Advanced Cardiopulmonary Support for the Critically Ill Adult

Cardiogenic Shock

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Advanced Heart Failure, Cardiac Transplant & Mechanical Circulatory Support

No Disclosures

Cardiogenic Shock: Definition

End-organ hypoperfusion secondary to cardiac failure

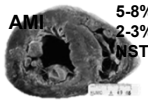
Hemodynamics

- **Persistent hypotension**
  - Systolic BP < 80-90 mmHg or
  - MAP 30 mmHg below baseline
- **Cardiac Index**
  - < 1.8 L/min/m^2 without support
  - < 2.0 L/min/m^2 with support
- **Elevated Filling Pressures**
  - LVEDP > 18 mmHg
  - RVEDP > 10-15 mmHg

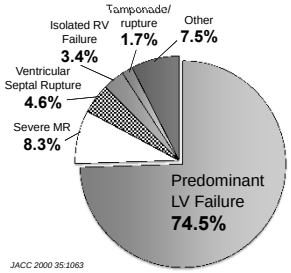
Clinical Signs/Symptoms

- **Poor urine output**
- **Altered mentation**
- **Cool periphery**
- **Abdominal pain/N/V**
- **Lactic acidosis and ↓HCO_3^-**
- **Pulmonary congestion**

Cardiogenic Shock: Incidence/Etiologies



AMI
5-8% of STEMIs
2-3% of NSTEMIs

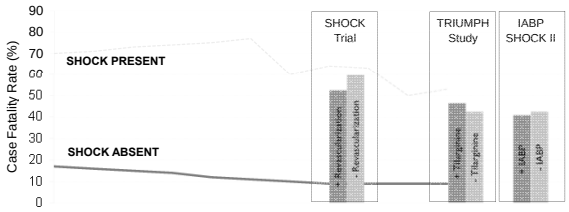


JACC 2000 35:1063

Other Etiologies

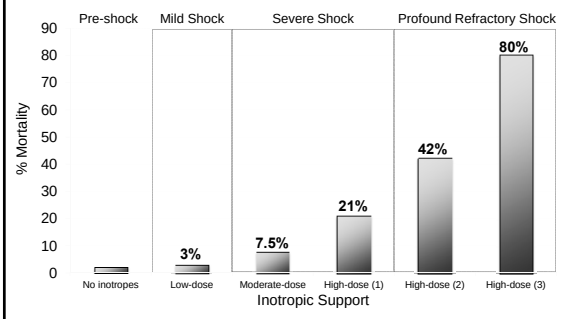
- **Postcardiotomy shock**
- **Fulminant myocarditis**
- **Tako-tsubo Cardiomyopathy**
  - 4.2% of cases complicated by CS
- **Acute valvular regurgitation**
  - Endocarditis
  - Trauma
  - Aortic dissection
- **Decompensated severe aortic/mitral stenosis**
- **Primary graft failure**
- **Pulmonary embolism**
- **Drug overdose**
- **Toxic cardiomyopathy of sepsis**

Cardiogenic Shock: Declining (But Still High) Case Fatality Rate



Adapted from Werdan et al. IEuropean Heart Journal (2014) 35, 156–167.
Goldberg et al. Circulation 2009;119: 1211 – 1219.

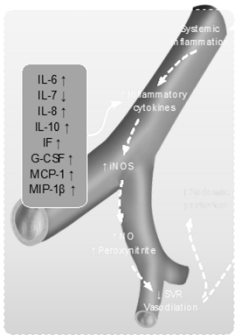
Cardiogenic Shock: A Spectrum of Disease

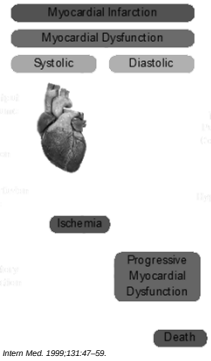


HIGH DOSE: *Epinephrine > 10 mcg/min; Dopamine > 10 mcg/kg/min; Dobutamine > 10 mcg/kg/min; Milrinone > 0.50 mcg/kg/min*

Samuels LE. J Card Surg 1999;14:288-93

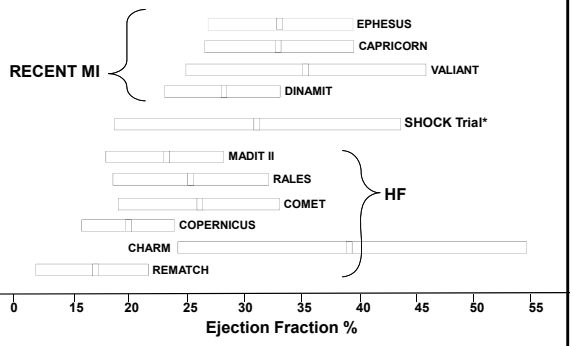
Cardiogenic Shock: Not Just Deranged Hemodynamics





Adapted from Hochman et al, Circulation. 2003;107:2998–3002 &Hollenberg et al, Ann Intern Med. 1999;131:47–59.

Cardiogenic Shock: Distribution of LV Systolic Function



*on support with IABP or inotropic therapy

Ramanathan K, et al. J Am Coll Cardiol. 2004;43:241A.

Cardiogenic Shock: Prognostic Biomarkers

Biomarker	Area Under the Curve (Selejan et al, 2012)* (Prodzinsky et al, 2010)¶	
RAGE expression on monocytes	0.943, p < 0.001*	Markers of inflammation and MSOF are better predictors of survival than the best hemodynamic variables.
SAPS score	0.873, p < 0.001*	
APACHE score	0.850, p < 0.001¶	
Soluble RAGE in plasma	0.815, p = 0.004*	
Interleukin-6 in plasma	0.769, p = 0.011*¶	
Cardiac power index	0.742, p = 0.025*	Not predictive of survival beyond 96 hours
Cardiac index	0.771, p = 0.88¶	
BNP	0.502, p = 0.987¶	
CRP	0.505, p = 0.963*	

Werdan et al. Crit Care Med. 2012;40:1669-1670.

Prondzinsky et al. Crit Care Med 2010;38:152-160.
Selejan, et al. Crit Care Med 2012;40:1513-1522.

Inotropic Therapy: A Necessary Evil

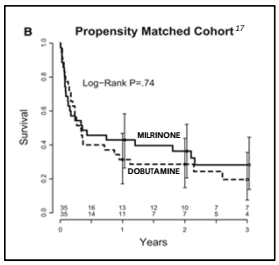
Increased mortality
- Milrinone [1,2]
- Enoximone [3]
- Imazodan [4]
- Vesnarinone [5]
- Dobutamine [6,7]
- Xamoterol [8]
- Ibopamine [9]

Increased risk of admission[1]

Arrhythmia
- Milrinone [10,11]
- Dobutamine [12]
- Dopamine [13]

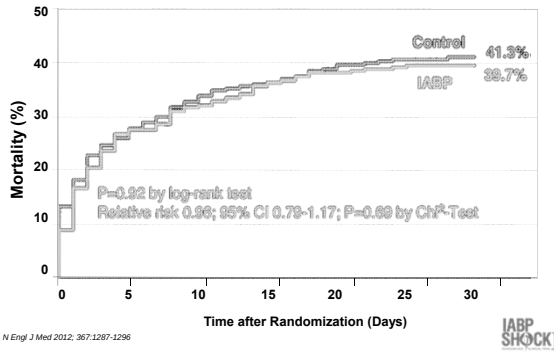
Tachyphylaxis[15]

Neurohormonal activation[16]



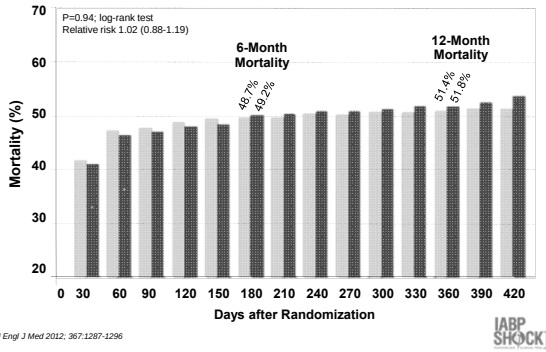
[1] Packer M, et al. *New Engl J Med* 1991; 325: 1468-75.
[2] DiBianco R, et al. *New Engl J Med* 1989; 320: 677-83.
[3] Uretsky BF, et al. *Circulation* 1990; 82: 774-80.
[4] Goldberg AD, et al. *Circulation* 1990; 82: Suppl III: III-673.
[5] Cohn JN, et al. *New Engl J Med* 1998; 339: 1810-16.
[6] Dies F, et al. *Circulation* 1986;74: Suppl II: II-38.
[7] O' Connor CM, et al. *Am Heart J* 1999; 138: 78-86.
[8] Xamoterol in Heart Failure Group. *Lancet* 1990; 336: 1-6.
[9] Hampton JR, et al. *Lancet* 1997; 349: 971-7.
[10] Kleiman NS, et al. *J Am Coll Cardiol* 2000; 36; 310-25
[11] Thackray S, et al. *Eur J Heart Fail* 2000; 2: 209-212
[12] Burger AJ, et al. *Am J Cardiol* 2001 Jul 1;88(1):35-9
[13] Chiolero, et al, *Cardiovasc Surgeon* 1991; 39: 81-84
[14] Colucci WS. *J Card Fail* 2001;7(1):92-100.
[15] B. Hoffman and R. Lefkowitz. Goodman and Gilman, Eds, 9th. Edition. 1996.
[16] Aronson D, et al. J Card Fail 2001; 7 (No. 3 Suppl 2): 28.
[17] Gorodeski et al. *Circ Heart Fail. 2009;2:320-324.*

Cardiogenic Shock: Short-term Survival with IABP



N Engl J Med 2012; 367:1287-1296

Cardiogenic Shock: Long-term Survival with IABP



N Engl J Med 2012; 367:1287-1296

Cardiogenic Shock: IABP in the Guidelines

Class I B → IIa B

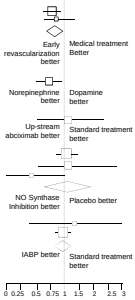
Antman et al. Circulation 2004;110:82-292
O'Gara et al. Circulation. 2013;127:e362-e425

Class I C → IIb B

Van de Werf et al. Eur Heart J 2008;29:2909-2945
Steg et al. Eur Heart J.2012;33:2569-2619

Randomized Trials in Cardiogenic Shock

Trial	Follow-up	n/N	n/N	Relative Risk 95% CI	Relative-Risk 95% CI
Revascularization					
SHOCK	1-year	76/152	83/149		0.80 (0.66;0.98)
SMACH	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 Inhib	In-hospital	15/40	13/40		1.15 (0.59;2.27)
PRAGUE-7					
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)



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

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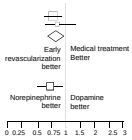
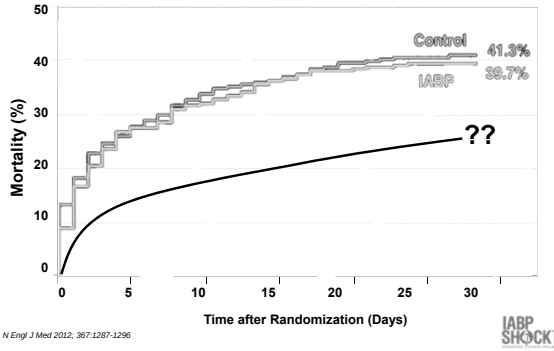


Paucity of Randomized Controlled Data
Clinical Trials are Extremely Challenging to Perform

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

What About More Robust Mechanical Support?



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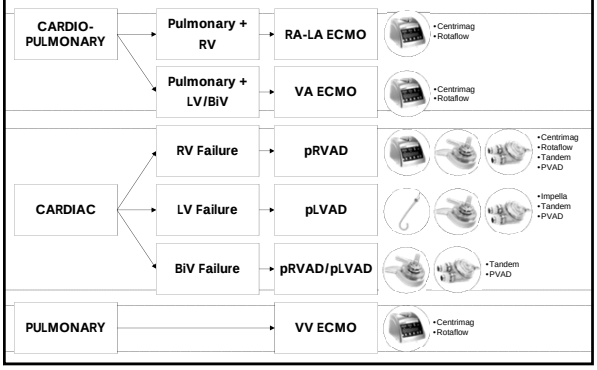
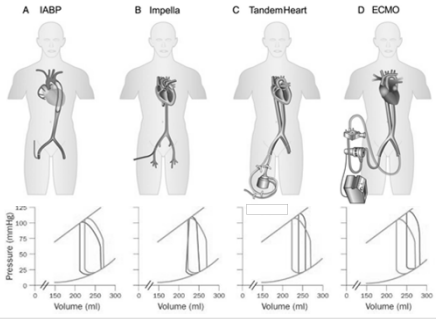
IABP SHOCK II

Tailored Approach to Temporary MCS in Refractory Failure



Hemodynamic Effects and Ventricular Unloading with pVADs



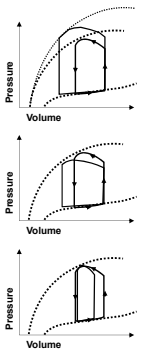
Burkhoff, D. (2015) Where next in cardiogenic shock owing to myocardial infarction?
Nat. Rev. Cardiol. doi:10.1038/nrcardio.2015.81

Optimal MCS Should Reduce Stroke Work and Myocardial O_2 Consumption

Inotropic drugs
- Increase peak systolic pressure
- Stroke volume increase

Balloon pump
- **Reducing systolic aortic pressure**
- **Stroke volume increase**

Impella
- **Unloads from ventricle**
- **Reduces diastolic volume**



Work reduction
Reduced area of PV loop?

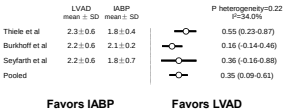
No: increases PV loop area

No: stroke volume increase offsets pressure reduction

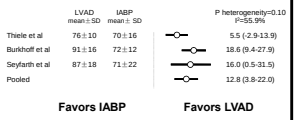
Yes: volume reduction reduces PV loop area

Meta-Analysis of IABP vs. Temporary Left Ventricular Assist Devices: Hemodynamics

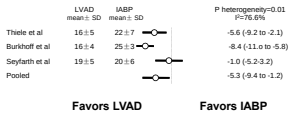
Cardiac Index



Mean Arterial Pressure



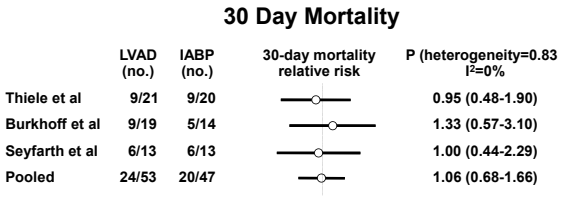
Pulmonary Capillary Wedge Pressure



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

Meta-Analysis of IABP vs. Temporary Left Ventricular Assist Devices: Mortality

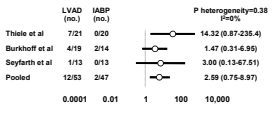
30 Day Mortality



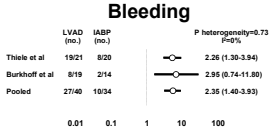
Cheng et al: Eur Heart J 2009;30:2102-2108.

Meta-Analysis of IABP vs. Temporary Left Ventricular Assist Devices

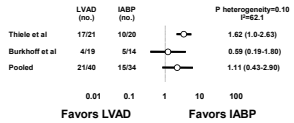
Limb Ischemia



Bleeding

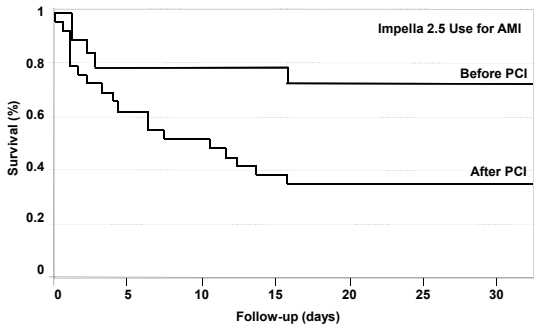


Sepsis



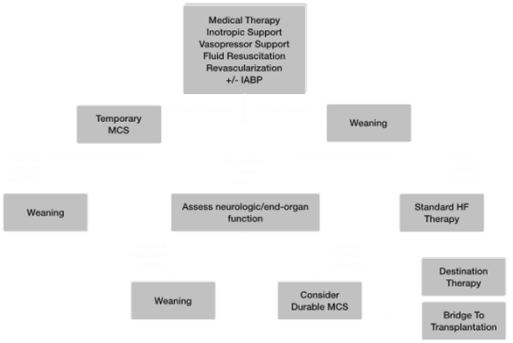
Cheng et al: Eur Heart J 2009;30:2102-2108.

Whatever the Modality of Support… Earlier Is Better



W. O'Neill for the USPELLA Investigators TCT 2010

Algorithmic Approach to Patients with Refractory Cardiogenic Shock



Thiele et al, EAPCI 2012; Kapitel 23

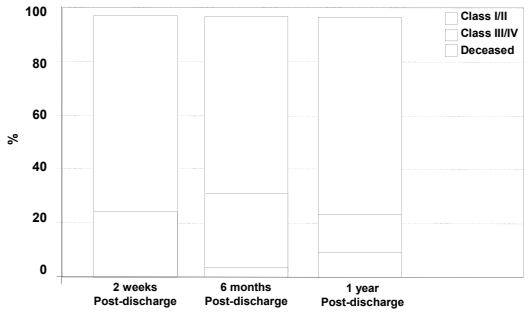
"How Long Does The Storm Last?"

Majority of Added Morbidity/Mortality Occurs in the first 2 months following discharge.

After this period, outocmes are comparable to patients without shock.

The Majority of Cardiogenic Shock Survivors Enjoy Good Functional Status/QOL

SHOCK Trial (Patients having undergone urgent revascularization)



Sleeper et al. J Am Coll Cardiol. 2005;46:266–273.

Cardiogenic Shock: Summary

- **Cardiogenic shock continues to be associated with high morbidity/mortality.**
- **There is a spectrum of disease severity with nearly uniform mortality in those with the most severe shock.**
- **While historically considered a complication of AMI, increasingly seen in other clinical contexts.**

Cardiogenic Shock: Summary

- **Markers of end-organ dysfunction and inflammation may be more predictive of survival than hemodynamic variables.**
- **There few proven therapies and high quality clinical trial data is difficult to obtain.**
- **Guideline recommendations for IABP support have been downgraded due to recent trial results.**
- **Whether more robust mechanical support (Impella, Tandem Heart, VA ECMO, etc.) achieves superior survival has yet to be conclusively demonstrated and is critically dependent on patient selection.**

Cardiogenic Shock: Summary

- **In patients with adequate end-organ function (most critically neurologic function), temporary MCS may serve as a bridge to durable MCS/transplant.**
- **The first two months after hospitalization for cardiogenic shock represent the highest risk period for increased hospitalization/mortality.**
- **The majority of long-term survivors of cardiogenic shock have acceptable quality of life and functional status.**