THE NORTHERN HOSPITAL

ATRIAL FIBRILLATION

"Cesare Borgia", Altobello Melone, c. 1520, Bergamo Accademia Carrara Italy

"…no government should ever imagine that it can always adopt a safe course; rather it should regard all possible courses of action as risky. This is the way things are: whenever one tries to escape one danger one runs into another. Prudence consists in being able to assess the nature of a particular threat and in accepting the lesser evil."

Niccolo Machiavelli, The Prince, XX1 , 1513-14.

Though not widely read during his life time Niccolo Machiavelli's "The Prince" has become one of the iconic literary masterpieces of the Western world. Many works before his, beginning with Plato's "Republic" and many since such as Jean Jacques Rousseau's "Emile" have tried to define what the "perfect society" ought to be. These works were based however on the wishful thinking of philosophers with little understanding of the real world.

Machiavelli's genius lay in his ability to assess and understand human nature as it truly is. Shocking to many of his time and since, it was a work that for the first time in history told of how a prince could attain and maintain a "perfect society" not based on a starry eyed ideal but within the constraints of the real world. Drawing on his own vast experience as a diplomat within the treacherous and turbulent world of Renaissance Italy he stated uncompromisingly what to varying degree most governments actually do, but none profess to do. Having dealt at first hand with all levels of society from the Emperor Maximilian of the Holy Roman Empire, King Louis XII of France, Leonardo da Vinci, Pope Julius II, the infamous Pope Alexander VI and his equally infamous son Cesare Borgia, upon whom his prince was modelled, to the common artisan, local farm workers, actresses of ill repute, soldiers and prostitutes, he came to know human nature well enough.

His earliest biographer Pasquale Villari, wrote of him, "Of middle height, slender figure, sparkling eyes, dark hair, rather a small head, a slightly aquiline nose, a tightly closed mouth. All about him bore the impress of a wry accurate observer and thinker. He could not easily rid himself of the sarcastic expression continually playing round his mouth and flashing from his eyes, which gave him the air of a cold impassable calculator..."

One of his most recent biographers, Michael White, wrote of him, "...Machiavelli was a commanding presence in any company. He was cool calm astute, probing and wise. He could size up others very quickly with very little to go on. Most of the time he played his cards close to his chest, but he was never afraid to express a sincerely held opinion…he understood how the world worked and he could make piercing critical judgments with apparent ease"

When confronting the problem of AF in the Emergency Department we must recognize that there is no ideal treatment that will cover all scenarios and situations. Like the history of humanity's attempts to define the perfect society many medical textbooks describe their "perfect" treatment of AF, but rarely if ever in practice will this be the ideal treatment for a particular individual case. We can only heed the wise words of Niccolo Machiavelli, that no course of action will be without some measure of risk, this is currently "the way things are". We must therefore be prudent, assessing each case on its merits, recognizing the nature of any threat for any particular treatment we choose. In the final event we must make a "piercing critical judgment" to do the best we can for our patients, accepting it as the "lesser evil" of other possible alternatives.

ATRIAL FIBRILLATION

Introduction

Atrial fibrillation (**AF**) is a very common presenting problem to the ED.

Management is often problematic, there being no ideal treatment to cover all cases or all situations.

The major issues within the ED for *rapid* AF will be:

- The decision of rate versus rhythm control.
- Prophylaxis against thromboembolic complications.

Treatment decisions will be based on:

- The chronicity of the problem
- The clinical symptoms of the patient
- The actual rate of the AF
- The exact cause of the AF.

Epidemiology

AF is the most common recurrent arrhythmia faced in clinical practice, and it causes substantial morbidity and mortality.

Current estimates of AF prevalence in developed countries such as Australia range from 2% - 4%, and there is a steep gradient with increasing age.

However, *true* prevalence is underestimated because subclinical AF is frequent

Pathophysiology

Causes

Atrial fibrillation (AF) is a common arrhythmia, with a prevalence that increases markedly with increasing age.

1. Primary:
    - AF can be seen in younger patients with no evidence of comorbid cardiopulmonary disease - this condition is termed “lone AF”. Estimates of its incidence range from 1.6 - 30 % of patients.

      Given the absence of comorbidities, it carries a lower risk of stroke.
2. Secondary causes:

The most important causes include:

- Ischemic heart disease, including acute coronary syndromes.
- Valvular heart disease, (i.e usually **mitral** valve).
- Hypertension
- Cardiomyopathies
- Cardiac channelopathies:

  Examples include:

  - ♥ Long QT syndrome / Short QT syndrome
  - ♥ Brugada syndrome
- Thyrotoxicosis, especially in the elderly.
- Congenital aberrant pathways, especially WPW.
- Hypothermia, (common)
- Obstructive sleep apnoea
- Obesity
- Alcohol and caffeine, (digoxin toxicity is **not** a cause)

Less commonly:

- Pulmonary embolism.
- Pericardial disease.
- Electrolyte deficiencies:

  - ♥ Hypokalemia / hypomagnesaemia
- Myocarditis.
- Electrocution.
- Myocardial injury e.g. contusion.

Complications:

The principle complications of AF include:

1. Loss of atrial contraction component of stroke volume, hence reduced cardiac output.

2. Excessively rapid ventricular response, leading to reduced cardiac filling times, and reduction of cardiac output.

3. Blood stasis within the atria, leading to clot formation and the risk of thromboembolism.

    - Atrial fibrillation itself rarely causes death or serious morbidity except through **thromboembolic** complications.

Clinical Presentations

In many patients, AF progresses from short paroxysmal episodes to more frequent and persistent attacks, and then often to permanent AF.

However, progression can be mitigated by aggressive targeting of modifiable cardiovascular risk factors.

Four main clinical patterns of AF have been described, based on duration and termination of AF episodes

Paroxysmal AF:

- Episodes come on suddenly and self revert spontaneously, even if no intervention is undertaken, usually within **48 hours**, or are cardioverted within 7 days.

  Episodes may occur with variable frequency.

Persistent AF:

- Episodes of continuous AF that last >7 days and do not self-terminate, including episodes that are cardioverted 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 (or chronic) AF:

- This applies when a decision has been made jointly by the physician and patient to accept the presence of AF and stop further attempts to restore or maintain sinus rhythm.

  This represents *clinical acceptance* rather than an inherent pathophysiological attribute of AF and, should a rhythm-control strategy be adopted, the arrhythmia should be re-classified as "long-standing persistent AF".

"**Non-Valvular AF**" refers to AF in the **absence of moderate to severe mitral stenosis** or the presence of a **mechanical heart valve**.

Investigations

The following investigations should be considered:

Blood tests:

1. FBE
2. U&Es / glucose:
    - Hypokalemia, in particular.
3. Thyroid function tests:
    - This should be done for all new cases.

      Note that patients who are on **amiodarone** and who present with rapid AF, should also have their TFTs repeated, as thyroid dysfunction, both *hyper* and *hypo* are possible side effects of this drug.
4. Cardiac enzymes:
    - These are not routinely required unless the patient presents with a suspected ACS.

      They should be *considered* in patients with *high-risk* co-morbidity for ACS, even if they do not present with chest pain.

ECG:

ECG features of AF include:

- Absence of P waves (replaced by fibrillory waves, these can be coarse or fine).
- The QRS complexes are irregularly irregular.
- QRS complexes may be narrow or wide (if there is pre-existing bundle branch pathology or aberrant pathways)
- The rate may be slow or fast. (If > 180 and with variable morphology, WPW may be the underlying cause).

CXR:

Look for cardiomegaly, suggestive of unsuspected cardiomyopathy.

If this is found flecainide and sotolol are best **avoided.**

Echocardiography:

A transthoracic echocardiogram should be performed in all patients with newly diagnosed AF.

A transthoracic echocardiogram can assist patient management by identifying valvular heart disease, and quantifying left ventricle (LV) function and atrial size.

Transthoracic echocardiogram will yield data on some key parameters:

1. Mitral stenosis and regurgitation:

    - Both of these conditions can lead to increased atrial size and hence AF

      Mitral stenosis can also increase thromboembolic risk, and DOACs are contraindicated in patients with moderate or severe mitral stenosis.

2. LA size and volume:

    - LA volume may be a stronger predictor than LA size for predicting AF and stroke risk.

3. LV systolic dysfunction:

    - Moderate to severe LV systolic dysfunction leads to a 2.5-fold increase in the risk of thromboembolism, reversible LV dysfunction may develop in patients with uncontrolled AF.

Transoesophageal echocardiography (TOE) can be considered when findings might affect patient management, primarily where electrical or pharmacological cardioversion is indicated and the presence of thrombus may affect timing.

Management

Management of the patient presenting with AF in the **ED**, will depend on the following:

1. The hemodynamic status of the patient.
2. The age of the patient.
3. The exact cause of the AF.
4. The rate of the ventricular response, (i.e. too slow or too fast)
5. The chronicity of the AF

    - Has it been present for less than or greater than **48 hours.**

6. Any associated cardiac/medical conditions of the patient.

There is no current ideal treatment or drug for all patients or situations.

Each case must therefore be treated on its merits in the light of the above considerations.

The major initial decision in the ED will be between rate control or reversion to sinus rhythm.

Two trials in 2002, the American **AFFIRM trial** and a second European study demonstrated that there was no longer term difference in mortality and morbidity between rate control and anticoagulation and rhythm control with anticoagulation in patients with persistent or chronic AF. So whilst it may be desirable to attempt reversion to sinus rhythm in some patients with significant symptoms or cardiovascular compromise, there is no overall absolute necessity to do so.

These studies concentrated predominantly on older patients (> 65 years of age) with cardiovascular risk factors and with persistent or chronic AF.

The situation however is less clear in younger patients without significant associated risk factors or known structural heart disease and who present with apparent **de novo paroxysmal AF of < 48 hours onset**.

Whilst many will revert spontaneously within the following 24 - 48 hours, some may in fact be persistent which cannot be known at the initial time of presentation.

An editorial in the NEJM edition that published the above two studies suggested that at an attempt at rhythm control in this group was justifiable though not imperative. Advantages of restoring sinus rhythm in this group would include resolution of symptoms and the avoidance of the need for *long term* anti-coagulation.

The following are scenarios that may be encountered in the ED.

1. **The unstable patient**:

   Cardioversion is the best treatment in the very unstable patient in whom it is thought that reversion to sinus rhythm would be beneficial in order to restore cardiac output.

   Note however that AF, even if rapid, is usually well tolerated and that if a patient is unstable it may not be the **AF that is the primary problem.**

   For example in a patient with hypotension look for another cause (e.g. **hypovolemia, pulmonary embolism, sepsis**) before attributing the problem to the AF.

2. **New Onset Paroxysmal Rapid AF (< 48 hours)**:

   If the AF is a recurrent event, there may be a relevant history and pattern to take into account, but if a first episode a pattern will not yet be evident.

   In cases of paroxysmal AF of less than **48 hours** duration, it is generally considered safe to attempt reversion to sinus rhythm without the need for an echocardiogram, as the risk of embolism in this group is very low.

   A judgment on this time frame can only be made if there is a clear and unambiguous history of a time of onset.

   Anticoagulation should nonetheless be commenced for these patients as well. Even in very recent onset AF there is a risk of **atrial "stunning"** following reversion, (be it

electrically, pharmacologically or spontaneous) to sinus rhythm. Stunning is an unpredictable failure of the atria to contract which may follow AF. It can occur even after a brief episode, (but is more common after longer attacks) and may persist for hours to days. During this time fresh thrombus can form within the non contracting atria and constitute an embolic risk.

3. **Rapid AF where the patient has been in AF > 48 hours:**

In this situation there is a clear risk of embolism if the patient is reverted to sinus rhythm and initial treatment is therefore aimed at rate control only.

The AFFIRM trial and others mentioned above have shown that for those over 65 years with persistent or chronic AF, rate control is equal to rhythm control (in both cases with anticoagulation). There is therefore no imperative need to achieve rhythm control, unless symptoms are severe.

Initial treatment in the ED therefore will primarily be aimed at rate control, (as well as attention to any underlying precipitating factors).

A decision can be made later by the cardiology department as to whether an attempt at reversion to sinus rhythm is warranted.

If sinus rhythm restoration is to be attempted in these cases then the risk of thromboembolism must first be minimized by TOE examination to exclude intracardiac thrombus (which will obviate the need for prolonged anticoagulation) or a period of anticoagulation for 4 - 6 weeks should be undertaken.

Either way a period of anticoagulation will still be required post reversion in view of the atrial stunning phenomenon.

A "**lenient**" **rate-control strategy** (i.e. resting heart rate < 110 - as opposed to one of < 80) may be reasonable as long as patients remain asymptomatic and left ventricular systolic function is preserved.

Rate Control:

Options for rate control (i.e. < 110) in the ED include:

Oral therapy:

Stable patients who are not distressed by their symptoms and have only moderately fast rates and are otherwise stable may be treated with oral therapy, (but a response will take longer than IV therapy)

Options include:

- **Metoprolol** 25 - 100 mg orally, b.d
- **Non-dihydropyridine calcium channel blockers**:
  - ♥ **Diltiazem** controlled-release 180 - 360 mg orally, daily

- ♥ **Verapamil** sustained-release 160 - 480 mg orally, daily.

- **Digoxin**:

  Digoxin may be considered to aid in acute control of ventricular rate either as **add-on** therapy to beta adrenoceptor antagonists or non-dihydropyridine calcium channel antagonists, or as stand-alone therapy if these agents and amiodarone are contraindicated.

  Note however, that it has a **delayed onset of action**, has only a **weak effect** in terms of rate control, and has a **narrow therapeutic index**. Digoxin **monotherapy** may *not* result in effective rate control.

Intravenous therapy:

When more rapid control of the heart rate is required such as unstable patients or who are distressed by symptoms or have very high ventricular rates:

Options include:

1. **IV beta adrenergic blocker**:

   Metoprolol:

   - 5 mg (1 mg/min) IV, repeated at 5 minute intervals up to a maximum 20 mg.

   IV Esmolol infusion:

   - 500 micrograms/kg IV, over 1 minute, then titrate to achieve desired ventricular rate, typically 50 to 200 micrograms/kg/minute

2. **IV Verapamil**:

   - IV verapamil can be given in 1 mg boluses at a rate of about 1 mg per minute, (to a maximum of 15 mg)

     Note it is best to avoid combined calcium channel blockers and beta blockers if possible because of the increased risk of the development of complete heart block.

     This agent should be used with caution however because of its negative inotropic effects, and *avoided* in those with impaired LV function.

3. **IV Amiodarone**:

   - IV Amiodarone is recommended for acute control of the ventricular rate in highly symptomatic AF patients, or in those with known left ventricular systolic dysfunction, who are not unstable enough to require immediate electrical cardioversion.

     Amiodarone is more likely to achieve rate control than rhythm control

In patients with marginal haemodynamic reserve, established heart failure, or other significant structural heart disease, amiodarone may be the most effective (and only) rate control option.

4. **IV Digoxin**:

   - An initial intravenous dose of **0.25 to 0.5 mg** of digoxin is given over **several minutes.**

   Followed by:

   - **0.25 mg every 6 hours** for a **total loading dose of 0.75 to 1.5 mg** (i.e. 10 to 12 mcg/kg lean body weight) - over a period of **24 hours.**

5. **IV $MgSO_4$**:

   The role and efficacy of $MgSO_4$ for rate control of rapid AF is uncertain.

   Considerations for use may include:

   - Where significant contra-indications exist to the use of beta-blockers or calcium channel blockers or amiodarone.
   - As an *adjunctive* agent, where other agents have not been effective.
   - The presence of significant hypomagnesaemia.

   The optimal dosing is not established, but the following is suggested in the Emergency Medicine Therapeutic Guidelines:

   - **Magnesium sulfate 50%, 5 to 10 mL (= 2.5 to 5 g or 10 to 20 mmol) IV over 20 to 60 minutes.**

     (Or as per Kg dosing: Magnesium sulfate 50% 0.1 mL/kg (= 50 mg/kg or 0.2 mmol/kg) IV over 20 minutes)

Rhythm Control:

Factors favoring a strategy of **rhythm control over** rate control include:

1. AF < 48 hours in duration
2. Highly symptomatic patients
3. Physically active patients
4. Difficulty in achieving adequate rate control
5. LV dysfunction (mortality benefit)
6. Absence of severe atrial enlargement

7. Patient preference

Pharmacological Reversion:

As many of the rhythm-control drugs and some of those used for rate control have myocardial depressant or proarrhythmic potential, it is very useful to have an assessment of left ventricular function and of the presence of coronary disease. However, this information is not always available on first presentation.

Initial pharmacological reversion treatment options include:

1. Flecainide:

    - Flecainide is the best option in younger patients for rapid reversion to sinus rhythm, *providing they have normal left ventricular function, no structural heart disease or coronary artery disease.*

    - **Give flecainide 2 mg/kg, up to 150 mg, IV over 30 minutes.**

    Note that if using flecainide, there is a possibility of accelerating the ventricular rate (higher proportion of atrial impulses being conducted through the atrioventricular (AV) node, if the diagnosis is **atrial flutter,** rather than AF

Alternatively:

2. IV Amiodarone:

    Amiodarone administered intravenously may be considered for delayed conversion to sinus rhythm in patients with structural heart disease, *including patients with heart failure and coronary artery disease.*

    - **Give a loading dose of 5 mg/kg (or generally 150 - 300 mg) IV over 20 - 30 minutes.**

    - **Ongoing infusions of amiodarone can also be given for difficult to control rapid AF.**

3. Sotolol:

    - Although sometimes used in the past for attempted pharmacological reversion, the evidence suggests it is no more effective than placebo (in contrast to its well documented efficacy in maintaining sinus rhythm in the **long term**)

      In view of this uncertainty, current National Heart Foundation Guidelines do **not** recommend the use of sotalol for the acute reversion to sinus rhythm.

Electrical Cardioversion:

If sinus rhythm has not been achieved following attempted pharmacological reversion, electrical cardioversion may be considered.

A period of observation in a monitored Short Stay Ward, may be considered initially as many cases will revert spontaneously, even without treatment.

If still in AF at 24 hours then cardioversion in the ED should be considered.

The patient should be fasted for at least 4 hours.

Cardioversion can then be done under appropriate sedation.

150 Joules of synchronize biphasic energy counter shock should be used.

Anticoagulation post Cardioversion in Patients with AF < 48 hours:

This is not currently well defined in the setting of de novo paroxysmal (< 48 hours) presentations.

eTG recommends that anticoagulant therapy should be used **at the time of cardioversion**

An initial dose of enoxaparin 1.5 mg/kg SC can be given.

Longer term, anticoagulation may then be commenced depending on the patient's CHADS-VA thromboembolic risk

All patients who have been reverted by cardioversion or drug treatment should be observed in the ED/SSU for a minimum of 4 hours ECG monitoring before discharge.

Long term anticoagulation for patients with Chronic AF:

The **CHA_2DS_2-VA Score** can be used to assess the risk of thromboembolism in patients with **non-valvular** AF, and together with the **HAS-BLED Score**, which assesses the risk of bleeding in a patient on anticoagulation, can be used to inform decisions on initiating anticoagulation in patients with non-valvular AF.

See also separate documents on:

- **CHA_2DS_2-VA Score, (in CVS folder)**
- **HAS-BLED Score, (in CVS folder)**

Current National Heart Foundation Guidelines recommend the following:

SCORE	RISK	TREATMENT
0	**Low**	No therapy (antiplatelet *or* oral anticoagulant) is indicated.
1	**Moderate**	Consider oral anticoagulation therapy

≥ 2	**High**	Oral anticoagulation therapy is recommended if there are no contraindications. Patient values and preferences should also be taken into account.

When oral anticoagulation is initiated in a patient with Non-Valvular AF, a DOAC - (apixaban, dabigatran, or rivaroxaban) - is recommended in preference to warfarin.

Warfarin is recommended and DOACs should not be used in patients with valvular AF (i.e. mechanical heart valves or moderate to severe mitral stenosis).

Antiplatelet therapy is not recommended for stroke prevention in Non-Valvular AF patients, regardless of stroke risk.

Note that the final decision to treat (and with what) will also depend on patient's risk factors for bleeding. In this regard the HAS - BLED Score will also be useful in guiding the final decision to commence oral anticoagulation therapy.

Note that the final decision to treat (and with what) will also depend on a patient's risk factors for bleeding. In this regards the HAS - BLED Score will also be useful.

One suggestion is that a **HAS-BLED score** of **≥ 3 points** constitutes high risk, sufficient to justify caution in prescribing oral anticoagulants or at least more regular review.

Rapid AF due to underlying WPW (or other Pre-excitation syndrome):

Suspect this condition when the ventricular rate is very fast (> 180) and there is **variation** in the morphology of the QRS complexes.

The following ("A,B,C,D") drugs are potentially dangerous in this condition and are best **avoided:**

- **A**denosine
- **B**eta blockers
- **C**alcium channel blockers (i.e verapamil)
- **D**igoxin

Blockade of the A-V node by these agents will allow an unrestricted pathway via the bundle of Kent into the ventricles.

The following may be considered:

- Flecainide:
    - ♥ This is virtually the only anti-arrhythmic (available in Australia) considered safe to use in this rhythm.

Amiodarone and sotalol: These are *no longer* recommended in **WPW AF**. Both these agents have specific **beta blocking** effects.

If the patient is unstable then DC cardioversion is the treatment of choice.

DC cardioversion is the *best* option in all cases of WPW AF.

(**See also separate WPW document**)

Rapid AF due to Hyperthyroidism:

Beta blockers are recommended to control ventricular rate with AF complicating thyrotoxicosis unless contraindicated

When beta blockers cannot be used, a non-dihydropyridine calcium channel antagonist (i.e **verapamil** or **diltiazem**) is recommended to control ventricular rate

Slow AF:

AF with an excessively slow ventricular response rate may be seen in cases of:

- **Drug effect in patients with pre-existing AF.**
- As part of the syndrome of sinus nodal dysfunction.
- Hypothermia.

Management in these cases will consist of:

- Treatment of the underlying cause.
- Atropine or pacing to improve the ventricular rate, (note that bradyarrhythmias should **not** be cardioverted, because of the risk of severe bradyarrhythmia or asystole.)

Disposition:

All patients with newly diagnosed AF, but particularly those who are younger (i.e, aged < 65 years) and with more severe symptoms, should be referred to Cardiology for review.

If the patient is able to be discharged then an outpatient echocardiogram to look for structural disease, should be organized if the patient has not had one in the recent past.

In selecting patients for **catheter ablation of AF**, consideration should be given to the patient's age, duration of AF, left atrial size and the presence of significant structural heart disease. Best results are obtained in younger patients with paroxysmal AF, no structural heart disease and smaller atria.

Techniques include:

- MAZE procedure
- AV node ablation with ventricular pacing

- Ablation of accessory pathways

References

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