THE LINQ BETWEEN CRYPTOGENIC STROKE AND AF

Atrial fibrillation detection and treatment matters for improved stroke outcomes
CRYPTOGENIC STROKE IS A CHALLENGE

1 in 4
Stroke survivors will experience another stroke within 5 years.4

25%
Despite a comprehensive diagnostic workup, about 25% of ischemic stroke patients remain cryptogenic.2

Up to 30% of patients with cryptogenic stroke may have previously undetected paroxysmal AF.3

697,650
Americans experience ischemic strokes every year.1

5x
There is a 5-fold increase in ischemic stroke risk for AF patients.10

2x
More likely for AF-related ischemic stroke to be fatal than non-AF stroke.11

79%
of first AF episodes are asymptomatic at 12 months.3

AF Detection and Treatment Matters

Detection of AF in Cryptogenic Stroke Patients Changes Treatment

RE-SPECT ESUS and NAVIGATE ESUS trial results highlight the importance of detecting AF and tailoring treatment for cryptogenic stroke or ESUS patients.

Study Outcome

<table>
<thead>
<tr>
<th>Study</th>
<th>Outcome</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>NAVIGATE ESUS</td>
<td>NEGATIVE*</td>
<td>Increase in bleeding in the rivaroxaban arm</td>
</tr>
<tr>
<td>RE-SPECT ESUS</td>
<td>FAILED PRIMARY OUTCOME*</td>
<td>Dabigatran was not superior to ASA</td>
</tr>
</tbody>
</table>

AF Detection and Treatment

Cryptogenic stroke

- Atrial Fibrillation
- Anticoagulation* or other management
- Antiplatelet until AF is identified*5-7

*: If the patient is an appropriate candidate.

*1 in 4 Stroke survivors will experience another stroke within 5 years.4

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*697,650 Americans experience ischemic strokes every year.1

*5x There is a 5-fold increase in ischemic stroke risk for AF patients.10

*2 more likely for AF-related ischemic stroke to be fatal than non-AF stroke.11

*79% of first AF episodes are asymptomatic at 12 months.3

**CRYPTOGENIC STROKE**

SECONDARY STROKE PREVENTION IS ESSENTIAL

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SECONDARY STROKE PREVENTION IS ESSENTIAL
Atrial fibrillation after cryptogenic stroke was most often asymptomatic and paroxysmal and thus likely to be detected by strategies based on symptom-driven monitoring or intermittent short-term recordings.


The CRYSTAL-AF Study Demonstrates the Superiority of ICM for AF Detection

As published in the New England Journal of Medicine³

CRYSTAL-AF study results

<table>
<thead>
<tr>
<th>Months since Randomization</th>
<th>0</th>
<th>6</th>
<th>12</th>
<th>18</th>
<th>24</th>
<th>30</th>
<th>36</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atrial Fibrillation Detected (% of patients)</td>
<td>1.4%</td>
<td>2%</td>
<td>4.9%</td>
<td>8.9%</td>
<td>12.4%</td>
<td>18%</td>
<td>24%</td>
</tr>
</tbody>
</table>

Hazard ratio, 8.8 (95% CI, 3.5–22.2)  P < 0.001 by log-rank test

8.8X

30-DAY CARDIAC MONITORING IS NOT ENOUGH

Short-term and intermediate-term cardiac monitoring may miss many patients with paroxysmal AF³

30-DAY CARDIAC MONITORING IS NOT ENOUGH

Short-term and intermediate-term cardiac monitoring may miss many patients with paroxysmal AF³

Considerations for monitoring of cryptogenic stroke patients:

- 30% AF detected at 3 years vs. 3% for SOC.
- Multiple studies show that short-term monitoring is NOT sufficient for AF detection in cryptogenic stroke.¹²,¹³

“"Atrial fibrillation after cryptogenic stroke was most often asymptomatic and paroxysmal and thus likely to be detected by strategies based on symptom-driven monitoring or intermittent short-term recordings.”

Study objective: Evaluate the impact of prolonged cardiac rhythm monitoring (PCM) on secondary stroke prevention using data from available to date randomized clinical trials (RCTs) and observational studies.

The above forest plot represents the differences between prolonged (favors PCM) and conventional (favors non-PCM) cardiac rhythm monitoring in the risk of recurrent stroke.

The meta-analysis included 4 studies for a total of 1,102 patients:

<table>
<thead>
<tr>
<th>Study Name</th>
<th>Study Type</th>
<th>Conventional Cardiac Monitor Method</th>
<th>Total Number of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brown ESUS-AF</td>
<td>OS</td>
<td>30-day noninvasive ambulatory ECG monitoring</td>
<td>117</td>
</tr>
<tr>
<td>CRYSTAL-AF</td>
<td>RCT</td>
<td>ECG monitoring at scheduled and unscheduled visits at the discretion of the site investigator</td>
<td>441</td>
</tr>
<tr>
<td>FIND-AF</td>
<td>RCT</td>
<td>At least 2 hours ECG monitoring</td>
<td>398</td>
</tr>
<tr>
<td>Rodriguez-Campello, et al.</td>
<td>OS</td>
<td>24–36 hours ECG monitoring</td>
<td>146</td>
</tr>
</tbody>
</table>
INFORM YOUR CLINICAL DECISIONS WITH THE REVEAL LINQ™ ICM SYSTEM

Up to 3 YEARS of continuous cardiac monitoring

The Reveal LINQ insertable cardiac monitoring system transforms your ability to diagnose atrial fibrillation with its proven AF detection algorithm.

The world's smallest, most accurate insertable cardiac monitor\(^{17,18}\)

1.5T & 3T MRI CONDITIONAL

No post-insertion wait time or patient positioning restrictions\(^*\)

99.7% AF episode detection accuracy

Industry's highest AF episode detection accuracy rate\(^{19,20}\)

PATIENTS ARE MORE SATISFIED WITH ICMs THAN EXTERNAL WEARABLE MONITORS\(^21\)

Percentage of patients “very satisfied” with monitoring strategy was higher in ILR vs. ELR arm (21% vs. 10%)\(^21\)

Patient Satisfaction with Monitoring Strategy

- The Reveal LINQ ICM is inserted just under the skin of the patient’s chest in a short and simple procedure.
- The heart monitor is one-third the size of a AAA battery (1.2 cc) and is not visible in most patients.
- Use of the Reveal LINQ system doesn’t require a change in daily activities.

\(^*\) Reveal LINQ has been demonstrated to pose no known hazards in a specified MRI environment with specified conditions of use. Please see the Reveal ICM clinician manual or MRI technical manual for more details.

Overall Chi-square = 34.4; p < 0.001.

\(^*\) Bonferroni-adjusted pairwise comparison of column proportions p < 0.05.
GUIDELINES RECOMMEND ICM FOR PATIENTS WITH CRYPTOGENIC STROKE

2019 AHA/ACC/HRS Atrial Fibrillation Guidelines

Recommends use of implantable loop recorder (ILR) in patients with cryptogenic stroke (Class IIa, LOE B-R”).

RECOMMENDATIONS
In patients with cryptogenic stroke (i.e., stroke of unknown cause) in whom external ambulatory monitoring is inconclusive, implantation of a cardiac monitor (loop recorder) is reasonable to optimize detection of silent AF.

2016 ESC AF Guidelines

ICM recommendation for cryptogenic stroke (Class IIa, LOE B”).

RECOMMENDATIONS
In stroke patients, additional ECG monitoring by long-term, noninvasive ECG monitors or implanted loop recorders should be considered to document silent AF.

WHEN TO CONSIDER LOOKING FOR AF IN CRYPTOGENIC STROKE PATIENTS

Reveal LINQ ICM Indications*

- Patients with clinical syndromes or situations at increased risk of cardiac arrhythmias
- Patients who experience transient symptoms such as dizziness, palpitation, syncope, and chest pain, that may suggest a cardiac arrhythmia

Appropriate

- Stroke detected by CT or MRI that is not lacunar
- Absence of extracranial or intracranial atherosclerosis causing ≥ 50% luminal stenosis in arteries supplying the area of ischaemia
- No major-risk cardioembolic source of embolism
- No other specific cause of stroke identified (e.g., arteritis, dissection, migraine/vasospasm, drug misuse)
- First event — stroke or high-risk TIA
- CHADS₂ score ≥ 2 (minimal risk factors)

Not Appropriate

- Indication for chronic anticoagulation or already on anticoagulation
- Patients with a relative contraindication for long-term anticoagulation and not appropriate for LAA closure device

*Class IIa is Benefit >> Risk and LOE B-R is moderate quality of evidence from 1 or more RCTs or meta-analysis of moderate-quality RCTs.
†Endorsed by the European Stroke Organization (ESO). Class IIa is weight of evidence/opinion is in favor of usefulness/efficacy. LOE B is data derived from a single randomized clinical trial or large nonrandomized studies.

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*See full brief statement for complete indications for use.
†ABCD² Score > 5.
Pathway based on the consensus of the Cryptogenic Stroke Pathway steering committee. February 2016.
PLANNING THE CRYPTOGENIC STROKE PATHWAY

Many cryptogenic stroke patients are lost to follow-up. Pathways for transition of care and follow-up help to ensure these patients receive better care.

Why establish a cryptogenic stroke pathway?

Establishing a monitoring pathway to detect and treat AF can significantly reduce a patient’s risk for another stroke. When developing a cryptogenic stroke pathway, it is important to include all stakeholders involved in the care of the patient.

PATHWAY TIPS

- Less than 4% of ischemic stroke patients who initially receive short-term external cardiac monitoring (up to 30 days) go on to receive an ICM.16
- Ischemic stroke patients seen by an electrophysiologist are 4x more likely to receive an ICM than a patient seen by a practitioner from a different specialty.16
- The diagnostic yield of 30 days of monitoring is likely to be limited. Data suggest a rationale for proceeding directly to ILR prior to hospital discharge in cryptogenic stroke patients.23
CRYSTAL-AF study found that continuous monitoring with Reveal LINQ ICM is superior to standard monitoring for the detection of AF in cryptogenic stroke patients. 

30% AF DETECTED AT 3 YEARS WITH ICM vs. 3% for SOC

SHORT-TERM MONITORING IS NOT ENOUGH

88% of patients who had AF would have been missed if only monitored for 30 days*

PROLONGED CARDIAC MONITORING AND SECONDARY STROKE PREVENTION

55% Lower stroke recurrence in patients with cryptogenic stroke/TIA undergoing prolonged vs. conventional cardiac monitoring.**

*Based on Kaplan-Meier estimates.