Emergency Response for the Pharmacist: Cardiac Arrest Management

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OhioHealth Grant Medical Center

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Objectives

- Pharmacists:
  - Discuss the evidence and practical considerations for the use of pharmacologic therapy in cardiac arrest
  - Define the role of the pharmacy department in promoting quality patient care during cardiac arrest
- Pharmacy Technicians:
  - Define the role of the pharmacy department in promoting quality patient care during cardiac arrest

Financial Disclosure / CE Accreditation

- The speakers and planners have indicated that they do not have any financial interest or relationship with any defined commercial interest

ACPE	
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For questions regarding Pharmacy CE, contact Monica Climer or Jamie Summerlin

Introduction

The American Heart Association (AHA) updated the Guidelines for Cardiopulmonary Resuscitation (CPR) and Emergency Cardiovascular Care in 2020

Quality chest compressions and early defibrillation remain the mainstay of cardiac arrest treatment

Pharmacologic therapy is emphasized in cardiac arrest despite limited evidence

Panchal AR, et al. *Circulation*. 2020;142(suppl 2):S366-S468.

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Class of Recommendation

Class I	Strong Recommendation Benefit >>> Risk
Class IIa	Moderate Recommendation Benefit >> Risk
Class IIb	Weak Recommendation Benefit ≥ Risk
Class III: No Benefit	Moderate Recommendation Benefit = Risk
Class III: Harm	Strong Recommendation Risk > Benefit

Panchal AR, et al. *Circulation*. 2020;142(suppl 2):S366-S468.

Level of Evidence

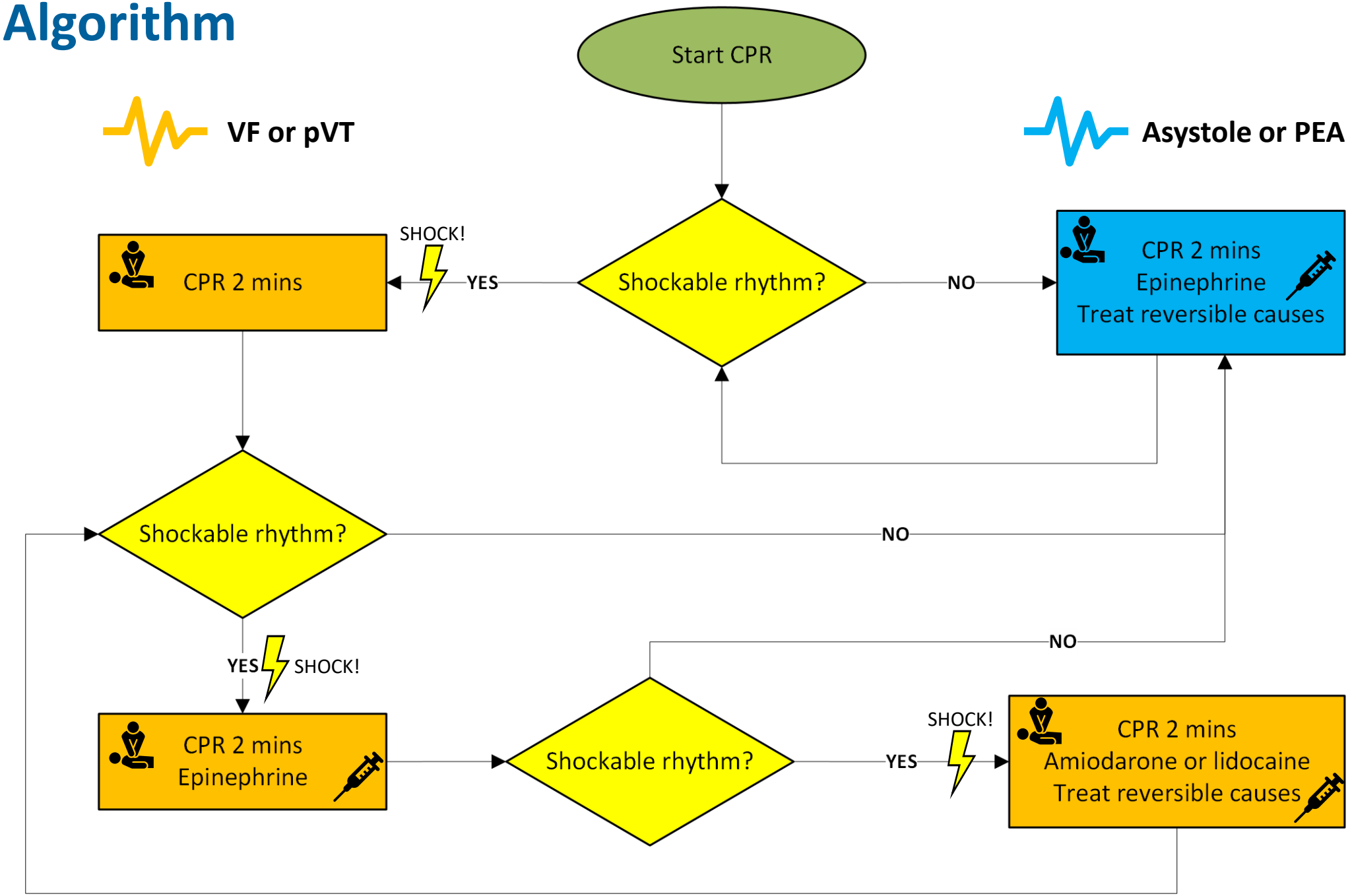
Level A	High-quality evidence from >1 RCT
Level B-R	Moderate-quality evidence from ≥1 RCT
Level B-NR	Moderate-quality evidence from nonrandomized studies, observational studies, or registry studies
Level C-LD	Randomized or nonrandomized observational or registry studies with limitations of design or execution
Level C-EO	Expert opinion based on clinical experience

Panchal AR, et al. *Circulation*. 2020;142(suppl 2):S366-S468.

Patient Case

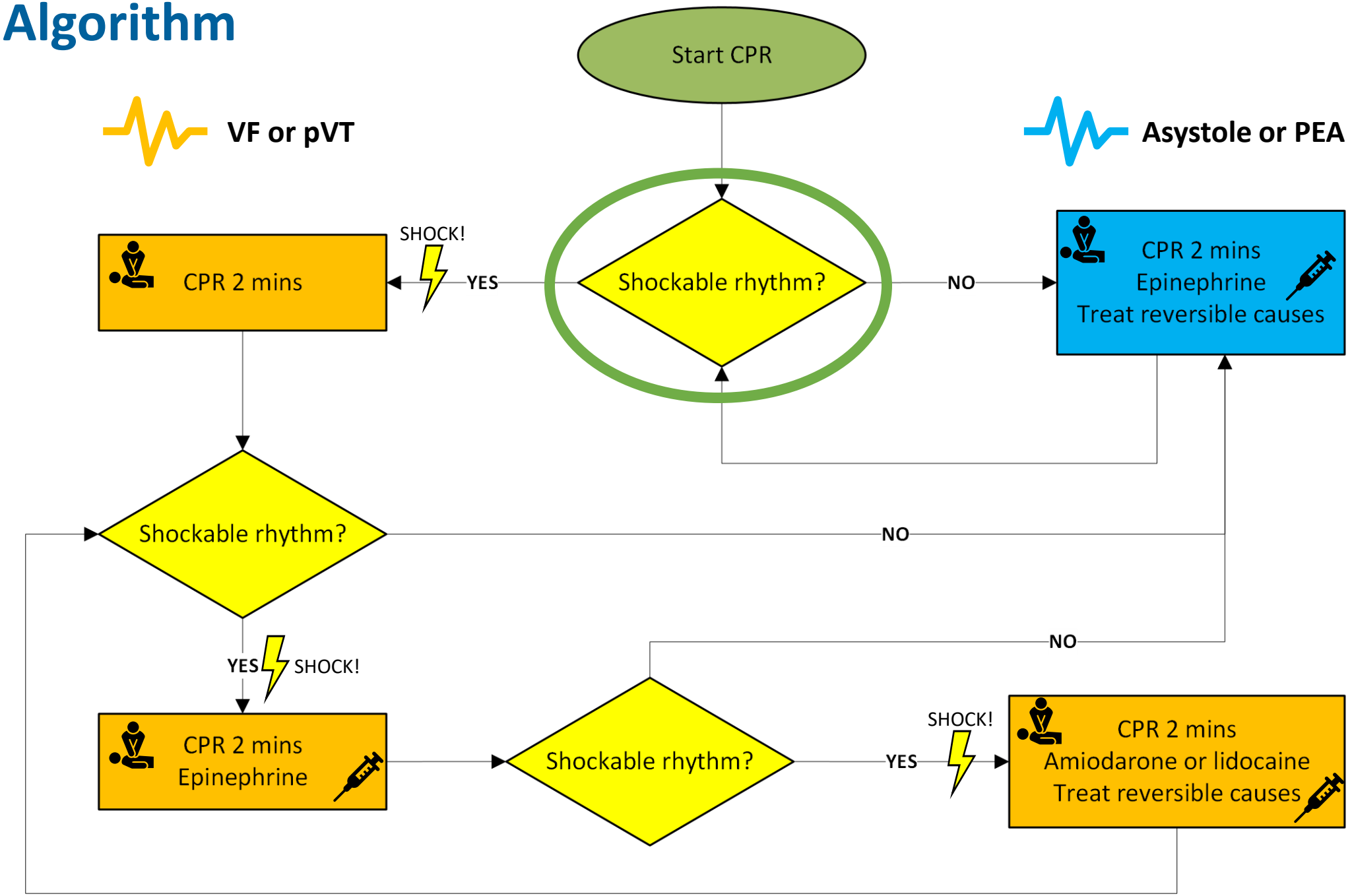
- 63 YOM was found on the floor at home by his wife. He was unconscious and unresponsive. She called 911 and began CPR.
- EMS arrives and the patient is found to have the following rhythm:

ACLS Algorithm



Adapted from: Panchal AR, et al. *Circulation*. 2020;142(suppl 2):S366-S468.

ACLS Algorithm



Adapted from: Panchal AR, et al. *Circulation*. 2020;142(suppl 2):S366-S468.

Epinephrine

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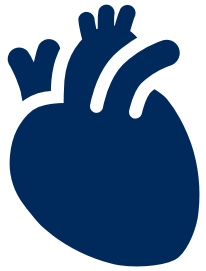
Epinephrine



Beneficial effects in cardiac arrest:
Alpha-adrenergic stimulation → increased coronary perfusion pressure and cerebral perfusion pressure during CPR

Value of beta-adrenergic effects are controversial
Increased myocardial stress
Reduced subendocardial perfusion

Link MS, et al. *Circulation*. 2015;132:S444-S464.

Epinephrine

Indications & Dosing	Cardiac arrest	1 mg IVP every 3-5 mins
	Hypotension & Symptomatic bradycardia	1-10 mcg/min IV; titrate to effect
	Anaphylaxis	0.2-0.5 mg IM; repeat every 5-15 mins
Crash Cart	• Epinephrine 1 mg/10 mL syringes • Epinephrine 1 mg/mL multidose vial (30 mL)	
Practical Considerations	• May use the multidose vial to make more syringes (dilute syringe to 1 mg/10 mL) or compound epinephrine IVPB (4 mg/250 mL) • Must use 1 mg/mL for IM administration	

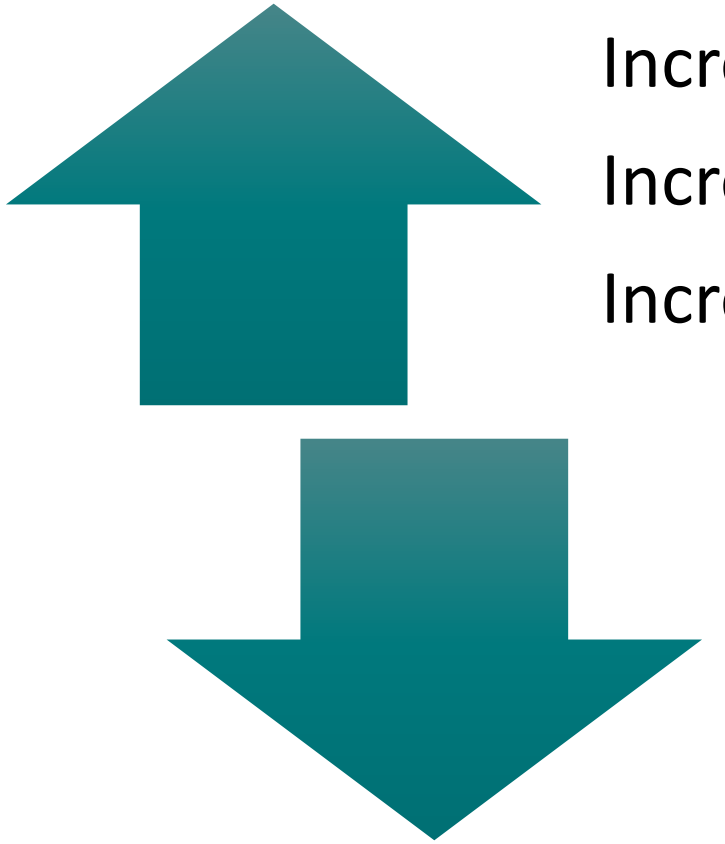
Panchal AR, et al. *Circulation*. 2020;142(suppl 2):S366-S468.

PARAMEDIC2 Trial 2018

Study Design	Multicenter, double-blind, randomized controlled trial	
Population	8014 patients with out-of-hospital cardiac arrest (OHCA)	
Interventions	Epinephrine (n=4015) 1 mg IVP every 3-5 mins	Placebo (n=3999)
Results	• Epinephrine increased rate of 30-day survival (epinephrine 3.2% vs. placebo 2.4%, p=0.02) • No difference in survival to hospital discharge with favorable neurologic outcome (epinephrine 2.2% vs. placebo 1.9%, 95% CI 0.86-1.61) • Severe neurologic impairment more common at hospital discharge in epinephrine group (epinephrine 31% vs. placebo 17.8%)	

Perkins GD, et al. *N Engl J Med*. 2018;379:711-721.

Epinephrine



Increased survival to hospital admission

Increased ROSC

Increased 30-day survival

No increase in good neurologic outcome

ROSC: return of spontaneous circulation

Jacobs IG, et al. *Resuscitation*. 2011;82:1138-1143.
Perkins GD, et al. *N Engl J Med*. 2018;379:711-721.

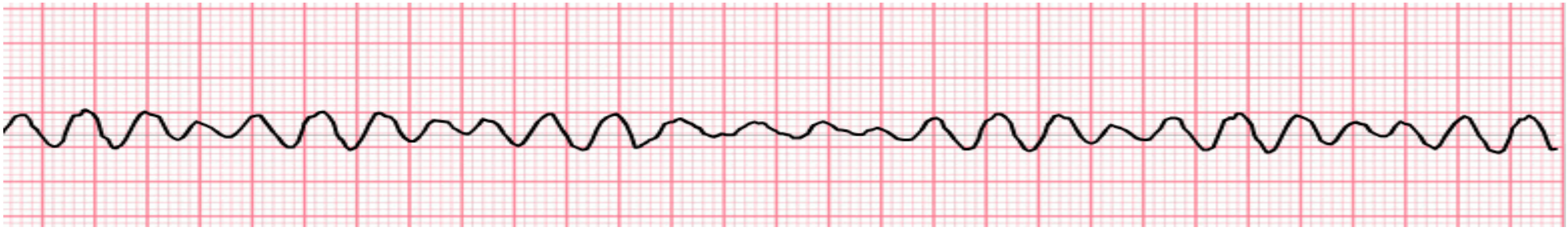
AHA 2020 Recommendations

- Recommend epinephrine in cardiac arrest (Class I, LOE B-R)
- Epinephrine 1 mg every 3-5 mins is reasonable for cardiac arrest (Class IIa, LOE B-R)
- Timing of epinephrine:
  - **Nonshockable rhythm:** as soon as feasible (Class IIa, LOE C-LD)
  - **Shockable rhythm**: after failing defibrillation (Class IIb, LOE C-LD)
- Vasopressin offers no advantage over epinephrine (Class IIb, LOE C-LD)

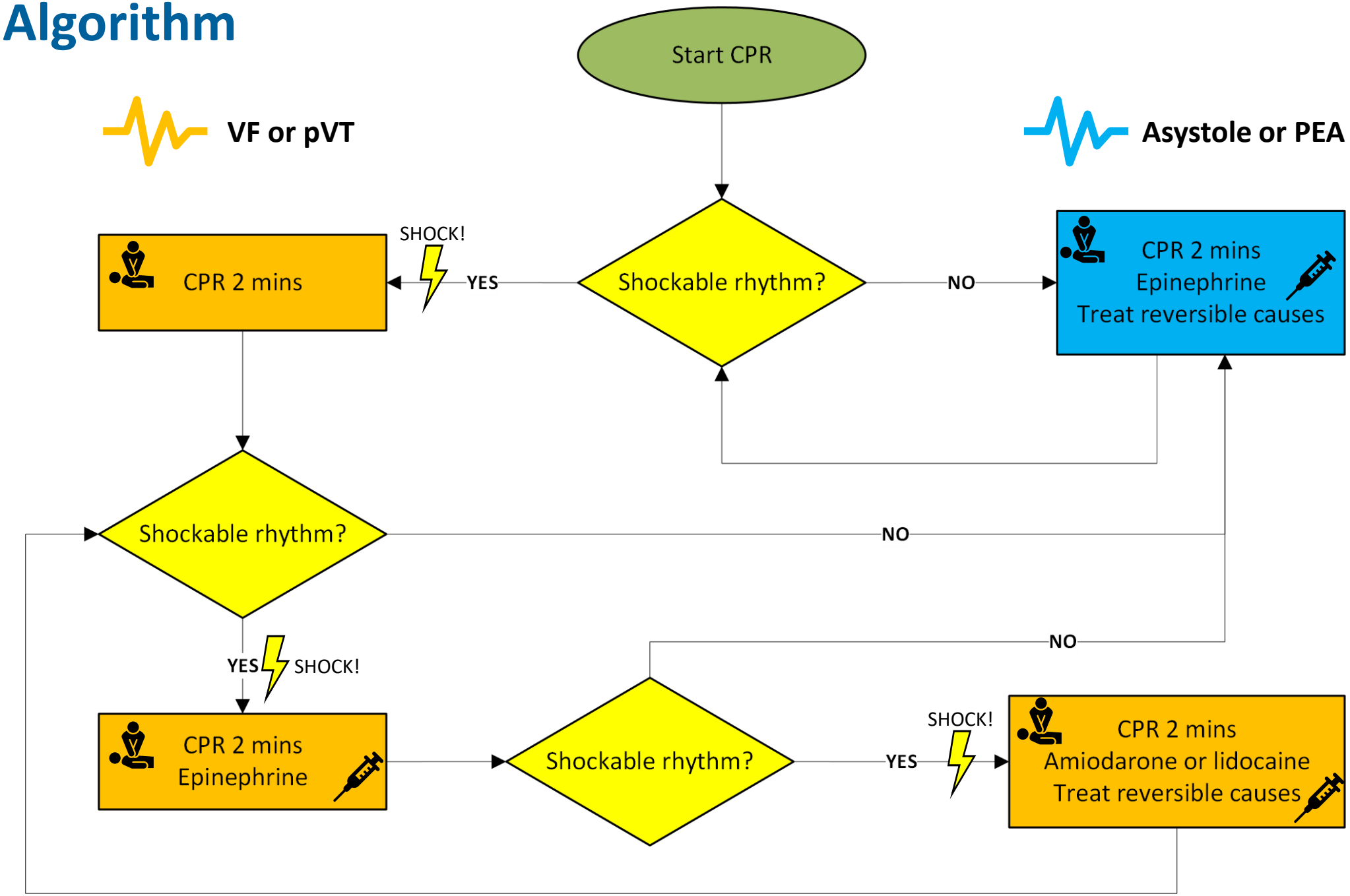
Panchal AR, et al. *Circulation*. 2020;142(suppl 2):S366-S468.

Patient Case (continued)

- Patient arrives in the ED. EMS established IV access and intubated the patient prior to arrival.
- Patient was shocked three times and received epinephrine 1 mg IVP prior to arrival. The following rhythm is on the monitor:



ACLS Algorithm



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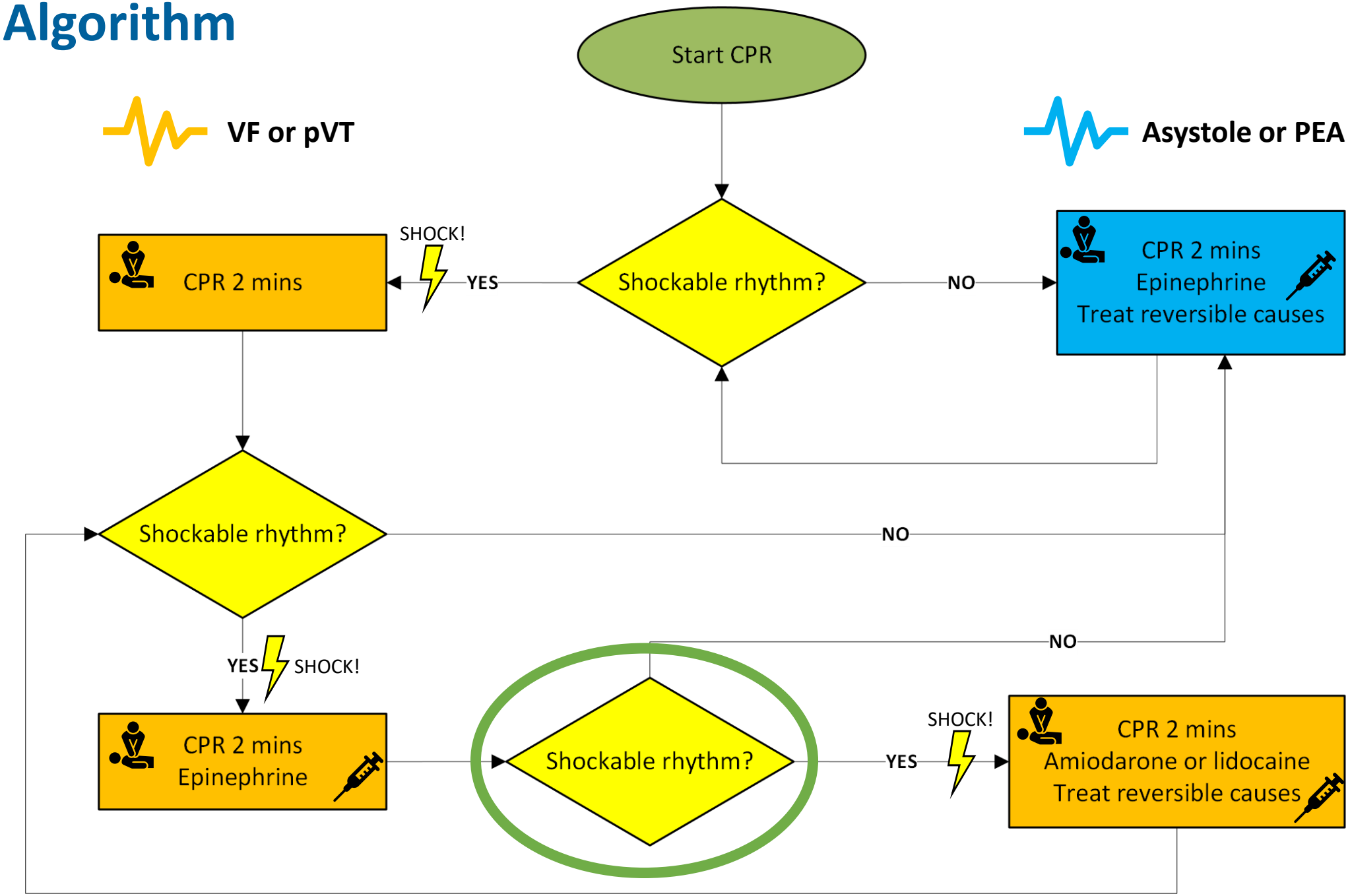
ACLS Algorithm



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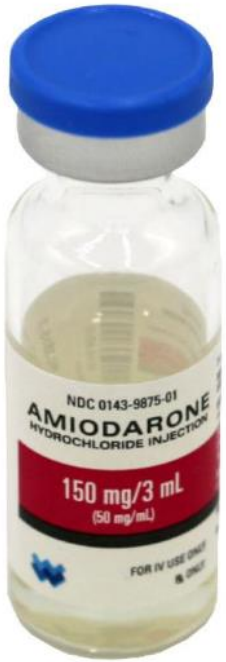
Antiarrhythmic Drugs



Antiarrhythmic Drugs

Used for refractory VF or pVT

Facilitate restoration and maintenance of an organized perfusing rhythm

Lidocaine and amiodarone are the most used antiarrhythmics in cardiac arrest

Link MS, et al. *Circulation*. 2015;132:S444-S464.

Amiodarone

Indications & Dosing	pVT VF	300 mg IVP; may repeat 150 mg IVP once
		Upon ROSC: 1 mg/min for 6 hours, then 0.5 mg/min thereafter
	Stable VT Atrial fibrillation SVT	150-300 mg IV bolus over 10 mins, then 1 mg/min for 6 hours, then 0.5 mg/min thereafter
Crash Cart	• Amiodarone 150 mg/3 mL vials • Amiodarone 360 mg/200 mL IV premix	
Practical Considerations	• 0.22-micron filter required, stocked in crash cart • Bolus from bag if patient is stable, administer undiluted IVP if patient is pulseless • May cause hypotension or bradycardia	

SVT: supraventricular tachycardia

Panchal AR, et al. *Circulation*. 2020;142(suppl 2):S366-S468.

Lidocaine

Indications & Dosing	pVT VF	1-1.5 mg/kg IVP (max 100 mg); may repeat 0.5-0.75 mg/kg IVP
		Upon ROSC: 1-4 mg/min IV infusion
Crash Cart	• Lidocaine 2% 100 mg/5 mL syringe	
Practical Considerations	• Added back to the ACLS algorithm in 2018 as an equivalent alternative to amiodarone	

Panchal AR, et al. *Circulation*. 2020;142(suppl 2):S366-S468.

ALIVE Study 2002

Study Design	Multicenter, double-blind, randomized controlled trial	
Population	347 patients with non-traumatic OHCA & recurrent VF or VF after 4 shocks + epinephrine	
Interventions	Amiodarone (n=180) 5 mg/kg IVP, then 2.5 mg/kg IVP	Lidocaine (n=167) 1.5 mg/kg IVP, then 1.5 mg/kg IVP
Results	• Amiodarone increased survival to hospital admission (amiodarone 22.8% vs. lidocaine 12%, p=0.009) • No difference in survival to hospital discharge (amiodarone 5% vs. lidocaine 3%, p=0.34)	

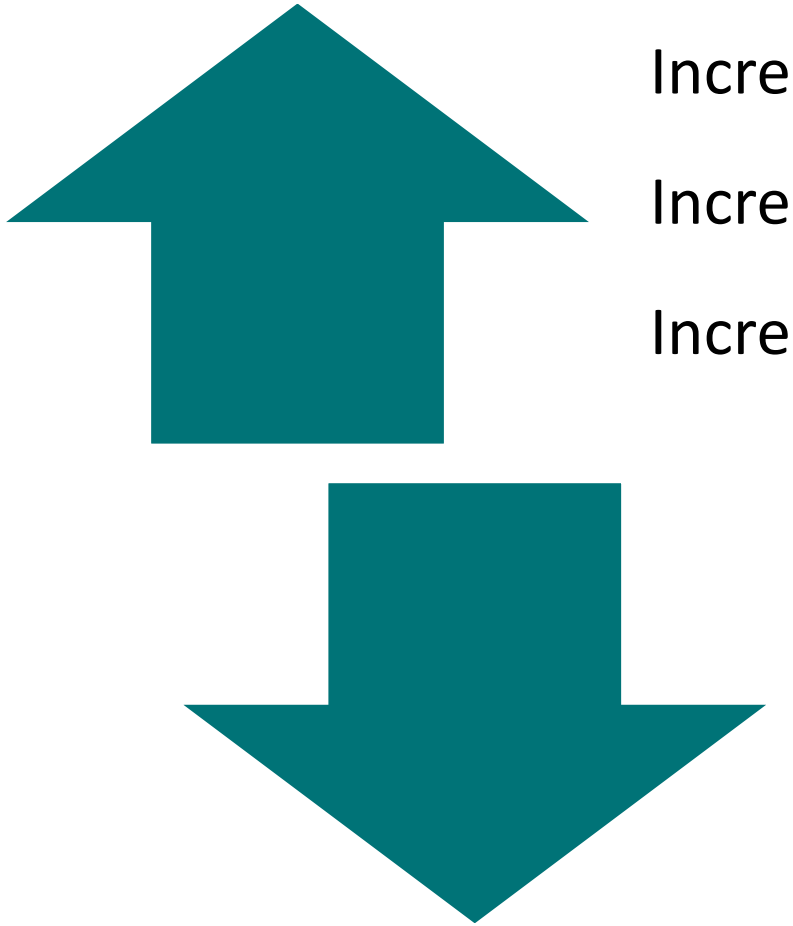
Dorian P, et al. *N Engl J Med*. 2002;346:884-890.

ROC-ALPS Study 2016

Study Design	Multicenter, double-blind, randomized controlled trial		
Population	3026 patients with non-traumatic OHCA and shock-refractory VF/pVT		
Interventions	Amiodarone (n=974) 300 mg IVP, then 150 mg IVP	Lidocaine (n=993) 120 mg IVP, then 60 mg IVP	Placebo (n=1059)
Results	• No significant difference in survival to hospital discharge (amiodarone 24.4% vs. lidocaine 23.7% vs. placebo 21%) • Significantly higher survival rate in amiodarone and lidocaine groups vs. placebo in witnessed arrest • Significantly higher survival to hospital admission in amiodarone and lidocaine groups vs. placebo (amiodarone 45.7% vs. lidocaine 47% vs. placebo 39.7%) • Neurologic outcomes were similar between groups		

Kudenchuk PJ, et al. *N Engl J Med*. 2016;374(18):1711-1722.

Amiodarone & Lidocaine



Increased survival to hospital admission

Increased ROSC

Increased survival in witnessed cardiac arrest

No increase in survival to hospital discharge

No increase in good neurologic outcome

Dorian P, et al. *N Engl J Med*. 2002;346:884-890.
Kudenchuk PJ, et al. *N Engl J Med*. 2016;374(18):1711-1722.

AHA 2020 Recommendations

- Consider amiodarone or lidocaine for VF/pVT unresponsive to defibrillation (Class IIb, LOE B-R)

- Antiarrhythmics may be particularly useful in witnessed cardiac arrest (Class IIb, LOE B-R)

Panchal AR, et al. *Circulation*. 2020;142(suppl 2):S366-S468.

Magnesium Sulfate

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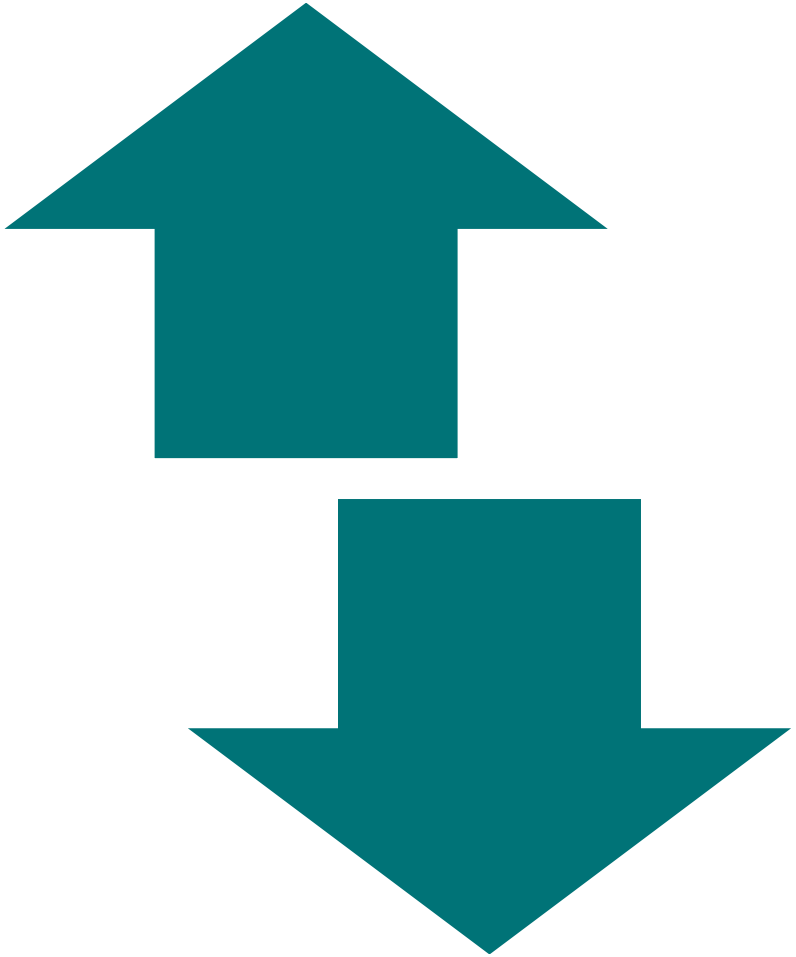
Magnesium Sulfate

Indications & Dosing	Torsades de pointes	1-2 g IV over 10-20 mins
	pVT VF	1-2 g IV over 1-2 mins
Crash Cart	• Magnesium sulfate 500 mg/mL (2 mL) vials	

Practical Considerations	• Must dilute prior to administration
	  • Dilute 1 g → 10 mL with 0.9% NaCl
	  • Dilute 2 g → 20 mL with 0.9% NaCl	

Link MS, et al. *Circulation*. 2015;132:S444-S464.

Magnesium Sulfate



No increase in ROSC

No increase in survival to hospital discharge

No increase in good neurologic outcome

Link MS, et al. *Circulation*. 2015;132:S444-S464.

AHA 2020 Recommendations

- Routine use of magnesium for cardiac arrest is not recommended (Class III: No Benefit, LOE B-R)
- Magnesium is recommended for cardiac arrest with severe hypomagnesemia (Class I, LOE C-LD)
- Consider magnesium for the treatment of torsades de pointes (Class IIb, LOE C-LD)

Panchal AR, et al. *Circulation*. 2020;142(suppl 2):S366-S468.

Assessment Question

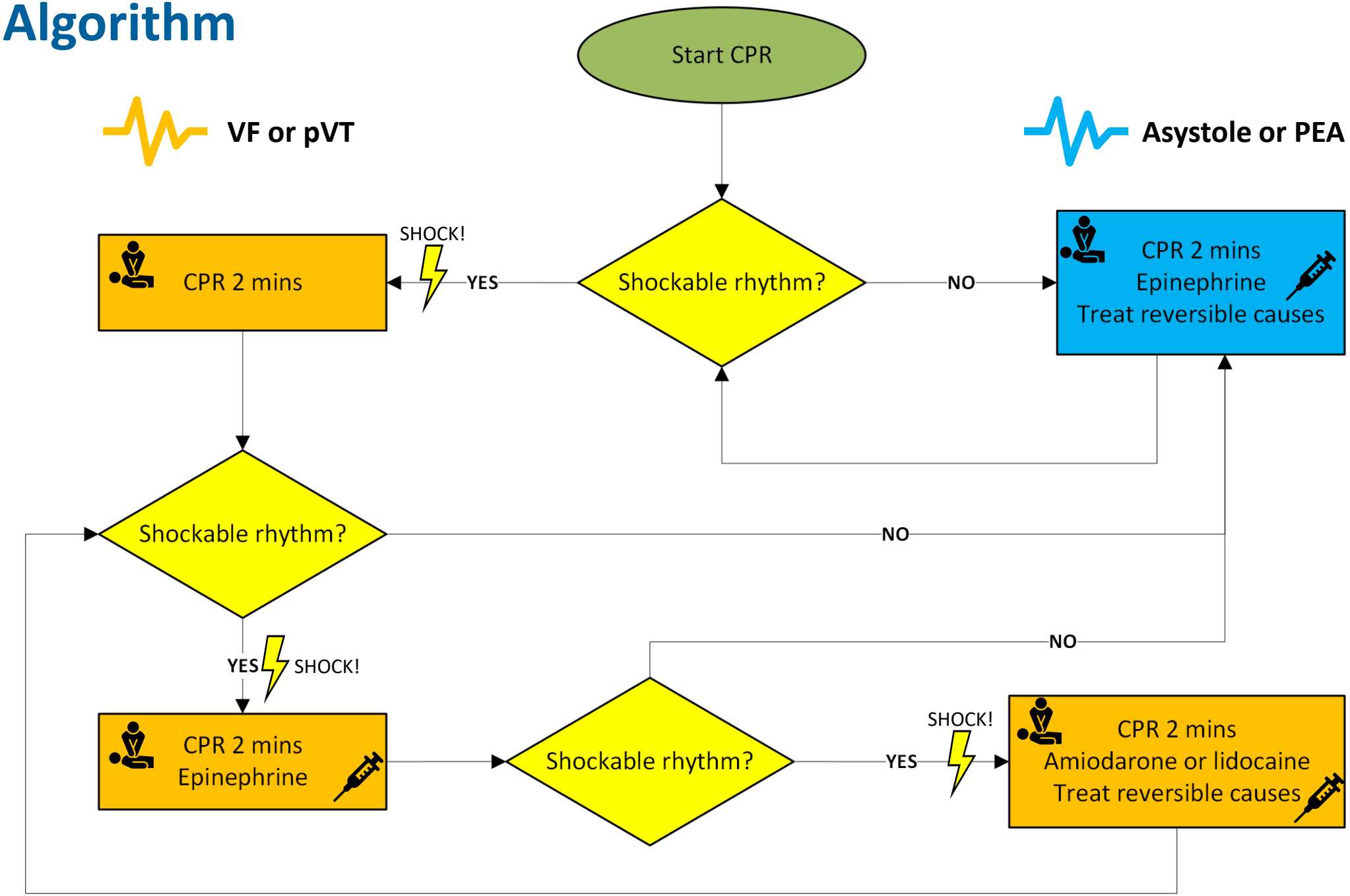
Which of the following statements is true about antiarrhythmic drugs for ventricular fibrillation or pulseless ventricular tachycardia?

A. Amiodarone and lidocaine are considered equivalent
B. Amiodarone is the preferred agent
C. Lidocaine is the preferred agent
D. Magnesium sulfate is the preferred agent

Patient Case (continued)

- Patient received amiodarone 300 mg IVP, was shocked again, and received another dose of epinephrine 1 mg IVP.
- The patient does not have a pulse. The monitor displays the following rhythm:

ACLS Algorithm



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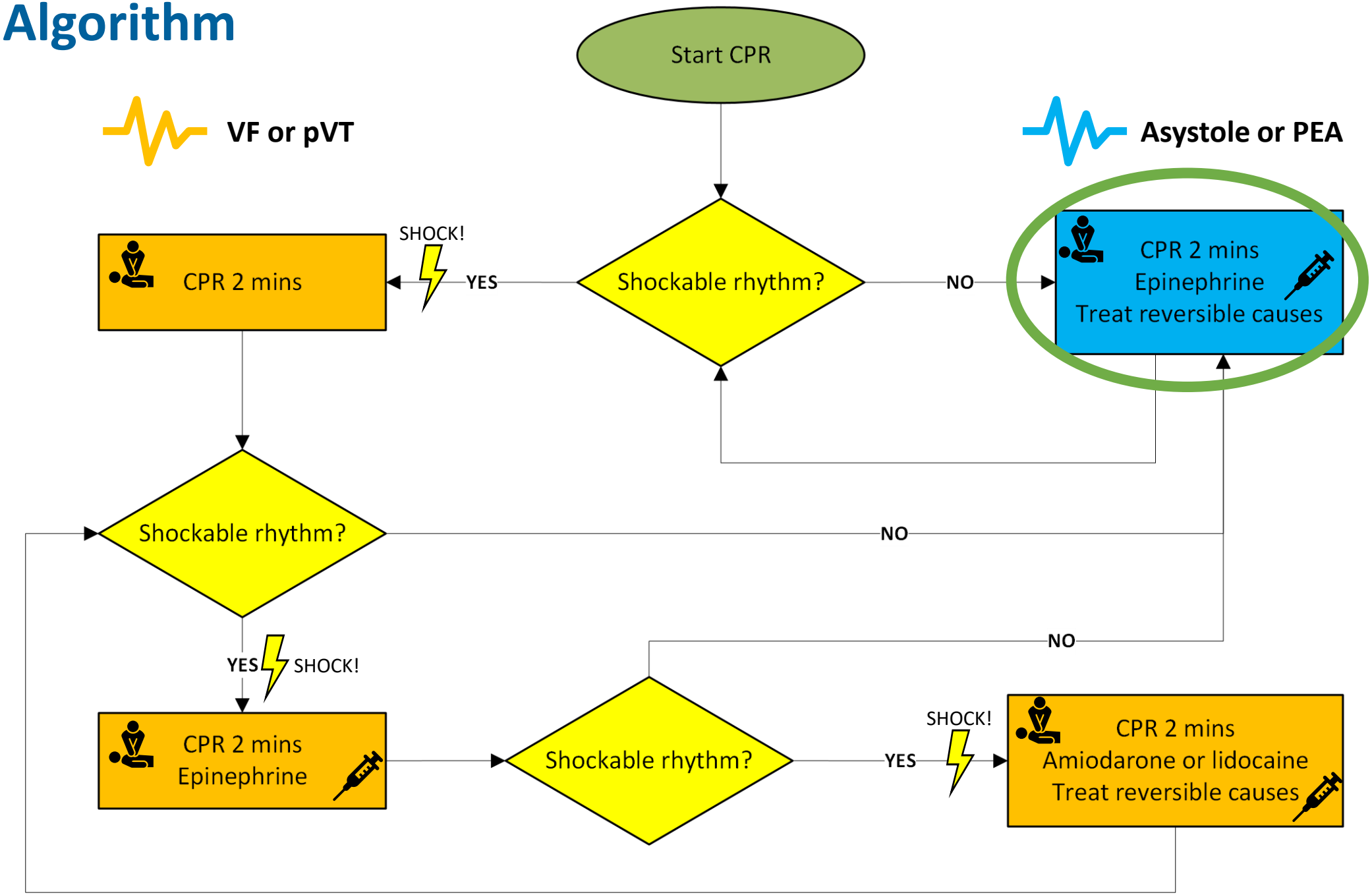
ACLS Algorithm



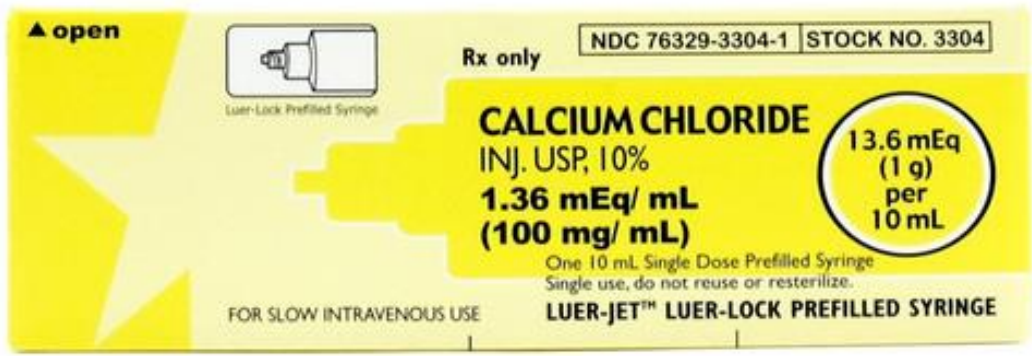
Adapted from: Panchal AR, et al. *Circulation*. 2020;142(suppl 2):S366-S468.

Reversible Causes | “Hs & Ts”

Hypovolemia	Toxins
Hypoxia	Thrombosis (coronary)
~~Hypoglycemia~~	Thrombosis (pulmonary)
Hyperkalemia	Tamponade (cardiac)
Hypokalemia	~~Trauma~~
Hypothermia	Tension pneumothorax
Hydrogen ion (acidosis)	

Panchal AR, et al. *Circulation*. 2020;142(suppl 2):S366-S468.

Calcium



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Calcium

Hyperkalemia

Stabilizes the cardiac membrane
Does not lower serum potassium level

Beta-blocker & calcium channel blocker (CCB) overdose

Increases extracellular calcium concentrations, allowing calcium influx via unblocked channels

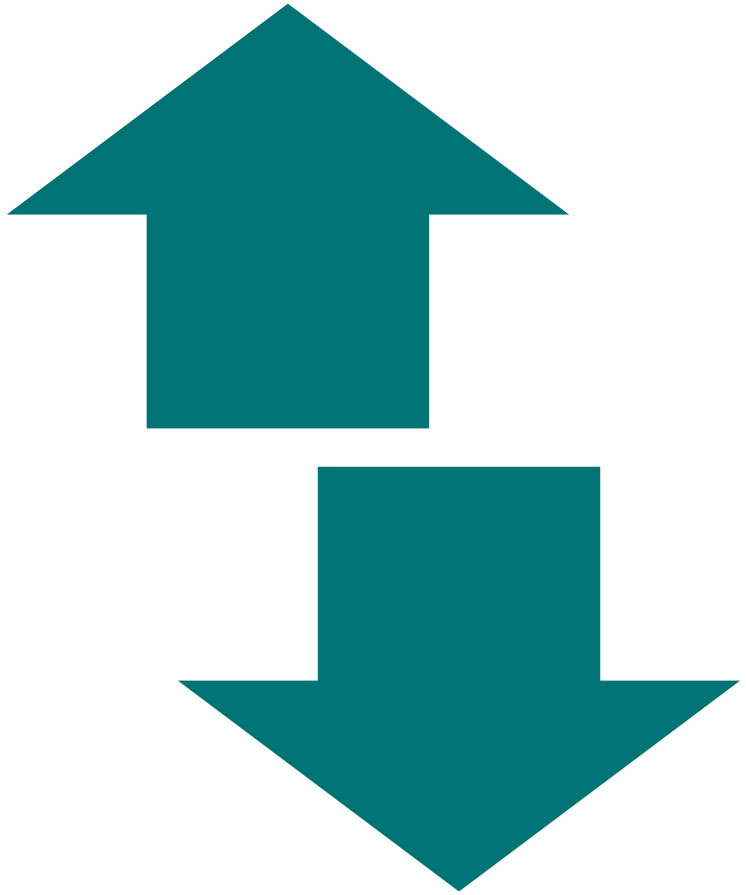
Link MS, et al. *Circulation*. 2015;132:S444-S464.

Calcium Gluconate

Indications & Dosing	Cardiac arrest due to hyperkalemia	1.5-3 g IVP over 2-5 mins
	CCB overdose Beta-blocker overdose	3 g IVP over 5-10 mins; repeat every 15 mins as needed
Crash Cart	• Calcium gluconate 1 g/10 mL vials	
Practical Considerations	• Rapid administration in stable patients can cause hypotension, bradyarrhythmias, and cardiovascular collapse • Calcium gluconate contains 1/3rd of the amount of elemental calcium of calcium chloride • May be administered peripherally	

Neumar RW, et al. *Circulation*. 2010;122:S729-S767.

Calcium



Variable effects on ROSC

No increase in survival in in-hospital or out-of-hospital cardiac arrest

Neumar RW, et al. *Circulation*. 2010;122:S729-S767.

AHA 2020 Recommendations

- Routine use of calcium for cardiac arrest is not recommended (Class III: No Benefit, LOE B-NR)
- Calcium should be used for cardiac arrest with hyperkalemia (Class I, LOE C-LD)
- Calcium is reasonable for CCB overdose (Class IIa, LOE C-LD) or beta-blocker overdose (Class IIb, LOE C-LD)

Panchal AR, et al. *Circulation*. 2020;142(suppl 2):S366-S468.

AHA 2020 Recommendations

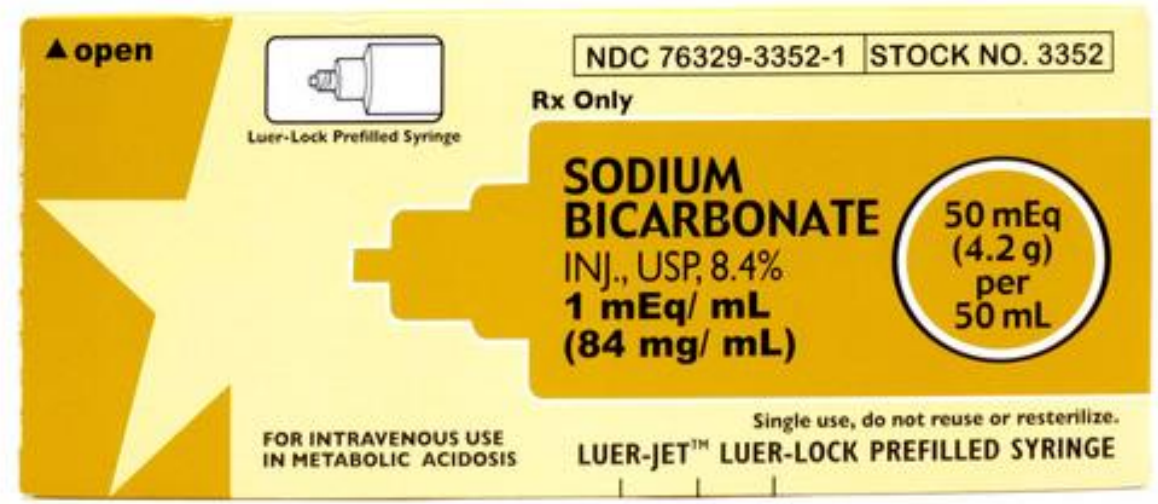
- Routine us
  (Class III: N
- Calcium sh
  (Class I, LC
- Calcium is
  -blocker
  overdose

COCA trial assessed calcium compared to placebo in patients with OHCA without a known indication for calcium (i.e. hypocalcemia or hyperkalemia). Treatment with calcium did not improve ROSC and the trial was stopped early due to concerns for harm.

Vallentin MF, et al. *JAMA*. 2021;326(22):2268-2276.

Panchal AR, et al. *Circulation*. 2020;142(suppl 2):S366-S468.

Sodium Bicarbonate



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Sodium Bicarbonate

- Metabolic acidosis
  - $NaHCO_3 + H^+ \rightleftarrows Na^+ + H_2CO_3 \rightleftarrows Na^+ + H_2O + CO_2$
- Hyperkalemia
  - Shifts potassium into the cell via the Na^+-H^+ exchanger and Na^+-K^+-ATPase pump
- Tricyclic antidepressant (TCA) overdose
  - Alkalinization
  - Increases extracellular sodium concentration

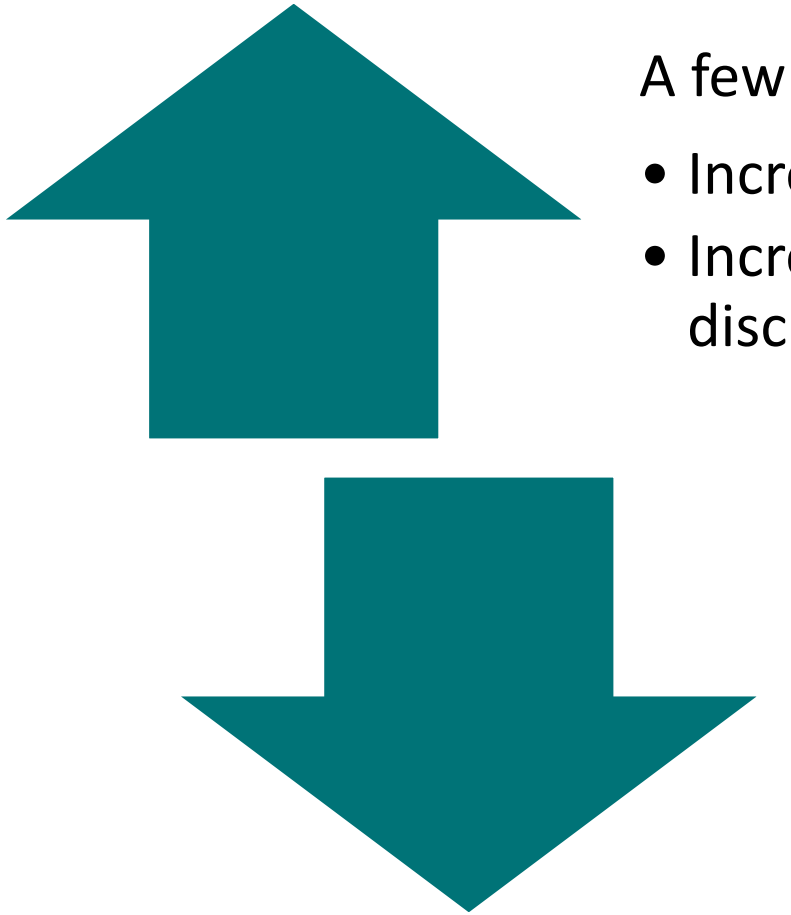
Kerr GW, et al. *Emerg Med J*. 2001;18:236-241.
Aronson PS, et al. *J Am Soc Nephrol*. 2011;22:1981-1989.

Sodium Bicarbonate

Indications & Dosing	Cardiac arrest	1 mEq/kg/dose IVP; repeat doses based on ABG
	Cardiac arrest due to hyperkalemia	50 mEq IVP over 5 mins
	TCA overdose	100 mEq IVP; titrate to pH 7.45-7.55
Crash Cart	• Sodium bicarbonate 8.4% 1 mEq/mL (50 mL) syringes or vials	
Practical Considerations	• Unclear efficacy in cardiac arrest • Flush line between calcium and sodium bicarbonate administration to avoid precipitation	

Neumar RW, et al. *Circulation*. 2010;122:S729-S767.

Sodium Bicarbonate



A few studies demonstrated:

- Increased ROSC
- Increased survival to hospital admission and discharge

Most studies found no benefit or a correlation with a poor outcome

Neumar RW, et al. *Circulation*. 2010;122:S729-S767.

Sodium Bicarbonate | Adverse Effects

- Decreased coronary perfusion pressure
- Extracellular alkalosis
- Hypernatremia and hyperosmolarity
- Paradoxical intracellular acidosis

Kette F, et al. *JAMA*. 1991;266:2121-2126.
Graf H, et al. *Science*. 1985;227:754-756.

Sodium Bicarbonate | Adverse Effects

D

E

H

$$NaHCO_3 + H^+ \rightleftarrows Na^+ + H_2CO_3 \rightleftarrows Na^+ + H_2O + CO_2$$

Paradoxical intracellular acidosis

Kette F, et al. *JAMA*. 1991;266:2121-2126.
Graf H, et al. *Science*. 1985;227:754-756.

AHA 2020 Recommendations

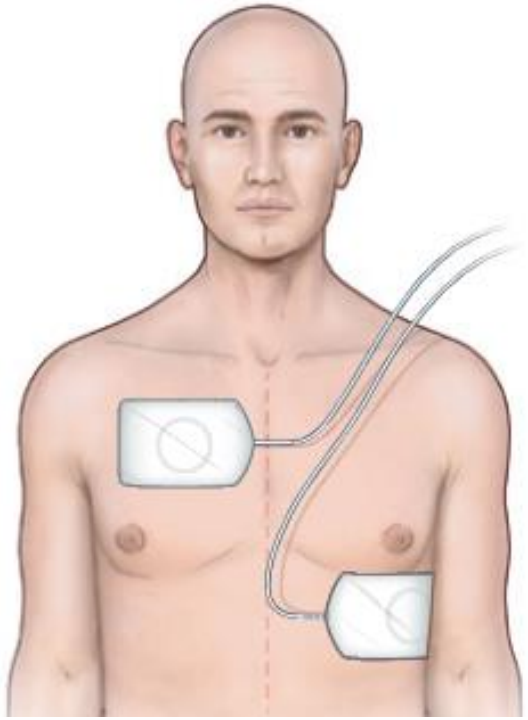
- Routine use of sodium bicarbonate for cardiac arrest is not recommended (Class III: No Benefit, LOE B-R)
- Sodium bicarbonate can be beneficial for cardiac arrest due to sodium channel blocker or TCA overdose (Class IIa, LOE C-LD)

Panchal AR, et al. *Circulation*. 2020;142(suppl 2):S366-S468.

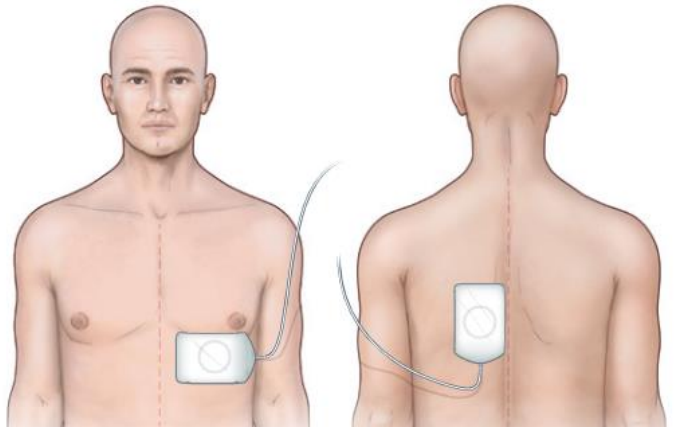
Additional Medication Options

- Epinephrine + vasopressin + methylprednisolone
- Thrombolytics
- Esmolol
- Lipid emulsion therapy

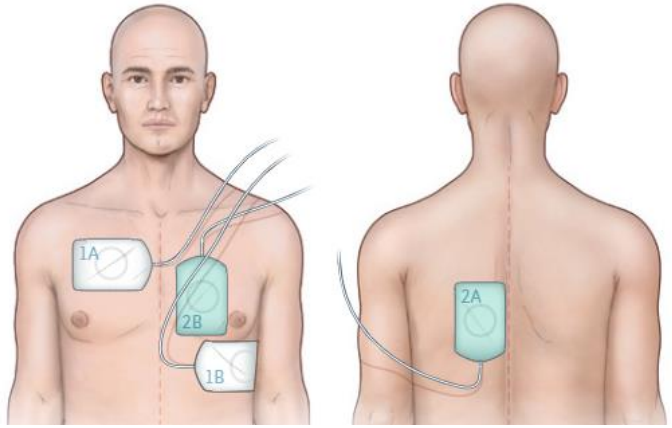
Defibrillation Strategies



Standard
Defibrillation



Vector-Change
Defibrillation



Double Sequential
External Defibrillation

Cheskes S, et al. *N Engl J Med*. 2022;387:1947-1956

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Summary

ACLS drugs have failed to consistently demonstrate a mortality benefit

Optimal timing of drug administration in cardiac arrest is unknown

Chest compressions and defibrillation remain the primary focus in cardiac arrest treatment

Assessment Question

Which of the following roles can the pharmacy department take on to promote quality care for patients in cardiac arrest?

A. Provide medication recommendations and delivery
B. Optimize pharmacy operations to promote rapid drug administration in emergency situations
C. Serve as timekeeper during ACLS
D. Identify shockable rhythms
E. All of the above

Post-Cardiac Arrest Management

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Considerations

Airway, breathing, circulation!

Advanced airway is an adjunct in ACLS, but typically required post-arrest (crash intubation vs. RSI)

Patients are commonly comatose with minimal sedation requirements post-intubation

BP often normal/elevated immediately post-arrest, but drops quickly as epi is metabolized

Cause of cardiac arrest drives ongoing management

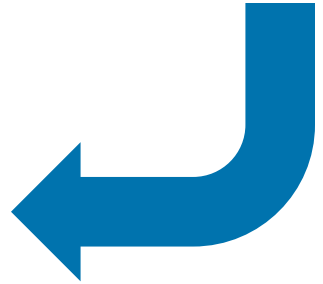
Target normothermia (prevent hyperthermia)

Considerations

TTM2 Trial compared all-cause mortality 6 months after OHCA in patients randomized to hypothermia (33°C) vs. normothermia (early treatment of fever). There was no difference in mortality or functional outcomes between the groups, but significantly higher incidence of arrhythmias resulting in hemodynamic compromise in the hypothermia group.

Dankiewicz J, et al. *N Engl J Med.* 2021;384:2283-2294.

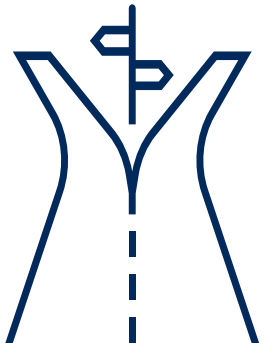
Target normothermia (prevent hyperthermia)



immediately post-arrest, but drops quickly as epi is metabolized

Vasopressors

- Agent selection
  - Availability and logistics
  - Heart rate
  - Comorbidities



- Administration
  - Central line preferred
  - Peripheral line reasonable acutely
  - Intraosseous access if no other option
  - IV compatibility

Push-Dose Vasopressors

- Commonly used in the perioperative setting
- Place in therapy:
  - Bridge to vasopressor infusion in crashing patient
  - Anticipate transient hypotension (e.g. RSI)
- Epinephrine and phenylephrine commonly used in the ED

Antiarrhythmic Drugs

OhioHealth

Amiodarone

Indications & Dosing	pVT VF	300 mg IVP; may repeat 150 mg IVP once
		Upon ROSC: 1 mg/min for 6 hours, then 0.5 mg/min thereafter
	Stable VT Atrial fibrillation SVT	150-300 mg IV bolus over 10 mins, then 1 mg/min for 6 hours, then 0.5 mg/min thereafter
Crash Cart	• Amiodarone 150 mg/3 mL vials • Amiodarone 360 mg/200 mL IV premix	
Practical Considerations	• 0.22-micron filter required, stocked in crash cart • Bolus from bag if patient is stable, administer undiluted IVP if patient is pulseless • May cause hypotension or bradycardia	

SVT: supraventricular tachycardia

Panchal AR, et al. *Circulation*. 2020;142(suppl 2):S366-S468.

Lidocaine

Indications & Dosing	pVT VF	1-1.5 mg/kg IVP (max 100 mg); may repeat 0.5-0.75 mg/kg IVP
		Upon ROSC: 1-4 mg/min IV infusion
Crash Cart	• Lidocaine 2% 100 mg/5 mL syringe	
Practical Considerations	• Added back to the ACLS algorithm in 2018 as an equivalent alternative to amiodarone	

Panchal AR, et al. *Circulation*. 2020;142(suppl 2):S366-S468.

Other Considerations

- Medications aren’t the only option!
  - Transcutaneous pacing
  - Cardioversion
- “Plans within plans within plans”
- Don’t be a hero! Ask your colleagues for help when you need it

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