FSHP
49th Annual Meeting

Atrial Fibrillation

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OWNING CHANGE: Taking Charge of Your Profession

Disclosure

- I do not have a vested interest in or affiliation with any corporate organization offering financial support or grant monies for this continuing education activity, or any affiliation with an organization whose philosophy could potentially bias my presentation

Objectives

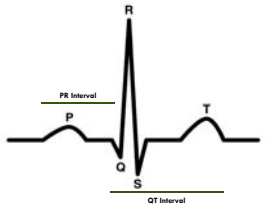
- Summarize pathophysiologic mechanisms underlying atrial fibrillation
- Describe atrial fibrillation signs and symptoms
- Characterize antiarrhythmic drugs according to effects on ion channels
- Discuss the decision to anticoagulate in atrial fibrillation using CVA prediction tools
- Highlight rate and rhythm control strategies
- Outline pharmacotherapy for atrial fibrillation

Electrocardiogram (ECG)

- P wave – atrial depolarization
- QRS complex – ventricular depolarization
- T wave – ventricular repolarization

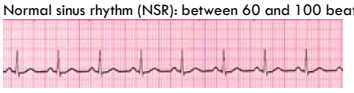
Corrected QT (QTc) = QT interval/√RR interval

RR interval = 60/HR

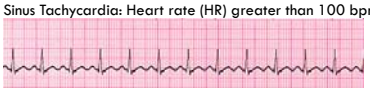


Arrhythmia Classification

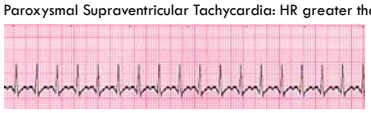
- Normal sinus rhythm (NSR): between 60 and 100 beats per minute (bpm)



- Sinus Tachycardia: Heart rate (HR) greater than 100 bpm (narrow QRS)

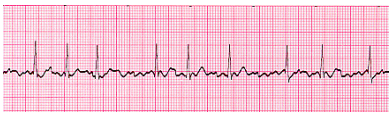


- Paroxysmal Supraventricular Tachycardia: HR greater than 100 bpm

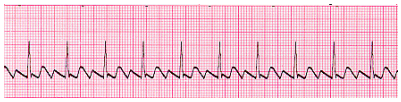


Arrhythmia Classification

- Atrial fibrillation: rapid ventricular rate (rvr) - HR above 100; controlled ventricular rate (cvr) – HR 60-100; slow ventricular rate (svr) : HR less than 60



- Atrial flutter: can also be classified as rvr, cvr and svr



Atrial Fibrillation/Flutter

- Atrial fibrillation (AF)
  - Loss of coordinated atrial activation
  - Loss of atrial mechanical function
  - ECG-replacement of P waves with fibrillatory waves
  - Irregular and frequently rapid ventricular response
- Atrial flutter
  - Saw-tooth pattern of regular atrial activation
  - Reduced atrial function, but not entirely lost
  - Commonly occurs with 2:1 AV block, resulting in a regular or irregular ventricular rate (most often 150 bpm)

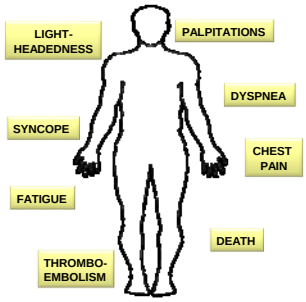
January CT, Wann LS, Alpert JS et al. 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the Heart Rhythm Society. J Am Coll Cardiol 2014; 64: e1-76.

Causes of Atrial Fibrillation

- **Noncardiovascular causes**
  - Acute/chronic alcohol ingestion
  - Autonomic
  - Diabetes
  - Genetics
  - Obesity
  - Pulmonary embolism
  - Severe lung disease
  - Sleep apnea
  - Thyroid disorders
- **Cardiovascular causes**
  - Coronary artery disease
  - Heart failure
  - Hypertension
  - Valvular heart disease
- **Iatrogenic causes**
  - Beta-agonists
  - Cardiac and non-cardiac surgery
  - Intracardiac catheters
  - Local anesthetics, caffeinated beverages, other stimulants
  - OTC cold remedies

January CT, Wann LS, Alpert JS et al. 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the Heart Rhythm Society. J Am Coll Cardiol 2014; 64: e1-76.

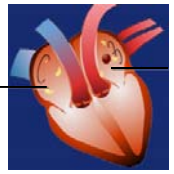
Clinical Presentation



- AF presents with a wide range of symptoms
- Asymptomatic AF = Potential for underlying electrical and structural damage to atrial myocardium
- While AF symptoms alone may not always be severe, untreated disease can result in significant morbidity and mortality

January CT, Wann LS, Alpert JS et al. 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the Heart Rhythm Society. J Am Coll Cardiol 2014; 64: e1-76.

Consequences of Atrial Fibrillation



→Loss of atrial systolic function (atrial contribution to ventricular filling is lost)

→Irregular rapid ventricular contractions

↓

Cardiac output reduced

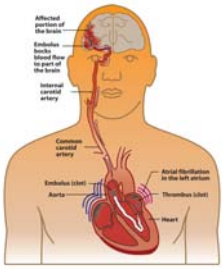
Abnormal blood flow and stasis in the atria

↓

Formation of intra-atrial thrombus

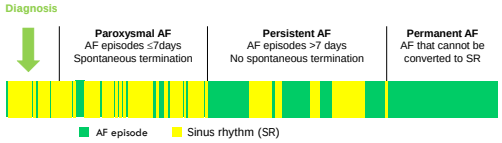
Stroke

- All-cause stroke rate with atrial fibrillation is 5% per year
- Atrial fibrillation is an independent risk factor for stroke:
  - ~5-fold increase in stroke risk
  - ~15% of all strokes caused by AF
  - Stroke risk increases with age
- Stroke risk persists with asymptomatic AF
- Stroke risk with atrial flutter is not well characterized



January CT et al. J Am Coll Cardiol 2014;64: e1-76.
Wolf PA, et al. Stroke. 1991;22:983-988.
Page RL, et al. Circulation. 2003;107:1141-1145.
Hart RG, et al. J Am Coll Cardiol. 2000;35:183-187.

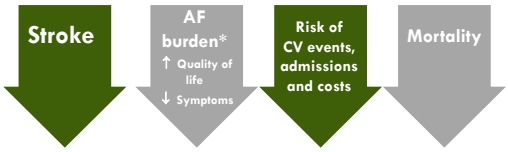
Atrial Fibrillation Continuum



Kirchhof et al. Europace 2007;9:1006-1023.

Goals of Therapy

Comprehensive management of AF includes a reduction in:



* Total percentage of time a patient has AF, as determined by the number and duration of AF episodes.

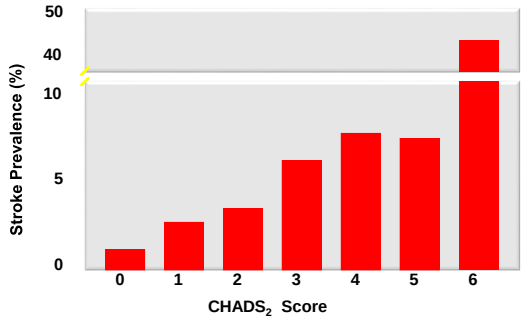
Wolf PA, et al. Stroke. 1991;22:983-988.
Singh SN, et al. J Am Coll Cardiol. 2006;48:721-730.
Prystowsky EN. J Cardiovasc Electrophysiol. 2006;17(Suppl 2):S7-S10.
Hohnloser S, et al. J Cardiovasc Electrophysiol. 2008;19:69-73.
Camm AJ, et al. Eur Heart J Suppl. 2008;10(Suppl H):H5S-H78.
January CT et al. J Am Coll Cardiol 2014;64: e1-76.

Stroke Risk: $CHADS_2$ Score

	Risk Factor	Points
C	Chronic Heart Failure	1
H	Hypertension	1
A	Age > 75	1
D	Diabetes	1
S_2	Prior Stroke/TIA	2

Gage BF, et al. JAMA. 2001;285:2864-2870.

Risk of Stroke Without Warfarin: National Registry of Atrial Fibrillation (NRAF) by $CHADS_2$ Score



Gage BF, et al. JAMA. 2001;285:2864-2870.

CHA_2DS_2-VASc

	Risk Factor	Points
C	Chronic Heart Failure	1
H	Hypertension	1
A_2	Age > 75	2
D	Diabetes	1
S_2	Prior Stroke/TIA	2
V	Vascular Disease	1
A	Age 65 - 74	1
Sc	Sex: female	1

Lip GY, et al. CHEST 2010;137:263-72

Anticoagulation Therapy

$CHADS_2$/CHA_2DS_2-VASc Score	Risk	Treatment
0	Low	Aspirin
1	Moderate	Aspirin or oral anticoagulant[1]
≥ 2	High	Oral anticoagulant

1. Treatment with an oral anticoagulant is preferred

If not a candidate for oral anticoagulation… aspirin + clopidogrel may be considered

January CT et al. J Am Coll Cardiol 2014;64: e1-76
You JJ, et al. CHEST 2012;141(2)(Suppl):e531S–e575S

Oral Anticoagulation Therapy

	Apixaban	Dabigatran	Edoxaban	Rivaroxaban	Warfarin
Mechanism	Factor Xa inhibitor	Direct thrombin inhibitor	Factor Xa inhibitor	Factor Xa inhibitor	Vitamin K antagonist
Dose for stroke prevention secondary to a. fib	5mg twice daily	150mg twice daily	60mg once daily	20mg once daily	Dosed to achieve an INR between 2 and 3
Renal dose adjustment	2.5mg twice daily (AF only)	75mg twice daily (AF only)	30mg once daily *Do not use if CrCL is greater than 95ml/min*	15mg once daily (AF only)	Not required

In a nutshell...

	RE-LY	ROCKET-AF	ARISTOTLE
Inclusion criteria	AF and at least 1 additional risk factor for stroke	AF and at least ≥3 or more risk factors or previous thromboembolism (90% of subjects)	AF and at least 1 additional risk factor for stroke
Exclusion criteria	CrCl <30 mL/min, liver disease, recent stroke	CrCl <30 mL/min, Plt <90 000, uncontrolled HTN, recent stroke	CrCl <25 mL/min, mitral valve stenosis, recent stroke
Design	PROBE	Randomized double-blind, double dummy	Randomized double-blind
Primary stroke	Any stroke or systemic embolism	Any stroke or systemic embolism	Any stroke or systemic embolism
Mean age, y	71.5	73	70
Mean time in treatment range TTR	64%	55%	62%

RE-LY indicates Randomized Evaluation of Long-Term Anticoagulation Therapy; ROCKET-AF, Rivaroxaban versus Warfarin in Nonvalvular Atrial Fibrillation; ARISTOTLE, Apixaban versus Warfarin in Patients with Atrial Fibrillation; AF, atrial fibrillation; CrCl, creatine clearance; PROBE, prospective, randomized, open-label, blinded end point evaluation; Plt, platelets; HTN, hypertension.

ENGAGE-AF TIMI 48	
Inclusion	AF and CHADS2 of 2 or higher
Exclusion	Reversible AF, CrCL < 30ml/min, dual antiplatelet therapy, ACS/PCI/stroke within 30 days of randomization, mitral valve stenosis
Design	Three group, randomized, double-blind, double-dummy trial
Primary Outcome	Time to first stroke or systemic embolism
Median age	72
TTR	68.4%

Kotecha D et al. Circulation 2012;125: 1577-1583
Giugliano et al. NEJM 201;369(22): 2093-2104.

Rhythm Versus Rate Control

- Major trials include:
  - AFFIRM[1]
  - RACE[2]
  - PIAF, STAF, HOT CAFE[3-5]
  - AF-CHF[6]
- Major overall findings:[1-7]
  - Rhythm-control strategy not superior to rate-control strategy
  - Therapy based on each patient's symptoms and disease
  - Management options for AF include rate control, stroke prevention, and maintenance of NSR

1. AFFIRM Investigators. N Engl J Med 2002;347:1825-1833.
2. Van Gelder IC, et al. N Engl J Med. 2002;347:1834-1840.
3. Hohnloser SH, et al. Lancet. 2000;356:1789-1794.
4. Carlsson J, et al. J Am Coll Cardiol. 2003;41:1690-1696.
5. Opolski G, et al. Chest. 2004;126:476-486.
6. Roy D, et al. N Engl J Med. 2008;358:2667-2677
7. January CT et al. J Am Coll Cardiol 2014;64: e1-76

Goals of Rate Control

- Outcomes
  - Reduce symptomatic palpitations
  - Improve ventricular performance, exercise capacity, hemodynamics
  - Prevent (reverse) tachycardia-related cardiomyopathy
- Goal HR
  - Less than 80 bmp at rest
    -- Or --
  - Less than 110 bmp at rest IF asymptomatic and left ventricular systolic function is preserved

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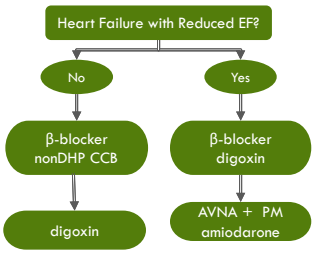
Rate Control



- HFrEF – avoid non-DHP CCBs; start low, go slow with β-blockers
- Digoxin does not prevent activity-related increases in HR; useful in sedentary patients
- Digoxin + β-blocker is a useful combination if additional HR control needed

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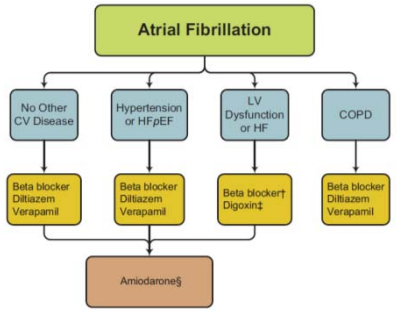
Rate Control Considerations



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Goals of Rhythm Control

- Restore NSR
- Maintain NSR, prevent recurrence of AF
- Reduce frequency of AF episodes, suppress symptoms, improve tolerability of recurrence, improve exercise capacity, maintain hemodynamics
- Prevent (reverse) tachycardia-related cardiomyopathy
- Limit drug toxicity

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Cardioversion

- Indications
  - Hemodynamic compromise, HF, worsening angina → immediate cardioversion
  - Symptomatic, persistent AF → elective cardioversion
- Electrical versus chemical
  - Electrical
    Pros: more effective than pharmacological
    Cons: requires conscious sedation/general anesthesia
  - Chemical
    Pros: effective if conversion attempted within 7 days, more so if < 48 hours, convenient
    Cons: drug toxicity (e.g., proarrhythmia), delayed onset

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Cardioversion

Is anticoagulation required?

Yes, (due to stunning of the myocardium) if duration of AF is unknown or greater than 48 hours and …

- *Hemodynamically stable* – anticoagulate for 3 weeks before and at least 4 weeks after cardioversion, control rate in the interim
  - *TEE-guided approach*
    1. Perform TEE prior to cardioversion to detect thrombus
    2. If no thrombus give parenteral anticoagulant, cardiovert and follow with oral anticoagulation therapy
    3. If thrombus present, give oral anticoagulation therapy as usual and do not cardiovert
- *Hemodynamically unstable* – administer parenteral anticoagulant, proceed with cardioversion, initiate oral anticoagulation and continue for at least 4 weeks after cardioversion
- If subtherapeutic after cardioversion within 4 weeks, may consider bridging with parenteral anticoagulant

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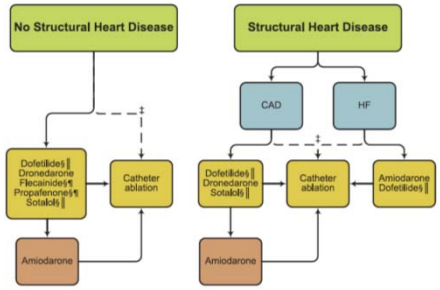
Table 8-1 Classification of Antiarrhythmic Drugs

Class	Drug	Conduction Velocity[a]	Refractory Period	Automaticity	Ion Block
Ia	Quinidine	↓	↑	↓	Sodium (intermediate) Potassium
	Procainamide				
	Disopyramide				
Ib	Lidocaine	0/↓	↓	↓	Sodium (fast on-off)
	Mexiletine				
Ic	Flecainide	↓↓	0	↓	Sodium (slow on-off)
	Propafenone[b]				
II[c]	β-Blockers	↓	↑	↓	Calcium (indirect)
III	Amiodarone[d]	0	↑↑	0	Potassium
	Dofetilide				
	Dronedarone[d]				
	Sotalol[b]				
	Ibutilide				
IV[c]	Verapamil	↓	↑	↓	Calcium
	Diltiazem				

[a]Variables for normal tissue models in ventricular tissue.
[b]Also has β-blocking actions.
[c]Variables for sinoatrial (SA) and atrioventricular (AV) nodal tissue only.
[d]Also has sodium, calcium, and β-blocking actions; see Table 8-2 (for amiodarone).

Rhythm Control Considerations



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Amiodarone Safety Monitoring

	Baseline	1 month	q 3 and 6 months	q 12 months	Prn for symptoms
ECG	X	X[a]		X	
CXR	X			X	
PFTs[b]	X				X
LFTs	X	X	X		
TFTs	X	X	X		
Eye[c]	X				X

[a]ECG is not required at 1 month, but is preferred and often done as part of routine clinical care [b]PFTs may be obtained more frequently if reduction in DLCO from previous or poor lung function at baseline; [c] Eye exam should be performed promptly for any new or worsening vision abnormality

Non-pharmacologic Therapy

- Catheter ablation
  - RF is applied to isolate the PV (PVI)
  - More successful than AADs
  - Complications: catheter-site bleeding, CVA, MI, puncture, PV sclerosis
- Maze procedure
  - PVI and LAA removal
  - Done in conjunction with CT surgery (e.g. valve repair/replacement, CABG)
- AV nodal ablation with pacemaker
  - Induce complete heart block
  - Pace with a DC or BiVentricular PM

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Final Thoughts

- Which type of AF has the highest stroke risk?
- Is there data regarding quality of life + anticoagulation therapy?
- If a patient has an ICD, which shows brief periods of AF, should you anticoagulate?

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- Summarize pathophysiologic mechanisms underlying atrial fibrillation
- Describe atrial fibrillation signs and symptoms
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- Discuss the decision to anticoagulate in atrial fibrillation using CVA prediction tools
- Highlight rate and rhythm control strategies
- Outline pharmacotherapy for atrial fibrillation