Atrial Fibrillation
Based on ESC Guidelines

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Epidemiology

- AF affects 1–2% of the population, and this figure is likely to increase in the next 50 years.
- AF may long remain undiagnosed (silent AF), and many patients with AF will never present to hospital.
- Hence, the ‘true’ prevalence of AF is probably closer to 2% of the population.
- The prevalence of AF increases with age
  - 0.5% at 40–50 years, to 5–15% at 80 years.
- Men are more often affected than women.
- The lifetime risk of developing AF is 25% in those who have reached the age of 40.
- The incidence of AF appears to be increasing (13% in the past two decades).

Atrial fibrillation - cardiovascular outcomes

- **AF is associated with increased rates**
  - -Death (doubled)
  - -Stroke and other thrombo-embolic events
  - -Heart failure
  - -Hospitalizations
  - -Degraded quality of life
  - -Reduced exercise capacity
  - -Left ventricular (LV) dysfunction

Death

- Death rates are doubled by AF, independently of other known predictors of mortality
- Only antithrombotic therapy has been shown to reduce AF-related deaths.

Stroke

- Stroke in AF is often severe and results in long-term disability or death
- Approximately every fifth stroke is due to AF
- Paroxysmal AF carries the same stroke risk as permanent or persistent AF

Hospitalizations

- Hospitalizations due to AF account for one-third of all admissions for cardiac arrhythmias
- The main causes are:
  - Acute coronary syndrome
  - Aggravation of heart failure
  - Thrombo-embolic complications
  - Acute arrhythmia management

Quality of life and exercise capacity

- Quality of life and exercise capacity are impaired in patients with AF
- Patients with AF have a significantly poorer quality of life compared with
  - healthy controls
  - the general population
  - Or patients with coronary heart disease in sinus rhythm

Left ventricular (LV) function

- Left ventricular (LV) function is often impaired by
  - the irregular, fast ventricular rate
  - by loss of atrial contractile function
  - and by increased end-diastolic LV filling pressure
- Both rate control and maintenance of sinus rhythm can improve LV function in AF patients

Cardiovascular and other conditions associated with atrial fibrillation

- Ageing
- Hypertension
- Symptomatic heart failure
- Tachycardiomyopathy
- Valvular heart diseases
- Cardiomyopathies
- Atrial septal defect
- Coronary artery disease
- Thyroid dysfunction
- Obesity
- Diabetes mellitus
- COPD
- Chronic renal disease

Ageing

- Ageing increases the risk of developing AF, possibly through
  - age-dependent loss and isolation of atrial myocardium
  - and associated conduction disturbances

Hypertension

- Hypertension is a risk factor for incident (first diagnosed) AF and for AF-related complications such as:
  - stroke
  - and systemic thrombo-embolism

Symptomatic heart failure

- Symptomatic heart failure (NYHA classes II–IV) is found in 30% of AF patients
- AF is found in up to 30–40% of heart failure patients
- Heart failure can be both:
  - a consequence of AF
  - and a cause of the arrhythmia due to:
    - increased atrial pressure and volume overload

Valvular heart diseases

- Valvular heart diseases are found in 30% of AF Patients
- AF caused by left atrial (LA) distension is an early manifestation of mitral stenosis and/or regurgitation
- AF occurs in later stages of aortic valve disease
- ‘rheumatic AF’ was a frequent finding in the past, it is now relatively rare in Europe

Cardiomyopathies

- Cardiomyopathies, including primary electrical cardiac diseases, carry an increased risk for AF, especially in young patients
- Relatively rare cardiomyopathies are found in 10% of AF patients
- A small proportion of patients with ‘lone’ AF carry known mutations for ‘electrical’ cardiomyopathies

Sleep apnea

- Sleep apnoea, especially in association with hypertension, diabetes mellitus, and structural heart disease, may be a pathophysiological factor for AF because of apnea-induced increases
  - in atrial pressure and size
  - or autonomic changes

Mechanisms of atrial fibrillation

- Atrial factors
  - -Structural
  - -Pathophysiological changes as a consequence of atrial fibrillation
  - -Contractile function
- Electrophysiological mechanisms
  - -Focal mechanisms
  - -Multiple wavelet
- Genetic predisposition
- Clinical correlates
  - -Atrioventricular conduction
  - -Haemodynamic changes
  - -Thrombo-embolism

Atrial factors associated with AF

Table 4 **Structural abnormalities associated with AF**

Extracellular matrix alterations
Interstitial and replacement fibrosis
Inflammatory changes
Amyloid deposit
Myocyte alterations
Apoptosis
Necrosis
Hypertrophy
Dedifferentiation
Gap junction redistribution
Intracellular substrate accumulation (haemocromatosis, glycogen)
Microvascular changes
Endocardial remodelling (endomyocardial fibrosis)

AF = atrial fibrillation.

Detection, ‘natural’ history, and acute management

- Definition
- Detection
- ‘Natural’ time course
- Electrocardiogram techniques to diagnose and monitor atrial fibrillation
- Types of atrial fibrillation
- Initial management
- Clinical follow-up

Definition

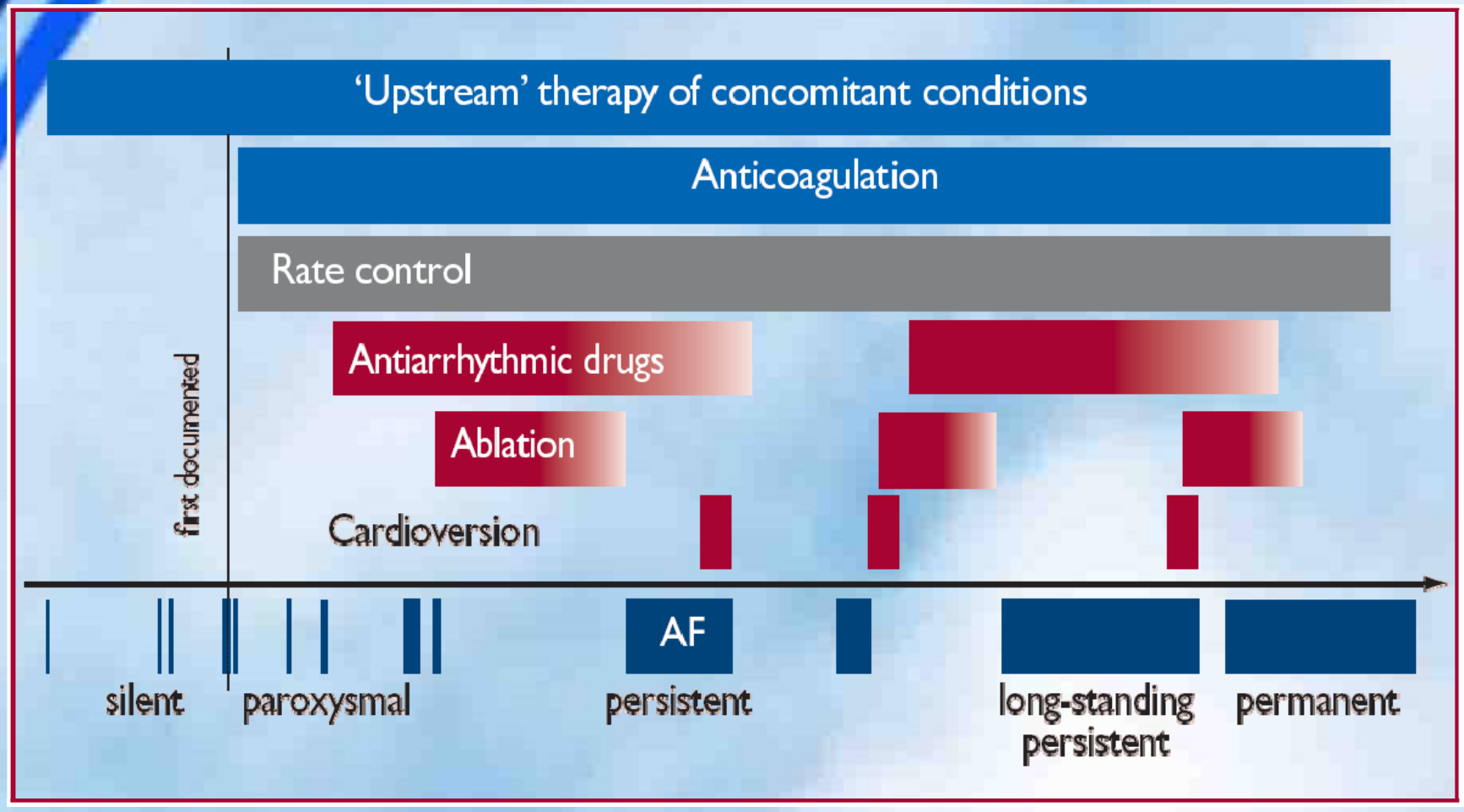
- **AF is defined as a cardiac arrhythmia with the following characteristics:**

  -(1) The surface ECG shows ‘absolutely’ irregular RR intervals

  -(2) There are no distinct P waves on the surface ECG

  -(3) The atrial cycle length (when visible) is usually variable and <200 ms (>300 bpm)

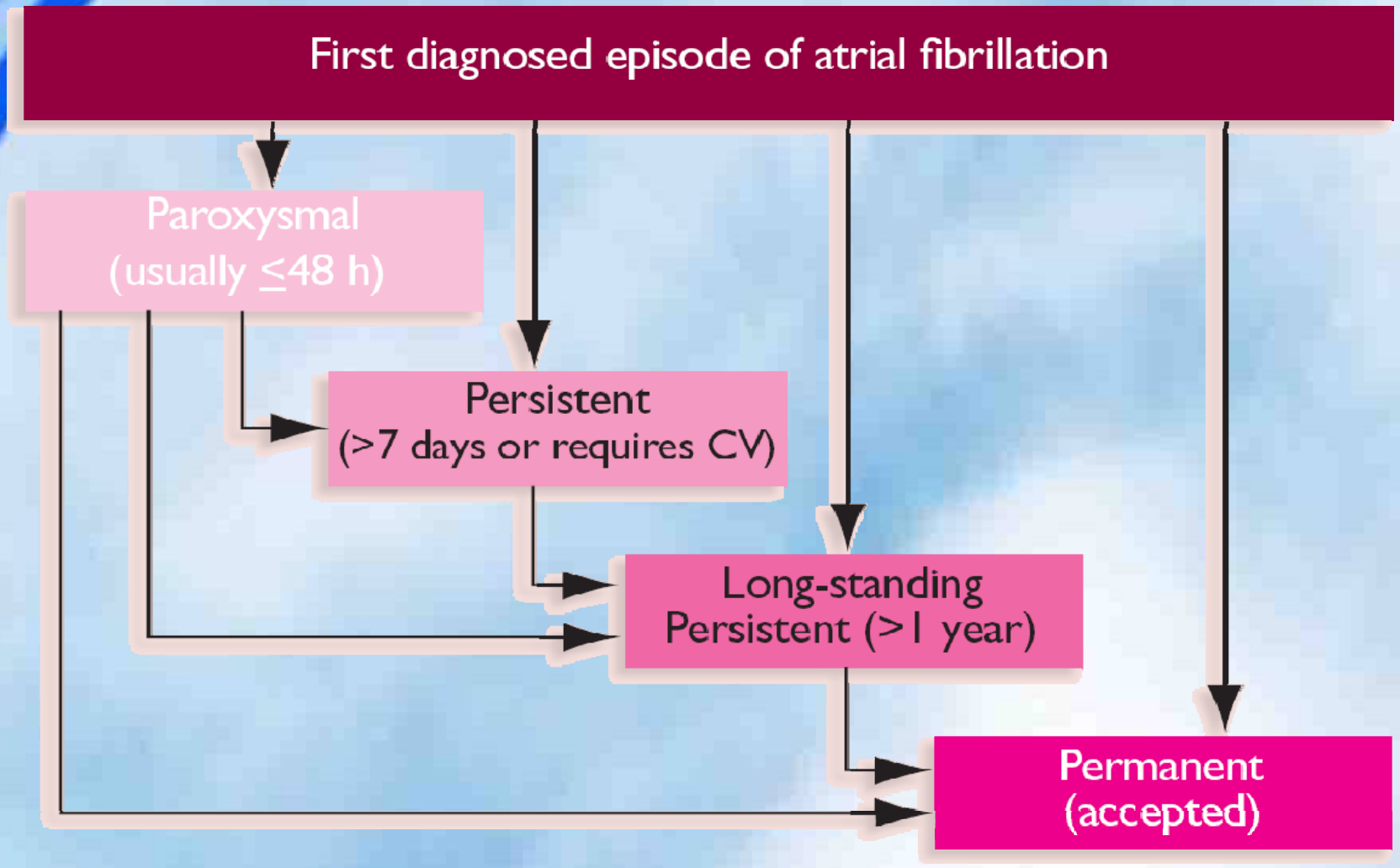
‘Natural’ time course



Types of atrial fibrillation

- First diagnosed AF
- Paroxysmal AF
- Persistent AF
- Long-standing persistent AF
- Permanent AF

Types of atrial fibrillation



Initial management

- A thorough medical history should be obtained from the patient with suspected or known AF
- The acute management of AF patients should concentrate on relief of symptoms and assessment of AF-associated risk
- Clinical evaluation should include
  - -determination of the EHRA score
  - -Estimation of stroke risk
  - -and search for:
    - conditions that predispose to AF
    - and for complications of the arrhythmia

Initial management

- **The 12-lead ECG should be inspected for signs of structural heart disease:**
  - -acute or remote myocardial infarction
  - -LV hypertrophy
  - -bundle branch block
  - -ventricular pre-excitation
  - -signs of cardiomyopathy, or ischemia

Table 6 EHRA score of AF-related symptoms

Classification of AF-related symptoms (EHRA score)	
EHRA class	**Explanation**
EHRA I	'No symptoms'
EHRA II	'Mild symptoms'; normal daily activity not affected
EHRA III	'Severe symptoms'; normal daily activity affected
EHRA IV	'Disabling symptoms'; normal daily activity discontinued

AF = atrial fibrillation; EHRA = European Heart Rhythm Association.

The EHRA score only considers symptoms that are attributable to AF and reverse or reduce upon restoration of sinus rhythm or with effective rate control

Clinical follow-up

- Has the risk profile changed?
- Is anticoagulation now necessary?
- Have the patient's symptoms improved on therapy?
- Are there signs of proarrhythmia or risk of proarrhythmia?
- Has paroxysmal AF progressed to a persistent/permanent form?
- Is the rate control approach working properly?

Clinical follow-up

- 12-ECG to document:
  - the rhythm and rate
  - to assess potential proarrhythmic ECG precursors such as:
    - lengthening of:
      -PR, QRS, or QT intervals
    - non-sustained ventricular tachycardia
    - or pauses
- The patient should be fully informed about the pros and cons of the different treatment options, whether it is anticoagulation, rate control drugs, antiarrhythmic drugs, or interventional therapy

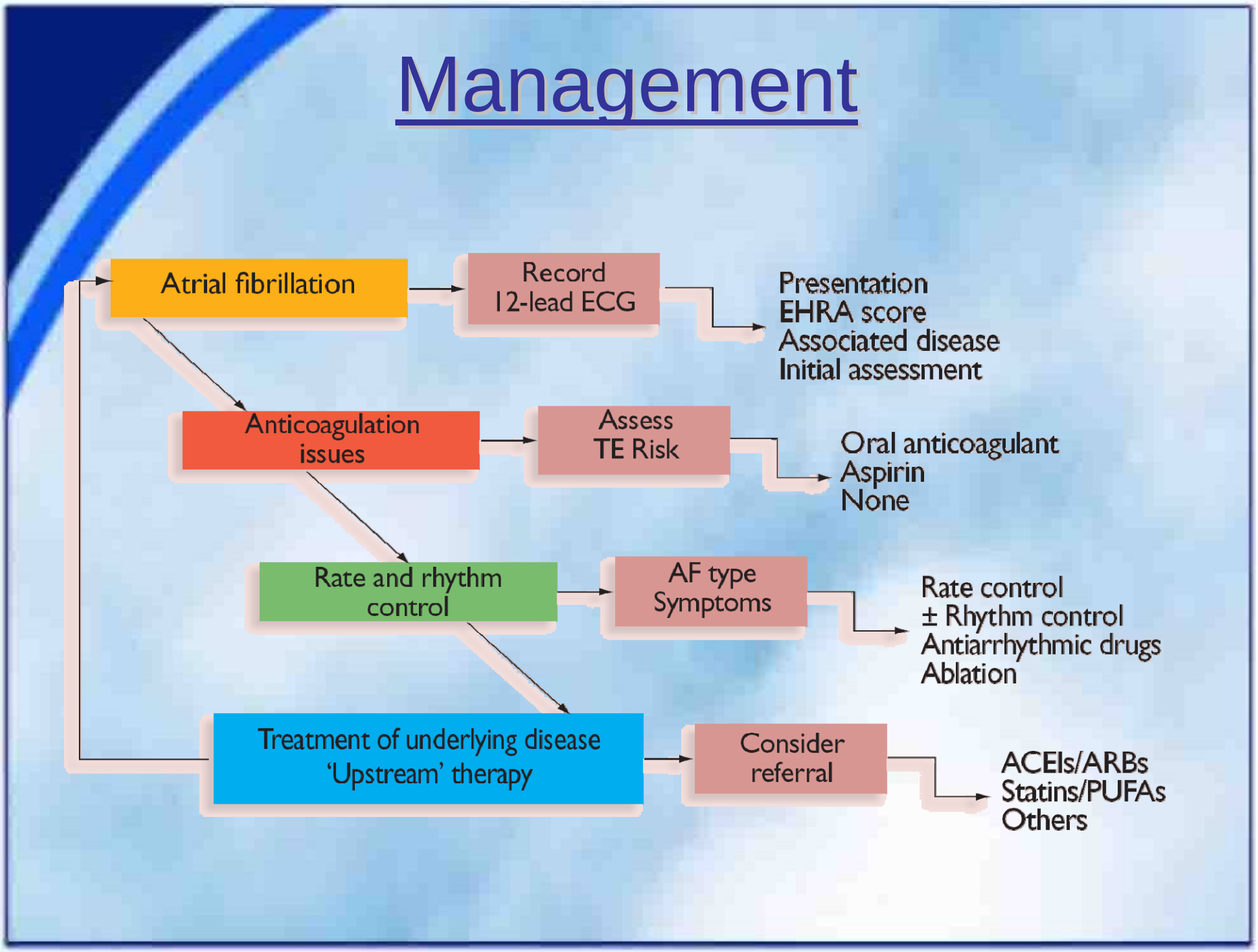
Management

- Antithrombotic management
- Rate and rhythm management
- Long-term management
- Upstream therapy

Management

- **Management of AF patients is aimed at:**
  - -reducing symptoms
  - -and preventing severe complications associated with AF
- **Prevention of AF-related complications relies on:**
  - -antithrombotic therapy
  - -control of ventricular rate
  - -and adequate therapy of concomitant cardiac diseases
- **These therapies may already alleviate symptoms, but symptom relief may require additional**
  - -rhythm control therapy by cardioversion
  - -antiarrhythmic drug therapy
  - -or ablation therapy

Management


Atrial fibrillation
Record 12-lead ECG
Presentation
EHRA score
Associated disease
Initial assessment
Anticoagulation issues
Assess TE Risk
Oral anticoagulant
Aspirin
None
Rate and rhythm control
AF type
Symptoms
Rate control
± Rhythm control
Antiarrhythmic drugs
Ablation
Treatment of underlying disease
'Upstream' therapy
Consider referral
ACEIs/ARBs
Statins/PUFAs
Others

Antithrombotic management

- Risk stratification for stroke and thrombo-embolism
- Antithrombotic therapy
- Current recommendations for antithrombotic therapy
- Risk of bleeding
- Optimal INR
- Special situations
- Cardioversion
- Non-pharmacological methods to prevent stroke

CHADS2 and CHA2DS2VASc score

(a) Risk factors for stroke and thrombo-embolism in non-valvular AF	
'Major' risk factors	**'Clinically relevant non-major' risk factors**
Previous stroke, TIA, or systemic embolism Age ≥75 years	Heart failure or moderate to severe LV systolic dysfunction (e.g. LV EF ≤40%) Hypertension - Diabetes mellitus Female sex - Age 65–74 years Vascular disease[a]
(b) Risk factor-based approach expressed as a point based scoring system, with the acronym CHA_2DS_2-VASc (Note: maximum score is 9 since age may contribute 0, 1, or 2 points)	

Risk factor	Score
Congestive heart failure/LV dysfunction	1
Hypertension	1
Age ≥75	2
Diabetes mellitus	1
Stroke/TIA/thrombo-embolism	2
Vascular disease[a]	1
Age 65–74	1
Sex category (i.e. female sex)	1
Maximum score	**9**

CHADS2 and CHA2DS2VASc score and stroke rate

$CHADS_2$ score	Patients (n = 1733)	Adjusted stroke rate (%/year)[a] (95% confidence interval)
0	120	1.9 (1.2–3.0)
1	463	2.8 (2.0–3.8)
2	523	4.0 (3.1–5.1)
3	337	5.9 (4.6–7.3)
4	220	8.5 (6.3–11.1)
5	65	12.5 (8.2–17.5)
6	5	18.2 (10.5–27.4)

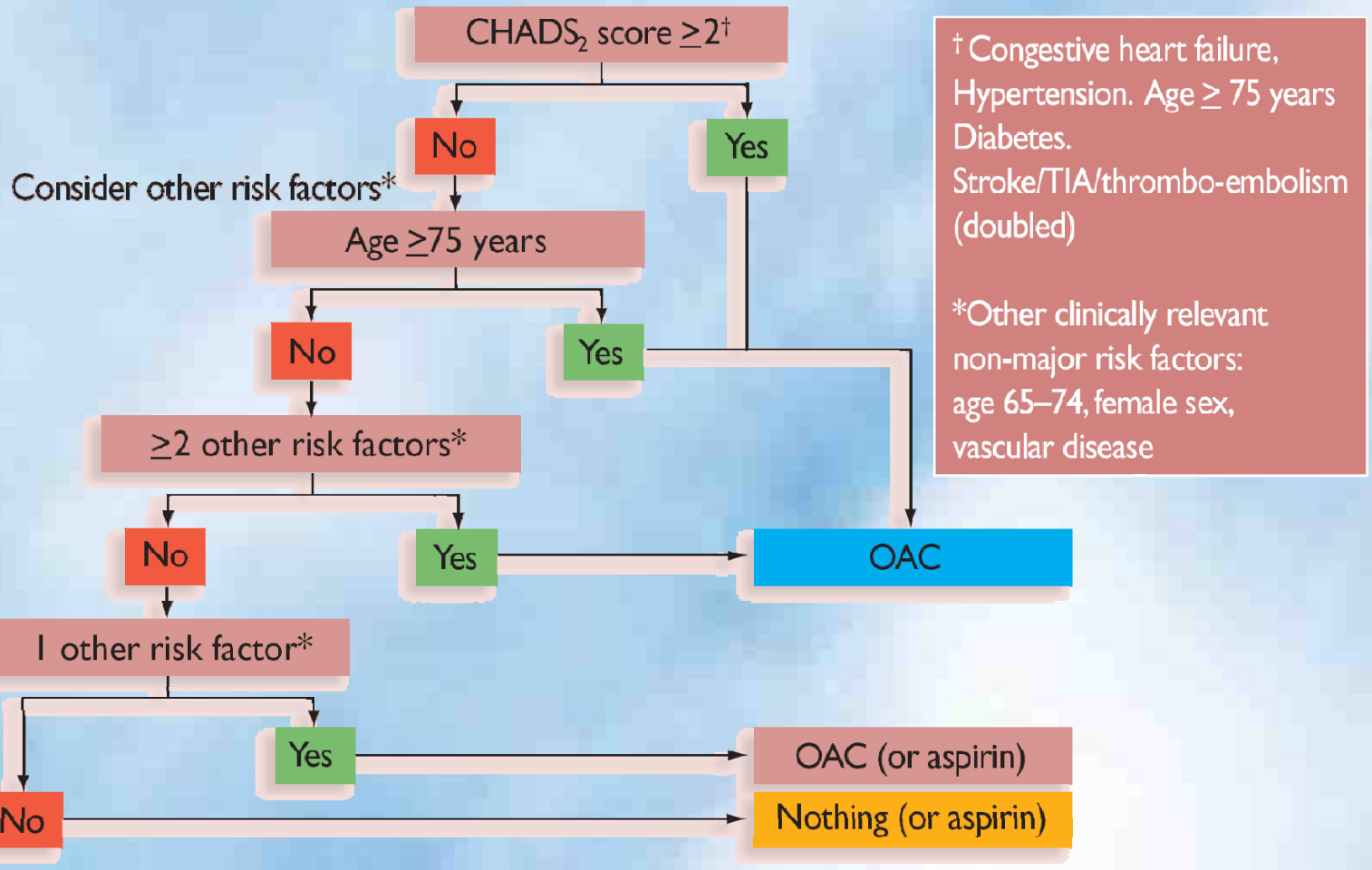
(c) Adjusted stroke rate according to CHA_2DS_2-VASc score

CHA_2DS_2-VASc score	Patients (n = 7329)	Adjusted stroke rate (%/year)[b]
0	1	0%
1	422	1.3%
2	1230	2.2%
3	1730	3.2%
4	1718	4.0%
5	1159	6.7%
6	679	9.8%
7	294	9.6%
8	82	6.7%
9	14	15.2%

Antithrombotic therapy

- Anticoagulation therapy with vitamin K antagonist vs. control
- Antiplatelet therapy vs. control
- Anticoagulation therapy with vitamin K antagonist vs. antiplatelet therapy
- Other antithrombotic drug regimens
- Investigational agents

Current recommendations for antithrombotic therapy



Current recommendations for antithrombotic therapy

Risk category	CHA_2DS_2-VASc score	Recommended antithrombotic therapy
One 'major' risk factor or ≥2 'clinically relevant non-major' risk factors	≥ 2	OAC[a]
One 'clinically relevant non-major' risk factor	1	Either OAC[a] or aspirin 75–325 mg daily. Preferred: OAC rather than aspirin.
No risk factors	0	Either aspirin 75–325 mg daily or no antithrombotic therapy. Preferred: no antithrombotic therapy rather than aspirin.

- OAC:
  - -Coumadin (INR 2-3)
  - -Dabigatran:
    - Patient with low risk of bleeding (HAS-BLED score of 0–2) dabigatran 150 mg b.i.d
    - Patient with high risk (HAS-BLED score of ≥3), dabigatran etexilate 110 mg b.i.d
    - Patients with one 'clinically relevant non-major' stroke risk factor, abigatran 110 mg b.i.d
- Patients with no stroke risk factors (CHA2DS2-VASc = 0) aspirin 75–325 mg daily or no antithrombotic

HAS-BLED bleeding risk score

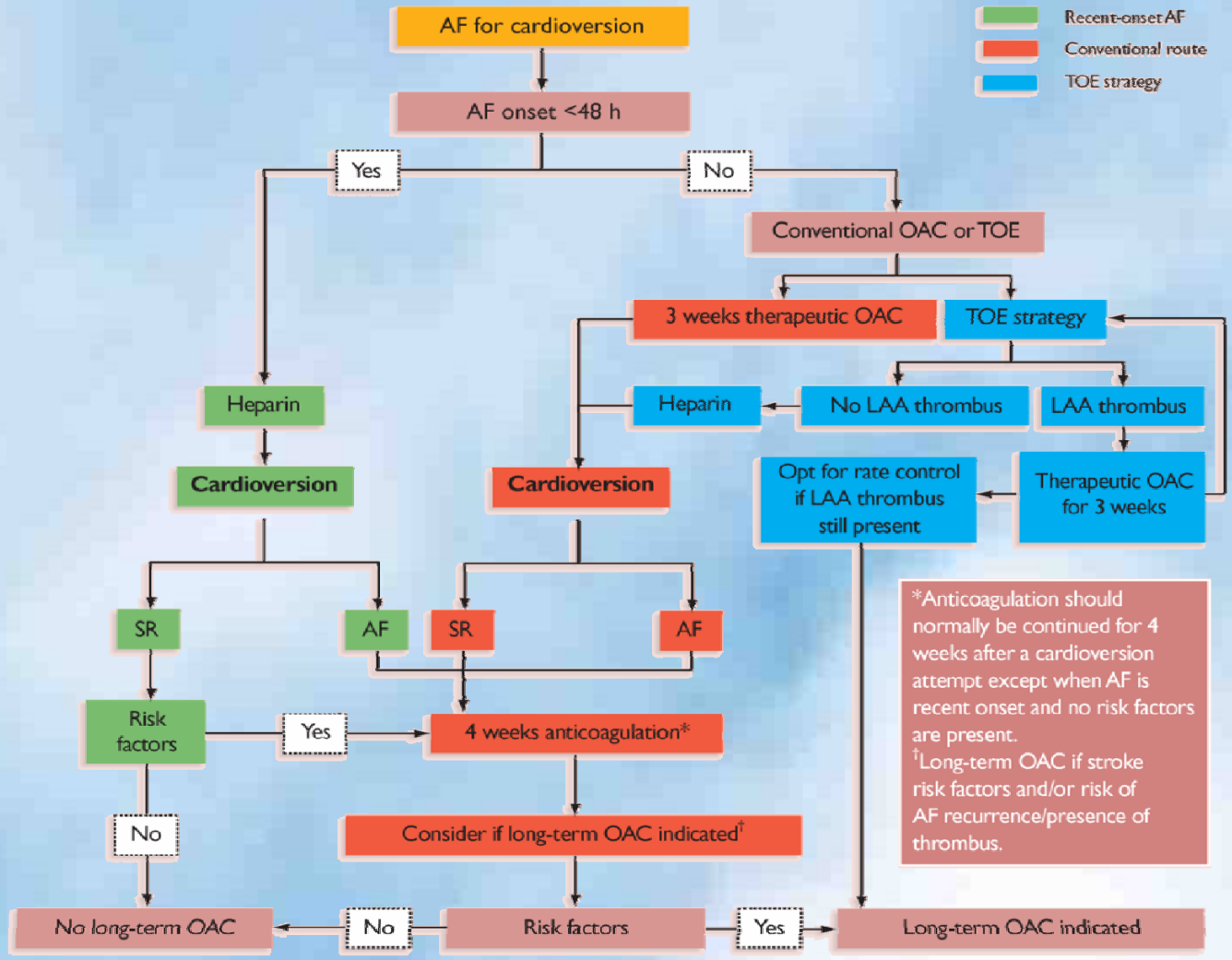
Letter	Clinical characteristic[a]	Points awarded
H	Hypertension	1
A	Abnormal renal and liver function (1 point each)	1 or 2
S	Stroke	1
B	Bleeding	1
L	Labile INRs	1
E	Elderly (e.g. age >65 years)	1
D	Drugs or alcohol (1 point each)	1 or 2
		Maximum 9 points

- Hypertension' systolic BP>160 mmHg
- 'Abnormal kidney function' - chronic dialysis or renal transplantation or serum creatinine ≥200 mmol/L
- 'Abnormal liver function' - cirrhosis or bilirubin >2 x and AST/ALT/ALP >3
- 'Bleeding' - previous bleeding history and/or predisposition to bleeding, e.g. bleeding diathesis, anaemia, etc.
- 'Labile INRs' - unstable/high INRs or poor time in therapeutic range (<60%)
- Drugs/alcohol use refers to concomitant use of drugs, such as antiplatelet agents, non-steroidal anti-inflammatory drugs, or alcohol abuse, etc

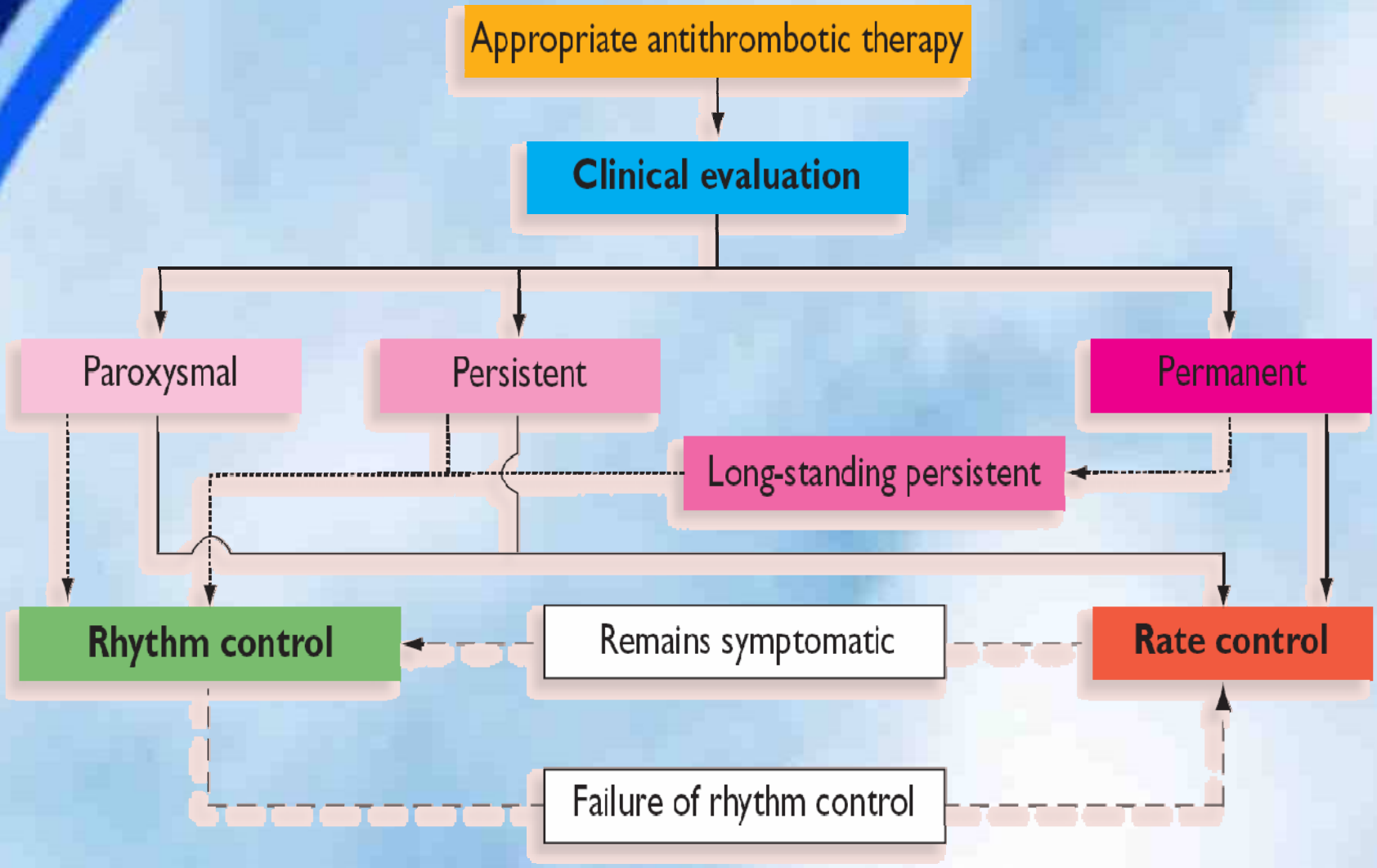
Special situations

- Paroxysmal atrial fibrillation
- Perioperative anticoagulation
- Stable vascular disease
- Acute coronary syndrome and/or percutaneous
- coronary intervention
- Elective percutaneous coronary intervention
- Non-ST elevation myocardial infarction
- Acute ST segment elevation myocardial infarction with primary percutaneous intervention
- Acute stroke
- Atrial flutter

Cardioversion of hemodynamically stable AF



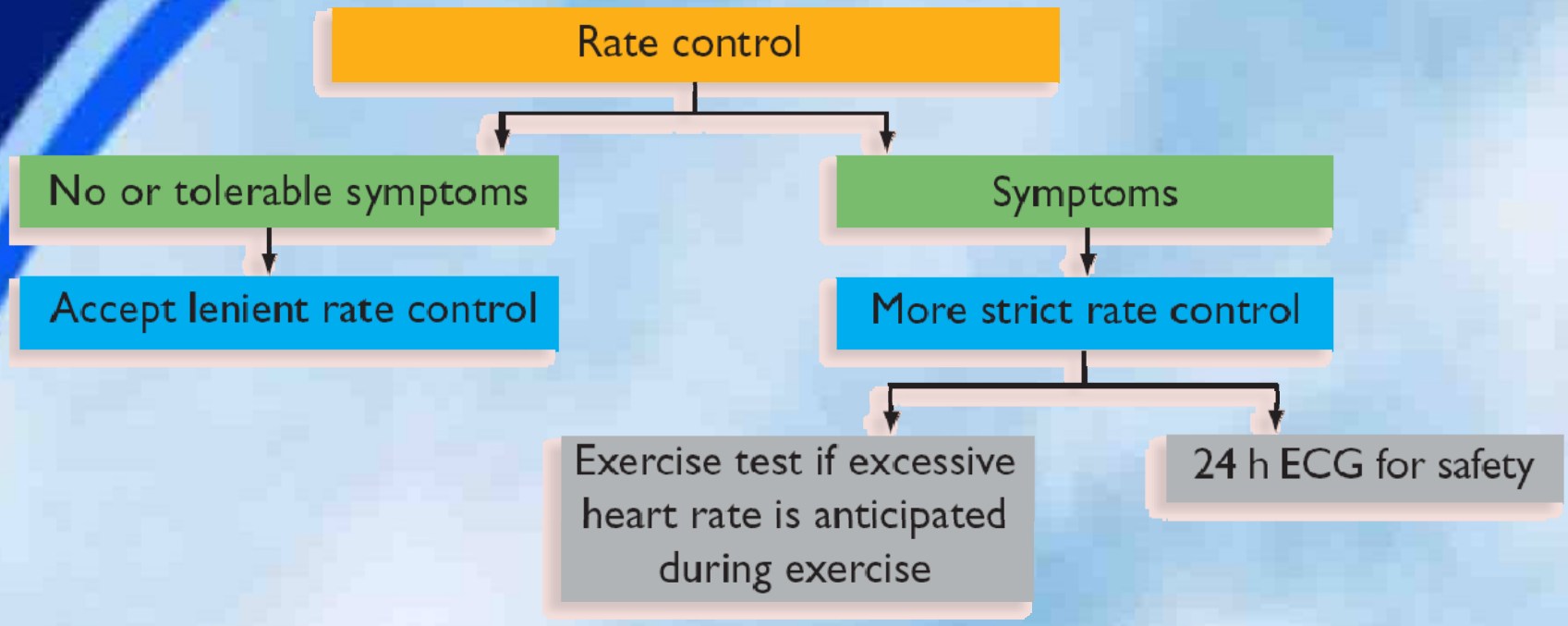
Rate and rhythm control



Rate and rhythm management

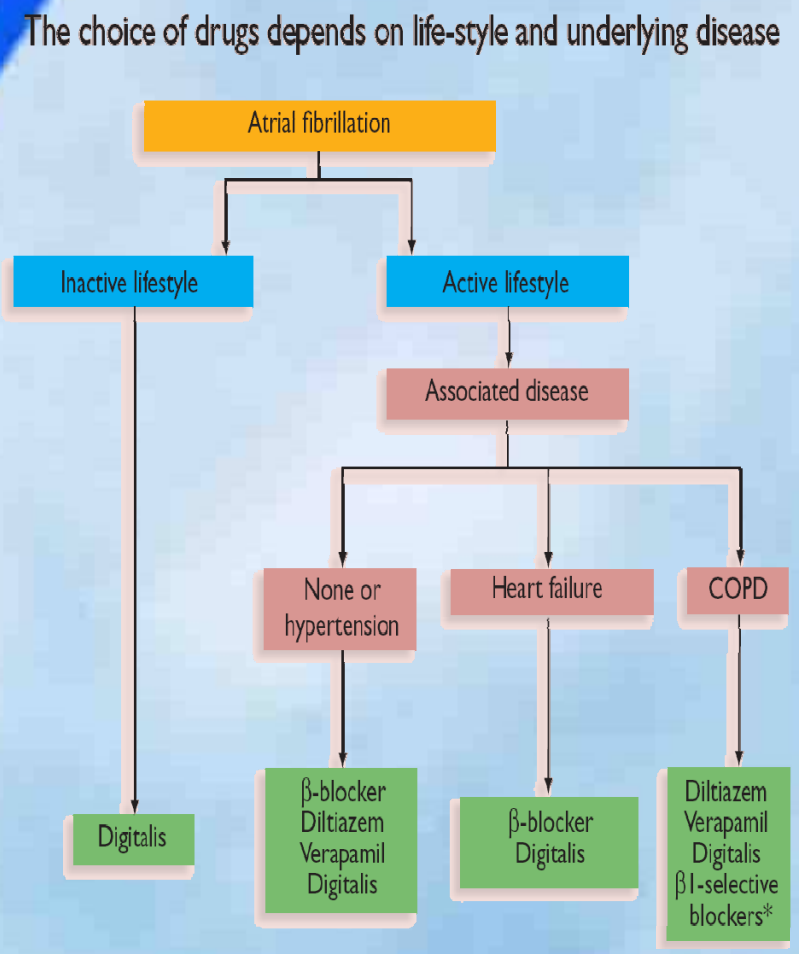
- Rate control
  - -Pharmacological rate control
  - -AVN ablation and modification
- Rhythm control
  - -Antiarrhythmic drugs to maintain sinus rhythm
  - -Left atrial catheter ablation
  - -Surgical ablation

Intensity of rate control therapy



- An irregular rhythm and a rapid ventricular rate in AF can cause symptoms including:
  -palpitations, dyspnoea, fatigue, and dizziness
- Adequate control of the ventricular rate may reduce symptoms and improve hemodynamics
- Previous guidelines recommended strict rate control (HR of 60-80 at resting and 90–115 bpm during exercise
- RACE II trial did not identify a benefit of stringent rate control over lenient rate control therapy in 614 patients

Choice of Drugs for Rate control

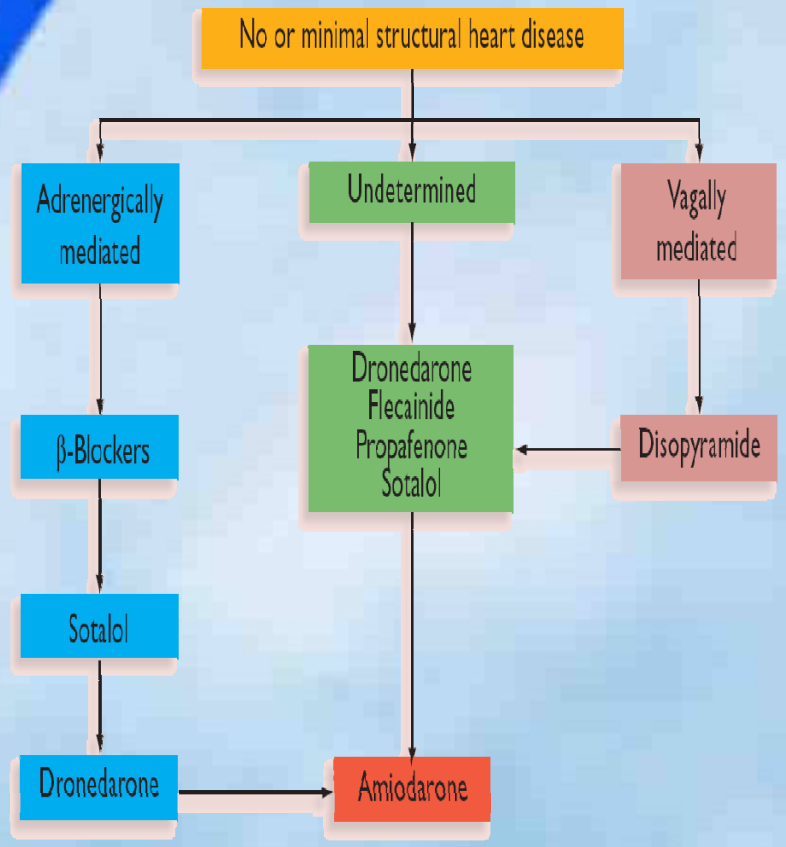


- Small doses of beta1-selective blockers may be used in COPD
- Amiodarone is used for rate control in patients who do not respond to:
  - -glycosides, b-blockers or non-dihydropyridine calcium antagonists
- Dronedarone may be used for rate control in patient with recurrent AF

Rhythm Control

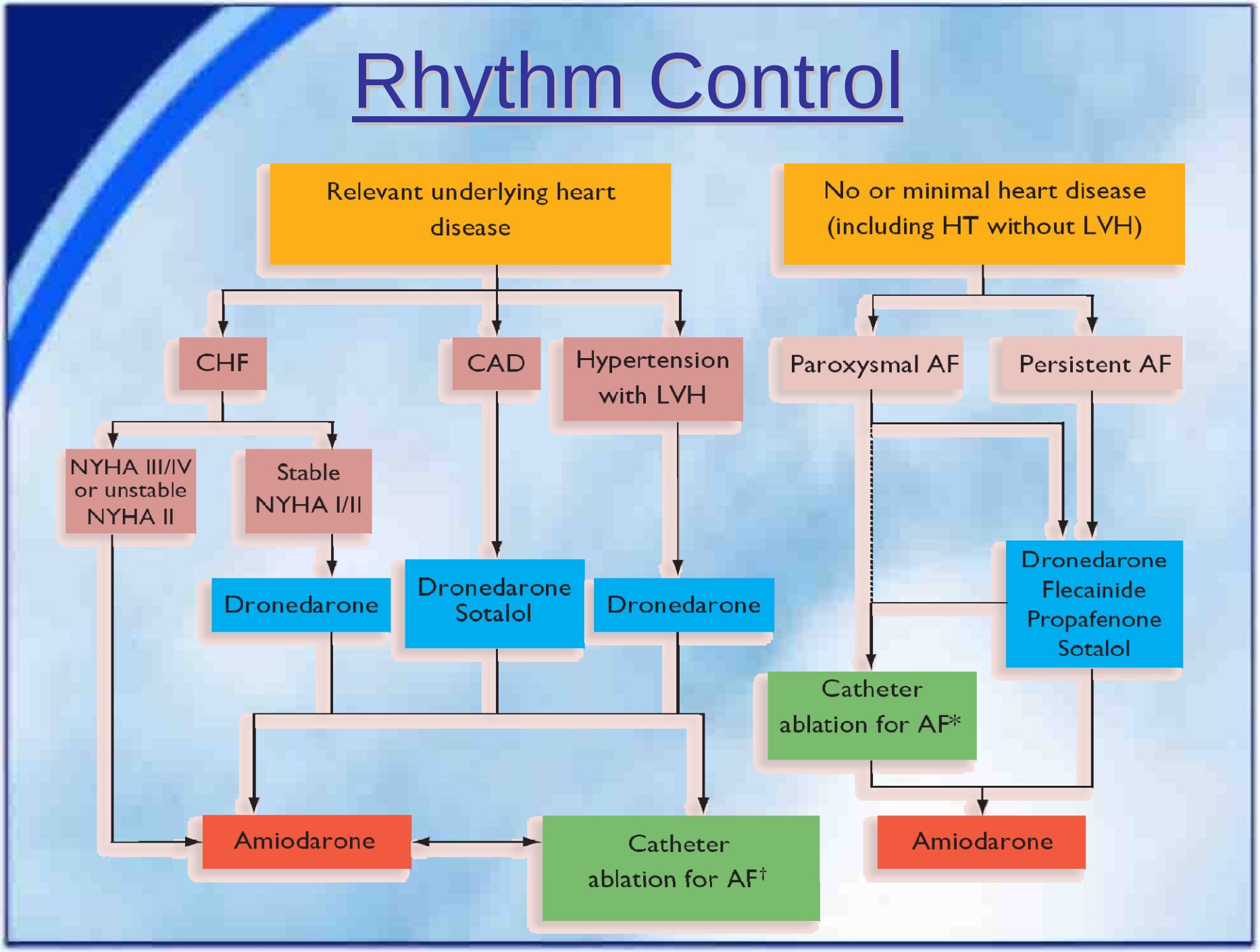
- The main motivation to initiate rhythm control therapy is relief of AF-related symptoms
- Asymptomatic patients (or those who become asymptomatic with adequate rate control therapy) should **not** generally receive AAD
- Principles of AAD therapy to maintain sinus rhythm in AF:
  - Aimed to rreduce AF-related symptoms
  - Efficacy of AAD to maintain SR is modest
  - Clinically successful AAD may reduce rather than eliminate recurrence of AF
  - If one AAD ‘fails’, a clinically acceptable response may be achieved with another agent
  - Drug-induced proarrhythmia or extra-cardiac side effects are frequent
  - Safety rather than efficacy considerations should primarily guide the choice of AAD

Rhythm control for lone AF



- Adrenergic AF - b-blockers, for prevention of AF
- 'lone AF', without response to b-blockers:
  - -flecainide, propafenone, sotalol, or dronedarone is usually prescribed
- Disopyramide, (with marked anticholinergic effects), may be useful in vagally mediated AF

Rhythm Control



Upstream therapy

- ACE inhibitors and ARB
- Aldosterone antagonists
- Statins
- Polyunsaturated fatty acids

Recommendations for primary prevention of AF with 'upstream' therapy

Recommendations	Class[a]	Level[b]	Ref.[c]
ACEIs and ARBs should be considered for prevention of new-onset AF in patients with heart failure and reduced ejection fraction.	IIa	A	145–149
ACEIs and ARBs should be considered for prevention of new-onset AF in patients with hypertension, particularly with left ventricular hypertrophy.	IIa	B	147, 150, 151
Statins should be considered for prevention of new-onset AF after coronary artery bypass grafting, isolated or in combination with valvular interventions.	IIa	B	161, 162
Statins may be considered for prevention of new-onset AF in patients with underlying heart disease, particularly heart failure.	IIb	B	164, 165
Upstream therapies with ACEIs, ARBs, and statins are not recommended for primary prevention of AF in patients without cardiovascular disease.	III	C	

Recommendations for secondary prevention of AF with 'upstream' therapy

Recommendations	Class[a]	Level[b]	Ref.[c]
Pre-treatment with ACEIs and ARBs may be considered in patients with recurrent AF *and* receiving antiarrhythmic drug therapy.	IIb	B	145–147, 152–153
ARBs or ACEIs may be useful for prevention of recurrent paroxysmal AF or in patients with persistent AF undergoing electrical cardioversion in the absence of significant structural heart disease if these agents are indicated for other reasons (e.g. hypertension).	IIb	B	145, 155–156

Specific populations

- Heart failure
- Athletes
- Valvular heart disease
- Acute coronary syndromes
- Diabetes mellitus
- The elderly
- Pregnancy
- Post-operative atrial fibrillation
- Hyperthyroidism
- Wolff–Parkinson–White syndrome
- Hypertrophic cardiomyopathy
- Pulmonary disease

Recommendations for rate control during AF with heart failure

Recommendations	Class[a]	Level[b]	Ref.[c]
β-Blockers are recommended as first-line therapy to control the ventricular rate in patients with heart failure and low LVEF.	I	A	169, 171
Where monotherapy is inadequate for heart rate control, digoxin should be added.	I	B	171, 172
In haemodynamically unstable patients with acute heart failure and low LVEF, amiodarone is recommended as the initial treatment.	I	B	173
If an AP is excluded, digoxin is recommended as an alternative to amiodarone to control the heart rate in patients with AF and acute systolic heart failure.	I	C	
AV node ablation should be considered to control the heart rate when other measures are unsuccessful or contraindicated in patients with permanent AF and an indication for CRT (NYHA class III–IV, LVEF ≤35%, and QRS width ≥130 ms).	IIa	B	105, 109, 110, 174
In patients with heart failure and preserved LVEF, a non-dihydropyridine calcium channel antagonist may be considered.	IIb	C	
A β-blocker may be considered as an alternative to a non-dihydropyridine calcium channel antagonist in heart failure with preserved ejection fraction.	IIb	C	
A non-dihydropyridine calcium channel antagonist is not recommended to control the heart rate in patients with systolic heart failure.	III	C	

Recommendations for rhythm control of AF in heart failure

Recommendations	Class[a]	Level[b]	Ref.[c]
DCC is recommended when a rapid ventricular rate does not respond to pharmacological measures in patients with AF and ongoing myocardial ischaemia, symptomatic hypotension, or symptoms of pulmonary congestion.	I	C	
In patients with AF and severe (NYHA class III or IV) or recent (≤4 weeks) unstable heart failure, the use of antiarrhythmic therapy to maintain sinus rhythm should be restricted to amiodarone.	I	C	
Administration of amiodarone is a reasonable option for pharmacological cardioversion of AF, or to facilitate electrical cardioversion of AF.	IIa	B	46, 74, 80, 175
In patients with AF and stable heart failure (NYHA class I, II) dronedarone should be considered to reduce cardiovascular hospitalizations.	IIa	C	
For patients with heart failure and symptomatic persistent AF despite adequate rate control, electrical cardioversion and rhythm control may be considered.	IIb	B	90, 93, 94, 97, 176
Catheter ablation (pulmonary vein isolation) may be considered in heart failure patients with refractory symptomatic AF.	IIb	B	93, 94

Recommendations for AF in valvular heart disease

Recommendations	Class[a]	Level[b]	Ref.[c]
OAC therapy (INR 2.0–3.0) is indicated in patients with mitral stenosis and AF (paroxysmal, persistent, or permanent).	I	C	
OAC therapy (INR 2.0–3.0) is recommended in patients with AF and clinically significant mitral regurgitation.	I	C	
Percutaneous mitral balloon valvotomy should be considered for asymptomatic patients with moderate or severe mitral stenosis and suitable valve anatomy who have new-onset AF in the absence of LA thrombus.	IIa	C	
Early mitral valve surgery should be considered in severe mitral regurgitation, preserved LV function, and new-onset AF, even in the absence of symptoms, particularly when valve repair is feasible.	IIa	C	

Recommendations for AF in athletes

Recommendations	Class[a]	Level[b]	Ref.[c]
When a 'pill-in-the-pocket' approach with sodium channel blockers is used, sport cessation should be considered for as long as the arrhythmia persists, and until 1–2 half-lives of the antiarrhythmic drug used have elapsed.	IIa	C	
Isthmus ablation should be considered in competitive or leisure-time athletes with documented atrial flutter, especially when therapy with flecainide or propafenone is intended.	IIa	C	
Where appropriate, AF ablation should be considered to prevent recurrent AF in athletes.	IIa	C	
When a specific cause for AF is identified in an athlete (such as hyperthyroidism), it is not recommended to continue participation in competitive or leisure time sports until correction of the cause.	III	C	
It is not recommended to allow physical sports activity when symptoms due to haemodynamic impairment (such as dizziness) are present.	III	C	

Recommendations for AF in acute coronary syndrome

Recommendations	Class[a]	Level[b]	Ref.[c]
DCC is recommended for patients with severe haemodynamic compromise or intractable ischaemia, or when adequate rate control cannot be achieved with pharmacological agents in patients with ACS and AF.	I	C	
Intravenous administration of amiodarone is recommended to slow a rapid ventricular response to AF in patients with ACS.	I	C	
Intravenous β-blockers are recommended to slow a rapid ventricular response to AF in patients with ACS.	I	C	
Intravenous administration of non-dihydropyridine calcium antagonists (verapamil, diltiazem) should be considered to slow a rapid ventricular response to AF in patients with ACS and no clinical signs of heart failure.	IIa	C	
Intravenous administration of digoxin may be considered to slow a rapid ventricular response in patients with ACS and AF associated with heart failure.	IIb	C	
Administration of flecainide or propafenone is not recommended in patients with AF in the setting of ACS.	III	B	124

Recommendations for AF in WPW

Recommendations	Class[a]	Level[b]	Ref.[c]
Catheter ablation of an overt AP in patients with AF is recommended to prevent SCD.	I	A	30
Immediate referral to an experienced ablation centre for catheter ablation is recommended for patients who survived SCD and have evidence of overt AP conduction.	I	C	
Catheter ablation is recommended for patients with high risk professions (e.g. pilots, public transport drivers) and overt but asymptomatic AP conduction on the surface ECG.	I	B	30
Catheter ablation is recommended in patients at high risk of developing AF in the presence of an overt but asymptomatic AP on the surface ECG.	I	B	198
Asymptomatic patients with evidence of an overt AP should be considered for catheter ablation of the AP only after a full explanation and careful counselling.	IIa	B	198

Recommendations for AF in HCMP

Recommendations	Class[a]	Level[b]	Ref.[c]
Restoration of sinus rhythm by DCC or pharmacological cardioversion is recommended in patients with HCM presenting with recent-onset AF.	I	B	200
OAC therapy (INR 2.0–3.0) is recommended in patients with HCM who develop AF unless contraindicated.	I	B	200
Amiodarone (or alternatively, disopyramide plus β-blocker) should be considered in order to achieve rhythm control and to maintain sinus rhythm in patients with HCM.	IIa	C	
Catheter ablation of AF should be considered in patients with symptomatic AF refractory to pharmacological control.	IIa	C	
Ablation procedures (with concomitant septal myectomy if indicated) may be considered in patients with HCM and refractory AF.	IIa	C	