What You Need to Know about Undiagnosed Atrial Fibrillation

An Under-Recognized Stroke Risk Factor

Approved for CME and ABIM MOC Points

Major Lecture Themes

• Need to know that AFib, even if it is undiagnosed or asymptomatic, is still a risk factor for stroke
• Need to identify patients who do not have AFib, but are at higher risk of stroke if they do develop it
• Need to know about new and emerging approaches for prolonged or intermittent ECG screening in patients likely to have undiagnosed AFib
• Need to prescribe oral anticoagulation for those high-risk patients with newly identified AFib
What You Need to Know about Undiagnosed Atrial Fibrillation

What We Know

• AFib with risk factor(s) and diagnosed in routine care has 5X risk of stroke
• Even short episodes (>6 min) of “silent” AFib is a risk factor for stroke
• Silent AFib is common: 30% of pts with pacers, 1.4% of population ≥ 65 y/o (500,000 in US alone)
• CHA2DS2VASc features are risk factors for stroke with or without AF

What We Do Not Know

• Is the risk of silent AFib detected by pacers and screening reduced by oral anticoagulants?
• If so, what is the threshold for when treatment should be used?
• What is the role of monitoring devices and detection strategies?
AFib, even if it is undiagnosed or asymptomatic, is still a risk factor for stroke.
Permanent AFib is a greater risk factor than paroxysmal AFib

Pattern of AFib and Embolic Stroke
6563 Aspirin-treated Patients from ACTIVE-A and AVERROES Trials

Permanent, persistent, paroxysmal AFib
AFib vs normal sinus rhythm at enrollment

Vanassehe T. Eur Heart J 2015;36:281-287
Even modest AFib is enough to increase risk of stroke?

**Studies Evaluating Risk of Stroke Versus AFib Burden**

*Even Small AFib Burden Increases Stroke Risk*

<table>
<thead>
<tr>
<th>Year</th>
<th>Study</th>
<th>n</th>
<th>AFib Burden Measure</th>
<th>HR for stroke</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>2003</td>
<td>MOST</td>
<td>312</td>
<td>5 min</td>
<td>6.7</td>
<td>0.02</td>
</tr>
<tr>
<td>2005</td>
<td>Capucci</td>
<td>725</td>
<td>&gt;24 hrs</td>
<td>3.1</td>
<td>0.04</td>
</tr>
<tr>
<td>2009</td>
<td>Botto</td>
<td>568</td>
<td>CHADS + AF burden</td>
<td>6.2</td>
<td>0.8%</td>
</tr>
<tr>
<td>2012</td>
<td>Home monitor CRT</td>
<td>560</td>
<td>3.8 hrs</td>
<td>9.4</td>
<td>0.006</td>
</tr>
<tr>
<td>2012</td>
<td>TRENDS</td>
<td>2486</td>
<td>5.5 hrs</td>
<td>2.4</td>
<td>0.06</td>
</tr>
<tr>
<td>2012</td>
<td>ASSERT</td>
<td>2580</td>
<td>6 min</td>
<td>2.5</td>
<td>0.008</td>
</tr>
</tbody>
</table>

New Models of AFib Diagnosis and Management

- New Approaches for AFib
- New technologies – eg AliveCor, Reveal LINQ, WatchBP Home, Health Stations
  - Long-term and intermittent monitoring
  - Self-monitoring
- Management of newly diagnosed AFib; guides to anticoagulant treatment
  - Assessment of stroke risk
  - Assessment of disease burden

Atrial Fibrillation Burden

- Current guidelines recommend using vascular risk factors (as measured by the CHA2DS2-VASc score) and not considering AFib burden when making decisions regarding anticoagulation for stroke prevention in AFib

- The strongest evidence, however, suggests that patients with persistent AFib are at higher risk of stroke than those with paroxysmal AFib

Chen LY et al. Circulation. 2018;137:00–00. DOI: 10.1161/CIR.0000000000000568
AFib Burden: What We Don’t Know

- Optimal monitoring frequency and duration to measure AFib burden
- Threshold of AFib burden that results in an increased risk of stroke, heart failure, dementia, and other AFib-related outcomes
- Prevalence of subclinical AFib and effects of AFib burden in community-based cohorts
- Risk factors and determinants of AFib burden in broad community-based cohorts
- Lack of temporal relationship between AFib burden and stroke in AFib patients
- How AFib burden will need to be redefined in the era of widespread, long-term continuous cardiac monitoring
- Threshold of AFib burden that indicates need for anticoagulation in patients with higher risk of stroke (eg, CHA2DS2-VASc score ≥2)

Chen LY et al. Circulation. 2018;137:00–00. DOI: 10.1161/CIR.0000000000000568

Screening for Undiagnosed AFib Is Effective

- Screening can increase detection rate of new cases of AFib: 1.63% a year compared with 1.04% without systematic or opportunistic screening¹
- Systematic screening: invitation for electrocardiography
- Opportunistic screening: pulse taking and electrocardiography if the pulse is irregular
- Use of new technologies for large-scale population screening
  - Hand-held ECG devices; personal-monitoring devices
- Incidence of previously unknown AFib was found to be 1.4% in ≥65 year olds²

What You Need to Know about Undiagnosed Atrial Fibrillation

Who to Screen

• People over 65 years of age
• People at high cardiovascular disease risk
• People with predisposing conditions:
  – Hypertension
  – Heart failure
  – Coronary artery disease
  – Obesity
  – Diabetes mellitus
  – Chronic kidney disease
  – Obstructive sleep apnoea


CHA₂DS₂-VASc Risk Score
This Can Be Useful to Identify Patients At-risk for Stroke

<table>
<thead>
<tr>
<th>Condition</th>
<th>Points</th>
<th>CHA₂DS₂-VASc Risk Score</th>
<th>Annual Stroke Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>C</td>
<td>1</td>
<td>0</td>
<td>0.8%</td>
</tr>
<tr>
<td>H</td>
<td>1</td>
<td>1</td>
<td>2.0%</td>
</tr>
<tr>
<td>A2</td>
<td>2</td>
<td>3</td>
<td>3.7%</td>
</tr>
<tr>
<td>D</td>
<td>1</td>
<td>4</td>
<td>5.9%</td>
</tr>
<tr>
<td>S2</td>
<td>2</td>
<td>5</td>
<td>9.3%</td>
</tr>
<tr>
<td>V</td>
<td>1</td>
<td>6</td>
<td>15.3%</td>
</tr>
<tr>
<td>A</td>
<td>1</td>
<td>7</td>
<td>19.7%</td>
</tr>
<tr>
<td>Sc</td>
<td>1</td>
<td>8</td>
<td>21.5%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>9</td>
<td>23.6%</td>
</tr>
</tbody>
</table>

It is important to consider new and emerging approaches for prolonged or intermittent ECG screening in patients likely to have undiagnosed AFib.

**ASSERT: Study Design**

*Do Device-detected Atrial Tachyrhythmias Predict Increase Stroke Risk?*

**PROSPECTIVE COHORT DESIGN**

- 2580 pts enrolled after pacemaker or ICD
- Age ≥ 65 years
- History of hypertension
- Excluded if any history of AF or on VKA
- Minimum follow up 1.75 yrs
- Maximum follow up 5 yrs

Enrolled 0-8 wks post implant | Arrhythmia Detection | Follow Up Period | Primary Outcome: Ischemic Stroke or Systemic Embolism

Visits | Months -3 | 0 | 3 | 9 | 15 | 21 | 27 | 33 | 39 | 45 | 51 | 57

**ASSERT Trial: Subclinical AFib and Risk of Stroke**

*Atrial Tachyarrhythmia > 6 min ≤ 3 Months After Pacemaker or Defibrillator Implantation*

![Graph showing the risk of stroke or systemic embolism](image)

- **HR 2.49 (1.28 – 4.85)**
- Subclinical atrial tachyarrhythmias present

**ASSERT Trial**

*Un-adjudicated Atrial High Rate Episodes (AHRE)*

<table>
<thead>
<tr>
<th>AHRE Duration</th>
<th>RR of clinical AFib</th>
<th>P-value</th>
<th>RR of Primary Outcome (Ischemic Stroke and Non-CNS Embolism)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 6 min</td>
<td>5.25</td>
<td>&lt;0.001</td>
<td>2.04</td>
<td>0.04</td>
</tr>
<tr>
<td>&gt; 30 min</td>
<td>5.37</td>
<td>&lt;0.001</td>
<td>2.10</td>
<td>0.04</td>
</tr>
<tr>
<td>&gt; 6 hrs</td>
<td>7.83</td>
<td>&lt;0.001</td>
<td>4.32</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

# ASSERT Trial

**Clinical Outcomes by CHADS\textsubscript{2}**

<table>
<thead>
<tr>
<th>CHADS\textsubscript{2} Score</th>
<th>Total Pts.</th>
<th>Sub-clinical Atrial Tachyarrhythmia between enrollment and 3 months</th>
<th>Sub-clinical Atrial Tachyarrhythmia Present vs. absent</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Present</td>
<td>Absent</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Pts.</td>
<td>Events</td>
</tr>
<tr>
<td>1</td>
<td>600</td>
<td>68</td>
<td>1</td>
</tr>
<tr>
<td>2</td>
<td>1129</td>
<td>119</td>
<td>4</td>
</tr>
<tr>
<td>&gt;2</td>
<td>848</td>
<td>72</td>
<td>6</td>
</tr>
</tbody>
</table>


How close is the temporal relationship between AFib episodes and stroke?
ASSERT Trial
Timing of Atrial Arrhythmia and Stroke

- Of 51 patients with stroke/SE, 26 (51%) had Subclinical AFib (SCAF).
- In 18 patients (35%), SCAF was before stroke.
- Only 4 patients (8%) had SCAF within 30 days before stroke, and only 1 of 4 patients had SCAF at time of stroke (B).
- In 14 patients with SCAF detected >30 days before stroke, most recent episode was median of 339 days (25th to 75th percentile, 211–619) earlier.
- Eight patients (16%) had SCAF detected only after stroke, despite continuous monitoring for median of 228 days before event.

Duration of Device-Detected Subclinical AFib and Occurrence of Stroke in ASSERT

Van Gelder IC et al. Eur Heart J. 2017;38:1339-1344
## ARTESIA Study

**Protocol Overview**

<table>
<thead>
<tr>
<th>Objective:</th>
<th>To test if apixaban is superior to aspirin for prevention of stroke and systemic embolism in patients with device detected subclinical AF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Design:</td>
<td>Double-blind, double-dummy randomized clinical trial</td>
</tr>
<tr>
<td>Sample Size:</td>
<td>4000 patients</td>
</tr>
<tr>
<td>Population:</td>
<td>Patients with at least one episode of SCAF ≥ 6 min but none &gt; 24 hrs; CHADs-Vasc ≥ 4; without clinical AFib and without any contraindication to NOAC or aspirin.</td>
</tr>
<tr>
<td>Intervention:</td>
<td>5 mg bid apixaban vs 81 mg daily aspirin</td>
</tr>
<tr>
<td>Follow-up:</td>
<td>Event driven; estimated 3 years average</td>
</tr>
</tbody>
</table>
| Outcomes:            | 1º efficacy: composite of stroke/TIA with imaging and systemic embolism  
|                      | 1º safety: ISTH major bleeding                                                                                                 |


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**What proportion of patients with cryptogenic stroke have underlying undetected AFib?**
What You Need to Know about Undiagnosed Atrial Fibrillation

**AFib in Patients with Cryptogenic Stroke**

![Graph showing the percentage of patients with atrial fibrillation detected over time.](Gladstone DJ et al; N Engl J Med. 2014;370:2467-2477)

**CRYSTAL AF**

*Study of Continuous Cardiac Monitoring to Assess AFib After Cryptogenic Stroke*

- **Phase 3,** randomized, prospective study in patients with cryptogenic stroke
- **Sample size:** ~ 450 patients

**Inclusion criteria:**
- Recent cryptogenic symptomatic transient ischemic attack (TIA) or cryptogenic ischemic stroke

**Continuous cardiac monitoring:** Reveal XT™ insertable cardiac monitor

**Control arm:** Follow-up at the same frequency, but with no insertable cardiac monitor

**Primary outcome:** Time to first documented episode of AF within 6 mo after stroke
**Secondary outcomes:** Time to first documented episode of AF by 12 mo of CRIM, incidence of stroke and transient ischemic attack (TIA); cardiovascular drug changes (oral anticoagulation and antiarrhythmic drugs); quality of life; clinical disease burden and care pathway; patient assistant impact on AF diagnosis

ClinicalTrials.gov website.
Risk of Stroke
By Quartiles of N-terminal Pro B-type Natriuretic Peptide (NT-proBNP)

Cryptogenic Stroke and Underlying AFib

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There is a need to know about new and emerging approaches for prolonged or intermittent ECG screening in patients likely to have undiagnosed AFib.

Should we screen for asymptomatic AFib? If so, how?
What You Need to Know about Undiagnosed Atrial Fibrillation

Screening to Identify Unknown Atrial Fibrillation
A Systematic Review

<table>
<thead>
<tr>
<th></th>
<th>Total cohort</th>
<th>≥65 years</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number of studies</td>
<td>Number of participants</td>
</tr>
<tr>
<td>All settings</td>
<td>14</td>
<td>67,772</td>
</tr>
<tr>
<td>GP/Outpatient clinic</td>
<td>5</td>
<td>13,533</td>
</tr>
<tr>
<td>Community</td>
<td>8</td>
<td>54,239</td>
</tr>
</tbody>
</table>

* p<0.001; † p = not significant = 0.7.

- 1.4% of population ≥ 65 years have AF on screening
- 34,991,753 people in US ≥ age 65
- This translates into 490,000 Americans

http://www.census.gov/prod/cen2010

Prognosis of Asymptomatic AFib Detected Incidentally
A Case for Screening

European Guidelines
2016 Update

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Class of Recommendation</th>
<th>Level of Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Opportunistic screening for AFib is recommended by pulse taking or ECG rhythm strip in patients &gt;65 years of age</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>Systematic ECG screening may be considered to detect AFib in patients aged &gt;75 years, or those at high stroke risk</td>
<td>IIb</td>
<td>B</td>
</tr>
</tbody>
</table>


Canadian Cardiovascular Society Guidelines
2014 Update

- New recommendations for Investigation and Management of silent AFib (conditional recommendation)
- Oral anticoagulation (OAC) for patients ≥ 65 years or CHADS2 ≥ 1 with Silent AFib > 24 hours or for shorter episodes in high risk patients (e.g. recent cryptogenic stroke)
- All patients with AFib, whether paroxysmal or persistent, should be stratified for stroke risk and that OAC therapy be prescribed for most patients aged 65 years or CHADS2 score > 1

Verma A et al., Canadian Journal of Cardiology. 2014;30:1114-1130
U.S. Preventive Services Task Force (UPSTF)

Conclusion: Insufficient evidence to determine whether benefits of screening for AFib outweigh harms

• Benefit
  – Screening with ECG detected more new AFib than no screening
• Potential risks linked to misdiagnosis of abnormal ECG results
  – Avoidable patient anxiety
  – Unnecessary testing
  – Inappropriate treatments or invasive procedures
• Patient management considerations involve more than clinical evidence alone
• Future Work
  – Need for more controlled trial data on asymptomatic patients

Curry SJ et al. JAMA 2018;320:478-484

Representative Screening Devices
AliveCore ECG Analyzer in Mobile Health

“Consumerised” ECG Analysis

• Check heart health anywhere, anytime on a mobile device
• Share information with patients that typically only doctors could see
• Backed up by professional healthcare services
• Large database (~2.5 million) of ECGs
• More accurate and consistent than human interpretations

Provider Dashboard

• For health professionals with patients who use the heart monitor
• Helps provider to review patients’ ECG data
• Free secure web-based portal
• Simply “invite” a patient by entering their email address

http://www.alivecor.com/posts/the-provider-dashboard
Reveal LINQ: A Revolutionary System
The Complete Monitoring Solution

Reveal LINQ™ ICM
MyCareLink™ Patient Monitor
Simplified Insertion Procedure

Cellular

Mobile Alerts
Streamlined Reports

Improved CareLink® User Interface

All patient and clinical data are fictitious and for demonstration purposes only

Easy-to-Use, Clinically Actionable Reports
The Information You Need When You Need It

Comprehensive
Get the full picture with diagnostic trends on simplified reports

Customizable
Optional CareAlert® Notifications with auto-generated reports
95% of physicians found the Reveal LINQ reports easy to use and clinically actionable

Device-Detected AFib

How much AF is necessary to warrant treatment?

- Depending on their clinical characteristics, 10% to 25% of people with implantable devices have AF detected over time[^13].
- Continuous monitoring devices are finding more AF than ever before[^12].
- The greater the severity of associated disease, the less AF it took to be associated with stroke (REACH registry)[^11].


Even small amounts of AF have been associated with an elevated risk of stroke.[^11]

REVEAL AF: Detection Rates

- Median time from device insertion to the first detection of an AF episode was 123 days (~4 months).
  - At 18 months, AF incidence did not differ among patients with CHADS2 scores of 2, 3, 4, or greater.

Time to First Episode of AF > 6 minutes

![Graph showing time to first episode of AF > 6 minutes](chart.png)

- Short-term (30 days) monitoring is not enough time for first detection of AF episode.

What You Need to Know about Undiagnosed Atrial Fibrillation

Value of Long Term Continuous Monitoring: Detect Intermittent AFib
*TRENDS* Study Subgroup Analysis

- Newly Detected AFib ("NDAF") in Patients with Thromboembolic Events
  - 163 patients with previous ischemic stroke/TIA, no known AFib, were continuously monitored via pacemaker or Implantable Cardioverter Defibrillator
  - NDAF > 5 minute duration were found in 28% patients
  - 73% of patients had newly detected atrial tachycardia/AFib on <10% of follow-up days

  ![Graph showing time from device implant and freedom from AFib](image)
  - 89% of NDAF patients identified beyond 1 day
  - 78% of NDAF patients identified beyond 7 days
  - 60% of NDAF patients identified beyond 30 days


Community AFib Screening: AFinder Program
*Opportunistic screening in Hong Kong*

- 11,574 citizens; aged 50 years or older
- 10,735 had interpretable smartphone ECG records
- 244 (2.3%) had AFib
- 74 (0.69%) had newly diagnosed AFib
- Number needed to screen for 1 newly diagnosed AFib: 145

There is a need to prescribe oral anticoagulation (and anticoagulant options) for those high-risk patients with newly identified AFib.

Drugs Approved for Stroke Prevention in Patients with AFib

- Warfarin (vitamin K antagonist)
- Apixaban (factor Xa inhibitor)
- Dabigatran (thrombin inhibitor)
- Edoxaban (factor Xa inhibitor)
- Rivaroxaban (factor Xa inhibitor)
Efficacy of Warfarin to Prevent Stroke in AF
*Warfarin vs Placebo (Pooled Analysis of 2900 Participants)*


**Non-vitamin K Antagonist Oral Anticoagulants**

Which anticoagulant?

Efficacy and Safety of DOACs

*Meta-analysis of Randomized Trials*

<table>
<thead>
<tr>
<th>Trial</th>
<th>Stroke and Systemic Embolism</th>
<th>P Value</th>
<th>Major Bleeding</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>RE-LY</td>
<td></td>
<td>.0001</td>
<td></td>
<td>.34</td>
</tr>
<tr>
<td>ROCKET AF</td>
<td></td>
<td>.12</td>
<td></td>
<td>.72</td>
</tr>
<tr>
<td>ARISTOTLE</td>
<td></td>
<td>.012</td>
<td></td>
<td>&lt; .0001</td>
</tr>
<tr>
<td>ENGAGE AF-TIMI 48</td>
<td></td>
<td>.10</td>
<td></td>
<td>.0002</td>
</tr>
<tr>
<td>Combined</td>
<td></td>
<td>&lt; .0001</td>
<td></td>
<td>.06</td>
</tr>
</tbody>
</table>

What You Need to Know about Undiagnosed Atrial Fibrillation

### All DOACS: Stroke or Systemic Embolic Event (SEE)

<table>
<thead>
<tr>
<th>Study</th>
<th>Risk Ratio (95% CI)</th>
<th>Heterogeneity</th>
</tr>
</thead>
<tbody>
<tr>
<td>RE-LY ( dabigatran 150 mg)</td>
<td>0.66 (0.53 - 0.82)</td>
<td></td>
</tr>
<tr>
<td>ROCKET AF ( rivaroxaban)</td>
<td>0.88 (0.75 - 1.03)</td>
<td></td>
</tr>
<tr>
<td>ARISTOTLE ( apixaban)</td>
<td>0.80 (0.67 - 0.95)</td>
<td></td>
</tr>
<tr>
<td>ENGAGE AF-TIMI 48 ( edoxaban 60 mg)</td>
<td>0.88 (0.75 - 1.02)</td>
<td></td>
</tr>
<tr>
<td>Combined (Random Effects Model)</td>
<td>0.81 (0.73 - 0.91)</td>
<td>Heterogeneity P=0.13</td>
</tr>
</tbody>
</table>


### Secondary Efficacy Outcomes

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Risk Ratio (95% CI)</th>
<th>Heterogeneity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ischemic Stroke</td>
<td>0.92 (0.83 - 1.02)</td>
<td>P=0.10</td>
</tr>
<tr>
<td>Hemorrhagic Stroke</td>
<td>0.49 (0.38 - 0.64)</td>
<td>P&lt;0.0001</td>
</tr>
<tr>
<td>MI</td>
<td>0.97 (0.78 - 1.20)</td>
<td>P=0.77</td>
</tr>
<tr>
<td>All-Cause Mortality</td>
<td>0.90 (0.85 - 0.95)</td>
<td>P=0.0003</td>
</tr>
</tbody>
</table>

What You Need to Know about Undiagnosed Atrial Fibrillation

### All DOACS: Major Bleeding

<table>
<thead>
<tr>
<th>Trial</th>
<th>Risk Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>RE-LY (dabigatran 150 mg)</td>
<td>0.94 (0.82 - 1.07)</td>
</tr>
<tr>
<td>ROCKET AF (rivaroxaban)</td>
<td>1.03 (0.90 - 1.18)</td>
</tr>
<tr>
<td>ARISTOTLE (apixaban)</td>
<td>0.71 (0.61 - 0.81)</td>
</tr>
<tr>
<td>ENGAGE AF-TIMI 48 (edoxaban 60 mg)</td>
<td>0.80 (0.71 - 0.90)</td>
</tr>
<tr>
<td>Combined (Random Effects Model)</td>
<td>0.86 (0.73 - 1.00)</td>
</tr>
</tbody>
</table>

Risk Ratio $= 0.06$

### Secondary Safety Outcomes

<table>
<thead>
<tr>
<th>Event</th>
<th>Risk Ratio (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ICH</td>
<td>0.48 (0.39 - 0.59)</td>
<td>$&lt;0.0001$</td>
</tr>
<tr>
<td>GI Bleeding</td>
<td>1.25 (1.01 - 1.55)</td>
<td>0.043</td>
</tr>
</tbody>
</table>

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What You Need to Know about Undiagnosed Atrial Fibrillation

2016 ESC Guidelines for the Management of AFib
Developed in Collaboration with EACTS*

Important changes:

• Avoid the misleading term “non-valvular AF”

• No recommendation to use bleeding scores to withhold oral anticoagulation (only to identify modifiable factors)

• NOACs preferred over warfarin (IA)

• Aspirin is a class III LOE A recommendation (harm) for stroke prevention in AFib

*EACTS: European Association for Cardio-Thoracic Surgery

DOAC Dosing

<table>
<thead>
<tr>
<th>DOAC</th>
<th>Standard Dose</th>
<th>Reduced Dose</th>
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</thead>
<tbody>
<tr>
<td>Dabigatran¹</td>
<td>150 mg BID (CrCl &gt;30 mL/min)</td>
<td>75 mg BID (CrCl 15–30 mL/min; dronedarone or ketoconazole)</td>
</tr>
<tr>
<td>Rivaroxaban²</td>
<td>20 mg QD with evening meal (CrCl &gt;50 mL/min)</td>
<td>15 mg QD with evening meal (CrCl 15–50 mL/min; ESRD on dialysis) Avoid use with P-gp + CYP 3A4 inhibitor</td>
</tr>
<tr>
<td>Apixaban³</td>
<td>5 mg BID (Most patients)</td>
<td>2.5 mg BID (≥2 of the following: age ≥80 y; weight ≤60 kg; SCr ≥1.5 mg/dL OR strong dual inhibitors P-gp and CYP 3A4) Avoid use with strong dual inducers of P-gp and CYP 3A4</td>
</tr>
<tr>
<td>Edoxaban⁴</td>
<td>60 mg QD</td>
<td>30 mg QD (CrCl 15–50 mL/min) Avoid use with rifampin; only applies to patients with AF</td>
</tr>
</tbody>
</table>

¹No dosage adjustment needed for patients with end-stage renal disease on dialysis
²Dabigatran [prescribing information]. Ridgefield, CT: Boehringer Ingelheim Pharmaceuticals Inc; 11/2015.
Doses of DOACs According to Renal Function


2016 ESC/EACTS Guidelines for Management of AFib

What You Need to Know about Undiagnosed Atrial Fibrillation

**NOAH-AFNET 6 Trial Design**

- Pre-Study Screening
  - Patients at risk for cardiovascular events
    - Age ≥65 years
    - ≥1 additional CHA₂DS₂-VASc factor
  - AHRE documented by an implanted device
- Study Procedures
  - Stratification by indication of antiplatelet therapy
  - Randomisation
  - NOAC group (edoxaban)
  - Usual Care group
    - No oral anticoagulation
    - (aspirin or placebo)
  - Outpatient follow-up for events


**Summary**

- Undetected or silent AFib is relatively common
- It is associated with risk of stroke, related to burden and risk factors
- Whether treating with oral anticoagulant has overall benefit is being investigated in trials
- For the time being:
  - Treat if > 6 to 24 hours, depending on risk factors
  - After cryptogenic stroke, generally treat if > 30 seconds to 2 minutes of AFib
- Whether, when, whom and how to screen is being studied
- In the meantime, patient preferences should be considered for screening
Conclusions

• Screen-detected AFib is not a benign condition and with additional stroke risk factors warrants consideration of OAC
• The setting for AFib screening should be both country and health-system specific

Based on current knowledge

“This white paper provides a strong case for AFib screening now while recognizing that large randomized outcomes studies would be helpful to strengthen the evidence-base.”

Freedman et al: Circ, 2017

Conclusions

• Reducing stroke risk is essential, regardless of whether a patient is symptomatic or not
• Screening for AF has been made easier by the development of new affordable technology and should be encouraged
• Oral anticoagulants have demonstrated a reduction in stroke risk in patients with AFib, and are superior to no treatment or aspirin
• The prescription of anticoagulation should be based on stroke risk assessed using the CHA2DS2-VASc scoring system