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# TREATMENT OF VENTRICULAR DYSRHYTHMIAS

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# I report no conflicts of interest

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# Objectives

- Recognize mechanisms, types, and clinical presentations of ventricular dysrhythmias
- List different diagnostic approaches to ventricular dysrhythmias
- Analyze different pharmacological options for treating ventricular dysrhythmias

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# Outline

1. **Mechanisms & Etiology** of Ventricular Dysrhythmia
2. Synchronized Cardioversion vs Defibrillation
3. Stable Ventricular Tachycardias
4. Torsades de Pointes
5. pVT and VF (treatment strategies)
    - lidocaine vs amiodarone
6. Refractory VF strategies

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# Dysrhythmias

## Tachydysrhythmias

**QRS complex**

Narrow(<120ms)

### Supraventricular

- Atrial flutter (one ectopic focus)
- Atrial Fibrillation (multiple foci)
- pSVT
  - AVNRT
  - AVRT

**Wide > 120ms**

- SVT w aberrancy

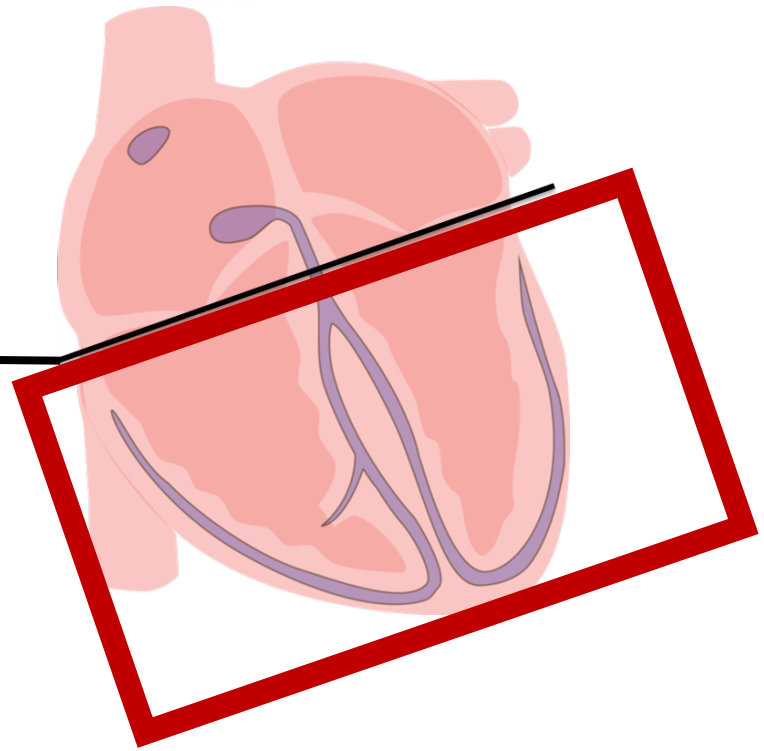
### Ventricular

- VT
- VF

## Bradydysrhythmias

– AV block

- 1st, 2nd, 3rd degree



Ray L, Geier C, DeWitt KM. Am J Health Syst Pharm. 2023 Aug 18;80(17):1123-1136.

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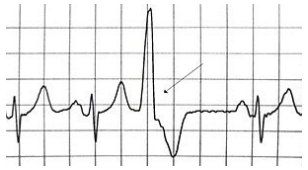
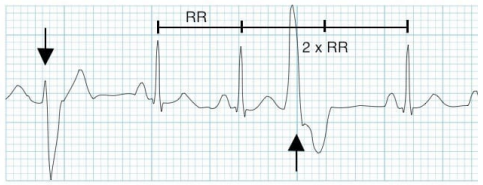
# PVC premature ventricular contraction

Why is a normal QRS complex narrow?

PVC: QRS is wide because it is slow



Unifocal vs multifocal PVCs



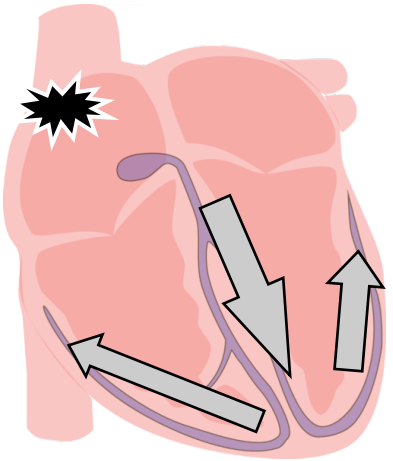

Definition of VT:

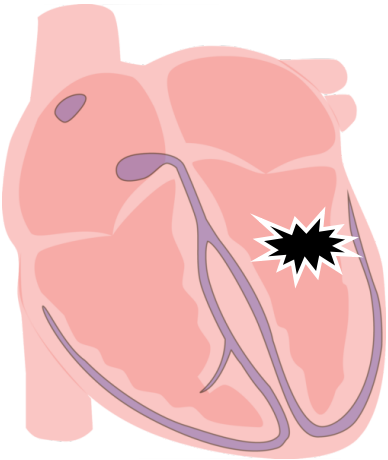
≥ 3 consecutive PVCs

Monomorphic vs polymorphic

Sustained VT:

VT ≥ 30 sec (or requiring cardioversion)





Ventricular Tachyarrhythmias. Ed. Brian Olshansky, Arrhythmia Essentials. 2nd Ed. Elsevier, 2017, p 219-277,

Images: Wikipedia commons

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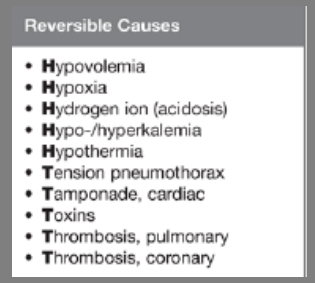
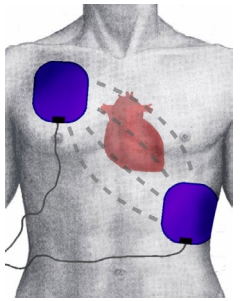
# Out-of-Hospital Cardiac Arrest

| Initial rhythm | Cause | Survival [1,2,3] |
|---|---|---|
| OHCA overall survival[1] | | 10% |
| pVT/VF | Coronary | 25% - *74%* |
| PEA |  | 8% |
| asystole | ??? | 1 % |





1. Daya MR, et al. Resuscitation Outcomes Consortium (ROC). Resuscitation. 2015 Jun;91:108-15.
2. Valenzuela TD, N Engl J Med. 2000 Oct 26;343(17):1206-9
3. Kudenchuck PJ. N Engl J Med. ALPS Trial. 2016 May 5;374(18):1711-22.

Images: https://commons.wikimedia.org/wiki/

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# Etiology of Ventricular Arrhythmias

~1/3 of OHCA patients have initial pVT/VF[1]

ventricular dysrhythmia associated w 3-6x higher rate of MI[3,4]

*Pediatric/adolescent VT/VF:*
HCM, ARVD, LQTS…
Brugada… toxicology…
Congenital and high risk of SCD

18% of initial pVT/VF requires medication[2]

(refractory to shock)

Initial shockable rhythm[5,6]
50% have evidence of acute MI


1. Oving I et al. Resuscitation. 2020 Jun;151:67-74
2. Kudenchuck PJ. N Engl J Med. ALPS Trial. 2016 May 5;374(18):1711-22.
3. Henkel DM, et al. Am Heart J. 2006 Apr;151(4):806-12
4. Zeyons F, et al. Eur Heart J Acute Cardiovasc Care. 2017 Mar;6(2):103-111
5. Resuscitation. 2012 Dec;83(12):1444-50.
6. Zeyons F et al. Eur Heart J Acute Cardiovasc Care. 2017 Mar;6(2):103-111.

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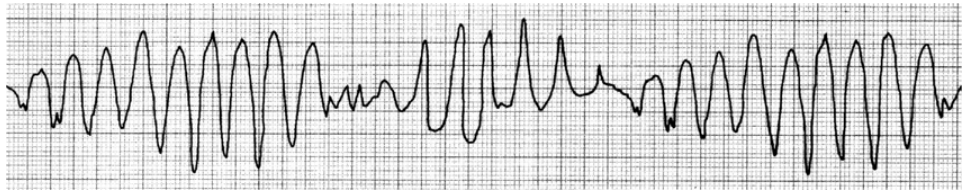
# monomorphic

## Adult cardiovascular disease



# polymorphic

## Torsades de Poines (TdP)

Brugada syndrome

Long-QT syndrome (LQTS)

pediatric / congenital

95% of non-sustained VT
have cardiomyopathy

Idiopathic Fascicular Left Ventricular Tachycardia

(Verapamil-Sensitive VT)

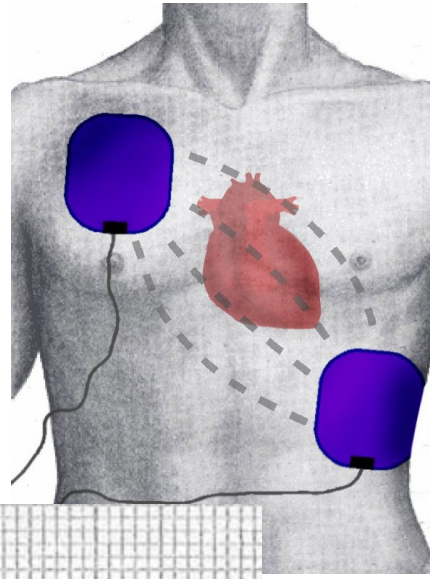
Catecholaminergic Polymorphic VT (CPVT)

Accessory pathways?

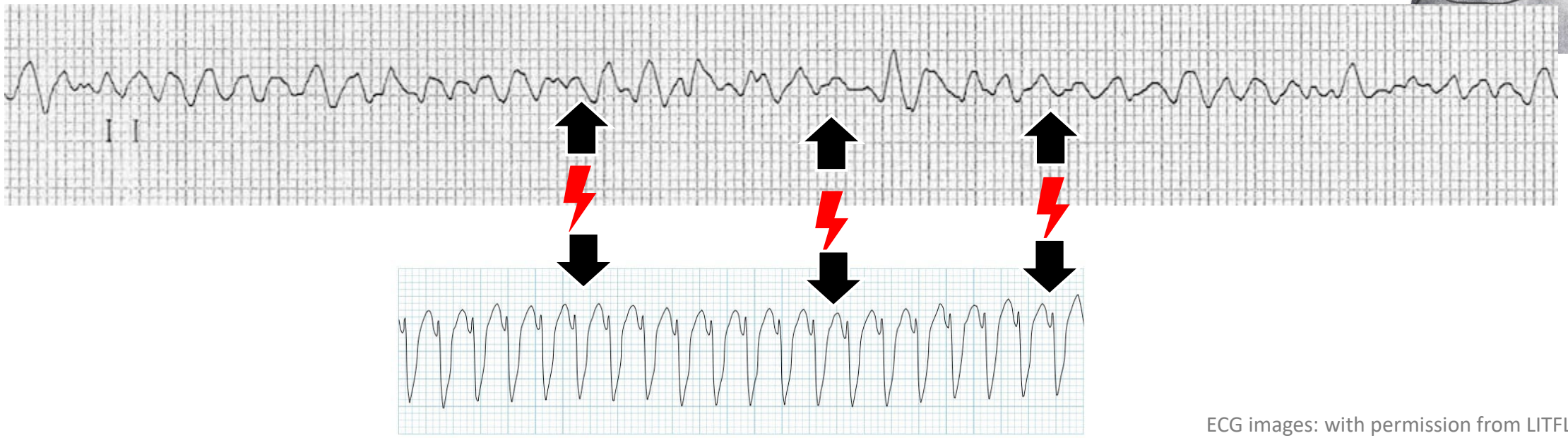
Ventricular Tachyarrhythmias. Ed. Brian Olshansky, Arrhythmia Essentials. 2nd Ed. Elsevier, 2017, p 219-277.
Images: litflecglibrary.com

# SYNCHRONIZED CARDIOVERSION –

## FOR RHYTHMS WITH PULSE



## DEFIBRILLATION - FOR PULSELESS VT & VF



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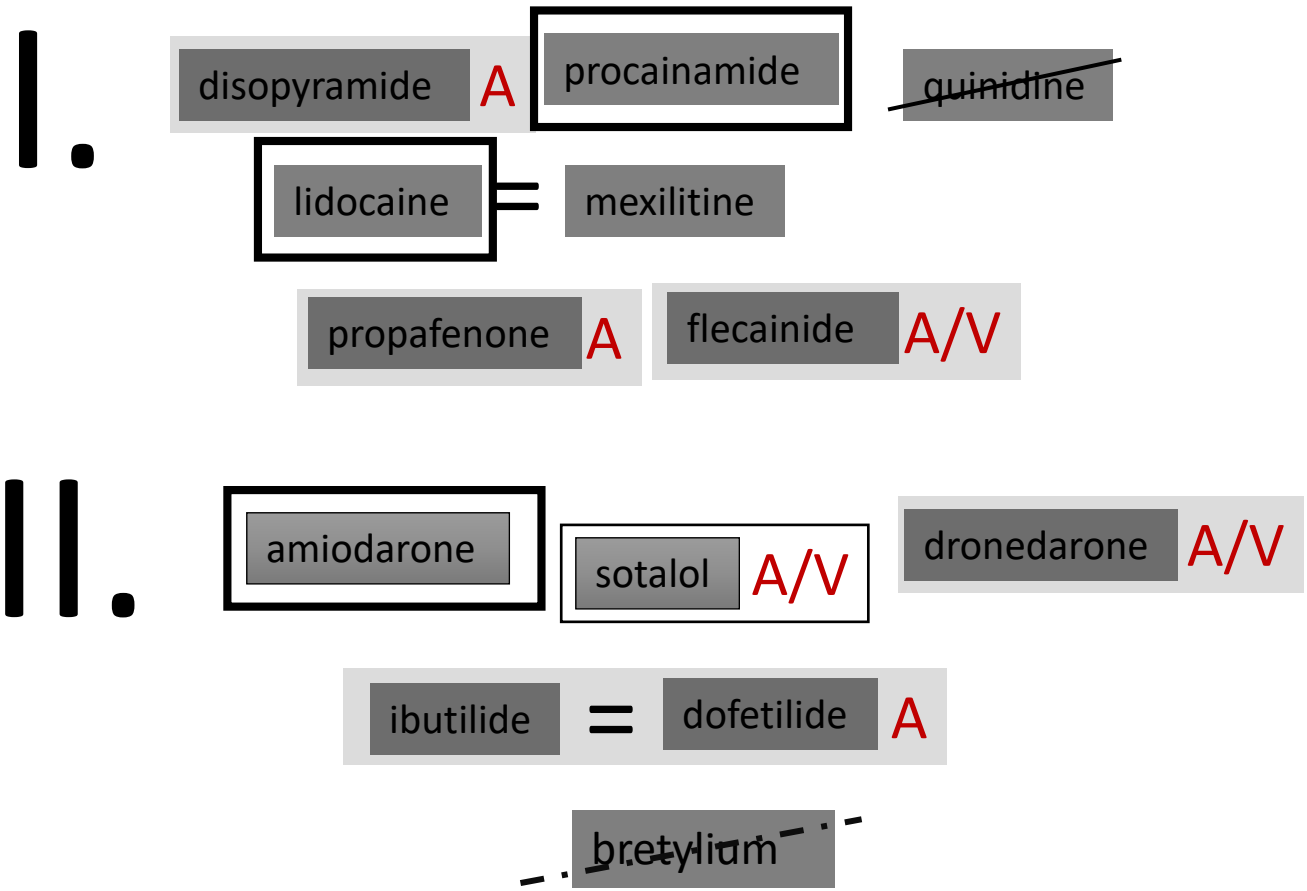
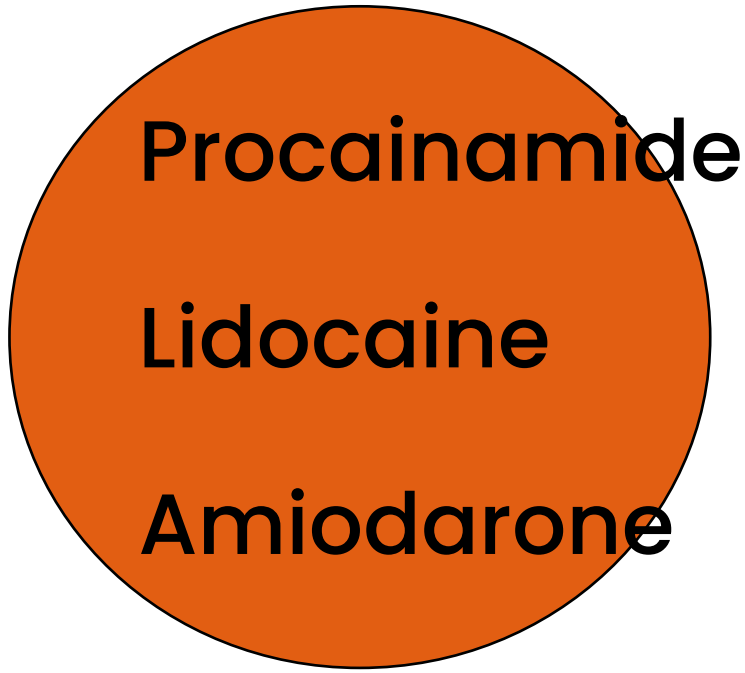
# MAKING SENSE OF ANTI-ARRHYTHMICS




PO

IV

IV or PO

A Atrial

V Ventricular

# STABLE VT

# STABLE VT

Literature review

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# STABLE MONOMORPHIC VT

## Prospective Randomized Trials

Gorgels 1996

- (n = 29) Procainamide superior to lidocaine[2] 80% vs 21%

Lidocaine "0 for 3"

Ho 1994

- (n = 33) Sotalol superior to lidocaine[3] 69% vs 20%

Manz 1988

- (n = 31*) amjaline superior to lidocaine 67% vs 13%

Ortiz 2017

- (n = 62) procainamide superior to amiodarone

Gorgels AP, et al. Am J Cardiol. 1996 Jul 1;78(1):43-6.
Ho DSW, et al. Lancet 1994;344:18–23.)
Manz et al. Dtsch Med Wochenschr. 1988 Aug 26;113(34):1317-21.
Marill KA, et al. Acad Emerg Med 2010;17:297–306
Ortiz M et al. PROCAMIO study. Eur Heart J. 2017 May 1;38(17):1329-1335

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# PROCAMIO Trial

Multicenter
Prospective
Randomized

Amiodarone 5mg/kg (n = 29)
over 20 min
Procainamide 10mg/kg (n = 33)

26 centers
6 years
n = 74

Endpoint: major cardiac adverse events
Amiodarone 41%
Procainamide 9 %
p = 0.006

VT Terminated*:
38% (amio)
67% (procainamide)

Adverse events*:
Amiodarone 48%
Procainamide 24 %

Most common ADR:
Hypotension
(amiodarone 7; procainamide 3)

*p < 0.05

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# STABLE VENTRICULAR TACHYCARDIA

- **Literature is sparse and small**
- **Procainamide**
  - Often best choice
- **Amiodarone**
  - Common choice
- **Lidocaine**
  - weakest literature
  - For patients taking amiodarone

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# STABLE VENTRICULAR TACHYCARDIA
# DOSING

## Procainamide

- 100mg q 5 min
- 10 – 17 mg/kg
- or 20 to 50mg/min until:

Max dose: 17 mg/kg[1] or 1 g[2]

1. Arrhythmia is suppressed
2. Hypotension ensues
3. QRS complex prolonged by 50% of original duration*

Maintenance Infusion: 1 – 4 mg/min

Active metabolite: N-acetylprocainamide (NAPA)

K-channel blocking activity

*not relevant in VT


1. Al-Khatib SM,, et al: 2017 AHA/ACC/HRS Guideline. Heart Rhythm 2018; 15(10):e73-e189.
2. Product Information: Procainamide HCl. Hospira Inc. Lake Forest, IL, 2019.

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# STABLE VENTRICULAR TACHYCARDIA

# DOSING

## Amiodarone

- 150mg over 10 minutes
- Maintenance:

Maintenance Infusion:
1 mg/min x 6h, then 0.5mg/min x 18h
$T_{1/2}$: 26 – 107 d
ADRs: eye, thyroid, pulmonary, skin, neuro, hepatitis, ~~renal~~


Al-Khatib SM,, et al: 2017 AHA/ACC/HRS Guideline. Heart Rhythm 2018; 15(10):e73-e189.

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# STABLE VENTRICULAR TACHYCARDIA
# DOSING

## Lidocaine

- 1-1.5 mg/kg bolus (IVP)
- Repeat 0.5-0.75mg/kg IVP q 5-10 min (max 3 mg/kg)
- Maintenance infusion: 1 – 4 mg/min
  - Hepatically metabolized
  - Renally excreted

Accumulation of active MGEX
Lidocaine serum levels [1.5 – 5 mcg/mL]


1. Al-Khatib SM,, et al: 2017 AHA/ACC/HRS Guideline. Heart Rhythm 2018; 15(10):e73-e189.
2. Product Information: Procainamide HCl. Hospira Inc. Lake Forest, IL, 2019.

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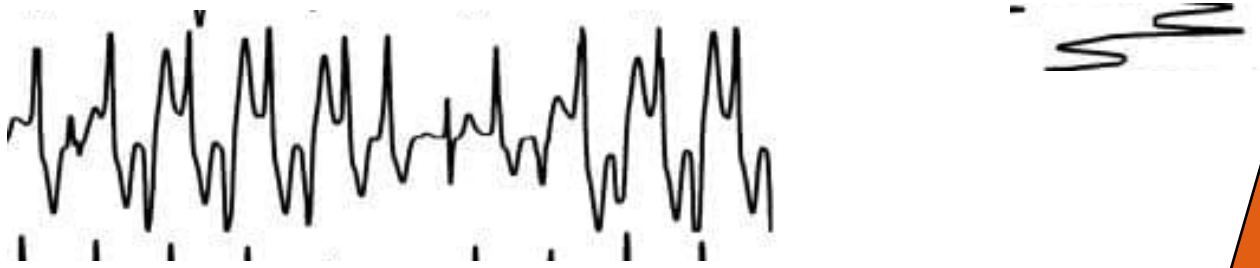
# VERAPAMIL-SENSITIVE VENTRICULAR TACHYCARDIA

WHAT !?

- a.k.a. Belhassen Ventricular Tachycardia
- Right Bundle Branch Block + R/L Axis Deviation
- Verapamil: 5 – 10 mg IVP
- **Challenging diagnosis** *(known history?)*

## CATECHOLAMINERGIC POLYMORPHIC VT (CPVT)

- Genetic, Diagnosed early in life
- Mortality > 30% if later
- Stress- or Exercise-Induced
- Beta-blocker
- **Challenging diagnosis**



Pérez-Riera AR, et al. Ann Noninvasive Electrocardiol. 2018 Jul;23(4):e12512.

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# UNUSUAL CASES:
## VT IN SEVERE HEART FAILURE

MI → LV heart failure + ventricular dysrhythmia → transplant?

ICD → amiodarone or sotalol → +/- mexiletine

Ablation of VT and ICD better than drug escalation[2]

Procainamide Infusion??


1. Santangeli P, et al. J Am Coll Cardiol. 2017 Apr 11;69(14):1842-1860
2. Sapp JL: N Engl J Med. 2016 Jul 14;375(2):111-21

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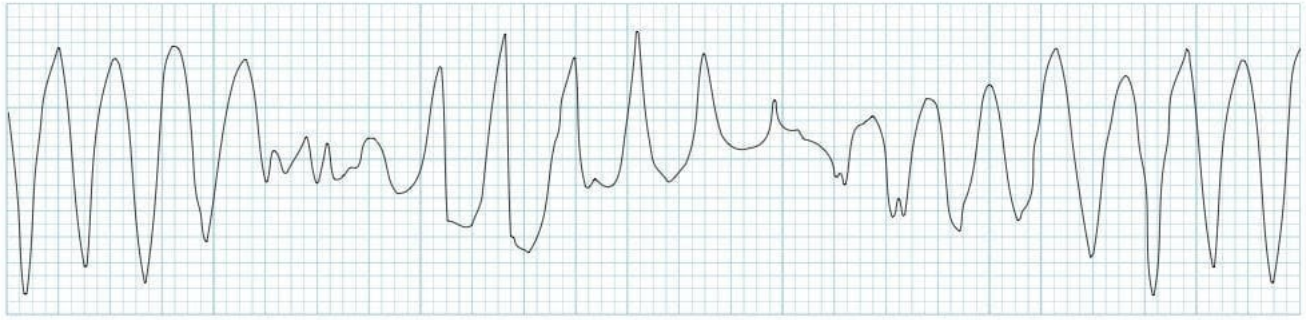
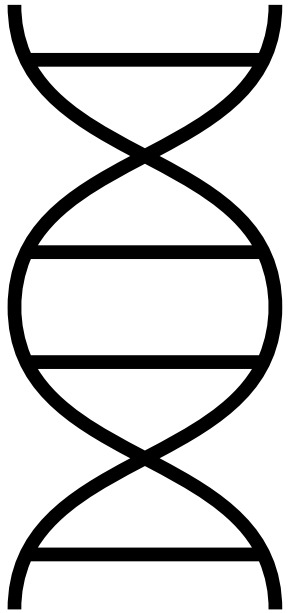
# TORSADES DE POINTES

- Acquired LQTS
  - Electrolytes
  - Medications (≈ 250)
  - Sex (F), advanced age, HF/MI
- Up to 20% of TdP cases linked to LQTS
  - LQTS
  - Type 1 LQTS ($\downarrow I_{Ks}$)
  - Type 2 LQTS ($\downarrow I_{kr}$)
  - Type 3 LQTS ($\uparrow I_{Na,L}$)





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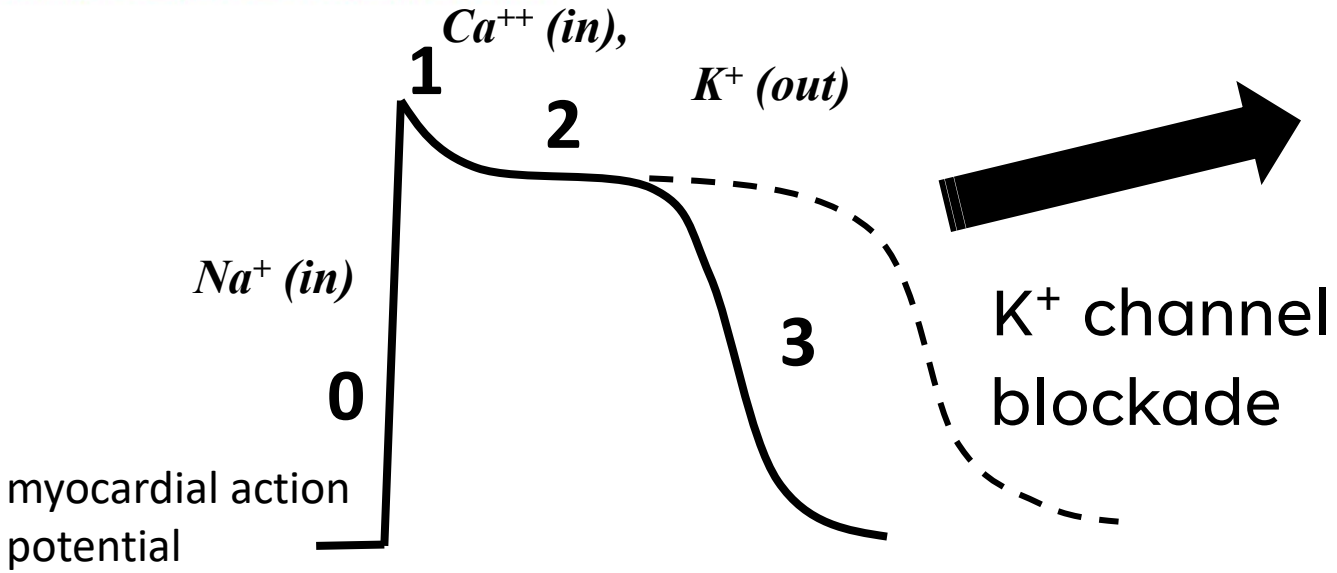
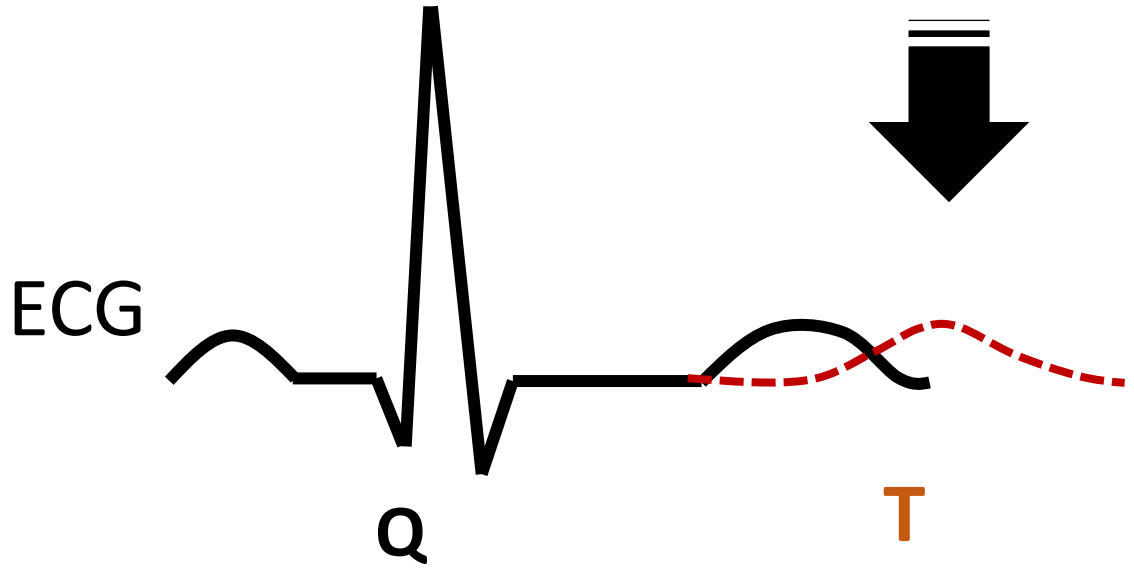



$I_{Kr}$

Delayed rectifier potassium current (Rapid component)




CLASS III (K-BLOCKING) ANTIARRHYTHMICS ARE ***SUPPOSED TO*** PROLONG QT

| | | |
|---|---|---|
| Dofetilide (1) | 25-50 ms | 2.1% |
| Sotalol (2,3) | 25-60 ms | 1.8-4.8 (1) |
| Ibutilide (4,5,6) | 39ms (+/- 28) | 0.6 – 2.7% |
| Amiodarone (7,8) | 35-199* (QT dispersion) | 0.34-0.7 % (2) |
| Methadone (doses > 60-100mg) (9,10) | 42 +/- 8 ms | 3.5 % |
| Fluconazole (11)<br>Fluconazole + ciprofloxacin (12) | 10.1 ms<br>10.7 ms | 0.30 % |
| Fluoroquinolones: (13,20,21) | 14-16 ms | <0.0001 %<br>Moxifloxacin >> Levofloxacin >Ciprofloxacin |
| **Macrolides**<br>Erythromycin) (14)<br>Azithromycin (15) | <br>~ 50 ms<br>5-14 ms | <br>Many cases<br>Rare |
| Haloperidol (16) | 4.7 ms | 0.14 % |
| Ondansetron (17,18,19) | 5.6 ms (8mg IV)<br>19.5ms (32mg) | 0 – case reports |
| Olanzapine (16) | 6.8 ms | <0.001 % |
| Ziprasidone (16) | 20.3 ms | <.0001 % |

Highly dependent on baseline QT, electrolytes, renal insufficiency, DDI

TdP risk dramatically increases when QTc is > 60ms above baseline

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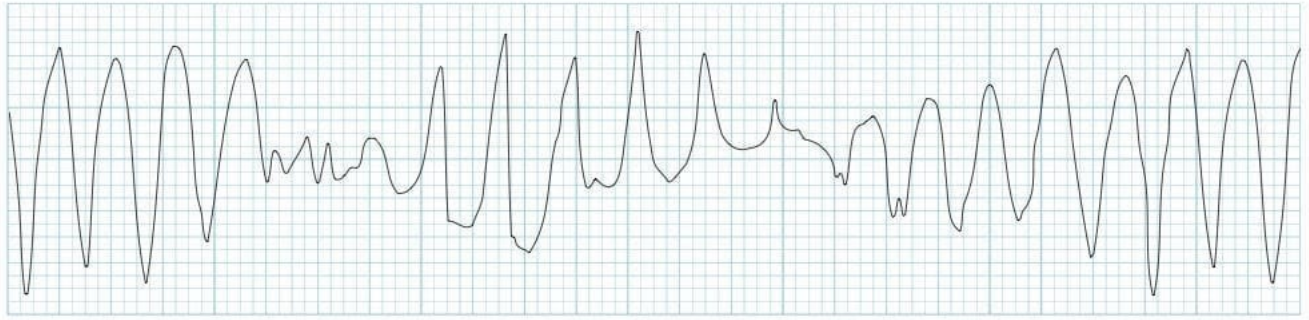
# TORSADES DE POINTES



Immediate treatment = unstable or stable VT

- Electrical cardioversion
- Antiarrhythmic therapy
  - Lidocaine or amiodarone?

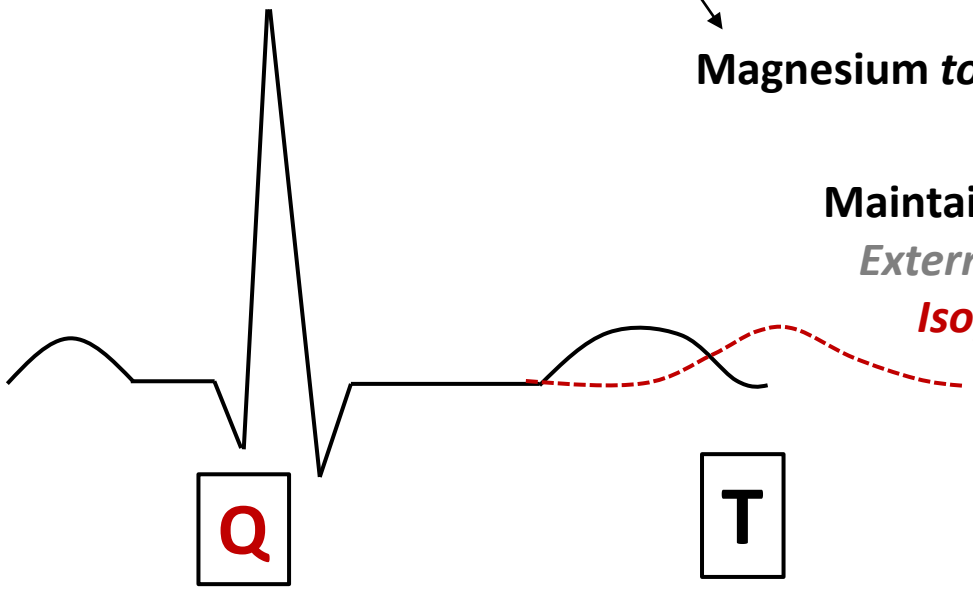
**Magnesium *to prevent recurrence***

**Maintain HR > 100**

***External/internal pacing***

***Isoproterenol infusion***

***0.5 – 5 mcg/min***




Panchal AR, et al. ACLS Guidelines *Circulation*. 2020;142(16_suppl_2):S366-S468.

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# ANTIARRHYTHMICS FOR STABLE VT

| Drug | Bolus | Maintenance | Notes |
|---|---|---|---|
| Amiodarone | 150mg over 10 min | 1 mg/min x 6h<br>0.5 mg/min x 18h | Hypotension |
| Procainamide | 10 mg/kg over 20 min<br>100mg q 5 min<br>10-17 mg/kg over 30 min | 1 – 4 mg/min | NAPA metabolite (monitor) |
| Lidocaine | 1.5 mg/kg<br>additional 0.75 mg/kg | 1 – 4 mg/min | Hepatic metabolism (MGEX) is renally excreted |
| Sotalol | 100mg IV over 5 min | 75-150mg IV q12h<br>(infused over 5 h) | Recently available IV (for AF) $$$ |
| Magnesium | 2g over 20-30 min | - | Only “for prevention of TdP” |

Ray L, Geier C, DeWitt KM. Am J Health Syst Pharm. 2023 Aug 18;80(17):1123-1136.
Neumar RW, et al. . Circulation 2010; 122(18 Suppl.3):S729-S767.

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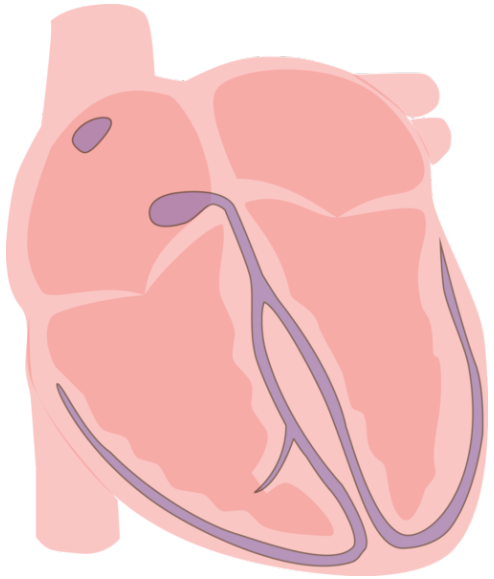
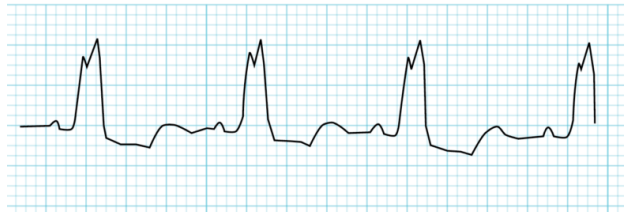
**Wide > 120ms**

SVT w aberrancy
Ventricular
VT
VF



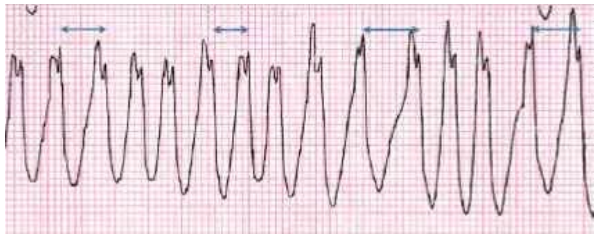


Bundle branch block

+

AFib

=



(80%) SVT with aberrancy
(20%) Ventricular tachycardia

Issa ZF et al. Clinical Arrhythmology and Electrophysiology. In: Braunwald's Cardiology. 21, 730 - 747

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# WIDE COMPLEX TACHYCARDIA

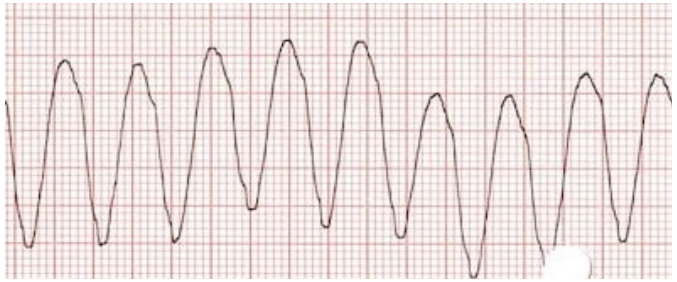
HR > 100 bpm

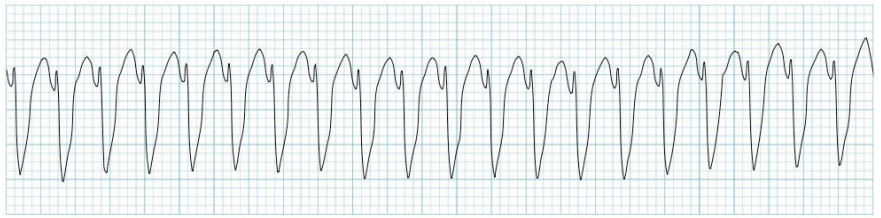
QRS > 120 ms

Stable WCT ?

Consider adenosine if **regular** and **monomorphic**

SVT with bundle branch block (aberrancy) ?





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# PULSELESS VT
# PULSELESS VF

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# pulseless VT/VF → ACLS

| COR | LOE |
|---|---|
| 1 | B-NR |
| 1 | B-NR |
| 1 | B-R |

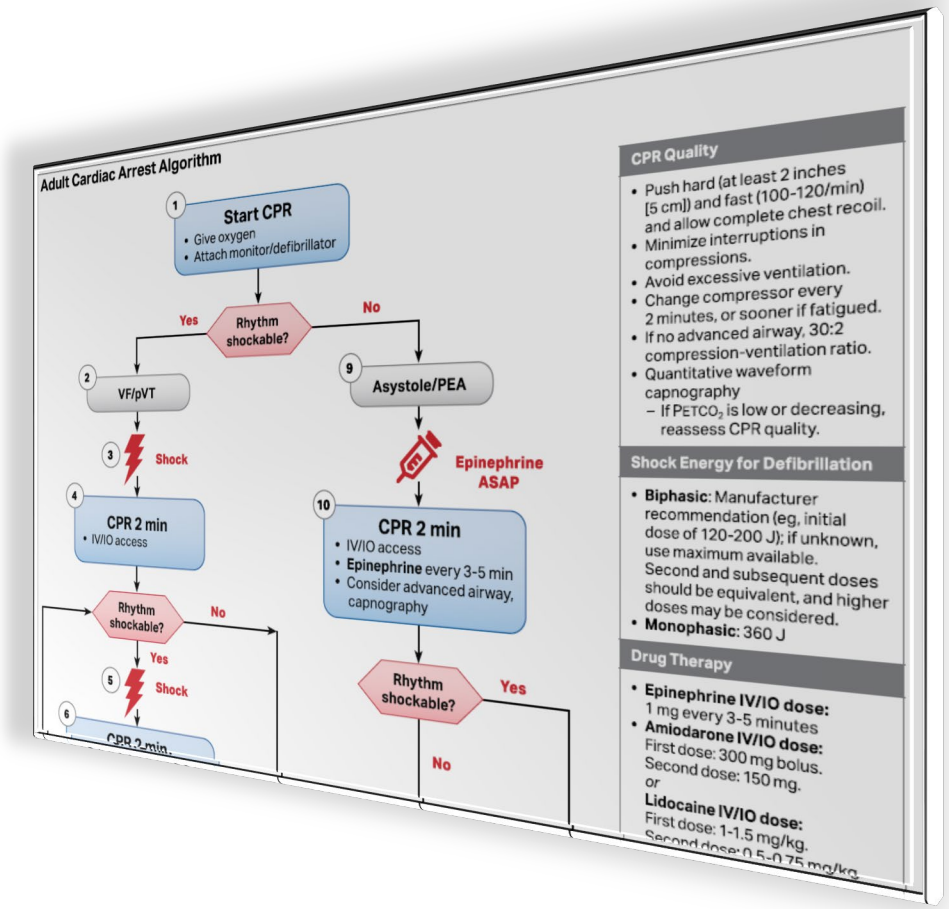
High quality CPR
Early shock
Epinephrine → BP support

| | |
|---|---|
| 2b | B-R |
| 2b | B-R |

*"May Consider"*

**After 3 shocks:**
Amiodarone
or
Lidocaine

"May continue Infusion"



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# VT/pVF arrest

## Out-of-Hospital Cardiac Arrest Landmark Trials

Clinical Trial > N Engl J Med. 2002 Mar 21;346(12):884-90. doi: 10.1056/NEJMoa013029.

**Amiodarone as compared with lidocaine for shock-resistant ventricular fibrillation**

Paul Dorian [1], Dan Cass, Brian Schwartz, Richard Cooper, Robert Gelaznikas, Aiala Barr

Affiliations + expand

PMID: 11907287 DOI: 10.1056/NEJMoa013029

### ALIVE (2002)

- N = 347 (92% VF)
- Witnessed (77%)
- Bystander CPR (27%)
- Amio 5mg/kg vs lido 1.5 mg/kg
- **survival to admission**
- **23% vs 20% (p = 0.009)**
- **aOR 2.46 [95% CI, 1.3-4.9]**

3%

Procainamide and Survival in Ventricular Fibrillation Out-of-hospital Cardiac Arrest

David T. Markel, Laura S. Gold, MSPH, Judith Allen, MPH, Carol E. Fahrenbruch, MSPH, Thomas D. Rea, MD, MPH, Mickey S. Eisenberg, MD, PhD, and Peter J. Kudenchuk, MD

### Markel et. Al 2010

- Observational retrospective
- n = 95
- Rates of termination equal
- *"Procainamide and amiodarone were equally ineffective"*

Randomized Controlled Trial > N Engl J Med. 2016 May 5;374(18):1711-22.

doi: 10.1056/NEJMoa1514204. Epub 2016 Apr 4.

**Amiodarone, Lidocaine, or Placebo in Out-of-Hospital Cardiac Arrest**

Peter J Kudenchuk [1], Siobhan P Brown [1], Mohamud Daya [1], Thomas Rea [1], Graham Nichol [1], Laurie J Morrison [1], Brian Leroux [1], Christian Vaillancourt [1], Lynn Wittwer [1], Clifton W Callaway [1], James Christenson [1], Debra Egan [1], Joseph P Ornato [1], Myron L Weisfeldt [1], Ian G Stiell [1], Ahamed H Idris [1], Tom P Aufderheide [1], James V Dunford [1], M Riccardo Colella [1], Gary M Vilke [1], Ashley M Brienza [1], Patrice Desvigne-Nickens [1], Pamela C Gray [1], Randal Gray [1], Norman Seals [1], Ron Straight [1], Paul Dorian [1]; Resuscitation Outcomes Consortium Investigators

### ALPS ROC (2016)

- N = 4653
- Amio vs lido vs placebo
- No survival difference
- Lidocaine > ROSC at ED arrival
- Survival 74% if witnessed

Rahimi M, et al. *J Am Heart Assoc*. 2022;11(6):e023958. doi:10.1161/JAHA.121.023958

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# ROC-ALPS TRIAL

| | Amiodarone (n=974) | Lidocaine (n=993) | placebo (n=1059) |
|---|---|---|---|
| Survival to discharge | 24.4% | 23.7% | 21.0% |
| P value vs placebo | 0.08 | 0.16 | - |

N = 3000; 90% to detect 6.3% difference
N= 3026 total

If true difference was ~ 3%
Underpowered to detect difference

- Time-to-first dose trial drug: 19 minutes
- Prefilled amiodarone (without polysorbate-80)
- Only positive finding:
  Lidocaine increased ROSC (p=0.01)

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# VT/pVF arrest

## In-Hospital Cardiac Arrest

## Landmark Trial

› Chest. 2023 May;163(5):1109-1119. doi: 10.1016/j.chest.2022.10.024. Epub 2022 Nov 2.

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

Deborah Wagner [1], S L Kronick [2], H Nawer [3], J A Cranford [2], S M Bradley [4], R W Neumar [2]

Affiliations + expand

PMID: 36332663 DOI: 10.1016/j.chest.2022.10.024

Several Limitations:
Observational
Registry Level

2023 Wagner et al.
Retrospective (2000 – 2014)
696 Hospitals

- N = 14,630
- Amiodarone (10,058) vs lidocaine (4,572)

**Lidocaine:**

↑ ROSC: aOR 1.15 [95%CI 1.03 – 1.30]
↑ 24-survival: aOR 1.16 [95%CI 1.05 – 1.28]
↑ survival to DC: aOR 1.19 [95%CI 1.08 – 1.30]
↑ favorable neuro at DC: aOR 1.18 [95%CI 1.07 – 1.30]

Wagner D, et al. *Chest*. 2023;163(5):1109-1119. doi:10.1016/j.chest.2022.10.024

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# pVT/VF ANTIARRHYTHMICS

## amiodarone Vs. lidocaine

2b B-R

- Historical favorite
  - Training, “practice”
- Multi-modal MOA
  - All types of anti-arrhythmic
  - Beta-blocker + NDP-CCB properties
- ROC-ALPS Subanalysis
  - Amiodarone worked better early ($p<0.05$)
- Long half-life
- Polysorbate 80 diluent ?
  - No current syringe or vial product available

2b B-R

- ROC-ALPS Study:
  - More ROSC at ED arrival ($p=0.01$)
- ROC-ALPS Subanalysis:
  - Non-shockable → shockable
    - Lidocaine superior to amio ($p<0.05$)
  - Longer time-to-antiarrhythmic
    - Lidocaine with sustained action
- IHCA Trial ($n > 14,000$)
  - Lidocaine superior in *all outcomes*
- Convenient dosage form
- Favorable pharmacokinetics ?

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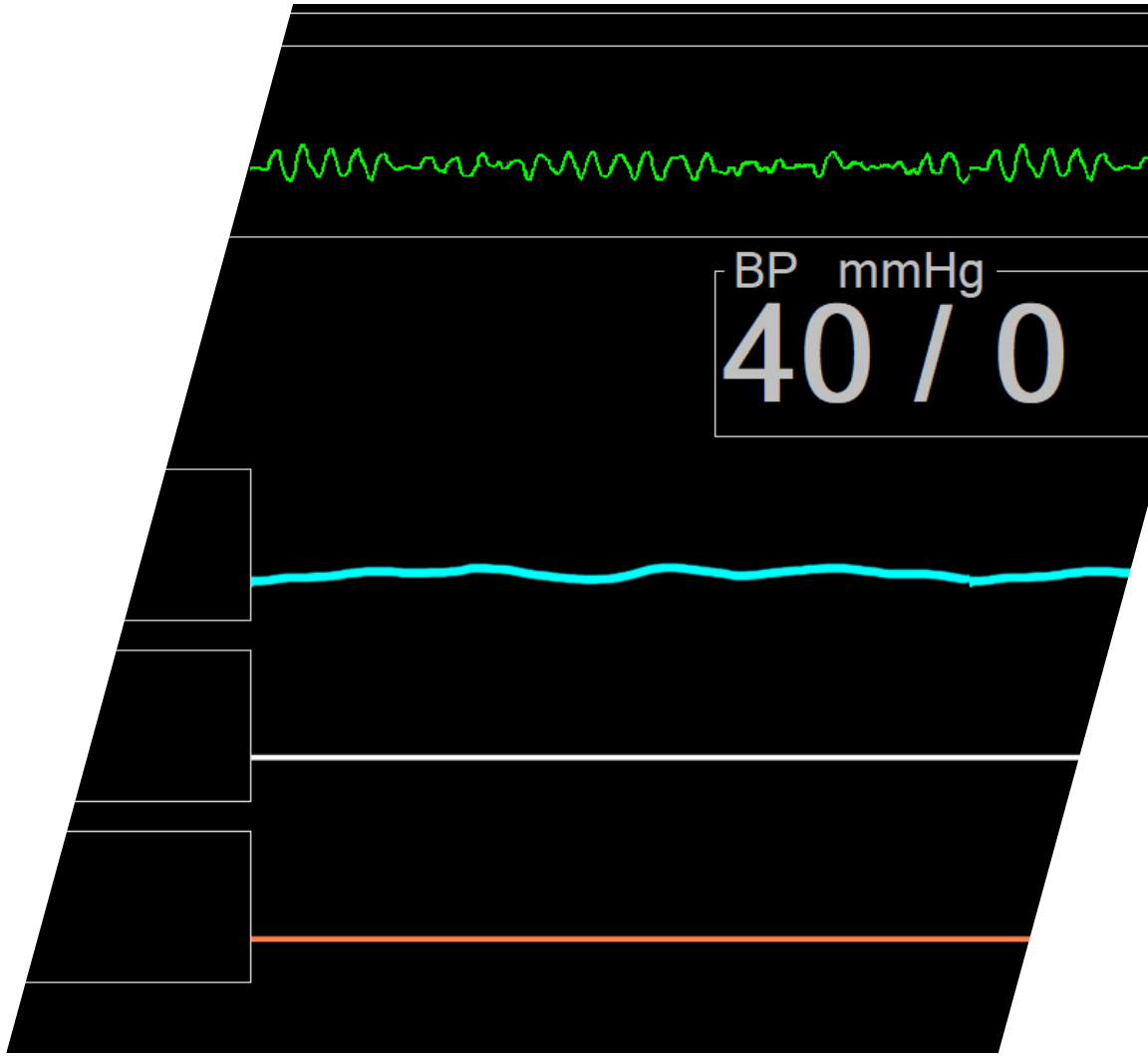
# REFRACTORY VF

"Electrical Storm"
"Malignant VF"
"Incessant VF"

## Definition:




≥ 3 defibrillation attempts

≥ 3 mg epinephrine

**≥ 300mg admiodarone (450mg?)**

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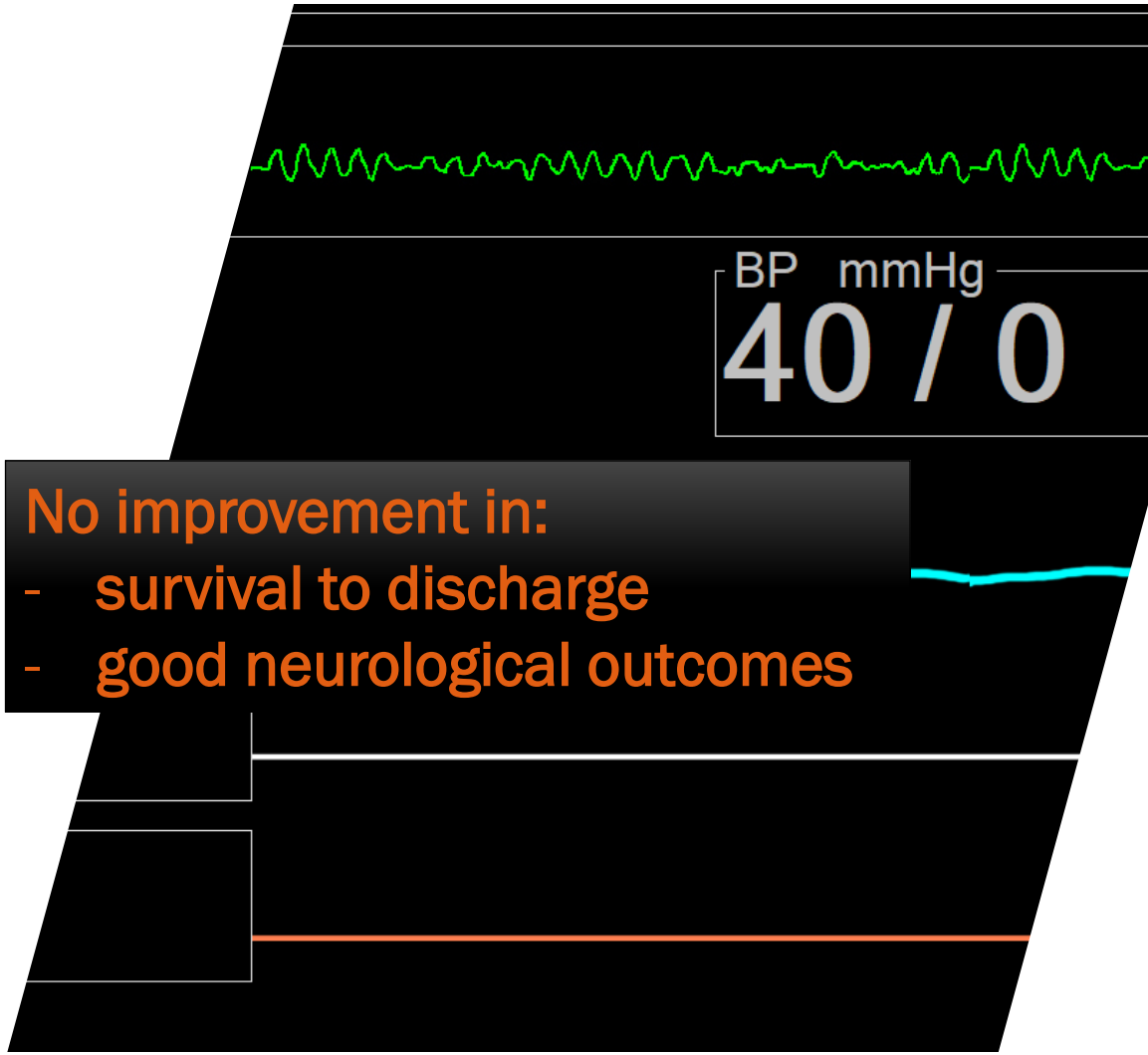
# REFRACTORY VF

## Literature

<u>Driver et al. 2014</u>
Retrospective single center
N = 25
Sustained ROSC
Esmolol (66.7%) control (31.6%)

<u>Lee et al. 2016</u>
Retrospective single center pre/post study
N = 41
Sustained ROSC
Esmolol (56.0%) control (16.0%) p=0.007



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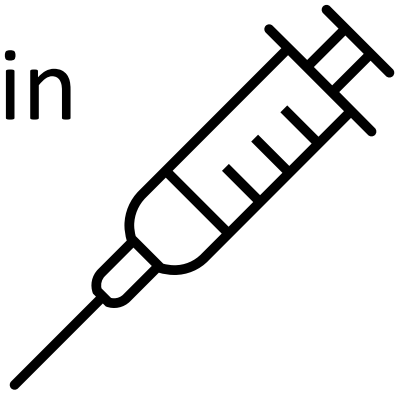
# REFRACTORY VF

## Esmolol Dosing

500 mcg/kg bolus

0 – 100 mcg/kg/min



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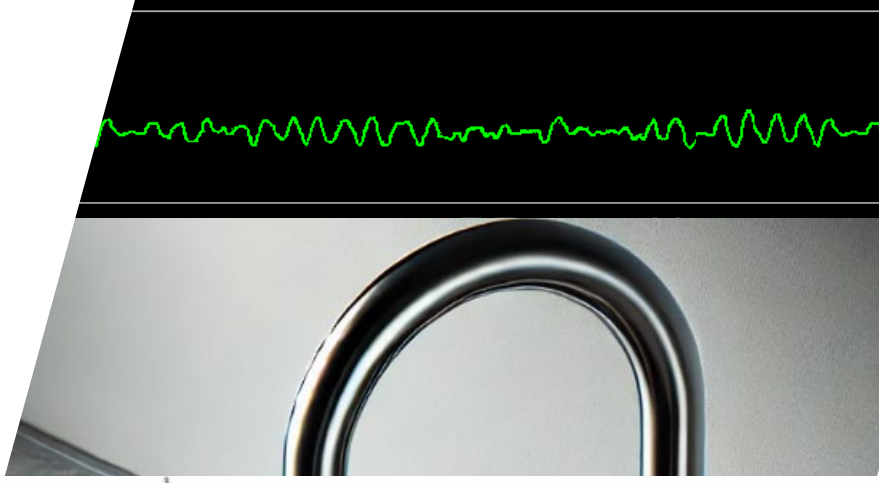
# REFRACTORY VF

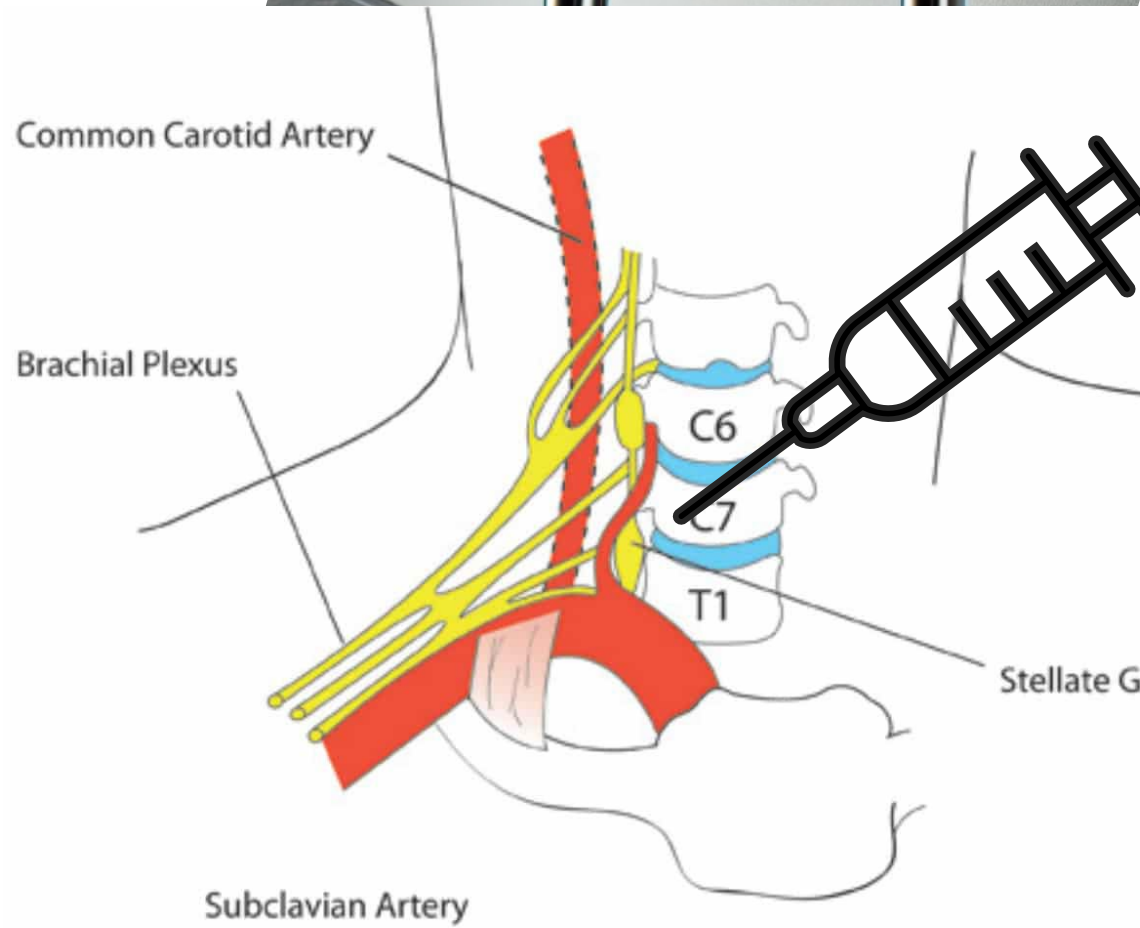
## Stellate Ganglion Block



Ultrasound guided, bedside procedure

- 8-12 cc local anesthetic
  - lidocaine 1-2%
  - bupivacaine 0.5%

Suppress sympathetic activity




Current Study: GANGSTER-VT

(GANGlion Stellate Block for Treatment of Electric storRm) RCT (NCT05078684)

Chouairi F, et al. *JACC Clin Electrophysiol*. 2024;10(4):750-758

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# TREATMENT OF VENTRICULAR DYSRHYTHMIAS

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