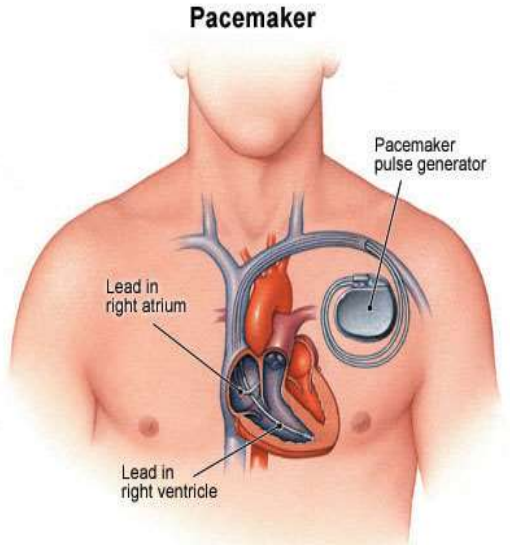
Dept.of Clinical Pharmacy
Therapeutics (I)/ 5th level

Arrhythmias (II): Treatment

1-Nonpharmacologic therapy of bradyarrhythmias: cardiac pacemakers

Artificial cardiac pacemakers are devices that deliver **a small electrical impulse** to a localized region of the heart, thus initiating an action potential that then spreads to the remainder of the heart. These devices can be used ***temporarily*** to treat a transient bradyarrhythmia resulting from **a reversible** cause or can be implanted ***permanently*** to treat **irreversible** disorders of impulse formation or conduction that result in recurrent or persistent bradyarrhythmias[(1)].



Permanentpacemaker systems are implanted in a skin "pocket" below the collar bone. Leads are inserted via a vein into the heart [(2)].

2-Nonpharmacologic therapy of tachyarrhythmias

A-Direct current cardioversion and defibrillation

Cardioversion refers to the process of restoring the heart's normal rhythm. This can be done chemically using drugs (**chemical or pharmacological cardioversion**) or by application of an electric shock across the chest (**electrical cardioversion**). This involves the delivery of a low voltage shock to the heart through the chest wall (eg, using paddles). The aim is to **disrupt the abnormal electrical conduction pathways** in order to convert an arrhythmia to sinus rhythm [(2, 3)].

B-Radiofrequency Catheter Ablation and Implantable Cardioverter-Defibrillators

1-Radiofrequency (RF) ablation is a procedure whereby a catheter with an electrode at its tip is guided to the effected site on the myocardium. **RF energy is then transmitted locally to destroy the affected tissue and remove the conduction pathway**. The procedure has a high success rate and patients can return to normal activities in a few days [(3)].

2-The **implantable cardioverter-defibrillator (ICD)** is the antitachycardic equivalent of a pacemaker and is used for the treatment of ventricular tachyarrhythmias. Like the pacemaker, the ICD has a generator that is implanted in a skin "pocket" and is connected via vein into the heart. The device monitors heart rate[(2)] and can detect and terminate life-threatening ventricular tachyarrhythmias[(9)].

Pharmacologictherapy

Classification of antiarrhythmic drugs

A-VaughnWilliams classification

Table 2 Vaughn Williams Classification System
Ia: Quinidine, procainamide, disopyramide
Ib: Lidocaine, mexiletine, tocainide
Ic: Flecainide, propafenone, moricizine
II: Beta-blockers
III: Amiodarone, bretylium, sotalol, ibutilide, dofetilide
IV: Verapamil, diltiazem

The most frequently used classification system is the Vaughn Williams classification, which categorizes these drugs on the basis of their in vitro electrophysiologic effect on normal Purkinje fibers.
There are four antiarrhythmic drug classes. Class I drugs, ***Na^{+}-channel blockers***, Class II drugs are ***β-adrenergic blocker***s, class III drugs are ***K^{+}-channel blockers,*** and class IV drugs are ***Ca^{++}-channel blockers***[4, 5].

B-Classification according to site of action

A more simple classification system used in clinical practice is to consider the principal ***site or sites of action*** of anti-arrhythmic drugs [2]

Panel 2: Classification of drug according to principal site of action

Site of action	Anti-arrhythmic drug	Action
AV node	Verapamil, dilatiazem, adenosine, digoxin, beta-blockers	Delay AV nodal conduction Useful for control of supra-ventricular tachycardias
Ventricles	Lignocaine, mexelitine, phenyoin	Control of ventricular arrhythmias
Atria, ventricles and accessory pathways	Quinidine, disopyramide, amiodarone, flecainide, procainamide, propafenone	Effective in both supra-ventricular tachycardias and ventricular arrhythmias

Bradycardia

1-In patients with sinus bradycardia due to underlying correctable disorders (such as electrolyte abnormalities or hypothyroidism), management consists of correcting those disorders[6].

2-Treatment of sinus bradycardia is only necessary in patients who become symptomatic. If the patient is taking any medication(s) that may cause sinus bradycardia, ***the drug(s) should be discontinued*** whenever possible[6]. In certain circumstances, however, discontinuation of the medication(s) may be undesirable .In these patients, a **permanent pacemaker** may be implanted in order to allow the patient to maintain therapy with β-blockers[6].
3-Acute treatment of the symptomatic patient consists primarily of administration of the anticholinergic drug ***atropine***, which may be given in doses of 0.5 mg intravenously (IV) every 3 to 5 minutes. The maximum recommended total dose of atropine is 3 mg[6].

4-In patients with hemodynamically unstable or severely symptomatic sinus bradycardia that is unresponsive to atropine and in whom temporary pacing is not available or is ineffective, **epinephrineor dopamine infusion** may be administered to increase heart rate[6].

5-Long-term management of patients with sick sinus syndrome requires implantation of a permanent pacemaker [6].

AV-Block

1-Treatment of **first-degree AV nodalblockade** is rarely necessary, because symptoms rarely occur.

2-Second or third-degree AV nodal blockade requires treatment, because bradycardia usually results in symptoms[6].

A- In patients with second- or third-degree AV block due to **underlying correctable disorders** (such as electrolyte abnormalities or hypothyroidism), management consists of correcting those disorders [6].

B-If the patient is taking any medication(s) that may cause AV nodal blockade, the **drug(s) should be discontinued** whenever possible.
However, in certain circumstances, discontinuation of a medication may be undesirable. In these patients, a permanent pacemaker may be implanted in order to allow the patient to maintain therapy with β-blockers[6].

C-Acute treatment of patients with second- or third-degree AV nodal blockade consists primarily of administration of **atropine**(as above)[6].
In patients with hemodynamically unstable or severely symptomatic AV nodal blockade that is unresponsive to atropine and in whom temporary pacing is not available or is ineffective, **epinephrineor dopamine infusion** may be administered[6].

D-Long-term management of patients with AV nodal blockade due to idiopathic degeneration of the AV node requiresimplantation of a **permanent pacemaker**[6].

Tachycardias

A-Sinus tachycardia

1-In most cases, Sinus tachycardia (ST) can be addressed by treating the underlying cause, for example, using antibiotics to treat infections, fluid replacement to correct hypotension and hypovolaemia and beta-blockers and antithyroid agents to manage thyrotoxicosis[3].

2-Management of inappropriate ST relies on the use of rate-controlling agents such as **beta-blockers** or **calcium channel blockers**. In some cases, RF ablation may be necessary to modify the **sinus node** activity[3].

B-Atrial ectopic beats (extrasystoles, premature beats)

1-They are frequently asymptomatic and require no specific therapy other than treatment of the underlying disease or avoidance of precipitants[1].

2-Symptomatic cases usually produce palpitations or the sensation of skipped beats and can usually be controlled with ***β-blockers***[1].

C- Atrial fibrillation (AF):

Hemodynamically Unstable AF

1-For patients who present with an episode of AF that is hemodynamicallyunstable (patients with shock or severe hypotension,pulmonary edema, or ongoing myocardial infarction orischemia), emergent conversion to sinus rhythm isnecessary using **direct current cardioversion**(DCC)[6, 10].

2-There is a potential risk of thromboembolism inpatients undergoing cardioversion who have not receivedanticoagulation therapy if atrial fibrillation has been present**for > 48** hours; however, in hemodynamically unstablepatients the need for immediate rate control outweighsthat risk[10].

Hemodynamically stable AF patient

Rate Control Versus Rhythm Control

A-Ventricular Rate Control is achieved by inhibiting the proportion of electrical impulses conducted from the atria tothe ventricles through the AV node. Therefore, drugs thatare effective for ventricular rate control are those thatinhibit AV nodal impulse conduction: β-blockers, diltiazem,verapamil, and digoxin[6].

B-Rhythm Control(Restoration of sinus rhythm)can be achieved with DCC or with antiarrhythmic agents (pharmacological cardioversion) (typeIc, and III agents are effective)[7, 8]. DCC is generally more effective than drug therapy for conversion to sinus rhythm [6].

C-The treatment strategy for most patients should be a rate control strategy. However, rhythm control is necessary when patients experience symptoms despite adequate rate control, or if patients cannot tolerate the adverse effects of rate-controlling medications [4].

Conversion To Normal Sinus Rhythm

1-The cardioversion decision strategydepends greatly on the duration of AF. If the AF is **less than 48 hours** in duration, then the likelihood of atrial clot formation is low and conversion to sinus rhythm is safe and maybe attempted with elective DCC or specific drug therapy[4, 6].

2-However, if the duration of the AF episode is longer than 48 hours or if there is uncertainty regarding the duration of the episode, two strategies for conversion may be considered[6]**:**

A-Anticoagulate patientswith warfarin, maintaining a therapeutic International Normalized Ratio (INR) for 3 weeks, after which cardioversionmay be performed[6].

B-Alternatively, a trans esophageal echocardiogram (TEE) can be used todetermine whether atrial clots have formed. If no clot is observed on TEE, then there is low risk for strokewith cardioversion of AF. However, if an atrial clot is evidenton TEE, the patient need to be adequately anticoagulated for3 weeks before cardioversion to prevent embolization of the clotand stroke[4].

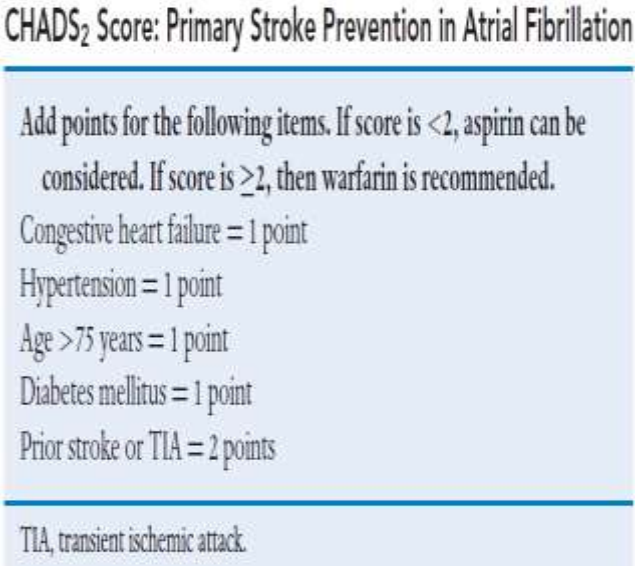
3-If cardioversion is successful, patients should remainon warfarin for at least 4 weeks after cardioversion because normalatrial contraction may not return for up to 3 weeks, andpatientsmay be at risk of late embolization[4].

Stroke Prevention

1-Patients with AF have an increased risk for stroke compared with patients without AF[4].

2-Selection of an antithrombotic regimen for thepatient with AF must be based on assessment of stroke risk which is performedwith the use of the $CHADS_2$ scoring system[4].

3-$CHADS_2$is an acronymderived from stroke risk factors:**[C**ongestive heart failure, **H**ypertension,**A**ge >75 y, **D**iabetes, and prior **S**troke ortransient ischemic attack][7].



A CHADS2 scoreis calculated by assigning **1** point each for the presence ofcongestive heart failure, hypertension, age older than 75 years,or diabetes and **2**points for a history of stroke[4].

A-Generally, patients with a $CHADS_2$ score of 2 or greater should receive oralanticoagulation for stroke prophylaxis[4].

B-If $CHADS_2$ score is 1, oral anticoagulation or aspirin should be used, taking into account risk, benefit, and patient preferences[10].

Note: In addition to vitamin K antagonists such as warfarin,**three** additional **oral** anticoagulants have been shown to beat least as effective as warfarin for stroke prevention: **dabigatran**,**rivaroxaban**, and **apixaban**[10].

C-Those at low risk forstroke ($CHADS_2$ score of 0)should be treated with aspirin 81–325 mg daily orno antithrombotic therapy, with the choice of no antithromboticherapy preferred[10].

Premature ventricular complexes

In apparently healthy individuals, drug therapy is unnecessary because PVCs without associated heart disease carry little or no risk. In patients with **risk factors for arrhythmic death** (recent MI, LV dysfunction), chronic drug therapy should be restricted to ***β-blockers*** because only they have been proven to prevent mortality in these patients [8].

Ventricular tachycardia

A-Acute Ventricular Tachycardia

1-Hemodynamically unstable VT should beterminated immediately using direct current cardioversion (DCC)[6].
2-A decision algorithm for management of hemodynamicallystable VT is presented in Fig. 2.

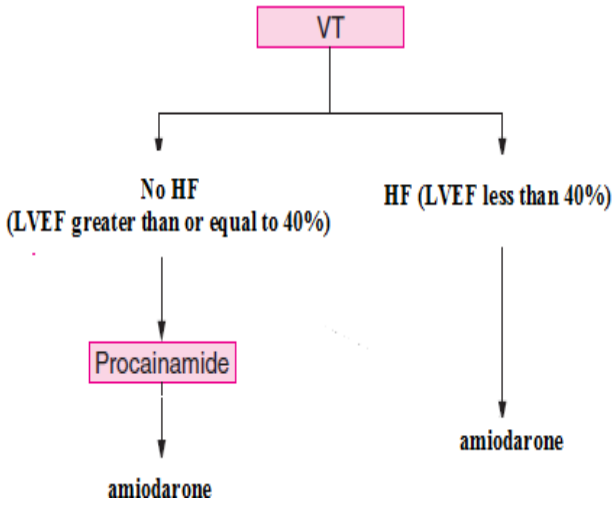


Fig. 2.

Procainamide isconsidered the first-line agent formanagement of VT in patients with normal left ventricular function, whileamiodarone may be used for refractory cases[6].

3-However, in patients with HFdue to LV dysfunction, procainamide should be avoided, due tonegative inotropic activity[6].

B-Sustained Ventricular Tachycardia

Patients with chronic recurrent sustained VT are at extremely high risk for death. The ***ICD*** is a highly effective method for preventing sudden death due to recurrent VT or VF [8].

Torsade de Pointes

1-Management of drug-induced torsade de pointes includes discontinuation of the potentially causative agent.

2-Patients with hemodynamically unstable torsades de pointes should undergo immediate DCC [6].

3-Hemodynamically stable torsade depointes is often treated with I.V magnesium, irrespectiveof whether the patient is hypomagnesemic; magnesiumhas been shown to terminate torsade de pointes in normomagnesemicpatients[6].

Ventricular fibrillation [6]

1-Ventricular fibrillation is by definition **hemodynamically unstable**, due to the absence of pulse and blood pressure.

2-Initial management includes provision of basic life support,including calling for help and initiation of cardiopulmonaryresuscitation (CPR).

3-Oxygen should be administered as soon as it is available.

4-The only means of successfully terminatingVF and restoring sinus rhythm is electrical defibrillation (DCC).

5-If VF persists following one or two defibrillation shocks,drug therapy may be administered. *The purpose of drugadministration for treatment of VF is to facilitate successful defibrillation.Drug therapy alone will not result in termination of VF.**A** defibrillation attempt should be made after every dose of drug*.

6-The **vasopressor agents** epinephrine or vasopressin areadministered initially, because it has been shown that a criticalfactor in successful defibrillation is maintenance of coronaryperfusion pressure, which is achieved via the vasoconstrictingeffects of these drugs.

7-A decision algorithm for the treatment of VF is presented in Fig.3. Drugs that are used for facilitation of defibrillation in patients with VF are listed in Table 4.
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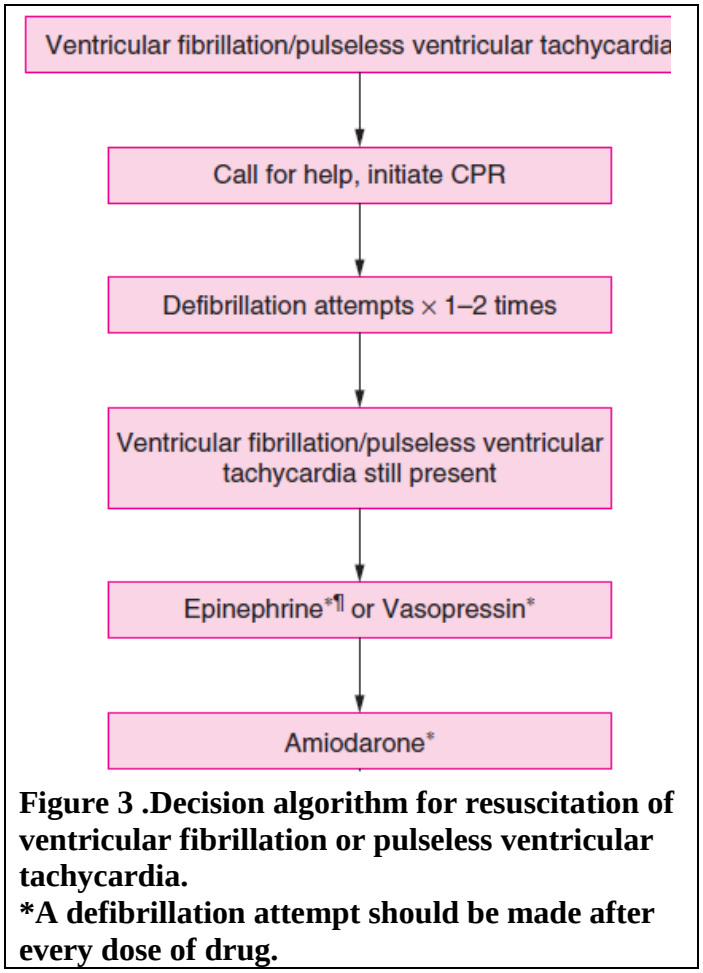

Figure 3 .Decision algorithm for resuscitation of ventricular fibrillation or pulseless ventricular tachycardia.
***A defibrillation attempt should be made after every dose of drug.**

References

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