ATRIAL FIBRILLATION
(RATE VS RHYTHM CONTROL)

By

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**AF Classification:**

<table>
<thead>
<tr>
<th>Term</th>
<th>Definition</th>
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</table>
| Paroxysmal AF               | • AF that terminates spontaneously or with intervention within 7 d of onset.  
                             | • Episodes may recur with variable frequency.                              |
| Persistent AF               | • Continuous AF that is sustained >7 d.                                   |
| Longstanding persistent AF  | • Continuous AF of >12 mo duration.                                       |
| Permanent AF                | • Permanent AF is used when there has been a joint decision by the patient and clinician to cease further attempts to restore and/or maintain sinus rhythm.  
                             | • Acceptance of AF represents a therapeutic attitude on the part of the patient and clinician rather than an inherent pathophysiological attribute of the AF.  
                             | • Acceptance of AF may change as symptoms, the efficacy of therapeutic interventions, and patient and clinician preferences evolve. |
| Nonvalvular AF              | • AF in the absence of rheumatic mitral stenosis, a mechanical or bioprosthetic heart valve, or mitral valve repair. |
Mechanisms of AF:

- **Extracardiac Factors:** Hypertension, Obesity, Sleep apnea, Hyperthyroidism, Alcohol/drugs
- **Atrial Structural Abnormalities:** Fibrosis, Dilation, Ischemia, Infiltration, Hypertrophy
- **Atrial tachycardia remodeling**
- **Genetic Variants:** Channelopathy, Cardiomyopathy
- **Atrial Electrical Abnormalities:**
  - ↑Heterogeneity
  - ↓Conduction
  - ↓Action potential duration/Refractoriness
  - ↑Automaticity
  - Abnormal intracellular Ca** handling
- **Inflammation, Oxidative stress**
- **RAAS activation**
- **Autonomic Nervous system activation**
Selected Risk Factors and Biomarkers for AF:

<table>
<thead>
<tr>
<th>Clinical Risk Factors</th>
<th>Electrocardiographic</th>
<th>Echocardiographic</th>
<th>Biomarkers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increasing age</td>
<td>LVH</td>
<td>LA enlargement</td>
<td>Increased CRP</td>
</tr>
<tr>
<td>Hypertension</td>
<td></td>
<td>Decreased LV fractional shortening</td>
<td>Increased BNP</td>
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<tr>
<td>Diabetes mellitus</td>
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<td>Increased LV wall thickness</td>
<td></td>
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<tr>
<td>MI</td>
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<td></td>
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<tr>
<td>VHD</td>
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<tr>
<td>HF</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Obesity</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Obstructive sleep apnea</td>
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<td></td>
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<tr>
<td>Cardiothoracic surgery</td>
<td></td>
<td></td>
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<tr>
<td>Smoking</td>
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<td></td>
<td></td>
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<tr>
<td>Exercise</td>
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<td></td>
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<tr>
<td>Alcohol use</td>
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<tr>
<td>Hyperthyroidism</td>
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<td></td>
<td></td>
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<tr>
<td>Increased pulse pressure</td>
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<td></td>
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<tr>
<td>European ancestry</td>
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<tr>
<td>Family history</td>
<td></td>
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<td></td>
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<tr>
<td>Genetic variants</td>
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</tbody>
</table>
WHY AF?
• 1. Atrial fibrillation is the most common sustained cardiac arrhythmia occurring in 1-2% of the general population
2. AF confers a 5-fold risk of stroke and one in five of all strokes is attributed to this arrhythmia.
3. In the majority of patients there appear to be an exorable progression of AF to persistent or permanent forms, associated with further development of the disease that underlie the arrhythmia.
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5. Some advance has been made in the understanding of the dynamic development of AF from its preclinical state as an arrhythmia-in-waiting to its final expression as an irreversible and end-stage cardiac arrhythmia associated with serious adverse cardiovascular events.
### Clinical events (outcomes) affected by AF

<table>
<thead>
<tr>
<th>Outcome parameter</th>
<th>Relative change in AF patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Death</td>
<td>Death rate doubled.</td>
</tr>
<tr>
<td>2. Stroke (includes haemorrhagic stroke and cerebral bleeds)</td>
<td>Stroke risk increased; AF is associated with more severe stroke.</td>
</tr>
<tr>
<td>3. Hospitalizations</td>
<td>Hospitalizations are frequent in AF patients and may contribute to reduced quality of life.</td>
</tr>
<tr>
<td>4. Quality of life and exercise capacity</td>
<td>Wide variation, from no effect to major reduction. AF can cause marked distress through palpitations and other AF-related symptoms.</td>
</tr>
<tr>
<td>5. Left ventricular function</td>
<td>Wide variation, from no change to tachycardiomyopathy with acute heart failure.</td>
</tr>
</tbody>
</table>
Cardiovascular and other conditions associated with AF:

1. Ageing

2. Hypertension

3. Heart failure (NYHA class II-IV) 30-40% of HF patients.

4. Tachycardiomyopathies.
5. Valvular heart disease: 30% of AF patients

6. Cardiomyopathies

7. Cardiac syndromes:
   - Short and Ion Q-T syndromes
   - Brugada syndrome
   - Hypertrophic cardiomyopathy
   - Abnormal LV hypertrophy
• 8. Atrial septal defect (ASD)

• 9. Other congenital defects
e.g. single ventricle after Mustard operation or after fontain surgery.

• 10. Coronary artery disease: 20% of AF patients

• 11. Thyroid dysfunction: hyperthyroidism and hypothyroidism.
12. Obesity in 25% of AF patients.

13. Diabetes mellitus: in 20% of AF patients

14. COPD in 10-15% of AF patients

15. Sleep apnoea

CONDITIONS PREDISPOSING TO, OR ENCOURAGING PROGRESSION OF AF

- Hypertension
- Symptomatic heart failure (NYHA II - IV) including tachycardiomyopathy
- Valvular heart disease
- Cardiomyopathies including primary electrical cardiac disease
- Atrial septal defect and other congenital heart defects
- Coronary artery disease
- Thyroid dysfunction and possibly subclinical thyroid dysfunction
- Obesity
- Diabetes mellitus
- Chronic obstructive pulmonary disease (COPD) and sleep apnoea
- Chronic renal disease
Clinical management of patients with AF involves the following five objectives:

1. Prevention of thromboembolism
2. Optimal management of concomitant cardiovascular disease
3. Symptom relief
4. Rate control
5. Correction of the rhythm disturbance
General rules in control of AF

• In patient with chronic or paroxysmal AF with rapid ventricular response → pharmacological therapy

• In patient with chronic or paroxysmal AF who don’t respond to or are intolerant of pharmacological therapy → AV nodal ablation and pacing

• CRT should be considered in other conditions
AF DECISION TREE AND STRATEGY

- **PAROXYSMAL AF**: RHYTHM CONTROL
- **PERSISTENT AF**: RATE OR RHYTHM CONTROL
- **PERMANENT AF**: RATE CONTROL
- **RATE CONTROL** more likely if:
  - Older – CAD – CI to AAD – Unsuitable CV
- **RHYTHM CONTROL** more likely if:
  - Symptomatic – Younger – First of Lone AF
  - Secondary to correctable cause – Heart Failure
RATE Vs RHYTHM CONTROL
2012 ESC guidelines Rhythm Vs Rate control

- Rate control **strongly preferred** as the initial approach in elderly patients with minor symptoms
- Rhythm control is strongly preferred in patients with symptoms despite rate control including those with HF
- Rhythm control is weakly preferred in young asymptomatic patients
- Rhythm control is weakly preferred in AF 2ry to a trigger or substrate that has been corrected
Why a Rate control?

- To avoid
  - Hemodynamic instability
  - Tachycardia mediated CM

- General principles
- 2 decisions
  - Determine the urgency of treatment
  - Choose between rate and rhythm control
Rate or Rhythm control

- **Preference of rate control**
  - The result of AFFIRM & RACE trials showed better outcome with rate control
  - Proarrythmia associated with anti-arrhythmic drugs

- Rate of recurrent AF and frequent crossover to a rate control strategy when anti arrhythmic are used to maintain a sinus rhythm

- Rate control is preferred in
  - HF
  - Newly detected AF
  - Elderly with AF
Preference for Rhythm control

- Should be considered
  - Limited efficacy
  - Side effects specially proarhythymia
Failure of Rate Control

• 2 manifestations
  • Persistent symptoms
  • Inability to attain adequate rate control:
    • Resting HR < 80
    • During exercise < 110
    • 6MWT
Control of Ventricular rate in AF

I) Non pharmacological methods
   - AV nodal ablation
   - AV nodal conduction modification

Investigational methods
   - Parahissian Pacing
   - Low atrial isolation
   - Ventricular rate regularization
   - Gene therapy
CRT in AF

- It improves some potential risk factor as LA size & LV systolic function
- However incident of new AF is not decreased
- Indication in
  - AF with EF $< 35\%$, QRS $> 0.12$ sec & NYHA III or ambulatory NYHA IV
  - Most patient who satisfy either of the above criteria are also candidate for ICD & should receive a combined device
Control of Ventricular rate in AF

• II) Pharmacological methods
Approach to Selecting Drug Therapy for Ventricular Rate Control

Atrial Fibrillation

- No Other CV Disease
  - Beta blocker
  - Diltiazem
  - Verapamil

- Hypertension or HFpEF
  - Beta blocker
  - Diltiazem
  - Verapamil

- LV Dysfunction or HF
  - Beta blocker†
  - Digoxin‡

- COPD
  - Beta blocker
  - Diltiazem
  - Verapamil

Amiodarone§
مكيفه Disea ولا مش مكيفه
يا متعلمين يا بتوع المدارس
New drugs for rate control of AF

I) Adenosine A1 receptor agonist.

**Tecadenson:**

- It is an adenosine derivative with high specificity to A1 receptors and a potency to prolong AVN conduction at dose that does that do not reduce BP or cause bronchospasm by stimulation of A2 receptors.
- It has no effect on ventricular conduction and very little effect on atrial action potential duration.
• It is used as an urgent rate control of possibly cardio version of AF.

• It is successful in terminating about 87% in SVT.
Selodenson:

- It is an adenosine like agent which differ from Tecadenson in that it has a longer half life (150 min)
Other new Drugs:

- **New Class III agents:**
  - Azimilide.
  - Dronedaron.
  - Tedisamid.
  - Celivarone.
  - Other Amiodaron derivatives.
  - Nitekalmt.
Novel drugs:

**New Class III agents:**
- Adenosine agonist.
- Ranolazine.
- Connexin modulators.
- SAC Blockers.
- 5-HT4.
- Na+/H+ Inhibitors.
- Na+/Ca++ inhibitors.
- Ry p2 modifiers.

*Gap junction modifiers.*
Choice of Pharmacological treatment of AF (2012)

- A) Acute Rate control
  - IV medications
    - IV diltiazem, Bblockers or amiodarone should be considered in the following order
    - IV digoxin should be considered if there is
      - Hypotension or HF
      - Inadequate response to 1st line drugs
    - Not tolerated previous combination → IV amiodarone should be considered
Choice of Pharmacological treatment of AF (2012)

• B) Chronic rate control
  • Oral therapy with B Blokers or CCBs in such patient
  • Oral digoxin may be combined if the response to 1\textsuperscript{st} line inadequate
  • Triple therapy of B Blokers or CCBs and digoxin if response to BB or CCB alone is inadequate
<table>
<thead>
<tr>
<th>Medication</th>
<th>Intravenous Administration</th>
<th>Usual Oral Maintenance Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Beta blockers</strong></td>
<td></td>
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<tr>
<td>Metoprolol tartrate</td>
<td>2.5–5.0 mg IV bolus over 2 min; up to 3 doses</td>
<td>25–100 mg BID</td>
</tr>
<tr>
<td>Metoprolol XL (succinate)</td>
<td>N/A</td>
<td>50–400 mg QD</td>
</tr>
<tr>
<td>Atenolol</td>
<td>N/A</td>
<td>25–100 mg QD</td>
</tr>
<tr>
<td>Esmolol</td>
<td>500 mcg/kg IV bolus over 1 min, then 50–300 mcg/kg/min IV</td>
<td>N/A</td>
</tr>
<tr>
<td>Propranolol</td>
<td>1 mg IV over 1 min, up to 3 doses at 2 min intervals</td>
<td>10–40 mg TID or QID</td>
</tr>
<tr>
<td>Nadolol</td>
<td>N/A</td>
<td>10–240 mg QD</td>
</tr>
<tr>
<td>Carvedilol</td>
<td>N/A</td>
<td>3.125–25 mg BID</td>
</tr>
<tr>
<td>Bisoprolol</td>
<td>N/A</td>
<td>2.5–10 mg QD</td>
</tr>
<tr>
<td><strong>Nondihydropyridine calcium channel antagonists</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Verapamil</td>
<td>(0.075–0.15 mg/kg) IV bolus over 2 min, may give an additional 10.0 mg after 30 min if no response, then 0.005 mg/kg/min infusion</td>
<td>180–480 mg QD (ER)</td>
</tr>
<tr>
<td>Diltiazem</td>
<td>0.25 mg/kg IV bolus over 2 min, then 5–15 mg/h</td>
<td>120–360 mg QD (ER)</td>
</tr>
<tr>
<td><strong>Digitalis glycosides</strong></td>
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</tr>
<tr>
<td>Digoxin</td>
<td>0.25 mg IV with repeat dosing to a maximum of 1.5 mg over 24 h</td>
<td>0.125–0.25 mg QD</td>
</tr>
<tr>
<td><strong>Others</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amiodarone</td>
<td>300 mg IV over 1 h, then 10–50 mg/h over 24 h</td>
<td>100–200 mg QD</td>
</tr>
</tbody>
</table>

AF indicates atrial fibrillation; BID, twice daily; ER, extended release; IV, intravenous; N/A, not applicable; QD, once daily; QID, four times a day; and TID, three times a day.
# Summary of Recommendations for Rate Control

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>COR</th>
<th>LOE</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control ventricular rate using a beta blocker or nondihydropyridine calcium channel antagonist for paroxysmal, persistent, or permanent AF</td>
<td>I</td>
<td>B</td>
<td>(93-95)</td>
</tr>
<tr>
<td>IV beta blockers or nondihydropyridine calcium channel blocker recommended to slow ventricular heart rate in the acute setting in patients without pre-excitation. In hemodynamically unstable patients, electrical cardioversion is indicated</td>
<td>I</td>
<td>B</td>
<td>(96-99)</td>
</tr>
<tr>
<td>For AF, assess heart rate control during exertion, adjusting pharmacological treatment as necessary</td>
<td>I</td>
<td>C</td>
<td>N/A</td>
</tr>
<tr>
<td>A heart rate control (resting heart rate &lt;80 bpm) strategy is reasonable for symptomatic management of AF</td>
<td>IIa</td>
<td>B</td>
<td>(95, 100)</td>
</tr>
<tr>
<td>IV amiodarone can be useful for rate control in critically ill patients without pre-excitation</td>
<td>IIa</td>
<td>B</td>
<td>(101-103)</td>
</tr>
<tr>
<td>AV nodal ablation with permanent ventricular pacing is reasonable when pharmacological management is inadequate and rhythm control is not achievable</td>
<td>IIa</td>
<td>B</td>
<td>(104-106)</td>
</tr>
<tr>
<td>Lenient rate control strategy (resting heart rate &lt;110 bpm) may be reasonable with asymptomatic patients and LV systolic function is preserved</td>
<td>IIb</td>
<td>B</td>
<td>(100)</td>
</tr>
<tr>
<td>Oral amiodarone may be useful for ventricular rate control when other measures are unsuccessful or contraindicated</td>
<td>IIb</td>
<td>C</td>
<td>N/A</td>
</tr>
<tr>
<td>AV nodal ablation should not be performed without prior attempts to achieve rate control with medications</td>
<td>III: Harm</td>
<td>C</td>
<td>N/A</td>
</tr>
<tr>
<td>Nondihydropyridine calcium channel antagonists should not be used in decompensated HF</td>
<td>III: Harm</td>
<td>C</td>
<td>N/A</td>
</tr>
<tr>
<td>With pre-excitation and AF, digoxin, nondihydropyridine calcium channel antagonists, or amiodarone, should not be administered</td>
<td>III: Harm</td>
<td>B</td>
<td>(107)</td>
</tr>
<tr>
<td>Dronedarone should not be used to control ventricular rate with permanent AF</td>
<td>III: Harm</td>
<td>B</td>
<td>(108, 109)</td>
</tr>
</tbody>
</table>
THANK YOU