Mr. DW

RFC: Cryptogenic Stroke; ?AF
74 yo-WM
*Presented to Bryan West 3/23 with acute left MCA stroke and small right subcortical stroke (aphasia, right sided ataxia)
*Was working in his shop when he developed weakness, expressive aphasia, and facial droop. Denies palpitations, CP, syncope.
*TPA given with near resolution of symptoms
*EKG: SR, LAD
* Normal TTE/TEE
*Mild bilateral carotid stenosis
*No arrhythmias on telemetry
DW’s story, continued

*Remote history of MVA 2011, complicated by left hydropneumothorax, required thoracentesis, VATS and decongestion bronchoscopy

*Wife states “I wonder if he didn’t have a stroke back then…”

*MPS stress testing was normal at the time

*No arrhythmias had been documented at any point during his extensive hospital stay

*Medtronic REVEAL LINQ implanted 3/26
Cardiac Diagnostics Landscape

Indications for Cardiac Monitoring

- Evaluation of syncope
  - Bradycardia or tachycardia mediated
- Atrial fibrillation
  - Diagnosis
  - Determine rate and rhythm control/burden/duration
  - Post AF ablation surveillance
- Cryptogenic stroke
  - Asymptomatic atrial arrhythmias
Types of Monitors Available

- Continuous telemetry monitors
- External event activated recorders
- Mobile Cardiac Monitors
- Implantable loop recorders

---

Holter Monitors

**Uses**
- Patients experiencing daily symptoms
- Quantifying arrhythmias

**Drawbacks**
- Short duration of data recording (24-48 hrs)
- Patient must experience arrhythmia during 24-48 hr period
- No real-time physician notification

*Diagnostic yield: 5% - 13%*¹

---

Looping Event Monitors

- Requires external leads
- Patient must be able to recognize symptoms and trigger device
  - Equates to ability to use an ATM machine
- Optimal monitoring duration: 2 weeks¹
- "Autotrigger" (AT-LR): record arrhythmias without patient trigger
  - Algorithm based, asymptomatic arrhythmias
  - AT-LR increased diagnostic yield in both symptomatic and asymptomatic arrhythmias compared to Holter/EM²

---
Post Event Recorders

- Easier to tolerate
- Initiation and termination of a symptomatic event is often not recorded
- Patient needs to activate device during an arrhythmia
- Best use in patients with prolonged symptoms

Mobile Cardiac Telemetry Monitors

- Device automatically records based on preset parameters for arrhythmia acquisition
  - Sensor either transmits automatically or via handheld device to a central monitoring station using cellular system
  - Symptoms can also be added to transmission
- Direct contact between patient and monitoring company

As Cardiac Monitoring Evolves, Diagnostic Yield Improves
Follow-up AF Detection Depends on Monitoring Strategy

Heart Rhythm Society on Long Term Continuous Monitoring

Implantable Loop Recorders

CRYptogenic STroke And underLying Atrial Fibrillation (CRYSTAL AF)

As Published in the New England Journal of Medicine

Clinical Study Summary
Background

• 30% of ischemic strokes are of unknown mechanism (cryptogenic stroke)
• Detection of AF usually prompts long-term anticoagulation instead of antiplatelet therapy
• Optimal monitoring duration to detect AF is currently undetermined
• AF may be paroxysmal, occur rarely, and be asymptomatic, making detection with routine methods difficult

Objectives of CRYSTAL AF

• To assess whether a long-term monitoring strategy with an insertable cardiac monitor (ICM) is superior to standard medical care for the detection of AF in patients with a cryptogenic stroke at 6 months (primary end point) and 12 months follow-up (secondary end point)
• Determine the proportion of patients with cryptogenic stroke that have underlying AF.
• Determine actions taken after patient is diagnosed with AF

Key Inclusion/Exclusion Criteria

Inclusion:
• ≥40 years of age
• Cryptogenic stroke (or clinical TIA), with infarct seen on MRI or CT, within the previous 90 days, and no mechanism (including AF) determined after:
  • 12-lead ECG
  • 24-hour ECG monitoring (e.g. Holter)
  • Transesophageal echocardiography (TEE)
  • CTA or MRA of head and neck to rule out arterial source
  • Screening for hypercoagulable states in patients <55 years old

Exclusion:
• History of AF or Atrial Flutter
• Permanent indication or contraindication for anticoagulation
• Indication for pacemaker or implantable cardioverter defibrillator
Comparison of Monitoring Strategies

Continuous Monitoring Arm: Insertion of REVEAL® XT
- Minimally invasive outpatient procedure
- Local anesthetic and no leads or fluoroscopy
- 15-30 minute procedure
- Device can be followed remotely
- MRI conditional
- 3 year device longevity
- Automatic AF detection algorithm

Standard Monitoring Arm
- Cardiac monitoring performed according to local standards, after mandated testing completed
- Symptoms consistent with AF were evaluated by study physicians

Patient Follow-up
- Patients in both arms received scheduled follow-up visits at:
  - 1 month
  - 6 months
  - 12 months
  - Every 6 months thereafter until study closure
- Follow-up visits recorded:
  - Cardiac symptoms
  - Treatment modifications
  - Recurrence of stroke or TIA
  - Modified Rankin Scale
  - Health status (EQ-5D)

Methods
- AF defined as an episode of irregular heart rhythm, without detectable p waves, greater than 30 seconds
- AF episodes were identified by patient’s physician and adjudicated by an independent committee
Baseline Characteristics:

<table>
<thead>
<tr>
<th></th>
<th>ICM</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>61.9 ± 11.4 years</td>
<td>61.4 ± 11.3 years</td>
</tr>
<tr>
<td>Gender - Male</td>
<td>142 (64.3%)</td>
<td>138 (62.7%)</td>
</tr>
<tr>
<td>Index Event – Stroke</td>
<td>200 (90.5%)</td>
<td>201 (91.4%)</td>
</tr>
<tr>
<td>Index Event – TIA</td>
<td>21 (9.5%)</td>
<td>19 (8.6%)</td>
</tr>
<tr>
<td>Pre-enrollment AF screening – Holter Monitoring</td>
<td>71.5% of patients (IQR 21-34)</td>
<td>70.9% of patients (IQR 22-34)</td>
</tr>
<tr>
<td>Pre-enrollment AF screening – Telemetry</td>
<td>29.9% of patients (IQR 36-96)</td>
<td>29.5% of patients (IQR 48-96)</td>
</tr>
<tr>
<td>Time between index event and randomization</td>
<td>36.6 ± 28.2 days</td>
<td>39.6 ± 26.9 days</td>
</tr>
<tr>
<td>Time between randomization and device insertion</td>
<td>8.7 ± 27.6 days</td>
<td>n/a</td>
</tr>
</tbody>
</table>

Primary Endpoint: Detection of AF at 6 months
ICM finds 6x more patients with AF

Rate of detection in ICM arm was 8.4% vs 1.4% in control arm
### 6 Month Endpoints

<table>
<thead>
<tr>
<th></th>
<th>ICM</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median time from randomization to AF Detection</td>
<td>41 days</td>
<td>32 days</td>
</tr>
<tr>
<td>Patients found to have AF</td>
<td>19</td>
<td>3</td>
</tr>
<tr>
<td>% Asymptomatic Episodes</td>
<td>74%</td>
<td>33%</td>
</tr>
<tr>
<td>Oral Anticoagulation (OAC) Usage, overall</td>
<td>10.1%</td>
<td>4.6%</td>
</tr>
<tr>
<td>OAC use in patients with detected AF</td>
<td>94.7%</td>
<td>66.7%</td>
</tr>
<tr>
<td>Recurrent Stroke/TIA</td>
<td>5.2%</td>
<td>8.6%</td>
</tr>
<tr>
<td>Proportion of patients with AF ≥ 6 minutes on one day</td>
<td>93.8%</td>
<td>N/A</td>
</tr>
<tr>
<td>Tests required to detect AF</td>
<td>Automatic AF detection</td>
<td>88 ECGs, 20 24-hour Holters, 1 event recorder</td>
</tr>
</tbody>
</table>

### Secondary Endpoint: Detection of AF at 12 months

ICM finds 7x more patients with AF

Rate of detection in ICM arm was 12.4% vs 2.0% in control arm

### 12 Month Endpoints

<table>
<thead>
<tr>
<th></th>
<th>ICM</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median time from randomization to AF Detection</td>
<td>84 days</td>
<td>52.5 days</td>
</tr>
<tr>
<td>Patients found to have AF</td>
<td>29</td>
<td>4</td>
</tr>
<tr>
<td>% Asymptomatic Episodes</td>
<td>79%</td>
<td>50%</td>
</tr>
<tr>
<td>Oral Anticoagulation (OAC) Usage, overall</td>
<td>14.7%</td>
<td>6.0%</td>
</tr>
<tr>
<td>OAC use in patients with detected AF</td>
<td>96.6%</td>
<td>100%</td>
</tr>
<tr>
<td>Recurrent Stroke/TIA</td>
<td>7.1%</td>
<td>9.1%</td>
</tr>
<tr>
<td>Proportion of patients with AF ≥ 6 minutes on one day</td>
<td>92.3%</td>
<td>N/A</td>
</tr>
<tr>
<td>Tests required to detect AF</td>
<td>Automatic AF detection</td>
<td>121 ECGs, 32 24-hour Holters, 1 Event Recorder</td>
</tr>
</tbody>
</table>
Detection of AF at 36 months
ICM finds 8.8x more patients with AF

Rate of detection in ICM arm was 30% vs 3% in control arm.

36 Month Data

<table>
<thead>
<tr>
<th></th>
<th>ICM</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median time from randomization to AF Detection</td>
<td>255 days</td>
<td>72 days</td>
</tr>
<tr>
<td>Patients found to have AF</td>
<td>42</td>
<td>5</td>
</tr>
<tr>
<td>% Asymptomatic Episodes</td>
<td>81%</td>
<td>40%</td>
</tr>
<tr>
<td>Oral Anticoagulation (OAC) Usage, overall</td>
<td>38.5%</td>
<td>8.3%</td>
</tr>
<tr>
<td>OAC use in patients with detected AF</td>
<td>90%</td>
<td>80%</td>
</tr>
<tr>
<td>Recurrent Stroke/TIA</td>
<td>11.1%</td>
<td>12.7%</td>
</tr>
<tr>
<td>Proportion of patients with AF ≥ 6 minutes on one day</td>
<td>94.9%</td>
<td>N/A</td>
</tr>
<tr>
<td>Tests required to detect AF</td>
<td>Automatic AF detection</td>
<td>202 ECGs, 52 Holter Monitors, 1 Event Recorder</td>
</tr>
</tbody>
</table>

Conclusions

Continuous monitoring with Reveal ICM is superior to standard medical care for the detection of AF in patients with a cryptogenic stroke.

The study demonstrated that:

1. Continuous monitoring detected over 7 times more patients with AF at the 12-month end point.
2. At 3 years, AF was detected at a rate of 30% in the ICM arm vs. only 3% in the Standard Monitoring arm.
3. Short-term monitoring is not sufficient, as the median time to AF detection over 12 months of follow-up was 84 days.
4. 97% of patients who had AF detected were prescribed OAC.
Reference


Brief Statement

Indications

The Reveal XT Insertable Cardiac Monitor is an implantable patient-activated and automatically-activated monitoring system that records subcutaneous ECG 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, palpitation, syncope and chest pain, that may suggest a cardiac arrhythmia.

Reveal XT Patient Assistant

The Reveal XT and Reveal Patient Assistant is intended for unsupervised patient use away from a hospital or clinic. The Patient Assistant activates one or more of the data management features in the Reveal Insertable Cardiac Monitor:

- To verify whether the implanted device has detected a suspected arrhythmia or device related event.
- To initiate recording of cardiac event data in the implanted device memory.

Contraindications

There are no known contraindications for the implant of the Reveal XT 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 XT Insertable Cardiac Monitors

Patients with the Reveal XT should avoid sources of diathermy, high sources of radiation, electrosurgical cautery, external defibrillation, lithotripsy, therapeutic ultrasound and radiofrequency ablation to avoid electrical reset of the device, and/or inappropriate sensing. MRI scans should be performed only in a specified MR environment under specified conditions as described in the device manual.

Reveal XT Patient Assistants

Operation of the Model 9539 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.

For further information, please call Medtronic at 1-800-328-2518 and/or consult Medtronic's website at www.medtronic.com.

Caution:

Federal law (USA) restricts this device to sale by or on the order of a physician.

World Headquarters

Medtronic, Inc.
710 Medtronic Parkway
Minneapolis, MN 55432-5604
USA
Tel: (763) 514-4000
Fax: (763) 514-4879
www.medtronic.com

Now, back to our patient...
AF was Mr. DW’s “Missing Link”

*Started on Apixaban
*LINQ explant
*Dual Chamber Pacer Implant

Thanks for your attention
Go Big Red!