Atrial Fibrillation: It’s Not so Simple Anymore

Karen Marzlin DNP, RN, CCNS, CCRN-CMC, CHFN

PESI Health Care Cardiac Essentials Conference

2014 Key Choice / CNEA
Just a Thought

Link your roots deeply into whatever task you are doing, for commitment and enthusiasm transform monotony into freshness and routine into joy and discovery.
Organized Atrial Tachycardias

- Focal ectopic atrial tachycardia

- Typical “isthmus - dependent” flutter
  - Isthmus: Tricuspid valve annulus and inferior vena cava
  - Typical: Clockwise flutter
  - Counterclockwise flutter

- Macroreentry “non-isthmus dependent” flutter
- Prior atrial surgery or scarring
- Lateral wall RA
- Left atrial flutter
Paroxysmal Atrial Tachycardia (PAT) with Block
Multi Focal Paroxysmal Atrial Tachycardia
Atrial Flutter 2:1 Conduction
Atrial Fibrillation

- Rapid, irregular fib waves
- Atrial rate > 350
- Fib wave seen best in V1

Irregularly irregular ventricular rate

- QRS usually normal
- If QRS is wide and rate > 200 then consider WPW with conduction over accessory pathway
ECG Recognition of AF

♥ Lack of coordinated atrial activity (no consistent P waves)
♥ Irregular, chaotic atrial “f” waves
♥ Irregularly irregular ventricular response
Atrial fibrillation can be Coarse or Fine
Fast or Slow
Conduct Aberrantly
Not conduct at all
Occurs intermittently
The Scope

❤️ The most frequently occurring arrhythmia
❤️ 2.2 million adults in the US have AF

- 0.4% - 1% of the general population
- 70% of cases occur in people 65-85 years old
  - < 0.1% in people < 55 years old
  - 9% - 10% in people > 80 years old
- More common in men than women
- More common in Caucasians

Many people have it, it’s a chronic problem, and what do you do about it?
Classifications

♥ Recurrent
  • Two or more episodes of AF

♥ Paroxysmal
  • Terminates spontaneously

♥ Persistent
  • When sustained beyond 7 days

♥ Permanent
  • Accepted as permanent or when it lasts longer than one year.

♥ “Lone AF”
  • Young adults without clinical or echocardiographic evidence of cardiopulmonary disease
Mechanisms of AF
Requires a “trigger” and an anatomic substrate capable of initiating and maintaining AF

♥ Enhanced automaticity
  • Rapid firing of foci in or near the pulmonary veins in LA (most common site)
  • Other common sites: in posterior wall of LA, RA, SVC, coronary sinus

♥ Reentrant circuits
  • One or more reentry circuits within the atria with “wavelets” that spread in multiple directions
♥ Paroxysmal AF
• Pathological triggers repeatedly initiate AF
• Triggers often related to autonomic nervous system
• Patients often younger and without structural heart disease
• About 25% of patients with paroxysmal AF progress to permanent AF within 5 years

♥ Persistent & Permanent AF
• Involve abnormal atrial substrate that perpetuates AF
• Atrial enlargement with fibrosis
• Multiple reentry circuits
• Abnormal triggers located in extra-atrial sites (i.e. pulmonary veins)
Trigger Sites

Posterior view of atria

- Left superior pulmonary vein
- Left inferior pulmonary vein
- Right superior pulmonary vein
- Right inferior pulmonary vein
- Coronary Sinus
- SVC
- IVC
Reentry Circuits

Left superior pulmonary vein
Left inferior pulmonary vein
Coronary Sinus
SVC
IVC
Right superior pulmonary vein
Right inferior pulmonary vein
Pathophysiology

♥ Atrial fibrosis and loss of atrial muscle mass.
♥ Triggers of fibrosis include
  • Inflammation
  • Autoimmune disorders
  • Atrial dilation
♥ AF itself causes alterations in atrial architecture and function contributing to atrial remodeling
  • Dilation causing loss of contractility
♥ “Atrial fib begets atrial fib”
  • Atrial electrical remodeling
  • Progressive shortening of effective refractory periods
Pathophysiology

♥ Inflammation
  • C-reactive protein levels higher in persistent AF patients

♥ Autonomic nervous system
  • Stimulation of parasympathetic system shortens atrial and PV refractory periods

♥ Atrial ischemia

♥ Atrial dilation from volume overload

♥ Structural changes associated with aging
Causes

♥ Reversible
- Acute, temporary causes
- Alcohol intake
- Surgery (common in cardiac surgery)
- Electrocution
- AMI
- Pericarditis
- Myocarditis
- Pulmonary embolism
- Other pulmonary diseases
- Obstructive sleep apnea
- Hyperthyroidism
- A flutter
- WPW
- AVNRT

♥ Obesity
- LA size increases as BMI increases

♥ Without associated Heart Disease
- “Lone AF”
- Familial arrhythmia
Causes: Associated Heart Disease

♥ Valvular heart disease
  • Most often mitral valve
♥ HF
♥ CAD
♥ HTN
  • Especially if LVH present

♥ Hypertrophic cardiomyopathy
♥ Dilated cardiomyopathy
♥ Restrictive cardiomyopathy
♥ Constrictive pericarditis
♥ Cardiac tumors
♥ Congenital diseases
  • Atrial septal defects
Hemodynamic Consequences

♥ Loss of synchronous atrial mechanical activity
  • Loss of atrial contraction
  • Compounded in cases of mitral stenosis, HTN, HCM, restrictive cardiomyopathy

♥ Irregular ventricular response
  • Cardiac output falls

♥ Rapid heart rate

♥ Impaired coronary arterial blood flow
  • Diastolic duration inconsistent and unreliable
  • Increased coronary vascular resistance
Stroke: The Most Devastating Complication of AF

♥ Atrial fibrillation is an independent risk factor for stroke: increases risk about five-fold.
♥ AF is responsible for >15% of all strokes
♥ Strokes associated with AF are more severe and TIAs last longer than those due to carotid disease
♥ Strokes associated with AF have more disability and higher mortality than strokes that occur in absence of AF
# Atrial Fibrillation

<table>
<thead>
<tr>
<th>Rate Control</th>
<th>Rhythm Control</th>
<th>Prevention of Thromboembolism</th>
</tr>
</thead>
</table>
| - Calcium Channel Blockers (2)  
- Beta Blockers  
- **Always first priority**  
- **Strict versus lenient rate control**  
  - Less than 110 bpm at rest (new lenient control – RACE II)  
  - Does not apply to patients with HF  
- AV node ablation if pharmacological therapy cannot control rate | - Electrical or chemical cardioversion  
  - Chemical effective if atrial fib < 7 days  
  - TEE guided or full anticoagulation  
- **Class I and Class III antiarrhythmics**  
  - AFFIRM and RACE trials  
- Registry data supports slowing progression of disease | - **All patients regardless of rate or rhythm control**  
- Amount of time in atrial fibrillation is not deciding factor  
- Decision based on stroke risk  
  - CHADS2  
  C – CHF  
  H – Hypertension  
  A – Age  
  D – Diabetes  
  S₂ – Stroke or TIA  
- CHADS Vasc Score |
Rate Control

❤ Avoid development of tachycardia-induced cardiomyopathy

❤ Accomplished through medications that slow conduction through the AV node
  • Beta blockers, calcium channel blockers (verapamil, diltiazem) most common
  • Digoxin only effective at rest

❤ Pacemaker may be required if HR becomes too low

❤ AV Ablation is an option if pharmacological therapy is unsuccessful in controlling rate

❤ Continued anticoagulation required

❤ Avoid toxic effects of antiarrhythmics
Pharmacological Considerations in Rate Control

❤ Calcium channel blockers versus beta blockers

❤ Pros and Cons of Digoxin
  • Blood pressure effect
  • Heart rate control at rest versus exercise

❤ Pros and Cons of Amiodarone
  • Limiting use of other antiarrhythmics (terminal half-life elimination 40 to 55 days)
  • Use in heart failure
# A Closer Look at Calcium Channel Blockers

<table>
<thead>
<tr>
<th></th>
<th>Verapamil</th>
<th>Dihydropyridines</th>
<th>Diltiazem</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart Rate</td>
<td>▼▼▼</td>
<td>▲</td>
<td>▼</td>
</tr>
<tr>
<td>AV Nodal Conduction</td>
<td>▼▼▼</td>
<td>▼▼▼▼▼</td>
<td>▼</td>
</tr>
<tr>
<td>Contractility</td>
<td>▼▼▼</td>
<td>▼▼▼▼</td>
<td>▼</td>
</tr>
<tr>
<td>Arterial Vasodilatation</td>
<td>▲▲▲</td>
<td>▲▲▲▲▲</td>
<td>▲</td>
</tr>
</tbody>
</table>
Additional Rate Control Information

RACE II

❤ Strict versus lenient rate control

❤ Strict
• Resting HR < 80
• Exercise < 110

❤ Lenient
• Resting HR < 110

❤ No benefit of strict rate control

❤ **Note:** Study population did not include patients with heart failure.
Class III Recommendation:

Treatment to achieve strict rate control of heart rate (<80 bpm at rest or <110 bpm during a 6-minute walk) is not beneficial compared to achieving a resting heart rate <110 bpm in patients with persistent AF who have stable ventricular function (left ventricular ejection fraction >0.40) and no or acceptable symptoms related to the arrhythmia, though uncontrolled tachycardia may over time be associated with a reversible decline in ventricular performance (Level of Evidence: B)
Rhythm Control

♥ Prevention of thrombus formation
♥ Prevention of atrial myopathy
♥ Relief of symptoms
♥ Initially mechanical cardioversion without antiarrhythmics
♥ Subsequent occurrences attempt cardioversion with antiarrhythmics
♥ Antiarrhythmics – toxic side effects
**AFFIRM Trial (2002)**

❤ Compared rate control and rhythm control in patients with AF to determine which approach was associated with better survival outcome

❤ Results

- **Mortality rate nearly equal in the two groups**
- More ischemic strokes in rhythm control group (anticoagulation often DC’d with NSR)
- More adverse drug effects in rhythm control group
- More hospitalizations in rhythm control group
Conclusions:

- Rhythm control offers no survival advantage over rate control
  - Trend toward increased mortality with rhythm control
- Potential advantages to rate control: fewer adverse drug effects
- Anticoagulation should be continued in all AF patients at risk for stroke regardless of rate or rhythm control strategies
**RACE (2002)**

♥ Compared rate control and rhythm control in patients with recurrent persistent AF

- End point was composite of CV death, admission for HF, thromboembolic event, severe bleeding, severe side effects from drugs

♥ Results:

- Primary end point occurred in 17.2% of rate control group and 22.6% of rhythm control group (trend in favor of rate control)
- Thromboembolism more frequent in rhythm control group
- More adverse drug effects in rhythm control group
Conclusions:

• Rate control is not inferior to rhythm control for prevention of death and morbidity from CV causes in patients with persistent AF

• Cardiovascular risk (including risk of stroke) is not reduced with rhythm control even when sinus rhythm is maintained

• Anticoagulation therapy should continue in all AF patients at risk for stroke regardless of rate or rhythm control therapy
Rate Vs Rhythm Control Recommendations

♥ Data from 7 trials do not support a routine strategy of rhythm control in patients with atrial fibrillation with or without HF

♥ Rate control recommended in most patients with AF

♥ Rhythm control can be considered based on specific patient considerations
  • Continuing symptoms on rate control
  • Exercise intolerance with rate control drugs
  • Patient preference
Registry data showing support for rhythm control in select patients to decrease disease progression. (Registry on Cardiac Rhythm Disorders Assessing the Control of Atrial Fibrillation)

HOWEVER!
Anticoagulation Decision Making

❤ Chronic anticoagulation is recommended in both groups in patients at high risk for stroke

❤ C – HF / LVEF ≤ 35%
❤ H – Hypertension
❤ A – Age
❤ D – Diabetes Mellitus
❤ S₂ - Stroke or TIA
CHA$_2$DS$_2$VASc

- **C** – HF or LVEF $\leq$ 35%
- **H** – Hypertension
- **A$_2$** – $< 65$, $65$ to $74$, and $\geq 75$
- **D** – Diabetes Mellitus
- **S$_2$** – Stroke, TIA, or Thromboembolism
- **VA** – Vascular Disease
- **Sc** – Gender
General Principles for Atrial Arrhythmias

❤ Atrial Fibrillation

• Rate control is first priority
• Optimize rate control based on clinical assessment of perfusion
• Hemodynamic instability
  – BP < 90 systolic or HR > 150 BPM

❤ Anticipate need for rhythm control with atrial flutter

❤ Critical care setting associated with increased catecholamine levels

• Treat infection
• Treat inflammation
• Correct electrolytes
# Antiarrhythmic in Atrial Fibrillation

<table>
<thead>
<tr>
<th>Class</th>
<th>Specific Medications</th>
<th>Purpose of Medication</th>
<th>Major Cardiac Side Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Class I A</td>
<td>Disopyramide</td>
<td><strong>Rhythm Control</strong></td>
<td>Torsade de pointes, HF</td>
</tr>
<tr>
<td></td>
<td>Procainamide</td>
<td><strong>Rhythm Control</strong></td>
<td>Torsade de pointes</td>
</tr>
<tr>
<td></td>
<td>Quinidine</td>
<td><strong>Rhythm Control</strong></td>
<td>Torsade de pointes</td>
</tr>
<tr>
<td>Class I B</td>
<td>Not used in atrial fibrillation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Class I C</td>
<td>Flecainide</td>
<td><strong>Rhythm Control</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Propafenone</td>
<td><strong>Rhythm Control</strong></td>
<td>Ventricular tachycardia, HF, Atrial Flutter</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Class II</td>
<td>Beta Blockers</td>
<td><strong>Rate Control</strong></td>
<td></td>
</tr>
<tr>
<td>Class III</td>
<td>Amiodarone</td>
<td><strong>Rhythm / Rate Control</strong></td>
<td>Torsade de pointes (rare)</td>
</tr>
<tr>
<td></td>
<td>Dronedarone</td>
<td></td>
<td>* <strong>Organ toxicity</strong></td>
</tr>
<tr>
<td></td>
<td>Dofetilide</td>
<td><strong>Rhythm Control</strong></td>
<td>Torsade de pointes</td>
</tr>
<tr>
<td></td>
<td>Ibutilide</td>
<td><strong>Rhythm Control</strong></td>
<td>Torsade de pointes</td>
</tr>
<tr>
<td></td>
<td>Sotalol (Also contains beta blocker)</td>
<td><strong>Rhythm Control (also controls rate)</strong></td>
<td>Torsade de pointes, HF, Beta blocker side effects</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Class IV</td>
<td>Calcium Channel Blockers</td>
<td><strong>Rate Control</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Medications Used to Maintain Sinus Rhythm in Patients with Atrial Fibrillation

- Amiodarone
- Disopyramide
- Dofetilide
- Dronedarone
- Flecainide
- Procainamide
- Propafenone
- Quinidine
- Sotalol
Recommendations for therapy in the maintenance of sinus rhythm

Therapy to maintain sinus rhythm in patients with recurrent paroxysmal or persistent atrial fibrillation. Drugs are listed alphabetically and not in order of suggested use. The seriousness of heart disease progresses from left to right, and selection of therapy in patients with multiple conditions depends on the most serious condition present. LVH indicates left ventricular hypertrophy. Adapted from Wann 2011.
Class I: Na⁺ Channel Blockers

Class III: K⁺ Channel Blockers

Class IV: Calcium Channel Blockers

TP

TRP

ECG complex

QRS

TP

RP

T wave

Seconds

0

0.04

0.08

0.12

0.18

0.20

0.40
Class I
Slow conduction (widen QRS).
Some prolongation of refractory period (prolong QT interval).

Class III
Marked prolongation of refractory period (prolong QT interval).
Dronedarone

❤ Similar to amiodarone without iodine component and less fat soluble

❤ Class III antiarrhythmic (K⁺ channel blocker) with effects from all four classes

❤ Less effective than amiodarone at maintaining sinus rhythm but also less toxic

❤ Elimination half-life 13-19 hours

❤ Has both rate and rhythm control effects but is primarily indicated for rhythm control

❤ May reduce incidence of stroke (mechanism uncertain)
Dronedarone (ATHENA)

♥ Approved for maintenance of sinus rhythm in patients with history of paroxysmal or persistent AF or flutter with EF > 35% who are in sinus rhythm or will be cardioverted

♥ Dose: 400 mg PO bid with meals (no grapefruit juice)

♥ Contraindicated in patients with NYHA Class IV HF or NYHA Class II-III HF with recent decompensation requiring hospitalization or referral to a specialized HF clinic
  • > twofold increase in mortality in HF patients

♥ Side Effects
  • GI, skin disorders
  • Can prolong QTc but low risk of Torsades
  • Increases serum creatinine
  • Interferes with digoxin metabolism

Concern: LIVER Dysfunction: 1/2011
ACCF/AHA/HRS Atrial Fibrillation Guidelines

Class II A Recommendation:

Dronedarone is reasonable to decrease the need for hospitalization for cardiovascular events in patients with paroxysmal AF or after conversion of persistent AF. Dronedarone can be initiated during outpatient therapy (Level of Evidence: B)

Reduces risk of recurrent atrial fibrillation after cardioversion by 25%.
ACCF/AHA/HRS Atrial Fibrillation Guidelines

Class III Recommendation:
Dronedarone should not be administered to patients with class IV heart failure or patients who have had an episode of decompensated heart failure in the past 4 weeks, especially if they have depressed left ventricular function (left ventricular ejection fraction 35%)
(Level of Evidence: B)
Evidence to Support the Recommendation

**ANDROMEDA** (Antiarrhythmic Trial with Dronedarone in Moderate to Severe CHF Evaluating Morbidity Decrease)

Dronedarone increased mortality after a median follow-up of only 2 months; 8.1% in the dronedarone group died compared to 6.3% in the placebo group.

HR: 2.13; 95% CI: 1.07 to 4.25; p=0.03)
Preventing Thromboembolism

♥ Consideration in all patients with atrial fibrillation of atrial flutter

Warfarin

♥ Target INR of 2.0-3.0

♥ Target INR adjusted in those with mechanical heart valve – at least 2.5

♥ Surgical amputation of left atrial appendage
Dabigatran (Pradaxa)

❤ Oral direct thrombin inhibitor
  • Is a prodrug (dabigatran etexilate) that is converted in liver to active form
  • Peak plasma levels in 1.5 hours; half-life 12 to 18 hours
  • Eliminated mostly by kidneys (reduced dose for moderate renal failure, not recommended in severe renal failure)

❤ Predictable dose-response relationship so no lab monitoring of coagulation status needed

❤ Drug to drug interactions exist

❤ Dose:
  • 150 mg PO BID
  • 75 mg PO BID with creatinine clearance 15 to 30 mL/minute
    – These patients and this dose not tested in clinical trials
Dabigatran

♥ No known antidote
♥ For surgeries with a high risk for bleeding (i.e. CABG), recommended hold time is 3 to 5 days. For urgent cases of major surgery delay until clotting times are normal or until four half-lives has passed
  ♥ Hold times for surgery are dependent on renal function
  ♥ Minimum hold time for low risk surgery and normal renal function is > 24 hours
♥ Bleeding risk can be assessed by an ecarin clotting time if available
  ♥ If not available, a PTT can be assessed to determine clearance of the drug because dabigatran has been shown to prolong aPTT (aPTT not used for quantitative assessment)
  ♥ > 2 x upper normal limit 12 to 24 hours after drug may be indicative of high risk for bleeding
♥ Thrombin time is most sensitive test. Diluted thrombin time (DTT) is a quantitative test (calibrated Hemoclot®)

DO NOT USE INR. Can be falsely elevated.
Dabigatran

♥ RE-LY trial (Connolly et al, 2009)
♥ Study results (stroke / systemic embolism) compared to warfarin:
  • 110 mg BID non-inferior to warfarin (p < 0.001)
  • 150 mg BID superior to warfarin (p< 0.001)
♥ Rate of major bleeding
  • 110 mg BID lower than warfarin (p=0.003)
  • 150 mg BID no different from warfarin dose of dabigatran (p=0.31)
    – One area of concern GI Bleed
♥ Ischemic stroke
  • Statistically lower with dabigatran at 150 mg PO BID
♥ Hemorrhagic stroke
  • Statistically lower with dabigatran at both doses (p < 0.001).
♥ Approved for reduction of stroke in patients with AF at intermediate or high risk of stroke.
♥ Specific patient characteristics
  • 30.9% to 32.6% CHADS2 score = 0-1
  • 34.7% to 37.0% CHADS2 score = 2
Rivaroxaban (Xarelto)

❤ Oral direct factor Xa inhibitor
• Maximum plasma level in 3 hours
• Half-life 5-9 hours (up 11 to 13 hrs if > 75 years old)
• Dose 20 mg PO daily
• Should be taken with food
• Hepatic and renal excretion
  – Contraindicated in severe renal failure

❤ Predictable dose-response relationship
so no lab monitoring needed
Rivaroxaban

♥ Recommended hold time prior to high bleeding risk surgeries is 2 to 4 days depending on the patient’s age and renal function

♥ Minimum hold time for low risk surgery in patients with normal renal function is ≥ 24 hours

♥ With severe hepatic impairment the elimination half-life is not known - recommended the drug be held for 7 days prior to major surgery

♥ No known reversal agent
Rivaroxaban

♥ ROCKET AF (Patel et al., 2011)

• Double-blind randomized trial
• 14,264 patients with nonvalvular atrial fibrillation (at increased risk for stroke)
• **Mean CHADS2 score 3.5**
  – 87% to 86.9% had CHADS2 score ≥ 3
• Rivaroxaban (at a daily dose of 20 mg) or dose-adjusted warfarin
• Composite of stroke (ischemic or hemorrhagic) and systemic embolism
• P<0.001 for non-inferiority of rivaroxaban
• No significant between-group difference in the risk of major bleeding, although intracranial and fatal bleeding occurred less frequently in the rivaroxaban group
Apixaban (Eliquis)

♥ Oral factor Xa inhibitor
♥ Rapid absorption; 8 to 15 hour elimination ½ life
♥ 25% renal excretion
♥ Dose: 5 mg BID
♥ Dose: 2.5 mg BID

- Creatinine > 1.5 mg/dL and either
- Age ≥ 80 years
- Weight ≤ 60 kg
Apixaban

❤ Recommended to be held for at least 48 hours prior to surgery with a moderate to high risk for bleeding.

❤ Minimum hold time for low risk surgery in patients with normal renal function is $\geq$ 24 hours

❤ No known reversal agent
Apixaban

♥ ARISTOTLE (Granger et al., 2011.)
♥ Randomized, double blind, double dummy
♥ 18,201 patients; median age 70 years; 35% female
♥ Apixaban 5 mg BID versus warfarin (INR 2.0 to 3.0)
  • 2.5 mg BID used in subset of patients
♥ Primary objective evaluated for non-inferiority for primary endpoint of Ischemic stroke/ hemorrhagic stroke / systemic embolism
  • Found to be non inferior to warfarin (p = <0.001)
♥ Secondary objective evaluated for superiority for primary endpoint of Ischemic stroke/ hemorrhagic stroke / systemic embolism
  • Found to be superior to warfarin (p= 0.01)
♥ Primary safety outcome: Major bleeding
  • Statistically less with apixaban (p<0.001)
♥ Delayed by FDA for review of data management and verification
♥ No statistical difference in ischemic stroke.
Apixaban

**AVERROES**: Apixaban versus ASA.

**APPRAISE – 2**: Apixaban added to DAPT in ACS in high risk patient.
Enoxaban

♥ ENGAGE AF-TIMI 48
♥ Randomized, double-blind, double-dummy trial
♥ 21,105 patients, follow up 2.8 years
♥ Tested for non-inferiority for stroke or systemic embolism
♥ $P = < 0.001$ for high dose and $P = 0.005$ for low dose
♥ Significantly lower rates of bleeding and cardiovascular death compared to warfarin at both doses
More on Factor Xa Inhibitors

♥ PT may provide qualitative assessment of presence of factor Xa
♥ Not sensitive for quantitative anticoagulation effect
♥ Point of care INR should not be used to gauge anticoagulation effects
♥ Chromogenic assay can provide quantitative assessment – not widely available, not fully studied, not recommended at this time
♥ Not all drug to drug interactions are known
♥ Factor Xa inhibitor antidote, andexanet alfa – breakthrough therapy designation by FDA
Electrical Cardioversion

❤️ Direct current cardioversion
❤️ Involves delivery of an electrical shock synchronized with the intrinsic activity of the heart
❤️ Usually is done by sensing R wave on the EKG.
Electrical Cardioversion

♥ Assures no electrical stimulation from 60–80 ms before to 20-30 ms after the apex of the T wave
  • vulnerable phase of cardiac cycle
♥ Used to normalize all abnormal cardiac rhythms except for ventricular fibrillation or pulseless VT
♥ Rhythms due to re-entry are more suitable for cardioversion
♥ Rhythms due to automaticity do not respond to cardioversion
Electrical Cardioversion

♥ Often performed electively
♥ Need for anesthesia
♥ Immediate need for hemodynamically unstable rhythms
♥ Anticoagulation prophylaxis (same with pharmacological cardioversion)
♥ Full anticoagulation versus TEE / Heparin strategy
♥ Risk for thromboembolism greatest when atrial fibrillation present greater than 48 hours
Indications for Emergent DC Cardioversion

❤ Active ischemia
❤ Symptomatic hypotension
❤ Severe heart failure
❤ Preexcitation via an accessory pathway

Contraindicated in presence of digitalis toxicity or hypokalemia
This is a pre-thrombosis state in which the enlarged/inefficient atrium allows blood flow to become sluggish, with the RBC's visible as swirling "smoke" under echo imaging. The slowly moving blood has the potential to form thrombus, especially in the crescent shaped atrial appendage.
Electrical Cardioversion: Technical Issues

- Need for good R wave and good P wave visualization
- AP placement preferred (short axis)
- Initial energy delivered (monophasic) for atrial flutter may be as low as 50 J
- Higher energy is needed for atrial fibrillation starting at least 200 J
- Initial higher energy produces more immediate success and may reduce total energy delivered
- Maximum J is 400
- Biphasic waveforms use less energy
- Time between shocks not less than one minute
## Energy Levels for Cardioversion

<table>
<thead>
<tr>
<th>Rhythm</th>
<th>Initial Energy Level (monophasic)</th>
<th>Subsequent Energy Levels</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atrial Flutter</td>
<td>50 J</td>
<td>100, 200, 300, 360 J</td>
</tr>
<tr>
<td>SVT</td>
<td>50 J</td>
<td>100, 200, 300, 360 J</td>
</tr>
<tr>
<td>Atrial Fibrillation</td>
<td>100 – 200 J</td>
<td>300, 360 J</td>
</tr>
<tr>
<td>Monomorphic VT</td>
<td>100 J</td>
<td>200, 300, 360 J</td>
</tr>
</tbody>
</table>
Treatment: Electrical Cardioversion

♥ Factors Predicting Success:
♥ Short duration of atrial fibrillation
♥ Atrial flutter
♥ Young Age

♥ Factors Predicting Failure:
♥ Left atrial enlargement
♥ Underlying heart disease
♥ Cardiomegaly

Success rates vary from 70% to 90%

The relapse rate is high without continuation of antiarrhythmic drug therapy
Understanding Therapy Options

- Biphasic waveform
  - Less energy required compared to monomorphic
- Transvenous cardioversion
  - Superior to external in obese patients and those with COPD
  - Frequency of reoccurrence not superior to external
  - Biphasic waveform will decrease the need for internal cardioversion
  - Future indications might include implantable pacemakers or defibrillators or drug infusion pumps
Cardioversion in Patients with Devices

♥ Can be safe when appropriate precautions are taken
♥ Generators are designed to protect themselves but programmed data can still be altered
♥ Device should be interrogated before and after procedure
♥ Electricity conducted along an implanted lead can cause myocardial damage leading to exit block and failure of ventricular capture
♥ Paddle should be positioned away from implanted devices
♥ Internal cardioversion does not interfere with pacemaker function
Nursing Considerations in Cardioversion

♥ Emergency cart
  • Intubation supplies / ambu bag
  • Emergency drugs (lidocaine, epinephrine, amiodarone, atropine)

♥ Sedation reversal agent

♥ O2 delivery equipment

♥ Suction equipment

♥ O2 saturation monitor, and non-invasive BP monitoring equipment
Electrical Cardioversion

Complications

- Embolism (1%-7% without prophylactic anticoagulation)
- Benign arrhythmias
- Ventricular arrhythmias with hypokalemia and digitalis toxicity
- Myocardial damage has not been confirmed
- Reoccurrence of atrial fibrillation
  - Prophylactic antiarrhythmic drug therapy before cardioversion for patients at risk
Pharmacological Cardioversion

♥ Works best if AF present for < 7 days
♥ Most effective drugs are
  • Ibutilide (Corvert)
  • Flecainide (Tambocor)
  • Dofetilide (Tycosin)
  • Propafenone (Rhythmol)
  • Amiodarone
♥ Associated with side effects
  • Bradycardia (8%)
  • QT prolongation (1.5%)
  • Ventricular arrhythmias (1.3%)
Drugs Proven Most Effective for Pharmacological Cardioversion of Atrial Fibrillation (Class I Recommendation from ACC / AHA Guidelines Duration of Less than or Equal to 7 Days)

Dofetilide *
Flecainide
Ibutilide
Propafenone

(* Also-class I recommendation for duration of Atrial Fibrillation > 7 days)
Recommendations for Pharmacological Cardioversion of Atrial Fibrillation

♥ Administration of flecainide, dofetilide, propafenone, or ibutilide is recommended for pharmacological cardioversion of AF

♥ Class IIa recommendations:

- Amiodarone
- “Pill-in-the-pocket” single oral dose of propafenone or flecainide to terminate persistent AF outside the hospital in selected patients (no sinus node or AV node dysfunction, LQT, Brugada, or structural heart disease)
Ablation for AF

♥ Paroxysmal AF is triggered by ectopic foci localized to the PVs in about 90% of patients with structurally normal hearts

- Most patients have one or two foci 2 to 4 cm inside the pulmonary veins (the remaining foci are usually in the right or left atrium)
- Pulmonary vein isolation procedure is successful in 60% to 70%

♥ Patients cardioverted from chronic AF often have multiple ectopic sites in both atria
- More difficult to ablate multiple foci successfully
Pulmonary Vein Isolation Procedures

Focus on isolating the triggers in the PVs from the left atrial myocardium

- **Segmental ostial ablation** targets isolated sites of ectopic foci in PVs and ablates the connection between those sites and atrial myocardium

- **Circumferential ablation** creates lesions that encircle the ostia of all four pulmonary veins and completely isolates them from atrial myocardium – most common procedure
Complications of PV Isolation

- Cardiac tamponade
- Pulmonary vein stenosis (can lead to pulmonary hypertension)
- Esophageal injury or atrio-esophageal fistula
- Phrenic nerve injury
- Thromboembolism
- Mitral valve trauma
- Radiation exposure due to long procedures
Ablation for Atrial Fibrillation

Potential energy sources:
• Radiofrequency (heats tissue)
• Cryothermy (freezes tissue)
• Focused ultrasonography
AV Node Ablation

♥ Creates complete AV block to prevent conduction of AF into ventricles (requires insertion of permanent pacemaker)
Ablation for Permanent Atrial Fibrillation
Cox-Maze III

❤️ “Cut & sew” method developed in 1987

• Considered the gold standard for surgical treatment of AF
• Isolates the pulmonary veins
• Isolate the posterior left atrium
• Interrupts the macro reentrant circuits responsible for atrial fibrillation and atrial flutter
• Amputates the left atrial appendage
Creates a pathway from sinus node to AV node and allows all of atrium to be activated
Technical challenges of procedure limited its use.
Cox-Maze IV Using Ablation

♥ Creation of lesions using ablation technology

- Unipolar or bipolar energy sources

- Unipolar
  - Unipolar radiofrequency (RF) (heats tissue)
  - Cryothermia (freezes tissue)
  - High frequency ultrasound

- Bipolar
  - Bipolar radiofrequency (RF)
  - Delivered between two electrodes held in place inside a jaw like clamp
Cox-Maze IV Using Ablation

♥ Must create transmural lesions from epicardial or endocardial surface
  • Unipolar sources don’t consistently create transmural lesion
  • Unipolar cryosurgery or radiofrequency ablation can also cause unintended cardiac injury

♥ Bipolar RF clamps most widely used device
  • Limitation: Only tissue fitting between clamp can be ablated, particularly limiting when performed on beating heart
  • Right atrial isthmus and left atrial isthmus are not able to be fully ablated
Role of the Isthmus

Right Atrial Isthmus

Left Atrial Isthmus

Performed through median sternotomy or right mini thoracotommy with patient on CPB

Uses combination of unipolar and bipolar RF or cryothermia ablations delivered through small atrial incisions to achieve desired lesions

Left atrial appendage is also amputated

Results similar to Cox-Maze III

The term “Maze” procedure implies entire bi-atrial lesion set of the Cox-Maze procedure (includes ablation of both the right and left atrial isthmuses)
Surgical Procedures for Atrial Fibrillation

♥ Cox-Maze IV: Cox-Maze III lesion set using ablation technology
♥ Pulmonary vein isolation
♥ Pulmonary vein isolation with a left atrial lesion set connecting to the mitral valve annulus

♥ Amputation of left atrial appendage
   Usually done in conjunction
Percutaneous Left Atrial Appendage Occlusion

♥ The LAA is a multi-lobed structure of variable anatomy that is attached to the LA
♥ More than 90% of clots in patients with non-rheumatic AF form in the LAA
♥ Many patients are unable to take coumadin and are at risk for stroke in chronic AF
♥ Mechanical occlusion of LAA can prevent thrombus embolization
LAA Occlusion Devices

Watchman

Amplatzer
LAA Occlusion Devices: Watchman

♥ Protect AF Trial
  • 2009: Non inferior but safety concern: Pericardial effusion
  • May 2013: New long term data (45 month follow up of 800 patients) superior to warfarin with respect to all-cause and CV mortality and hemorrhagic stroke in patients with nonvalvular atrial fibrillation and stroke risk factors

♥ Prevail Trial – 2013
  • Did not meet 1st primary endpoint
    – Non inferiority to warfarin for composite of stroke, systemic embolism, or cardiovascular or unexplained death
  • Met 2nd primary endpoint
    – Non inferiority to warfarin for prevention of ischemic stroke or systemic embolism

♥ FDA status
  • 2010 FDA denied approval
  • December 2013 – advisory board 13 to 1 recommended approval
LAA Occlusion Devices: Amplatzer

❤️ AMPLATZER Cardiac Plug
❤️ European CE Mark Approval January 2013
❤️ The AMPLATZER™ Cardiac Plug Clinical Trial (ACP Trial)
  • First patient enrolled in March 2013
Atrial Defibrillators (IAD)

- Good efficacy – however:
- Limitations
  - Poor patient tolerance for energy levels > 1 J
  - Many candidates are also candidates for catheter ablation
- Implanted devices are limited to patients with poor LV function who also meet criteria for ventricular defibrillator
- Several devices have capability for atrial and ventricular sensing and pacing; and atrial cardioversion and ventricular defibrillation
Pacemakers and Atrial Fibrillation

❤ Standard RV pacing effects:
• Loss of AV synchrony
• Causes “iatrogenic LBBB” and intraventricular dysynchrony
• Is associated with increased incidence of AF
  – Risk increases linearly with cumulative % of RV pacing

❤ Atrial pacing supresses PACs and prevents retrograde V to A conduction
Observations from Clinical Trials

- Annual rate of paroxysmal or chronic AF was significantly lower with DDD or AAI pacing compared to VVI pacing (CTOPP trial)
- Significantly lower first occurrence of AF or chronic AF with DDDR vs VVIR pacing (MOST trial)
- Significant reduction in both % of ventricular paced beats and rate of occurrence of persistent AF with minimal ventricular pacing compared to standard RV pacing (SAVE PACe trial)

Patients who are predominantly RV paced have a higher likelihood of developing AF.
More on Pacing and Atrial Fibrillation

❤ Mode Switching
- DDD/DDDR pacer switches to non-tracking mode when rapid atrial rates occur.
- Prevents pacer from pacing RV rapidly

❤ Managed Ventricular Pacing (MVP) Mode to minimize RV ventricular pacing

❤ Permanent pacing is not indicated solely to prevent AF
Postoperative CABG AF

- 20% to 50% of patients
- Almost always within 5 days
- Peak time: 2 days
- Increased risk morbidity
  - Up to 4 x risk for disabling embolic stroke
- Increased risk mortality
  - Up to 3 x risk for cardiac related mortality
- Most patients (without pre-existing AF) convert within 6 weeks

Hillis et al., 2011
Postoperative CABG AF

♥ Class I Recommendations

• Unless contraindicated, treatment with an oral beta blocker at least 24 hours before CABG to prevent post-operative AF is recommended for patients undergoing cardiac surgery.
  – Continued post operatively and at hospital discharge
• Administration of AV nodal blocking agents is recommended to achieve rate control in patients who develop post-operative AF.

♥ Class Ila Recommendations

• Preoperative administration of amiodarone is appropriate prophylactic therapy for patients at high risk for postoperative AF.
• Digoxin and calcium channel blockers can be used for rate control

Hillis et al., 2011
Atrial Fibrillation Clinical Considerations: Case Examples

38 year old female with palpitations and light headedness

No past medical history

Monitor – AVNRT and infrequent short (seconds) runs atrial fibrillation

AVNRT associated with symptoms. Atrial fibrillation incidental finding.

86 year old male presenting with TIA symptoms.

Found in atrial fibrillation of unknown origin.

History of HTN and debilitating arthritic pain and spinal stenosis.

Options?
From Chaos to Clarity
Reflection and Gratitude