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Ventricular Arrhythmias Part 2

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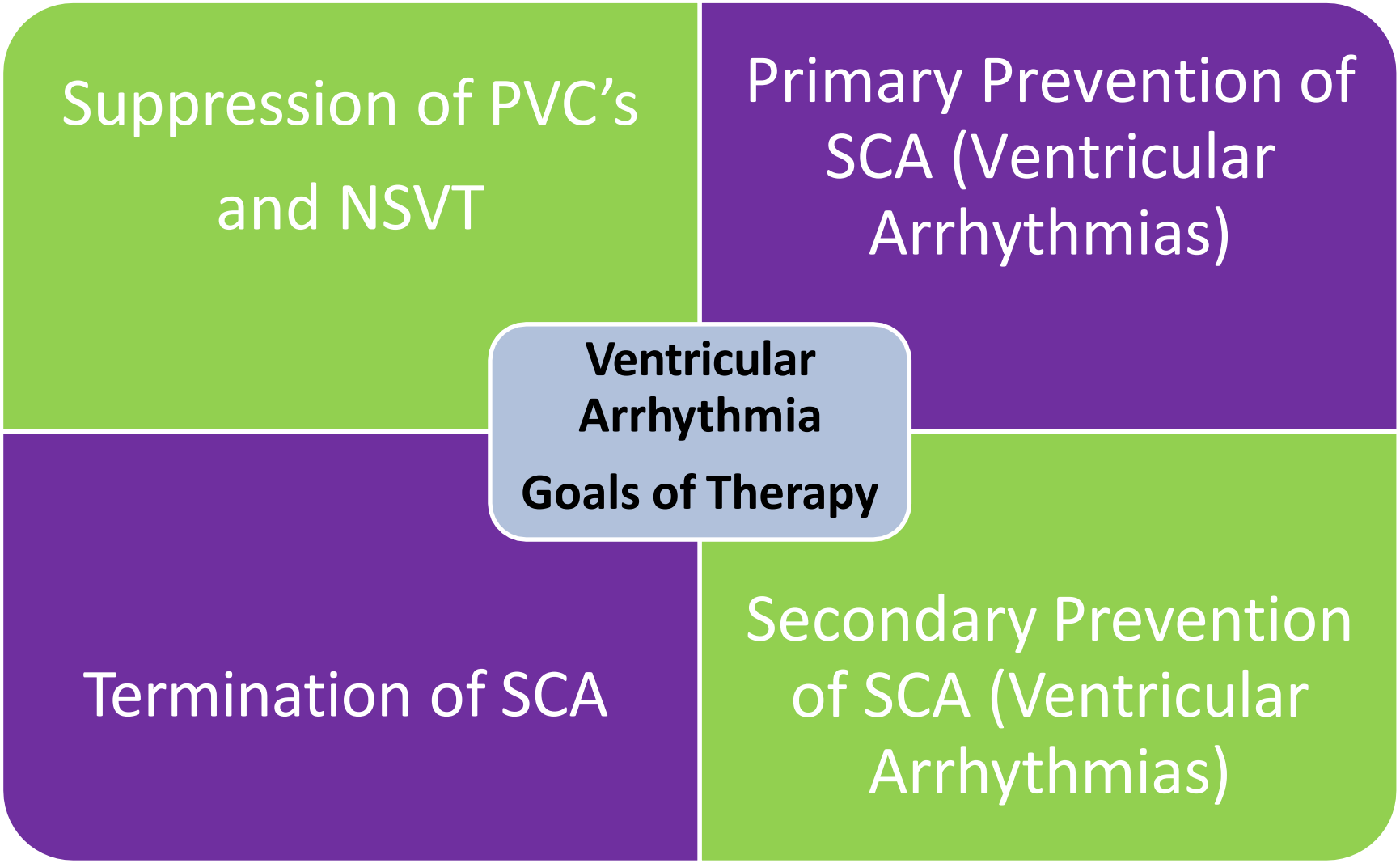
Objectives (Part 2)

- Develop treatment plans for non life-threatening ventricular arrhythmias (PVC, NSVT)
- Compare antiarrhythmic medications with non-drug therapies for the primary and secondary prevention of sudden cardiac arrest
- Evaluate treatment options for patients with implantable cardioverter defibrillators receiving multiple shocks


Suppression of PVC's and NSVT
Primary Prevention of SCA (Ventricular Arrhythmias)
Ventricular Arrhythmia
Goals of Therapy
Termination of SCA
Secondary Prevention of SCA (Ventricular Arrhythmias)

Risk Factors for Ventricular Arrhythmias

Cardiac (SHD)	Non-Cardiac
CHD (Acute MI)	**Electrolyte abnormalities**
Cardiomyopathy: dilated, hypertrophic	**Medications**
LV dysfunction (EF < 40%)	Hyperthyroidism
Congenital heart abnormalities	Surgery
Valvular heart disease	Acidosis
	Hypothermia
	Illicit drugs: cocaine, amphetamines

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Therapies for Ventricular Arrhythmias

Treatment Options for Ventricular Arrhythmias

Medication Therapies	Non-Drug Therapies
1. Beta blockers	Internal cardioverter defibrillator (ICD)
2. Calcium channel blockers	External cardioverter defibrillators and AEDs
3. Class I antiarrhythmics: Procainamide, lidocaine	Radio frequency ablation
4. Class III antiarrhythmics: Amiodarone, sotalol	
5. Electrolytes: Potassium, magnesium	

Non-drug therapy > Drug therapy

1. Beta Blockers

- Beta blockers are safe and effective antiarrhythmic agents that can be considered the mainstay of antiarrhythmic drug therapy
- Overall, the available antiarrhythmic drugs other than beta blockers should not be used as primary therapy in the management of ventricular arrhythmias and prevention of SCA
- All beta blockers are equally effective
  - Consider patient comorbidities (HF)
  - Consider patient's ability to eliminate drug
    - Renal clearance – atenolol
    - Hepatic clearance- metoprolol, carvedilol

J Am *Coll Cardiol*. 2006;48:1064-1108

2. Calcium Channel Blockers

- Indication- suppression of PVCs and non-sustained ventricular tachycardia (NSVT) only
- Non-dihydropyridine CCBs only!
- Avoid use in patients with decompensated HF

Class I Antiarrhythmics: Sodium Channel Blockers

Class	Channel Effects	Repolarization Time	Drugs
IA	Sodium blocking effect: ++	Prolongs	Procainamide Quinidine Disopyramide
IB	Sodium blocking effect: +	Shortens	Lidocaine Mexilitine Tocainide
IC	Sodium blocking effect: +++	Unchanged	Propafenone Flecainide

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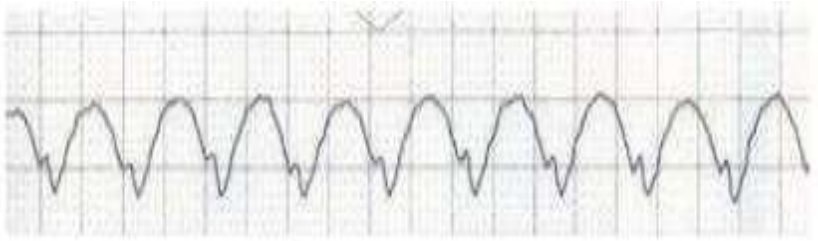
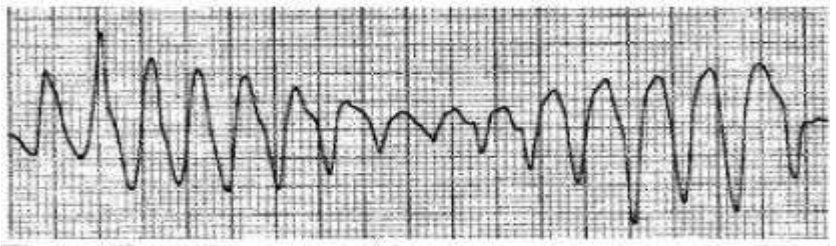
+ = inhibitory effect; ++ = markedly inhibitory effect;
+++ = major inhibitory effect

3. Class 1A Antiarrhythmics: Procainamide

- Class IA antiarrhythmic agent
  - Sodium channel blocking properties (primary)
  - Potassium channel blocking properties (secondary)
- Indication (IV formulation):
  - **Termination** of hemodynamically stable monomorphic VT
- Side effects common
  - Bradycardia, hypotension
  - Proarrhythmic
- **Contraindications**
  - QT prolongation
  - Heart failure





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Circulation. 2010;122:s729-s767

3. Class 1A Antiarrhythmics: Procainamide Continued

- Dose: (do not need to know)
  - 20-50 mg/min IV infusion until arrhythmia suppressed or rate limiting factors met **OR**
  - 100 mg every 5 minutes IV until arrhythmia suppression or rate limiting factor present
- **Rate limiting factors:**
  - Hypotension
  - QRS prolongation of 50% or more
  - Total cumulative dose of 17 mg/kg

Circulation. 2010;122:s729-s767

3. Class IB Antiarrhythmics: Lidocaine

- Indication
  - **Termination** of hemodynamically stable monomorphic VT (especially post myocardial infarction)
- Little effect on hemodynamic parameters
- Side effects
  - Altered mental status, seizures (check lidocaine levels)
  - Bradycardia
- Initial dose: 1-1.5 mg/kg injection
  - Repeat with 0.5-0.75 mg/kg IV every 5-10 minutes to a maximum cumulative dose of 3 mg/kg
- Maintenance infusion: 1-4 mg/min (30-50 mcg/kg/min)

3. Class 1C Antiarrhythmics

- Oral agents: propafenone, flecainide
- Indication: **<u>suppression</u>** of PVC's and monomorphic VT
- **Side effects:**
  - Proarrhythmic
  - Negative inotropic effects

4. Class III Antiarrhythmics: Amiodarone

- Indications
  - **(acute/chronic) Termination and suppression** of hemodynamically stable monomorphic VT and polymorphic VT with normal QT interval
  - **(acute) Termination** of sudden cardiac arrest due to pVT/VF after defibrillation
  - **(chronic) Prevention** of sustained VT to decrease ICD shock
- Side effects (acute)
  - Bradycardia
  - ~~Hypotension – due to solvent in old IV preparation~~
  - Phlebitis (IV formulation)

4. Class III Antiarrhythmics: Amiodarone Continued

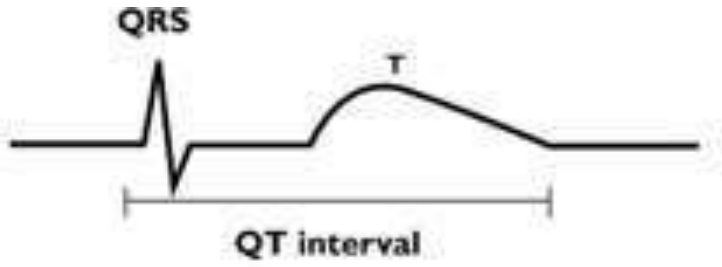
- Acute IV dosing for **stable** monomorphic and polymorphic VT (not pVT/VF dosing):
  - 150 mg IV over 10 minutes
  - Repeat 150 mg bolus if needed
  - Infusion 1 mg/min x 6 hours, then 0.5 mg/min
  - Convert to oral therapy if chronic treatment warranted
  - Recommend coadministration with a beta-blocker
- Can be used safely in patients with HF
- Amiodarone offers no benefit – SCD-HeFT
- Complex drug interactions: CYP 450, p-glycoprotein
- Dose- and duration-dependent adverse drug events

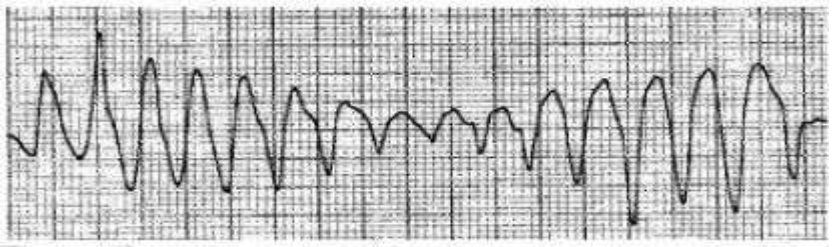
4. Class III Antiarrhythmics: Amiodarone Continued

- Oral dosing: 400mg po q8-12 hours for 1-2 weeks, then 300-400mg daily
  - Reduce dose to 200mg daily if possible
- Side effects (long term): bradycardia, heart block, TdP, corneal microdeposits, thyroid abnormalities (hyper- or hypothyroidism), nausea, vomiting, constipation, photosensitivity, skin discoloration, rash, ataxia, dizziness, peripheral neuropathy, tremor, hepatitis, cirrhosis, pulmonary fibrosis, or pneumonitis
  - Regular eye exams, chest xray, labs (liver fxn test, TSH), EKG, skin exam

4. Class III Antiarrhythmics: Sotalol

- Indication:
  - **(acute) Termination** of hemodynamically stable monomorphic VT
  - **(chronic) Prevention** of sustained VT, decrease ICD shock
- Side effects
  - Bradycardia, hypotension
  - Proarrhythmic
- **Contraindications**
  - QT prolongation
  - Heart failure



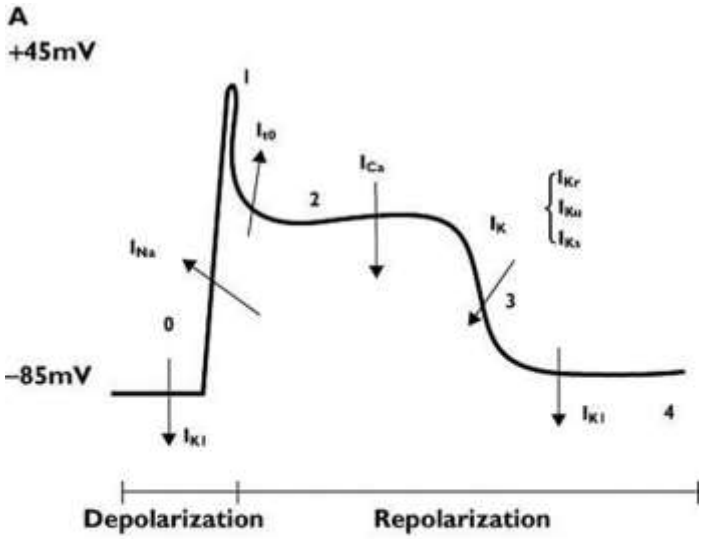


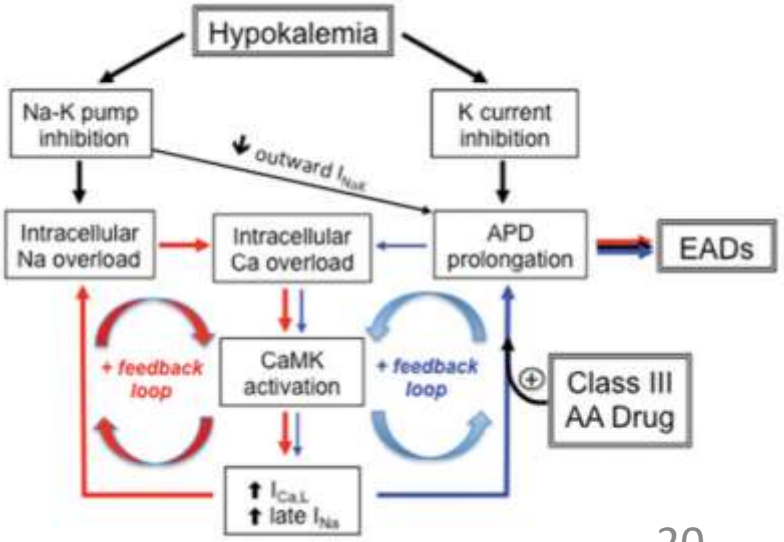
4. Class III Antiarrhythmics: Sotalol Continued

- Dosing (IV) (do not need to know):
  - Studied dose: 1.5 mg/kg infused over 5 minutes
  - US labeling: 1.5 mg/kg infused over 5 hours
- Dosing (PO):
  - Initial: 80 mg BID; if VT returns and excessive QTc prolongation does not occur after 3 days (QTc < 500 msec), increase to 120mg BID; if response not adequate after 3 days and QTc no excessively prolonged (QTc < 500 msec), increase to 160 mg BID (max dose)
- Caution with impaired renal function!
  - Requires adjusting dosing interval in CrCl < 60 ml/min

5. Electrolytes: Potassium

- Indication:
  - **(acute) Suppression** of EADs that lead to PVCs and polymorphic VT associated with QT prolongation (TdP)
- Dosing: based on serum potassium levels (ave 20-60 mEq total)
  - Oral: no more than 40 meq/dose
  - IV: 10 meq IV over 60 min (peripheral line)
  - IV: 20 meq IV over 60 min (central line)





Weiss et al. Circ Arrhythm Electrophysiol 2017;10:10-21

5. Electrolytes: Magnesium

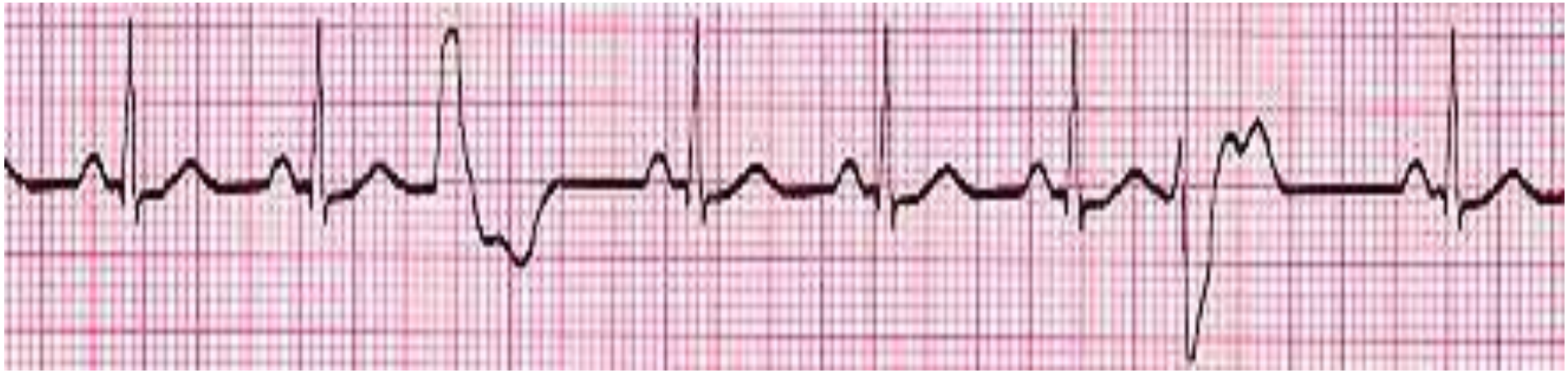
- Cofactor for sodium and potassium transport
- Indication:
  - **(acute) Suppression and termination** of polymorphic VT associated with QT prolongation (TdP)
- Side effects (rare)
  - Hypotension
  - CNS toxicity
  - Respiratory depression
- Dose
  - 1-2 grams IV over 15 minutes; over 5 min in SCA

Ventricular Arrhythmia

Goals of Therapy

- Suppression of PVC's and NSVT
- Primary Prevention of SCA (Ventricular Arrhythmias)
- Termination of SCA
- Secondary Prevention of SCA (Ventricular Arrhythmias)

Premature Ventricular Contraction (PVC)



- Abnormal depolarization originating from the ventricles
- Wide QRS >120msec
- Couplet is two successive PVCs in a row
- R on T phenomenon
- Risk factors: caffeine, tobacco, alcohol, illicit drugs, exercise, HTN, anxiety, heart disease (CHD, HF, ACS, cardiomyopathy, congenital heart disease)

PVC Treatment Algorithm

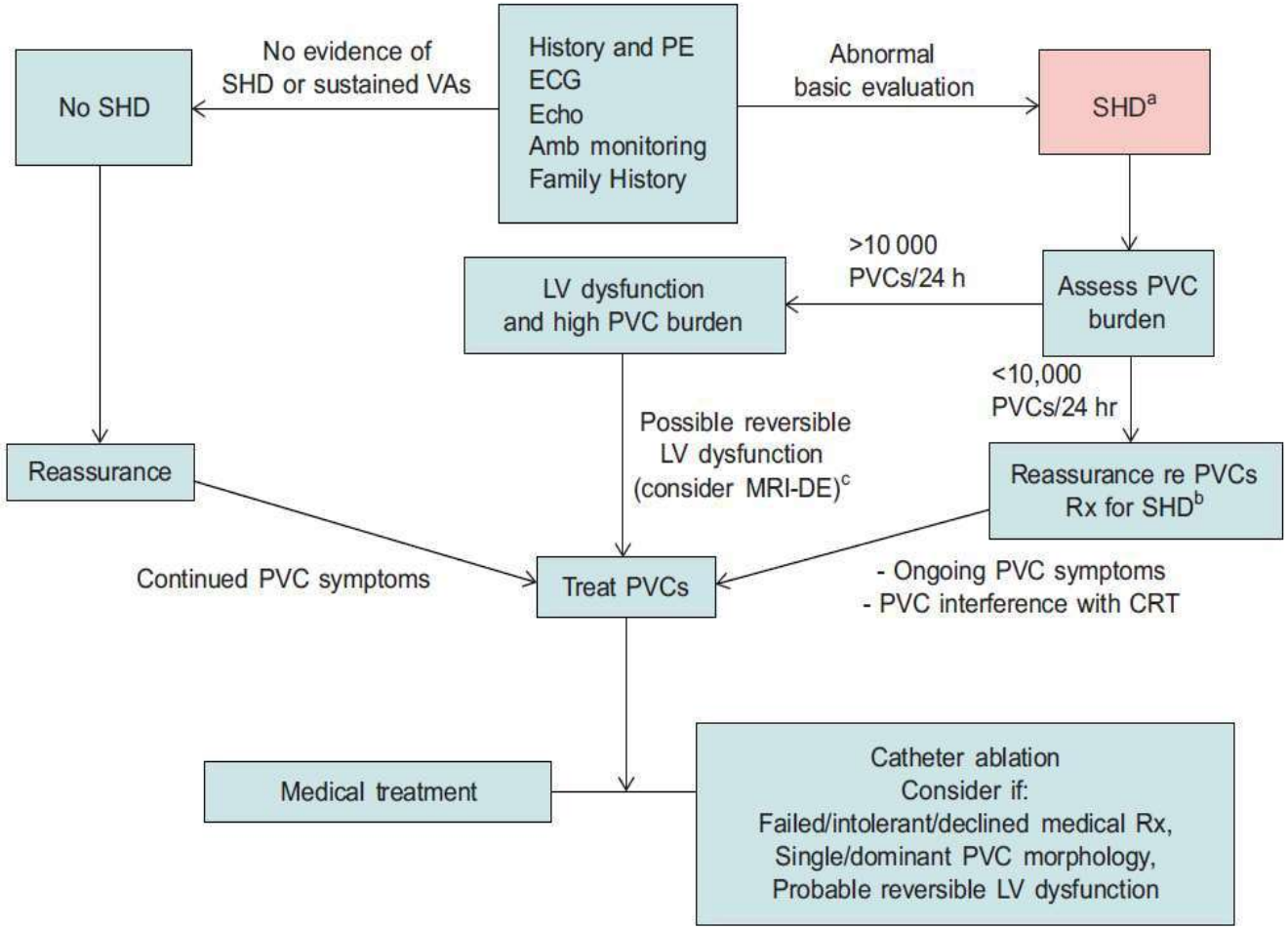


Figure 1 Management of PVCs. a. See table for definitions of structural heart disease; b. Medical therapy + ICD; c. Absence of high scar burden suggests reversibility. CRT = cardiac resynchronisation therapy; ICD = implantable cardioverter-defibrillator; LV = left ventricular; MRI-DE = magnetic resonance imaging with delayed enhancement; PE = physical examination; PVC = premature ventricular complexes; Rx = therapy; SHD = structural heart disease; VAs = ventricular arrhythmias.

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Heart Rhythm 2014;1:e166-e196

First Line Therapy for Suppression of PVCs

	No Structural Heart Disease (or LVEF >40%)	Structural Heart Disease (or LVEF <40%)
Asymptomatic	No Treatment	Beta-blocker
Symptomatic	Beta-blocker or non-DHP CCB	Beta-blocker

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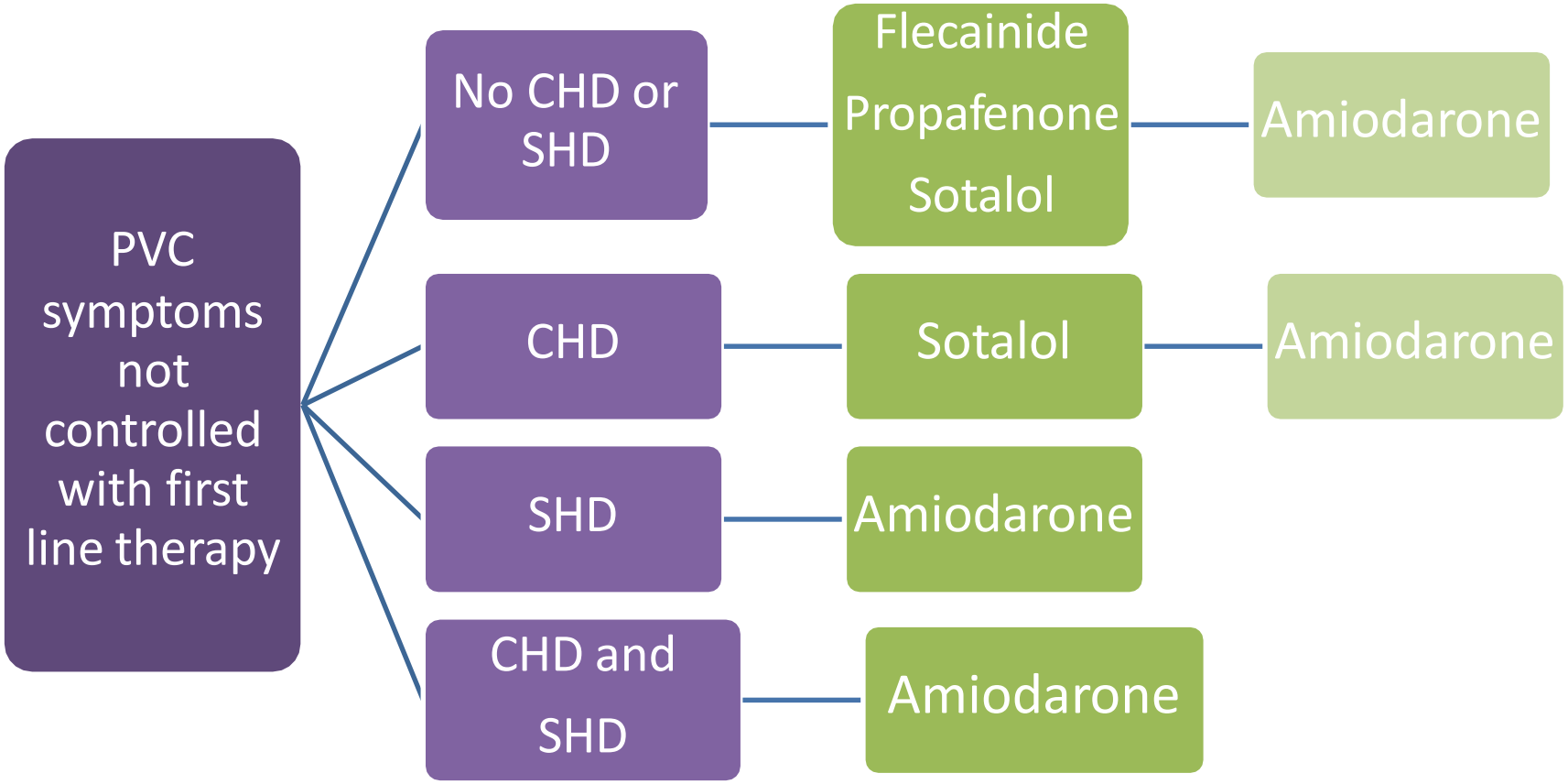
Heart Rhythm 2014;1:e166-e196

Second Line Therapy for Suppression of PVCs



CHD = coronary heart disease
SHD = structural heart disease

Patient Case Question

BT is a 54 yo man who suffered a myocardial infarction yesterday. He has been having intermittent premature ventricular contractions on ECG but is not experiencing symptoms. Recent TTE shows a LVEF of 50%. What is the best therapy to suppress his PVCs?

a. amiodarone
b. amiodarone + metoprolol
c. metoprolol
d. propafenone
e. no treatment

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a. amiodarone
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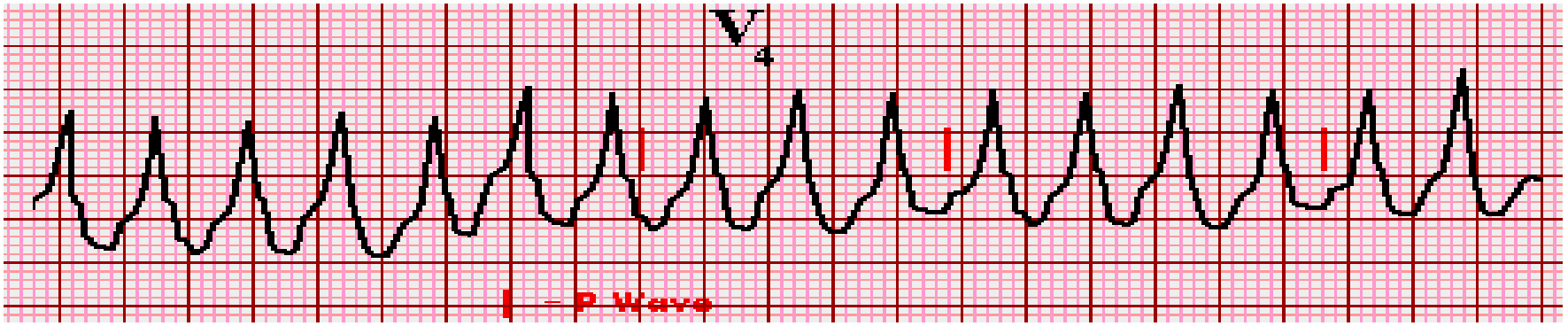
c. metoprolol
d. propafenone
e. no treatment

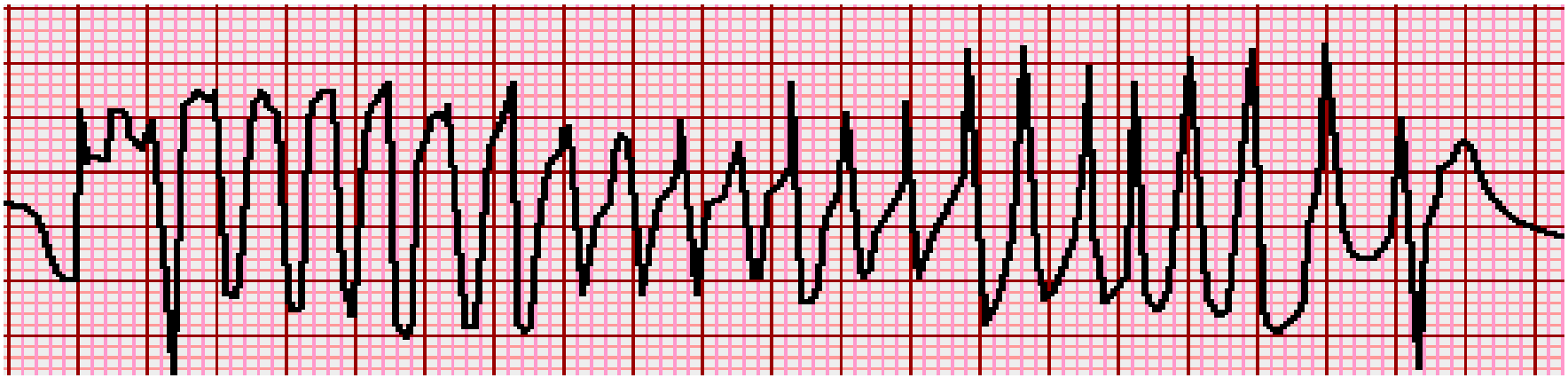
Ventricular Tachycardia (VT)

≥ 3 successive ventricular beats (PVC) at a rate of >100 bpm



- Non-sustained VT- terminates within 30 seconds
- Sustained VT- persists for >30 seconds or requires CV due to symptoms of syncope and palpitations
- Monomorphic- nonsustained or sustained VT with a single QRS morphology
- Polymorphic- nonsustained or sustained VT with a changing QRS morphology (torsades de pointes)

Torsades de Pointes (TdP)



- A form of polymorphic VT
- “twisting of points”
- Associated with prolonged QT or QTc interval
- QTc prolongation is caused by delayed ventricular repolarization as a result of abnormal conduction through potassium channels (Ikr)
- **Often self-limiting, but may deteriorate to VF**

V Tach Clinical Features

NSVT

- Asymptomatic or symptoms are transient

VT

- Symptoms include: palpitations, diaphoresis, chest pain, dizziness, syncope, presyncope, hemodynamic instability
- Requires prompt treatment: drugs, DC cardioversion

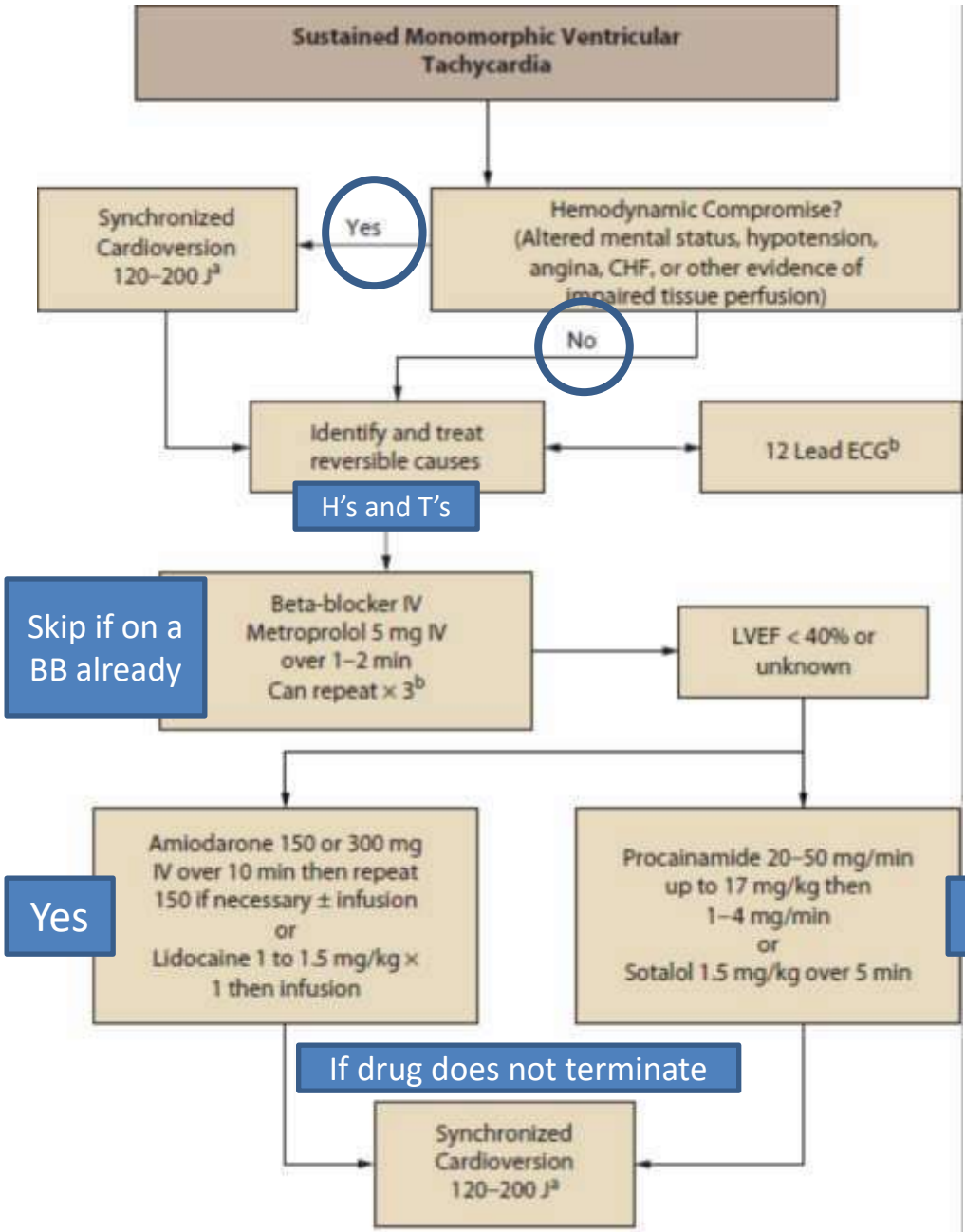
SCA

- Requires prompt life support measures (pVT/VF algorithm)

Treatment of Non-Sustained Monomorphic V Tach

- **Structurally normal heart**: treat only if symptomatic!
  - Beta blocker or non-DHP CCB
  - Class 1C antiarrhythmic
  - Radiofrequency ablation
- **Structural heart disease**:
  - Beta blocker
  - Optimize underlying heart disease or cause
  - Evaluate patient for ICD placement

Termination of Sustained Monomorphic V Tach



Source: Jesse B. Hall, Gregory A. Schmidt, John P. Kress: *Principles of Critical Care*, 4th Edition: www.accessmedicine.com

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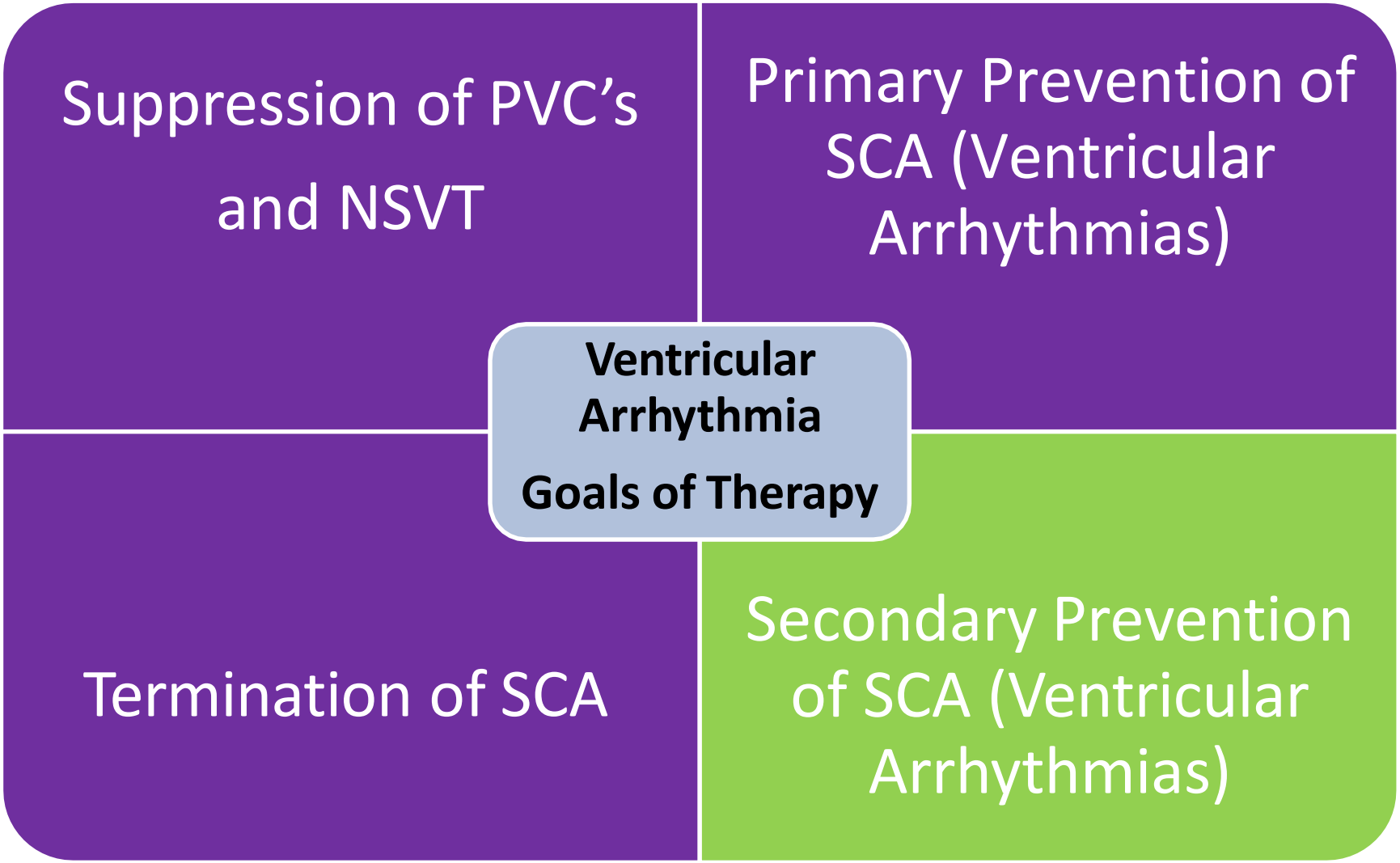
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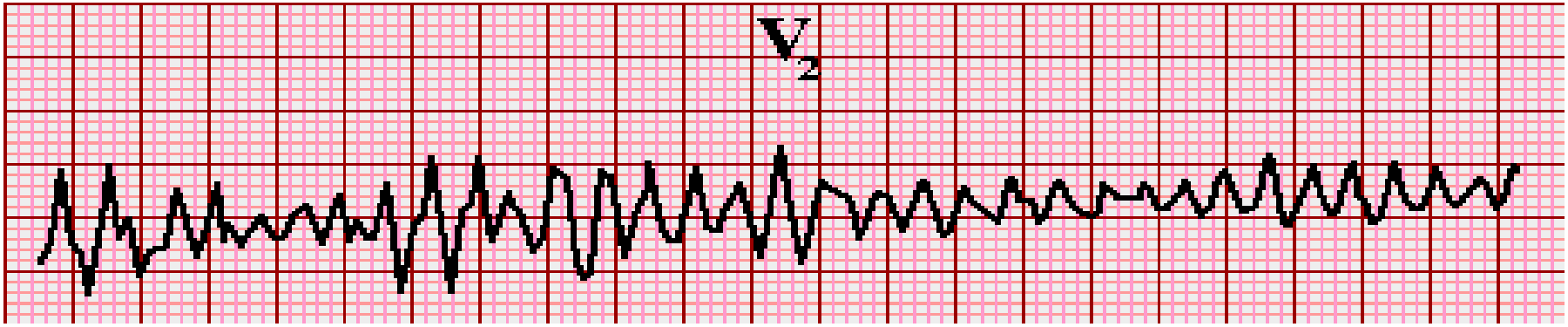
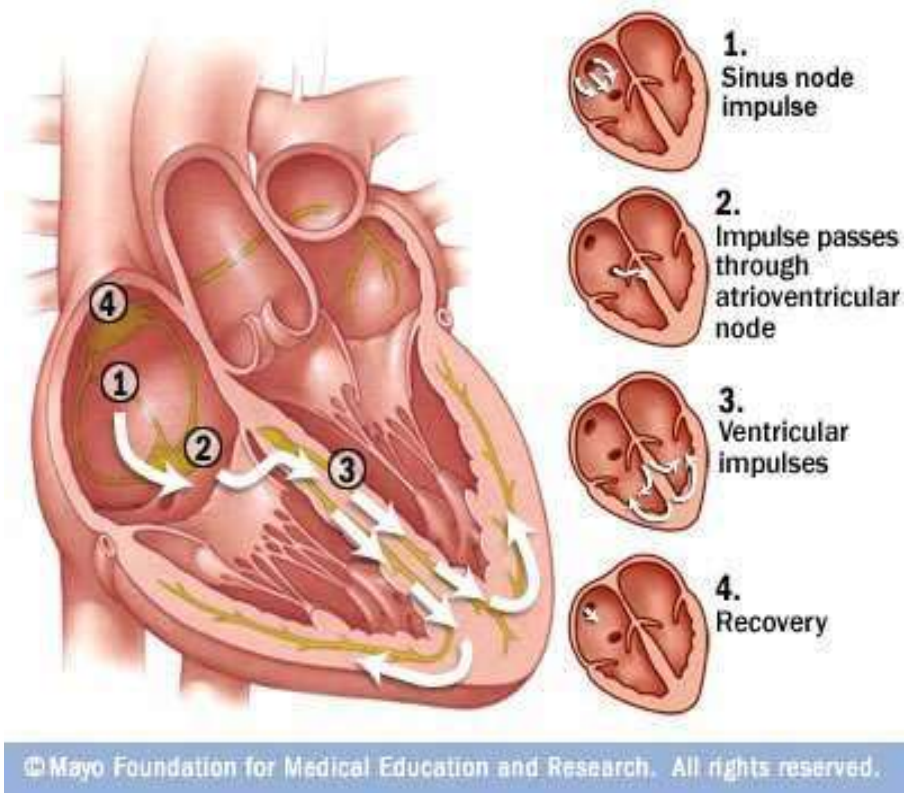
Ventricular Fibrillation

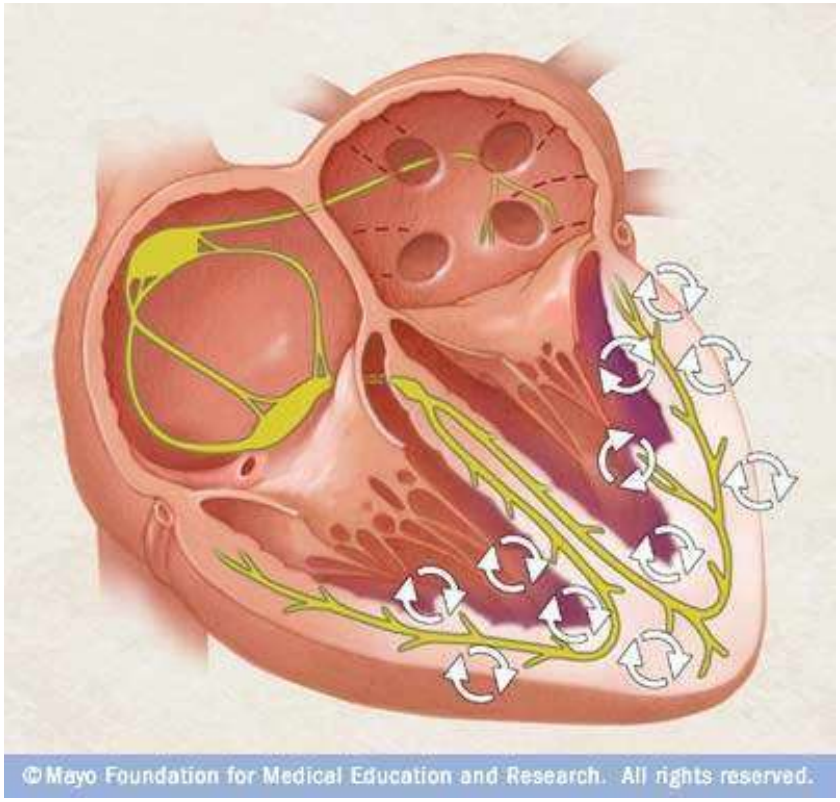


- Absence of organized electrical activity in the heart
- Ventricular rate >300 bpm
- Lack of recognizable P waves, QRS Complexes, and T waves
- Complete loss of cardiac output

Mechanism of VF



http://www.mayoclinic.com/health/medical/IM02485



http://www.mayoclinic.com/health/medical/IM02524

Mechanism of VF Continued

- The mechanism responsible for ventricular fibrillation is the degeneration of electrical impulses into multiple small reentry circuits/wavelets that travel through the myocardium

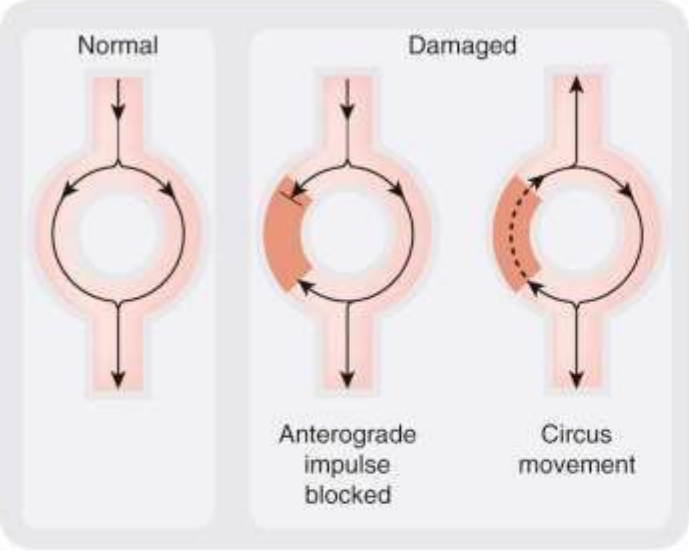


Fig. 21.3

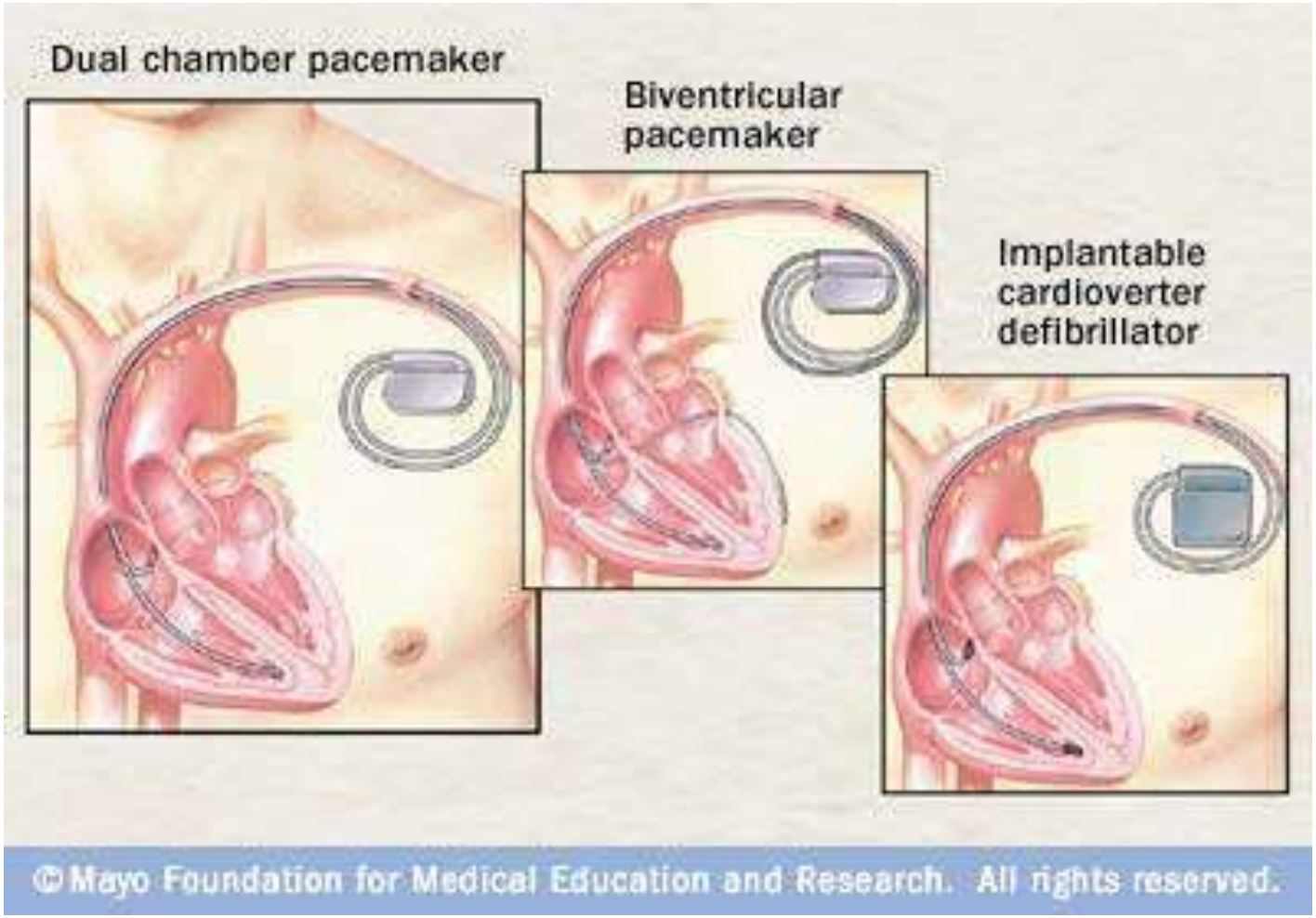
Generation of a re-entrant rhythm by a damaged area of myocardium.

The damaged area (brown) conducts in one direction only. This disturbs the normal pattern of conduction and permits continuous circulation of the impulse to occur.

Clinical features: loss of consciousness, convulsions, and death

Treatment: prompt defibrillation, anti-arrhythmic drugs and ICD placement to prevent recurrences.

Internal Cardioverter Defibrillator (ICD)



http://www.mayoclinic.com/health/medical/IM02119

Risks of ICD Implantation

- Procedural sedation
- Surgical site infection
- Sensitivity to the device material
- Hematoma
- ICD storm
  - Misfiring or failing to fire
- Financial burden

ICD therapy is superior to medication therapy for primary prevention of SCA

Trial	Patients	End Point	Results
MADIT n=196 Drug vs. ICD	Hx MI, LVEF <36%, inducible VT	All-cause mortality, 27-month follow-up	54% mortality reduction with ICD (p=0.009)
MUSTT n=704 Drug vs. ICD	CAD, LVEF <40%, inducible sustained VT	Cardiac arrest 5-year follow-up	27% mortality reduction with ICD (p=0.04)

N Engl J Med. 1996;335(26):1933; N Engl J Med. 1999;341(25):1882

ICD therapy is superior to medication therapy for primary prevention of SCA

Trial	Patients	End Point	Results
MADIT II n=1232 Drug vs ICD	Hx MI, LVEF <30%,	All-cause mortality, 20-month follow-up	19.8% mortality in drug group vs. 14.2% mortality in ICD group (p=0.016)
SCD HeFT n=2521 Amio vs ICD	NYHA class II or III HF, LVEF <35%, +/- inducible VT	All-cause mortality, 5-year follow-up	Placebo 29% Amio 28% ICD 22%

N Engl J Med. 2002;346(12):877; N Engl J Med. 2005;352(3):225

Class I Indications for ICD Therapy for Primary Prevention of SCA

- LVEF ≤ 35% due to prior MI who are at least 40 days post-MI and are NYHA Functional Class II or III (IA)
- LVEF ≤ 30% due to prior MI who are at least 40 days post-MI and are NYHA Functional Class I (IA)
- LVEF ≤ 35% with nonischemic DCM and who are in NYHA Functional Class II or III (IB)
- LVEF < 40% with nonsustained VT due to prior MI, and inducible VF or sustained VT at electrophysiological study (IB)
- Structural heart disease and spontaneous sustained VT (IB)
- Syncope of undetermined origin with clinically relevant, hemodynamically significant sustained VT or VF induced at electrophysiological study (IB)

Circulation. 2008; 117: 2820-2840

ICD therapy is superior to medications therapy for secondary prevention of SCA

Trial	Patients	End Point	Results
AVID n=1016 ICD vs. Drug	SCA, Mean LVEF 32%	All-cause mortality, f/u 3 years	31% RRR mortality with ICD
CIDS n=659	SCA	All-cause mortality, f/u 3 years	13.7% RRR mortality with ICD
CASH n=349	SCA Mean LVEF 46%	All-cause mortality, mean f/u 57 months	8% decrease absolute mortality (p=0.08)

*pts with EF <35% derived the most benefit from ICDs

N Engl J Med. 1997; 337:1576-1584
Circulation. 2000; 101: 1297-1302
Circulation. 2000; 102: 748-754

Class 1 Indication for ICD Therapy for Secondary Prevention of SCA

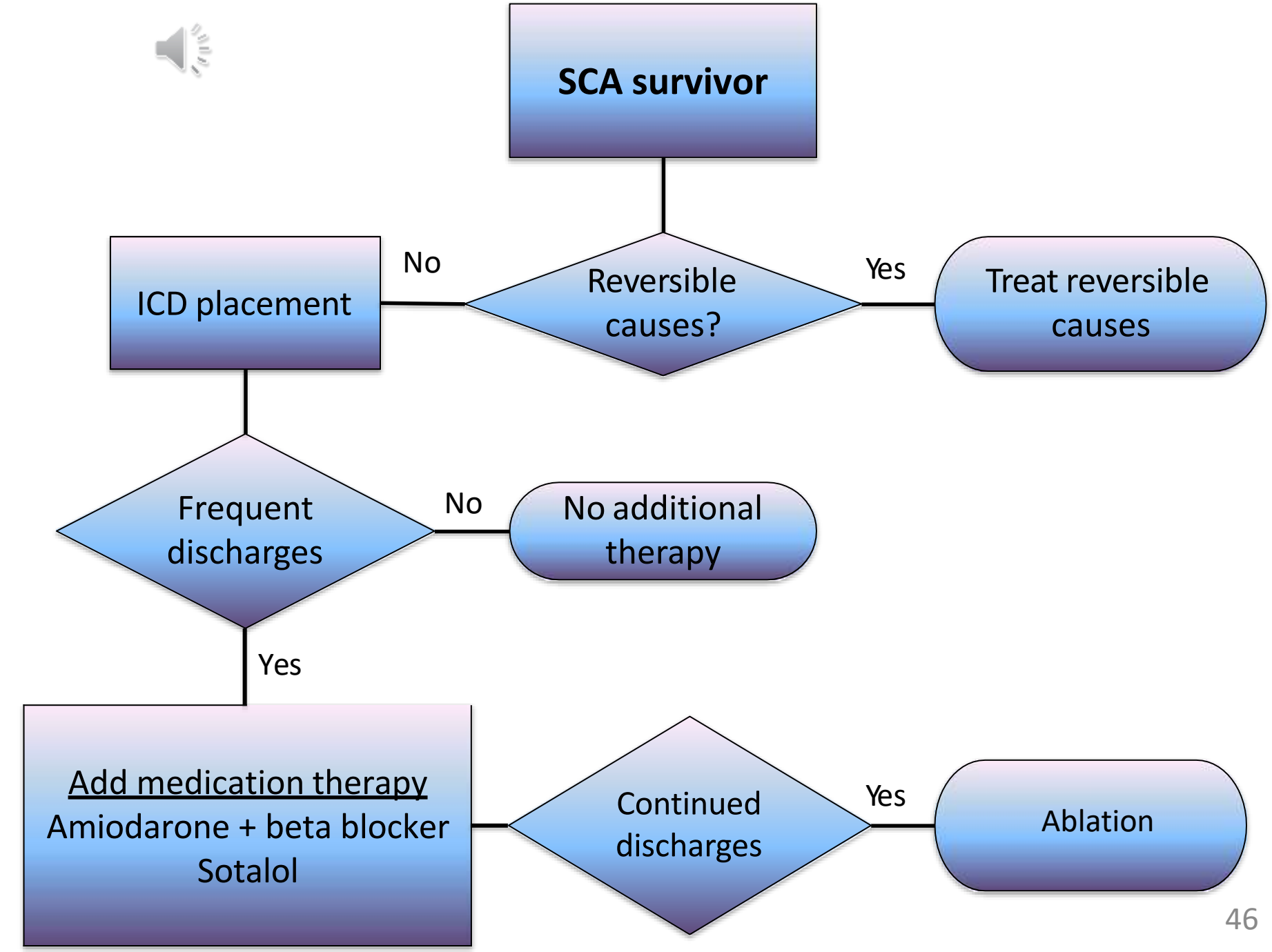
- Survivors of cardiac arrest due to VF or hemodynamically unstable sustained VT after evaluation to define the cause of the event and to exclude any completely reversible causes (IA)

Circulation. 2008; 117: 2820-2840

Defibrillator Storm

Patients who have recurrent VT/VF with frequent *appropriate* ICD firing

- Sotalol useful
- **Amiodarone plus beta blocker** better
- Ablation may be indicated


SCA survivor
Reversible causes?
No
Yes
ICD placement
Treat reversible causes
Frequent discharges
No
No additional therapy
Yes
Add medication therapy
Amiodarone + beta blocker
Sotalol
Continued discharges
Yes
Ablation

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End of Part 2