Feel the Rhythm! Feel the Rhyme! Give it up, it's Lidocaine's Time:

Lidocaine vs Amiodarone for Shock Refractory VF/pVT

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Financial Disclosures

- This speaker has no financial conflicts of interest to disclose

Pharmacist Objectives

1. Discuss the role of pharmacologic treatment options for shockable versus non-shockable rhythms

2. Compare and contrast lidocaine and amiodarone for pulseless ventricular tachycardia (VT)/ventricular fibrillation (VF) in terms of mechanisms of action (MOA), pharmacokinetics (PK), and dosing

3. Interpret primary literature to compare the safety and efficacy of lidocaine versus amiodarone for pulseless VT/VF

4. Using a patient case, develop a treatment plan for a patient in shock-refractory pulseless VT/VF

Pharmacy Technician Objectives

1. Identify differences in drug preparation for lidocaine and amiodarone during advanced cardiac life support (ACLS)

2. Using the ACLS algorithm, identify when antiarrhythmic drugs may be indicated

3. Discuss primary literature comparing the use of lidocaine vs amiodarone for shock-refractory pulseless VT/VF

Abbreviations

Abbreviation	Meaning	Abbreviation	Meaning
ACLS	Advanced cardiac life support	pVT	Pulseless ventricular tachycardia
OHCA	Out-of-hospital cardiac arrest	VF	Ventricular fibrillation
IHCA	In-hospital cardiac arrest	PEA	Pulseless electrical activity
CPR	Cardiopulmonary resuscitation	IV/IO	Intravenous, intraosseous
EKG	Electrocardiogram	SA/AV node	Sinoatrial/Atrioventricular
ERP	Effective refractory period	CVD	Cardiovascular disease
EMS	Emergency medical services	ROSC	Return of spontaneous circulation
mRS	Modified rankin scale	GWTG-R	Getting with the guidelines registry

Knowledge Check 1

TS is a 32-year-old female admitted for concerns of an NSTEMI. A CODE BLUE is called, and you are the pharmacist who responds. CPR is in progress, defibrillator/monitor pads are attached, rhythm check shows VF, and a shock is deployed followed by epinephrine 1mg. Which medication do you recommend to the team? (TS weighs 54kg and height is 69 inches)

A. Amiodarone 150 mg IVP

B. Amiodarone 300 mg IVP

C. Lidocaine 40 mg IVP

D. Lidocaine 80 mg IVP

Overview of ACLS

What is ACLS?

ACLS = Advanced Cardiac Life Support

- Guidelines to treat life-threatening cardiovascular conditions
- Resuscitation efforts aimed to restore spontaneous circulation and retain intact neurological function

Sudden cardiac arrest

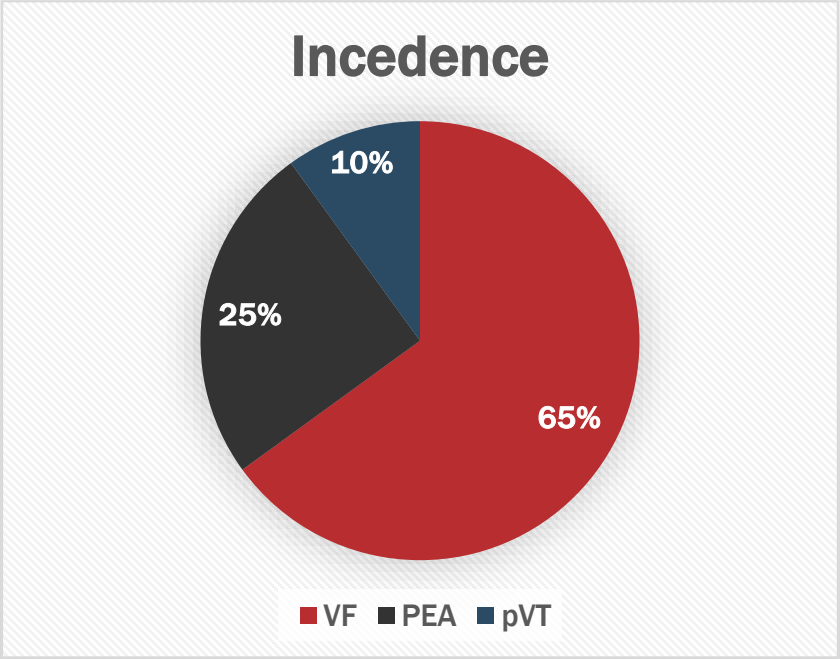
- Cessation of cardiac activity with hemodynamic collapse

Arrhythmias of sudden cardiac arrest

- Pulseless ventricular tachycardia (pVT)/ventricular fibrillation (VF)
- Pulseless electrical activity (PEA)
- Asystole

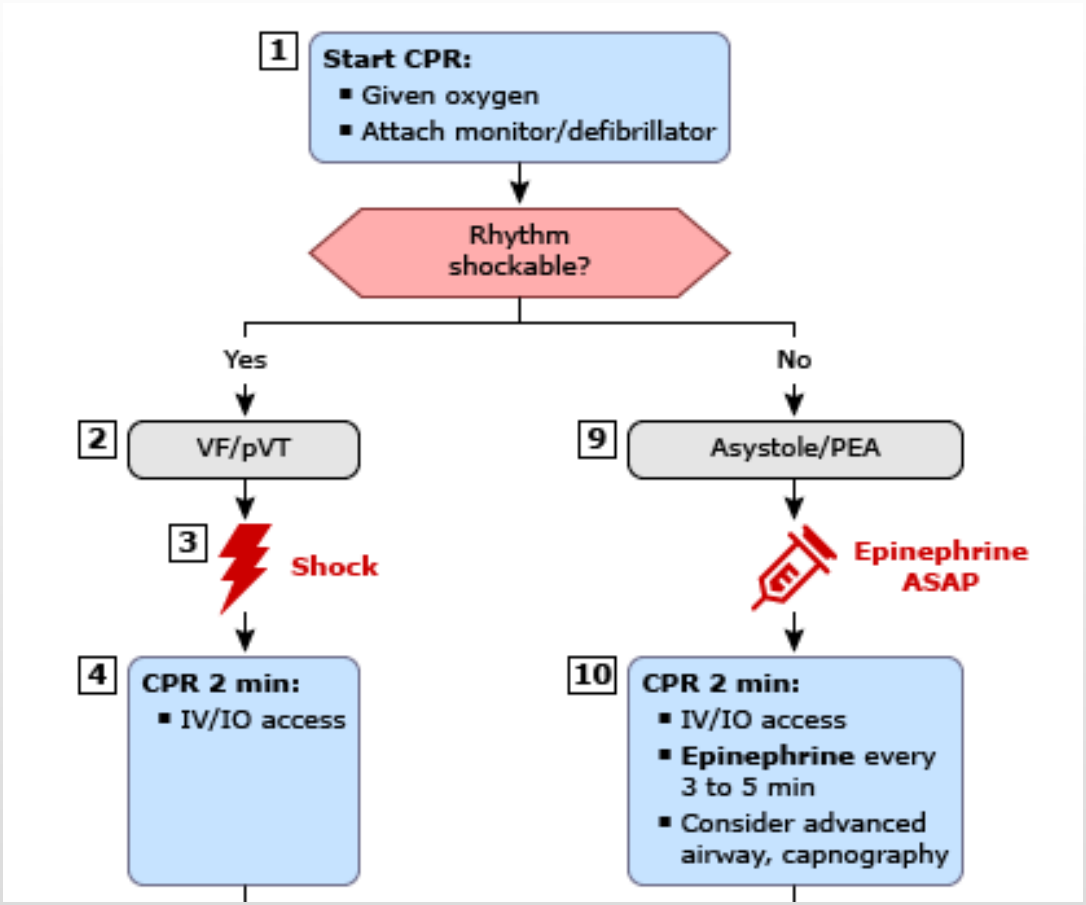
Epidemiology

- >135 million cardiovascular deaths each year
- Rates of OHCA range from 20 to 140 per 100,000 people
  - Survival ranges from 2% to 11%
- IHCA has median survival rate of ~25%

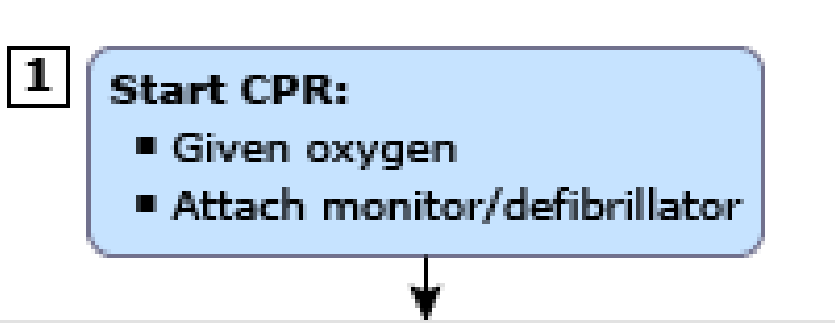


Circulation. 2013 Jul 23;128(4):417-35.
Circulation. 2020;141(9):e139-e596.

ACLS Algorithm



Step 1: CPR ASAP



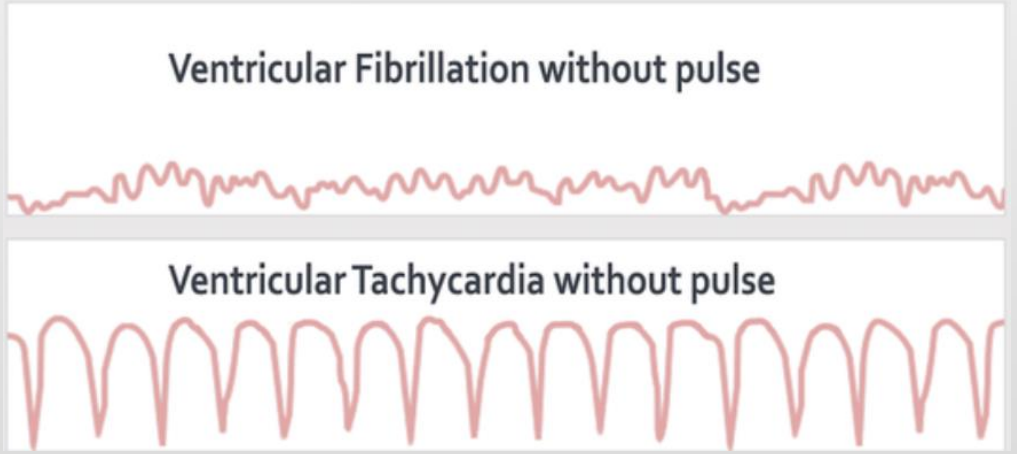
- High quality CPR is the single-most important intervention
- 30-day survival with CPR 10.5%
- 30-day survival without CPR 4%

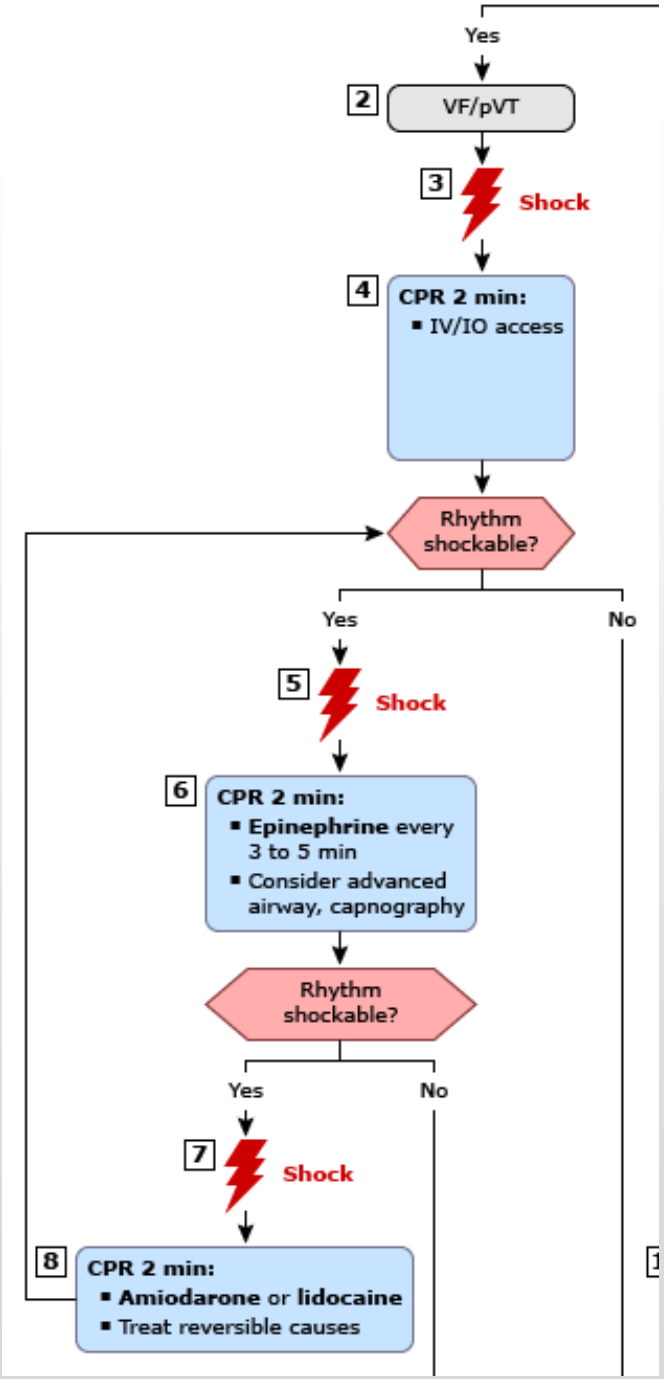
N Engl J Med. 2015;372(24):2307-2315.

Shockable vs Non-shockable Rhythms

Non-shockable - Asystole and PEA

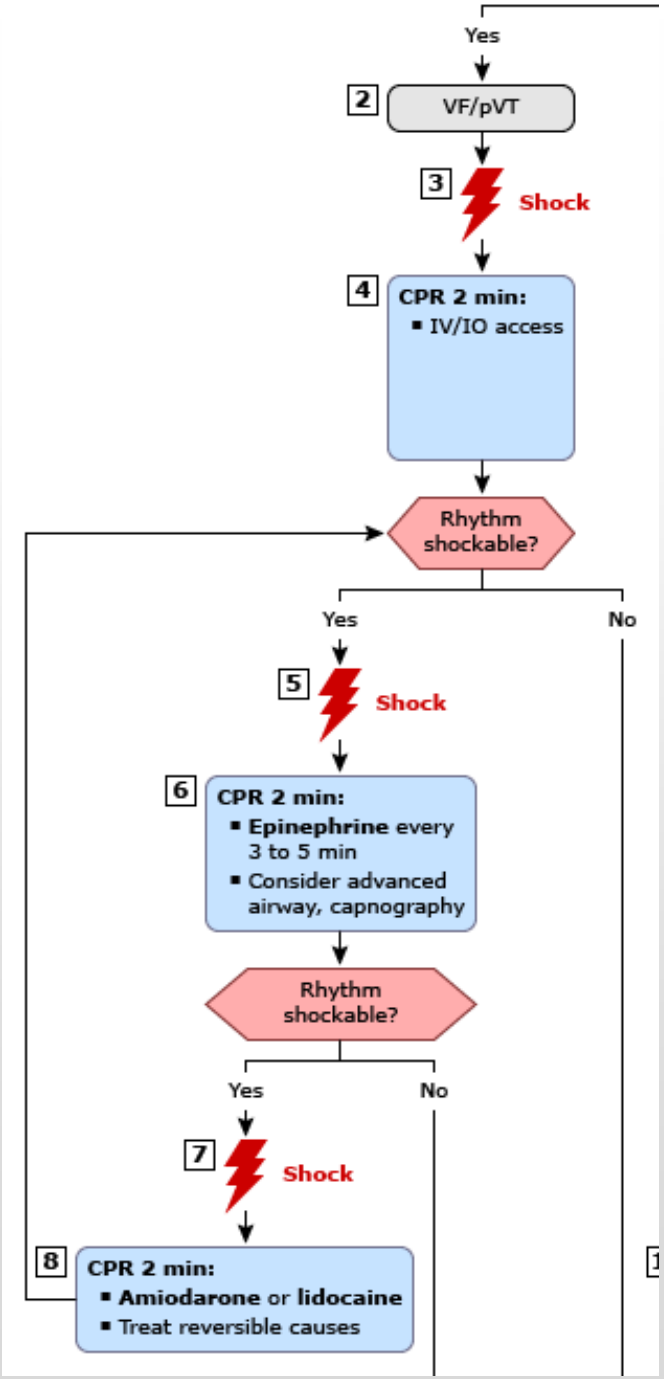
Shockable - VF and pVT





Steps 2 – 4: Shock

- Attach defibrillator pads while CPR performed
- During rhythm check, briefly stop CPR
- Shockable rhythm detected → allow defibrillator to charge and resume CPR
- Stop compressions when charged and SHOCK
- Resume CPR and gain IV/IO access



Shocking Outcomes

Success of defibrillation and patient survival depends on duration of the arrhythmia

Patients shocked within two minutes:

- Survival at 1 year 25.7% vs 15.5%
- Survival at 3 years 19.1% vs 11%
- Survival at 5 years 14.7% vs 7.9%

Circulation. 2018;137(19):2041-2051.

Shock-Refractory VF/pVT

Refractory after 2 shocks

- >50% of VF
- Assess shockable rhythm
- CPR 2 minutes
- Administer:
  - Epinephrine 1mg IV/IO every 3 – 5 minutes (every other pulse check)

Refractory after 3 shocks

- >20% of VF
- Assess shockable rhythm
- CPR 2 minutes
- Administer:
  - Amiodarone 300mg bolus, repeat with 150mg bolus or
  - Lidocaine 1 – 1.5mg/kg, repeat with 0.5 – 0.75mg/kg

Repeat steps as necessary

Resuscitation. 2021;161:115-151.

Knowledge Check 2

Which two rhythms are shockable during ACLS?

A. PEA, Asystole
B. VF, pVT
C. PEA, VF
D. PEA, pVT

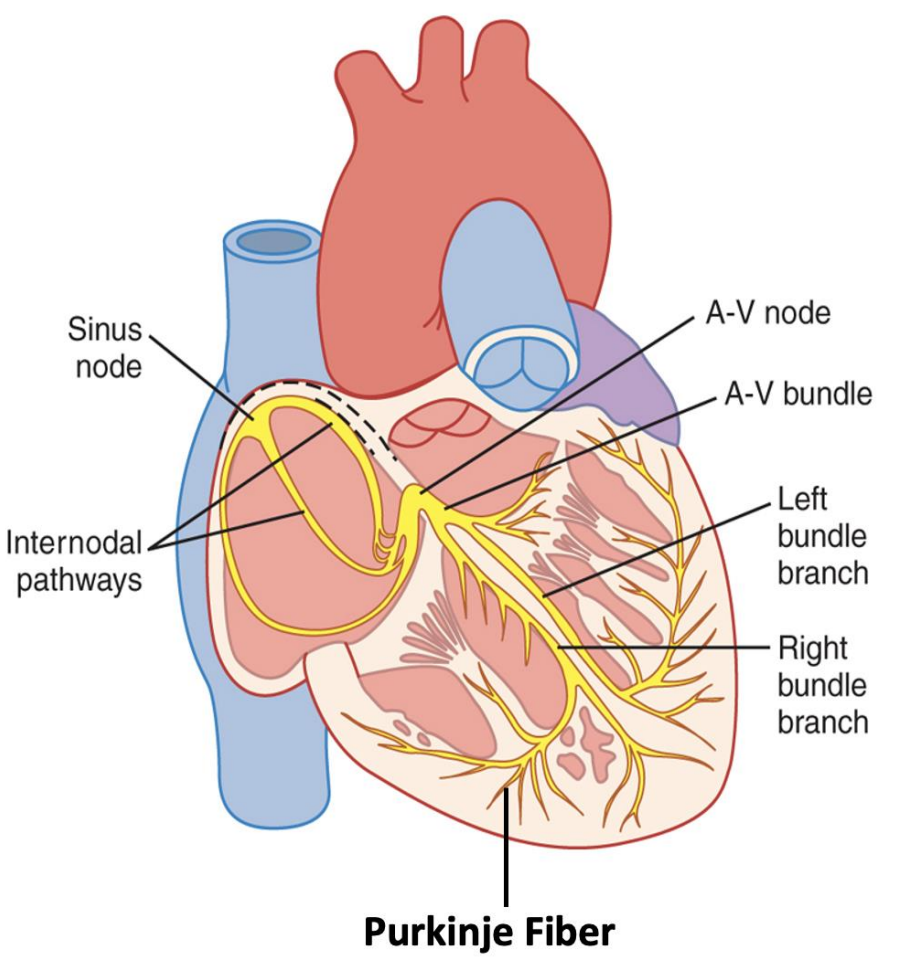
Knowledge check 2

Which two rhythms are shockable during ACLS?

A. PEA, Asystole
B. VF, pVT
C. PEA, VF
D. PEA, pVT

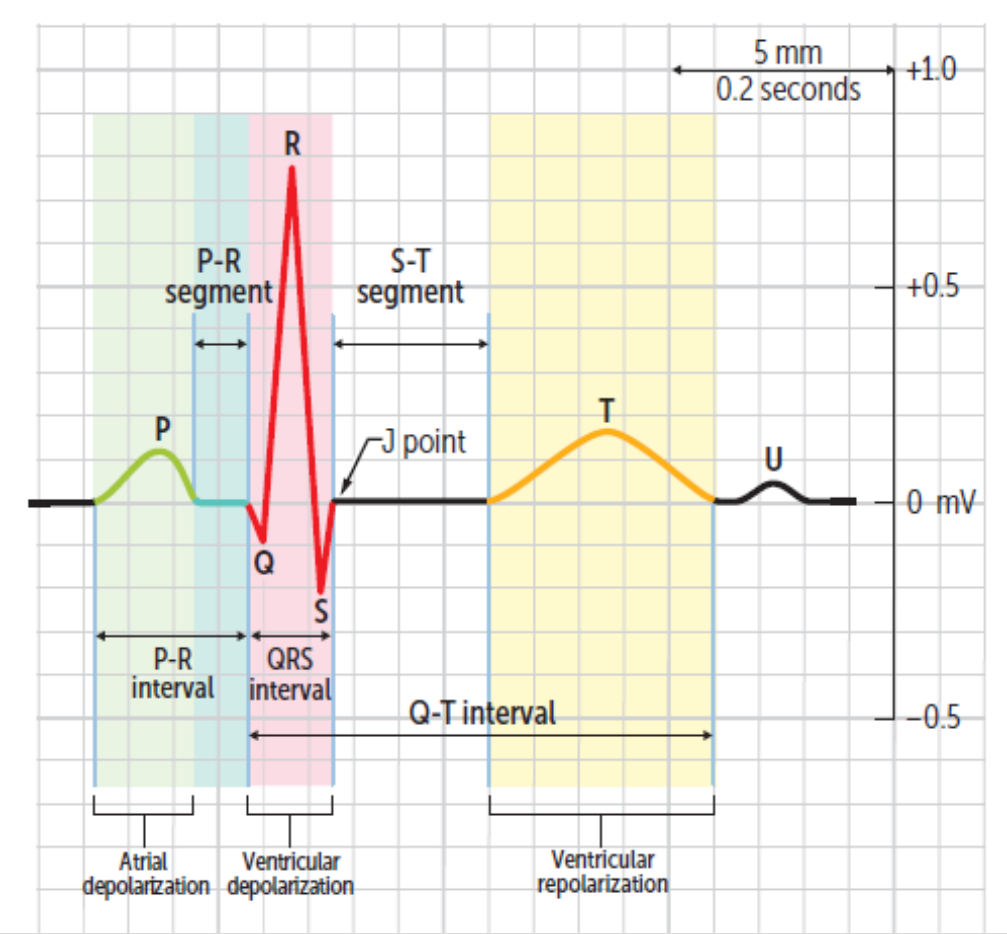
Review of the Rhythms

Normal Conduction System



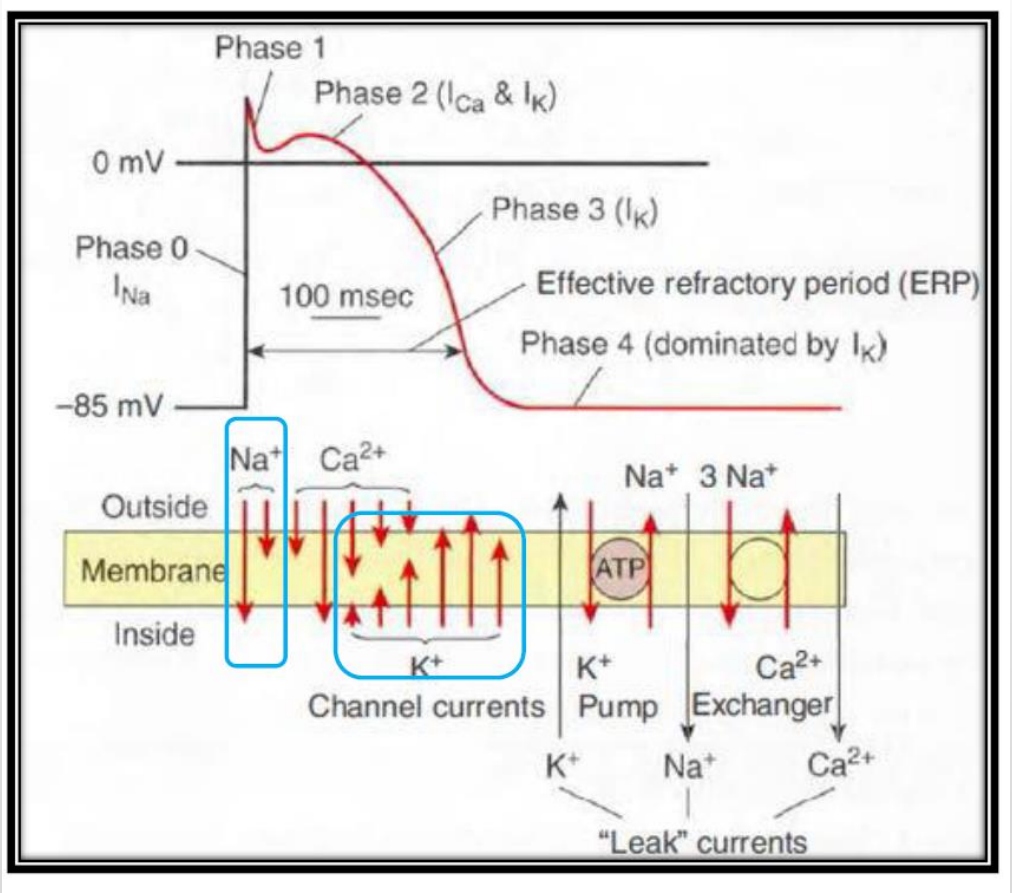
- Sinus Node
- Internodal Pathways
- AV Node
- AV Bundle
- Bundle Branches
- Purkinje Fibers

Review of a Normal EKG



EKG Basics	
P wave	Atrial depolarization; repolarization masked by QRS
QRS complex	Ventricular depolarization
T wave	Ventricular repolarization

Action Potentials

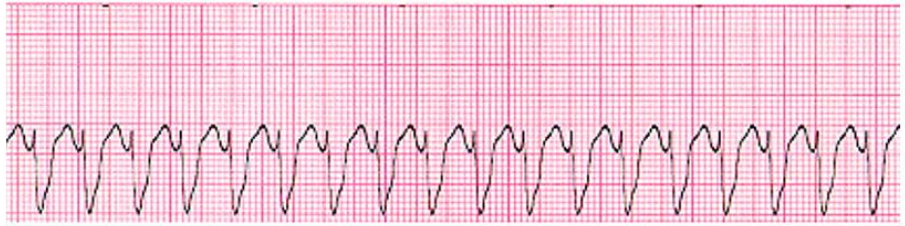


- Phase 0, 1, 2, part of 3
  - Cell is refractory to initiation of new action potentials
- Effective Refractory Period (ERP)
  - Stimulation of the cell does not produce a new action potential
- Damaged cells promote reentry circuits → shorter ERP and arrythmias
- Prolonging ERP makes irregular impulses disappear

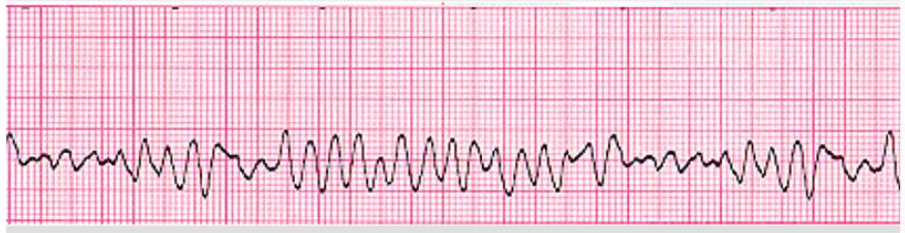
Ventricular Arrythmias

Sinus Rhythm

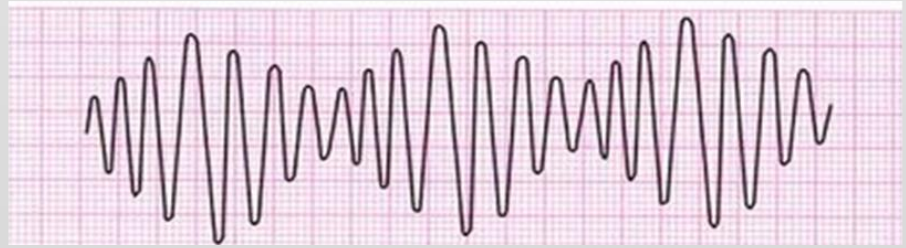
Ventricular Tachycardia



Ventricular Fibrillation



Torsade de Pointes



Risk Factors for VF/pVT

Myocardial Infarction

- Ischemia → myocardial scarring

CVD

- Ventricular hypertrophy
- HTN
- RAAS activation

Increased Sympathetic Tone

- Hyperthyroidism
- Exercise

Metabolic Disturbances

- Diabetes
- Obesity

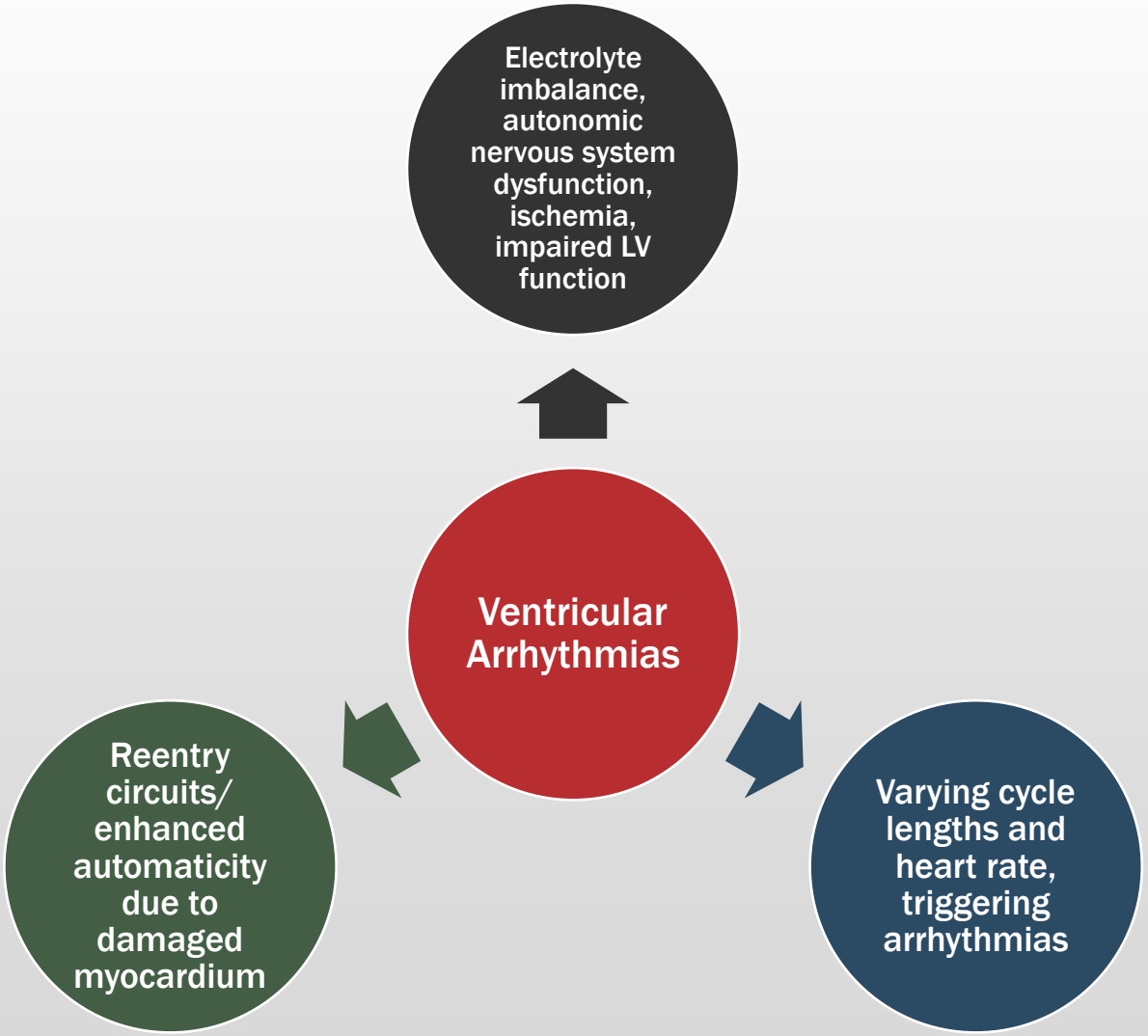
Oxidative Stress

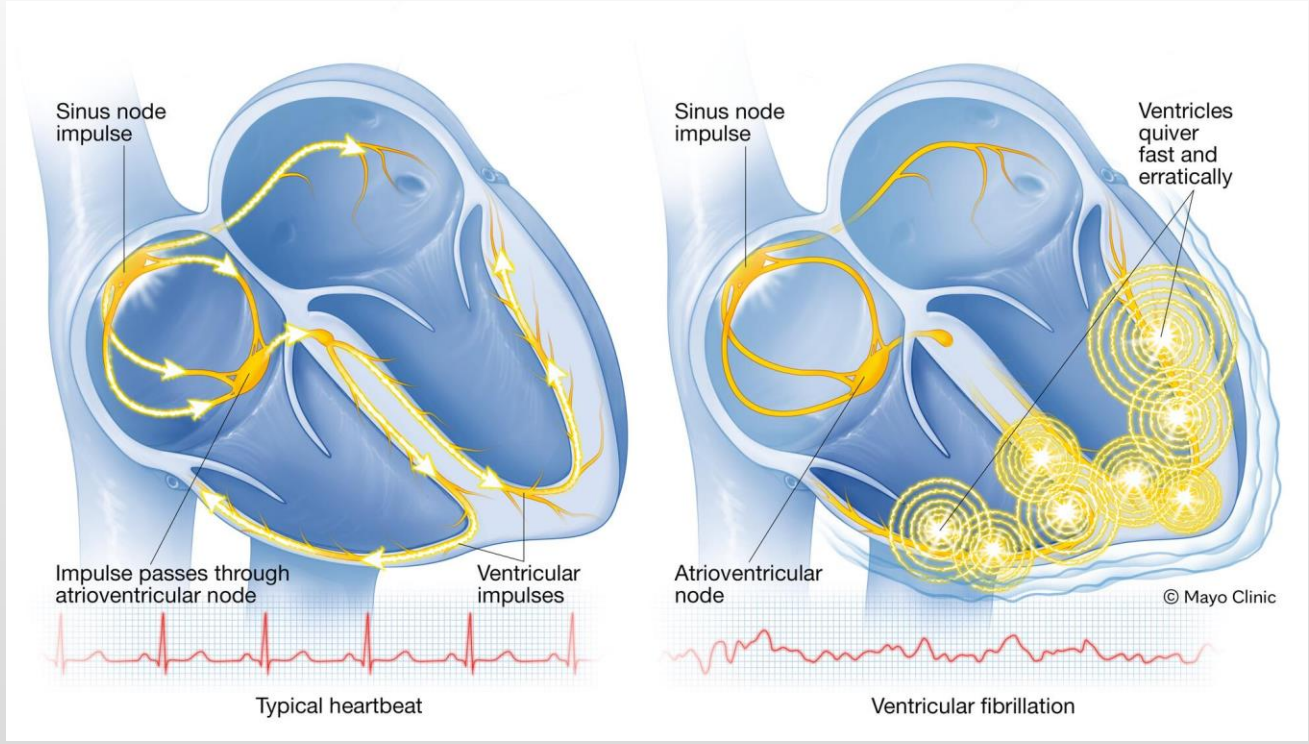
- Smoking
- Alcohol use

Non-Modifiable Factors

- Age
- Genetic mutation/ polymorphism

Ventricular Arrythmias

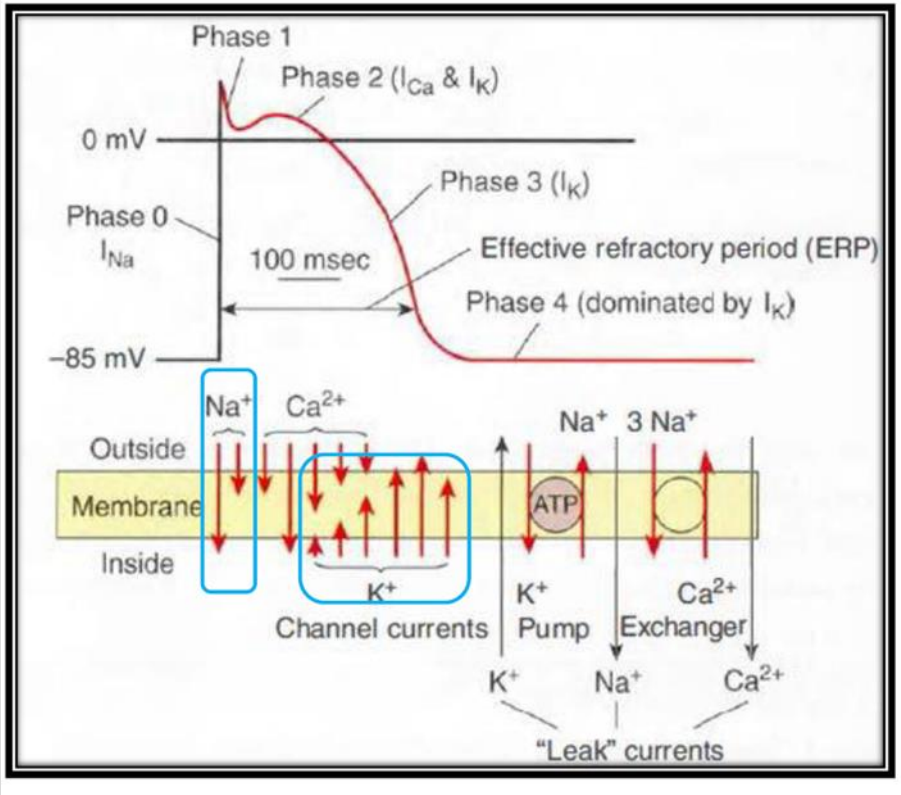




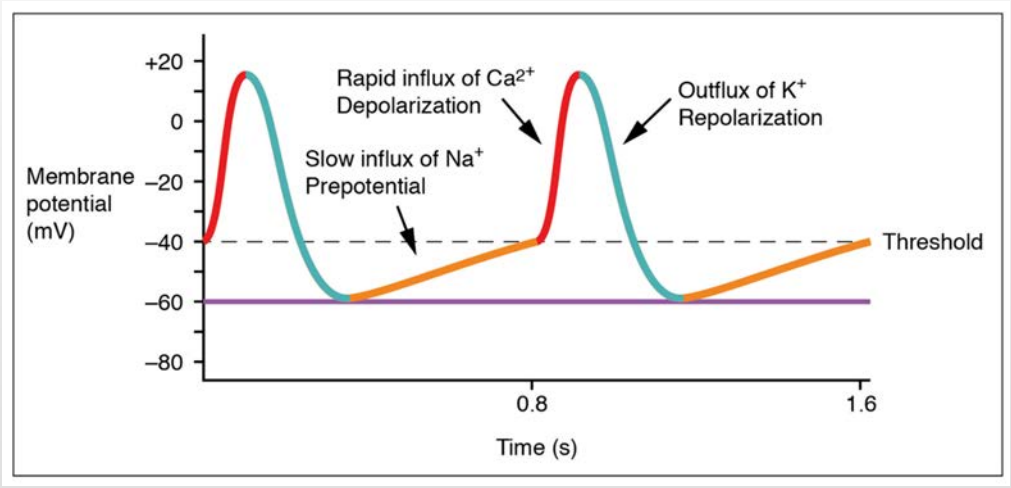
Physiol Rev. 1989;69(4):1049-1169.

What can we do to Stabilize Arrhythmias?

Ventricular Cells



AV Node



Prolong ERP

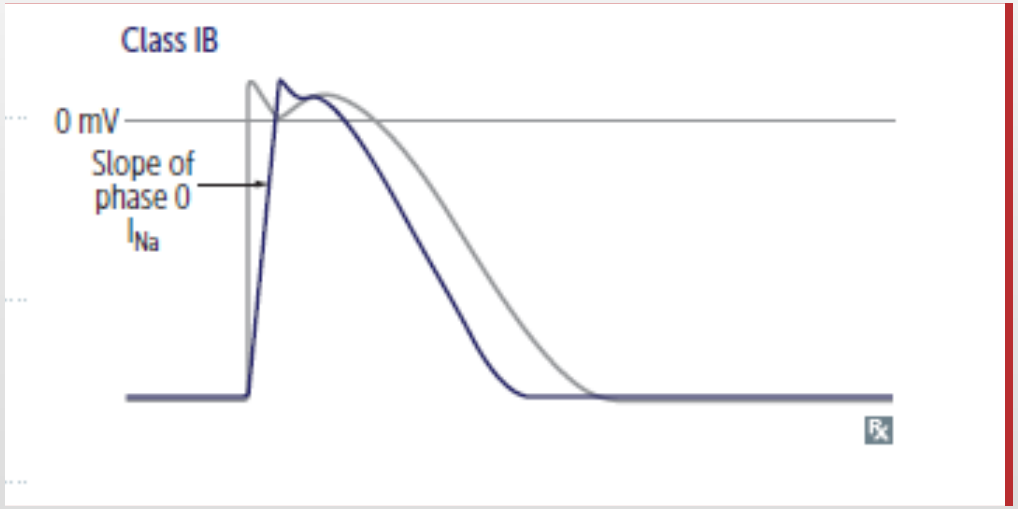
Three Major Players: Na^+, Ca^{2+}, K^+

2020 AHA Guidelines for CPR and Emergency Cardiovascular Care

Amiodarone or lidocaine may be considered for VF/pVT that is unresponsive to defibrillation

Circulation. 2020;142(16_suppl_1):S92-S139.

Lidocaine



- ↓ Action potential duration
- Preferentially affects ischemic or depolarized Purkinje fibers and ventricular tissue

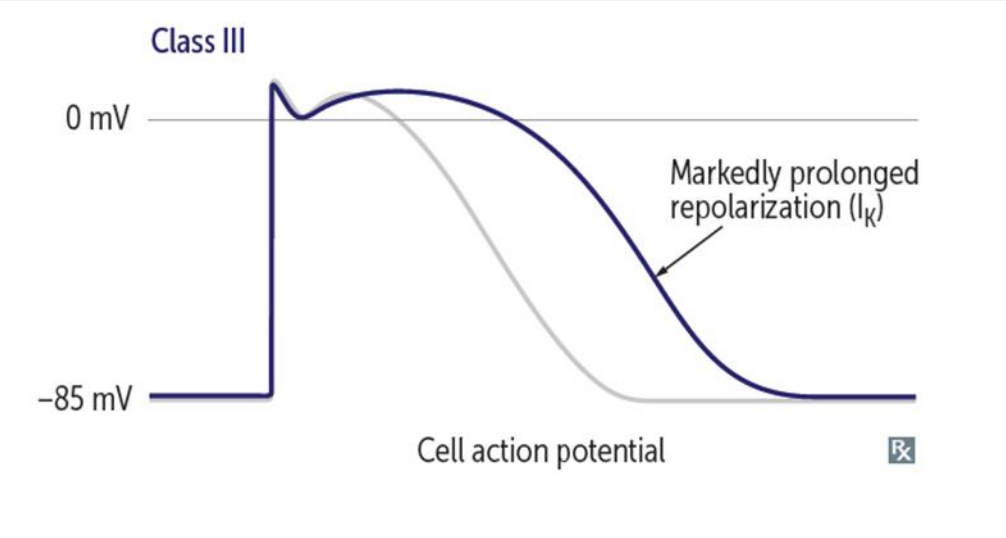
Lidocaine

Class	Class Ib antiarrhythmic agent
MOA	• Blocks initiation/conduction of nerve impulses by decreasing membrane's permeability to Na ions • Increases electrical stimulation threshold of ventricle • Inhibits depolarization

Dosing in VF/pVT	• **1 - 1.5 mg/kg IVP**
	  • **Repeat: 0.5 – 0.75 mg/kg IVP**
	  • Max dose: 3 mg/kg
	• 2 – 4 mg/kg ET

Kinetics	• Metabolism: 90% via CYP1A2 and CYP3A4 • Duration: 10 – 20 minutes
Adverse Events	• Less proarrhythmic effects compared to other class I antiarrhythmics • Hypotension in patients with pre-existing heart failure • Sedation, nausea, confusion, dizziness

Amiodarone



- ↑ Action Potential
- ↑ ERP
- ↑ QT interval

Amiodarone

Class	Class III antiarrhythmic agent	
MOA	• Inhibits ion flux through Na^+, K^+, Ca^{2+} channels • Inhibits adrenergic stimulation (α- and β-blocking activities) • Prolongs action potential and ERP in myocardial tissue	
Dosing	• **300 mg IVP/IO** • **Repeat: 150 mg IVP/IO** • Max Dose in 24 hours: 2.2 g	
Adverse Events	• Hypotension • Bradycardia • QTc prolongation	• Liver toxicity • Thyroid toxicity
Kinetics	• Metabolism: CYP2C8 and CYP3A4 to active metabolite • Half-life: 9 – 36 days (IV); 9 – 30 days for active metabolite	
DDI	• P-gp inhibitor • Inhibits 2C9, 2C19, 3A4, 2D6	

Knowledge Check 3

What is the initial dose of lidocaine for shock refractory VF/pVT?

A. 150 mg IVP

B. 300 mg IVP

C. 0.5 – 0.75 mg/kg IVP

D. 1 – 1.5 mg/kg IVP

Knowledge Check 3

What is the initial dose of lidocaine for shock refractory VF/pVT?

A. 150 mg IVP

B. 300 mg IVP

C. 0.5 – 0.75 mg/kg IVP

D. 1 – 1.5 mg/kg IVP

Lidocaine vs amiodarone in VF/pVT

Lidocaine

- Bristojet prefilled syringe
- Open the box
- Remove caps
- Twist together
- Administer

Amiodarone

- Prepared using 2 vials of 150mg/3mL
- Bubbles may accumulate when drawing up

The Eras of Antiarrhythmics' in the ACLS Guidelines

1974

- AHA publishes the first ACLS guidelines

AHA 1986 update

- Lidocaine preferred over bretylium

AHA 1992 update

- Lidocaine, amiodarone, bretylium

1999

- ARREST trial

Amiodarone for Resuscitation after Out-of-hospital Cardiac Arrest due to Ventricular Fibrillation (ARREST)

Population	Intervention	Outcome	Conclusion
OHCA due to VF/pVT refractory to ≥3 shocks Double-blind, Placebo-controlled, Randomized Control Trial N=504	Amiodarone 300mg (n=246) vs Placebo (n=258)	Primary: Hospital Admission 44% v 34%; p=0.03 Adjusted OR 1.6 (95% CI 1.1 – 2.4; p=0.02) Secondary: Survival to discharge: 13.4% v 13.2% HOTN: 59% v 48% Bradycardia: 41% v 25%	• Amiodarone improves survival to hospital admission in shock-refractory VF. • Survival to admission was 39% • Survival to discharge was ~13%

N Engl J Med. 1999;341(12):871-878.

The Eras of Antiarrhythmics' in the ACLS Guidelines

1974

- AHA publishes the first ACLS guidelines

AHA 1986 update

- Lidocaine preferred over bretylium

AHA 1992 update

- Lidocaine, amiodarone, bretylium

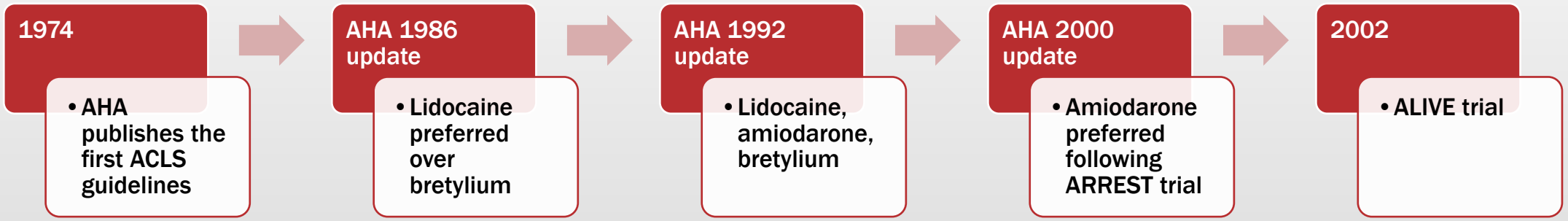
AHA 2000 update

- Amiodarone preferred following ARREST trial

CLINICAL QUESTION:

Should amiodarone or lidocaine be the antiarrhythmic of choice for shock refractory ventricular fibrillation/ pulseless ventricular tachycardia?

The Eras of Antiarrhythmics' in the ACLS Guidelines



Amiodarone as compared with lidocaine for shock-resistant ventricular fibrillation (ALIVE)

DORIAN ET AL. 2002

ALIVE

Objective

- To determine the efficacy of lidocaine compared to amiodarone for the treatment and prevention of OHCA due to VF

Study Design

- Investigator initiated, double-blind, randomized control trial
- 347 patients

N Engl J Med. 2002;346(12):884-890.

ALIVE Inclusion and Exclusion

Inclusion

- Age >18
- EKG documented VF
- Resistant VF (≥3 shocks)
- ≥1 dose of Epinephrine + 4th shock
- Recurrent VF after successful initial defibrillation

Exclusion

- VF due to trauma
- Other cardiac rhythms that converted to VF

N Engl J Med. 2002;346(12):884-890.

ALIVE Interventions

Amiodarone (n=180)

- 5 mg/kg in polysorbate-80 and 30 mL of D5W
- Repeat dose: 2.5 mg/kg

Lidocaine (n=167)

- 1.5 mg/kg (10 mg/mL)
- Repeat dose: 1.5 mg/kg

N Engl J Med. 2002;346(12):884-890.

ALIVE Outcomes

Primary

- Survival to hospital admission

Secondary

- Survival to hospital discharge
- Adverse events

N Engl J Med. 2002;346(12):884-890.

ALIVE Baseline Characteristics

Baseline Characteristics	Amiodarone (n=180)	Lidocaine (n=167)
Age, mean, yr	68	66
History of cardiac disease (%)	61%	59%
Witnessed arrest (%)	76%	78%
CPR by bystander (%)	26%	28%
VF as initial rhythm (%)	91%	93%
pVT as initial rhythm (%)	1%	2%
Supraventricular rhythm (%)	2%	1%
Time from dispatch to response/procedure:		
First shock, mean, min (SD)	8 ± 3	9 ± 4
Intubation, mean, min (SD)	11 ± 4	11 ± 4
Administration of study drug, mean, min (SD)	25 ± 8	24 ± 7

N Engl J Med. 2002;346(12):884-890.

ALIVE Primary Outcomes

Primary Outcome	Amiodarone (n=180)	Lidocaine (n=167)	Unadjusted OR for survival (95% CI)	Adjusted OR for survival (95% CI)
Survival to hospital admission – N (%)	41 (22.8%)	20 (12%)	2.17 (1.21 – 3.83); p=0.009	2.49 (1.28 – 4.85); p=0.007

N Engl J Med. 2002;346(12):884-890.

ALIVE Effect of Study Drug on Survival

Treatment factor	Unadjusted OR for survival (95% CI)	Adjusted OR for survival (95% CI)
ROSC before drug administration	3.6 (1.7 – 7.3); p < 0.001	5.93 (2.46 – 14.26); p < 0.001
Time from dispatch to drug administration (per 1-min increase)	0.91 (0.86 – 0.96); p < 0.001	0.88 (0.83 – 0.93); p < 0.001
Treatment assignment (amiodarone vs lidocaine)	2.17 (1.21 – 3.83); p=0.009	2.49 (1.28 – 4.85); p=0.007

N Engl J Med. 2002;346(12):884-890.

ALIVE Outcomes After Study Drug

Outcomes after study drug	Amiodarone (n=180)	Lidocaine (n=167)	P-value
Survival to hospital discharge – No. (%)	9 (5%)	5 (3%)	0.32
Treatment for bradycardia (atropine use) – No. (%)	43 (24%)	38 (23%)	>0.05
Treatment for hypotension (dopamine use) – No. (%)	13 (7%)	6 (4%)	>0.05

N Engl J Med. 2002;346(12):884-890.

ALIVE Strengths

Strengths

- Short time from dispatch to first shock
- Found association between survival and time to drug administration
- Adjusted baseline characteristics to make groups evenly matched

N Engl J Med. 2002;346(12):884-890.

ALIVE Limitations

Limitations

- Survival to discharge < 5%
- Time to drug administration compared to ACLS algorithm
- Amiodarone weight-based dosing not consistent with the recommended 300 mg IVP in the guidelines
- Repeat lidocaine dose 1.5 mg/kg vs 0.5 - 0.75 mg/kg recommended in the guidelines
- No average number of doses administered recorded
- No outcomes on neurologic status
- Initial rhythm of pVT only in 3 patients

N Engl J Med. 2002;346(12):884-890.

ALIVE Takeaways

Big loss for lidocaine

Survival to discharge < 5% (overall)

Time to drug administration ~24 minutes

Patients in amiodarone group were twice as likely to achieve ROSC prior to administration

Overall, study found association with survival and earlier drug administration

N Engl J Med. 2002;346(12):884-890.

The Eras of Antiarrhythmics' in the ACLS Guidelines

AHA 2000 update
- Amiodarone preferred following ARREST trial

2002
- ALIVE trial shows benefit over lidocaine

AHA 2005, 2010, 2015 update
- Amiodarone preferred agent

2016
- ROC-ALPS trial

Amiodarone, Lidocaine, or Placebo in Out-of-Hospital Cardiac Arrest (ROC-ALPS)

KUDENCHUK ET AL. 2016

ROC-ALPS

Objective

- Compare effects of amiodarone, lidocaine, or placebo after OHCA due to VF/pVT on survival to hospital discharge

Study Design

- Multicenter, randomized, double-blind, placebo-controlled, pre-hospital trial
- 3026 patients

N Engl J Med. 2016;374(18):1711-1722.

ROC-ALPS Inclusions and Exclusion

Inclusion

- Age > 18
- Shock-refractory VF/pVT
- At least one shock
- Vascular access (IV or IO)

Exclusion

- Already receiving open-label IV lidocaine or amiodarone
- Known hypersensitivity to lidocaine or amiodarone
- Known advanced directive
- Protected populations

N Engl J Med. 2016;374(18):1711-1722.

ROC-ALPS Interventions

Amiodarone

- 300 mg (150 mg/3mL syringe)
- Repeat 150 mg

Lidocaine

- 120 mg (60 mg/3mL syringe)
- Repeat 60 mg

Placebo

N Engl J Med. 2016;374(18):1711-1722.

ROC-ALPS Outcomes

Primary Outcome

- Survival to hospital discharge (amiodarone vs placebo)

Secondary Outcome

- Favorable neurologic function at discharge (mRS ≤ 3)

Mechanistic Outcomes

- ROSC at ED arrival
- Hospital admission

N Engl J Med. 2016;374(18):1711-1722.

ROC-ALPS Baseline Characteristics

Baseline Characteristics	Amiodarone (n=974)	Lidocaine (n=993)	Placebo (n=1059)
Age, mean, yr	63.7	63.0	62.7
Cardiac arrest witnessed by EMS (%)	6.0%	4.6%	5.3%
Bystander-initiated shock (%)	6.9%	5.5%	5.8%
Bystander-initiated CPR (%)	61.4%	59.2%	60.2%
Time from initial call to EMS arrival, mean, min (SD)	5.8 ± 2.6	5.6 ± 2.4	5.8 ± 2.6
Time from initial call to first dose of trial drug in non-EMS witnessed arrest, min	19.3 ± 7.1	19.3 ± 7.6	19.3 ± 7.3
Time from cardiac arrest to first dose of trial drug in EMS witnessed arrest, min	11.7 ± 5.8	12.1 ± 6.6	12.1 ± 6.6
Number of EMS shocks, median (IQR)	5 (3 – 7)	5 (3 – 7)	6 (4 – 9)
Number of shocks after first dose of trial drug, median (IQR)	2 (1 – 4)	2 (1 – 3)	3 (1 – 6)

N Engl J Med. 2016;374(18):1711-1722.

ROC-ALPS Outcomes: Amiodarone vs Placebo

Primary Outcome	Amiodarone (n=974)	Placebo (n=1059)	Absolute Risk Difference (95% CI)
Survival to discharge – N (%)	237 (24.4%)	222 (21.0%)	3.2 (-0.4 – 7.0); p=0.08

Secondary Outcome	Amiodarone (n=974)	Placebo (n=1059)	Absolute Risk Difference (95% CI)
mRS ≤ 3 – N (%)	182 (18.8%)	175 (16.6%)	2.2 (-1.1 – 5.6); p=0.19
ROSC at ED arrival – N (%)	350 (35.9%)	366 (34.6%)	1.4 (-2.8 – 5.5); p=0.52
Hospital admission – N (%)	445 (45.7%)	420 (39.7%)	6.0 (1.7 – 10.3); p=0.01

N Engl J Med. 2016;374(18):1711-1722.

ROC-ALPS Outcomes: Lidocaine vs Placebo

Primary Outcome	Lidocaine (n=993)	Placebo (n=1059)	Absolute Risk Difference (95% CI)
Survival to discharge – N (%)	233 (23.7%)	222 (21.0%)	2.6 (-1.0 – 6.3); p=0.16

Secondary Outcome	Lidocaine (n=993)	Placebo (n=1059)	Absolute Risk Difference (95% CI)
mRS ≤ 3 – N (%)	172 (17.5%)	175 (16.6%)	0.9 (-2.4 – 4.2); p=0.59
ROSC at ED arrival – N (%)	396 (39.9%)	366 (34.6%)	5.4 (1.2 – 9.5); p=0.01
Hospital admission – N (%)	467 (47.0%)	420 (39.7%)	7.4 (3.1 – 11.6); p<0.001

N Engl J Med. 2016;374(18):1711-1722.

ROC-ALPS Outcomes: Amiodarone vs Lidocaine

Primary Outcome	Amiodarone (n=974)	Lidocaine (n=993)	Absolute Risk Difference (95% CI)
Survival to discharge – N (%)	237 (24.4%)	233 (23.7%)	0.7 (-3.2 – 4.7); p=0.70

Secondary Outcome	Amiodarone (n=974)	Lidocaine (n=993)	Absolute Risk Difference (95% CI)
mRS ≤ 3 – N (%)	182 (18.8%)	172 (17.5%)	1.3 (-2.1 – 4.8); p=0.44
ROSC at ED arrival – N (%)	350 (35.9%)	396 (39.9%)	-4.0 (-8.3 – 0.3); p=0.07
Hospital Admission – N (%)	445 (45.7%)	467 (47.0%)	-1.3 (-5.7 – 3.1); p=0.55

N Engl J Med. 2016;374(18):1711-1722.

ROC-ALPS Adverse Events

Event	Amiodarone (n=974)	Lidocaine (n=993)	Placebo (n=1059)	P-value
Clinical seizure activity within 24 hours – N (%)	31 (3.2%)	51 (5.1%)	39 (3.7%)	0.07
Temporary cardiac pacing within 24 hours – N (%)	48 (4.9%)	32 (3.2%)	29 (2.7%)	0.02

N Engl J Med. 2016;374(18):1711-1722.

ROC-ALPS Strengths

Strengths

- Double-blind, randomized trial
- Large sample size
- Equal baseline characteristics and evenly matched groups
- 99.5% patient follow-up
- No differences in pre-shock pauses, compression rate/depth, CPR fraction between groups

N Engl J Med. 2016;374(18):1711-1722.

ROC-ALPS Limitations

Limitations

- Utilized non-weight-based dosing for lidocaine
- Post-cardiac arrest care not standardized between hospitals
- Enrolled patients at randomization who (at baseline) had little to no chance of survival
- Selection bias

N Engl J Med. 2016;374(18):1711-1722.

ROC-ALPS Takeaways

No difference in hospital discharge or favorable neurologic outcome

Lidocaine associated with higher rates of ROSC at ED arrival

Lidocaine and amiodarone associated with higher rates of hospital admission

Patients given either drug required fewer shocks

Amiodarone required more cardiac pacing

Utilized pre-made syringes

N Engl J Med. 2016;374(18):1711-1722.

The Eras of Antiarrhythmics' in the ACLS Guidelines

AHA 2000 update
- Amiodarone preferred following ARREST trial

2002
- ALIVE trial shows benefit over lidocaine

AHA 2005, 2010, 2015 update
- Amiodarone preferred agent

2016
- ROC-ALPS trial

AHA 2018 focus update
- Amiodarone or lidocaine

2022
- ROC-ALPS post-hoc analysis

Effect of Time to Treatment With Antiarrhythmic Drugs on Return of Spontaneous Circulation in Shock-Refractory Out-of-Hospital Cardiac Arrest

RAHIMI ET AL. 2022

ROC-ALPS Post-hoc

Primary Objective

- Explore the relationship between time to antiarrhythmic treatment and ROSC

Study Design

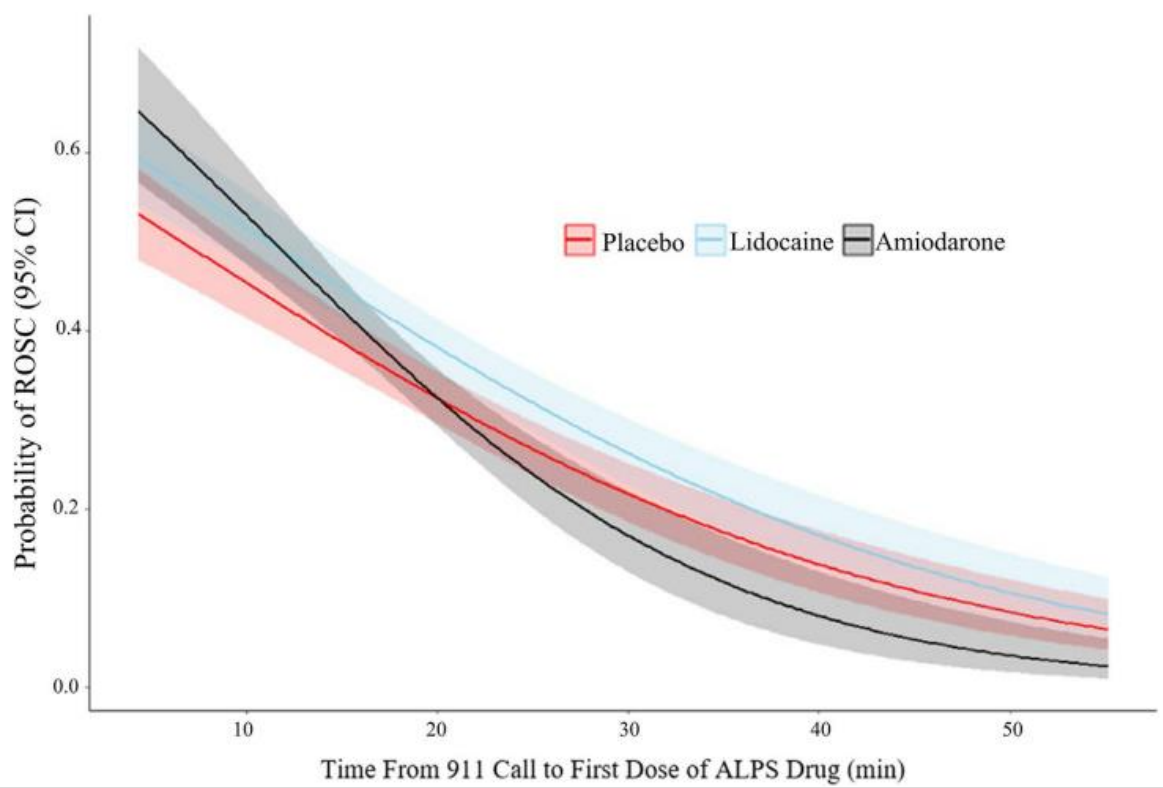
- Individual patient-level secondary analysis in the per-protocol population
- 2994 patients with known drug administration

Primary Outcome

- **ROSC at hospital arrival**

J Am Heart Assoc. 2022;11(6):e023958..

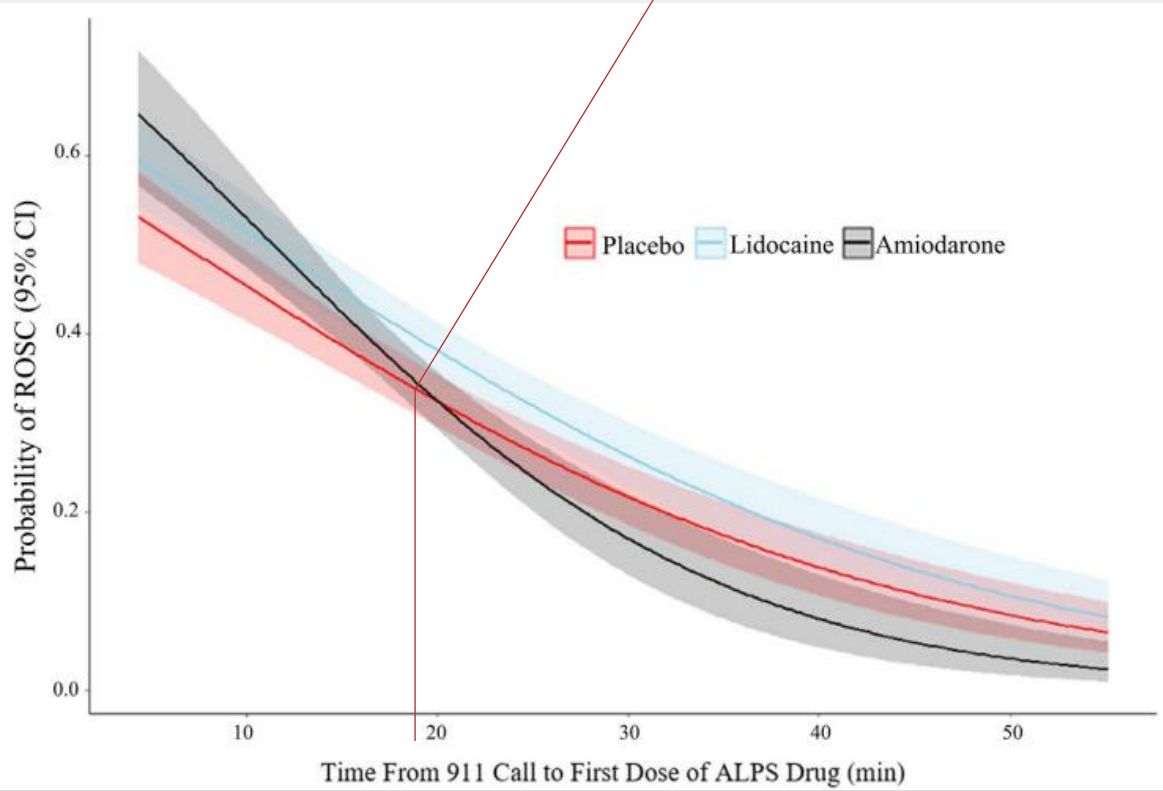
ROC-ALPS Post-hoc: Primary Outcome



J Am Heart Assoc. 2022;11(6):e023958..

Primary Outcome: Amiodarone vs Placebo

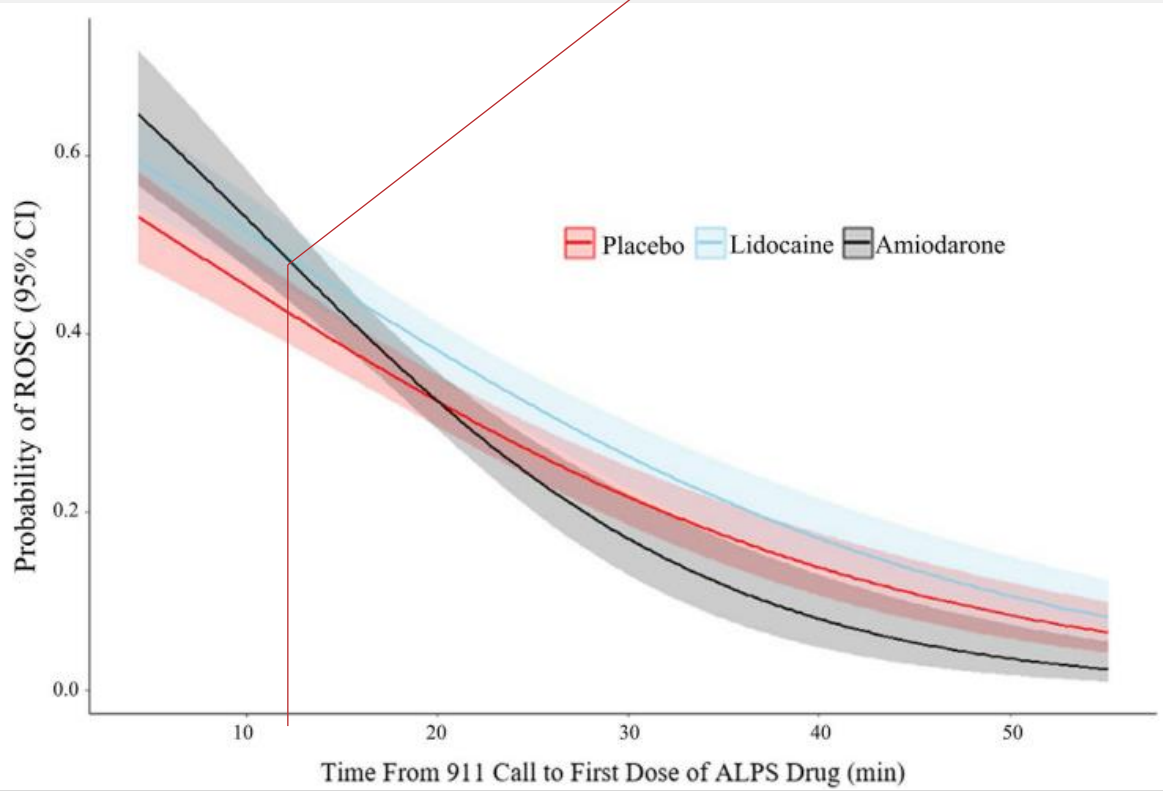
Treatment with amiodarone is more likely to lead to ROSC vs placebo until ~19.5 minutes



J Am Heart Assoc. 2022;11(6):e023958..

Primary Outcome: Amiodarone vs Lidocaine

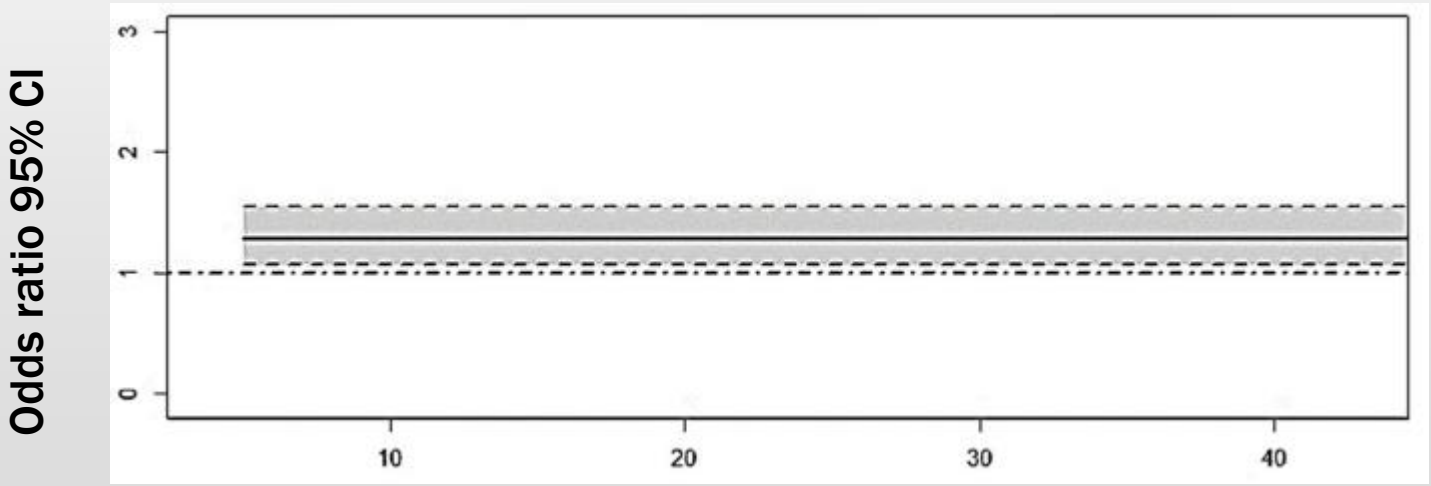
Treatment with amiodarone is more likely to lead to ROSC vs lidocaine until ~13.5 minutes



J Am Heart Assoc. 2022;11(6):e023958..

Primary Outcome: Lidocaine vs Placebo

Time	OR of ROSC at hospital arrival
All time points	1.29 (1.07 – 1.59); p=0.004



J Am Heart Assoc. 2022;11(6):e023958..

ROC-ALPS Post-hoc Takeaways

Amiodarone appears superior to lidocaine if given early (< 13.5 minutes)

Lidocaine appears superior to amiodarone if given later (>13.5 minutes)

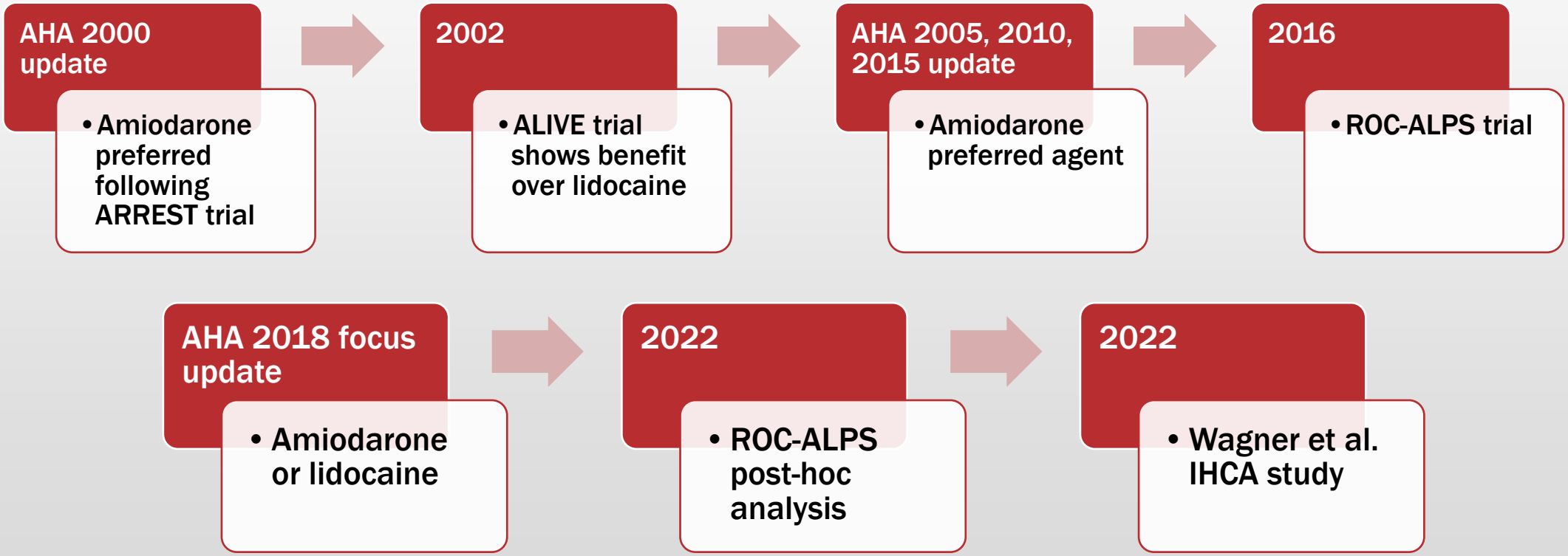
Placebo appears superior to amiodarone if given later (>19.5 minutes)

Early administration of antiarrhythmics appears more beneficial compared to later

Early administration may be a marker for early CPR/defibrillation

J Am Heart Assoc. 2022;11(6):e023958..

The Eras of Antiarrhythmics' in the ACLS Guidelines



Comparative Effectiveness of Amiodarone and Lidocaine for the Treatment of In-Hospital Cardiac Arrest

WAGNER ET AL. 2022

Wagner et al.

Objective

- Compare outcomes of patients with IHCA due to VF/pVT treated with amiodarone or lidocaine

Study Design

- Retrospective cohort study
- Data from GWTG-R registry
- 14,630 Patients

Chest. 2023;163(5):1109-1119.

Wagner et al. Inclusion and Exclusion

Inclusion

- Age > 18
- IHCA secondary to VF/pVT
- Received defibrillation
- Received either amiodarone or lidocaine

Exclusion

- Arrest began in outpatient or ambulatory care setting
- Did not receive defibrillation
- Did not receive amiodarone or lidocaine
- Received both antiarrhythmics
- Missing data on treatment
- Incomplete documentation

Chest. 2023;163(5):1109-1119.

Wagner et al. Interventions

- Amiodarone (n=10,058)
- Lidocaine (n=4572)

Chest. 2023;163(5):1109-1119.

Wagner et al. Outcomes

Primary Outcome

- ROSC

Secondary Outcome

- 24-hour survival post arrest
- Survival to hospital discharge
- Favorable neurologic outcome

Chest. 2023;163(5):1109-1119.

Wagner et al. Statistics

- Utilized propensity score methods (PSMs) and multivariable logistic regression to balance covariates between groups
- Average marginal effect (AME) calculated to predict the probability of an outcome with consistent covariates
  - Often referred to as the average treatment effect (ATE)
- Risk differences were estimated using inverse probability of treatment weighting (IPTW)
  - Potential benefits of IPTW for PSMs:

Lower statistical errors	Approximately correct CIs	Minimize type I error rates

Chest. 2023;163(5):1109-1119.

Wagner et al. Baseline Characteristics

Baseline Characteristics	Amiodarone (n=10058)	Lidocaine (n=4572)
Age, mean, yr (SD)	65.2 ± 14.7	65.7 ± 14.3
Diabetes (%)	30.8%	27.1%
Renal insufficiency or dialysis (%)	29.0%	22.9%
Event location: Adult ICU (%)	50.6%	43.2%
Event location: ED (%)	14.0%	19.6%
Event witnessed (yes) (%)	87.5%	87.7%
Continuous vasopressor (%)	32.9%	26.2%
Time to defibrillation (min)	2.4	2.2

Chest. 2023;163(5):1109-1119.

Wagner et al. Primary Outcome

Primary Outcome	Unadjusted Outcome with Amiodarone (n=10058)	Unadjusted Outcome with Lidocaine (n=4572)	Absolute risk difference (95% CI)
ROSC (%)	76.6%	77.3%	0.7 (-1.2 – 2.7); p=0.47

Primary Outcome	Adjusted Outcome with Amiodarone (n=10058)	Adjusted Outcome with Lidocaine (n=4572)	Absolute Risk Difference	Average Marginal Effect (95% CI)
ROSC (%)	76.1%	79.0%	1.15; p = 0.01	2.3% (0.5 – 4.2)

Chest. 2023;163(5):1109-1119.

Wagner et al. Adjusted Secondary Outcomes

Secondary Outcomes	Adjusted risk with Amiodarone (n=10058)	Adjusted risk with Lidocaine (n=4572)	Adjusted Odds Ratio	Average Marginal Effect (95% CI)
24-hour survival	59.9%	62.5%	1.16; p=0.004	3.0% (0.9 – 5.1)
Survival to discharge	43.0%	46.3%	1.19; p<0.001	3.3% (1.5 – 5.2)
Favorable neurologic outcome at hospital discharge	39.4%	42.5%	1.18; p<0.001	3.1% (1.3 – 4.9)

Chest. 2023;163(5):1109-1119.

Wagner et al. Strengths

Strengths

- Large sample size
- Adjusted results due to confounders
- Unadjusted results favor lidocaine
- Benefit in neurologic outcomes
- Discuss potential mechanisms that favor use of lidocaine

Chest. 2023;163(5):1109-1119.

Wagner et al. Limitations

Limitations

- Observational, retrospective cohort analysis
- 70% of sample received amiodarone
- Data limited to hospitals who participate in the GWTG-R registry
- Limited data on: reasons for admission, **etiology of IHCA**, **duration of CPR**, hemodynamic parameters at ROSC, amount of drug administered
- No data on administration of either treatment
- Favorable neurologic outcome based on cerebral performance (more of an estimation versus mRS)
- Complex statistics

Chest. 2023;163(5):1109-1119.

Wagner et al. Takeaways

Only study looking at IHCA

Utilized ROSC as a primary outcome

Adjusted results favored lidocaine in achieving ROSC, 24-hour survival, survival to discharge, and neurologic survival

Only study to find that lidocaine is associated with improved survival vs amiodarone

Only study finding improvement in neurologic status (though based on cerebral performance)

Survival rate >40%

Chest. 2023;163(5):1109-1119.

Summary

	ALIVE		ROC ALPS		Wagner et al.	
Antiarrhythmic	Amiodarone	Lidocaine	Amiodarone	Lidocaine	Amiodarone	Lidocaine
Survival to hospital admission*	✓	✗	=		✗	✓
Survival to discharge**	n/a	n/a	=		✗	✓
ROSC***	n/a	n/a	✓	✓	✗	✓
Favorable neurologic outcome	n/a	n/a	=		✗	✓

*ALIVE Primary Outcome
**ROC-ALPS Primary Outcome
***Wagner et al. Primary Outcome

CLINICAL QUESTION:

Should amiodarone or lidocaine be the antiarrhythmic of choice for shock refractory ventricular fibrillation/ pulseless ventricular tachycardia?

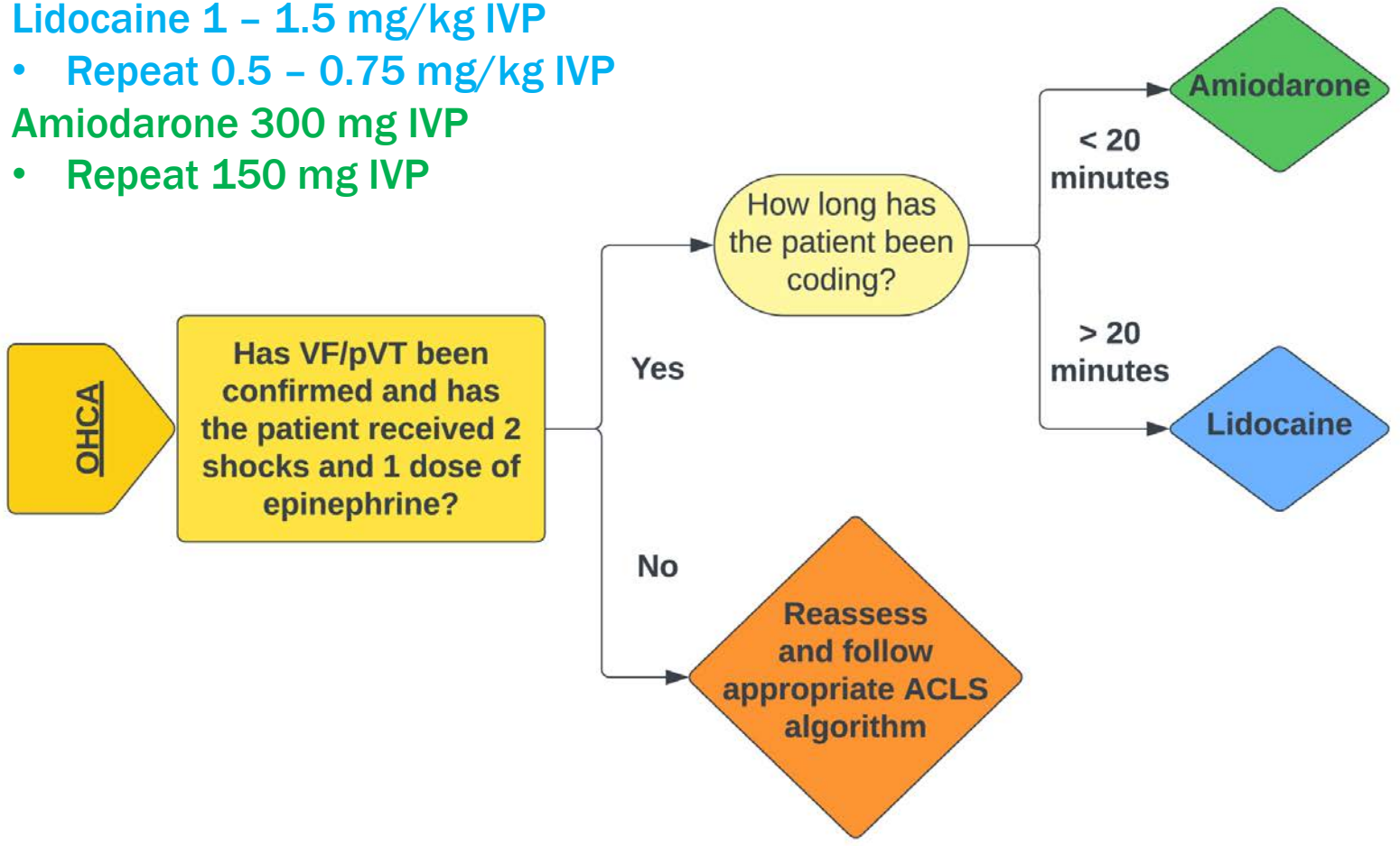
OHCA Algorithm

Lidocaine 1 – 1.5 mg/kg IVP

- Repeat 0.5 – 0.75 mg/kg IVP

Amiodarone 300 mg IVP

- Repeat 150 mg IVP



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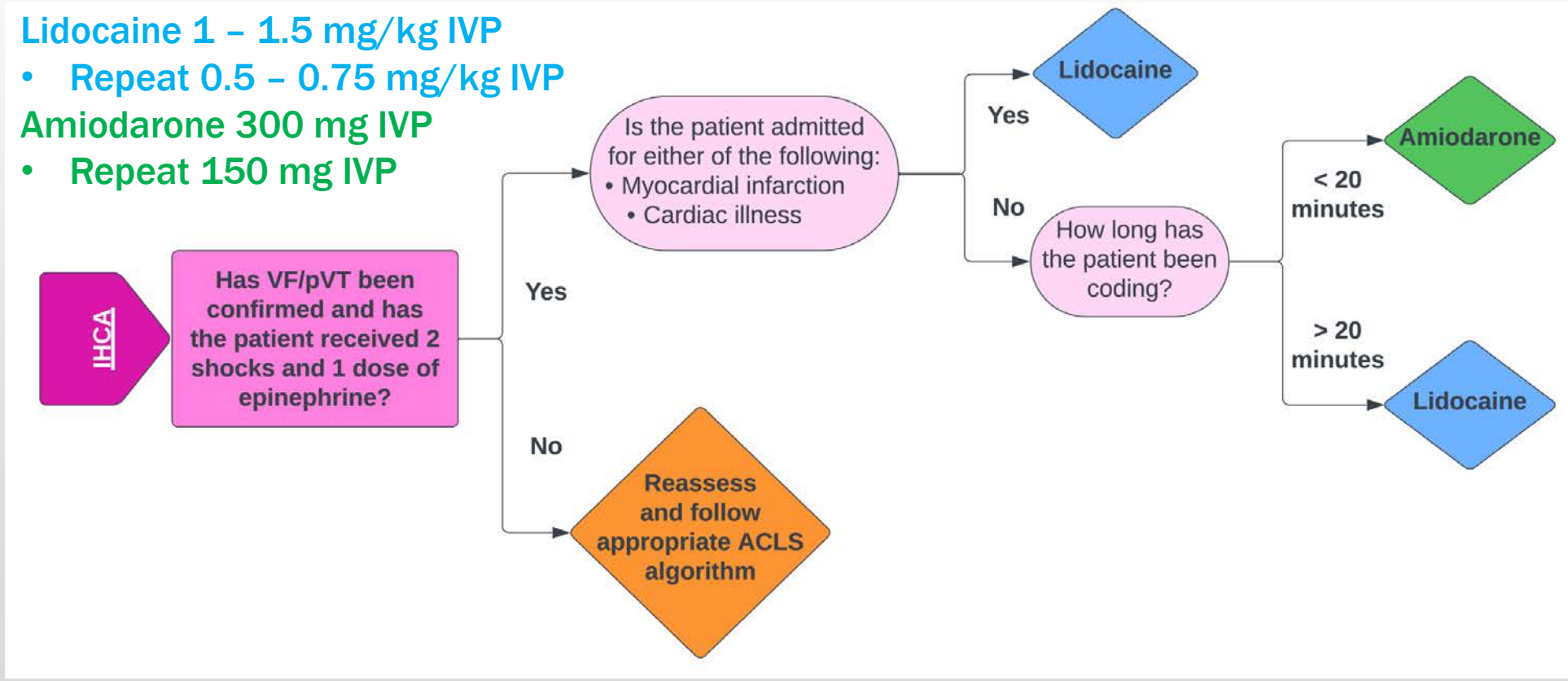

Feel the Rhythm! Feel the Rhyme! Give it up, it's Lidocaine's Time:

Lidocaine vs Amiodarone for Shock Refractory VF/pVT

Markus Reedy, PharmD.
PGY 2 Pharmacotherapy Resident
University of the Incarnate Word
Feik School of Pharmacy

Resources for Pharmacists

2020 AHA Guidelines for ACLS – Executive Summary

- Merchant RM, Topjian AA, Panchal AR, et al. Part 1: Executive Summary: 2020 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. Circulation. 2020;142(16_suppl_2):S337-S357. doi:10.1161/CIR.0000000000000918

2020 AHA Guidelines for ACLS – Basics of Emergency Cardiovascular Care

- Panchal AR, Bartos JA, Cabañas JG, et al. Part 3: Adult Basic and Advanced Life Support: 2020 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. Circulation. 2020;142(16_suppl_2):S366-S468. doi:10.1161/CIR.0000000000000916

Find an ACLS course near you!

- Advanced cardiovascular life support (ACLS). cpr.heart.org. May 25, 2023. Accessed November 10, 2023. https://cpr.heart.org/en/cpr-courses-and-kits/healthcare-professional/acls.

Post-test Questions

Post-test Question 1

What is the initial dose of amiodarone for shock refractory ventricular fibrillation (VF)/pulseless ventricular tachycardia (pVT)?

A. 150 mg IVP

B. 300 mg IVP

C. 1 – 1.5 mg/kg IVP

D. 150 mg IV bolus over 10 minutes

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D. 150 mg IV bolus over 10 minutes

Post-test Question 2

You are the pharmacist who responded to a CODE BLUE. CPR is in progress. Defibrillator/monitor pads are attached which shows the rhythm above, and the physician states the patient is in ventricular fibrillation. What is the correct treatment algorithm?

A. Shock, CPR for 2 minutes, recheck rhythm, shock, CPR for 2 minutes and epinephrine, recheck rhythm, shock, CPR and lidocaine

B. Shock, CPR for 2 minutes, recheck rhythm, shock, CPR for 2 minutes and amiodarone, recheck rhythm, shock, CPR and repeat amiodarone

C. CPR for 2 minutes, epinephrine every 3 – 5 minutes (every other pulse check)

D. CPR for 2 minutes, epinephrine every 3 – 5 minutes (every other pulse check), lidocaine after third pulse check

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You are the pharmacist who responded to a CODE BLUE. CPR is in progress. Defibrillator/monitor pads are attached which shows the rhythm above, and the physician states the patient is in ventricular fibrillation. What is the correct treatment algorithm?

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Post-test Question 3

Regarding the primary literature reviewed in this presentation, the study by Wagner et al found higher rates of ROSC with lidocaine and amiodarone compared to the ROC-ALPS trial. What major difference between the two studies could have led to higher rates of ROSC in Wagner et al study?

A. Wagner et al compared lidocaine to amiodarone for OHCA which has a higher rate of survival compared to IHCA

B. Wagner et al compared lidocaine to amiodarone for IHCA which has a higher rate of survival compared to OHCA

C. ROC ALPS utilized the GWTG-R data base which is limited by only hospitals participating in the registry

D. ROC ALPS utilized PSM to adjust for baseline differences between groups which could negatively affect outcome results

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Post-test Question 4

TS is a 32-year-old female with an extensive cardiovascular history. She is currently admitted to the CVICU for concerns of an NSTEMI with plans for a staged PCI tomorrow. A CODE BLUE is called, and you are the pharmacist who responds. CPR is in progress, defibrillator/monitor pads are attached, first rhythm check shows VF, and a shock is deployed followed by epinephrine 1mg. Based on the algorithm, which medication do you recommend to the team? (TS weighs 54kg and height is 69 inches)

A. Amiodarone 150 mg IVP

B. Amiodarone 300 mg IVP

C. Lidocaine 40 mg IVP

D. Lidocaine 80 mg IVP

Post-test Question 4

TS is a 32-year-old female with an extensive cardiovascular history. She is currently admitted to the CVICU for concerns of an NSTEMI with plans for a staged PCI tomorrow. A CODE BLUE is called, and you are the pharmacist who responds. CPR is in progress, defibrillator/monitor pads are attached, first rhythm check shows VF, and a shock is deployed followed by epinephrine 1mg. Based on the algorithm, which medication do you recommend to the team? (TS weighs 54kg and height is 69 inches)

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D. Lidocaine 80 mg IVP

Special Thanks

Faculty Mentor

- Sarah Berman, PharmD, BCCCP

Critique

- Lauren Lozano, PharmD, BCCCP

Claiming Co-curricular Credit

Use this QR code to claim co-curricular credit

Feel the Rhythm! Feel the Rhyme! Give it up, it's Lidocaine's Time:

Lidocaine vs Amiodarone for Shock Refractory VF/pVT

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