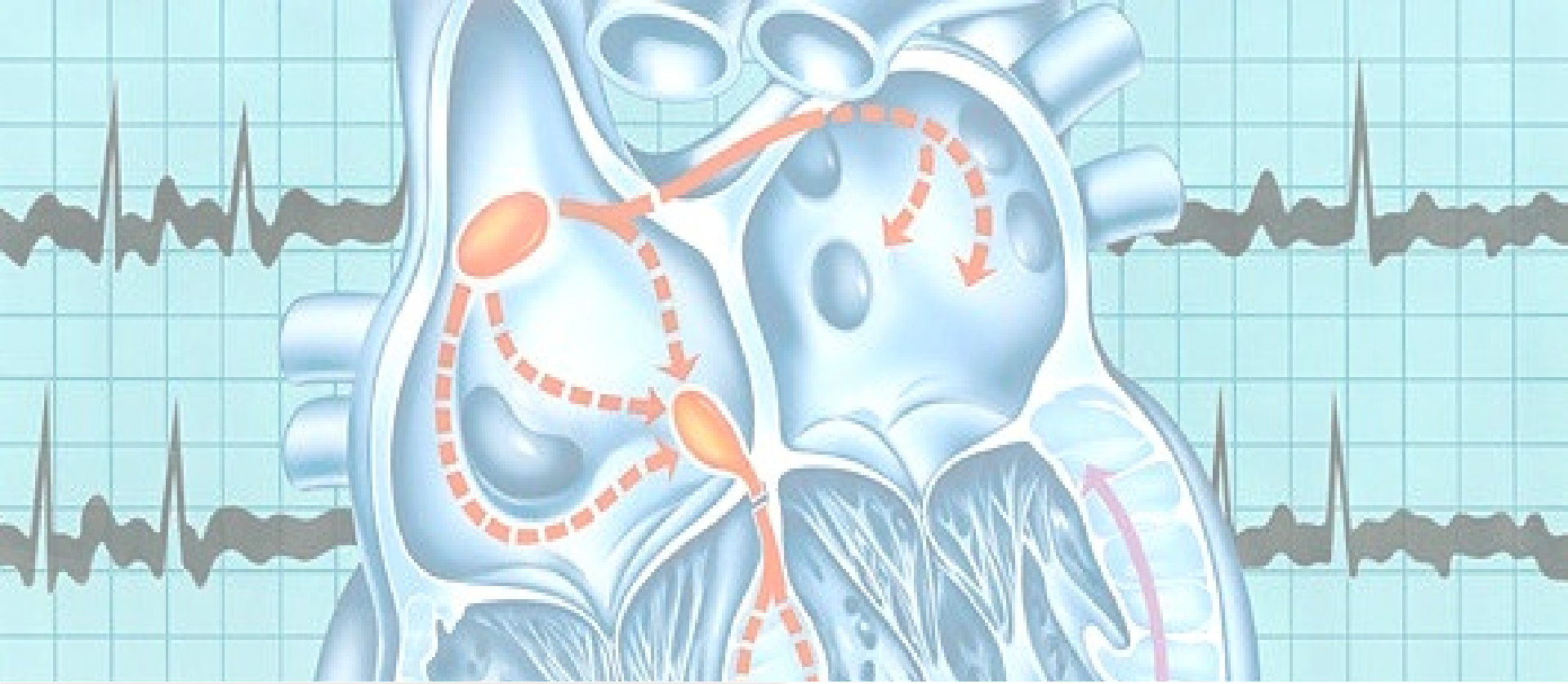
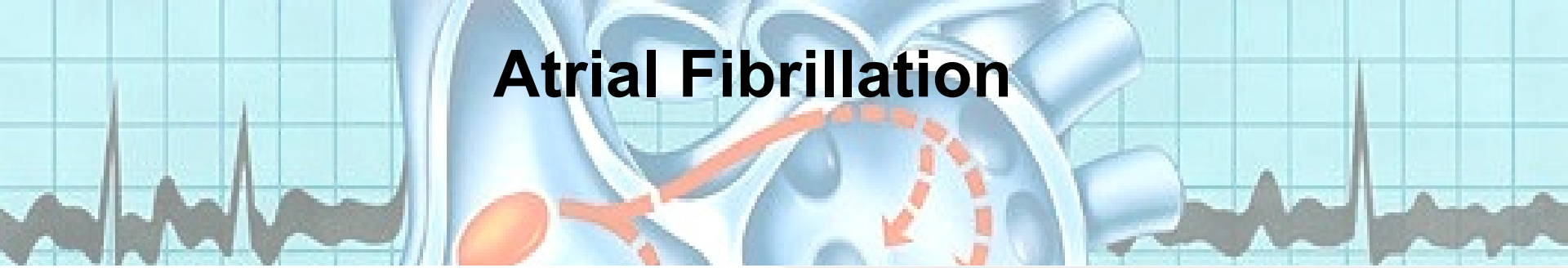


A tale of two atria

Atrial Fibrillation



Prevalence

- 1-2% of population
- AF may long remain undiagnosed/asymptomatic/silent AF
- 'True' prevalence is probably closer to 2% of population
- Prevalence increases with age

  <0.5% at 40-50yo

  5-15% at 80yo
- AF is associated with increased risks of death, stroke and other thrombo-embolic events, heart failure and hospitalisations, degraded QOL, reduced exercise capacity, and LV dysfunction

Natural Hx

- Progression from short, rare episodes, to longer, more frequent episodes
- Many pts develop sustained forms of AF over time
- Only a small proportion of pts remain in paroxysmal AF over several decades
- Distribution of paroxysmal AF recurrences is clustered
- Asymptomatic AF is common even in symptomatic patients - irrespective of initial presentation being paroxysmal or persistent

A tale of two atria

65yo M

Retired farmer

MHx: Hypertension (Ramipril 5mg)

Benign Prostatic Hyperplasia

BCCs face

27yo M

Mine FIFO worker

Looks fit, works out & plays contact rugby

Drinks 20-30 std drink/weekend

Occasional speed use

65yo M
MHx: Hypertension (Ramipril 5mg)
Benign Prostatic Hyperplasia
BCCs face

27yo M
Mine FIFO worker
Looks fit, works out & plays contact rugby
Drinks 20-30 std drink/weekend
Occasional speed use

Tuesday Morning
Both pts present to ED with AF @ 160bpm with 36hr Hx of palps + lightheadedness

65yo M
MHx: Hypertension (Ramipril 5mg)
Benign Prostatic Hyperplasia
BCCs face

27yo M
Mine FIFO worker
Looks fit, works out & plays contact rugby
Drinks 20-30 std drink/weekend
Occasional speed use

Tuesday Morning
Both pts present to ED with AF @ 160bpm
with 36hr Hx of palps + lightheadedness
2 Echos available

LVEF 45%
No valve pathology

LVEF 59%
No valve pathology

Considerations for each patient:

Rate or Rhythm???

Rhythm: Acute or Delayed?

Anticoagulation

Prevalence @ Age
Underlying conditions
Natural Hx of AF

Rx Options

Rhythm Control

considerations:

- Pharmacological cardioversion

or

- DC cardioversion

- Acute

or

- Delayed

Rate Control

- Beta blockers
- Calcium Channel blockers
- Digoxin

- Ablation therapy

Anticoagulation

- Heparin
- Aspirin/ Clopidogrel
- Warfarin
- Dabigatran

NICE Guidelines suggest:

Paroxysmal AF=> Rhythm control 1st line

Permanent AF => Rate control 1st line

Persistent AF= > Rhythm vs rate???

Consider Rhythm Control for patients:

- who are symptomatic
- who are younger
- presenting for the first time with lone AF
- secondary to a treated or corrected precipitant
- with congestive heart failure

Consider Rate Control for Patients:

- over 65
- with coronary artery disease
- with contraindications to antiarrhythmic drugs
- unsuitable for cardioversion
  - Anticoagulation contraindicated
  - Unlikely to maintain sinus rhythm due to structural abnormalities

Rhythm Control

Ottawa Aggressive Protocol suggests

http://www.google.com.au/url?sa=t&rct=j&q=ottawa%20aggressive%20protocol&source=web&cd=6&ved=0CGoQFjAF&url=http%3A%2F%2Femed.wustl.edu%2Fcontent%2Fjournalclub%2Farticles%2Fdocuments%2FPGYII_OttawaAggressiveProtocolAFibMgt_CJEM2010.pdf&ei=gpLOT_TkG86viQeUwJCHDA&usg=AFQjCNFpdTJIlEGuw8THK-53lLmYDannjg&cad=rja

For pts presenting to ED with recent onset AF

Exclusion criteria

- permanent AF (chronic, persistent or long standing)
- symptoms > 48hrs or unknown duration (unless therapeutically anticoagulated with warfarin for 3 weeks)
- another primary diagnosis necessitating admission (eg cardiac ischemia, CCF, hypotensive)

Do both our patients fit the bill?

Ottawa Aggressive Protocol suggests

Exclusion criteria

- permanent AF (chronic, persistent or long standing)
- symptoms > 48hrs or unknown duration (unless therapeutically anticoagulated with warfarin for 3 weeks)
- another primary diagnosis necessitating admission (eg cardiac ischemia, CCF, hypotensive)

Pharmacological

Attempted first

Procainamide IV 1g in 250mL dextrose and water over 1Hr

(stopped if BP falls below 100mmHg; continued if 250mL bolus normal saline corrects)

Electrical

If chemical fails

Procedural sedation + analgesia (propofol IV + fentanyl IV)

150-200J biphasic synchronised

Ottawa Aggressive Protocol suggests

Exclusion criteria

- permanent AF (chronic, persistent or long standing)
- symptoms > 48hrs or unknown duration (unless therapeutically anticoagulated with warfarin for 3 weeks)
- another primary diagnosis necessitating admission (eg cardiac ischemia, CCF, hypotensive)

Pharmacological

Attempted first

Procainamide IV 1g in 250mL dextrose and water over 1Hr

(stopped if BP falls below 100mmHg; continued if 250mL bolus normal saline corrects)

Electrical

If chemical fails

Procedural sedation + analgesia (propofol IV + fentanyl IV)

150-200J biphasic synchronised

Home 1 hr after cardioversion

No antiarrhythmic prophylaxis or anticoagulation given

If CHADS score $\geq$ 1 consider warfarin and early follow-up

Cardiology follow-up 1st episode or multiple episodes

Ottawa Aggressive Protocol suggests

Exclusion criteria

- permanent AF (chronic, persistent or long standing)
- symptoms > 48hrs or unknown duration (unless therapeutically anticoagulated with warfarin for 3 weeks)
- another primary diagnosis necessitating admission (eg cardiac ischemia, CCF, hypotensive)

Pharmacological

Attempted first

Procainamide IV 1g in 250mL dextrose and water over 1Hr

(stopped if BP falls below 100mmHg; continued if 250mL bolus normal saline corrects)

Electrical

If chemical fails

Procedural sedation + analgesia (propofol IV + fentanyl IV)

150-200J biphasic synchronised

Consider TOE if onset unclear

What % of people have asymptomatic episodes?

GISSI - AF study found

Disertori M et al (2011) Clinical characteristics of patients with asymptomatic recurrences of atrial fibrillation in the Gruppo Italiano per lo Studio della Sopravvivenza nell'Infarto Miocardico-Atrial Fibrillation (GISSI-AF) trial. American heart journal. 162:2 (382-9)

http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/438/CN-00798438/frame.html

Atrial fibrillation (AF) is a common arrhythmia that frequently recurs after restoration of sinus rhythm. In a consistent percentage of cases, AF recurrences are asymptomatic, thus making its clinical management difficult in relation to both therapeutic efficacy and thromboembolic risk.

The GISSI-AF trial enrolled 1,442 patients in sinus rhythm with previous AF episodes and followed for 12 months.

Asymptomatic AF recurrences were present in 49.5% of patients.

Association of the Ottawa Aggressive Protocol

- 628 patients with AF
- 376 converted with procainamide
- 243 electrically cardioverted (223 successful)
- 29 no cardioversion attempted
- No significant adverse events (stroke/death)
- Aggressive Protocol significantly reduced hospital admissions and time in ED care

Outcomes of Rhythm Control

Cochrane review:
Pharmacological cardioversion versus rate control(AFFIRM, PIAF)

- No difference in mortality between rhythm control and rate control
- Higher rates of hospitilisation and adverse events in rhythm control
- No difference in QOL between treatment groups

Electrical cardioversion versus rate control (Hot Cafe; RACE; STAF; J-RHYTHM)

- Rhythm control lead to a non-significant increase in stroke risk (OR 1.9, 95% CI 0.99 to 3.64)
- Quality of life (physical functioning, physical role function and vitality) significantly better in the rhythm control group

Use of antiarrhythmics after cardioversion

One year after DC cardioversion ~ 25% will still be in sinus rhythm

- Increases to 50-75% at one year with antiarrhythmics
- Class 1A (disopyramide, quinidine), 1C (flecainide, propafenone) and III (amiodarone, sotalol) drugs and beta blockers significantly reduce AF recurrence - NNT 3-16

- Increased adverse events - pro-arrhythmia for most drugs except amiodarone
- Disopyramid, quinidine and sotalol may increase mortality

http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD005049.pub3/abstract

Rate Control

Why Control the Rate?

A high rate in AF can reduce cardiac output by up to 30% via:

- Reduced atrial refractory period and filling
- AV asynchrony
- Reduced ventricular filling

Reducing the heart rate should theoretically allow a more effective atrial refractory period, ventricular filling and therefore increase cardiac output.

Efficacy of Rate Control Agents

The AFFIRM Trial

- Maintenance of rate control (<80bpm) during rest and exercise:
  - Beta blockers: 59%
  - Ca channel blockers: 38%
  - Digoxin: 58%
  - Beta blocker plus digoxin: 75%

- Lower mortality than rhythm control: 23.8% v 21.3%

  HR 1.15, 95% CI 0.99-1.34

- Lower rate of drug side effects than with rhythm control

Efficacy of Rate Control Agents

The RACE Study (2002)

- Rate control of <80bpm v >80bpm: no difference in quality of life, cardiovascular mortality, thromboembolic complications, pacemaker implantation or serious drug side effects. (Follow-up 2 yrs)

- 5% of rate controlled patients underwent spontaneous cardioversion

- 5% of rate controlled patients required active cardioversion for intolerable symptoms.

Rate Control in the Acute Setting

Beta Blockers

- Often considered as first line therapy for symptom reduction
- There is little evidence for it's efficacy

Safety and Efficacy Trial of Diltiazem (1995)

- 20mg IV bolus: 94% immediate HR control
- 10h continuous infusion at 15mg/h:
  - 74% maintained response
  - 8% conversion to sinus rhythm
  - 13% became hypotensive, 3.6% symptomatic
- 10h continuous infusion at 5mg/h:
  - 47% maintained response

Rate Control in the Acute Setting

Digoxin

Rate control with digoxin takes on average 10hr

AFFIRM Trial substudy- elevated mortality risk with Digoxin

- Increased overall mortality with use:
  - Without low EF or CHF: HR 1.45, 95% CI 1.17-1.8
  - With low EF or CHF: HR 1.42. 95% 1.11-1.82

- Increased cardiovascular mortality with use:
  - Without low EF or CHF: HR 1.36, 95% CI 0.98-1.91
  - With low EF or CHF: HR1.49, 95% CI 1.08-2.06

Which Rate Control Agent?

We don't know!

- Comorbidities
- Contraindications
- Drug Interactions
- Side Effects

Beta Blockers

Relative Contraindications

- Asthma
- COPD
- CHF

Drug Interactions

Amiodarone	incr serum conc	bradycardia	incr SEs
Cimetidine	incr serum conc	bradycardia	incr SEs
Paroxetine	incr serum conc	bradycardia	incr SEs
Rifampicin	decr serum conc	decr therapeutic effects	

Side Effects

- Common: Hypotension, bradycardia, fatigue, dizziness, nausea, cold extremities, heart failure, heart block
- Uncommon: Rash, impotence, urinary retention, liver function abnormalities

Calcium Channel Blockers

Relative Contraindications

- CHF
- Myasthenia-type neuromuscular disease
- Hepatic impairment- lower dose
- Elderly- lower starting dose

Drug Interactions

- Carbemazepine, Statins, Colchicine, Midazolam, Phenytoin

Side Effects

- Common: Dizziness, headaches, nausea, swelling of hands and feet
- Uncommon: Rash, paresthesia, pulmonary oedema, SJS, hepatitis, gingival hyperplasia

Digoxin

Relative Contraindications

- Renal Failure (70% renal clearance)
- Hyper/Hypothyroidism
- Hypokalaemia, hypomagnesaemia, acidosis, hypoxia
- Acute MI, WPW, HOCM

Drug Interactions

- Amiodarone, Macrolides, Rifampicin, Spironolactone, Ca Channel blockers

Side Effects

- Common: Anorexia, n/v/d 3%, visual disturbance, dizziness 5%, drowsiness, nightmares, headaches 3%
- Uncommon: Psychosis, delirium, VF, VT, gynaecomastia

Digoxin has less negative inotropic effects and is more likely to be considered in CHF.

Antithrombotic therapy in AF

- Embolic stroke main risk following AF

- Anticoagulation or antiplatelet therapy effective in reducing the incidence of stroke following AF
  - Vitamin K antagonists: RRR 62 %, 95% CI: 48-72%
  - Aspirin: RRR 22%, 95% CI:3-38%
  - Clopidogrel plus aspirin: RRR 40%; 95% CI 18–56%

- Risk of bleeding with antithrombotic therapy
  - Risk of stroke vs risk of major bleed
  - Stroke risk assessment: CHADS2 / CHA2D S2VASc
  - Major bleed risk assessment: HAS-BLED

CHADS2 -> CHA2DS2VASc

http://www.mdcalc.com/cha2ds2-vasc-score-for-atrial-fibrillation-stroke-risk/

CHADS2 Risk	Score
CHF	1
Hypertension	1
Age > 75	1
Diabetes	1
Stroke or TIA	2

From ESC AF Guidelines
http://www.escardio.org/guidelines-surveys/esc-guidelines/GuidelinesDocuments/guidelines-afib-FT.pdf

CHA2DS2- VASc Risk	Score
CHF or LVEF ≤ 40%	1
Hypertension	1
Age ≥ 75	**2**
Diabetes	1
Stroke/ TIA/ Thromboembolism	2
Vascular Disease	**1**
Age 65-74	**1**
Female	**1**

CHADS2 -> CHA2DS2VASc

CHADS 2 score	Patients (*n* = 1733)	Adjusted stroke rate %/year
0	120	1.9
1	463	2.8
2	523	4.0
3	337	5.9
4	220	8.5
5	65	12.5
6	5	18.2

From ESC AF Guidelines: http://www.escardio.org/guidelines-surveys/esc-guidelines/GuidelinesDocuments/guidelines-afib-FT.pdf

CHA2D- VASc score	Patients (n= 7329)	Adjusted Stroke Rate (%/year)
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 using CHA2DS2VASc

Risk category	CHA2DS2-VASc score	Risk of embolic stroke in one year	Recommended antithrombotic therapy
One ‘major’ risk factor or >2 ‘clinically relevant non-major’ risk factors	≥2	≥2.2%	OAC
One ‘clinically relevant non-major’ risk factor	1	1.3%	Either OAC or aspirin 75–325 mg daily. Preferred: OAC rather than aspirin.
No risk factors	0	0%	Either aspirin 75–325 mg daily or no antithrombotic therapy. Preferred: no antithrombotic therapy rather than aspirin.

HASBLED- Risk of major bleed in one year

http://www.mdcalc.com/has-bled-score-for-major-bleeding-risk/

Letter	Clinical Characteristic	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	1
D	Drugs or alcohol (1 point each)	1 or 2

HASBLED Score	Risk of major bleed in 1 year
0	0.9%
1	3.4%
2	4.1%
3	5.8%
4	8.9%
5	9.1%
>5	Unknown

Bleeding rates only exceed thrombotic events at an HAS BLED score >3

Caution and regular review needed in patients with HAS BLED ≥ 3

Risk vs benefit to be weighed with risk of embolic stroke- CHA2D- VASc score

Antithrombotic therapy in AF

- Heparin
  - Activates antihrombin III
  - 5000- 10000 IU IV bolus for immediate effect at initial presentation
  - Can use LMWH in non acute setting subcut
- Aspirin
  - Anti-platelet via inhibition of thromboxane
  - Used following full risk assessment
  - 75-300mg daily in low risk patients, moderate risk patients depending on patient preference
- Warfarin
  - Vitamin K antagonist
  - Moderate and high risk patients
  - Effective in reducing risk of embolic stroke
  - Needs regular monitoring
  - Significant side effects and contraindications
- Dabigatran
  - Direct thrombin inhibitor
  - Reduced rates of life threatening bleeding, intracranial bleeding, major and minor bleeds cf. wafarin (Connelly SJ et al. Dabigatran versus Warfarin in Patients with Atrial Fibrillation, NEJM 2009)
  - Monitoring and antidote note yet available

Warfarin

- Vitamin K antagonist
- RRR 62 %, 95% CI: 48-72%
- Living on Warfarin
  - Need for regular blood tests
  - Interactions with many medications
  - Not able to easily change diet (particularly foods high in vitamin K, dark green leafy vegetables)
  - Limited alcohol consumption - 1-2 standard drinks
  - Not able to play contact sport
  - C/I in pregnancy

Warfarin vs. Dabigatran

The RE-LY Trial

- Dabigatran 150mg bd reduces risk of haemorrhagic stroke, thromboembolic stroke and systemic emboli following AF by 34% more than warfarin (1.11% v 1.71%), RR 0.65, 95% CI 0.52-0.81

- 110mg bd has similar outcome to warfarin but reduces yearly bleeding risk by 20% (3.57% v 2.87%), P=0.003 for superiority

- Risk of MI possibly higher with Dabigatran: 0.82% v 0.64%, RR 1.29, 95% CI 0.94-1.75

Benefits

- **Less risk of bleeding**
- **Dosing options 110mg, 150mg**
- **Regular monitoring not required**

Disadvantages

- **Possible increase risk of ACS**
- **Not reversible**
- **Acute monitoring not available**

65yo M
MHx: Hypertension (Ramipril 5mg)
Benign Prostatic Hyperplasia
BCCs face

27yo M
Mine FIFO worker
Looks fit, works out & plays contact rugby
Drinks 20-30 std drink/weekend
Occasional speed use

Tuesday Morning
Both pts present to ED with AF @ 160bpm
with 36hr Hx of palps + lightheadedness
2 Echos available

LVEF 45%
No valve pathology

LVEF 59%
No valve pathology

Your Thoughts ???

There are vast gaps in evidence for AF management:

ESC Essential Messages: Adapted from the ESC Guidelines for the Management of Atrial Fibrillation (2010 Version) (European Heart Journal 2010;31:2369-2429;doi:10.1093/eurheartj/ehq278)

1. Epidemiology and mechanisms

- Biomarkers for prediction of thromboembolic risk.
- Differences in aetiology in other (non-western) world regions. Characterization of the population with "silent", undiagnosed AF.

2. Diagnosis and general management

- It is likely that systematic ECG screening for AF would result in earlier diagnosis of silent AF and may help to prevent AF-related complications. This would require formal validation of screening methods in different populations.
- The diagnostic value of any monitoring strategy for AF detection is not clear.
- So far, there is no signal that progression of AF can be stopped by rhythm control interventions. The benefit of a comprehensive, multimodal therapy of AF awaits formal testing.
- The diagnostic accuracy especially the specificity of implantable loop recorders for AF detection is not known.

3. Anticoagulation

- The full role of new oral anticoagulants in AF is not established.
- While trial data suggest that the newer anticoagulants may be safer and/or more effective in preventing strokes in AF, there is so far no experience in clinical practice outside controlled trials.
- It is uncertain whether the complete absence of any AF in patients post-ablation or post-cardioversion, represents a 'low risk' state for thromboembolism, allowing cessation of oral anticoagulation therapy. Emerging data suggest that late AF recurrence may occur even in these patients.
- It is uncertain if the new oral anticoagulants have adequate safety and efficacy for thrombo-prophylaxis in AF patients undergoing cardioversion, or in those with prosthetic heart valves, etc.
- It is not known how combination therapy of newer anticoagulants with antiplatelet drugs (e.g. after stenting) compares with combination therapy with VKAs.

4. Conversion

- The role of antiarrhythmic agents to enhance the success of DCC remains unclear.
- It is uncertain if new atrial selective antiarrhythmic drugs will offer better outcomes compared to sodium channel blockers.

5. Rate and rhythm control

- There is a lack of trials using hard clinical endpoints and newer rhythm control interventions in patients with AF.
- The impact of rate control by AV node ablation on prognosis in symptomatic AF patients is unknown.
- There are no trials on the effects of antiarrhythmic drug therapy in patients with permanent AF.

6. LA ablation therapy

- The long term success of LA ablation for prevention of AF recurrence is not yet documented.
- The long-term effect of LA ablation on mortality and hospitalizations is not yet known.

7. Upstream therapy

- It remains unclear if upstream therapy per se (alone) is useful for secondary prevention of AF. Apart from patients with heart failre or left ventricular hypertrophy, the patient groups who will benefit from upstream therapy are not well defined at present.
- The interaction of antiarrhythmic drugs with therapeutic agents used for upstream therapy remains to be elucidated.

http://www.escardio.org/guidelines-surveys/esc-guidelines/GuidelinesDocuments/Essential_Messages_Afib.pdf