קוים מנחים לפרפור פרוזדורים - עדכון

משה סויסה

מרכז רפואי קפלן

INTRODUCTION

- The prevalence of atrial fibrillation (AF) is approximately 1.5–2% of the general population
- The arrhythmia is associated:
  - with a five-fold risk of stroke
  - a three-fold incidence of CHF
  - higher mortality
  - higher hospitalization rate
- Fortunately a number of valuable treatments have been devised in recent years that may offer some solution to this problem

INTRODUCTION

- In 2010, when the ESC Guidelines for AF were first issued it was already realized that an update would be necessary in 2012
  - Approvals of new drugs vernakalant and dabigatran
  - In addition, reports from major clinical trials of the novel oral anticoagulants
    - AVERROES
    - ROCKET-AF
    - ARISTOTLE
  - What was not expected was the early discontinuation of the PALLAS of dronedarone nor the reports of hepatotoxicity associated with this drug

New / Modified Recommendation

Topic	A	B	C	I	IIa	IIb	III
Anticoagulation risk stratification	6	7		6	7		
Anticoagulation	2	5	1	3	4		1
Left atrial appendage occlusion		1	1			2	
Pharmacological cardioversion	1	2		1	2		
Oral antiarrhythmic therapy	1	2		1		1	1
Left atrial catheter ablation	2	3		1	4		
Total n (%)	12 (35%)	20 (59%)	2 (9%)	12 (35%)	17 (50%)	3 (9%)	2 (9%)

Opportunistic Screening

- Diagnosing AF before the first complications is important recognized priority for the prevention of strokes
  - ASSERT in patients with implanted devices
  - Holter ECGs in epidemiological studies
  - **even short episodes of 'silent' AF convey an increased risk for stroke**

Recommendations for screening AF		
Recommendations	**Class[a]**	**Level[b]**
Opportunistic screening for AF in patients ≥65 years of age using pulse-taking followed by an ECG is recommended to allow timely detection of AF.	I	B

2012 focused update of the ESC Guidelines for the management of AF

- Stroke and bleeding risk assessment
- Novel oral anticoagulants
- Left atrial appendage closure
- Cardioversion with pharmacological agents
- Oral antiarrhythmic drug therapy
- Catheter ablation of atrial fibrillation

European Heart Journal (2012) 33, 2719–2747

Stroke and bleeding risk assessment

- Risk factors for ischemic stroke/TIA/ systemic embolism in patients with AF: the Swedish Cohort Atrial Fibrillation study
- Multivariate analysis, based on 90,490 patients without anticoagulant treatment during follow-up

	Multivariate hazard ratios (95% CI)
Age (years) <65 65–74 ≥75	 1.0 (Reference) 2.97 (2.54–3.48) 5.28 (4.57–6.09)
Female sex	1.17 (1.11–1.22)
Previous ischaemic stroke	2.81 (2.68–2.95)
Intracranial bleeding	1.49 (1.33–1.67)
Vascular disease (any) • Myocardial infarction • Previous CABG • Peripheral artery disease	1.14 (1.06–1.23) 1.09 (1.03–1.15) 1.19 (1.06–1.33) 1.22 (1.12–1.32)
Hypertension	1.17 (1.11–1.22)
Heart failure (history)	0.98 (0.93–1.03)
Diabetes mellitus	1.19 (1.13–1.26)
Thyroid disease Thyrotoxicosis	1.00 (0.92–1.09) 1.03 (0.83–1.28)

Friberg L et al, Eur Heart J 2012;33:1500–10

$CHADS_2 = 0$

- $CHADS_2 = 0$ (Stroke rate > 1.5%)
- $CHADS_2 = 0$
  - $CHA_2DS_2VASC = 0$ (lone Afib), stroke rate of 0.84%
  - $CHA_2DS_2VASC = 1$ (>65), stroke rate of 0.1.75%
  - $CHA_2DS_2VASC = 2$ (>65, female) stroke rate of 2.69%
  - $CHA_2DS_2VASC = 3$ (>65, femal, vasc) stroke rate of 3.2%

CHA_2DS_2VASc score

		CHA_2DS_2-VASc Score
C	Congestive heart failure	1
H	Hypertension	1
A	Age ≥ 75 years	2
D	Diabetes mellitus	1
S	Stroke (or TIA)	2
V	Vascular disease*	1
A	Age 66-74 years	1
Sc	Sex category (female)	1

* Prior MI, peripheral artery disease, aortic plaque

HAS-BLED Score

HAS-BLED Score

	Clinical Characteristic	Score
H	Hypertension	1
A	Abnormal renal or liver function (1 each)	1 or 2
S	Stroke	1
B	Bleeding	1
L	Labile INR	1
E	Elderly age	1
D	Drugs or alcohol (1 each)	1 or 2
	Maximum Score	**9**

Hypertension, SBP > 160 mmHg; Abnormal renal function: chronic dialysis, renal transplant, serum creatinine ≥ 200 µmol/L; Abnormal liver function: chronic hepatitis, bilirubin > 2x upper limit of normal (ULN) in association with AST/ALT/ALP > 3 x ULN; Bleeding, previous history, predisposition; Labile INRs, unstable/high INRs in therapeutic range < 60%; Age > 65 years; Drugs/alcohol: concomitant use of antiplatelet agents, NSAIDs, etc.

Rates of Intracranial Bleeding

ARISTOTLE[a]	Apixaban (n = 9088)	Warfarin (n = 9052)	*P* Value
%/y	0.33	0.80	< .001

RE-LY[b]	Dabigatran 110 mg (n = 6015)	Dabigatran 150 mg (n = 6076)	Warfarin (n = 6022)	
Rate/y, %	0.2	0.3	0.7	< .001

ROCKET AF[c]	Rivaroxaban (n = 7111)	Warfarin (n = 7125)	
%	0.8	1.2	.02

AVERROES

Outcome	Apixaban Annual Rate	Aspirin Annual Rate	Apixaban vs Aspirin HR (95% CI)	Apixaban vs Aspirin *P* Value
Stroke or systemic embolism	1.6	3.7	0.45 (0.32-0.62)	< .001
Stroke	1.6	3.4	0.46 (0.33-0.65)	< .001
• Ischemic	1.1	3.0	0.37 (0.25-0.55)	< .001
• Systemic embolism	0.1	0.4	0.15 (0.03-0.69)	.01
Major bleeding	**1.4**	**1.2**	**1.13 (0.74-1.75)**	**.57**

Anticoagulation - General

Recommendations for prevention of thromboembolism in non-valvular AF - general		
Recommendations	**Class**	**Level**
Antithrombotic therapy to prevent thromboembolism is recommended for all patients with AF, except in those patients (both male and female) who are at low risk (aged <65 years and lone AF), or with contraindications.	I	A
The choice of antithrombotic therapy should be based upon the absolute risks of stroke/thromboembolism and bleeding and the net clinical benefit for a given patient.	I	A
The CHA_2DS_2-VASc score is recommended as a means of assessing stroke risk in non-valvular AF.	I	A

Anticoagulation - General

Recommendations	Class	Level
In patients with a CHA2DS2-VASc score of 0 (i.e., aged <65 years with lone AF) who are at low risk, with none of the risk factors, no antithrombotic therapy is recommended.	I	B
In patients with a CHA_2DS_2-VASc score ≥2, OAC therapy with: • adjusted-dose VKA (INR 2–3); or • a direct thrombin inhibitor (dabigatran); or • an oral factor Xa inhibitor (e.g., rivaroxaban, apixaban …. is recommended, unless contraindicated.	I	A
In patients with a CHA_2DS_2-VASc score of 1, OAC therapy with: • adjusted-dose VKA (INR 2–3); or • a direct thrombin inhibitor (dabigatran); or • an oral factor Xa inhibitor (e.g., rivaroxaban, apixaban)[d] …. should be considered, based upon an assessment of the risk of bleeding complications and patient preferences.	IIa	A

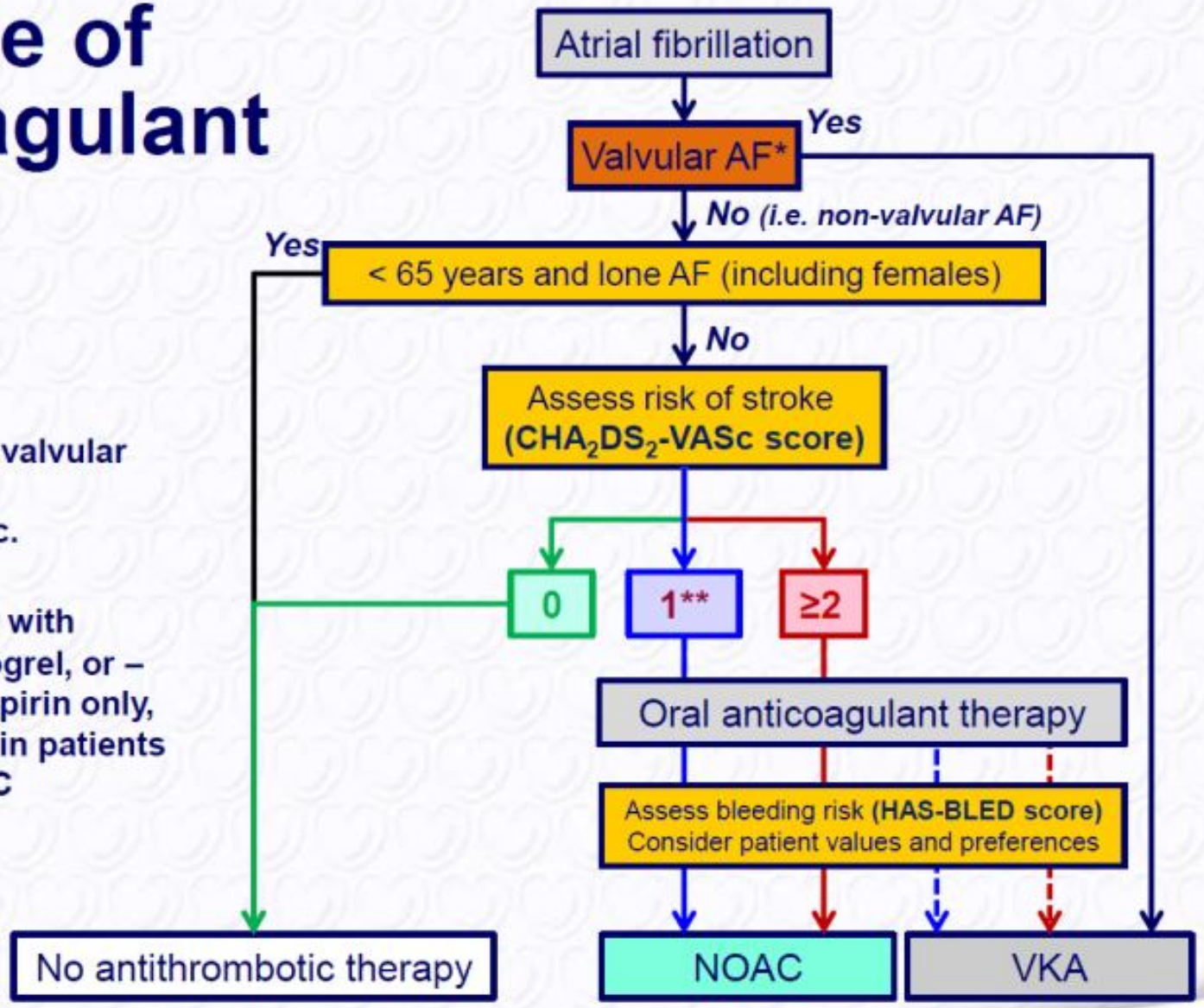
Anticoagulation - General

Recommendations for prevention of thromboembolism in non-valvular AF - general		
Recommendations	**Class**	**Level**
When patients refuse the use of any OAC (whether VKAs or NOACs), antiplatelet therapy should be considered, using combination therapy with aspirin 75–100 mg plus clopidogrel 75 mg daily (where there is a low risk of bleeding) or – less effectively – aspirin 75–325 mg daily.	**IIa**	**B**

Anticoagulation - NOACs

Recommendations for prevention of thromboembolism in non-valvular AF - NOACs		
Recommendations	**Class**	**Level**
When adjusted-dose VKA (INR 2–3) cannot be used in a patient with AF where an OAC is recommended, due to difficulties in keeping within therapeutic anticoagulation, experiencing side effects of VKAs, or inability to attend or undertake INR monitoring, one of the NOACs, either: • a direct thrombin inhibitor (dabigatran); or • an oral factor Xa inhibitor (e.g., rivaroxaban, apixaban)d … is recommended.	I	B
Where OAC is recommended, one of the NOACs, either: • a direct thrombin inhibitor (dabigatran); or • an oral factor Xa inhibitor (e.g., rivaroxaban, apixaban)d … should be considered rather than adjusted-dose VKA (INR 2–3) for most patients with non-valvular AF, based on their net clinical benefit.	IIa	A

Choice of Anti-coagulant



- Includes rheumatic valvular AF, hypertrophic cardiomyopathy, etc.

** Antiplatelet therapy with aspirin plus clopidogrel, or – less effectively – aspirin only, may be considered in patients who refuse any OAC

Anticoagulation - Summary

- The efficacy of stroke prevention with aspirin is weak, and the risk of major bleeding (and ICH) with aspirin is not significantly different to that of OAC, especially in the elderly
- The use of antiplatelet therapy (as aspirin/clopidogrel or less effectively aspirin monotherapy) for stroke prevention in AF should be limited to the few patients who refuse any form of OAC
- The CHA_2DS_2-VASc score is better at identifying 'truly low-risk' patients with AF and is as good as—and possibly better than $CHADS_2$ score

LAA Closure/Occlusion/Excision

- The LAA is considered the main (but not the only) site of thrombus formation in patients with AF
- Surgical excision or stapling of the LAA
- Percutaneous LAA occlusion (PROTECT AF, PREVAIL, Amplatzer Cardiac Plug Trial)

Recommendations for LAA closure/occlusion/excision

Recommendations	Class	Level
Interventional, percutaneous LAA closure may be considered in patients with a high stroke risk and contraindications for long-term oral anticoagulation.	IIb	B
Surgical excision of the LAA may be considered in patients undergoing open heart surgery.	IIb	C

Pharmacological Cardioversion

- Vernakalant atrial effect
- AC Trail - vernakalant was:
  - significantly more effective than placebo in converting AF of ≤7 days (51.7% vs 3.6%)
  - The median time to conversion was 8–11 minutes
  - AF post cardiac surgery (47% vs 14%)
- Vernakalant is superior to IV amiodarone in converting AF within 90 min (51.7% vs. 5.2%)
- Vernakalant is ineffective in converting AF of more than 7 days duration or typical atrial flutter

Pharmacological Cardioversion

- Vernakalant in IHD, HTN, HF
- Safety:
  - Hypotension in patients with HF
  - Bradycardia
  - no excess in ventricular arrhythmia
  - No drug-related torsades de pointes
  - However, in HF patients NSVT occurred more often on treatment (7.3% vs. 1.6% on placebo)
  - The QTc and QRS prolonged by 25 and 8ms

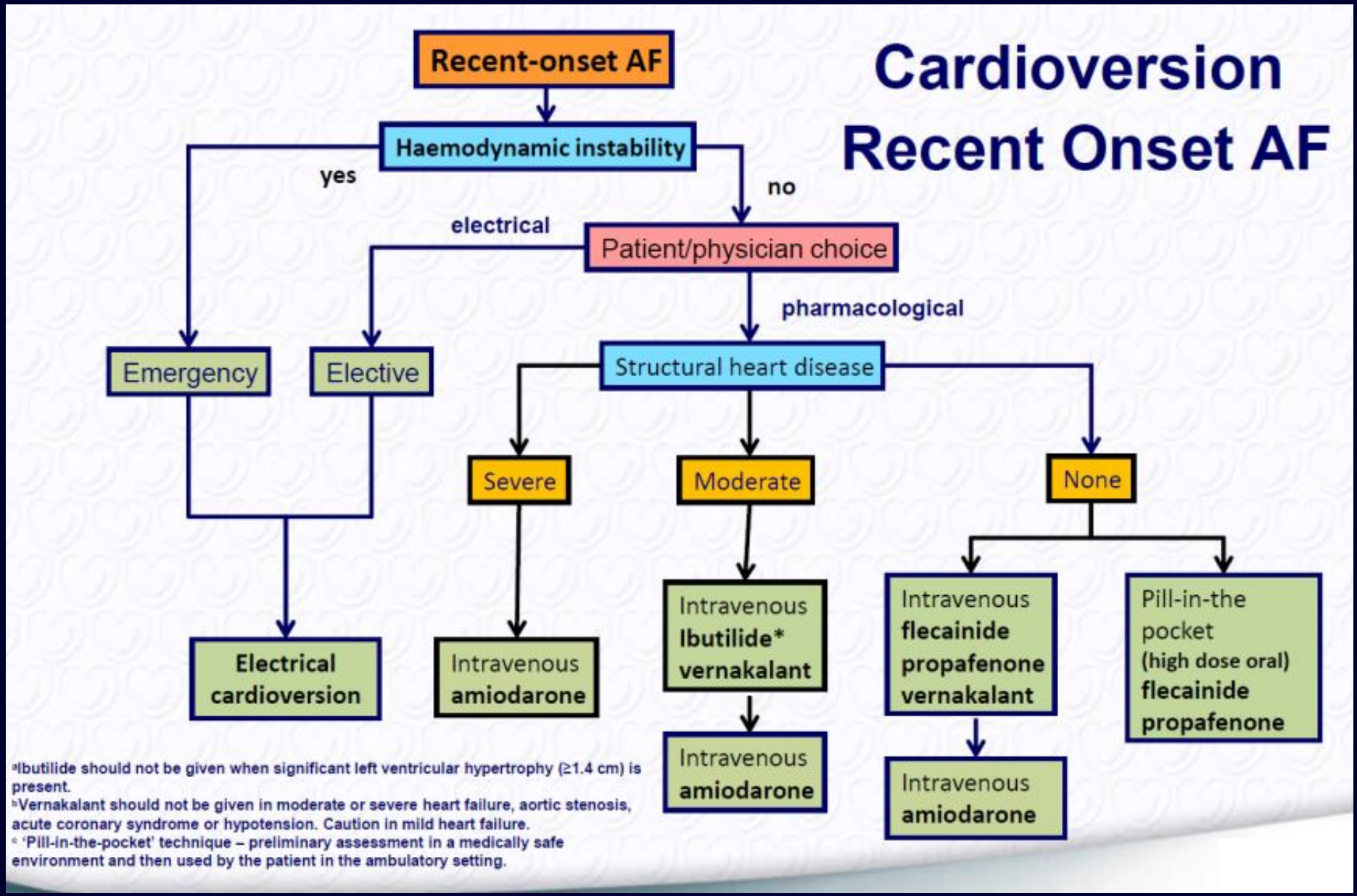
Pharmacological Cardioversion

- Vernakalant is contraindicated
  - hypotension < 100 mmHg
  - ACS within 30 days
  - CHF NYHA class III and IV
  - severe aortic stenosis
  - Prolonged QT >440 ms
- Should be used with caution inpatients with NYHA I or II heart failure because of increased risk of hypotension
- Should be avoided in patients LVEF ≤35

Pharmacological Cardioversion

Recommendations for pharmacological cardioversion of recent-onset AF		
Recommendations	**Class**	**Level**
When pharmacological cardioversion is preferred and there is no or minimal structural heart disease, intravenous flecainide, propafenone, ibutilide, or vernakalant are recommended.	I	A
In patients with AF ≤7 days and moderate structural heart disease (but without hypotension <100 mm Hg, NYHA class III or IV heart failure, recent [<30 days] ACS, or severe aortic stenosis) intravenous vernakalant may be considered. Vernakalant should be used with caution in patients with NYHA class I–II heart failure.	IIb	B
Intravenous vernakalant may be considered for cardioversion of postoperative AF ≤3 days in patients after cardiac surgery.	IIb	B

Cardioversion Recent Onset AF

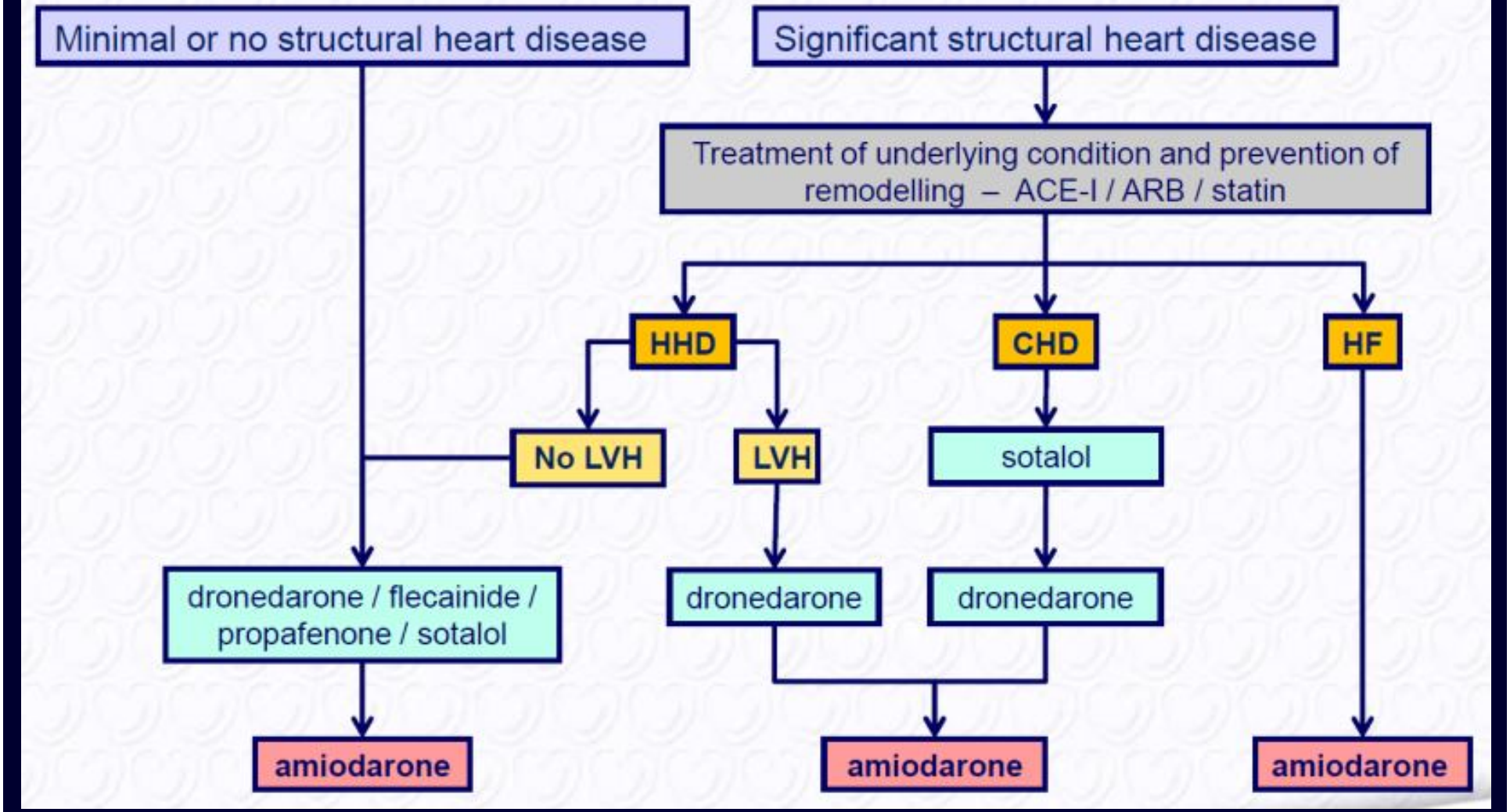


[a]Ibutilide should not be given when significant left ventricular hypertrophy (≥1.4 cm) is present.
[b]Vernakalant should not be given in moderate or severe heart failure, aortic stenosis, acute coronary syndrome or hypotension. Caution in mild heart failure.
[c] 'Pill-in-the-pocket' technique – preliminary assessment in a medically safe environment and then used by the patient in the ambulatory setting.

Oral Antiarrhythmic Drugs

Recommendations for oral antiarrhythmic agents		
Recommendations	**Class**	**Level**
Dronedarone is recommended in patients with recurrent AF as a moderately effective antiarrhythmic agent for the maintenance of sinus rhythm.	I	A
Short-term (4 weeks) antiarrhythmic therapy after cardioversion may be considered in selected patients e.g., those at risk for therapy associated complications.	IIb	B
Dronedarone is not recommended in patients with permanent AF.	III	B

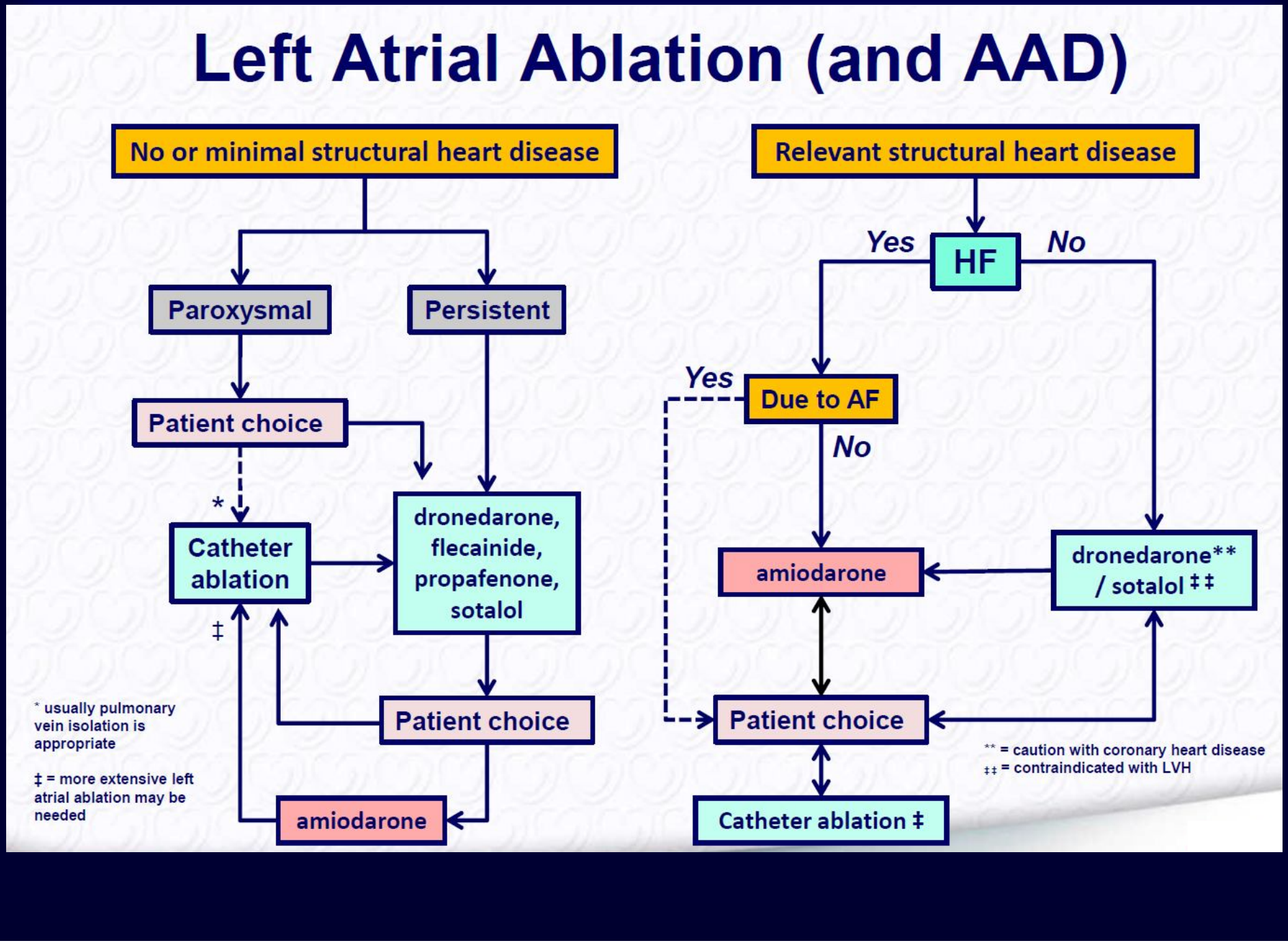
Choice of Oral Antiarrhythmic Drug



Left Atrial Ablation

Recommendations for left atrial ablation		
Recommendations	**Class**	**Level**
Catheter ablation of symptomatic paroxysmal AF is recommended in patients who have symptomatic recurrences of AF on antiarrhythmic drug therapy (amiodarone, dronedarone, flecainide, propafenone, sotalol) and who prefer further rhythm control therapy, when performed by an electrophysiologist who has received appropriate training and is performing the procedure in an experienced centre.	I	A
Catheter ablation of AF should be considered as first-line therapy in selected patients with symptomatic, paroxysmal AF as an alternative to antiarrhythmic drug therapy, considering patient choice, benefit, and risk.	IIa	B

Left Atrial Ablation (and AAD)



תודה רבה

לא כפייתי מידי

לא מבלבל מידי