מרכז רפואי רבין
Rabin Medical Center

Update on the Role of IABP in Acute Heart Failure

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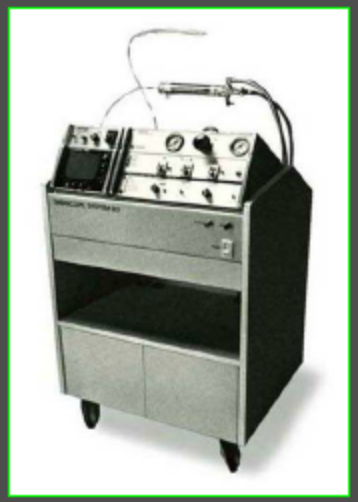
Background

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

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INTRA-AORTIC BALLOON COUNTERPULSATION IN CARDIOGENIC SHOCK

Report of a Co-operative Clinical Trial

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Abstract Eighty-seven patients with cardiogenic shock were treated with the intra-aortic counterpulsating balloon in 10 institutions according to a common protocol. Clinical and physiologic responses were favorable in most patients. Heart rate fell from 110 ± 24 (mean ± S.D.) to 103 ± 21 beats per minute, systolic arterial pressure ("afterload") fell from 76 ± 22 to 57 ± 17 mm Hg, diastolic arterial pressure increased from 53 ± 12 to 83 ± 19 mm Hg, and mean arterial pressure did not change. Cardiac output increased 500 ml per minute, and a decrease in lactate production or increase in lactate extraction by the myocardium occurred in 18 of 19 patients with metabolic studies. Fifty-two patients died during balloon assistance, and 35 survived; 15 of the survivors left the hospital, and eight have lived for more than one year. Attempts to predict survival in advance, or from response to balloon counterpulsation, were generally unsuccessful, and precise indications for initiation and termination of balloon counterpulsation remain in doubt. (N Engl J Med 288:979-984, 1973)

REMOVING volume from the aortic root during systole and returning it during diastole, counterpulsation, decreases left ventricular work but maintains mean perfusion pressure. Arterial pressure is reduced during systole and augmented during diastole.[1-3] Early experimental[4-6] and clinical trials[7-32] suggested that the intra-aortic counterpulsating balloon could effectively render circulatory assistance to the failing heart. To obtain a wider experience, the Co-operative Study was organized in 1969 to carry out large-scale clinical testing of the counterpulsating balloon. It was decided that the intra-aortic balloon would be tested in treatment of patients with cardiogenic shock, a clinical syndrome associated with mortality in excess of 85 per cent.[33,34]

From the Department of Medicine, Albany Medical College, Cornell University Medical College–New York Hospital, Harvard Medical School–Peter Bent Brigham Hospital, Washington University School of Medicine–Barnes Hospital; Department of Surgery, Baylor College of Medicine, Duke University Medical Center; departments of Medicine and Surgery, Cedars-Sinai Medical Center (Los Angeles), Sinai Hospital of Detroit–Wayne State University School of Medicine, St. Vincent's Hospital and Medical Center (New York) and State University of New York–Downstate Medical Center (Brooklyn) (address reprint requests to Dr. Scheidt, at Division of Cardiology, F-436, New York Hospital–Cornell Medical Center, 525 E. 68th Street, New York, N.Y. 10021).

Other participating investigators in the Co-operative Study include (A. Kantrowitz, Chairman) S. Bondurant, J. T. Doyle and D. Brown (Albany), E. Leffrak, E. Diethrich and M. E. DeBakey (Baylor), E. Corday, T. Lang, A. Goldman and S. Meerbaum (Cedars–Sinai), M. Wolk and J. Bloch (Cornell – supported in part by a contract [PH-43-67-1439]), R. Nachi, B. Wechsler, R. Rubin and P. Sawyer (Downstate), D. Subiston and R. Cline (Duke), A. Aris, S. Phillips, M. Ciborski, M. Lipsius, D. Jaron, W. Waiszczuk and P. Freed (Sinai–Detroit), E. Sonnenblick and R. Gorlin (Peter Bent Brigham), S. Ayres, E. F. Conklin and S. Gianelli (St. Vincent's) and J. Collins (Washington University).

Supported by the John A. Hartford Foundation and a planning grant from the David and Minnie Berk Foundation.

MATERIALS AND METHODS

Each of the 10 institutions participating in the Co-operative Study agreed to treat cardiogenic shock resulting from acute myocardial infarction according to a common protocol. All patients had definite acute myocardial infarction as documented either by the appearance of new electrocardiographic Q waves (73 patients) or by a typical history followed by characteristic changes in serum activity of glutamic oxalacetic transaminase or creatine phosphokinase (14 patients).

The diagnosis of cardiogenic shock was made only when all the following criteria were satisfied. The first was that the arterial systolic pressure was less than 80 mm Hg, as determined by direct intra-arterial measurement. Secondly, urine flow from an indwelling bladder catheter of less than 20 ml per hour or impairment of mental status not attributable to drugs or previous cardiopulmonary arrest was present. Thirdly, hypovolemia was excluded as a cause of shock – unless left ventricular filling pressure was more than 12 mm Hg as determined by direct measurement, pulmonary capillary "wedge" pressure or pulmonary-artery diastolic pressure or clinical signs of pulmonary congestion were apparent, a trial expansion of intravascular volume was attempted (69 patients met these criteria, and in 18 others only a measurement of central venous pressure was available). In spite of the serious limitations of extrapolating from central venous to left ventricular filling pressure,[35] central venous pressure over 7 mm Hg (over 10 cm of water) was assumed for the purposes of the present report to exclude the presence of hypovolemia. The final requirement was correction of possible contributory or potentiating factors, such as arrhythmia of possible hemodynamic consequence, severe pain, hypoxemia, hypoventilation or acidemia.

All patients received a trial of "standard" medical therapy in an attempt to restore normal blood pressure. *L*-norepinephrine was administered by intravenous infusion to 73 patients. Occasionally,

52 of 87 pts died (60%)
At that time expected death 85%

Benchmark Registry (2001)

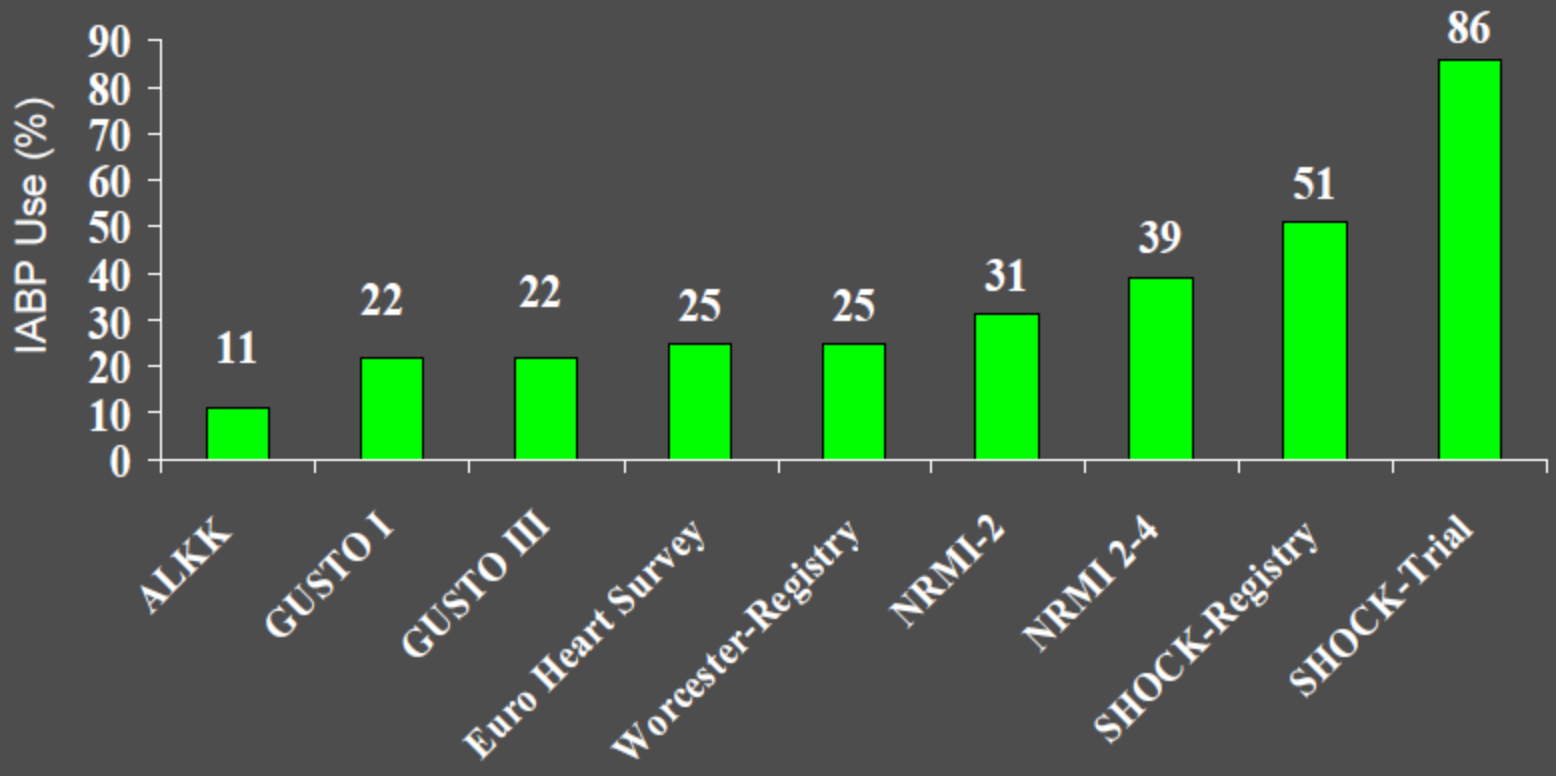
- **1996-2000, 203 hospitals worldwide (90% U.S), 16,909 patient case records (68.8% men, 31.2% women; mean age 65.9 +/- 11.7 years).**
- **The most frequent indications for use of IABP were**
  - **hemodynamic support during/after cardiac cath (20.6%)**
  - **cardiogenic shock (18.8%)**
  - **weaning from cardiopulmonary bypass (16.1%)**
  - **preoperative use in high risk patients (13.0%)**
  - **refractory unstable angina (12.3%)**
- **Major IABP complications (major limb ischemia, severe bleeding, balloon leak, death directly due to IABP insertion or failure) occurred in 2.6% of cases**
- **In-hospital mortality was 21.2% (11.6% with the balloon in place).**
- **Female gender, high age and peripheral vascular disease were independent predictors of a serious complication.**

Hemodynamic Basis For Use in Cardiogenic Shock

- Reduce afterload
- Increase diastolic coronary perfusion pressure
- Modestly increase coronary blood flow
- Have minimal effects on cardiac output
- Have an excellent safety profile
- Are easy to use
- Help stabilize patients with cardiogenic shock and provide hemodynamic support for patients undergoing PCI

Background

IABP-Use in Cardiogenic Shock



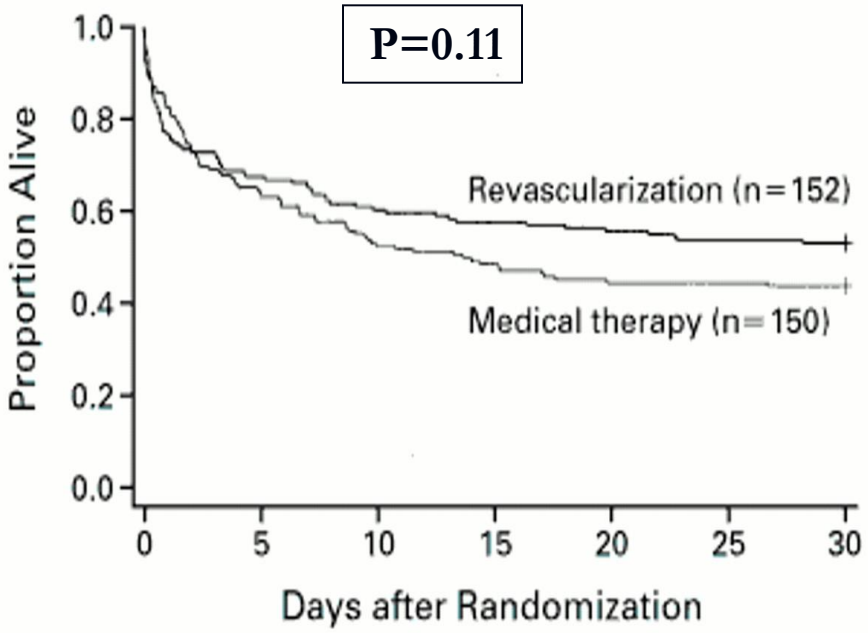
Thiele et al. Eur Heart J 2010,31:1828-1835

Management of CS: Mechanical revascularization

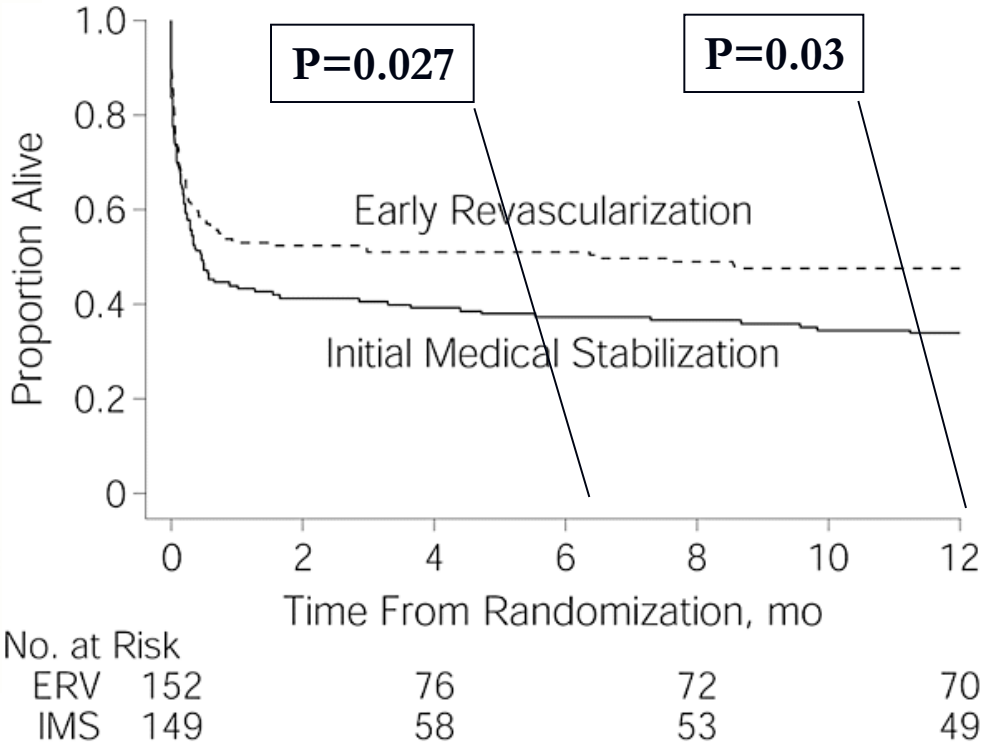
- SHOCK trial
  - Randomized pts. to emergency revascularization (within 6 hrs of randomization, IABP recommended) versus initial medical stabilization (IABP and Tx recommended).
  - SHOCK Registry (April 1993-August 1997)
  - Of 1492 pts screened, 152 pts assigned to revascularization vs. 150 to medical treatment (1190 nonrandomized pts).
  - Included:
    - CS with STEMI or new LBBB within 36 hours from infarction and randomization up to 12 hours from the CS diagnosis, IABP use was encouraged.
  - Excluded:
    - Severe systemic illness
    - Mechanical causes of shock
    - Severe valvular disease
    - Inability of revascularization

Hochman et al., NEJM, 1999

Benefit of early revascularization

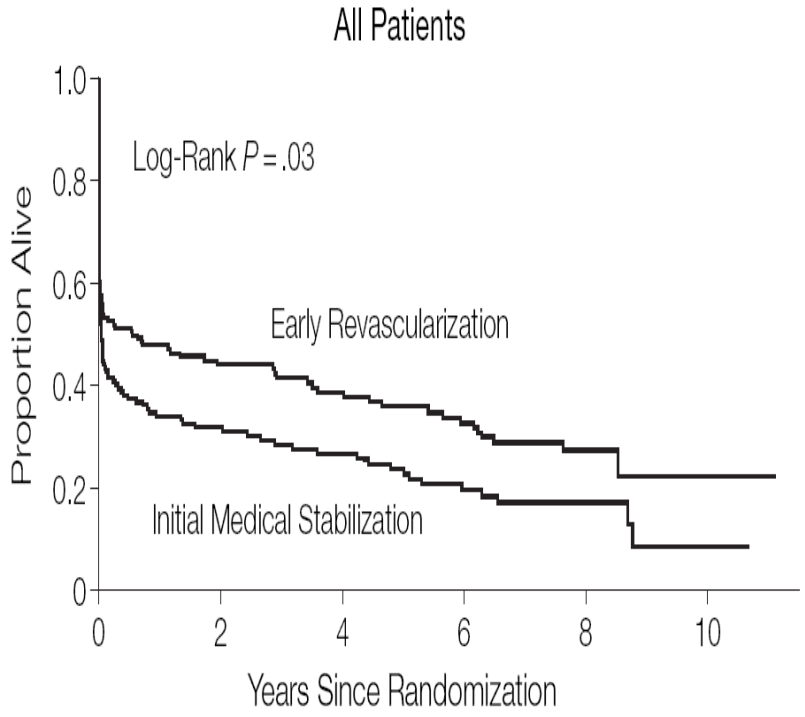


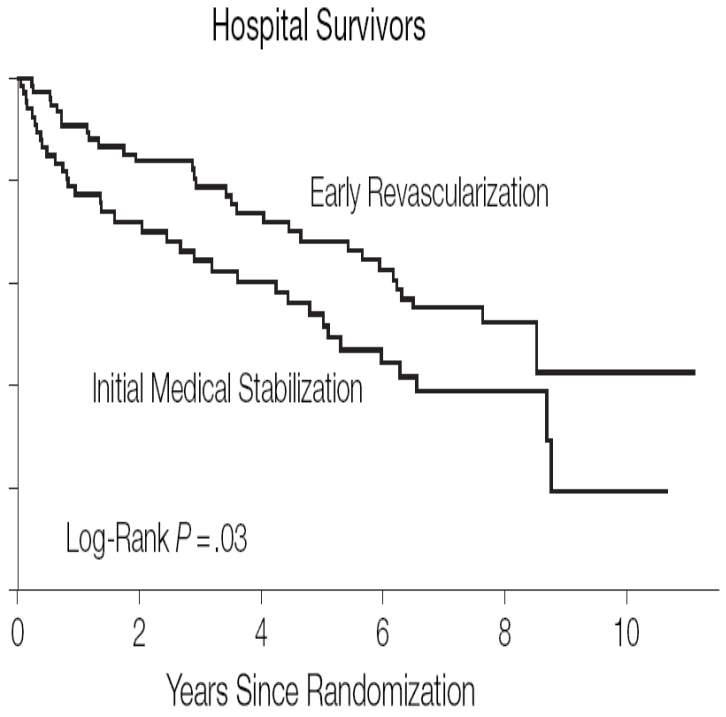
Hochman et al. NEJM, 1999



Hochman et al. JAMA, 2001

Long-term survival of CS after early revascularization





NNT= 8

No. at Risk						
ERV	152	56	42	33	18	3
IMS	150	38	29	18	9	2

77	56	42	33	18	3
66	38	29	18	9	2

Hochman et al., JAMA, 2006

The previously reported differential treatment effect at 1y for patients>75 years no longer statistically significant.

Guideline Recommendations for IABP in AMI Complicated by Cardiogenic Shock

Class Ic

EUROPEAN SOCIETY OF CARDIOLOGY®

IC → IIB

EUROPEAN SOCIETY OF CARDIOLOGY

Class Ib

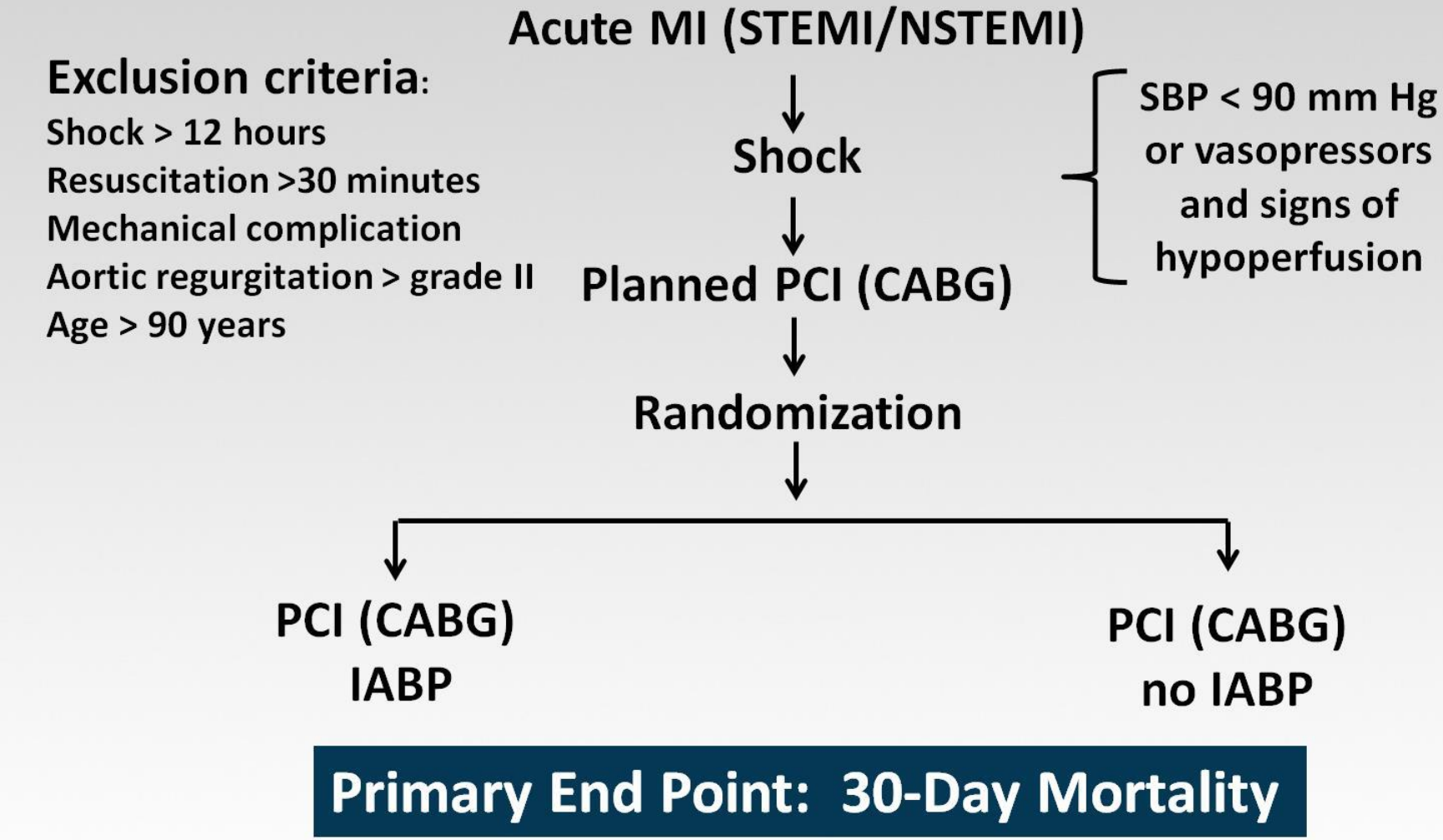
ACC/AHA

IB → IIA

American Heart Association

O'Gara PT, et al. *Circulation* 2013;127:e362-e425[1]; b. Antman E, et al. *Circulation*. 2004;110:588-636[4]; c. Steg PG, et al. *Eur Heart J.* 2012;33:2569-2619[2]; d. Wijns W, et al. *Eur Heart J.* 2010;31:2501-2555.[3]

IABP-Shock-II Trial

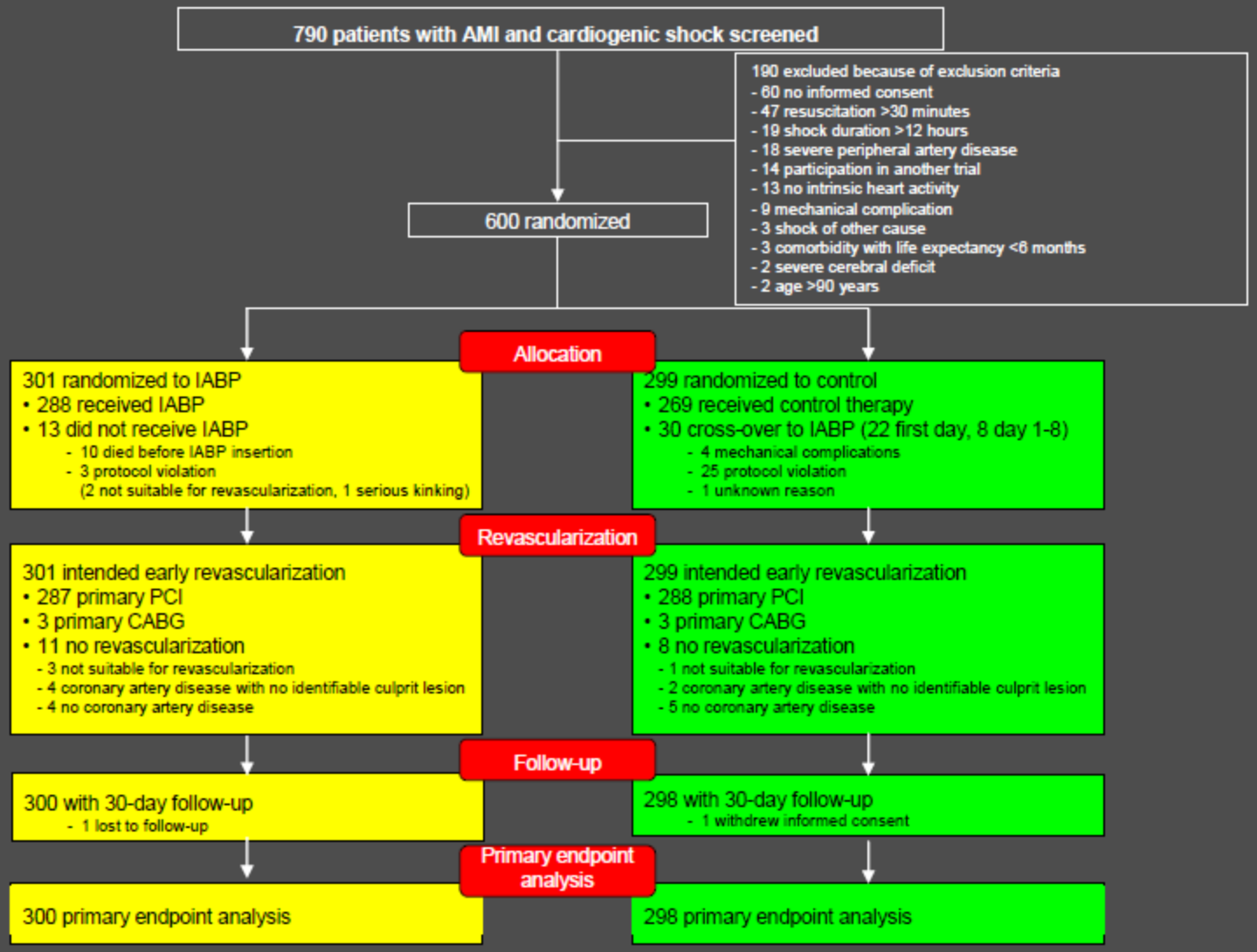


Thiele H, et al. *N Engl J Med.* 2012;367:1287.[5]

Results

Trial Flow and Treatment

IABP SHOCK II RANDOMIZED CLINICAL TRIAL



Results

Patient Characteristics

IABP SHOCK II RANDOMIZED CLINICAL TRIAL

	IABP (n=301)	Control (n=299)
Age (years); median (IQR)	70 (58-78)	69 (58-76)
Male sex; n (%)	202 (67.1)	211 (70.6)
Current Smoking; n/total (%)	96/295 (32.5)	108/299 (36.1)
Hypertension; n/total (%)	213/296 (72.0)	199/299 (66.6)
Hypercholesterolemia; n/total (%)	122/295 (41.4)	105/299 (35.1)
Diabetes mellitus; n/total (%)	105/297 (35.4)	90/299 (30.1)
Prior myocardial infarction; n/total n (%)	71/300 (23.7)	61/299 (20.4)
Fibrinolysis < 24 h before randomization; n/total (%)	28/301 (9.3)	20/299 (6.7)
STEMI/LBBB; n/total (%)	200/300 (66.7)	212/298 (71.1)
NSTEMI; n/total (%)	96/300 (32.0)	81/298 (27.2)
Resuscitation before randomization; n/total (%)	127/301 (42.2%)	143/299 (47.8)
Signs of impaired organ perfusion; n/total (%)		
Altered mental status	215/300 (71.7)	232/299 (77.6)
Cold, clammy skin and extremities	257/300 (85.7)	245/299 (81.9)
Oliguria	90/300 (30.0)	99/299 (33.1)
Serum lactate >2.0 mmol/l	226/300 (75.3)	218/298 (73.2)
Creatinine clearance (ml/min); median (IQR)	60.7 (43.4-86.6)	56.8 (39.7-78.1)
Infarct related artery; n/total (%)		
LAD	132/293 (45.1)	121/293 (41.3)
LCX	55/293 (18.8)	57/293 (19.5)
RCA	73/293 (24.9)	79/293 (27.0)
Left main	26/293 (8.9)	28/293 (9.6)
Bypass graft	7/293 (2.4)	8/293 (2.7)
Multivessel disease; n/total (%)	235/296 (79.4)	228/293 (77.9)
Left ventricular ejection fraction (%); median (IQR)	35 (25-45)	35 (25-45)

Results

Treatment + Process of Care Outcomes

IABP SHOCK II

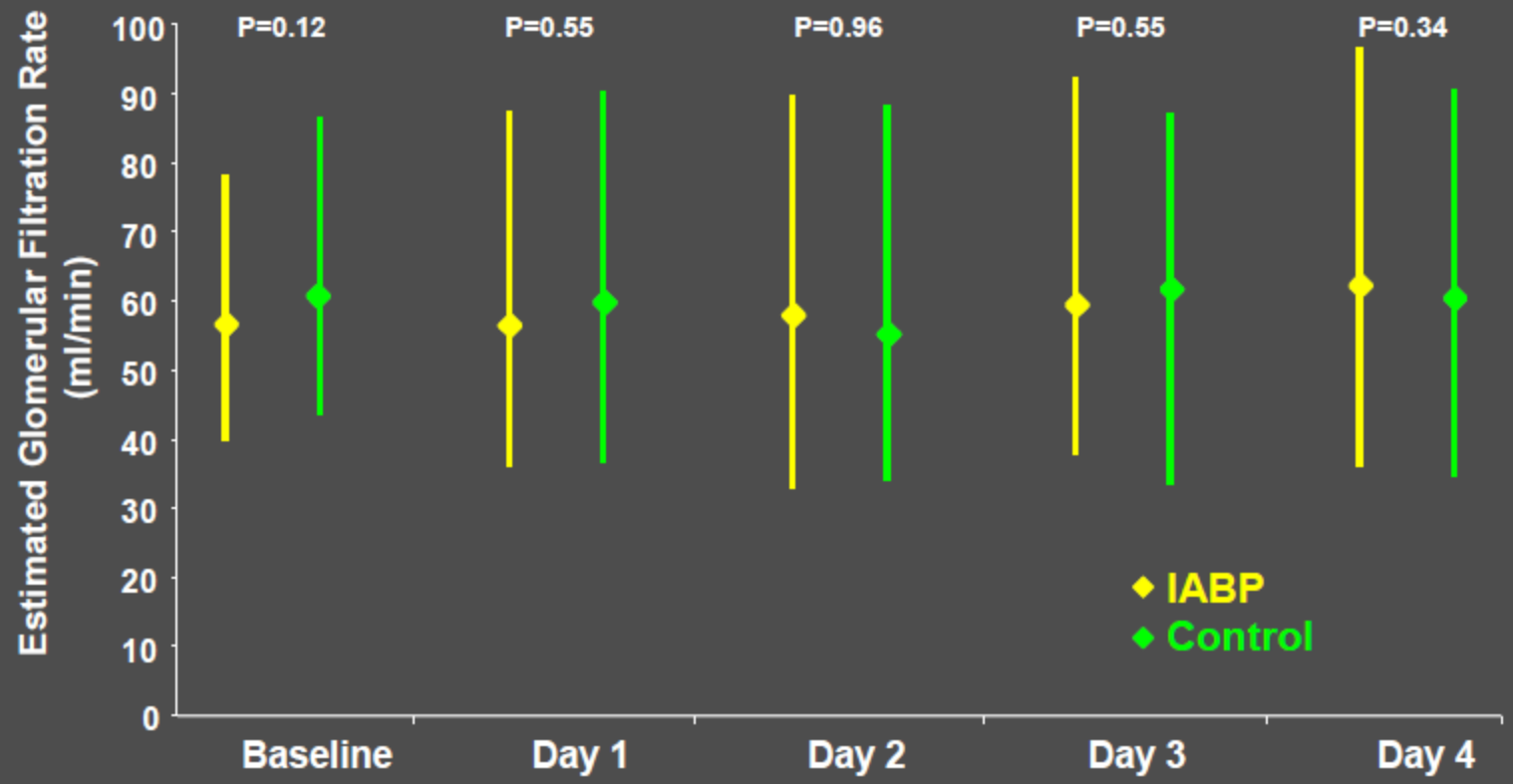
Variable	IABP (n=301)	Control (n=299)	p
Primary PCI; n/total (%)	287/301 (95.3)	288/299 (96.3)	0.55
Stent implanted; n/total (%)	273/301 (90.7)	266/299 (89.0)	0.48
Drug-eluting stent; n/total (%)	126/301 (41.9)	123/299 (41.1)	0.86
Immediate PCI of non-culprit lesions; n/total (%)	90/301 (29.9)	81/299 (27.1)	0.45
Immediate bypass surgery; n/total (%)	8/301 (2.7)	10/299 (3.3)	0.62
Staged bypass surgery; n/total (%)	3/301 (1.0)	4/299 (1.3)	0.72
Active left ventricular assist device; n/total (%)	11/301 (3.7)	22/299 (7.4)	0.053
Mild hypothermia; n/total (%)	106/301 (35.2)	120/299 (40.1)	0.21
Mechanical ventilation; n/total (%)	240/301 (79.7)	252/299 (84.3)	0.15
Mechanical ventilation duration (days); median (IQR)	3.0 (1.0-8.0)	3.0 (1.0-8.0)	0.44
ICU treatment (days); median (IQR)	6.0 (3.0-12.0)	6.0 (3.0-13.0)	0.34
Renal replacement therapy; n/total (%)	62/301 (20.6)	47/299 (15.7)	0.12
Catecholamines (µg/kg per minute); median (IQR)			
Dopamine	4.1 (2.9-7.7)	4.2 (3.6-8.3)	0.76
Norepinephrine	0.3 (0.1-1.2)	0.4 (0.1-1.1)	0.73
Epinephrine	0.3 (0.1-1.3)	0.3 (0.2-1.4)	0.59
Dobutamine	10.2 (4.9-20.6)	9.0 (4.8-17.6)	0.25
Duration of catecholamines (days), median (IQR)	3.0 (1.0-5.0)	3.0 (1.0-6.0)	0.81
Time - hemodynamic stabilization (days); median (IQR)	3.0 (1.0-5.0)	3.0 (1.0-6.0)	0.50

Results

Simplified Acute Physiology Score-II

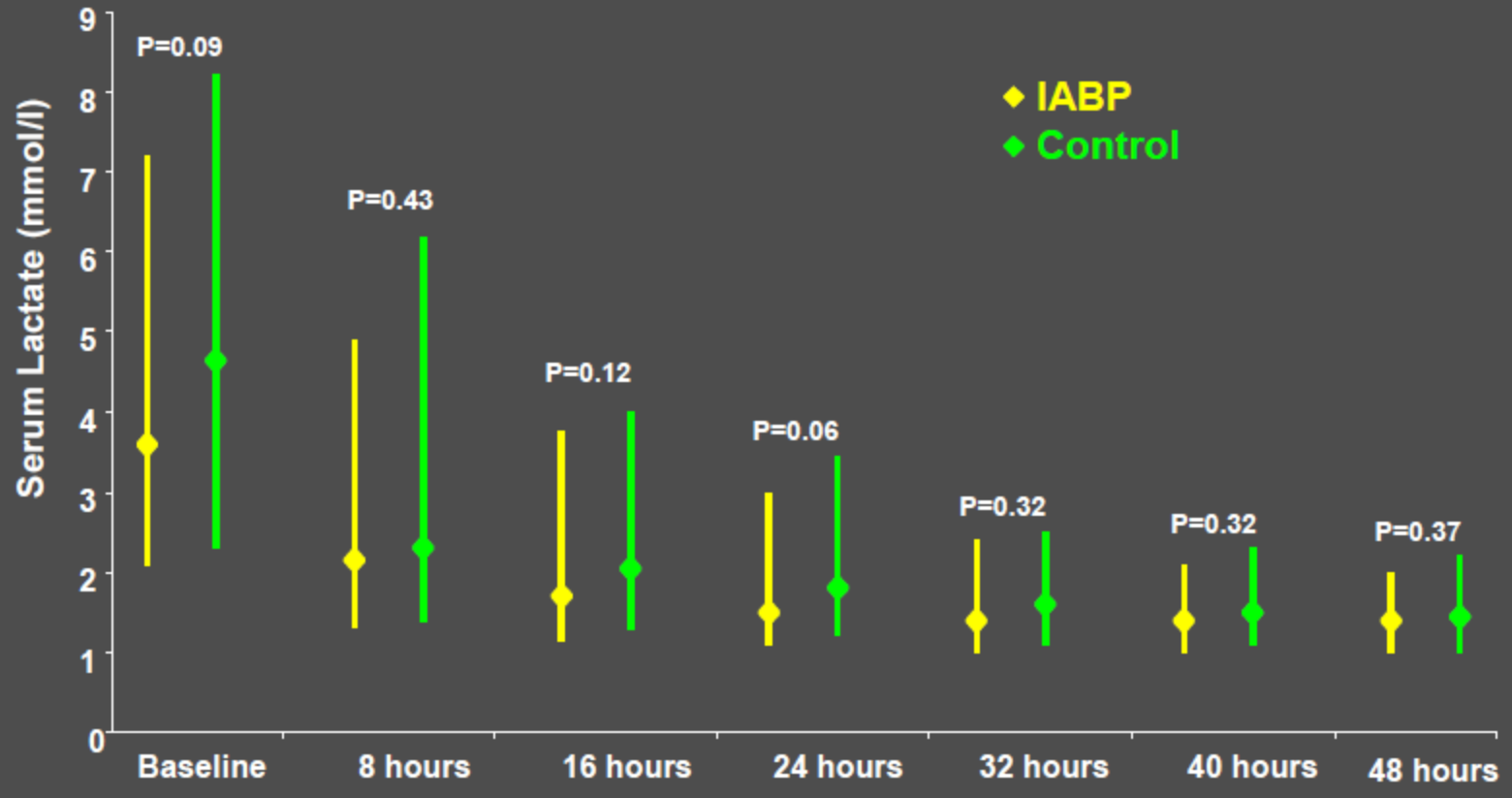
Results

Renal Function (eGFR)



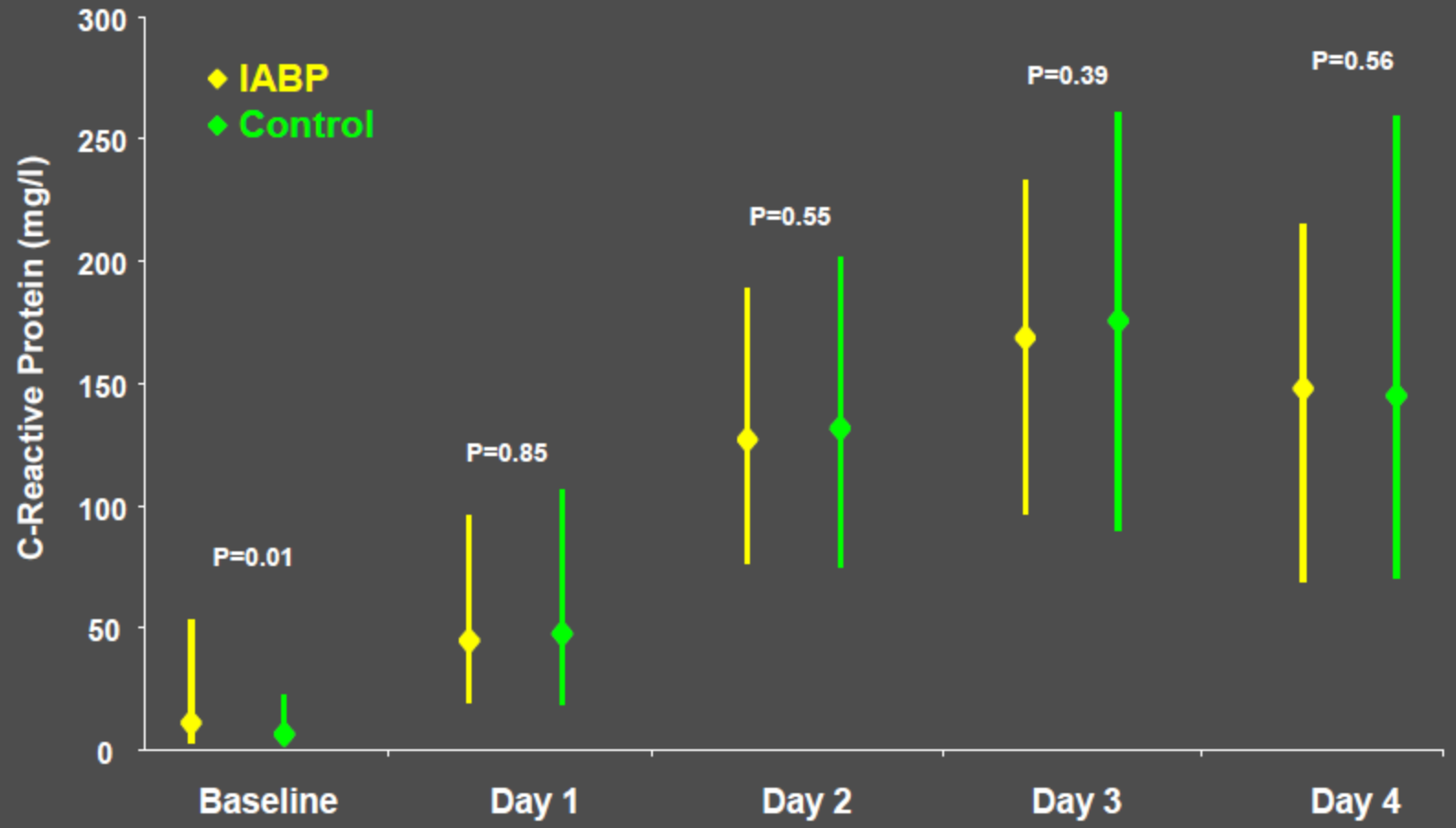
Results

Serum Lactate



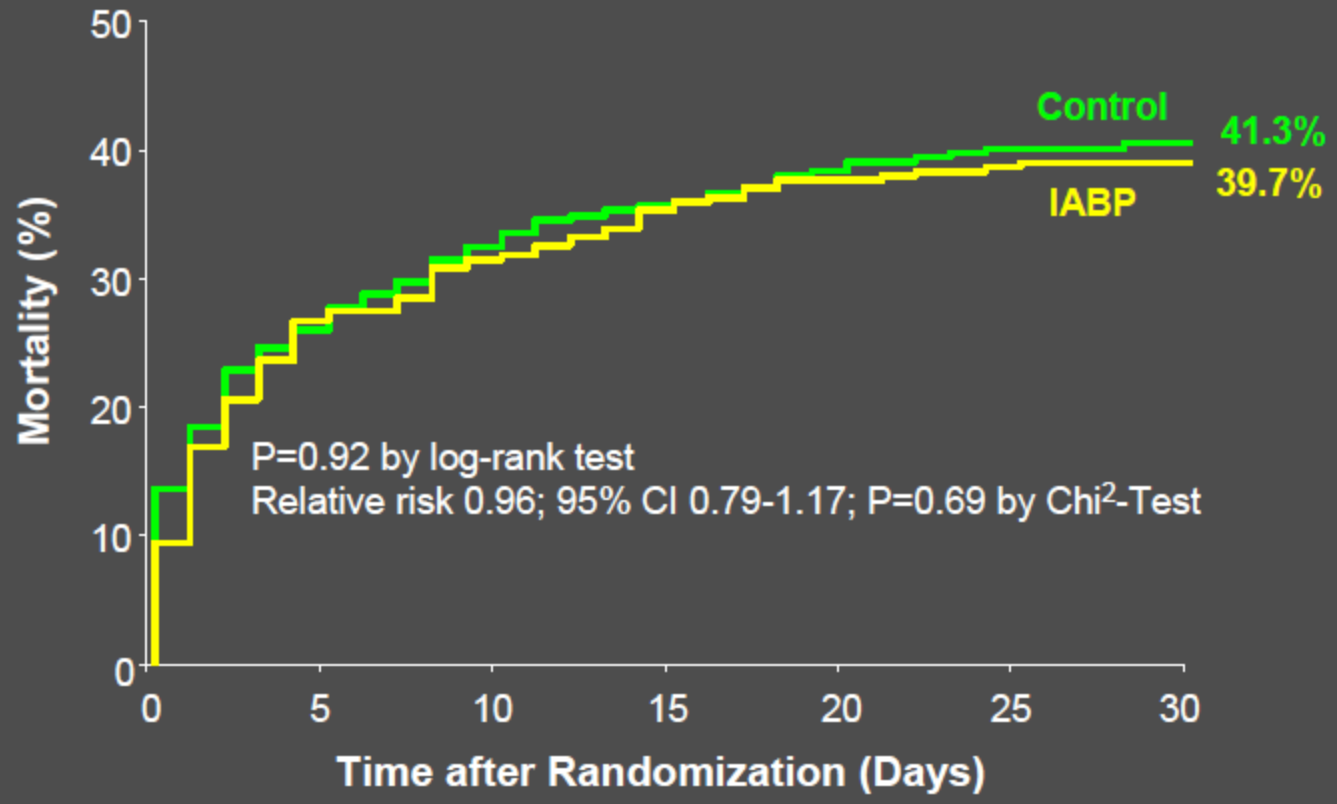
Results

Inflammatory Reaction (CRP)



Results

Primary Study Endpoint (30-Day Mortality)

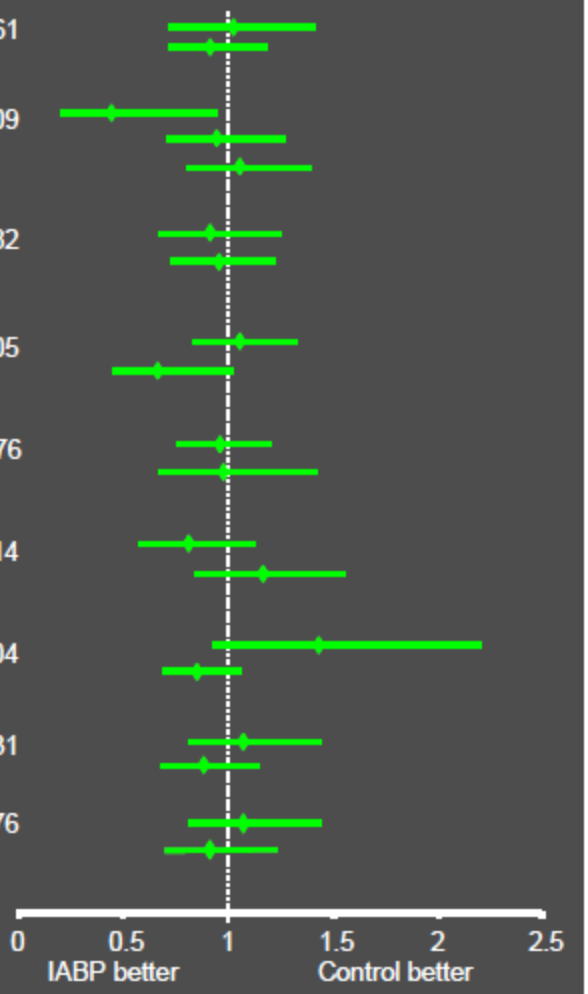


Results

Subgroups (30-Day Mortality)

IABP SHOCK II RANDOMIZED CLINICAL TRIAL

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)	



Results

Safety

IABP SHOCK II

	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

IABP-SHOCK II Trial: No Benefit/No Harm

Strengths:

- Largest randomized shock trial ever performed
- 600 patients included within 32 months
- 12-month follow-up: 99.2%

Limitations:

- No hemodynamic shock assessment
- 10% crossover to IABP
- Majority of patients received IABP following PCI

Patients in IABP-SHOCK II Trial

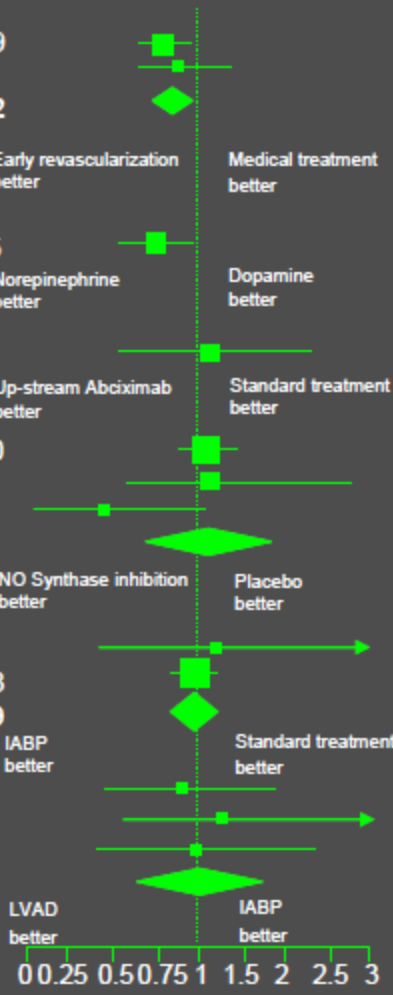
- Mortality rate lower than expected -- 40% vs expected 56%
- Ejection fractions relatively high
- Relatively high blood pressures; median 90/55 mm Hg
- Mild to moderate cardiogenic shock
- 86% did not require hemodynamic support (IABP) during PCI
- One-third of patients were NSTEMI
- 40% of patients had previous CPR and cardiac resuscitation

Clinical Implications

- In mild to moderate cardiogenic shock use catecholamine/pressors rather than IABP?
  - Catecholamines increase myocardial oxygen demand
- Start IABP early
- Consider severity of cardiogenic shock
- Little to no downside risk -- safety of IABPs
- IABP use may allow for more complete revascularization

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

Cardiogenic Shock

- A spectrum of a disease with varying degrees of severity
- Some but not all patients respond to IABP therapy
- Possible reasons for lack of response
  - Hypovolemia
  - Tachycardia
- Need to select appropriate patients/identify if IABP has unloaded the heart

Goals of Percutaneous Circulatory Support In Acute Myocardial Infarction and Cardiogenic Shock

1. Stabilize systemic perfusion and improve multi-organ function at the time of emergent revascularization
2. Reduce LV wall stress and stroke work
3. Augment coronary perfusion
4. Potentially allow for more complete revascularization (ie, thrombectomy, multivessel intervention, bifurcation therapy, and left main PCI)