

ASSERT Sub Study
Temporal relationship between
Subclinical Atrial Fibrillation and
Embolic Event

Michela Brambatti, MD
Universita' Politecnica delle Marche
Ancona, Italy



BACKGROUND

- Atrial fibrillation (AF) increases the risk of stroke (Wolf PA, Stroke 1991)
- A significant proportion of AF is asymptomatic and may reveal itself only after stroke occurred (Ziegler P, Stroke 2010)
- Modern dual chamber pacemakers (PM) are able to document and quantify individual episodes of atrial tachyarrhythmias (AT) for prolonged periods of time
- Device-detected ATs correlate well with ECG documentation of AF (subclinical atrial fibrillation-SCAF) (Pollak WM, PACE 2001) and occur in over 40% of PM patients without previous history of AF (Healey JS, NEJM 2012)

ASSERT TRIAL

| Event | SCAF (>6min, >190 bpm) | | | | SCAF Detected vs. not detected | | |
|---|-------------------------|------------|--------------------|--------|-----------------------------------|-------------|--------|
| | Not detected N= 2319 | | Detected N= 261 | | RR | 95% CI | p |
| | events | %/ year | events | %/year | | | |
| Ischemic Stroke or Systemic Embolism | 40 | 0.69 | 11 | 1.69 | 2.50 | 1.28 – 4.89 | 0.008 |
| Vascular Death | 153 | 2.62 | 19 | 2.92 | 1.14 | 0.71 – 1.84 | 0.59 |
| Stroke / MI / Vascular Death | 206 | 3.53 | 29 | 4.45 | 1.27 | 0.86 – 1.88 | 0.23 |
| Clinical Atrial Fibrillation or Flutter | 71 | 1.22 | 41 | 6.29 | 5.75 | 3.89 – 8.47 | <0.001 |

UNRESOLVED QUESTION

Are SCAF causally implicated in stroke or simply a marker of risk?

PREVIOUS FINDINGS



Europace (2012) 14, 230–237
doi:10.1093/europace/eur293

CLINICAL RESEARCH
Pacing and Resynchronization Therapy

Detection of atrial high-rate events by continuous Home Monitoring: clinical significance in the heart failure–cardiac resynchronization therapy population

Nesan Shanmugam¹, Annegret Boerdlein², Jochen Proff², Peter Ong¹, Oswald Valencia¹, Sebastian K.G. Maier³, Wolfgang R. Bauer³, Vince Paul^{4*}, and Stefan Sack⁵

- 560 CRT patients followed with REMOTE MONITORING for 370 days
- Stroke patients (n= 11)
- 27 % of patients were in AT/AF at the time of the stroke
- 73% of patients did not show a temporal association of AT/AF and stroke

« Previous

Heart Rhythm

Volume 8, Issue 9, Pages 1416-1423, September 2011

Temporal relationship of atrial tachyarrhythmias, cerebrovascular events, and systemic emboli based on stored device data: A subgroup analysis of TRENDS

[Emile G. Daoud, MD](#), [Taya V. Glotzer, MD](#), [D. George Wyse, MD, PhD, FHRS](#), [Michael D. Ezekowitz, MD, PhD](#), [Christopher Hilker, MS](#), [Jodi Koehler, MS](#), [Paul D. Ziegler, MS](#), TRENDS Investigators

- Stroke patients (n= 40)
- 20 pts with SCAF detected prior to the stroke
 - 30% was in SCAF at the time of the stroke
 - 70 % did not show a temporal association SCAF and stroke (mean interval 168± 199 days earlier)

STUDY AIM

Circulation
JOURNAL OF THE AMERICAN HEART ASSOCIATION



Temporal Relationship between Subclinical Atrial Fibrillation and Embolic Events
Michela Brambatti, Stuart J. Connolly, Michael R. Gold, Carlos A. Morillo, Alessandro Capucci, Carmine Muto, Chu Lau, Isabelle C. Van Gelder, Stefan H. Hohnloser, Mark Carlson, Eric Fain, Juliet Nakamya, Georges H. Mairesse, Marta Halytska, Wei Q. Deng, Carsten W. Israel and Jeff S. Healey
on behalf of the ASSERT Investigators

Circulation, published online March 14, 2014;
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2014 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

Understand the stroke mechanism among the ASSERT study population, by evaluating the **Temporal Relationship** between subclinical atrial fibrillation (SCAF) and ischemic stroke/systemic embolism

METHODS

Patient Eligibility:

- Enrolled after new dual-chamber pacemaker or ICD
- Age \geq 65 years
- History of hypertension
- Excluded if any history of AF
- Excluded if on Vitamin K antagonists

Device programmed according to protocol-specific setting:

- Atrial lead sensitivity (0.1-0.5 mV)

Threshold for SCAF episode detection was:

- Atrial rate $>$ 190 beats per minute
- Lasting $>$ 6 minutes

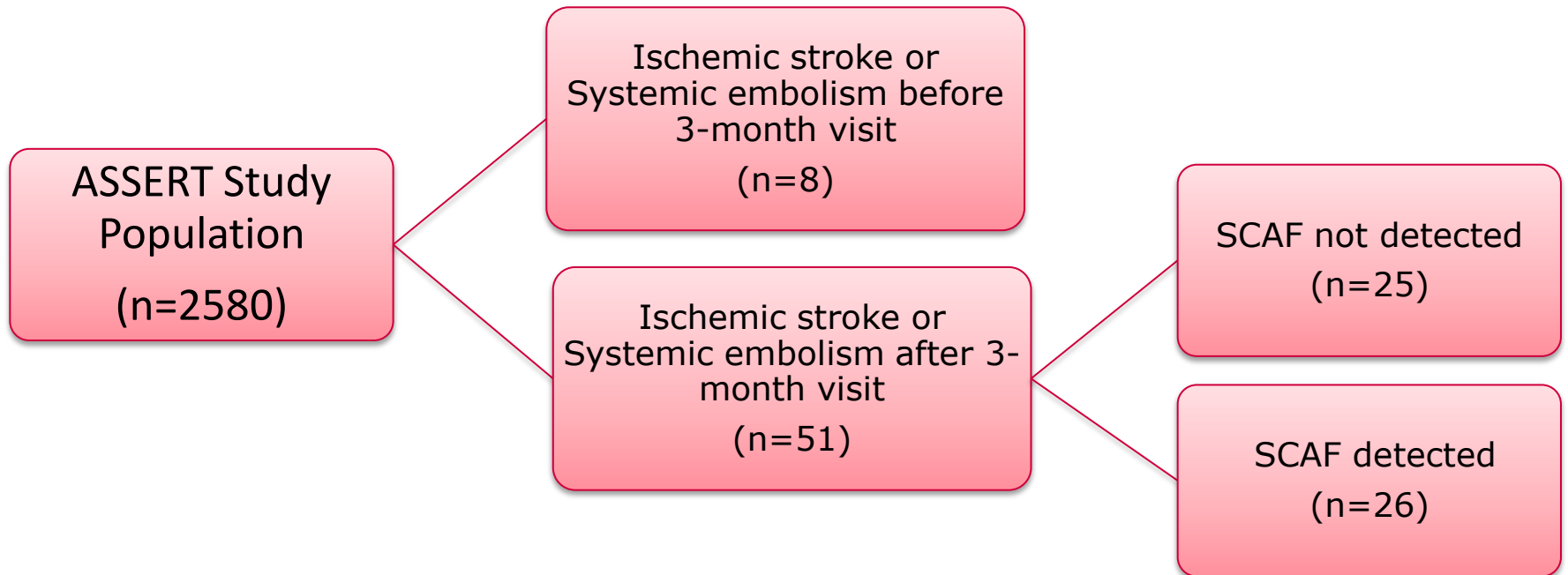
Stored Device Data (Date, Time of onset and duration*) of all SCAF events detected for the entire FU

*For multiple SCAF events occurring in a single day, total duration was considered

Outcome

- Ischemic stroke or systemic embolism

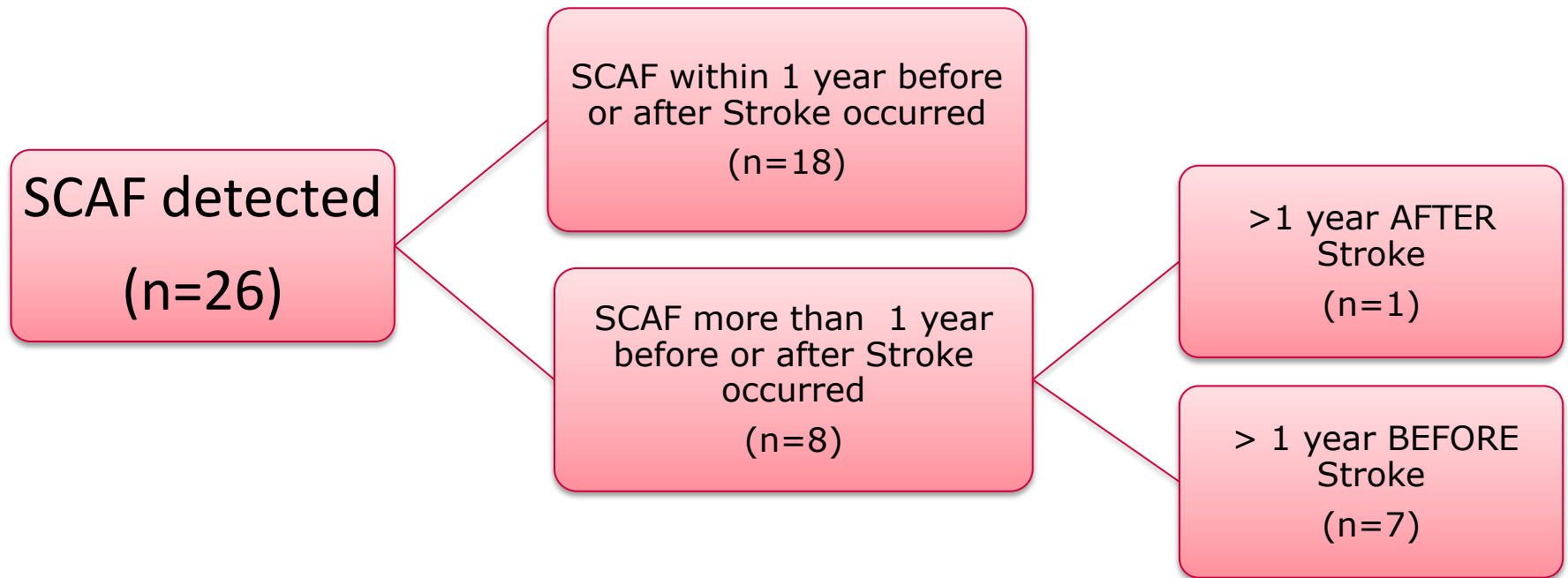
STUDY FLOW CHART



BASELINE CHARACTERISTICS

| | | SCAF not detected (n=25) | SCAF detected (n=26) | Overall (n=51) |
|---|--------------------------------|-----------------------------|-----------------------------|-----------------------------|
| Age ~ years* | Mean (SD) | 75.4 ± 6.7 | 80.3 ± 7.1 | 77.9 ± 7.3 |
| Male sex ~ no. (%) | | 20 (80) | 8 (31) | 28 (55) |
| Ischemic Stroke ~ no. (%) | | 21 (84) | 25 (96) | 46 (90) |
| Systemic Embolism ~ no. (%) | N (%) | 4 (16) | 1 (4) | 5 (10) |
| CHADS2 score | Mean (SD) | 2.8 ± 1.2 | 2.7 ± 1.1 | 2.8 ± 1.1 |
| | Median (P25-P75) | 2 (2-4) | 2 (2-4) | 2 (2-4) |
| CHA2DS2-VASc score | Mean (SD) | 4.3 ± 1.4 | 4.7 ± 1.0 | 4.5 ± 1.2 |
| | Median (P25-P75) | 5 (3-5) | 5 (4-5) | 5 (4-5) |
| Risk factors for stroke ~ no. (%) | | | | |
| Prior stroke | | 5 (20) | 4 (15) | 9 (18) |
| Prior TIA | | 4 (16) | 2 (8) | 6 (12) |
| History of HF | | 2 (8) | 5 (19) | 7 (14) |
| Diabetes Mellitus | | 9 (36) | 7 (27) | 16 (31) |
| Prior MI | | 6 (24) | 1 (4) | 7 (14) |
| Sinus node disease w or w/o AV node disease ~ no. (%) | | 11 (44) | 12 (46) | 23 (45) |
| Aspirin ~ no. (%) | | 13 (52) | 15 (58) | 28 (55) |
| <u>Time from Device Implant to Stroke (days)</u> | <u>Mean (SD)</u> | <u>580 ± 357</u> | <u>703 ± 394</u> | <u>643 ± 377</u> |
| | <u>Median (P25-P75)</u> | <u>570 (263-816)</u> | <u>670 (456-900)</u> | <u>612 (293-890)</u> |
| <u>Time from Stroke to last follow up (days)</u> | <u>Mean (SD)</u> | <u>477 ± 399</u> | <u>452 ± 480</u> | <u>464 ± 438</u> |
| | <u>Median (P25-P75)</u> | <u>404 (93-866)</u> | <u>350 (41-731)</u> | <u>398 (71-825)</u> |

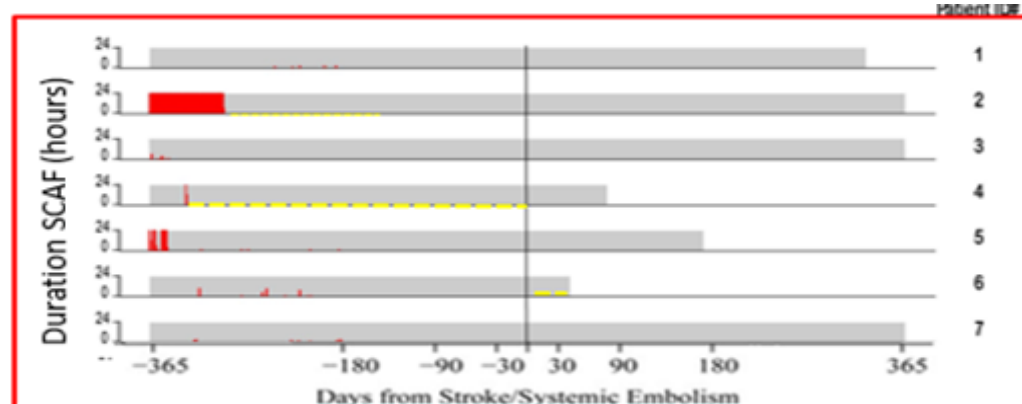
STUDY FLOW CHART



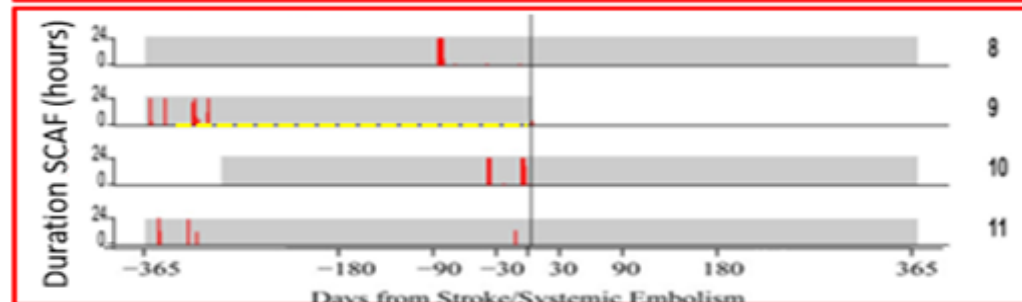
Results: SCAF occurring within 1 year before or after Stroke



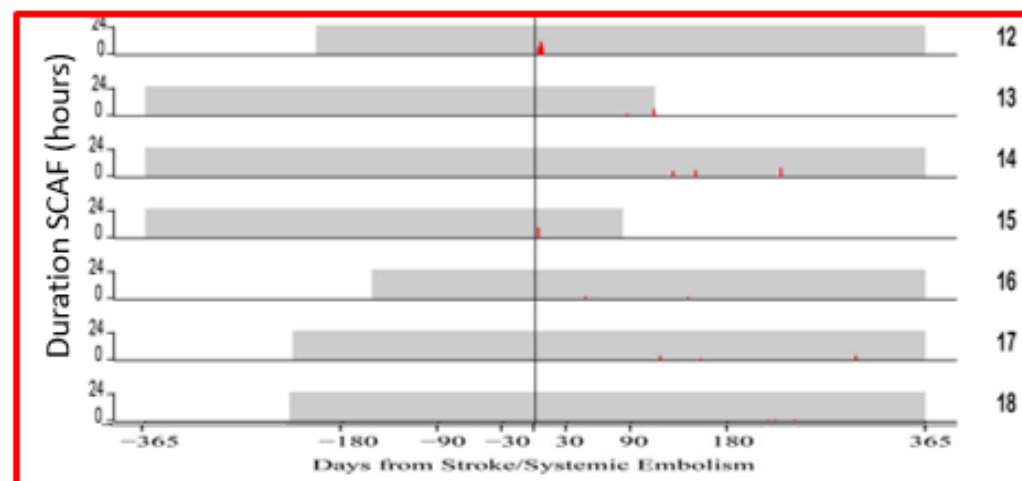
SCAF detected
> 30 days BEFORE the Stroke



SCAF detected
< 30 days BEFORE the Stroke

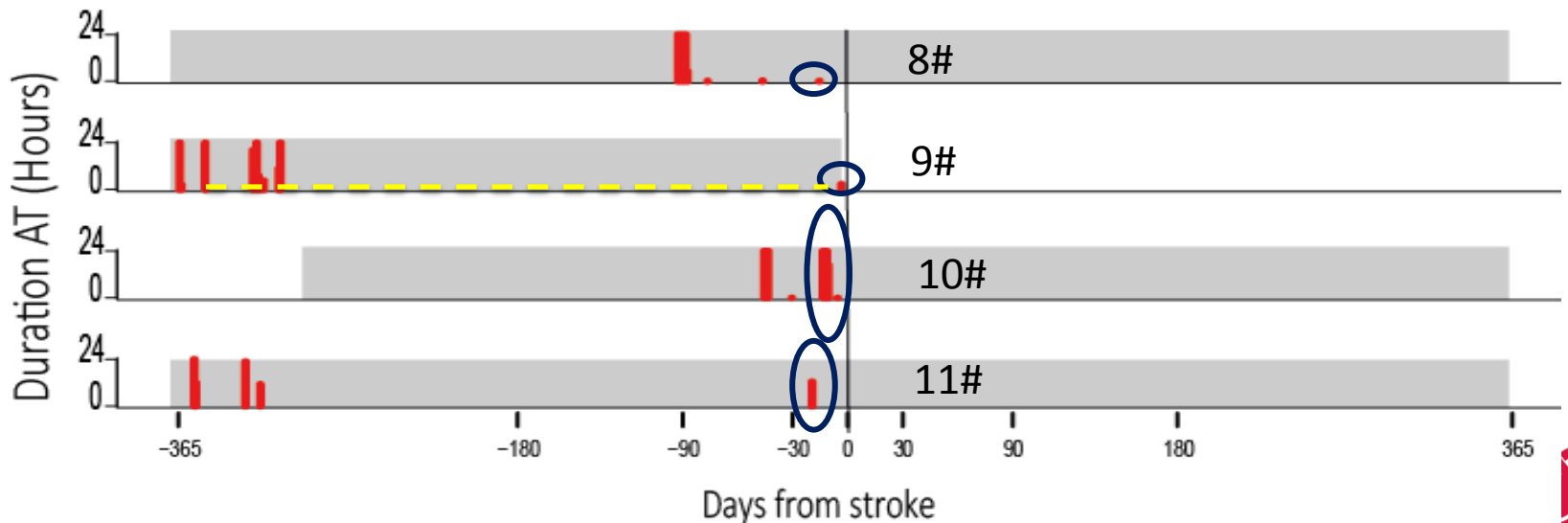


SCAF detected AFTER Stroke



Results: SCAF occurring PRIOR to the Stroke

- In **14 PATIENTS (27%)** SCAF occurred > 30 days prior to the STROKE
 - The most recent episode of SCAF
 - > median interval of 339 days (P25-P75:211-619 days) before
 - > median duration of 4.2 hours (P25-P75:0.80-466 hours)
- In **ONLY 4 PATIENTS (8%)** SCAF occurred within 30 days prior to the STROKE
 - 8# had last SCAF 11 days before (6 minutes)
 - 9# had SCAF at the time of his stroke (2.7 hours)
 - 10# had last SCAF 9 days before (4 days)
 - 11# had last SCAF 15 days before (12 hours)



Results: SCAF occurring AFTER the Stroke

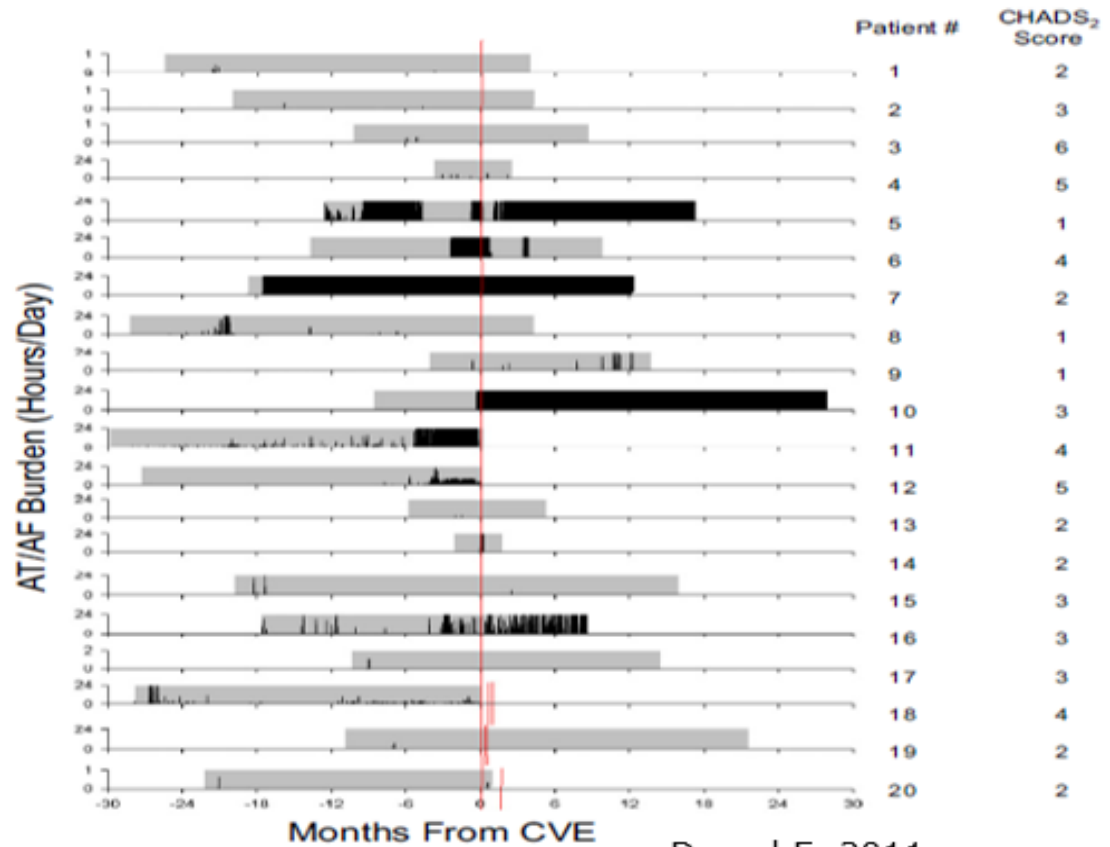
- In 8 patients (16%), SCAFs were detected only AFTER the stroke at a median interval of 101 days (P25-P75:14-196).
- The maximum median SCAF duration on a single day was 6.3 hours (P25-P75:1.9-10.3).

CONCLUSIONS I

TRENDS SUBSTUDY

40 stroke patients:

- 20 pts with AT/AF detected prior to the embolic events
 - ✓ 45% pts with no AT/AF within 30 days of stroke
 - ✓ 15% pts with AT/AF within 30 days
 - ✓ 30% pts was in AT/AF at the time of their stroke
 - ✓ 55% with diagnosis of AF prior to the enrolment



Daoud E, 2011

→ INDIRECT MECHANISM OF STROKE?

→ SCAF AS A RISK MARKER?

CONCLUSIONS II

| Study | Groups | N | Onset of Monitoring after stroke (days) | Duration of monitoring (days) | Proportion with AF (%) | Use of oral anticoagulant (%) |
|----------------------------------|------------------------|-----|---|-------------------------------|------------------------|-------------------------------|
| EMBRACE (NEMJ 2014) | Usual* | 285 | 75.1±38.6 | 90 | 3.2 | 11.1 |
| | Intensive ^o | 286 | | | 16.1 | 18.6 |
| CRYSTAL AF (NEMJ 2014) | Usual* | 220 | 38.1±27.6 | 180 | 1.4 | 4.6 |
| | Intensive [§] | 221 | | | 8.9 | 10.1 |

*12-lead ECG and Holter ECG monitoring for 24-48 h. ^o Continuous surface ECG for 4 weeks. [§]Subcutaneous ECG monitoring with an implanted device for up to 3 years.

Modified from Camm J,2014

-> SCAF AFTER CRYPTOGENETIC STROKE STILL THE CAUSE OF THE EMBOLIC EVENT?

THANK YOU
FOR YOUR
ATTENTION