



Atrial Fibrillation and Flutter

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Learning Objectives

- ▶ Identify and interpret the ECG for both atrial fibrillation and atrial flutter
- ▶ Understand risk factors and mechanisms for atrial fibrillation/flutter
- ▶ Management of atrial fibrillation/flutter (Rate and Rhythm Control)
- ▶ Understanding risk stratification for thromboembolic complications
- ▶ Indications for chronic systemic anticoagulation (Antithrombin therapy) as well as the choice of systemic anticoagulant

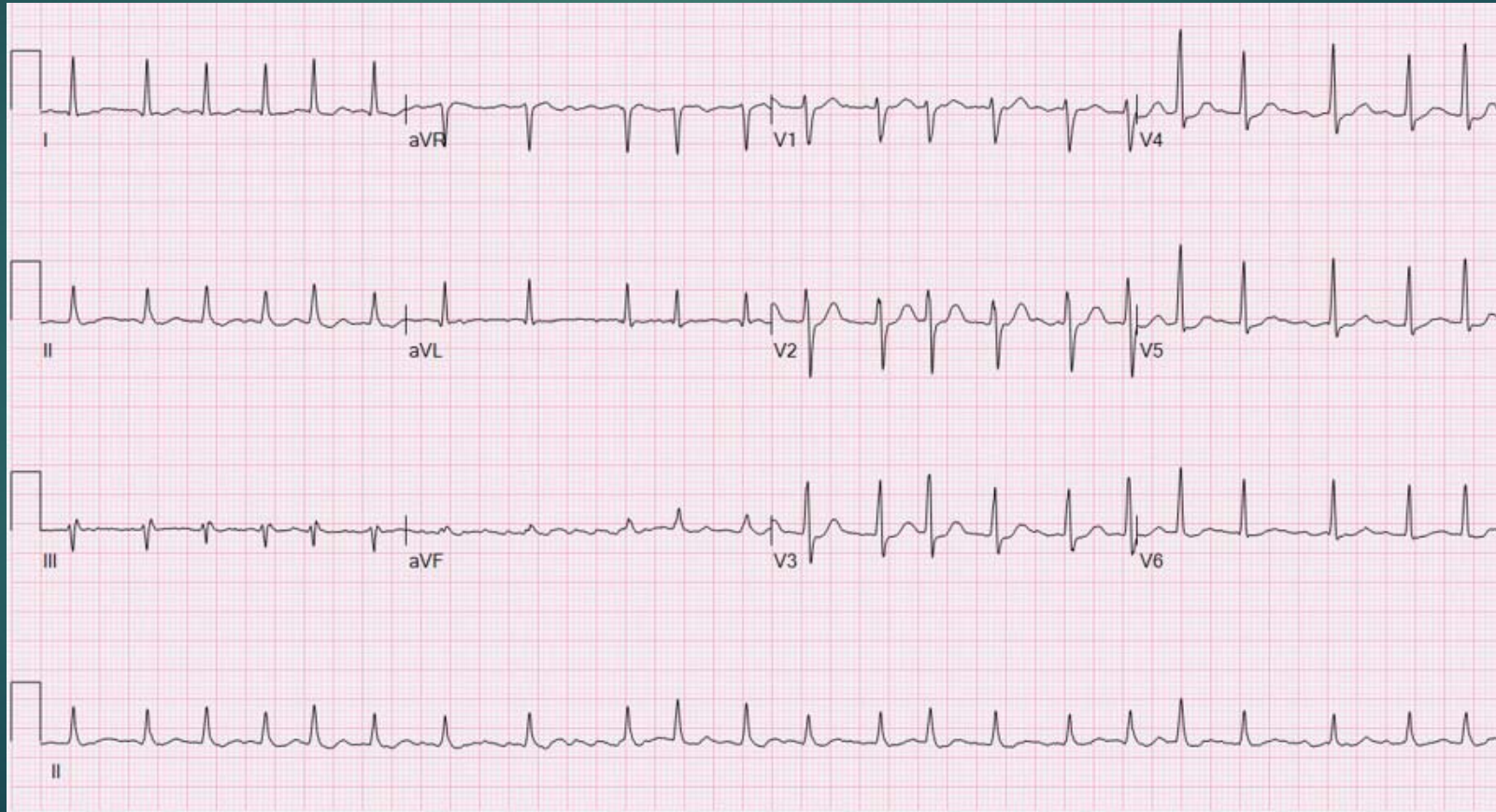
Sources

**2019 AHA/ACC/HRS Focused Update of the
2014 Guideline for Management of Patients
with Atrial Fibrillation**

**2014 AHA/ACC/HRS Guideline for the
Management of Patients With Atrial
Fibrillation**

Case #1

- ▶ 71-year-old female with a history of HTN presents to the ED with complaints of palpitations for the past several days. On presentation the patient is alert and oriented. Does not appear to be in distress. Vital signs demonstrate a heart rate of 121 bpm, blood pressure is 148/60. ECG is obtained and shown below:



Case #1

Which of the following is the most appropriate initial therapy for the patient's arrhythmia:

- A. Adenosine
- B. Diltiazem
- C. Digoxin
- D. Amiodarone
- E. Sotalol



Atrial Fibrillation

Atrial Fibrillation Classifications

Paroxysmal Atrial Fibrillation

- ▶ (self-terminating within 1 week)

Persistent Atrial Fibrillation

- ▶ (lasting more than a week, or requires medication/cardioversion)

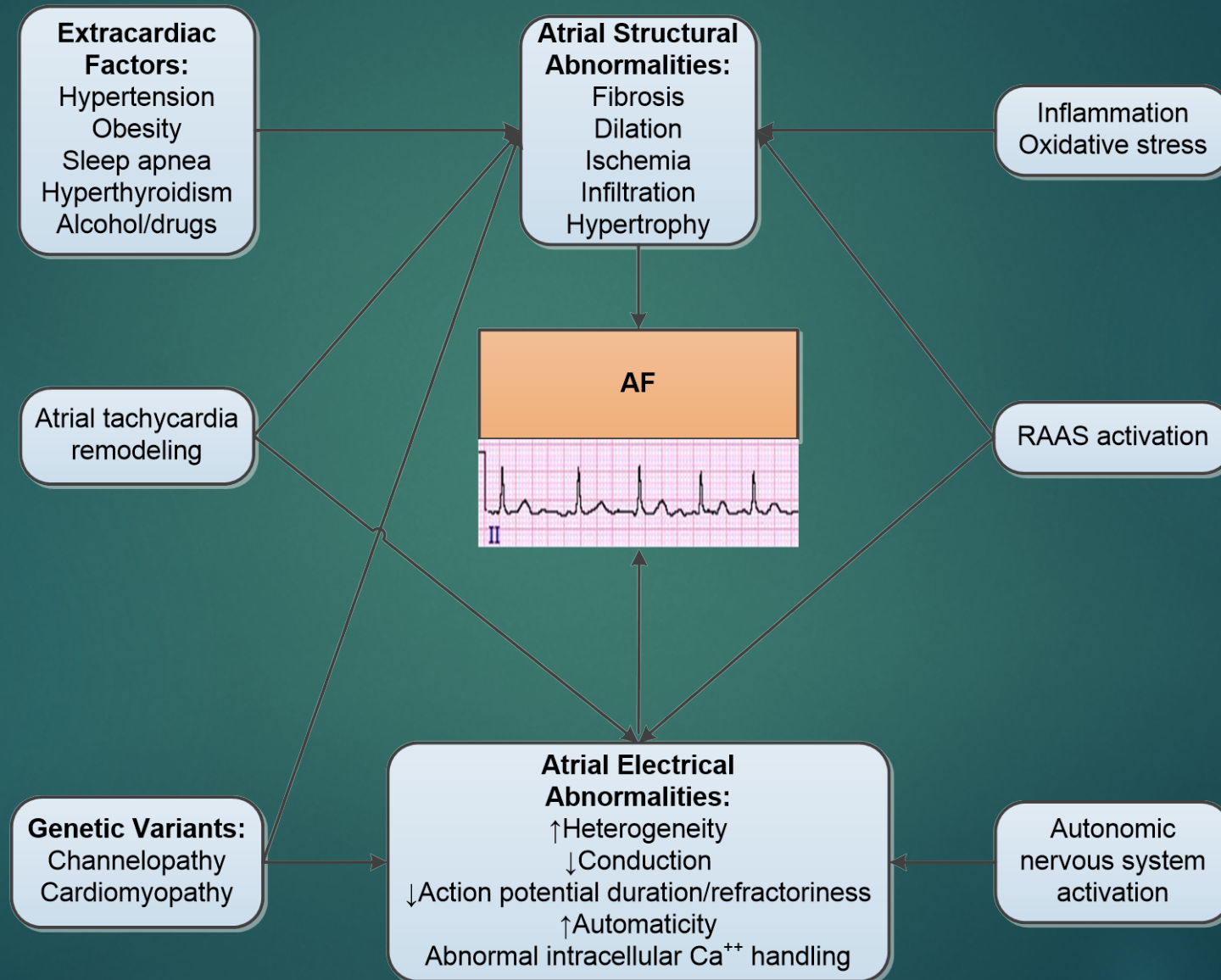
Long-standing Persistent Atrial Fibrillation

- ▶ (lasting more than 1 year)

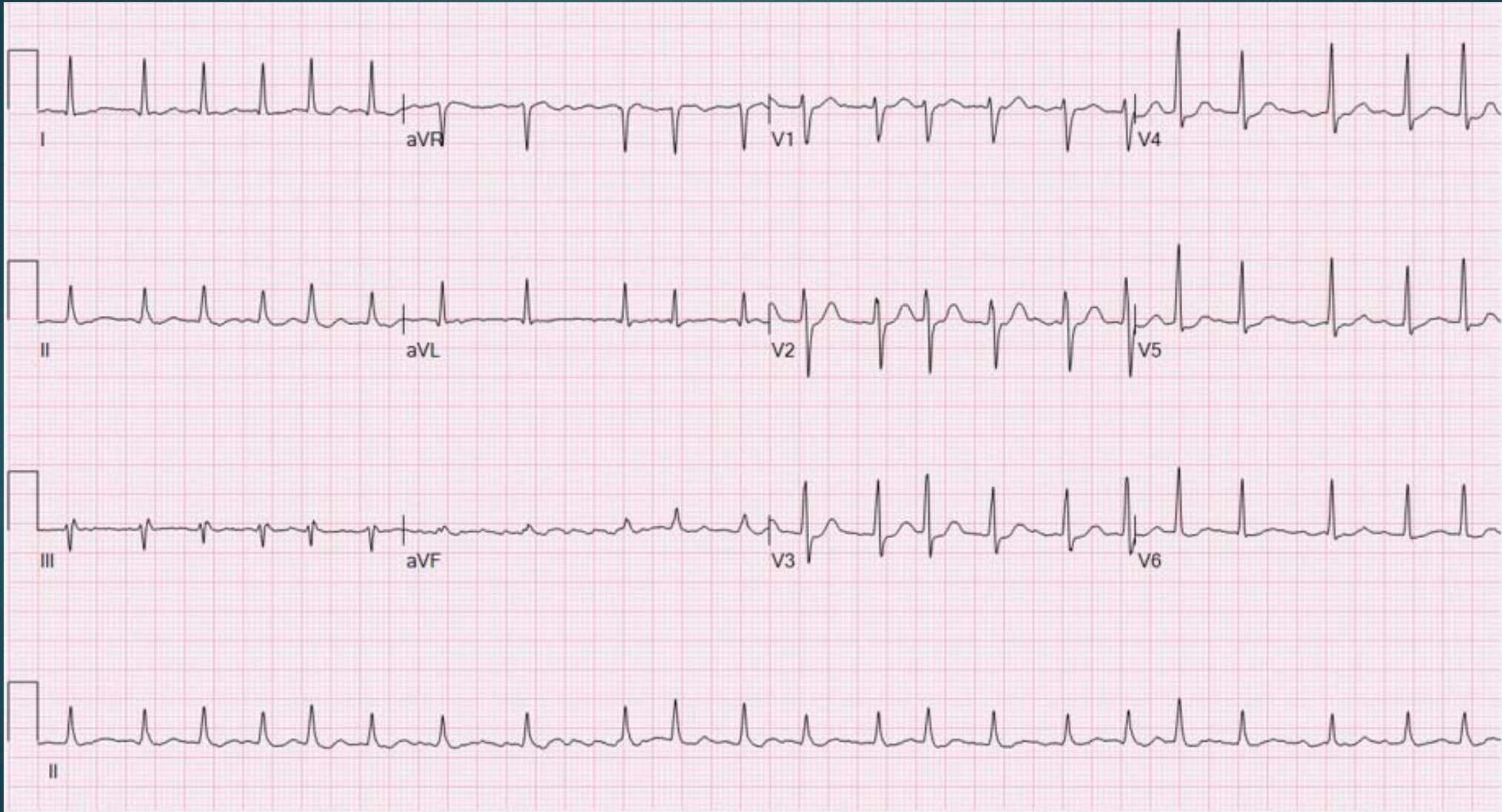
Permanent or Chronic Atrial Fibrillation.

- ▶ (unlikely to be converted to normal rhythm)

Risk factors and Mechanisms of AF



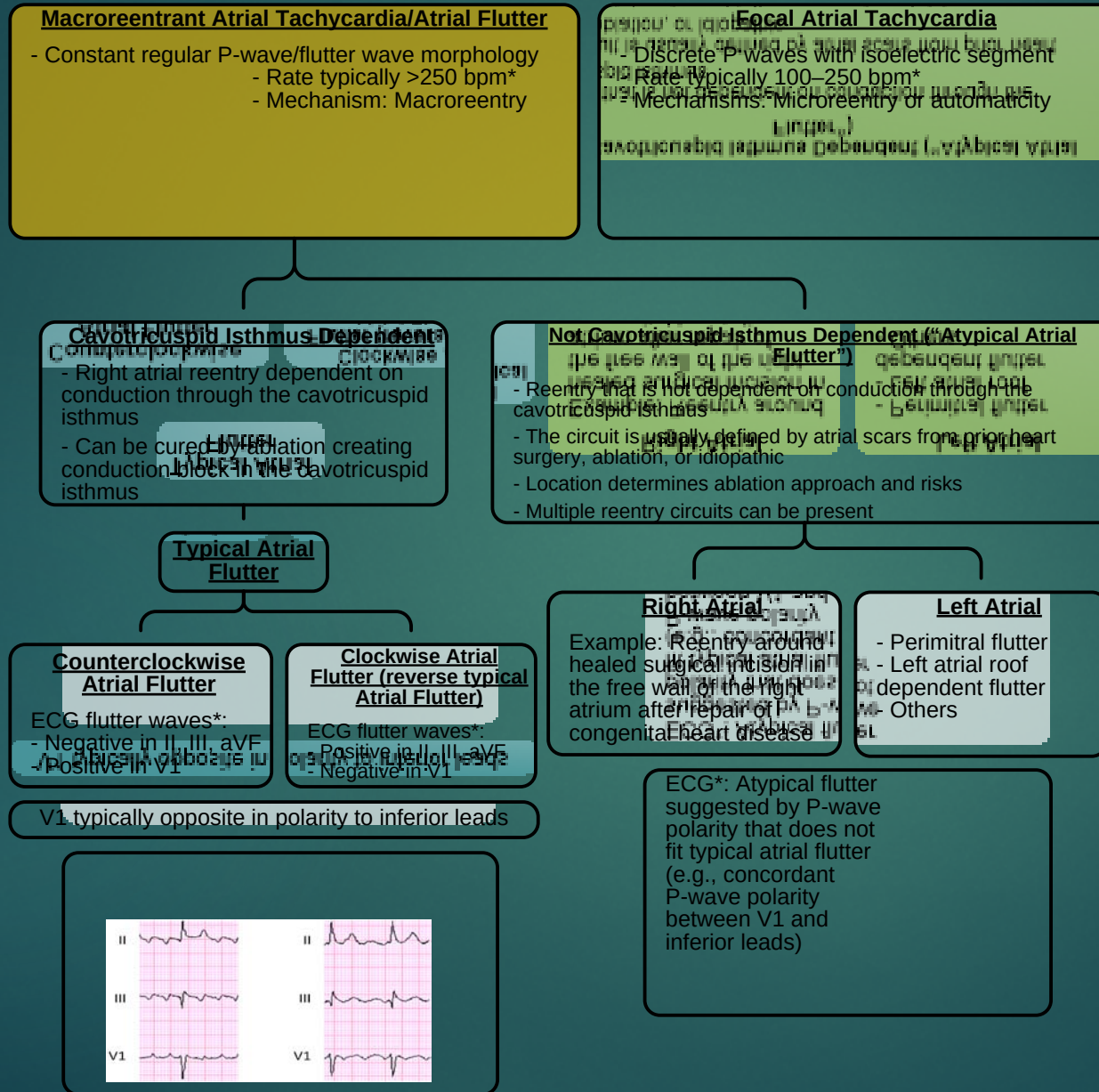
ECG for Atrial Fibrillation:





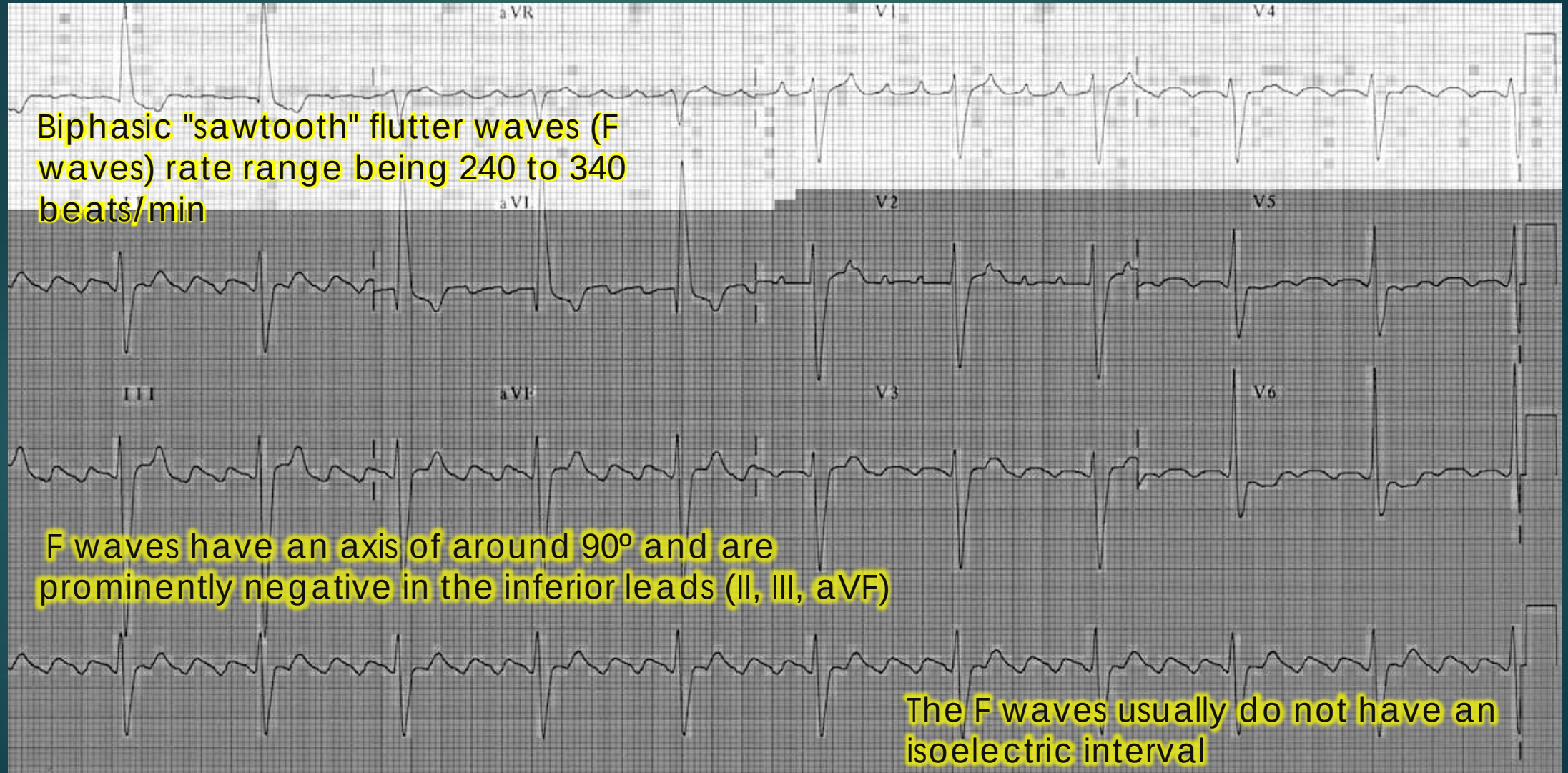
Atrial Flutter

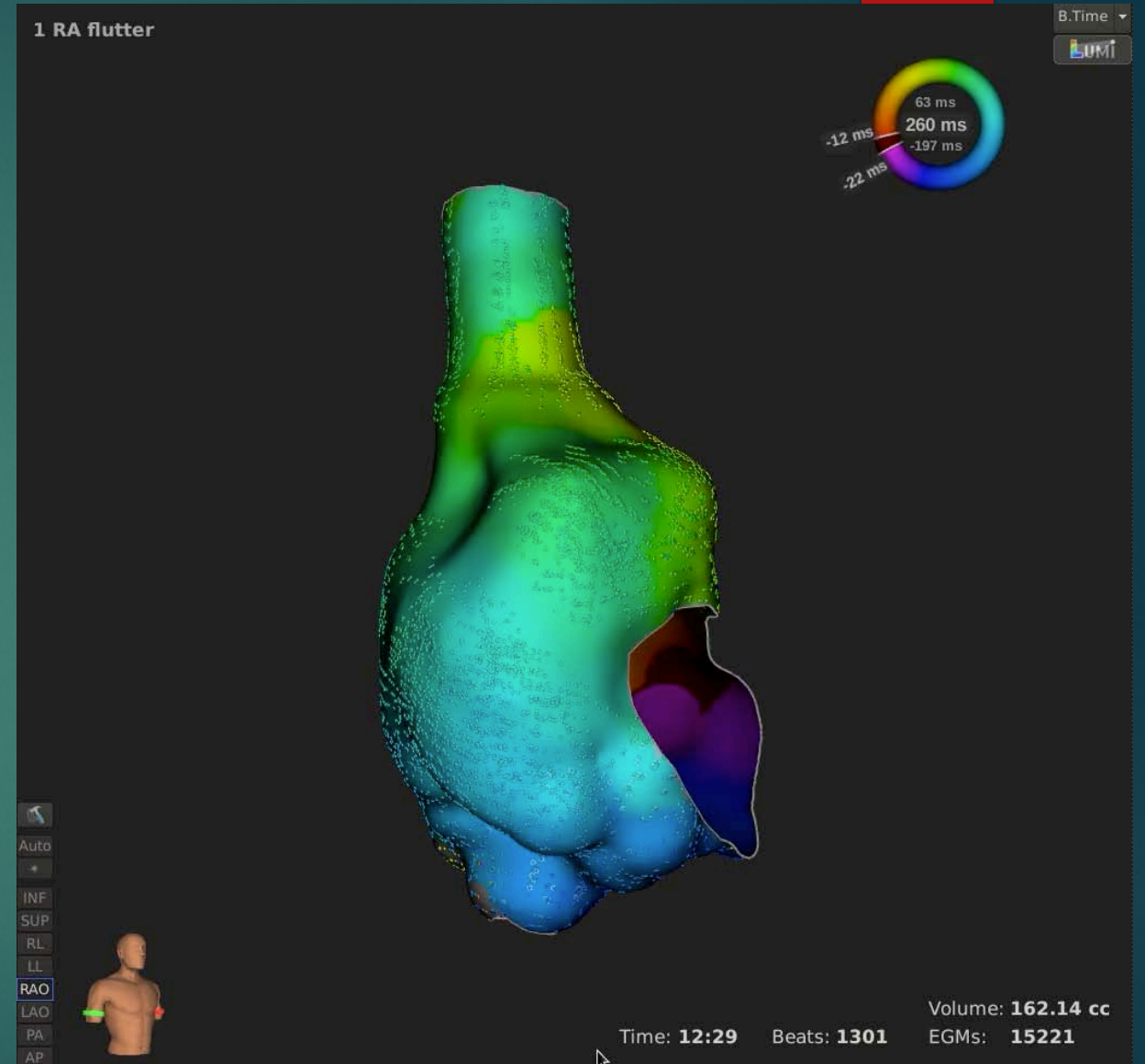
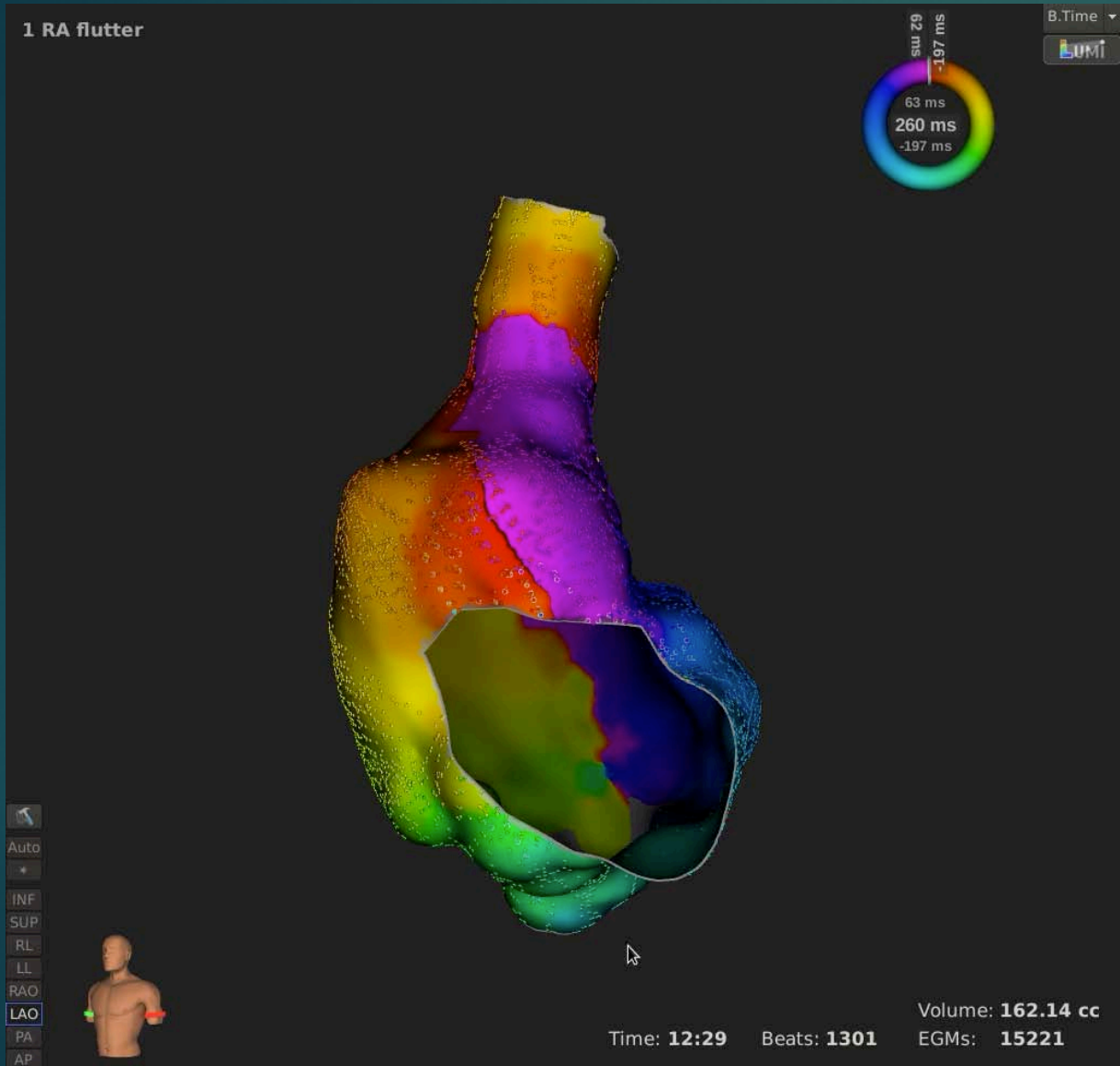
Atrial Tachycardias/Flutter



- Diagram summarizing types of atrial tachycardias often encountered in patients with a history of AF.
- P-wave morphologies are shown for common types of atrial flutter; however, the P-wave morphology is not always a reliable guide to the re-entry circuit location or the distinction between common atrial flutter and other macroreentrant atrial tachycardias.

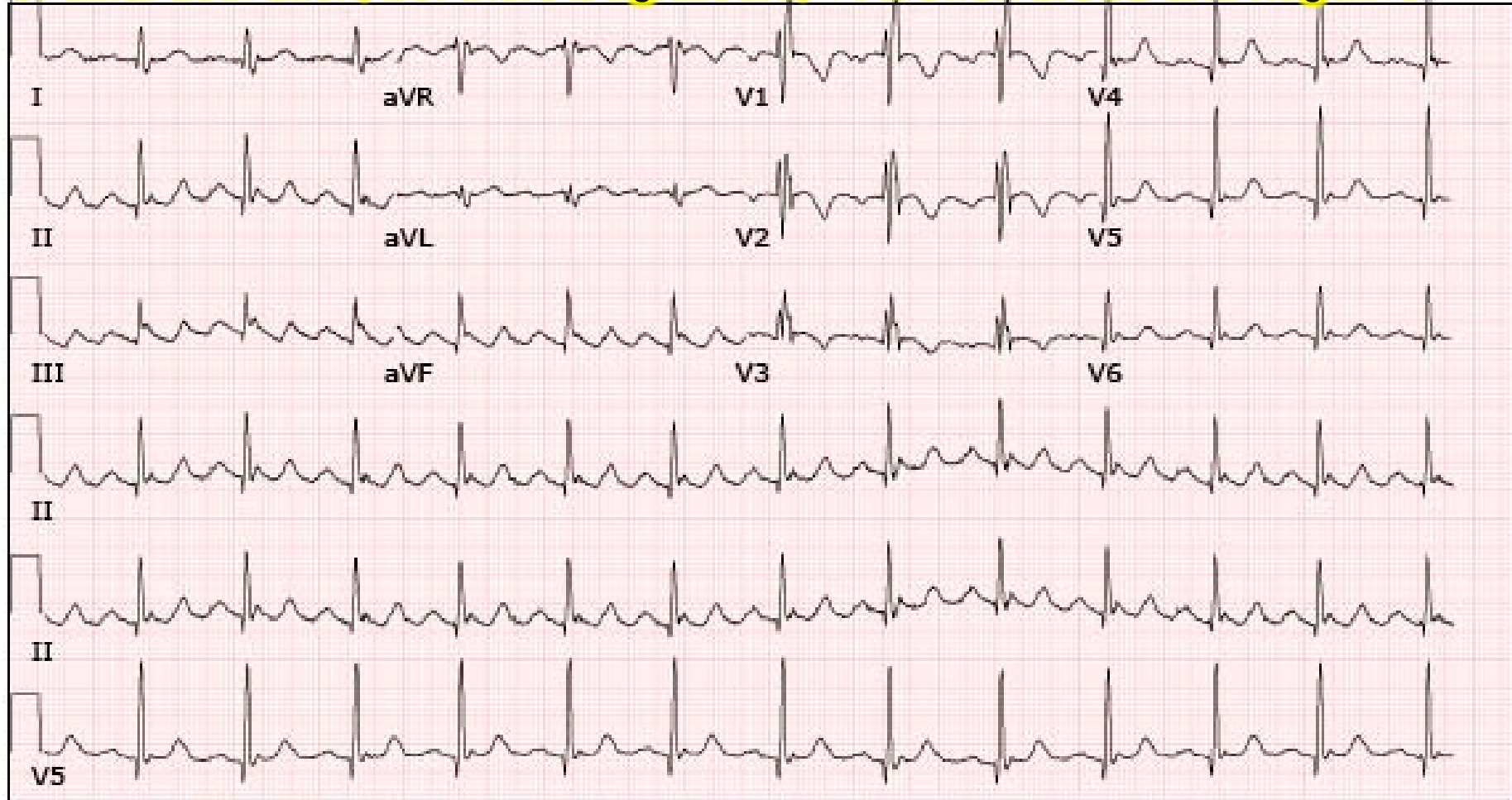
ECG for Counterclockwise Typical Atrial Flutter:



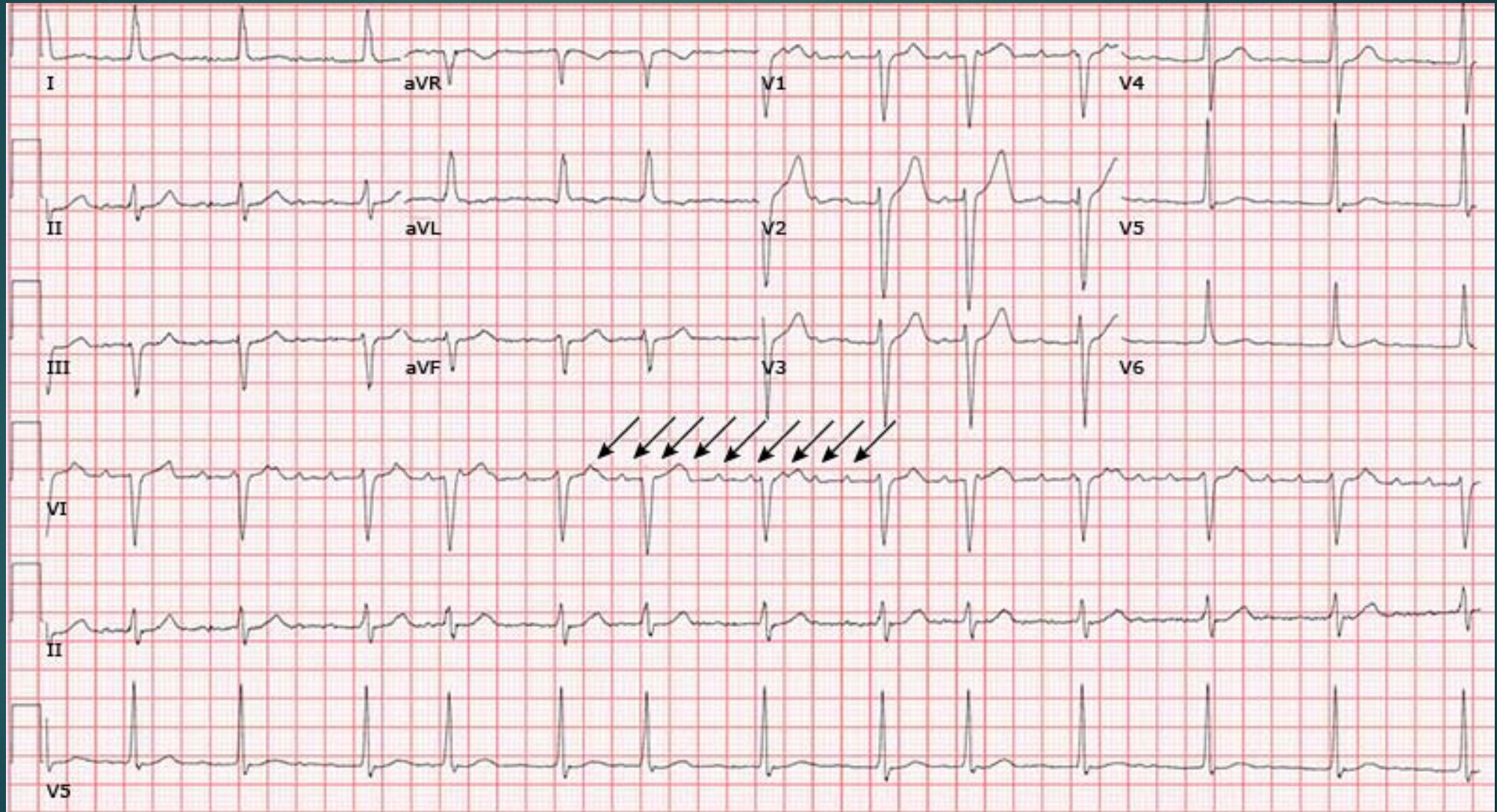


ECG for Clockwise Typical Atrial Flutter:

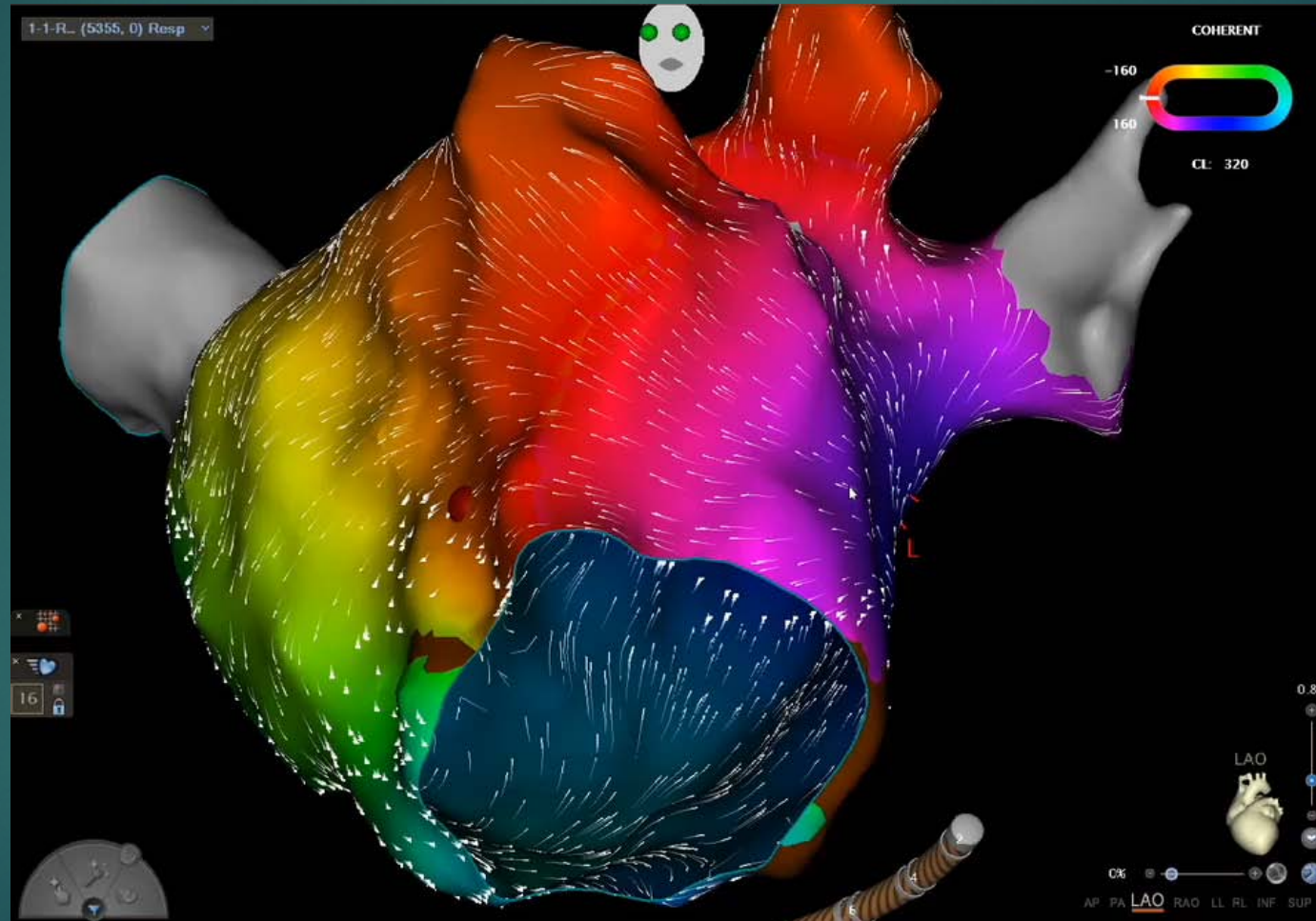
F waves are usually positive in the inferior leads due to an opposite direction of atrial activation, but there is significant, V1 is often broad and negative



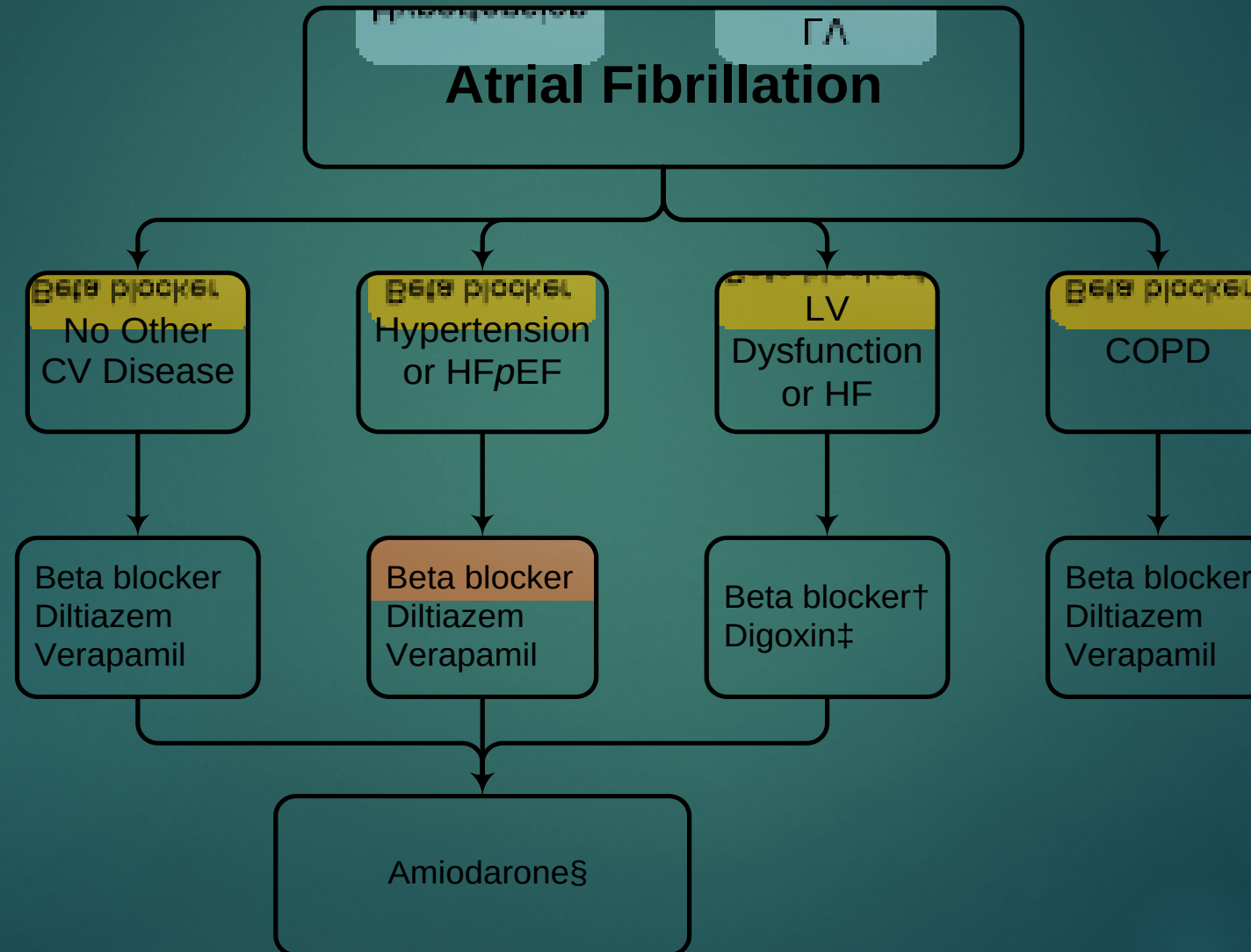
ECG for Atypical Atrial Flutter:



Peri-Mitral Flutter (counter clockwise)



Approach to Selecting Drug Therapy for Ventricular Rate Control



Management of Atrial Fibrillation/Flutter – Rate Control

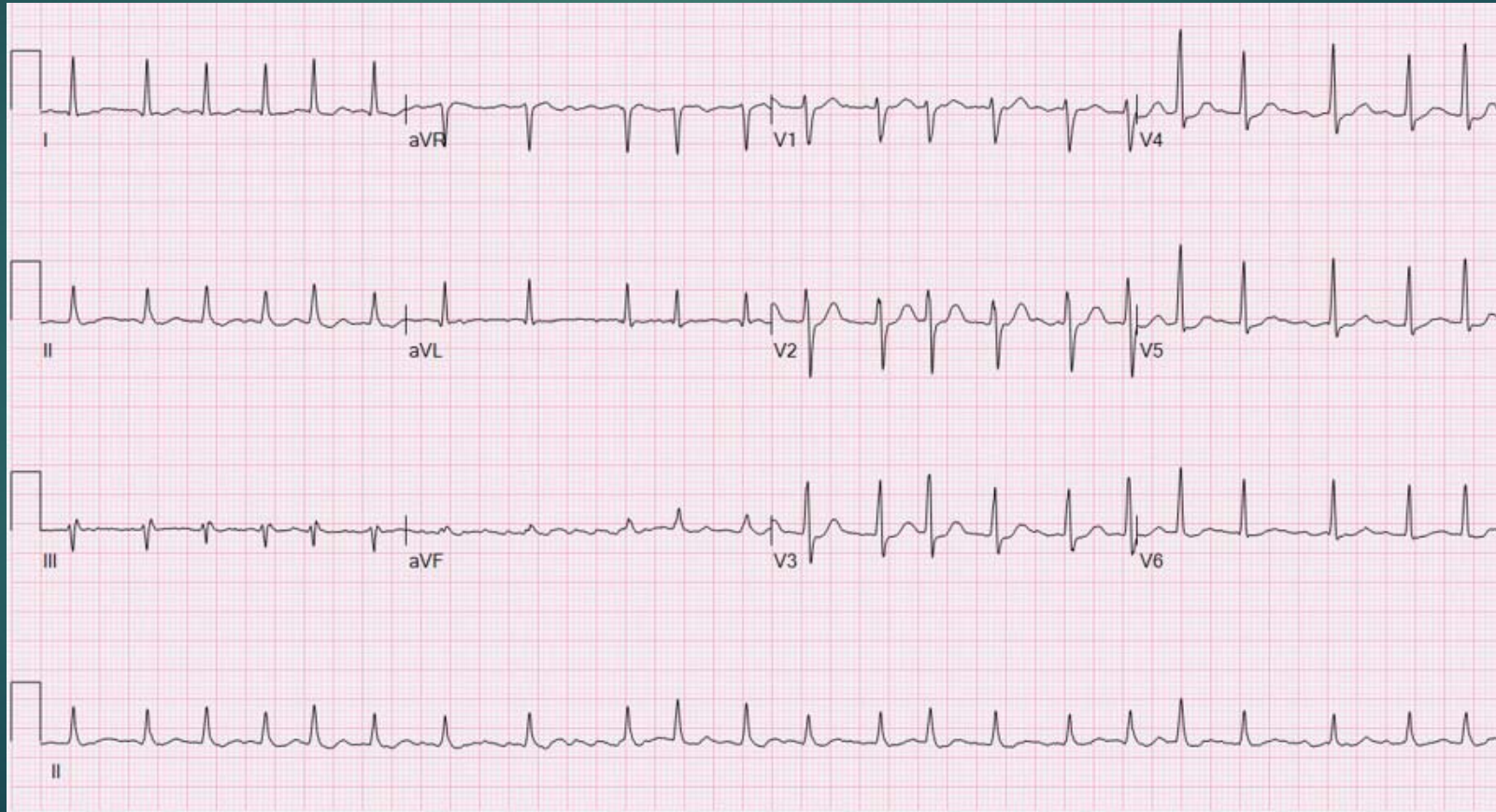
- ▶ A heart rate control (resting heart rate <80 bpm) is reasonable for symptomatic management of AF
- ▶ A lenient rate-control strategy (resting heart rate <110 bpm) may be reasonable in asymptomatic patients and LV systolic function is preserved.

Management of Atrial Fibrillation/Flutter – Rate Control

- ▶ Non-dihydropyridine CCA should not be used in patients with decompensated HF
- ▶ In patients with pre-excitation and AF, digoxin, non-dihydropyridine CCA, or intravenous amiodarone should not be administered

Case #1

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Case #2

78-year-old female presents to your office with a new diagnosis of atrial fibrillation. This diagnosis was made during a recent visit to the ED with palpitations and tachycardia. In the office today your patient is in NSR. The patient has a history of well controlled hypertension on amlodipine and HCTZ as well as diabetes mellitus on oral hypoglycemic agents. Which of the following is indicated for long term prevention of thromboembolic stroke:

- ▶ Aspirin
- ▶ Aspirin and Plavix
- ▶ Warfarin
- ▶ Apixaban
- ▶ Non are indicated as the patient is low risk for CVA



OK, So Who
Should Be on
Long Term
Systemic
Anticoagulation?

Thrombo-embolic Risk Stratification in Atrial Fibrillation: CHADS₂ vs CHA₂DS₂-VASc

Definition and scores for CHADS ₂ and CHA ₂ DS ₂ -VASc	
CHADS ₂ acronym	Score
Congestive HF	1
Hypertension	1
Age ≥75 years	1
Diabetes mellitus	1
Stroke/TIA/TE	2
Maximum score	6
CHA ₂ DS ₂ -VASc acronym	Score
Congestive HF	1
Hypertension	1
Age ≥75 years	2
Diabetes mellitus	1
Stroke/TIA/TE	2
Vascular disease (prior MI, PAD, or aortic plaque)	1
Age 65 to 74 years	1
Sex category (ie, female sex)	1
Maximum score	9

Stroke risk stratification with the CHADS ₂ and CHA ₂ DS ₂ -VASc scores	
CHADS ₂ acronym	Unadjusted ischemic stroke rate (% per year)*
0	0.6%
1	3.0%
2	4.2%
3	7.1%
4	11.1%
5	12.5%
6	13.0%
CHA ₂ DS ₂ -VASc acronym	Unadjusted ischemic stroke rate (% per year)*
0	0.2%
1	0.6%
2	2.2%
3	3.2%
4	4.8%
5	7.2%
6	9.7%
7	11.2%
8	10.8%
9	12.2%

Thrombo-embolic Risk and Anticoagulation

- ▶ Selection of anticoagulant therapy should be based on the risk of thromboembolism
CHA₂DS₂-VASc:
 - ▶ **Irrespective** of whether the AF pattern is paroxysmal, persistent, or permanent.
 - ▶ **Irrespective** of suppression of AF with Anti-Arrhythmic Drug therapy or Ablation.

Female Gender and CHA2DS2-VASc score

Most studies support the finding that females with AF are at increased risk of stroke, however:

- ▶ Recent studies have suggested that female sex, in the absence of other AF risk factors (CHA2DS2-VASc score of 0 in males and 1 in females), carries a low stroke risk that is similar to males.
- ▶ The excess risk for females was especially evident among those with advanced age and/or ≥ 2 non-sex related stroke risk factors

What CHA₂DS₂-VASc is considered of significant risk:

CHA₂DS₂-VASc of 2 in Males and CHA₂DS₂-VASc of 3 in Females is considered a significantly increased risk of thromboembolic events and long-term systemic anticoagulation is recommended

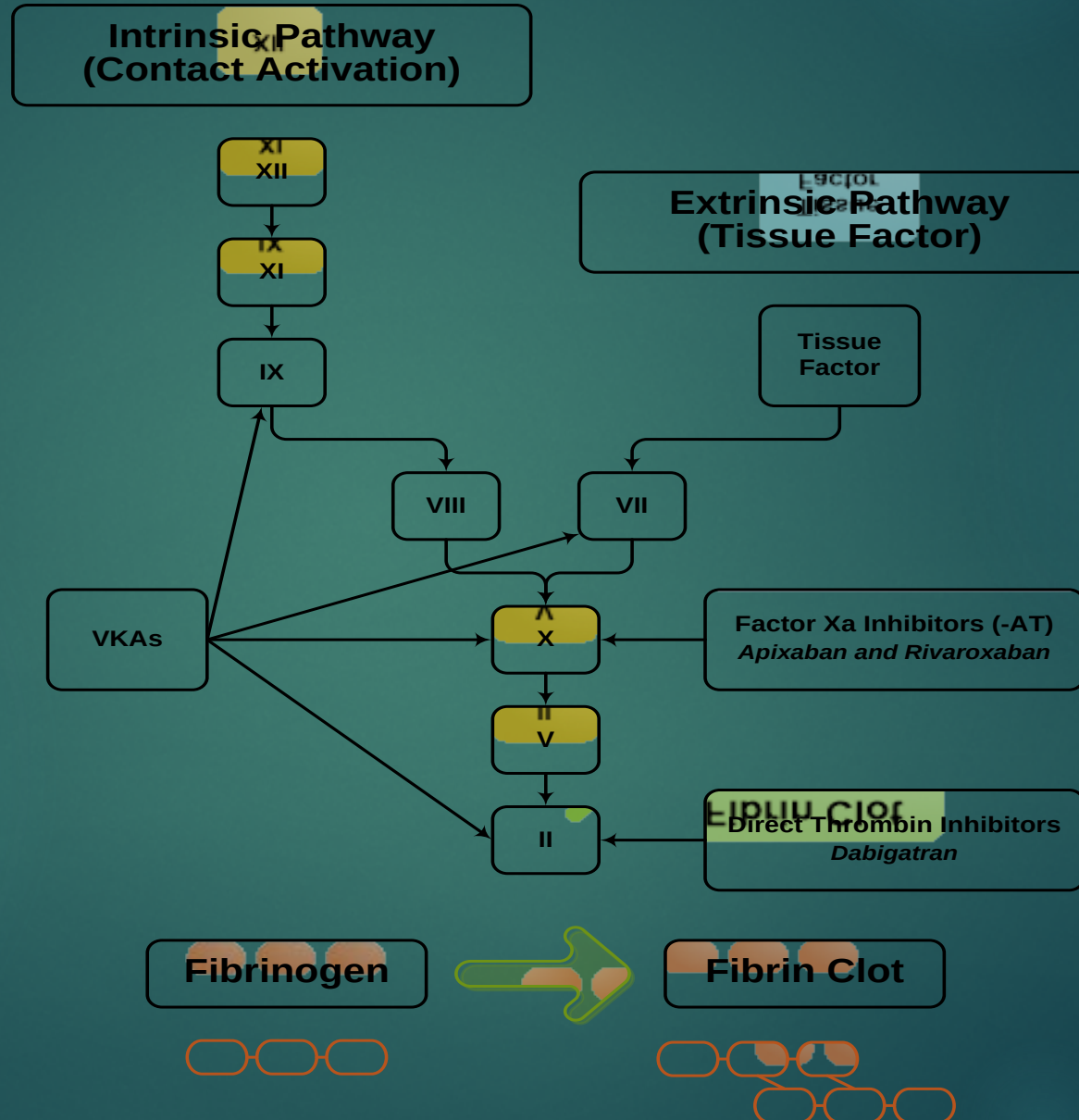
Exceptions to The Rule

- ▶ Mitral Valve Stenosis (Moderate/Severe)
- ▶ Hypertrophic Cardiomyopathy
- ▶ Untreated Hyperthyroidism or Hypothyroidism

NOACs and DOACs

In newest guideline update : DOACs are recommended as first-line therapy for stroke prevention in patient with AF who are eligible to receive DOACs

Coagulation Cascade:



Adapted from
Nutescu et al.

Stroke Prevention in Atrial Fibrillation

-Limitations of Warfarin Therapy in Atrial Fibrillation

Unpredictable
response

Narrow therapeutic
window
(INR range 2-3)

Routine coagulation
monitoring

Frequent dose
adjustments

**Warfarin
therapy has
several
limitations
that make it
difficult to use
in practice**

Slow onset/offset
of action

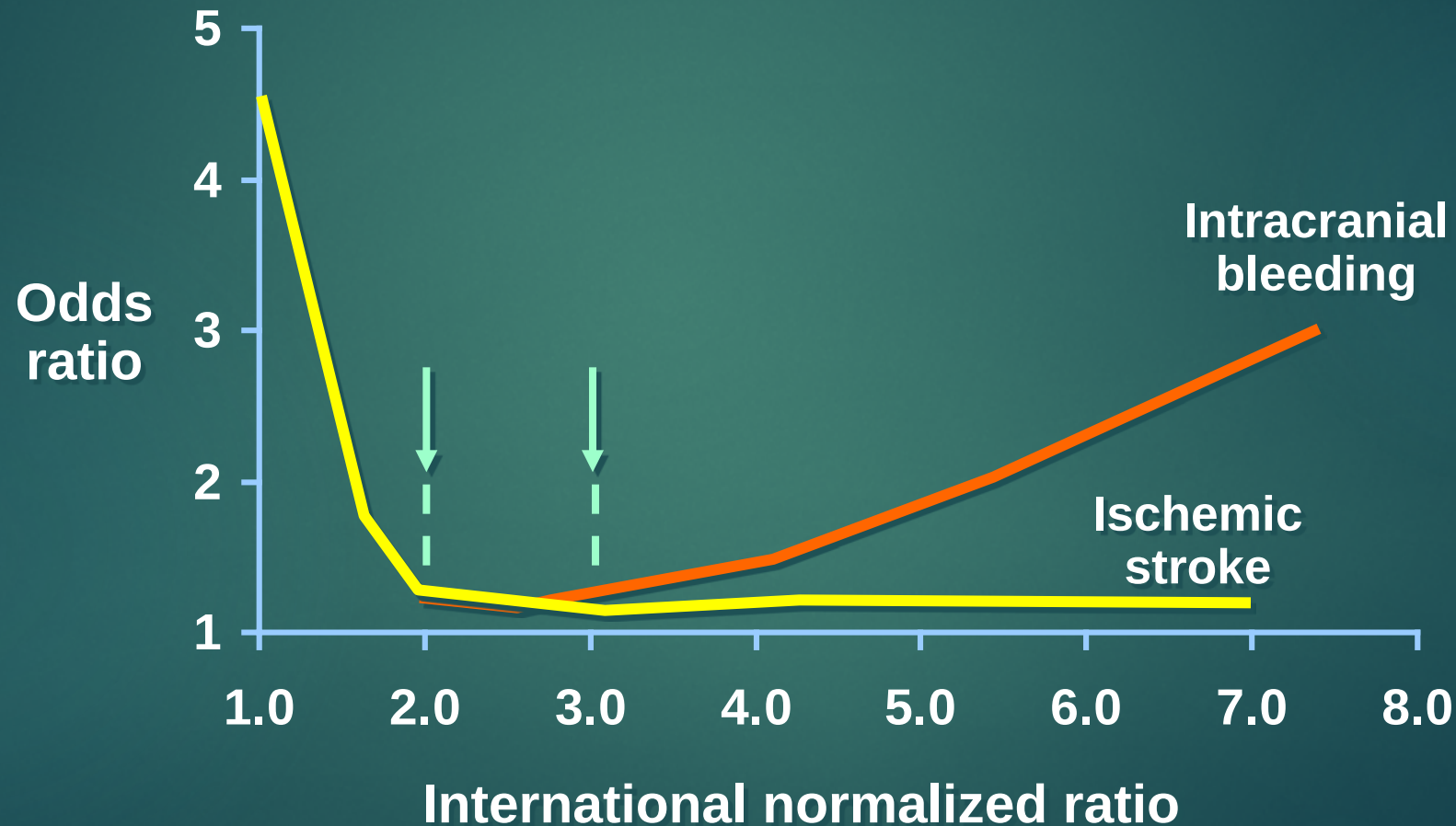
Numerous food-drug
interactions

Numerous drug-drug
interactions

Risk of Bleeding
Complications

- Warfarin was #1 in 2003 and 2004 in the number of mentions of “deaths for drugs causing adverse effects in therapeutic use”
- Warfarin caused 6% of the 702,000 ADEs treated in the ED/year; 17% required hospitalization
- J Thromb Thrombolysis 2008; 25: 52-60.

Adjusted Odds Ratios for Ischemic Stroke and Intracranial Bleeding in Relation to Intensity of Anticoagulation in Randomized Trials of Antithrombotic Therapy for Patients with Atrial Fibrillation



Why NOACs:

- ▶ The DOAC AF trials demonstrated that DOACs are noninferior or superior to warfarin in preventing stroke.
- ▶ DOACs reduce intracranial bleeding as compared with warfarin
- ▶ Specific DOACs, such as apixaban, may have lower risks of bleeding (including intracranial hemorrhage) and improved efficacy for stroke prevention, whereas the risk of bleeding for rivaroxaban is comparable to that of warfarin

Case #2

78-year-old female presents to your office with a new diagnosis of atrial fibrillation. This diagnosis was made during a recent visit to the ED with palpitations and tachycardia. In the office today your patient is in NSR. The patient has a history of well controlled hypertension on amlodipine and HCTZ as well as diabetes mellitus on oral hypoglycemic agents. Which of the following is indicated for long term prevention of thromboembolic stroke:

- ▶ Aspirin
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Case #3

54-year-old male presents to your office with a new diagnosis of atrial fibrillation. In the office today your patient is in atrial fibrillation with well controlled ventricular rate. The patient has a history of dyslipidemia and well controlled hypertension. He has a history of rheumatic fever as a child and known to have moderate mitral valve stenosis. Which of the following is indicated for long term prevention of thromboembolic stroke:

- ▶ Dabigatran
- ▶ Aspirin and Plavix
- ▶ Warfarin
- ▶ Rivaroxaban
- ▶ Non are indicated as the patient is at low risk for CVA

Who Are NOAC Eligible Patients?

Valvular vs Non-Valvular AF

What is Non-Valvular AF anyway

Very Confusing Terminology

Valvular vs Non-Valvular AF

- ▶ Classically - Valvular AF refers to AF in the setting of **moderate to severe mitral stenosis** or in the presence of an artificial (**mechanical**) heart valve.
- ▶ Valvular AF is considered an indication for long-term anticoagulation with **Warfarin** **regardless of CHA2DS2-VASc Score**
- ▶ Nonvalvular AF does not imply the absence of valvular heart disease

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Case #4

81-year-old male presents with atrial fibrillation. The patient has a history of dyslipidemia, coronary artery disease, previous MI, mild chronic kidney disease and hypertension. Which of the following is the best option for long term prevention of thromboembolic stroke:

- ▶ Dabigatran
- ▶ Apixaban
- ▶ Warfarin
- ▶ Rivaroxaban
- ▶ Aspirin

Pharmacokinetics and drug interactions of direct oral anticoagulants

Anticoagulant	Bioavailability	Metabolism and clearance* ¶	Half-life	Potential for pharmacokinetic drug interactions* ¶
Dabigatran (Pradaxa)	3 to 7% bioavailable - Unaffected by food - Capsule must be taken intact and requires gastric acidity for absorption	- Over 80% renally cleared - P-gp substrate*	12 to 17 hours - Prolonged in renal impairment and older adults	- P-gp inhibitors can increase dabigatran effect - P-gp inducers can decrease dabigatran effect - Avoidance of some combinations or dose adjustment may be needed
Apixaban (Eliquis)	50% bioavailable - Unaffected by food	27% renally cleared - Metabolized, primarily by CYP3A4 ¶ - P-gp substrate*	12 hours - Prolonged in older adults	- Strong CYP3A4 inhibitors and/or strong P-gp inhibitors can increase apixaban effect - Strong CYP3A4 inducers and/or strong P-gp inducers can decrease apixaban effect - Avoidance of some combinations or dose adjustment may be needed
Edoxaban (Savaysa, Lixiana)	62% bioavailable - Unaffected by food	50% renally cleared - Reduced efficacy in patients with NVAf and CrCl >95 mL/minute^Δ - Undergoes minimal CYP metabolism ¶ - P-gp substrate*	10 to 14 hours - Prolonged in renal impairment	- P-gp inhibitors can increase edoxaban effect - P-gp inducers can decrease edoxaban effect - Avoidance of some combinations or dose adjustment may be needed
Rivaroxaban (Xarelto)	10 mg dose: 80 to 100% bioavailable - Unaffected by food 20 mg dose: 66% bioavailable if taken when fasting; increased if taken with food	36% renally cleared - Metabolized, primarily by CYP3A4 ¶ - P-gp substrate*	7 to 11 hours^[1] - Prolonged in renal impairment and older adults	- Strong CYP3A4 inhibitors and/or strong P-gp inhibitors can increase rivaroxaban effect - Strong CYP3A4 inducers and/or strong P-gp inducers can decrease rivaroxaban effect - Avoidance of some combinations or dose adjustment may be needed

Renal and Hepatic Function

- ▶ All 4 NOACs with FDA approval for use in patients with AF have dosing defined by renal function (Creatinine or CrCl using the Cockcroft-Gault equation). Apixaban adds additional dosing considerations of age ≥ 80 years or weight ≤ 60
- ▶ Renal function should be regularly monitored and CrCl calculated at an interval that depends on the individual degree of renal dysfunction and likelihood of fluctuation, and dose adjustments should be made according to FDA dosing guidelines.
- ▶ In addition, for the factor Xa inhibitors, hepatic function should occasionally be monitored. NOACs are not recommended for use in patients with severe hepatic dysfunction.

Renal and Hepatic Function

- ▶ Edoxaban is not approved for use in patients with poor renal function ($\text{CrCl} < 30 \text{ mL/min}$) or upper-range renal function ($\text{CrCl} > 95 \text{ mL/min}$).
- ▶ For patients with AF who have a CHA2DS2-VASc score of 2 or greater in men or 3 or greater in women and who have end-stage CKD or are on dialysis, it might be reasonable to prescribe warfarin (INR 2.0 to 3.0) or apixaban for oral anticoagulation

Case #4

81-year-old male presents with atrial fibrillation. The patient has a history of dyslipidemia, coronary artery disease, previous MI, mild chronic kidney disease and hypertension. Which of the following is the best option for long term prevention of thromboembolic stroke:

- ▶ Dabigatran
- ▶ Apixaban
- ▶ Warfarin
- ▶ Rivaroxaban
- ▶ Aspirin

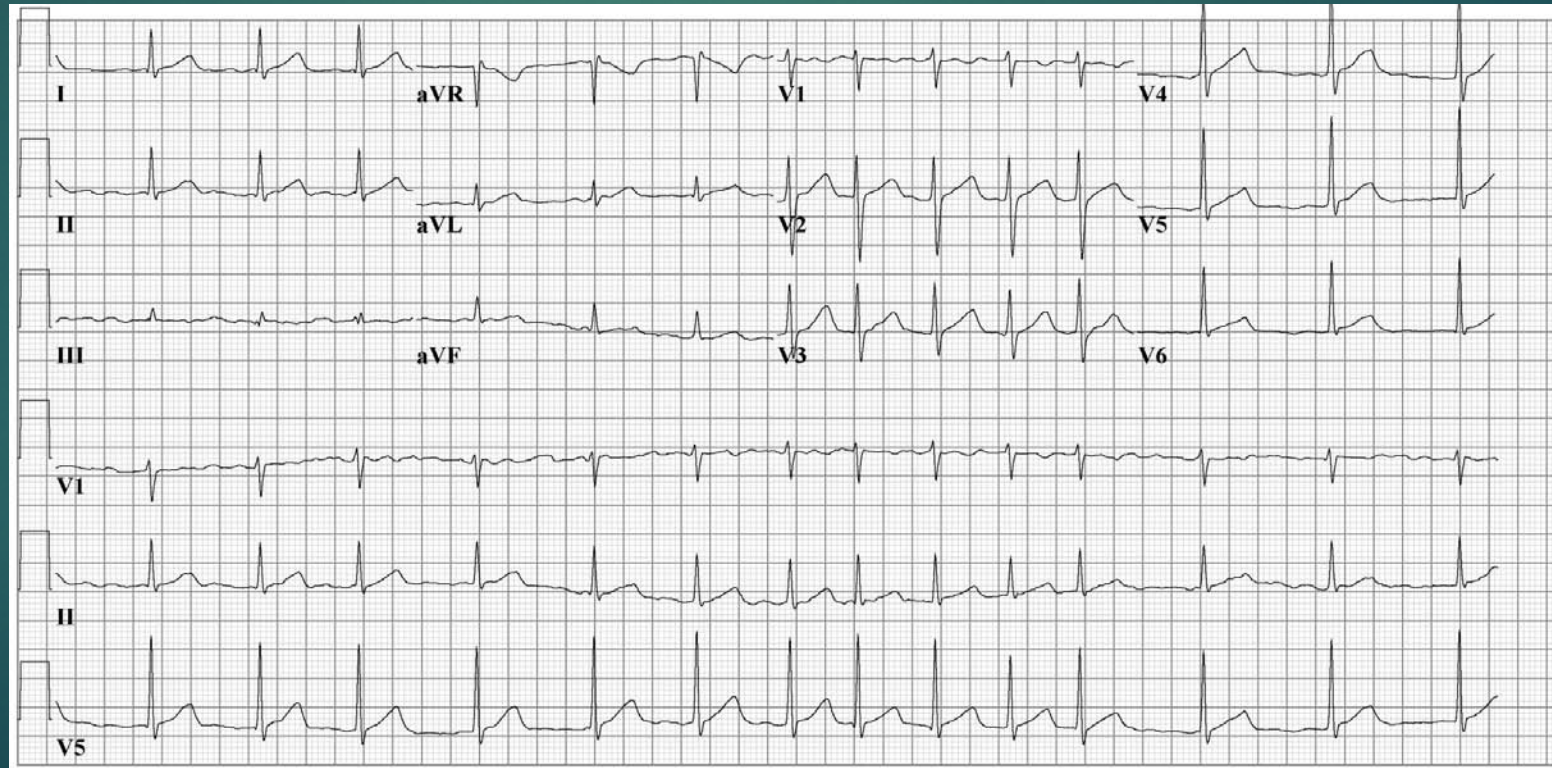
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CASE #5

66-year-old male with a history of Atrial Fibrillation presents to your office with complaints of 2 weeks of dyspnea and fatigue with occasional palpitations. He feels like “he’s back in Afib”. He doesn’t feel “great”. His BP in the office is 131/72. His HR is in the 80’s. His only other cardiovascular history is Hypertension. His home medications include Metoprolol, Lisinopril, Aspirin 81 mg and Omeprazole. ECG shown below:



Case #5

In hopes to restore sinus rhythm which of the following is the most appropriate course of action:

- A. Increase dose of Aspirin to 325mg and schedule Cardioversion
- B. Start Flecainide in attempt of chemical cardioversion
- C. Start Apixaban and schedule Cardioversion tomorrow given degree of symptoms
- D. Start rivaroxaban and schedule cardioversion after 4 weeks of therapy, continue rivaroxaban long term post cardioversion
- E. Schedule TEE guided cardioversion, no need for systemic anticoagulation

Direct-Current Cardioversion

- ▶ Rhythm-control strategy (Symptomatic patients), cardioversion is recommended for patients with AF or atrial flutter as a method to restore sinus rhythm
- ▶ Cardioversion is recommended when a rapid ventricular response does not respond promptly to pharmacological therapies and associated with ongoing **myocardial ischemia, hypotension, or HF**
- ▶ Cardioversion is recommended for patients with AF or atrial flutter and **pre-excitation** when associated with hemodynamic instability.

Anticoagulation and Cardioversion

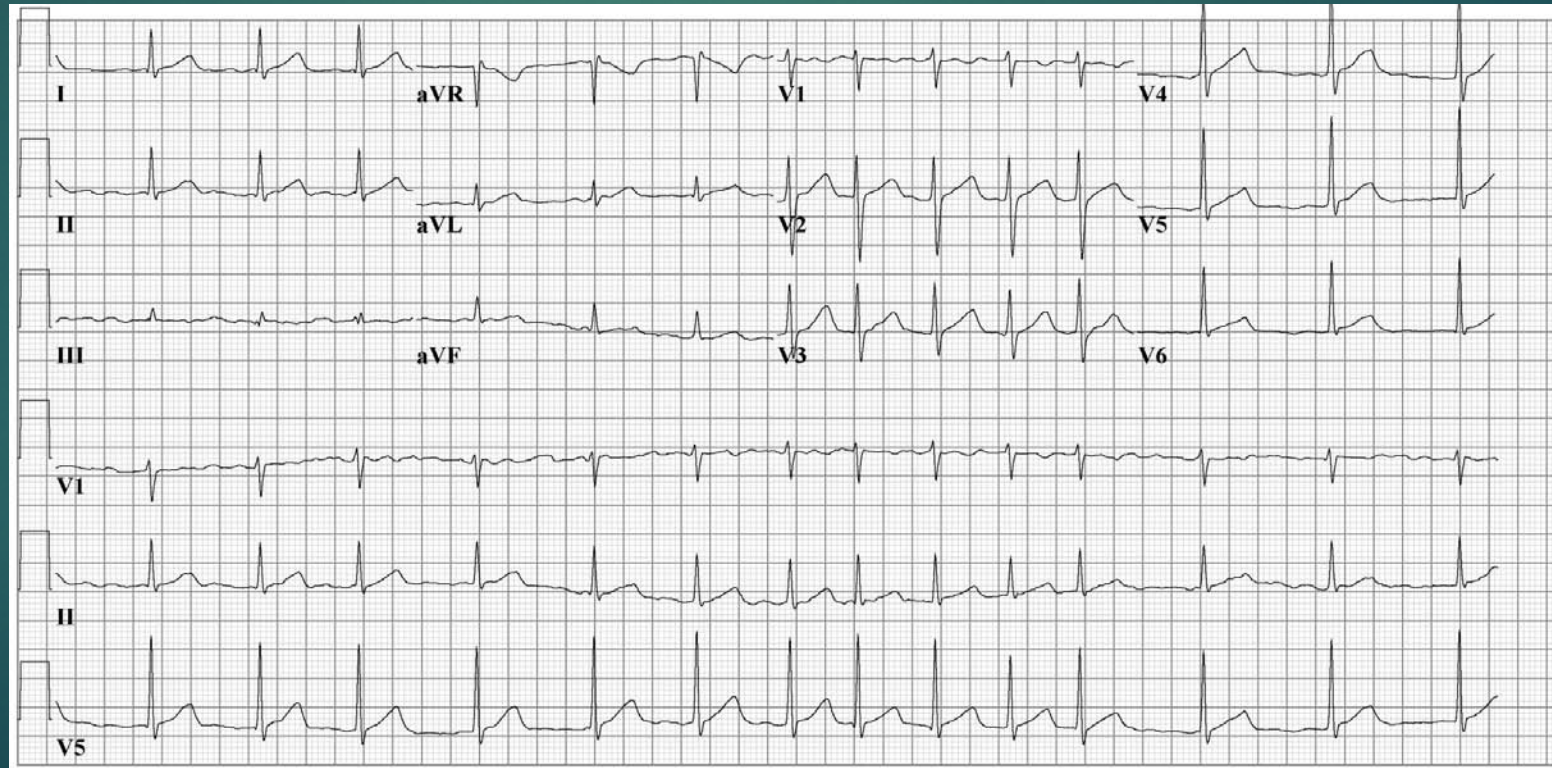
Recommendations	COR	LOE
For patients with AF or atrial flutter of 48 hours' duration or longer, or when the duration of AF is unknown, anticoagulation with warfarin (INR 2.0 to 3.0) is recommended for at least 3 weeks before and 4 weeks after cardioversion, <u>regardless of the CHA₂DS₂-VASc score and the method (electrical or pharmacological) used to restore sinus rhythm.</u>	I	B
For patients with AF or atrial flutter of more than 48 hours' duration or unknown duration that requires <u>immediate cardioversion</u> for hemodynamic instability, anticoagulation should be initiated as soon as possible and continued for at least 4 weeks after cardioversion unless contraindicated.	I	C
For patients with AF or atrial flutter of <u>less than 48 hours' duration and with high risk of stroke</u> , intravenous heparin or LMWH, or administration of a factor Xa or direct thrombin inhibitor, is recommended as soon as possible before or immediately after cardioversion, followed by long-term anticoagulation therapy.	I	C

Anticoagulation and Cardioversion

Recommendations	COR	LOE
Following cardioversion for AF of any duration, the decision about <u>long-term anticoagulation therapy should be based on the thromboembolic risk profile.</u>	I	C
For patients with AF or atrial flutter of 48 hours' duration or longer or of unknown duration who <u>have not been anticoagulated for the preceding 3 weeks, it is reasonable to perform TEE before cardioversion</u> and proceed with cardioversion if no LA thrombus is identified, including in the LAA, provided that anticoagulation is achieved before TEE and maintained after cardioversion for at least 4 weeks.	IIa	B
For patients with AF or atrial flutter of 48 hours' duration or longer or when duration of AF is unknown, anticoagulation with dabigatran, rivaroxaban, or apixaban is reasonable for at least 3 weeks before and 4 weeks after cardioversion.	IIa	C

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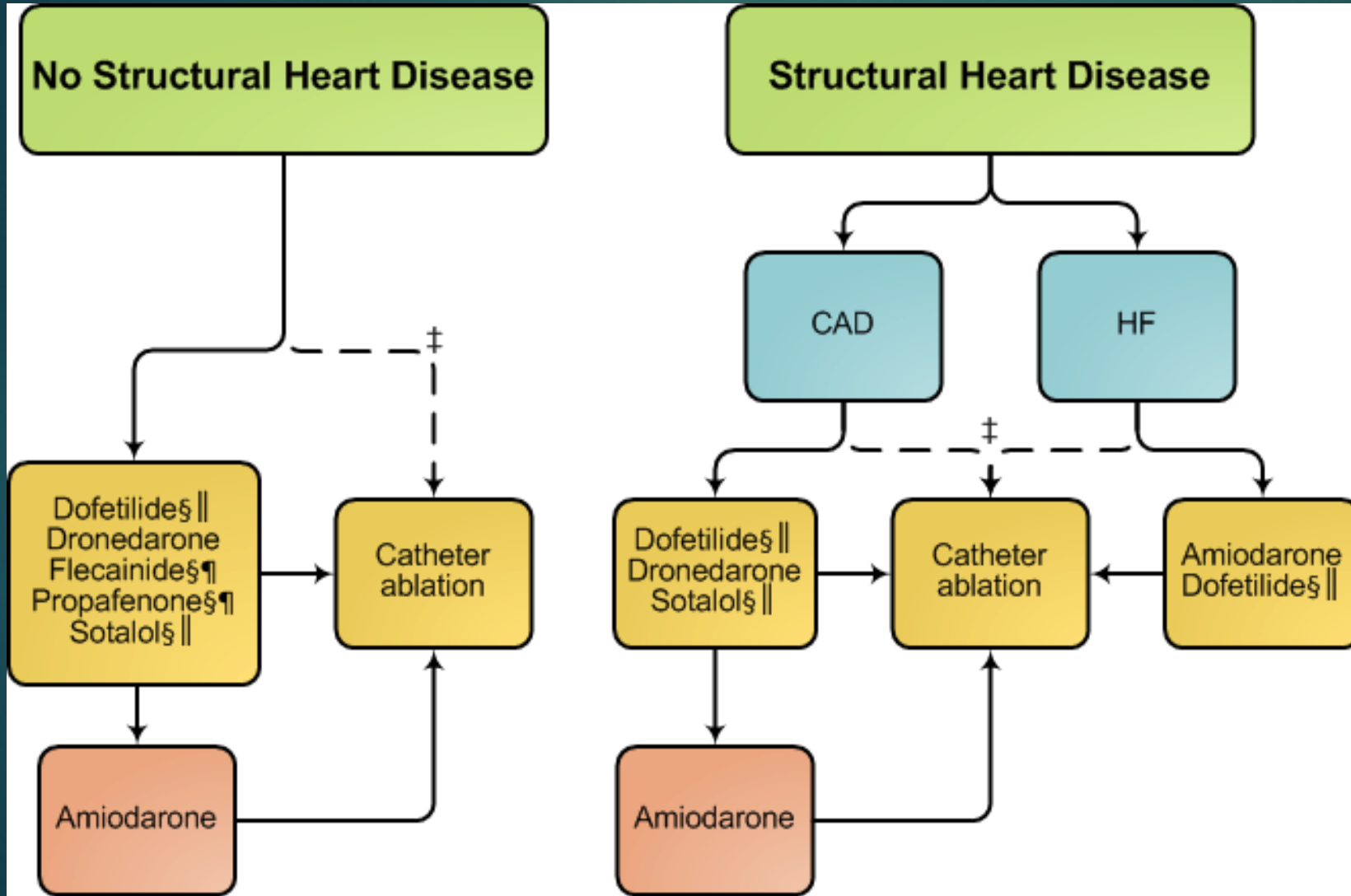


Rhythm Control Antiarrhythmic Drug Therapy

Rhythm Control - Antiarrhythmic Drug Therapy

- ▶ Before initiating antiarrhythmic drug therapy, treat precipitating or reversible causes of AF is
- ▶ The risks of the antiarrhythmic drug, including pro-arrhythmia, should be considered and discussed with patients.
- ▶ Amiodarone should only be used after consideration of risks and when other agents have failed or are contraindicated (Class I)

Strategies for Rhythm Control in Patients with Paroxysmal and persistent AF



§ Not recommended with severe LVH (wall thickness >1.5 cm)

|| Should be used with caution in patients at risk for Torsades de Pointes ventricular tachycardia

¶ Should be combined with AV nodal blocking agents

Rhythm Control - Antiarrhythmic Drug Therapy

- ▶ Dronedarone **should not** be used for treatment of AF in patients with active or recent NYHA class III and IV HF
- ▶ Antiarrhythmic drugs for rhythm control **should not** be continued when AF becomes permanent

Cryptogenic Stroke

- ▶ The cause of ischemic stroke remains unknown in up to 40% of patients with a diagnosis of cryptogenic stroke.
- ▶ Prolonged electrocardiogram monitoring with an implantable cardiac monitor in these patients (age >40 years) has the advantage of increasing the likelihood of detecting silent AF that would escape detection with short-term monitoring.
- ▶ Role in screening with a “smart” worn or handheld WiFi-enabled devices



Thank You!

Questions?