MHIF FEATURED STUDY:

CLBS16-P02 FREEDOM Study

OPEN and ENROLLING:

EPIC message to *Research MHIF Patient Referral*

CONDITION:	PI:	RESEARCH CONTACTS:	SPONSOR:
Coronary Microvascular Dysfunction without obstructive Coronary Artery Disease (CAD)	Jay Traverse, MD	**Jane Fox, RN** Jane.Fox@allina.com | 612-863-6289	Caladrius Bioscience

DESCRIPTION: Blinded randomized study comparing IC delivery of apheresis derived (after G-CSF administration) autologous CD34+ cells versus placebo.

Reduced CFR is a risk factor and these are patients with chronic chest pain thought to be secondary to microvascular dysfunction. This disease adversely affects women; typical patients experience angina without obstructive coronary artery disease (CAD).

CRITERIA LIST/ QUALIFICATIONS:

Inclusion

- Age > 18
- Experiencing angina > 3 times a week
- No obstructive CAD
- CCS Class II-IV

Exclusion

- Active Inflammatory or autoimmune disease
- Sickle Cell disease
- LVEF < 30%

Minneapolis Heart Institute Foundation®

Creating a world without heart and vascular disease

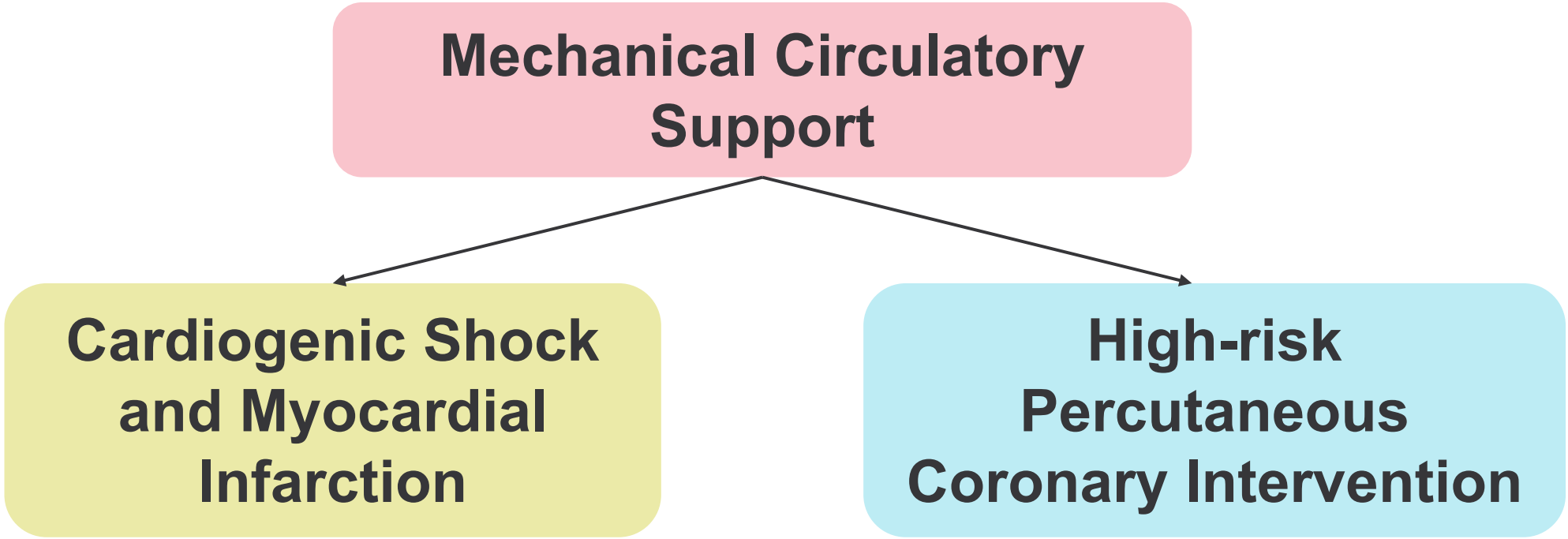
Mechanical Circulatory Support in the Cath Lab: *Where are We Now?*

Raviteja R. Guddeti, MD

Interventional Cardiology Fellow

Objectives

- To understand the indications for mechanical circulatory support in the cath lab
- To review evidence for mechanical circulatory support
- To identify patient selection criteria for mechanical circulatory support



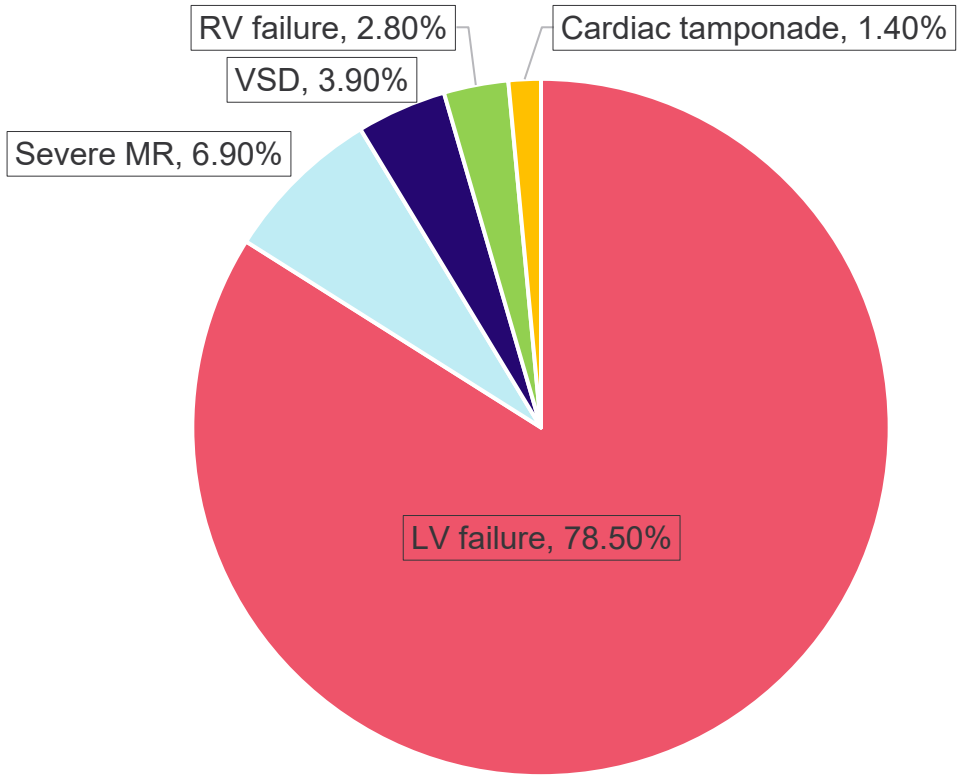
Mechanical Circulatory Support in Cardiogenic Shock secondary to AMI

Cardiogenic Shock

- "A state of critical end-organ hypoperfusion primarily due to cardiac dysfunction"

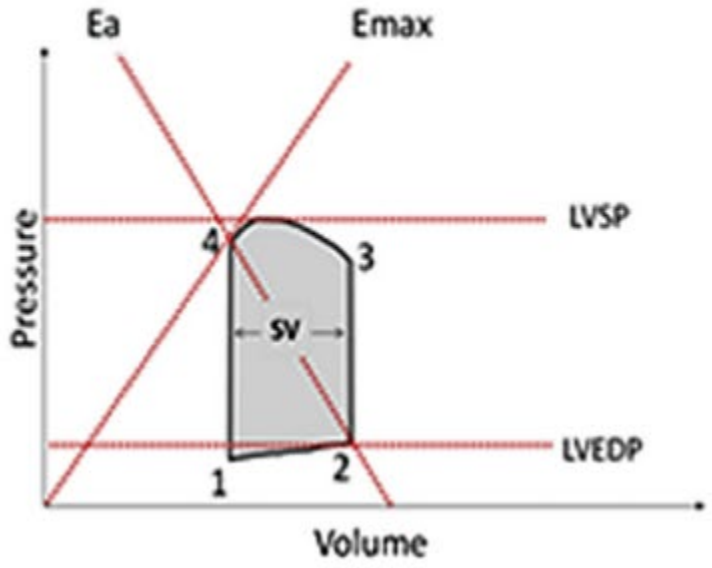
- Hypotension (**SBP <90 mmHg** or need for vasopressors) and signs of impaired organs perfusion, reduced cardiac index (**CI <1.8 or <2.2 L/min/m^2 with cardiac support**) or increased left ventricular filling pressure (**PCWP >15 mmHg**)

- Cardiogenic shock complicates **5% to 10%** of acute MI cases
- Common causes of cardiogenic shock in acute MI

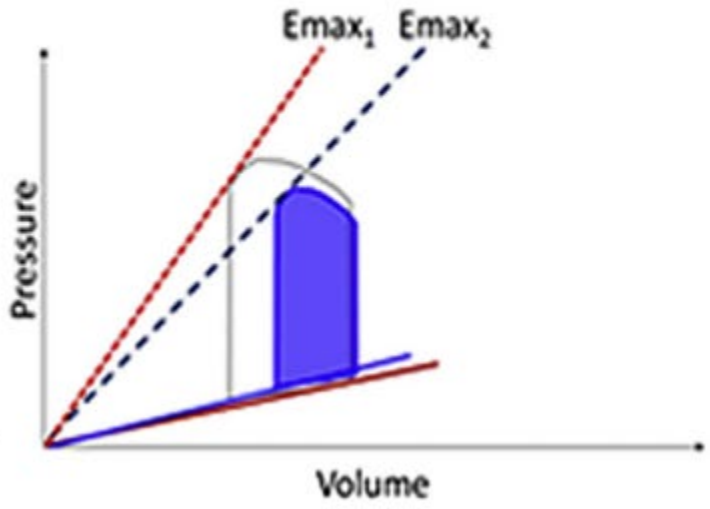


Hochman et al; J Am Coll Cardiol. 2000 Sep;36(3 Suppl A):1063-70.

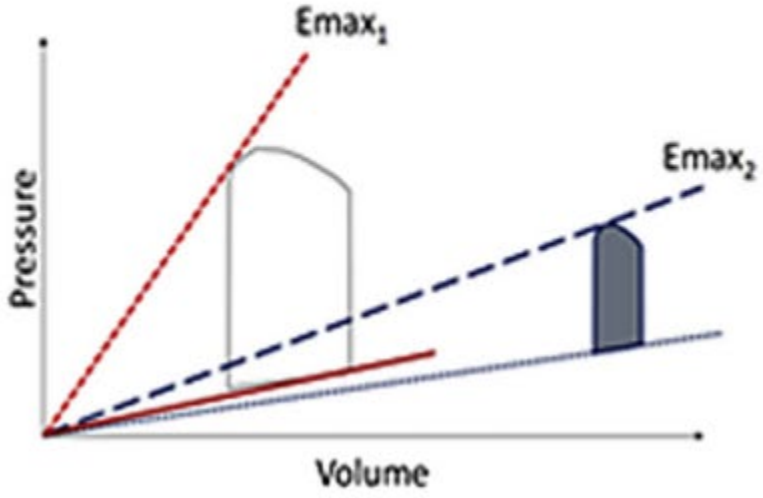
A. Steady State



B. Acute Myocardial Infarction



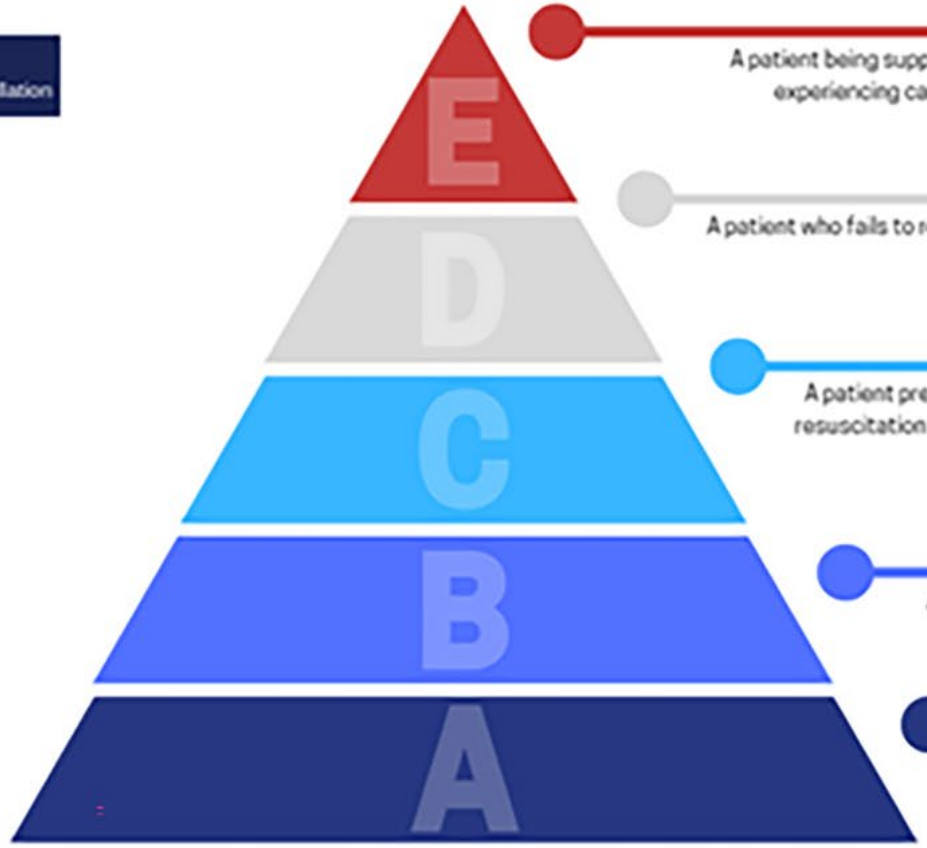
C. Cardiogenic Shock



SCAI Stages of Cardiogenic Shock

Adapted from the SCAI Clinical Expert Consensus Statement on the Classification of Cardiogenic Shock
Endorsed by ACC, AHA, SCCM, and STS

Arrest (A) Modifier:
CPR, including defibrillation



EXTREMIS

A patient being supported by multiple interventions who may be experiencing cardiac arrest with ongoing CPR and/or ECMO.

DETERIORATING

A patient who fails to respond to initial interventions. Similar to stage C and getting worse.

CLASSIC

A patient presenting with hypoperfusion requiring intervention beyond volume resuscitation (inotrope, pressor, or mechanical support including ECMO). These patients typically present with relative hypotension.

BEGINNING

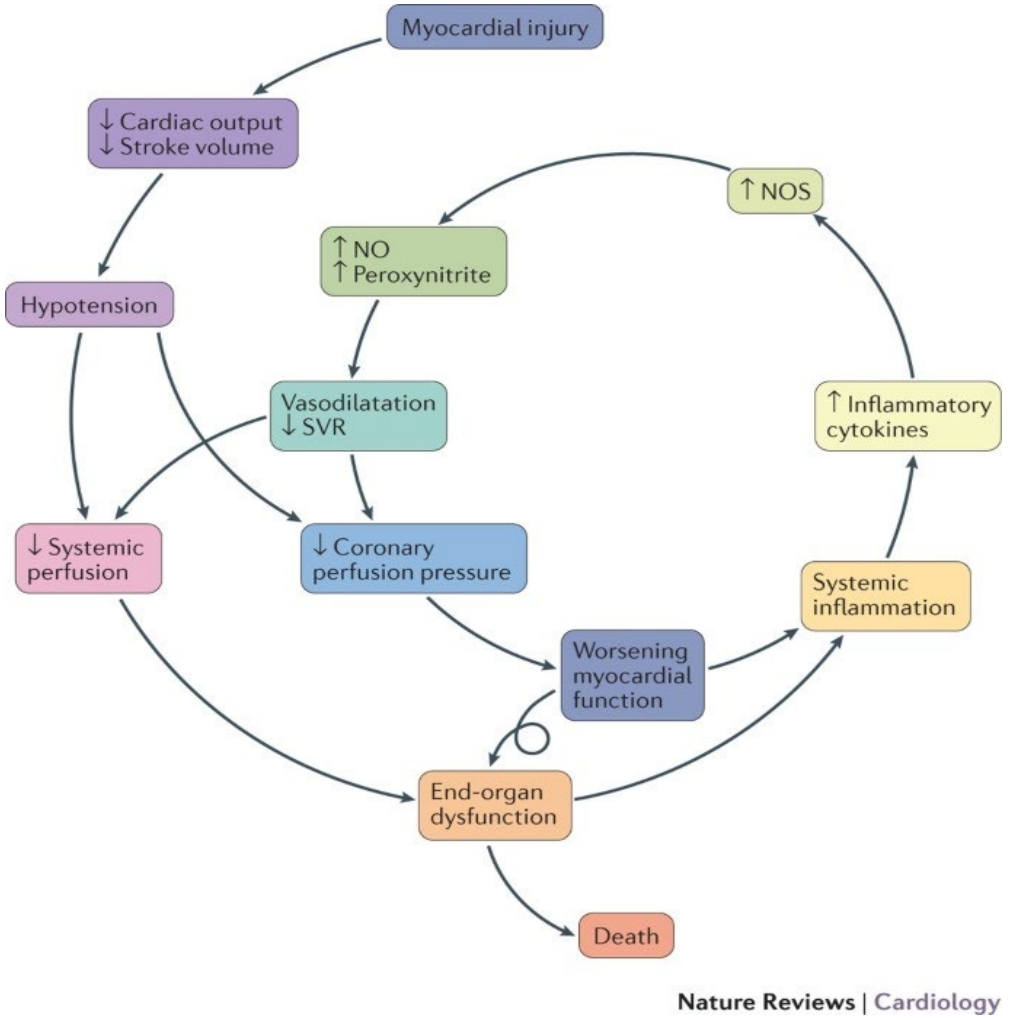
A patient who has clinical evidence of relative hypotension or tachycardia without hypoperfusion.

AT RISK

A patient with risk factors for cardiogenic shock who is not currently experiencing signs or symptoms. For example, large acute myocardial infarction, prior infarction, acute and/or acute on chronic heart failure.

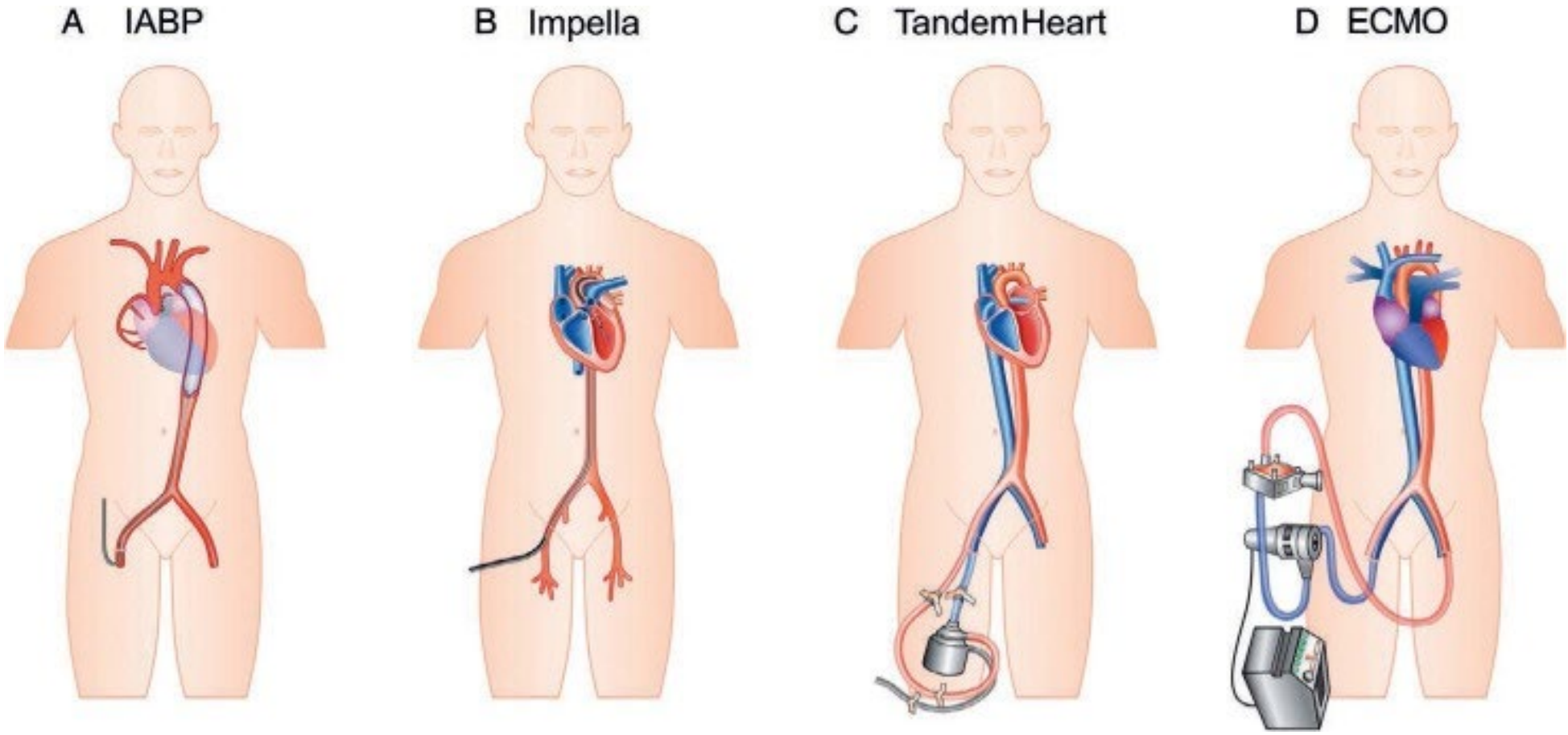
Baran DA, Grines CL, Bailey S, et al. SCAI clinical expert consensus statement on the classification of cardiogenic shock. Catheter Cardiovasc Interv. 2019;1-9. https://doi.org/10.1002/ccd.28329
For more information, please visit: www.scai.org/shockdefinition

Pathophysiology of Cardiogenic Shock



Reyentovich et al; *Nature Reviews Cardiology* volume 13, pages 481–492(2016)

Options for Mechanical Circulatory Support



Potential Benefits of Mechanical Circulatory Support

- Maintain vital **organ perfusion**, thereby preventing systemic shock syndrome
- Reduce intracardiac **filling pressures**, thereby reducing congestion and/or pulmonary edema
- Reduce **left ventricular volumes**, wall stress, and myocardial oxygen consumption
- Augment **coronary perfusion**
- Support the circulation during complex interventional procedures
- Limit infarct size

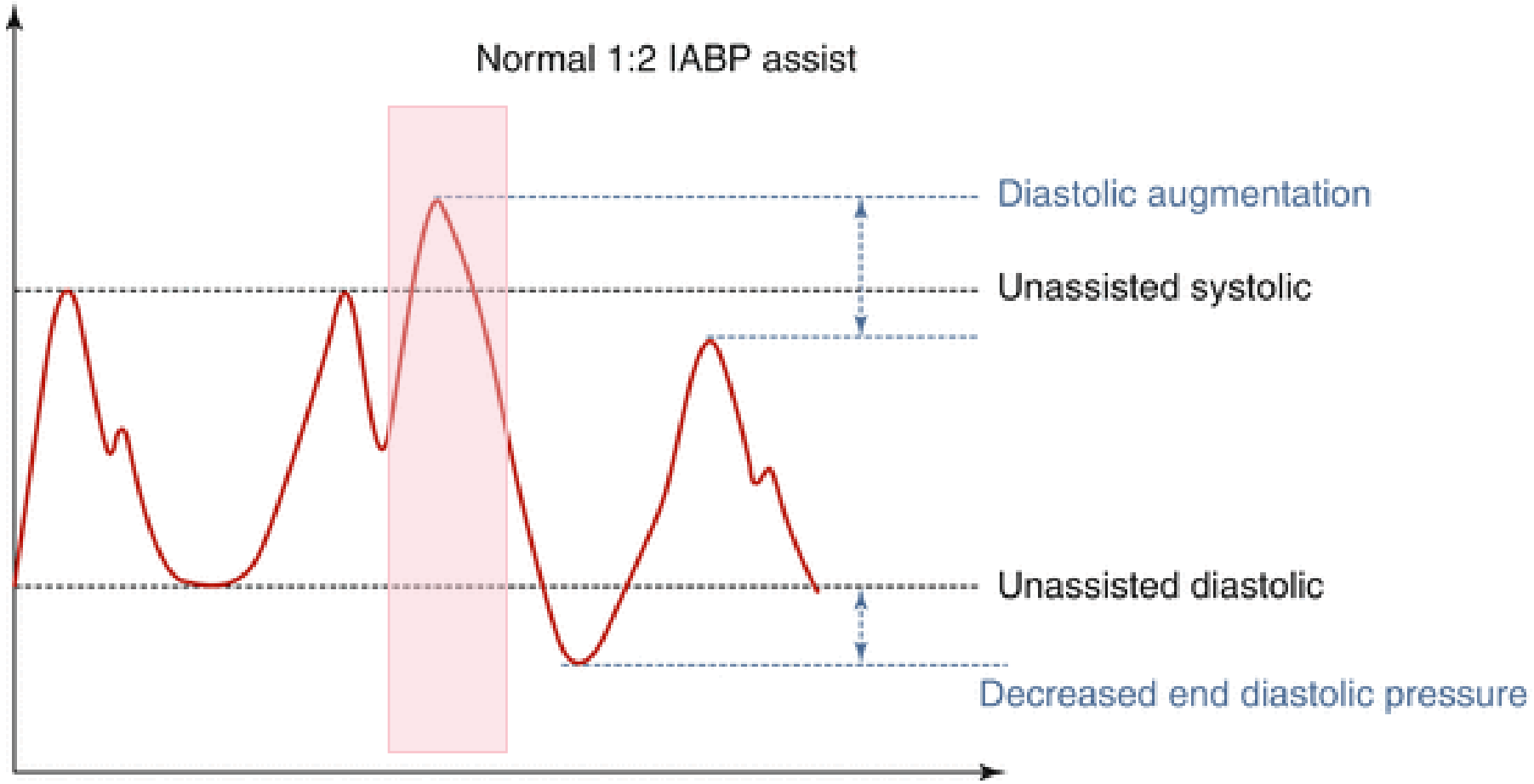
Intra-aortic Balloon Pump

Case

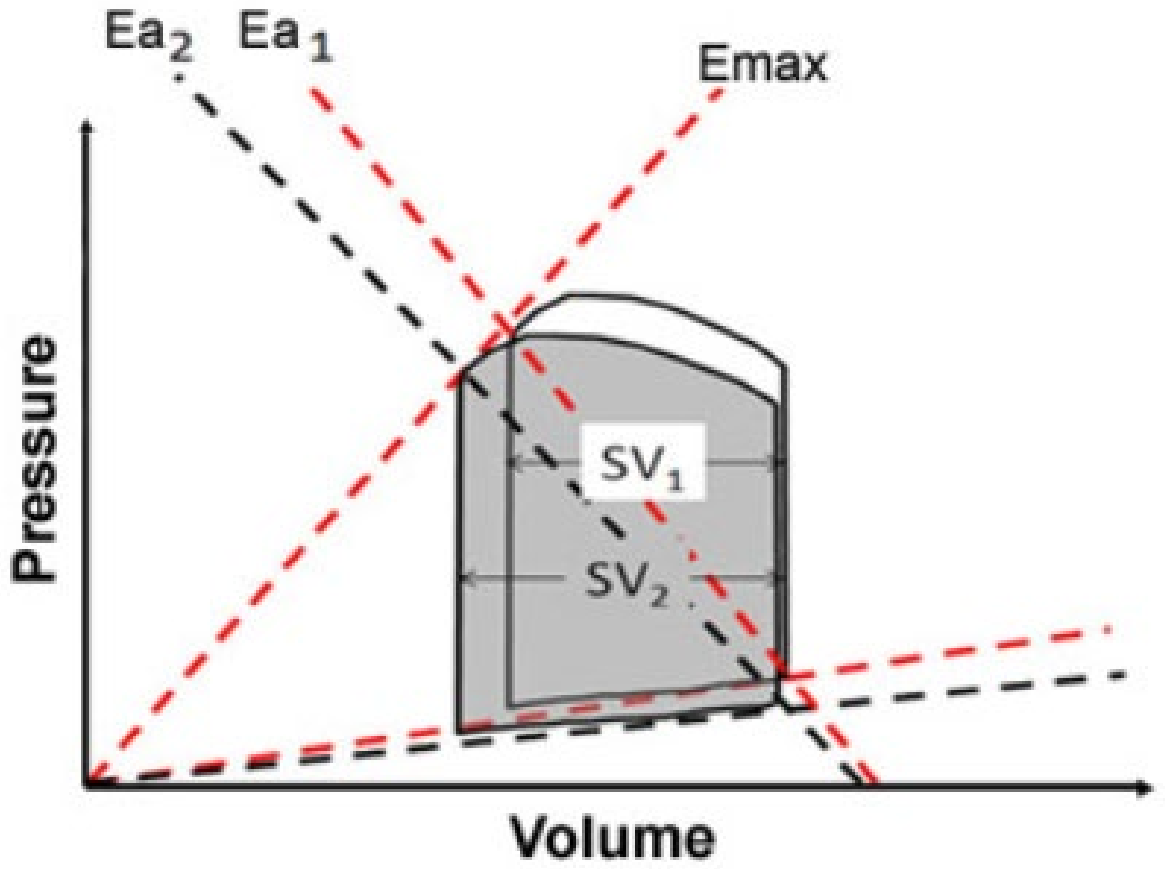
- A 90 y.o. male with history of CAD s/p multiple stents to LAD, D1, rPDA, and hyperlipidemia, presents with chest pain.
- **Acute inferior STEMI** with **complete heart block** with junctional escape rate at 43 bpm and on-going symptoms.
- **Deteriorating** with systolic blood pressure of 80 mmHg and acute distress.
- Multiple V fib episodes needing shocks, amiodarone, pressors

Coronary Angiogram

- Most basic of all MCS devices
- Has been in use since the 1960s
- Inflation of **helium** filled balloon during diastole (counter pulsation) and actively deflating in systole



- ↑ Coronary perfusion
- ↓ LV afterload
- ↓ Myocardial O_2 demand
- ↑ Myocardial O_2 supply



IABP SHOCK II Trial

Design	Randomized, prospective, open label, multicenter trial
Patients	600 patients with **cardiogenic shock complicating acute MI**
Intervention	**IABP** (301) vs. **no IABP** (299)
Primary Outcomes	30-day all cause mortality
Secondary Outcomes	Serum lactates, creatinine clearance, CRP, SAPS II

Thiele et al; N Engl J Med. 2012;367:1287–1296

Table 3. Clinical Outcomes.

Outcome	IABP (N=300)	Control (N=298)	P Value	Relative Risk with IABP (95% CI)
	number (percent)			
Primary end point: all-cause mortality at 30 days	119 (39.7)	123 (41.3)	0.69	0.96 (0.79–1.17)
Reinfarction in hospital	9 (3.0)	4 (1.3)	0.16	2.24 (0.70–7.18)
Stent thrombosis in hospital	4 (1.3)	3 (1.0)	0.71	1.32 (0.30–5.87)
Stroke in hospital	2 (0.7)	5 (1.7)	0.28	0.40 (0.08–2.03)
Ischemic	2 (0.7)	4 (1.3)	0.45	0.49 (0.09–2.71)
Hemorrhagic	0	1 (0.3)	0.50	—
Peripheral ischemic complications requiring intervention in hospital	13 (4.3)	10 (3.4)	0.53	1.29 (0.58–2.90)
Bleeding in hospital*				
Life-threatening or severe	10 (3.3)	13 (4.4)	0.51	0.76 (0.34–1.72)
Moderate	52 (17.3)	49 (16.4)	0.77	1.05 (0.74–1.50)
Sepsis in hospital	47 (15.7)	61 (20.5)	0.15	0.77 (0.54–1.08)

Thiele et al; N Engl J Med. 2012;367:1287–1296

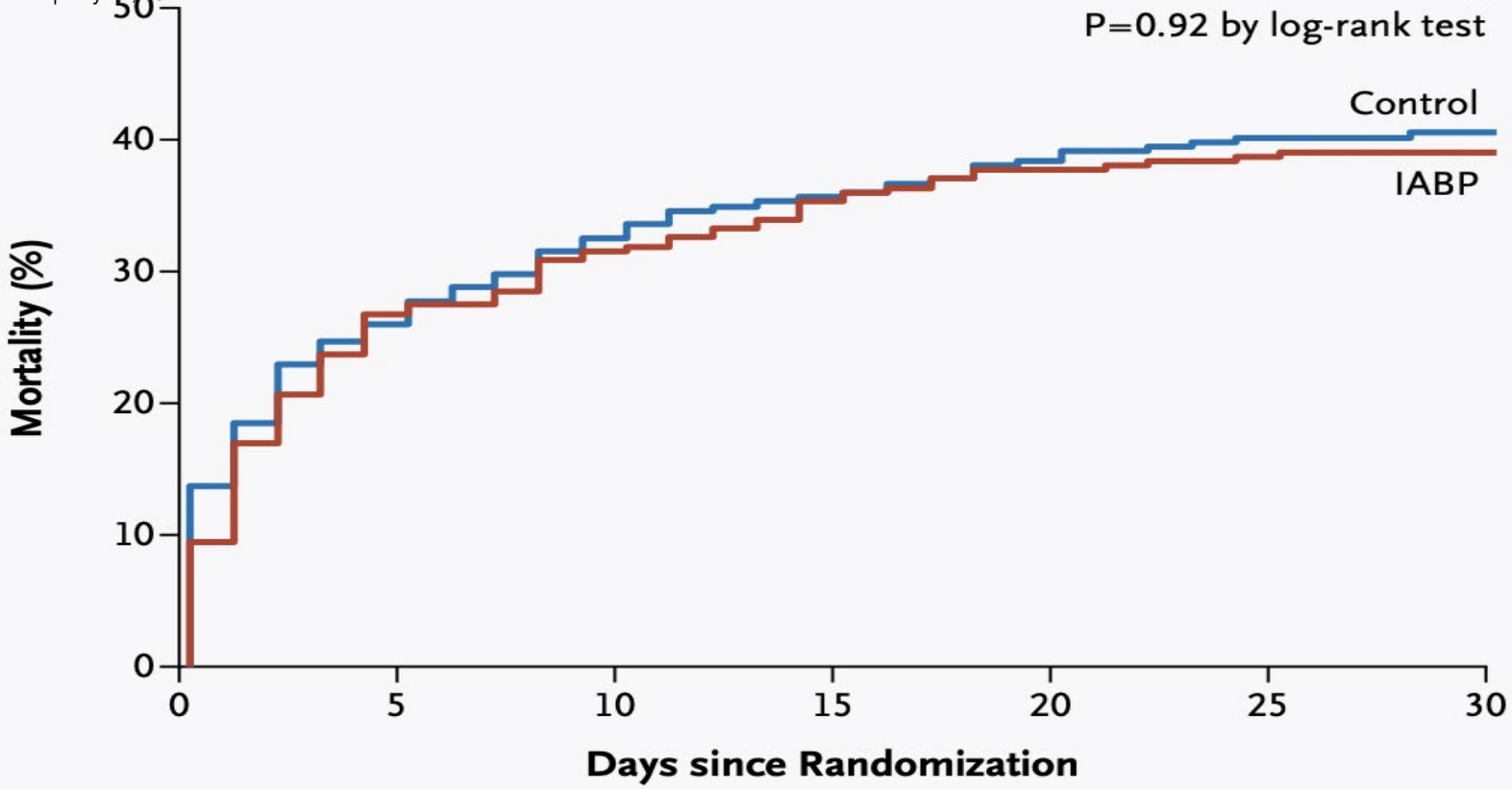


Figure 1. Time-to-Event Curves for the Primary End Point.

Time-to-event curves are shown through 30 days after randomization for the primary end point of all-cause mortality. Event rates represent Kaplan–Meier estimates.

Thiele et al; N Engl J Med. 2012;367:1287–1296

- Long-term outcomes:
  - No difference between the groups for all-cause mortality (66.3% vs 67%), recurrent MI, repeat revascularization

- Cross over rate: **14.2%**
- Relatively under-powered
- Timing of IABP insertion: at the discretion of the operator
  - **83%** had IABP inserted after PCI

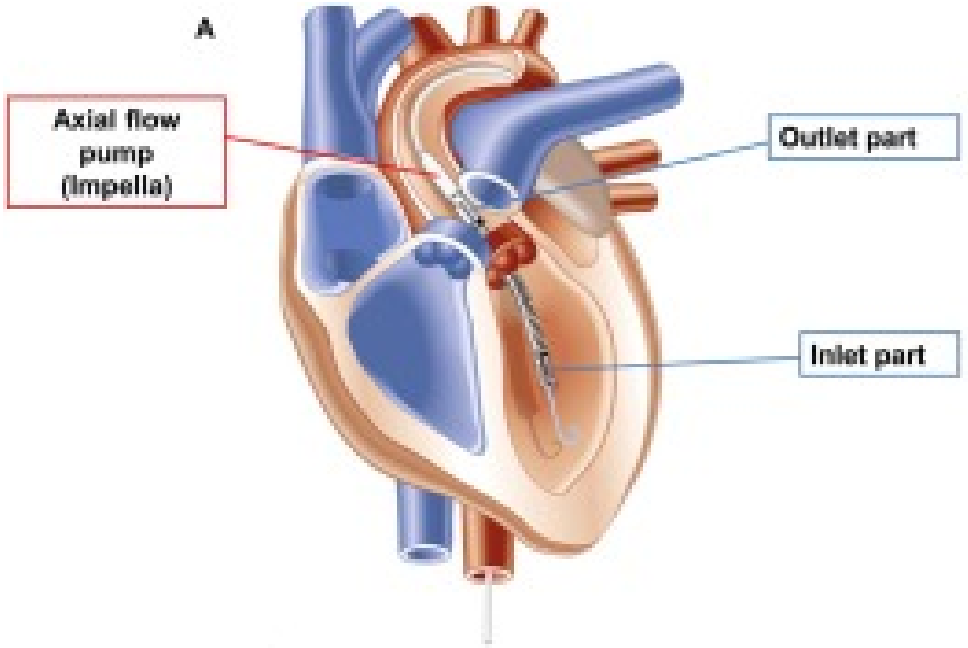
Thiele et al; Circulation. 2019;139:395–403

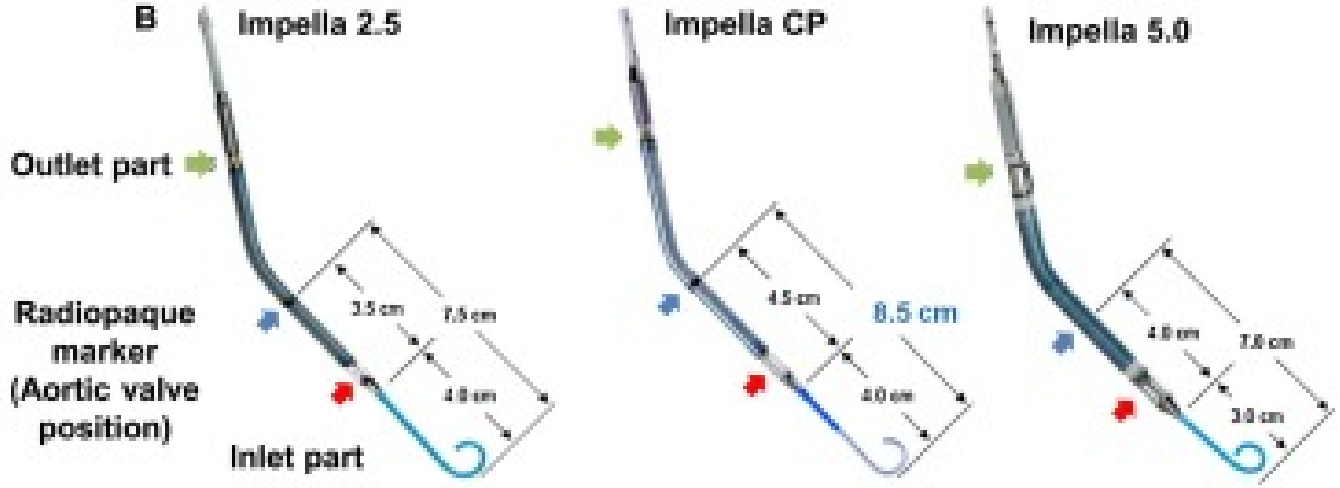
- Abdel-Wahab et al:
  - 48 patients (26 pts IABP **before PCI** and 22 controls IABP **after PCI**) with shock and acute MI
  - Patients with IABP before PCI had significantly **lower** CKMB, in-hospital mortality and CVA

Abdel-Wahab M et al; *Am J Cardiol* . 2010 Apr 1;105(7):967-71.

- In conclusion
  - Still the **most commonly** used MCS device
  - IABP **modestly** improve cardiac output
  - Increases **coronary blood flow** and decreases LV afterload
  - Clinical outcomes **unfavorable** to IABP for routine use

Impella





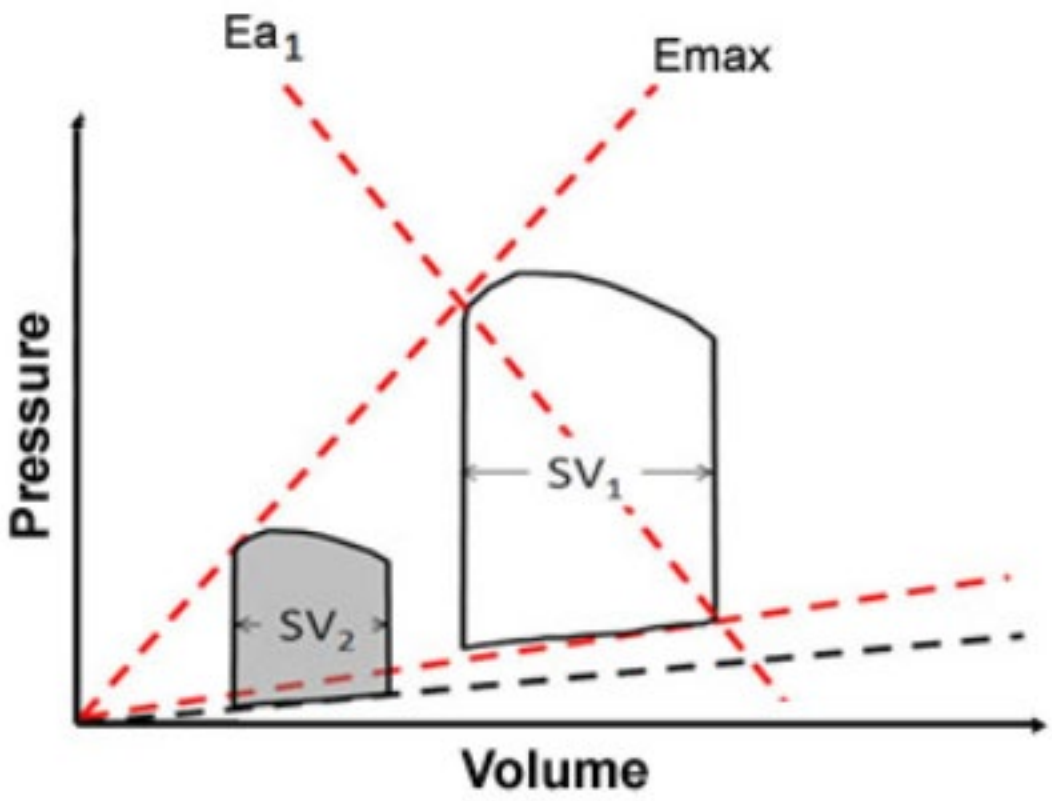
Unloading of LV

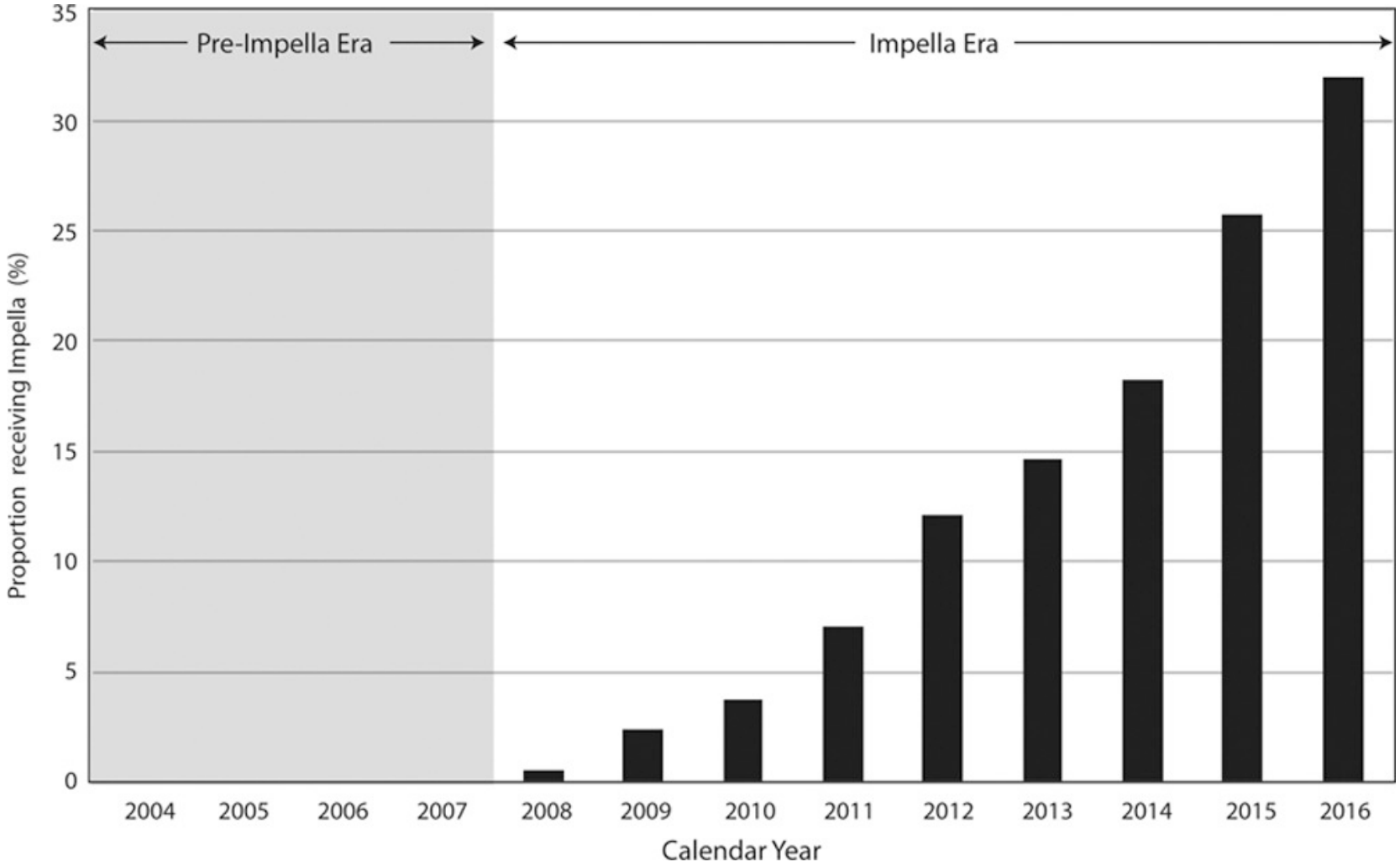
↑ Forward flow

↓ LV size, pressure and wall stress

↓ Myocardial O2 demand

↓ PCWP

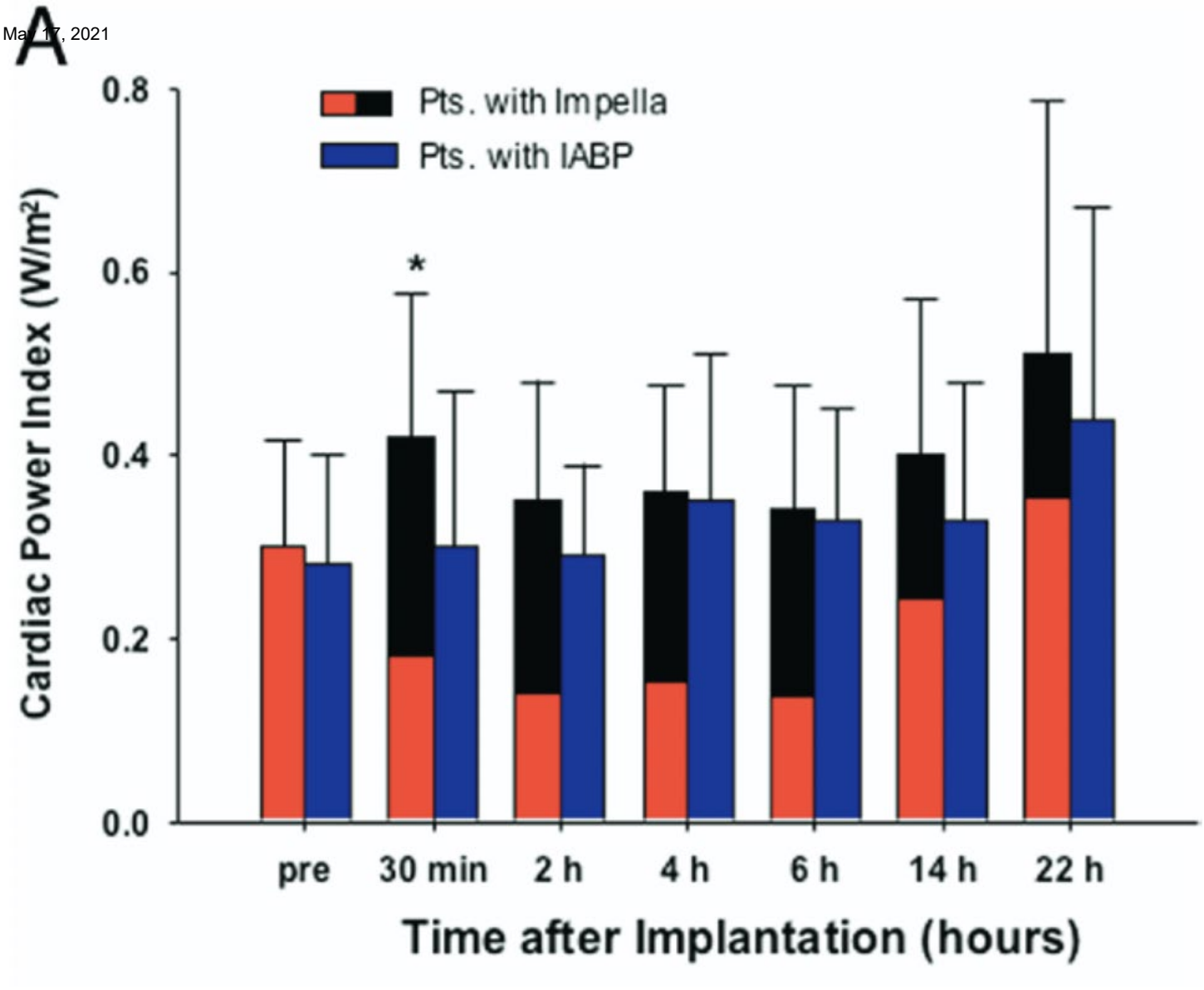


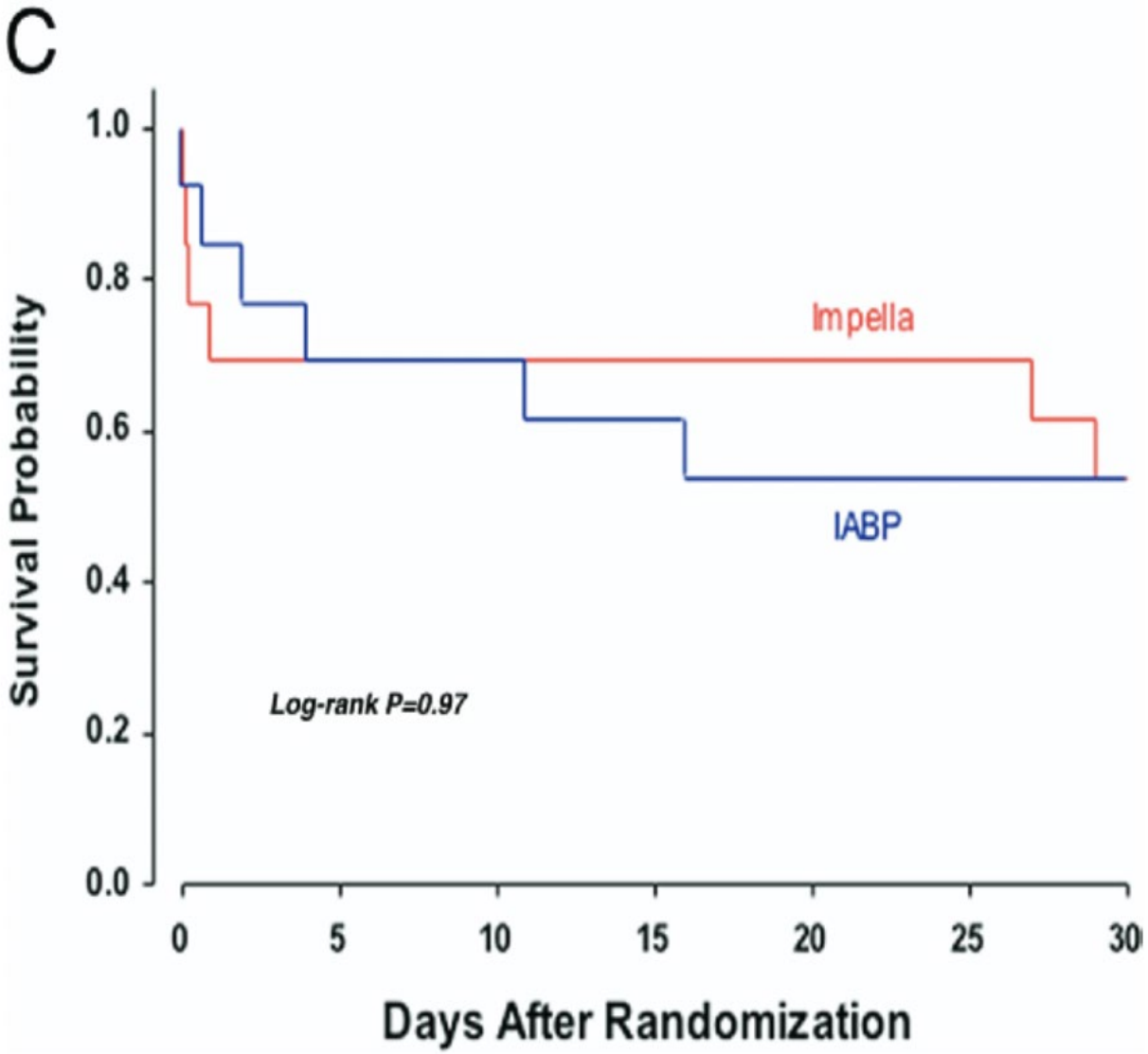


ISAR-SHOCK Trial

Design	Randomized, prospective, open label, multicenter trial
Patients	25 patients with **cardiogenic shock complicating acute MI**
Intervention	**Impella 2.5 (n=12)** vs. **IABP (n=13)**
Primary Outcomes	Change in CI from baseline to 30 mins after time of implantation
Secondary Outcomes	Lactic acidosis, hemolysis, and mortality after 30 days

Seyfarth M et al; *J Am Coll Cardiol*. 2008 Nov 4;52(19):1584-8





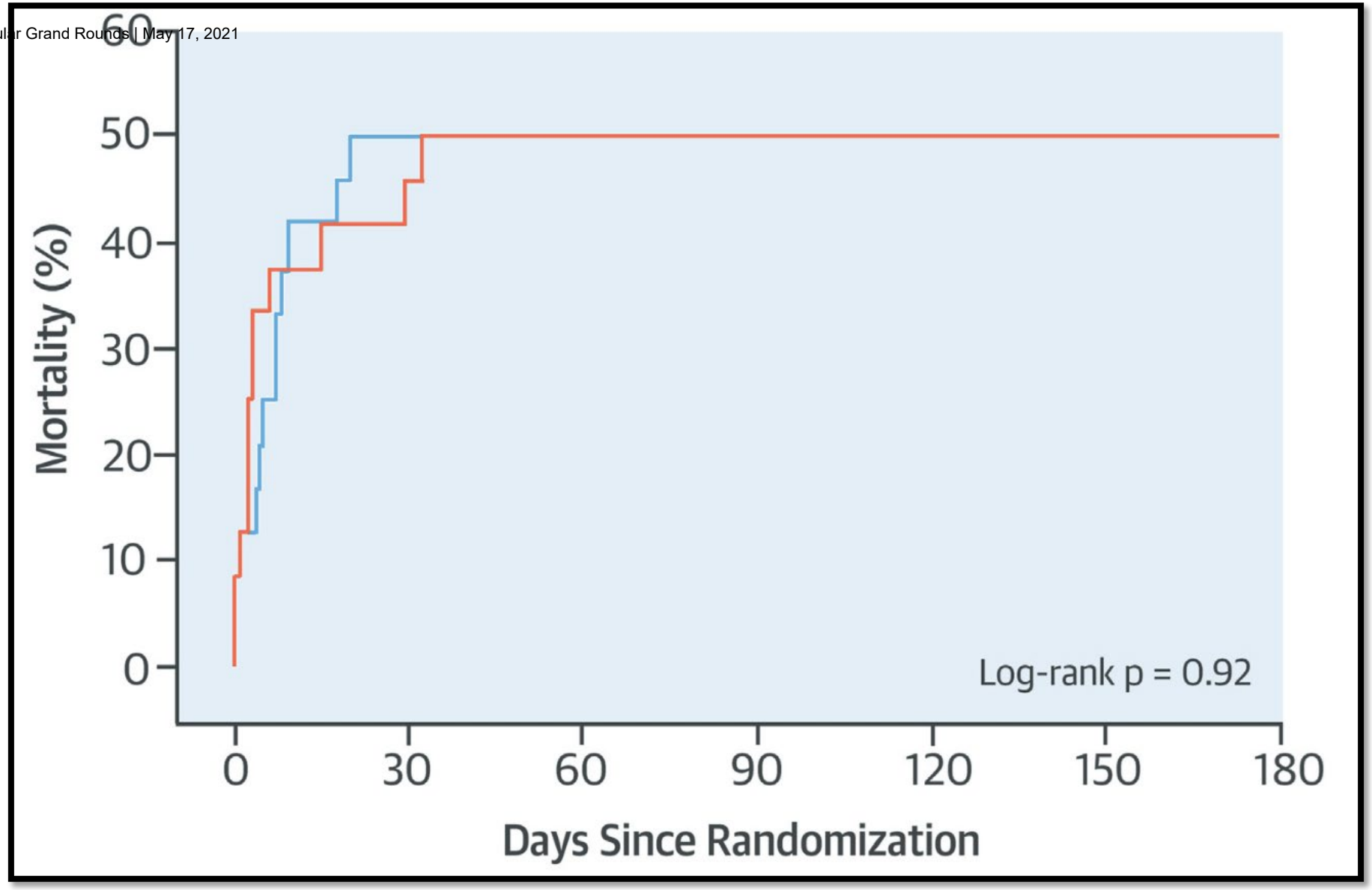
IMPRESS Trial

Design	Randomized, prospective, open label, multicenter trial
Patients	48 patients with **cardiogenic shock complicating acute MI**
Intervention	**Impella CP (24)** vs. **IABP (24)**
Primary Outcomes	**30-day all cause mortality**
Secondary Outcomes	60-day all cause mortality, duration of mechanical ventilation, ionotropic and vasopressor therapy, renal replacement therapy, hospital length of stay, stroke, repeat revascularization, vascular and bleeding complications

Ouweneel DM etal; J Am Coll Cardiol . 2017 Jan 24;69(3):278-287

- 30-day all-cause mortality:
  - 46% in Impella vs 50% in IABP: 0.96 (0.42-2.18)

- 6-month all-cause mortality:
  - 50% in Impella vs 50% in IABP: 1.04 (0.47-2.32)



- Ventilated (100%), post-arrest (92% cardiac arrest), largely comatose patients with advanced hemo-metabolic shock as evidenced by their baseline lactate of 8 → **Extremely sick patients**

- Most patients (**83%**) in IMPRESS underwent MCS implantation **after revascularization**.

USPella Registry

Design	Prospective, consecutive cohort from USPella registry over 38 sites between 2009 and 2012
Patients	154 patients with **cardiogenic shock complicating acute MI**
Groups	Impella initiated **pre-PCI** (63) vs. **post-PCI** (91)
Primary Outcomes	Survival to discharge
Secondary Outcomes	Changes in hemodynamics, incidence of MI, stroke, repeat vascularization, AKI, bleeding and vascular complications

O'Neill WW et al; J Interv Cardiol. 2014;27(1):1-11.

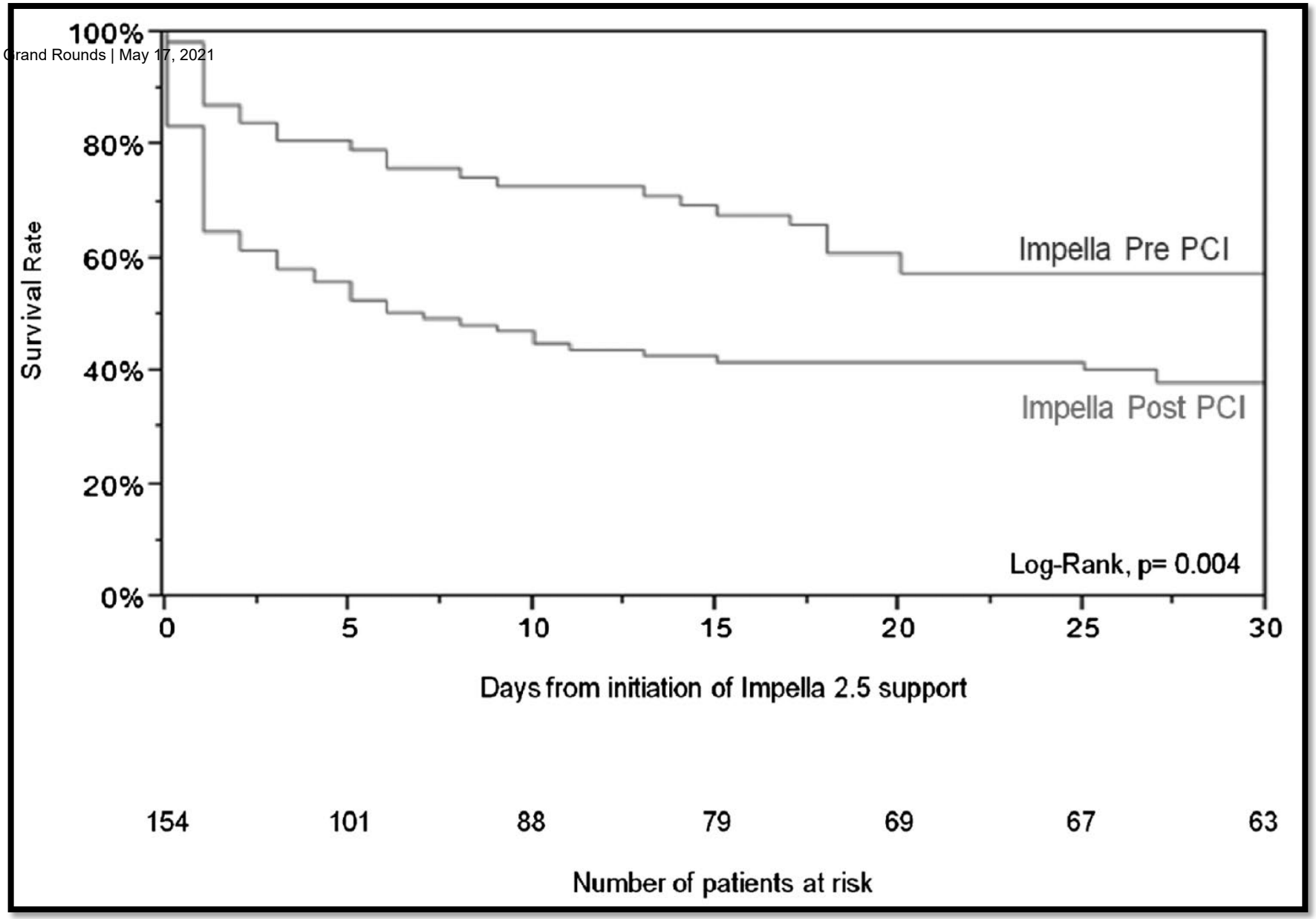


Table 4. Multivariate Analysis for Predictors of In-Hospital Mortality

	Odds Ratio	95% Confidence Interval	P-Value
Initiation of Impella support prior to PCI	0.37	0.17–0.79	0.01
Age	1.05	1.02–1.08	0.003
Number of inotropes	1.56	11–2.18	0.01
Cardiogenic shock onset prior to admission	2.42	1.12–5.24	0.03
Mechanical ventilation	4.59	2.02–10.42	0.0003

Study	Year	Patients	Outcomes
DCSI	2018	41 AMICS pts Impella CP **prior to PCI** (n=41) vs. historic controls	Survival to explant was **85%** vs. **51%** in historic controls Post-procedure CPO was significantly higher than pre-procedure CPO (**0.95 vs 0.57**; p <0.001)
NCSI	2019	171 AMICS pts Impella CP **prior to PCI**	Survival to discharge was **72%**
INOVA	2019	204 AMI/ADHF CS pts **Shock team-based** approach vs. historic controls	Survival at 30-days: **57.9% (2017)** to **76.6% (2018)** vs. **47% in 2016** historic controls

Basir et al; Catheter Cardiovasc Interv 2018; 91:454-461
Basir et al; Catheter Cardiovasc Interv 2019: 93:1173-1183
Tehrani et al; J Am Coll Cardiol 2019; 73:1659-1669

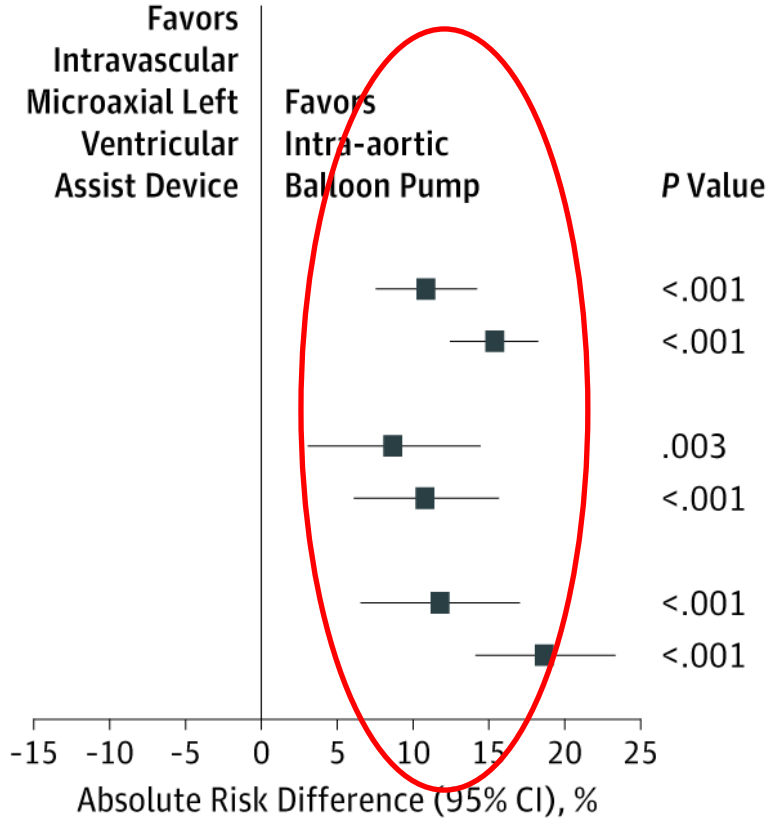
- Schrage B et al:
  - Matched 237 patient on Impella for CS and acute MI to 237 patients with IABP (IABP cohort was taken from IABP-SHOCK II trial database)
  - No difference in 30-day mortality (48.5% vs. 46.4%)
  - **More bleeding** and **vascular complications** with Impella

Schrage B et al; *Circulation.* 2019 Mar 5;139(10):1249-1258.

Study	Year	Patients	Outcomes
Amin et al	2020	48,306 pts from the Premier Healthcare database; 4782 received Impella	Impella pts had more **death**: OR 1.24; **bleeding**: OR 1.10; and **stroke**: OR 1.34
Dhruva et al	2020	28,304 pts undergoing PCI for AMI and CS from the CathPCI and Chest Pain MI registries; 1680 propensity matched pairs Impella vs. IABP	More **mortality** and **major bleeding** with Impella compared to IABP

Amin AP et a; *Circulation*. 2020;141:273–284
Dhruva SS et al; *JAMA*. 2020;323(8):734-745

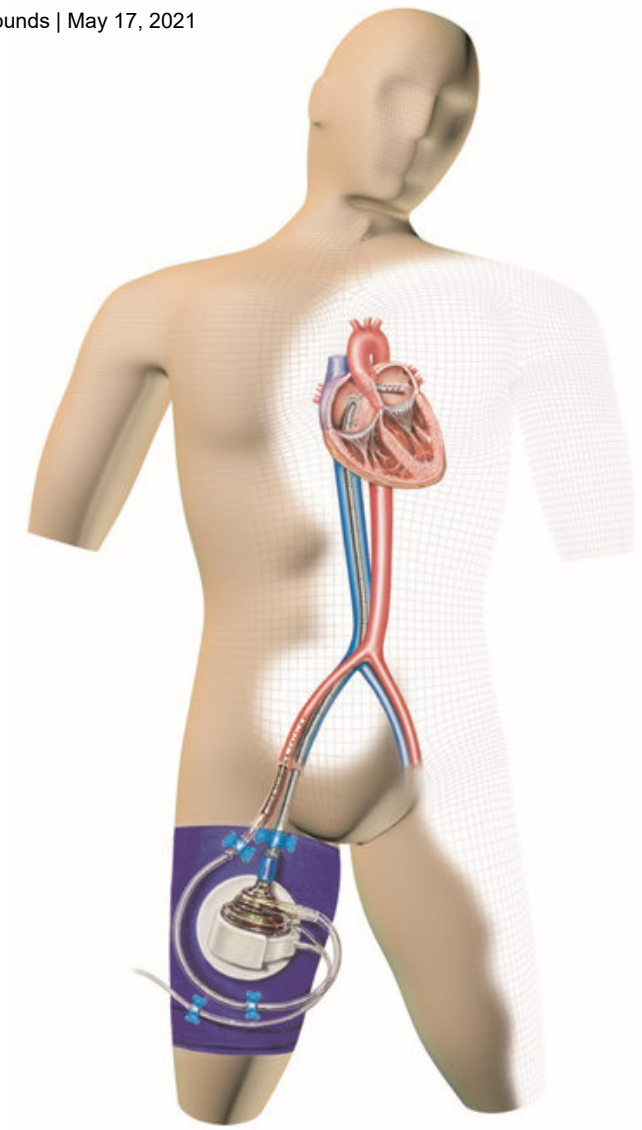
	Intravascular Microaxial Left Ventricular Assist Device		Intra-aortic Balloon Pump		Absolute Risk Difference (95% CI), %	*P* Value
	No. of Patients	Patients, %	No. of Patients	Patients, %		
Overall (n = 1680 matched pairs)						
Mortality	756	45.0	573	34.1	10.9 (7.6-14.2)	<.001
Major bleeding	526	31.3	268	16.0	15.4 (12.5-18.2)	<.001
Device placement before initiation of percutaneous coronary intervention (n = 573 matched pairs)						
Mortality	261	45.5	211	36.8	8.7 (3.1-14.4)	.003
Major bleeding	157	27.4	95	16.6	10.8 (6.1-15.6)	<.001
Device placement after initiation of percutaneous coronary intervention (n = 662 matched pairs)						
Mortality	291	44.0	213	32.2	11.8 (6.6-17.0)	<.001
Major bleeding	228	34.4	104	15.7	18.7 (14.2-23.3)	<.001

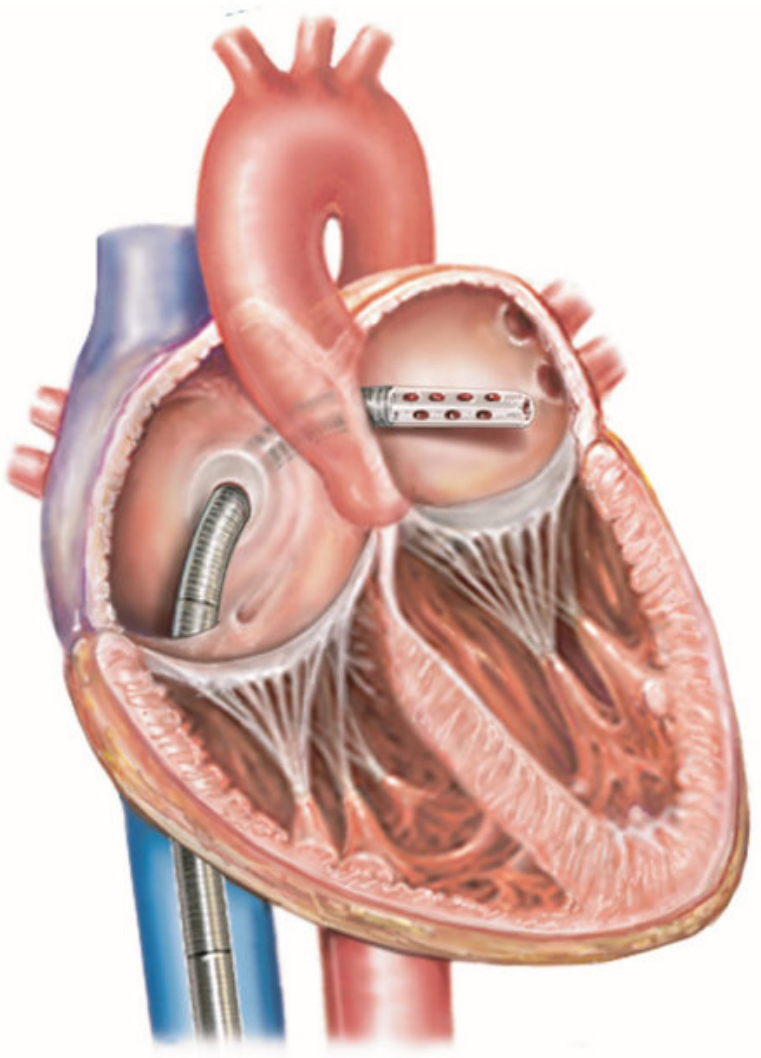


Dhruva SS et al; *JAMA*. 2020;323(8):734-745

- In conclusion:
  - Impella improves axial flow by actively unloading the LV, decreasing wall stress and myocardial O2 demand
  - Use in cardiogenic shock complicating acute MI is limited based on lack of evidence
  - **Timing of initiation** of Impella may play a role in outcomes

TandemHeart





↓ LV preload

LV workload

LV filling pressures

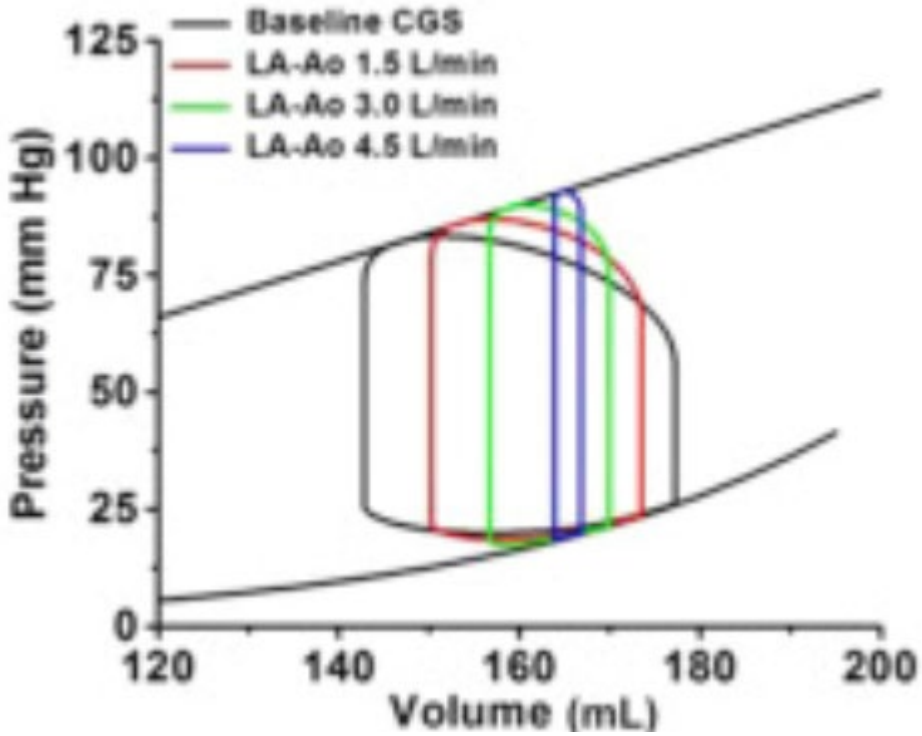
LV wall stress

Myocardial O2 demand

↑ Blood pressure

Cardiac output

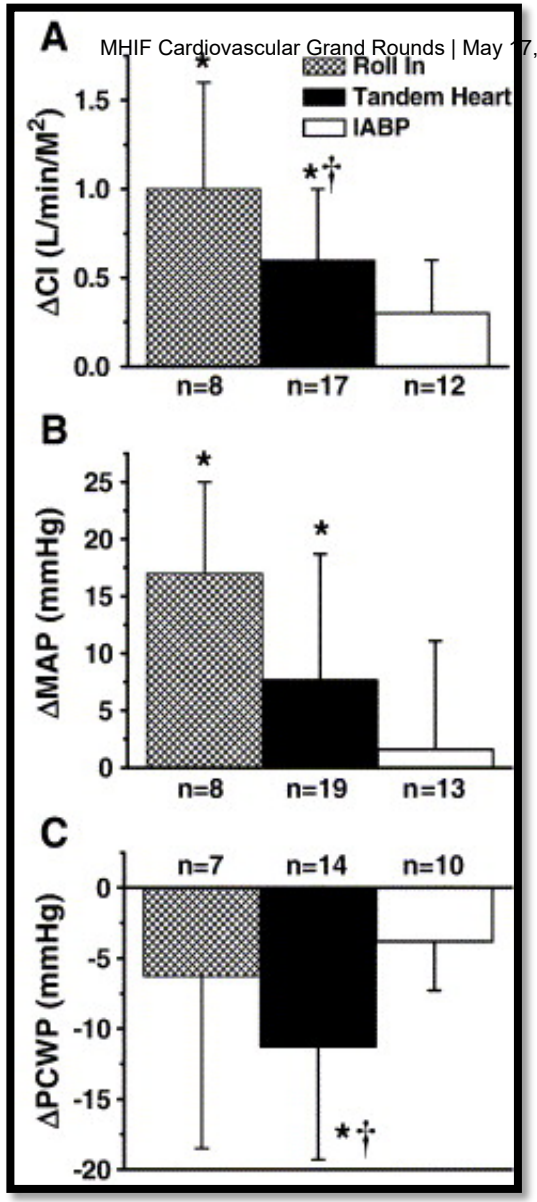
LV afterload

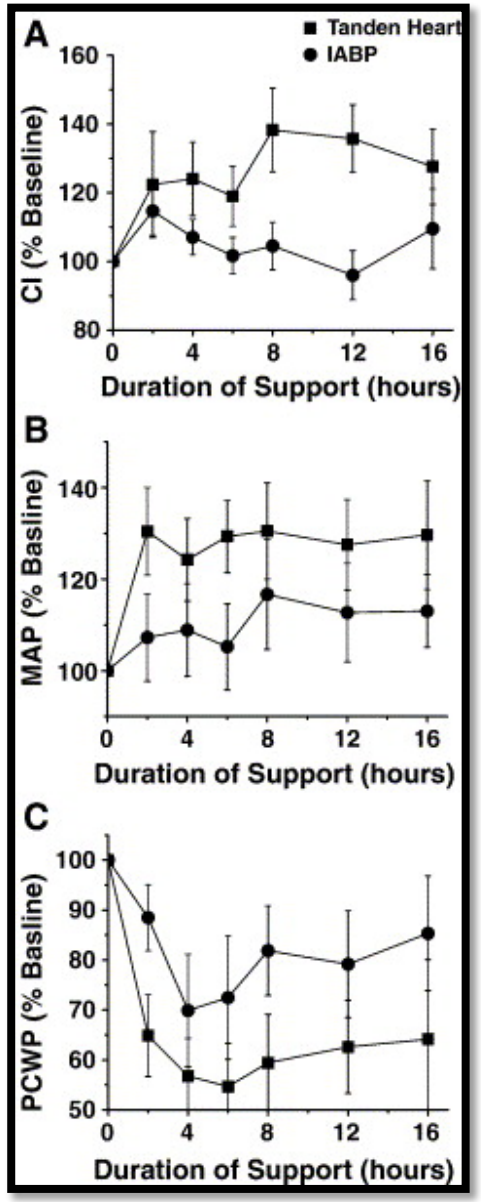


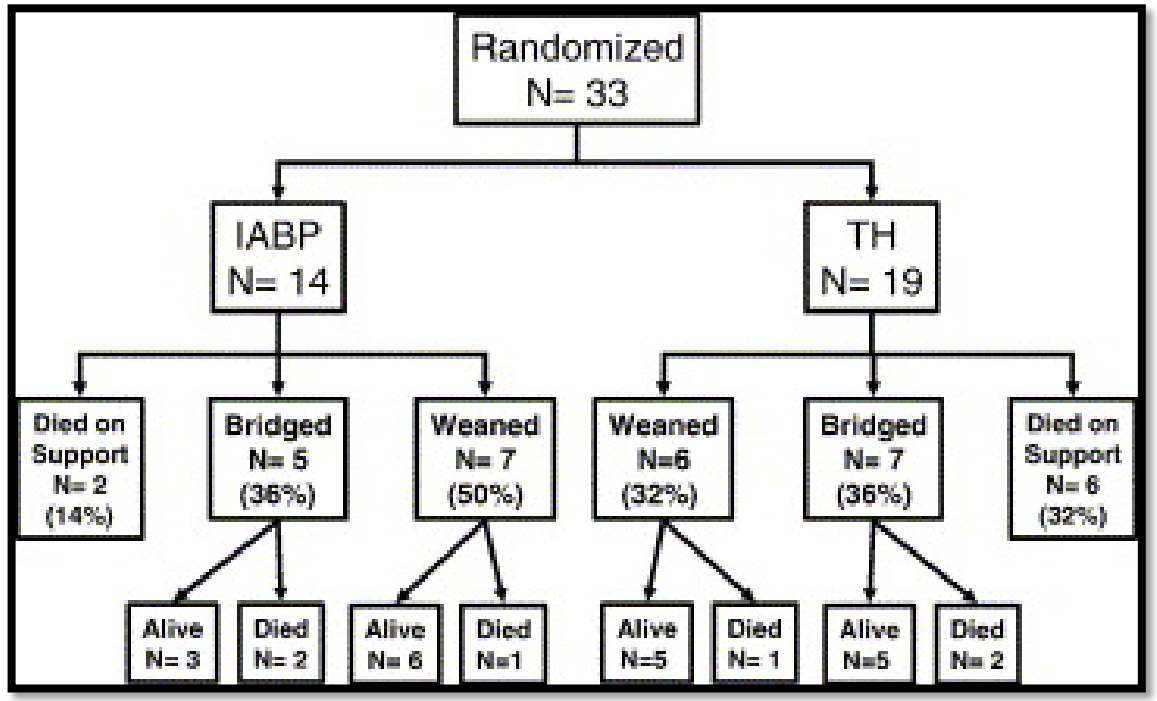
TandemHeart Investigators Group

Design	Randomized, prospective, multicenter trial
Patients	42 patients from 12 centers with **cardiogenic shock** (**70% from AMI**)
Intervention	**IABP** versus **Tandem Heart**
Primary Outcomes	Hemodynamics
Secondary Outcomes	30-day all-cause mortality

Burkhoff D; *Am Heart J*. 2006 Sep;152(3):469.e1-8.







No survival benefit

European TandemHeart Trial

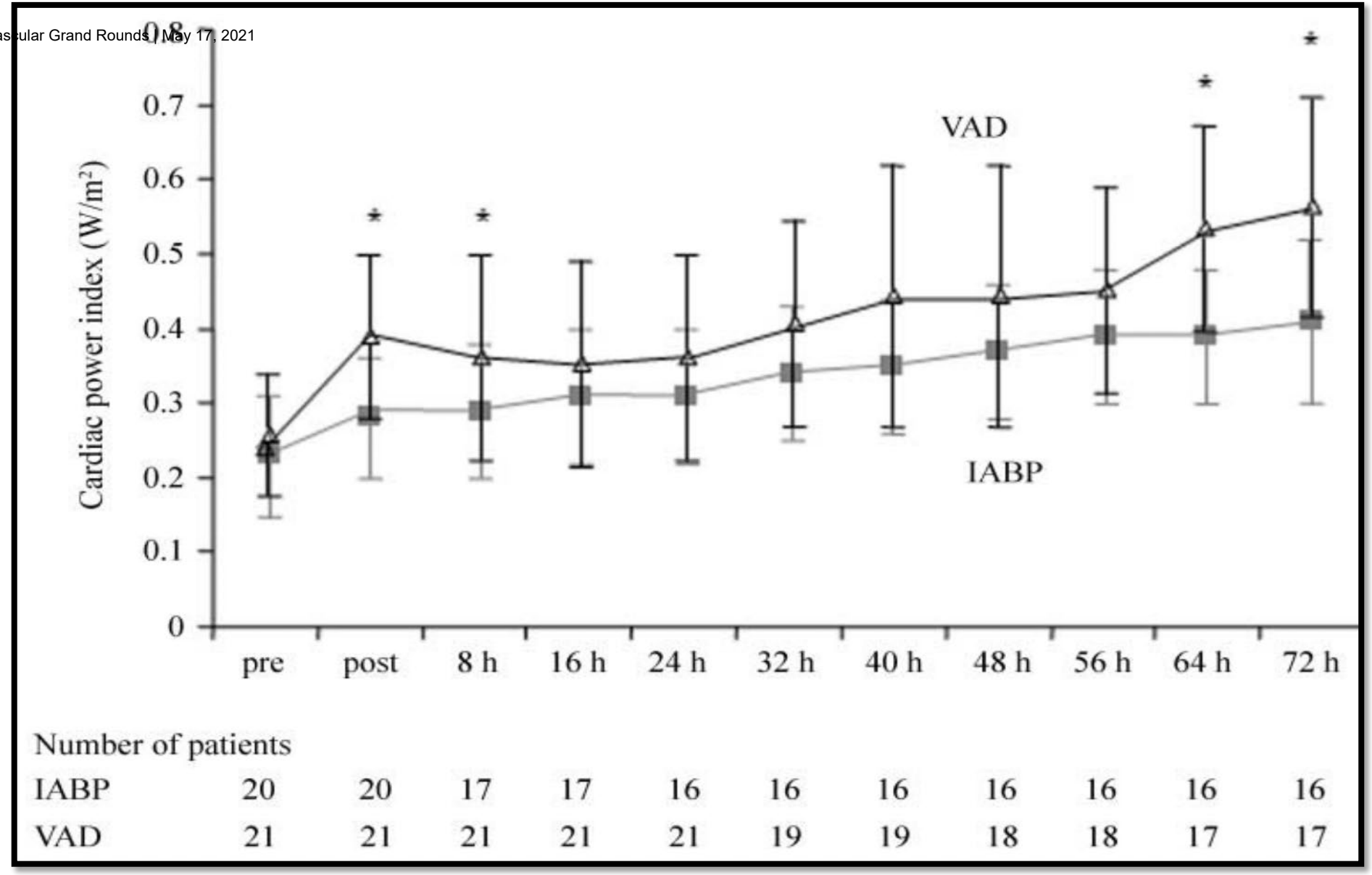
Design	Randomized, prospective, multicenter trial (2000-2003)
Patients	41 patients with **cardiogenic shock complicating AMI**
Intervention	**IABP** (20) versus **TandemHeart** (21)
Primary Outcomes	Change in cardiac power index 2 hours after device implantation
Secondary Outcomes	30-day mortality, hemodynamic, metabolic and clinical parameters

Thiele et al. European Heart Journal (2005) 26, 1276–1283

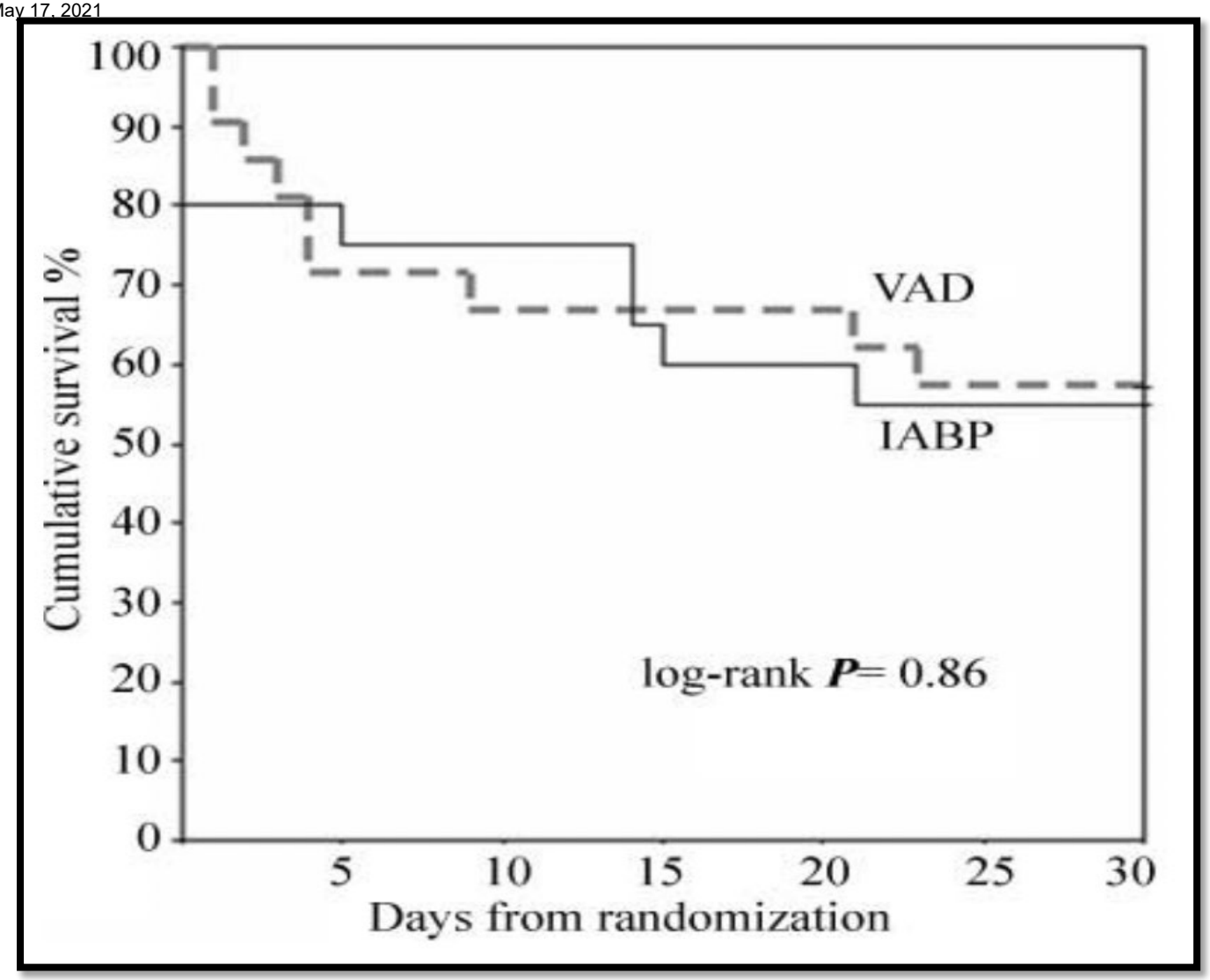
Table 3 Haemodynamic parameters pre- and post-IABP and VAD implantation

	Pre-implantation IABP	Pre-implantation VAD	*P*-value	Post-implantation IABP	Post-implantation VAD	*P*-value
Cardiac output (L/min)	3.0 (2.5–4.0)	3.5 (3.3–4.2)	0.29	3.3 (2.9–4.3)	4.5 (4.0–5.4)	0.007
CI (L/min/m^2)	1.5 (1.3–2.0)	1.7 (1.5–2.1)	0.35	1.7 (1.5–2.1)	2.3 (1.9–2.7)	0.005
Blood pressure mean (mmHg)	64 (57–74)	63 (51–70)	0.50	67 (62–84)	74 (70–84)	0.38
CPI (W/m^2)	0.22 (0.18–0.30)	0.22 (0.19–0.30)	0.72	0.28 (0.24–0.36)	0.37 (0.30–0.47)	0.004
SVR (dyn × s × cm^{-5})	1440 (1034–1758)	1049 (852–1284)	0.16	1388 (998–1809)	1153 (844–1425)	0.08
Heart rate (beats/min)	122 (92–130)	113 (107–121)	0.57	115 (90–125)	105 (100–116)	0.94
PCWP (mmHg)	27.0 (20.0–30.0)	20.0 (18.0–23.0)	0.02	21.5 (17.0–26.0)	16.0 (12.5–19.0)	0.003
Central venous pressure (mmHg)	13.0 (11.0–16.5)	11.0 (9.0–15.3)	0.29	12.0 (10.0–17.5)	10.0 (8.0–12.0)	0.06
PAP mean (mmHg)	32.5 (27.5–38.0)	28.0 (24.5–34.8)	0.45	28.5 (25.5–33.5)	24.5 (20.0–26.0)	0.007
Serum lactate (mmol/L)	3.8 (3.5–6.7)	4.5 (3.1–6.5)	0.53	3.25 (2.7–7.0)	2.8 (2.3–3.5)	0.03
Standard base excess (mmol/L)	−6.8 [−8.3–(−3.9)]	−5.1 [−7.5–(−4.4)]	0.74	−4.3 [−8.8–(−2.3)]	−4.3 [−6.1–(−3.3)]	0.28
pH	7.34 (7.28–7.38)	7.28 (7.24–7.36)	0.50	7.36 (7.28–7.41)	7.33 (7.31–7.40)	0.49

SVR, systemic vascular resistance; PAP, pulmonary artery pressure; values are given as median (IQR).



Number of patients											
IABP	20	20	17	17	16	16	16	16	16	16	16
VAD	21	21	21	21	21	19	19	18	18	17	17

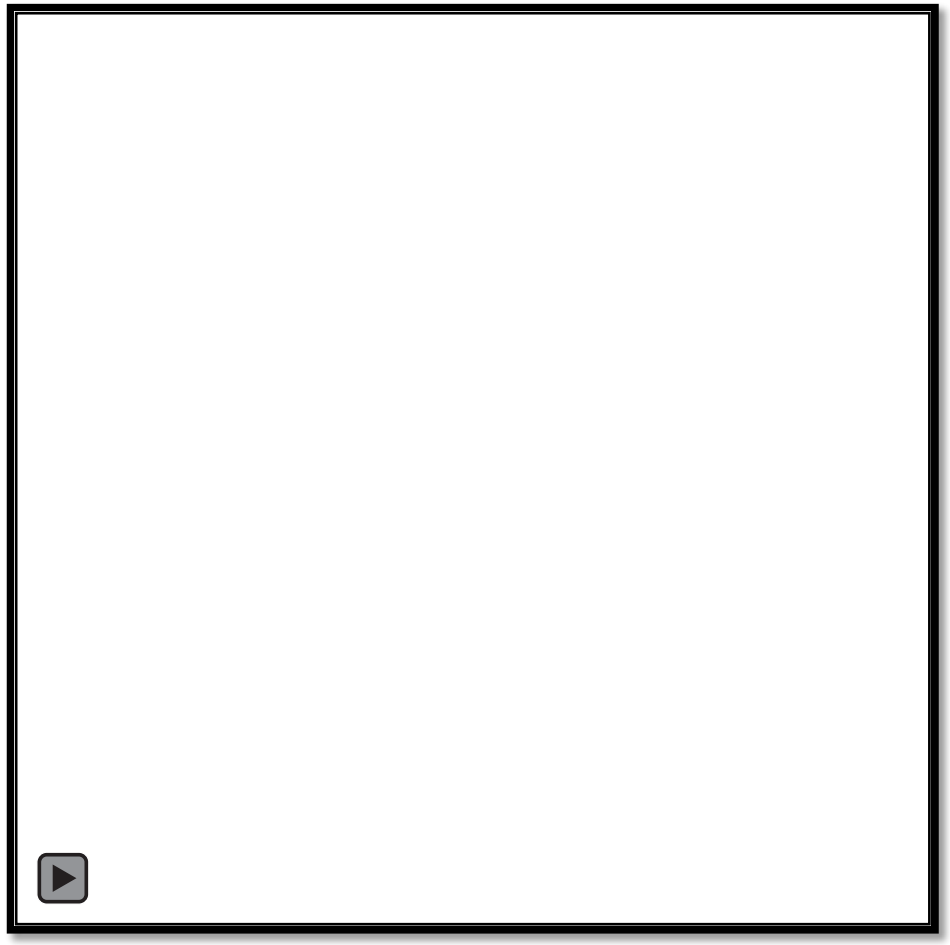


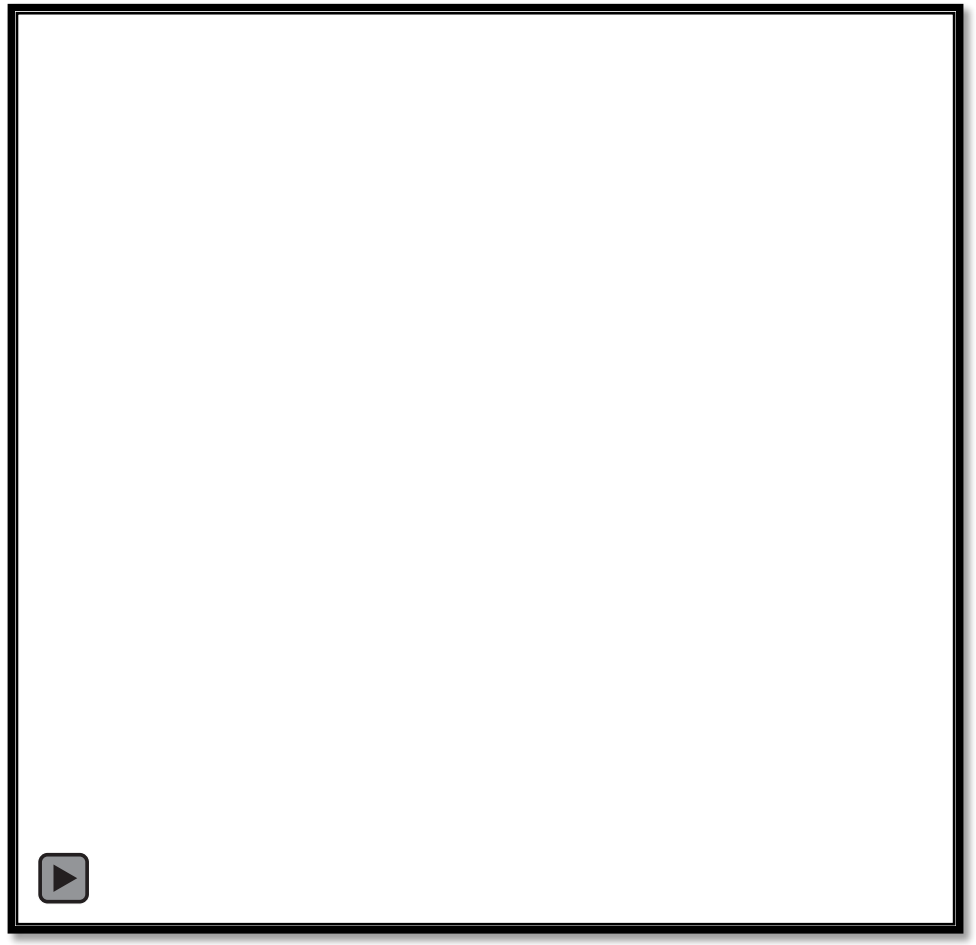
- In conclusion:
  - TandemHeart significantly improves hemodynamics in CS + AMI patients
  - Evidence for TandemHeart is not convincing for routine use in CS with AMI

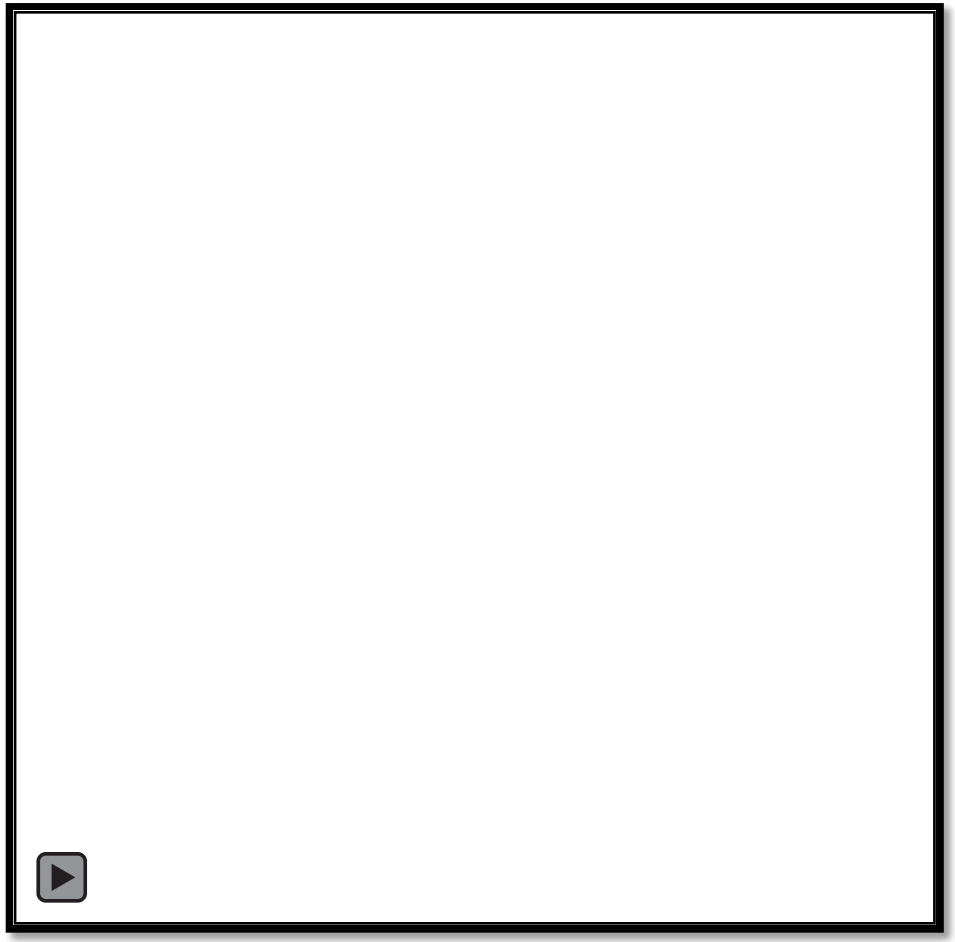
Extra Corporeal Membrane Oxygenation

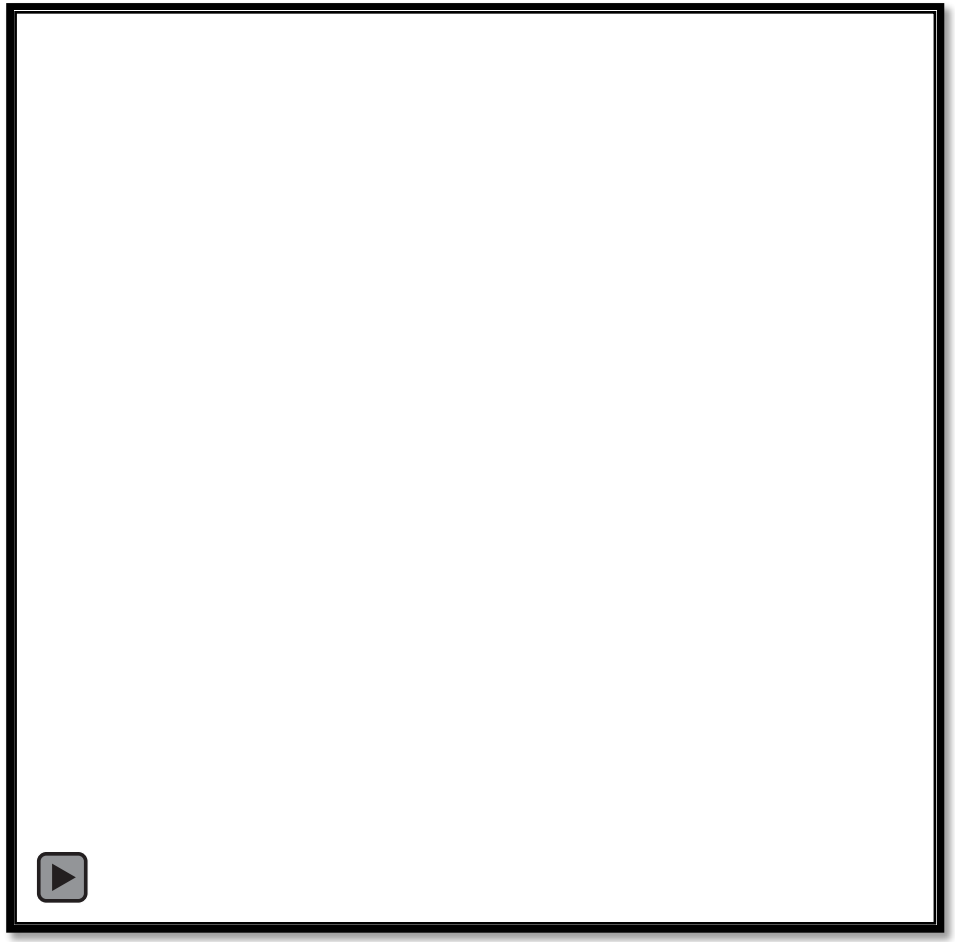
Case

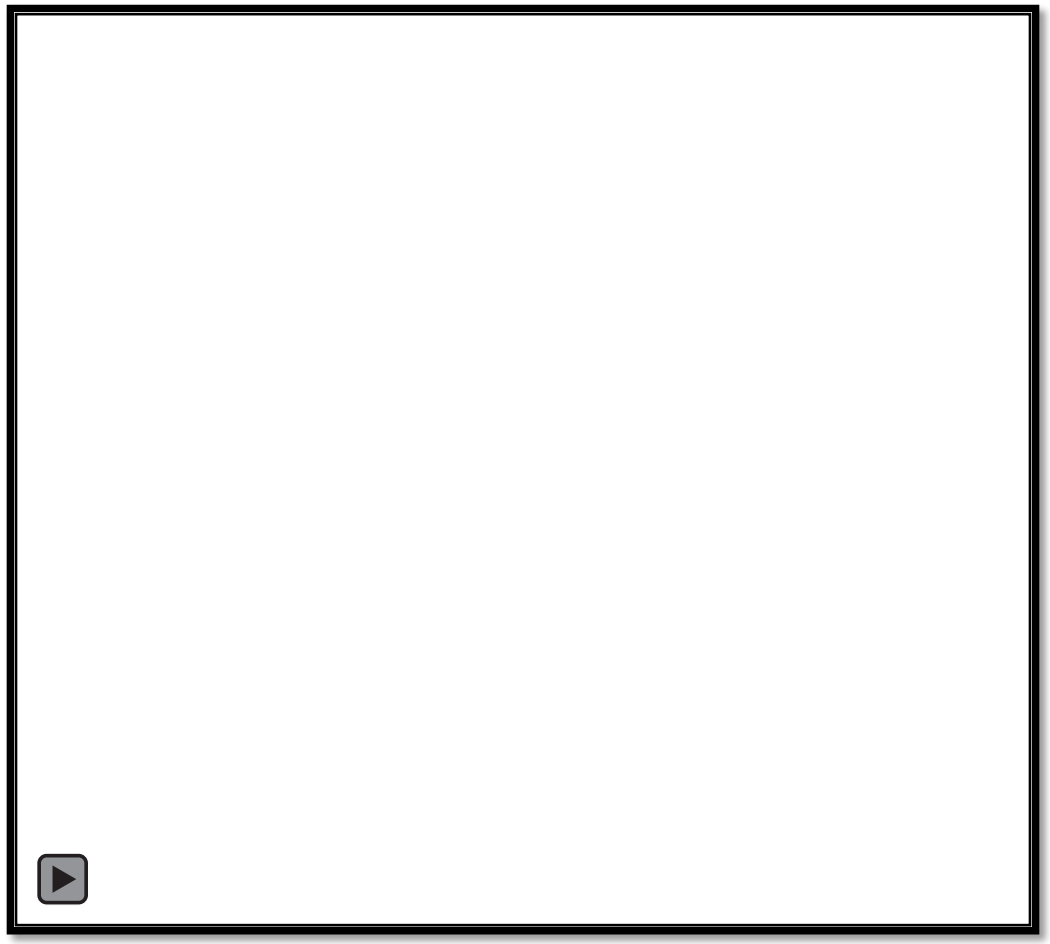
- 48-year-old male with no significant past medical history came in with chest pain (for 2 weeks). Negative stress echo few days prior.
- EKG: sinus bradycardia with nonspecific ST changes in lateral leads.
- Unresponsive, initial rhythm was **v. fib** → several shocks. ACLS protocol with active CPR using Lucas device.
- Bedside TEE was performed which showed **incessant ventricular fibrillation**





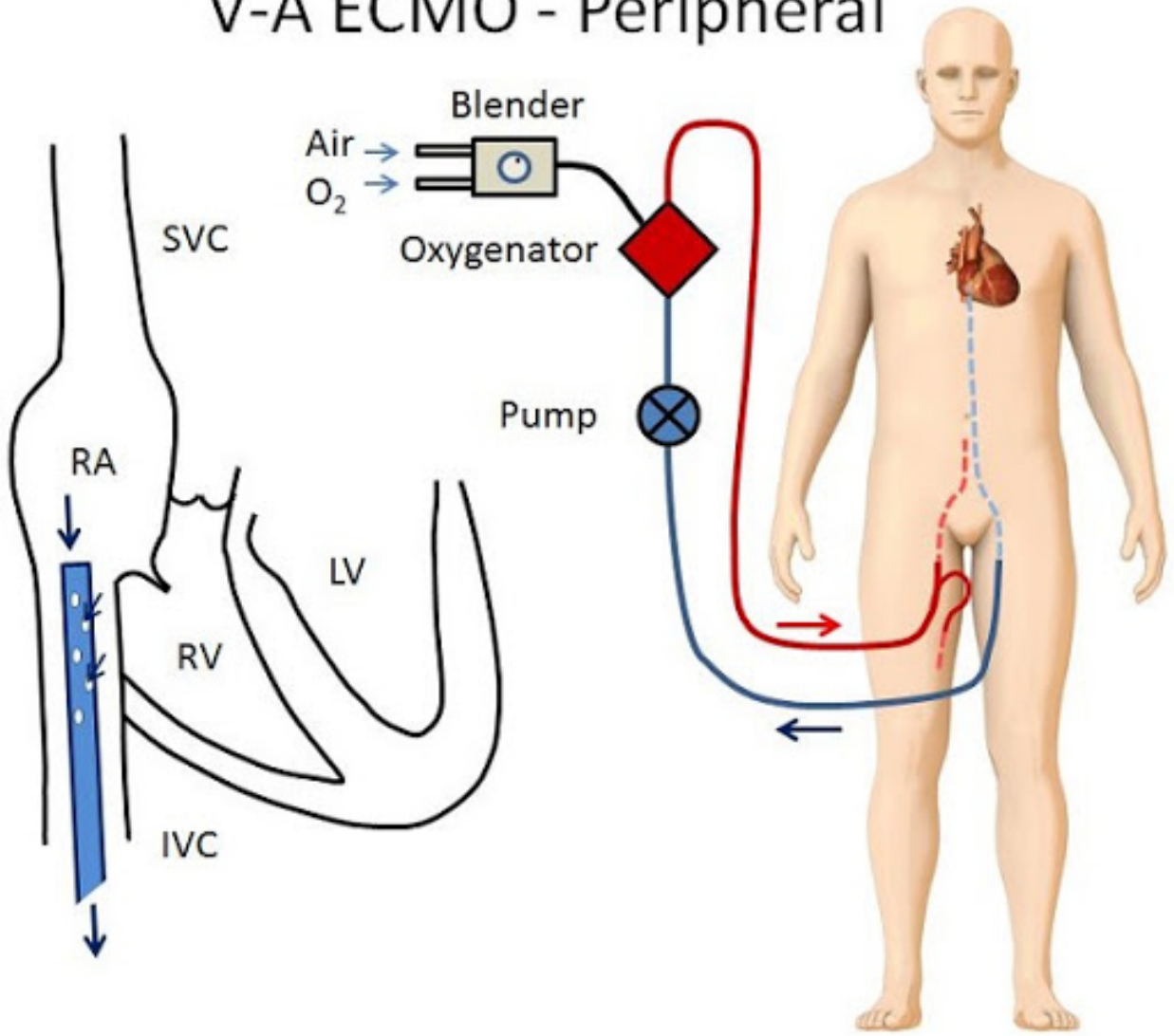




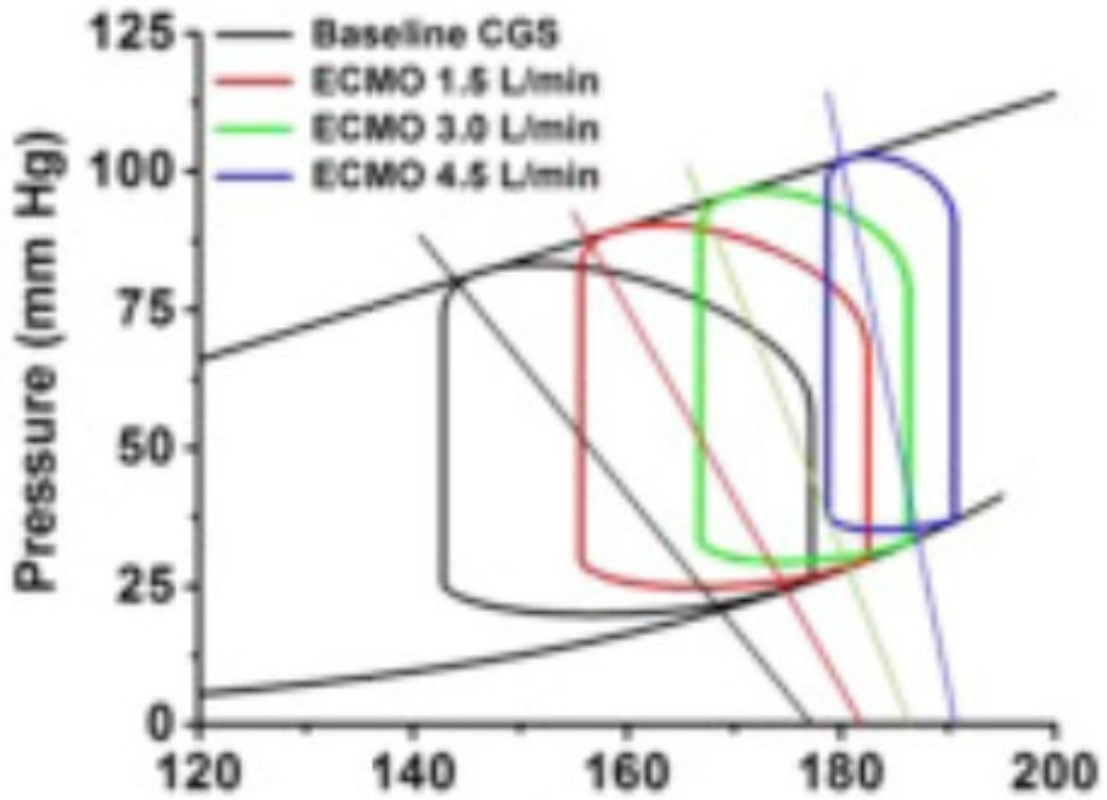


- VA-ECMO
- Use of ECMO is rapidly evolving
- Mostly retrospective observation data and meta-analysis
- Provides up to 5-6 liters/min of cardiac output

V-A ECMO - Peripheral

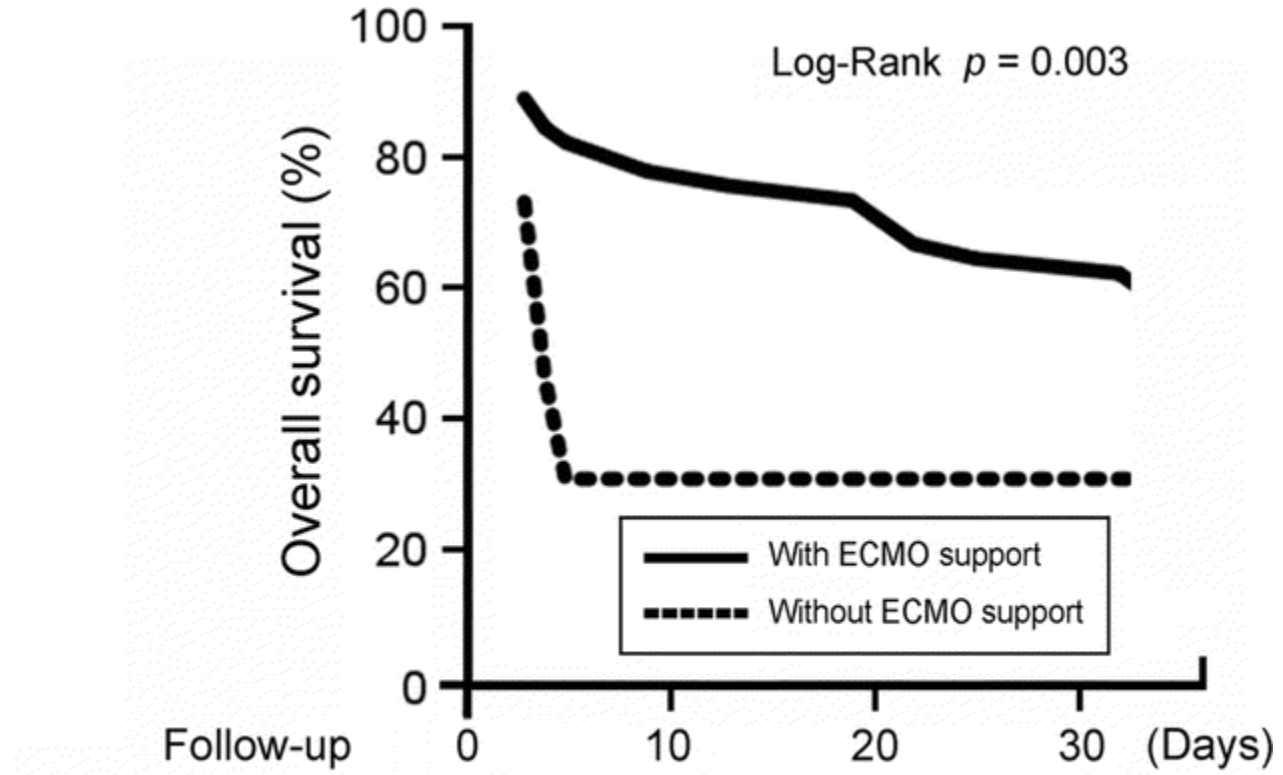


- ↓ RV end-diastolic volume
- ↑ Mean arterial pressure
- ↑ LV afterload



- Sheu J et al:
  - 115 patients (group 1 [between 1993 and 2002]) vs. 219 patients (group 2) with acute STEMI and shock (between 2002 and 2009)
  - ECMO use only in patients with profound shock in group 2 (46 patients)
  - 30-day survival: 39% vs **72%**

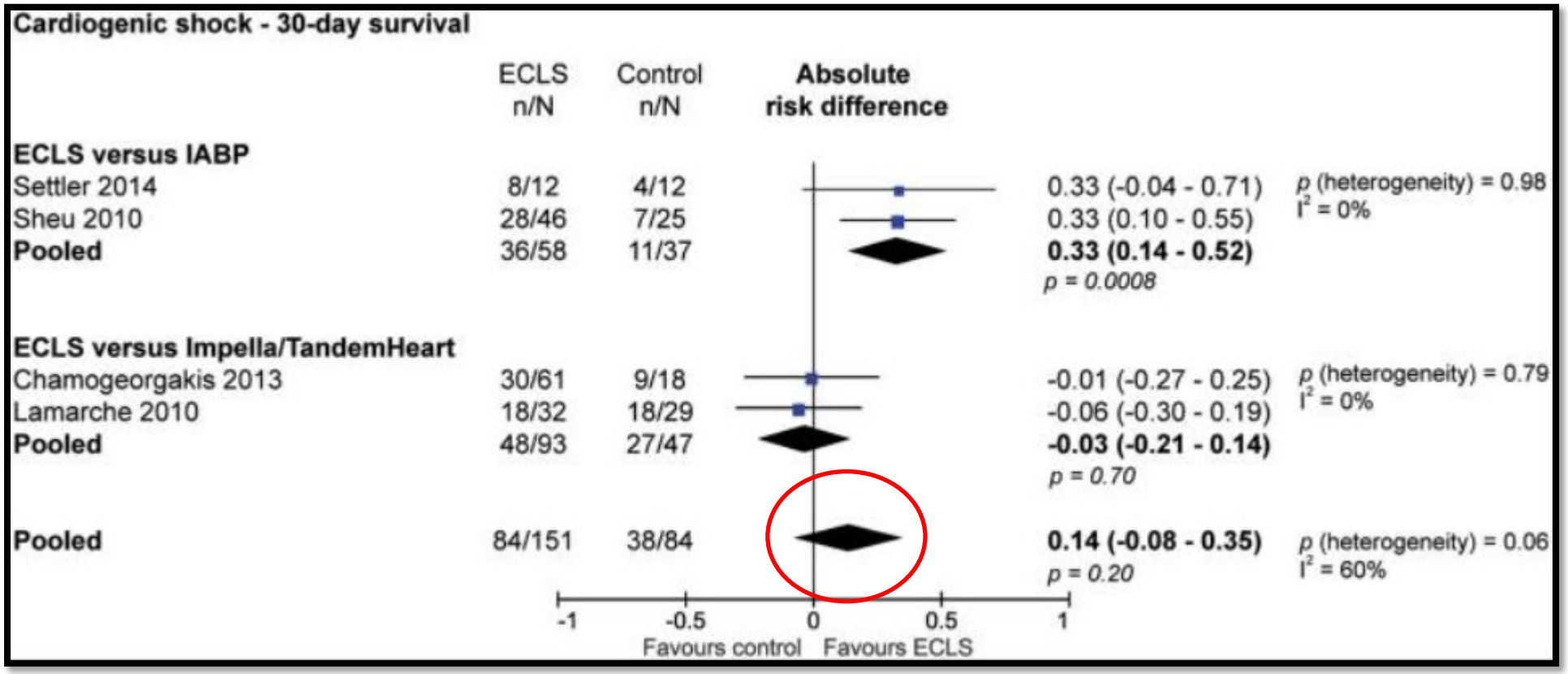
Sheu JJ et al. *Crit Care Med* 2010; 38: 1810–17



At risk (n)	With ECMO	46	32	31	28
	Without ECMO	25	7	7	7

- Ouweneel DM et al:
  - Meta-analysis of 4 studies of patients with acute MI and cardiogenic shock
  - **33% higher survival** in patients with VA-ECMO compared to IABP at 30 days
  - **No difference in survival** compared to TandemHeart or Impella

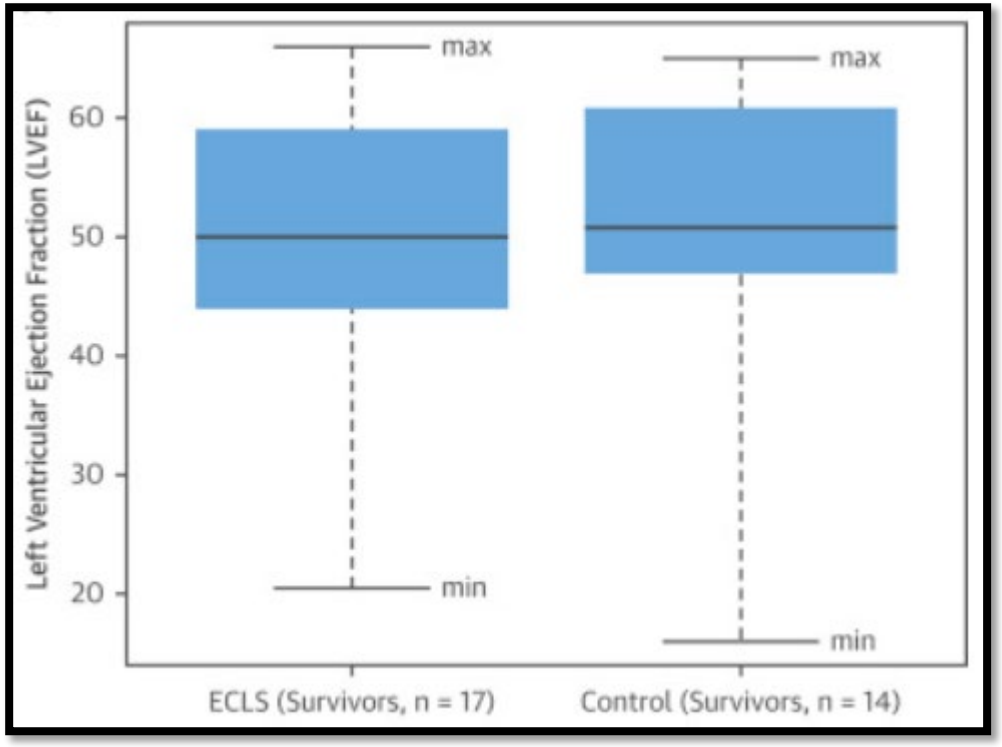
Ouweneel D et al; *Intensive Care Med* . 2016 Dec;42(12):1922-1934

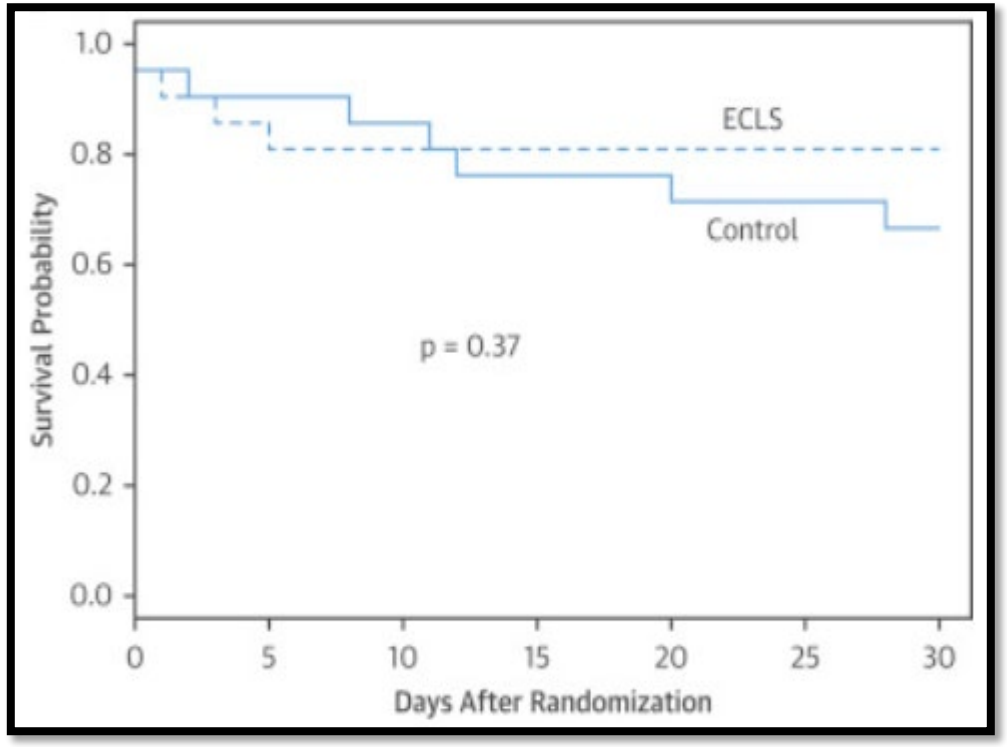


Brunner S et al:

Design	Single-center, randomized, open-labeled
Patients	42 patients with **cardiogenic shock complicating AMI**
Intervention	**ECLS** (21) vs. **no MCS** (21)
Primary Outcomes	**LVEF at 30 days**
Secondary Outcomes	pH values, lactate, cumulative catecholamine doses

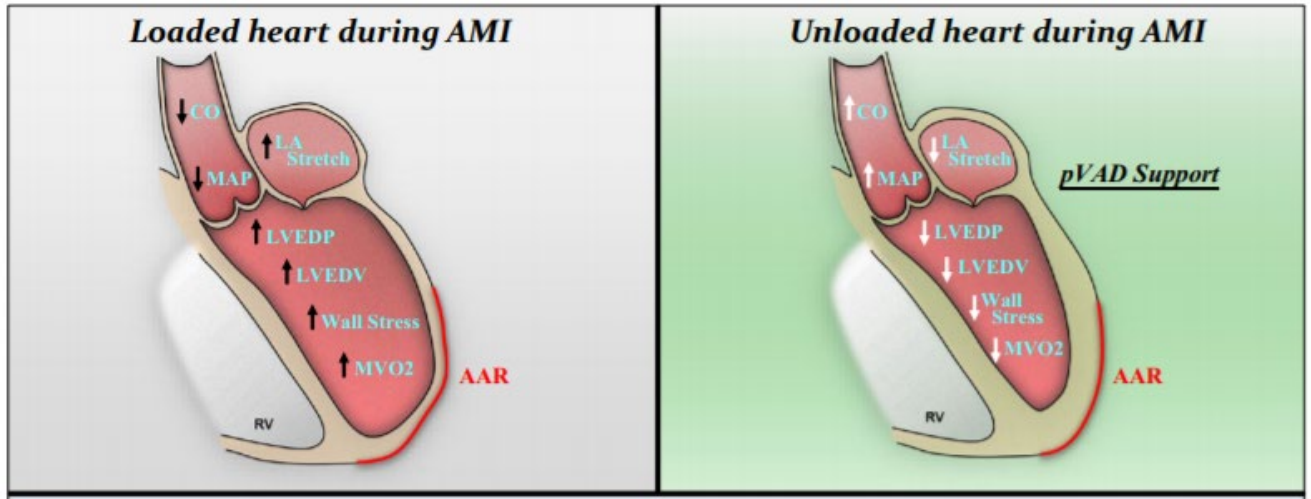
Brunner S et al; J Am Coll Cardiol 2019; 73:2355–2357





- In conclusion:
  - VA-ECMO is used increasingly, especially in patients who present with cardiac arrest secondary to AMI
  - Provides the maximal support for cardiac output
  - High quality evidence is lacking

MCS in STEMI



Cardioprotective Effects of Unloading

Decreased myocardial oxygen consumption

Activation of cardioprotective signaling (i.e., SDF1a/CXCR4 and RISK pathway)

Increased cardiac microvascular perfusion into infarct zone

Hemodynamic stabilization through reperfusion-dependent arrhythmia

Bridge through reperfusion-induced myocardial stunning

Reduced acute infarct size and subsequent scar size

Curran et al J Cardiovasc Transl Res. 2019; 12(2): 95–106

CRISP AMI Trial

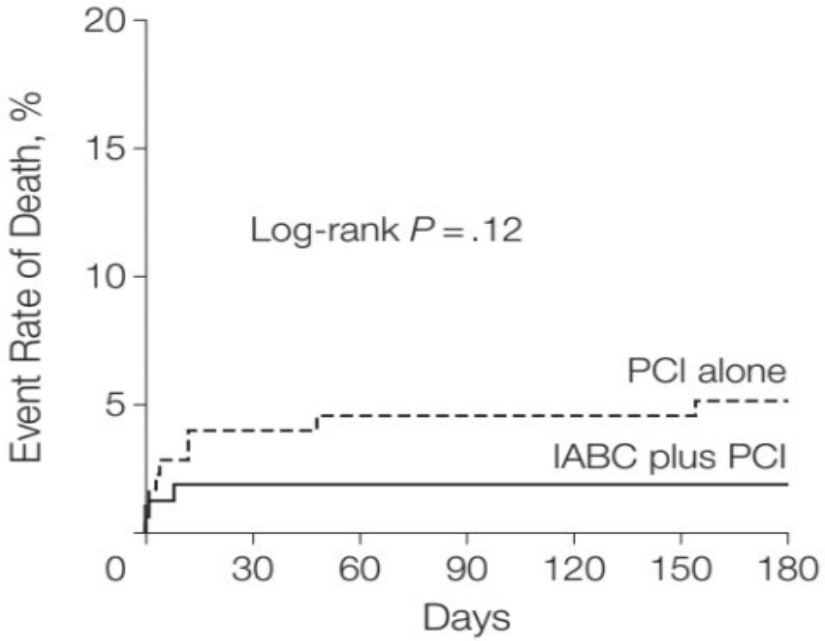
Design	Randomized, open, multicenter trial
Patients	337 patients with acute **anterior STEMI without shock**
Intervention	**IABP** versus no IABP pre-vascularization
Primary Outcomes	**Infarct size** measured by Cardiac MRI 3-5 days after revascularization
Secondary Outcomes	All-cause mortality at 6 months
	Vascular and bleeding complications at 30-days

Patel M et al; JAMA. 2011;306(12):1329-1337

Table 3. Cardiac Magnetic Resonance Imaging (MRI) Findings

	Total (N = 337)	IABC Plus PCI (n = 161)	PCI Alone (n = 176)	*P* Value
Time from symptom onset to MRI, median (IQR), d	4.0 (3.0-5.0)	4.0 (3.0-5.0)	4.0 (3.0-4.0)	.20
Primary End Point				
Infarct size, % of left ventricular mass				
Per-protocol analysis, No. (%)	275 (81.6)	133 (82.6)	142 (80.7)	
Mean (95% CI)	39.8 (37.4-42.1)	42.1 (38.7-45.6)	37.5 (34.3-40.8)	.06
Median (IQR)	38.8 (26.0-52.2)	42.8 (27.2-54.7)	36.2 (25.9-49.4)	
Multiple imputation analysis				
Mean (95% CI)	39.7 (37.3-42.1)	42.1 (38.6-45.6)	37.6 (34.3-40.9)	.07
Median (IQR)	39.0 (26.0-52.3)	42.5 (27.1-55.9)	36.4 (24.9-49.9)	
Proximal left anterior descending and TIMI flow score of 0 or 1				
Per-protocol analysis, No. (%)	192 (57.0)	93 (57.8)	99 (56.3)	
Mean (95% CI)	44.4 (41.7-47.1)	46.7 (42.8-50.6)	42.3 (38.6-45.9)	.11
Median (IQR)	42.1 (30.3-54.7)	45.1 (32.7-60.8)	38.6 (29.6-51.6)	
Multiple imputation analysis				
Mean (95% CI)	44.4 (41.7-47.1)	46.8 (42.9-50.8)	42.1 (38.4-45.7)	.08
Median (IQR)	42.5 (30.3-55.9)	45.3 (32.3-61.6)	39.2 (29.5-51.9)	

Figure 2. Event Rate of Death From 0 to 180 Days



No. at risk

PCI alone	174	167	165	165	165	165	164
IABC plus PCI	157	154	153	153	153	153	153

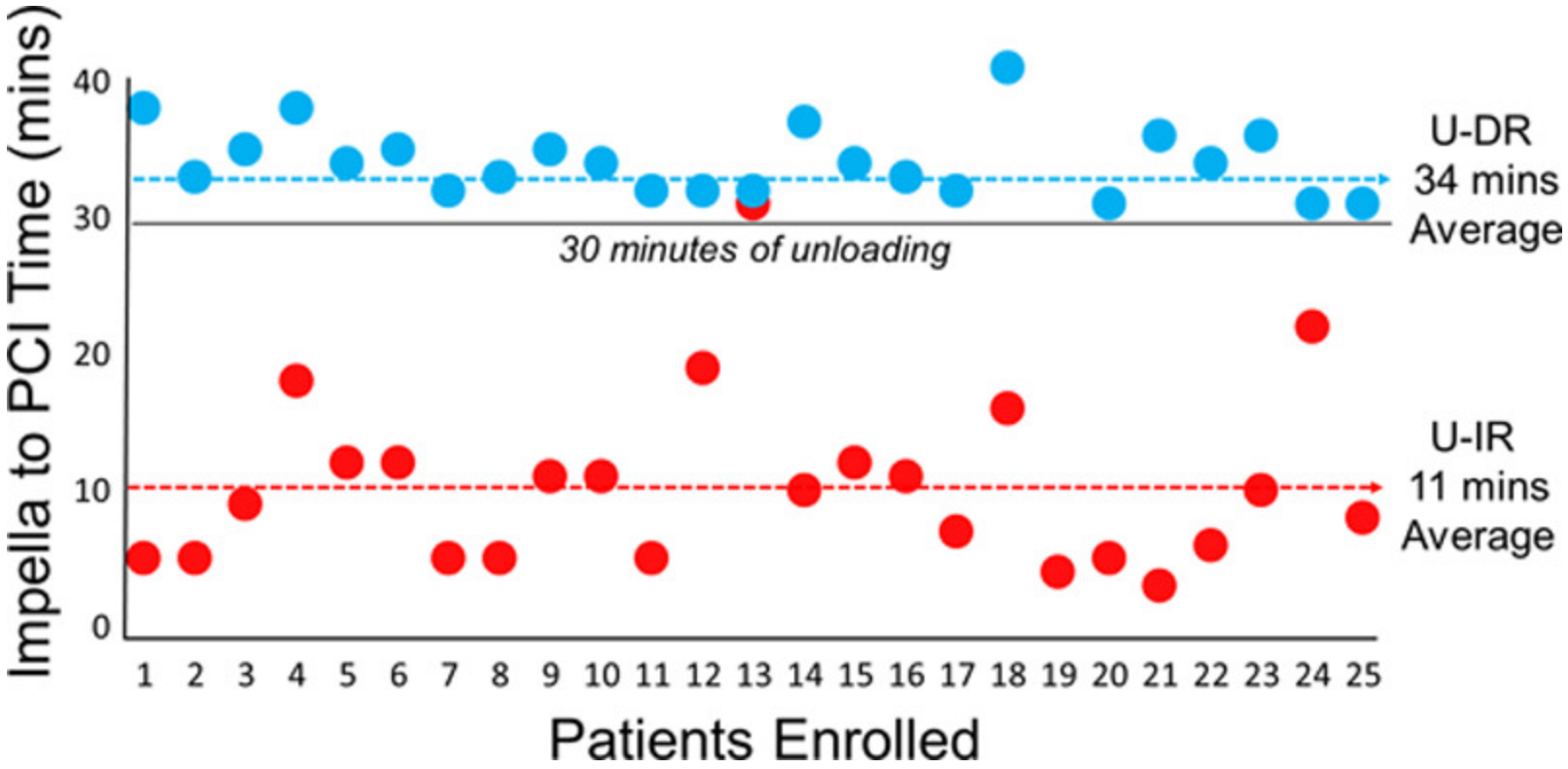
IABC indicates intra-aortic balloon counterpulsation; PCI, percutaneous coronary intervention.

- No difference in major vascular or bleeding complications

DTU-STEMI Trial

Design	Multicenter, prospective, randomized exploratory safety and feasibility trial
Patients	50 patients with **acute anterior STEMI without shock**
Intervention	Unloading by Impella CP followed by **immediate revasc** (U-IR) vs. unloading followed by **delayed revasc** after 30 min (U-DR)
Primary Outcomes	MACCE and **infarct size** at 30 days
Secondary Outcomes	Infarct size measured by Cardiac MRI 3-5 days after revasc and 30-days

Kapur NK et al; *Circulation*. 2019 Jan 15;139(3):337-346.



- 30-day MACCE: 12% in U-DR vs 8% in U-IR
- Infarct size at 30 days: not different

- **More data is needed to consider MCS before PCI to unload LV in STEMI**

Guidelines

- ESC 2017 STEMI guidelines: among patients with STEMI and cardiogenic shock:

Short-term mechanical support may be considered in patients with **refractory** shock	IIb	C
Routine intra-aortic balloon pumping is **not recommended**	III	B

- ACC/AHA 2013 STEMI guidelines:

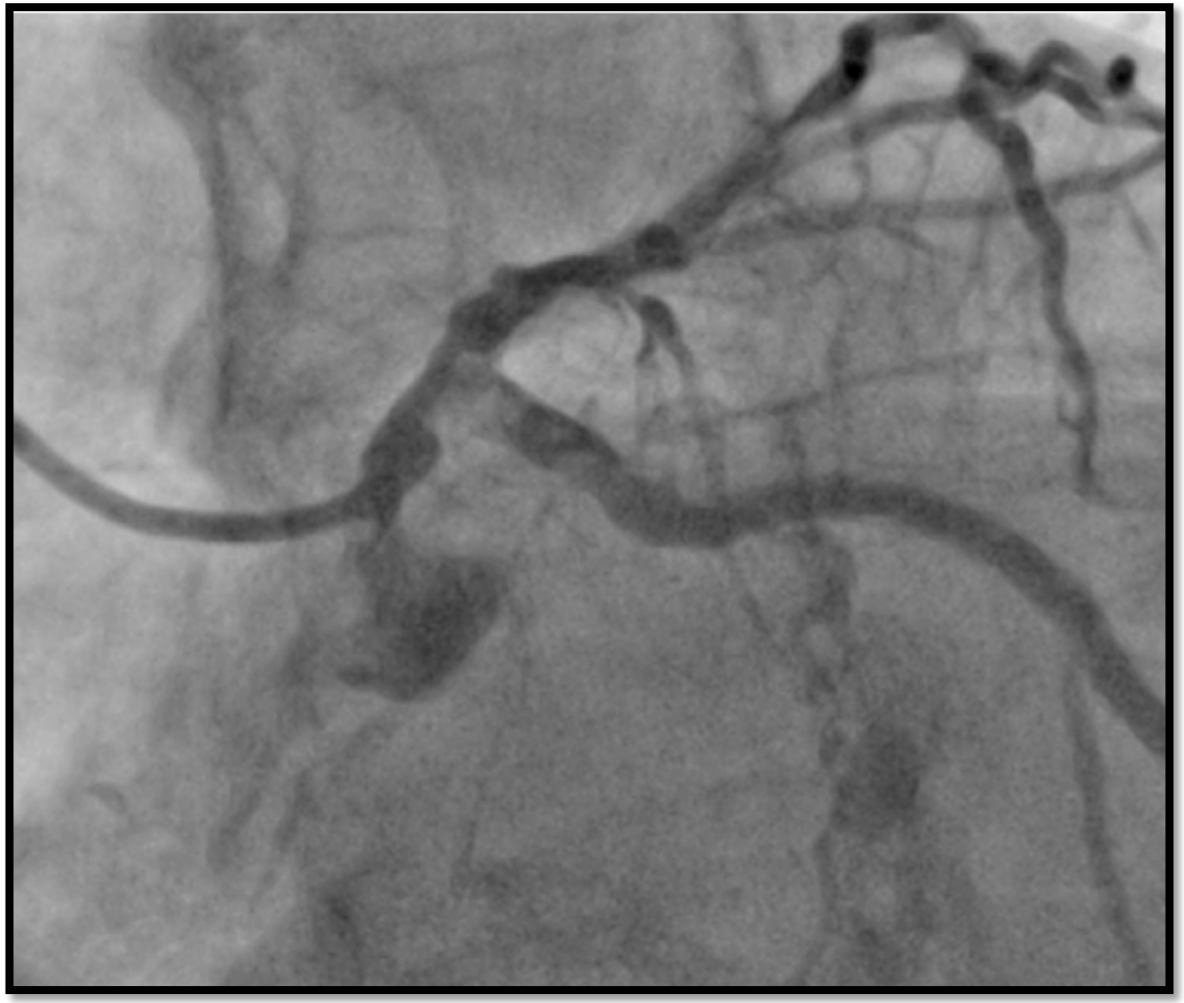
The use of intra-aortic balloon pump counterpulsation can be useful for patients with cardiogenic shock after STEMI **who do not quickly stabilize with pharmacological therapy**	IIa	B
Alternative left ventricular (LV) assist devices for circulatory support may be considered in patients with **refractory** cardiogenic shock	IIb	C

Mechanical Circulatory Support in High-risk PCI

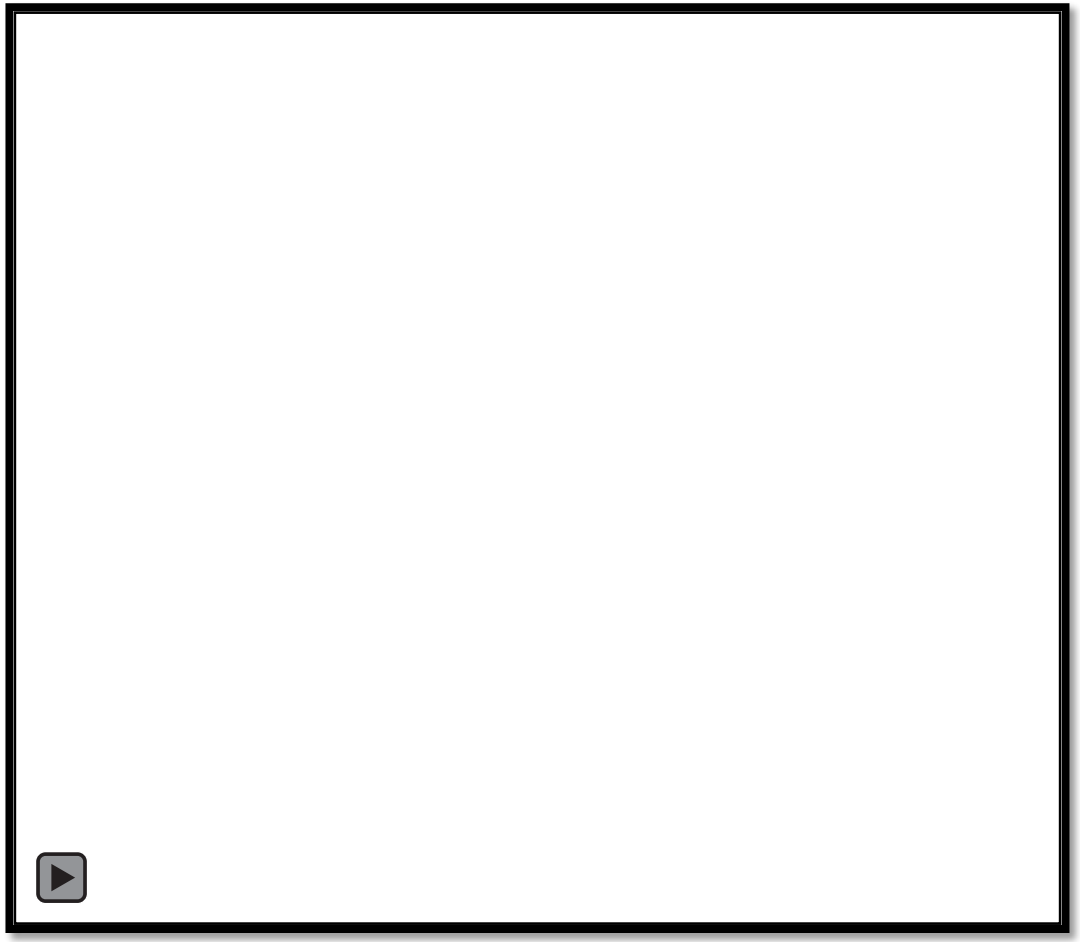
Case

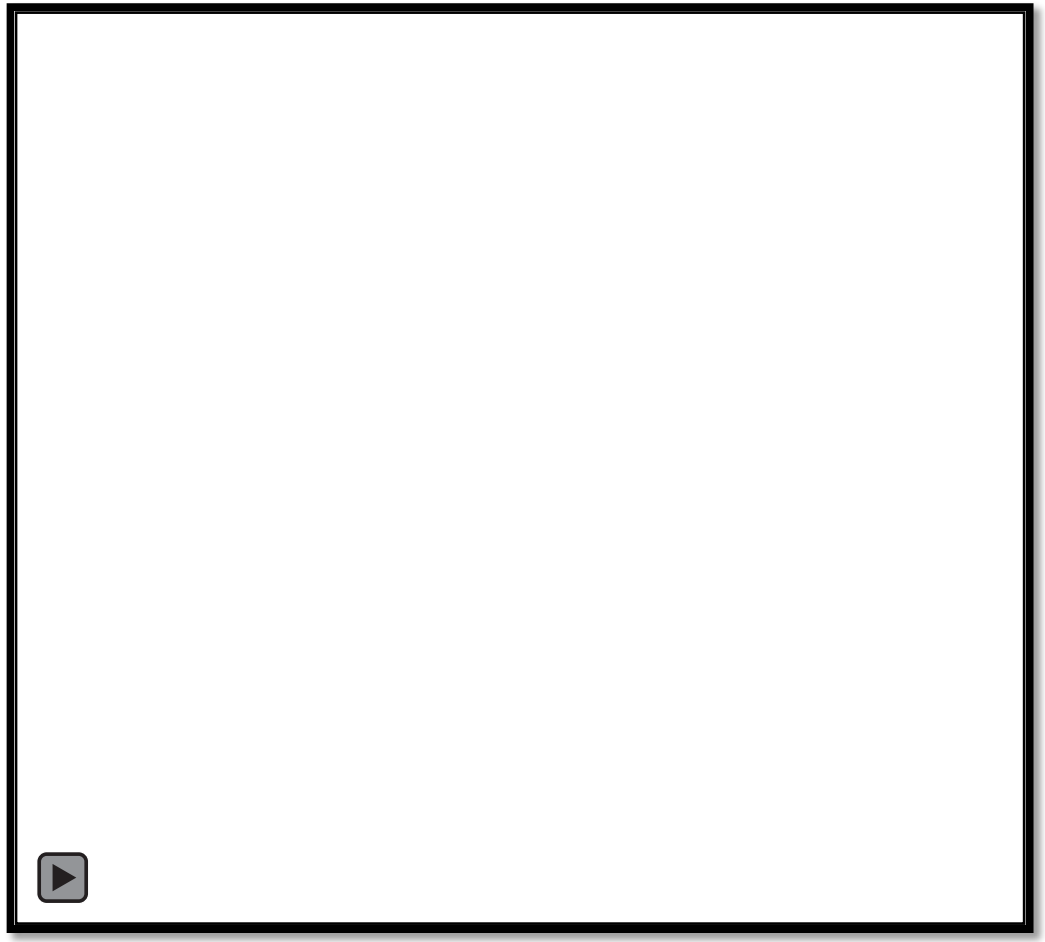
- 84 y/o female with H/O CAD s/p PCI to LCx in 2007, LAD in 2014 and 2020, **severe AS** came in with NSTEMI.

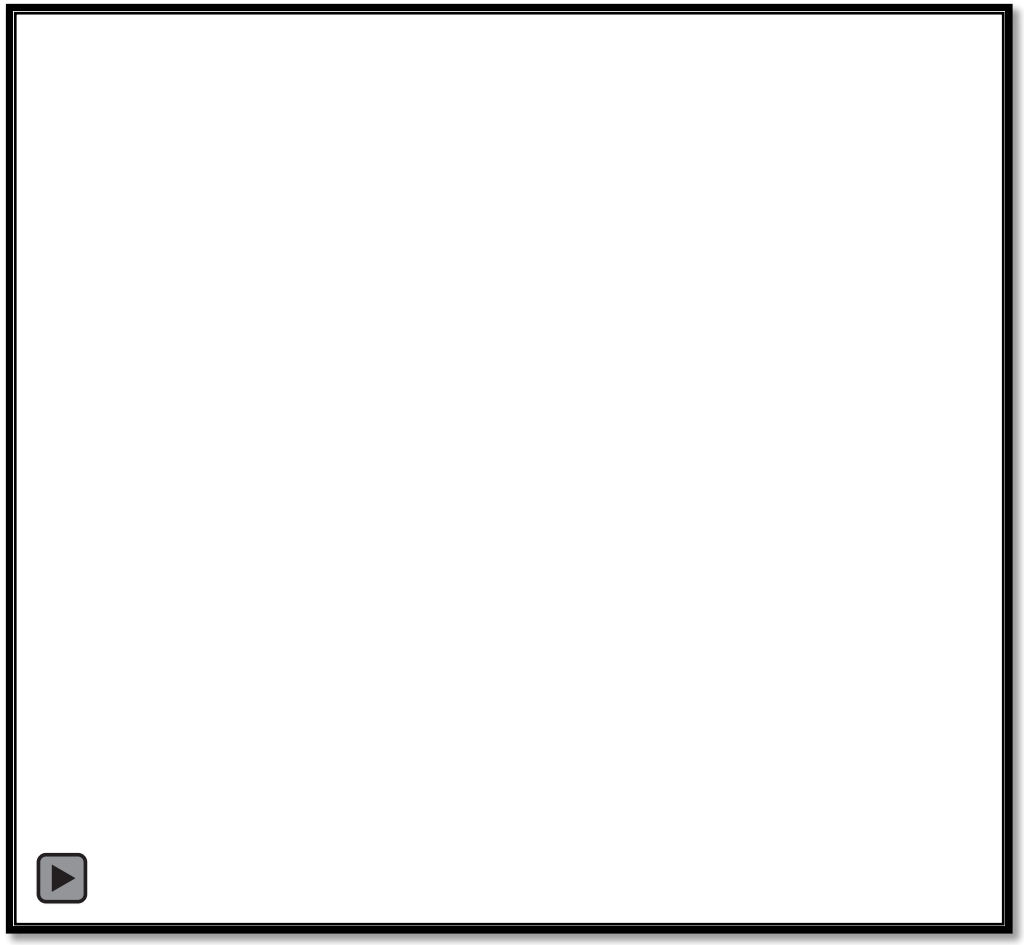
- Echo: Peak velocity 4.6 m/sec, mean gradient 58 mm Hg, LVEF 70%

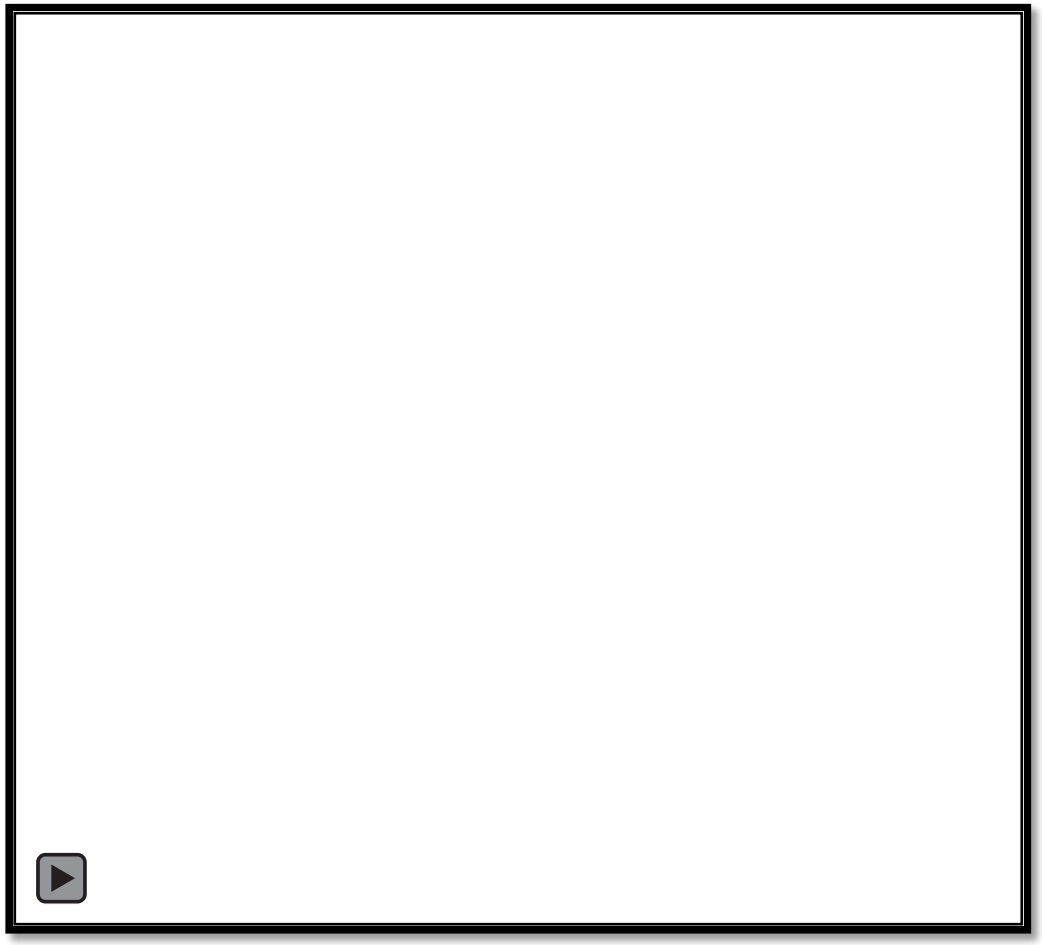


- Not a surgical candidate given her age, frailty
- Patient was not interested in surgical options either









What is high-risk PCI?

CLINICAL CHARACTERISTICS

- LVEF <35%
- Electrical instability
- Congestive heart failure

COMORBIDITIES

- Severe AS, MR
- Severe COPD
- ACS
- CKD
- DM II
- PVD
- H/o CVA

ANATOMICAL CHARACTERISTICS

- Unprotected LM
- Last remaining vessel
- 3v disease with SYNTAX score >33
- Distal LM bifurcation

Important Considerations for Hemodynamic Support in High-risk PCI

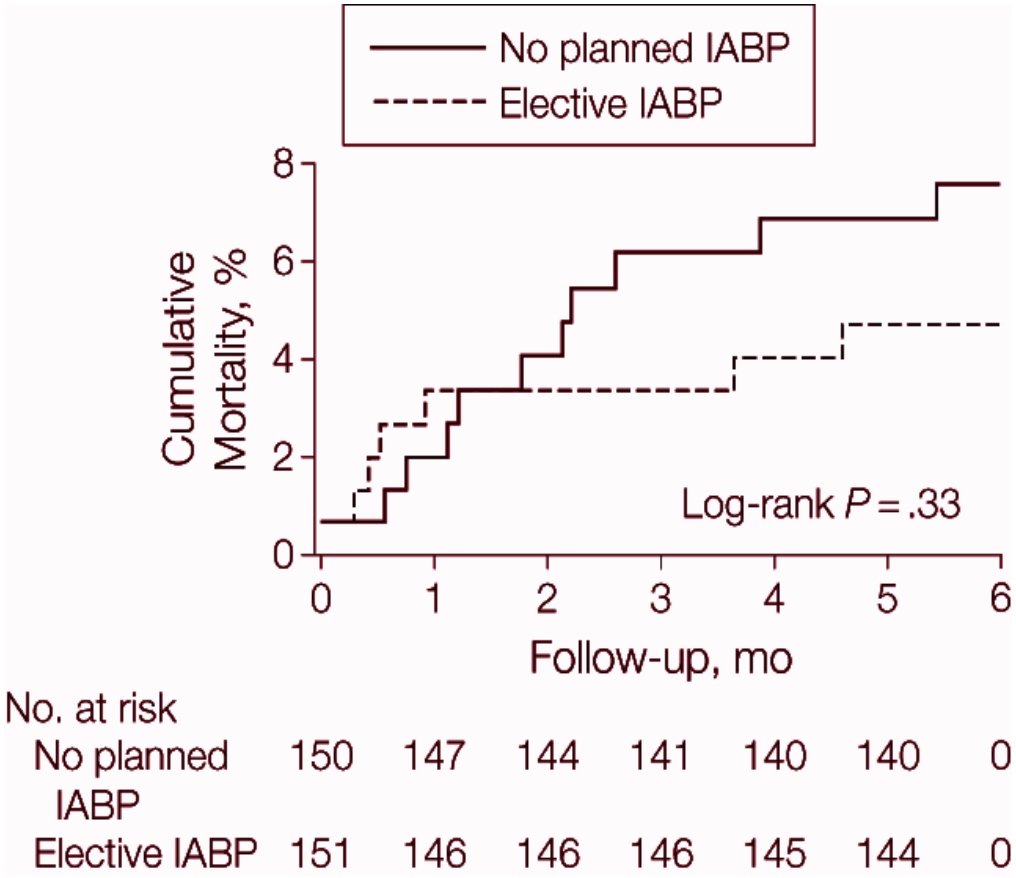
- Is the patient hemodynamically stable?
  - Low blood pressure
  - Active CHF
- Does the patient have enough reserve to sustain a brief ischemic insult during PCI?
  - **Last remaining vessel**
  - Borderline blood pressure
  - Severe pulmonary hypertension
  - Low cardiac index
  - Very **low LVEF <20%**
- Risk of prolonged ischemic insult risking LV injury?
  - Extensive **atherectomy**
  - Left dominant system with **complex bifurcation lesion**
  - Retrograde CTO with dual system compromise

BCIS-1 Trial

Design	Prospective, open, multicenter, RCT between Dec 2005 and Jan 2009
Patients	301 pts with **severe LV dysfunction (EF ≤30%)** and **extensive CAD** (Jeopardy Score ≥8/12)
Intervention	Elective **IABP** (151) before PCI vs. no IABP (150)
Primary Outcomes	MACCE at hospital discharge (capped at 28 days)
Secondary Outcomes	All-cause mortality at 6 months, major procedural complications, bleeding, and access-site complications

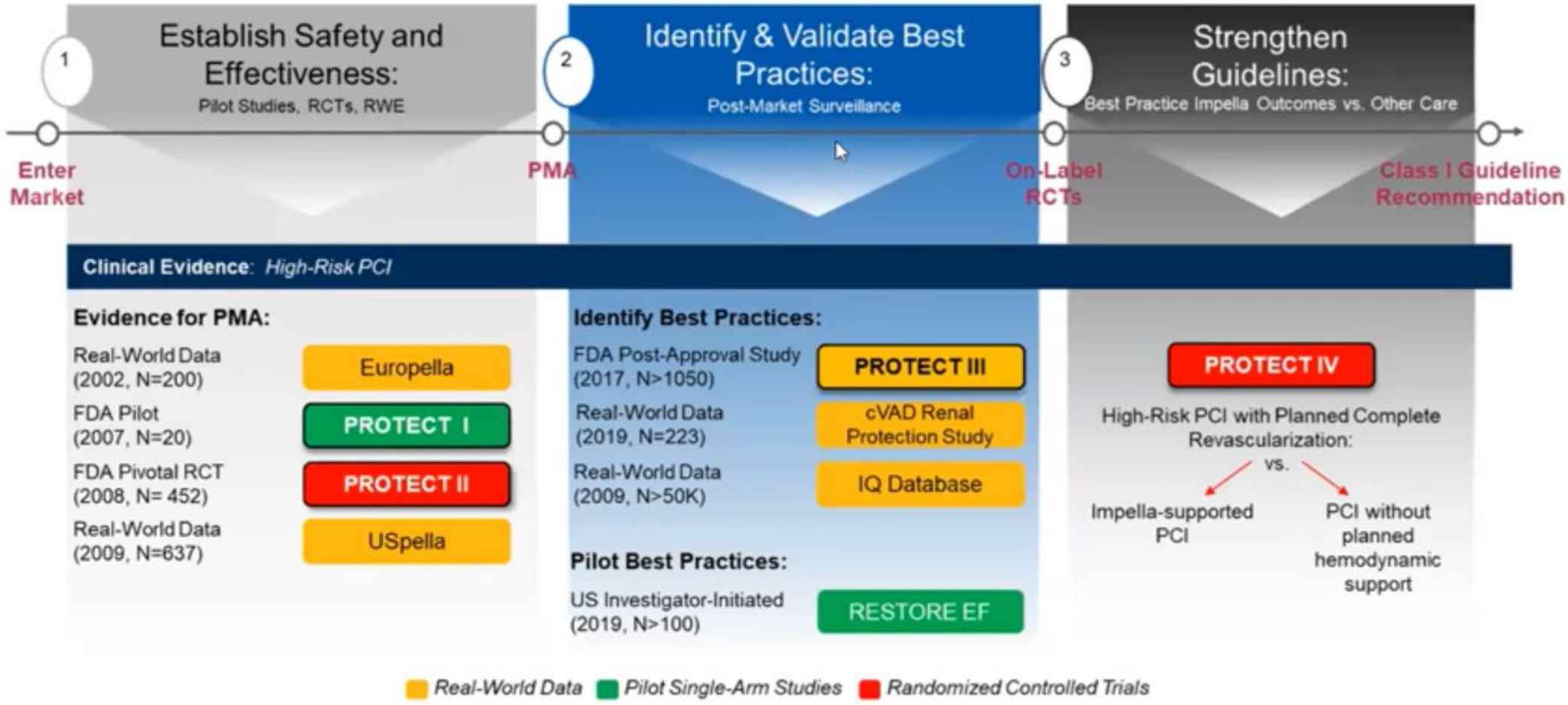
Perera D et al; *JAMA.* 2010;304(8):867-874.

- In-hospital MACCE: 15.2% (23/151) in elective IABP vs. 16.0% (24/150) in the no planned IABP group
- All-cause mortality at 6 months: 4.6% vs. 7.4% ($P = 0.32$).
- Major procedural complications: 1.3% vs 10.7%, $P < 0.001$).
- Major or minor bleeding: 19.2% vs. 11.3% ($P = 0.06$)



Perera D et al; *JAMA.* 2010;304(8):867-874.

Impella in High-risk PCI



Protect I Trial

Design	Prospective multicenter **feasibility** trial
Patients	20 patients with **LVEF <35%** and undergoing **high-risk PCI**
Intervention	**Impella 2.5**
Primary Outcomes	Safety endpoint: MACCE at 30 days Efficacy endpoint: hemodynamic compromise during PCI (MAP <60 mm Hg for >10 min)

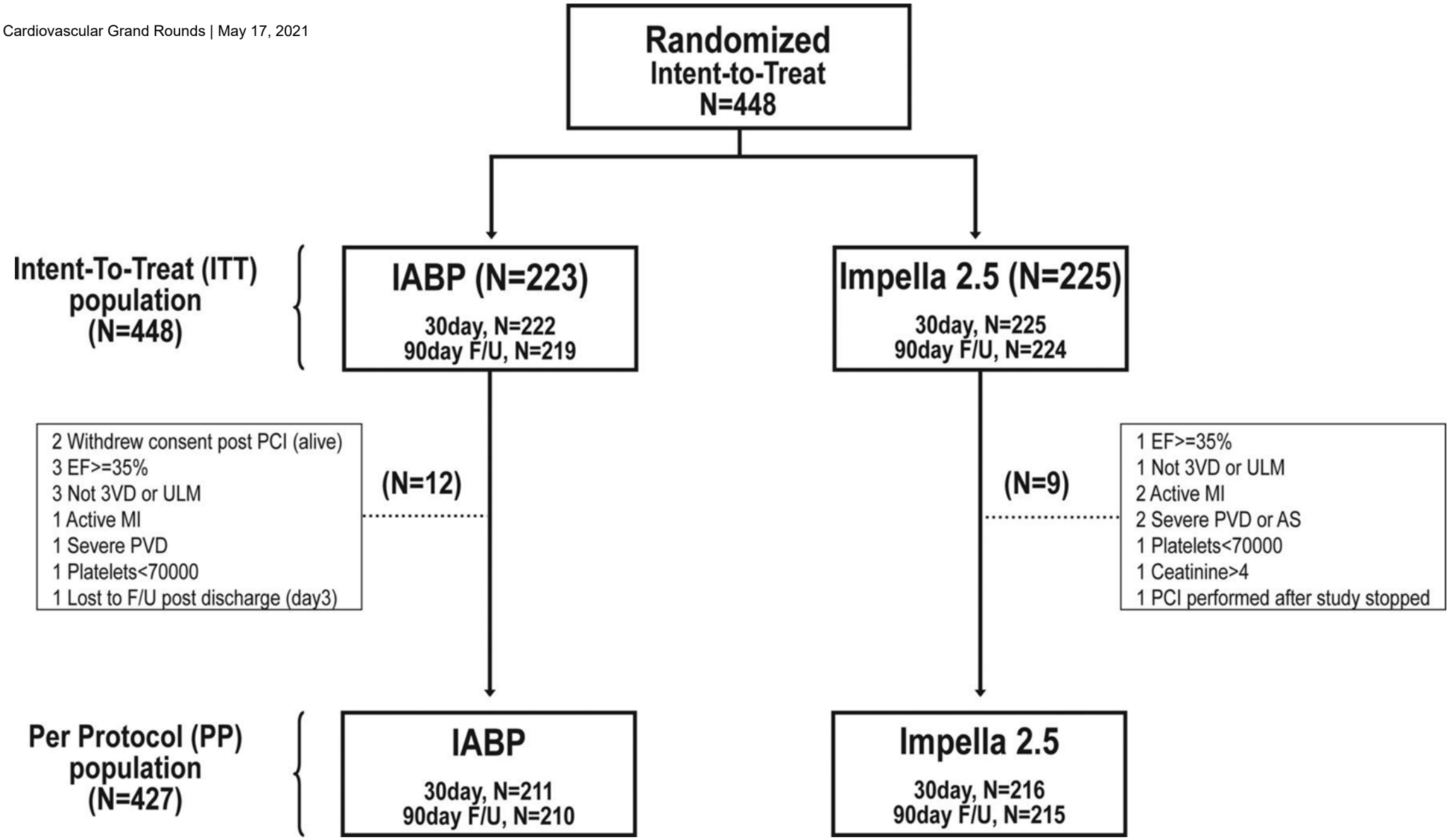
Dixon et al; *JACC Cardiovasc Interv*. 2009 Feb;2(2):91-6

- Primary safety endpoint: 20% of patients
- No hemodynamic compromise in any patient

Protect II Trial

Design	Prospective, multicenter RCT
Patients	448 symptomatic patients with **LVEF <35%** and **complex 3v CAD** or **unprotected LM** undergoing non-emergent high-risk PCI
Intervention	**IABP** (n=225) vs. **Impella 2.5** (n=223)
Primary Outcomes	MACCE at 30 days

O'Neill W et al. *Circulation.* 2012;126:1717-1727



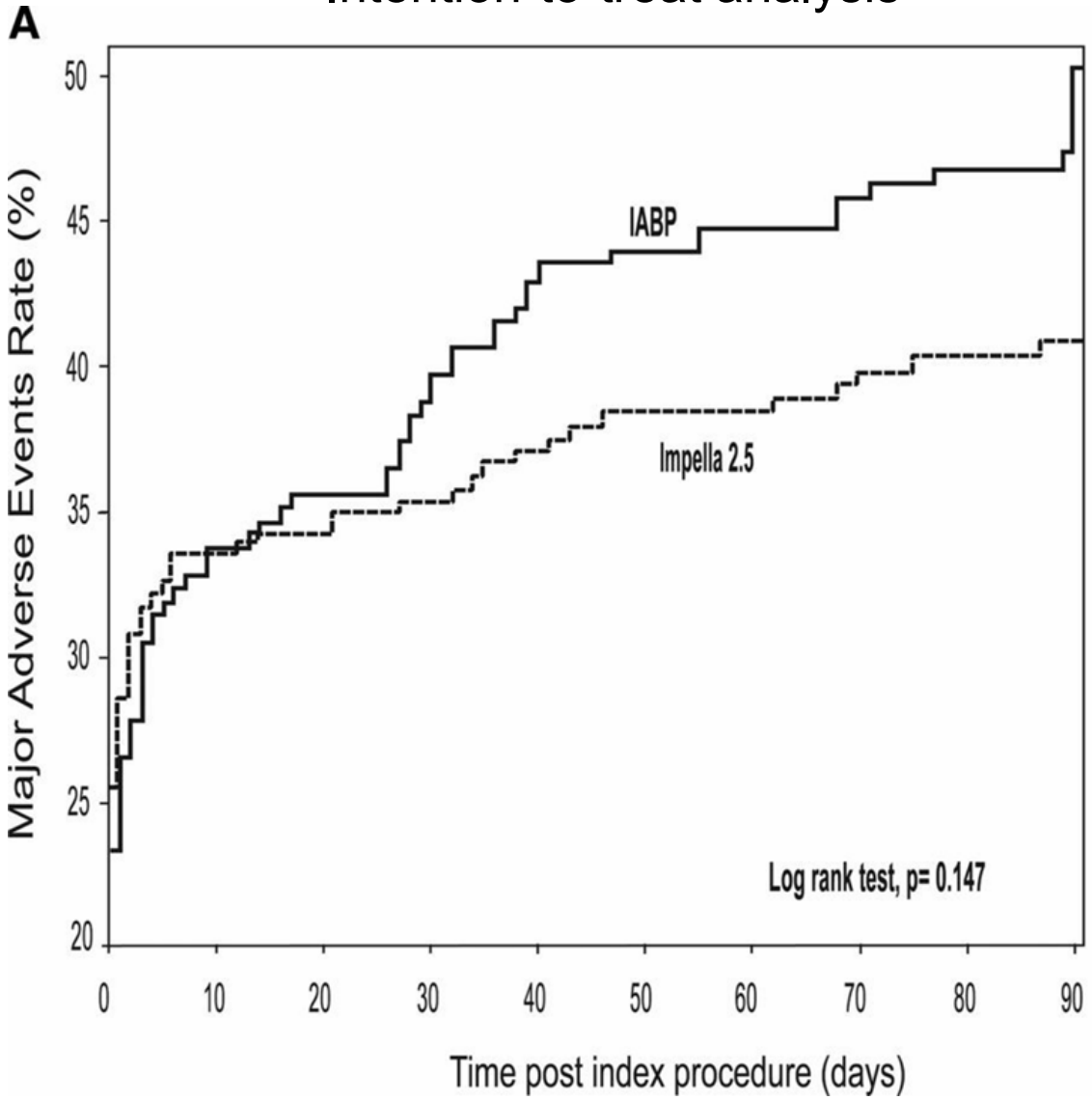
Intention to Treat Analysis

	30 Days			90 Days		
	IABP (n=222)	Impella 2.5 (n=225)	*P*	IABP (n=219)	Impella 2.5 (n=224)	*P*
Composite of major adverse events	40.1	35.1	0.277	49.3	40.6	0.066
Death	5.9	7.6	0.473	8.7	12.1	0.244
Stroke/TIA	1.8	0.0	0.043	2.7	0.9	0.144
Myocardial Infarction	10.4	13.8	0.268	14.2	12.1	0.512
Repeat revascularization	4.1	1.3	0.075	7.8	3.6	0.056
Need for cardiac or vascular operation*	1.4	0.9	0.642	1.8	1.3	0.681
Acute renal dysfunction	4.5	4.0	0.792	4.6	4.0	0.776
Cardiopulmonary resuscitation/ventricular arrhythmia†	3.2	2.2	0.543	4.1	2.2	0.259
Aortic valve damage/increase in aortic insufficiency	0.0	0.0	...	0.0	0.0	...
Severe hypotension requiring treatment	8.6	4.9	0.121	5.5	4.0	0.469
Angiographic failure	0.5	0.4	0.992	0.0	0.4	0.322

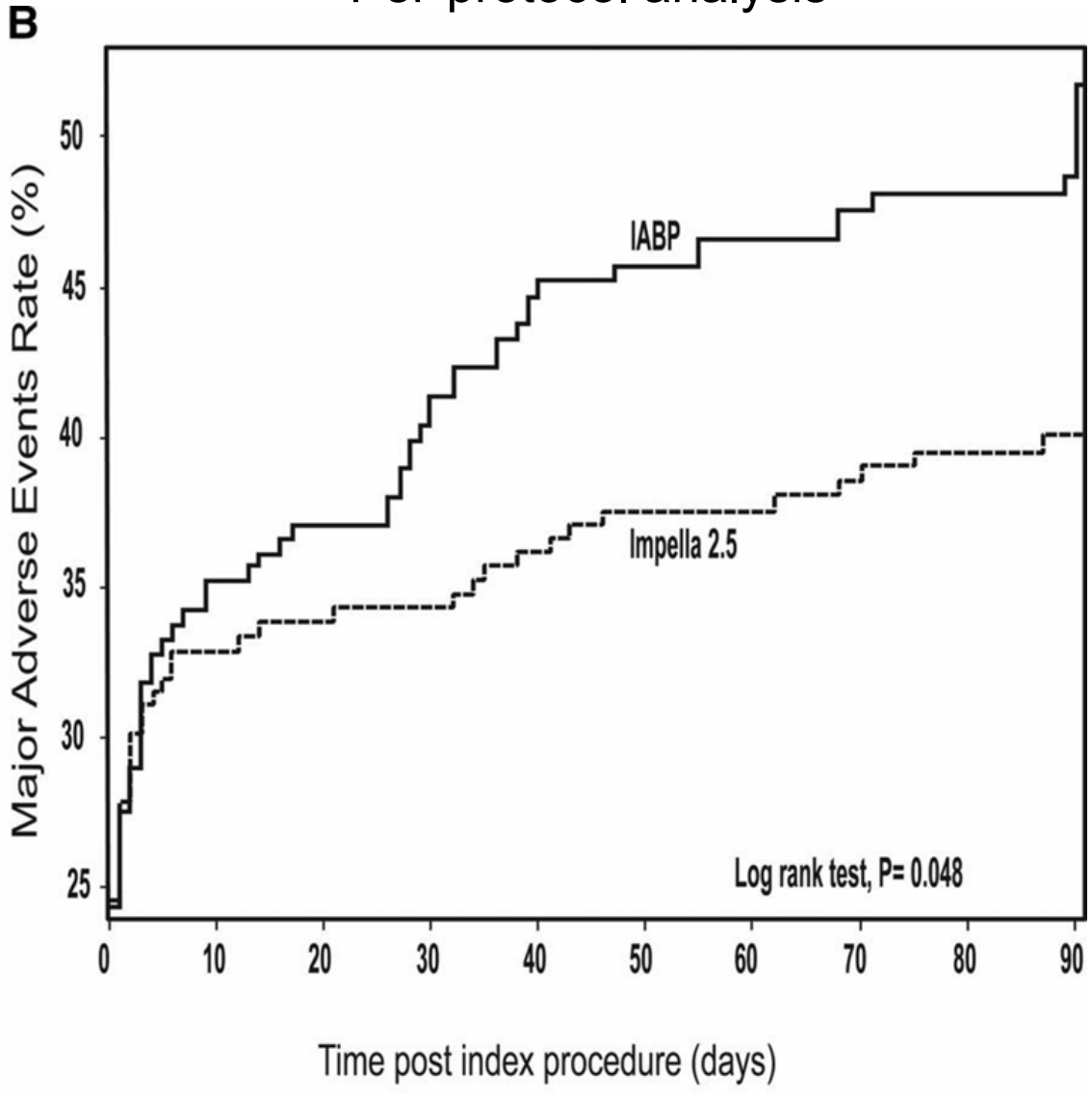
Per Protocol Analysis

	30 Days			90 Days		
	IABP (n=211)	Impella 2.5 (n=216)	*P*	IABP (n=210)	Impella 2.5 (n=215)	*P*
Composite of major adverse events	42.2	34.3	0.092	51.0	40.0	0.023
Death	6.2	6.9	0.744	9.0	11.6	0.383
Stroke/TIA	1.9	0.0	0.042	2.4	0.9	0.240
Myocardial infarction	10.9	13.4	0.425	14.8	11.6	0.340
Repeat revascularization	4.3	1.4	0.072	8.1	3.7	0.055
Need for cardiac or vascular operation*	1.4	0.9	0.634	1.9	1.4	0.680
Acute renal dysfunction	4.7	4.2	0.774	4.8	4.2	0.774
Cardiopulmonary resuscitation/ventricular arrhythmia†	3.3	2.3	0.531	4.3	2.3	0.258
Aortic valve damage/increase in aortic insufficiency	0.0	0.0	...	0.0	0.0	...
Severe hypotension requiring treatment	9.0	4.6	0.072	5.7	3.7	0.332
Angiographic Failure	0.5	0.5	0.987	0.0	0.5	0.322

Intention-to-treat analysis



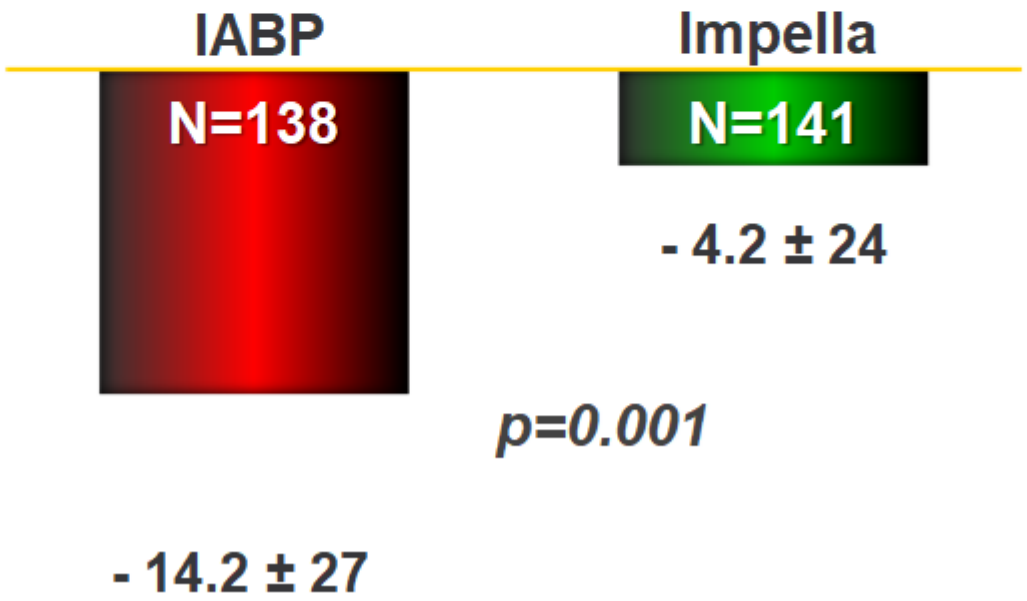
Per-protocol analysis



Hemodynamic Support Effectiveness

Cardiac Power Output
(Secondary Endpoint)

Maximal Decrease in CPO on device Support from Baseline (in x0.01 Watts)

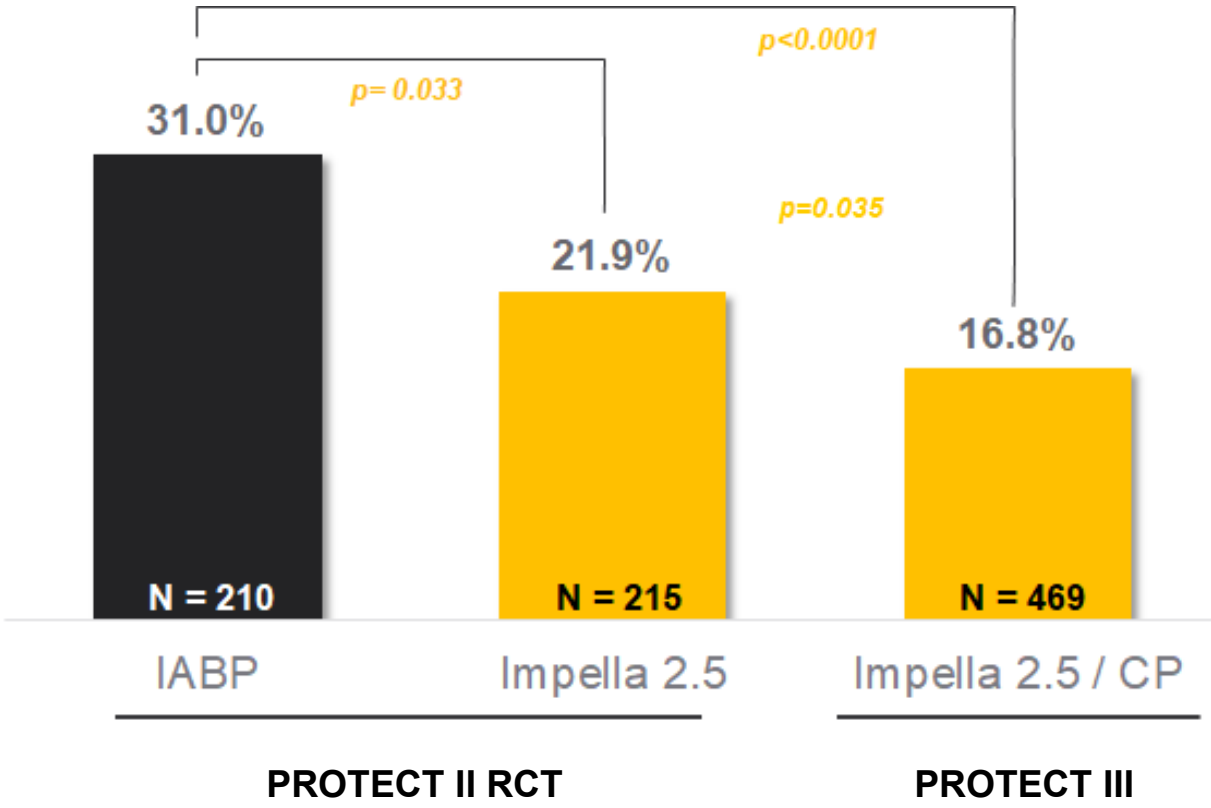


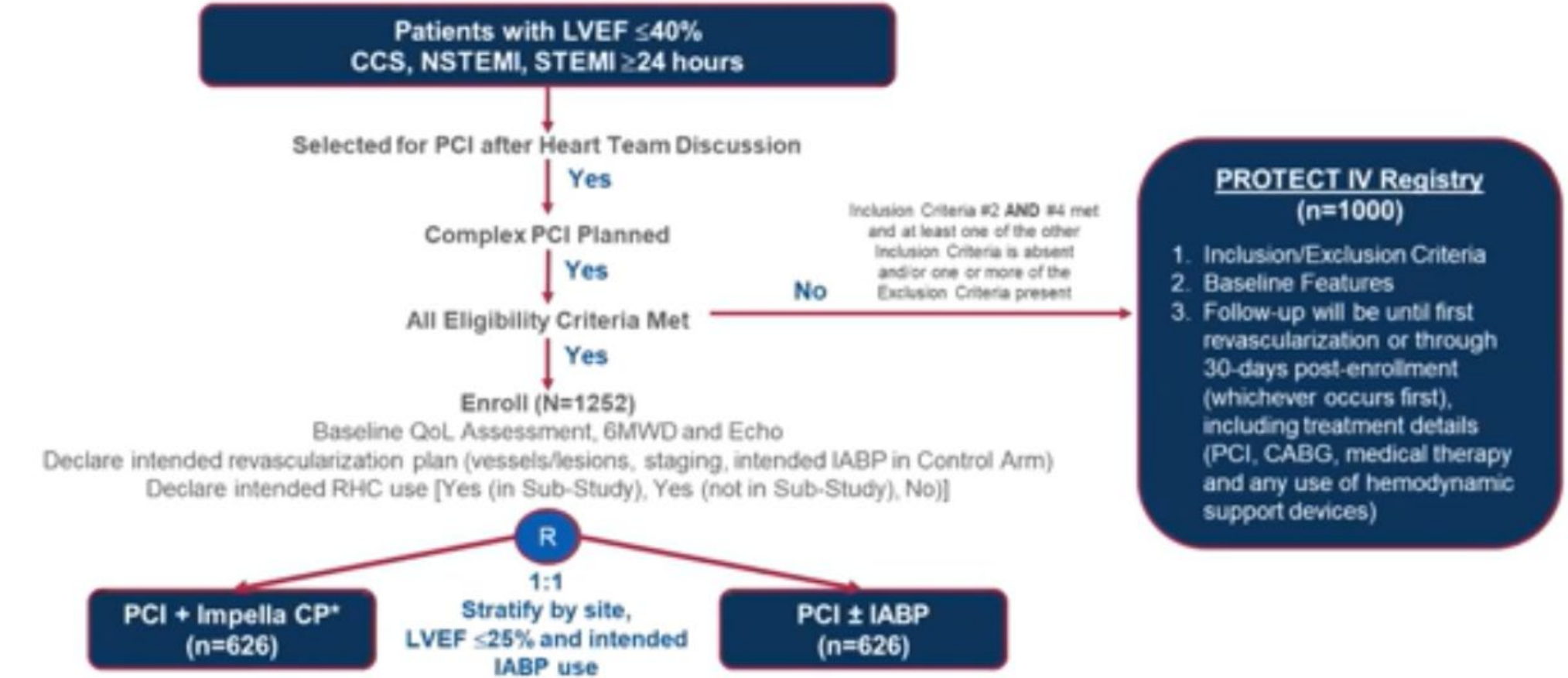
- Few important observations in this study:
  - Impella 2.5 group had **more patients with CHF and h/o CABG**
  - Glycoprotein IIb/IIIa inhibitor use was less in the Impella group
  - Significantly **more contrast use** in the Impella group (267±142 cc vs. 241±114 cc)
  - Use of **rotational atherectomy** was more frequent in the Impella group with longer duration and more runs (14.2% vs. 9%)
  - **Support time was much lower** in the Impella group (1.9±2.7 h vs. 8.4±21.8 h)

Protect III Post-approval Study

- Prospective, multicenter single-arm FDA post-approval study
- Interim analysis of 898 patients (571 Impella CP vs 327 Impella 2.5) presented in TCT 2019. Enrollment ongoing.
- Compared findings with Protect II data
  - Patients much older than those in Protect II
  - More pts with 3 vessel PCI
  - Significantly **higher use of atherectomy** 43.3% vs 14.2% in Protect II trial
  - **More left main PCI** 15.7% vs 11.5%
  - Much longer duration of support 6.79±21.1 h vs 1.9±2.7 h
  - Much **less contrast** use 204±105.6 cc vs 267±141.7 cc

- MACCE at 90 days

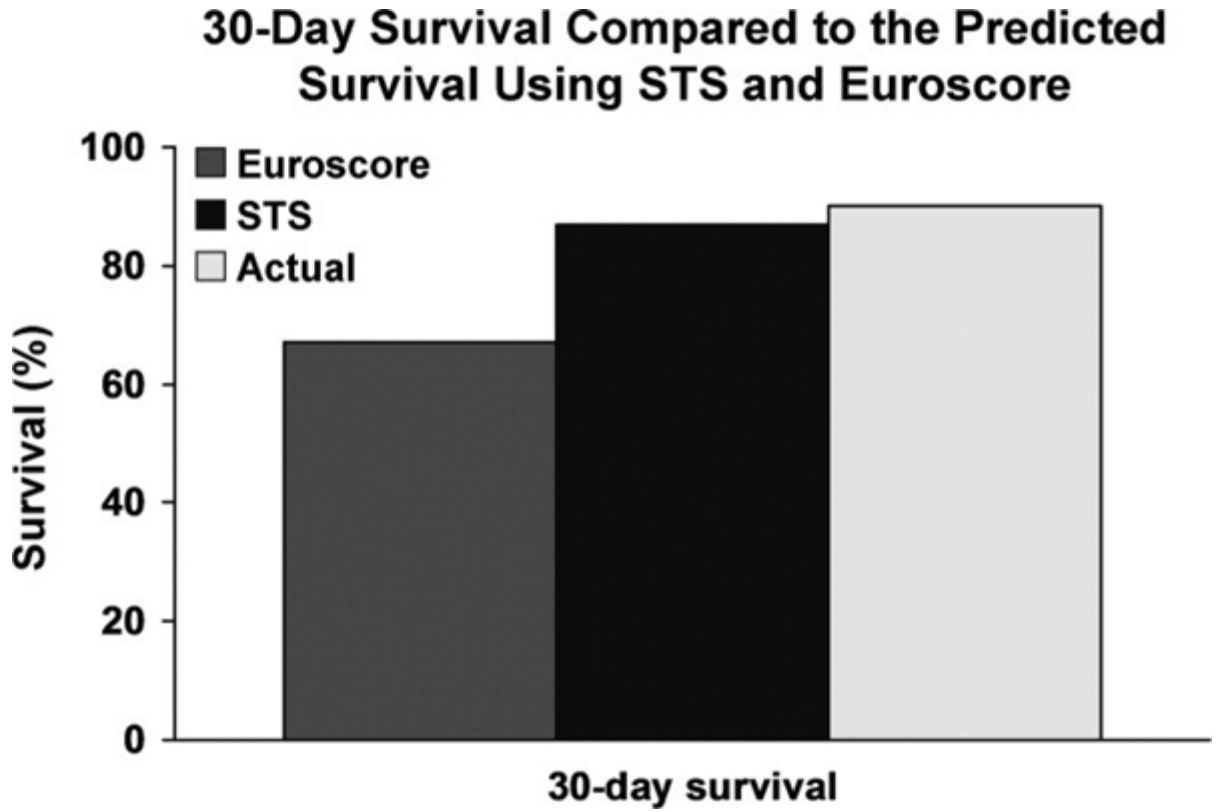




Clinical Follow-Up: 1-month post-discharge and 6-months, 1-year, annually through 3-years post-RND (+sweep visit when last patient enrolled reaches 1-year follow-up post-RND); Echocardiography at 6-months, 1-year and 3-years post-RND; QOL, 6MWD and cost assessment at 30-day post-discharge and 1- and 3-years post-RND

Primary Endpoint: All-cause death, stroke, MI or hospitalization for cardiovascular causes measured through 3-year follow-up, min. 1-year follow-up in all patients

- Mayo clinic single-center data
  - 54 nonsurgical patients undergoing **high-risk PCI** - **TandemHeart**
  - The median SYNTAX score was 33 with high predicted surgical revascularization mortality
  - Left main and multivessel PCI in 62% of patients, and rotablation in 48%.
  - Improvement in right and left heart pressures, cardiac output increased from 4.7 to 5.7 L/min during support.
  - Procedural success rate was 97% and **30-day** and **6-month survival** were **90%** and **87%**, respectively. Major vascular complications occurred in 13% of cases.



Algorithmic Approach to MCS

Practical Approach to Percutaneous MCS

- **Step 1**: Prompt recognition of patients with cardiogenic shock or impending shock, and high-risk PCI features
- **Step 2**: Multidisciplinary team approach (critical care, advanced heart failure, interventional cardiology and cardiothoracic surgery)
- **Step 3**: Identifying disease severity from shock or PCI perspective to pick the right device

Comparison of Devices

FIGURE 2 Comparison of MCS Devices and Their Impact on Cardiac Flow

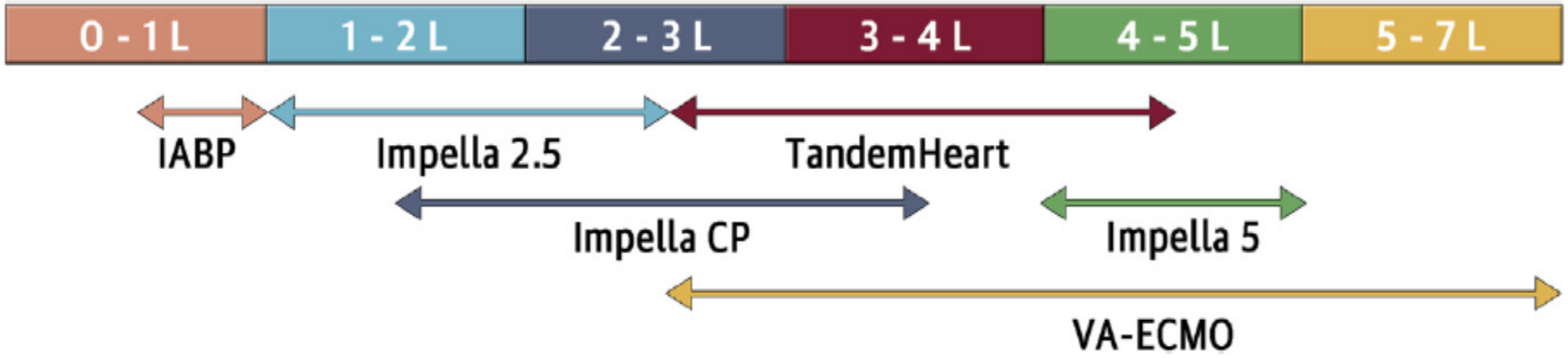
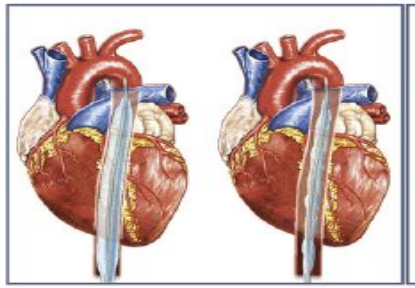
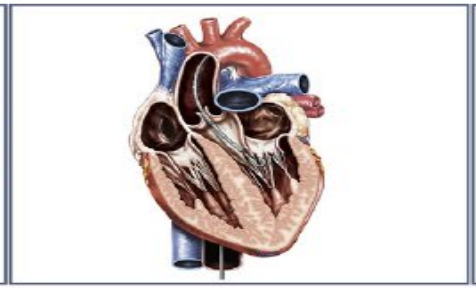
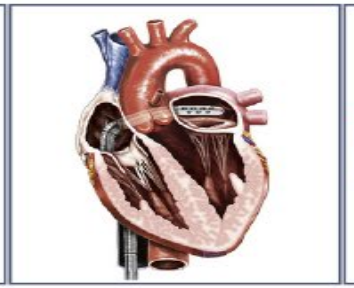
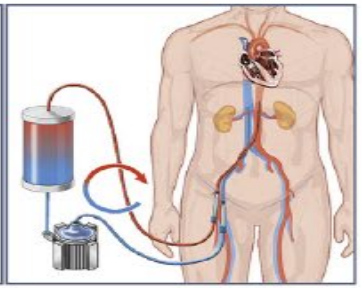
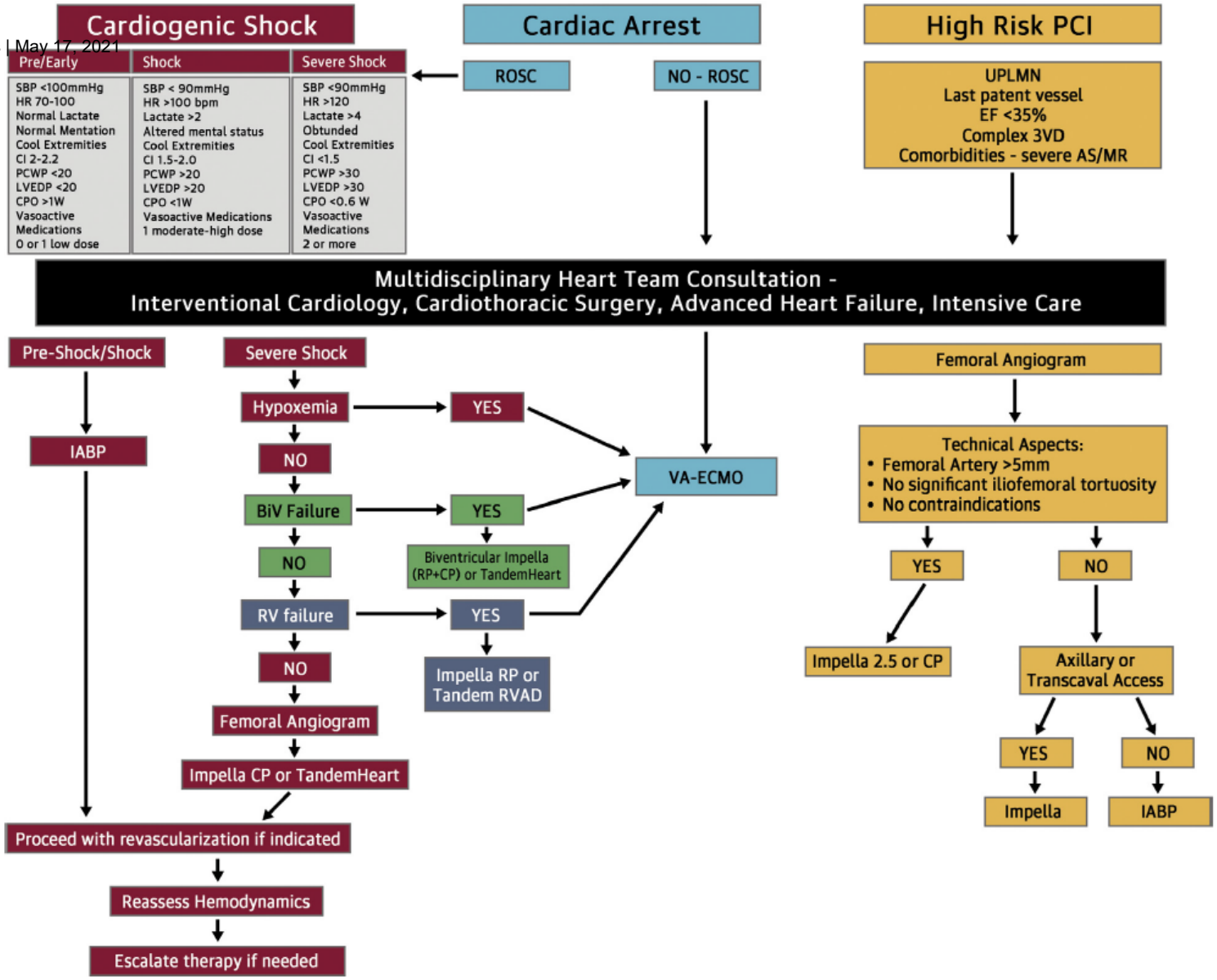


FIGURE 1 Comparison of MCS Devices

	IABP	IMPELLA	TANDEMHEART	VA-ECMO
Cardiac Flow	0.3-0.5 L/ min	1-5L/ min (Impella 2.5, Impella CP, Impella 5)	2.5-5 L/ min	3-7 L-min
Mechanism	Aorta	LV → AO	LA → AO	RA → AO
Maximum implant days	Weeks	7 days	14 days	Weeks
Sheath size	7-8 Fr	13-14 Fr Impella 5.0 - 21 Fr	15-17 Fr Arterial 21 Fr Venous	14-16 Fr Arterial 18-21 Fr Venous
Femoral Artery Size	>4 mm	Impella 2.5 & CP - 5-5.5 mm Impella 5 - 8 mm	8 mm	8 mm
Cardiac synchrony or stable rhythm	Yes	No	No	No
Afterload	↓	↓	↑	↑↑↑
MAP	↑	↑↑	↑↑	↑↑
Cardiac Flow	↑	↑↑	↑↑	↑↑
Cardiac Power	↑	↑↑	↑↑	↑↑
LVEDP	↓	↓↓	↓↓	↔
PCWP	↓	↓↓	↓↓	↔
LV Preload	---	↓↓	↓↓	↓
Coronary Perfusion	↑	↑	---	---
Myocardial oxygen demand	↓	↓↓	↔↓	↔

Atkinson TM, et al. A Practical Approach to Mechanical Circulatory Support in Patients Undergoing PCI: An Interventional Perspective. JACC Cardiovasc Interv. 2016 May 9;9(9):871-83.



Atkinson, T.M. et al. J Am Coll Cardiol Intv. 2016;9(9):871–83.

Contraindications and Complications

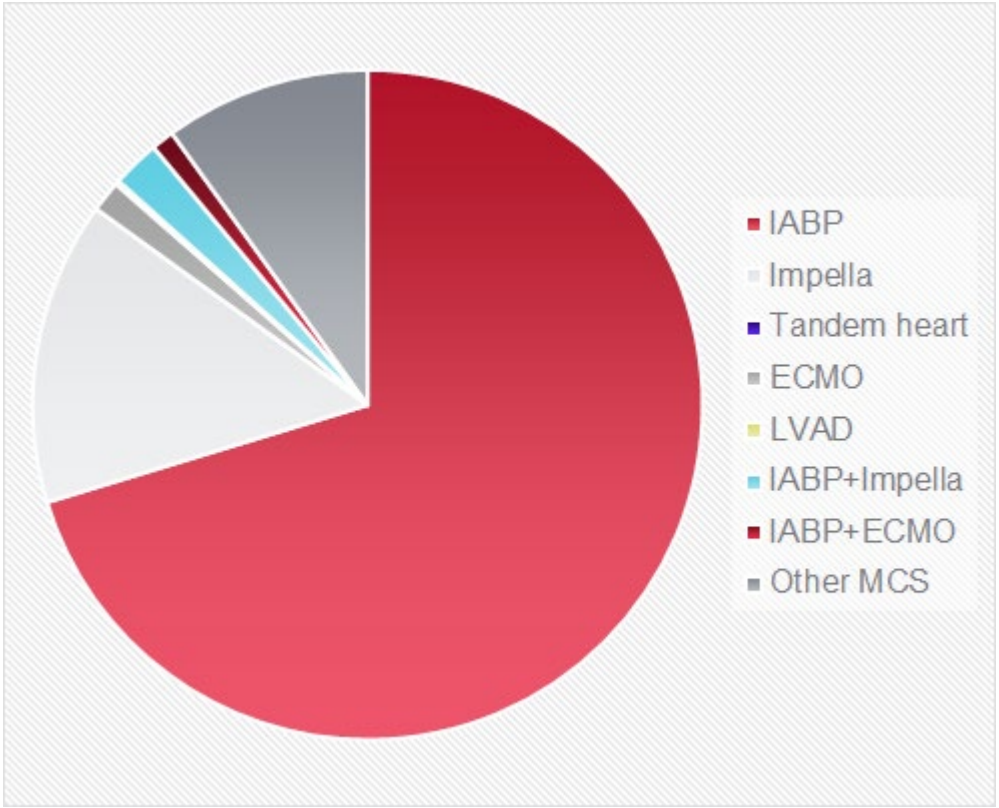
	IABP	Impella	TandemHeart	VA-ECMO
Contraindications	Moderate to severe AR Severe PAD Aortic disease	LV thrombus Mechanical aortic valve Aortic stenosis with AVA <0.6 Moderate to severe AR Severe PAD Contraindication to anticoagulation	Severe PAD HIT DIC Contraindications to anticoagulation LA thrombus VSD Moderate to severe AR	Contraindications to anticoagulation Moderate to severe AR Severe PAD
Complications	Stroke Limb ischemia Vascular trauma Balloon rupture Thrombocytopenia Acute kidney injury Bowel ischemia Infection	Device migration Device thrombosis Limb ischemia Vascular trauma Hemolysis Infection Stroke	Air embolism Thromboembolism Device Dislodgement Cardiac tamponade Limb ischemia Vascular trauma Hemolysis Infection Stroke	Bleeding Vascular trauma Limb ischemia Compartment syndrome Acute kidney injury Hemolysis Thromboembolism Air embolism Infection Neurological Injury
Bleeding/hemolysis	+	++	++	++
Vascular complications	+	++	+++	++++

Conclusions

- Use of mechanical circulatory support devices should be **individualized** based on patient characteristics
- Multidisciplinary heart team approach preferably a "**Shock team**" is vital to the success of the program.
- More research and evidence are needed, due to paucity of high-quality evidence.

Trends in use of MCS in AMI and CS

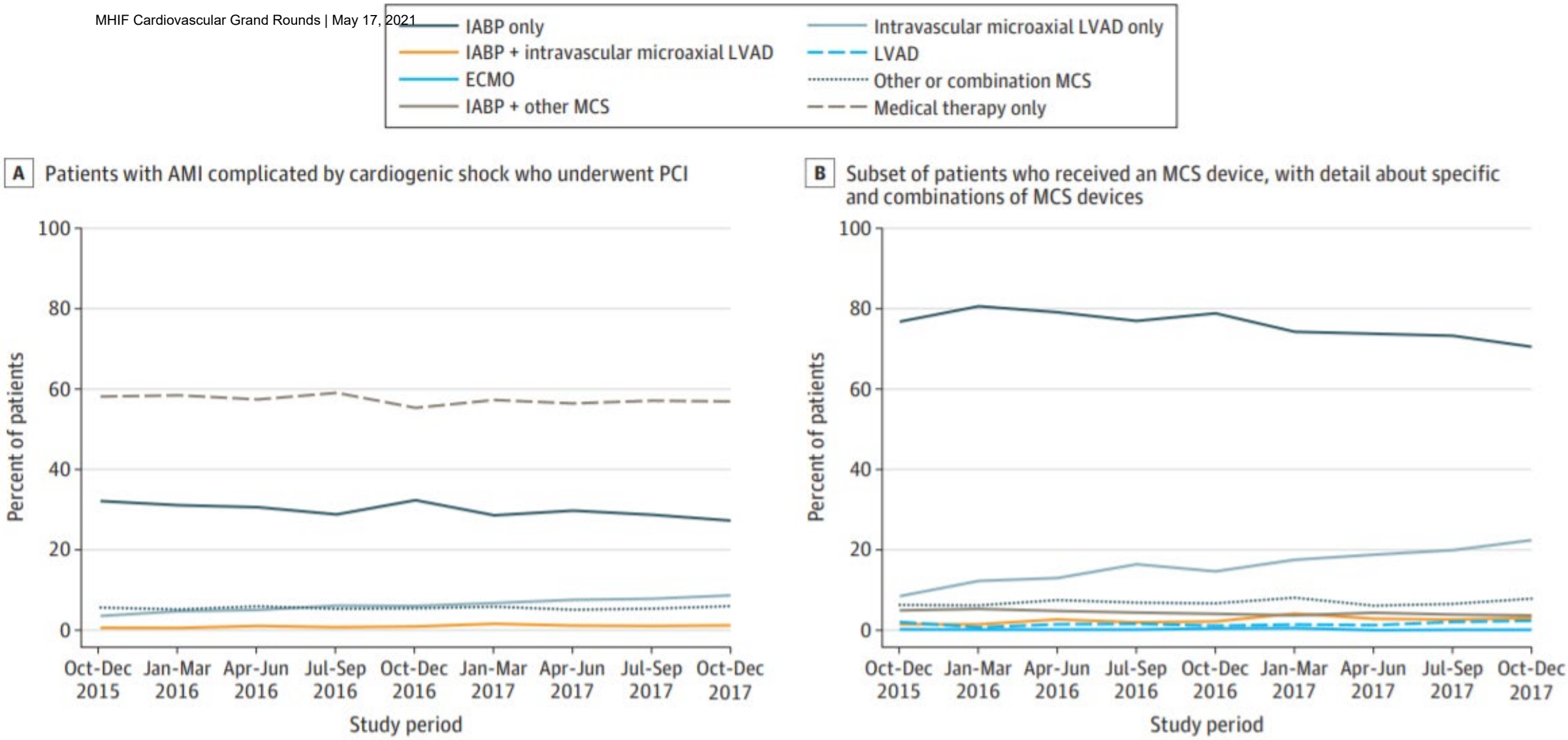
- Recent trends show a decline in use of IABP and increase in use of Impella
- Combining CathPCI and Chest Pain-MI registries
- 42.7% received an MCS device



Sandhu A et al; *Circulation*. 2015;132(13):1243-1251
Dhruva S et al; *JAMA Netw Open.* 2021;4(2):e2037748

- MCS use in cardiogenic shock and acute MI remained similar from 2015 to 2017 (41.9% to 43.1%)
- Impella use increased from 4.1% to 9.8%
- IABP use decreased from 34.8% to 30%

- **More than half the hospitals did not use any MCS device for these patients**



Timing of MCS Relative to Reperfusion in AMI and Shock

No shock

- SBP >90 mm Hg
- Warm and dry
- CI >2.5 L/min/m2
- PCWP <15

→ Primary reperfusion

Impending shock

- SBP >90 mm Hg
- Cool and dry/wet
- CI >2.2 L/min/m2

→ Primary reperfusion
Monitor Swan data

Shock

- SBP <90 mm Hg
- SBP >90 mm Hg while on pressors
- CI <2.2 L/min/m2

→ MCS
Reperfusion

- Options for LV venting in ECMO