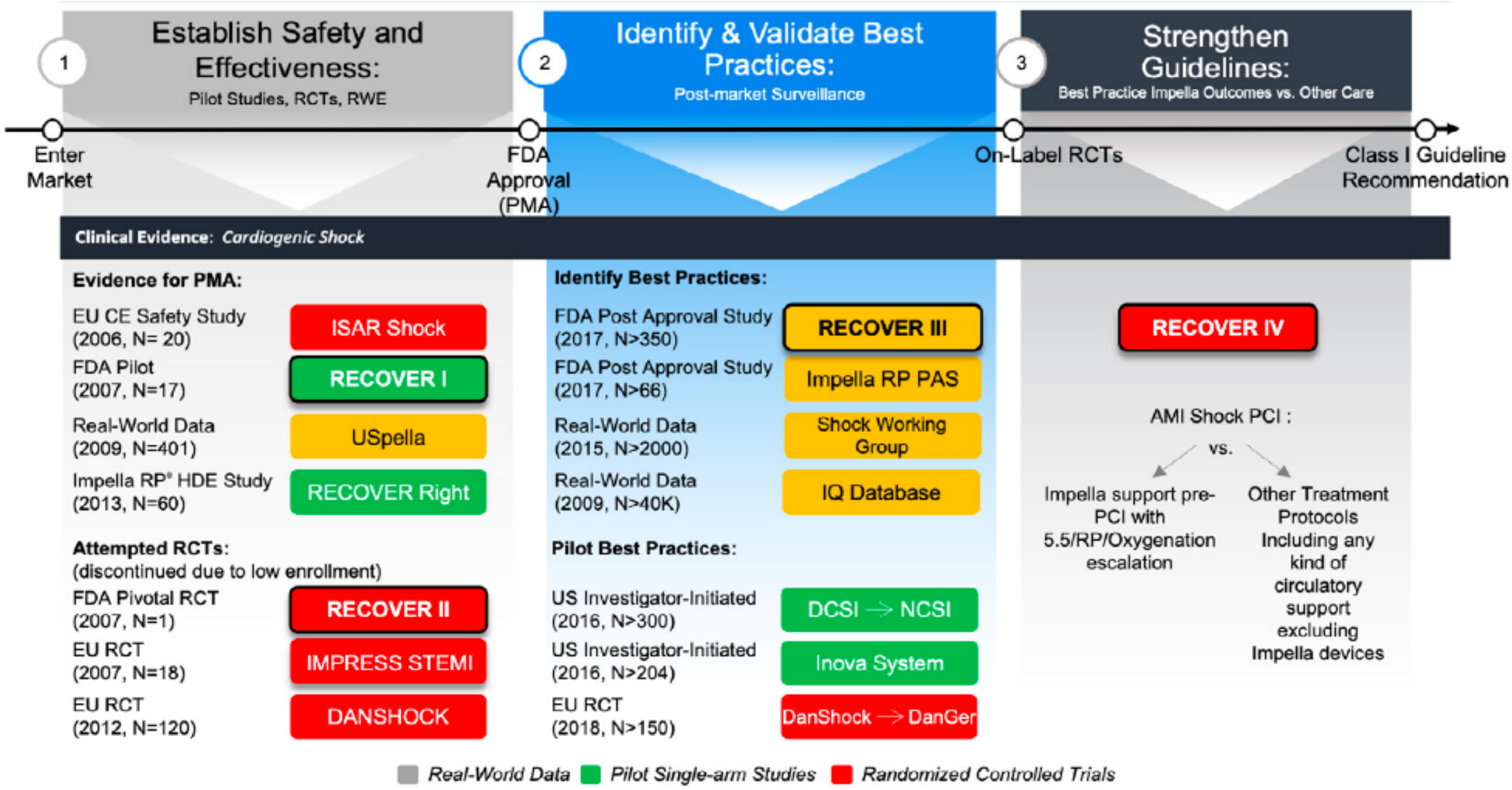
Multi-Center, Prospective clinical registry led by Impella Committee

Three-year interim analysis[1]
Enrollment period: Oct 2017 – Jan 2020

Major Adverse Events

(Impella-related or undeniable)




1
Establish Safety and Effectiveness:
Pilot Studies, RCTs, RWE
2
Identify & Validate Best Practices:
Post-market Surveillance
3
Strengthen Guidelines:
Best Practice Impella Outcomes vs. Other Care
Enter Market
FDA Approval (PMA)
On-Label RCTs
Class I Guideline Recommendation
Clinical Evidence: Cardiogenic Shock
Evidence for PMA:
EU CE Safety Study (2006, N= 20)
ISAR Shock
FDA Pilot (2007, N=17)
RECOVER I
Real-World Data (2009, N=401)
USpella
Impella RP® HDE Study (2013, N=60)
RECOVER Right
Attempted RCTs:
(discontinued due to low enrollment)
FDA Pivotal RCT (2007, N=1)
RECOVER II
EU RCT (2007, N=18)
IMPRESS STEMI
EU RCT (2012, N=120)
DANSHOCK
Identify Best Practices:
FDA Post Approval Study (2017, N>350)
RECOVER III
FDA Post Approval Study (2017, N>66)
Impella RP PAS
Real-World Data (2015, N>2000)
Shock Working Group
Real-World Data (2009, N>40K)
IQ Database
Pilot Best Practices:
US Investigator-Initiated (2016, N>300)
DCSI → NCSI
US Investigator-Initiated (2016, N>204)
Inova System
EU RCT (2018, N>150)
DanShock → DanGer
RECOVER IV
AMI Shock PCI :
vs.
Impella support pre-PCI with 5.5/RP/Oxygenation escalation
Other Treatment Protocols Including any kind of circulatory support excluding Impella devices
Real-World Data
Pilot Single-arm Studies
Randomized Controlled Trials

Conclusions

- Mortality rates in AMI cardiogenic shock have not improved in 20 years
- Know your tool box!
- Protocols (NCSI or Inova) are they way to improve practice:
  - Reduction of toxic inotropes
  - Impella Pre-PCI
  - Invasive hemodynamic monitoring
- Hemodynamic support with Impella devices promotes myocardial recovery
- Data from the National CSI Inova initiative – utilizing a best practices protocol – is demonstrating a significant improvement in survival


THANK
You!