Michael Spooner MD MBA FACC FHRS
Electrophysiology
Mercy One North Iowa Heart Center

# Approaches to Post-Stroke Monitoring for Atrial Fibrillation

# Disclosures

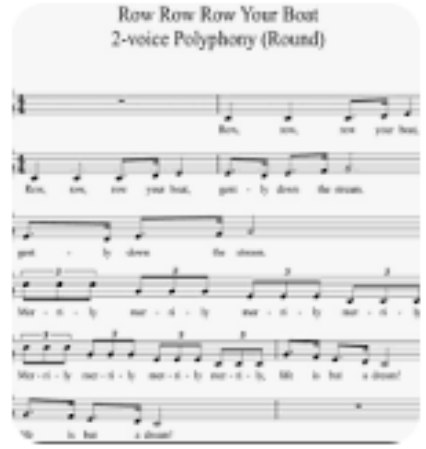
NONE PERTINENT TO THIS TALK

# Introduction

1. Lots of discussion about primary stroke prevention, but want to take a secondary stroke perspective
2. Discuss different situations of stroke that may make us consider monitoring from different perspectives
3. When and how do we monitor?

# Game – Point & Counterpoint

Counterpoint begins with the cantus firmus, or the fixed melody. The counterpoint is then composed against, note for note (point against point), the cantus firmus. In its simplest form, first species counterpoint is a single note against a single note.



1. **Team A and Team B**
2. **Case will be Presented**
3. **Position Assignment**:
   - Team A will make an argument for a specific answer
   - Team B will be required to make an argument for a different answer
4. **Rebuttal**:
   - Each team has a chance to rebut the opposing team's argument.
   - The spokespersons from each team may directly address the points made by the other team.
5. **Judging and Point Allocation**:
   - Points are awarded based on the strength of the arguments, clarity of presentation, logical reasoning, and persuasiveness.
6. **Winner Declaration**:
   - After all arguments are presented and points are allocated, the moderator declares the winning team. Remember, the key to a successful game of Point Counterpoint is respectful and constructive argumentation. Players should focus on presenting strong, evidence-based arguments while listening attentively to the opposing team's points.

# WARM UP

# Should this meeting be always held in Des Moines?

Team A:  Yes
Team B:  No, it should rotate between sites

# CASE 1

Patient is a 75 year old male with a history of T1DM, CAD, now re-admitted with worsening symptoms of recent stroke. Four days prior, patient had a diagnosed right PCA stroke with left sided weakness, and facial droop.  While in rehab, patient developed slurred speech and worsening left sided weakness.

Physical examination verified left sided arm/leg weakness with some slurred speech.

Repeat MRI demonstrated progressive right PCA infarct as well as new 5 mm inferior/posterior left occipital lobe lesion.

Echo shows LVEF 60-65%; late positive bubble study

Patient started on aspirin and ticagrelor

1. Monitor or no monitor?
2. How do we monitor and for how long?

Team A:  Yes, a 2 week Patch
Team B:  Yes, an Implantable Loop Recorder

The patient has had a cryptogenic stroke and we are looking for AF -- ”Secondary Prevention”

1. What is the yield of detecting AF utilizing different monitors?
2. Does changing treatment (adding an OAC) depend on the diagnosis of AF?

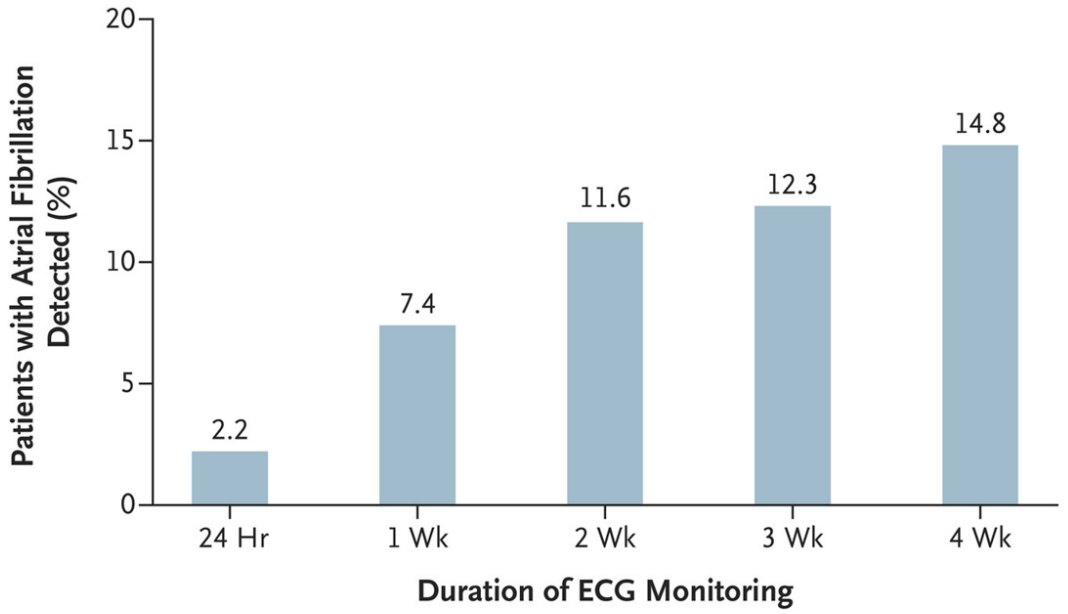
ORIGINAL ARTICLE

# Atrial Fibrillation in Patients with Cryptogenic Stroke

**Authors**: David J. Gladstone, M.D., Ph.D., Melanie Spring, M.D., Paul Dorian, M.D., Val Panzov, M.D., Kevin E. Thorpe, M.Math., Judith Hall, M.Sc., Haris Vaid, B.Sc., +24, for the EMBRACE Investigators and Coordinators* Author Info & Affiliations

Published June 26, 2014 | N Engl J Med 2014;370:2467-2477 | DOI: 10.1056/NEJMoa1311376 | VOL. 370 NO. 26

572 post-stroke/TIA patients with 30 day vs. 24 hour monitoring

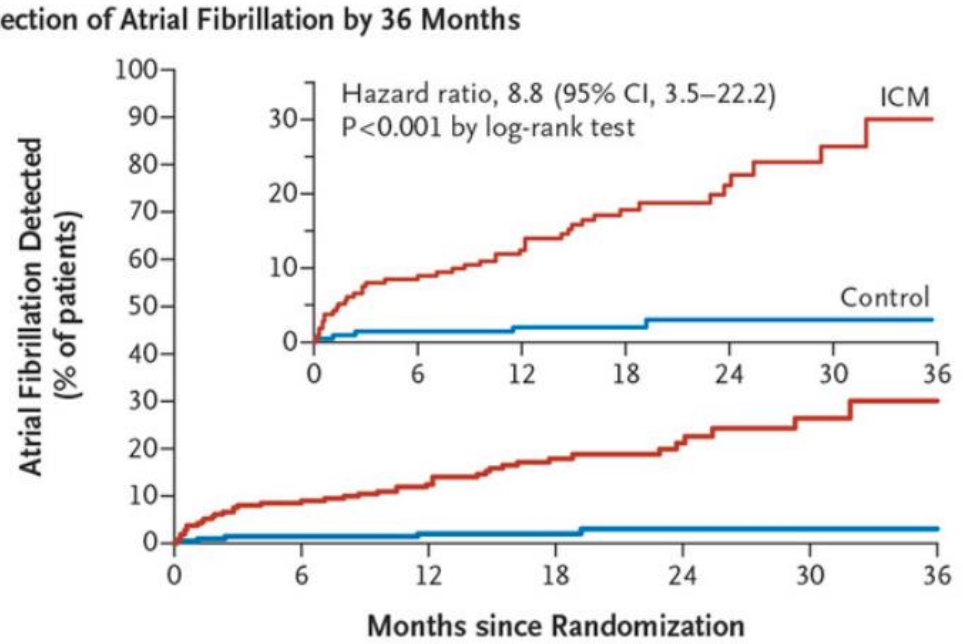



ORIGINAL ARTICLE

# Cryptogenic Stroke and Underlying Atrial Fibrillation

Tommaso Sanna, M.D., Hans-Christoph Diener, M.D., Ph.D., Rod S. Passman, M.D., M.S.C.E., Vincenzo Di Lazzaro, M.D., Richard A. Bernstein, M.D., Ph.D., Carlos A. Morillo, M.D., Marilyn Mollman Rymer, M.D., Vincent Thijs, M.D., Ph.D., Tyson Rogers, M.S., Frank Beckers, Ph.D., Kate Lindborg, Ph.D., and Johannes Brachmann, M.D., for the CRYSTAL AF Investigators*

441 post-stroke/TIA patient with ILR vs. conventional monitoring



1. Does treatment of detected AF by switching therapy to OAC make a difference?
   - SPAF 1991: warfarin versus placebo, 2.3% versus 7.4% per year; p = 0.01; mortality benefit noted
   - Other stroke risk calculation studies

Meta-Analysis > Ann Intern Med. 2007 Jun 19;146(12):857-67.
doi: 10.7326/0003-4819-146-12-200706190-00007.

## Meta-analysis: antithrombotic therapy to prevent stroke in patients who have nonvalvular atrial fibrillation

Robert G Hart [1], Lesly A Pearce, Maria I Aguilar

**Data synthesis:** Twenty-nine trials included 28,044 participants (mean age, 71 years; mean follow-up, 1.5 years). Compared with the control, adjusted-dose warfarin (6 trials, 2900 participants) and antiplatelet agents (8 trials, 4876 participants) reduced stroke by 64% (95% CI, 49% to 74%) and 22% (CI, 6% to 35%), respectively. Adjusted-dose warfarin was substantially more efficacious than antiplatelet therapy (relative risk reduction, 39% [CI, 22% to 52%]) (12 trials, 12 963 participants). Other randomized comparisons were inconclusive. Absolute increases in major extracranial hemorrhage were small (< or =0.3% per year) on the basis of meta-analysis.

JAMA | Original Investigation

# Apixaban to Prevent Recurrence After Cryptogenic Stroke in Patients With Atrial Cardiopathy

## The ARCADIA Randomized Clinical Trial

Hooman Kamel, MD; W. T. Longstreth Jr, MD; David L. Tirschwell, MD; Richard A. Kronmal, PhD;

**DESIGN, SETTING, AND PARTICIPANTS** Multicenter, double-blind, phase 3 randomized clinical trial of 1015 participants with cryptogenic stroke and evidence of atrial cardiopathy, defined as P-wave terminal force greater than 5000 µV × ms in electrocardiogram lead $V_1$, serum N-terminal pro-B-type natriuretic peptide level greater than 250 pg/mL, or left atrial diameter index of 3 cm/m$^2$ or greater on echocardiogram. Participants had no evidence of atrial fibrillation at the time of randomization. Enrollment and follow-up occurred from February 1, 2018, through February 28, 2023, at 185 sites in the National Institutes of Health StrokeNet and the Canadian Stroke Consortium.

**INTERVENTIONS** Apixaban, 5 mg or 2.5 mg, twice daily (n = 507) vs aspirin, 81 mg, once daily (n = 508).

**MAIN OUTCOMES AND MEASURES** The primary efficacy outcome in a time-to-event analysis was recurrent stroke. All participants, including those diagnosed with atrial fibrillation after randomization, were analyzed according to the groups to which they were randomized. The primary safety outcomes were symptomatic intracranial hemorrhage and other major hemorrhage.

**DESIGN, SETTING, AND PARTICIPANTS** Multicenter, double-blind, phase 3 randomized clinical trial of 1015 participants with cryptogenic stroke and evidence of atrial cardiopathy, defined as P-wave terminal force greater than 5000 µV × ms in electrocardiogram lead $V_1$, serum N-terminal pro-B-type natriuretic peptide level greater than 250 pg/mL, or left atrial diameter index of 3 cm/m$^2$ or greater on echocardiogram. Participants had no evidence of atrial fibrillation at the time of randomization. Enrollment and follow-up occurred from February 1, 2018, through February 28, 2023, at 185 sites in the National Institutes of Health StrokeNet and the Canadian Stroke Consortium.

**INTERVENTIONS** Apixaban, 5 mg or 2.5 mg, twice daily (n = 507) vs aspirin, 81 mg, once daily (n = 508).

**MAIN OUTCOMES AND MEASURES** The primary efficacy outcome in a time-to-event analysis was recurrent stroke. All participants, including those diagnosed with atrial fibrillation after randomization, were analyzed according to the groups to which they were randomized. The primary safety outcomes were symptomatic intracranial hemorrhage and other major hemorrhage.

The patient has had a cryptogenic stroke and we are looking for AF -- ”Secondary Prevention”

1. Longer monitoring – probably at least 30 days (for around 15% yield) post-stroke recommended

**Recommendation for Silent AF and Stroke of Undetermined Cause**
**Referenced studies that support the recommendation are summarized in the Online Data Supplement.**

| COR | LOE | Recommendation |
|---|---|---|
| 2a | B-R | 1. In patients with stroke or TIA of undetermined cause, initial cardiac monitoring and, if needed, extended monitoring with an implantable loop recorder are reasonable to improve detection of AF.[1] |

2. It is still necessary to demonstrate AF before the efficacy of OAC’s are seen in secondary prevention efficacy

Joglar JA, Chung MK, Armbruster AL, et al. *J Am Coll Cardiol*. 2024;83:109-279.

# CASE 2

A 68 year-old female with a history of HTN, HLP, hiatal hernia was admitted for acute right arm and right leg weakness with “stumbling gait.” No speech or facial involvement.

Physical examination verified mild right sided arm and leg weakness with paresthesias

MRI demonstrated acute/subacute lacunar infarct in left thalamus with some small vessel white matter disease

Echo shows LVEF 60-65%; negative bubble study; possible hiatal hernia compressing on left atrium

Patient started on DAPT and discharged with 2 week Zio patch monitor

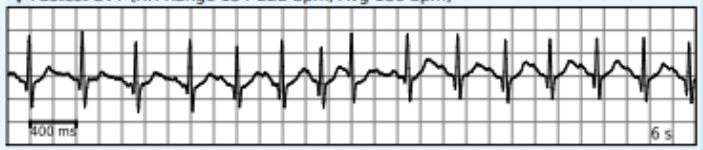
## Supraventricular Tachycardia (4 beats or more)

Episodes **26**

HR Range **86-222 bpm**

Avg **132 bpm**

▼ Fastest SVT (HR Range 154-222 bpm, Avg 186 bpm)




## Ventricular Tachycardia (4 beats or more)

None found

## Pauses (3 secs or longer)

None found

## AV Block (2nd° Mobitz II, 3rd°)

None found

## Atrial Fibrillation

**None found**

## Heart Rate

| | | | |
|---|---|---|---|
| **Overall** | Max | **222 bpm** | 02:58pm, 09/15 |
| | Min | **46 bpm** | 06:29am, 09/11 |
| | Avg | **77 bpm** | |
| **Sinus** | Max | **138 bpm** | 03:02pm, 09/15 |
| | Min | **46 bpm** | 06:29am, 09/11 |
| | Avg | **77 bpm** | |

## Patient Events

**Total Triggers: 0** **Total Diaries: 0**

Findings within ± 45 sec of triggered events or diary entries:

| | Range | Trigger | Diary |
|---|---|---|---|

None found

## Ectopics

| | Rare <1% | Occasional 1% to 5% | Frequent >5% |
|---|---|---|---|

### Supraventricular Ectopy (SVE/PACs)

| | | | |
|---|---|---|---|
| Isolated | **Rare** | <1.0% | |
| Couplet | **Rare** | <1.0% | |
| Triplet | **Rare** | <1.0% | |

### Ventricular Ectopy (VE/PVCs)

| | | | |
|---|---|---|---|
| Isolated | **Occasional** | 2.5% | 16469 |
| Couplet | **Rare** | <1.0% | 29 |
| Triplet | **0** | | |

| | |
|---|---|
| Longest Ventricular Bigeminy Episode | 5.1 s |
| Longest Ventricular Trigeminy Episode | 37.2 s |

## Preliminary Findings

Patient had a min HR of 46 bpm, max HR of 222 bpm, and avg HR of 77 bpm. Predominant underlying rhythm was Sinus Rhythm. Slight P wave morphology changes were noted. 26 Supraventricular Tachycardia runs occurred, the run with the fastest interval lasting 4 beats with a max rate of 222 bpm, the longest lasting 16 beats with an avg rate of 107 bpm. Isolated SVEs were rare (<1.0%), SVE Couplets were rare (<1.0%), and SVE Triplets were rare (<1.0%). Isolated VEs were occasional (2.5%, 16469), VE Couplets were rare (<1.0%, 29), and no VE Triplets were present. Ventricular Bigeminy and Trigeminy were present.

### Final Interpretation

Agree with Findings.
PSVT episodes - most likely paroxysmal atrial tachycardia. Longest episode - 8.8 seconds.

MERCYONE

1. Long-term monitoring or no monitoring?
2. How do we monitor and for how long?

Team A: Yes, a 30 day event recorder
Team B: No need for monitoring

The patient has had a small vessel non-embolic stroke as the proposed cause of stroke -- ”Secondary Prevention” – Case 3

1. What is benefit of long-term monitoring for AF?
2. What is the benefit of changing therapy to OAC if AF is detected?

J Am Heart Assoc. 2016 Sep 26;5(9):e004151. doi: 10.1161/JAHA.116.004151.

## Detection of Atrial Fibrillation Among Patients With Stroke Due to Large or Small Vessel Disease: A Meta-Analysis

Jelle Demeestere [1], Steffen Fieuws [2], Maarten G Lansberg [3], Robin Lemmens [4]

Affiliations + expand

PMID: 27671319 PMCID: PMC5079054 DOI: 10.1161/JAHA.116.004151

- Meta-analysis of 30 studies and 5687 patients demonstrated AF with short-term monitoring (max 7 days): 2.2% (large-vessel stroke), 2.4% (small-vessel stroke), 9.2% (cryptogenic stroke)

JAMA Neurology | Original Investigation

## Atrial Fibrillation In Patients With Stroke Attributed to Large- or Small-Vessel Disease

### 3-Year Results From the STROKE AF Randomized Clinical Trial

Richard A. Bernstein, MD, PhD; Hooman Kamel, MD; Christopher B. Granger, MD; Jonathan P. Piccini, MD; Jeffrey M. Katz, MD; Pramod P. Sethi, MD; Erika Pouliot, MS; Noreli Franco, PhD; Paul D. Ziegler, MS; Lee H. Schwamm, MD; for the STROKE AF Investigators

- STROKE-AF study – increased rate of AF detected by ILR in individuals with prior large or small vessel stroke (12.1% vs. 1.8%)

# Does treatment of AF events discovered during monitoring make a difference when other stoke etiologies (large/small vessel) suggested?

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 SEPTEMBER 28, 2023 VOL. 389 NO. 13

## Anticoagulation with Edoxaban in Patients with Atrial High-Rate Episodes

P. Kirchhof, T. Toennis, A. Goette, A.J. Camm, H.C. Diener, N. Becher, E. Bertaglia, C. Blomstrom Lundqvist, M. Borlich, A. Brandes, N. Cabanelas, M. Calvert, G. Chlouverakis, G.-A. Dan, J.R. de Groot, W. Dichtl, B. Kravchuk, A. Lubiński, E. Marijon, B. Merkely, L. Mont, A.-K. Ozga, K. Rajappan, A. Sarkozy, D. Scherr, R. Sznajder, V. Velchev, D. Wichterle, S. Sehner, E. Simantirakis, G.Y.H. Lip, P. Vardas, U. Schotten, and A. Zapf, for the NOAH-AFNET 6 Investigators*

**CONCLUSIONS**

Among patients with AHREs detected by implantable devices, anticoagulation with edoxaban did not significantly reduce the incidence of a composite of cardiovascular death, stroke, or systemic embolism as compared with placebo, but it led to a higher incidence of a composite of death or major bleeding. The incidence of stroke was low in both groups. (Funded by the German Center for Cardiovascular Research and others; NOAH-AFNET 6 ClinicalTrials.gov number, NCT02618577; ISRCTN number, ISRCTN17309850.)

ORIGINAL ARTICLE

## Apixaban for Stroke Prevention in Subclinical Atrial Fibrillation

J.S. Healey, R.D. Lopes, C.B. Granger, M. Alings, L. Rivard, W.F. McIntyre, D. Atar, D.H. Birnie, G. Boriani, A.J. Camm, D. Conen, J.W. Erath, M.R. Gold, S.H. Hohnloser, J. Ip, J. Kautzner, V. Kutyifa, C. Linde, P. Mabo, G. Mairesse, J. Benezet Mazuecos, J. Cosedis Nielsen, F. Philippon, M. Proietti, C. Sticherling, J.A. Wong, D.J. Wright, I.G. Zarraga, S.B. Coutts, A. Kaplan, M. Pombo, F. Ayala-Paredes, L. Xu, K. Simek, S. Nevills, R. Mian, and S.J. Connolly, for the ARTESIA Investigators*

**CONCLUSIONS**

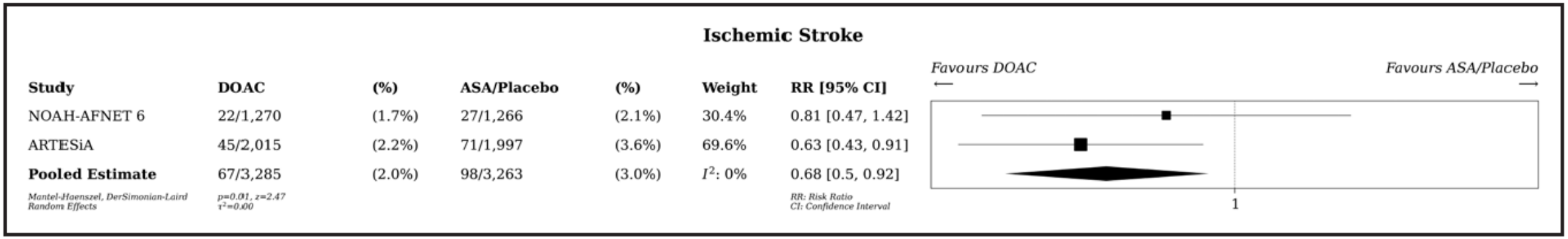
Among patients with subclinical atrial fibrillation, apixaban resulted in a lower risk of stroke or systemic embolism than aspirin but a higher risk of major bleeding. (Funded by the Canadian Institutes of Health Research and others; ARTESIA ClinicalTrials.gov number, NCT01938248.)

*Circulation*. 2024;149:981–988. DOI: 10.1161/CIRCULATIONAHA.123.067512

ORIGINAL RESEARCH ARTICLE

# Direct Oral Anticoagulants for Stroke Prevention in Patients With Device-Detected Atrial Fibrillation: A Study-Level Meta-Analysis of the NOAH-AFNET 6 and ARTESiA Trials

William F. McIntyre, MD, PhD; Alexander P. Benz, MD, MSc; Nina Becher, MD; Jeffrey S. Healey, MD, MSc; Christopher B. Granger, MD; Lena Rivard, MD, MSc; A. John Camm, MD; Andreas Goette, MD; Antonia Zapf, PhD; Marco Alings, MD, PhD; Stuart J. Connolly, MD, MSc; Paulus Kirchhof, MD; Renato D. Lopes, MD, MHS, PhD




**CONCLUSIONS:** The results of the NOAH-AFNET 6 and ARTESiA trials are consistent with each other. Meta-analysis of these 2 large randomized trials provides high-quality evidence that oral anticoagulation with edoxaban or apixaban reduces the risk of stroke in patients with device-detected atrial fibrillation and increases the risk of major bleeding.

# Further clarification in post-stroke population…

1. FIND AF2 – Germany - 2026/2027
2. ARTESIA Stroke Cohort – 2024/2025

The patient has had a small vessel non-embolic stroke as the proposed cause of stroke -- ”Secondary Prevention” – Case 3

For Now:

1. Long-term monitoring for AF could be considered for all strokes regardless of type
2. There appears to be some OAC treatment benefit of treating AF events > 6 minutes as seen by monitoring in patients of higher CHADS2VASC (stroke risk) scores

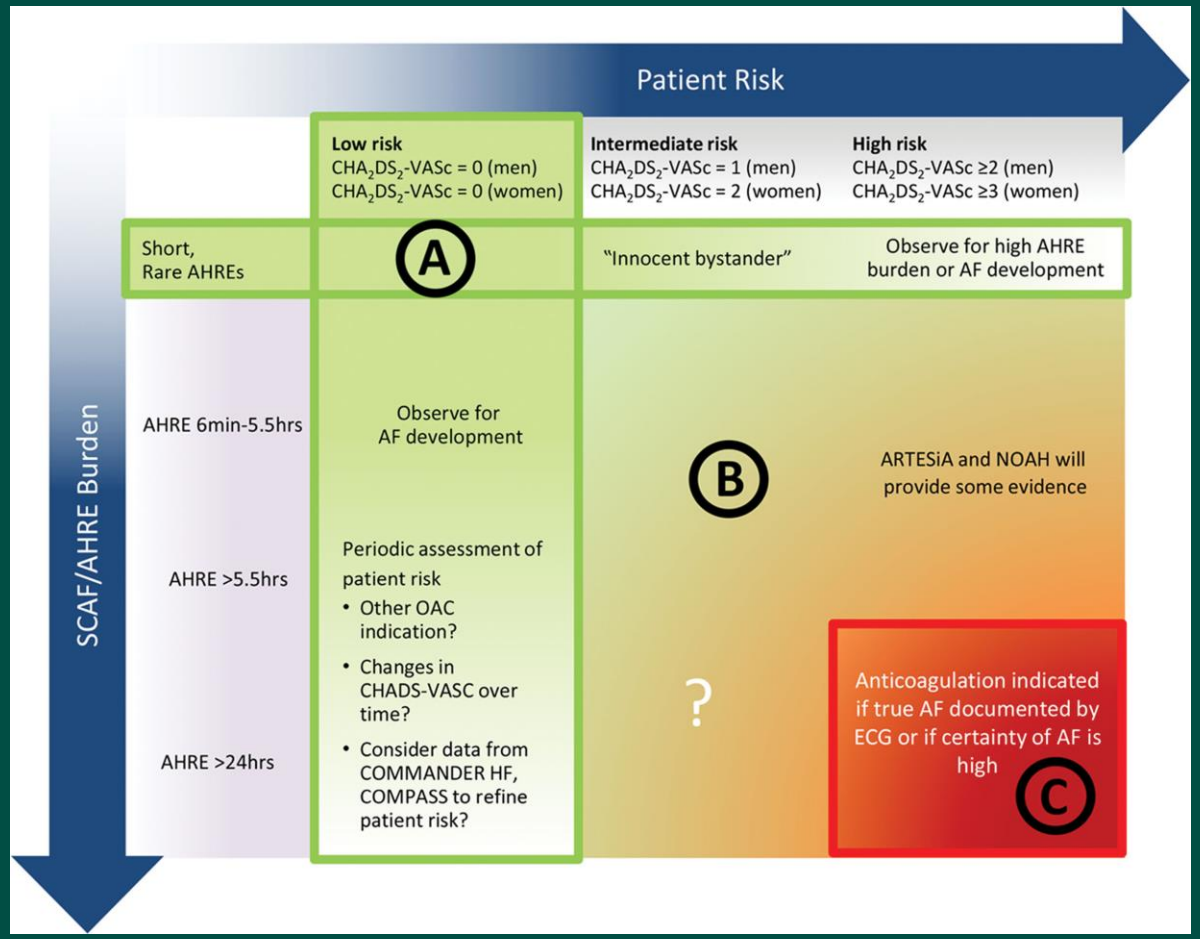
Summary

# How much AF should warrant anticoagulation?

# 2023 AF Guidelines

**Recommendations for Oral Anticoagulation for Device-Detected Atrial High-Rate Episodes Among Patients Without a Previous Diagnosis of AF**
**Referenced studies that support the recommendations are summarized in the Online Data Supplement.**

| COR | LOE | Recommendations |
|---|---|---|
| 2a | B-NR | 1. For patients with a device-detected atrial high-rate episode (AHRE) lasting ≥24 hours[1] and with a $CHA_2DS_2$-VASc score ≥2 or equivalent stroke risk,[2] it is reasonable to initiate oral anticoagulation[3] within a SDM framework that considers episode duration and individual patient risk. |
| 2b | B-NR | 2. For patients with a device-detected AHRE lasting between 5 minutes and 24 hours and with a $CHA_2DS_2$-VASc score ≥3 or equivalent stroke risk,[2] it may be reasonable to initiate anticoagulation within a SDM framework that considers episode duration and individual patient risk. |
| 3: No Benefit | B-NR | 3. Patients with a device-detected AHRE lasting <5 minutes and without another indication for oral anticoagulation should not receive oral anticoagulation.[4,5] |




Joglar JA, Chung MK, Armbruster AL, et al. *J Am Coll Cardiol*. 2024;83:109-279.

# Summary

1. Long-term monitoring recommended for most cryptogenic strokes
2. Monitoring plays less of a role when there is already an established need for anticoagulation
3. Monitoring may play a role in detection of AF in all post-stroke patients, regardless of type
4. Starting to see the integration of length of AF episode with baseline stroke risk when deciding need for anticoagulation