

Cardiogenic Shock



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Equations to know....

- Cardiac Output

$$CO = HR \times LVSV$$

- Flow

$$Q = (P_{in} - P_{out}) \left(\frac{\pi r^4}{8\mu L} \right)$$

- Vascular Resistance

$$R = (P_{in} - P_{out})/Q$$

$$SVR = MAP - RAP/CO$$

- Cardiac Performance

$$LVEF = \frac{LVSV}{LVEDV}$$

Q = flow rate

P = pressure

μ = viscosity

r = inner radius

L = length

RAP = Rt atrial pressure

CO = Cardiac Output

SVR = Systemic resistance

LVSV = LV SV

EDV = end diastolic volume

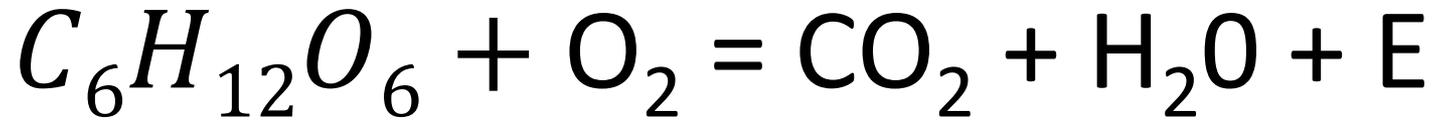
Definition of Shock

- In 1852, shock was defined as “a rude unhinging of the machinery of life.” Probably no better definition exists to describe the devastating effects of this process on a patient, but a more recent definition calls shock “the collapse and progressive failure of the cardiovascular system.”
- Shock left untreated may be fatal. It must be recognized and treated immediately, or the patient will likely die.

Perfusion

- What is the purpose of the cardiovascular system?
 - Perfusion
 - Definition
 - The injection of fluid into a blood vessel in order to reach an organ or tissues, usually to supply nutrients and oxygen.





- Perfusion ultimately is the sum of
 - Substrate delivery
 - Oxygen delivery
 - Carbon dioxide removal
 - Removal of metabolic waste
 - Systemic and/or local energetics (ATP etc...)

Remember... this is cellular energetics from physiology class.

Definition of Shock

- The definition of shock does not involve low blood pressure, rapid pulse or cool clammy skin - these are merely the signs. Simply stated, shock results from inadequate perfusion of the body's cells with oxygenated blood.

Cardiogenic Shock

- Definition

- General definition- Inadequate tissue perfusion resulting from cardiac dysfunction.
- Clinical definition - decreased cardiac output and tissue hypoxia in the presence of adequate intravascular volume.
- Hemodynamic definition - sustained systolic BP < 90 mm Hg, cardiac index < 2.2 L/min/m², PCWP > 15 mm Hg

Cardiogenic Shock

- Cardiogenic shock is characterized by a decreased pumping ability of the heart causing a shock-like state with inadequate perfusion to the tissues.
- It occurs most commonly in association with, and as a direct result of, acute ischemic damage to the myocardium.

Etiology

- Intrinsic
 - Myocardial injury*****
 - Tachycardia
 - Bradycardia
 - Valvular defect
- Extrinsic
 - Pericardial tamponade
 - Tension pneumothorax
 - Large pulmonary embolus

Common Etiology

- Acute myocardial infarction***
- Heart failure
- Cardiomyopathy
- Arrhythmias
- Valvular disorders
- Prolonged cardio-pulmonary bypass
- Septic Shock (toxic ventricular dysfunction)

Ventricular Failure

- Systolic dysfunction (decreased contractility)
 - Ischemia/MI
 - Global hypoxemia
 - Valvular disease
 - Myocardial depressant drugs (eg, beta-blockers, calcium channel blockers, antiarrhythmics)
 - Myocardial contusion
 - Respiratory acidosis
 - Metabolic derangements (eg, acidosis, hypophosphatemia, hypocalcemia)
- Diastolic dysfunction/increased myocardial diastolic stiffness
 - Ischemia
 - Ventricular hypertrophy
 - Restrictive cardiomyopathy
 - Consequence of prolonged hypovolemic or septic shock
 - Ventricular interdependence
 - External compression by pericardial tamponade
- Greatly increased afterload
 - Aortic stenosis
 - Hypertrophic cardiomyopathy
 - Dynamic aortic outflow tract obstruction
 - Coarctation of the aorta
 - Malignant hypertension
- Valvular or structural abnormality
 - Mitral stenosis
 - Endocarditis
 - Mitral aortic regurgitation
 - Obstruction due to atrial myxoma or thrombus
 - Papillary muscle dysfunction or rupture
 - Ruptured septum or free wall arrhythmias
- Decreased contractility
 - RV infarction
 - Ischemia
 - Hypoxia
 - Acidosis

Ventricular Failure

- Greatly increased afterload
 - Pulmonary embolism
 - Pulmonary vascular disease (eg, pulmonary arterial hypertension, veno-occlusive disease)
 - Hypoxic pulmonary vasoconstriction
 - Peak end-expiratory pressure
 - High alveolar pressure
 - Acute respiratory distress syndrome
 - Pulmonary fibrosis
 - Sleep disordered breathing
 - Chronic obstructive pulmonary disease
- Arrhythmias
 - Atrial and ventricular arrhythmias (tachycardia-mediated cardiomyopathy)
 - Conduction abnormalities (eg, atrioventricular blocks, sinus bradycardia)

Mortality/Morbidity

- The historic mortality rates from cardiogenic shock are 80-90%; more recent studies have reported somewhat lower in-hospital mortality rates, in the range of 56-67%.

- Hard-core measurements

- Blood pressure changes ↑ or ↓
- Pulse rate ↑
- Urine output ↓
- Electrocardiogram
- Arterial blood gas
- Pulmonary artery wedge pressure**
- Cardiac output**
- Cardiac index**
- Central venous pressure**

- Soft-core measurements

- Skin changes (cool, pale or damp)
- Altered Sensorium (depressed or apprehensive)
- Thirst
- Vein changes
- Hyperventilation

** requires invasive procedure

Signs/Symptoms

- Anxiety
- Confusion
- Agitation
- Fatigue
- Tachycardia
- Tachypnea
- Sweating
- Decreased Urine
- Pale skin
- Cool skin (especially in arms/legs)

Physical Exam

- Physical examination will often reveal a patient in the middle of an AMI.
- Patients appear in frank extremis, profoundly diaphoretic and complaining of severe shortness of breath and chest pain.
- Clinical assessment begins with attention to the ABCs and vital signs.

Physical Exam

- Neck examination may reveal jugular venous distention. This is evidence of right ventricular failure and may be prominent.
 - With increasing degrees of ventricular dysfunction, florid pulmonary edema and severe hypotension may develop.
 - Auscultation of the chest may reveal varying degrees of congestive heart failure (CHF).

Physical Examination

- Careful attention should be directed toward the cardiac examination, as there are mechanical causes of cardiogenic shock which are readily amenable to surgical intervention, and without which the mortality is dismal.
 - These include papillary rupture, valvular dysfunction, myocardial wall or septal rupture, cardiac tamponade and aortic aneurysm.
 - Loud murmurs may indicate a valvular dysfunction while muffled heart tones with JVD and pulsus paradoxus may suggest tamponade.

Differentiating Shock vs HF

- Cardiogenic Shock
 - High CVP
 - Low CI
 - High SVRI
 - Low VO₂
- Heart Failure
 - High CVP
 - Low CI
 - High SVRI
 - Normal VO₂

Identifying Types of HF

Congestion at Rest

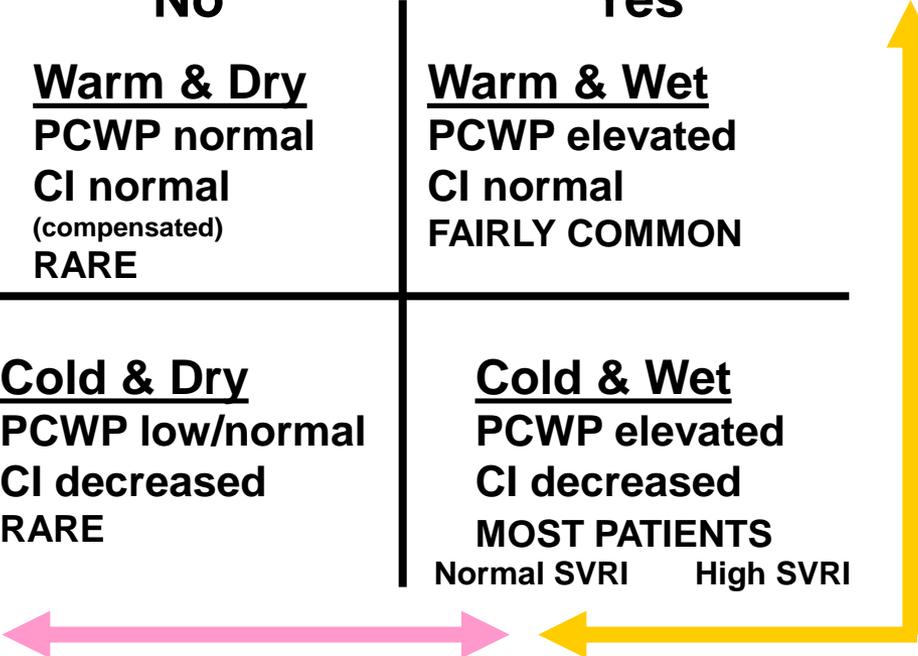
		NO	YES
Low Perfusion at Rest	NO	Warm & Dry	Warm & Wet 67%
	YES	Cold & Dry 5%	Cold & Wet 28%

Nohria, J Cardiac Failure 2000;6:64

Patient Types

Congestion at Rest

		No	Yes
Low Perfusion at Rest	No	<p><u>Warm & Dry</u> PCWP normal CI normal (compensated) RARE</p>	<p><u>Warm & Wet</u> PCWP elevated CI normal FAIRLY COMMON</p>
	Yes	<p><u>Cold & Dry</u> PCWP low/normal CI decreased RARE</p>	<p><u>Cold & Wet</u> PCWP elevated CI decreased MOST PATIENTS</p> <p>Normal SVRI High SVRI</p>



Compensation

- Early Compensatory systems
 - SNS (Fight or flight activation)
 - Vasoconstriction
 - Increased chronotropy
 - Increased inotropy
- Late Compensatory systems
 - RAAS
 - ET
 - Immune/inflammatory

Evolution of Shock from AMI

Frequently, shock develops after presentation for myocardial infarction.

- **SHOCK Registry**

- At presentation 25% in shock
- Within 24 hours 75%
(median delay = 7 hours)

- **GUSTO Trial**

- At presentation 11% in shock
- After admission 89%

SHOCK Registry, Circulation. 1995;91:873-81.

GUSTO J Amer Coll Cardiol. 1995;26:668-74

Cardiogenic Shock

TREATMENT

Cardiac shock made easy

- $CO = SV \times HR$

Where CO is cardiac output in liters per minute

SV is stroke volume in cubic centimeters

HR is heart rate in beats per minute

Normal range at rest (~5.0 lpm in males, and ~4.5 lpm in females)

Measuring CO

- Fick Principle (Oxygen consumption rule)
 - Thermodilution (PA catheter)
 - Echocardiography (estimation of flow)
 - Calibrated Pulse Pressure (Lidco)
-
- **You should strive to learn the differences in these techniques as a critical care provider.

- FICK equation

$$VO_2 = (CO \times C_a) - (CO \times C_v)$$

CO= Cardiac Output

C_a = Arterial oxygen concentration

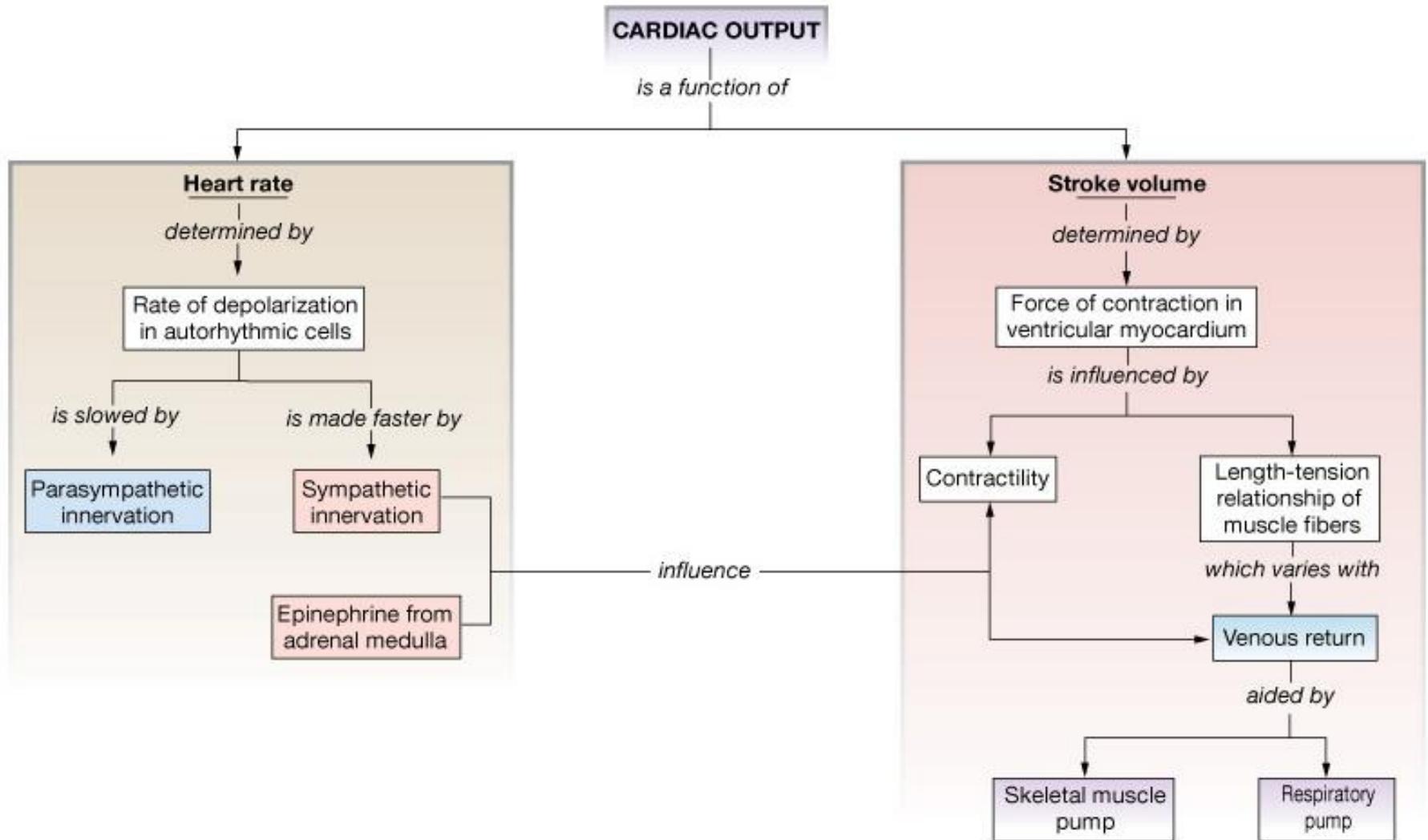
C_v = Venous oxygen content

VO_2 = Oxygen consumption

$$CO = \frac{VO_2}{C_a - C_v}$$

A commonly-used value for O_2 consumption at rest is 125ml O_2 per minute per square meter of body surface area.***

Regulators of the Heart: Factors Influencing Cardiac Output



Initial Management

- Assure oxygenation
 - Intubation and ventilation if needed
- Venous access (consider CV placement)
- Continuous EKG monitoring
- Continuous BP monitoring
- Consider CO monitoring

Heart Rate

- Heart rate modification
 - Intrinsic heart rate (~60-100 bpm)
 - Sympathetic
 - Parasympathetic

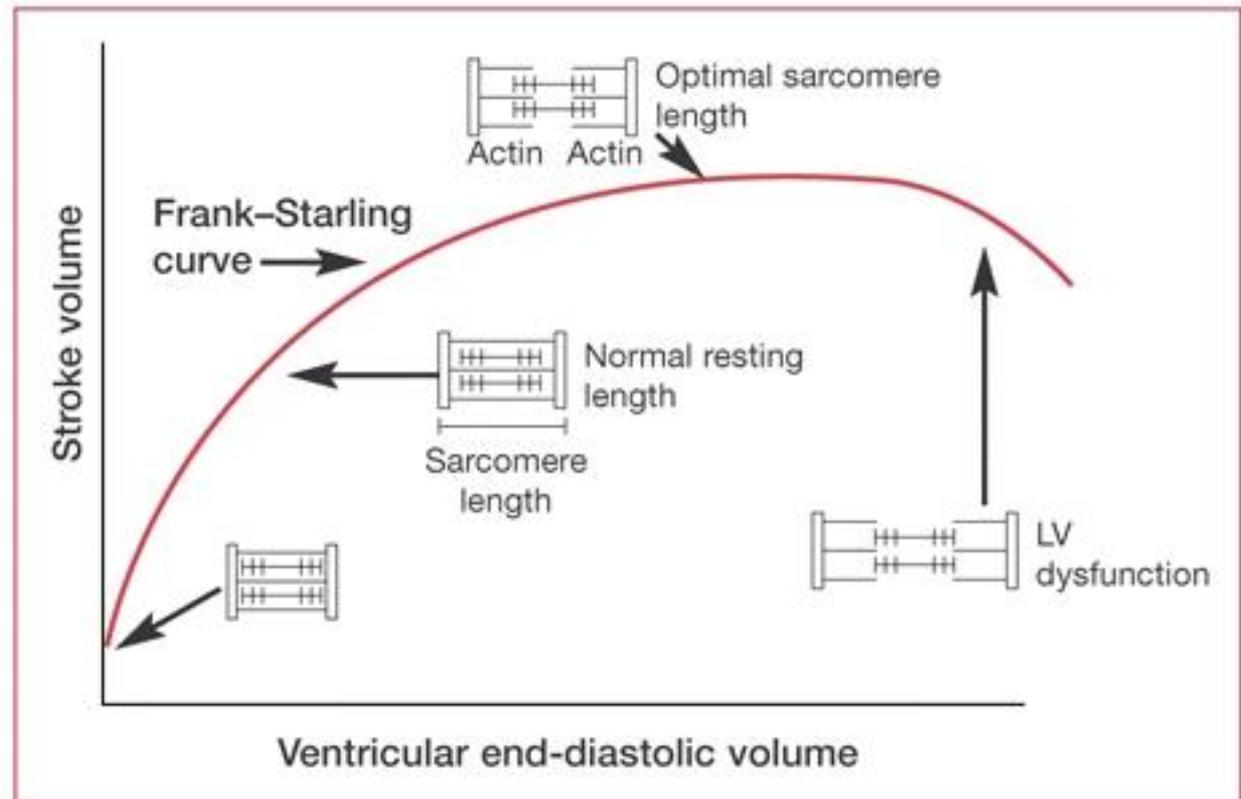
Other HR modification?

Stroke Volume

- Stroke volume
 - $SV = EDV - ESV$
 - Average exemplar, 70kg man with EDV of 120ml and a ESV of 50ml, has a SV of 70 ml
- Influenced by...
 - Preload
 - Afterload
 - Contractility
 - Lusitropy
 - Duration of Contraction

Modifying Preload

- Optimization of Volume status
 - Aim for Euvolemia



Modifying Afterload

- Vasodilators (ie.. Modification of SVR)
 - Nipride
 - Nitroglycerine
 - BNP
 - NO
 - Nicardipine

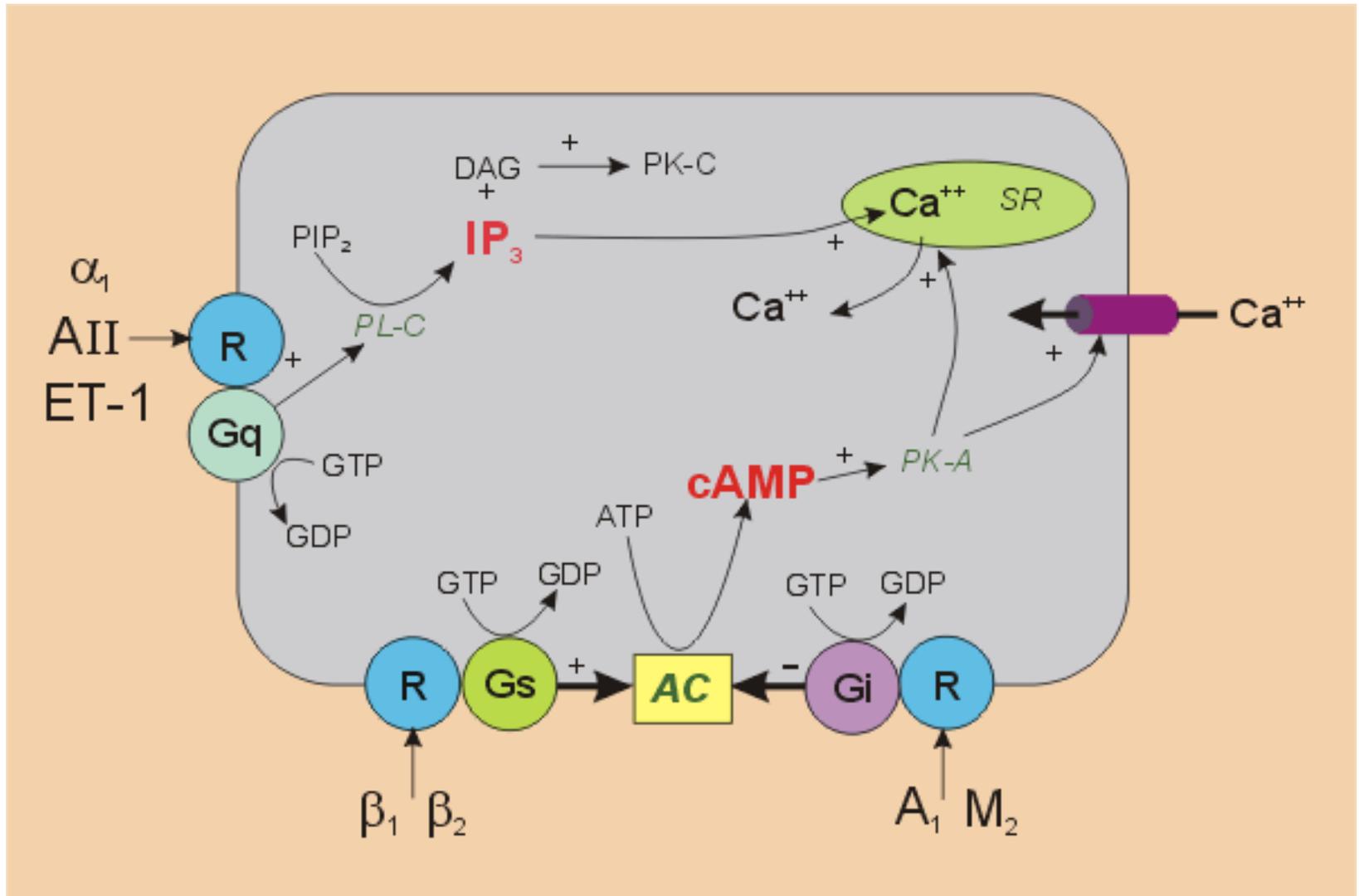
Modifying Contractility

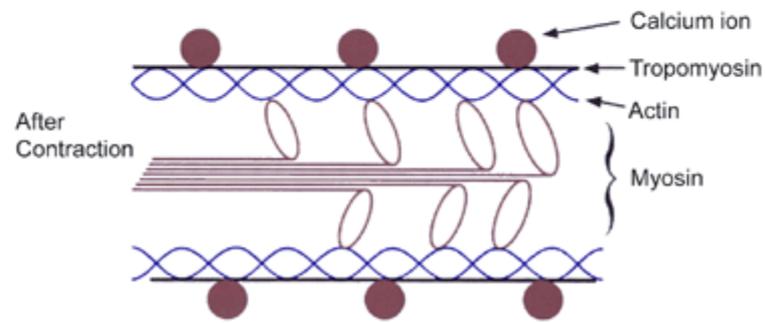
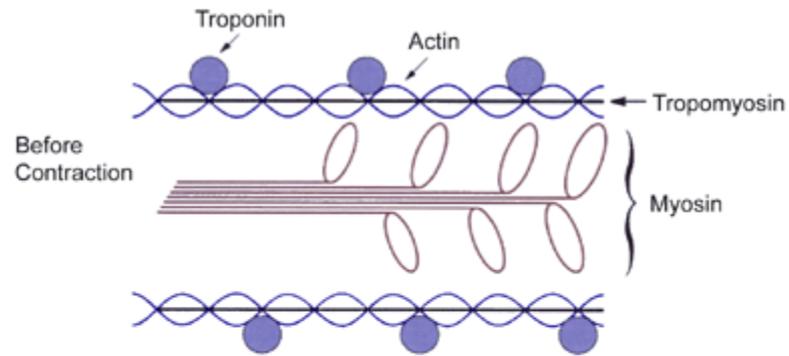
- An inotrope is an agent, which increases or decreases the force or energy of muscular contractions.
- In 1785 the first inotrope-Digitalis was discovered & used for CCF.
- As science advanced, other inotropes were developed which were more potent and have different chemical properties and physiological effects.
- All inotropes are successful because they increase the myocardial contractility of the heart.
- By enhancing myocardial contractility, cardiac output, the amount of blood ejected by the heart with each beat, will also increase.

Inotropes

- Atropine
- Ca^{2+}
- Dopamine
- Dopexamine
- Dobutamine
- Epinephrine
- Noradrenaline
- Isoprenaline
- Enoximone
- Milrinone
- Aminophylline
- Vasopressin
- Methylene blue

Receptors





Drug Classifications

- Cardiac Glycosides:
 - Digitalis Derivatives
 - Digoxin
- Sympathomimetics: -
 - Epinephrine
 - Dopamine (Intropin)
 - **Dobutamine (dobutrex)**
 - **Norepinephrine (levophed)**
 - **Isoproterenol (isuprel)**
- Phosphodiesterase Inhibitors:
 - Amrinone (Inocor)
 - Milirinone (Primacor)

<u>Receptor</u>	<u>Agonist potency order</u>	<u>Selected action of agonist</u>	<u>Mechanism</u>	<u>Agonists</u>	<u>Antagonists</u>
α_1 : A, B, D [†]	Norepinephrine > epinephrine >> isoprenaline	Smooth muscle contraction	G_q : phospholipase C (PLC) activated, IP_3 and DAG, rise in calcium	(Alpha-1 agonists) •Noradrenaline •Phenylephrine •Methoxamine •Cirazoline •Xylometazoline	•(Alpha-1 blockers) <u>Doxazosin</u> •Phenoxybenzamine •Prazosin •Tamsulosin •Terazosin <u>Amitriptyline</u> •Clomipramine •Doxepin
α_2 : A, B, C	Epinephrine \geq norepinephrine >> isoprenaline	Smooth muscle relaxation and neurotransmitter inhibition	G_i : adenylate cyclase inactivated, cAMP down	(Alpha-2 agonists) •Dexmedetomidine •Romifidine •Clonidine •Detomidine •Lofexidine •Xylazine •Tizanidine	•(Alpha-2 blockers) <u>Phentolamine</u> •Yohimbine •Idazoxan •Atipamezole
β_1	Isoprenaline > epinephrine = norepinephrine	Heart muscle contraction	G_s : adenylate cyclase activated, cAMP up	•Noradrenaline •Isoprenaline •Dobutamine	•(Beta blockers) <u>Metoprolol</u> •Atenolol
β_2	Isoprenaline > epinephrine >> norepinephrine	Smooth muscle relaxation	G_s : adenylate cyclase activated, cAMP up (also G_i , see β_2)	•(Short/long) <u>Salbutamol</u> (<u>Albuterol</u> in USA) •Bitolterol mesylate •Formoterol •Isoprenaline •Levalbuterol •Metaproterenol •Salmeterol •Terbutaline •Ritodrine	•(Beta blockers) <u>Butoxamine</u> •Propranolol
β_3	Isoprenaline = norepinephrine > epinephrine	Enhance lipolysis	G_s : adenylate cyclase activated, cAMP up	•L-796568 [2] •Amibegron •Solabegron	• <u>SR 59230A</u>

SYMPATHOMIMETICS (ADRENERGIC)

- Sympathomemetic drugs exert potent inotropic effects by stimulating beta (B1 and B2), alpha (A1 and A2) and dopaminergic receptors in the myocardium, blood vessels, and sympathetic nervous system.

Adrenergic Receptor Types

- ALPHA 1 (A1):
 - A1 receptors are in vascular smooth muscle & also in the myocardium, which mediate positive inotropic and negative chronotropic effects.
 - Stimulation of A1 receptors leads to vasoconstriction.
- ALPHA 2 (A2):-
 - A2 receptors are located in large blood vessels.
 - Stimulation of A2 receptors mediates arterial and venous vasoconstriction.

Adrenergic Receptor Types

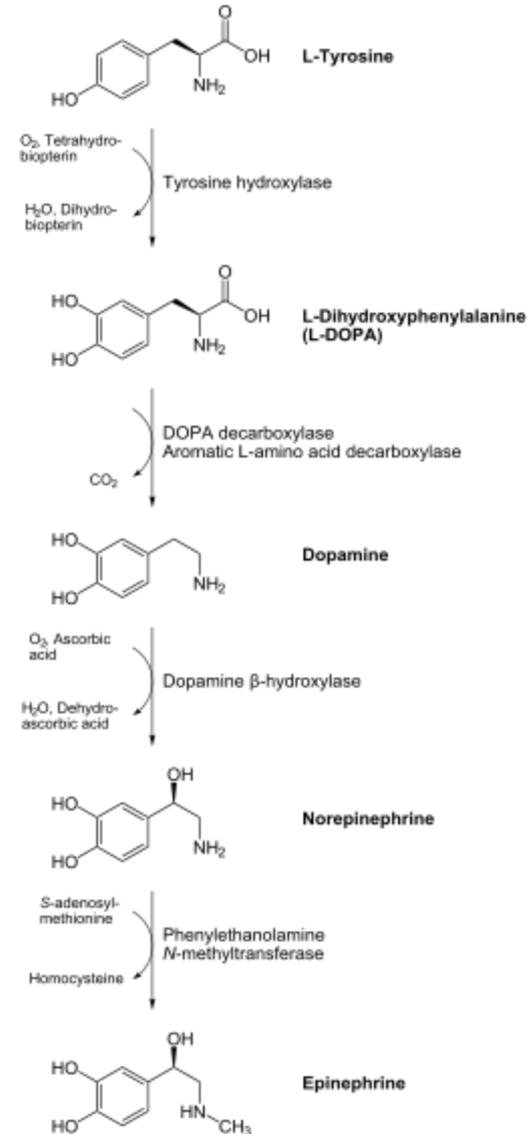
BETA 1 (B1):-

- Beta 1 receptors increase heart rate and myocardial contractility.

BETA 2 (B2):-

- Beta 2 receptors enhance vasodilation; relax bronchial, uterine and gastrointestinal smooth muscle

DOPAMINERGIC: Related to the effect of dopamine.



Phosphodiesterase Inhibitors

- Inhibits phosphodiesterase, an enzyme that degrades (CAMP) Cyclic Adenosine Monophosphate.
- There is no effect on alpha or beta-receptors.
- Increase contractile force and velocity of relaxation of cardiac muscle.
- Increasing cardiac output without increasing myocardial oxygen consumption.
- They cause vasodilation and a decrease in SVR (systemic vascular resistance) and PVR (Pulmonary vascular resistance & in afterload (resistance to ventricular ejection))

Risks of Inotrope therapy Drug Therapy

- Increased mortality
 - Milrinone ^{1,2}
 - Enoximone ³
 - Imazodan ⁴
 - Vesnarinone ⁵
 - Dobutamine ^{6,7}
 - Xamoterol ⁸
 - Ibopamine ⁹
- Increased risk of hospitalization ¹
- **Aggravation and induction of arrhythmias (need telemetry)**
 - Milrinone ^{10,11}
 - Dobutamine ¹²
 - Dopamine ¹³
- **Tachycardia** ¹⁴
- **Tachyphylaxis (dobutamine)**¹⁵
- **Neurohormonal activation and/or lack of suppression** ¹⁶
- **Physiologic effects antagonized by b-blockade (dobutamine, dopamine)**

¹Packer M, et al. *New Engl J Med* 1991; 325: 1468-75.

²DiBianco R, et al. *New Engl J Med* 1989; 320: 677-83.

³Uretsky BF, et al. *Circulation* 1990; 82: 774-80.

⁴Goldberg AD, et al. *Circulation* 1990; 82: Suppl III: III-673.

⁵Cohn JN, et al. *New Engl J Med* 1998; 339: 1810-16.

⁶Dies F, et al. *Circulation* 1986; 74: Suppl II: II-38.

⁷O'Connor CM, et al. *Am Heart J* 1999; 138: 78-86.

⁸The Xamoterol in Severe Heart Failure Group. *Lancet* 1990; 336: 1-6.

⁹Hampton JR, et al. *Lancet* 1997; 349: 971-7.

¹⁰Kleiman NS, et al. *J Am Coll Cardiol* 2000; 36: 310-25

¹¹Thackray S, et al. *Eur J Heart Fail* 2000; 2: 209-212

¹²Burger AJ, et al. *Am J Cardiol* 2001 Jul 1; 88(1):35-9

¹³Chiolero, et al, *Cardiovasc Surgeon* 1991; 39: 81-84

¹⁴Colucci WS. *J Card Fail* 2001; 7(1):92-100.

¹⁵B. Hoffman and R. Lefkowitz. Chapter 10, *The Pharmacologic Basis of Therapeutics*, Goodman and Gilman, Eds, 9th. Edition (CD-ROM) 1996.

¹⁶Aronson D, et al. *J Card Fail* 2001; 7 (No. 3 Suppl 2): 28.

Hemodynamic Management

- Think modification of the CO equation....
 - Questions to ask...
 - Adequate Preload? - Consider fluid challenge
 - Adequate Afterload? - Consider afterload reduction
 - Adequate HR? – Consider pacing
 - Adequate Inotropy? – Consider Inotropes

Advanced therapies

- Intra-aortic Balloon Pump (IABP)
- Surgical:
 - CABG
 - Valve surgery
 - Ventricular assist device
 - Cardiac transplantation

Intra-aortic Balloon Counterpulsation

- Reduces afterload and augments diastolic perfusion pressure
- Beneficial effects occur without increase in oxygen demand
- Only minor improvement in blood flow distal to critical coronary stenosis
- No improvement in survival when used alone
- May be essential support mechanism to allow for definitive therapy

Hypotension in Cardiac Shock

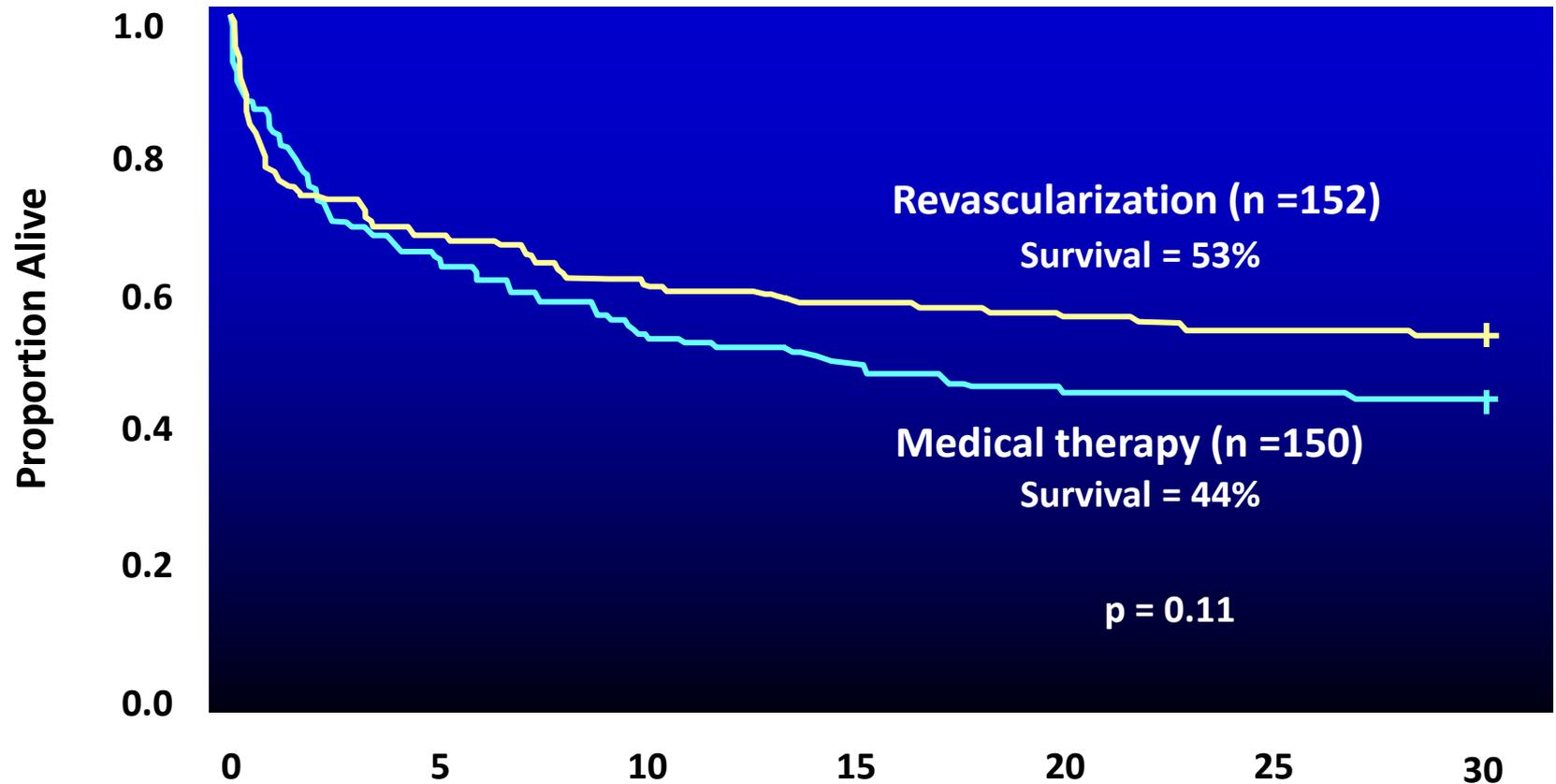
- Hypotension....
 - Consider vasoconstriction, but remember that increasing afterload may reduce CO.

Focusing on the Cause

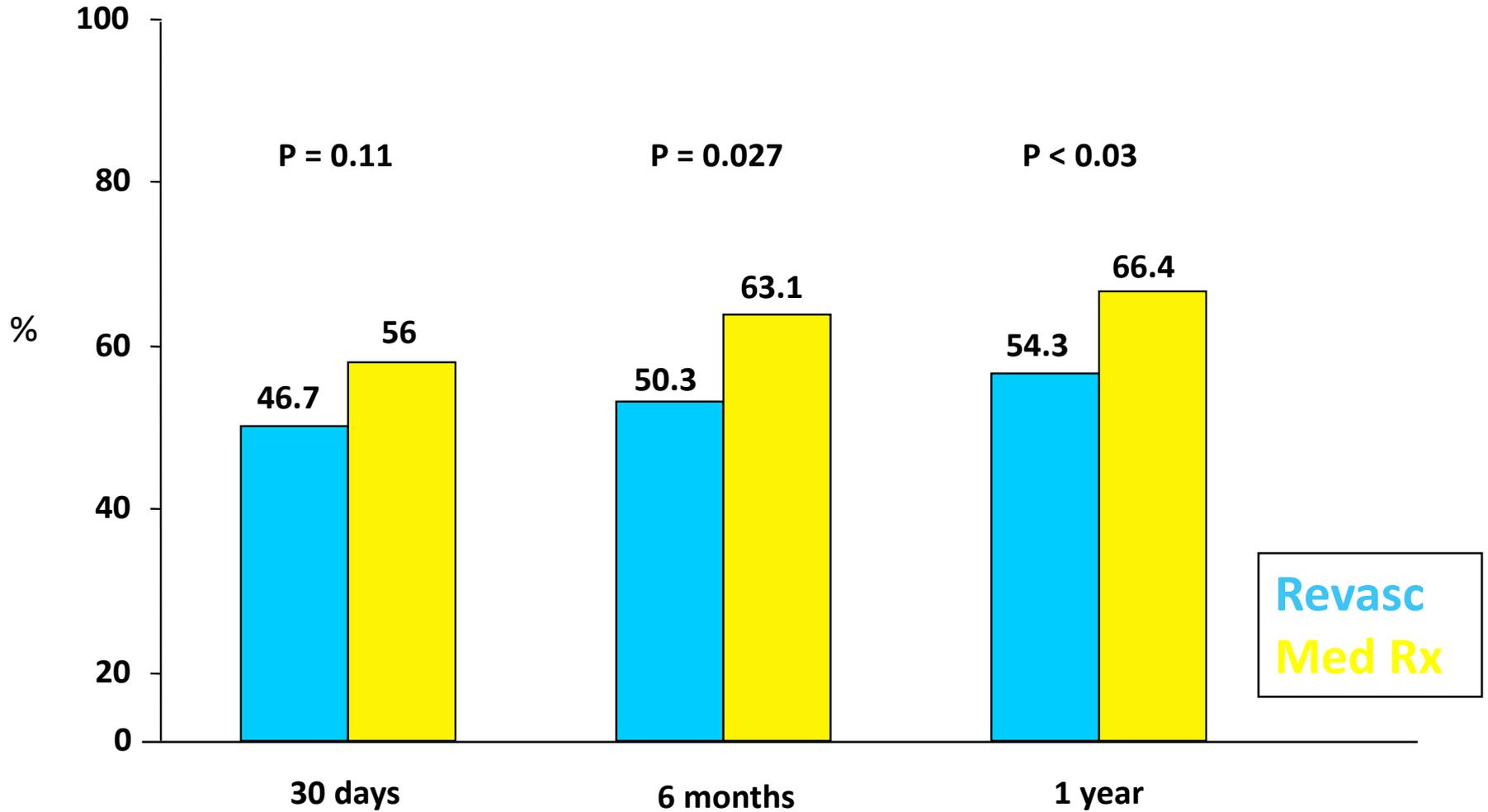
- Treat the AMI....
- Treat the Cardiac failure...

Early Revascularization in Acute Myocardial Infarction Complicated by Cardiogenic Shock

Overall 30-Day Survival in the Study



SHOCK Trial Mortality



ACC/AHA Class I Indication

- Patients with ST segment elevation MI who have cardiogenic shock and are less than 75 years of age should be brought immediately or secondarily transferred to facilities capable of cardiac catheterization and rapid revascularization (PCI or CABG) if it can be performed within 18 hours of onset of shock. (Level of Evidence: A)

National Registry of MI Early Revascularization is Underutilized in Cardiogenic Shock

- Despite ACC/AHA recommendation to treat patients < 75 years of age aggressively with early mechanical revascularization, in 2001, two years after the guidelines were published, only 41% of patients with cardiogenic shock complicating AMI were treated with primary PTCA and only 3.1% underwent early CABG.
- These data demonstrate significant underutilization of guideline recommended therapy.

Case Scenario #1

- A 60yo man with a PMH of HTN and HLP. He was admitted to the ICU following aortic valve replacement with extubation in OR. His BP is 82/48, HR 112, oxygen sat of 91% on 4L. Echo reveals an EF of 30%. CVP 15, PA 52/26, PCWP 22, CO 1.6.
- Diagnosis?
- Etiology?
- Initial management?

Case Scenario #2

- A 61yo female with h/o HTN, HLP and previous MVA 5years ago. Admitted from OSH for flail mitral valve and severe pulm HTN. She was intubated at OSH and initiated on Levophed at 16mcg/min for hypotension. She arrives at your ICU with TLC in place, oxygenating well. SBP 135/45, HR 120, CVP 4, SaO2 96% on 0.6% FiO2. Cold clammy extremities. Rales throughout. Pulmonary edema on CXR.
- Diagnosis?
- Etiology?
- Management?