Stroke Prevention in Atrial Fibrillation

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St. Mary’s Electrophysiology
Stroke Prevention in Atrial Fibrillation

- Preventing first stroke
  - Known history of atrial fibrillation

- Preventing subsequent stroke
  - No prior history of atrial fibrillation
  - Diagnosing atrial fibrillation
Stroke Prevention in Atrial Fibrillation

- Preventing first stroke
  - Known history of atrial fibrillation

- Preventing subsequent stroke
  - No prior history of atrial fibrillation
  - Diagnosing atrial fibrillation
Ever Felt Like This?
Introduction

- Most common arrhythmia.
- > 5.1 million people

- Heart's 2 upper chambers (the atria) beat chaotically & irregularly, out of coordination with the 2 lower chambers (the ventricles).
  - Heart is not filled completely and pumping function is reduced
  - Blood stays in upper chambers that get dilated
  - Clot formation- can go to brain and cause stroke
What does afib cause?

- **Symptoms**
  - Palpitations
  - Shortness of breath
  - Fatigue/tiredness
  - Weakness
  - Chest pain

- **Stroke**
  - Increases mortality

- **Congestive heart failure**
  - Increases mortality
The incidence of AF is

- 670/100,000 white men
- 400/100,000 white women
- 390/100,000 African American men
- 300/100,000 African American women
AF: an age related condition

Go et al JAMA 2001;285:2370-2375
AF: a growing problem

Doubling of patients with AF from 1995 to 2030

Go et al JAMA 2001;285:2370-2375
Risk Factors

- Clinical:
  - Non-modifiable: Age, Sex, Ethnicity, Genetic
  - Modifiable:
    - Hypertension, Diabetes
    - Obesity, OSA
    - Coronary artery disease, Tobacco use
Obesity and AF Risk

Adjusted HR 1.5 with obesity, attributable to increased LA size

Wang et al, JAMA 2004; 292:2471
Causes of AF

- Anything that damages or stretches the atria:
  - Hypertension, Aging
  - Obstructive Sleep Apnea, Lung Disease
  - Ischemia, CHF, Myocarditis, Valvular Dz (MS, MR), CABG
  - Thyrotoxicosis, Ethanol (Holiday Heart)
  - Obesity BMI>30
  - Accessory Pathway
  - Genetics
Therapeutic Options
Treatment involves

1. Restoration of the normal heart rate
   - Medication +/- electrical shock

2. Slow the ventricular response with medications

3. Prevention of blood clots that may cause a stroke.

4. Look for reversible causes
Rate Control vs Rhythm Control

- Favor attempts to maintain SR:
  - First or infrequent episodes of persistent AF
  - Young active patient
  - Significant symptoms
  - Difficult to rate control
  - Contraindication to long term warfarin

- Favor rate control:
  - Asymptomatic sedentary elderly patient
  - Contraindication to anti-arrhythmics or ablation
Management

➤ Medical therapy
  - Rate control: AVN blockers
  - Rhythm control: Anti-arrhythmic drugs
  - CVA prevention:
    ▪ Warfarin
    ▪ New antithrombotics
    ▪ LAA occlusion vs resection.
      • PROTECT-AF (Watchman)

➤ Ablation
  - Catheter Ablation:
    ▪ AF ablation: Pulm Vein Isolation, Substrate modification
    ▪ AVN ablation and PPM implant
  - Surgical Ablation
Electrical Cardioversion
AV Node Ablation

Normal condition

Chaotic and irregular conduction

Atrial fibrillation

Image courtesy of Medtronic, Inc.
Who needs a blood thinner like coumadin? An afib patient with significant risk of stroke i.e. CHADS-VASC score of 2 or more

**CHA\textsubscript{2}DS\textsubscript{2}-VASc**

<table>
<thead>
<tr>
<th>Condition</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>C</td>
<td>Congestive heart failure (or Left ventricular systolic dysfunction)</td>
</tr>
<tr>
<td>H</td>
<td>Hypertension: blood pressure consistently above 140/90 mmHg (or treated hypertension on medication)</td>
</tr>
<tr>
<td>A\textsubscript{2}</td>
<td>Age ≥75 years</td>
</tr>
<tr>
<td>D</td>
<td>Diabetes Mellitus</td>
</tr>
<tr>
<td>S\textsubscript{2}</td>
<td>Prior Stroke or TIA or thromboembolism</td>
</tr>
<tr>
<td>V</td>
<td>Vascular disease (eg. peripheral artery disease, myocardial infarction, aortic plaque)</td>
</tr>
<tr>
<td>A</td>
<td>Age 65-74 years</td>
</tr>
<tr>
<td>S\textsubscript{e}</td>
<td>Sex category (i.e. female gender)</td>
</tr>
</tbody>
</table>
How does CHADS-VASC score determine stroke risk?

### Annual Stroke Risk[^2]

<table>
<thead>
<tr>
<th>CHADS_2 Score</th>
<th>Stroke Risk %</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>1.9</td>
<td>1.2–3.0</td>
</tr>
<tr>
<td>1</td>
<td>2.8</td>
<td>2.0–3.8</td>
</tr>
<tr>
<td>2</td>
<td>4.0</td>
<td>3.1–5.1</td>
</tr>
<tr>
<td>3</td>
<td>5.9</td>
<td>4.6–7.3</td>
</tr>
<tr>
<td>4</td>
<td>8.5</td>
<td>6.3–11.1</td>
</tr>
<tr>
<td>5</td>
<td>12.5</td>
<td>8.2–17.5</td>
</tr>
<tr>
<td>6</td>
<td>18.2</td>
<td>10.5–27.4</td>
</tr>
</tbody>
</table>

Score of 2 or more means that the benefit of coumadin or pradaxa outweighs the risk
## Anticoagulation

<table>
<thead>
<tr>
<th>Score</th>
<th>Risk</th>
<th>Anticoagulation Therapy</th>
<th>Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Low</td>
<td>None or Aspirin</td>
<td>Aspirin daily</td>
</tr>
<tr>
<td>1</td>
<td>Moderate</td>
<td>Aspirin or Warfarin</td>
<td>Aspirin daily or raise INR to 2.0-3.0, depending on patient preference</td>
</tr>
<tr>
<td>2 or greater</td>
<td>Moderate or High</td>
<td>Warfarin</td>
<td>Raise INR to 2.0-3.0, unless contraindicated</td>
</tr>
</tbody>
</table>

Score of 2 or more means that the benefit of coumadin or pradaxa outweighs the risk
# Coumadin vs. Pradaxa

<table>
<thead>
<tr>
<th>Coumadin (Warfarin)</th>
<th>Pradaxa (Dabigatran)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood testing required (INR)</td>
<td>No blood testing required</td>
</tr>
<tr>
<td>Generic</td>
<td>Non-generic</td>
</tr>
<tr>
<td>Once a day</td>
<td>Twice a day</td>
</tr>
<tr>
<td>Antidote available</td>
<td>No antidote available</td>
</tr>
</tbody>
</table>
Pradaxa (Dabigatran)

**Figure 1.** Cumulative Hazard Rates for the Primary Outcome of Stroke or Systemic Embolism, According to Treatment Group.
Pradaxa: Label Update
June 7, 2012

The Clinical Studies section of the label will now read,

"Pradaxa 150-mg twice daily was superior in reducing ischemic and hemorrhagic strokes relative to warfarin."
Stroke Reduction in Atrial Fibrillation

- By eliminating atrial fibrillation, can ablation reduce the risk of stroke and stroke-related deaths?
Maintenance of sinus rhythm with an ablation strategy in patients with atrial fibrillation is associated with a lower risk of stroke and death

Ross J Hunter,1 James McCready,2 Ihab Diab,1 Stephen P Page,1 Malcolm Finlay,2 Laura Richmond,1 Antony French,3 Mark J Earley,1,4 Simon Sporton,1,4 Michael Jones,5 Jubin P Joseph,5 Yaver Bashir,5 Tim R Betts,5 Glyn Thomas,3 Andrew Staniforth,6 Geoffrey Lee,7 Peter Kistler,7 Kim Rajappan,5 Anthony Chow,2 Richard J Schilling1,4

ABSTRACT

Objective To investigate whether catheter ablation of atrial fibrillation (AF) reduces stroke rate or mortality.

Methods An international multicentre registry was compiled from seven centres in the UK and Australia for consecutive patients undergoing catheter ablation of AF. Long-term outcomes were compared with (1) a cohort with AF treated medically in the Euro Heart Survey, and (2) a hypothetical cohort without AF, age and gender matched to the general population. Analysis of stroke and death was carried out after the first procedure (including peri-procedural events) regardless of success, on an intention-to-treat basis.

Results 1273 patients, aged 58±11 years, 56% paroxysmal AF, CHADS2 score 0.7±0.9, underwent 1.8±0.9 procedures. Major complications occurred in 5.4% of procedures, including stroke/TIA in 0.7%. Freedom from AF following the last procedure was 85% (76% off antiarrhythmic drugs) for paroxysmal AF, and 72% (60% off Catheter ablation is now successful in maintaining freedom from AF long term in the majority of patients without the need for AADs,7–12 raising the possibility that it might reduce rates of stroke and death. Several single-centre registries7–9,11–13 and two large multicentre registries10,14 have demonstrated low rates of stroke and death after catheter ablation of AF. Data from one large multicentre registry suggested that risk of stroke and death after catheter ablation of AF is reduced compared with patients treated medically, and is the same as that of the general population.10

Since randomised data to confirm this effect remain some years away, we sought to investigate the impact of catheter ablation of AF on long-term outcomes by compiling an international multicentre registry. Outcomes were compared with (1) a real-world cohort of patients with AF treated medically in the Euro Heart Survey on AF, and (2) a

### Table 1  Patient demographics and stroke risk factors

<table>
<thead>
<tr>
<th>Factor</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>58 ± 11</td>
</tr>
<tr>
<td>Paroxysmal AF (%)</td>
<td>56</td>
</tr>
<tr>
<td>Months since AF diagnosed</td>
<td>36 (24—70)</td>
</tr>
<tr>
<td>Left atrial diameter (mm)</td>
<td>41 ± 8</td>
</tr>
<tr>
<td>CHADS&lt;sub&gt;2&lt;/sub&gt;/CHA&lt;sub&gt;2&lt;/sub&gt;DS&lt;sub&gt;2&lt;/sub&gt; VASc constituents</td>
<td></td>
</tr>
<tr>
<td>Congestive heart failure (%)</td>
<td>13</td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>42</td>
</tr>
<tr>
<td>Age ≥75 years (%)</td>
<td>5</td>
</tr>
<tr>
<td>Diabetes (%)</td>
<td>5</td>
</tr>
<tr>
<td>Stroke or TIA before enrolment (%)</td>
<td>5</td>
</tr>
<tr>
<td>Vascular disease (%)</td>
<td>9</td>
</tr>
<tr>
<td>Age ≥65 years (%)</td>
<td>28</td>
</tr>
<tr>
<td>Female sex (%)</td>
<td>26</td>
</tr>
<tr>
<td>Mean CHADS&lt;sub&gt;2&lt;/sub&gt; score</td>
<td>0.7 ± 0.9</td>
</tr>
<tr>
<td>(48% scored 1, 35% scored 2, 12% scored 3, 4% scored 4 and 1% scored ≥4)</td>
<td></td>
</tr>
<tr>
<td>Mean CHA&lt;sub&gt;2&lt;/sub&gt;DS&lt;sub&gt;2&lt;/sub&gt; VASc score</td>
<td>1.4 ± 1.3</td>
</tr>
<tr>
<td>(29% scored 0, 32% scored 1, 21% scored 2, 11% scored 3 and 8% scored ≥4)</td>
<td></td>
</tr>
</tbody>
</table>

Proportions are given as a percentage, other figures are mean ± SD if normally distributed or median (range) if not.

AF, atrial fibrillation; TIA, transient ischaemic attack.
Table 2  Procedural complications

<table>
<thead>
<tr>
<th>Complication</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any major</td>
<td>5.4</td>
</tr>
<tr>
<td>Procedural death</td>
<td>0</td>
</tr>
<tr>
<td>Death within 30 days</td>
<td>0.1</td>
</tr>
<tr>
<td>Tamponade</td>
<td>3.1</td>
</tr>
<tr>
<td>Stroke or TIA</td>
<td>0.7</td>
</tr>
<tr>
<td>Haematoma</td>
<td>2.1</td>
</tr>
<tr>
<td>Vascular access complication</td>
<td>0.1</td>
</tr>
<tr>
<td>Pulmonary vein stenosis</td>
<td>0.2</td>
</tr>
<tr>
<td>Other major</td>
<td>0.4</td>
</tr>
</tbody>
</table>

Values are shown as percentages.
Haematomas were included only if they prolonged hospital stay or required re-admission. The sum of complications exceeds the ‘any major’ complication rate, since some patients had more than one complication. The 10 complications grouped under ‘other major’ include a femoral arteriovenous fistula which was repaired surgically, a deep vein thrombosis, a pulmonary embolus, a renal embolism, a pulmonary artery perforation, three burns from grounding plates, gastric stasis (presumed due to phrenic denervation) and a re-admission at 7 days with cardiac failure.
TIA, transient ischaemic attack.
AF Free Survival After Last Ablation

Figure 1  Freedom from atrial fibrillation (AF). Kaplan–Meier curve showing freedom from AF following the last procedure for patients with paroxysmal AF (PAF) and persistent AF. Comparison of curves was by the log-rank test. The number in brackets is the proportion free from AF and not receiving antiarrhythmic drugs (AADs).
Figure 2  Maintenance of sinus rhythm and stroke-free survival. Kaplan-Meier curve showing stroke-free survival for patients who remained free from atrial fibrillation (AF) compared with those with recurrent AF. Comparison of curves was by the log-rank test. The number at the bottom is the number of patients still followed up at each time point.
Comparison with medically treated afib patients and general population (without afib)

Figure 4  Outcome after catheter ablation of atrial fibrillation (AF) compared with medical treatment in the Euro Heart Survey and controls without AF in the general population. Bars show rates of stroke, death, or a composite of both as a percentage of patients per 100 years of patient follow-up for the study cohort, for the Euro Heart Survey on AF and for a hypothetical cohort matched to the study cohort for age and gender from UK national statistics. *Denotes a significant difference between the Euro Heart Survey cohort and the other two groups.
Stroke/TIA in patients who stopped taking warfarin after a-fib ablation

<table>
<thead>
<tr>
<th>CHADS&lt;sub&gt;2&lt;/sub&gt; score</th>
<th>Patient number</th>
<th>Patient-years</th>
<th>Stroke or TIA, n (%)</th>
<th>Expected annual rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>462</td>
<td>1132</td>
<td>2 (0.2)*</td>
<td>1.9</td>
</tr>
<tr>
<td>1</td>
<td>278</td>
<td>649</td>
<td>2 (0.3)*</td>
<td>2.8</td>
</tr>
<tr>
<td>2</td>
<td>46</td>
<td>112</td>
<td>0</td>
<td>4.0</td>
</tr>
<tr>
<td>≥3</td>
<td>14</td>
<td>38</td>
<td>0</td>
<td>≥5.9</td>
</tr>
<tr>
<td>CHA&lt;sub&gt;2&lt;/sub&gt;DS&lt;sub&gt;2&lt;/sub&gt; VASc score</td>
<td>Patient number</td>
<td>Patient-years</td>
<td>Stroke or TIA, n (%)</td>
<td>Expected annual rate (%)</td>
</tr>
<tr>
<td>------------------------</td>
<td>---------------</td>
<td>---------------</td>
<td>----------------------</td>
<td>-------------------------</td>
</tr>
<tr>
<td>0</td>
<td>298</td>
<td>756</td>
<td>2 (0.3)</td>
<td>0</td>
</tr>
<tr>
<td>1</td>
<td>287</td>
<td>670</td>
<td>0</td>
<td>0.7</td>
</tr>
<tr>
<td>2</td>
<td>132</td>
<td>300</td>
<td>2 (0.7)</td>
<td>1.9</td>
</tr>
<tr>
<td>≥3</td>
<td>88</td>
<td>205</td>
<td>0*</td>
<td>≥4.7</td>
</tr>
</tbody>
</table>

The number of patient-years of follow-up and the number of strokes or TIA, broken down by CHADS<sub>2</sub> score and CHA<sub>2</sub>DS<sub>2</sub> VASc score.

The expected rate of stroke or TIA is taken from the studies describing these algorithms.\textsuperscript{23,24} Difference between groups denoted by *(p<0.01 for all).
Stroke/TIA in patients who stopped taking warfarin after afib ablation

- Results need to be confirmed in a randomized controlled trial
- For now, Heart Rhythm Society recommends continuation of warfarin for CHADS 2 or more, regardless of the result of ablation
Conclusion

- Similar to prior multicenter and single-center registry studies (9 total)
  - AF ablation strategy, regardless of results, substantially reduces stroke and death as compared to medically treated afib patients
  - Incidence of stroke and death after AF ablation is no different than general population

- Results need to be confirmed in randomized controlled trials (CABANA, EAST)
Impact of Ablation on Mortality and Stroke

- 37,908 Intermountain Healthcare patients

Mortality

4,212 AF abl pts  16,848 age/gender matched controls with AF

Stroke

16,848 age/gender matched controls w/o AF

Bunch et al, Manuscript in Press
Stroke Prevention in Atrial Fibrillation

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- Preventing subsequent stroke
  - No prior history of atrial fibrillation
  - Diagnosing atrial fibrillation
TRENDS Trial Subanalysis

Incidence of Newly Detected Atrial Arrhythmias via Implantable Devices in Patients With a History of Thromboembolic Events

Paul D. Ziegler, MS; Taya V. Glotzer, MD; Emile G. Daoud, MD; D. George Wyse, MD, PhD; Daniel E. Singer, MD; Michael D. Ezekowitz, MD, PhD; Jodi L. Koehler, MS; Christopher E. Hilker, MS

Background and Purpose—Evidence of atrial tachycardia/atrial fibrillation (AT/AF) is often sought in patients with ischemic stroke or transient ischemic attack. We studied patients with previous thromboembolic events (TE) who were implanted with devices capable of continuous arrhythmia monitoring to comprehensively quantify the incidence and duration of newly detected AT/AF.

Methods—This study represents a subgroup analysis of the TRENDS trial, which included patients with clinical indications for pacemakers or defibrillators and ≥1 stroke risk factors (heart failure, hypertension, age 65 or older, diabetes, or previous TE). A history of AF was not required. All implanted devices were capable of continuously monitoring the cumulative time spent in AT/AF each day. This analysis focuses primarily on the incidence and duration of newly detected AT/AF (defined as ≥5 minutes of AT/AF on any day) in patients with previous TE, no documented history of AF, and no warfarin or antiarrhythmic drug use.

Results—A total of 319 patients had a history of TE and ≥1 day of device data. Patients with a documented history of AF (n=80), warfarin use (n=56), or antiarrhythmic drug use (n=20) were excluded from analysis. Of the remaining 163 patients, newly detected AT/AF was identified via the device in 45 patients (28%) over a mean follow-up of 1.1±0.7 years. AT/AF recurred infrequently, with only 12 patients experiencing AT/AF on >10% of follow-up days.

Conclusion—Newly detected episodes of AT/AF were found via continuous monitoring in 28% of patients with previous TE. Most episodes would not have been detected by standard intermittent monitoring techniques. (Stroke. 2010;41:256-260.)

Key Words: ambulatory electrocardiography ■ atrial fibrillation ■ diagnostic methods ■ stroke
TRENDS study

319 patients with
- prior TE
- Implanted device

• Excluded:
  - prior h/o AF
  - prior h/o AAD Rx
  - prior h/o warfarin use

• 28% had newly detected
  - Atrial tachycardia
  - Atrial fibrillation
  (of remaining 169 pts)

Majority detected after 30 days
SURPRISE study
Preliminary Results

- 52 patients with cryptogenic stroke
- Implantable loop recorder (Reveal XT)
- 18.6% had afib documented on monitoring and were started on anticoagulation
- Average time from stroke to detection of the first afib episode: 133 days
Sandin et al

- 42 patients with cryptogenic stroke
- Implantable loop recorder
- 17% were found to have paroxysmal atrial fibrillation
- Average time from stroke to afib diagnosis: 185 days

- CRYSTAL-AF trial is being conducted: 450 pts with cryptogenic stroke will be randomized to standard monitoring vs ILR
Left Atrial Appendage Closure (Watchman)

- 707 patients
- Randomized to
  - Warfarin
  - LAA closure
- LAA closure non-inferior to warfarin
  - Stroke
  - Cardiac death
  - Systemic embolism
- 3 vs 4.9 events per 100 patient-years
Questions