

**Summit** Angioplasty TCT Asia Pacific 2009

April 22-24, 2009

The Convention Center of Sheraton Grande Walkerhill Hotel, Seoul, Korea

# Acute Myocardial Infarction - Expanding the Therapeutic Paradigm

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# **DISCLOSURE**

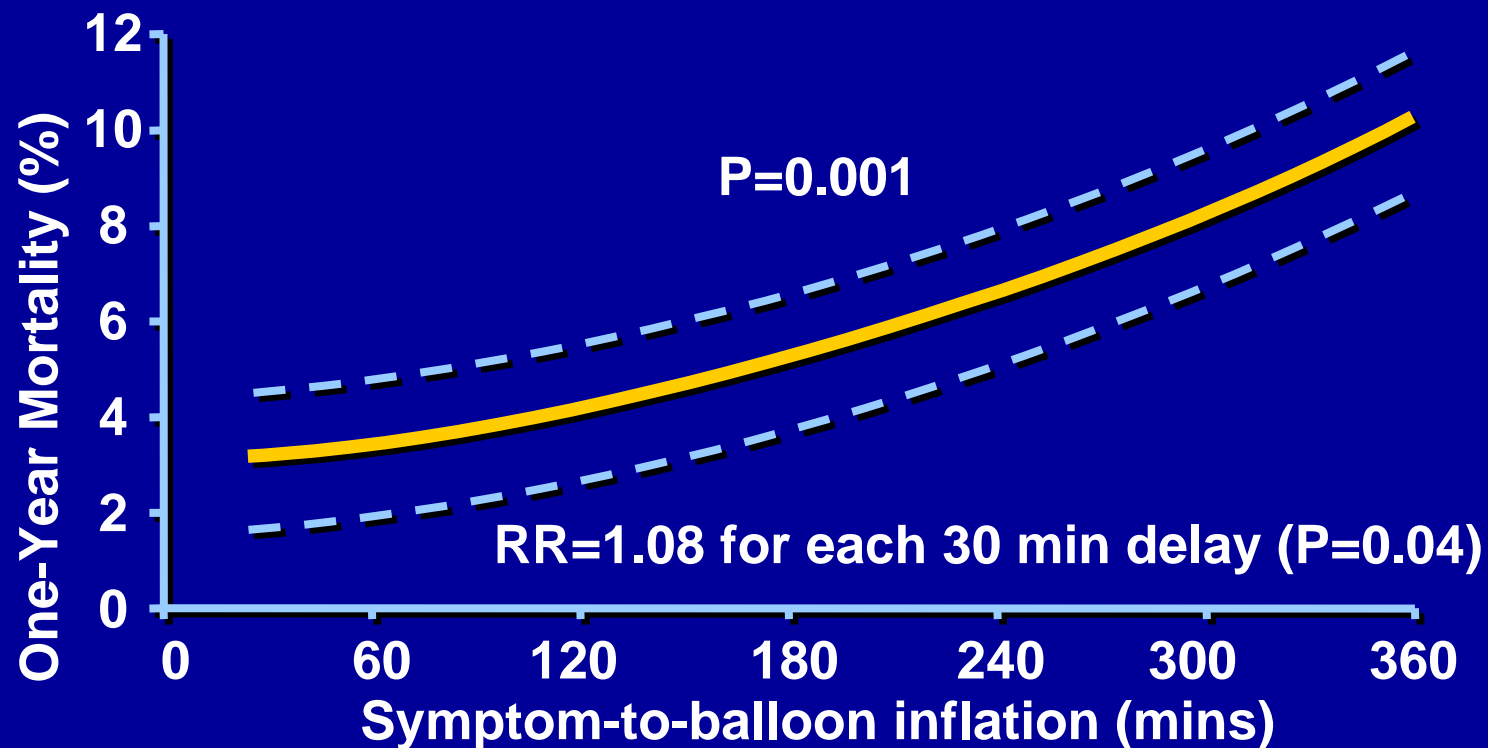
Consultant, CardiacAssist, Inc  
Stock options, CardiacAssist, Inc

**Lenox Hill Heart and Vascular Institute**



## Time is Outcome: Primary PCI

6 RCTs of Primary PCI by Zwolle Group 1994-2001



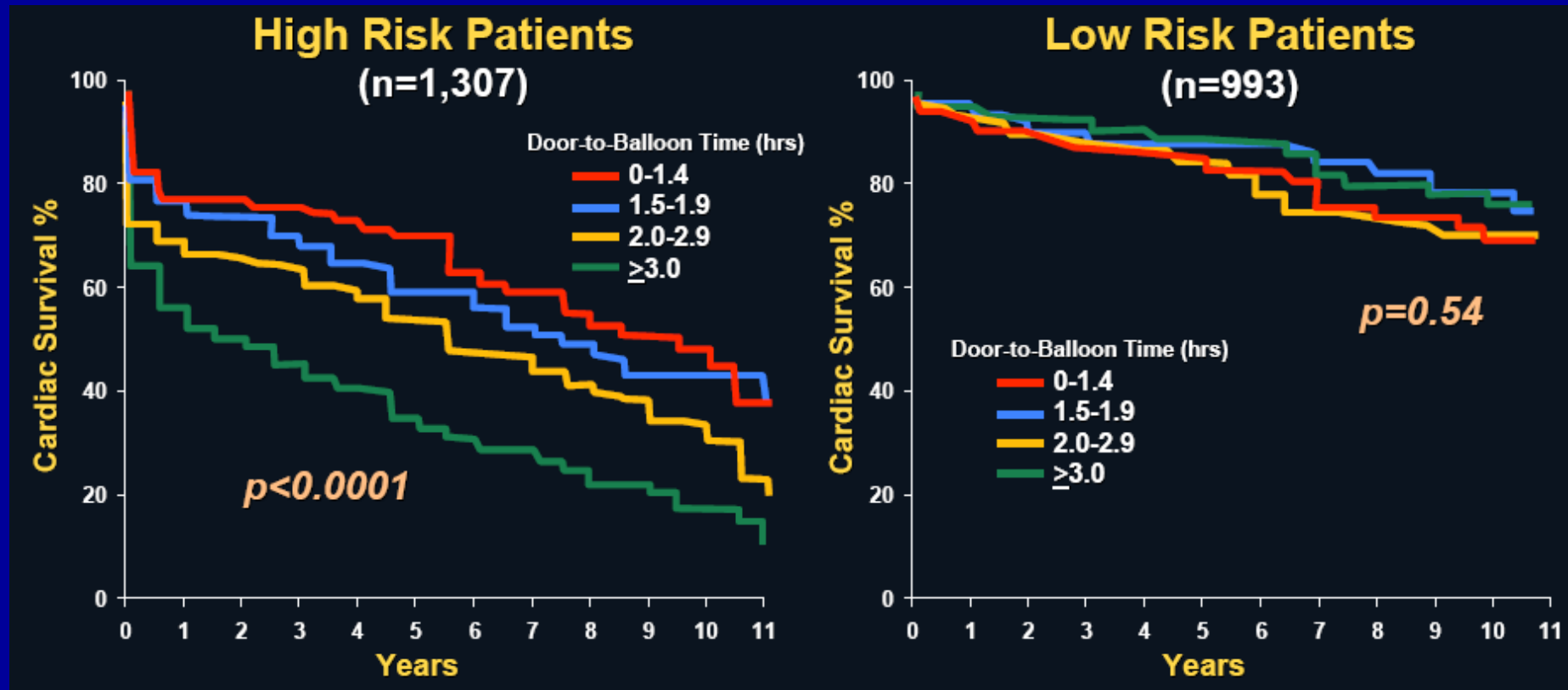
DeLuca G et al. *Circulation* 109:1223, 2004

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# D2B Time And Mortality

2300 Patients



High risk = Killip class 3 or 4, age >70, anterior MI



# **New Devices and Strategies to Manage AMI**

## **REPERFUSION IN AMI AND LV FUNCTION**

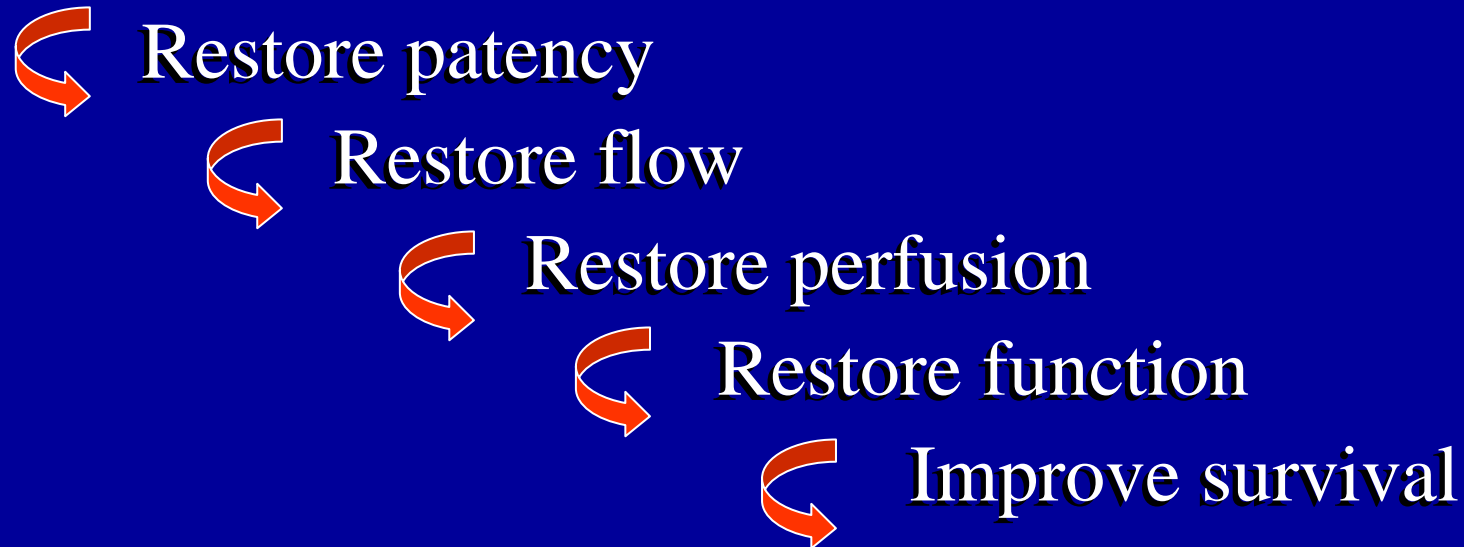
- Reperfusion Rx has resulted in dramatic improvement in survival post MI and has become the standard of care
- Despite improved survival, no significant improvement in LV systolic function has been consistently demonstrated
- This has led to the “open artery hypothesis” to explain improved survival with presumed favorable effects on remodeling, infarct expansion and arrhythmogenesis



# New Devices and Strategies to Manage AMI

## TREATMENT OF ACUTE MI

### Goal of Therapy



# New Devices and Strategies to Manage AMI

## MICROVASCULAR FLOW IN ACUTE MYOCARDIAL INFARCTION

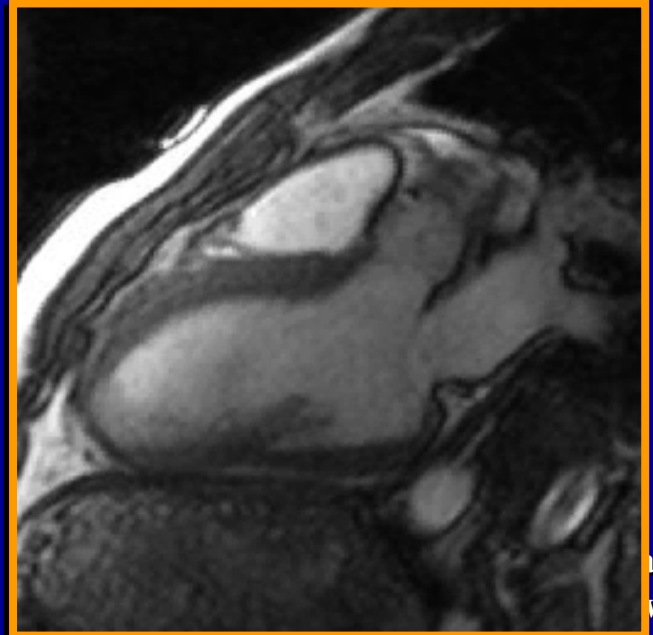
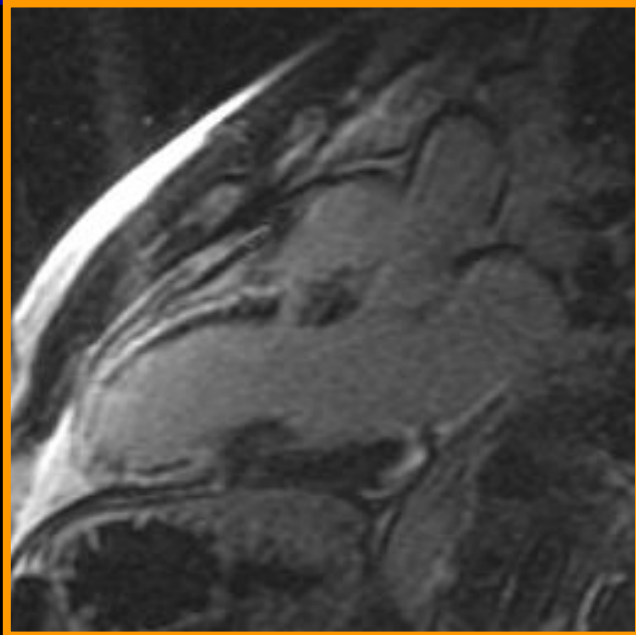
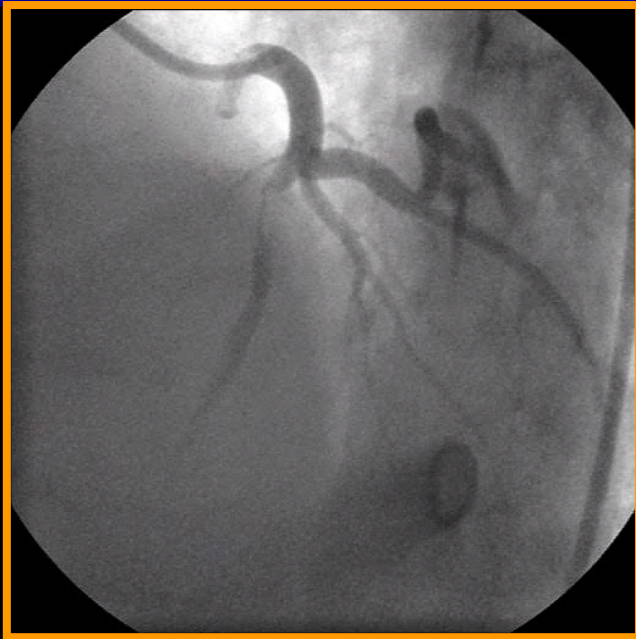
### Microvascular Flow as a Predictor of LV Functional Recovery in Acute Anterior MI

- 39 patients with acute anterior MI, *all with restoration of TIMI III flow*
- *Angiographic successful reflow  $\neq$  successful myocardial perfusion.* The MCE defect in the risk area predicts poor functional recovery

Ito et al. Circulation 85(5); 1992:1699-1705



# Acute MI – The Illusion of Reperfusion





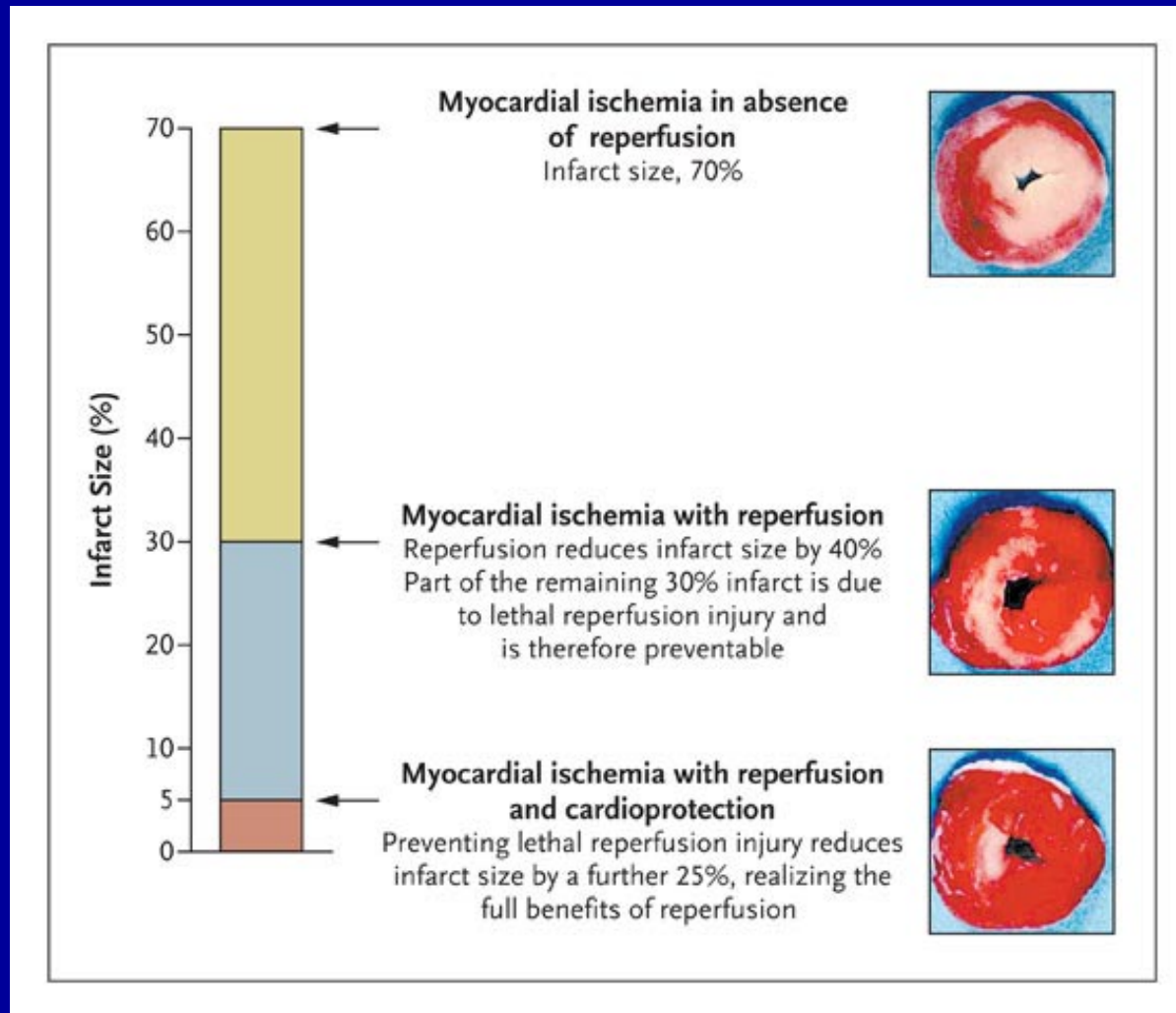
# **New Devices and Strategies to Manage AMI**

Is there a better way?

- Earliest possible intervention
- Improve microvascular flow
- Prevent lethal myocardial reperfusion injury
- Pharmacologic rx?
- LV support?
- Resultant improved LV function and decreased morbidity and mortality



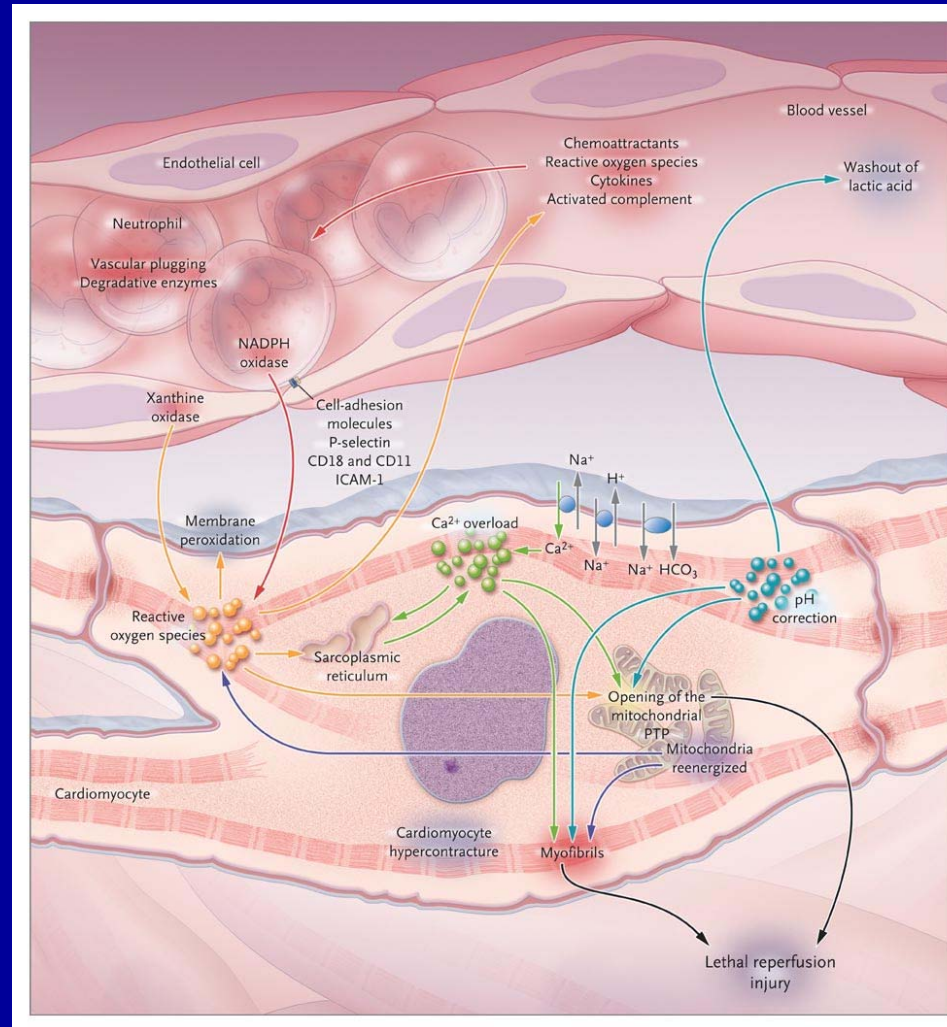
# Contribution of Lethal Reperfusion Injury to Final MI Size



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



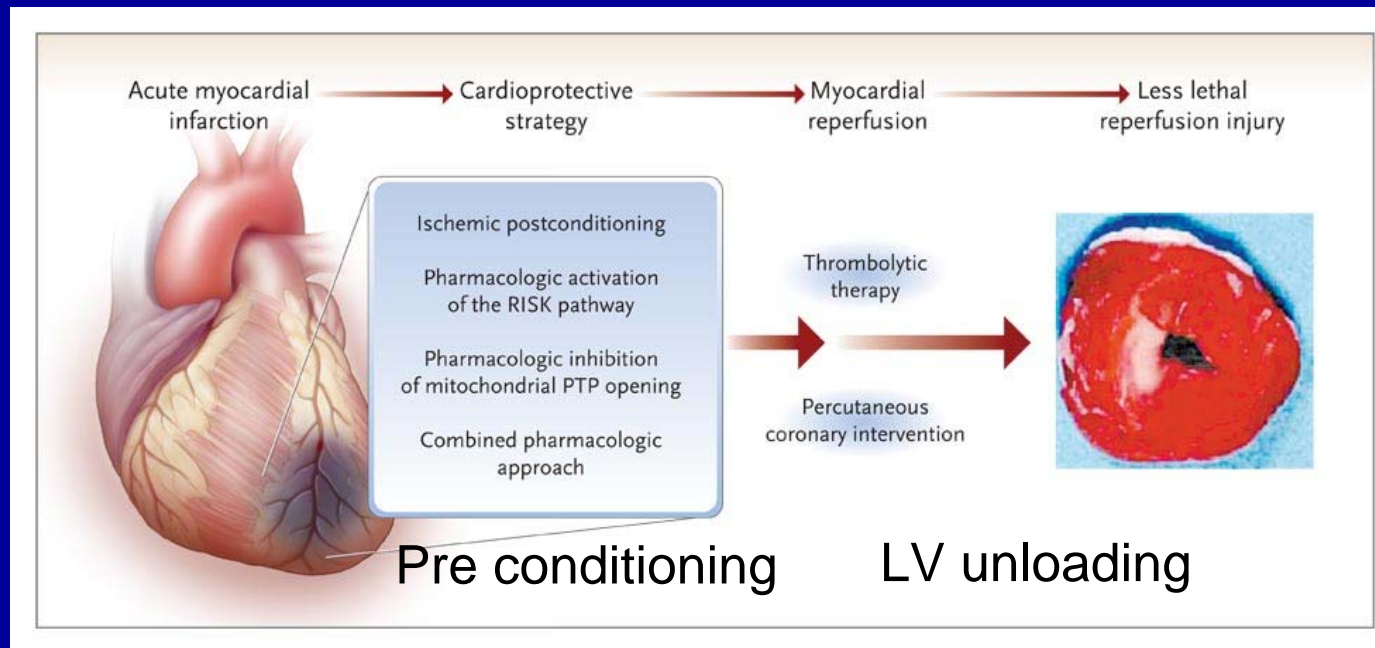
# Major Mediators of Lethal Reperfusion Injury



Yellon D and Hausenloy 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



# Effect of Cyclosporine on Reperfusion Injury in Acute Myocardial Infarction

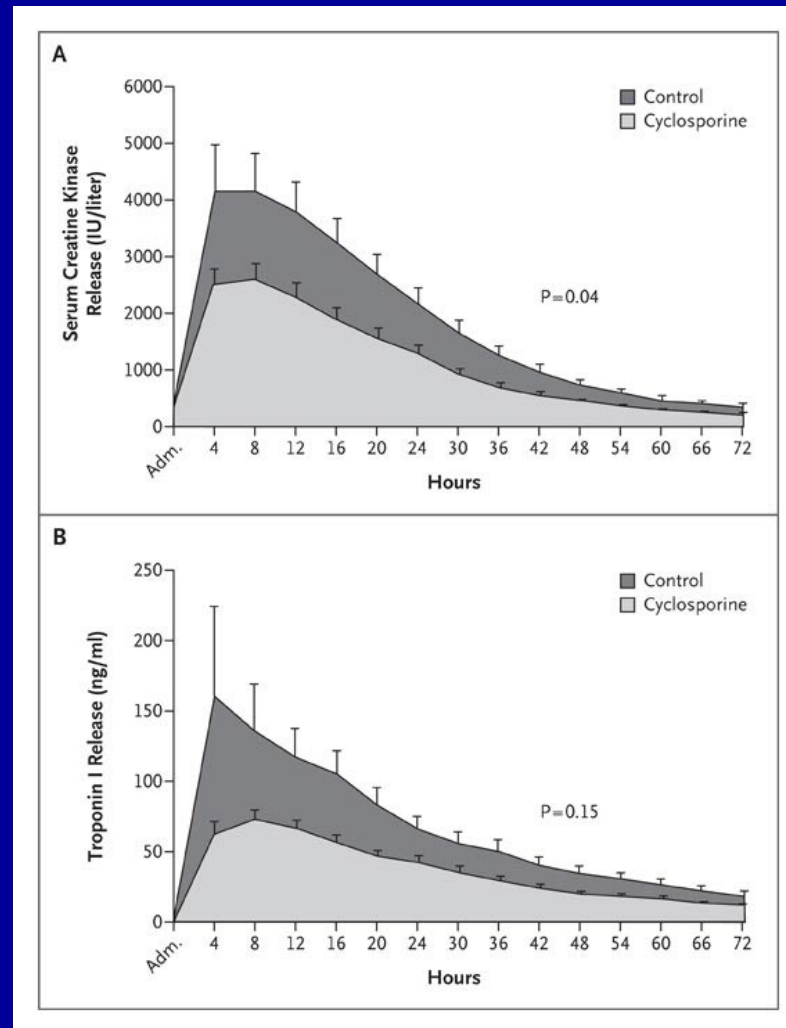
Christophe Piot, M.D., Ph.D., Pierre Croisille, M.D., Patrick Staat, M.D., H el ene Thibault, M.D., Gilles Rioufol, M.D., Ph.D., Nathan Mewton, M.D., Rachid Elbelghiti, M.D., Thien Tri Cung, M.D., Eric Bonnefoy, M.D., Ph.D., Denis Angoulvant, M.D., Christophe Macia, M.D., Franck Raczka, M.D., Catherine Sportouch, M.D., Gerald Gahide, M.D., G erard Finet, M.D., Ph.D., Xavier Andr e-Fou et, M.D., Didier Revel, M.D., Ph.D., Gilbert Kirkorian, M.D., Ph.D., Jean-Pierre Monassier, M.D., Genevi eve Derumeaux, M.D., Ph.D., and Michel Ovize, M.D., Ph.D.

N Engl J Med  
Volume 359(5):473-481  
July 31, 2008

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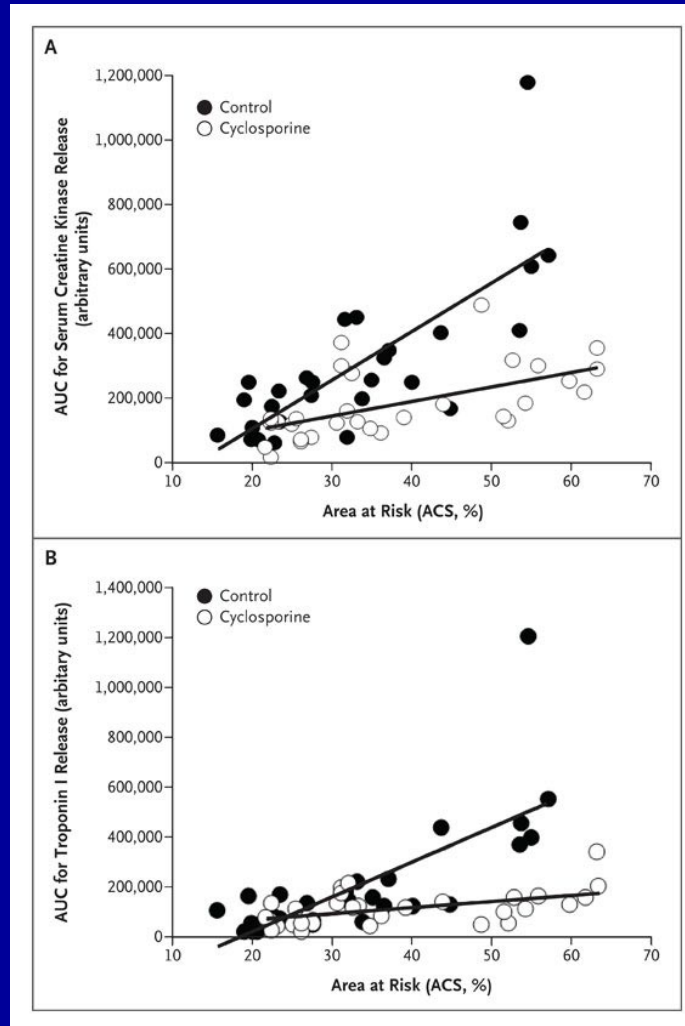
# Infarct Size by Biomarker Measurement



Piot C et al. N Engl J Med 2008;359:473-481



# Infarct Size as a Function of the Area at Risk



Piot C et al. N Engl J Med 2008;359:473-481





# New Devices and Strategies to Manage AMI

## LVAD THEORETICAL ADVANTAGES

- Superior LV *pressure and volume* unloading with enhanced remodeling capability
- Decreased wall tension with improved *endocardial blood flow*
- Beating, non-working heart has *low metabolic requirement*
- Presumed enhanced ability for *cellular repair and survival*





# New Devices and Strategies to Manage AMI

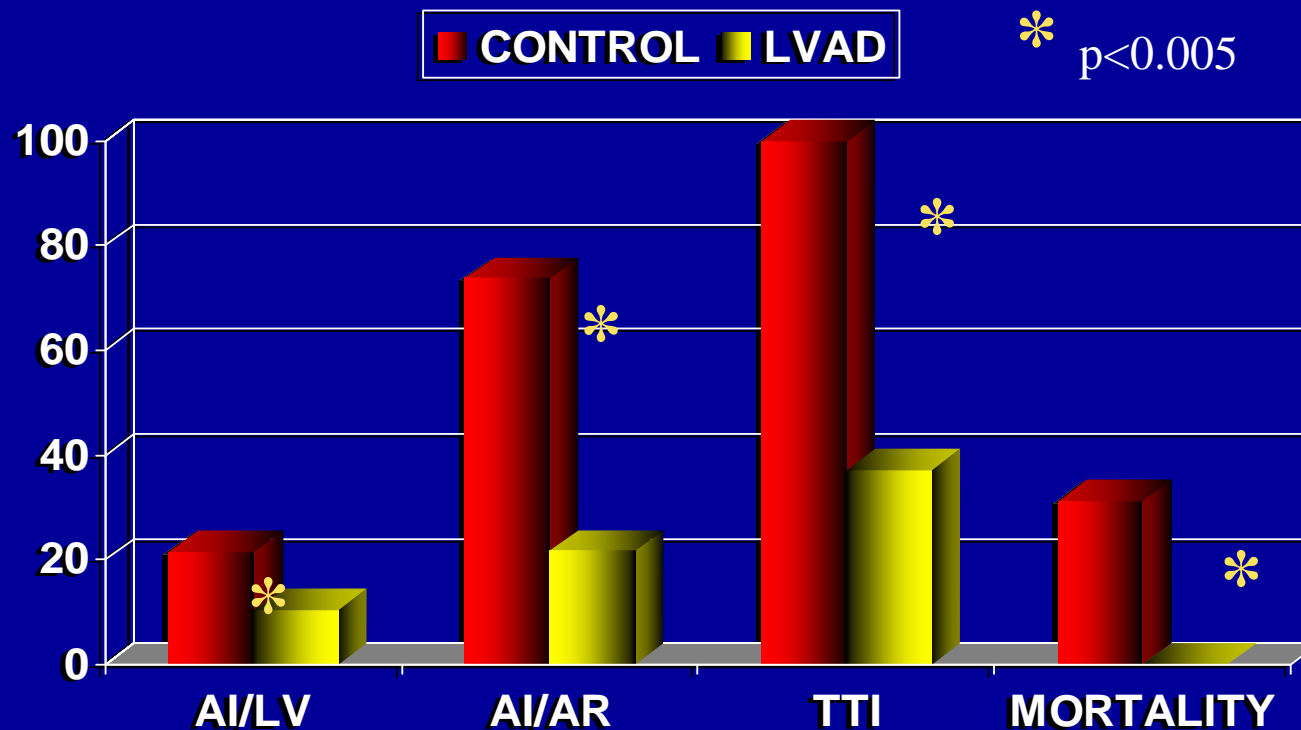
## LVAD THEORETICAL ADVANTAGES

- Release of cytokines by the heart have been documented in patients post PCI in AMI and implicated in the pathophysiology of CGS
- LVAD support may allow for resolution of these inflammatory and neurohormonal abnormalities with recovery of LV function and hemodynamics – patients who recover are frequently NYHA Class I



# PERCUTANEOUS LEFT VENTRICULAR ASSIST

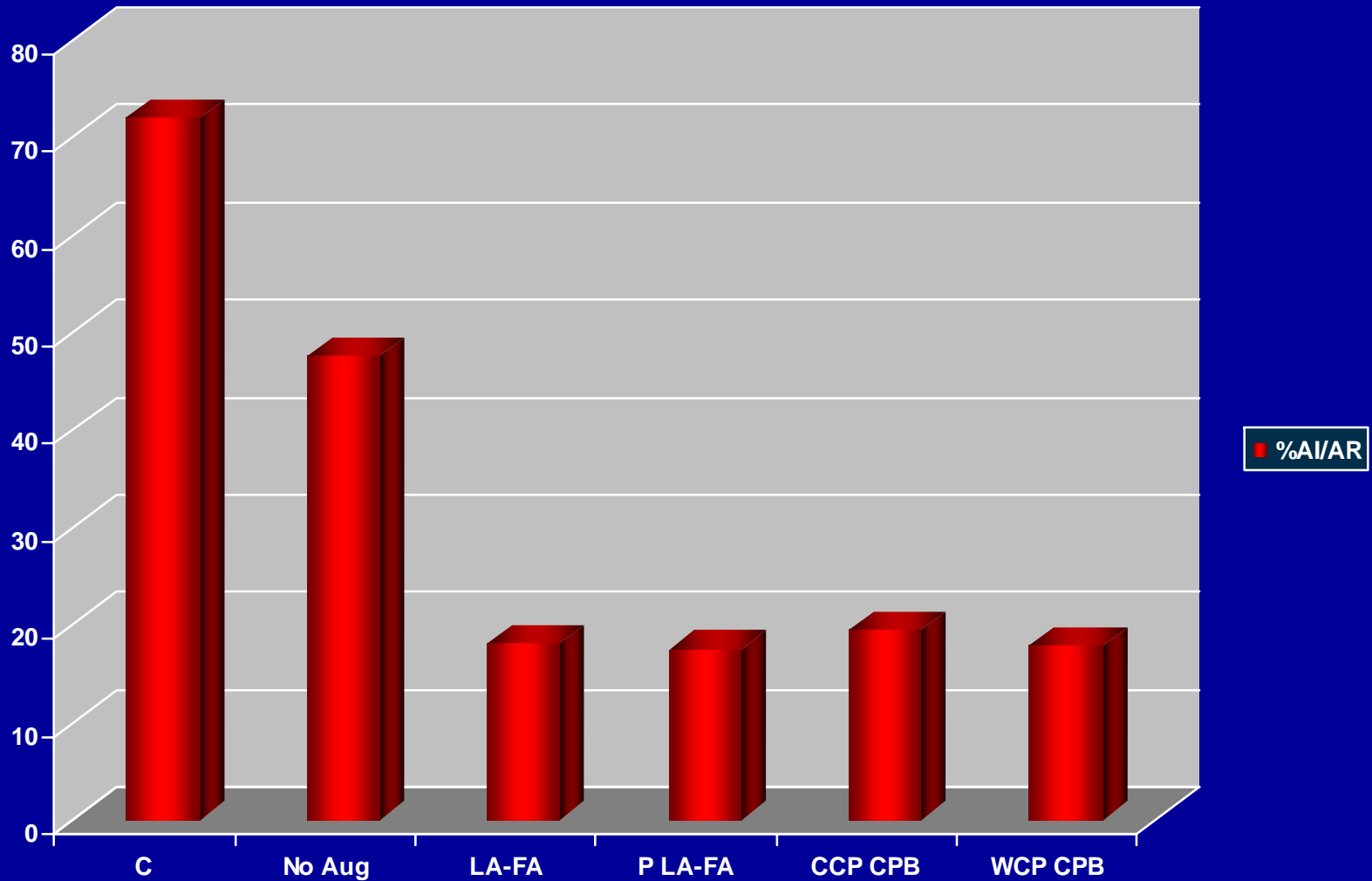
## LA-FA BYPASS EFFECTIVENESS IN REDUCTION OF EXPERIMENTAL AMI



Catinella et al. *J of Thoracic & Cardiovasc Surgery*. 86(6):887-96, 1983



# Methods for Limiting MI Expansion During Reperfusion

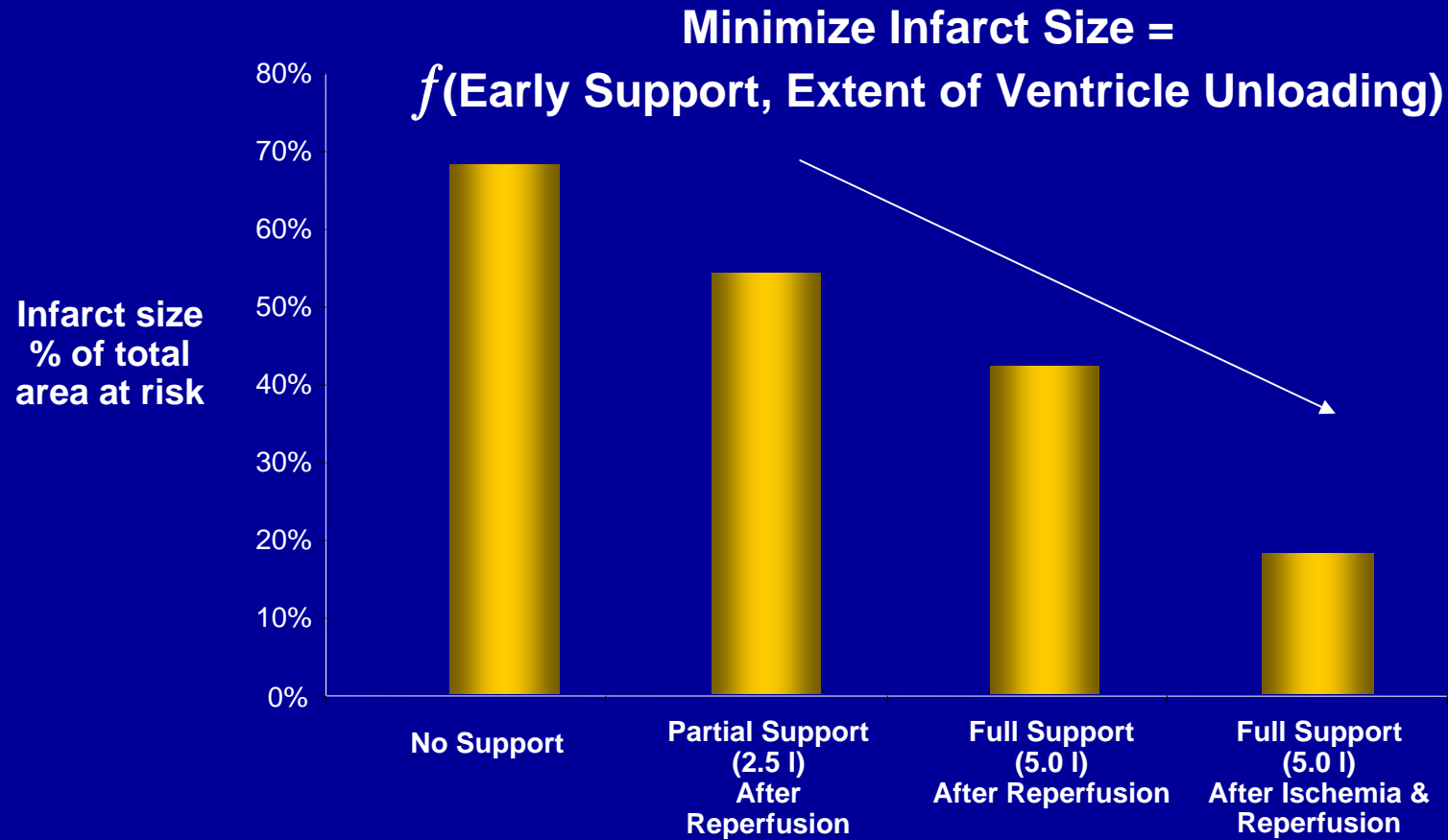


Axelrod et al *Circulation* 76(supplV);28-32,1987

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# Early LV Support Reduces Infarct Size with Impella®



Meyns, B. et al. J Am Coll Cardiol 2003;41:1087-1095

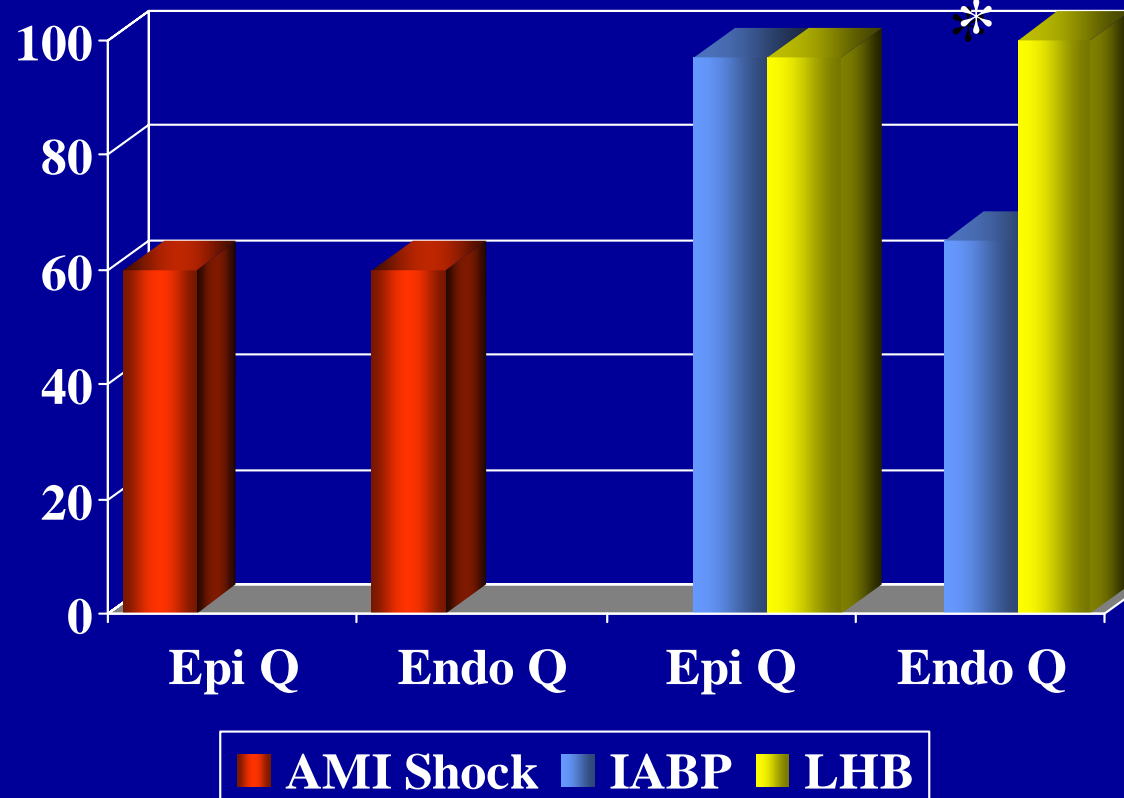


# New Devices and Strategies to Manage AMI

PIG MODEL CGS - LVAD vs IABP

EFFECT on MIRCOCIRCULATION

\* P < .05



Modified from Hata et al. Artificial Organs. 20(6); 1996:678-680

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# TANDEMHEART TO REDUCE INFARCT SIZE

## TRIS TRIAL

- Expanding the Paradigm
  - Single center safety/feasibility trial
  - Five patients with anterior MI
  - LV unloading (TandemHeart) prior to reperfusion
  - Infarct size at 30 days measured by MRI
  - PI – Kirk Garratt
  - DSMB – Chair, David Holmes



# THERAPY FOR AMI FUTURE DIRECTIONS

## Conclusions: In AMI

- The “up-stream” problems have been solved to a great extent and now the focus is “down-stream”
- Earlier intervention – clearly beneficial, decrease D to B
- Preemptive therapy for protection and restoration of microvascular flow – Prevent Reperfusion Injury!
  1. Pharmacology – *vasodilators, adenosine, protein kinase inhibition, cyclosporine, RISK pathway activation*
  2. Myocardial protection- mechanical and metabolic – *distal protection, thrombus removal, cooling and enhanced oxygen delivery, pre and post conditioning*
  3. Left ventricular assistance/unloading – *pVAD*
- Multi-faceted approach required



THANK YOU

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