REVEAL AF IN YOUR CRYPTOGENIC STROKE PATIENTS

Are You Looking Long Enough?

Medtronic
ONE-THIRD OF ISCHEMIC STROKES ARE CRYPTOGENIC (UNEXPLAINED) \(^1-^6\)

Each year, at least 200,000 cryptogenic strokes occur in the United States \(^7\).

Cryptogenic stroke accounts for approximately one-third of ischemic strokes in the majority of modern stroke registries and databases \(^1-^6\).

- Cryptogenic stroke is as prevalent as large vessel stroke.

AF DETECTION AND TREATMENT MATTERS

2016 ESC Guidelines for the management of atrial fibrillation \(^11\)

- Guidelines developed by the Task Force for the management of atrial fibrillation of the European Society of Cardiology (ESC).
- Developed with the special contribution of the European Heart Rhythm Association (EHRA) of the ESC.
- Endorsed by the European Stroke Organisation (ESO).

Guideline Recommendation

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

Class IIa

Level B

AF detection and monitoring modality selection matters for cryptogenic stroke patients

- The ability to identify AF in patients with cryptogenic stroke has profound implications for long-term medical management \(^12\).
- Recurrence was more frequent and functional deficits were more likely to be severe among survivors of AF-related ischemic stroke \(^9\).
- Guidelines also recommend anticoagulant therapy for stroke prevention in most patients with AF \(^13\).

5-FOLD

Increase in ischemic stroke risk for AF patients \(^8\).

2X

More likely for AF-related ischemic stroke to be fatal as non-AF stroke \(^9\).

67%

Decrease in AF patient stroke risk with oral anticoagulants \(^10\).
ARE YOU MONITORING CRYPTOGENIC STROKE PATIENTS LONG ENOUGH?

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

AF episode
Repeated short-term monitoring

Long-term, continuous monitoring (up to 3 years)

84 DAYS

Median time to detect AF following cryptogenic stroke:

30 days 12 months 24 months 36 months

Short-term monitoring (up to 1 week)
Intermediate-term monitoring (up to 30 days)

Note: Illustration purposes only

84 DAYS is the median time to AF detection in cryptogenic stroke patients.

79% of first AF episodes were asymptomatic at 12 months.

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

*Based on Kaplan-Meier estimates.

INFORM YOUR CLINICAL DECISIONS WITH THE REVEAL LINQ™ ICM SYSTEM

Up to 3 YEARS of continuous cardiac monitoring

The revolutionary Reveal LINQ Insertable Cardiac Monitoring System transforms your ability to diagnose atrial fibrillation with its proven AF detection algorithm.

Simple, minimally invasive insertion procedure

- The Reveal LINQ ICM is placed just under the skin of the patient's chest in a simple procedure
- The ultra-discreet heart monitor is not visible in most patients
- Patients prefer the Reveal LINQ ICM over external wearable monitors

Safe for use in MRI setting same day at 1.5 and 3.0 Tesla*

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

The clinic receives easy-to-use and clinically actionable Reveal LINQ reports via the CareLink™ Network.

The world's smallest insertable cardiac monitor

TheReveal LINQ ICM continuously records heart rhythm data and sends them wirelessly to the MyCareLink™ Patient Monitor.

The MyCareLink Patient Monitor transmits data from the Reveal LINQ ICM to the clinic via a global cellular connection.
THE CRYSTAL-AF STUDY DEMONSTRATES THE SUPERIORITY OF ICM FOR AF DETECTION IN PATIENTS WITH CRYPTOGENIC STROKE

As published in the New England Journal of Medicine

<table>
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<tr>
<th>STUDY DESIGN</th>
<th>PATIENT INCLUSION CRITERIA</th>
<th>END POINTS</th>
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<tr>
<td>Randomized, controlled clinical trial with 441 patients</td>
<td>≥ 40 years of age</td>
<td>Primary</td>
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<td>Compared continuous, long-term monitoring with Reveal™ ICM vs. conventional follow-up</td>
<td>Cryptogenic stroke (or clinical TIA) with infarct seen on MRI or CT within the previous 90 days and no mechanism identified after:</td>
<td>Time to first detection of AF at 6 months of follow-up</td>
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<td>Assessment at scheduled and unscheduled visits</td>
<td>– 12-lead ECG</td>
<td>Secondary</td>
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<td>ECG monitoring performed at the discretion of the site investigator</td>
<td>– 24-hour ECG monitoring (e.g., Holter)</td>
<td>Time to first detection of AF at 12 months of follow-up</td>
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<tr>
<td>ECG monitoring performed at the discretion of the site investigator</td>
<td>– Transesophageal echocardiography</td>
<td>Recurrent stroke or TIA</td>
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<td>– CTA or MRA of head and neck to rule out arterial source</td>
<td>Actions taken after patient diagnosed with AF</td>
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<td></td>
<td>– Screening for hypercoagulable states in patients &lt; 55 years old</td>
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The CRYSTAL-AF Study found that continuous monitoring with Reveal ICM is superior to standard medical care for the detection of AF in cryptogenic stroke patients.

Visit CRYSTAL-AF.com for complete study information.

Clinical impact: More appropriate care

Short-term cardiac monitoring is NOT sufficient for AF detection in cryptogenic stroke

- Extensive external monitoring found few patients with AF
  - In the control group at 6 months, only 3 patients were found to have AF; yet there were 88 conventional ECGs, 20 24-hour Holters, and 1 event recorder used
  - RevealICM detected over 7 times more patients with AF at the 12-month end point

Conclusions:

- Reveal ICM detected over 7 times more patients with AF at the 12-month end point
- More AF detected at 36 months: 30% in ICM group vs. 3.0% in control

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

**CRYSTAL-AF study results**

- More AF detected at 6 months: 8.9% in ICM group vs. 1.4% in control
- More AF detected at 12 months: 12.4% in ICM group vs. 2.0% in control
- More AF detected at 36 months: 30% in ICM group vs. 3.0% in control

**END POINTS**

<table>
<thead>
<tr>
<th>at risk</th>
<th>Months since randomization</th>
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<tr>
<td>Control</td>
<td>220 194 167 114 72 36 7</td>
</tr>
<tr>
<td>ICM</td>
<td>221 191 173 102 57 29 8</td>
</tr>
</tbody>
</table>

Hazard ratio, 8.8 (95% CI, 3.5 - 22.2) P < 0.001 by log-rank test
**ISCHEMIC STROKE PATHWAY**

**Ischemic Stroke/TIA**

- Lacunar infarction: small vessel disease
- Embolic appearing stroke with no history of AF:
  - Multiple foci of infarction
  - Cortical watershed distribution
  - Cerebellar
- History of AF
  - Standard stroke work-up
  - Antiplatelet agent

  - MRA or CTA of intracranial vessels
  - Transesophageal Echocardiogram (TEE)

  - Standard stroke work-up
  - LUM or CTA of intracranial vessels
  - Transesophageal Echocardiogram (TEE)

  - Medical management
  - Antiplatelet agents

  - Anticoagulant

- Symptomatic carotid stenosis: greater than 50%
  - CEA or stent
  - Inpatient
  - Intracranial stenosis
  - Positive TEE
  - Anticoagulant
  - Medical management
  - Antiplatelet agents

- Glucose control
- Blood pressure management
- Hypercoagulation labs if age < 50

**Lacunar infarction**

**Standard stroke work-up**

**Cryptogenic Stroke PATHWAY**

**Patient Diagnosed with Cryptogenic Stroke/TIA**

- Could detection of suspected AF impact patient management?
  - YES
  - Refer to cardiology to insert Reveal LINQ ICM
  - Insert Reveal LINQ ICM prior to discharge
   - If unable to insert prior to discharge, potential external monitor bridge and schedule Reveal LINQ ICM expeditiously
   - Enroll in CareLink Network & perform remote monitoring
   - Schedule clinical follow-up with treating physician and ensure long-term adherence to monitoring
   - AF detected
   - AF not detected
  - Insert Reveal LINQ ICM
  - Outpatient
  - Bridge with external monitor

- NO
  - Not a candidate

Pathway based on the consensus of the Cryptogenic Stroke Pathway steering committee. February 2016.

Medtronic Disclosure Statement: This pathway is provided for educational purposes and should not be considered the exclusive source for this type of information. It is the responsibility of the practitioner to exercise independent clinical judgment.

Refer to the brief statement for indications, warnings/precautions, and complications for the Reveal LINQ ICM.
References


Brief Statement

Indications

Reveal LINQ® LNQ11 Insertable Cardiac Monitor and Patient Assistant

The Reveal LINQ Insertable Cardiac Monitor is an implantable patient-activated and automatically-activated monitoring system that records subclinical EEG and is indicated in the following cases:

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

This device has not specifically been tested for pediatric use.

Patient Assistant

The Patient Assistant is intended for unsupervised patient use away from a hospital or clinic. The Patient Assistant activates the data management feature in the Reveal Insertable Cardiac Monitor to initiate recording of cardiac event data in the implanted device memory.

Contraindications

There are no known contraindications for the implant of the Reveal LINQ Insertable Cardiac Monitor. However, the patient’s particular medical condition may dictate whether or not a subcutaneous, chronically implanted device can be tolerated.

Warnings/Precautions

Reveal LINQ LNQ11 Insertable Cardiac Monitor

Patients with the Reveal LINQ Insertable Cardiac Monitor should avoid sources of diathermy, high sources of radiation, electrocautery, microwave diathermy, lithotripsy, therapeutic ultrasound, and radiofrequency ablation to avoid electrical reset of the device, and/or inappropriate sensing as described in the Medical procedure and EMI precautions manual.

MRI scans should be performed only in a specified MRI environment under specified conditions as described in the Reveal LINQ-MRI Technical Manual.

Patient Assistant

Operation of the Patient Assistant near sources of electromagnetic interference, such as cellular phones, computer monitors, etc., may adversely affect the performance of this device.

Potential Complications

Potential complications include, but are not limited to, device rejection phenomena (including local tissue reaction), device migration, infection, and erosion through the skin.

Medtronic MyCareLink™ Patient Monitor, Medtronic CareLink™ Network and CareLink™ Mobile Application

Intended Use

The Medtronic MyCareLink Patient Monitor and CareLink Network are indicated for use in the transfer of patient data from some Medtronic implantable cardiac devices based on physician instructions and as described in the product manual. The CareLink Mobile Application is intended to provide current CareLink Network customers access to CareLink Network data via a mobile device for their convenience. The CareLink Mobile Application is not replacing the full workstation, but can be used to review patient data when a physician does not have access to a workstation. These products are not a substitute for appropriate medical attention in the event of an emergency and should only be used as directed by a physician. CareLink Network availability and mobile device accessibility may be unavailable at times due to maintenance or updates, or due to coverage being unavailable in your area. Mobile device access to the Internet is required and subject to coverage availability. Standard text messaging rates apply.

Contraindications

There are no known contraindications.

Warnings and Precautions

The MyCareLink Patient Monitor must only be used for interrogating compatible Medtronic implantable devices.

See the device manual for detailed information regarding the implant procedure, indications, contraindications, warnings, precautions, and potential complications/adverse events. For further information, please call Medtronic at 1-800-328-2518 and/or consult the Medtronic website at www.medtronic.com.

Cautions

Federal law (USA) restricts these devices to sale by or on the order of a physician.
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84 Days

is the median time to AF detection in cryptogenic stroke patients

30%

AF-Detection Rate at 3 Years

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