MedStar Heart Institute

Cleveland Clinic
Heart and Vascular Institute

STEMI intervention
Left Ventricular Assist Devices
Against
Dispelling the Myths, No Benefits in Reality

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Main reasons for the use of Left Ventricular Assist Devices for STEMI Intervention

Reduce infarct size

Save Life

Study Design

Anterior STEMI without Shock

Inclusion Criteria
- Anterior STEMI
  2 mm in 2 contiguous leads or at least 4 mm in the anterior leads
- Planned Primary PCI within 6 hrs
- Adult able to consent

Intra-aortic Balloon Counterpulsation prior to PCI

Randomize
Open Label
(n ~ 300)

Standard of Care Primary PCI

At least 12 hours of IABC post PCI

Routine Post PCI care

Cardiac MRI performed day 3-5 post PCI

Primary Endpoint: Infarct Size on CMR
1. All Patients with CMR data
2. Patients with Prox LAD occlusion TIMI 0/1 flow

Clinical Events – 6 months

clinicaltrials.gov as # NCT00833612.
Also at controlled-trials.com #ISRCTN89012474

Primary outcome

	All (N=337)	IABC (N=161)	SOC (N=176)	P Value
Primary endpoint				
Infarct size (% LV), modified ITT all patients with CMR data				**0.060**
N	275	133	142	
Mean	39.8	42.1	37.5	
Median	38.8	42.8	36.2	
Infarct size (% LV), modified ITT patients prox. LAD and TIMI flow 0/1				**0.110**
N	192	93	99	
Mean	44.4	46.7	42.3	
Median	42.1	45.1	38.6	

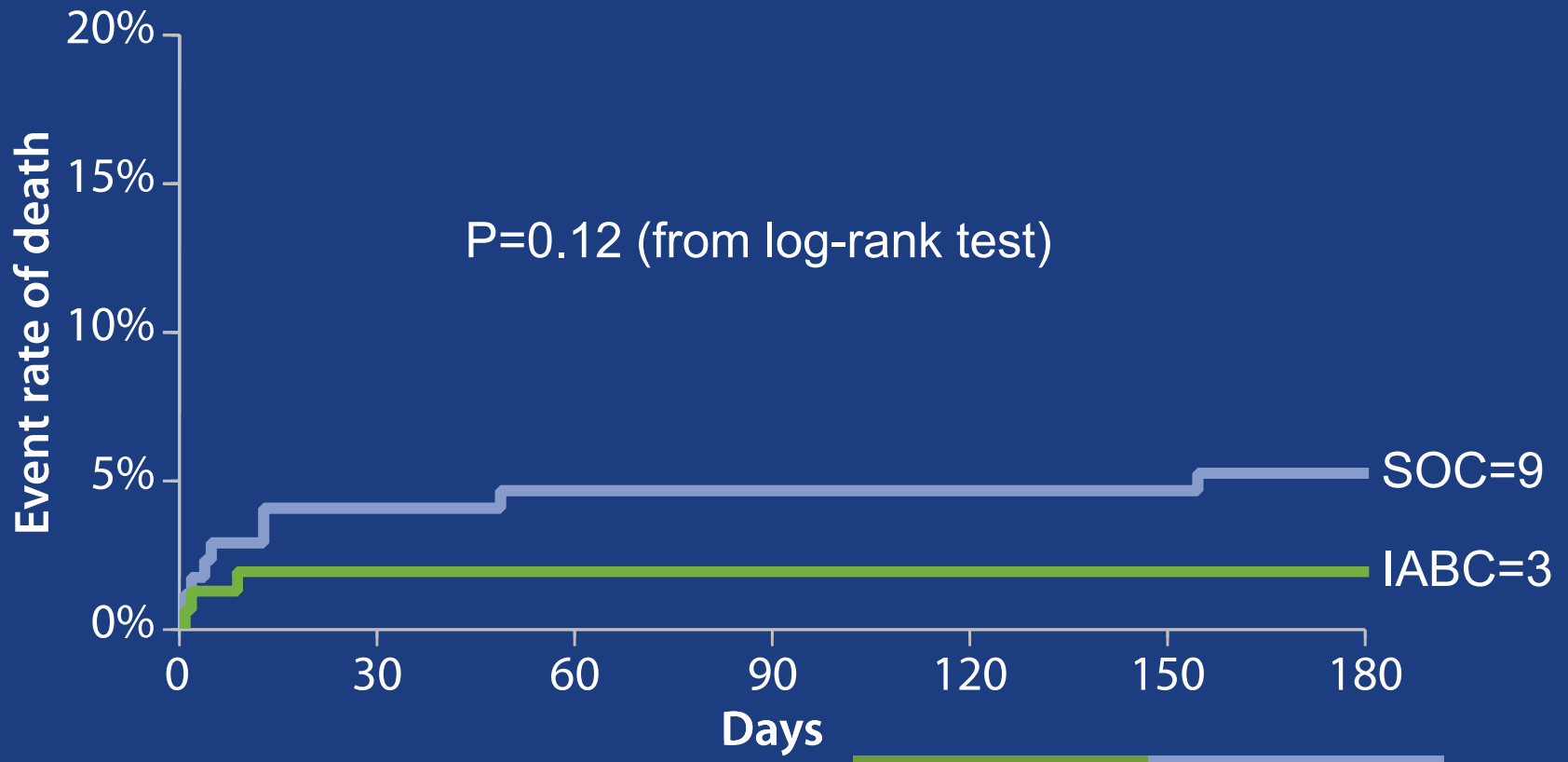
Co-primary endpoint: 2-sided p=0.025

30-day Clinical Events

	IABC (N=161)	SOC (N=176)	P Value
Death, %	1.9*	4.0*	0.26*
Stroke, %	1.9	0.6	0.35
Major bleed per GUSTO 1 definition or transfusion, %	3.1	1.7	0.49
Vascular complications, (n) %	7(4.3)	2 (1.1)	0.09
Major limb ischemia requiring operative intervention (n)	0	0	
Distal embolization (n)	0	0	
Major dissection (n)	2	0	
Pseudoaneurysm or AV fistula (n)	3	2	
Hematoma >5 cm (n)	3	0	

*From KM curves and log-rank test.

All Cause Death – 6 months



	IABC (N=161)	SOC (N=176)	P Value
Death, %	1.9*	5.2*	0.12*
Death/recurrent MI/new or worsening CHF, %	6.3*	10.9*	0.15*
Death/shock/new or worsening CHF, %†	5.0*	12.0*	0.03*

**From KM curves and log-rank test.* *†Exploratory analysis.*

Conclusion

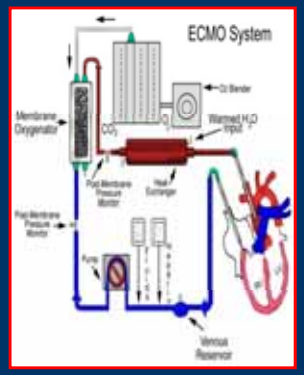
Among Patients with Acute Anterior STEMI without cardiogenic shock use of Intra-aortic counterpulsation prior to PCI compared with standard of care PCI:

1. Does not reduce infarct size
2. All cause mortality at 6 months was not different
3. Exploratory composite clinical endpoint favored IABC

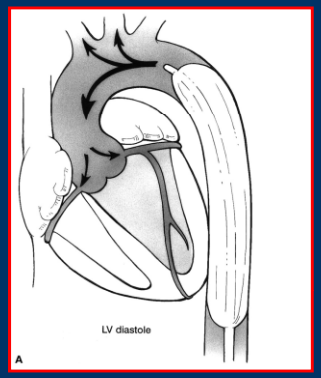
These findings do not support the routine use of IABC prior to PCI in Anterior STEMI patients without cardiogenic shock

Do Left Ventricular Assist Devices useful for the management of AMI with cardiogenic shock?

Historical Perspectives of Cardiac Support Devices

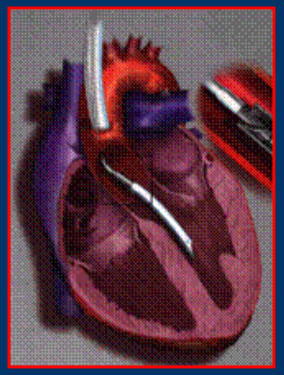


ECMO

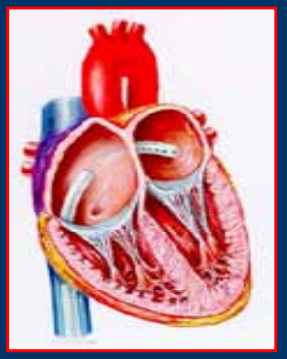


IABP

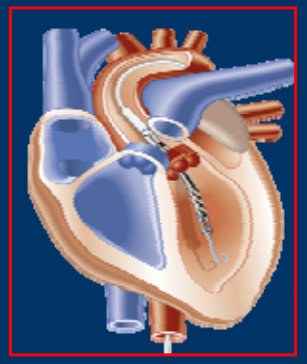
CPS



Hemopump



TandemHeart



Impella

1970's 1980's 1990's 2000's

Percutaneous MSC in Cardiogenic Shock Consumer Report

Device	Ease of Insertion	Duration of use	Flow L/min	MVF	Cost	Available	LV Unloading
IABP	++++	Days to weeks	±	±	$	++++	±
ECMO	++	Hours to Days	6.0	NA	$$$	++	++
Impella 2.5	+++	Hours to days	2.5	+	$$$	+++	+
LA-FA Bypass	+	Days to weeks	5.0	+++	$$$	++	+++

IABP in Cardiogenic Shock

History:

1962 Animal studies

Moulopoulos et al. Am Heart J 1962;63:669-675

1968 First clinical description in shock

Kantrowitz et al. JAMA 1968;203:135-140

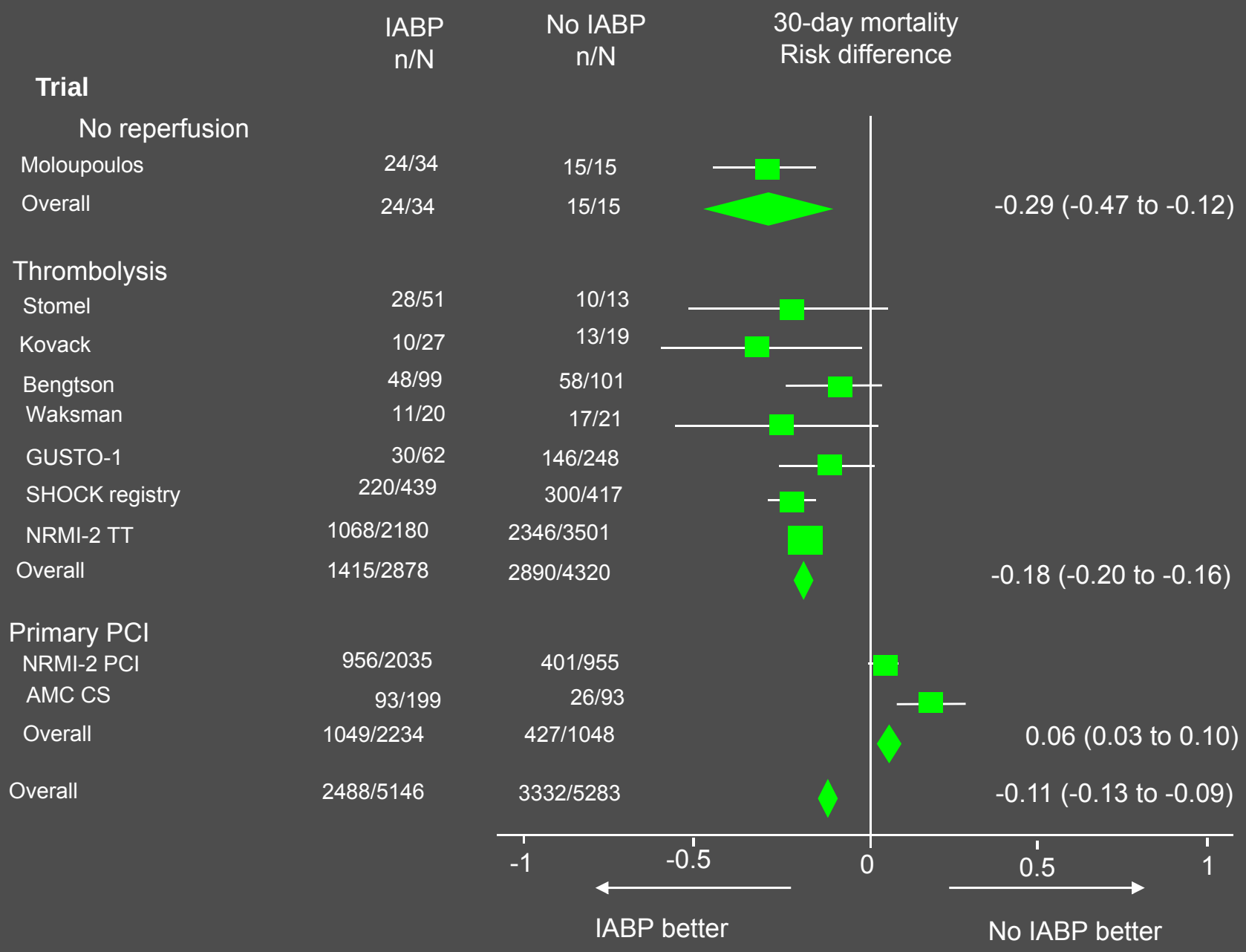
1973 Hemodynamic effects in shock, Mortality unchanged

Scheidt et al. NEJM 1973;288:979-984

> 40 years > 1 Million patients treated, low complication rate, Benchmark registry

Ferguson et al. JACC 2001;38:1456-1462

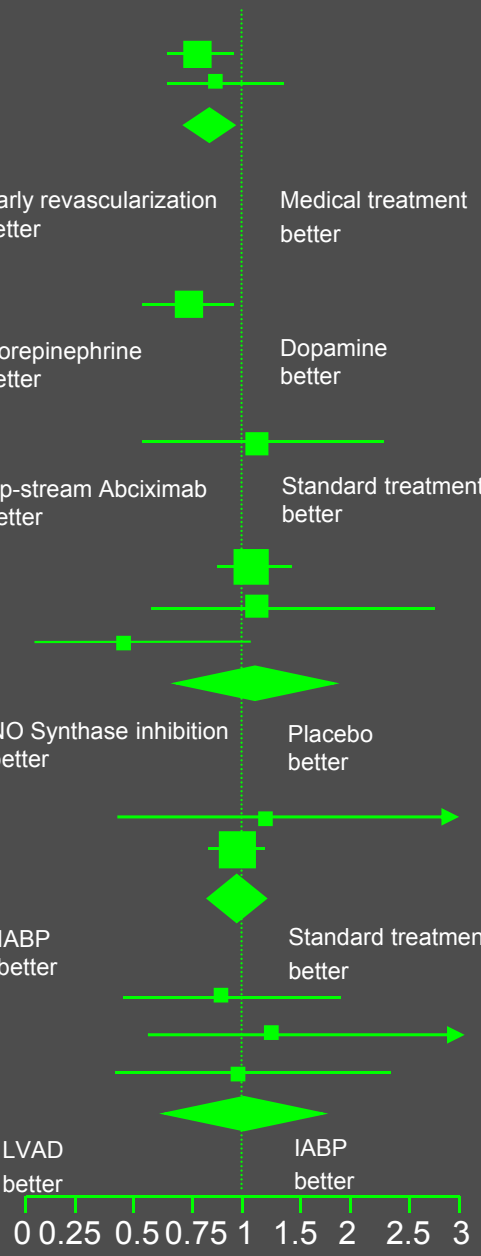
Mortality IABP vs no IABP - Metaanalysis



Sjauw et al. Eur Heart J 2009;30:459-468

Randomized Studies in Cardiogenic Shock

Trial	Follow-up	n/N	n/N	Relative Risk 95% CI	Relative Risk 95% CI
Revascularization (PCI/CABG)					
SHOCK	1-year	76/152	83/149		0.80 (0.66;0.98)
SMASH	30 days	22/32	18/23		0.87 (0.66;1.29)
Total		**103/184**	**117/172**		**0.82 (0.70;0.98)**
Catecholamines					
SOAP II (CS Subgroup)	28 days	64/145	50/135		0.75 (0.55;0.93)
Glycoprotein IIb/IIIa-Inhibitors					
PRAGUE-7	In-hospital	15/40	13/40		1.15 (0.59;2.27)
NO Synthase Inhibitors					
TRIUMPH	30 days	97/201	76/180		1.14 (0.91;1.45)
SHOCK-2	30 days	24/59	7/20		1.16 (0.59;2.69)
Cotter et al	30 days	4/15	10/15		0.40 (0.13;1.05)
Total		**125/275**	**93/215**		**1.05 (0.85;1.29)**
IABP					
IABP-SHOCK I	30 days	7/19	6/21		1.28 (0.45;3.72)
IABP-SHOCK II	30 days	119/300	123/298		0.96 (0.79;1.17)
Total		**126/319**	**129/319**		**0.98 (0.81;1.18)**
LVAD					
Thiele et al	30 days	9/21	9/20		0.95 (0.48;1.90)
Burkhoff et al	30 days	9/19	5/14		1.33 (0.57-3.10)
Seyfarth et al	30 days	6/13	6/13		1.00 (0.44-2.29)
Total		**24/53**	**20/47**		**1.06 (0.68-1.66)**



Updated from Thiele et al. Eur Heart J 2010,31:1828-1835

Randomized comparison of intraaortic balloon counterpulsation versus optimal medical therapy in addition to early revascularization in acute myocardial infarction complicated by cardiogenic shock

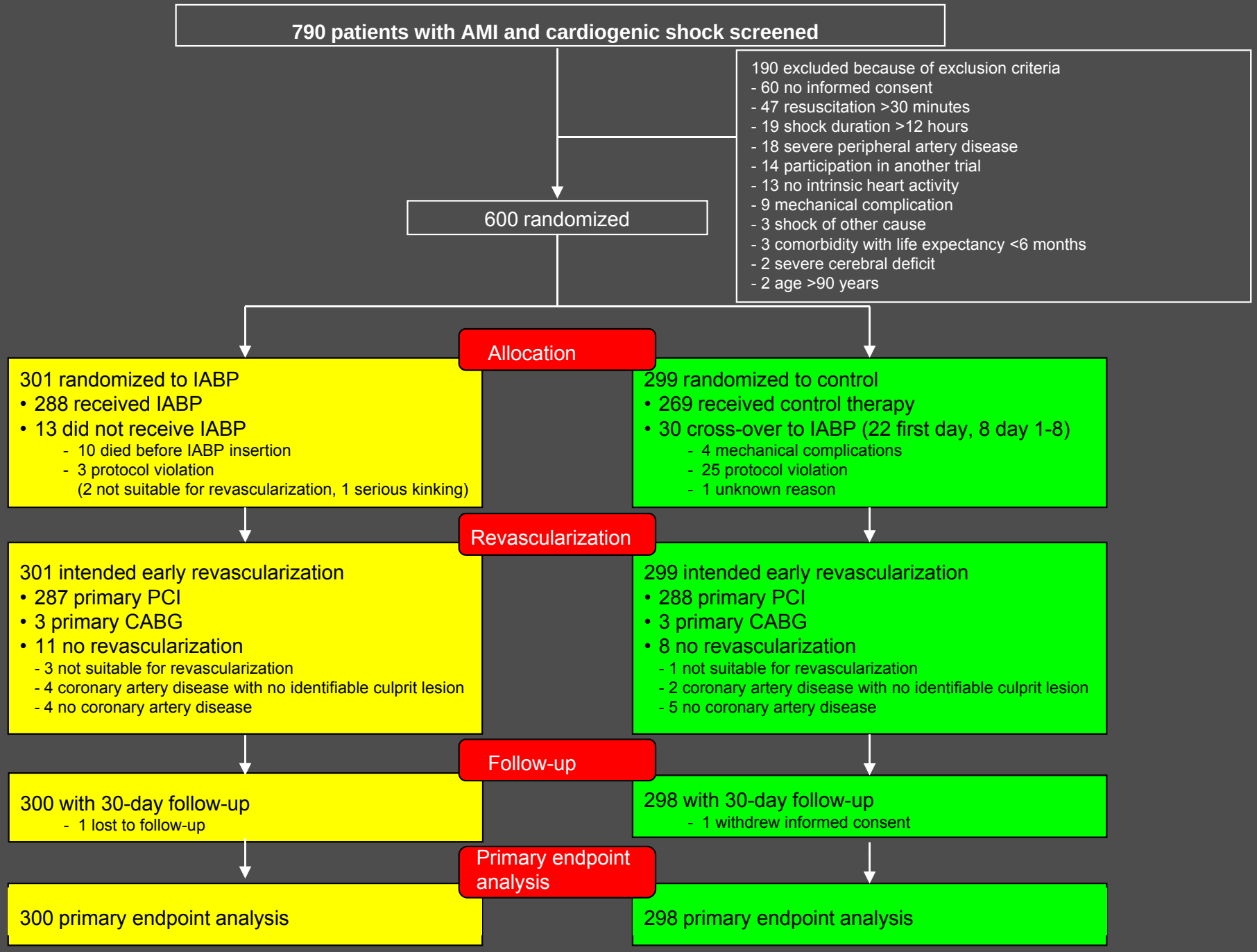
Holger Thiele, MD

Uwe Zeymer, MD; Franz-Josef Neumann, MD; Miroslaw Ferenc, MD; Hans-Georg Olbrich, MD; Jörg Hausleiter, MD; Gert Richardt, MD; Marcus Hennersdorf, MD; Klaus Empen, MD; Georg Fuernau, MD; Steffen Desch, MD; Ingo Eitel, MD; Rainer Hambrecht, MD; Jörg Fuhrmann, MD; Michael Böhm, MD; Henning Ebelt, MD; Steffen Schneider, PhD; Gerhard Schuler, MD; Karl Werdan, MD

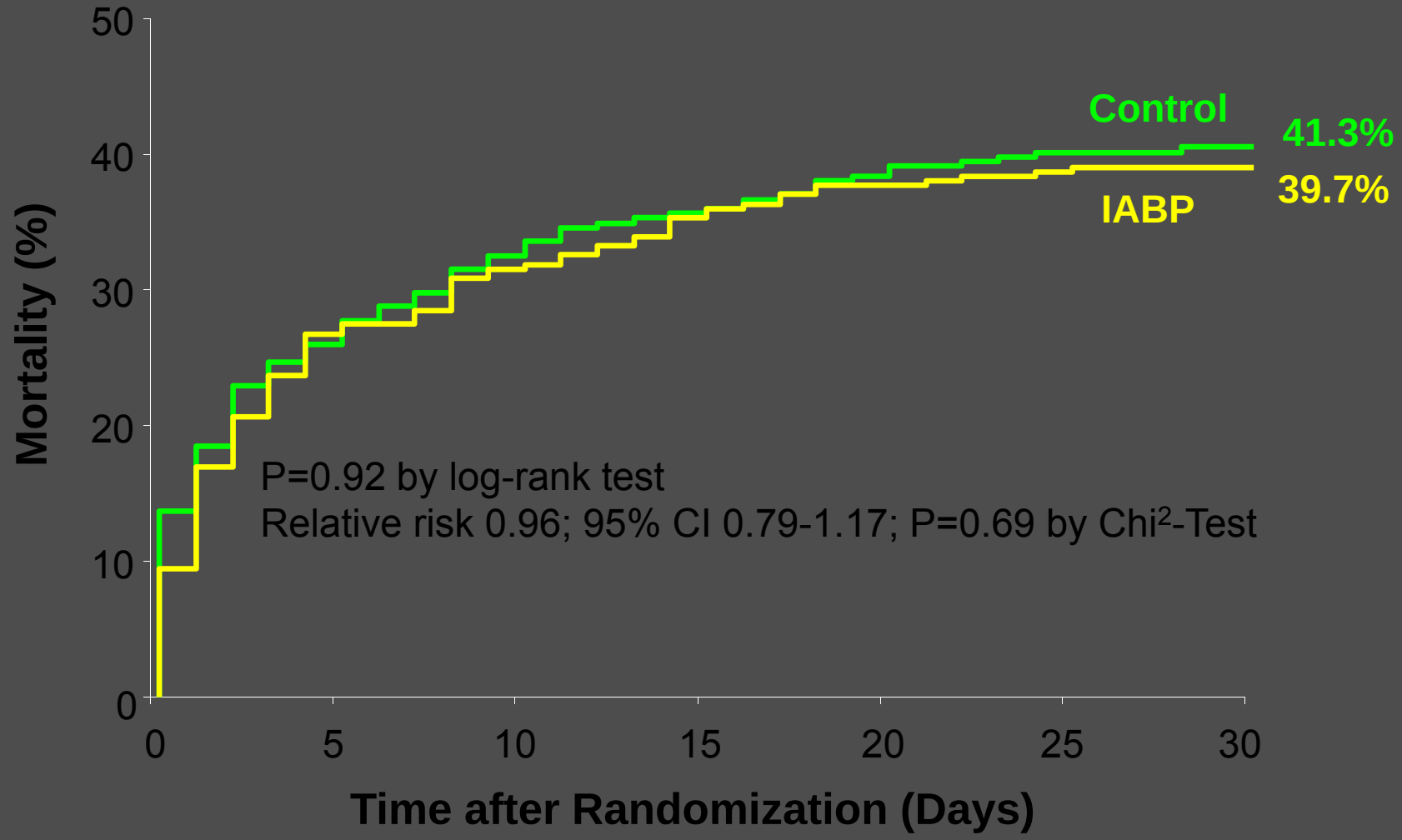
on behalf of the **IABP-SHOCK II Trial** Investigators

University of Leipzig – Heart Center

Trial Flow and Treatment

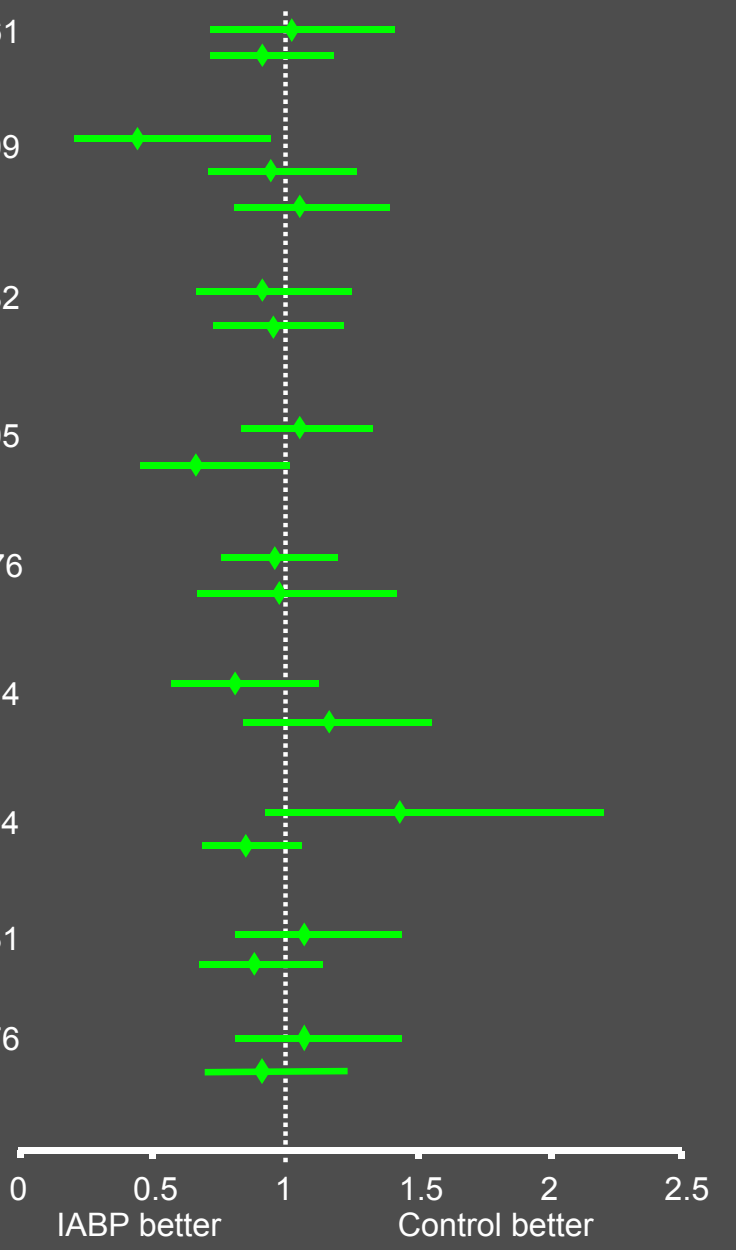


Primary Study Endpoint (30-Day Mortality)



Subgroups (30-Day Mortality)

Baseline Variable	N	30-Day Mortality (%) IABP	30-Day Mortality (%) Control	Relative Risk (95% CI)	P-Value for Interaction
Female	187	44.4	43.2	1.03 (0.74-1.43)	0.61
Male	411	37.3	40.5	0.92 (0.72-1.18)	
Age <50 years	70	19.4	44.1	0.44 (0.21-0.95)	0.09
Age 50-75 years	334	34.6	36.5	0.95 (0.71-1.27)	
Age >75 years	194	53.7	40.0	1.07 (0.81-1.41)	
Diabetes	195	42.9	46.7	0.92 (0.67-1.26)	0.82
No diabetes	399	37.2	38.9	0.96 (0.74-1.23)	
Hypertension	410	42.9	40.4	1.06 (0.84-1.34)	0.05
No hypertension	183	28.9	43.0	0.67 (0.45-1.01)	
STEMI/LBBB	412	41.0	42.9	0.96 (0.77-1.21)	0.76
NSTEMI	177	37.5	38.3	0.98 (0.67-1.43)	
Anterior STEMI	216	35.4	43.7	0.81 (0.58-1.13)	0.14
Non-anterior STEMI	196	48.3	42.2	1.16 (0.85-1.57)	
Previous infarction	131	47.9	33.3	1.44 (0.93-2.21)	0.04
No previous infarction	466	37.3	43.3	0.86 (0.69-1.07)	
Hypothermia	226	48.1	44.2	1.09 (0.82-1.44)	0.31
No hypothermia	372	35.1	39.3	0.89 (0.68-1.16)	
Blood pressure <80 mmHg	161	50.7	46.4	1.09 (0.79-1.50)	0.76
Blood pressure ≥80 mmHg	432	35.9	39.2	0.92 (0.72-1.17)	



Safety

	IABP (n=300)	Control (n=298)	P
Stroke in-hospital n/total (%)	2/300 (0.7)	5/298 (1.7)	0.28
GUSTO bleeding; n/total n (%)			
Life-threatening/severe	10/300 (3.3)	13/298 (4.4)	0.51
Moderate	52/300 (17.3)	49/298 (16.4)	0.77
Peripheral ischemic complication requiring intervention; n/total n (%)	13/300 (4.3)	10/298 (3.4)	0.53
Sepsis; n/total n (%)	47/300 (15.7)	61/298 (20.5)	0.15

Summary + Conclusions

- IABP support in cardiogenic shock is safe without significant inherent complications.
- However, IABP support did not reduce 30-day mortality in this large, randomized, multicenter trial in cardiogenic shock patients complicating myocardial infarction undergoing early revascularization.
- The primary study endpoint results are supported by a lack of benefit in secondary endpoints.

Guidelines

IABP in AMI complicated by cardiogenic shock

ESC

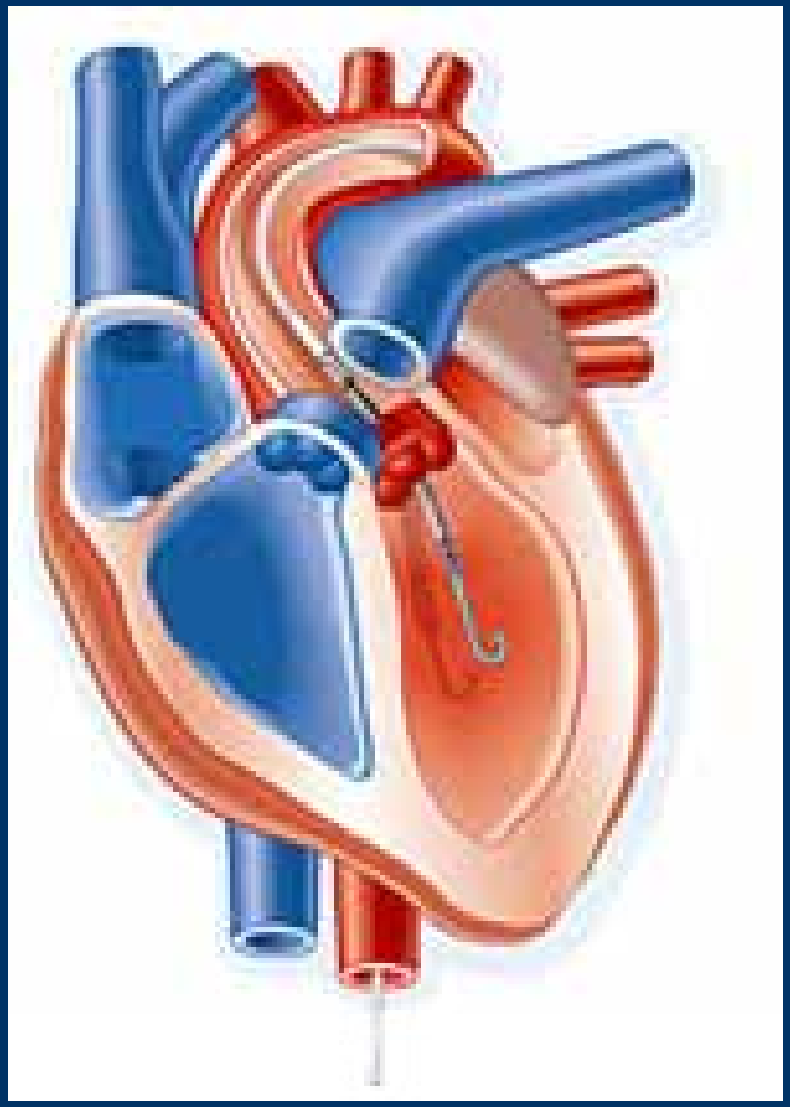
Class IC

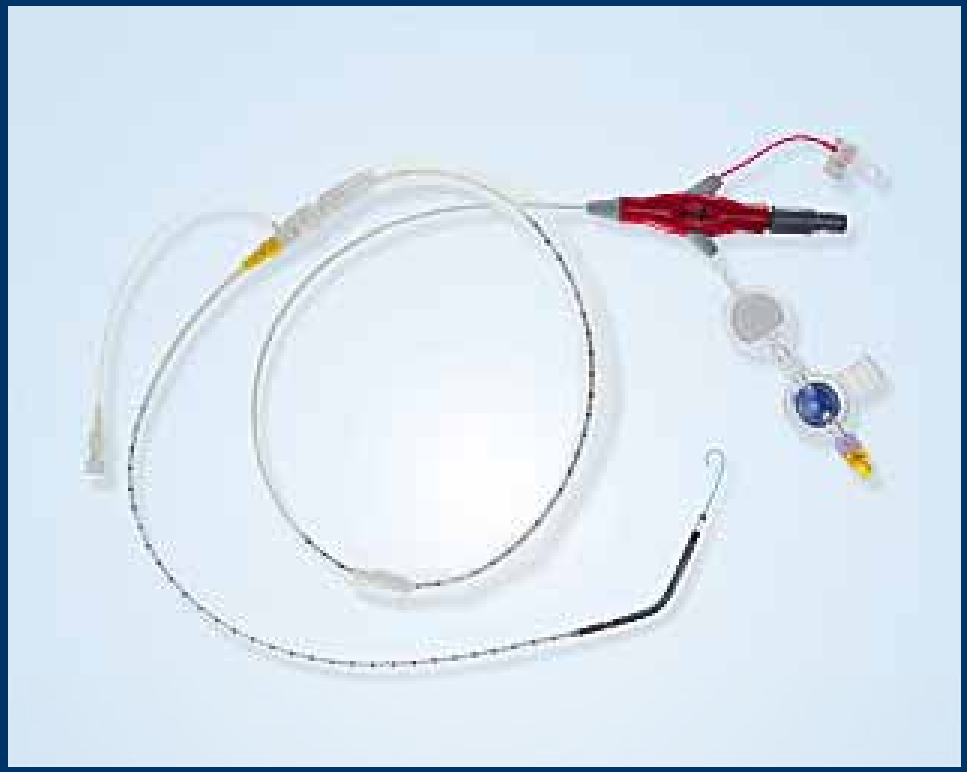
ACC/AHA

Class IB

Van de Werf et al. Eur Heart J 2008;29:2909-2945
Wijns et al. Eur Heart J 2010;31:2501-2555
Antman et al. Circulation 2004;110:82-292

Catheter Mounted Micro Axial Flow Pump





- 6.4 mm device (21F via surgical cutdown) results in 4.2-5.0 L/min output (33,000 RPM)
- 4.0 mm device (13F percutaneous) results in 2.5 L/min output (25,000 RPM)

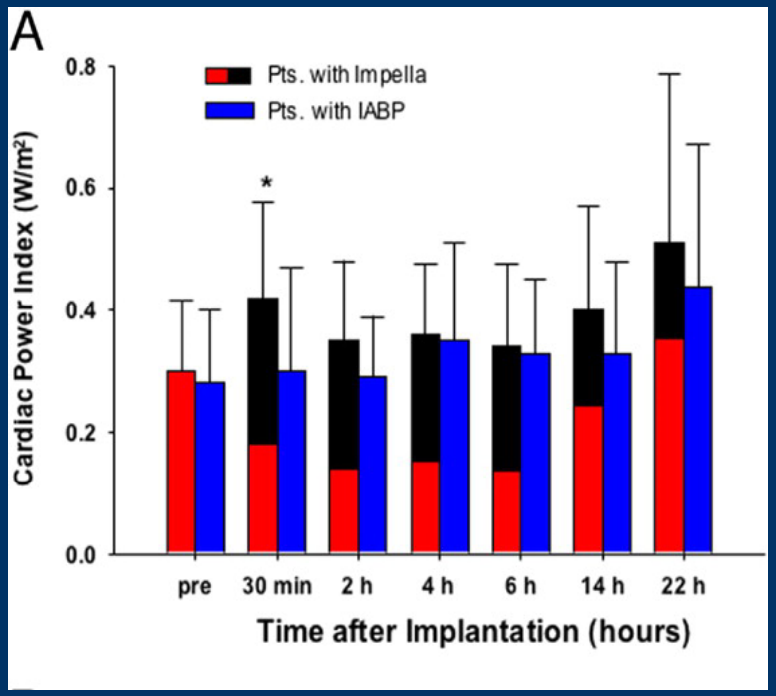
A RCT to Evaluate Safety and Efficacy of a pLVAD vs IABP for Rx of CGS Caused by MI

- Prospective RCT to test whether the Impella 2.5 provides superior hemodynamic support compared to IABP
- Primary EP Cardiac Power Index from baseline to 30 minutes after implantation
- Secondary EP included lactic acidosis, hemolysis and mortality after 30 days

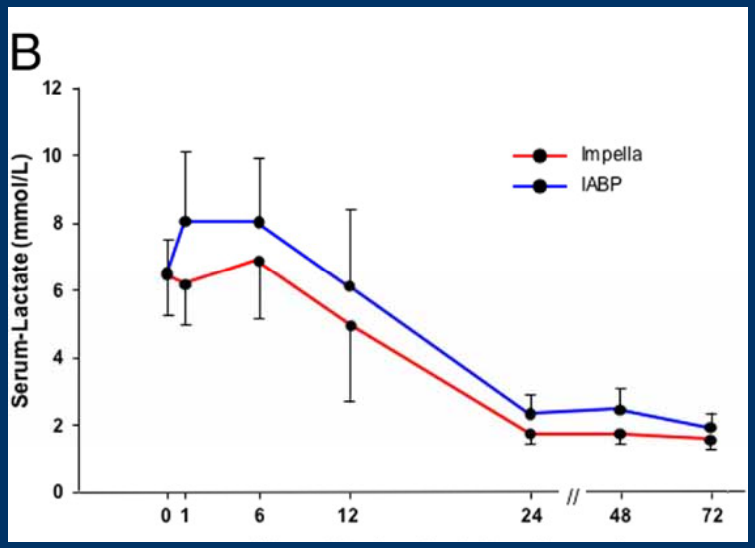
Seyfarth, M. et al. J Am Coll Cardiol 2008;52:1584-1588

IMPELLA 2.5

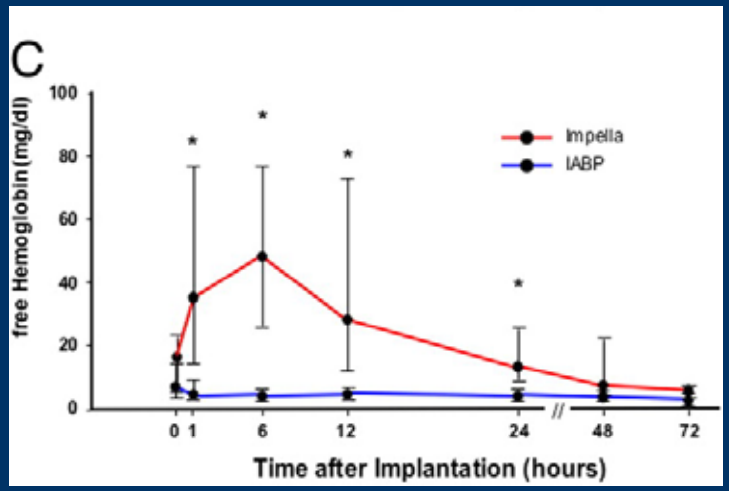
Time Course of CPI Serum Lactate, and Hemolysis



Cardiac Power Index



Serum Lactate



Plasma Free Hgb

Seyfarth, M. et al. J Am Coll Cardiol 2008;52:1584-1588

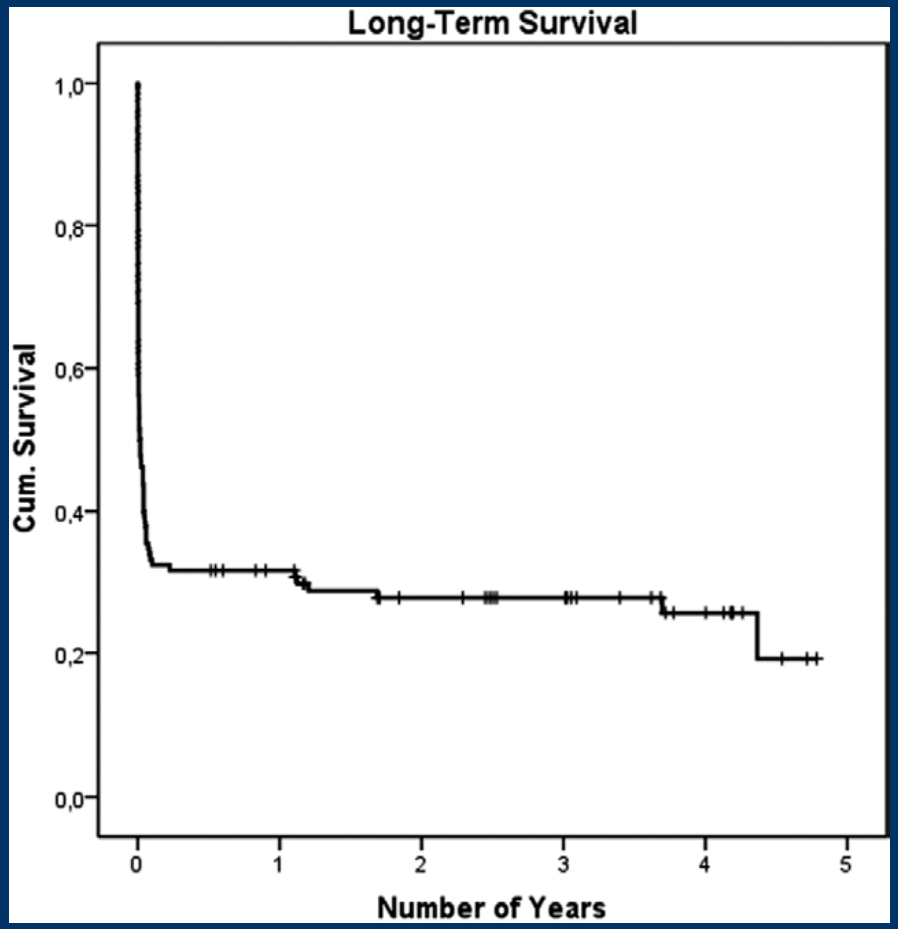
Percutaneous LV Support With the Impella-2.5–Assist Device in Acute CGS Results of the Impella–EUROSHOCK-Registry

- Retrospective multicenter registry 120 CGS AMI pts, 14 centers, 5 countries (2005-2010)
- Primary endpoint – 30 day mortality
- Secondary endpoints
  - Change in Lactate after institution of support
  - MACCE and long-term survival

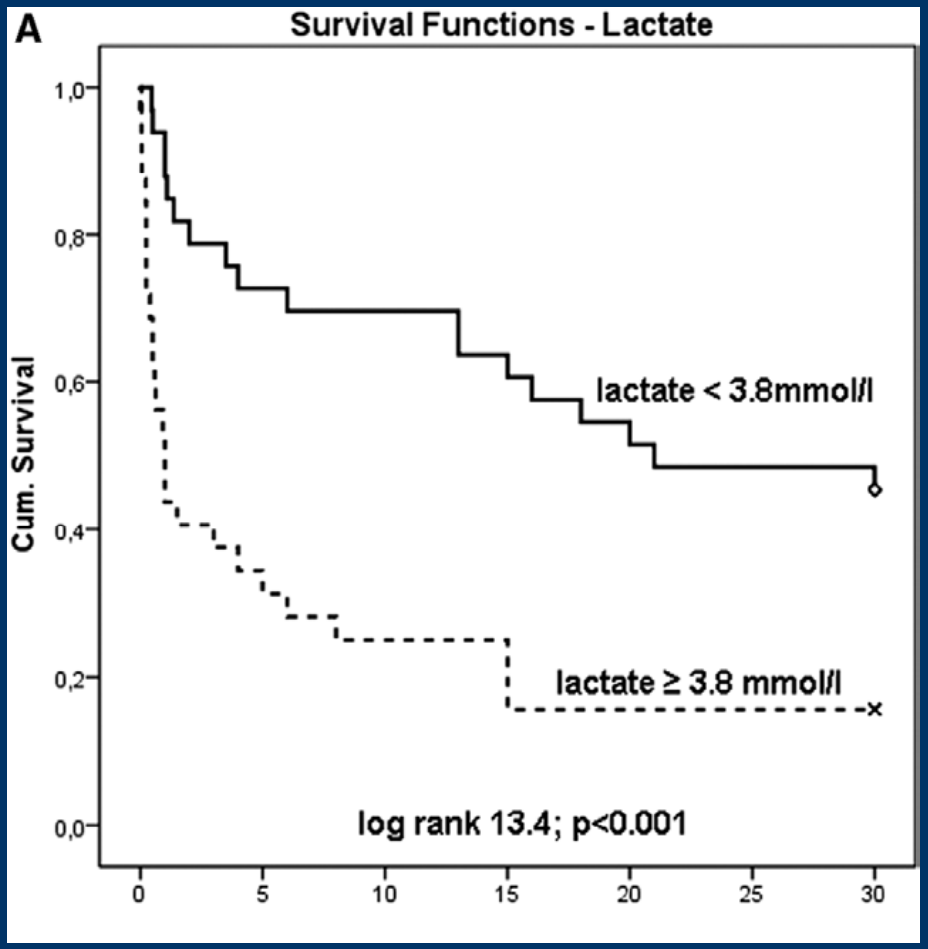
Latten et al – EUROShock Registry; *Circ Heart Fail* 2013;6;23-30

Lactate and age only predictors for survival

Overall Survival



Survival and Lactate



Variable	Odds Ratio(95% CI)	p
Age > 65yo	5.245 (1.473-18.677)	0.011
Lactate > 3.38 mmol	5.245 (1.473-18.677)	0.011

Mortality at 30 Days

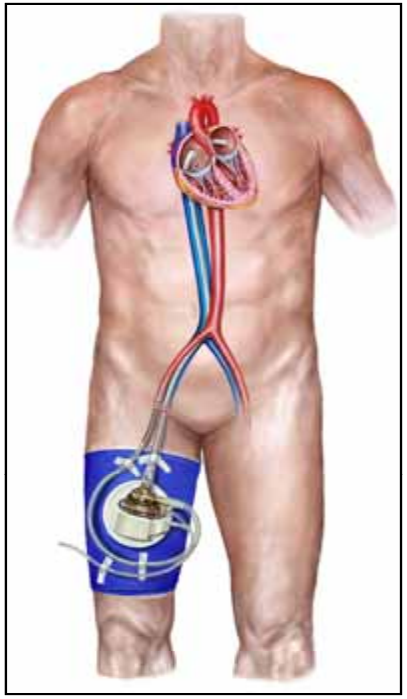
Latten et al – EUROShock Registry;Circ Heart Fail 2013;6;23-30	Baseline (N=120)
Primary Endpoint	
Mortality at 30 days	77 (64.2)
Death on circulatory support	50 (40.0)
Successfully weaned from support	53 (44.5)
Long-term survival (after 317±526d)	34 (28.3)
Secondary Endpoints	
Successful implantation procedure	119 (99.2)
Procedure related easy or suitable	114 (95)

The Use of Impella 2.5 in CGS Patients Does It Save Lives?

- Based in the foregoing data – NO
- in severe shock the device does not unload the LV sufficiently or provide enough systemic support, or increase MVF
- Not as a bridge to recovery but as a bridge to decision
- Decisions needs to be made rapidly and in an environment where all therapeutic alternatives are available (pVAD, VAD, TAH, Transplant)

Tandem Heart PVAD

TandemHeart Enhanced Flow Cannula



TandemHeart Pump

TandemHeart Escort™ Controller

Percutaneous LVAD in CGS

Reversal of Cardiogenic Shock by Percutaneous Left Atrial–to–Femoral Arterial Bypass Assistance

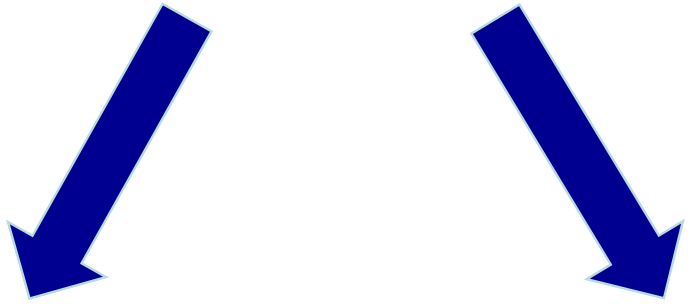
Holger Thiele, MD; Bernward Lauer, MD; Rainer Hambrecht, MD; Enno Boudriot, MD; Howard A. Cohen, MD; Gerhard Schuler, MD

Circulation 104:2917-2922, 2001

- 18 Consecutive patients with CGS and AMI (44-89yo)
- 5/18 Ventricular septal rupture
- Mean duration of support 4 ± 3 days
- Survival at 30 days 56% (77% excluding VSD pts)

Severe Refractory Cardiogenic Shock

Ischemic and Non Ischemic 117 Patients
Mortality - 30 Day 40.2%, 6 Month 45.3%

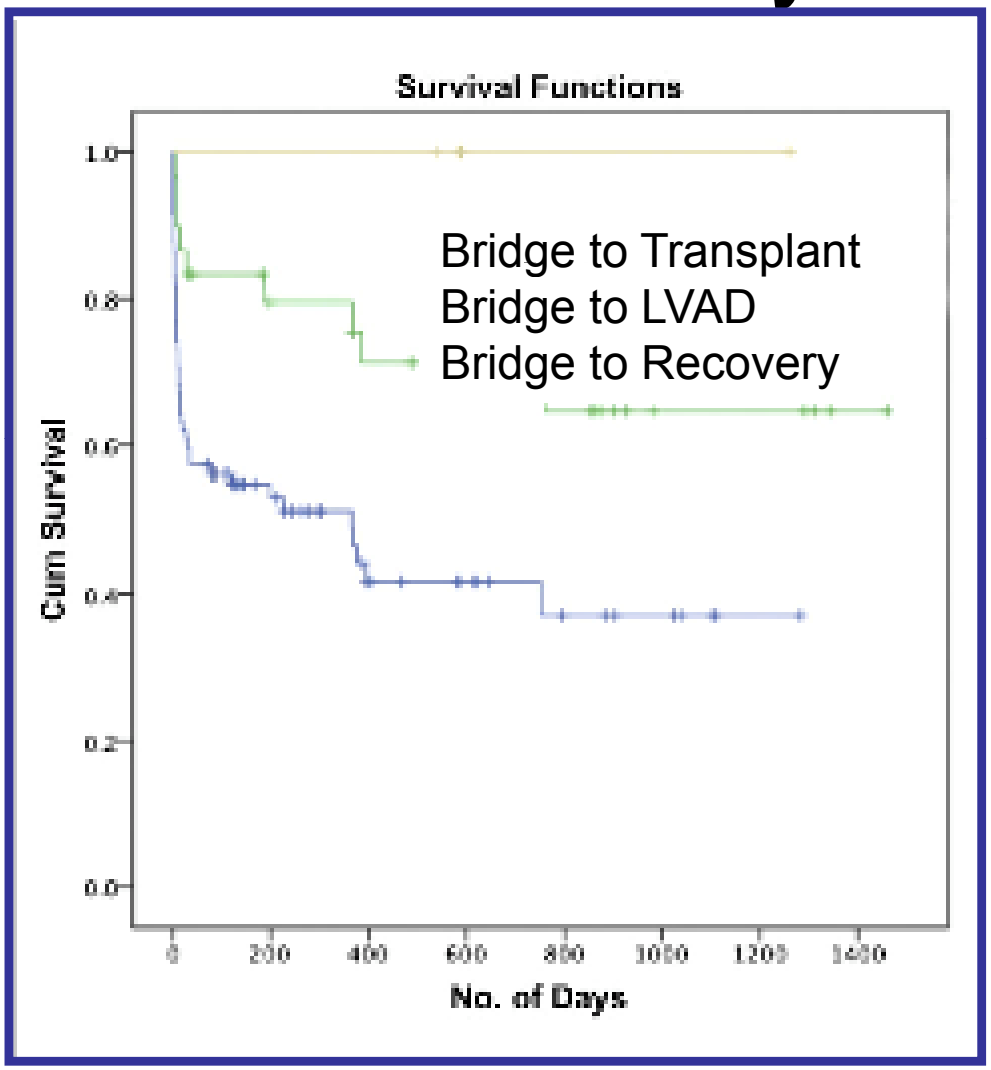


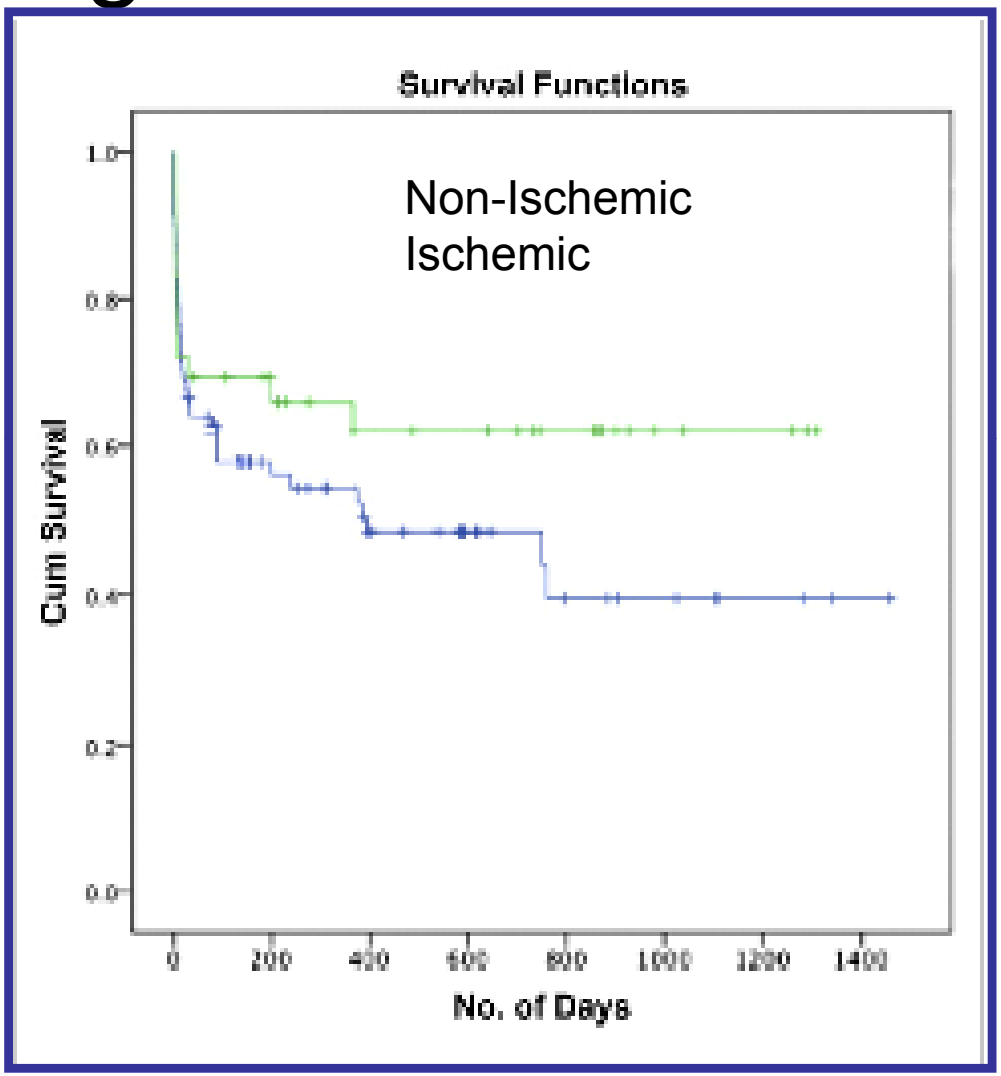
Ischemic 80 Patients
30 Day 43.8%, 6 Month 50%

Non Ischemic 37 Patients
30 Day32%, 6 Month 35%

Kar et al. *J Am Coll Cardiol* 2010

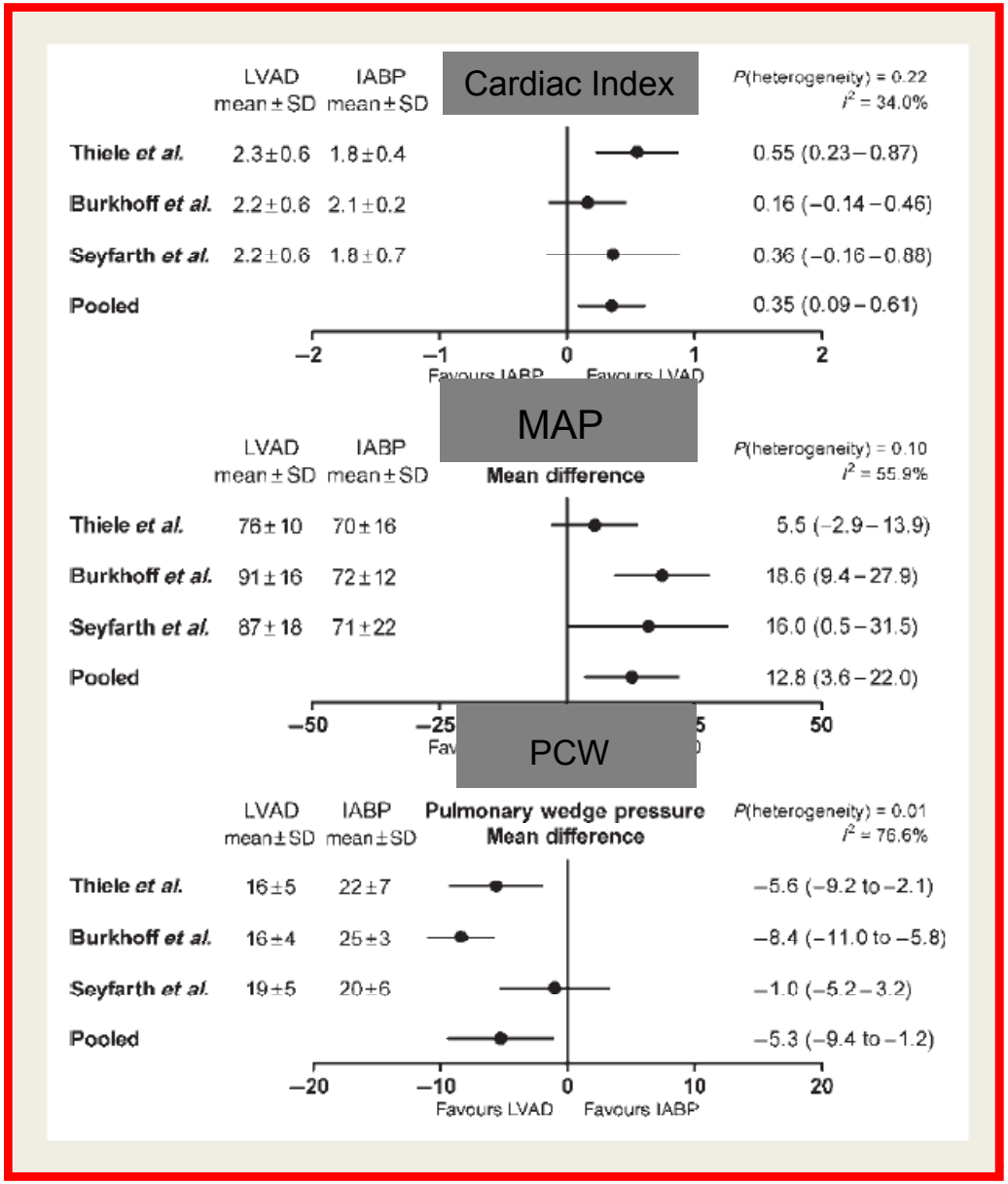
Percutaneous LVAD in Severe Refractory Cardiogenic Shock





Kar et al. *J Am Coll Cardiol* 2010

META-ANALYSIS of IABP vs LVAD in CGS



Cheng et al. *Eur Heart J* 2009;30:2102-2108

Conclusions – STEMI - SHOCK

1. Coordinated Efforts for Reperfusion have improved outcomes in patients with STEMI
2. Future Efforts for patients with SHOCK and STEMI may involve – mechanical support and transfer for more intensive therapies
3. Routine IABP placement does not reduce 30-day mortality
   - Percutaneous LVAD
   - Surgical LVAD