Acute Restoration Of Sinus Rhythm in Atrial Fibrillation (ESC Guidelines 2016)

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Learning Objectives

- The new gender and genetic aspects that guide management of AF in 2016 guidelines .
- The recent classification of AF; patterns, and clinical types.
- Be aware of acute management of AF according to the 2016 guidelines.
- Be able to determine when patients should be evaluated for curative ablation versus treatment with medical therapy.

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ESC GUIDELINES

2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS

The Task Force for the management of atrial fibrillation of the European Society of Cardiology (ESC)

Developed with the special contribution of the European Heart Rhythm Association (EHRA) of the ESC

Endorsed by the European Stroke Organisation (ESO)

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Table 3 Cardiovascular morbidity and mortality associated with atrial fibrillation

Event	Association with AF
Death	Increased mortality, especially cardiovascular mortality due to sudden death, heart failure or stroke.
Stroke	20–30% of all strokes are due to AF. A growing number of patients with stroke are diagnosed with 'silent', paroxysmal AF.
Hospitalizations	10–40% of AF patients are hospitalized every year.
Quality of life	Quality of life is impaired in AF patients independent of other cardiovascular conditions.
Left ventricular dysfunction and heart failure	Left ventricular dysfunction is found in 20–30% of all AF patients. AF causes or aggravates LV dysfunction in many AF patients, while others have completely preserved LV function despite long-standing AF.
Cognitive decline and vascular dementia	Cognitive decline and vascular dementia can develop even in anticoagulated AF patients. Brain white matter lesions are more common in AF patients than in patients without AF.

Gender in AF

- In both developed and developing countries, the age-adjusted incidence and prevalence of AF are lower in women, while the risk of death in women with AF is similar to or higher than that in men with AF **(Chug et al., 2014).**
- Female AF patients who have additional stroke risk factors (particularly older age) are also at greater risk than men of having a stroke **(Pancholy et al., 2014)**
- Women with diagnosed AF can be more symptomatic than men and are typically older with more co morbidities.

Recommendations relating to gender

Recommendations	Class[a]	Level[b]	Ref[c]
AF clinicians must offer effective diagnostic tools and therapeutic management to women and men equally to prevent stroke and death.	I	A	39, 46, 57
Catheter or surgical ablation techniques should be regarded as equally effective in women and men.	IIa	B	55, 56

Genetic predisposition in AF:

- Early-onset AF, has a strong heritable component that is independent of concomitant cardiovascular conditions. Up to one-third of AF patients carry common genetic variants that predispose to AF.
- The most important variants are located close to the paired-like homeodomain transcription factor 2 (Pitx2) gene on chromosome 4q25.
- These variants modify the risk of AF up to seven-fold. Genetic variants could, in the future, become useful for patient selection of rhythm or rate control.

The 2016 Classifications of AF

1- Atrial fibrillation patterns.

2- Atrial fibrillation clinical types.

3- Symptom burden in atrial fibrillation.

Table 5 Patterns of atrial fibrillation

AF pattern	Definition
First diagnosed AF	AF that has not been diagnosed before, irrespective of the duration of the arrhythmia or the presence and severity of AF-related symptoms.
Paroxysmal AF	Self-terminating, in most cases within 48 hours. Some AF paroxysms may continue for up to 7 days.[a] AF episodes that are cardioverted within 7 days should be considered paroxysmal.[a]
Persistent AF	AF that lasts longer than 7 days, including episodes that are terminated by cardioversion, either with drugs or by direct current cardioversion, after 7 days or more.
Long-standing persistent AF	Continuous AF lasting for ≥1 year when it is decided to adopt a rhythm control strategy.
Permanent AF	AF that is accepted by the patient (and physician). Hence, rhythm control interventions are, by definition, not pursued in patients with permanent AF. Should a rhythm control strategy be adopted, the arrhythmia would be re-classified as 'long-standing persistent AF'.

AF = atrial fibrillation.
[a]The distinction between paroxysmal and persistent AF is often not made correctly without access to long-term monitoring.[163] Hence, this classification alone is often insufficient to select specific therapies. If both persistent and paroxysmal episodes are present, the predominant pattern should guide the classification.

Table 6 Clinical types of atrial fibrillation[a]

AF type	Clinical presentation	Possible pathophysiology
AF secondary to structural heart disease	AF in patients with LV systolic or diastolic dysfunction, long-standing hypertension with LVH, and/or other structural heart disease. The onset of AF in these patients is a common cause of hospitalization and a predictor of poor outcome.	Increased atrial pressure and atrial structural remodelling, together with activation of the sympathetic and renin-angiotensin system.
Focal AF	Patients with repetitive atrial runs and frequent, short episodes of paroxysmal atrial fibrillation. Often highly symptomatic, younger patients with distinguishable atrial waves (coarse AF), atrial ectopy, and/or atrial tachycardia deteriorating in AF.	Localized triggers, in most cases originating from the pulmonary veins, initiate AF. AF due to one or a few re-entrant drivers is also considered to be part of this type of AF.
Polygenic AF	AF in carriers of common gene variants that have been associated with early onset AF.	Currently under study. The presence of selected gene variants may also influence treatment outcomes.
Post-operative AF	New onset of AF (usually self-terminating) after major (typically cardiac) surgery in patients who were in sinus rhythm before surgery and had no prior history of AF.	Acute factors: inflammation, atrial oxidative stress, high sympathetic tone, electrolyte changes, and volume overload, possibly interacting with a pre-existing substrate.
AF in patients with mitral stenosis or prosthetic heart valves	AF in patients with mitral stenosis, after mitral valve surgery and in some cases other valvular disease.	Left atrial pressure (stenosis) and volume (regurgitation) load are the main drivers of atrial enlargement and structural atrial remodelling in these patients.
AF in athletes	Usually paroxysmal, related to duration and intensity of training.	Increased vagal tone and atrial volume.
Monogenic AF	AF in patients with inherited cardiomyopathies, including channelopathies.	The arrhythmogenic mechanisms responsible for sudden death are likely to contribute to the occurrence of AF in these patients.

AF = atrial fibrillation; LV = left ventricular; LVH = left ventricular hypertrophy. It is recognized that these types of AF will overlap in clinical practice, and that their impact for management needs to be evaluated systematically.

Table 7 Modified European Heart Rhythm Association symptom scale (modified from Wynn *et al.*[199])

Modified EHRA score	Symptoms	Description
1	None	AF does not cause any symptoms
2a	Mild	Normal daily activity not affected by symptoms related to AF[a]
2b	Moderate	Normal daily activity not affected by symptoms related to AF, but patient troubled by symptoms[a]
3	Severe	Normal daily activity affected by symptoms related to AF
4	Disabling	Normal daily activity discontinued

AF = atrial fibrillation; EHRA = European Heart Rhythm Association.
[a]EHRA class 2a and 2b can be differentiated by evaluating whether patients are functionally affected by their AF symptoms. AF-related symptoms are most commonly fatigue/tiredness and exertional shortness of breath, or less frequently palpitations and chest pain.[42,194,200–202]

Recommendation on use of the modified European Heart Rhythm Association symptom scale

Recommendation	Class[a]	Level[b]	Ref[c]
Use of the modified EHRA symptom scale is recommended in clinical practice and research studies to quantify AF-related symptoms.	I	C	192, 199

AF = atrial fibrillation; EHRA = European Heart Rhythm Association.
[a]Class of recommendation.
[b]Level of evidence.
[c]Reference(s) supporting recommendations.

Cardiovascular and other conditions independently associated with AF

Characteristic/comorbidity	Association with AF
Genetic predisposition (based on multiple common gene variants associated with AF)[64]	HR range 0.4–3.2
Older age[19] 50–59 years 60–69 years 70–79 years 80–89 years	HR: 1.00 (reference) 4.98 (95% CI 3.49–7.10) 7.35 (95% CI 5.28–10.2) 9.33 (95% CI 6.68–13.0)
Hypertension (treated) vs. none[19]	HR 1.32 (95% CI 1.08–1.60)
Heart failure vs. none[19]	HR 1.43 (95% CI 0.85–2.40)
Valvular heart disease vs. none[205]	RR 2.42 (95% CI 1.62–3.60)
Myocardial infarction vs. none[19]	HR 1.46 (95% CI 1.07–1.98)
Thyroid dysfunction[206, 207] Hypothyroidism Subclinical hyperthyroidism Overt hyperthyroidism	(reference: euthyroid) HR 1.23 (95% CI 0.77–1.97) RR 1.31 (95% CI 1.19–1.44) RR 1.42 (95% CI 1.22–1.63)
Obesity[19, 208] None (BMI <25 kg/m²) Overweight (BMI 25–30 kg/m²) Obese (BMI ≥31 kg/m²)	HR: 1.00 (reference) 1.13 (95% CI 0.87–1.46) 1.37 (95% CI 1.05–1.78)
Diabetes mellitus vs. none[19]	HR 1.25 (95% CI 0.98–1.60)
Chronic obstructive pulmonary disease[209] FEV1 ≥80% FEV1 60–80% FEV1 <60%	RR: 1.00 (reference) 1.28 (95% CI 0.79–2.06) 2.53 (95% CI 1.45–4.42)
Obstructive sleep apnoea vs. none[210]	HR 2.18 (95% CI 1.34–3.54)
Chronic kidney disease[211] None Stage 1 or 2 Stage 3 Stage 4 or 5	OR: 1.00 (reference) 2.67 (95% CI 2.04–3.48) 1.68 (95% CI 1.26–2.24) 3.52 (95% CI 1.73–7.15)

Cardiovascular and other conditions independently associated with AF

Smoking[212]	HR:
Never	1.00 (reference)
Former	1.32 (95% CI 1.10–1.57)
Current	2.05 (95% CI 1.71–2.47)
Alcohol consumption[213]	RR:
None	1.00 (reference)
1– 6 drinks/week	1.01 (95% CI 0.94–1.09)
7–14 drinks/week	1.07 (95% CI 0.98–1.17)
15–21 drinks/week	1.14 (95% CI 1.01–1.28)
>21 drinks/week	1.39 (95% CI 1.22–1.58)
Habitual vigorous exercise[214]	RR:
Non-exercisers	1.00 (reference)
<1 day/week	0.90 (95% CI 0.68–1.20)
1–2 days/week	1.09 (95% CI 0.95–1.26)
3–4 days/week	1.04 (95% CI 0.91–1.19)
5–7 days/week	1.20 (95% CI 1.02–1.41)

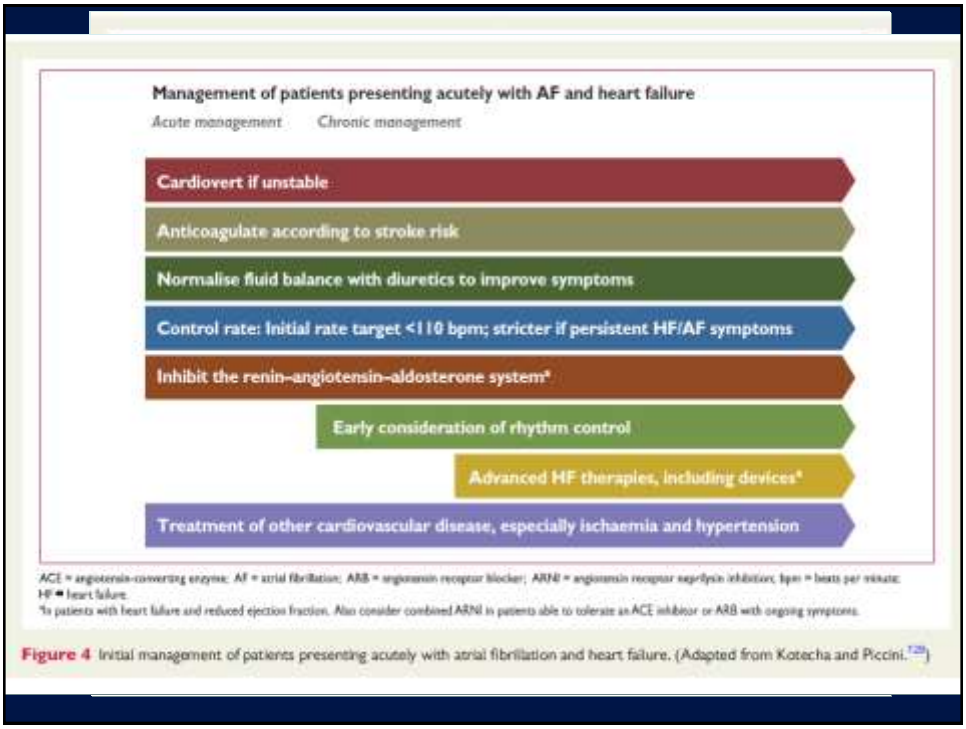
Atrial Fibrillation & Heart Failure

- Heart failure and AF can cause and exacerbate each other through:

- structural cardiac remodelling.
- activation of neurohormonal mechanisms.
- rate-related impairment of left ventricular LV function

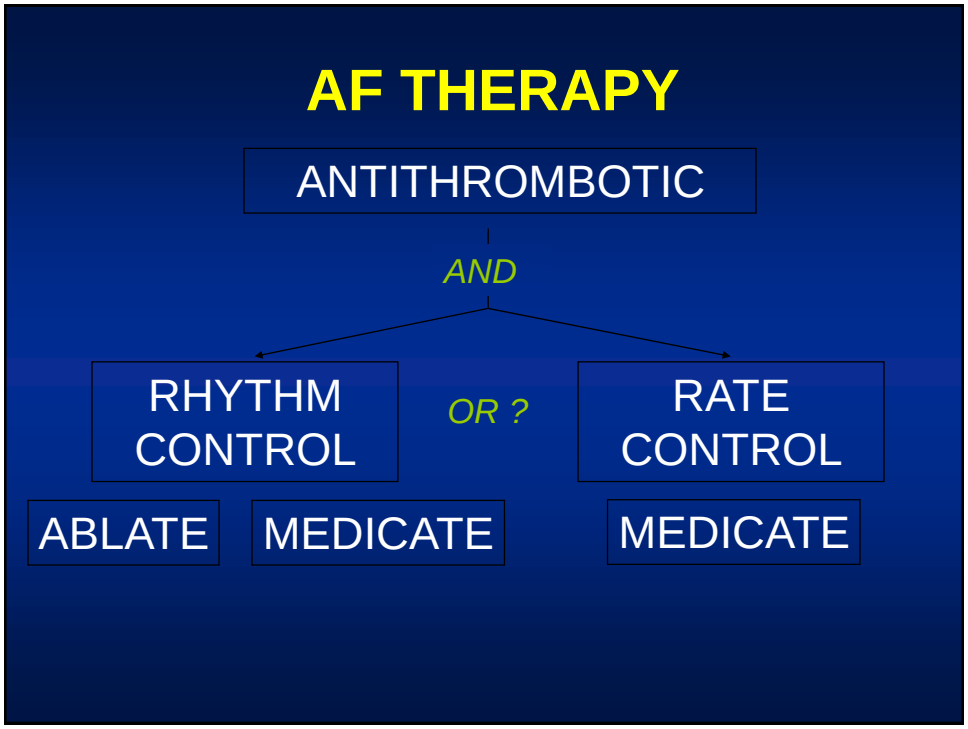
AF and HFrEF:

- ACEI or ARBs.
- Mineralocorticoid antagonists.
- Defibrillators, cardiac resynchronization therapy.
- Rhythm control in severe symptomatizing patients and those who developed HF due to AF(tachycardiomyopathy). Ablation is used to restore LV function.
- Rate control using BB and or digoxin.



ACE = angiotensin-converting enzyme; AF = atrial fibrillation; ARB = angiotensin receptor blocker; ARNI = angiotensin receptor–neprilysin inhibitor; bpm = beats per minute; HF = heart failure.
*In patients with heart failure and reduced ejection fraction. Also consider combined ARNI in patients able to tolerate an ACE inhibitor or ARB with ongoing symptoms.

Figure 4 Initial management of patients presenting acutely with atrial fibrillation and heart failure. (Adapted from Kotecha and Piccini.[728])



Acute Rate Control in Atrial Fibrillation

Acute Rate Control

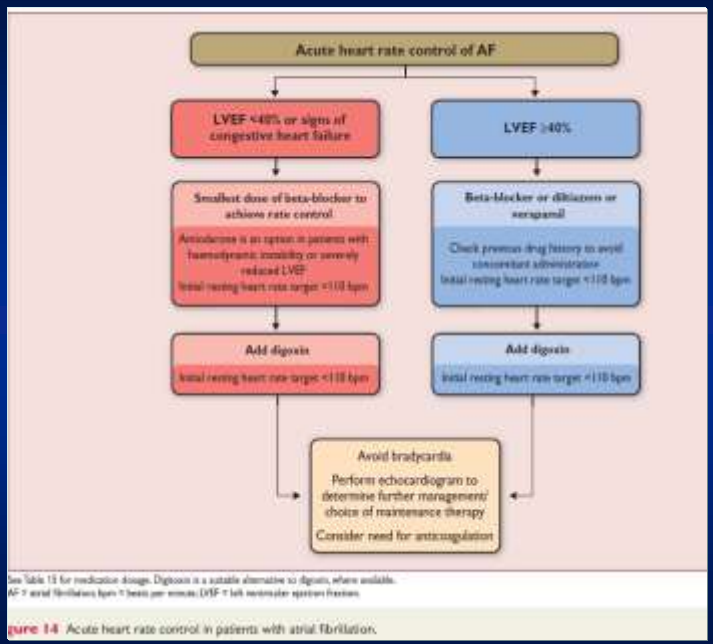
- Evaluate underlying causes of elevated heart rate, such as infection, endocrine imbalance, anaemia, and pulmonary embolism.
- In hemodynamicaly stable patients, beta-blockers and diltiazem/ verapamil are preferred over digoxin because of their rapid onset of action and effectiveness at high sympathetic tone.
- Combination therapy may be required.
- In critically ill patients & severely impaired LV systolic function patients, IV amiodarone can be used where excess HR leads to haemodynamic instability.

Acute rate control therapy in AF

Therapy	Acute intravenous rate control
Beta-blockers*	
Bisoprolol	Not available
Carvedilol	Not available
Metoprolol	2.5–10 mg intravenous bolus (repeated as required).
Nebivolol	Not available
Esmolol	0.5 mg/kg intravenous bolus over 1 min; then 0.05–0.25 mg/kg/min.
Calcium-channel blockers	
Diltiazem	15–25 mg intravenous bolus (repeated as required).
Verapamil	2.5–10 mg intravenous bolus (repeated as required).
Cardiac glycosides	
Digoxin	0.5 mg intravenous bolus (0.75–1.5 mg over 24 hours in divided doses).
Digitoxin	0.4–0.6 mg intravenous bolus.
Specific indications	
Amiodarone	300 mg intravenously diluted in 250 mL 5% dextrose over 30–60 minutes (preferably via central venous cannula).*

Heart rate targets in AF:

- The RACE (Rate Control Efficacy in Permanent Atrial Fibrillation) II study randomized 614 patients with AF to either a target HR 80 b.p.m. at rest and ,110 b.p.m. during moderate exercise, or to a lenient heart rate target of ,110 b.p.m.
- There was no difference in a composite of clinical events (14.9% in the strict rate control group, 12.9% in the lenient group), NYHA class, or hospitalizations.
- Nonetheless, lenient rate control is an acceptable initial approach, regardless of heart failure status, unless symptoms call for stricter rate control.



gure 14 Acute heart rate control in patients with atrial fibrillation.

Alternative Complete AVN Ablation and pacing

Advantages:

- 100% efficacy
- 85% symptomatic improvement
- Improved EF (LV remodeling)
- Eliminates need for rate control drugs

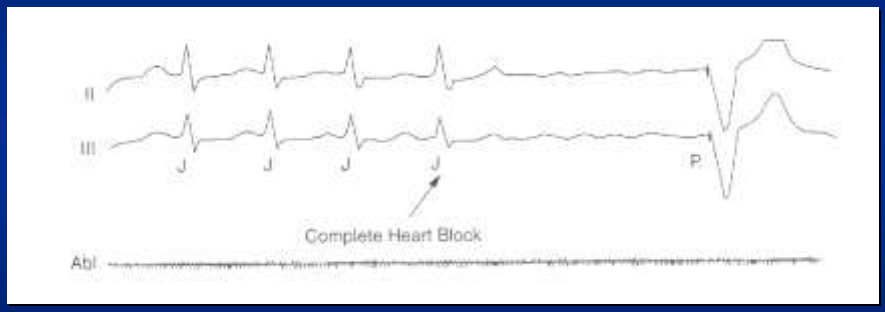
Disadvantages:

- Pacemaker dependant
- Risk of LV dysfunction with RV pacing
- Some pts still have symptoms

Good Candidates:

- Tachy / Brady Syndrome
- PCMK in Place – CHF with BiV device
- Medication refractory / intolerant
- Elderly

AVN RF ablation



Acute Restoration of Sinus Rhythm in Atrial Fibrillation

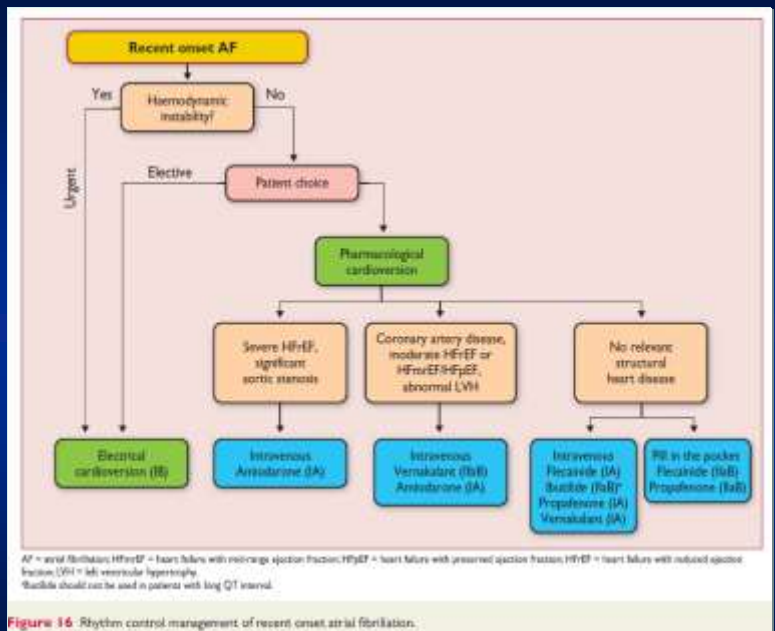


Figure 16 Rhythm control management of recent onset atrial fibrillation.

Pharmacological Cardioversion

- Pharmacological cardioversion restores sinus rhythm in approximately 50% of patients with recent-onset AF.
- In the short-term, electrical cardioversion restores sinus rhythm quicker and more effectively than pharmacological cardioversion and is associated with shorter hospitalization.
- Pharmacological cardioversion, conversely, does not require sedation or fasting.

Table 16 Antiarrhythmic drugs for pharmacological cardioversion

Drug	Route	I* dose	Follow-up dose	Risks	Reference
Flecainide	Oral IV	200–300 mg 1.5–2 mg/kg over 10 min	N/A	Hypotension, atrial flutter with 1:1 conduction, QT prolongation. Avoid in patients with IHD and/or significant structural heart disease.	595, 598
Amiodarone	IV*	5–7 mg/kg over 1–2 hours	50 mg/hour to a maximum of 1.0 g over 24 hours	Phlebitis, hypotension, bradycardia/AV block. Will slow ventricular rate. Delayed conversion to sinus rhythm (8–12 hours).	596–601
Propafenone	IV Oral	1.5–2 mg/kg over 10 min 450–600 mg		Hypotension, atrial flutter with 1:1 conduction, QRS prolongation (mild). Avoid in patients with IHD and/or significant structural heart disease.	622, 625
Ibutilide†	IV	1 mg over 10 min	1 mg over 10 min after waiting for 10 min	QT prolongation, polymorphic ventricular tachycardia/torsades de pointes (3–4% of patients). Will slow ventricular rate. Avoid in patients with QT prolongation, hypokalemia, severe LVH or low ejection fraction.	614, 615
Vernakalant	IV	3 mg/kg over 10 min	2 mg/kg over 10 min after waiting for 15 min	Hypotension, non-sustained ventricular arrhythmias, QT and QRS prolongation. Avoid in patients with SBP <100 mmHg, recent (<30 days) ACS, NYHA Class III and IV heart failure, QT interval prolongation (uncorrected QT >440 ms) and severe aortic stenosis.	602–605, 618

ACS = acute coronary syndromes; AV = atrio-ventricular; IHD = ischaemic heart disease; i.v. = intravenous; LVH = left ventricular hypertrophy; NYHA = New York Heart Association; SBP = systolic blood pressure.
*Use a large peripheral vessel and change to oral amiodarone within 24 h of i.v. (central line) administration.
†Ibutilide is only available in selected European countries.

Recommendations for Rhythm Control Therapy

General recommendations		
Rhythm control therapy is indicated for symptom improvement in patients with AF.	I	B
Management of cardiovascular risk factors and avoidance of AF triggers should be pursued in patients on rhythm control therapy to facilitate maintenance of sinus rhythm.	IIa	B
With the exception of AF associated with haemodynamic instability, the choice between electrical and pharmacological cardioversion should be guided by patient and physician preferences.	IIa	C

Cardioversion of AF		
Electrical cardioversion of AF is recommended in patients with acute haemodynamic instability to restore cardiac output.	I	B
Cardioversion of AF (either electrical or pharmacological) is recommended in symptomatic patients with persistent or long-standing persistent AF as part of rhythm control therapy.	I	B
Pre-treatment with amiodarone, flecainide, ibutilide, or propafenone should be considered to enhance success of electrical cardioversion and prevent recurrent AF.	IIa	B
In patients with no history of ischaemic or structural heart disease, flecainide, propafenone, or vernakalant are recommended for pharmacological cardioversion of new-onset AF.	I	A
In patients with no history of ischaemic or structural heart disease, ibutilide should be considered for pharmacological conversion of AF.	IIa	B
In selected patients with recent-onset AF and no significant structural or ischaemic heart disease, a single oral dose of flecainide or propafenone (the 'pill in the pocket' approach) should be considered for patient-led cardioversion, following safety assessment.	IIa	B
In patients with ischaemic and/or structural heart disease, amiodarone is recommended for cardioversion of AF.	I	A
Vernakalant may be considered as an alternative to amiodarone for pharmacological conversion of AF in patients without hypotension, severe heart failure or severe structural heart disease (especially aortic stenosis).	IIb	B

Antiarrhythmic effects of non-antiarrhythmic drugs			
ACE-Is, ARBs and beta-blockers should be considered for prevention of new-onset AF in patients with heart failure and reduced ejection fraction.	IIa	A	23, 219, 236, 237, 239, 250, 714
ACE-Is and ARBs should be considered for prevention of new-onset AF in patients with hypertension, particularly with LV hypertrophy.	IIa	B	238, 246, 686, 714
Pre-treatment with ACE-Is or ARBs may be considered in patients with recurrent AF undergoing electrical cardioversion and receiving antiarrhythmic drug therapy.	IIb	B	236, 237, 248, 249
ACE-Is or ARBs are not recommended for the secondary prevention of paroxysmal AF in patients with little or no underlying heart disease.	III (no benefit)	B	241, 697

E = angiotensin-converting enzyme; AF = atrial fibrillation; ARB = angiotensin receptor blocker; CHA_2DS_2-VASc = Congestive Heart failure, hypertension, Age ≥75 abled), Diabetes, Stroke (doubled), Vascular disease, Age 65–74, and Sex (female); ECG = electrocardiogram; LV = left ventricular; LVH = left ventricular hypertrophy; VAC = non-vitamin K antagonist oral anticoagulant; TOE = transoesophageal echocardiography.

Catheter Ablation

Rationale for eliminating AF with ablation

- Improvement of quality of life.
- Decrease stroke risk.
- Decrease heart failure risk.
- Improve survival.

(HRS/EHRA/ECAS Expert Consensus Statement on AF Ablation, 2012)

Afib ablation in 2016 Guidelines

AF ablation is effective in restoring and maintaining sinus rhythm in patients with symptomatic paroxysmal, persistent, and probably long-standing persistent AF, in general as second-line treatment after failure of or intolerance to antiarrhythmic drug therapy.

As first-line treatment for paroxysmal AF, randomized trials showed only modestly improved rhythm outcome with catheter ablation compared to antiarrhythmic drug therapy.

Atrial Fibrillation Ablation

Who should be offered atrial fibrillation ablation?

- **The best results** for AF ablation are seen in patients with paroxysmal AF who are less than 70 years of age, have a left atrial size less than 5 cm, and do not have other significant co-morbities including severe obesity, sleep apnea, and heart failure.
- There are no absolute age or left atrial size cut offs that exclude a patient from consideration of AF ablation.
- AF ablation can also be offered to those with persistent and long standing persistent AF but the expected efficacy is less.

(HRS/EHRA/ECAS Expert Consensus Statement on AF Ablation, 2012)

Atrial Fibrillation Ablation

Who should be offered atrial fibrillation ablation?

- May be considered first-line therapy in:
  - Young, symptomatic patients.
  - Symptomatic patients with heart failure or reduced EF.

(HRS/EHRA/ECAS Expert Consensus Statement on AF Ablation, 2012)

Atrial Fibrillation Ablation

Which clinical factors are associated with lower efficacy of atrial fibrillation ablation?

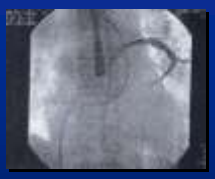
- Long standing persistent AF
- Sleep apnea
- Increased left atrial size (> 5.5 cm)
- Increased age (> 70 yrs)

There are no cut off levels to exclude a patient from consideration for AF ablation. But these factors should be considered when speaking with a patient about the risks and benefits of the procedure

(HRS/EHRA/ECAS Expert Consensus Statement on AF Ablation, 2012)

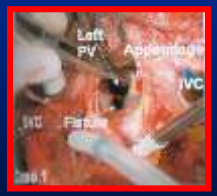
Atrial Fibrillation: Ablation vs Medications

Ablation	Medications.
70% success	40% success
PV stenosis	Proarrhythmia
AE fistula	End Organ Toxicity
TIA/CVA	

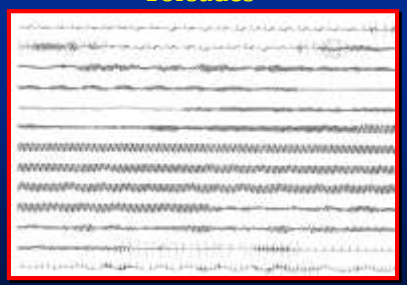


PV stenosis

AE fistula



Torsades



THANK YOU