Hemodynamics Under Fire: Pharmacologic and Device-Based Management of Cardiogenic Shock in the Intensive Care Unit

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Disclosure

I do not have a vested interest in or affiliation with any corporate organization offering financial support or grant monies for this continuing education activity, or any affiliation with an organization whose philosophy could potentially bias my presentation (within the last 12 months).

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Presentation Objectives

Pharmacist Objectives:

1. Describe the hemodynamic disturbances characteristic of cardiogenic shock and interpret key ICU monitoring parameters to guide therapeutic decision
2. Differentiate the pharmacologic roles, mechanisms and clinical indications of inotropes, vasopressors and afterload-modifying agents used in cardiogenic shock
3. Explain the function, indications and ICU considerations for commonly used mechanical circulatory support (MCS) devices and clarify how these devices interact with pharmacotherapy
4. Assess the pharmacokinetic and pharmacodynamic challenges associated with MCS support (such as altered drug clearance, anticoagulation needs, and circuit-related drug sequestration) and incorporate these into medication management plans

Technician Objectives:

1. Identify commonly used medication in cardiogenic shock and recognize their storage, labeling, and handling requirements in the ICU setting
2. Recognize the basic purpose of MCS devices and understand how they may influence medication preparation, urgency, or workflow in the pharmacy

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Cardiogenic Shock

40,000 – 50,000 patients annually in the United States

- 5-10% in MI patients
- >10% in patients >75 years old with AMI

Non-AMI-related cardiogenic shock now outnumbers AMI-related

- HF: 46%
- AMI: 30%
- Other: 17%
  - Structural heart disease, incessant VT, severe valve disease

JAMA. 2021;326(18):1840–1850
Circulation. 2024;149(14):e1051-e1065
N Engl J Med. 2026;394:62-77
Abbreviations: (AIMI, (acute) myocardial infarction; HF, heart failure; VT, ventricular tachycardia

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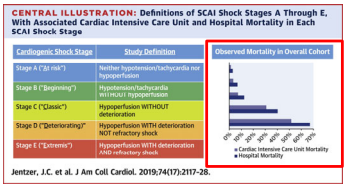
Outcomes in Cardiogenic Shock

- Leading cause of in-hospital death in AMI patients
  - 30-day mortality: ~40%
  - 1-year mortality: ~50%
- Mortality by etiology:
  - Mixed-cause: 48%
  - AMI: 41%
  - New HF: 31%
  - Secondary causes: 31%
  - Acute-on-chronic HF: 25%
- Increases incrementally with advancing age



Circulation. 2024;149(14):e1051-e1065

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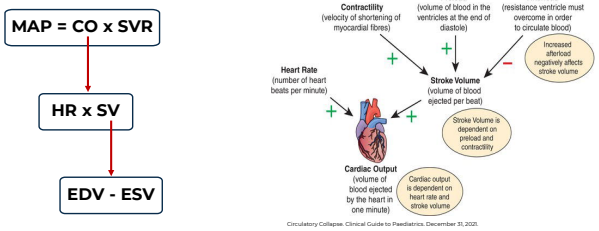
Hemodynamics Overview



Crit Care. 2008;12(4):174
Abbreviations: MAP, mean arterial pressure; CO, cardiac output; SVR, systemic vascular resistance; HR, heart rate; SV, stroke volume; EDV, end diastolic volume; ESV, end systolic volume

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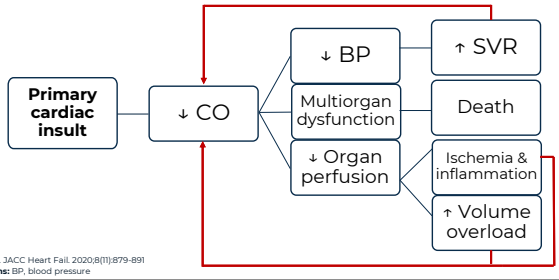
Pathophysiology



Tehrani et al. JACC Heart Fail. 2020;8(11):879-891
Abbreviations: BP, blood pressure

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Diagnosis

- Sustained hypotension
  - SBP ≤ 90 mmHg or MAP ≤ 65 mmHg for >30 minutes
  - or >30 mmHg decrease from baseline
  - Or need for pharmacological/mechanical support to maintain SBP >90 mmHg
- Evidence of end-organ hypoperfusion
  - Lactic acid >2 mmol/L
  - ALT >200 U/L or >3x ULN
  - SCr ≥2x ULN
  - pH 7.2 or metabolic acidosis without another known cause
  - Oliguria/anuria (≤30 mL/hr; ≤0.5 mL/kg/hr)
- Clinical signs and symptoms
  - Altered mental status
  - Cold and clammy extremities
  - Rapid pulse with low pulse pressure
  - Elevated JVP, lower extremity edema
  - Crackles, rales, orthopnea

J Am Coll Cardiol. 2025;85(16):1618-1641
Abbreviations: SBP, systolic blood pressure; MAP, mean arterial pressure; ALT, alanine aminotransferase; ULN, upper limit of normal; SCr, serum creatinine; JVP, jugular venous pressure

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Hemodynamic Criteria

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- ≥1 of the following criteria along with CI ≤ 2.0 L/min/m², SBP ≤ 90 mmHg or MAP ≤ 60 mmHg, and evidence of hypoperfusion:
  - PCWP >15 mmHg
  - Other hemodynamics:
    - Cardiac power output <0.6 W
    - Shock index (HR/SBP) >1
    - For RV shock: PAPI ≤0.9, CVP >15 mm Hg, or CVP-PCWP >0.6

ARC

- CI ≤ 2.2 L/min/m²
- SVR >2200 dynes/(cm sec^{-5})
- PCWP >15 mmHg

J Am Coll Cardiol. 2022;79(17):e263-e421
Lancet. 2024;404(10466):2006-2020
Abbreviations: CI, cardiac index; PCWP, pulmonary capillary wedge pressure; HR, heart rate; RV, right ventricular; PAPI, pulmonary artery pulsatility index; CVP, central venous pressure

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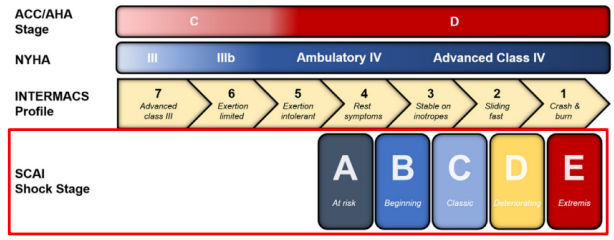
Risk Stratification



Circulation. 2018;138(24):2841-2851

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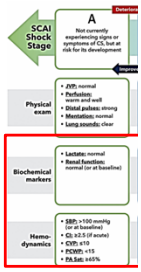
SCAI Shock Stages



J Am Coll Cardiol. 2025;85(16):1618-1641

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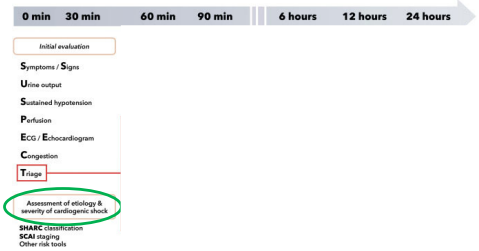
SUSPECT CS



J Am Coll Cardiol. 2025;85(16):1618-1641

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Pharmacologic Management

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Stevenson Classification

Dry and Warm (adequately perfused; hemodynamically stable)	Dry and Cold (hypoperfused ± hypovolemia)
Adjust oral therapy	Consider fluid challenge Inotropic agents if still hypoperfused
Wet and Warm (congestion with adequate perfusion)	**Wet and Cold (congestion and hypoperfused)**
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Curr Heart Fail Rep. 2017;14(5):385-392

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Goals of Pharmacological Management

Mitigate congestion → **Diuresis/ultrafiltration**

Optimize cardiac output; Enhance perfusion → **Vasopressors/inotropes**

J Am Coll Cardiol. 2025;85(16):1618-1641

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Hemodynamic Targets

CVP 8-12 mmHg | PCWP ≤ 15 mmHg | CI ≥ 2.2 L/min/m² | MAP > 65 mmHg

Clinical Assessment

Downtrending lactate | UOP ≥ 0.5 mL/kg/hr | SCr and LFT normalization | $ScvO_2$ >70%

Acidosis resolution | Neurologic improvement | Peripheral perfusion

Circulation. 2017;136(16):e232-e268
JACC Heart Fail. 2024;12(7):1141-1156
Abbreviations: SCr, serum creatinine; LFT, liver function test; $ScvO_2$, central venous oxygen saturation

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Volume Management

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Curr Heart Fail Rep. 2017;14(5):385-392

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Signs of Congestion ("Wet")

PCWP >15, Elevated CVP

Pulmonary congestion
- Orthopnea
- Paroxysmal nocturnal dyspnea
- Crackles/rales on auscultation
- Hypoxemia
- Frank pulmonary edema, pulmonary failure
- S3 gallop

Systemic venous congestion
- Elevated JVP
- Lower extremity edema
- Hepatomegaly, ascites, abdominal discomfort

Respiratory distress
- Tachypnea
- Decreased oxygenation
- Increased work of breathing

JAMA. 2021;326(18):1840-1850
J Am Coll Cardiol. 2025;85(16):1618-1641

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Assessment of Hemodynamic Phenotype

LV-Dominant Shock	RV-Dominant Shock	Biventricular Shock
PCWP >15 mmHg Normal/mildly elevated CVP	Normal PCWP **CVP typically elevated**	
Aggressive IV loop diuretic decongestion	**Decongestion** **assuming preload-dependence and giving volume is overly simplistic**	Requires the most **nuanced approach**
	If CVP low, can give small fluid bolus with close monitoring	

Circulation. 2018;137(20):e578-e622
Lancet. 2024;404(10466):2006-2020
J Am Coll Cardiol. 2025;85(16):1618-1641

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Initial Intravenous Loop Diuretic Dosing

Diuretics are recommended to improve symptoms and reduce morbidity

Assess outpatient diuretic use
- On loop diuretics → 1-2.5x home dose
- Diuretic-naïve → 40-80mg IV daily FE

	Oral (mg)	Intravenous (mg)	Duration (hr)
Furosemide	40	20	6 – 8
Torsemide	20	Not available in U.S.	6 – 8
Bumetanide	1	1	4 – 6

J Card Fail. 2022;28(5):e1-e167
J Am Coll Cardiol. 2024;84(13):1241-1267
Abbreviations: FE, furosemide equivalent

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Dose Escalation Strategy

- Double dose if UOP does not measurably increase within 2 hours
  Consider ordering **urine sodium** (<50 mEq/L at 2 hours after diuretic correlated with poor diuretic response in PUSH-AHF trial)
- If dose response is brisk but transient, **increase frequency** to 3-4x daily **or utilize continuous infusions**
- Continue until reaching **400-500 mg FE per day**
- Consider **sequential nephron blockade** with a thiazide-type diuretic (e.g., metolazone) for refractory congestion
- **Ultrafiltration** for severe refractory congestion

J Am Coll Cardiol. 2024;84(13):1241-1267
Eur J Heart Fail. 2024;26(6):1347-1357

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Sequential Nephron Blockade

	Metolazone	Chlorothiazide
Class	Thiazide-like	True thiazide
Route	Oral only	Oral or IV
Site of action	Distal convoluted and proximal tubule	Distal convoluted tubule
Onset	~1 hr (slow, erratic absorption)	Oral: ~2 hrs IV: **15 minutes**
Duration	**12 – 24 hrs**	**6 – 12 hrs**
Dosing	Initial: 2.5 – 5 mg once, 30 min prior to loop (max 20 mg/day in 1-2 divided doses)	500 – 1000 mg IV once/twice daily
Efficacy at low eGFR	Retains efficacy at eGFR 20 mL/min due to proximal tubule action	Lose efficacy at eGFR 30-40 mL/min
Cost	$	$$$

IV chlorothiazide was not superior to oral metolazone when added to loop diuretics (consistently has shown comparable 24-hour urine output)

Pharmacotherapy. 2016;36(8):852-860
J Am Coll Cardiol. 2020;75(10):1178-1195
J Am Coll Cardiol. 2024;84(13):1241-1267

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Diuretic Pearls

- **Do NOT underdose diuretics** out of concern for hypotension
  - Utilize vasoactives if needed
- **Modest rises in creatinine (≤0.5 mg/dL) are expected** and are associated with better, not worse, outcomes
  - When to consider a true AKI (tubular injury):
    - SCr >1.5x baseline or >50% in eGFR
    - Rising NT-proBNP and lactate
    - Oliguria despite adequate diuretic doses
    - Persistent congestion
- **Ceiling dose = 160 – 200 mg IV** furosemide equivalent
  - Dose more frequently rather than larger single doses

J Card Fail. 2016;22(10):753-760
J Am Coll Cardiol. 2020;75(10):1178-1195
Nephrol Dial Transplant. 2024;40(1):10-18.

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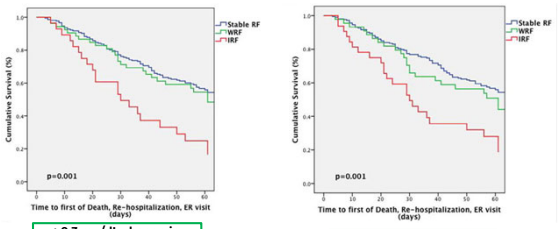

>0.3 mg/dL change in serum creatinine

≥20% change in eGFR

J Card Fail. 2016;22(10):753-760
Abbreviations: RF, renal function; WRF, worsening renal function; IRF, improvement in renal function

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Afterload-Modifying Agents

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Inodilators

- Dobutamine
- Milrinone

Pure vasodilators

- Nitroprusside
- Nitroglycerin

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Curr Heart Fail Rep. 2017;14(5):385-392

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Indications

Normotensive cardiogenic shock, especially if SVR elevated

Used as an **adjuvant to diuretics for relief of dyspnea** in patients admitted with acute decompensated HF (Class 2B recommendation)

- Lowest possible dose; shortest possible duration

Insufficient evidence to support superiority of any particular pure vasodilator

J Card Fail. 2022;28(5):e1-e167
J Am Coll Cardiol. 2025;85(16):1618-1641

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Feature	Nitroprusside	Nitroglycerin
Mechanism	Spontaneously releases NO → Activates GC → inc cGMP → vascular smooth muscle relaxation	Enzymatically converted to NO within vascular smooth muscle (same cGMP pathway)
Dosing	Start 0.3 mcg/kg/min Max dose 10 mcg/kg/min	Start 5-25 mcg/min Max dose 400 mcg/min ***non-weight based***
Primary vascular effect	**Balanced arterial/venous** vasodilator	**Predominantly venodilator** with modest vasodilation at higher doses (>100 mcg/min)
Afterload reduction	**Greater**	Moderate (less arteriolar effect)
Toxicity	**Cyanide toxicity** (doses >2 mcg/kg/min) **Thiocyanate toxicity** with prolonged use (especially with AKI/ESRD) **Methemoglobinemia**	Methemoglobinemia (rare; at very high doses)
Contraindication in ischemia	Not recommended in AMI **(coronary steal risk)**	Preferred in AMI **(improves collateral flow)**

J Appl Physiol. 2017;123(2):402-406
J Card Fail. 2022;28(5):e1-e167
Abbreviations: NO, nitric oxide; GC, guanylate cyclase; cGMP, cyclic guanosine monophosphate; AKI, acute kidney injury; ESRD, end-stage renal disease

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Inotropes

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Curr Heart Fail Rep. 2017;14(5):385-392

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Signs of Hypoperfusion ("Cold")

CI ≤ 2.2 L/min/m², MAP <65 mmHg, SBP <90 mmHg

Skin and extremities
- Cold, clammy, or mottled extremities
- Prolonged capillary refill time (>2 seconds)
- Weak or nonpalpable pulses

Neurologic
- Altered mentation
- Confusion
- Lethargy

Renal
- Oliguria (<30 ml/hr or <0.5 mL/kg/hr)
- Anuria

JAMA. 2021;326(18):1840-1850
J Am Coll Cardiol. 2025;85(16):1618-1641

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Receptor Overview

Receptor	Location	Activation - Effects	Inhibition - Effects
Alpha-1	Smooth muscle	Vasoconstriction	Vasodilation
Alpha-2	Smooth muscle, CNS	Inhibits release of norepinephrine in CNS – sedation, vasodilation	Hypertension, tachycardia
Beta-1	Heart	Chronotropy, dromotropy, inotropy	Bradycardia
Beta-2	Smooth muscle (blood vessels, lungs)	Vasodilation, bronchodilation	Vasoconstriction
Dopamine	Heart, kidney	Inotropy, dromotropy	
Vasopressin (V1)	Vascular smooth muscle	Vasoconstriction	Vasodilation
Vasopressin (V2)	Kidney	Sodium and water reabsorption	Diuresis, naturesis

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Inotropic Medications

Agent	MOA	Dosing	SVR	BP	CO	HR
Dobutamine	β1 (+++) β2 (++)	2-10 mcg/kg/min	↓↔	↓↔	↑↑	↑
Milrinone	PDE-3 Inhibitor	0.125-0.75 mcg/kg/min	↓↓	↓↓	↑↑	↔↑

J Am Coll Cardiol. 2025;85(16):1618-1641
Abbreviations: PDE, phosphodiesterase; MOA, mechanism of action; HR, heart rate

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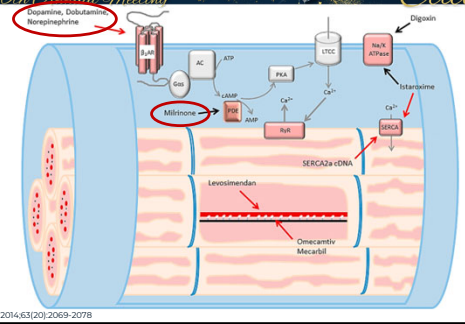

J Am Coll Cardiol. 2014;63(20):2069-2078

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Milrinone as Compared with Dobutamine in the Treatment of Cardiogenic Shock (DOREMI)

192 patients with cardiogenic shock (SCAI criteria)

- SBP <90 mm Hg with end-organ dysfunction
- Systemic and/or pulmonary congestion despite vasodilator/diuretic use
- ACS complicated by cardiogenic shock with CI <1.8 L/min/m² and LVEDP >18 mm Hg
- Clinical determination for need to augment CO

N Engl J Med. 2021;385:516-525
Abbreviations: ACS, acute coronary syndrome; LVEDP, left ventricular end diastolic pressure

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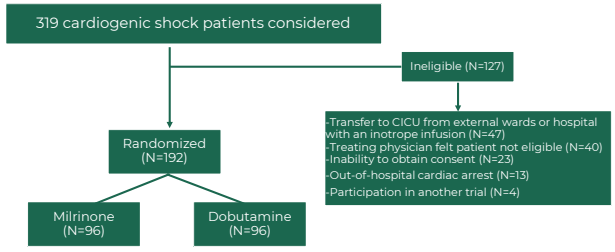
Randomization



N Engl J Med. 2021;385:516-525

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DOREMI Takeaways

Strengths

- Double-blinded, pragmatic design
- Clinical criteria to diagnose cardiogenic shock – reflects clinical practice
- Primarily SCAI C and D patients

Weaknesses

- Single-center study, limits generalizability
- Underpowered for smaller treatment effects
- Time to randomization from ICU admission was 17 – 24 hours; significant amount of time
- Dose adjustments based on physician judgement (no standardized protocol)

No significant differences in outcomes between milrinone and dobutamine

Challenges belief that dobutamine causes more dysrhythmias and milrinone causes more hypotension

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Vasopressors

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Curr Heart Fail Rep. 2017;14(5):385-392

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Vasopressors

- Epinephrine
- Norepinephrine
- Vasopressin
- Phenylephrine
- Dopamine

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Agent	Alpha-1	Beta-1	Beta-2	DA	Vasopressin	Clinical Effects
Norepinephrine	+++	++	0	0	0	SVR ↑↑ CO ↑
Epinephrine	+++	+++	++	0	0	SVR ↓ (<0.05 mcg/kg/min) SVR ↑↑ (≥0.05 mcg/kg/min) CO ↑↑
Phenylephrine	+++	0	0	0	0	SVR ↑ CO ↔/↓
Vasopressin	0	0	0	0	V1a (+++) V1b (++) V2 (++)	SVR ↑↑ CO ↔/↓
Dopamine (mcg/kg/min) -- 0.5 to 3 -- 5 to 10 -- 10 to 20	 0 + ++	 + ++ ++	 0 0 0	 ++ ++ ++	 0 0 0	 ↑ UOP CO ↑, SVR ↑ SVR ↑↑

J Am Coll Cardiol. 2025;85(16):1618-1641
Abbreviations: DA, dopamine; UOP, urine output

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Vasopressors

SOAP II trial (dopamine vs. norepinephrine)

- Significantly more arrhythmias with DA (24.1% vs. 12.4%) in shock
- Significantly higher 28-day mortality by Kaplan-Meier analysis in cardiogenic shock subgroup analysis (p=0.03)

OPTIMA-CC trial (epinephrine vs. norepinephrine)

- AMI-related cardiogenic shock
- Terminated early; significantly higher refractory shock with epinephrine (37% vs. 7%, p=0.008)

N Engl J Med. 2010;362(9):779-789
J Am Coll Cardiol. 2018;72(2):173-182

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Vasopressor Selection

Norepinephrine = standard of care for most patients
Titrate to MAP >65 mmHg

Phenylephrine discouraged as single first-line agent
(reflex bradycardia; CO reduction)

Scenario	Preferred Agent(s)	Rationale
Symptomatic bradycardia	Dopamine or epinephrine	Chronotropy
Dynamic LVOT obstruction	Phenylephrine or vasopressin	No inotropic stimulation
Refractory hypoxemia or acidosis	Vasopressin	Catecholamines may have attenuated efficacy
Pulmonary hypertension	Vasopressin	Lack of chronotropy Favorable PVR-SVR ratio

Circulation. 2021;143(15):e815-e829
Curr Opin Crit Care. 2021;27(4):426-432
Abbreviations: MAP, mean arterial pressure; LVOT, left ventricular outflow tract; PVR, pulmonary vascular resistance

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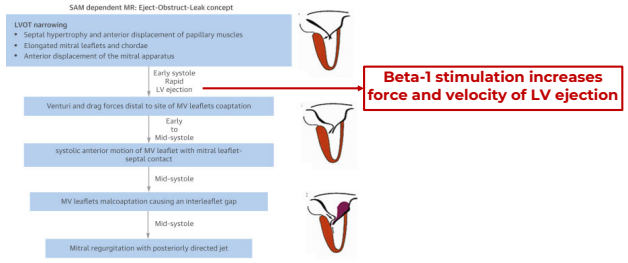
Left Ventricular Outflow Tract Obstruction



J Am Coll Cardiol. 2016;68(14):1505-1508

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Device Management

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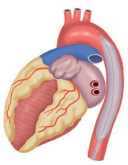
IABP



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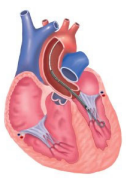

Fryer et al. *Chest.* 2019;156(5):1008-1021
Abbreviations: IABP, intra-aortic balloon pump

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Guideline Recommendations

2023 ACC/AHA/ACEP/NAEMSP/SCAI Guideline for the Management of Patients With Acute Coronary Syndromes: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines

Recommendations for MCS in Patients With ACS and Cardiogenic Shock
Referenced studies that support recommendations are summarized in the Online Data Supplement

COR	LOE	Recommendations
2a	B-R	1. In selected* patients with STEMI and severe or refractory cardiogenic shock, insertion of a microaxial intravascular flow pump is reasonable to reduce death.†
2a	B-NR	2. In patients with mechanical complication of ACS, short-term MCS devices are reasonable for hemodynamic stabilization as a bridge to surgery.‡,§
3: No benefit	B-R	3. In patients with AMI and cardiogenic shock, the routine use of intra-aortic balloon pump (IABP) or venoarterial extracorporeal membrane oxygenation (VA-ECMO) is not recommended due to a lack of survival benefit.‖,¶

2023 ESC Guidelines for the management of acute coronary syndromes

In patients with ACS and severe/refractory CS, short-term mechanical circulatory support may be considered.[402]	IIb	C
The routine use of an IABP in ACS patients with CS and without mechanical complications is not recommended.[399,405–407]	III	B

AHA/ACC/HFSA CLINICAL PRACTICE GUIDELINE

2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines

2a	B-NR	2. In patients with cardiogenic shock, temporary MCS is reasonable when end-organ function cannot be maintained by pharmacologic means to support cardiac function.[9–17]

Rao et al. *J Am Coll Cardiol.* 2025;85(22):2135-2237
Heidenreich et al. *Circulation.* 2022;145(18):e876-e894
Byrne et al. *Eur Heart J.* 2023;44(38):3720-3826

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Intra-Aortic Balloon Pump

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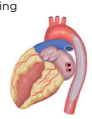
IABP Overview

Catheter-mounted balloon in the descending aorta

- Inflates during diastole, deflates during systole (counterpulsation)
- Augments **diastolic blood pressure** and **coronary perfusion**
- **Reduces LV afterload**

Device settings

- **Trigger mode**: inflation/deflation timed to ECG or to arterial pressure waveforms
  - Poor ECG quality, arrhythmias, or excessive tachycardia can impair timing, reducing effectiveness
- **Augmentation ratio**: typically 1:1 (mimics the cardiac cycle)
  - Weaning ratios are 1:2 or 1:3 before removal
- **Balloon volume**: 40 mL (50mL available)
  - Should be ~80-90% of the aortic diameter for optimal placement
- **Hemodynamic impact**: ~0.5 – 1.0 L/min
  - Depends on intrinsic ventricular function
  - Ineffective in pulseless rhythms (e.g., ventricular fibrillation)



J Am Coll Cardiol. 2015;65(19):e7-e26
Abbreviations: ECG, electrocardiogram

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IABP Anticoagulation

No definitive evidence guiding anticoagulation

Continuous balloon motion reduces thrombus risk (1:1)

- 1:2 and 1:3 augmentation ratios increase risk (more blood statis)
  - Can consider UFH

RCT of 153 IABP patients found no significant difference in limb ischemia between UFH and no-UFH groups

- Increased bleeding with UFH (14.1% vs. 2.4%)

ALTSHOCK-2 only used prophylactic-dose heparin unless therapeutic anticoagulation otherwise indicated

J Card Fail. 2023;29(3):304-374
J Am Coll Cardiol. 2025;85(16):1587-1597
Abbreviations: UFH, unfractionated heparin

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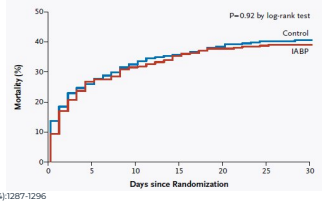
IABP-Shock II

- Acute NSTEMI or STEMI *complicated by* cardiogenic shock
- IABP + PCI (n = 300) vs. PCI alone (n = 298)
- 39.7% vs. 41.3% mortality



Thiele et al. *N Engl J Med.* 2012;367(14):1287-1296

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IABP-SHOCK II

Baseline Variable	No. of Patients	IABP	Control	Relative Risk (95% CI)	P Value for Interaction
		30-day mortality (%)			
Sex					0.61
Female	187	44.4	43.2	1.03 (0.74–1.43)	
Male	411	37.3	40.5	0.92 (0.72–1.18)	
Age					0.09
<50 yr	70	19.4	44.1	0.44 (0.21–0.95)	
50–75 yr	334	34.6	36.5	0.95 (0.71–1.27)	
>75 yr	194	53.7	50.0	1.07 (0.81–1.41)	
Diabetes					0.82
Yes	195	42.9	46.7	0.92 (0.67–1.26)	
No	399	37.2	38.9	0.96 (0.74–1.23)	
Hypertension					0.05
Yes	410	42.9	40.4	1.06 (0.84–1.34)	
No	183	28.9	43.0	0.67 (0.45–1.01)	
Type of MI					0.76
STEMI/LBBB	412	41.0	42.9	0.96 (0.77–1.21)	
Non-STEMI	177	37.5	38.3	0.98 (0.67–1.43)	
STEMI type					0.14
Anterior	216	35.4	43.7	0.81 (0.58–1.13)	
Nonanterior	196	48.3	42.2	1.16 (0.85–1.57)	

Thiele et al. *N Engl J Med.* 2012;367(14):1287-1296

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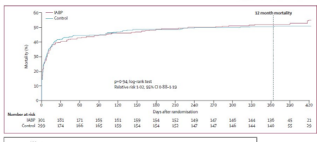
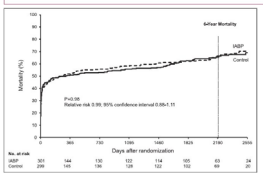
IABP-SHOCK II

12 months



6 years



Thiele et al. *Lancet*. 2013;382(9905):1638-1645
Thiele et al. *Circulation*. 2019;139(3):395-403

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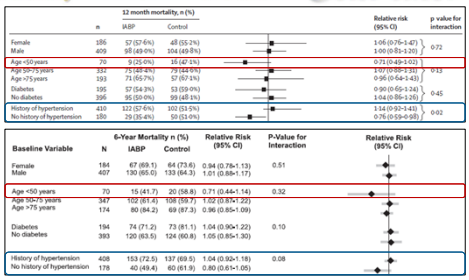
IABP-SHOCK II

12 months



6 years

Thiele et al. *Lancet*. 2013;382(9905):1638-1645
Thiele et al. *Circulation*. 2019;139(3):395-403

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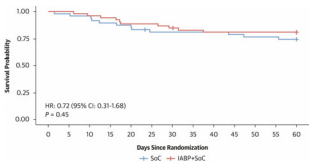
ALTSHOCK-2

- Prospective, multicenter, open-label RCT
- 101 patients randomized to early IABP + SOC vs. SOC alone
  - Acute decompensated HF complicated by cardiogenic shock
  - Excluded AMI as primary etiology
  - SCAI B (28%), C (57%), D (15%)
- Primary endpoint: survival or successful bridge to HRT at 60 days
  - No significant difference (IABP 81% vs. SOC 75%, CI 0.31-1.68, p=0.45)



J Am Coll Cardiol. 2025;85(16):1587-1597

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Impella

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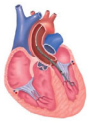
Impella Overview

Continuous axial flow pump
- Draws blood from LV and expels into ascending aorta

Key settings
- **Performance (P) levels**: P0 – P8/9
  - Increasing motor speeds and flow rates
  - P2 minimum
- **Flow rates by device**
  - Impella CP: 3.5 – 4.0 L/min
  - Impella 5.0/5.5: up to 5.0 – 6.2 L/min
- **Positioning**: inlet ~3.5 cm below aortic valve (CP/5.0) or ~5 cm (5.5)
  - Malpositioning causes suction events, hemolysis, reduced flow
- **SmartAssist technology**
  - Displays LV pressure waveform to differentiate:
    - Hypovolemia = negative diastolic pressure with normal systolic pressures
    - Malpositioning = negative diastolic and systolic pressures



JACC Cardiovasc Interv. 2023;16(14):1707-1720
J Card Fail. 2023;29(3):304-374

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Impella Anticoagulation

Anticoagulation **mandatory** due to shear force-induced coagulation activation and foreign body surfaces

Modes of anticoagulation:
- Purge solution heparin
  - Standard: UFH 50 U/mL in 5% dextrose
  - Controller automatically adjusts purge flow (2-30 mL/hr) to maintain purge pressure between 300-1000 mm Hg
  - Delivers variable systemic heparin dose (~8-10 units/kg/hr for an average patient)
- Systemic IV UFH
  - Often required to achieve anticoagulation targets in addition to purge

Monitoring targets
- aPTT: commonly 55-80 seconds
- Anti-Xa: 0.3-0.5 IU/mL (0.5-0.7 IU/mL if thrombosis suspected)
- ACT: 160-200 seconds (>250 seconds periprocedurally, used in PROTECT II)

Can use direct thrombin inhibitor (e.g., bivalirudin) if HIT suspected/confirmed

J Card Fail. 2023;29(3):304-374
J Am Coll Cardiol. 2022;79(19):1949-1962
Abbreviations: aPTT, activated partial thromboplastin time; ACT, activated clotting time; HIT, heparin-induced thrombocytopenia

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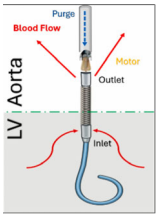
Purge Management

Purge solution flows from the motor housing in the opposite direction of blood flow, creating a **pressure barrier**
- Prevents blood from entering motor compartment

UFH 50 U/mL in 5% dextrose is recommended from manufacturer
- 25 U/mL or 12 U/mL available, can be used if bleeding a concern
  - Similar therapeutic aPTT and thrombotic event rates (low quality evidence)

Purge **must be dextrose based**
- Saline is corrosive to the pump's internal motor
- D5W preferred (less viscous, allows more UFH delivered systemically)
  - D10W/D20W more viscous → less systemic UFH delivery

Normal purge pressure = 300-1000 mmHg
- If persistently elevated (>800 mmHg) with decreased flow rates, consider occlusion or pump thrombosis



J Am Coll Cardiol. 2022;79(19):1949-1962
J Card Fail. 2023;29(3):304-374

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Use of Bicarbonate-Based Purge Solutions

Can be used because it provides two key protective mechanisms:
- Ionic charge-based antithrombotic properties
  - Sodium bicarbonate (25 mEq/L) has similar ionic charge to UFH
- Protein-stabilizing effects

Mimics heparin's role without contributing to systemic anticoagulation

Not yet standard practice, active area of investigation
- Single-center retrospective study found similar rates of pump thrombosis (16.3% vs. 12.2%, p=0.58) and significantly lower bleeding rates (27.9% vs. 65.3%, p<0.05)

J Card Fail. 2023;29(3):304-374
Ann Pharmacother. 2023;57(6):646-652

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Pump Thrombosis

Diagnosis suspected if:
- Elevated purge pressures (consistently >800 mmHg)
- Decreased purge flow rates
- **Hemolysis**:
  - Elevated LDH (2.5x ULN)
  - Elevated plasma-free Hgb (>20 mg/dL)
  - Decreased haptoglobin
  - Hematuria
  - Indirect hyperbilirubinemia

J Am Coll Cardiol. 2022;79(19):1949-1962
JACC Cardiovasc Interv. 2023;16(14):1707-1720

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Pump Thrombosis Management

Rule out other causes of hemolysis:
- Malpositioning of device (most common cause)
- Hypovolemia: causes suction events
- RV failure: reduces LV preload
- Reducing pump speed

If pump thrombosis confirmed:
- **Device exchange** (safest definitive intervention)
- Ensure **systemic anticoagulation** is therapeutic
- Evaluate for HIT if thrombocytopenia develops
  - Challenging given several confounders
- Alteplase (tPA) in purge solution (0.04 or 0.08 mg/mL in sterile water) as salvage
  - Hemorrhagic stroke and serious bleeding risk

J Card Fail. 2023;29(3):304-374
JACC Cardiovasc Interv. 2023;16(14):1707-1720
ASAIO J. 2025;71(12):e200-e204

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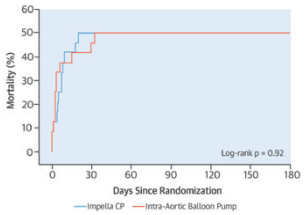
IMPRESS

- Acute MI with STEMI *complicated by* severe cardiogenic shock
  - All patients were mechanically ventilated and post-cardiac arrest
- Impella CP® vs. IABP
  - n = 24 in both groups



Ouweneel et al. *J Am Coll Cardiol.* 2017;69(3):278-287

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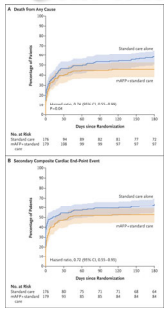
DanGer SHOCK

International, multicenter, open-label RCT

360 patients randomized 1:1 to Impella CP® + SOC vs. SOC alone
- STEMI complicated by cardiogenic shock
- Shock onset to randomization ≤24 hours
- Without suspected anoxic brain injury

Primary outcome: all-cause mortality at 180 days
- Significantly lower in Impella group (45.8% vs. 58.5%, CI 0.55-0.99, p=0.04)
- 7% absolute reduction at 30 days → 12.7% at 180 days
- Survival benefit sustained for up to 10 years

Moderate/severe bleeding, limb ischemia, and initiation of RRT all significantly higher in Impella group



N Engl J Med. 2024;390:1382-1393
Am J Cardiol. 2025;236:30-33

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Literature Summary

	Patients	Intervention	Outcome
IABP-SHOCK II (2012)	NSTEMI/STEMI	IABP + PCI vs. PCI alone	↔ overall mortality at 30d, 12 mos. and 6 years IABP: ↓ mortality at 30d if <50 yo. ↓ mortality at 12 mos. if no HTN
IMPRESS (2017)	STEMI	Impella CP® vs. IABP	↔ mortality at 30d and 6 mos.
DanGer Shock (2024)	STEMI	Impella CP® + SOC vs. SOC	↓ mortality at 180d
ALTSHOCK-2 (2025)	ADHF-CS	IABP + SOC vs. SOC	↔ mortality at 60d

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Contraindications to MCS Devices

IABP	Impella
• Severe PVD • Moderate-to-severe AR • Aortic disease/dissection • Abdominal aortic aneurysm • Tachyarrhythmias	• LV thrombus • Mechanical aortic valve • Severe AS • Moderate-to-severe AR • Severe PVD • Inability to anticoagulate

Fryer et al. *Chest.* 2019;156(5):1008-1021
Geller et al. *Circulation.* 2022;146:e50-e68
Abbreviations: PVD, peripheral vascular disease; AR, aortic regurgitation; LV, left ventricle; AS, aortic stenosis

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Complications

	IABP	Impella
Hemolysis	0.7 – 7.2%	10 – 46%
Limb ischemia	0.3 – 42%	0.07 – 10%
Major bleeding	0.8 – 47%	0.05 – 54%
Stroke	1 – 7%	2.4 – 6.3%

Subramaniam et al. *Cardiol Ther.* 2019;8:211-28

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Extracorporeal Life Support

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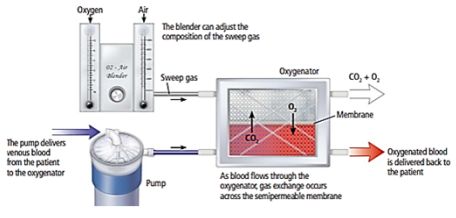
ECMO Review



Cleve Clin J Med. 2016;83(5):373-384
Abbreviations: ECMO, extracorporeal membrane oxygentation

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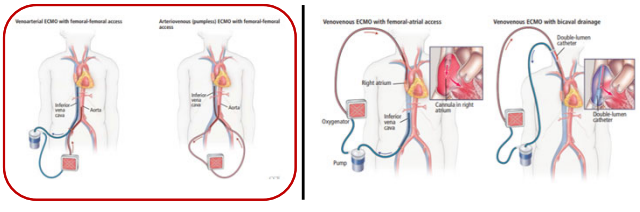
Venoarterial vs. Venovenous



Cleve Clin J Med. 2016;83(5):373-384

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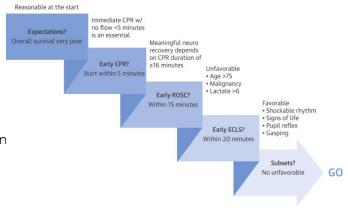
Selection Criteria (VA-ECMO)

- Cardiogenic shock refractory to medical therapy and/or MCS
  - Potentially reversible cause (e.g., acute fulminant myocarditis, AMI with planned revascularization, postcardiotomy shock)
- Refractory cardiac arrest (ECPR)
  - Witnessed arrest, shockable rhythm, no-flow time <5 minutes, early ECLS initiation within ~20 minutes
- Bridge to transplant or durable LVAD



Reversibility | **Survivability** | **Meaningful Recovery**

Circulation. 2017;136(16):e232-e268
J Am Coll Cardiol. 2019;73(6):698-716
Abbreviations: ECPR, extracorporeal cardiopulmonary resuscitation; LVAD, left ventricular assist device

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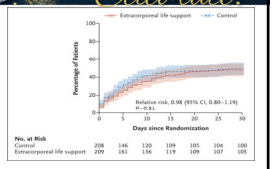
ECLS-SHOCK

- AMI *complicated by* cardiogenic shock
- ECLS + SOC vs. SOC alone (n = 417)
  - STEMI: ~67% of patients in each group
  - Impella CP: ~12% of patients in control group



	ECLS	SOC	RR (CI)
PV complications needing intervention	23 (11)	8 (3.8)	2.86 (1.31 – 6.25)
Moderate or severe bleeding	49 (23.4)	20 (9.6)	2.44 (1.50 – 3.95)

Thiele et al. *N Engl J Med* 2023; 389:1286-1297
Abbreviations: SOC, standard of care; PV, peripheral vascular

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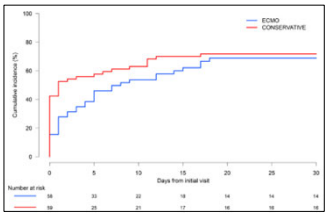
ECMO-CS

- Rapidly deteriorating or severe cardiogenic shock
  - Vasopressors to maintain MAP >50 mm Hg *and*
  - LVEF < 35% or LVEF 35 – 55% w/ severe MR or AS
- VA-ECMO vs. early conservative therapy (n = 117)
- STEMI: ~50% of patients in each group



Ostadal et al. *Circulation*. 2023;147:454-464

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Pharmacotherapy in ECMO

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Pharmacokinetic Considerations

Highly lipophilic (high log P) and **highly protein-bound** medications are most susceptible to adsorption

Volume of distribution is increased

- Circuit priming volume, hemodilution, inflammatory responses

Altered clearance

- Critical illness-related changes in hepatic and renal blood flow

Pharmacotherapy. 2019;39(3):355-368

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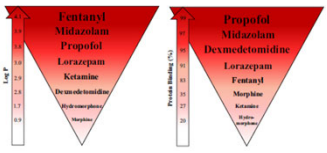
Analgesia and Sedation

- Fentanyl and morphine often used
  - **Hydromorphone** is a favorable alternative (low lipophilicity and protein binding)
- Light sedation with nonbenzodiazepine preferred when feasible
  - **Dexmedetomidine** may be favorable (higher doses often required)



At ECLS discontinuation, dose reductions should be anticipated!

Pharmacotherapy. 2019;39(3):355-368

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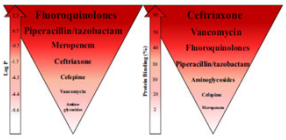
Antimicrobials

- Infectious complications in ~21% of ECLS patients (30.6 episodes per 1000 ECLS days)
  - Higher rates when ECLS >14 days (52% vs. 13%)
- Beta-lactams = hydrophilic with low-moderate protein binding
  - PK changes likely driven by critical illness rather than circuit sequestration
  - Prolonged/continuous infusion may help optimize time above MIC
- Vancomycin and aminoglycosides not significantly altered by ECLS circuits
  - Increased Vd may lead to insufficient AG peak concentrations (higher initial doses may be required)



Pharmacotherapy. 2019;39(3):355-368
Abbreviations: AG, aminoglycoside

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Anticoagulation

ELSO guidelines available to standardize and improve the quality of ECMO and ECLS
- Position unfractionated heparin as the primary anticoagulant

Anticoagulation targets generally less aggressive
- Pilot RCT (31 patients) using low-dose heparin (500 units/hr, aPTT <45s) found similar rates of thrombotic/bleeding events compared with aPTT 50-70s

Bivalirudin emerging as a potential agent; key considerations:
- Option when HIT suspected/confirmed
- No reversal agent
- Needs renal adjustment
- No RCTs exist comparing bivalirudin and unfractionated heparin

Blood. 2016;128:3822
Pharmacotherapy. 2019;39(3):355-368
Abbreviations: ELSO, extracorporeal life support organization

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Unfractionated Heparin vs. Bivalirudin

	UFH	Bivalirudin
Mechanism	Indirect thrombin inhibition (requires ATIII)	Direct thrombin inhibition (ATIII-independent)
Monitoring	aPTT, ACT, or anti-Xa	aPTT (goal 50-60s)
HIT risk	Present (~0.36% in VA-ECMO)	None
Reversal agent	Protamine	None available
Cost	Lower	Higher
Pericardial blood stagnation	Not affected	Diminished activity possible due to proteolysis

Crit Care Med. 2021;49(7):1129-1136
Pharmacotherapy. 2023;43(10):1084-1093

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Key Takeaways

Management of cardiogenic shock varies tremendously given patient-specific factors

Choice of pharmacologic agent depends on hemodynamics and clinical scenario

Mechanical support devices require careful attention and consistent monitoring to avoid adverse events

Altered pharmacokinetics of medications during ECMO needs to be considered to mitigate therapeutic effectiveness

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Key Pharmacy Technician Takeaways

Patients may require high doses of vasopressors for extended periods of time
- Concentrated vasopressors made in IV room made be required

Therapies change often given clinical scenarios

Concentrations matter for purge solutions
- UFH: 50 U/mL in 5% dextrose, sometimes 25 or 12.5 U/mL
- Sodium bicarb: 25 mEq/L

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Questions?

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Sparkle Shine Celebrate!
Hemodynamics Under Fire: Pharmacologic and Device-Based Management of Cardiogenic Shock in the Intensive Care Unit
Kyle Volland, PharmD, BCCCP
Email: kyle.volland95@gmail.com
Instagram: @icupharmdkyle
Thank you!

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