

Atrial Fibrillation

Where We've Been and What Lies Ahead

David Stultz, MD

Cardiology Fellow, PGY 5

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Patient Presentation

- A 76 year old male with history of hypertension and hyperlipidemia presents for routine examination. You detect an irregular pulse and heart rate. An EKG confirms atrial fibrillation with a heart rate of 85.
- New Diagnosis of Atrial Fibrillation
 - What tests?
 - What medications?

Atrial Fibrillation

- Most common sustained arrhythmia
- Estimated 2.3 million patients in the United States
- Incidence of 3.8% in patients >60 years
- Incidence of 9% in patients >80 years
- Increases relative risk of death 1.3-2x

CONDITIONS RELATED TO ATRIAL FIBRILLATION

Cardiac causes	Noncardiac causes
Hypertensive heart disease	Autonomically mediated (sympathetic or parasympathetic)
Valvular disease	Toxin exposure
Coronary heart disease	Endocrinopathy (especially thyroid disease)
Cardiomyopathy (all forms)	Pulmonary disease
Pericardial disease	Neurologic disorders
Intracardiac masses	Idiopathic
Electrical disease Sinus node dysfunction Tachycardia-induced Familial	
Cardiothoracic surgery	
Congenital heart disease	

Etiology - Hypertensive

- Hypertensive heart disease
 - Accounts for about 50% of cases in developed countries
 - May be due to LA dilatation secondary to decreased LV compliance
 - Associated CAD

Etiology - Valvular

- Valvular Heart Disease
 - Mitral stenosis due to rheumatic disease
 - Increased stroke risk – 20% of patients with AF and MS will have embolic event
 - Stroke risk 3-7x that of sinus rhythm with MS
 - AF is infrequent with isolated Aortic stenosis

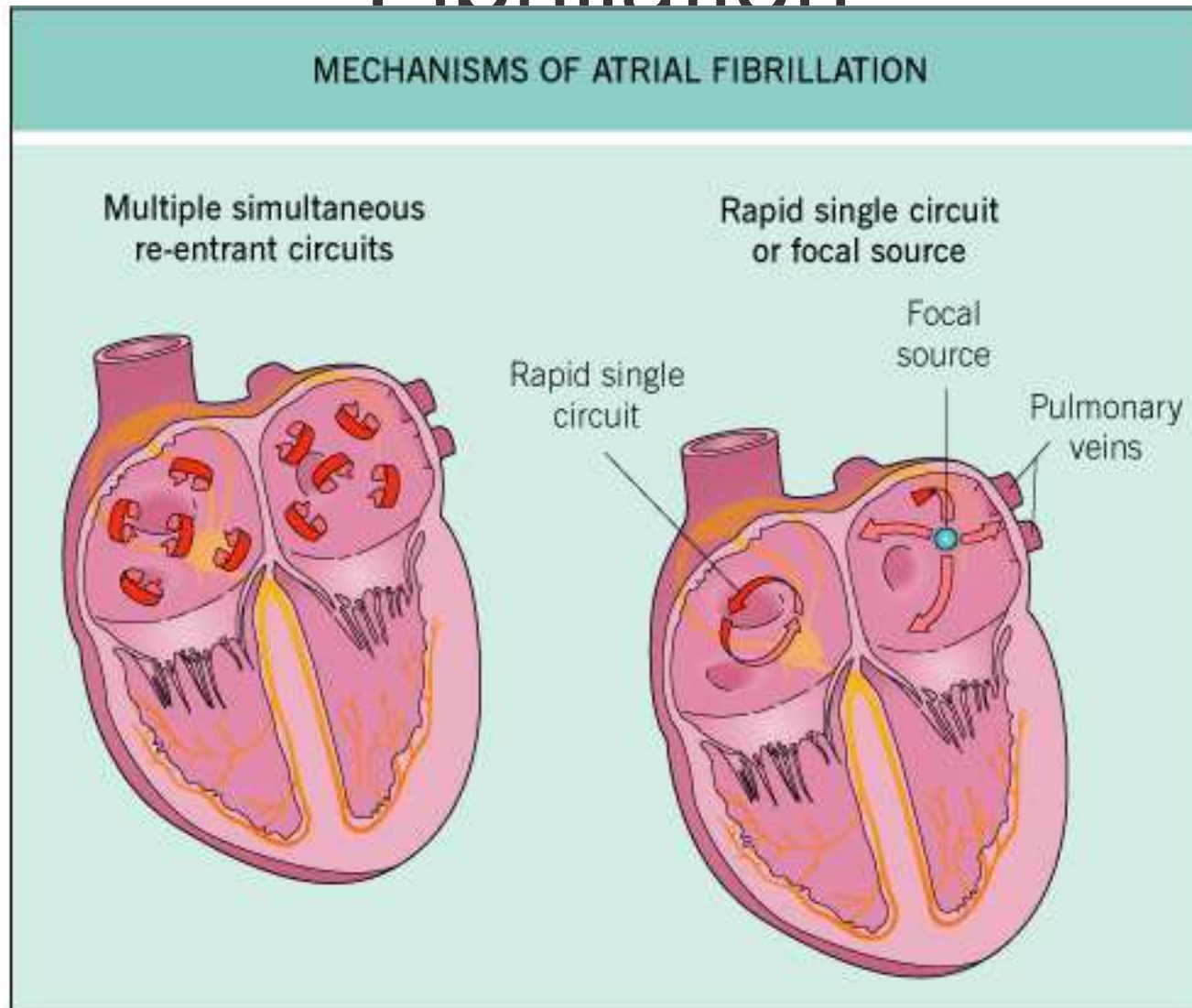
Etiology - Surgery

- Cardiac Surgery
 - Common complication of cardiac surgery
 - 20-40% incidence following CABG, often postoperative days 2-8
 - Risk of AF following surgery
 - Elderly
 - Prior AF
 - Right coronary artery stenosis
 - Beta blockers discontinued preoperatively

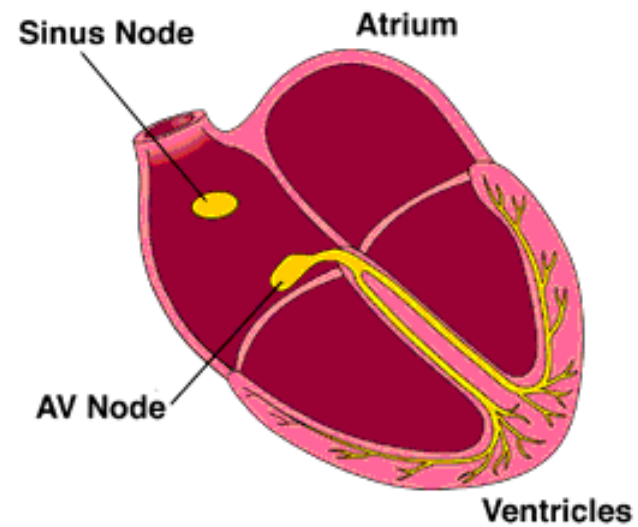
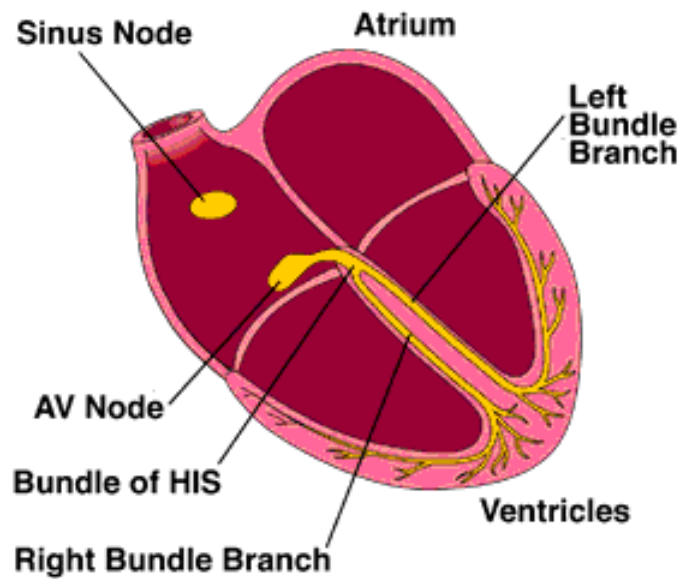
Etiology - Other

- Thyroid disease
 - Occurs in 20-25% of elderly with thyrotoxicosis
 - About 1% of new onset AF is due to hyperthyroidism
- Alcohol
 - Common cause of AF
 - Seen in up to 60% of binge drinkers
 - AF episodes coincide with heavy intake
- Cardiomyopathy
 - AF present in 28% of patients with hypertrophic cardiomyopathy
 - AF occurs in 20% of those with dilated cardiomyopathy
- Familial
 - Autosomal dominant – chromosome 10q22-q24

Mechanism of Atrial Fibrillation



Sinus Rhythm vs. Atrial Fibrillation



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Clinical Classification

- Acute – AF related to transient or reversible cause, or 1st episode of AF
- Chronic
 - Paroxysmal – self-terminating AF
 - Sustained
 - Persistent – AF that can be cardioverted
 - Permanent – AF that is resistant to cardioversion or inappropriate for cardioversion

Situational variants

- Vagal mediated – occurs at night or after meals
- Adrenergic mediated – AF during exercises, stress

Paroxysmal AF may become chronic

(8% at 1 year, 18% at 4 years)

Symptoms

- Asymptomatic – discovered by auscultation, pulse palpation, EKG, or Holter
- Major symptoms
 - Heart Failure
 - Angina
 - Hypotension
 - Presyncope
 - Syncope – usually with pre-excitation, hypertrophic cardiomyopathy, or aortic stenosis
 - Stroke
 - Systemic Embolization

Symptoms

- Minor symptoms
 - Palpations
 - Racing heart
 - Fatigue
 - Light-headedness
 - Increased urination
 - Shortness of breath

Initial Evaluation

INITIAL EVALUATION OF PATIENTS WITH ATRIAL FIBRILLATION

Minimum evaluation

History and physical exam

ECG

Chest X-ray

Echocardiogram

Laboratory studies – thyroid, renal function

Optional studies

Exercise testing or ambulatory ECG

Transesophageal echocardiogram

Electrophysiologic study

History

- Symptoms
- Sustained or intermittent
- Complications
- Precipitating factors
- Relief of symptoms
- Duration/Frequency
- Prior treatment

Blood Tests

- Complete Blood Count
- Electrolytes
- Renal function
- Thyroid function

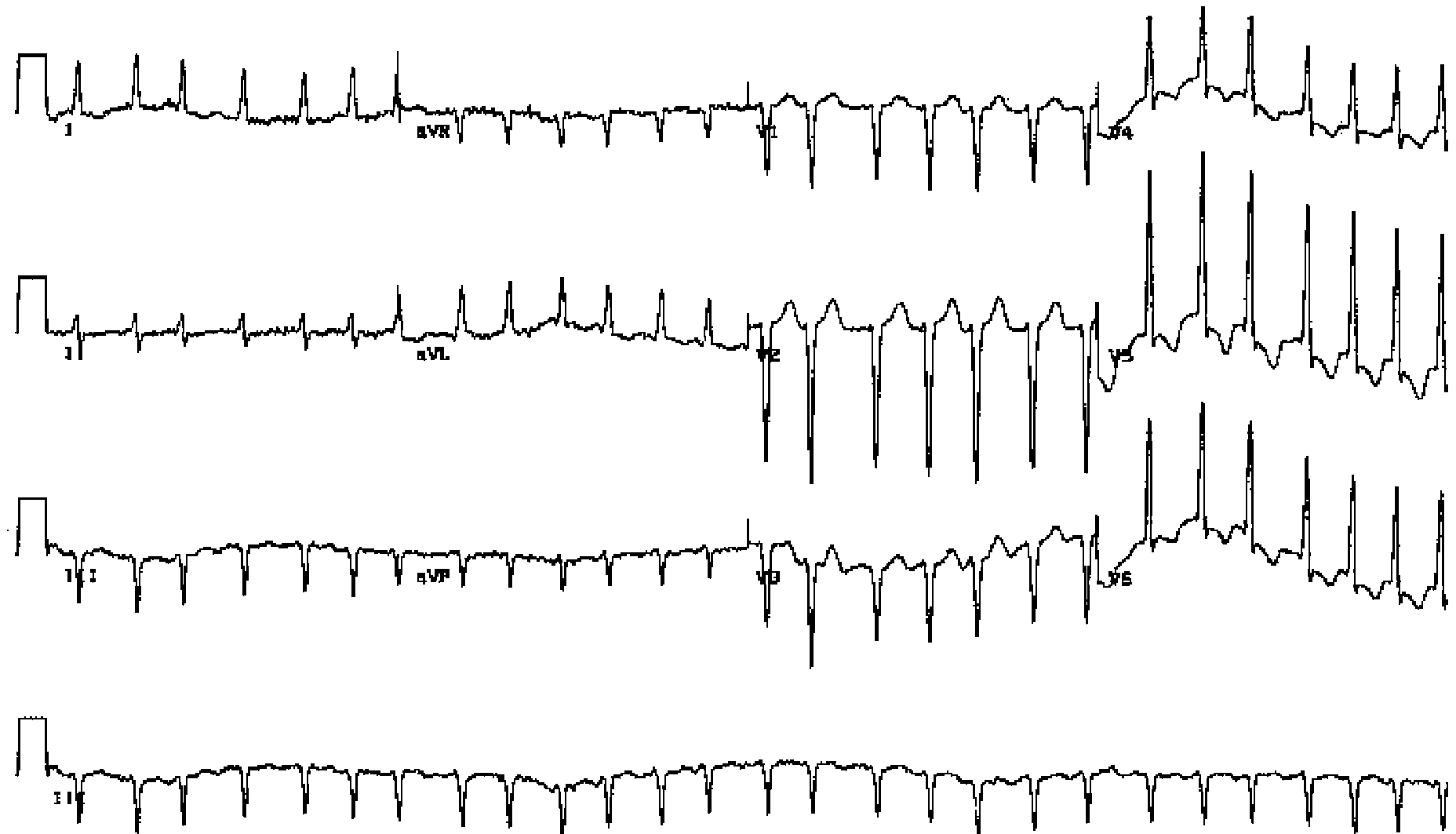
Chest X-ray

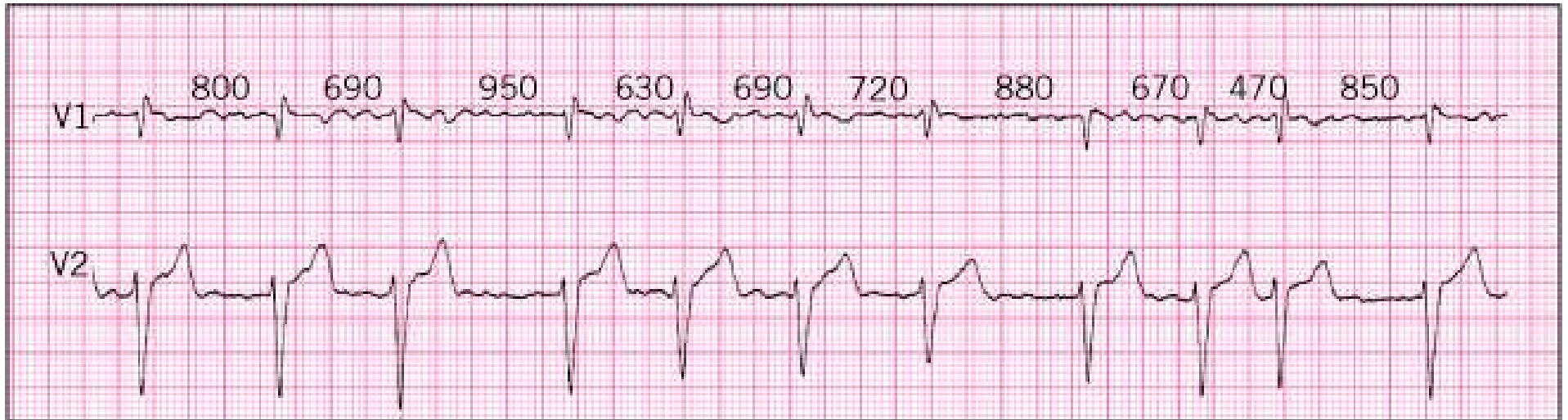
- May show congenital heart disease (ASD)
- Heart Size
- Presence of heart failure
- Coexisting intrathoracic pathology

EKG

- Rapid baseline oscillations
- Irregularly Irregular ventricular rate
- Absence of P waves
- ? Etiology
 - Left ventricular hypertrophy
 - Prior myocardial infarction
 - Pre-excitation

Atrial Fibrillation on EKG





Echocardiography

- Structural heart disease?
 - Valvular abnormalities
 - Congenital defects
 - Chamber size
 - Significant left atrial enlargement reduces success of cardioversion and long term maintenance of sinus rhythm. Also, LAE may increase risk of stroke
 - Pericardial thickening or effusion
 - Ventricular function

Electrophysiologic testing

- Limited role
- Atrial flutter or Supraventricular tachycardia is cause of atrial fibrillation
- Other symptoms (pre-excitation, sinus node dysfunction, syncope) need clarification
- Focal source amenable to ablation

Other studies

- Exercise stress testing
 - Anginal symptoms during episodic atrial fibrillation with rapid ventricular response or independent of atrial fibrillation
 - Assess for rate control during drug therapy
- Cardiac catheterization
 - Usually only indicated if symptoms or noninvasive tests suggest active ischemia

Pre-Management Assessment

- Are there any other associated arrhythmias or conduction abnormalities?
 - Pre-excitation
 - AV block
- Are there predisposing factors? Are they reversible or preventable?
- Is there a need for urgent intervention?
 - Hemodynamic instability
- Is there a need for rhythm control, or is rate control sufficient?

Acute Atrial Fibrillation Management

- Hemodynamic compromise – DC cardioversion
- Consider IV Heparin
- Rate control
 - Beta blockers
 - Calcium Channel Blockers
 - Digoxin
- Cardioversion if <48 hours duration

Paroxysmal Atrial Fibrillation Management

- Goals
 - Reduce frequency of paroxysms
 - Control rate during paroxysms
 - Prevent thromboembolism
- Digoxin may increase frequency and duration of paroxysms
- Calcium channel and Beta blockers may control ventricular rate, but not reduce frequency of attacks
- Antiarrhythmic therapy
 - Flecainide or propafenone considered in absence of structural heart disease
 - “Pill in the pocket” strategy

Chronic Atrial Fibrillation Management

- Underlying etiology?
- Rate control vs rhythm control
 - Heart rate 60-80 at rest, 90-115 during moderate exercise
- Thromboembolic prophylaxis

Risks for cardioversion failure and failure to maintain sinus rhythm

- Advanced age
- Duration of atrial fibrillation
 - Unlikely to maintain sinus rhythm when atrial fibrillation > 2 years duration
- Uncontrolled hypertension
- Severity of structural heart disease
 - Severe left atrial dilatation
- Other systemic diseases

Cardioversion

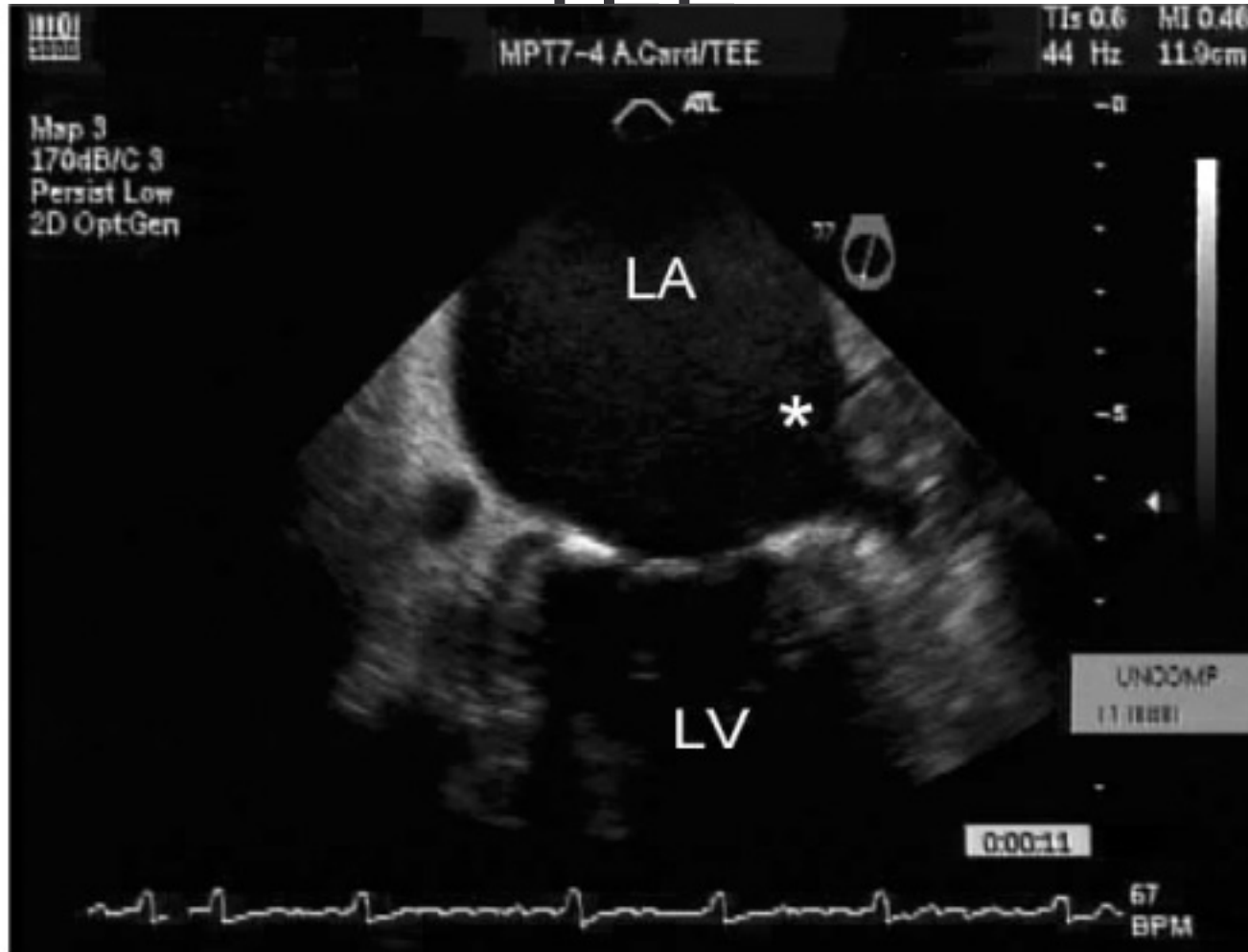
- Thromboembolism rare when AF duration is <48 hours
- When AF duration is >48 hours, thromboembolism occurs in 7% when no anticoagulation is used
- Most embolic events occur in 1st week after cardioversion

TEE before cardioversion

- Atrial fibrillation >48h or unknown
- Used to minimize duration of atrial fibrillation or reduce total anticoagulation time
- Evaluate for thrombus in the left atrial appendage
- If no thrombus, then may cardiovert followed by anticoagulation x 4 weeks
- If thrombus present, anticoagulation x 4 weeks then re-evaluate with TEE

Thrombus in left atrial appendage

TEE



Anticoagulation and Cardioversion

RECOMMENDATIONS FOR ANTICOAGULATION IN CARDIOVERSION OF ATRIAL FIBRILLATION		
Duration of arrhythmia	Anticoagulation before cardioversion	Anticoagulation after cardioversion
<48 hours	Not required	Optional based on risk for recurrence
>48 hours	Warfarin to achieve INR of 2–3 for 3 weeks, or	Warfarin to achieve INR of 2–3 for >4 weeks
	Transesophageal echocardiogram negative for thrombus	Heparin, then warfarin to achieve INR of 2–3 for >4 weeks

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Electrical Cardioversion

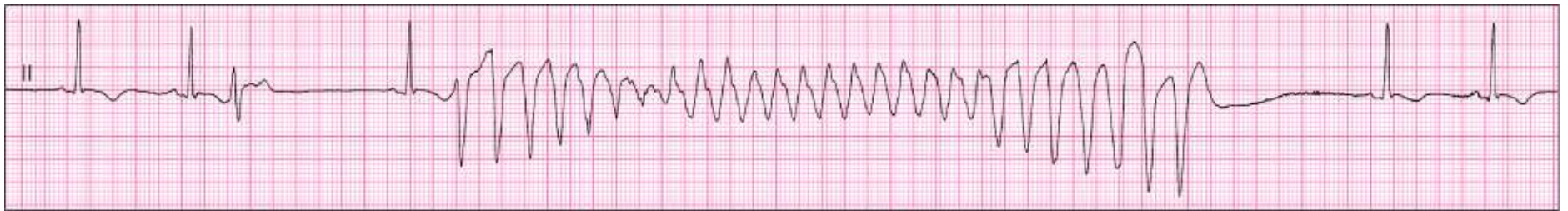
- Synchronized
- 200 J monophasic or 125J biphasic
- Ibutilide or other class III antiarrhythmic may facilitate cardioversion
- Reports of intracardiac shock or transthoracic shock up to 720J used in refractory cases

Nonembolic complications of electrical cardioversion

- Ventricular arrhythmia
- Sinus bradycardia
- Hypotension
- Pulmonary edema
- Skin burns
- Transient ST and T wave abnormalities

Torsades de Pointes

Following chemical cardioversion with ibutilide



Chemical cardioversion

- Many cases of new onset atrial fibrillation will spontaneously convert to sinus rhythm within 48

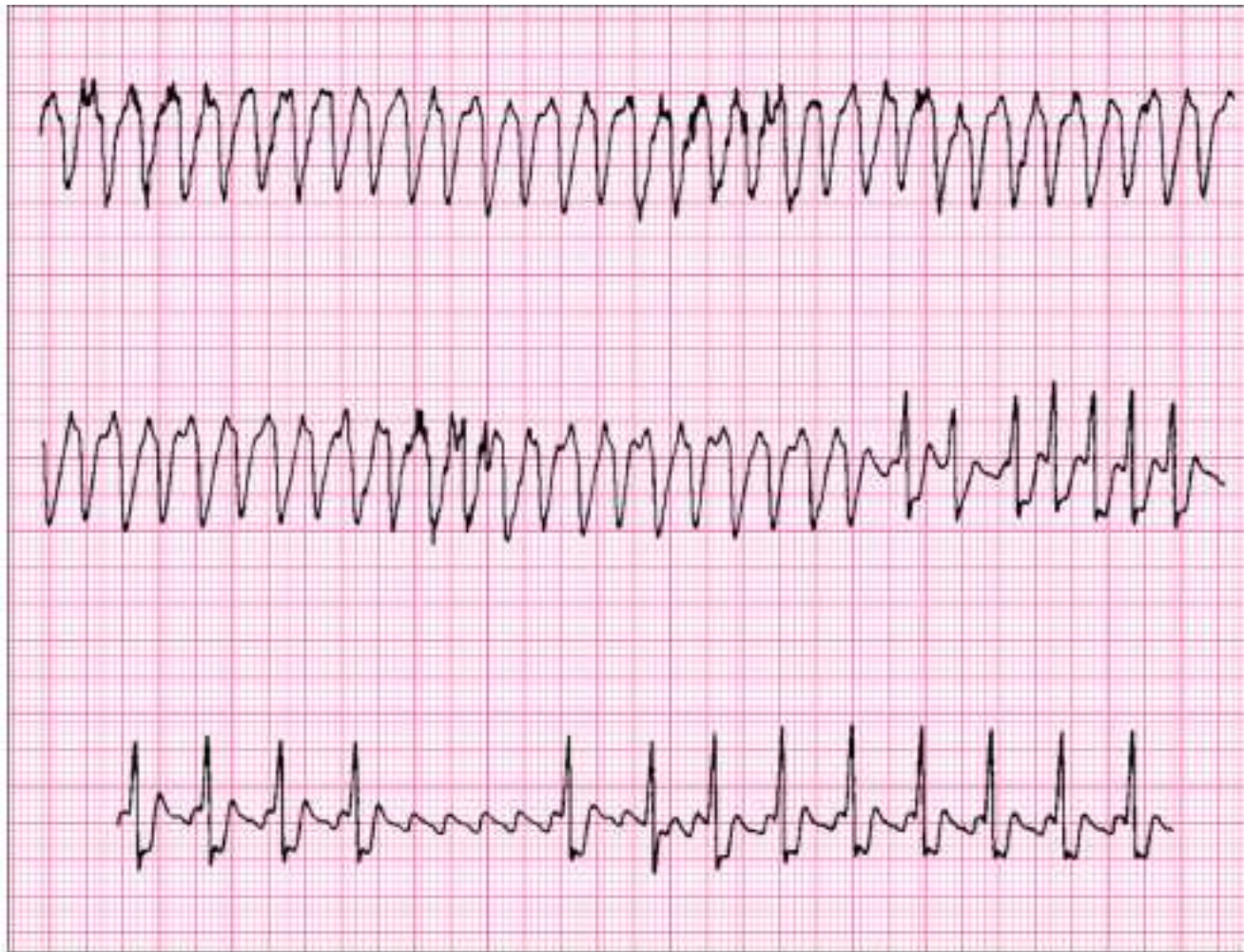
ANTIARRHYTHMIC DRUG DOSES FOR PHARMACOLOGICAL CARADIOVERSION AND PREVENTION OF ATRIAL FIBRILLATION RECURRENCES			
		iv or oral therapy for rapid conversion	Chronic oral drug therapy to prevent recurrence*
Class IA drugs	Procainamide	500–1200mg iv over 30–60 minutes	2000–4000mg/day
	Quinidine sulfate	Not recommended	600–1200mg/day
	Disopyramide	Not recommended	450–600mg/day
Class IC drugs	Flecainide	1.5–3.0mg/kg iv over 10 minutes [†] 200–400mg po	150–300mg/day
	Propafenone	1.5–2mg/kg IV over 10–20 minutes [†] 300–450 mg po	400–600mg/day
Class III drugs	Ibutilide	1mg iv over 10 minutes, repeat once	Not available
	Sotalol	Not recommended	160–320mg/day
	Amiodarone	5–7mg/kg iv over 30 minutes then 1.2–1.8g/day	400–1200mg/day for 7 days, then taper to 100–300mg/day
	Dofetilide	Loading not recommended	125–500µg q 12h

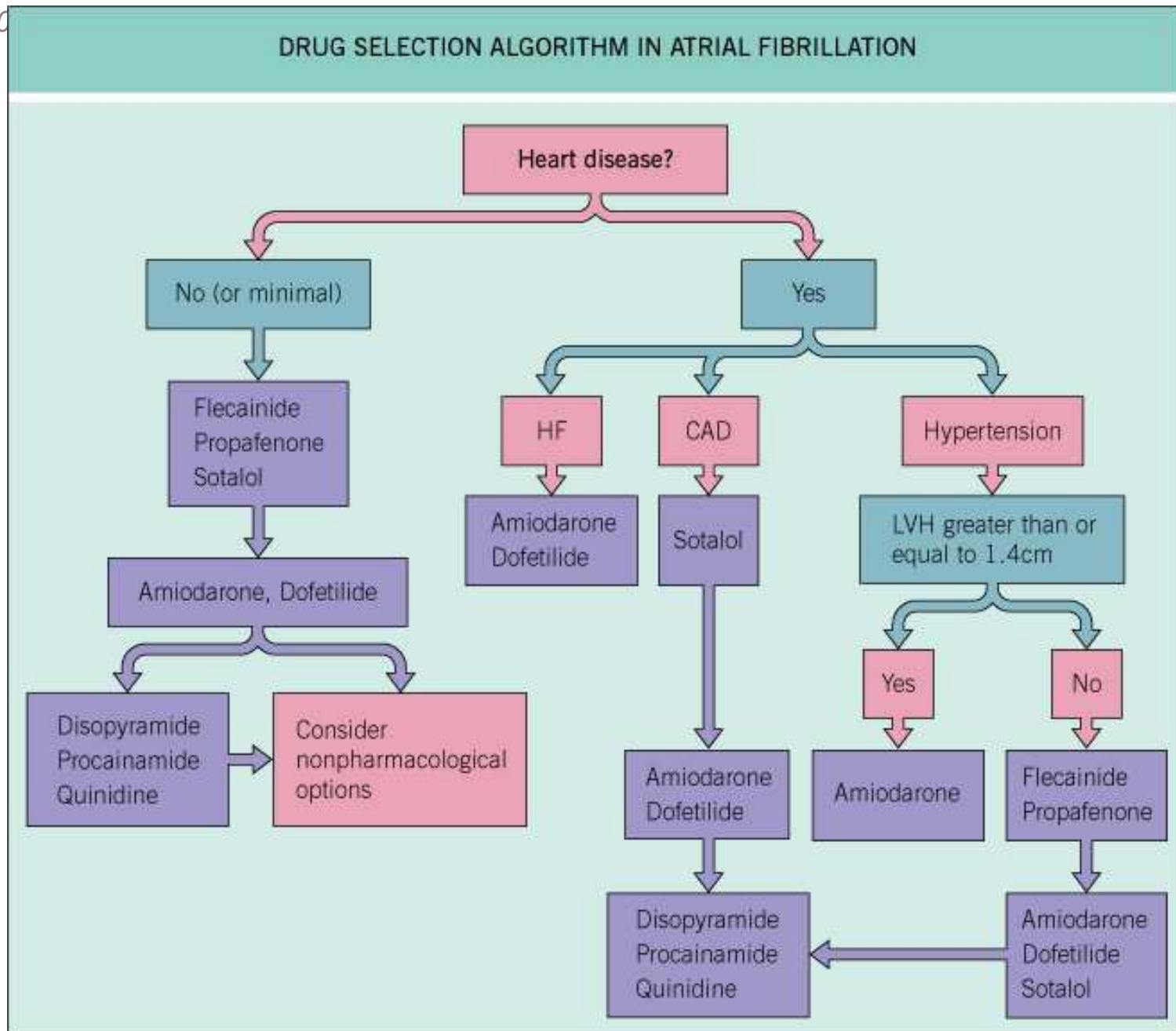
Antiarrhythmic therapy

Maintenance of sinus rhythm

- Amiodarone superior to sotalol and class I drugs
- Sotalol equivalent to class I drugs
- Risk of proarrhythmia
 - Sinus node dysfunction or AV block
 - Class IA and III prolong QT interval
 - Class IA, IC, and amiodarone can cause atrial flutter; in absence of AV blockade may cause hemodynamic collapse with 1:1 conduction

Flecainide (IC) causing atrial flutter with 1:1 conduction





Rate Control

- Digoxin
 - Enhances vagal tone, prolongs AV nodal refractory period
 - Less effect during stress, fever, etc.
 - Onset of action several hours (even IV)
- Beta Blockers
 - Decrease resting heart rate and blunt HR response to exercise
 - May worsen vagally mediated atrial fibrillation
- Calcium Channel Blockers
 - Slow conduction in the AV node
 - Negative inotropes (especially verapamil)

Medications for rate control

DRUG LOADING AND MAINTENANCE REGIMENS FOR CONTROL OF VENTRICULAR RATE IN ATRIAL FIBRILLATION			
		Acute intravenous therapy	Chronic oral therapy
Beta blockers	Metoprolol	2.5–5mg every 5 minutes up to 15mg	50–200mg/day
	Propranolol	0.15mg/kg (1mg every 2 minutes)	40–240mg/day
	Esmolol	0.5mg bolus, then 0.05–0.2mg/kg per minute	NA
	Pindolol	NA	7.5–30mg/day
	Atenolol	5mg over 5 minutes, repeat in 10 minutes	25–100mg/day
	Nadolol	NA	20–80mg/day
Calcium channel blockers	Verapamil	0.075–0.15mg/kg over 2 minutes; 0.005mg/kg per minute	120–360mg/day
	Diltiazem	0.25–0.35mg/kg followed by 5–15mg/hour	120–360mg/day
Cardiac glycoside	Digoxin	0.75mg–1.5mg in divided doses over 12–24 hours	0.125mg–0.375mg/day

Nonpharmacologic Therapies for rate control

- Pacemaker therapy
- Catheter ablation of AV node
- Catheter and surgical ablation

- Reserved for patients refractory to standard medical management

Pacemaker therapy

- Typically used in setting of sinus node dysfunction or AV block
- In sick sinus syndrome, atrial pacing results in much less atrial fibrillation than ventricular pacing
- In permanent atrial fibrillation, VVIR is the pacing mode of choice
- For selected patients atrial defibrillators are available to sense AF and either pace rapidly or shock to convert to sinus rhythm

Catheter ablation of AV node

- For patients resistant to medical rate control
- Requires implantation of pacemaker at time of ablation
 - VVIR mode for permanent atrial fibrillation
 - DDDR with mode switching for paroxysmal atrial fibrillation
- Must still risk stratify for thromboembolism and anticoagulate if indicated!

Surgical ablation

- Maze procedure (and variants) – multiple linear incisions in both atria, excision of both atrial appendages, and isolation of pulmonary veins
 - Complications of fluid retention, atrial arrhythmia
- Radiofrequency – lesion made on endocardium via atriotomy during open heart surgery

Pulmonary Vein Ablation (Percutaneous)

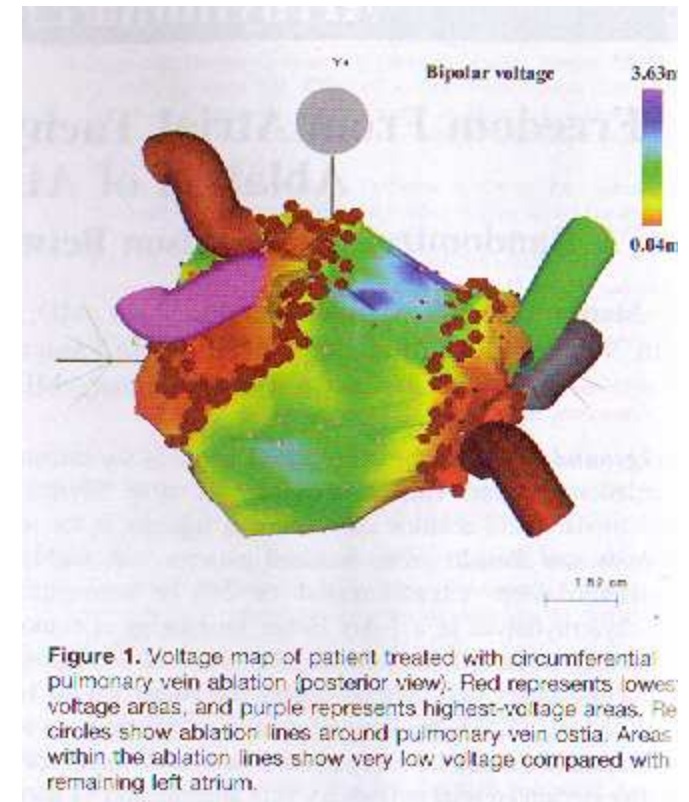
- 1,171 Symptomatic patients with AF
- 589 to ablation, 582 to antiarrhythmic therapy (not randomized)
 - Ablation patients off coumadin after 4 weeks
 - Amiodarone, flecainide, propafanon, sotalol most common antiarrythmics
- Median followup 900 days
- Ablation improved Mortality (92% vs 86% at 3 years), Morbidity (Heart failure, CVA, AF recurrence, and Quality of Life scores)

Worldwide Survey of Atrial Fibrillation Ablation

- 181 of 777 Worldwide centers surveyed
- 1995 – 18 procedures; 2002 – 5005 procedures
- Patient results
 - 52% asymptomatic without drugs
 - 24% asymptomatic with drugs
 - 27% required >1 procedure
 - 6% major complications
 - 0.05% death 1.22% Tamponade 0.28% Stroke
 - 1.6% Pulmonary vein stenosis

Atrial Fibrillation technique

- June 2005 German study
 - 50 patients circumferential PV ablation
 - 50 Segmental PV ablation
- Not much difference at 6 months
- Circumferential: More symptomatic Atrial **Flutter**
- Segmental: More pulmonary vein stenosis



Rate control vs Rhythm Control

- Previous belief that maintenance of sinus rhythm improved morbidity and mortality
- Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM)
 - 4060 patients, at 3.5 years trend toward lower mortality in rate control group
- 2 smaller trials also showed no stroke or mortality benefit to rhythm control
 - Pharmacological Intervention in Atrial Fibrillation (PIAF)
 - Rate Control vs. Electrical Cardioversion (RACE)
- In asymptomatic patients, either strategy is acceptable
- Lesson from trials: Anticoagulation must be continued with rhythm control

Risk of Stroke

- Thromboembolic stroke, typically due to thrombus in the left atrial appendage
- Risk of stroke 5-9% per year among high risk patients on aspirin (not coumadin)
- Duration of episodes and overall atrial fibrillation burden have not been useful to assess stroke risk

Stroke Prevention in Atrial Fibrillation Trials

Trial	Time Interval	Main Findings
SPAF I		
Warfarin vs. placebo	1987–1989	Warfarin substantially reduces stroke
Aspirin vs. placebo	1987–1990	Aspirin reduces stroke
SPAF II		
Warfarin vs. aspirin, age \leq 75 y	1987–1992	Small absolute reduction in stroke by warfarin over aspirin in unselected patients
Warfarin vs. aspirin, age $>$ 75 y	1989–1992	High rate of intracranial bleeding with warfarin (INR, 2–4.5) in patients $>$ 75 years of age offset reduction in ischemic stroke
SPAF III		
Warfarin INR 2–3 vs. aspirin plus low-intensity, fixed-dose warfarin in selected high-risk patients	1993–1995	Warfarin INR 2–3 offers large benefits over aspirin plus low-intensity, fixed-dose warfarin for high-risk patients
Aspirin-treated low-risk cohort	1993–1997	Patients whose stroke risk is low when given aspirin can be identified (validation of the SPAF risk stratification scheme)

* All were randomized trials, except the nonrandomized aspirin-treated low-risk cohort clinical trial in SPAF III, in which all participants were prescribed aspirin and followed to validate the stroke risk stratification scheme. INR = international normalized ratio; SPAF = Stroke Prevention in Atrial Fibrillation.

SPAF 3 Risk factors

Table 3. Stroke Prevention in Atrial Fibrillation III Stroke Risk Stratification Scheme*

Risk Strata and Criteria	Ischemic Stroke with Aspirin			
	Derivation Cohort (n = 854)	SPAF III Validation Cohort (n = 1936)	Hospital Discharge Cohort (28) (n = 1733)	Other Clinical Trials Cohort (11) (n = 2484)
	←————— %/y —————→			
High risk Previous stroke or transient ischemic attack Systolic blood pressure > 160 mm Hg Heart failure‡ Women > 75 y	5.9†	7.9	5.7	5.7
Moderate risk Hypertension No high-risk features	2.8	3.6	3.3	2.8
Low risk No hypertension No high-risk features	1.0	1.1	1.5	1.2

* SPAF = Stroke Prevention in Atrial Fibrillation.

† Excluding patients with previous stroke or transient ischemic attack, the annualized rates among remaining high-risk patients with atrial fibrillation (that is, for primary prevention) were 5.8% per year for the derivation data set (27), 5.3% per year for the test cohort (6), and 3.4% per year for the other clinical trials cohort (28).

‡ Congestive heart failure within the previous 3 months or left ventricular fractional shortening of $\leq 25\%$ by precordial echocardiography.

Risk Strata	Stroke Rate with Aspirin, %/y	Relative Risk Reduction: Warfarin vs. Aspirin, %†	NNT ₅ ‡	General Recommendation
Previous stroke or transient ischemic attack	10	60	17	Warfarin (INR, 2–3)
Primary prevention				
High risk	>4	55	35	Warfarin (INR, 2–3)
Moderate risk	2–4	45	75	Warfarin or aspirin§
Low risk	<2	35	>200	Aspirin (81–325 mg/d)

Risks of anticoagulation

- Intracranial hemorrhage – 0.1-0.3%/year
- Risk of major bleed – about 2%/year
 - 13-33% risk of death from major bleed
 - 15% risk of morbidity from major bleed

Anticoagulation Recommendations

ANTICOAGULATION IN CHRONIC NONVALVULAR ATRIAL FIBRILLATION			
Patient group	Risk factors	Estimated risk	Recommendation
Age <65 years	Present	High	Warfarin
	Absent	Low	Aspirin or nothing
Age 65–75 years	Present	High	Warfarin
	Absent	Moderate	Warfarin or aspirin
Age >75 years	Present	High	Warfarin
	Absent	Moderate to high	Warfarin

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- Anticoagulate all Valvular associated Atrial Fibrillation
- Assess risk factors (and review annually)
 - Prior TIA or stroke
 - Hypertension
 - Heart failure or Left ventricular dysfunction
 - Diabetes mellitus
 - * Clinical coronary artery disease (*not included as a risk factor in ACCP guidelines*)

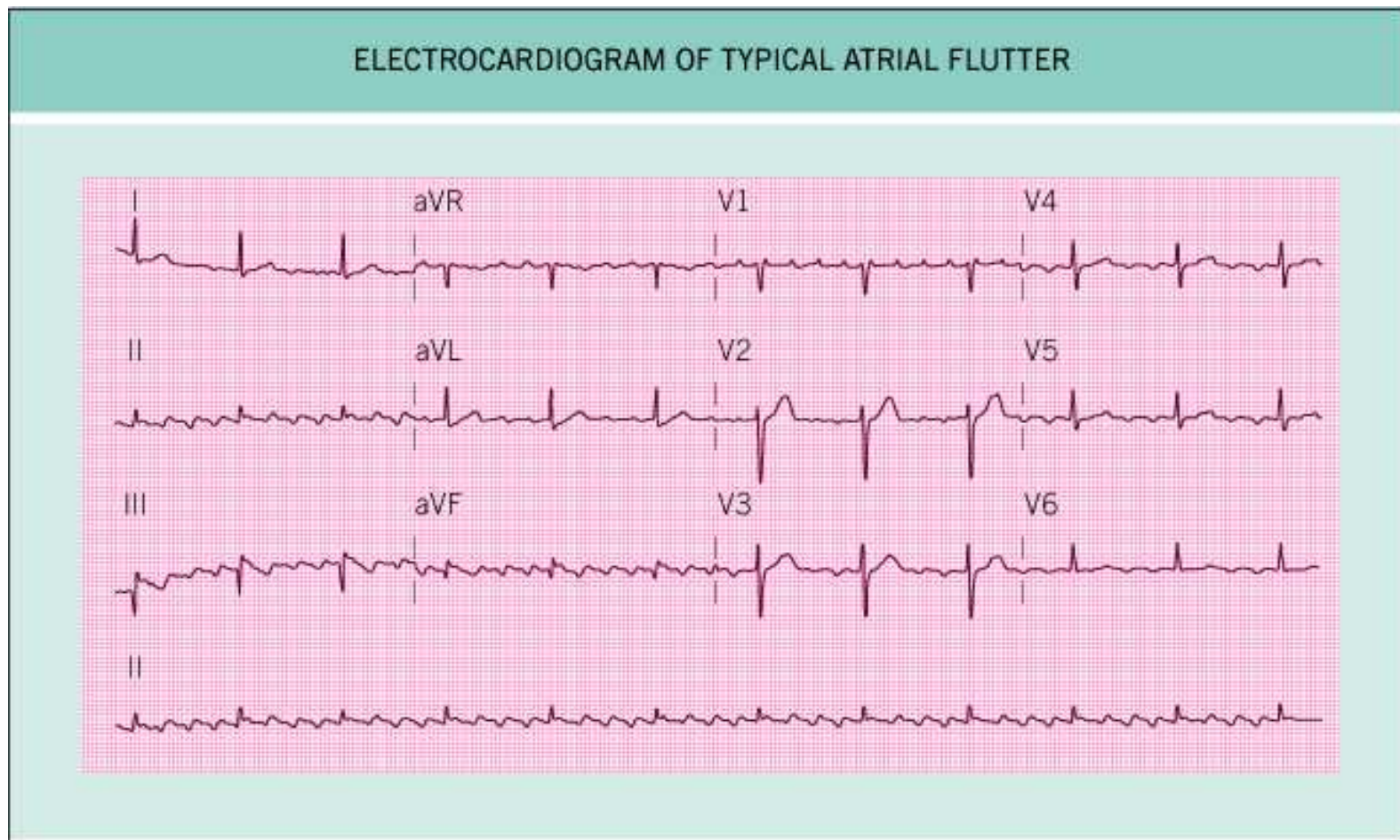
Prognosis

- Framingham study
 - Men: Odds ratio of death 1.5
 - Women: Odds ratio of death 1.9
- Greatest impact on those with advanced heart disease or other comorbidity

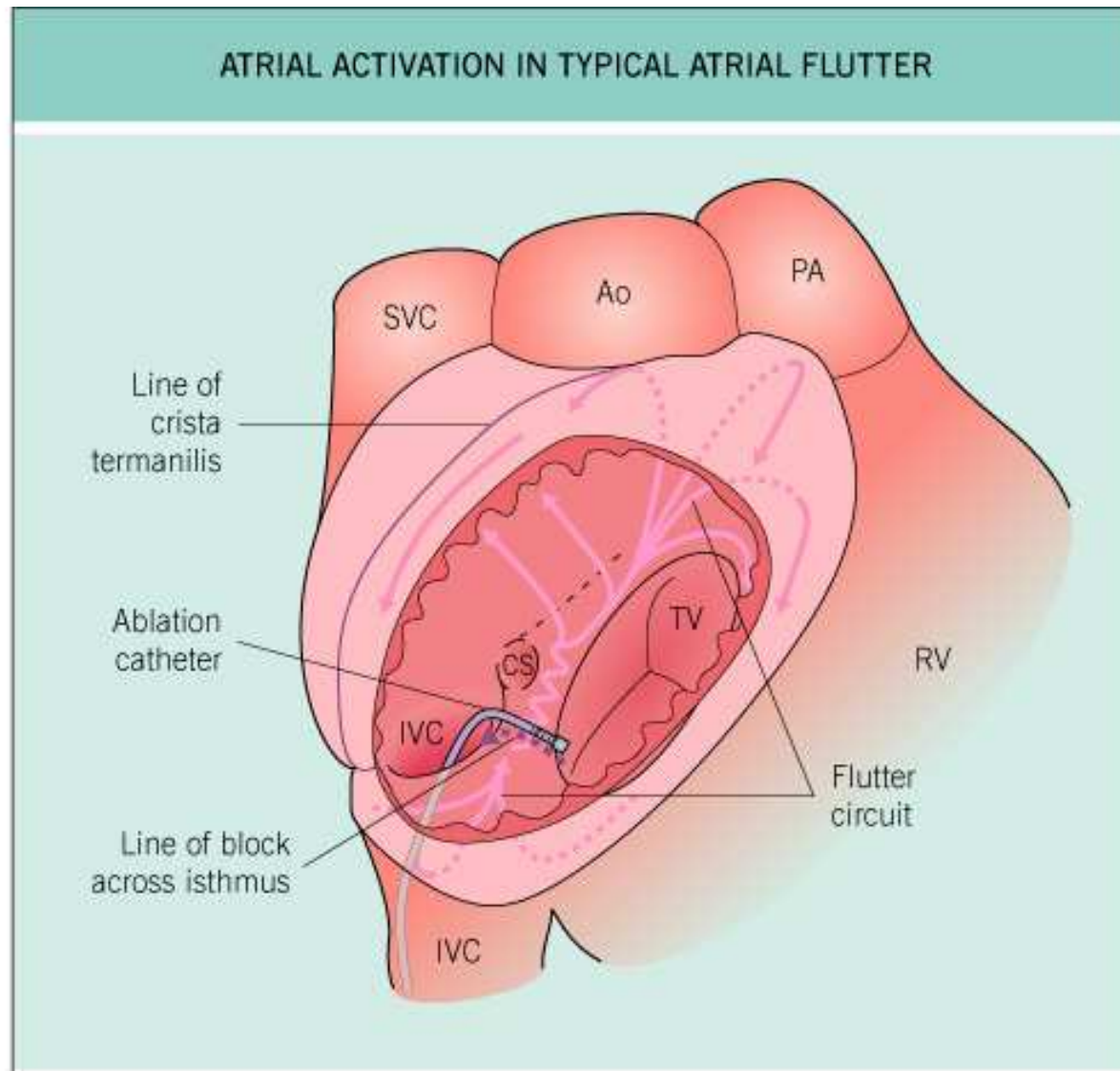
Atrial Flutter

- Digoxin, Beta Blockers, Calcium Channel blockers for rate control
- Electrical cardioversion (synchronized, 25-100J) preferred over medications
- Antiarrhythmic drugs have modest effect at preventing atrial flutter
- “Typical” atrial flutter very amenable to catheter ablation

Typical Atrial Flutter



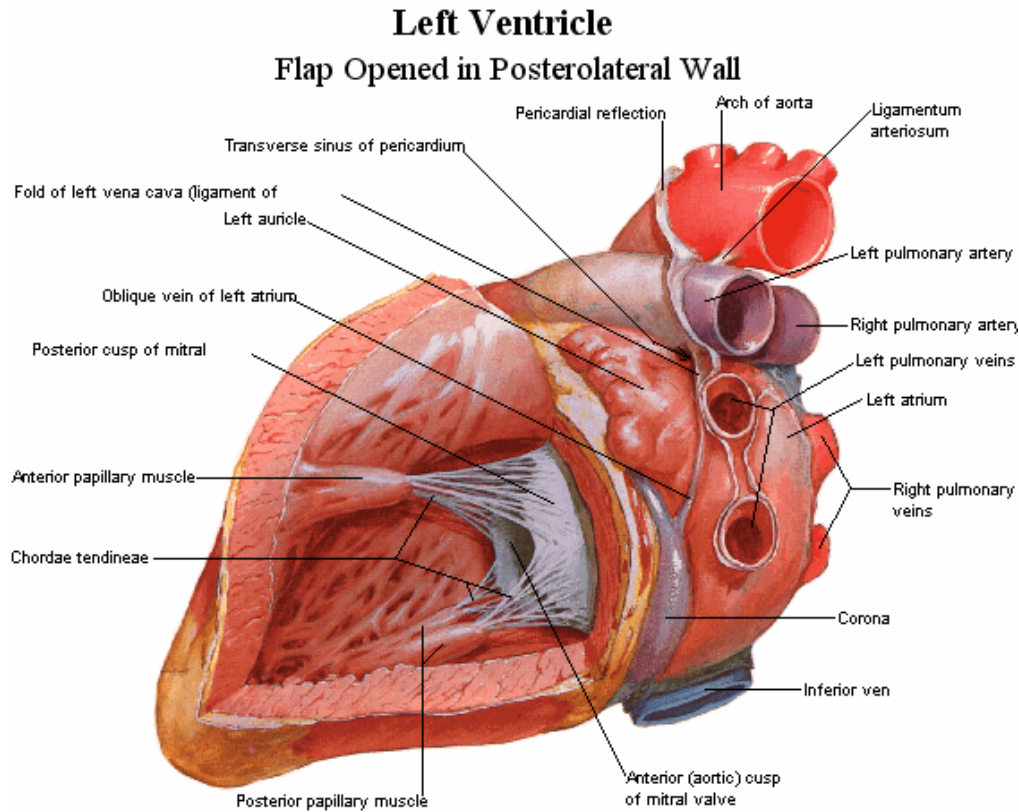
Mechanism of Typical Atrial Flutter



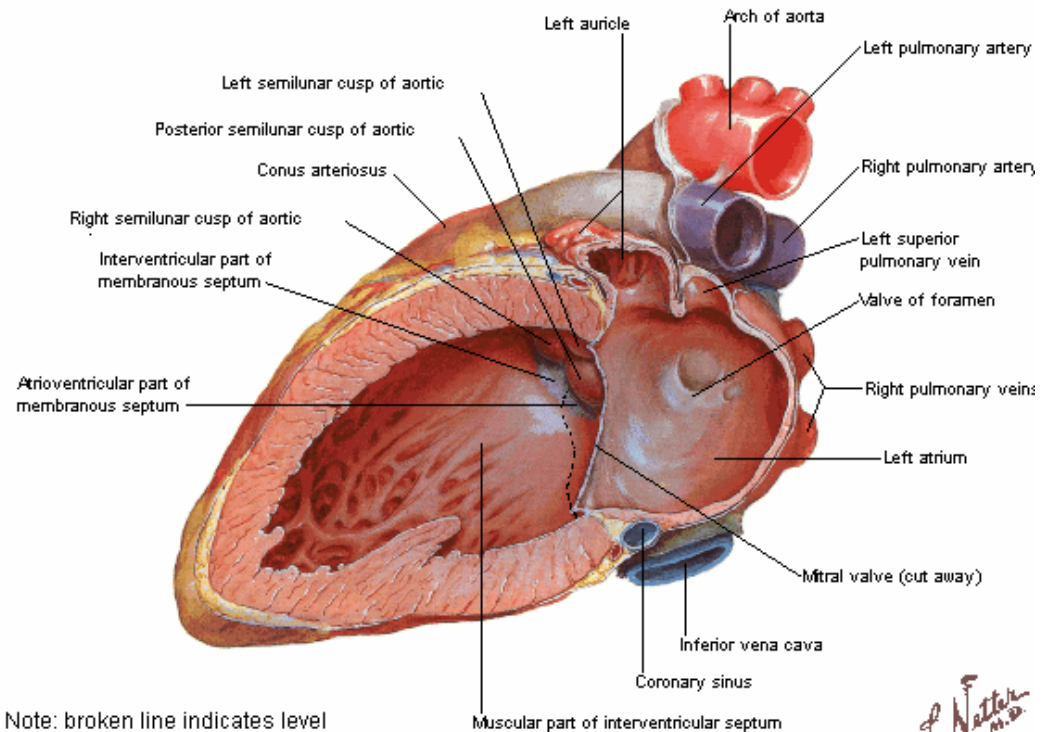
So What's New with Atrial Fibrillation?

- Recognition of upper pulmonary veins as major Atrial fibrillation focus (foci)
- Potential for Atrial Fibrillation Ablation
 - More effective for paroxysmal or persistent atrial fibrillation, rather than chronic sustained AF (25% success)
- Better antiarrhythmics?
 - AVEO118 is a novel K⁺ channel blocker that prolongs atrial refractory period without affecting the ventricles
- Novel direct thrombin inhibitors
 - Ximelagatran showed efficacy equivalent to coumadin in stroke prophylaxis for atrial fibrillation (SPORTIF III, SPORTIF V trials), however the FDA advisory panel recommended **against** drug approval due to hepatic toxicity
- Mechanical occlusion of left atrial appendage
- “Pill in the Pocket” for paroxysmal atrial fibrillation
 - Propafanone or flecainide for outpatient, episodic use

Left Atrial Appendage

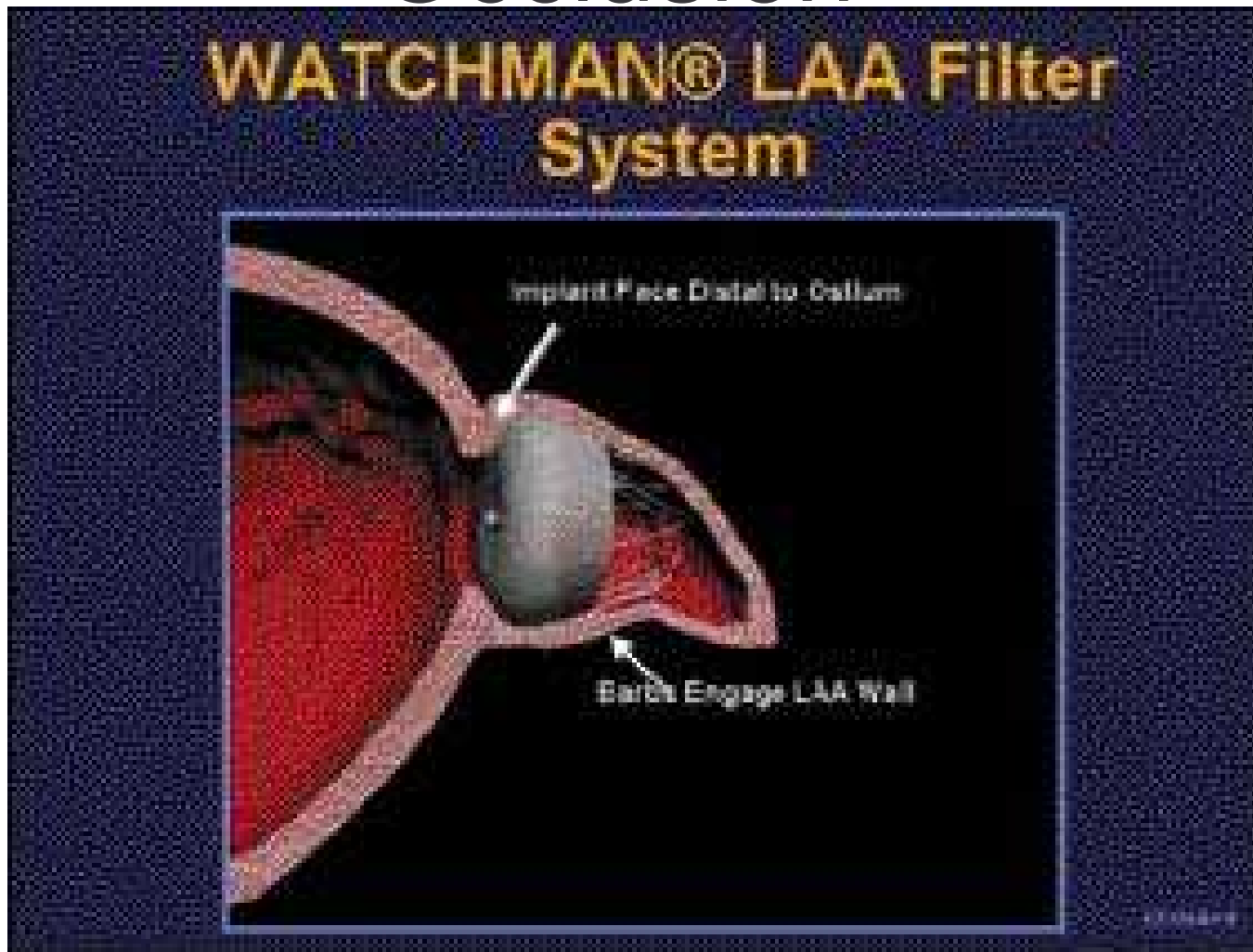


Left Atrium and Ventricle Sectioned with Mitral Valve Cut Away



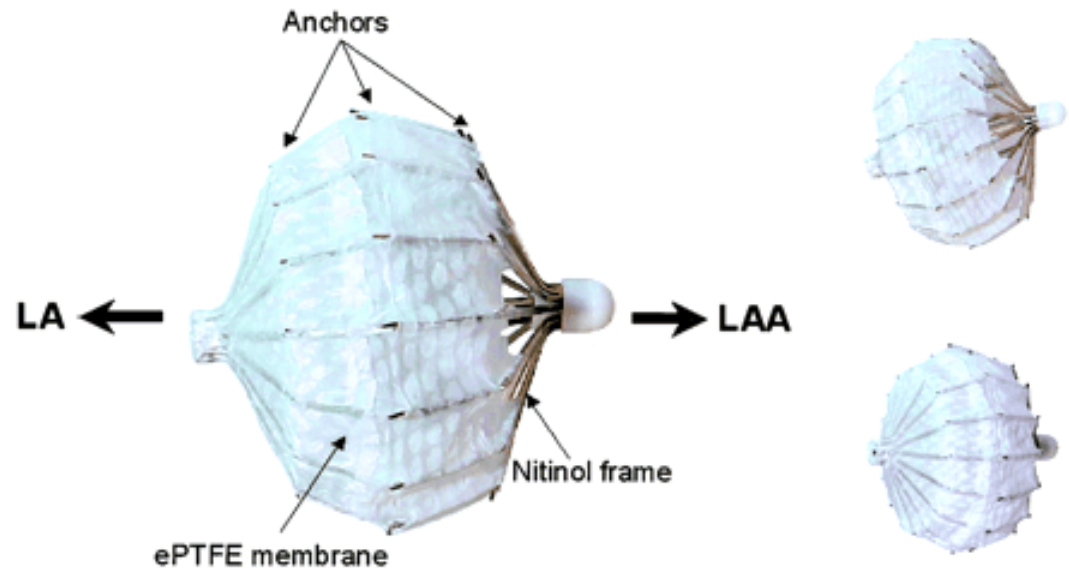
Note: broken line indicates level of origin of tricuspid valve

Left Atrial Appendage Occlusion



Percutaneous Left Atrial Appendage Transcatheter Occlusion (PLAATO)

- 15 patients with AF, high risk of stroke, poor coumadin candidates
- 1 month follow-up, implant stable by TEE



Back to the patient

- A 76 year old male with hypertension and hyperlipidemia diagnosed with asymptomatic atrial fibrillation, heart rate 85
 - EKG (done)
 - Echocardiography
 - Chest Xray
 - CBC, Renal panel, TSH
 - Rate control with Beta blocker (asymptomatic)
 - Assess adequacy with exercise monitoring if needed
 - May consider cardioversion after 3 weeks of anticoagulation
 - Anticoagulation with coumadin
 - Consider ischemic workup

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