RHYTHM DISTURBANCES ELECTRICAL ACTIVITY EKG

Kenneth Alonso, MD, FACP

Membrane potential

- Membrane potentials are always expressed as intracellular relative to extracellular potential.
- Resting membrane potential is primarily determined by K^+.
- When K^+ diffuses from intracellular to extracellular fluid down its concentration gradient, the inner membrane potential becomes negative relative to the outer membrane potential.
- The Na^+-K^+ pump is responsible for maintaining the K^+ concentration gradient that is responsible for the resting membrane potential.

Membrane potential

- Cl^- moves down its concentration gradient
- Extracellular fluid to intracellular fluid
- Cl^- moves against an electrical gradient (on the Na^+-K^+-Cl^- co-transporter),
- Energy is required
- Low extracellular Ca^{2+} levels alter the resting potential.

Action potential

- When Na^+ channels open, Na^+ diffuses down its concentration gradient (outside to inside).
- An action potential is generated.
- At the peak of the upstroke, the inner membrane potential becomes positive relative to the outer membrane potential.
- The Na^+-K^+ pump is responsible for maintaining the Na^+ concentration gradient that is responsible for the upstroke.
- 3 Na^+ are pumped out for every 2 K^+ (or 1 Ca^{2+}) pumped in.

Electrical activity

- Depolarization is achieved by the opening of Na^+ and Ca^{2+} channels and the closing of K^+ channels.
- Repolarization is achieved by the opening of K^+ channels and the closing of Na^+ and Ca^{2+} channels.

Cardiac muscle action potential

- In cardiac muscle, the rapid depolarization associated with the upstroke of the action potential is conducted down the T tubule system of the ventricular myocardium, where it causes the release of intracellular Ca^{2+} from the sarcoplasmic reticulum.
- In cardiac muscle, a large part of the Ca^{2+} released during rapid depolarization is from additional sarcoploasmic reticulum just inside the cell membrane.
- The principal role of the sarcoplasmic reticulum is in the rapid release, active uptake, storage, and buffering of cytosolic Ca^{2+}.

Cardiac muscle action potential

- Along with the Ca^{2+} released from the sarcoplasmic reticulum, a significant amount of Ca^{2+} enters the cell from outside during the upstroke and plateau phase of the action potential.
- The principal cause of the sustained depolarization of the plateau phase is the presence of a population of L-type voltage-gated membrane channels permeable to Ca^{2+}.
- These channels open relatively slowly
- While open, there is a net influx of Ca^{2+}, the slow inward current, moving down an electrochemical gradient.

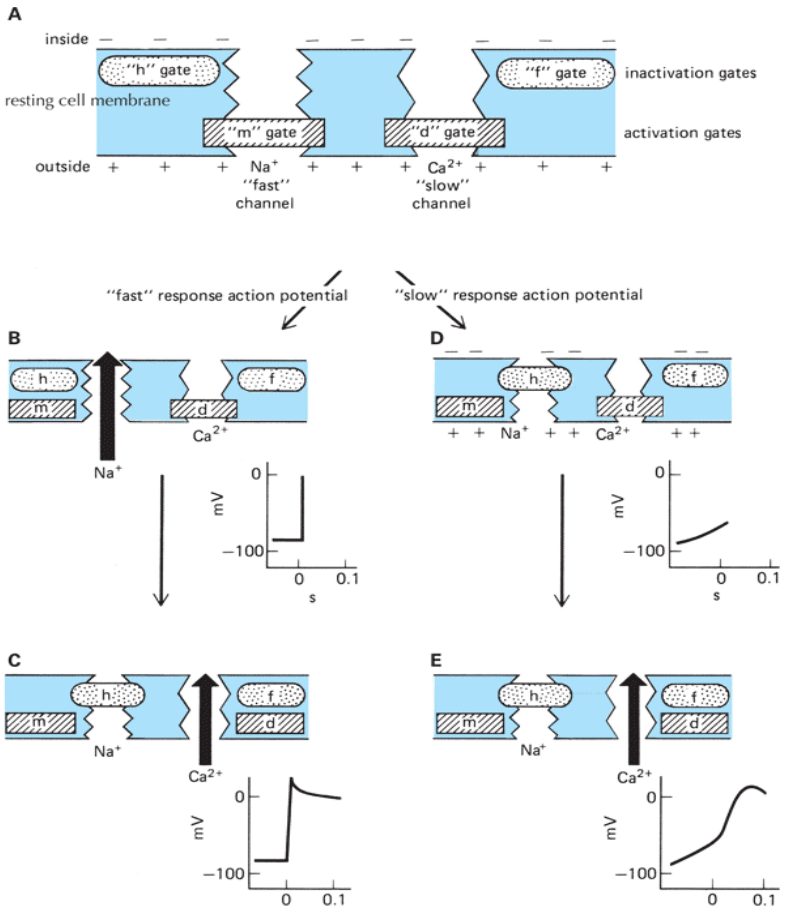
Cardiac muscle action potential

- Although the Ca^{2+} entering during an action potential does not directly affect that specific contraction, it affects the next contraction
- It increases the cellular Ca^{2+} content over time because of the repeated nature of the cardiac muscle contraction.
- In addition, even a small amount of Ca^{2+} entering through the sarcolemma causes the release of significant additional Ca^{2+} ion from the sarcoplasmic reticulum
- <u>Calcium-induced Calcium release</u>
- similar to that in smooth muscle.

Cardiac muscle action potential

- This constant influx of Ca^{2+} requires that there be a cellular system that can rid the cell of excess Ca^{2+}.
- The action of Ca^{2+} on the troponin- tropomyosin complex of the thin filaments is similar to that in skeletal muscle.

Conceptual model of myocardial membrane ion channels



Source: Mohrman DE, Heller LJ: *Cardiovascular Physiology*, 6th Edition: http://www.accessmedicine.com

Fig. 2-3 Accessed 02/01/2010

Rest (A); The initial phases of the fast response (B and C); The slow response action potentials (D and E).

Summary of ionic action potentials

- Phase 0. Rapid upstroke.
- Voltage gated Na^+ channels permit Na^+ entry.
- Massive influx of Na^+.
- Phase 1. Fast-action potential only.
- Partial repolarization.
- Voltage-gated Na^+ channels close.
- Voltage-gated K^+ channels open
- K^+ efflux.

Summary of ionic action potentials

- Phase 2. Plateau phase.
- Voltage-gated K^+ channels close.
- Voltage-gated Ca^{2+} channels open
- Ca^{2+} entry.
- Myocardial cell contracts.

Summary of ionic action potentials

- Phase 3. Rapid repolarization.
- Voltage-gated slow K^+ channels open.
- K^+ efflux is marked.
- Voltage gated Ca^{2+} channels close.
- Phase 4. Resting potential.
- Maintained by Na^+-K^+-ATPase pump.

Membrane and ion potentials

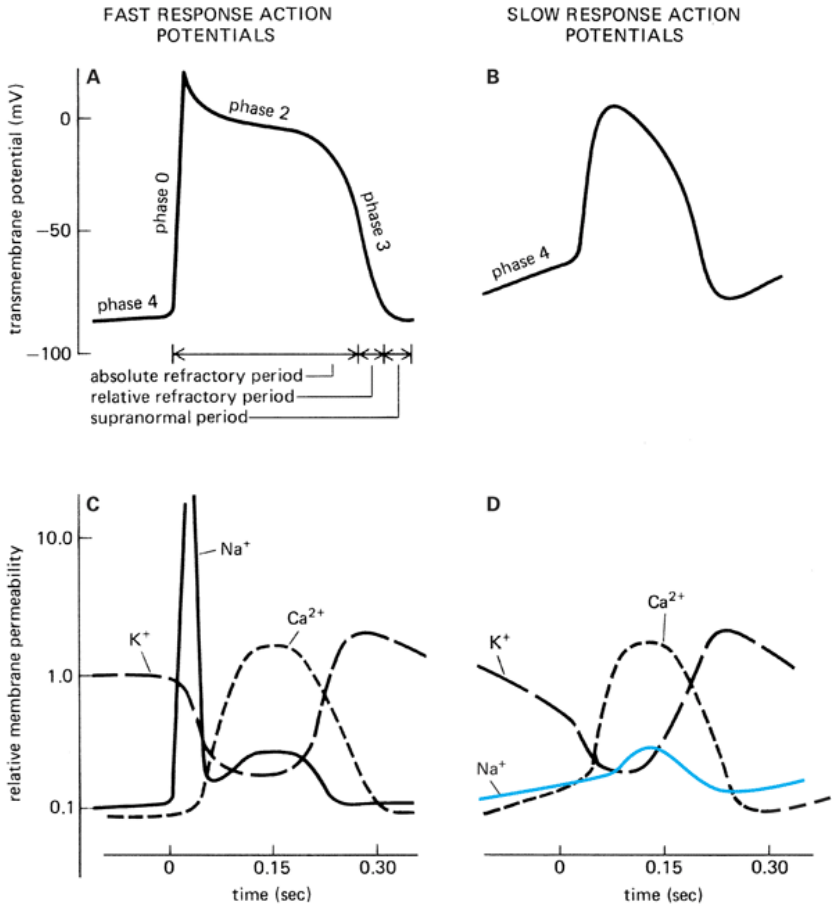


Fig. Accessed 02/01/2010

Automaticity

- Describes whether a myocardial cell can initiate its own action potential, depolarizing spontaneously.
- This behavior is seen in the:
- Sino-atrial (SA) node
- Atrial-ventricular (AV) node
- His-Purkinje system.

Excitability

- Describes how easily a myocardial cell fires an action potential in response to an inward depolarizing current from a neighboring cell that has fired an action potential
- Excitability is described by the refractory periods.

Refractory periods

- Absolute refractory period
- No Na^+ channels are available.
- Relative refractory period
- Na^+ channels become available and may respond to a larger stimulus to generate an action potential.
- Effective refractory period
- A larger stimulus may generate an action potential, but it is not sufficient to be conducted to a neighboring cell.

Autonomic nervous system effects

- Acetylcholine interacts with a G-protein linked muscarinic receptor on the SA nodal cell membrane which activates an inhibitory protein (G_i).
- An increase in K^+ conductance results from an increased opening of the K_{Ach} channels.
- A suppression of adenylate cyclase leads to a fall in intracellular cAMP
- Reduces the inward-going pacemaker current carried by Na^+.
- Acetylcholine decreases pacemaker activity and the speed of action potential conduction.

Autonomic nervous system effects

- Norepinephrine interacts with a G-protein linked α_1-adrenergic receptor on the SA nodal cell membrane which activates a stimulatory protein (G_s).
- Leads to an increase in adenylate cyclase
- Leads to an increase in intracellular cAMP
- Increases the open-state probability of the pacemaker Na^+ current channel.
- Norepinephrine increases pacemaker activity and the speed of action potential conduction.

Electrical activity

- Electrical activity is normally initiated in the sino-atrial (SA) node where pacemaker cells reach threshold first.
- Electrical activity spreads across the atria, through the atrio-ventricular (AV) node, through the Purkinje system, and to ventricular muscle.
- Conduction is unidirectional.

Heart conduction pathway

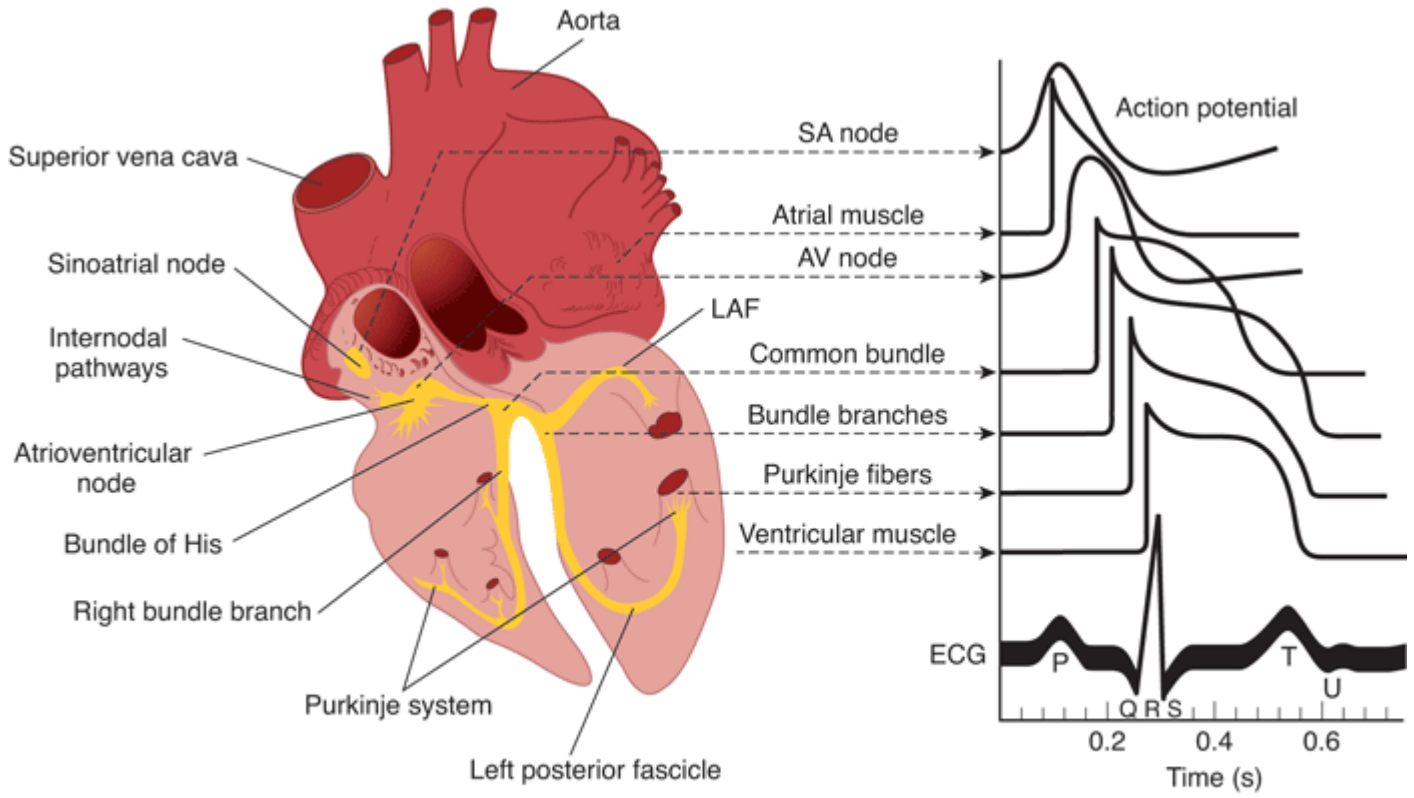


Fig. 30-1 Accessed 02/01/2010

Nodal action potential

- The SA node fires at 150ms
- The AV node fires at 250-300ms.
- Fast action potentials (fire at 100ms) occur in the myocytes as well as the Purkinje fibers.
- Conduction velocity depends on the size of the inward current during phase 0 (upward stroke of the action potential).
- A larger inward current means a faster conduction velocity.

Nodal action potential

- Conduction velocity is fastest in the Purkinje system and slowest in the AV node
- Atria empty fully into ventricles prior to depolarization of ventricles such that there is more time for ventricular filling

Node action potential

- Three major differences between the node and the myocardium are:
- (1) the presence of a pacemaker potential,
- (2) the slow rise of the action potential,
- (3) the lack of a well-defined plateau.
- The pacemaker potential results from changes in the permeability of the nodal cell membrane to all three of the major cations.

Node action potential

- First,
- K^+ channels, primarily responsible for repolarization, begin to close.
- Second,
- There is a steady increase in the membrane permeability to Na^+ as a cation channel opens.
- Third,
- Calcium moves in through a voltage gated Ca^{2+} channel early in diastole.

Node action potential

- These changes move the cell membrane potential to the Na^+ and Ca^{2+} equilibrium potentials.
- When that level is reached, an action potential is generated.
- In Purkinje cells, the rate of depolarization during phase 4 is much slower than that of nodal cells
- Thus, no pacemaker function.

Node action potential

- This action potential rises more slowly than the ventricular action potential because the fast voltage-gated Na^+ channels play an insignificant role.
- The opening of slow voltage-gated Ca^{2+} channels is primarily responsible for the upstroke of the action potential in nodal cells.
- The absence of a well-defined plateau (phase 2) occurs because K^+ channels open and pull the membrane potential toward the K^+ equilibrium potential.

Ventricular myocardium

- Area of depolarization resulting from artificial stimulus or pacemaker initiates process.
- Phase 0
- Positive charges displaced into adjacent areas of myocardium.
- Depolarization.
- Threshold is reached.
- Na^+ channels open.
- Membrane potential approaches Na^+ equilibrium potential.

Ventricular myocardium

- Phase 1.
- Na^+ channels inactivated and outward (transient) rectifying K^+ channel opens.
- Membrane potential nears zero.
- Phase 2.
- Ca^{2+} channels open and outward (transient) rectifying K^+ channel closes.
- Then, Ca^{2+} channels close and inward rectifying K^+ channel closes.
- Membrane potential stays near zero.

Ventricular myocardium

- Phase 3.
- Outward (delayed) rectifying K^+ channels open.
- Membrane potential approaches K^+ equilibrium potential.
- Phase 4.
- Outward (delayed) rectifying K^+ channels close and inward rectifying K^+ channels open.
- Na^+ channels activate.
- Resting membrane potential.

Ion channels in node

NAME	FUNCTION
Voltage gated long lasting Ca^{2+} channel	Inward movement of Ca^{2+} when membrane depolarizes at phase 0. Contributes to early pacemaker potential. β-adrenergic agents increase the probability of channel opening. Acetylcholine decreases the probability of channel opening.
Voltage gated short acting Ca^{2+} channel	Contributes to pacemaker potential.
Voltage gated mixed cation channel	Principally carries Na^{+} (and K^{+}) inward when activated by hyperpolarization. Contributes to pacemaker potential.

Ion channels in node

NAME	FUNCTION
Voltage gated outward (delayed) rectifying K^+ channel	Contributes to phase 3 of action potential. Closes early in phase 4. Contributes to pacemaker potential.
Ligand gated, G-protein activated K^+ channel	Opened by acetylcholine and adenosine. Hyperpolarizes membrane during phase 4, slowing pacemaker potential.

Ion channels involved in both His-Purkinje system and ventricular myocardium

NAME	FUNCTION
Voltage gated fast Na^+ channel	Permits influx of Na^+ at phase 0 of action potential.
Voltage gated long acting Ca^{2+} channel	Contributes to phase 2 of action potential by permitting Ca^{2+} influx when membrane is depolarized. (DHP sensitive) B-adrenergic agents increase probability of channel opening. Acetylcholine lowers probability of channel opening.
Voltage gated inward rectifying K^+ channel	Maintains resting membrane potential at phase 4 by permitting K^+ efflux at highly negative membrane potentials.

Ion channels involved in both His-Purkinje system and ventricular myocardium

NAME	FUNCTION
Voltage gated outward (transient) rectifying K^+ channel	Contributes briefly to phase 1 by transiently permitting K^+ efflux at positive membrane potentials.
Voltage gated outward (delayed) rectifying K^+ channel	Causes phase 3 of action potential by permitting efflux of K^+ after a delay when membrane depolarizes.
Ligand gated, G-protein activated K^+ channel	Opened by acetylcholine and adenosine. Hyperpolarizes membrane during phase 4 and shortens phase 2.

EKG

- Atrial excitation results from a wave of depolarization that originates in the SA node and spreads over the atria.
- The net dipole generated by this excitation has a magnitude proportional to the mass of the atrial musculature involved.
- The isoelectric period between the end of the P wave and the onset of the QRS complex is usually understood to represent AV conduction time.
- QRS complex indicates ventricular depolarization
- Conducted via the His-Purkinje system

EKG

- The ST segment is generally isoelectric as the action potential of the ventricle is in phase 2.
- Ventricular repolarization does not proceed in a synchronized propagated wave as does depolarization.
- The subendocardial myocardium depolarizes before the subepicardial myocardium
- BUT repolarizes after the subepicardial myocardium.
- Repolarization is a function of the properties of individual cells.
- The T wave, then, is longer than the QRS complex.

EKG

- The QT interval represents the total duration of ventricular activation.
- If ventricular repolarization is delayed, the QT interval lengthens.
- After delayed repolarization, the freshly repolarized myocardium may be subject to sudden, early depolarizations (after-polarizations)
- Because the membrane potential in a small region of myocardium begins to depolarize before it has stabilized at the resting value. (long QTc)

EKG

- Whenever the normal synchronized pattern of depolarization is interrupted (atrium or ventricle), chaotic depolarization and ineffective contraction results.

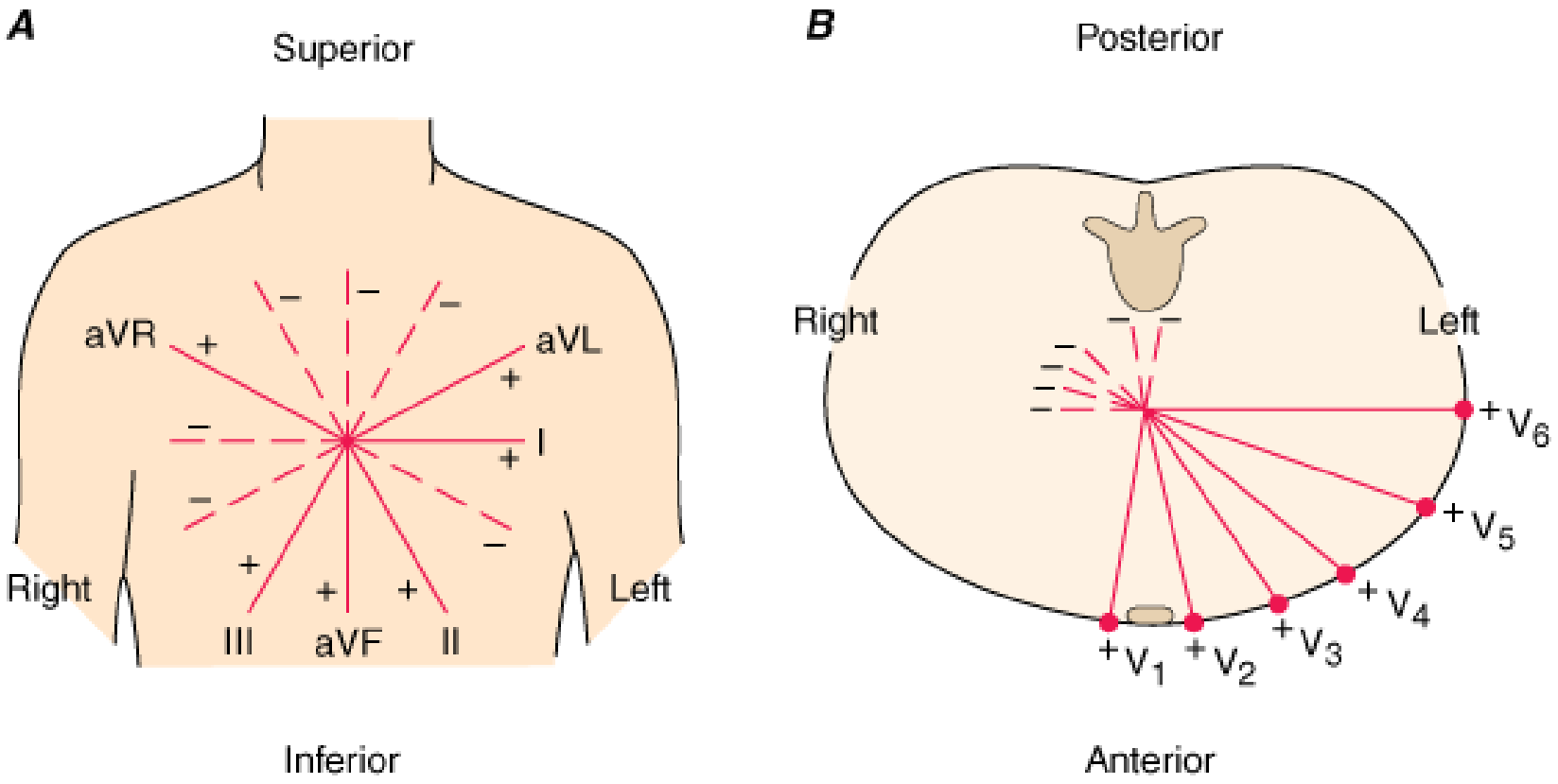
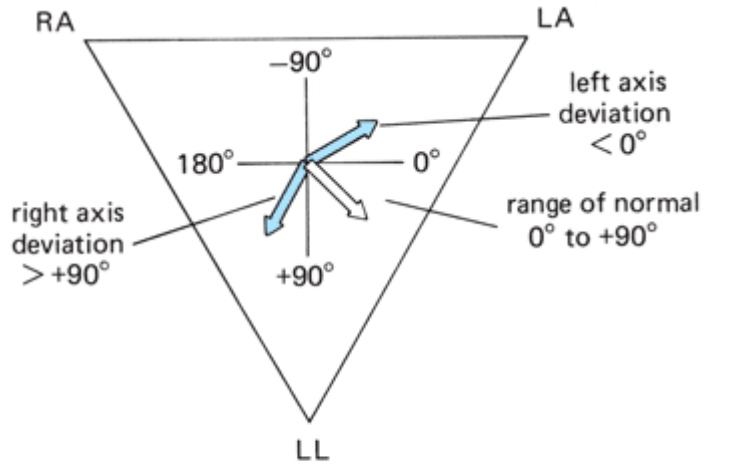
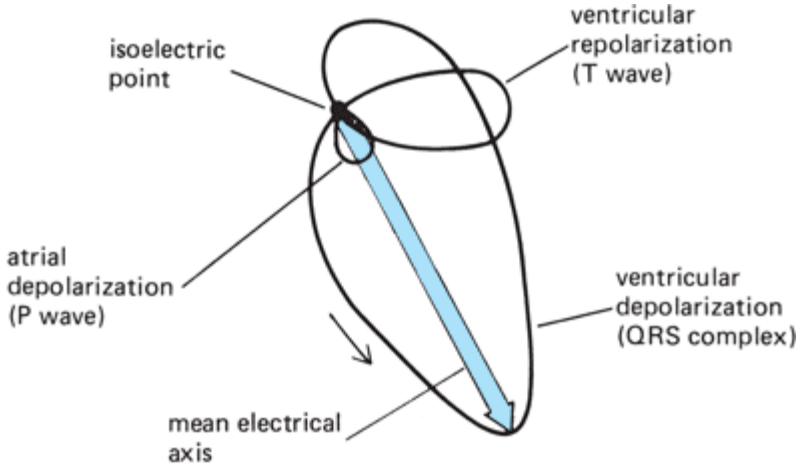


Fig. 221-3 Accessed 08/01/2010

Electrical dipole



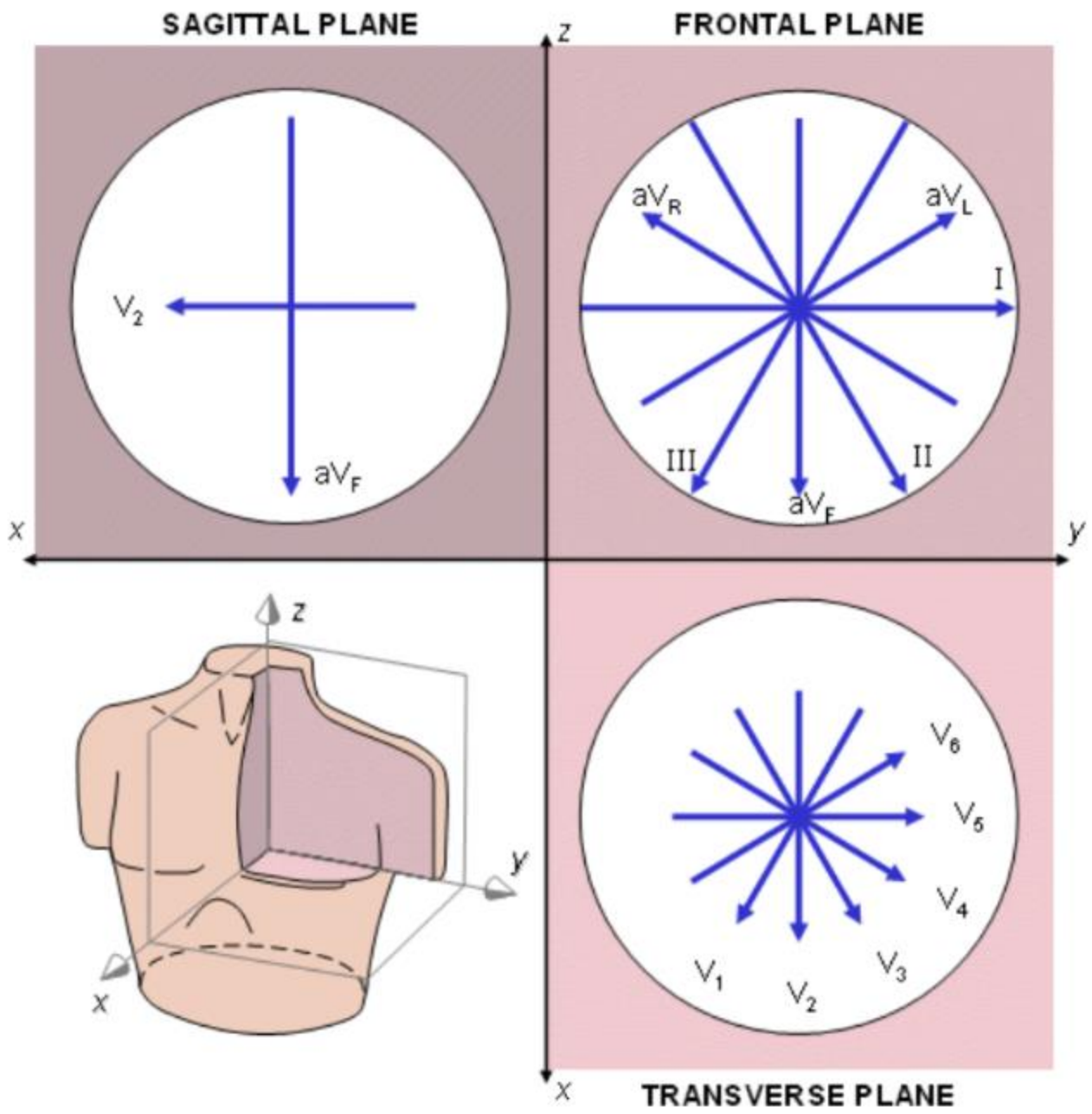
Source: Mohrman DE, Heller LJ: *Cardiovascular Physiology*, 6th Edition: http://www.accessmedicine.com

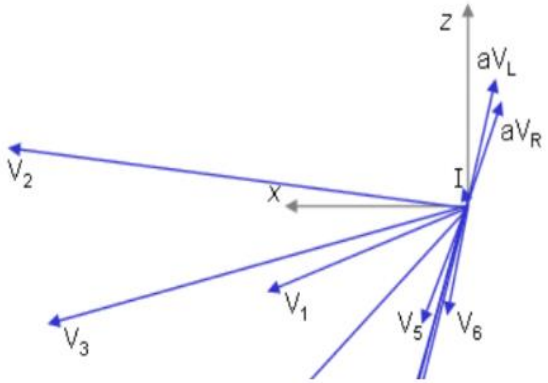


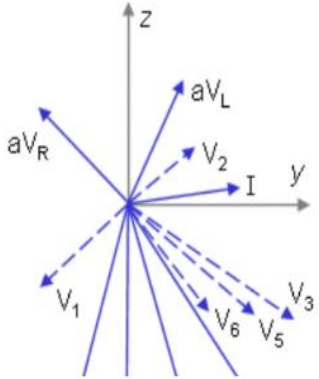
Source: Mohrman DE, Heller LJ: *Cardiovascular Physiology*, 6th Edition: http://www.accessmedicine.com

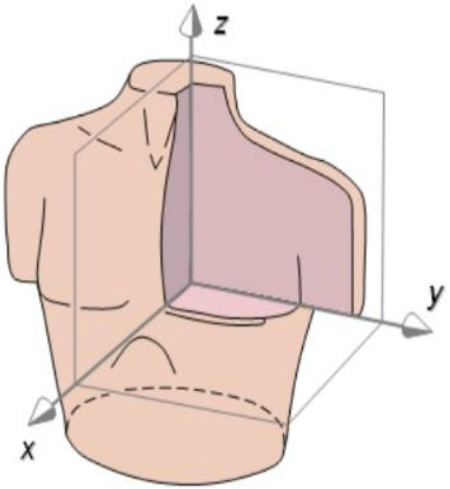
Figs. 4-5,6 Accessed 02/01/2010

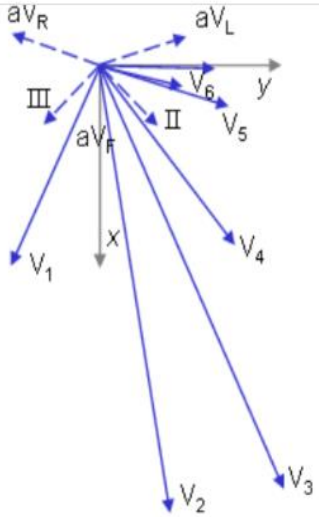
The electrical dipole is shown as a vector with its tail always positioned at the center of Einthoven's triangle.


SAGITTAL PLANE
FRONTAL PLANE
TRANSVERSE PLANE
z
x
y
V_2
aV_F
aV_R
aV_L
I
III
II
aV_F
V_6
V_5
V_4
V_3
V_1
V_2



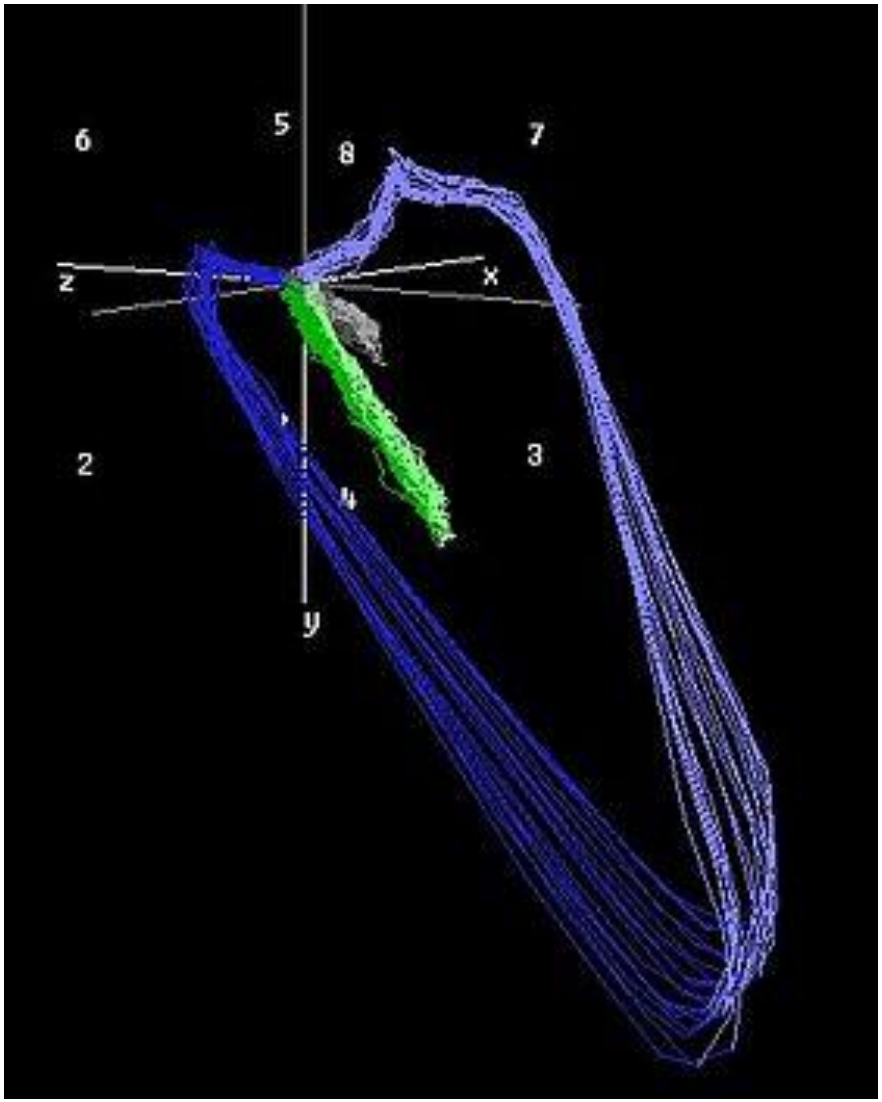






TRANSVERSE

forrás: BioLabor Biofizikai és Laboratóriumi Szolg. Kft. www.biolabor.hu



Vectorcardiogram

3D representation of depolarization and repolarization.

Blue: QRS
Green: T
Gray: P

May also be reconstructed from standard 12 lead EKG

https://en.wikipedia.org/wiki/Vectorcardiography
Accessed 01/20/2020

Mean axis

- If QRS is primarily positive in limb leads I and II, then axis is normal.
- Otherwise, find limb lead in which QRS is most isoelectric.
- The mean axis is perpendicular to that lead.
- If the QRS complex is positive in that perpendicular lead, then mean axis is in the direction of that lead
- If negative, then mean axis points directly away from that lead.

Axis deviation

- Left-axis deviation
- More negative than -30°
- Diffuse left ventricular disease
- Inferior myocardial infarction
- Left anterior hemiblock
- Small R, deep S in leads II, III, and aVF

Axis deviation

- Right-axis deviation
- >90°
- Right ventricular hypertrophy
- R>S in V1
- Left posterior hemiblock
- Small Q and tall R in leads II, III, and aVF
- Mild right-axis deviation is seen in thin, healthy individuals (up to 110°).

T-wave axis

- A marker of ventricular repolarization
- Calculation:
- $\alpha = \tan^{-1}(2/\sqrt{3}((II-I/2)/I))$ where α represents the T-wave axis in the frontal (XY) plane and I and II represent the signed areas of the vectors in leads I and II, respectively.
- When deviated from normal by more than 45 degrees in either direction in the frontal plane is left ventricular strain and a marker of ischemia
- Left ventricular strain has been strongly associated with an increased risk of fatal and non-fatal cardiac events in older adults.

PR intervals

- Short PR interval:
- <0.12s
- Pre-excitation syndrome of Wolff-Parkinson-White
- Look for slurred QRS upstroke due to “delta” wave
- Nodal rhythm
- Inverted P in aVF
- Long PR interval:
- >0.20s
- This is First-degree AV block.

QRS intervals

- A normal QRS interval is 0.06-0.10s
- Widened:
- >0.10s
- Ventricular premature beats
- Left bundle branch block
- RR’ in V6
- Right bundle branch block
- RsR’ in V1, deep S in V6
- Toxic levels of drugs (e.g., quinidine)
- Severe hypokalemia.

QT interval

- The normal QT duration is rate related
- 0.43 s or 50% of RR interval
- Bazett formula:

$$QTc = \frac{\text{QT interval (s)}}{\sqrt{\text{R} - \text{R interval (s)}}}$$

Table 20–7.

Causes of QT prolongation.[a]

Cardiac medications

- **Antiarrhythmics:** class IA (quinidine, procainamide, disopyramide) class III (amiodarone, sotalol)
- **Inotropic agents:** dobutamine, dopamine, epinephrine, isoproterenol

Noncardiac medications

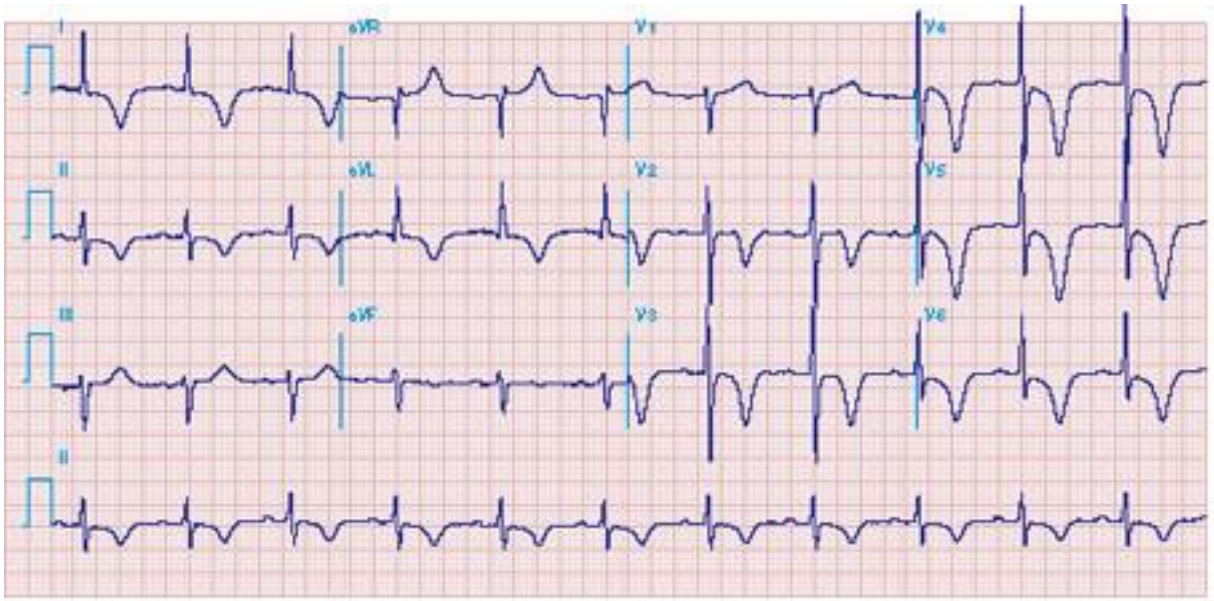
- **Antibiotics/antivirals:** azithromycin, clarithromycin, levofloxacin, amantadine
- **Antipsychotics:** risperidone, thioridazine, lithium, haloperidol
- **Sedatives:** chloral hydrate, methadone
- **Other:** albuterol, levalbuterol, ondansetron, phenytoin, pseudoephedrine
- **Electrolyte disturbances:** hypokalemia, hypomagnesemia, hypocalcemia

[a] Partial list only.

ST

- ST elevation:
- Acute myocardial infarction
- Coronary spasm
- Pericarditis (concave upward)
- LV aneurysm.
- ST depression:
- Digitalis effect
- Strain (due to ventricular hypertrophy)
- Ischemia
- Non-transmural myocardial infarction

Anterior wall myocardial ischemia

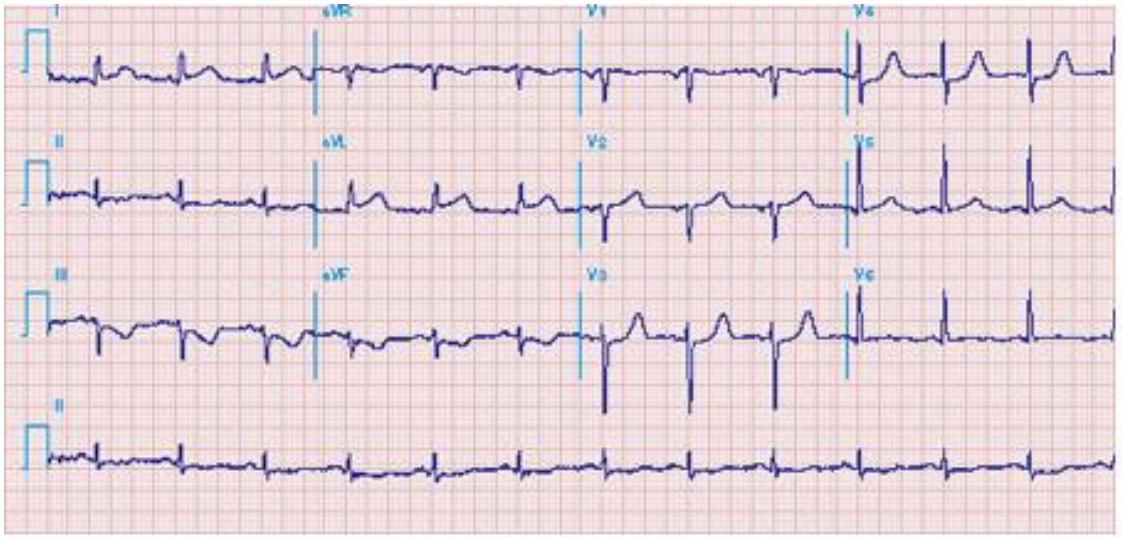


Deep T-wave inversions and ST-segment depressions in I, aVL, V_3–V_6 in a patient with LVH (increased voltage in V_2–V_5).

Source: Fauci AS, Kasper DL, Braunwald E, Hauser SL, Longo DL, Jameson JL, Loscalzo J: *Harrison's Principles of Internal Medicine*, 17th Edition: http://www.accessmedicine.com

Fig.e19-1 Accessed 03/17/2010

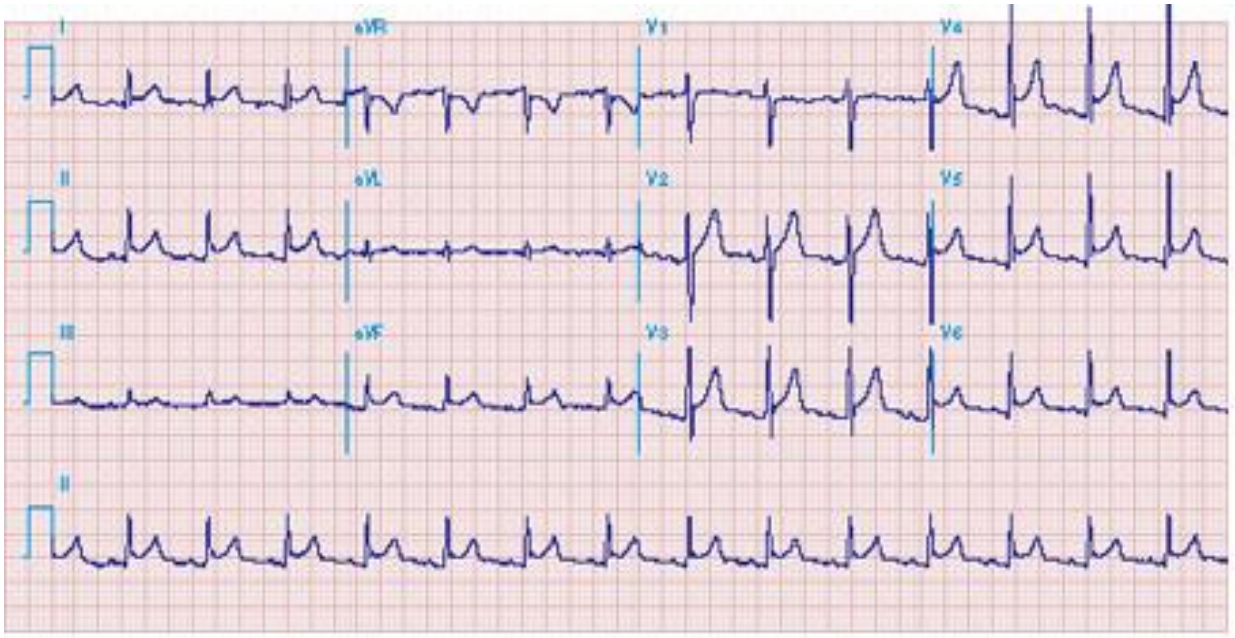
Lateral wall ischemia



ST elevations in I and aVL with probable reciprocal ST depressions inferiorly (II, III, and aVF). Ischemic ST depressions also in V_3 and V_4.

Fig. e19-4 Accessed 03/17/2010

Acute pericarditis



Source: Fauci AS, Kasper DL, Braunwald E, Hauser SL, Longo DL, Jameson JL, Loscalzo J: *Harrison's Principles of Internal Medicine*, 17th Edition: http://www.accessmedicine.com

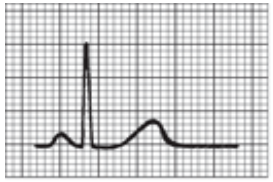
Diffuse ST elevations in I, II, III, aVF, V_3–V_6, without T-wave inversions. Also PR-segment elevation in aVR and PR depression in the inferolateral leads.

Fig. e19-13 Accessed 03/17/2010

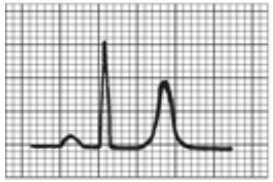
T waves

- Tall peaked T:
- Hyperkalemia
- Acute MI (“hyperacute T”).
- Inverted T:
- Non-Q-wave myocardial infarction
- Ventricular strain pattern
- Drug effect (e.g., digitalis)
- Hypokalemia
- Hypocalcemia
- Increased intracranial pressure (e.g., subarachnoid bleed).

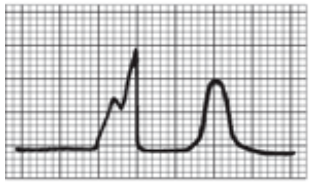
T waves



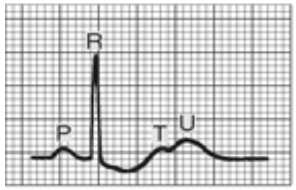
Normal tracing (plasma K^+ 4–5.5 meq/L). PR interval = 0.16 s; QRS interval = 0.06 s; QT interval = 0.4 s (normal for an assumed heart rate of 60).



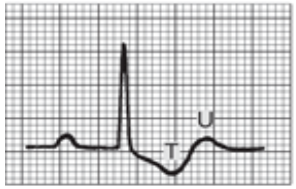
Hyperkalemia (plasma K^+ ±7.0 meq/L). The PR and QRS intervals are within normal limits. Very tall, slender peaked T waves are now present.



Hyperkalemia (plasma K^+ ±8.5 meq/L). There is no evidence of atrial activity; the QRS complex is broad and slurred and the QRS interval has widened to 0.2 s. The T waves remain tall and slender. Further elevation of the plasma K^+ level may result in ventricular tachycardia and ventricular fibrillation.



Hypokalemia (plasma K^+ ±3.5 meq/L). PR interval = 0.2 s; QRS interval = 0.06 s; ST segment depression. A prominent U wave is now present immediately following the T. The actual QT interval remains 0.4 s. If the U wave is erroneously considered a part of the T, a falsely prolonged QT interval of 0.6 s will be measured.



Hypokalemia (plasma K^+ ±2.5 meq/L). The PR interval is lengthened to 0.32 s; the ST segment is depressed; the T wave is inverted; a prominent U wave is seen. The true QT interval remains normal.

Source: Barrett KE, Barman SM, Boitano S, Brooks H: *Ganong's Review of Medical Physiology, 23rd Edition*: http://www.accessmedicine.com

Fig. 30-18 Accessed 02/01/2010

Electrolyte disorders

- Hyperkalemia may cause a wide QRS complex.
- It is distinguished by tall, peaked T waves and small P waves.
- Hypokalemia may cause a wide QRS complex.
- It is distinguished by flattened T waves, a U wave, and a prolonged QT interval.
- Hypercalcemia
- U wave
- The U wave is thought to represent repolarization by papillary muscles or Purkinje fibers

U waves

- U waves are also found with:
- Thyrotoxicosis
- Intracranial hemorrhage
- Digoxin
- Epinephrine
- Class Ia and class III antiarrhythmics
- The congenital prolonged QT syndrome

Hypertrophy

- Right atrium:
- P wave >2.5 mm in lead II.
- Left atrium:
- P biphasic (positive, then negative) in V1, with terminal negative force wider than 0.04 s.
- Right ventricle:
- R> S in V1 and R in V1> 5 mm; deep S in V6; right-axis deviation.
- Left ventricle:
- S in V1 plus R in V5 or V6 >35 mm or R in AVL> 11 mm.

Left atrial enlargement and left ventricular hypertrophy

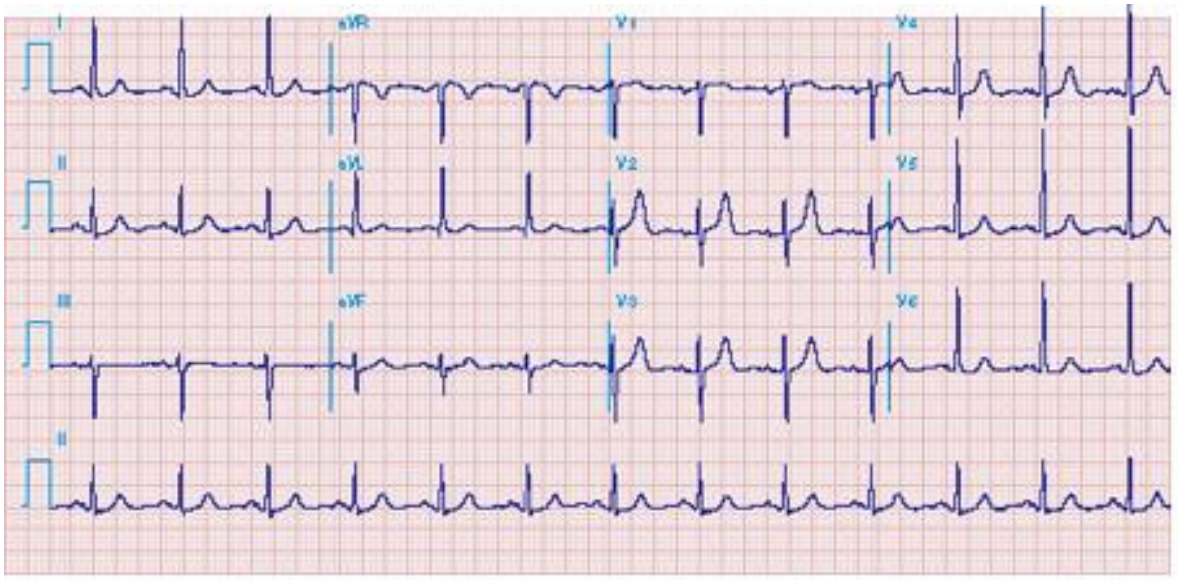


Fig. e19-28 Accessed 03/17/2010

Right atrial enlargement and right ventricular hypertrophy

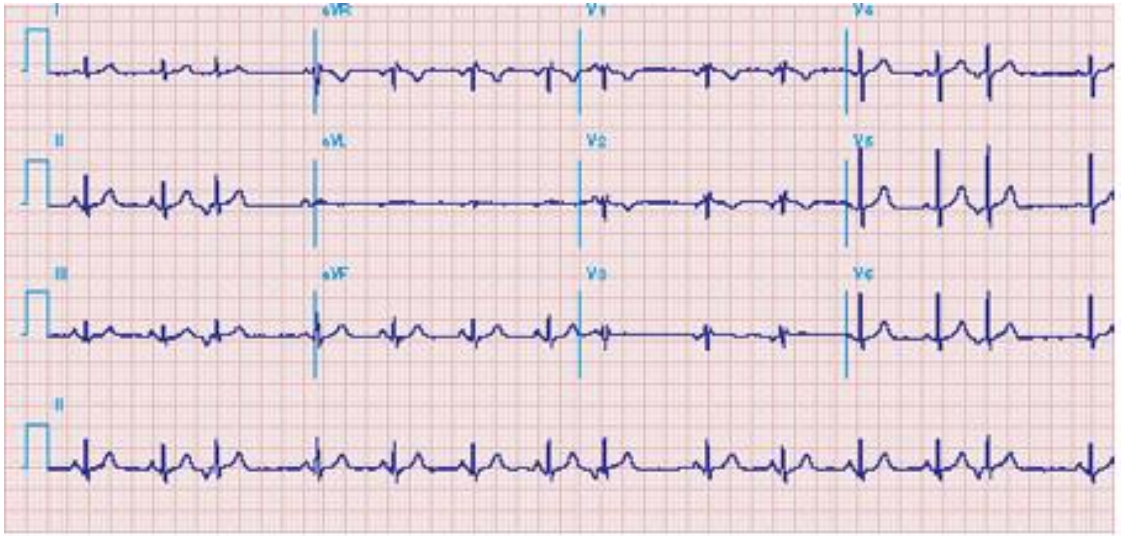


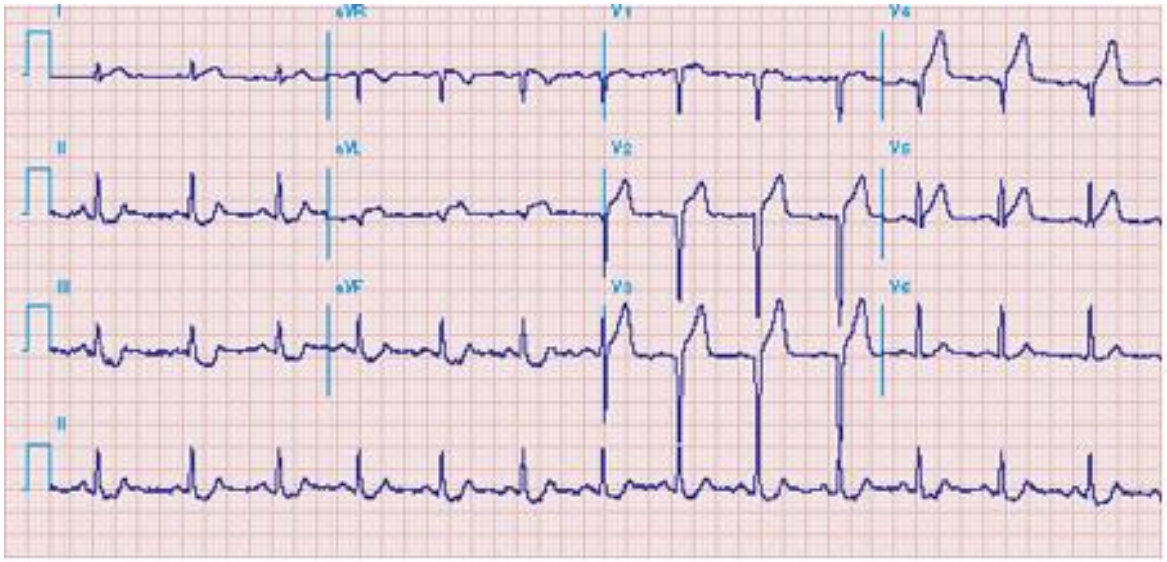
Fig. e19-23 Accessed 03/17/2010

Incomplete RBBB (rsr' in V_1–V_3); (3) borderline peaked P waves in lead II with vertical P-wave axis (probable right atrial overload); (4) slow R-wave progression in V_1–V_3; (5) prominent S waves in V_6 . superior axis deviation with an S_1-S_2-S_3 pattern

Abnormal Q waves

- V1-V2 Anteroseptal infarction
- V3-V4 Apical infarction
- I, aVL, V5-V6 Anterolateral infarction
- II, III, aVF Inferior infarction
- If shallow Q but deep R in V1-V2, posterior infarction

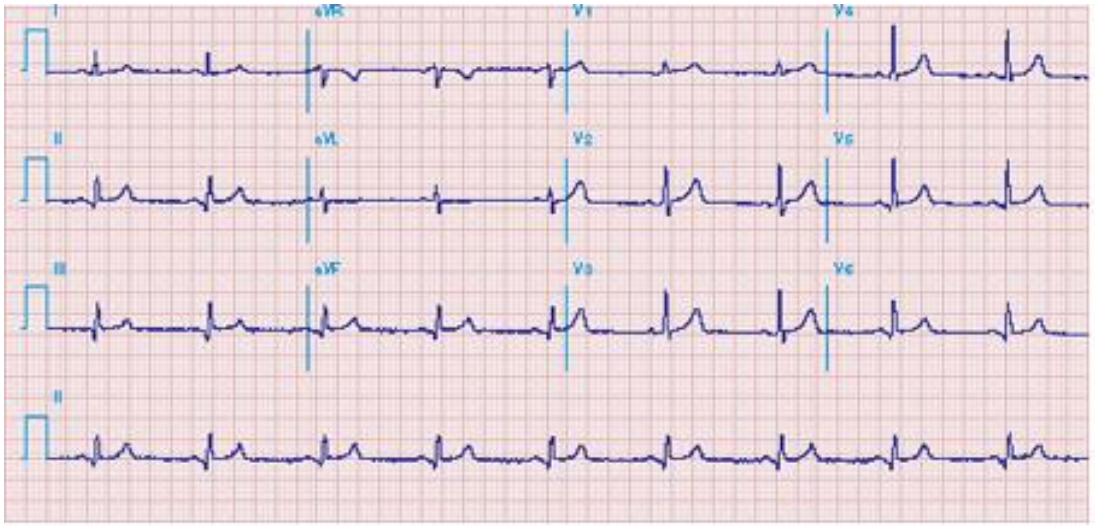
Acute anterior wall myocardial infarction



ST elevations and Q waves in V_1–V_4 and aVL and reciprocal inferior ST depressions.

Fig. e19-6. Accessed 03/17/2010

Old inferior-posterior myocardial infarction



Q waves in the inferior leads (II, III, aVF); broad R wave in V_1 (a Q wave equivalent). Absence of right-axis deviation and the presence of upright T waves in V_1–V_2 are also against RVH.

Fig. E19-11. Accessed 03/17/2010

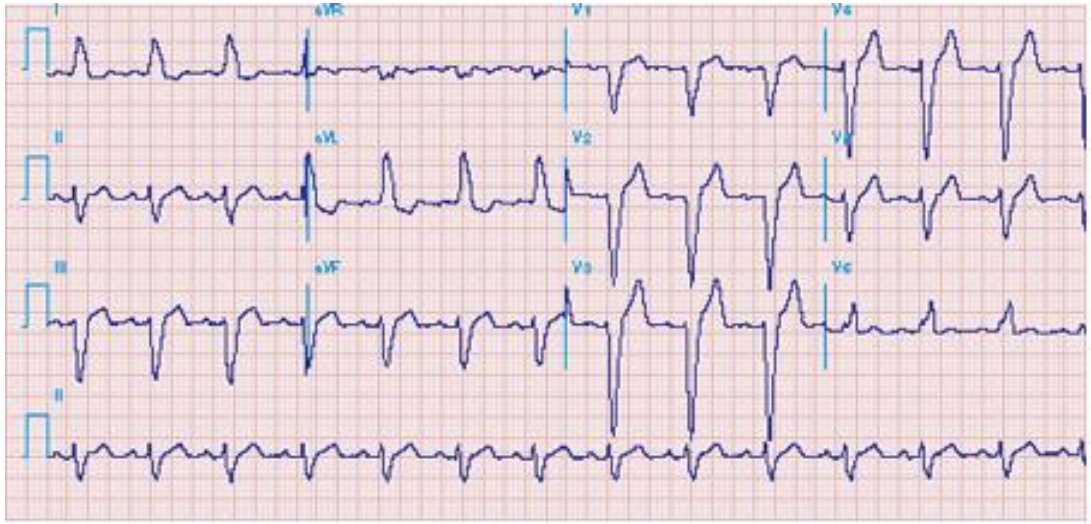
Bundle branch block

- Right bundle branch block
- Wide QRS complex with an RSR’ in V1 and inverted T waves in V1 and V2.
- Total left bundle branch blocks
- Wide QRS and T waves facing in the opposite direction from the QRS.
- They may also show notched QRS complexes in leads I, AVL, V5, and V6.

Bundle branch block

- Left anterior hemiblock
- Normal QRS duration with a left axis deviation > -45°.
- Left posterior hemiblock
- Normal QRS duration with a right axis deviation of +90° and no evidence of right ventricular hypertrophy or anterior wall infarction.

Left bundle branch block



Normal sinus rhythm with first-degree AV block (PR interval = 0.24 s), and complete left bundle branch block.

Fig. e19-30 Accessed 03/17/2010

Rhythm

- Sinus rhythm
- Present if every P wave is followed by a QRS
- PR interval >0.12 s
- Every QRS is preceded by a P wave
- The P wave is upright in leads I, II, and III.
- The P wave arising in the SA node is always upright in II, V5.

Rhythm

- Requisite for normal cell excitation are:
- A stable level of the resting potential (-80mV)
- A steep upstroke; and an adequately long duration of the action potential (refractory period).
- Rapid Na^+ channels cannot be activated if the resting potential is less negative (-55mV).
- Acidosis, hyperkalemia or hypokalemia, and cardiac glycosides affect the resting potential.

Rhythm

- If there is no rapid Na^+ current, depolarization is dependent upon the slow Ca^{2+} influx
- Amplified by norepinephrine and cell stretching
- Blocked by verapamil, Nifedipine
- The activation threshold is -40mV.
- The upstroke of the action potential is slower
- The amplitude is lower, and the plateau (phase 2) has disappeared.
- Spontaneous depolarization is possible.

Rhythm

- Women have longer QT intervals on electrocardiograms
- Increases their susceptibility to certain arrhythmias.
- Effects of sex steroids on cardiac repolarization
- Related to their effects on cardiac voltage-gated potassium channels
- There is a lower density of the rapid component (I_{Kr}) of the delayed rectifier potassium current (I_K) in females.

Table 12.6 Selected Examples of Causal Genes in Inherited Arrhythmogenic Diseases[a]

Disorder	Gene	Function
Long QT syndrome[b]	*KCNQ1*	K^+ channel (LOF)
	KCNH2	K^+ channel (LOF)
	SCN5A	Na^+ channel (GOF)
	CAV3	Caveolin, Na^+current (GOF)
Short QT syndrome[b]	*KCNQ1*	K^+ channel (GOF)
	KCNH2	K^+ channel (GOF)
Brugada syndrome[b]	*SCN5A*	Na^+ channel (LOF)
	CACNB2b	Ca^{++} channel (LOF)
	SCN1b	Na^+ channel (LOF)[a]
CPVT syndrome[b]	*RYR2*	Diastolic Ca^{++} release (GOF)
	CASQ2	Diastolic Ca^{++} release (LOF)

LOF, Loss-of-function mutations; *GOF,* gain-of-function mutations; *CPVT,* catecholaminergic polymorphic ventricular tachycardia.

[a]Different mutations can cause the same general syndrome, and mutations in some genes can cause multiple different phenotypes; thus, loss-of-function (LOF) mutations may cause long QT intervals, whereas gain-of-function (GOF) mutations result in short repolarization intervals.

[b]*Long QT syndrome* manifests as arrhythmias associated with excessive prolongation of the cardiac repolarization; patients often present with stress-induced syncope or sudden cardiac death (SCD), and some forms are associated with swimming. *Short QT syndrome* patients have arrhythmias associated with abbreviated repolarization intervals; they can present with palpitations, syncope, and SCD. *Brugada syndrome* manifests as ECG abnormalities (ST segment elevations and right bundle branch block) in the absence of structural heart disease; patients classically present with syncope or SCD during rest or sleep, or after large meals. *CPVT* does not have characteristic ECG changes; patients often present in childhood with life-threatening arrhythmias due to adrenergic stimulation (stress-related).

Modified from Cerrone M, Priori SG: Genetics of sudden death: focus on inherited channelopathies, *Eur Heart J* 32(17), 2109–2118, 2011.

Supraventricular arrhythimas

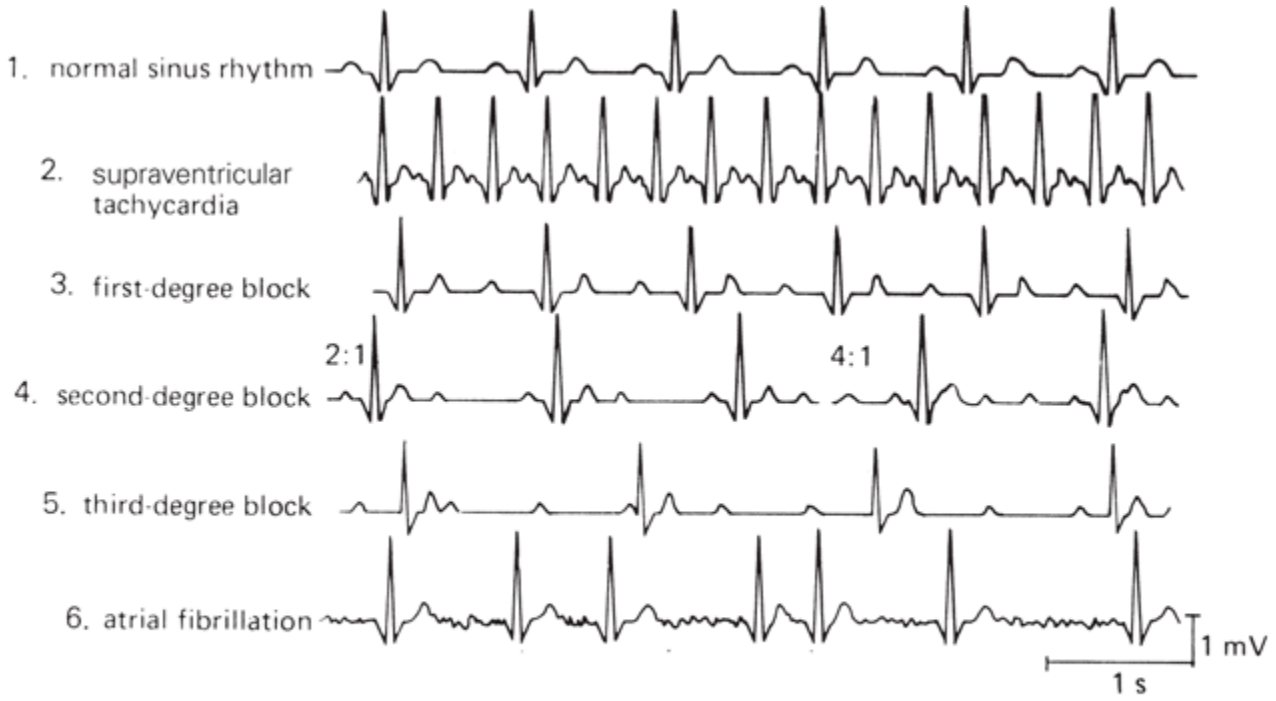


Fig. 5-1 Accessed 02/01/2010

Therapy

- Narrow complex tachyarrhythmias should first be treated with carotid massage (vagal maneuver).
- If this fails, adenosine is given as bolus.
- If rhythm converts, probable re-entry supraventricular tachycardia.
- Treat recurrence with adenosine or longer acting atrio-ventricular node blockers such as β-blockers or diltiazem.
- Synchronized cardioversion is indicated if heart rate is >150 beats/minute and the patient is unstable.
- If the rhythm does not convert, control the rate with diltiazem or β-blocker.

Therapy

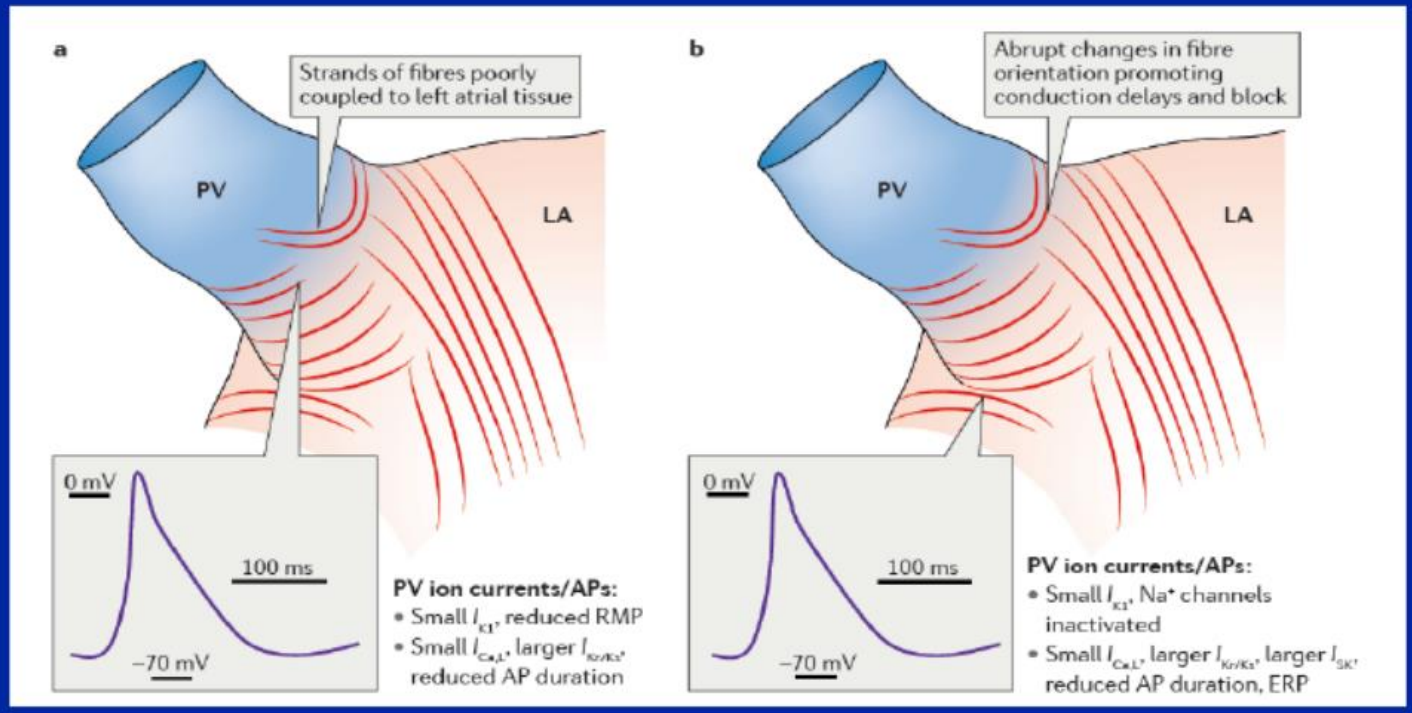
- Due to the potent negative inotropic action between these two classes of drugs, one switches between medications of the same class rather than switch from one class to another.
- Digoxin is useful in modulating the ventricular response to supraventricular tachycardia.
- Digoxin may work synergistically with beta blockers or calcium channel blockers.
- Digoxin toxicity can cause bradycardia, arrhythmia, nausea, visual disturbances, confusion.

Therapy

- Digoxin, adenosine, diltiazem, and β-blockers are not used with atrial fibrillation and Wolff-Parkinson-White syndrome as they cause slowing of conduction through the atrio-ventricular node.
- This may facilitate activation of alternate pathways.
- Amiodarone is the drug of choice.

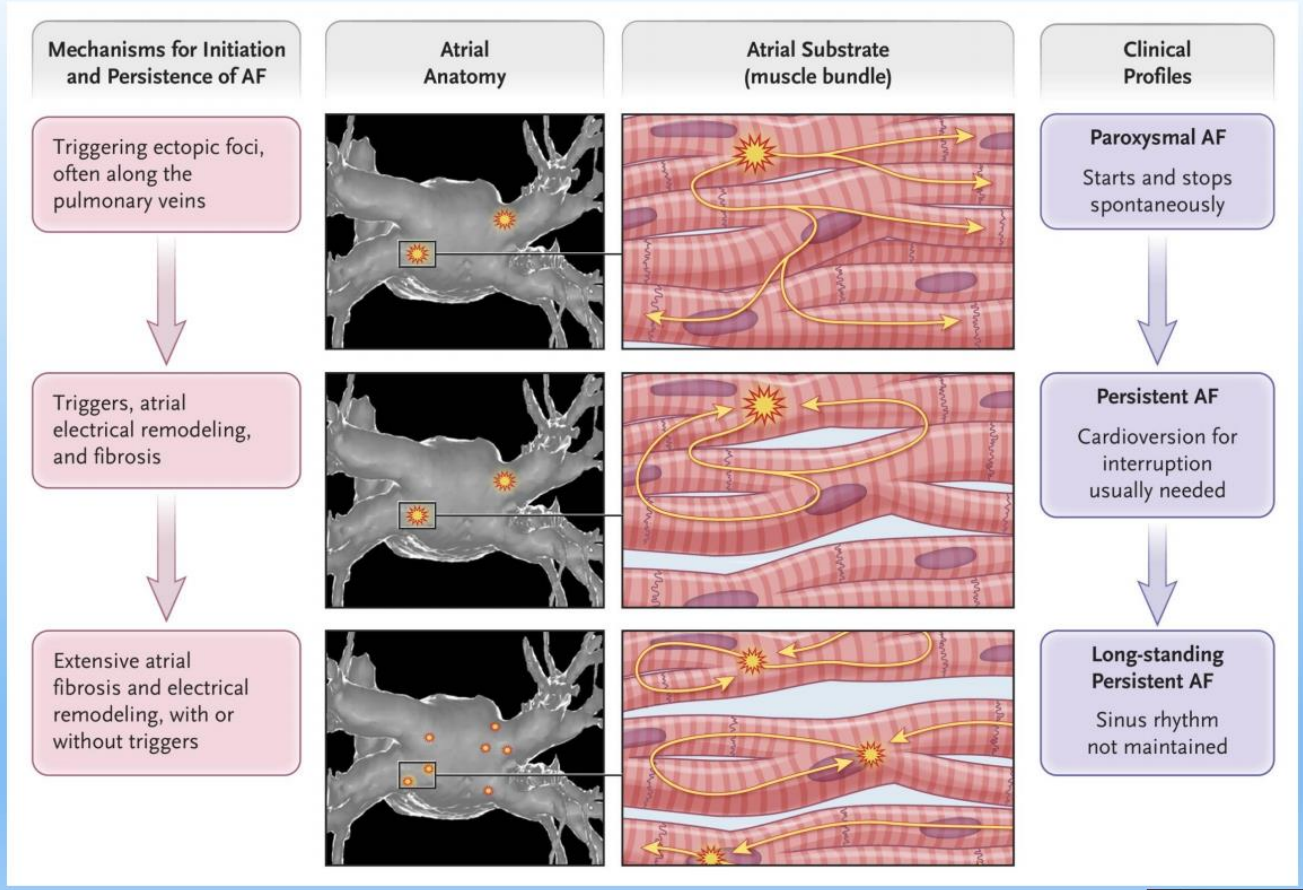
Atrial flutter

- COPD, valvular or structural heart disease, ASD, or surgically repaired congenital heart disease as risk factors
- Stroke risk is that of AF
- Catheter ablation is definitive therapy



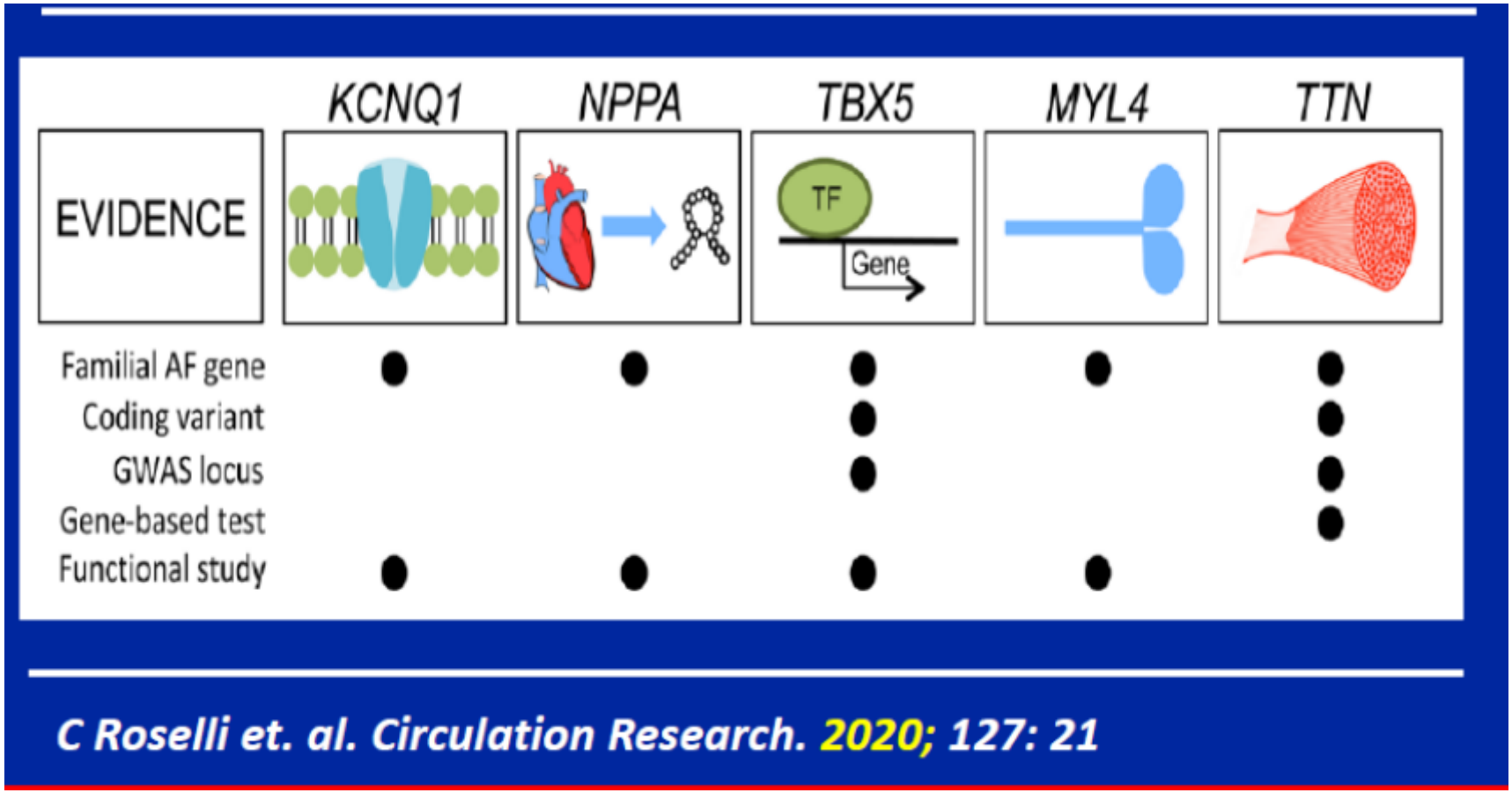
S Nattel et. al. Nat Rev Cardiol. 2016; 13: 575.

Types and Triggers of Atrial Fibrillation (AF).



Michaud GF, Stevenson WG. N Engl J Med 2021;384:353-361

The NEW ENGLAND JOURNAL of MEDICINE



C Roselli et. al. Circulation Research. 2020; 127: 21

Atrial fibrillation

- AF is the most common chronic arrhythmia
- 9% of those over 65 years of age
- 30% may be asymptomatic
- Hypertension increases risk 70-80%
- Each unit increase in BMI increases risk 4-5%
- Alcohol abuse or withdrawal (“holiday heart”), tobacco, obstructive sleep apnea increase risk 50%

Atrial fibrillation

- It may be the initial presenting sign in thyrotoxicosis
- Occurs in moderate-severe mitral stenosis,presence of a mechanical valve, dilated cardiomyopathy, ASD, hypertensive heart disease, congenital heart disease
- Other risks include pericarditis, pneumonia, pulmonary embolism, use of Theophylline and β-agonists
- Rate control is more important than rhythm control

Atrial fibrillation

- Atrial fibrillation often appears in a paroxysmal fashion before becoming the established rhythm.
- 5%/year risk of stroke
- 20%/year if over 75
- Thrombus formation
- Trans esophageal echocardiography (TEE) most sensitive imaging modality
- Myocardial ischemia
- Atrial fibrillation is the only common arrhythmia in which the ventricular rate is rapid and the rhythm very irregular.

Atrial fibrillation

- 30 seconds of atrial fibrillation is needed to establish the diagnosis
- Paroxysmal if duration less than 7 days
- Persistent if duration greater than 7 days
- Long standing if duration greater than 1 year
- Often associated with structural abnormality
- If left atrial appendage >5mm, cardioversion not useful
- If resistant to cardioversion, is permanent
- Proceed to AV node ablation

Therapy

- Rate control is the first-line treatment strategy
- Except in:
- Atrial fibrillation which has a reversible cause
- Heart failure thought to be primarily caused by atrial fibrillation
- New-onset atrial fibrillation
- Atrial flutter whose condition is considered suitable for an ablation strategy to restore sinus rhythm

Therapy

- <u>If hemodynamically stable, asymptomatic, and no LV dysfunction</u>:
- IV esmolol or metoprolol to control rate
- Follow with amiodarone for 4 weeks to 12 months as bridge to cardioversion
- Amiodarone can be administered on an outpatient basis
- Not associated with risk of torsade de pointes
- Increases prothrombin time with those on warfarin
- Risk of thyroid disorder
- Risk of pulmonary fibrosis
- Dronedarone has fewer complications than amiodarone

Therapy

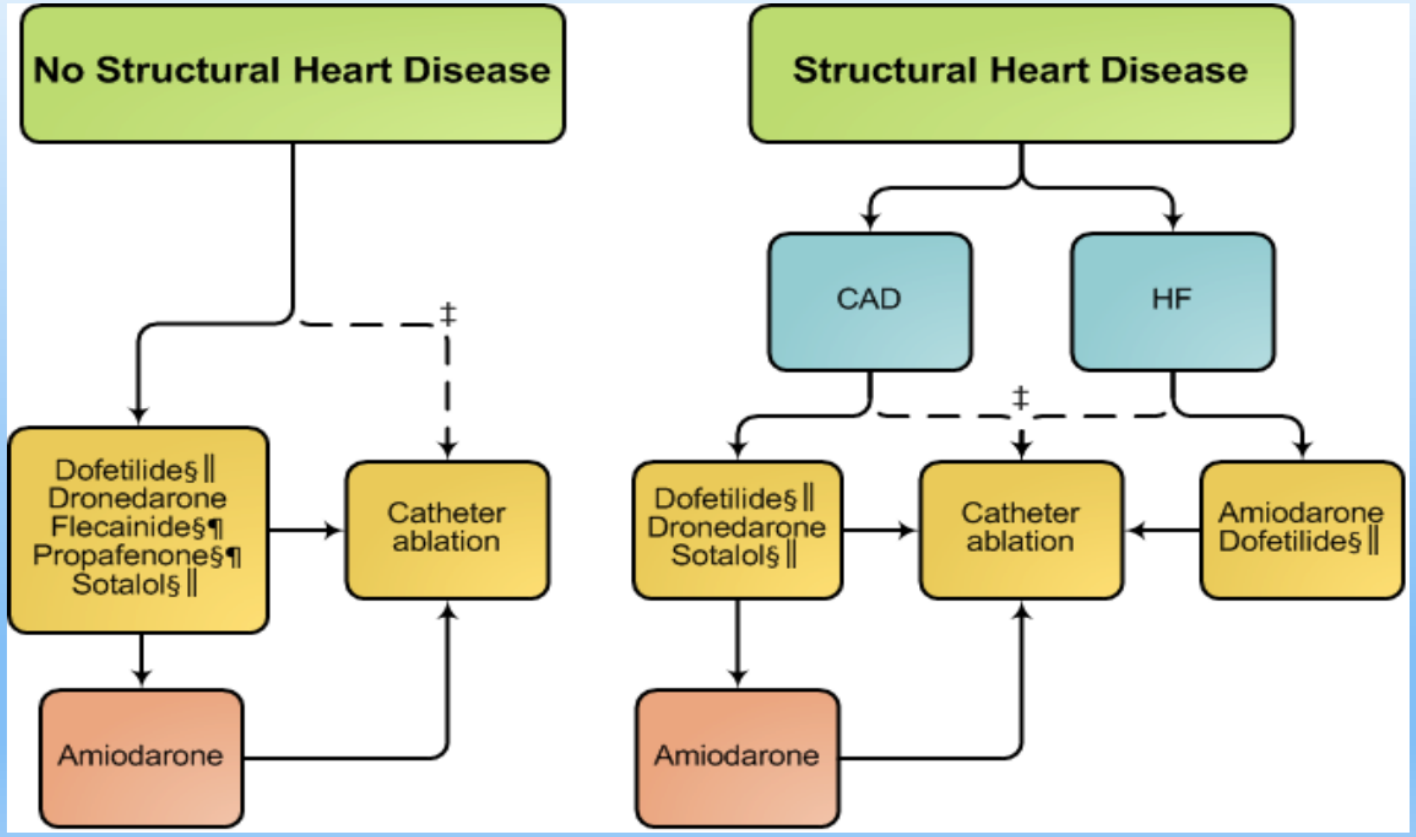
- If β-blockers contraindicated, diltiazem or verapamil to control the rate
- Diltiazem preferred if hypotension or LV dysfunction present
- But, avoid calcium channel blockers if concomitant heart failure
- No class Ic antiarrhythmic drugs (e.g., flecainide) if structural damage or ischemic heart disease
- Digoxin monotherapy in sedentary patients

Therapy

- 2/3 will spontaneously revert if onset <36 hours
- Else, cardioversion following 3 weeks of anticoagulation preparation
- Electric cardioversion more effective than pharmacologic cardioversion

Therapy

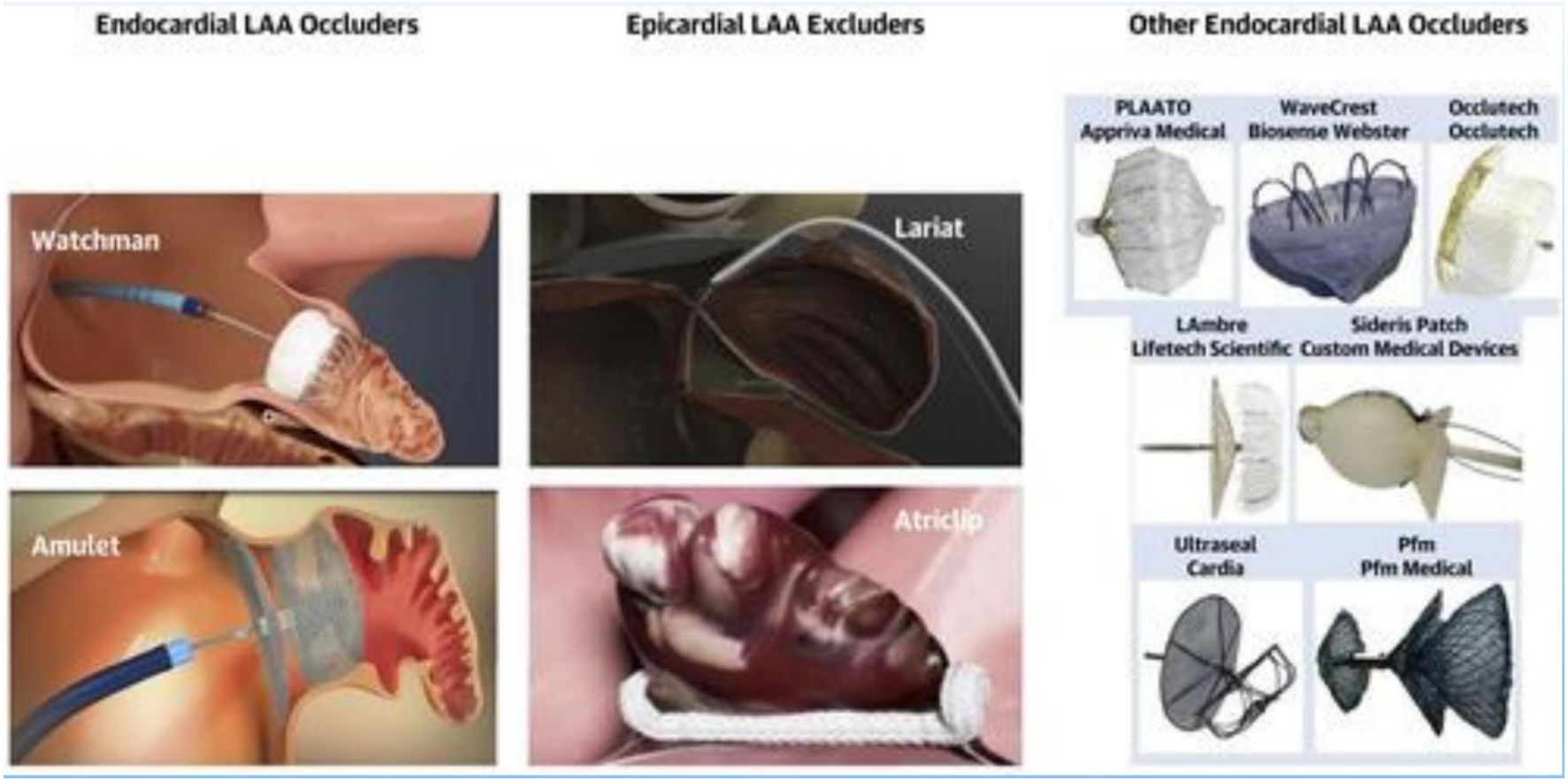
- If shock, pulmonary edema, severe hypertension, or severe ischemia/infarction, cardioversion is indicated.
- Increases risk of embolic disease if no prior anticoagulation
- Better result if cardioversion guided by TEE
- Cardioversion is contraindicated in the presence of hyperkalemia or digoxin toxicity.



J Am Coll Cardiol. 2019 Jan, 74 (1) 104–132

Therapy

- Left atrial ablation if drug therapy unsuccessful, unsuitable, or not tolerated.
- Left atrial catheter ablation before pacing and AV node ablation if symptoms or left ventricular dysfunction thought to be caused by high ventricular rates
- Cryoablation associated with fewer hospitalizations compared to radiofrequency ablation
- Antiarrhythmic therapy for 3 months following ablation


Endocardial LAA Occluders
Epicardial LAA Excluders
Other Endocardial LAA Occluders
Watchman
Lariat
Amulet
Atriclip
PLAATO
Appriva Medical
WaveCrest
Biosense Webster
Occlutech
Occlutech
LAmbre
Lifetech Scientific
Sideris Patch
Custom Medical Devices
Ultraseal
Cardia
Pfm
Pfm Medical

Chadsvasc risk factors [click on present risk factors]

RISK FACTORS	SCORE
Congestive heart failure	1
Hypertension	1
Age ≥ 75	2
Age 65-74	1
Diabetes mellitus	1
Stroke/TIA/thrombo-embolism	2
Vascular disease	1
Sex Female	1
Your score	0

view results

CHADSVASC clinical risk estimation. Adapted from Lip et al. See Van den Ham et al. below for actual risks in a larger population.

CHA_2DS_2VASc SCORE	PATIENTS (n=7329)	ADJUSTED STROKE RATE (% year)
0	1	0%
1	422	1,3%
2	1230	2,2%
3	1730	3,2%
4	1718	4,0%
5	1159	6,7%
6	679	9,8%
7	294	9,6%
8	82	6,7%
9	14	15,2%

HASBLED clinical characteristic [click on present risk factors]

CLINICAL CHARACTERISTIC	POINTS AWARDED
Hypertension	1
Abnormal liver function	1
Abnormal renal function	1
Stroke	1
Bleeding	1
Labile INRs	1
Elderly (Age >65)	1
Drugs	1
Alcohol	1
Your score	0

view results

HASBLED clinical risk estimation. Adapted from Pisters et al.

HAS BLED SCORE	NUMBER OF PATIENTS	NUMBER OF BLEEDING	BLEEDS PER 100 PATIENT YEARS
0	798	9	1,13
1	1286	13	1,02
2	744	14	1,88
3	187	7	3,74
4	46	4	8,70
5	8	1	12,50
6	2	0	0
7	---	---	---
8	---	---	---
9	---	---	---
Total	798	9	1,13

Classificaton of AF-related symptoms (EHRA score)

EHRA I	No symptoms
EHRA II	Mild symptoms; normal daily activity not affected
EHRA III	Severe symptoms; normal daily activity affected
EHRA IV	Disabling symptoms; normal daily activity discontinued

[CHADSVASC, CHA2DS2VASC and HASBLED risk score calculator for atrial fibrillation]

Downloaded 12/14/2021

2020 ESC Guidelines-Who Gets Anticoagulation?

	ACC/AHA 2019	ESC 2020
CHA_2DS_2-VASc = 0	No anticoagulant for 0 (men) or 1 (women)	
CHA_2DS_2-VASc = 1	Consider for 1 (men) or 2 (women)	
CHA_2DS_2-VASc ≥ 2	OAC for ≥2 (men) or ≥3 (women)	
AF < 48 hours with cardioversion	Pre: none Post: 4 weeks if CHA_2DS_2-VASc ≥ 2 (men) ≥3 (women)	Pre: none Post: 4 weeks (C-V 0/1), long-term otherwise
AF > 48 hours with cardioversion	Pre: 3 weeks (or imaging) Post: 4 weeks	Pre: 3 weeks (or imaging) Post: 4 weeks (C-V 0/1), long-term otherwise

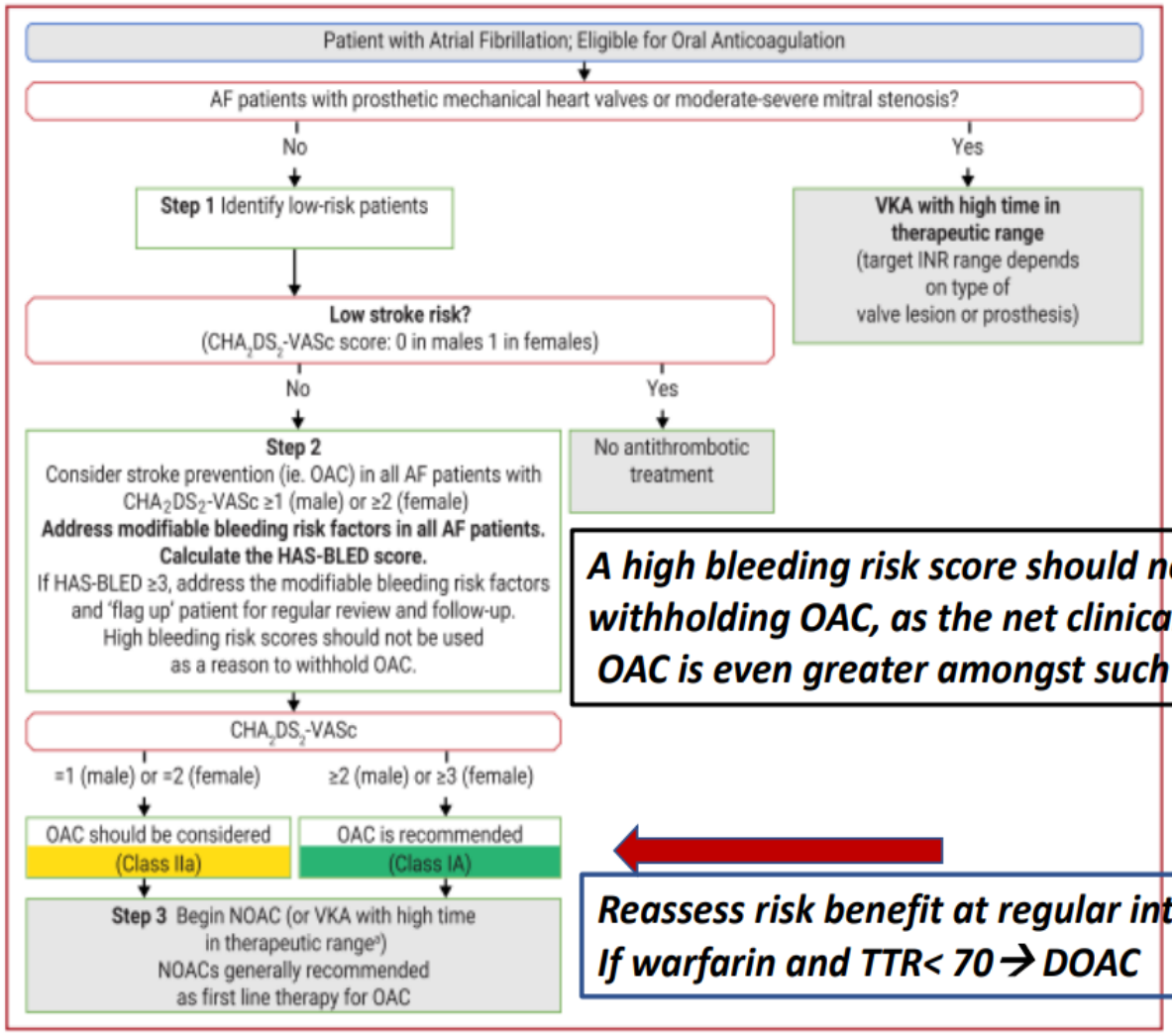
Reassess @ 4-6 months after initial assessment (IIa)

JACC 2019;74:104-132 & EHJ 10.1093/eurheartj/ehaa612

A history of falls is not an independent predictor of bleeding on OAC

EHJ 10.1093/eurheartj/ehaa612

AFIB 3-step patient pathway



A high bleeding risk score should not lead to withholding OAC, as the net clinical benefit of OAC is even greater amongst such patients (IIIB)

Reassess risk benefit at regular intervals (IB)
If warfarin and TTR< 70 → DOAC

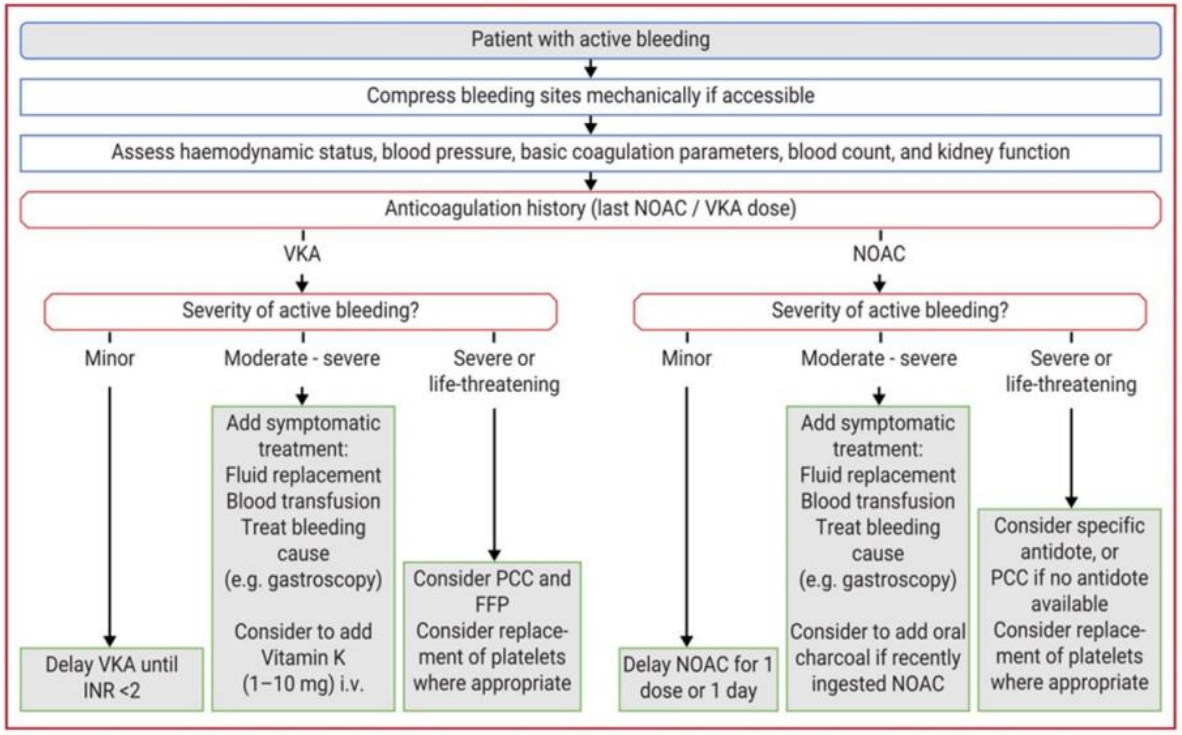
Anticoagulation

- If lone fibrillation (no underlying disease) in those <65 years of age, no anticoagulation may be needed
- Antiplatetelet therapy should not be used for stroke prevention
- Age 65–74 years, female sex, and no significant antecedent history, CHADSVASC score to decide upon anticoagulation
- If heart failure, hypertension, age 75 years or older, diabetes mellitus, and history of stroke or TIA (CHADSVASC score), oral anticoagulation
- No benefit to routine heparin-warfarin bridging

Anticoagulation

- DOACs pose less stroke risk and bleeding risk than use of Vitamin K antagonists
- Warfarin if prosthetic valve or severe renal disease or moderate-severe mitral stenosis
- Apixaban if cardiomyopathy
- Diminished risk of gastrointestinal or intracranial bleeding
- ASA not used with DOACs unless previous cardiac stent
- AV node ablation does not remove need for anticoagulation

Bleeding Management



JACC 2019;74:104-132 & EHJ 10.1093/eurheartj/ehaa612

- Dabigatran → Idarucizumab
- Rivaroxaban or apixaban → andexanet alpha

Mechanical Stroke Prevention?

- Surgical occlusion of LA appendage → consider during cardiac surgery in patients with AF (ACC & ESC)
- Percutaneous LA appendage occlude placement → consider if contraindication to long-term anticoagulation (ACC & ESC)

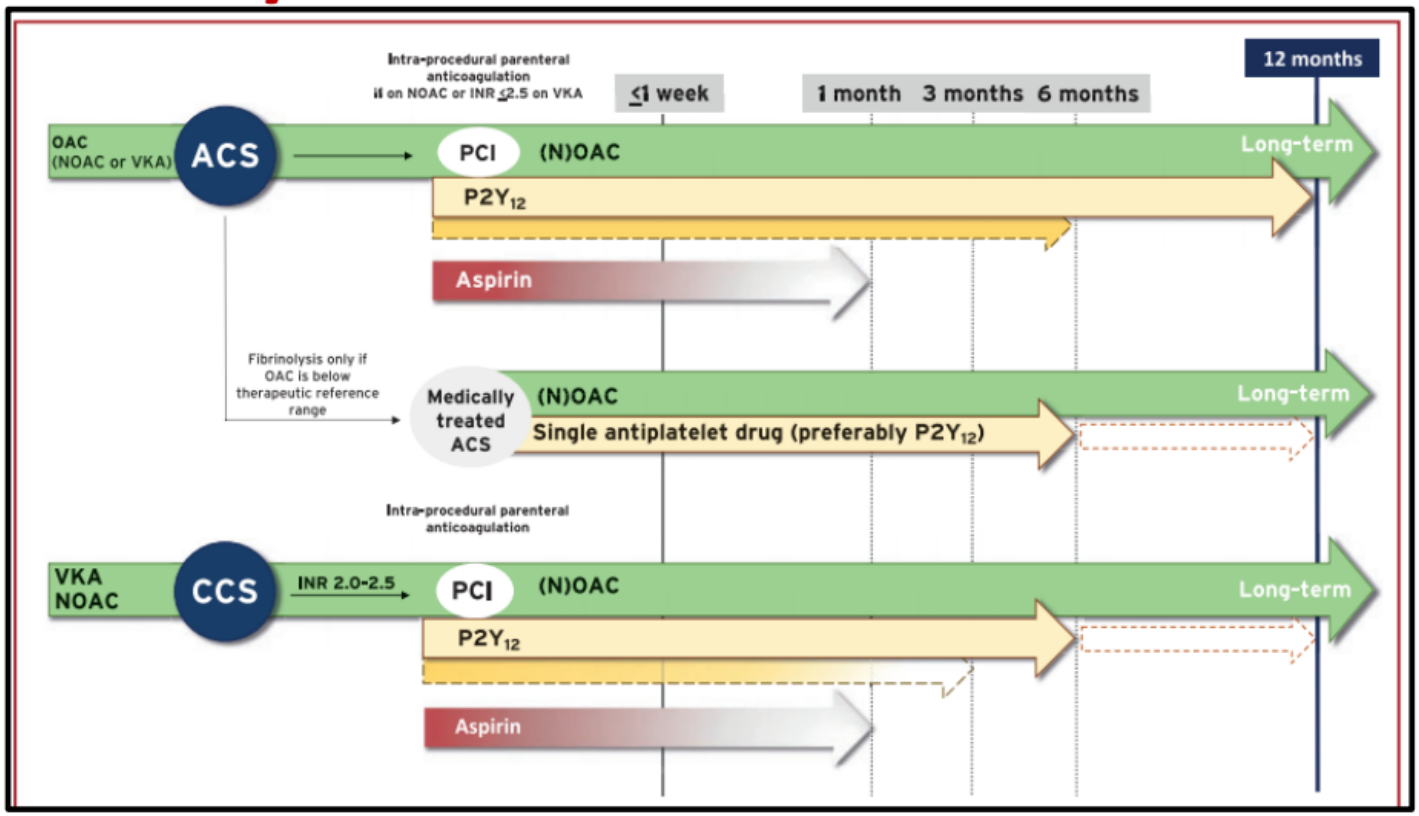
Table 12 **Antithrombotic therapy after left atrial appendage occlusion**

Device/patient	Aspirin	OAC	Clopidogrel	Comments
Watchman/low bleeding risk	75 - 325 mg/day indefinitely	Start warfarin after procedure (target INR 2 - 3) until 45 days or continue until adequate LAA sealing is confirmed[a] by TOE. NOAC is a possible alternative	Start 75 mg/day when OAC stopped, continue until 6 months after the procedure	Some centres do not withhold OAC at the time of procedure (no data to support/deny this approach)
Watchman/high bleeding risk	75 - 325 mg/day indefinitely	None	75 mg/day for 1 - 6 months while ensuring adequate LAA sealing[a]	Clopidogrel often given for shorter time in very high-risk situations
ACP/Amulet	75 - 325 mg/day indefinitely	None	75 mg/day for 1 - 6 months while ensuring adequate LAA sealing[a]	Clopidogrel may replace long-term aspirin if better tolerated

JACC 2019;74:104-132 & EHJ 10.1093/eurheartj/ehaa612

Closing a patent foramen ovale (PFO) reduces incidence of cryptogenic stroke

Post-procedural management of AFIB and ACS/PCI-2020 ESC



EHJ 10.1093/eurheartj/ehaa612

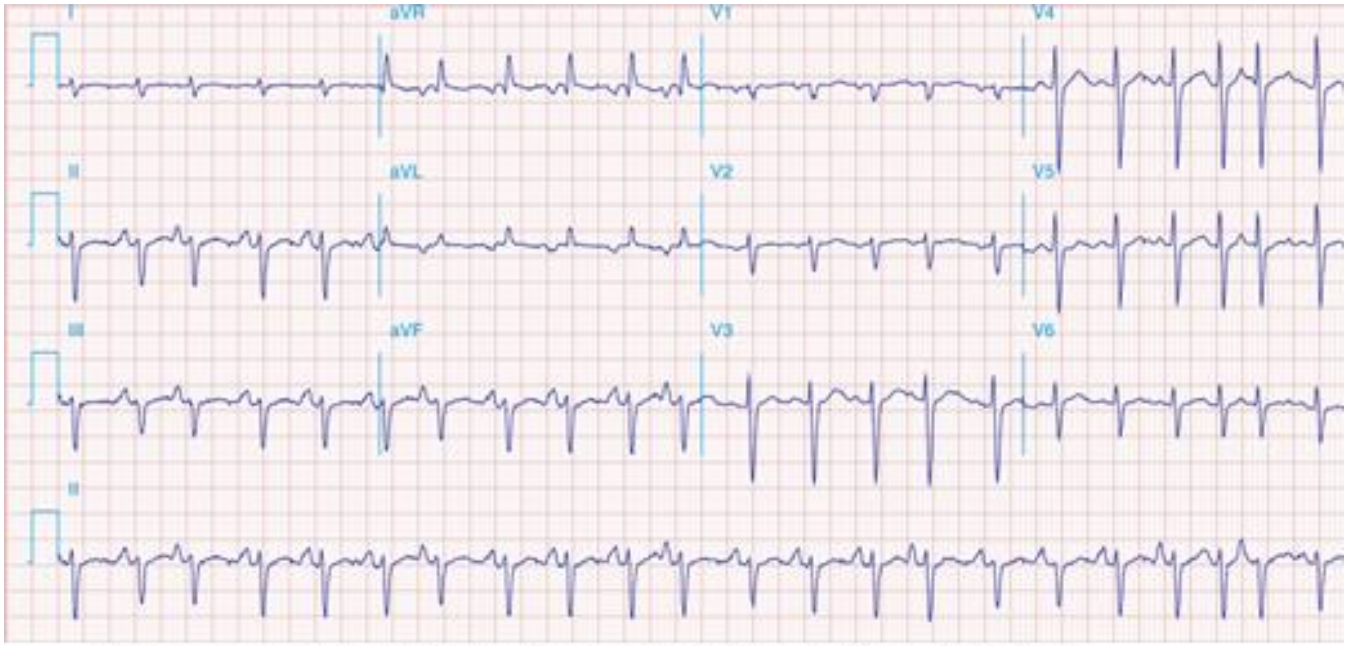
ESC Guidelines: New/Changed Rec

- Re-assess stroke and bleeding risk periodically → anticoagulation still appropriate?
- Estimated bleeding risk (e.g., HAS-BLED) should NOT be a sole deciding factor against anticoagulation
- Clinical pattern of AF (e.g., first detected, paroxysmal) should NOT influence anticoagulation decision
- Anticoagulation for 3 weeks (or imaging) recommended prior to catheter ablation procedure & at least 2 months after ablation
  - Do not interrupt anticoagulation for procedure
  - Continue OAC post ablation based on C-V score, not "success" of procedure
- If treated with VKA and TTR<70%, consider switching to DOAC
- After ICH if ischemic stroke risk high, (re-)initiation of OAC, with preference for NOACs over VKAs in NOAC-eligible patients, should be considered in consultation with a neurologist/ stroke specialist after considering risks/benefits

EHJ 10.1093/eurheartj/ehaa612

Multifocal atrial tachycardia

- Palpitations and edema
- Severe COPD
- Solitary atrial premature beats are benign
- Treat underlying pulmonary disease



Source: Maxine A. Papadakis, Stephen J. McPhee, Michael W. Rabow: Current Medical Diagnosis and Treatment 2021

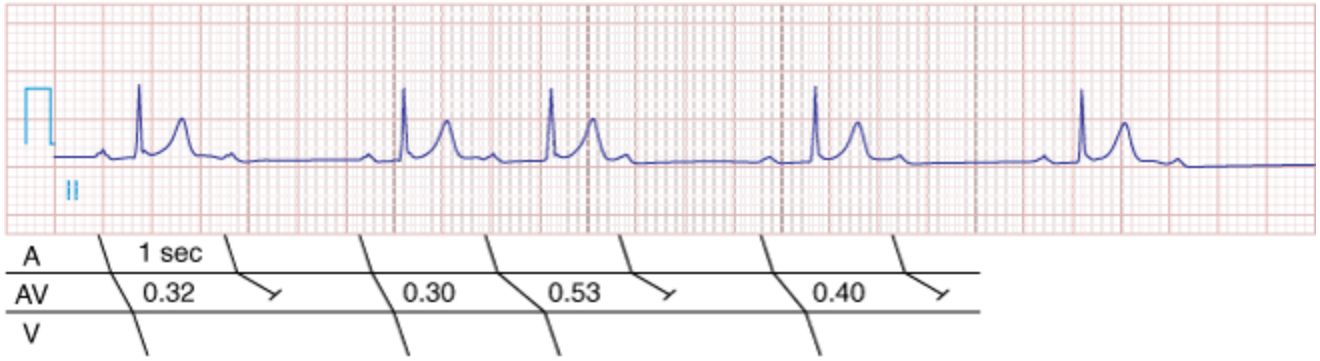
First degree atrio-ventricular block

- PR interval > 0.20s
- A slowing of conduction through the AV junction.
- The site of delay is typically in the AV node
- But may be in the atria, AV node bundle of His, or His-Purkinje system.
- A wide QRS complex favors distal conduction and narrow QRS complex delay in the node proper or, less commonly, in the bundle of His.

Second degree atrio-ventricular block

- There is an intermittent failure of electrical impulse conduction from atrium to ventricle.
- Two subclasses:
- Mobitz type 1 (Wenckebach)
- Progressively lengthening PR interval, shortening of the RR interval, and a pause that is less than two times the immediately preceding RR interval on the ECG.
- The ECG complex after the pause exhibits a shorter PR interval that that immediately preceding the pause

Mobitz type I atrio-ventricular block



Source: Fauci AS, Kasper DL, Braunwald E, Hauser SL, Longo DL, Jameson JL, Loscalzo J: *Harrison's Principles of Internal Medicine*, 17th Edition: http://www.accessmedicine.com

The PR interval prolongs prior to the pause as shown in the ladder diagram. The ECG pattern results from slowing of conduction in the AV node.

Fig. 225-6 Accessed 03/17/2010

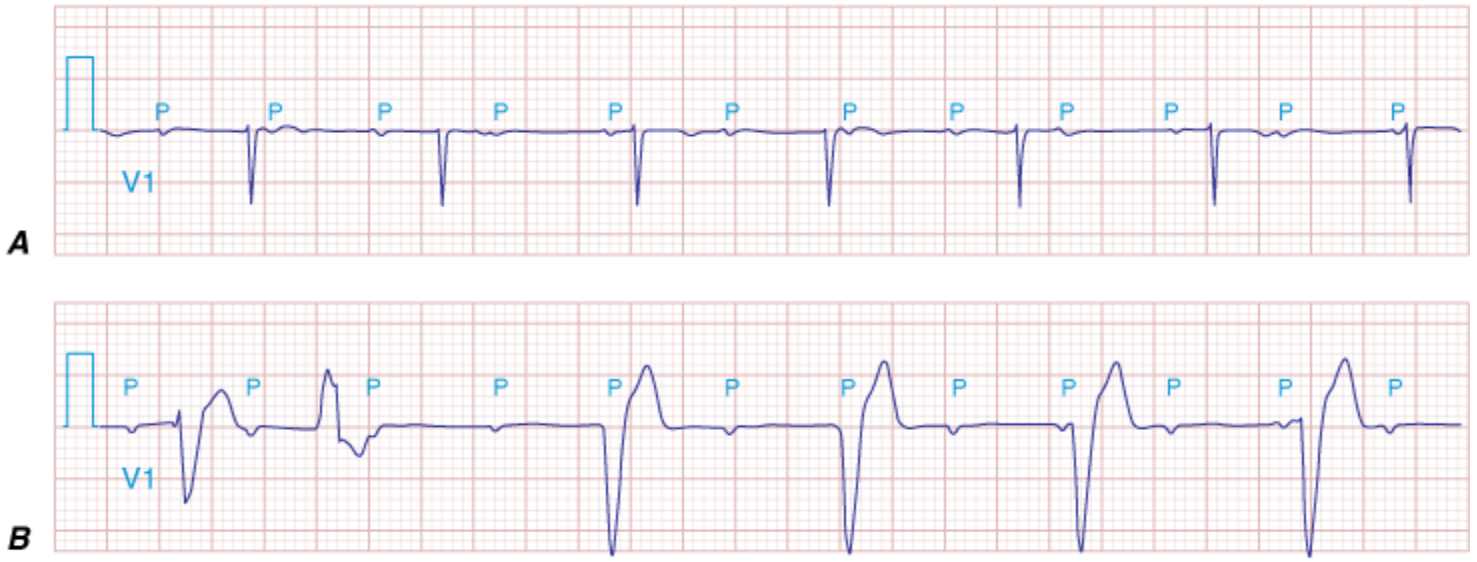
Second degree atrio-ventricular block

- Mobitz type 2
- Characterized by intermittent failure of conduction of the P wave without changes in the preceding PR or RR intervals.
- Typically occurs in the distal or infra-His conduction system
- Is often associated with intraventricular conduction delays (e.g., bundle branch block)
- More likely to proceed to higher grades of AV block than is type 1 second-degree AV block.

Atrio-ventricular block

- Second-degree AV block (particularly type 2) may be associated with a series of non-conducted P waves, referred to as paroxysmal AV block
- When AV block is 2:1 it may be difficult to distinguish type 1 from type 2 block.

High grade atrio-ventricular block



A. Multiple nonconducted P waves with a regular narrow complex QRS escape rhythm likely emanating from the AV junction. B. A wide complex QRS escape and a single PVC. In both cases there is no consistent temporal relationship between the P waves and QRS complexes. Fig. 225-8 Accessed 03/17/2010

Therapy

- Pacemakers are placed for treatment of:
- Symptomatic sinus bradycardia
- Symptomatic congenital complete heart block
- Symptomatic carotid sinus sensitivity
- Acquired complete heart block
- Sinus node dysfunction with life-threatening bradyarrhythmia
- Symptomatic type I heart block.
- Atropine may be used to increase transmission through the atrio-ventricular node pending pacemaker placement.

Rhythm

- A stimulus occurring in the relative refractory (vulnerable) period may trigger an extrasystole.
- Early depolarizing after-potentials occur when the action potential is markedly prolonged (long QTc).
- Following an extrasystole, 8 normal cycles are necessary to stabilize blood pressure.

Rhythm

- Predispositions to extrasystole:
- Bradycardia
- Hypothyroidism
- 1° and 2° AV block
- Hypokalemia
- Hypomagnesemia
- The Na^+ channel blockers quinidine, procainamide, disopyramide
- The Ca^{2+} channel blockers predispose to extra-systole.

Rhythm

- J-point elevation in V_4-V_6 is associated with increased risk of ventricular arrhythmia.
- The J point is the junction of the QRS and ST waves.
- If this occurs in the Purkinje cells, they trigger extra-systoles in the more distal myocardium as the myocardium has a shorter action potential than the Purkinje cell and is already depolarized.
- May see torsade de pointes.

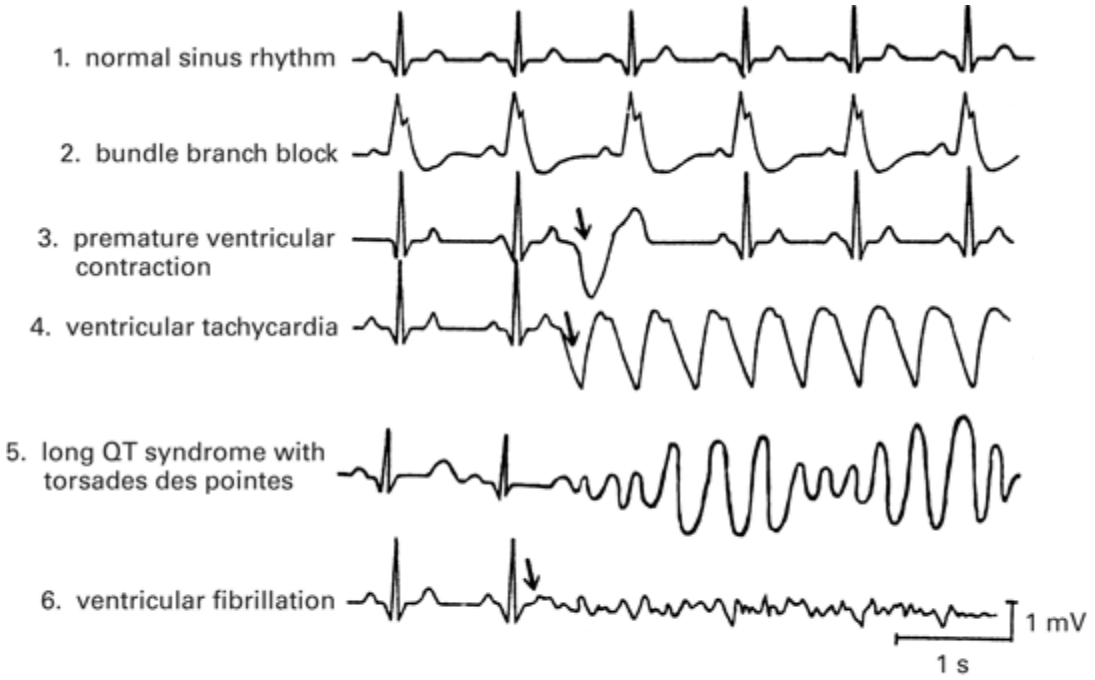
Rhythm

- Late depolarizing after-potentials are usually preceded by hyper-polarization.
- If the amplitude of the post-depolarization reaches threshold potential, a new action potential is triggered.
- This is seen with:
- High heart rates
- Digitalis intoxication
- Increased extracellular Ca^{2+} concentrations.

Rhythm

- Re-entry is the likely result (circular excitation) if there is ventricular hypertrophy (lengthened path)
- If the refractory period has shortened
- If the velocity of the spread of excitation is diminished.

Ventricular arrhythimas

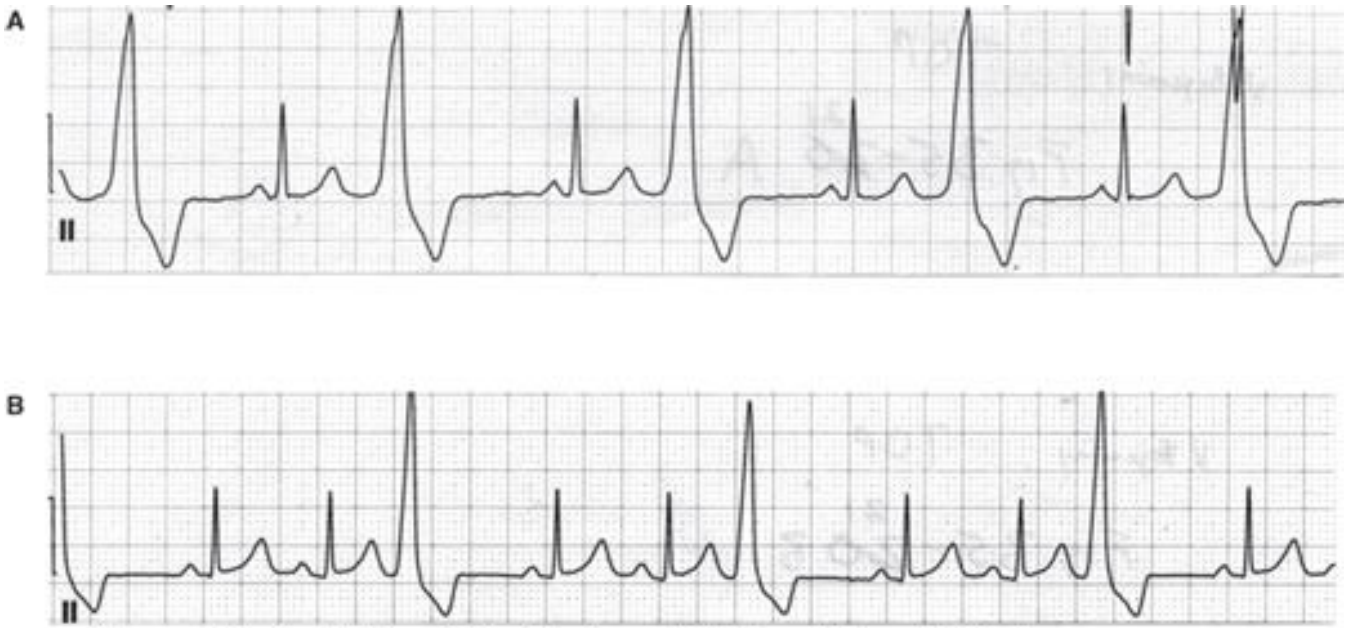


Source: Mohrman DE, Heller LJ: *Cardiovascular Physiology*, 6th Edition: http://www.accessmedicine.com

Fig. 5-3 Accessed 02/01/2010

Ventricular rhythms

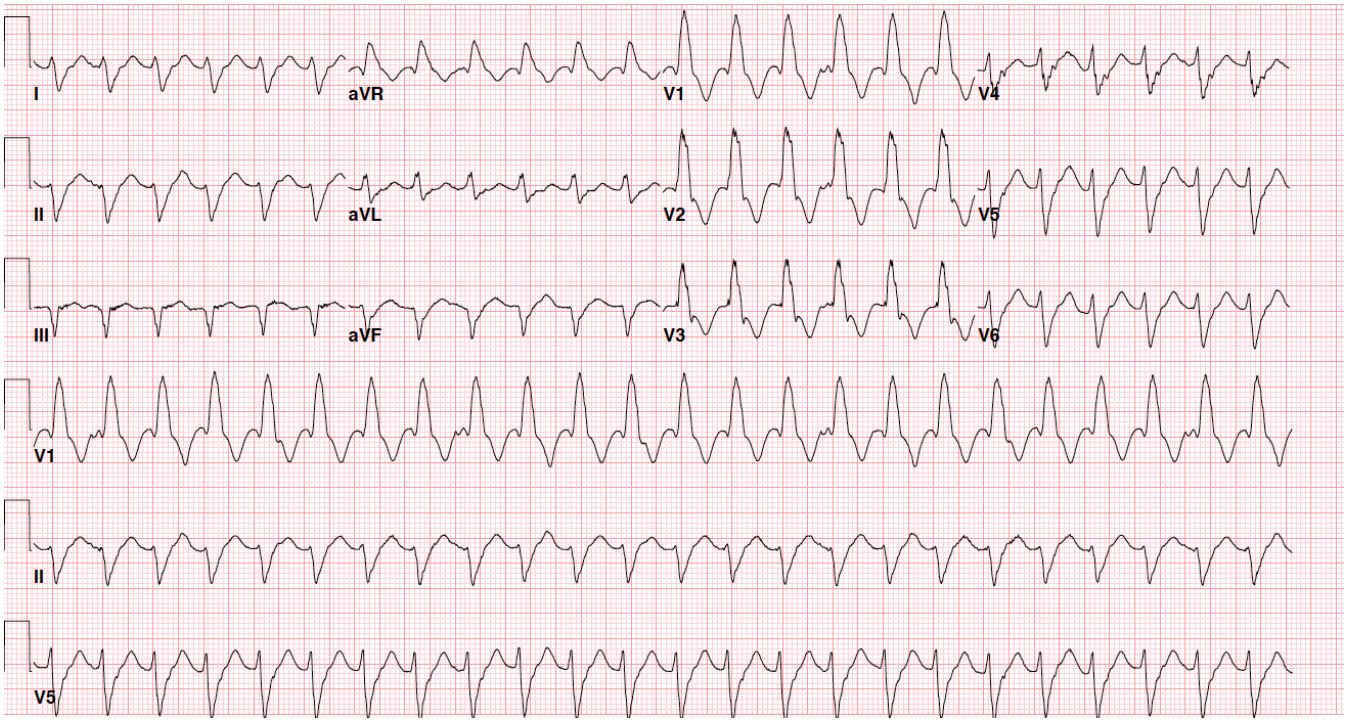
- Isolated premature ventricular complexes are benign
- If >10% on ambulatory EKG, may indicate LV dysfunction
- Bigeminy and trigeminy are arrhythmias in which every second or third beat is premature; these patterns confirm a reentry mechanism for the ectopic beat
- May be asymptomatic
- Beta-blockers or non-dihydropyridine calcium channel blockers as treatment choices



Source: Maxine A. Papadakis, Stephen J. McPhee, Michael W. Rabow: Current Medical Diagnosis and Treatment 2021

Ventricular rhythms

- Ventricular tachycardia is defined as three or more consecutive ventricular premature beats
- If no underlying heart disease, abnormal ventricular rhythm is often triggered by activity from the right or left ventricular outflow tract
- Palpitations, dyspnea, or lightheadedness,
- Hypokalemia or hypomagnesemia
- Nonsustained
- Lasting less than 30 seconds and terminating spontaneously
- Generally benign if not post MI



Source: Maxine A. Papadakis, Stephen J. McPhee, Michael W. Rabow:
Current Medical Diagnosis and Treatment 2021

Ventricular rhythms

- Sustained and rapid
- Frequent complication of MI or dilated cardiomyopathy
- Immediate treatment with a short-acting intravenous beta-blocker or verapamil may terminate the episode
- Idioventricular and <100bpm
- Common in cardiomyopathy or sleep apnea
- Treat underlying disorder

Therapy

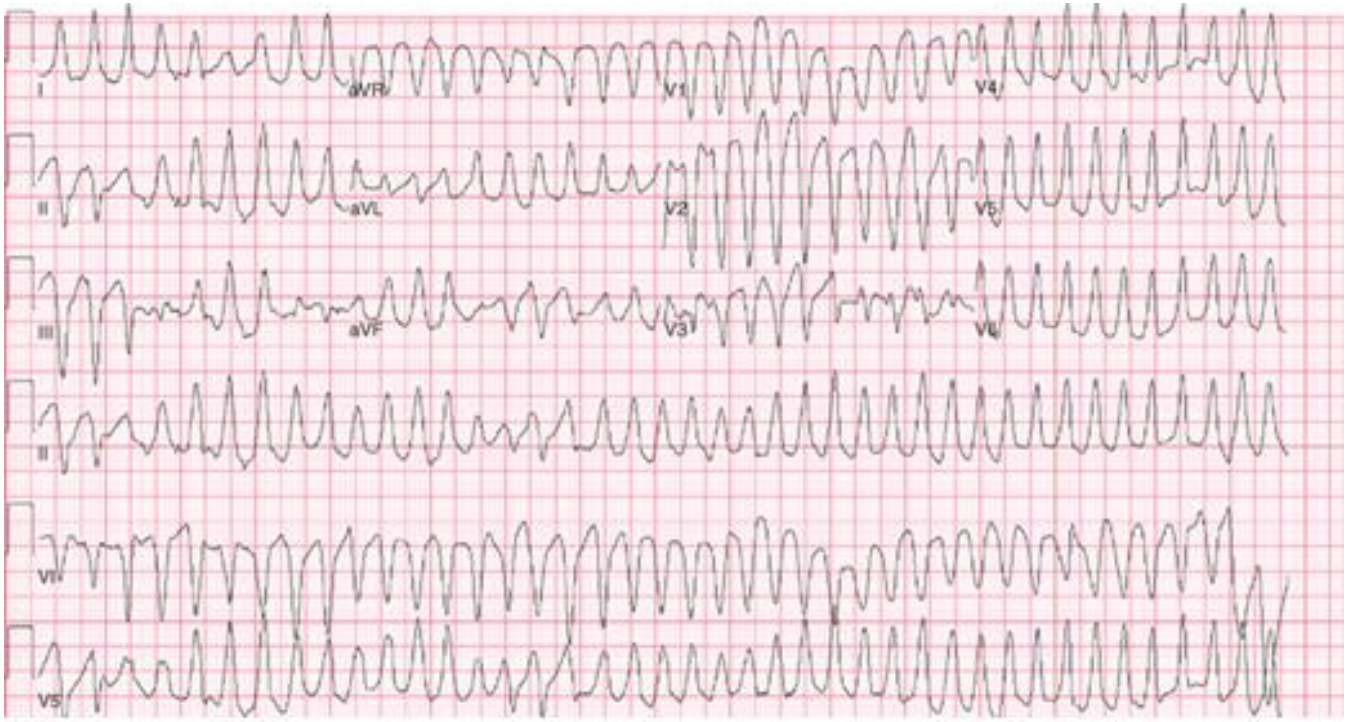
- If hypotension, heart failure, or myocardial ischemia, immediate synchronized direct current cardioversion
- A regular uniform wide-complex ventricular tachycardia is called monomorphic.
- Synchronized cardioversion should be attempted if the patient is unstable.
- An unstable patient with polymorphic ventricular tachycardia should be treated with unsynchronized shocks (as with ventricular fibrillation).

Therapy

- IV amiodarone to maintain rhythm
- IV magnesium as empirical therapy
- Long term management with β-blocker
- Non-hydropyridine calcium channel blocker if β-blocker not well tolerated
- Catheter ablation in those who fail medical therapy
- Implantable cardioverter defibrillator (ICD) if significant LV dysfunction

Ventricular rhythms

- Torsade de pointes
- Polymorphic
- QRS morphology twists around the baseline
- May also be precipitated by medication that prolongs QT interval
- Best treated with IV magnesium



Source: Maxine A. Papadakis, Stephen J. McPhee, Michael W. Rabow: Current Medical Diagnosis and Treatment 2021

Ventricular fibrillation

- 70% of cases of sudden cardiac death are attributable to underlying coronary artery disease
- In up to 40% of patients, sudden cardiac death may be the initial manifestation
- Presumed to be sustained monomorphic ventricular tachycardia, polymorphic ventricular tachycardia, or primary ventricular fibrillation (especially in the setting of acute ischemia)
- Complete heart block and sinus node arrest may also cause sudden death.
- A disproportionate number of sudden deaths occur in the early morning hours.

Heritable disorders

- Long QT syndrome
- Brugada syndrome
- Arrhythmogenic RV cardiomyopathy
- Catecholaminergic polymorphic ventricular tachycardia.
- Genetic testing for patients with suspected congenital long QT syndrome based on family history, ECG or exercise testing, or severely prolonged QT interval (greater than 500 msec) on serial ECGs.

Heritable disorders

- Patients with long QT syndrome or catecholaminergic polymorphic ventricular tachycardia should be treated long term with an oral beta-blocker (nadolol or propranolol).
- ICD is indicated for patients with ventricular arrhythmia or syncope despite medical treatment.

Anti-arrhythmic drugs

Class	Mechanism
IA **quinidine, procainamide, disopyramide**	**Reduce maximal velocity of depolarization phase by blocking inward Na+ current at all heart rates.** **Increase duration of action potential.**
IB **lidocaine, phenytoin**	**Little effect on maximal velocity of depolarization phase by blocking inward Na+ current at low heart rates.** **No change on action potential.**
IC **flecainide, propafenone**	**Reduce maximal velocity of depolarization phase by blocking inward Na+ current at normal rates.** **Minimal effect on action potential.**
II **β-adrenergic blockers**	**Diminish SA automaticity.** **Decrease AV nodal conduction velocity; Increase AV node refractory period.**

Anti-arrhythmic drugs

Class	Mechanism
III **amiodarone, sotalol, ibutilide, bretylium**	**Prolong action potential duration in tissues with fast-response (Na+) action potentials usually by blocking K+ channel action**
IV **verapamil, dilitazem**	**Decrease conduction velocity and increase refractory periods in tissues with slow Ca^{2+} channels (non-selective L type).**
Adenosine	**Activates acetylcholine sensitive K+ current in the SA and AV nodes, shortens the action potential by blocking intracellular cAMP, leading to hyperpolarization and slowing of normal automaticity.**
Glycosides	**Increase automaticity, particularly in hypokalemia. Increase intracellular Ca^{2+}. Prominent vagotonic actions inhibit Ca^{2+} currents in the AV node and activates acetylcholine sensitive K+ current in the atrium**

Sodium channel blockers

- Class Ia
- Quinidine is indicated for supraventricular and ventricular arrhythmias.
- As quinidine prolongs the QT, it should not be used for treatment of atrial flutter.
- Quinidine may cause hearing and vision problems, delerium, and hemolytic anemia.

Sodium channel blockers

- Class Ia
- Procainamide and disopyramide are indicated for ventricular arrhythmias.
- Procainamide can induce a lupus syndrome as well as cause psychosis.
- Disopyramide is an anticholinergic with negative inotropic effects and should not be used in patients with left ventricular dysfunction.

Sodium channel blockers

- Class Ib
- Lidocaine and mexiletine (lidocaine congener) are not effective for supraventricular arrhythmia.
- Class Ic
- In structurally normal hearts, flecainide and propafenone are useful in treatment of supraventricular and ventricular arrhythmias.
- Flecainide can cause ataxia and blurred vision.
- Propafenone may leave a metallic taste.

β-blockers

- Class II
- Beta blockers are indicated for the prevention of supraventricular arrhythmias
- For the prevention of sudden death due to ventricular ectopic depolarization in acute myocardial infarction.
- Contraindicated in patients with severe asthma, COPD, or heart block.
- Bradycardia is a side effect.

Potassium channel blockers

- Class III
- Amiodarone can be used for long-term suppression of both supraventricular and ventricular tachycardias.
- It is the drug of choice in patients with atrial fibrillation who are in heart failure.
- It is good for arrhythmia prevention following myocardial infarction.
- May be thyrotoxic (acts through common steroid receptor). Effects are transient.
- α and β blocker.
- Pulmonary fibrosis a long-term complication.

Potassium channel blockers

- Class III
- Sotalol can be used for atrial fibrillation and ventricular arrhythmias, but it can cause torsade de pointes.
- Ibutilide is used for chemical cardioversion in atrial flutter or fibrillation, but can cause torsade de pointes.
- Bretylium is indicated in ventricular fibrillation.
- Hypertension, tachycardia, and worsening of arrhythmias make it a last-line agent.

Other anti-arrhythmic drugs

- Class IV
- Calcium channel blockers are useful for supraventricular tachycardia but can exacerbate ventricular tachycardias.
- May lead to hypotension.

- Adenosine is useful for treatment of supraventricular tachycardias and re-entrant atrio-ventricular tachycardias, including Wolff-Parkinson-White syndrome.
- QT prolongation may be problematic with all anti-arrhythmics.