
بسم الله الرحمن الرحيم

Atrial Fibrillation:

Epidemiology, pathophysiology & diagnosis

By

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Agenda

- Definition
- Epidemiology
- Classification
- Etiology & pathogenesis
- Diagnosis

Definition

- **AF is a supraventricular tachyarrhythmia with uncoordinated atrial activation and consequently ineffective atrial contraction**
- **ECG characteristics include:**
  1. **irregular R-R intervals**
  2. **absence of distinct repeating P waves,**
  3. **irregular atrial activity**

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Epidemiology

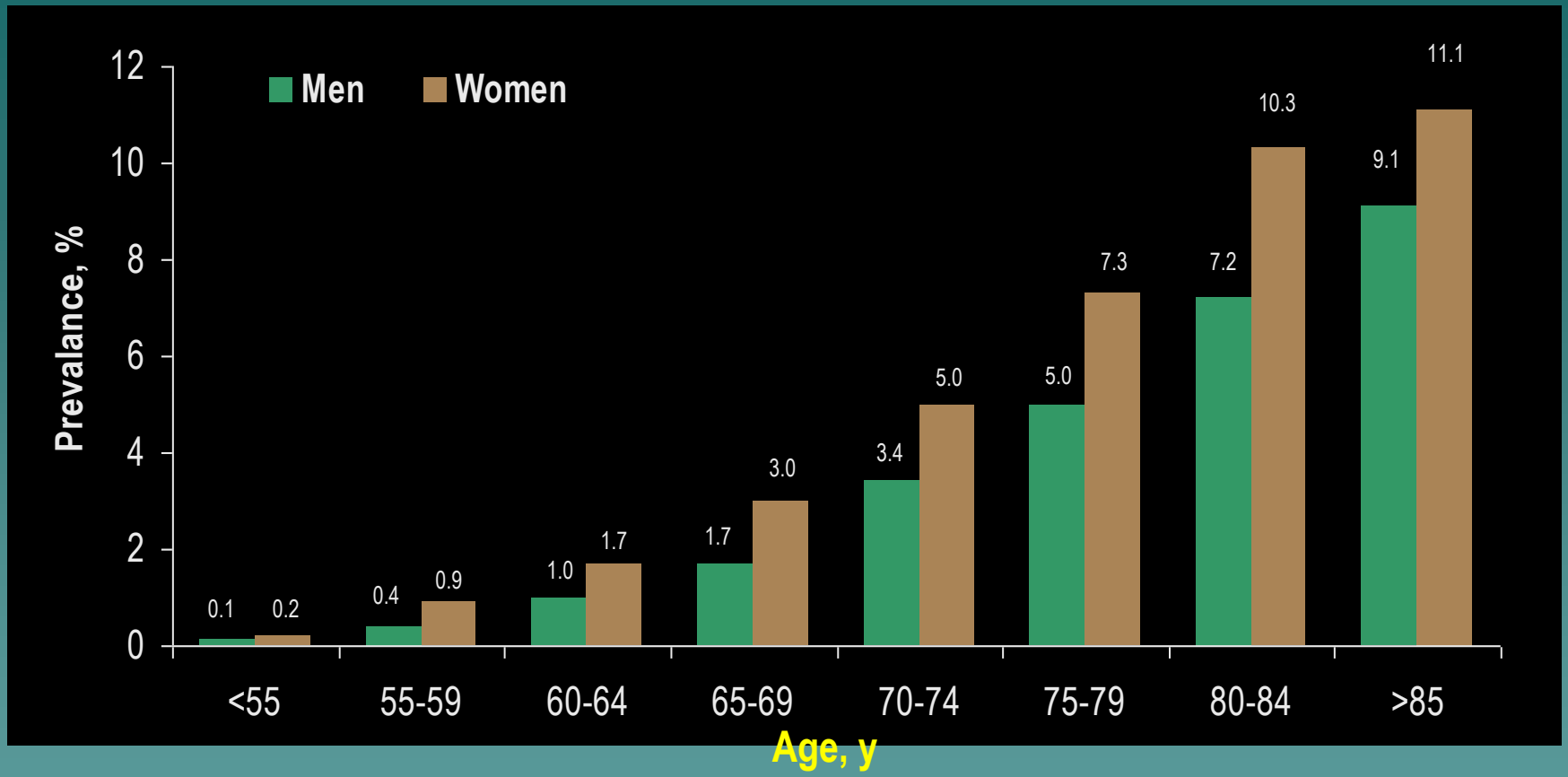
- AF is the most common arrhythmia in adult population
- The incidence of AF doubles with each decade of life; the prevalence of the disease increases as the longevity of the population increases
- In a large cross-sectional study (N = 1.89 million), AF prevalence increased from 0.1% of adults <55 years old to 9% of those ≥80 years; 3.8% of people older than 60 years had AF

Epidemiology

- The relative risk (RR) for death is **1.5** for men, **1.9** for women with AF; the primary cause of death is worsening heart failure[1]
- The annual incidence rate of ischemic stroke is **5%** among people with nonvalvular AF, **2 to 7 times** that of people without AF[2]

1. Benjamin EJ, et al. *Circulation*. 1998;98:946-952.
2. Fuster V, et al. ACC Guidelines *Circulation*. 2006;114:e257-e354

AF Prevalence by Age and Sex



Prevalence of AF in a population of 1.89 million members of a large health maintenance organization in California. The numbers represent the number of men and women with AF in each age category.

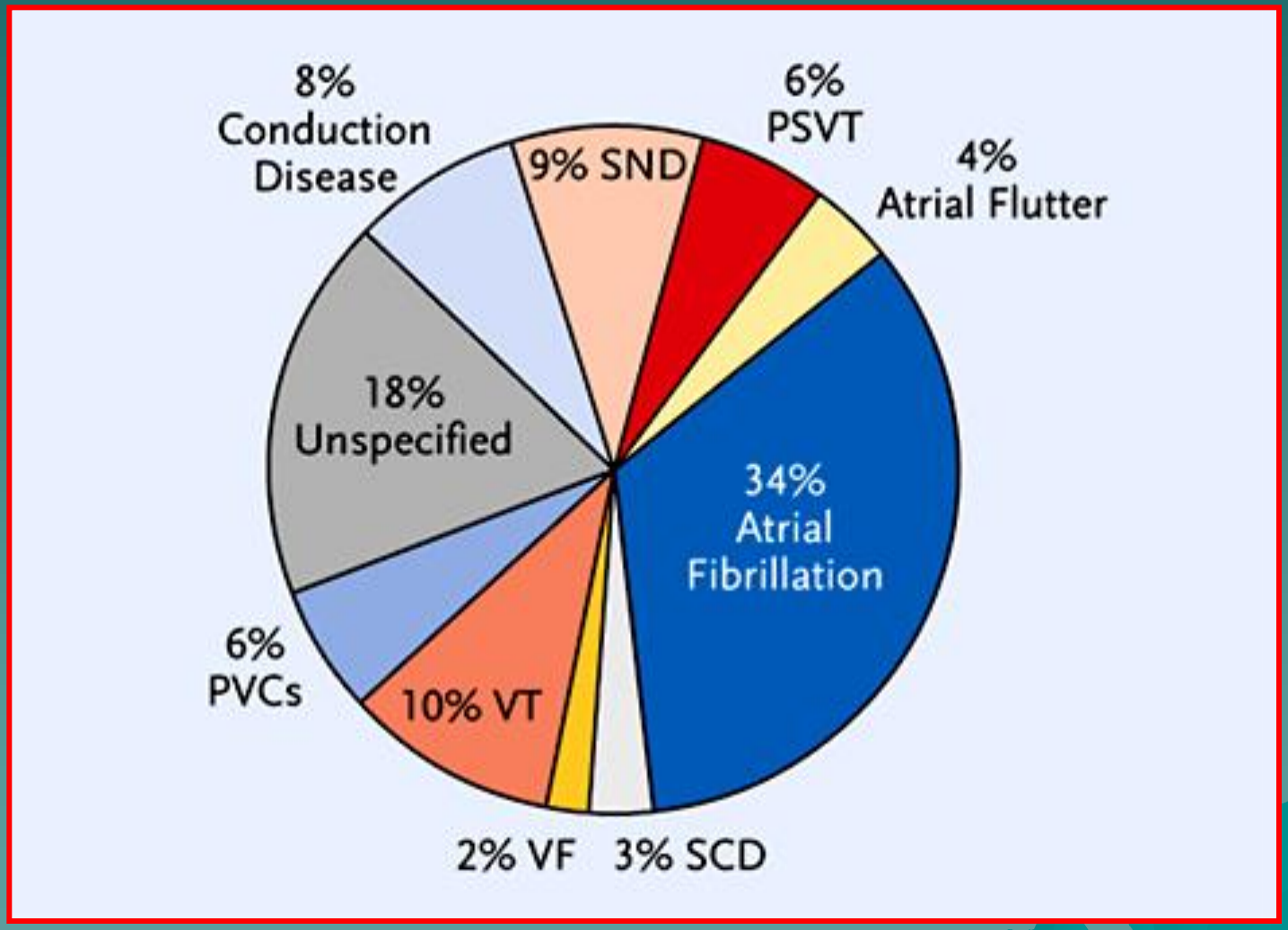
Go AS, et al. *JAMA.* 2001;285:2370-2375.

AF & CV risk

- 5 fold increase risk of stroke
- 3 fold increase risk of HF
- 2 Fold increase risk of both dementia and mortality

Impact on Healthcare

Hospital Discharges by Type of Arrhythmia[1]



[1]Bialy D, Lehmann MH, Schumacher DN. *JACC*. 1992;19:41A

Chronic comorbid conditions with AF

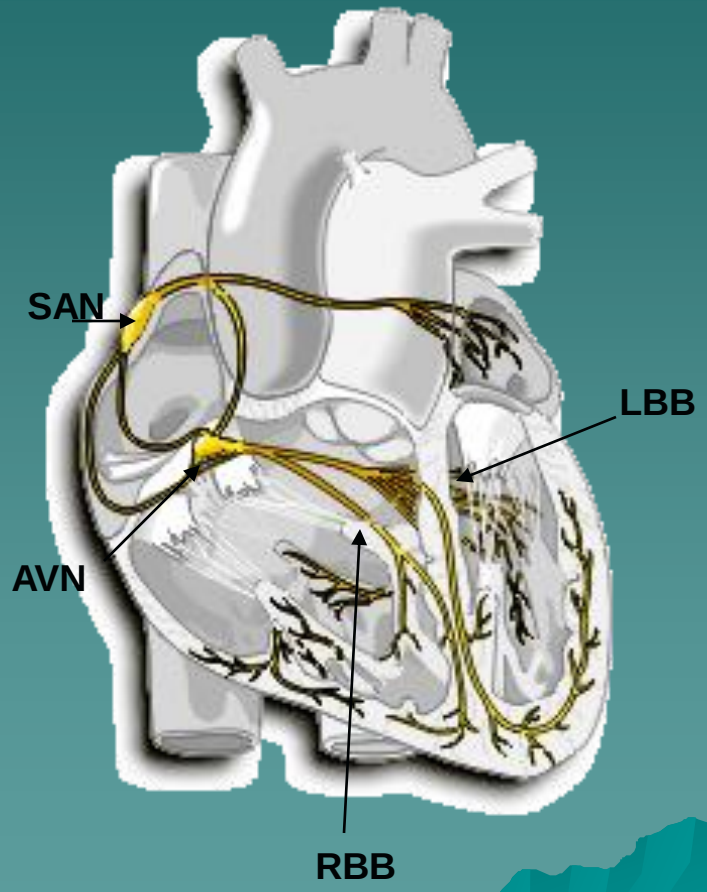
	> 65y	< 65y
HTN	83%	81.1%
IHD	63.8%	64.5%
Hyperlipidemia	62.1%	60.6%
HF	51.4%	59.3%
DM	36.5%	53.1%
Anemia	42.3%	45.6%
CKD	32.3%	40.3%
COPD	23.2%	31.4%

Classification

Term	Definition
Paroxysmal AF	• AF that terminates spontaneously or with intervention within 7 d of onset. • Episodes may recur with variable frequency.
Persistent AF	Continuous AF that is sustained >7 d.
Longstanding persistent AF	Continuous AF of >12 mo duration.
Permanent AF	• Permanent AF is used when there has been a joint decision by the patient and clinician to cease further attempts to restore and/or maintain sinus rhythm. • Acceptance of AF represents a therapeutic attitude on the part of the patient and clinician rather than an inherent pathophysiological attribute of the AF. • Acceptance of AF may change as symptoms, the efficacy of therapeutic interventions, and patient and clinician preferences evolve.
Non-valvular AF	AF in the absence of rheumatic mitral stenosis, a mechanical or bioprosthetic heart valve, or mitral valve repair.

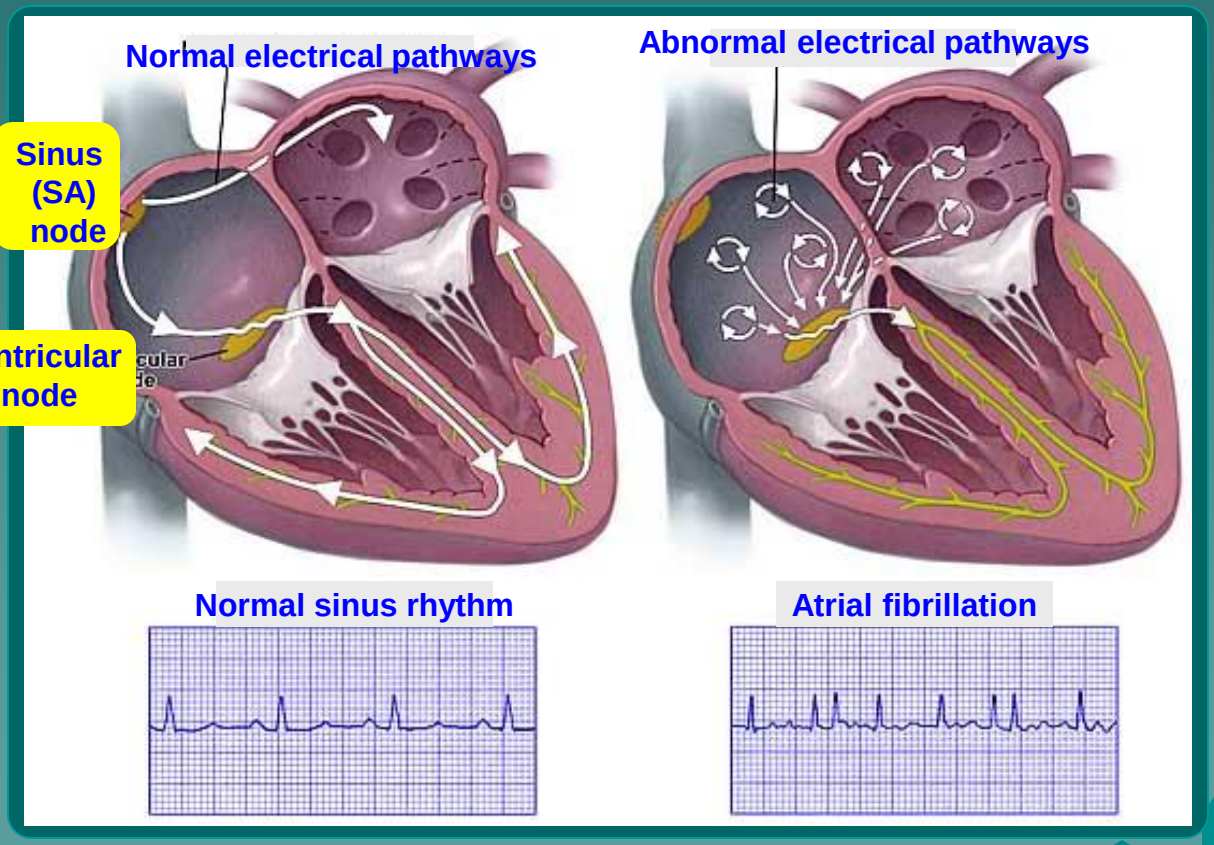
AF Pathophysiology

- Normal cardiac conduction is coordinated by rhythmic spontaneous depolarization of the sinoatrial node (SAN)
- SAN impulse causes atrial myocyte contraction, and conduction spreads across atrium toward the atrioventricular node (AVN)
- AVN slows conduction and coordinates rapid depolarization of the His-Purkinje system through the right and left bundle branches (RBB, LBB)
- Depolarization of endocardial to epicardial surface ensues with synchronous ventricular contraction and compressive ejection of stroke volume



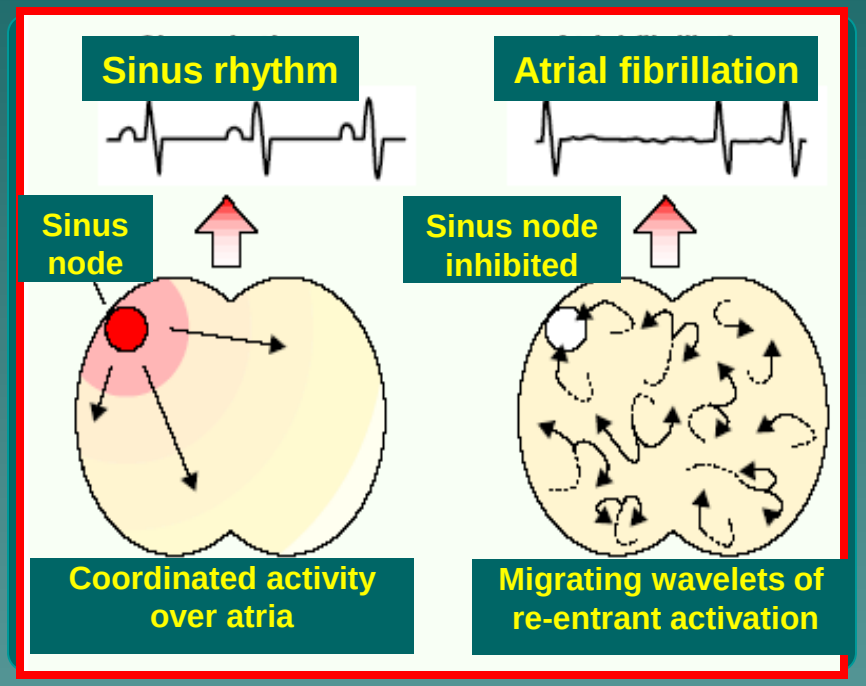
AF Pathophysiology (CONT'D)

- The hallmark of AF is chaotic atrial impulses leading to irregularly irregular ventricular contraction, usually with incessant tachycardia



AF Pathophysiology (CONT'D)

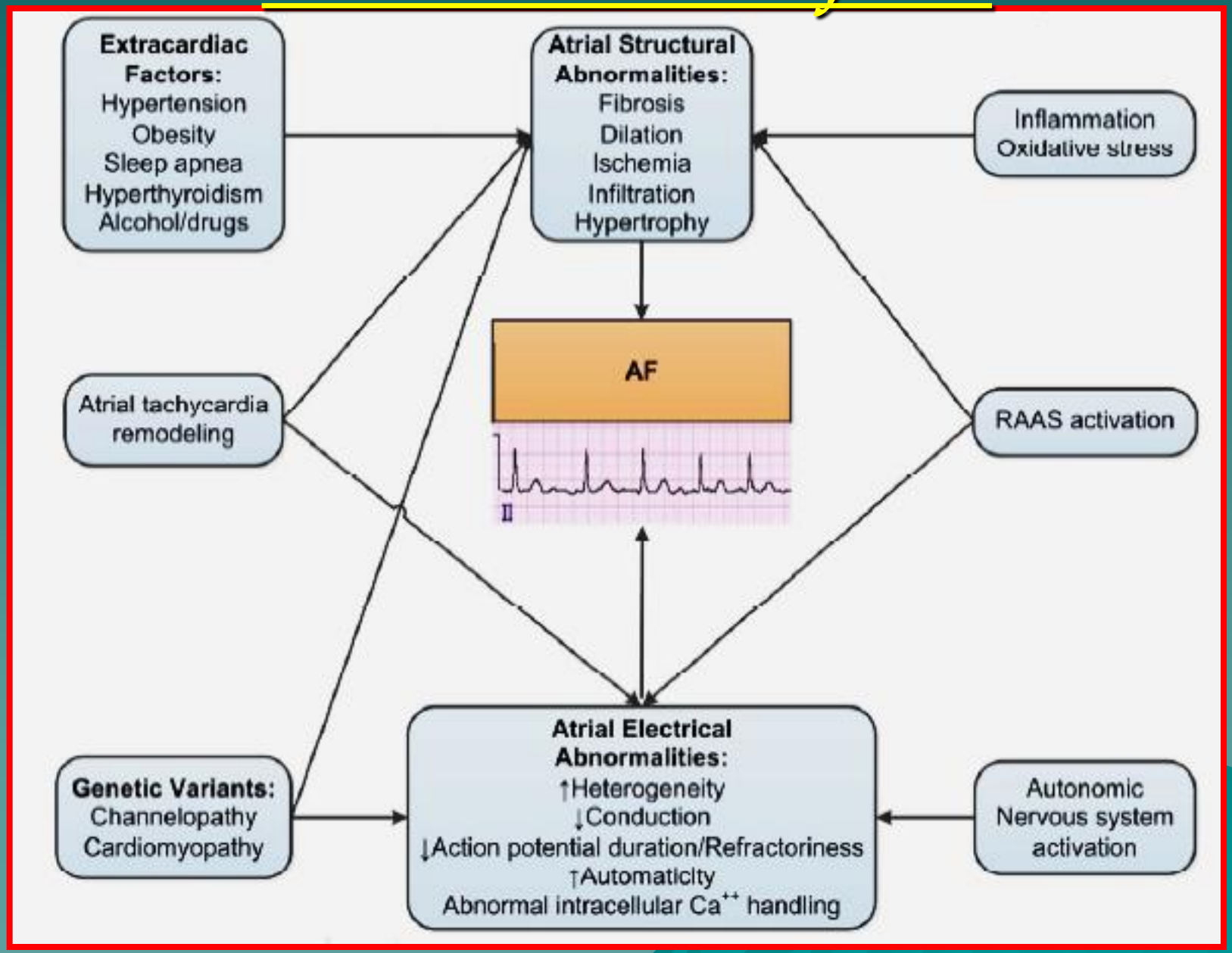
- During AF, the atria contract at a rate of 350 to 900 bpm, conducting to the ventricles at 90 to 170 bpm
- Traditional mechanism theory: AF is maintained by migrating wavelets of reentrant atrial activation
- Wavelet collisions cause chaotic reexcitation and "multiple propagating wavelets"



AF compared with sinus rhythm. AF is characterized by multiple electrical wavelets in the atria. Disorders that increase atrial size, decrease tissue wavelength, or affect both may increase the propensity for AF.

Adapted from Narayan SN, et al. *Lancet.* 1997;350:943-950.

Mechanisms of AF



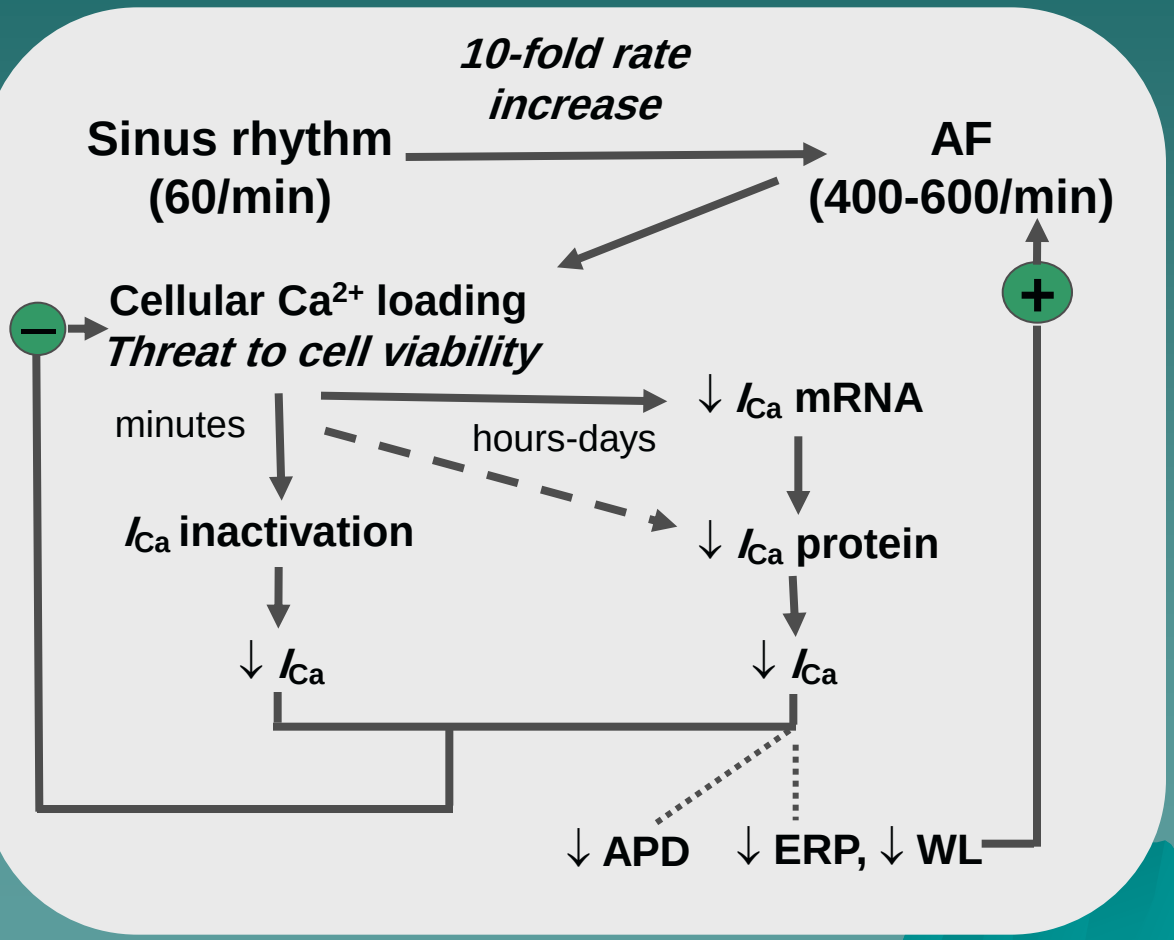
"AF Begets AF"

- With time, remodeling of atrial tissue and the conduction system causes chronic AF and makes conversion from AF to sinus rhythm more difficult
- Lack of contraction leads to increased left atrial diameter; "mechanical remodeling" may result from atrial fibrosis
- AF may also be triggered by premature atrial contractions, repetitive firing from pulmonary veins, or atrial flutter
- 1995: elegant studies in the goat model of AF prove that "AF begets AF"
- The longer atrial tissues experience chaotic electrical activity, the more likely they are to remain in AF

Wijffels MCEF, et al. *Circulation.* 1995;92:1954-1968.

Prolonged Tachycardia Leads to Ca^{2+} Overload in Atrial Myocytes, Causing "Electrical Remodeling"

A schema of the potential pathogenesis of atrial tachycardia remodeling. Ca^{2+} loading due to increased rates causes a threat to cell viability which is prevented by short- and long-term adaptations that reduc Ca^{2+} entry, providing protective negative feedback on Ca^{2+} loading, APD abbreviation, and positive feedback on AF likelihood by reducing ERP and WL.

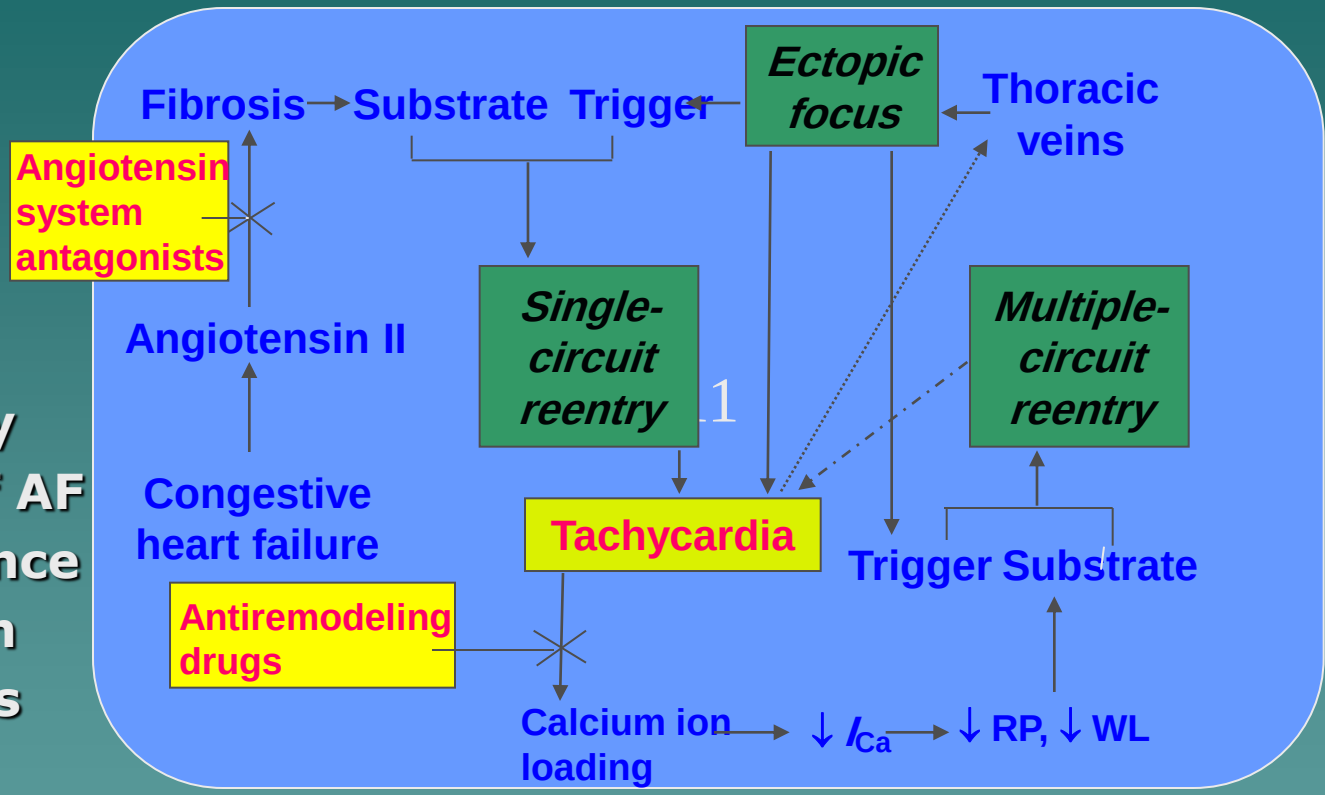


APD = action potential duration; ERP = effective refractory period; WL = wavelength.

Adapted from Shiroshita-Takeshita A, et al. *J Interv Card Electrophysiol.* 2005;13:181-193.

Atrial Remodeling

- Potential basis for suppression of AF in chronic CHF by ACE inhibitors and angiotensin receptor blockers
- Pulmonary vein ablation therapy may target ectopic foci of AF And prevent recurrence more effectively than rhythm-control drugs



Rapid atrial tachycardia causes atrial remodeling by down-regulating L-type calcium channel function (I_{Ca}), thereby accelerating atrial repolarization, reducing the refractory period and wavelength, and promoting reentry. Remodeling may also be able to promote ectopic activity in the thoracic veins. CHF activates the RAS and causes atrial fibrosis. Specific drug therapy might attenuate tachycardia-induced and fibrotic atrial remodeling and help prevent AF.

Shiroshita-Takeshita A, et al. *J Interv Card Electrophysiol.* 2005;13:181-193.

Pathophysiology: Ectopic AF Foci

- 1998 marks discovery that AF could be caused by a rapidly firing focus (usually in the superior pulmonary veins) and eliminated by focal ablation
- "Highest dominant frequency" may be the factor, originating in the pulmonary vein, inferior vena cava, or right atrium, that drives the AF wave front

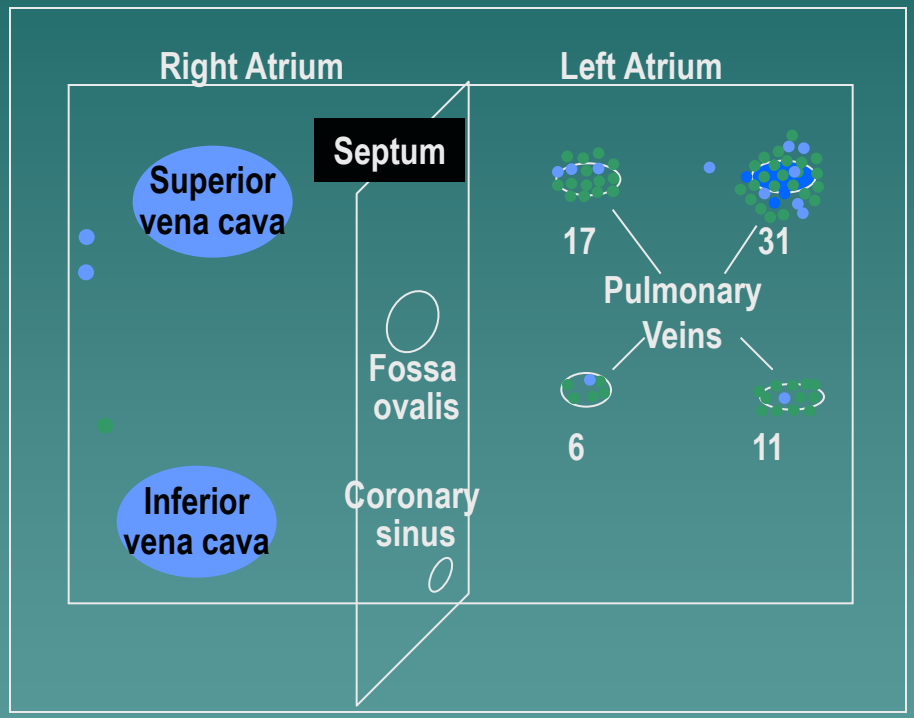
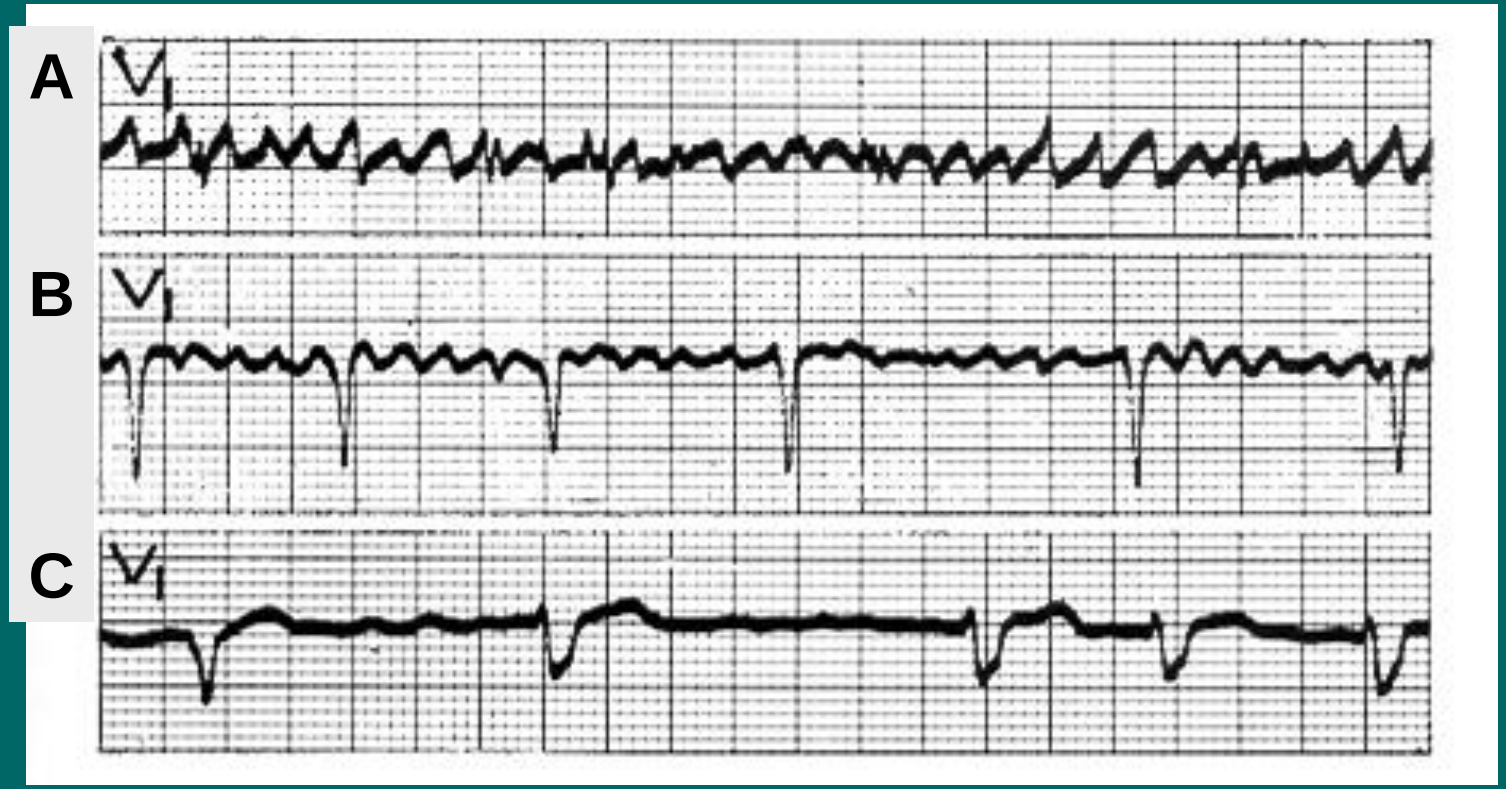


Diagram of the sites of 69 foci triggering AF in 45 patients. Note the clustering in the pulmonary veins, particularly in both superior pulmonary veins. Numbers indicate the distribution of foci in the pulmonary veins.

Adapted from Haissaguerre M, et al. *N Engl J Med.* 1998;339:659-666.

Atrial Fibrillatory Waveforms



Coarse (A), medium (B), and fine (C) atrial fibrillation, each with irregular ventricular response.

From Marriot HJL. *Practical Electrocardiography.* 7th ed. Baltimore: Williams & Wilkins; 1983.

Acute AF

- Acute AF = episode <48 hours
- In two thirds of patients with acute AF, conversion to sinus rhythm occurs spontaneously within 24 hours, and in half of the remaining third within 48 hours[1]
- Paroxysmal AF occurs in fits, accompanied by rapid ventricular conduction
- Permanent chronic AF is generally found to be a frequent outcome of paroxysmal AF, developing within a few years of the first arrhythmic episode[2]

Danias PG, et al. *J Am Coll Cardiol.* 1998;31:588-592.
Kerr CR, et al. *Am Heart J.* 2005;149:489-496.

AF Risk Factors and Causes

- **Electrophysiologic abnormalities**
  - Enhanced automaticity (focal AF)
  - Conduction abnormality (reentry)
- **Atrial pressure elevation**
  - M or T valve disease
  - Myocardial disease
  - Semilunar valvular disorders
  - Ventricular hypertrophy
  - Systemic or pulmonary hypertension
  - Pulmonary embolism
  - Intracardiac tumors or thrombi
- **Atrial ischemia**
  - Coronary artery disease
- **Inflammatory or infiltrative atrial disease**
  - Pericarditis
  - Amyloidosis
  - Myocarditis
  - Age-induced atrial fibrotic changes
- **Endocrine disorders**
  - Hyperthyroidism
  - Pheochromocytoma

AF Risk Factors and Causes (CONT'D)

- **Drugs**
  - Alcohol
  - Caffeine
- **Changes in autonomic tone**
  - Increased parasympathetic activity
  - Increased sympathetic activity
- **Neoplasm in or adjacent to atrial wall**
- **Postoperative**
  - Cardiac, pulmonary, esophageal surgery
  - Congenital heart disease
- **Neurogenic**
  - Subarachnoid hemorrhage
  - Major nonhemorrhagic stroke
- **Idiopathic (lone AF)**
- **Familial AF**

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Independent Risk Factors for AF: the Framingham Heart Study

Risk Factor	Relative Risk (95% CI)	
	Men	Women
Heart failure	4.5 (3.1-6.6)	5.9 (4.2-8.4)
Age (per decade)	2.1 (1.8-2.5)	2.2 (1.9-2.6)
Valve disease	1.8 (1.2-2.5)	3.4 (2.5-4.5)
Hypertension	1.5 (1.2-2.0)	1.4 (1.1-1.8)
Diabetes mellitus	1.4 (1.0-2.0)	1.6 (1.1-2.2)
Acute MI	1.4 (1.0-2.0)	1.2 (0.8-1.8)

In addition to traditional risk factors for AF, recent prospective studies show that the risk for developing AF is increased by the induction of atrial myocyte fibrosis under stimulation by angiotensin I and angiotensin II and by chronic inflammation as marked by elevated serum CRP levels.

Heist EK, Ruskin JN. *Prog Cardiovas Dis.* 2006;48:256-269.

Clinical Sequelae of AF

- Clinical sequelae of AF relate to loss of atrial "kick" and inadequate time for ventricular filling, with reduced cardiac output
- AF may lower stroke volume as much as 20%
- Cardiac output typically falls 0.8-1.0 L/min, and pulmonary artery occlusion pressure rises 3-4 mm Hg in human models of AF with rapid ventricular rate versus paced atrial tachycardia (conserved atrial contraction)
- Hemodynamics may be compromised by preexisting MS, LVH, restrictive cardiomyopathy, or diastolic heart failure. These conditions are dependent on atrial contraction to maintain cardiac output

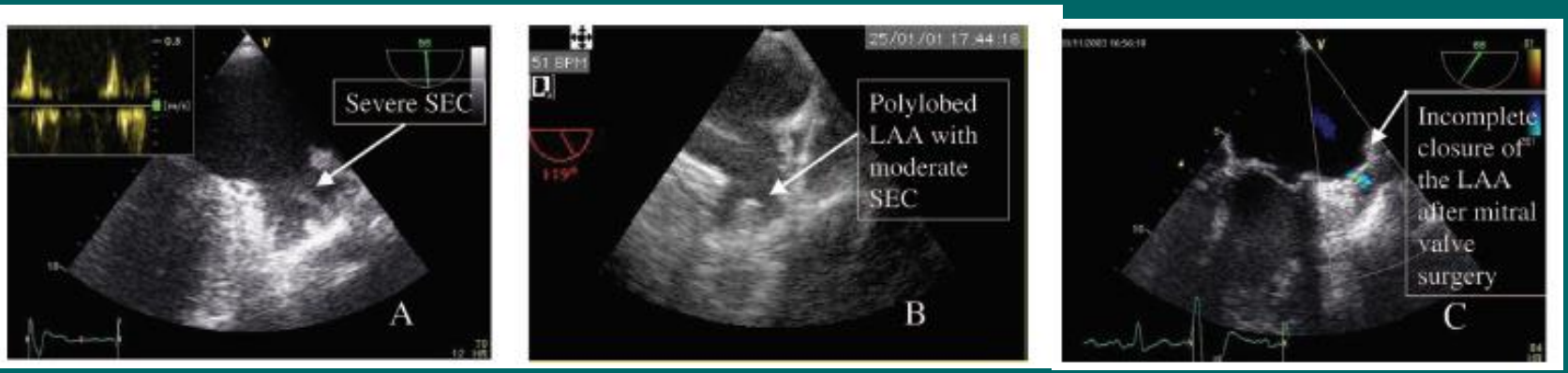
Clinical Sequelae of AF (CONT'D)

- Tachycardia-induced cardiomyopathy resulting from Ca^{2+} toxicity
- Rapid ventricular responses may be triggered by fever, sepsis, volume depletion, gastrointestinal bleeding, medication noncompliance, or uncontrolled hyperthyroidism
- Patients with Wolfe-Parkinson-White syndrome are at risk for AF (15% to 20% of patients) with conversion to ventricular fibrillation via relentless conduction across an accessory pathway
- 15% of patients with hypertrophic cardiomyopathy develop AF leading to rapid deterioration

AF and Stroke – Pathophysiology: LAA Thrombus

- More than 90% of all cardioembolic strokes in patients with AF arise from LAA thrombi
- With TEE, assess LAA size; presence of spontaneous echo contrast (SEC), representing turbulent blood pooling; and A-wave (active) and E-wave (passive) emptying of the LAA, which are reduced with elevated left ventricular end-diastolic pressures
- Left atrial cavity thrombus was found by TEE in 2% of patients with chronic AF (Cleveland Clinic study); LAA thrombus was found in 12% of patients and was strongly associated with SEC

Left Atrial Appendage (CONT'D)



A. Example of a polylobed LAA with severe SEC and the corresponding pulsed Doppler of LAA flows.
B. Second example of polylobed LAA.
C. Example of an LAA ligated by the surgeon at the time of mitral valvuloplasty. The ligature is incomplete and there is still flow between the LAA and the left atrial cavity.

Adapted from Donal E, et al. *Chest.* 2005;128:1853-1862.

Evaluation of Patients With AF

Minimum Evaluation

- **History and physical examination**
  - Presence and nature of AF symptoms
  - Clinical type of AF (first episode, paroxysmal, persistent, or permanent)
  - Onset (first symptomatic attack or date of discovery of AF
  - Frequency, duration, precipitating factors, and modes of termination of AF
  - Response to any drugs that have been given
  - Presence of underlying heart disease or other reversible condition
- **Electrocardiogram**
  - Rhythm (verify AF)
  - P-wave duration and morphology or fibrillatory waves
  - Preexcitation
  - Bundle-branch block
  - Prior MI
  - Other atrial arrhythmias
  - R-R, QRS, and QT intervals in conjunction with antiarrhythmic drug therapy

Evaluation of Patients With AF (CONT'D)

Minimum Evaluation

- **TTE to identify**
  - Valvular heart disease
  - LA and RA size
  - LV size and function
  - Peak RV pressure (pulmonary hypertension)
  - LV hypertrophy
  - LA thrombus (low sensitivity)
  - Pericardial disease
- **Blood tests of thyroid, renal, and hepatic function**
  - For first episode of AF, when ventricular rate is difficult to control

Additional Testing

- Six-minute walk test
  - If adequacy of rate control is in question
- Exercise testing
  - If adequacy of rate control is in question (permanent AF)
  - To reproduce exercise-induced AF
  - To exclude ischemia before treatment of selected patients with a type IC anti-arrhythmic drug
- Holter monitoring
  - If diagnosis of the type of arrhythmia is in question
  - As a means of evaluating rate control

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Evaluation of Patients With AF (CONT'D)

Additional Testing

- TEE:
  - To identify LA thrombus (in the LA appendage)
  - To guide cardioversion
- Electrophysiologic study
  - To clarify the mechanism of wide-QRS-complex tachycardia
  - To identify a predisposing arrhythmia such as atrial flutter or paroxysmal SVT
  - To seek sites for curative ablation or AV conduction block/modification
- Chest radiograph,

  to evaluate
  - Lung parenchyma, when clinical findings suggest an abnormality
  - Pulmonary vasculature, when clinical findings suggest an abnormality

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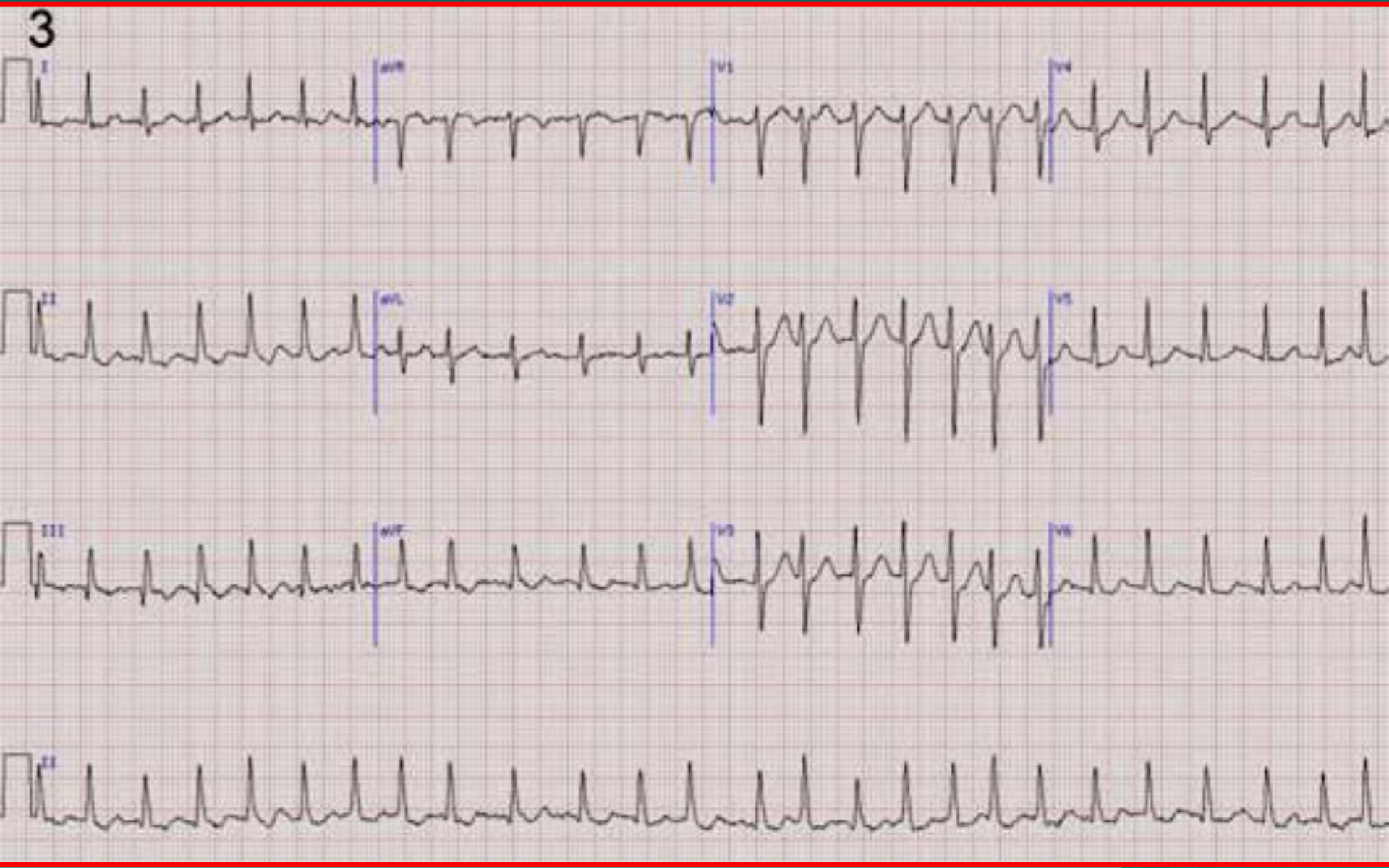
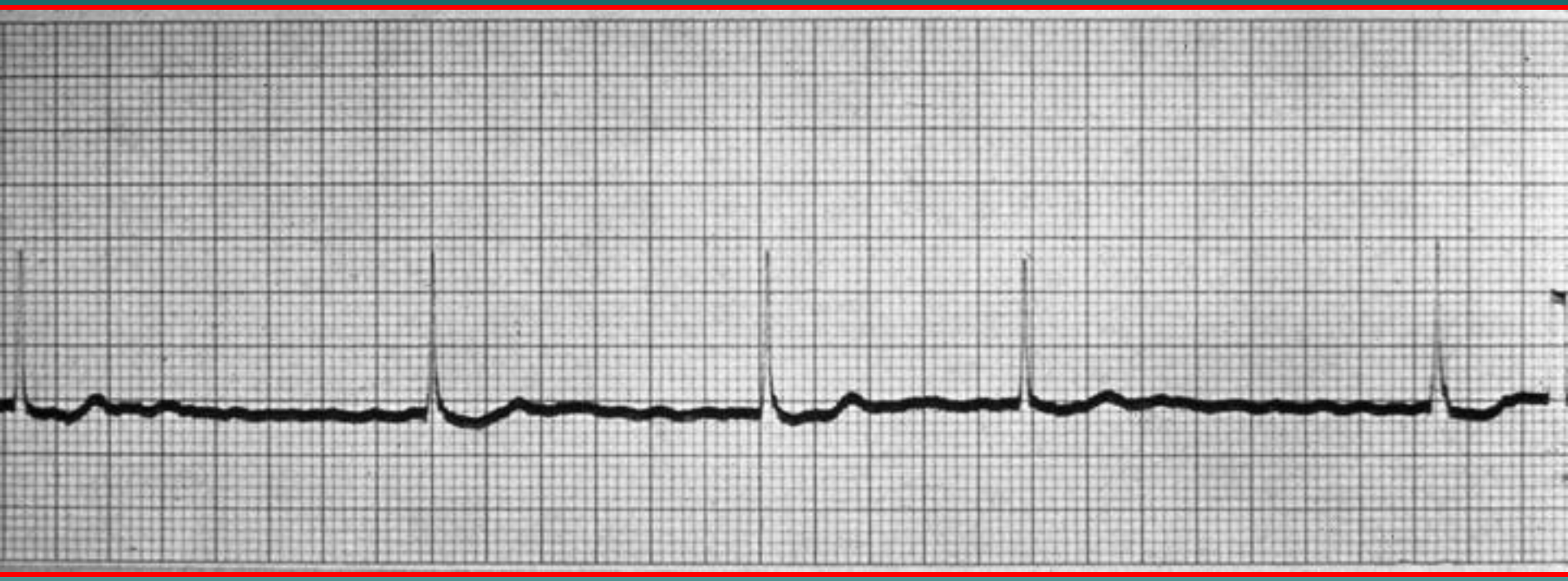
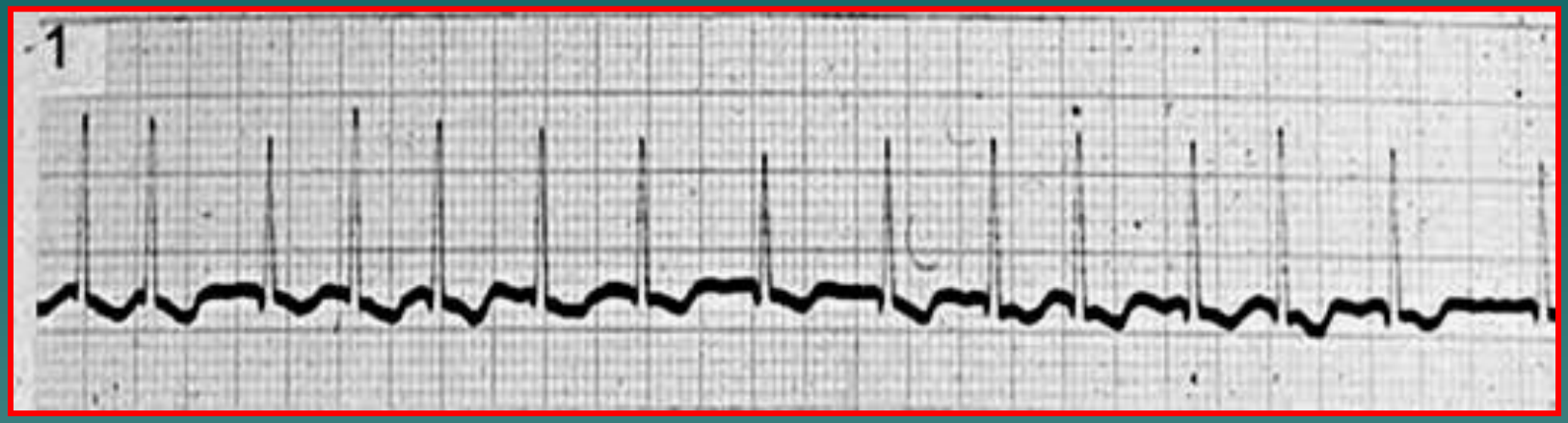
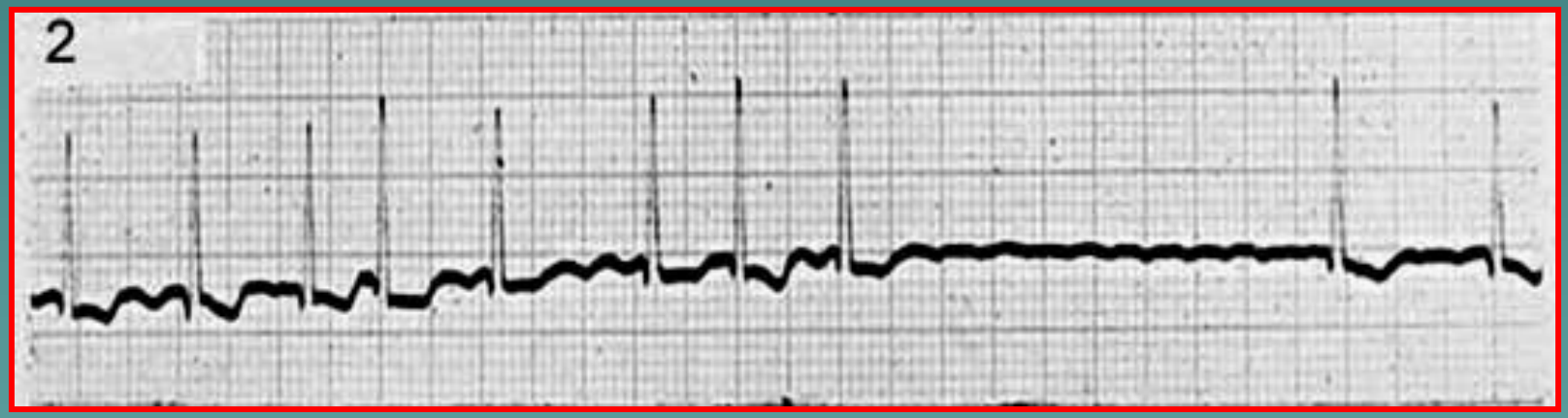


Rapid AF

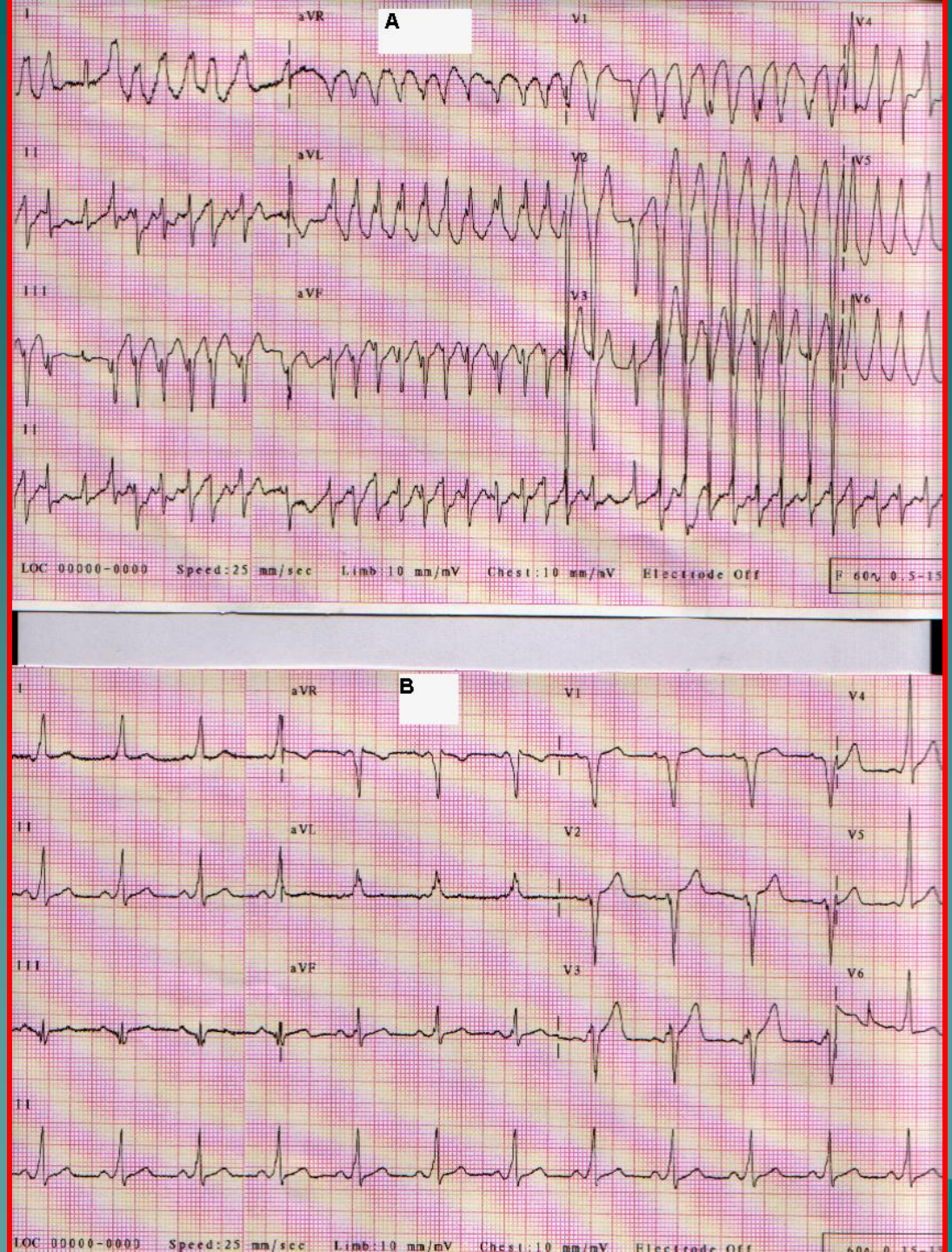


Slow AF





AF before 1 and after 2
IV adenosine


A
I
aVR
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V4
II
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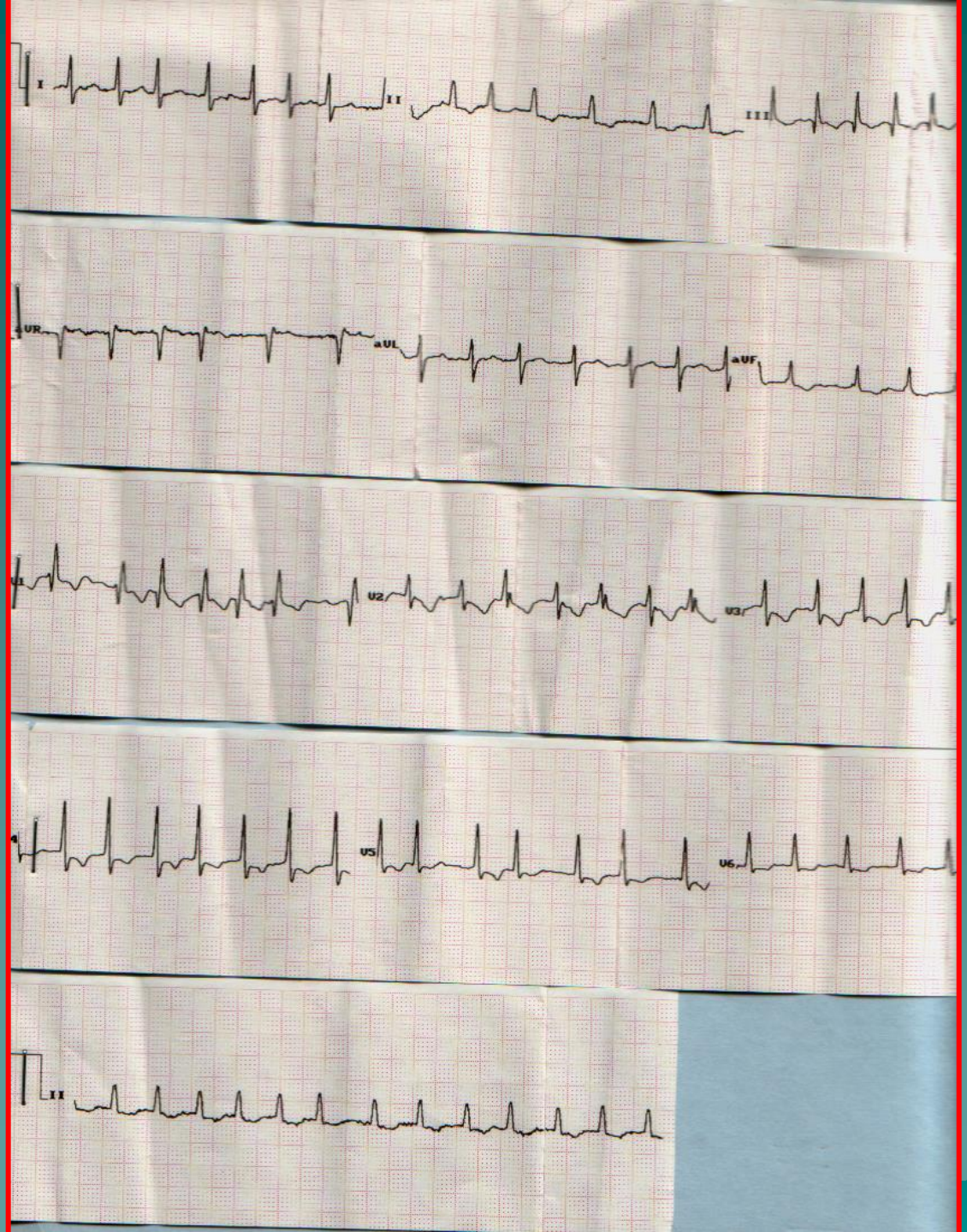
AF with WPW



AF in
? Pulmonary embolism

Risk score definitions

$CHADS_2$ acronym	
Congestive HF	1
Hypertension	1
Age ≥75 y	1
Diabetes mellitus	1
Stroke/TIA/TE	2
Maximum Score	6
CHA_2DS_2-VASc acronym	
Congestive HF	1
Hypertension	1
Age ≥75 y	2
Diabetes mellitus	1
Stroke/TIA/TE	2
Vascular disease (prior MI, PAD, or aortic plaque)	1
Age 65–74 y	1
Sex category (i.e., female sex)	1
Maximum Score	9

Stroke risk stratification

	Adjusted stroke rate (% per y)
$CHADS_2$ acronym*	
0	1.9%
1	2.8%
2	4.0%
3	5.9%
4	8.5%
5	12.5%
6	18.2%
CHA_2DS_2-VASc acronym†	
0	0%
1	1.3%
2	2.2%
3	3.2%
4	4.0%
5	6.7%
6	9.8%
7	9.6%
8	6.7%
9	15.20%

Thank You