ANGIOPLASTY SUMMIT

TCTAP 2011

TRANSCATHETER CARDIOVASCULAR THERAPEUTICS ASIA PACIFIC

Circulatory Support: From IABP to LVAD

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DISCLOSURES

- CardiacAssist Inc
  - Medical Director
  - Stock Options
  - Grant support
- Medtronic Inc
  - Grant Support
- Abbott Vascular
  - Grant Support
- Boston Scientific Corporation
  - Grant Support
- St. Jude, Inc
  - Grant Support

CIRCULATORY SUPPORT

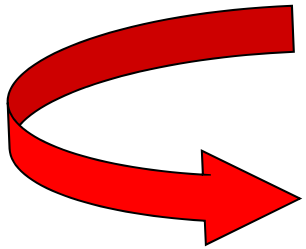
INDICATIONS

- High risk PCI
- Cardiogenic shock
- Mycocardial infarct size reduction (theoretical)
- Non CAD patients – acute and chronic severe LV dysfunction, acute and chronic valvular disease, RV dysfunction, VT ablation

Hemodynamic Support in the Cardiac Cath Lab

What Constitutes High Risk PCI

- High Risk Patient Severe LV/VALVE Dysfunction
  - Hemodynamically compromised
  - Last remaining vessel
  - Large amount of myocardium at risk
- High Risk Lesion
  - LMCA -complex
  - Complex lesion with or without thrombus (B2,C)
- Combination High Risk Patient/High Risk Lesion



LV ASSIST DEVICE

HIGH RISK PCI

HEMODYNAMIC SUPPORT

LV FUNCTION	SIMPLE PCI	COMPLEX PCI
NORMAL LV	NONE	IABP
POOR LV	IABP	LVAD

RIHAL, AICT, BANGKOK 2008

Mechanical Circulatory Support

Ideal Percutaneous Left Ventricular Assist

- Safety and efficacy
  - Freedom from thrombosis, bleeding, infection, hemolysis, vascular compromise
  - Flow rate – complete support
  - Improve systemic and myocardial perfusion
  - Improve Survival
  - Bridge to next therapy
- Ease of insertion, weaning and removal
- Cost
- Availability

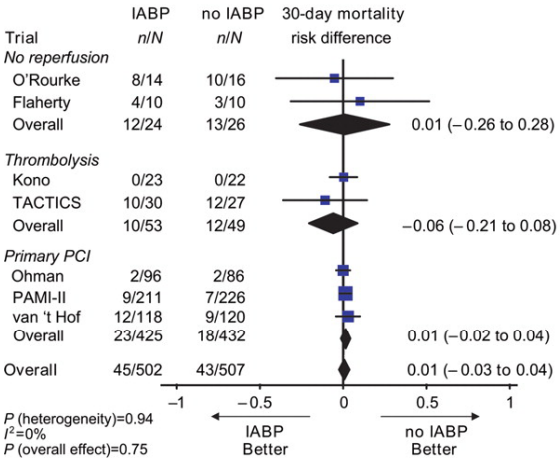
PERCUTANEOUS LEFT VENTRICULAR ASSIST

CIRCULATORY SUPPORT DEVICES

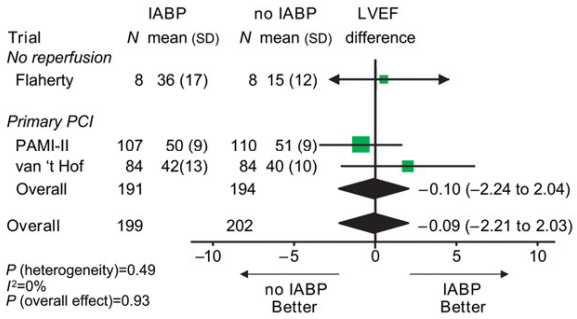
- Intra-aortic balloon pump ✓
- Catheter mounted miniature axial flow pump ✓
  Hemopump→A-Med →Impella
- CPS
- LA-FA bypass TandemHeart ✓
- ECMO
- Surgically implanted VAD
- Total artificial heart

RCT's of IABP Therapy in Acute MI

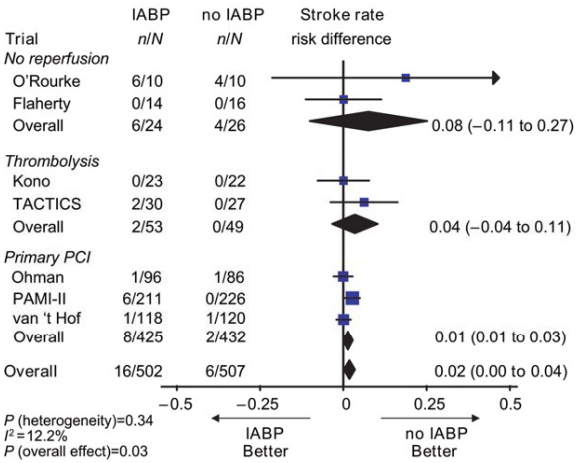
30 Day Mortality



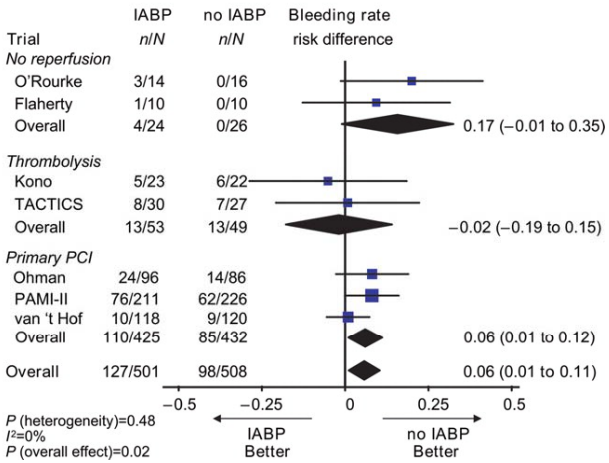
LVEF



Stroke Rate



Bleeding



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

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ELECTIVE IAB COUNTERPULSATION IN HIGH RISK PCI

Perera et al. *JAMA* 2010;304:867-874

Variable	No. (%) Elective IABP (n = 151)	No. (%) No Planned IABP (n = 150)	OR (95% CI)[a]	*P* Value
Primary end point				
MACCE[b]	23 (15.2)	24 (16.0)	0.94 (0.51-1.76)	.85
MI	19 (12.6)	20 (13.3)	0.93 (0.48-1.83)	.85
Death	3 (2.0)	1 (0.7)	3.02 (0.31-29.37)	.34
CVA	2 (1.3)	0		
Further revascularization	1 (0.7)	4 (2.7)	0.24 (0.03-2.20)	.21
Secondary end points				
6-mo mortality	7 (4.6)	11 (7.4)[c]	0.61 (0.24-1.62)	.32
Bleeding				
All	29 (19.2)	17 (11.3)	1.86 (0.93-3.79)	.06
Major	5 (3.3)	6 (4.0)	0.83 (0.20-3.36)	.77
Minor	24 (15.9)	11 (7.3)	2.39 (1.07-5.61)	.02
Procedural complications	2 (1.3)	16 (10.7)	0.11 (0.01-0.49)	<.001
Access-site complications	5 (3.3)	0		.06[d]

Mean EF=23.6% both groups

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PERCUTANEOUS LEFT VENTRICULAR ASSIST

CARDIOGENIC SHOCK AND THE USE OF HEMODYNAMIC SUPPORT DEVICES

ROLE OF IABP IN CGS

- Should *not* be viewed as an independent Rx of CGS
- Will allow *stabilization and support* until definitive therapeutic measures can be employed
- IABP use by itself *does not* result in preservation of LV function or improved survival

PERCUTANEOUS LEFT VENTRICULAR ASSIST

NEW 50 cc INTRA-AORTIC BALLOON

- Increased support
- Increased mean arterial pressure
- Increased LV unloading
- Increased cardiac output

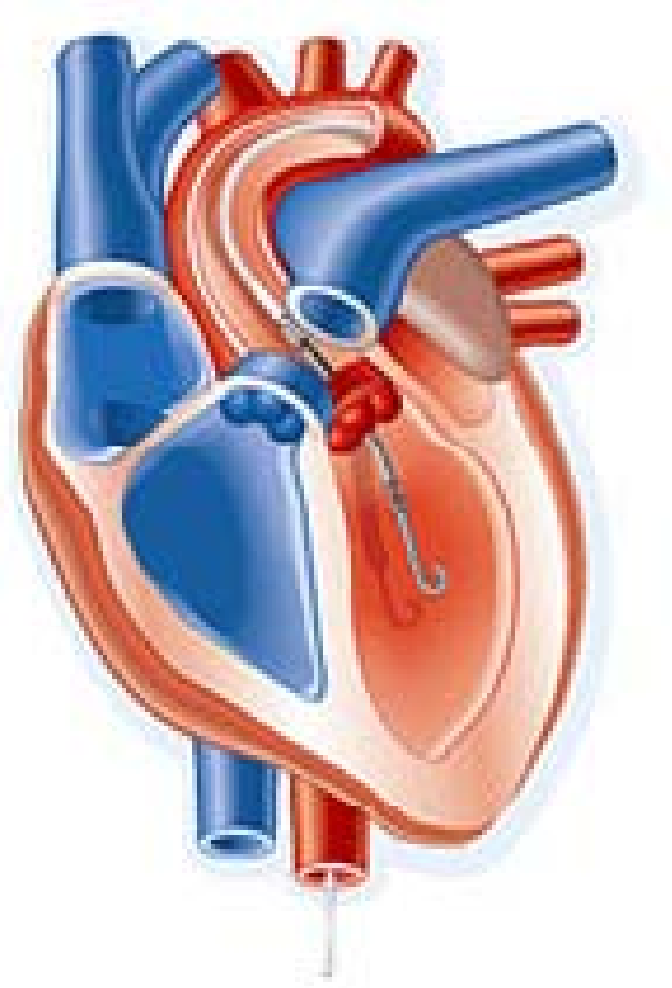
Catheter Mounted Micro Axial Flow Pump – IMPELLA

- Miniature axial flow pump
- Catheter mounted
- Placed retrograde across the aortic valve
- Blood withdrawn from the LV and expelled into the ascending Aorta

Catheter Mounted Miniature Axial Flow Pump

- 6.4 mm device (21F via surgical cutdown) results in 4.2-5.0 L/min output (32,000 RPM)
- 4.0 mm device (13F percutaneous) results in 2.2 L/min output (55,000 RPM)

Catheter Mounted Micro Axial Flow Pump



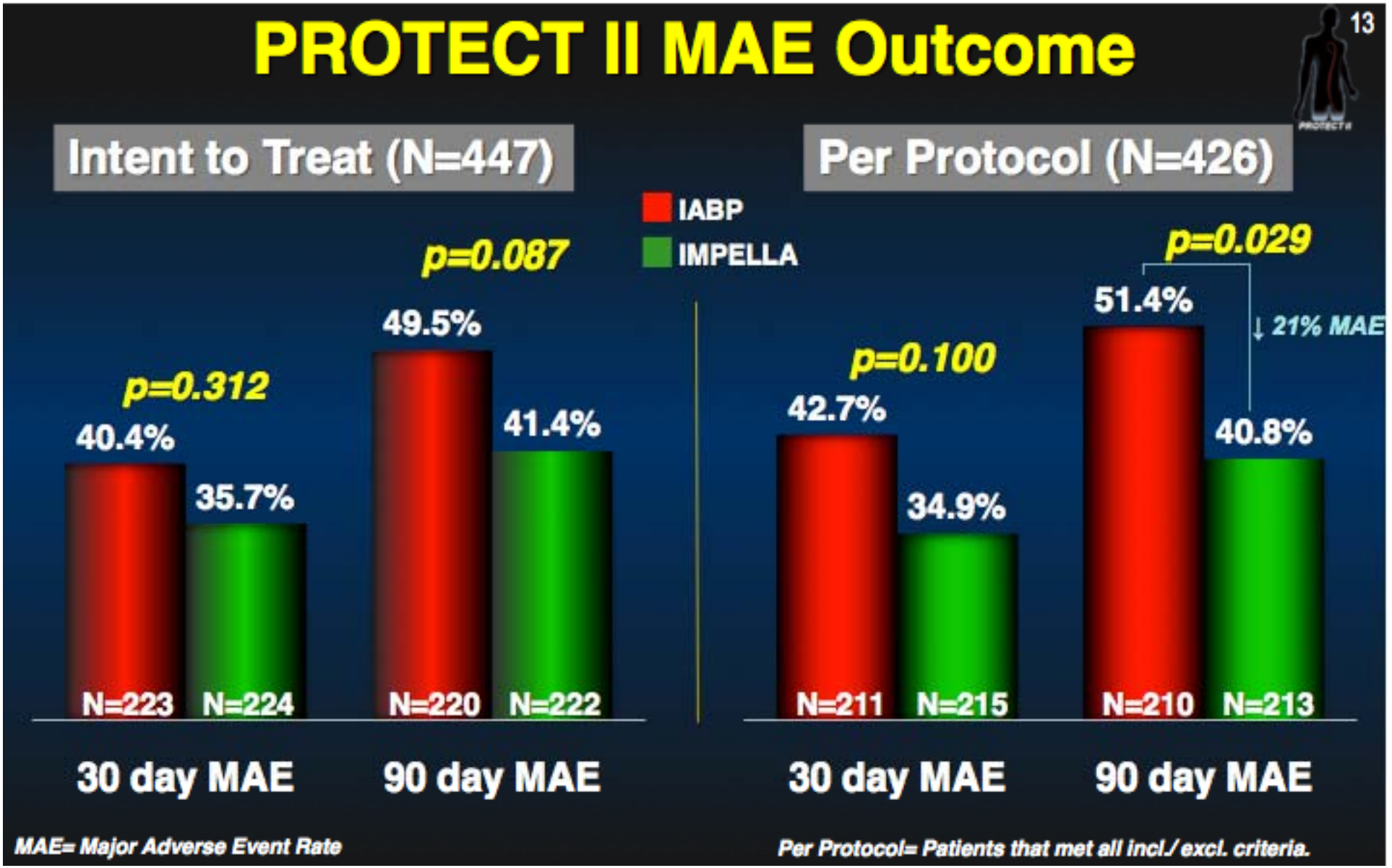
PROTECT II TRIAL

PROTECT II per protocol patients with and without RA at interim analysis

PATIENTS	% INTERIM POPULATION	MACCE RATE IMPELLA (%)	MA (%)	P
All Patients(n=305)	100	38	43	0.40
Patients w/o RA (n=237)	88		43	0.11
Patientsw RA (n=68)		72	46	0.12

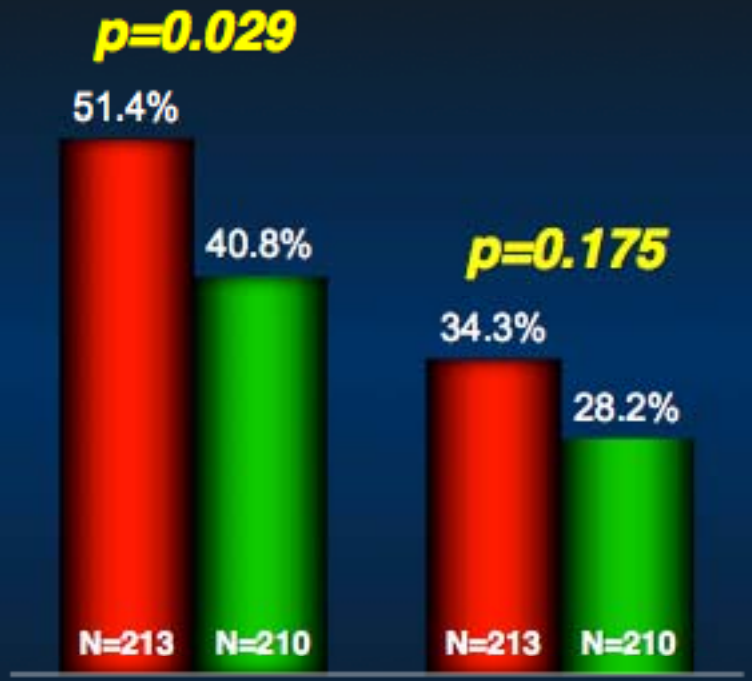
DSMB TERMINATES TRAIL DUE TO FUTILITY

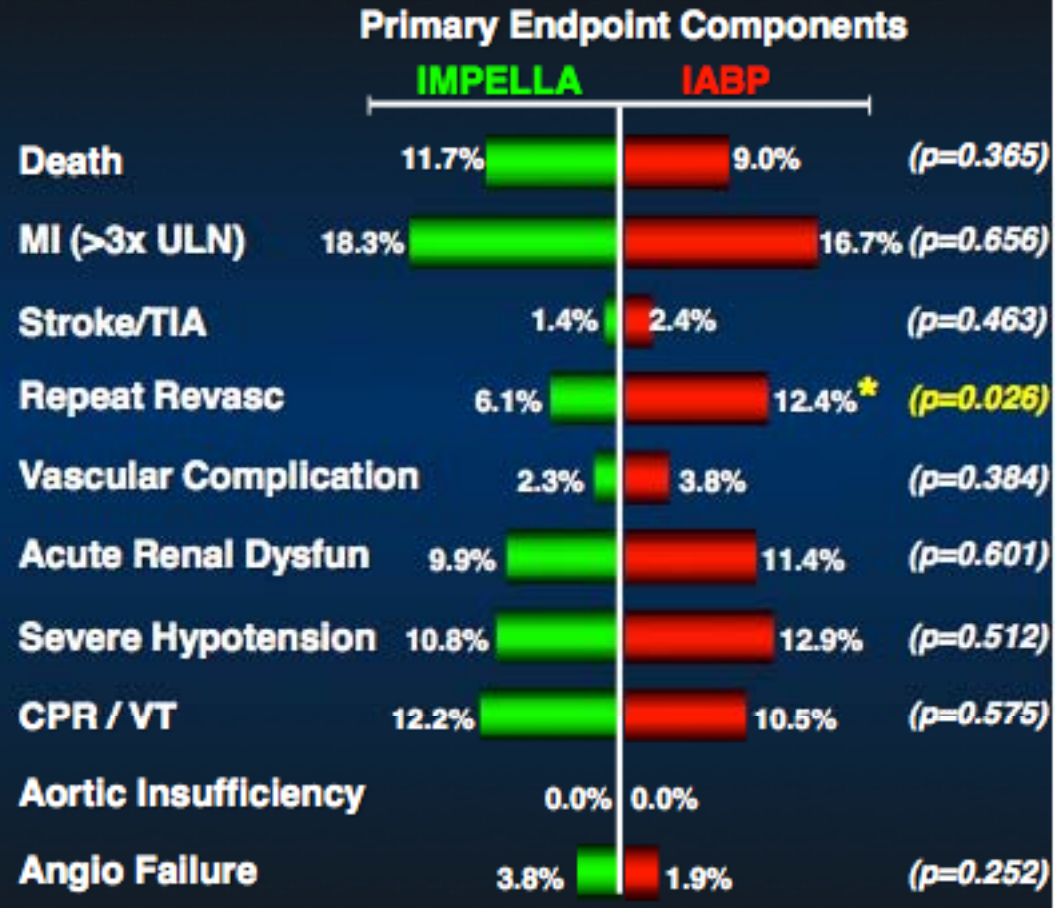
The Heart.org December 9,2010


PROTECT II MAE Outcome
13
Intent to Treat (N=447)
Per Protocol (N=426)
IABP
IMPELLA
p=0.312
40.4%
35.7%
N=223
N=224
30 day MAE
p=0.087
49.5%
41.4%
N=220
N=222
90 day MAE
p=0.100
42.7%
34.9%
N=211
N=215
30 day MAE
p=0.029
51.4%
40.8%
↓ 21% MAE
N=210
N=213
90 day MAE
MAE= Major Adverse Event Rate
Per Protocol= Patients that met all incl./ excl. criteria.

ACC 2011

PROTECT II 90-day Outcome (PP)





Per Protocol (PP)= Patients that met all incl./excl. criteria.

** Designates statistically significant difference (p<0.05).*
All other differences are non-significant

ACC 2011

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

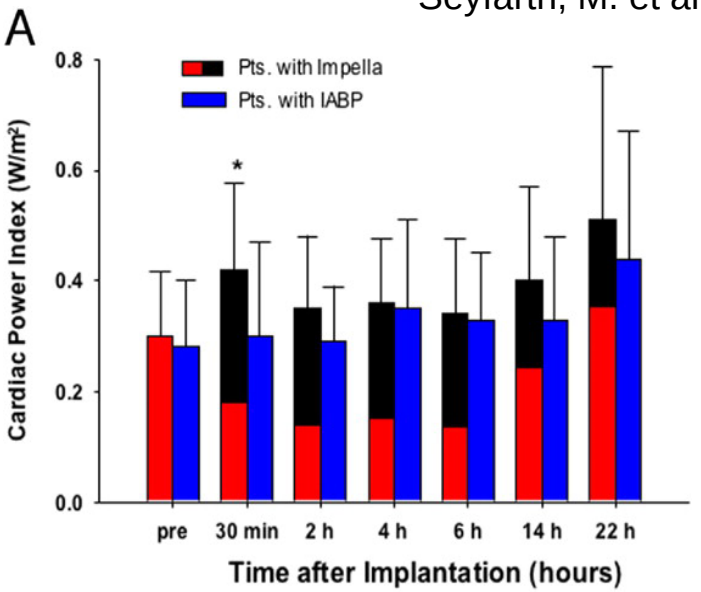
- Prospective RCT to test whether the Impella 2.5 provides superior hemodynamic support compared to IABP
- Primary EP Cardiac Power Index from baseline to 30 minutes after implantation
- Secondary EP included lactic acidosis, hemolysis and mortality after 30 days

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

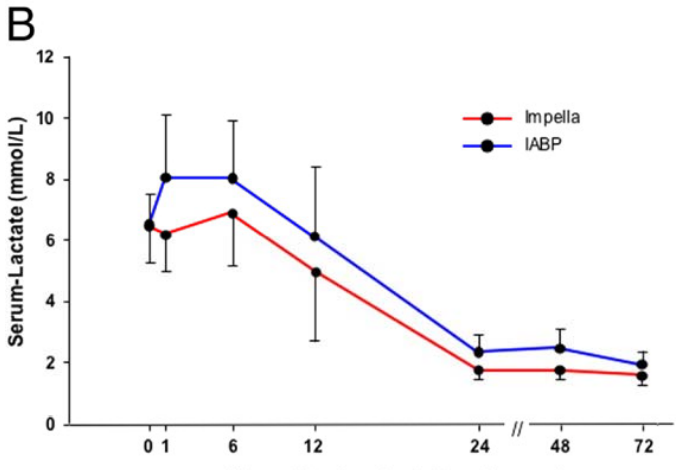
IMPELLA 2.5

Time Course of CPI Serum Lactate, and Hemolysis

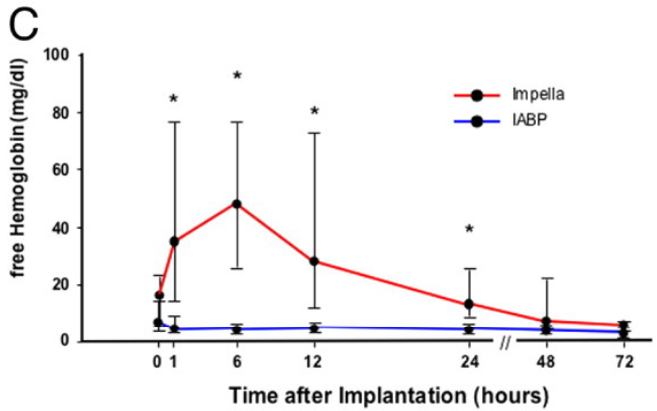
Seyfarth, M. et al. J Am CollCardiol 2008;52:1584-1588



Cardiac Power Index



Serum Lactate



Plasma Free Hgb

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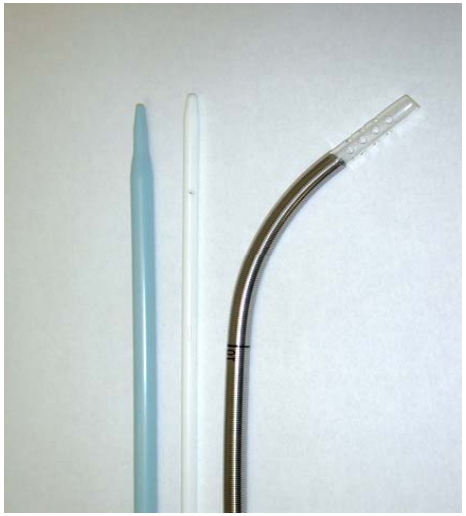
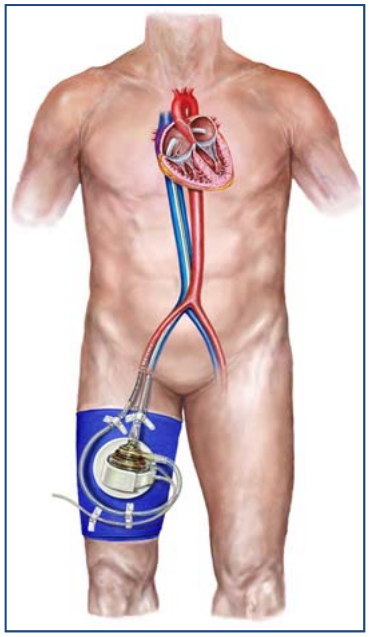
Tandem Heart PVAD



TandemHeart Enhanced Flow Cannula



TandemHeart Escort™ Controller

TandemHeart Pump

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CIRCULATORY SUPPORT

INDICATIONS

- High risk PCI (no RCT's)
- Cardiogenic shock (2 RCT's –small)
- Mycocardial infarct size reduction (theoretical)

Percutaneous LVAD in 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 CollCardiol*2010

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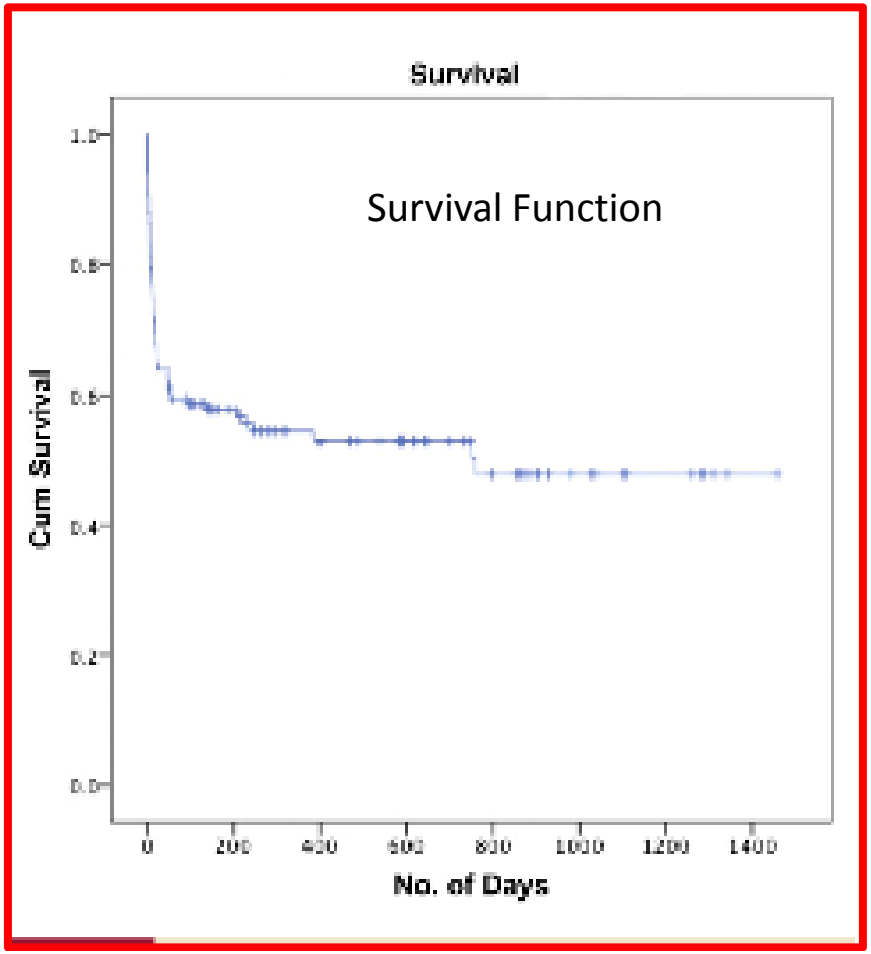
Percutaneous LVAD in Severe Refractory Cardiogenic Shock



Kar et al. *J Am CollCardiol*2010

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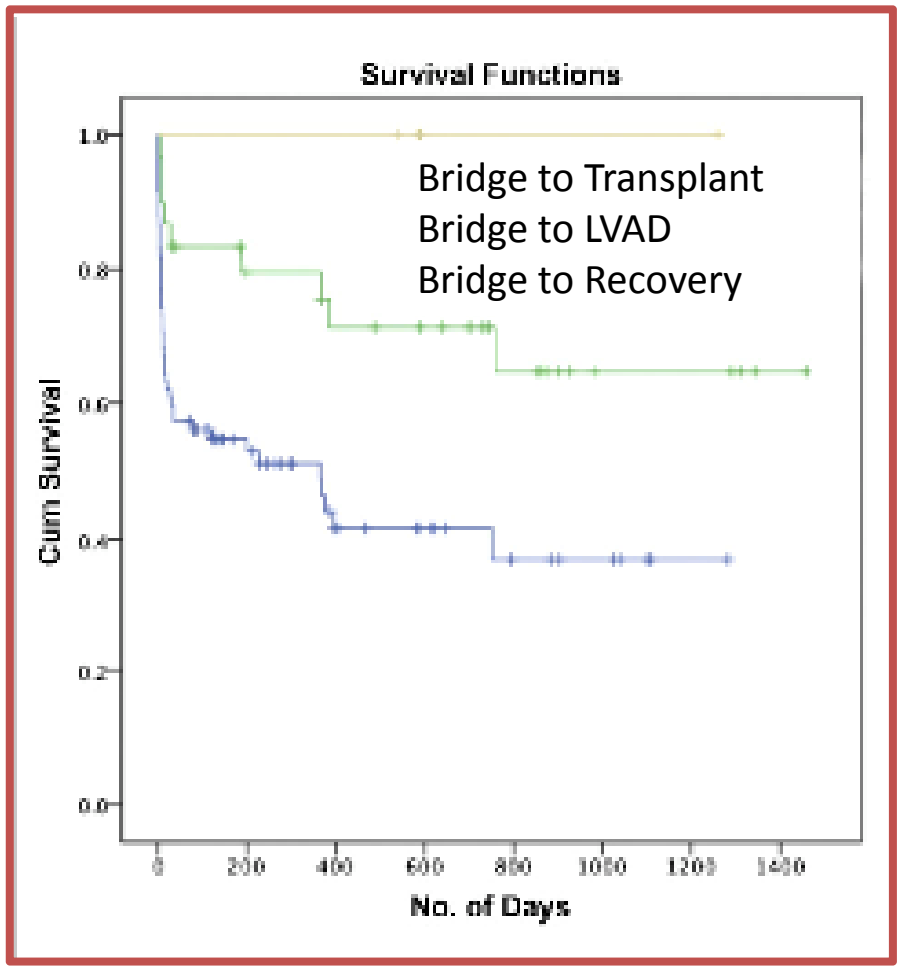
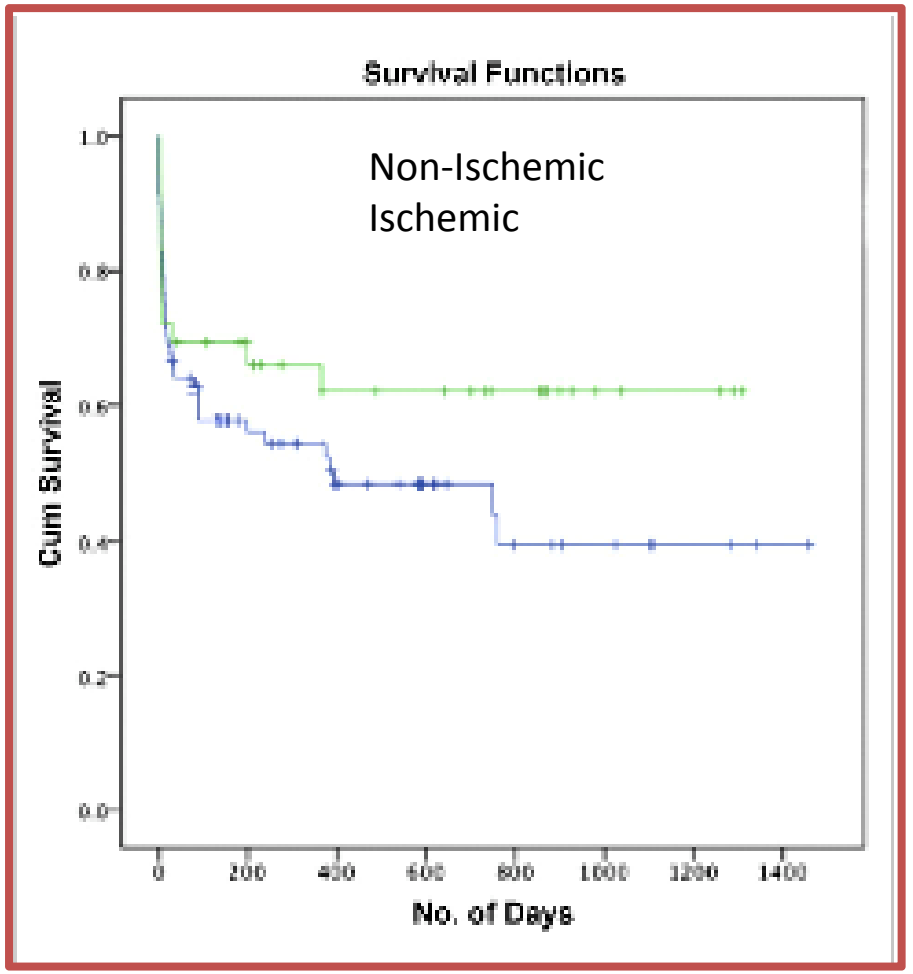
Percutaneous LVAD in Severe Refractory Cardiogenic Shock





Kar et al. *J Am CollCardiol*2010

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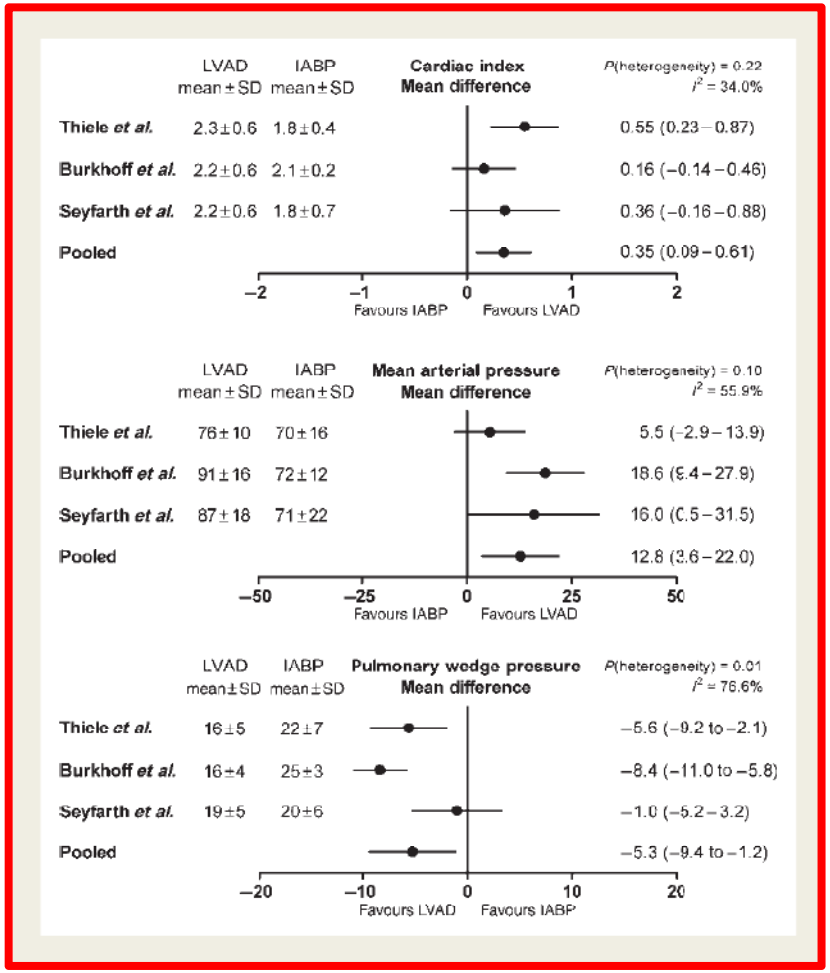
THI TandemHeart "Bridge to"

Kar BS et al; The J of Heart and Lung Transplantation 2009.28(2): S 256

	Recovery	LVAD	Surgery	Transplant
N	74	32	34	5
Support (DAYS)	5.6	6.4	3.0	6.4
Mortality RATE	57%	12%	43%	0%

META-ANALYSIS of IABP vs LVAD in CGS



Cardiac Index

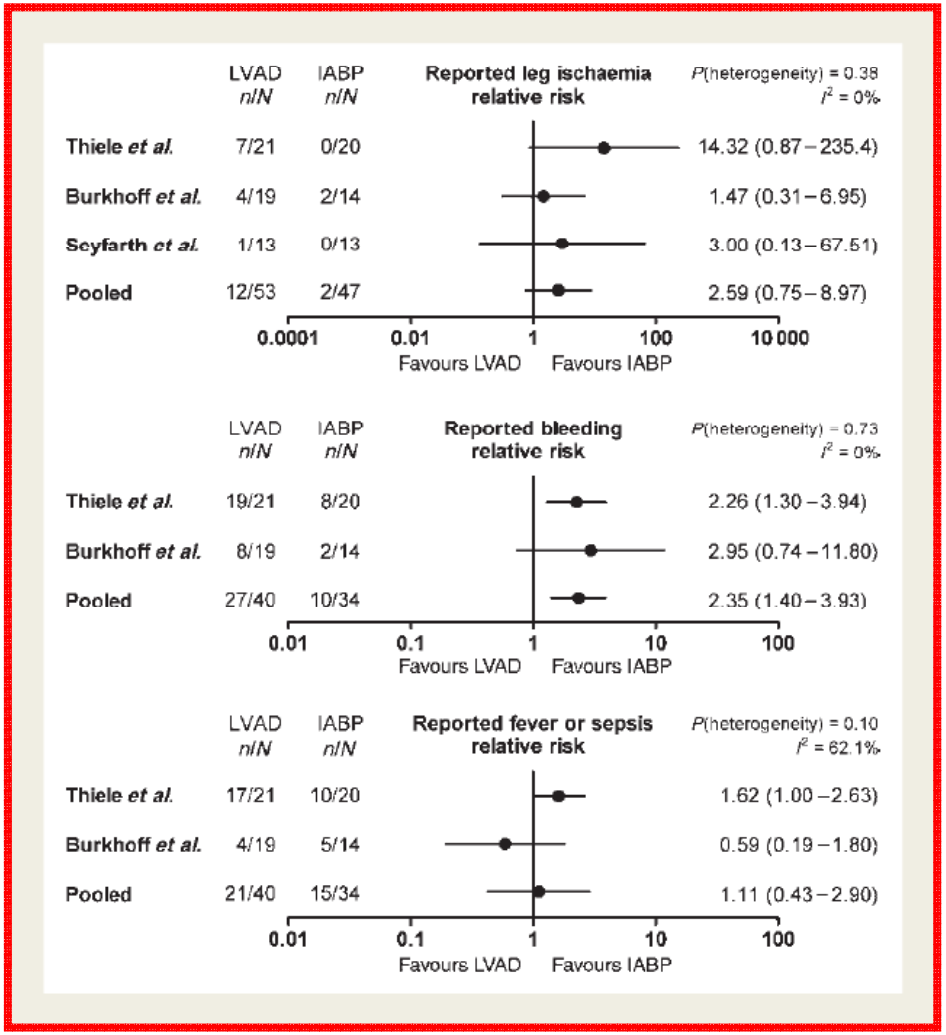
Mean Arterial Pressure

PCW Pressure

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

META-ANALYSIS of IABP vs LVAD in CGS

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



Leg Ischemia

Bleeding

Fever or Sepsis

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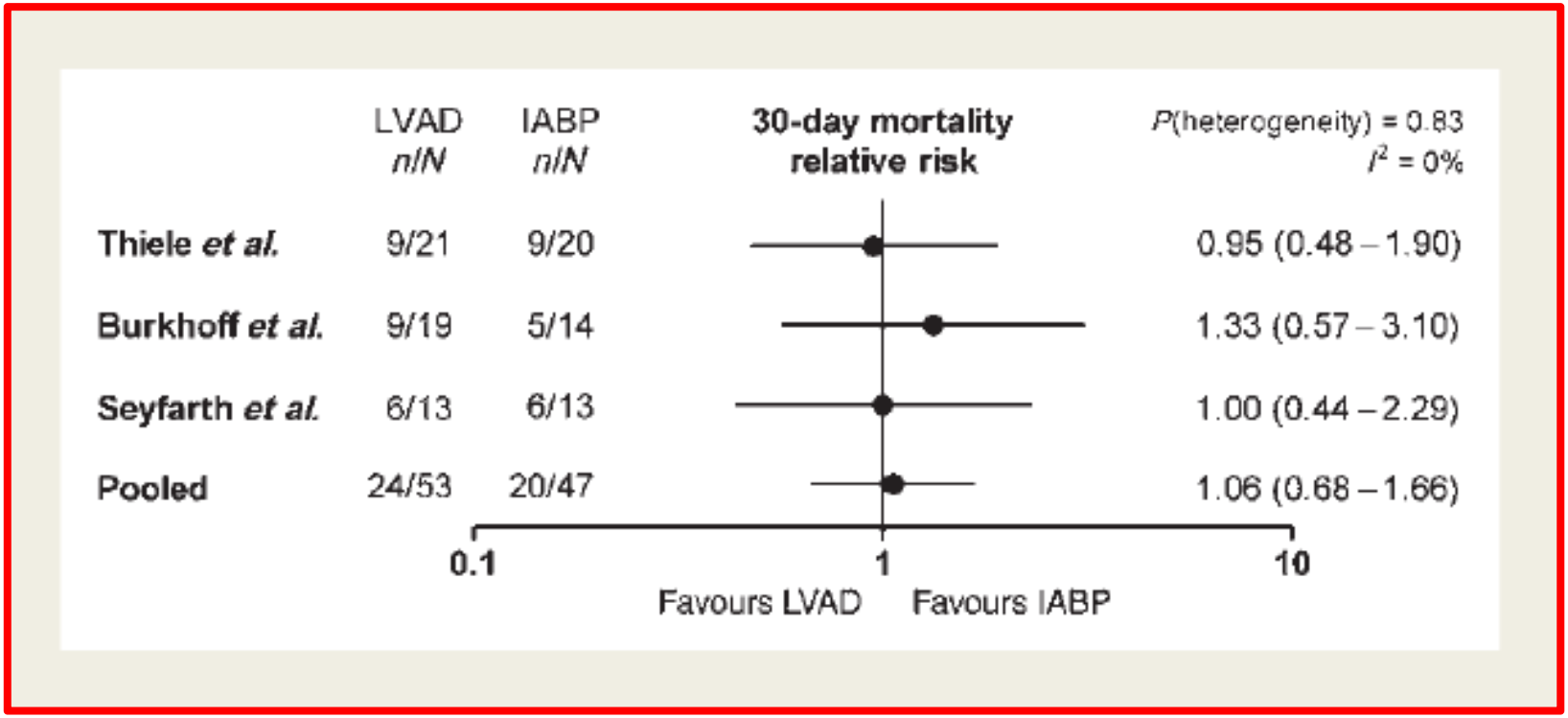
META-ANALYSIS of IABP vs LVAD in CGS

30 Day Mortality

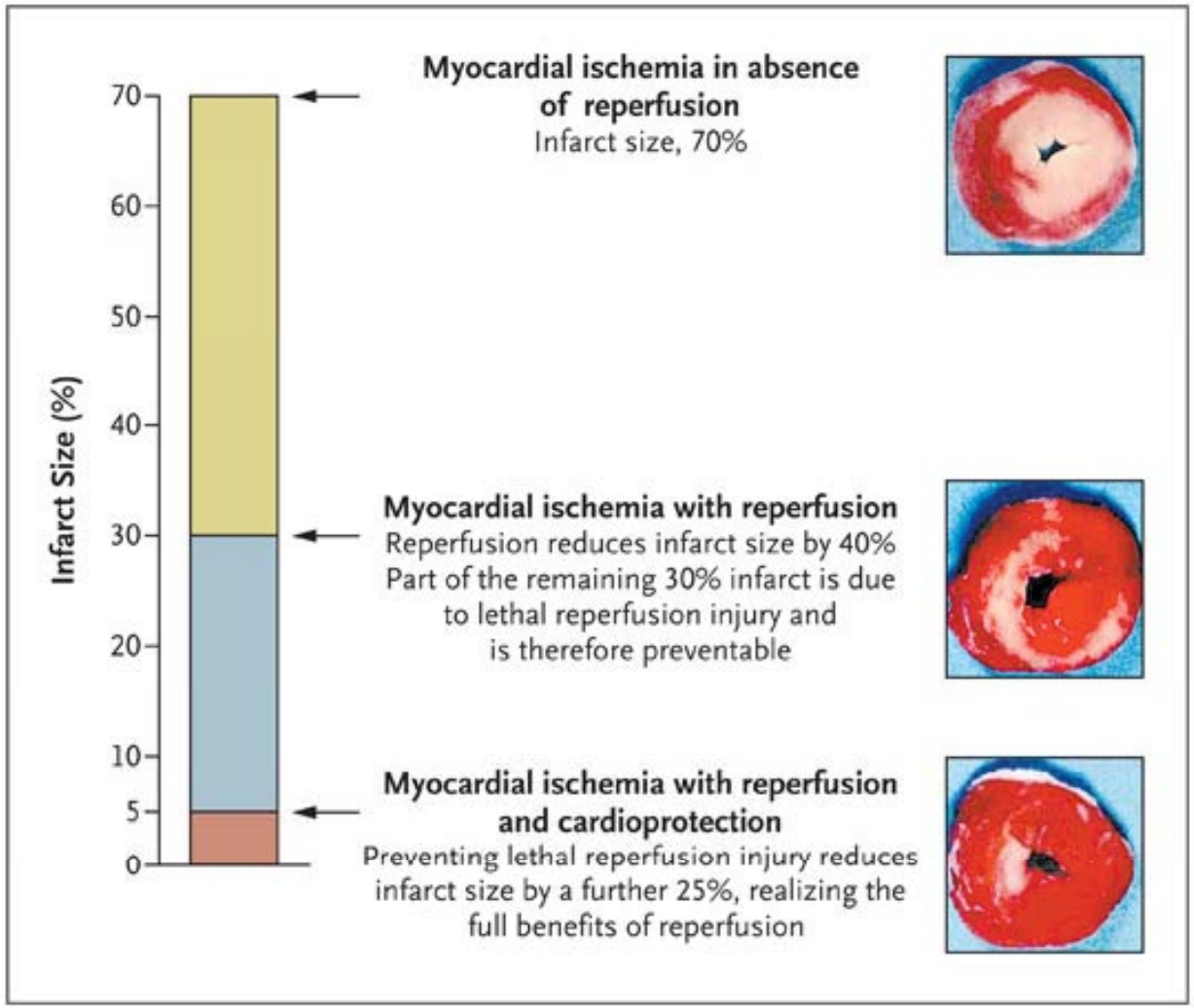


Cheng et al. *Eur Heart J* 2009;30:2102-2108

Mechanical Circulatory Assist in CGS

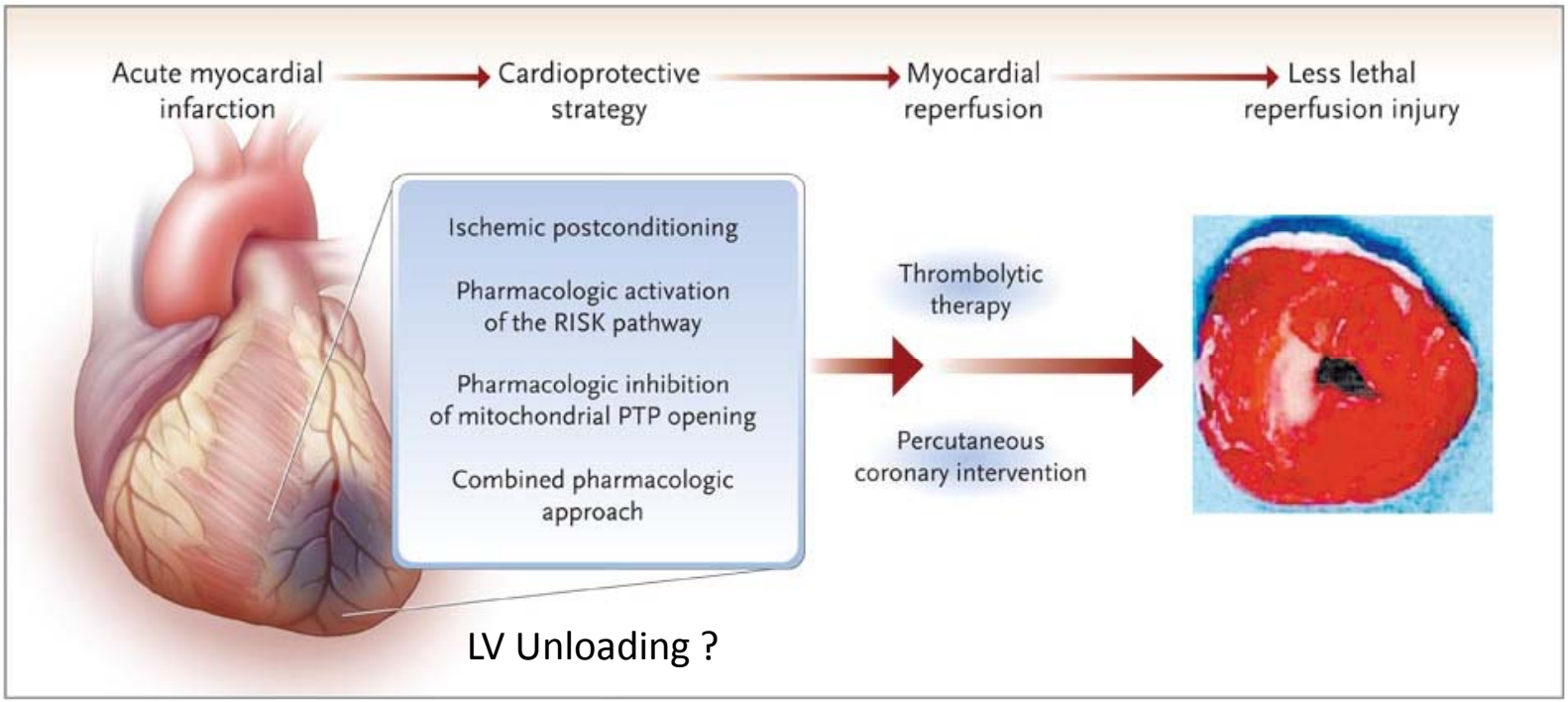
Device	Ease of Insertion	Duration of use	Flow L/min	MVF	Cost	Available
IABP	++++	Days to weeks	±	±	$	++++
Impella 2.5	+++	Hours to days	2.5	+	$$$$	+++
LA-FA Bypass	++	Days to weeks	5.0	++	$$$$	++

Contribution of Lethal Reperfusion Injury to Final MI Size



Yellon D andHausenloy D. N Engl J Med 2007;357:1121-1135

New Cardioprotective Strategies to Reduce Lethal Reperfusion Injury



Yellon D and Hausenloy D. N Engl J Med 2007;357:1121-1135

PLVAD and Reduction of Infarct Size

- Mini AMI - RCT Impella 2.5 vs Routine Medical Therapy to reduce infarct size
- TRIS TRIAL - RCT LA-FA Bypass (TandemHeart) vs Best Medical Therapy to reduce infarct size

THANK YOU