ECG monitoring after ischemic stroke of TIA of unknown source with an insertable monitor?

YES

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The Netherlands

ESC stroke council Prague January 2018
The problem: 25% of ischemic strokes is cryptogenic

Ischaemic stroke

- 25% large artery atherosclerotic stenosis
  - imaging echo-Doppler

- 25% small artery disease (lacunes)
  - specific neurology diagnosis

- 25% ESUS cryptogenic stroke
  - maybe AF

- 20% major risk source cardiogenic embolism
  - maybe AF previous AF LV aneurysm mitral stenosis

- 5% unusual e.g. dissections, arteritis
  - specific vascular diagnosis

ECG monitoring for >24h
ESUS

- Embolic Stroke of Unknown Source (ESUS) occurs frequently
- Now 24 hour Holter monitoring recommended
- But detection of AF has important therapeutic implications
- And not that this is secondary prevention!!
What are the data?

- High risk patients without clinical AF
ASSERT II

- Patients ≥ 65 years at cardiology or neurology department but NO history of AF
- Inclusion if:
  - CHA$_2$DS$_2$-VASc ≥ 2, or
  - OSAS, or
  - BMI > 30 kg/m$^2$, or
  - And LA ≥ 44mm or LAV ≥ 58 mL, or
  - NT-proBNP ≥ 290 pg/ml
- Primary endpoint: SCAF ≥ 5 min
ASSERT II

- 256 patients
- Mean age 74 years
- CHA$_2$DS$_2$-VASc = 4
- LA 47 mm
- 48% prior stroke or TIA or embolism
ASSERT II

- SCAF occurred in 90 pts: 34% per year
- 39% per year if previous stroke
- Baseline predictors:
  - Age
  - LA size
  - Blood pressure
Objectives

GOAL:
• To determine the incidence of previously undiagnosed AF with ICM* monitoring in a high-risk population.

PRIMARY ENDPOINT:
• Incidence of AF (adjudicated, ≥6 minutes) at 18 months in patients at high risk for, but without previously known AF.

* ICM = insertable cardiac monitor with AF detection capabilities
REVEAL AF study

Methods

DESIGN:
- Prospective, single-arm, open-label, multi-center, post-market study.

INCLUSION CRITERIA:
- CHADS<sub>2</sub> score of ≥ 3 or CHADS<sub>2</sub> = 2 and at least 1 of the following:
  - Coronary artery disease
  - Renal impairment (GFR 30-60 ml/min)
  - Sleep apnea
  - Chronic obstructive pulmonary disease

[ At least 70 pts were required for each CHADS<sub>2</sub> group (2, 3, ≥4 ) ]

Enrollment
Baseline
Successful Reveal
ICM insertion
Monthly device transmission
In-office follow-up visits every 6 months for a minimum of 18 and maximum of 30 months
The study population represents a common group of patients encountered in clinical practice.

### Baseline Demographics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Subjects with device insertion (N = 394)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Device inserted/attempted</td>
<td></td>
</tr>
<tr>
<td>Reveal LINQ™ ICM</td>
<td>272 (69.0%)</td>
</tr>
<tr>
<td>Reveal™ XT ICM</td>
<td>122 (31.0%)</td>
</tr>
<tr>
<td>Gender: male</td>
<td></td>
</tr>
<tr>
<td></td>
<td>206 (52.3%)</td>
</tr>
<tr>
<td>Age</td>
<td></td>
</tr>
<tr>
<td>Years (mean ± standard deviation)</td>
<td>71.6 ± 9.8</td>
</tr>
<tr>
<td>Under 65</td>
<td>88 (22.3%)</td>
</tr>
<tr>
<td>65 to 75</td>
<td>131 (33.3%)</td>
</tr>
<tr>
<td>75 and older</td>
<td>175 (44.4%)</td>
</tr>
<tr>
<td>Medical history</td>
<td></td>
</tr>
<tr>
<td>Renal dysfunction</td>
<td>64 (16.2%)</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>81 (20.6%)</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>233 (59.1%)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>369 (93.7%)</td>
</tr>
<tr>
<td>COPD</td>
<td>76 (19.3%)</td>
</tr>
<tr>
<td>Sleep apnea</td>
<td>104 (26.4%)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>248 (62.9%)</td>
</tr>
<tr>
<td>Vascular disease</td>
<td></td>
</tr>
<tr>
<td>Remote cerebrovascular accident (stroke)</td>
<td>80 (20.3%)</td>
</tr>
<tr>
<td>Remote transient ischemic attack</td>
<td>76 (19.3%)</td>
</tr>
</tbody>
</table>

36.5%
REVEAL AF study

Incidence of AF Lasting ≥ 6 Minutes

Median time to detection: 123 [IQR 41-330] days.

Detection rate at:
- **18 months** (primary endpoint): 29.3%.
- 30 days: 6.2%.
- 30 months: 40.0%.

AF may have gone undetected in over three-quarters of patients had monitoring been limited to 30 days.

Reiffel for the REVEAL AF Investigators JAMA Cardiology 2017
What are the data?

- Thus subclinical AF in patients at risk for stroke is high
- 30% per year
Monitoring in ESUS patients without known AF

- What show the studies in ESUS patients who are monitored for > 24 hours?
Long term monitoring in cryptogenic stroke
EMBRACE-AF

- 572 patients > 55 years with cryptogenic stroke
- No prior AF
- Randomized to 30 days event triggered monitoring (irregular rhythm) versus repeat 24 hour Holter monitoring
- Primary outcome: SCAF > 30 seconds detected during first 6 months
Long term monitoring in cryptogenic stroke
EMBRACE-AF

![Graph showing the percentage of patients with atrial fibrillation detected over different durations of ECG monitoring.]

- 24 Hr: 2.2%
- 1 Week: 7.4%
- 2 Weeks: 11.6%
- 3 Weeks: 12.3%
- 4 Weeks: 14.8%

Duration of ECG Monitoring
## Long term monitoring in cryptogenic stroke

### EMBRACE-AF

<table>
<thead>
<tr>
<th>Primary Outcome</th>
<th>Repeat Holter (n=285)</th>
<th>30-day Monitor (n=287)</th>
<th>p-value</th>
<th>Absolute Detection Difference (95% CI)</th>
<th>NNS</th>
</tr>
</thead>
<tbody>
<tr>
<td>AF ≥ 30 seconds</td>
<td>3%</td>
<td>16%</td>
<td>&lt;0.001</td>
<td>13% (9%-18%)</td>
<td>8</td>
</tr>
</tbody>
</table>

### Secondary Outcomes

<table>
<thead>
<tr>
<th>Secondary Outcome</th>
<th>Repeat Holter (n=285)</th>
<th>30-day Monitor (n=287)</th>
<th>p-value</th>
<th>Absolute Detection Difference (95% CI)</th>
<th>NNS</th>
</tr>
</thead>
<tbody>
<tr>
<td>AF ≥ 2.5 min</td>
<td>2%</td>
<td>10%</td>
<td>&lt;0.001</td>
<td>8% (4%-12%)</td>
<td>13</td>
</tr>
<tr>
<td>Any AF</td>
<td>4%</td>
<td>20%</td>
<td>&lt;0.001</td>
<td>16% (10%-21%)</td>
<td>6</td>
</tr>
</tbody>
</table>
Long term ILR in ESUS patients
CRYSTAL-AF

- 441 patients > 40 years with ESUS
- No prior AF
- Randomized to implantable loop recorder versus routine clinical care
- Primary endpoint: AF > 30 seconds detected < 6 months
Long term monitoring in cryptogenic stroke
CRYSTAL-AF

Rate of detection in ICM arm was 30.0% vs 3.0% in control arm after 36 months

AF > 30 seconds

Median time to detection 41 days

Sanna for the CRYSTAL-AF Investigators New Engl J Med 2014
Conclusion

ECG monitoring after ischemic stroke/ TIA of unknown source with an insertable monitor?

YES
Safety and benefit of ILR

- Infection: 1.4%
- ILR remained inserted in 97% at 1 year
- Number needed to implant to detect 1st episode AF 14 for 6 months, 4 for 36 months
High risk patients

AF can also occur asymptomatic: ‘silent AF’

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Class</th>
<th>Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Opportunistic screening for AF in patients $\geq 65$ years of age using pulse-taking followed by an ECG is recommended to allow timely detection of AF.</td>
<td>I</td>
<td>B</td>
</tr>
</tbody>
</table>
And cryptogenic ischemic strokes may be associated with AF

- 123 patients with ESUS using ILR
- AF in 23 patients (20%)
- First detection after 4 months
Risk of ischemic stroke or embolism in SCAF

- 2580 patients with hypertension, > 65 yrs
- no AF, pacemaker or ICD
- Follow-up: 2.5 years
- Subclinical AF: > 6 min > 190 bpm
Temporal disconnect

- Monitoring
- VKA therapy

stroke

Brambatti for the ASSERT Investigators Circulation 2014

Parekh et al. Circ 2006
AF: mechanism or marker for stroke?

SCAF episodes are associated with AF but only a minority had SCAF in the month before their stroke.
Continuous rhythm monitoring RACE V

Medtronic Advisa Pacemaker

Medtronic Reveal LINQ

CareLink system

FOCUSON™

University Medical Center Groningen

Medtronic

Advisa

Pacemaker

CareLink

system
All,

<table>
<thead>
<tr>
<th>Episode ID#</th>
<th>Episode Date and Time</th>
<th>Report type</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>7-16</td>
<td>maart 2017</td>
<td>Full 8 maart 2017 15:43</td>
<td>CareAlert AF, alle episodes tonen AF/PAF met snelle kamerspons. Terens zijn er een aantal breed complex tachycardieen zichtbaar max duur 20 seconden (#8) mogelijk VT, SVT/AT aberrante geleiding niet uitgesloten.</td>
</tr>
</tbody>
</table>
- 65 year old female
- Symptomatic atrial fibrillation
- Risk factor for AF hypertension
- Near collaps ~19.15 h
- 35 year old male
- Symptomatic atrial fibrillation
- Obesity, BMI 31, no other risk factors
Conclusions

- Remote monitoring of patients with implantable cardiac devices has benefits both for patients and physicians
  - Earlier detection of clinically relevant events not limited to SCAF
  - Probable a reduction of health care costs and consumption
- However, an issue is how to handle all those data efficiently
- The FOCUSON™ monitoring and triaging center may help to manage an adequate handling of all transmitted ECG data
- And it may potentially help to improve cardiovascular outcome
Thank you for your attention