RECENT ADVANCES IN ATRIAL FIBRILLATION

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UTHSC
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MEMORIAL HERMANN TEXAS MEDICAL CENTER
TOTAL HOSPITALIZATION DAYS BASED ON PRESENTING ARRHYTHMIA

<table>
<thead>
<tr>
<th>Presenting Arrhythmia</th>
<th>AF</th>
<th>Atrial Flutter</th>
<th>Cardiac arrest</th>
<th>Conduction disease</th>
<th>Junctional</th>
<th>Premature beats</th>
<th>Sick sinus syndrome</th>
<th>VF</th>
<th>VT</th>
<th>Unspecified</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>900</td>
<td>800</td>
<td>700</td>
<td>600</td>
<td>500</td>
<td>400</td>
<td>300</td>
<td>200</td>
<td>100</td>
<td>0</td>
</tr>
</tbody>
</table>
Dr. Oz answers a question on atrial fibrillation and other questions from the audience.
EPIDEMIOLOGY OF ATRIAL FIBRILLATION

Most common arrhythmia in Clinical Practice

> 5 million patients worldwide
  • 400,000 new cases diagnosed annually
  • 2.5 Million estimated patients in the United States

Major cause of stroke
  • 200,000 annually worldwide/80,000 in the U.S.
  • 25-30% of all strokes in the U.S.

U.S. cost to treat = $3.6 billion annually
  • Drug therapy + hospital admissions
ATRIAL FIBRILLATION: CARDIAC CAUSES

- Hypertensive heart disease
- Ischemic heart disease
- Valvular heart disease
  - Rheumatic: mitral stenosis
  - Non-rheumatic: aortic stenosis, mitral regurgitation
- Pericarditis
- Cardiac tumors: atrial myxoma
- Sick sinus syndrome
- Cardiomyopathy
  - Hypertrophic
  - Idiopathic dilated (cause vs. effect)
- Post-coronary bypass surgery
ATRIAL FIBRILLATION: NON-CARDIAC CAUSES

Pulmonary
- COPD
- Pneumonia
- Pulmonary embolism
- Sleep Apnea

Metabolic
- Thyroid disease: hyperthyroidism
- Pheochromocytoma
- Electrolyte disorders

Toxic: alcohol (‘holiday heart’ syndrome)
Why Do we need to Treat AF?

**STROKE**

**TACHYCARDIA**
- palpitations, cardiomyopathy, CHF

**Thromboembolism Prevention**

**Ventricular Rate Control**

**Rhythm Control**

**LOSS OF ATRIAL KICK**
- Dyspnea, fatigue, CHF

MANAGEMENT STRATEGIES

1. Anticoagulation strategies
2. Antiarrhythmic drugs
3. Ablation strategies
### CHADS₂ Score⁹,¹⁰

<table>
<thead>
<tr>
<th>Letter</th>
<th>Condition</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>C</td>
<td>Congestive Heart Failure</td>
<td>1 point</td>
</tr>
<tr>
<td>H</td>
<td>Hypertension</td>
<td>1 point</td>
</tr>
<tr>
<td>A</td>
<td>Age ≥ 75 y</td>
<td>1 point</td>
</tr>
<tr>
<td>D</td>
<td>Diabetes</td>
<td>1 point</td>
</tr>
<tr>
<td>S₂</td>
<td>Stroke</td>
<td>2 points</td>
</tr>
</tbody>
</table>

Maximum total score = 6 points.

American College of Cardiology/American Heart Association/Heart Rhythm Society 2006 Anticoagulation Recommendations: Score = 0 aspirin. Score = 1 aspirin or oral anticoagulation.

### CHA₂DS₂-VASc Score¹⁵,¹⁶

<table>
<thead>
<tr>
<th>Letter</th>
<th>Condition</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>C</td>
<td>Congestive Heart Failure</td>
<td>1 point</td>
</tr>
<tr>
<td>H</td>
<td>Hypertension</td>
<td>1 point</td>
</tr>
<tr>
<td>A₂</td>
<td>Age ≥ 75 y</td>
<td>2 points</td>
</tr>
<tr>
<td>D</td>
<td>Diabetes</td>
<td>1 point</td>
</tr>
<tr>
<td>S₂</td>
<td>Stroke</td>
<td>2 points</td>
</tr>
<tr>
<td>V</td>
<td>Vascular disease</td>
<td>1 point</td>
</tr>
<tr>
<td>A</td>
<td>Age ≥ 65 y</td>
<td>1 point</td>
</tr>
<tr>
<td>Sc</td>
<td>Sex category, female</td>
<td>1 point</td>
</tr>
</tbody>
</table>

Maximum total score = 9 points.

ESC 2010 Anticoagulation Recommendations: Score = 0 no therapy or aspirin (no therapy preferred). Score = 1 aspirin or oral anticoagulation (oral anticoagulation preferred). Score ≥ 2 oral anticoagulation.
MORE WOMEN ON AC

<table>
<thead>
<tr>
<th>Score</th>
<th>CHADS₂ (%/y)</th>
<th>CHA₂DS₂-VASc (%/y)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>1.9</td>
<td>0</td>
</tr>
<tr>
<td>1</td>
<td>2.8</td>
<td>1.3</td>
</tr>
<tr>
<td>2</td>
<td>4</td>
<td>2.2</td>
</tr>
<tr>
<td>3</td>
<td>5.9</td>
<td>3.2</td>
</tr>
<tr>
<td>4</td>
<td>8.5</td>
<td>4.0</td>
</tr>
<tr>
<td>5</td>
<td>12.5</td>
<td>6.7</td>
</tr>
<tr>
<td>6</td>
<td>18.2</td>
<td>9.8</td>
</tr>
<tr>
<td>7</td>
<td></td>
<td>9.6</td>
</tr>
<tr>
<td>8</td>
<td></td>
<td>6.7</td>
</tr>
<tr>
<td>9</td>
<td></td>
<td>15.2</td>
</tr>
</tbody>
</table>

CLINICAL SIGNIFICANCE

- The CHADS₂ score is commonly used for stroke risk stratification for atrial fibrillation, but it does not have great predictive value.
- The CHA₂DS₂-VASc schema has been validated and seems to have improved value.
- Adoption of the CHA₂DS₂-VASc schema may as much as double the number of patients recommended for oral anticoagulation.
- This change will be seen mostly in older women.
5791 Patients on warfarin

A large proportion of patients were outside the therapeutic range.
Approximately 50% loss of compliance at 3 years\(^1\)

Reasons: Dementia and inability to cope with the dose adjustments and monitoring required of warfarin\(^2\).

2. Khoo, Lip Initiation and persistence of warfarin or aspirin as thromboprophylaxis in chronic AF - J Thromb Haemost 2008; 6: 1622
NEWER ANTICOAGULANTS
## NEWER AC IN TRIALS

<table>
<thead>
<tr>
<th>Reference</th>
<th>Dabigatran dose</th>
<th>Comparator dose</th>
<th>Primary efficacy % (N=); [P value]</th>
<th>Primary safety % (N=); [P value]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atrial fibrillation</td>
<td>110 mg bid</td>
<td>Dabigatran, 150 mg—1.11%/y, (N=134/6076); P&lt;.001 for superiority</td>
<td>Dabigatran, 150 mg bid—3.11%/y, (N=375/6076); P=.31</td>
<td></td>
</tr>
<tr>
<td>N=18,113</td>
<td></td>
<td>Dabigatran, 110 mg—1.53%/y, (N=182/6015); P&lt;.001 for noninferiority</td>
<td>Dabigatran, 110 mg bid—2.71%/y, (N=322/6015); P=.003</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Reference</th>
<th>Rivaroxaban dose</th>
<th>Comparator dose</th>
<th>Primary efficacy % (N=); [P value]</th>
<th>Primary safety % (N=); [P value]</th>
</tr>
</thead>
<tbody>
<tr>
<td>ROCKET AF, 2011</td>
<td>20 mg qd</td>
<td>Warfarin</td>
<td>Composite VTE per year: Warfarin—2.4%/y, (N=306/7090)</td>
<td>All clinical bleeding events per year: Warfarin—14.5%/y, (N=1449/7125)</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>15 mg qd if CrCl ~30-49 mL/min/1.73 m²</td>
<td>Rivaroxaban—21%/y, (N=269/7081); P&lt;.001 for noninferiority</td>
<td>Rivaroxaban—14.9%/y, (N=1475/7111); P=.44</td>
<td></td>
</tr>
<tr>
<td>N=14,264</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Reference</th>
<th>Apixaban dose</th>
<th>Comparator dose</th>
<th>Primary efficacy % (N=); [P value]</th>
<th>Primary safety % (N=); [P value]</th>
</tr>
</thead>
<tbody>
<tr>
<td>AVERROES, 2011</td>
<td>5 mg bid</td>
<td>Aspirin (81-324 mg)</td>
<td>Composite VTE per year: Aspirin—3.7%/y, (N=113/2791)</td>
<td>Major bleeding per year: Aspirin—1.2%/y, (N=39/2791)</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td></td>
<td>Apixaban—1.6%/y, (N=51/2808); P&lt;.001 for superiority</td>
<td>Apixaban—1.4%/y, (N=44/2808); P=57</td>
<td></td>
</tr>
<tr>
<td>N=5599</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Reference</th>
<th>Apixaban dose</th>
<th>Comparator dose</th>
<th>Primary efficacy % (N=); [P value]</th>
<th>Primary safety % (N=); [P value]</th>
</tr>
</thead>
<tbody>
<tr>
<td>ARISTOTLE, 2011</td>
<td>5 mg bid</td>
<td>Warfarin</td>
<td>Composite VTE per year: Warfarin—1.60%/y, (N=265/9081)</td>
<td>Major bleeding per year: Warfarin—3.09%/y, (N=462/9052)</td>
</tr>
<tr>
<td>Postop TKA</td>
<td></td>
<td>Apixaban—1.27%/y, (N=212/9120); P=.01 for superiority</td>
<td>Apixaban—2.13%/y, (N=327/9088); P&lt;.001</td>
<td></td>
</tr>
</tbody>
</table>
ADVANCES IN ANTICOAGULANT THERAPY

Coumadin - greater use of home monitoring
  • Target INR in trials 55-64% of the time.

Dabigatran – PRADAXA 150/110/75 mg BID
  • RELY trial

Rivaroxaban – XARELTO 20/15/10 mg QD
  • ROCKET AF

Apixiban – ELIQUIS 5mg PO BID
  • ARISTOTLE

Edoxaban – LIXIANA 60/30 mg QD
  • ENGAGE AF-TIMI48

Betrixiban

- 10-12% mortality reduction
- 21% reduction in stroke/systemic embolism
- 31% reduction in major bleeding episodes

When compared with Warfarin

"The FDA hasn't approved these pills yet, but the CIA swears by them!"
# RX OF BLEEDING WITH NEWER AC

## Table 2: Possible measures to take in case of bleeding

<table>
<thead>
<tr>
<th>Non-life-threatening bleeding</th>
<th>Direct thrombin inhibitors (dabigatran)</th>
<th>FXa inhibitors (apixaban, edoxaban, rivaroxaban)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inquire last intake + dosing regimen</td>
<td>Inquire last intake + dosing regimen</td>
<td></td>
</tr>
<tr>
<td>Estimate normalization of haemostasis</td>
<td>Normalization of haemostasis: 12–24 h</td>
<td></td>
</tr>
<tr>
<td>Normal renal function: 12–24 h</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CrCl 50–80 mL/min: 24–36 h</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CrCl 30–50 mL/min: 36–48 h</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CrCl &lt;30 mL/min: ≥ 48 h</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maintain diuresis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Local haemostatic measures</td>
<td>Local haemostatic measures</td>
<td></td>
</tr>
<tr>
<td>Fluid replacement (colloids if needed)</td>
<td>Fluid replacement (colloids if needed)</td>
<td></td>
</tr>
<tr>
<td>RBC substitution if necessary</td>
<td>RBC substitution if necessary</td>
<td></td>
</tr>
<tr>
<td>Platelet substitution (in case of thrombocytopenia ≤ 60 x 10⁹/L or thrombopathy)</td>
<td>Platelet substitution (in case of thrombocytopenia ≤ 60 x 10⁹/L or thrombopathy)</td>
<td></td>
</tr>
<tr>
<td>Fresh frozen plasma as plasma expander (not as reversal agent)</td>
<td>Fresh frozen plasma as plasma expander (not as reversal agent)</td>
<td></td>
</tr>
<tr>
<td>Tranexamic acid can be considered as adjuvants</td>
<td>Tranexamic acid can be considered as adjuvants</td>
<td></td>
</tr>
<tr>
<td>Desmopressin can be considered in special cases (coagulopathy or thrombopathy)</td>
<td>Desmopressin can be considered in special cases (coagulopathy or thrombopathy)</td>
<td></td>
</tr>
<tr>
<td>Consider dialysis (preliminary evidence: −65% after 4h)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Charcoal haemoperfusion not recommended (no data)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Life-threatening bleeding</th>
<th>All of the above</th>
<th>All of the above</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prothrombin complex concentrate (PCC) 25 U/kg (may be repeated once or twice) (but no clinical evidence)</td>
<td>Prothrombin complex concentrate (PCC) 25 U/kg (may be repeated once or twice) (but no clinical evidence)</td>
<td></td>
</tr>
<tr>
<td>Activated PCC 50 IE/kg; max 200 IE/kg/day): no strong data about additional benefit over PCC. Can be considered before PCC if available</td>
<td>Activated PCC 50 IE/kg; max 200 IE/kg/day): no strong data about additional benefit over PCC. Can be considered before PCC if available.</td>
<td></td>
</tr>
<tr>
<td>Activated factor VII (rFVIIa; 90 µg/kg) no data about additional benefit + expensive (only animal evidence)</td>
<td>Activated factor VII (rFVIIa; 90 µg/kg) no data about additional benefit + expensive (only animal evidence)</td>
<td></td>
</tr>
</tbody>
</table>
TREATMENT STRATEGIES

RATE OR RHYTHM CONTROL......

its never that obvious
Sinus rhythm was associated with a 47% reduction in the risk of death whereas use of antiarrhythmic drug therapy was associated with a 49% increase in mortality. The toxicity of AADs counterbalances the benefits of SR.

RATE CONTROL - HOW SLOW DO YOU GO?

AFFIRM: HR <80bpm at rest and <110bpm with six minute hallway walk.

Digoxin (more for resting HR >100)

Beta blockade/Calcium channel blockade (more useful in ambulatory HR>120)
INTRACARDIAC ELECTROGRAMS: DURING RF ABLATION
Tachycardia Mediated Cardiomyopathy

Questions

1. Rate Control?

2. Pace and Ablate AVN?

3. Biventricular pace and ablate AVN?

4. Ablate the arrhythmia?
RATE CONTROL
BASELINE A FLUTTER TYPE 1 (2 TO 1 AV BLOCK)
Conversion of atrial flutter to NSR during RF ablation
RHYTHM CONTROL STRATEGIES

PILLS

ABLATION
AMIODARONE OR REFERRAL FOR ABLATION

Doctors may commit malpractice when prescribing Amiodarone as off-label treatment for atrial fibrillation

Many doctors routinely prescribe amiodarone for uses that the FDA has not approved — leading to disastrous outcomes for patients, and medical malpractice lawsuits against the doctors.

Because of the drug’s uniquely dangerous characteristics, amiodarone has been associated with severe side effects, especially when combined with simvastatin (Zocor). These side effects include muscle disease, lung diseases (interstitial lung disease and pulmonary fibrosis), thyroid disease, blindness, gastrointestinal disorders, and a skin disease called Toxic Epidermal Necrolysis (TEN). Amiodarone is often prescribed off-label, for uses that are not approved by the FDA.

Do I Have an Amiodarone Lawsuit? Colleen A. Clark is a true advocate.
WHO IS CANDIDATE FOR AF ABLATION?

Patients with symptomatic recurrent atrial fibrillation refractory to at least 1 antiarrhythmic medication

- No (or minimal) heart disease
  - Flecainide
  - Propafenone
  - Sotalol
  - Amiodarone
  - Dofetilide
  - Catheter ablation

- Hypertension
  - Substantial LVH
    - No
      - Flecainide
      - Propafenone
      - Sotalol
    - Yes
      - Amiodarone
  - Amiodarone
  - Dofetilide
  - Sotalol
  - Catheter ablation

- Coronary artery disease
  - Dofetilide
  - Sotalol
  - Amiodarone
  - Catheter ablation

- Heart failure
  - Amiodarone
  - Dofetilide
  - Catheter ablation

Natural History of AF
Dual Substrate Model

Paroxysmal
Self terminating AF episodes

Persistent
Sinus can be restored electrically or chemically

Permanent
Sinus cannot be maintained

AF begets more AF

Trigger initiation

Substrate maintenance
Atrial Fibrillation

Before Ablation

After Ablation

Impulses escape into the atrium

Impulses cannot pass the ablated tissue
CONTACT FORCE

- Irrigated Tip Electrode (7.5F, 3.5mm)
- Magnetic signal emitter
- 3 Magnetic signal sensors
- Force
- Spring coil
PV tachycardia
AFIB TERMINATION WITH ABLATION
Radiofrequency Ablation vs Antiarrhythmic Drugs as First-line Treatment of Symptomatic Atrial Fibrillation
A Randomized Trial

**Objective** To determine whether PVI is feasible as first-line therapy for treating patients with symptomatic AF.

**Design, Setting, and Participants** A multicenter prospective randomized study of 75 patients with symptomatic atrial fibrillation who were randomized to either PVI or antiarrhythmic drug therapy.

- **Better QoL**
- **Decreased Hospitalization (54% vs. 9%)**
RF CATHETER ABLATION IS SAFE AND EFFECTIVE IN OCTOGENARIANS

- Up to 10% of people over 80 have AF
- Up to 25% of strokes in this group are due to AF
- This study compared safety and efficacy of RF ablation in two groups; greater and less than 80 years
- Success rates and complications were similar between the two groups

“Your EKG showed atrial fibrillation, but we fixed it with ........ Photoshop”
STROKE PREVENTION WITH PERCUTANEOUS DEVICES
Clinical characteristics comprising the HAS-BLED bleeding risk score

<table>
<thead>
<tr>
<th>Letter</th>
<th>Clinical characteristic^a</th>
<th>Points awarded</th>
</tr>
</thead>
<tbody>
<tr>
<td>H</td>
<td>Hypertension</td>
<td>1</td>
</tr>
<tr>
<td>A</td>
<td>Abnormal renal and liver function (1 point each)</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 (e.g. age &gt;65 years)</td>
<td>1</td>
</tr>
<tr>
<td>D</td>
<td>Drugs or alcohol (1 point each)</td>
<td>1 or 2</td>
</tr>
</tbody>
</table>

Maximum 9 points
LEFT ATRIAL APPENDAGE: OCCLUDERS
LA APPENDAGE OCCLUDERS-THE LARIAT PROCEDURE

- Clinical Registry based approach.
- Need transseptal and epicardial access.
- Cannot use if adhesions from prior pericarditis or from heart surgery
- Does not need post procedure anticoagulation
POSITIONING THE TRANSSEPTAL SHEATH IN AP PROJECTION

Magnet “kissing”
LEFT ATRIAL APPENDAGE BY TEE PRIOR TO AND AFTER SUTURE DELIVERY
LA APPENDAGE OCCLUDERS
THE WATCHMAN DEVICE

The PROTECT AF (WATCHMAN Left Atrial Appendage System for Embolic PROTECTion in Patients with Atrial Fibrillation) trial.

- Need warfarin coverage until endothelialization of device occurs.
- Typically can stop warfarin in about 45 days.

Event rate 3/100 patient years in the Watchman Arm
Event rate 4.9/100 patient years in the Warfarin Arm

http://www.youtube.com/watch?v=ZFWMB42Y0KE

THE AMPLATZER DEVICE

- Currently part of research trial that we are enrolling in.
- Can be randomized to anticoagulation arm.
- Warfarin anticoagulation not necessary.
- Clopidogrel and aspirin for 1-3 months, followed by aspirin alone for ≥5 months for platelet inhibition.
TAKE HOME POINTS

[1] Stroke prevention with anticoagulation is KEY

[2] Newer options with blood thinners and percutaneous devices as an alternative to Coumadin

[3] Atrial Fibrillation is a curable arrhythmia in 75-80% of patients with ablation procedure if referred out relatively early in the disease process.
QUESTIONS ???

Sometimes I feel that I have the worst job in the world!

Ya... right!

MD

Please don’t waste the doctor’s time with questions