SUBCLINICAL ATRIAL FIBRILLATION IN PATIENTS WITH IMPLANTABLE DEVICES

ORAL ANTICOAGULANT THERAPY: TO GIVE OR NOT TO GIVE, THIS IS THE PROBLEM !!
Episodes of atrial tachyarrhythmias stored in device memory

Atrial tachycardia

Atrial fibrillation

.... but not all is true !!!

Repetitive Non-reentrant Ventriculoatrial Synchrony

Up to 20% of false positive so you need to check and confirm the episode

«ATRIAL HIGH RATES EPISODES» (AHREs)

Episodes of atrial tachyarrhythmias stored in device memory
«ATRIAL HIGH RATE EPISODES (AHRE) WITH A RATE > 190 bpm, DURATION BETWEEN 6 MINUTES AND 24 HOURS, WHICH LACK OF CORRELATED SYMPTOMS IN PATIENTS WITH CARDIAC IMPLANTABLE ELECTRONIC DEVICES, DETECTED WITH CONTINOUS ECG MONITORING (INTRACARDIAC) AND WITHOUT PRIOR DIAGNOSIS (ECG or HOLTER MONITORING) OF AF »

Device-detected subclinical atrial tachyarrhythmias: definition, implication and management – an European Heart Rhythm Association (EHRA) consensus document, endorsed by Heart Rhythm Society (HRS), Asia Pacific Heart Rhythm Society (APHRS), Sociedad Latinoamericana de Estimulación Cardiaca y Electrofisiologia (SOLEACE), Europace 2017, 19:1556-1578
DOCUMENTED ATRIAL FIBRILLATION

SUBCLINICAL ATRIAL FIBRILLATION

... MORE FREQUENT THAN WE IMAGINE (12 times more than symptomatic episodes)

... NOT LESS DANGEROUS THAN DOCUMENTED ONEs !!!
ASSOCIATION OF SCAF WITH INCREASED RISK OF ISCHEMIC STROKE AND SYSTEMIC TE

Glotzer et al, Circulation 2003

MOST trial

Healey et al, NEJM 2012

Subclinical Atrial Fibrillation and the Risk of Stroke

 ASSERT STUDY

Glotzer et al, Circ Arrhythm Electroph 2009

The Relationship Between Daily Atrial Tachyarrhythmia Burden From Implantable Device Diagnostics and Stroke Risk

THE TRENDS STUDY

Capucci et al, JACC 2005

Monitored Atrial Fibrillation Duration Predicts Arterial Embolic Events in Patients Suffering From Bradycardia and Atrial Fibrillation Implanted With Antitachycardia Pacemakers

AT 500 REGISTRY

<table>
<thead>
<tr>
<th>AT/AF Burden</th>
<th>Annualized TE Rate (95% CI), %</th>
<th>Excluding TIAs (95% CI), %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zero AT/AF burden</td>
<td>1.1 (0.8–1.6)</td>
<td>0.5 (0.3–0.9)</td>
</tr>
<tr>
<td>Low AT/AF burden (&lt;5.5 h)</td>
<td>1.1 (0.4–2.8)</td>
<td>1.1 (0.4–2.8)</td>
</tr>
<tr>
<td>High AT/AF burden (5.5 h)</td>
<td>2.4 (1.2–4.5)</td>
<td>1.8 (0.9–3.8)</td>
</tr>
</tbody>
</table>
WHAT ABOUT AHREs SHORTER THAN 5 MINUTES ?

Clinical Implications of Brief Device-Detected Atrial Tachyarrhythmias in a Cardiac Rhythm Management Device Population

Results from the Registry of Atrial Tachycardia and Atrial Fibrillation Episodes

<table>
<thead>
<tr>
<th>Clinical Event (Pts)</th>
<th>Exploratory Variable</th>
<th>Crude OR (95% CI)</th>
<th>P value</th>
<th>Adjusted OR (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Adverse Events (235)</td>
<td>Short AT/AF Only</td>
<td>0.72</td>
<td>0.55</td>
<td>9.61</td>
<td>0.57</td>
</tr>
<tr>
<td>Hosp. for AF, HT, VT, Stroke, TIA</td>
<td>Long AT/AF</td>
<td>1.60</td>
<td>0.006</td>
<td>1.25</td>
<td>0.28</td>
</tr>
<tr>
<td>Syncope, All-Cause Mortality</td>
<td>Short AT/AF Only</td>
<td>0.50</td>
<td>0.54</td>
<td>1.55</td>
<td>0.82</td>
</tr>
<tr>
<td>Long AT/AF</td>
<td>2.78</td>
<td>0.032</td>
<td>1.60</td>
<td>0.45</td>
<td></td>
</tr>
<tr>
<td>Hospitazation For AF (28)</td>
<td>Short AT/AF Only</td>
<td>0.30</td>
<td>0.30</td>
<td>1.78</td>
<td>0.51</td>
</tr>
<tr>
<td>Long AT/AF</td>
<td>1.24</td>
<td>0.44</td>
<td>2.22</td>
<td>0.66</td>
<td></td>
</tr>
<tr>
<td>Hospitazation For Heart Failure (56)</td>
<td>Short AT/AF Only</td>
<td>0.31</td>
<td>0.29</td>
<td>1.59</td>
<td>0.30</td>
</tr>
<tr>
<td>Long AT/AF</td>
<td>1.02</td>
<td>0.26</td>
<td>3.59</td>
<td>0.46</td>
<td></td>
</tr>
<tr>
<td>Stroke (24)</td>
<td>Short AT/AF Only</td>
<td>0.72</td>
<td>0.47</td>
<td>0.63</td>
<td>0.38</td>
</tr>
<tr>
<td>Long AT/AF</td>
<td>1.86</td>
<td>0.09</td>
<td>1.49</td>
<td>0.73</td>
<td></td>
</tr>
<tr>
<td>All-Cause Mortality (149)</td>
<td>Short AT/AF Only</td>
<td>0.31</td>
<td>0.29</td>
<td>1.59</td>
<td>0.30</td>
</tr>
<tr>
<td>Long AT/AF</td>
<td>1.02</td>
<td>0.26</td>
<td>3.59</td>
<td>0.46</td>
<td></td>
</tr>
</tbody>
</table>

Swiryn et al, Circulation 2016

« Short episodes of AT/AF in patients with PMK/ICD are not associated with increased risk of clinical events compared with patients without documented AT/AF but ……»
DEVELOPMENT OF LONG AT/AF DURING FOLLOW-UP IN PATIENTS WITH OR WITHOUT SHORT AT/AF

Swiryn et al, Circulation 2016

«…… patients with short AT/AF are more prone to develop longer episodes of AT/AF during 2 aa of follow-up»
THE DARK SIDE OF THE MOON …..

ABSOLUTE RISK OF STROKE/TE IN SCAF OFTEN LOWER THAN THAT OBSERVED IN CLINICAL AF …. BUT NOT SO DIFFERENT FROM ATRIA STUDY AND WELL-ABOVE THRESHOLD OF 1% FOR RECOMMENDED ANTICOAGULATION FOR STROKE PREVENTION

Stroke risk (per 100 person-y)

<table>
<thead>
<tr>
<th></th>
<th>NRAF Cohort</th>
<th>ATRIA Cohort</th>
<th>Subclinical AF</th>
<th>No Subclinical AF</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>4.0</td>
<td>2.54</td>
<td>2.76</td>
<td>0.93</td>
</tr>
<tr>
<td>CHAD$_2$ = 2</td>
<td>4.4</td>
<td>2.29</td>
<td>1.89</td>
<td>1.08</td>
</tr>
</tbody>
</table>

**SCAF DURATION AND RISK SCORE:**
Better To Take Them Together!!

**TE as a function of CHADS₂**

**Combination of CHADS₂ Score with AF Presence and Duration**
(in A – CHADS₂ score 0-1-2 and ≥ 3, in B – CHADS2 score 1-2)

- Low risk group
- High risk group

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from L. Botto et al., *Presence and duration of AF detected by Continuous Monitoring: Crucial Implications for the Risk of Thromboembolic Events*, *J Cardiovasc Electrop* 2009;20: 241-48
THE DARK SIDE OF THE MOON …..

POOR TEMPORAL RELATIONSHIP BETWEEN SCAF AND TE EVENTS (up to 94% of TE events without SCAF in the previous 30 days)

Table 6 Temporal relationship of device-detected atrial fibrillation to thromboembolic events

<table>
<thead>
<tr>
<th>Year</th>
<th>Trial</th>
<th>Number of patients with TE event</th>
<th>Definition of AF episode</th>
<th>Any AF detected prior to TE event</th>
<th>AF detected only after TE event</th>
<th>No AF in 30 days prior to TE event</th>
<th>Any AF in 30 days prior to TE event</th>
</tr>
</thead>
<tbody>
<tr>
<td>2011</td>
<td>TRENDS24</td>
<td>40</td>
<td>5 min</td>
<td>20/40 (50%)</td>
<td>6/40 (15%)</td>
<td>29/40 (73%)</td>
<td>11/40 (27%)</td>
</tr>
<tr>
<td>2014</td>
<td>ASSERT25</td>
<td>51</td>
<td>6 min</td>
<td>18/51 (35%)</td>
<td>8/51 (16%)</td>
<td>47/51 (92%)</td>
<td>4/51 (8%)</td>
</tr>
<tr>
<td>2014</td>
<td>IMPACT AF26</td>
<td>69</td>
<td>36/48 atrial beats ≥200 bpm</td>
<td>20/69 (29%)</td>
<td>9/69 (13%)</td>
<td>65/69 (94%)</td>
<td>4/69 (6%)</td>
</tr>
</tbody>
</table>

AF, atrial fibrillation; bpm, beats per minute; TE, thromboembolic; IMPACT AF, Randomized trial to IMProve treatment with AntiCoagulanTs in patients with Atrial Fibrillation. Other abbreviations as in Table 4.

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THE DARK SIDE OF THE MOON …..

UP TO 15% OF SCAF OBSERVED JUST AFTER ISCHEMIC STROKE !!
THE MORE WE SEE THE MORE WE FIND!

…. from memory of the device

<table>
<thead>
<tr>
<th>AP</th>
<th>AS</th>
<th>AS</th>
<th>AS</th>
<th>AS</th>
<th>AR</th>
<th>AS</th>
<th>AR</th>
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<th>AR</th>
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<tbody>
<tr>
<td>VP</td>
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<tr>
<td>013</td>
<td>441</td>
<td>538</td>
<td>363</td>
<td>668</td>
<td>410</td>
<td>443</td>
<td>457</td>
<td>788</td>
<td>541</td>
<td>862</td>
<td>948</td>
<td>748</td>
<td>748</td>
<td>748</td>
</tr>
</tbody>
</table>

ICM

PMK

ICD

CRT
BUT ... THE MORE WE TREAT THE MORE WE BENEFIT?

Randomized trial of atrial arrhythmia monitoring to guide anticoagulation in patients with implanted defibrillator and cardiac resynchronization devices

David T. Martin1, Malcolm M. Bersohn1, Albert L. Waldo2, Mark S. Wathen1, Wassim K. Choucair4, Gregory Y.H. Lip4, John Ip1, Richard Holcomb1, Joseph G. Akar5, and Jonathan L. Halperin16, on behalf of the IMPACT Investigators

IMPACT AF TRIAL

CONCLUSIONS

In patients with ICD (Implanted Cardioverter Defibrillator) the strategy of early initiation and interruption of anticoagulation (80% VKA) based on remote detected atrial tachyarrhythmias do not prevent thromboembolism and bleeding.

European Heart Journal 2015, 36:1660-1668
Probing oral anticoagulation in patients with atrial high rate episodes: Rationale and design of the Non–vitamin K antagonist Oral anticoagulants in patients with Atrial High rate episodes (NOAH–AFNET 6) trial

Paulus Kirchhof, MD, a,b,c,d, Benjamin F. Blank, b, Melanie Calvert, PhD, e,a John Camm, MD, g Gregory Chlouverakis, PhD, f Hans-Christoph Diener, MD, G Andreas Goege, MD, f,a Andrea Huening, MD, f Gregory Y. H. Lip, MD, a,b,1 Emmanuel Simantirakis, MD, a and Panos Vardas, MD a Birmingham, London, United Kingdom; Muenster, Essen, Paderborn, Munich, Germany; Crete, Greece; and Aalborg, Denmark

Trial Design

Rationale and design of the Apixaban for the Reduction of Thrombo-Embolism in Patients With Device-Detected Sub-Clinical Atrial Fibrillation (ARTESiA) trial

RCT# NCT01938248

Renato D. Lopes, MD, MHS, PhD, 1 Marco Alings, MD, PhD, 2 Stuart J. Connolly, MD, 3 Heather Bereski, 3 Christopher B. Granger, MD, 1 Juan Benezet Mazuecos, MD, 4 Giuseppe Boriani, MD, PhD, 2 Jens C. Nielsen, MD, DMSc, 6 David Conen, MD, MPH, 1, 2 Stefan H. Hohnloser, MD, 8 Georges H. Mairese, MD, 9 Philippe Mabo, MD, 10 A. John Camm, MD, 11 and Jeffrey S. Healey, MD, 3

Am Heart Journal 2017;189:137-145

Am Heart Journal 2017;190:12-18
2016 ESC Guidelines for the management of atrial fibrillation

Patient without known AF presenting with atrial high rate episode (AHRE, >5–6 min and >180 bpm) detected by an implanted device

Assess eligibility for oral anticoagulation using CHA₂DS₂-VASc score

Verify presence of AF by ECG documentation
- e.g. resting ECG
- Ambulatory ECG recorder
- Patient-operated devices
- Review device electrograms (if available) to determine whether it is AF

No AF detected

AF diagnosed

Grey zone

Consider patient characteristics (e.g. stroke risk score) and patient preference

No antithrombotic therapy (IB)

Initiate oral anticoagulation (IA)

AF = atrial fibrillation; AFNET = German Competence NETwork on Atrial Fibrillation; AHRE = atrial high rate episode; bpm = beats per minute; CHA₂DS₂-VASc = Congestive Heart failure, hypertension, Age ≥75 (doubled), Diabetes, Stroke (doubled), Vascular disease, Age 65–74, and Sex (female); ECG = electrocardiogram; EHRA = European Heart Rhythm Association.

*In rare individual circumstances, oral anticoagulation may be considered in patients with AHRE, but without diagnosed AF. This clearly needs discussion with the patient and careful evaluation of perceived benefit and risk.
*Adapted from the report of the 3rd AFNET/EHRA consensus conference.
Sintesi raccomandazioni TAO nei pazienti con SCAF

CHA₂DS₂-VaSC = 0 negli uomini
CHA₂DS₂-VaSC = 1 nelle donne

CHA₂DS₂-VaSC = 1 negli uomini
CHA₂DS₂-VaSC = 2 nelle donne

CHA₂DS₂-VaSC ≥ 2 negli uomini
CHA₂DS₂-VaSC ≥ 3 nelle donne

SCAF ≥ 5.5 ore/d

TAO non raccomandato, indipendentemente dalla durata degli AHREs

SCAF ≥ 5.5 ore/d

TAO può essere considerata/indicata (NOAC o VKA con TTR ≥ 70%)

SCAF ≥ 5.5 ore/d

TAO raccomandata (NOAC o VKA con TTR ≥ 70%)

* In caso di SCAF ≥ 5 minuti e ≤ 5.5 ore/d considerare la TAO solo in presenza di molteplici fattori di rischio per stroke ischemico. Episodi brevi e sporadici suggeriscono di proseguire il follow-up e rivalutare nel tempo il burden di FA prima di consigliare la TAO a vita.

∞ In caso di SCAF ≥ 24 h la TAO è raccomandata