CIED Detected
Subclinical AF: How to Monitor and to Treat?

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Disclosures

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AF Terminology

• Atrial high rate event (AHRE): atrial tachyarrhythmia episodes at >190 bpm detected by cardiac implantable electronic devices (CIED).

• Sub-clinical AF (SCAF): AHRE (>6 minutes and <24–hours) with lack of symptoms in patients with CIED, detected with continuous ECG (intracardiac) and without prior diagnosis of AF.

• Silent (asymptomatic) AF: documented AF in the absence of any symptoms or prior diagnosis often presenting with a complication related to AF e.g. stroke, heart failure.

B. Gorenhek et al. EHRA consensus document 2017
SCAF Detection

• Efficacy of SCAF detection depends on
• duration of ECG monitoring
• method of ECG monitoring; wearable vs implantable, AF detection algorithm

• 24-h Holter: sensitivity 44–66%
• CIEDs: sensitivity 91%
ASSERT II: Incidence of SCAF

256 patients age > 65
mean CHADSVASC 4

Rate per year (95% CI)

SCAF ≥ 5mins: 34.4% (27.7% – 42.3%)
SCAF ≥ 30mins: 21.8% (16.7% – 27.8%)
SCAF ≥ 6hours: 7.1% (4.5% – 10.6%)
SCAF ≥ 24hours: 2.7% (1.2% – 5.0%)

Reveal AF: AF > 6 mins

385 patients
Mean CHADS 2.9
Mean CHADSVASC 4.4

Reiffel et al. JAMA Cardiol. 2017;2(10):1120–1127
## ILR: Incidence of AF

<table>
<thead>
<tr>
<th>Study</th>
<th>N</th>
<th>Device</th>
<th>Inclusion</th>
<th>Rate of AF Detection</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASSERT</td>
<td>250</td>
<td>SJM Confirm</td>
<td>Age &gt; 65, and CHADSVASc &gt; 2, or OSA, or BMI &gt; 30; LA &gt; 58ml, or NT-ProBNP &gt; 290 pg/mL</td>
<td>&gt; 5 min 34% at 1 year</td>
</tr>
<tr>
<td>GRAF</td>
<td>200</td>
<td>REVEAL XT</td>
<td>Age &gt; 18</td>
<td>pending</td>
</tr>
<tr>
<td>REVEAL AF</td>
<td>450</td>
<td>REVEAL XT</td>
<td>Age &gt; 18, CHADS &gt; 3, or CKD/COPD/OSA/CAD</td>
<td>&gt; 6 mins 29% at 18 mos</td>
</tr>
<tr>
<td>PREDATE AF</td>
<td>245</td>
<td>REVEAL</td>
<td>Age &gt; 18, and CHADSVASc &gt; 2</td>
<td>&gt; 6 mins 22% at 451</td>
</tr>
<tr>
<td>DANISH LOOP</td>
<td>6000</td>
<td>REVEAL (1500)</td>
<td>Age &gt; 70, One of HTN, DM, HF, or</td>
<td>pending</td>
</tr>
</tbody>
</table>
Potential Alternatives to ILRs for AF detection
Overall Goal

To evaluate the ability of the irregular pulse notification algorithm to identify Afib and guide subsequent clinical evaluation

- Notification burden
- Subsequent Afib diagnosis
- Algorithm performance
- Safety
- Pragmatic and generalizable
- Scalable study procedures

Turakhia M, et al. ACC 2019
Conclusions

Study w/ Novel Virtual Design 419,297 in 8 months

Proportion Notified low Overall: 0.52% (0.49-0.54)

ECG patch 13 days after 34% had Afib

Positive predictive value Tachogram: 0.71 (0.69-0.74) Notification: 0.84 (0.76-0.92)

57% Notified (surveyed) Contacted Non-Study Provider

Exposure to the app was safe

Turakhia M, et al. ACC 2019
## Incidence of AF in CIED

<table>
<thead>
<tr>
<th>Study</th>
<th>Detection rate (bpm)</th>
<th>Detection time (min)</th>
<th>Incidence (n,%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gills AM et al. 2002</td>
<td>&gt;180</td>
<td>&gt; 1</td>
<td>157/231 (68%)</td>
</tr>
<tr>
<td>MOST 2003</td>
<td>&gt;220</td>
<td>&gt; 5</td>
<td>156/312 (50%)</td>
</tr>
<tr>
<td>Gonzales M, et al 2014</td>
<td>&gt;178</td>
<td>&gt; 5</td>
<td>39/224 (17%)</td>
</tr>
<tr>
<td>Benezet–M J et al 2015</td>
<td>&gt;225</td>
<td>&gt; 5</td>
<td>28/109 (26%)</td>
</tr>
<tr>
<td>ASSERT 2012</td>
<td>&gt;190</td>
<td>&gt; 6</td>
<td>895/2580 (35%)</td>
</tr>
<tr>
<td>Shanmugan N, et al 2012</td>
<td>&gt; 180</td>
<td>&gt; 14</td>
<td>223/560 (40%)</td>
</tr>
</tbody>
</table>
Questions

1. Risk of clinical AF
2. SE/Stroke risk
3. Risk of oral anticoagulation
4. Does she benefit from rhythm control strategy
### Meta-analysis

#### SCAF and clinical AF

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>log(Odds Ratio)</th>
<th>SE</th>
<th>Weight</th>
<th>Odds Ratio IV, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ancillary MOST</td>
<td>1.78</td>
<td>0.3685</td>
<td>22.5%</td>
<td>5.93 [2.88, 12.21]</td>
</tr>
<tr>
<td>ASSERT</td>
<td>1.7192</td>
<td>0.1987</td>
<td>77.5%</td>
<td>5.58 [3.78, 8.24]</td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td><strong>100.0%</strong></td>
<td></td>
<td></td>
<td><strong>5.66 [4.02, 7.97]</strong></td>
</tr>
</tbody>
</table>

Heterogeneity: $\tau^2 = 0.00$; $\chi^2 = 0.02$, df = 1 ($P = 0.88$); $I^2 = 0$

Test for overall effect: $Z = 9.91$ ($P < 0.000001$)

#### SCAF and stroke risk

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>log(Odds Ratio)</th>
<th>SE</th>
<th>Weight</th>
<th>Odds Ratio IV, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ancillary MOST</td>
<td>1.026</td>
<td>0.4096</td>
<td>14.2%</td>
<td>2.79 [1.25, 6.23]</td>
</tr>
<tr>
<td>ASSERT</td>
<td>0.9163</td>
<td>0.3416</td>
<td>20.5%</td>
<td>2.50 [1.28, 4.88]</td>
</tr>
<tr>
<td>Botto et al</td>
<td>0.9243</td>
<td>0.7674</td>
<td>4.1%</td>
<td>2.52 [0.56, 11.34]</td>
</tr>
<tr>
<td>Capucci et al</td>
<td>1.1314</td>
<td>0.5286</td>
<td>8.6%</td>
<td>3.10 [1.10, 8.74]</td>
</tr>
<tr>
<td>Shanmugam et al</td>
<td>2.2407</td>
<td>0.8433</td>
<td>3.4%</td>
<td>9.40 [1.80, 49.08]</td>
</tr>
<tr>
<td>SOS AF</td>
<td>0.6366</td>
<td>0.2579</td>
<td>35.9%</td>
<td>1.89 [1.14, 3.13]</td>
</tr>
<tr>
<td>TRENDS</td>
<td>0.7885</td>
<td>0.4231</td>
<td>13.4%</td>
<td>2.20 [0.96, 5.04]</td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td><strong>100.0%</strong></td>
<td></td>
<td></td>
<td><strong>2.41 [1.78, 3.26]</strong></td>
</tr>
</tbody>
</table>

Heterogeneity: $\tau^2 = 0.00$; $\chi^2 = 3.91$, df = 6 ($P = 0.69$); $I^2 = 0$

Test for overall effect: $Z = 5.68$ ($P < 0.000001$)

Stroke Risk for SCAF is Lower than AF

2. Gage BF et al. JAMA. 2001;285:2864–70
Asian and non-Asian populations

Primary efficacy endpoint:
Stroke or systemic embolism

Primary safety endpoint:
Major bleeding

There are no adequate and well-controlled head-to-head clinical trials comparing efficacy and safety of apixaban to any of the other NOACs. Hence, the analysis presented does not imply a comparison of efficacy, safety, or product interchangeability.

The rate of haemorrhagic stroke was consistently lower for all NOACs vs warfarin in Asian patients.

Key Secondary endpoint: Haemorrhagic Stroke (ICH)

Key observations from the meta-analysis:

- The efficacy and safety of standard dose NOACs over VKA were typically greater for Asian patients versus non-Asian patients.
- Standard dose NOACs also were more effective in reducing haemorrhagic stroke in Asian vs non-Asian patients.

There are no adequate and well-controlled head-to-head clinical trials comparing efficacy and safety of apixaban to any of the other NOACs. Hence, the analysis presented does not imply a comparison of efficacy, safety, or product interchangeability.

• Consider no antithrombotic therapy for any patient with \(\text{CHA}_2\text{DS}_2\text{-VASc score of 0}\) in males or 1 in females, irrespective of AHRE.

• Consider oral anticoagulation for AF burden (longest total duration of AF on any given day) of \(>5.5\ h\) in patients with one additional \(\text{CHA}_2\text{DS}_2\text{-VASc risk factor}\) (i.e. score=1 in males or =2 in females).

• For patients with two additional \(\text{CHA}_2\text{DS}_2\text{-VASc risk factors}\) (i.e. >2 in males, >3 in females) oral anticoagulation is recommended for AF burden \(>5.5\ h/\ day\) (if there are no contraindications). Lower duration may merit OAC if multiple risk factors are present.
Questions

1. Risk of clinical AF
2. SE/Stroke risk
3. Risk of oral anticoagulation
67/F, Hypertension, PPM for SND

Cardiac Compass Trends (Mar-2018 to May-2019)

AT/AF Durations
Duration  Episodes
>72 hr 0
48 hr to 72 hr 0
24 hr to 48 hr 0
12 hr to 24 hr 0
4 hr to 12 hr 0
1 hr to 4 hr 12
10 min to 1 hr 90
1 min to 10 min 541
<1 min 859


P = Program
I = Interrogate
= Remote

AT/AF total hours/day

V. rate during AT/AF (bpm)
max/day avg/day
>200
150
100
<50
Who benefits from rhythm control?

- LV dysfunction/ CHF/ Tachycardia mediated cardiomyopathy
- Symptomatic despite rhythm or rate control
- HCM or aortic stenosis
- Young age
Conclusion

• Wearable and implantable devices will increase detection rates of AF

• Patients with SCAF have an increase risk of stroke but the absolute stroke risk is not to be as high as with clinical AF.

• Role of anticoagulation: assuming that stroke risk reduction is similar to patients with clinical AF

• Identify those who may benefit from rhythm control strategy
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## TE risk with AHRE

<table>
<thead>
<tr>
<th>Study</th>
<th>Follow-up</th>
<th>Annualised TE rate</th>
<th>Hazard ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>MOST’03 (&gt;220 bpm)</td>
<td>27 months</td>
<td>&lt;5 min: 0.58% &gt;5 min: 2.22%</td>
<td>6.7 (p=0.02)</td>
</tr>
<tr>
<td>AT500 Reg’05 (&gt;174 bpm)</td>
<td>22 months</td>
<td>&lt;5 min: 0.9% &gt;24 hr: 1.8%</td>
<td>3.1 (p=0.04)</td>
</tr>
<tr>
<td>TRENDS’09 (&gt;175 bpm)</td>
<td>1.4 yrs</td>
<td>None: 1.1% &lt;5.5 hr: 1.1% &gt;5.5 hr: 2.4%</td>
<td>0.98 (p=NS) \2.2 (p=0.06)</td>
</tr>
<tr>
<td>ASSERT’12 (&gt;190 bpm)</td>
<td>2.5 yrs</td>
<td>&lt;6 min: 0.69% &gt;6 min: 1.69%</td>
<td>2.5 (p=0.007)</td>
</tr>
<tr>
<td>Van Gelder IC, et al. 2017</td>
<td>2.5 yrs</td>
<td>&lt;6min \6 min–6 hr \6 hr–24 hr &gt;24 hr</td>
<td>0.75 \1.32 \3.24</td>
</tr>
</tbody>
</table>

K. Miyazawa et al. Progress in Cardiovascular Diseases 60 (2018) 537–541