ATRIAL FIBRILLATION
CONSIDERATIONS AND MANAGEMENT
REVIEW OF RECENT UPDATES IN THE GUIDELINES

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Disclosures

• No financial disclosures
Case

- 82 yo F with prior stroke and diabetes mellitus type 2
- Multiple readmissions for permanent uncontrolled atrial fibrillation, resulting in heart failure.
- She has hypertension, chronic kidney disease, creatinine clearance 15 ml/min
- She undergoes pacemaker implantation and AV node ablation
- She is on warfarin – her CHA2DS2-VASc score is 8
Which is the correct therapy?

• She can be discharged with pacemaker lower rate 60
• Dabigatran 75 mg twice daily can substitute for warfarin
• ASA and clopidogrel can be substituted for warfarin
• Continue oral anticoagulation, lifelong with warfarin (INR 2.0-3.0)
• Left atrial appendage closure device should be implanted
• The CASE represent all the management issues we are going to talk about
• Atrial fibrillation – has a new terminology
• Anticoagulation issues – new recommendations in 2019 (AHA, ACC, ESC)
• Rhythm and rate control – who needs what and how to achieve it
• New procedures, new devices are available and will review the recommendations
• At the end we will solve our CASE!
What should be the goals to manage our patients?

• Quality of life – I would put this on the top – would include symptom management, avoidance of hospitalizations, choice of medications

• Prevention and reduction of the risk of thromboembolic events, including but not restricted to stroke prevention

• Preservation of left ventricular function

• Diagnosis and treatment of underlying, possible even causative cardiac and non cardiac risk factors for AF

• Education about preventable causes
In the US, how prevalent is Atrial fibrillation in individuals that are 60+ years old?

<table>
<thead>
<tr>
<th>Option</th>
<th>Probability</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 in 10</td>
<td></td>
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<tr>
<td>1 in 25</td>
<td></td>
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<tr>
<td>1 in 50</td>
<td></td>
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<tr>
<td>1 in 75</td>
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</tbody>
</table>
Why are we talking about Atrial fibrillation?

- Age is a major risk factor and prevalence of AF increases as we grow older
  - Age 60+ ➔ 1 in 25 in the US has AF
  - Age 80+ ➔ 1 in 10
- Most common sustained arrhythmia
- Significant morbidity and also mortality (1.2-2X)
- Important cause of stroke – especially in the elderly 20 % attributed
- One of the etiology of heart failure – tachycardia induced cardiomyopathy
Classification of Atrial Fibrillation

• Nonvalvular AF ➔ absence of rheumatic mitral stenosis and mechanical valve, bioprosthetic valve, mitral valve repair 2014 (AHA definition)

• The debate continues as more and more studies address the issue of anticoagulation with different valvular diseases

• 2019 Update of the ACC recommended not to use “nonvalvular AF”

• Exclusion criteria now defined as moderate to severe mitral stenosis and or mechanical valve in the use of DOAC* and CHA2DS2-VASCs

• NEED to speak the same “language” ➔ “lone AF” and “chronic AF” also to be avoided.

*Direct Oral Anticoagulants
AF first detected

Paroxysmal
Terminates within 7 days

Persistent
Continuous and sustained >7 days

Permanent
Long term decision for rate control

Long standing
Persistent > 1 yr
Classification of AF

• European Society of Cardiology

• Defined **clinical AF** ➔ symptomatic or asymptomatic AF documented on EKG

• Subclinical AF ➔ no symptoms, AF detected on pacemaker or ICD - but no surface EKG detected it. Recommendations for anticoagulation is not clear

• Recommendation made for screening with EKG

• Age >65 and Hypertension

• Or age >75
Prevention of Thromboembolism

- Left atrial thrombus formation – mainly in the left atrial appendage (LAA) is the main site for thrombus formation, low flow, stasis due to lack of contraction of the atrial wall
- Embolization to the brain, but also intestines, leg, even coronary arteries (myocardial infarction)
- We think after the new onset atrial fibrillation, it will take about 48 hours to have thrombus formation – not an exact science
- Our guidelines takes into consideration and the recommendations based on this
CHA2DS2-VASc score

Evaluates ischemic stroke risk in patients with atrial fibrillation

Developed prospectively, included patients from multiple countries

Patients were 18 and older. Both ambulatory and hospitalized

Followed for 12 months

CHADS2 – score is out – not enough to assess risk for thromboembolic events

Based on retrospective Medicare registry

Score 9 has a stroke risk of 15.2% /year
<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Congestive heart failure/LV dysfunction</td>
<td>1</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1</td>
</tr>
<tr>
<td>Age &gt;75 years</td>
<td>2</td>
</tr>
<tr>
<td>Diabetes</td>
<td>1</td>
</tr>
<tr>
<td>Stroke or transient ischemic attack</td>
<td>2</td>
</tr>
<tr>
<td>Vascular disease</td>
<td>1</td>
</tr>
<tr>
<td>Age 65–74 years</td>
<td>1</td>
</tr>
<tr>
<td>Sex group (female)</td>
<td>1</td>
</tr>
<tr>
<td><strong>Maximum points</strong></td>
<td><strong>9</strong></td>
</tr>
</tbody>
</table>
HAS-BLED score

- Not recommended to withhold anticoagulation even if it is elevated
- More monitoring for score >3
- Not a good predictor for hemorrhagic stroke

Table 2. The HAS-BLED score: The clinical characteristics contributing to the risk of bleeding

<table>
<thead>
<tr>
<th>Letter</th>
<th>Clinical characteristic</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>H</td>
<td>Hypertension</td>
<td>1</td>
</tr>
<tr>
<td>A</td>
<td>Abnormal renal and/or liver function</td>
<td>1 or 2*</td>
</tr>
<tr>
<td>S</td>
<td>Stroke</td>
<td>1</td>
</tr>
<tr>
<td>B</td>
<td>Bleeding</td>
<td>1</td>
</tr>
<tr>
<td>L</td>
<td>Labile INRs</td>
<td>1</td>
</tr>
<tr>
<td>E</td>
<td>Elderly (age &gt;65 years)</td>
<td>1</td>
</tr>
<tr>
<td>D</td>
<td>Drugs and/or alcohol</td>
<td>1 or 2*</td>
</tr>
</tbody>
</table>

Max. score: 9

INRs = international normalised ratios.
*1 point each.
NOACs (DOACs)

- Therapeutic safety compared to warfarin – in AF
- Non inferior preventing stroke and embolism
- Decreased intracranial bleeding (Apixaban especially)
- Head-to-head comparison of the different NOACs need careful assessment – need to be prospective
- Patient adherence is an issue – but now drug levels are available
Direct Oral Anticoagulants (DOAC)

**Direct thrombin inhibitor**
- Dabigatran (Pradaxa)
- Approved 10 yrs ago
- Twice daily dosing
- Parenteral form available (argatroban, bivalirudin)

**Direct factor Xa inhibitors**
- No parenteral form
- Rivaroxiban (Xarelto)
- Apixaban (Eliquis) - twice daily
- Edoxaban (Savaysa)
- Betrixaban (Bevyxxa) not in the US yet
• All 4 NOACs dosing defined by renal function
• Apixaban - also adds age >80 and weight <60 kg as dosing consideration
• Edoxaban not approved for either low creatine clearance or very high
• Severe hepatic dysfunction also a contraindication
• Monitoring both recommended periodically
• End stage CKD on dialysis a special population

• Increased prevalence of stroke and also increased bleeding risk

• Apixaban dosing examined recently and compared to warfarin.

• 5 mg standard dosing resulted the best clinical outcome (lower death and bleeding)

• Edoxaban 50% renally excreted – not recommended
• Different recommendations for women /men

• Sex without other risk factors – not an increased risk

• Recent data suggest if patient has 1 non-sex related risk factor, warfarin has small positive effect
• Based on trials like RE-ALIGN – dabigatran compared to warfarin in patients after mechanical heart valve placement dabigatran not recommended, neither any of the DOACs

• The study was discontinued early due to unacceptable thromboembolic and bleeding risk in the dabigatran group
New Reversal Drugs

• Idarucizumab — Dabigatran reversal

• Andexanet alfa — Rivaroxibban and Apixaban
Rhythm or rate control?

- No difference in survival or rate of embolism
- No difference in need for anticoagulation
- Again back to quality of life! → main goal is decreasing the frequency and duration of episodes – and decreasing the need for ED/hospital care
Rhythm control

• 2019 meta-analysis included 59 trials
• All of the known anti-arrhythmics lowered the AF recurrence rate
• Metoprolol also did
• Sotalol increased all-cause mortality compared with controls
• All drugs except propafenone increased pro-arrhythmia
• Amiodarone also not pro-arrhythmia, but has multiple side effects and toxicities
• Overall anti-arrhythmics can reduce recurrence of AF – with a price
Rhythm Control with Amiodarone

- The most effective medication maintaining sinus rhythm in 1 yr
- Trials – Canadian Trial of AF (CTAF), AFFIRM, SAFE-T
  - These studies compared amiodarone to placebo, sotalol and other antiarrhythmics
- Less effective with AF >1 yr duration and large LA
- Effective post cardiac surgery also
- Recommended regular monitoring of PFTs, TSH, Chest X-ray
- Known interactions with warfarin, digoxin – dose adjustment recommended
• Symptoms – usually related to higher HR
• Tachycardia “bad” – results in cardiomyopathy
• AV node has a major role – AV nodal blocking medications work well
• Recent trial RACE II compared lenient or strict control of permanent atrial fibrillation patients
• Lenient control, resting HR<110/min
• Strict rate control resting HR<80, exercise HR<110 /min
• There were no differences in outcome, the lenient control was non-inferior
• Again! Quality of life!
• Lenient rate control resulted in less medications, less outpatient visits
• These patient had permanent AF and minimal symptoms
• Average HR is the most valuable – it was 85/min in the lenient group
Rate-controlling Medications

• Large number (54) trial, but difficult to compare
• All of the known rate-controlling calcium channel blockers, beta blockers were successful to control HR
• Digoxin in combination with beta blockers and calcium channel blockers reduced HR at rest and stress

• Conclusions:
  • Pharmacologic therapy is effective, especially combination therapy
  • Amiodarone should only be used as a second line therapy for rate control
AV Node Ablation

• Produces complete heart block – pacemaker dependent
• The best candidates are older patients, previous pacemaker, permanent AF, marked LA dilation
• Post-ablation VF avoided by setting the HR > 90 immediately post ablation. It is decreases sympathetic activity.
• When the rate was set <70 ventricular fibrillation occurred post ablation
• Long term anticoagulation still required
AF-Catheter Ablation

- PVI (pulmonary vein isolation) – "freeze" it or "fry" it (Radio frequency, cryothermal, laser)
- Episodes of AF originates from electrical discharges from the pulmonary veins – isolating the PV – will not be able to activate atrial tissue
- Quality of life – main reason to do it to decrease symptoms – better than medical therapy
- Possible as first line therapy, not required "failed medical therapy"
- Based on recent data HFrEF (heart failure with reduced ejection fraction patient benefit from ablation( decreased mortality and hospitalizations) (NEJM 2018;378(5):417)
Success Rate of PVI

• Definition of “success” is difficult – depends on different factors

• Paroxysmal AF 70-80% - freedom from recurrent AF/AT for 1 year

• Persistent AF in 60-70%

• First 3 months anticoagulation is continued – also antiarrhythmic medications and might need cardioversion – “healing time”
Complications of PVI

• Pericardial effusion – tamponade
• Atrial-esophageal fistula
• Pulmonary vein stenosis
“Timing is everything”

Recently debated the previously practiced (but supported with very limited data) of cardioversion of AF <48 hours of duration without anticoagulation

- Risk of thromboembolic events increases significantly after cardioversion >12 hours of AF, mainly in pts >75 yo and in women
- <60 yo with low score and postop patients are lower risk
- Use of transesophageal echocardiography (TEE) to assess LA thrombus became a standard practice for recent but unknown time of onset AF, especially with symptomatic, hard to rate control scenarios
Coronary Artery Disease and AF

• Patients requiring stent placement – Clopidogrel preferred with ASA+ oral anticoagulant – “triple therapy”
• 4-6 weeks transition to Clopidogrel and oral anticoagulant (stop ASA)
• Warfarin and Clopidogrel – is an option to reduce bleeding – even immediately
• Clopidogrel and low dose 15 mg Rivaroxaban considered to be reasonable option
• Clopidogrel and Dabigatran 150 mg twice daily
• The bottom line ➔ “triple therapy” is very high risk for bleeding complications especially in the elderly
Cryptogenic Stroke

• Definition: stroke or transient ischemia without any definitive cause
• 1 in 4 ischemic strokes are cryptogenic
• Despite the unknown cause it has a better prognosis
• AF can be a source and recommendation made for long-term monitoring 30 days at least and loop recorder implantation is reasonable for these patients
• Present recommendations emphasize use of antithrombotic medications during the investigation and recommends anticoagulation only if atrial fibrillation is detected
Left Atrial Closure Devices

• LAA is a major source of thrombus formation and embolization

• If we mechanically prevent embolization of the LAA thrombi – can it replace anticoagulation?

• We have today two different ways of achieving it
  • Surgical (if patient requires surgery for other reasons, like mitral valve surgeries)
  • Percutaneous closure device

• Patients who are high risk of bleeding, falling, combined therapies are good candidates

• Most commonly used is the WATCHMAN device

• 2 large trials PROTECT-AF and PREVAIL
Different LAA closure devices
How can individuals prevent or control Atrial Fibrillation?
Prevention of Atrial Fibrillation

• New data demonstrated that in overweight and obese patients, weight loss combined with risk factor modifications can control atrial fibrillation.

• Obesity results in electro-structural remodeling of the atria

• Other risk factor modifications included treatment of sleep apnea, HTN, hyperlipidemia, glucose intolerance, and alcohol and tobacco use

• Also shown improved outcomes of AF ablation in those patients who also enrolled in weight loss program
Which is the correct therapy in our patient?

She can be discharged with pacemaker lower rate 60

Dabigatran 75 mg twice daily can substitute warfarin

ASA and clopidogrel can be substituted for warfarin

Continue oral anticoagulation, lifelong with warfarin (INR 2.0-3.0)

Left atrial appendage closure device should be implanted

A
B
C
D ✓ 0%
E ✓ 0%
Which is the correct therapy in our patient?

• She can be discharged with pacemaker lower rate 60------**NO**
• Dabigatran75 mg twice daily can substitute warfarin----**NO**
• ASA and clopidogrel can be substituted for warfarin----**NO**
• Continue oral anticoagulation, lifelong with warfarin
  (INR 2.0-3.0)---**YES**
• Left atrial appendage closure device should be implanted ---**MAYBE**