Κλινική σημασία βραχείας διάρκειας υποκλινικών επεισοδίων κολπικής μαρμαρυγής και κολπικών ταχυαρρυθμιών ανιχνευόμενων με καρδιακές συσκευές.

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Σεμινάρια Ομάδων Εργασίας ΕΚΕ 2019
Conflicts of interest

- Nothing to declare
The Clinical Presentation of AF

Asymptomatic Atrial Fibrillation
- Crypto Stroke
- Ischemic Stroke
- Sudden Death
- Heart Failure
  - Cognitive Decline
  - Dementia

Symptomatic Atrial Fibrillation
- Palpitations
- Hemodynamic
  - Dizziness
  - Heart Failure
  - Syncope
- Tachy Arrhythmias
  - Medical Attention
There is no evidence that asymptomatic AF patients have a different risk profile compared with symptomatic AF.
What are Atrial High-Rate Events (AHRE) or SCAF (Subclinical AF)?

Are AHRE synonymous with AF?

Are AHRE associated with stroke and thromboembolism?

How should we manage asymptomatic individuals with AHRE?
**Introduction**

- **AF detection** is critical in ischemic stroke survivors, often recommending a switch from antiplatelet therapy to oral anticoagulants for secondary prevention.

- Cardiac implantable electronic devices (CIEDs) with their **long-term recording capability** allows to document **subclinical AF** and to quantify the **arrhythmia burden**.

- Recent series in PPM and ICD recipients with no prior stroke showed that **short episodes of AF increased stroke risk** compared with those without AF recorded.

- Detection of AF by CIEDs represent a unique opportunity for prompt prevention of embolic risk in silent AF.
Atrial high rate event (AHRE): atrial high-rate episodes are defined as atrial tachyarrhythmia episodes with rate >190 beats/min detected by cardiac implantable electronic devices.

Subclinical atrial fibrillation (AF): atrial high-rate episodes (>6 minutes and <24-hours) with lack of correlated symptoms in patients with CIEDs, detected with continuous ECG monitoring (intracardiac) and without prior diagnosis (ECG or Holter monitoring) of AF.

Patients with CIEDs have an advantage over cardiac patients who do not have a continuous arrhythmia monitor in place because clinically silent arrhythmias can be detected.
False SCAF

Switch mode due to RNRVAS
repetitive non-reentrant VA synchrony

Note: R-R interval is regular; therefore this is not AF.
False AT/AF triggered due to PVC

Note: irregular R-R intervals.
The prevalence of AF in patients with CIEDs is reported to range from 30% to 60%. Overall, the incidence of subclinical AT/AF is 20% within 1 year of follow-up, but there have been no consistent predictors of SCAF in patients with PPMs and ICDs and without AF history.
Both the TRENDS and ASSERT studies have shown that SCAF is associated with an increased risk of stroke. However, unlike clinical AF where stroke risk is increased 4-5 times, the risk is only 2-2.5 times increased, and the absolute risk of stroke observed in these studies was much lower than expected based on the subjects’ CHADS-2 score.
SCAF burden (Time spent in AF per unit of time (day, w,mo) and stroke risk

- Are multiple shorter events (Greater AF burden) clinically equivalent to a single longer event of a similar cumulative duration?

Has yet to be determined.

- Are events >than 20 seconds but less than 5 minutes in duration clinically significant when compared to no events?

Has yet to be determined.

- Uncertainty still exists regarding the exact burden of AF that portends the highest risk, yet a minimum threshold associated with clinically events may be in the range of 5 or 6 minutes.

- The detection of shorter episodes should not be ignored as these herald a risk for developing a more significant AF burden over time and further study is required to identify stroke risk associated with these events.
Temporal relationship of device-detected AF 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>

It is also striking that **the majority of AF appears not to be linked with thromboembolic events in a temporal manner**, suggesting that atrial arrhythmias are **markers of a propensity towards stroke** as opposed to a direct etiology of LA thrombus.
AF is a risk marker and amplifier of underlying atrial fibrotic and prothrombotic pathology and not directly causal of the stroke.

The arrhythmia itself is not necessary condition for thrombus formation.
Ποια είναι η σημασία των ασυμπτωματικών κολπικών ταχυαρρυθμιών στην αύξηση του κινδύνου εμφάνισης ισχαιμικού ΑΕΕ ή συστηματικής εμβολής

- Η μελέτη ASSERT έδειξε ξεκάθαρα ότι υποκλινικές ταχυαρρυθμίες με κολπική συχνότητα >190 σφύξεις/min για περισσότερο από 6 min συσχετίστηκαν με αυξημένο κίνδυνο εμφάνισης κλινικής ΚΜ (hazard ratio, 5.56; 95% confidence interval [CI], 3.78-8.17; P<0.001) και ισχαιμικού ΑΕΕ ή συστηματικής εμβολής (hazard ration, 2.49; 95% CI, 1.28-4.85; P=0.007).

- Ωστόσο, δεν είναι διευκρινισμένο ακόμη το ποιά είναι επακριβώς η χρονική διάρκεια των επεισοδίων που αυξάνει τον θρομβοεμβολικό κίνδυνο.
2 εν εξελίξει μελέτες

- Επί του παρόντος 2 εν εξελίξει κλινικές τυχαιοποιημένες μελέτες φιλοδοξούν να δώσουν απάντηση όσον αφορά στο κλινικό όφελος από την αντιπηκτική θεραπεία ασθενών με επεισόδια κολπικής ταχυαρρυθμίας και να λυσουν το πρόβλημα της ετερογενούς πρακτικής.

- Η μόνη τυχαιοποιημένη προοπτική μελέτη με το ίδιο ερώτημα και χορήγηση αντιπηκτικού καθοδηγούμενη από remote rhythm monitoring σε ασθενείς με ICD και CRT-D devices (IMPACT μελέτη)

- Πιο συγκεκριμένα, η μελέτη NOAH-AFNET 6 θα εξετάσει αν η αντιπηκτική αγωγή με εντοξαμπάνη σε ασθενείς με επεισόδια κολπικής ταχυαρρυθμίας καταγεγραμμένα από εμφυτευμένες συσκευές είναι ανώτερη στη πρόληψη ΑΕΕ και καρδιαγγειακού θανάτου από τη χορήγηση ασπιρίνης ή καμίας αντιπηκτικής αγωγής.

- Η κλινική μελέτη ARTESiA θα επιχειρήσει να αξιολογήσει αν η αντιπηκτική θεραπεία με απιξαμπάνη έναντι της χορήγησης ασπιρίνης μειώνει τον κίνδυνο εκδήλωσης ΑΕΕ ή συστηματικής εμβολής σε ασθενείς με υποκλινική ΚΜ και παράγοντες θρομβοεμβολικού κινδύνου.
Among patients with SCAF, progression occurs at a rate of 9% per year and is independently associated with an increased risk of HF hospitalization. Progression of AF may be a suitable preventive and therapeutic target and is worthy of future studies.

SCAF progression associated with increased risk of HF hospitalization
[HR: 4.58; 95% CI: 1.64 - 12.8; p = 0.004]

Θεραπευτική αντιμετώπιση

- Μολονότι οι μελέτες MOST, TRENDS, ASSERT έχουν αναδείξει με σαφήνεια τον αυξημένο θρομβοεμβολικό κίνδυνο των ασθενών που παρουσιάζουν σιωπηλά επεισόδια κολπικών ταχυαρρυθμιών, στα καταγραφικά συσκευών για τη θεραπεία του καρδιακού ρυθμού, δεν έχει μέχρι τώρα ξεκαθαριστεί η καταλληλότερη θεραπευτική τους αντιμετώπιση.

- Variation in routine clinical practice due to evidence gap for a temporal relationship between AHRE and stroke and absence of guideline support for routine anticoagulation.
Device-detected subclinical atrial tachyarrhythmias: definition, implications and management—an European Heart Rhythm Association (EHRA) consensus document, endorsed by Heart Rhythm Society (HRS), Asia Pacific Heart Rhythm Society (APHRS) and Sociedad Latinoamericana de Estimulación Cardíaca y Electrofisiología (SOLEACE)

Bulent Gorenek (chair)\textsuperscript{1*}, Jeroen Bax\textsuperscript{2}, Giuseppe Boriani\textsuperscript{3}, Shih-Ann Chen\textsuperscript{4}, Nikolaos Dagres\textsuperscript{5}, Taya V. Glotzer\textsuperscript{6}, Jeff S. Healey\textsuperscript{7}, Carsten W. Israel\textsuperscript{8}, Gulmira Kudaiberdieva\textsuperscript{9}, Lars-Åke Levin\textsuperscript{10}, Gregory Y.H. Lip\textsuperscript{11,12}, David Martin\textsuperscript{13}, Ken Okumura\textsuperscript{14}, Jesper H. Svendsen\textsuperscript{15}, Hung-Fat Tse\textsuperscript{16}, and Giovanni L. Botto (co-chair)\textsuperscript{17}
<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Class</th>
<th>Supporting references</th>
</tr>
</thead>
<tbody>
<tr>
<td>If available, review stored intracardiac electrograms to confirm diagnosis and exclude artifact or reduce the effect of oversensing/undersensing by automated algorithms is recommended; solutions to correct inappropriate AF detection are provided in Table 7</td>
<td></td>
<td>6, 36, 37</td>
</tr>
</tbody>
</table>

**Facts**

The presence or absence of symptoms has no bearing on determining the need for anticoagulation.

13–15, 18–20, 22, 23
### Table 9: Recommendations for treatment of sub-clinical AF with oral anticoagulation

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Class</th>
</tr>
</thead>
<tbody>
<tr>
<td>Assessment of the patient’s stroke risk using the CHA2DS2-VASc score is recommended.</td>
<td><img src="https://via.placeholder.com/25" alt="Heart" /></td>
</tr>
<tr>
<td>No antithrombotic therapy for any patient with CHA2DS2-VASc score of 0 in males or 1 in females, irrespective of AHRE, is recommended. For patients with two additional CHA2DS2-VASc risk factors (i.e. ≥2 in males, ≥3 in females) oral anticoagulation is recommended for AF burden &gt;5.5 h/day (if there are no contraindications). Lower duration may merit OAC if multiple risk factors are present.</td>
<td><img src="https://via.placeholder.com/25" alt="Heart" /></td>
</tr>
<tr>
<td>For effective stroke prevention in patients with CHA2DS2-VASc score ≥2, oral anticoagulation, whether with well controlled vitamin K antagonist (VKA) with a time in therapeutic range &gt;70%, or with a non-VKA oral anticoagulant (NOAC, either dabigatran, rivaroxaban, apixaban or edoxaban) is recommended.</td>
<td><img src="https://via.placeholder.com/25" alt="Heart" /></td>
</tr>
</tbody>
</table>

Consider oral anticoagulation for AF burden (longest total duration of AF on any given day) of >5.5 h in patients with 1 additional CHA2DS2-VASc risk factor (i.e. score=1 in males or =2 in females).

Recognize that the data suggests risk is similarly increased by a mere 5-min episode, but it is reasonable to see a patient with only a single 5-min episode again in follow-up to observe their AF burden over time before committing them to life-long oral anticoagulation.

Bleeding risk should be assessed using validated scores, such as the HAS-BLED score.

- Patients at high risk (score≥3) should be identified for more regular review and follow-up, and the reversible bleeding risk factors addressed.
- A high HAS-BLED score is not a reason to withhold anticoagulation.
<table>
<thead>
<tr>
<th>CHA$_2$DS$_2$-VASc score</th>
<th>Duration of AHRE</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;2</td>
<td>&gt;5.5 h (lower duration if multiple stroke risk factors are present)*</td>
<td>![Heart icon]</td>
</tr>
<tr>
<td>1 (male) or 2 (female)</td>
<td>&gt;5.5 h*</td>
<td>![Yellow Heart icon]</td>
</tr>
</tbody>
</table>

*Data suggests risk is similarly increased by a mere 5 min. AHRE, atrial high rate episode.*
Consider no antithrombotic therapy for any patient with 
CHA$_2$DS$_2$-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 CHA$_2$DS$_2$-VASc risk factor (i.e. score=1 in males or = 2 in females)

For patients with two additional CHA$_2$DS$_2$-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.
2019 AHA/ACC/HRS Focused Update of the 2014 AHA/ACC/HRS Guideline for the Management of Patients With Atrial Fibrillation

### Recommendations for Device Detection of AF and Atrial Flutter

Referenced studies that support new recommendations are summarized in [Online Data Supplement 9](#).

<table>
<thead>
<tr>
<th>COR</th>
<th>LOE</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>B-NR</td>
<td>1. In patients with cardiac implantable electronic devices (pacemakers or implanted cardioverter-defibrillators), the presence of recorded atrial high-rate episodes (AHREs) should prompt further evaluation to document clinically relevant AF to guide treatment decisions (S7.12-1–S7.12-5).</td>
</tr>
<tr>
<td>Ila</td>
<td>B-R</td>
<td>2. In patients with cryptogenic stroke (i.e., stroke of unknown cause) in whom external ambulatory monitoring is inconclusive, implantation of a cardiac monitor (loop recorder) is reasonable to optimize detection of silent AF (S7.12-6).</td>
</tr>
</tbody>
</table>
Proposed approach to patients with AHRE detected by implanted devices.

AHRE detected by an implanted device

- Verify presence of AF to establish diagnosis
  - Review device electrograms during episodes
  - Attempt to document AF by surface ECG monitoring

AF confirmed?

Yes
- Initiate AF management including anticoagulation if appropriate based on clinical risk prediction models (ex. CHADS<sup>2</sup>)
- Follow device data to relate symptoms and guide rate and rhythm control strategy

No
- Discuss benefits and risks of anticoagulation with patient – threshold for initiation of anticoagulation may be lower in patients at high stroke risk or with higher AHRE burden (ex. >24 hours)
Synergism of AF and underlying disease

- There cannot be an absolute threshold for SCAF duration and embolic risk; rather, the risk must be dependent upon the AF burden and the number and magnitude of the comorbidities present.

- The greater the atrial pathophysiology created by the synergism of AF and underlying disease, the greater the risk.