ASSERT Sub Study

Temporal relationship between Subclinical Atrial Fibrillation and Embolic Event

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A Registered Branch of the ESC

EUROPEAN SOCIETY OF CARDIOLOGY®

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 (subclinal 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				
	events	%/ year	events	%/year	RR	95% CI	p
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 Shanmugam[1], Annegret Boerdlein[2], Jochen Proff[2], Peter Ong[1], Oswaldo Valencia[1], Sebastian K.G. Maier[3], Wolfgang R. Bauer[3], Vince Paul[4]*, and Stefan Sack[5]

- 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

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;
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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 ≥ 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

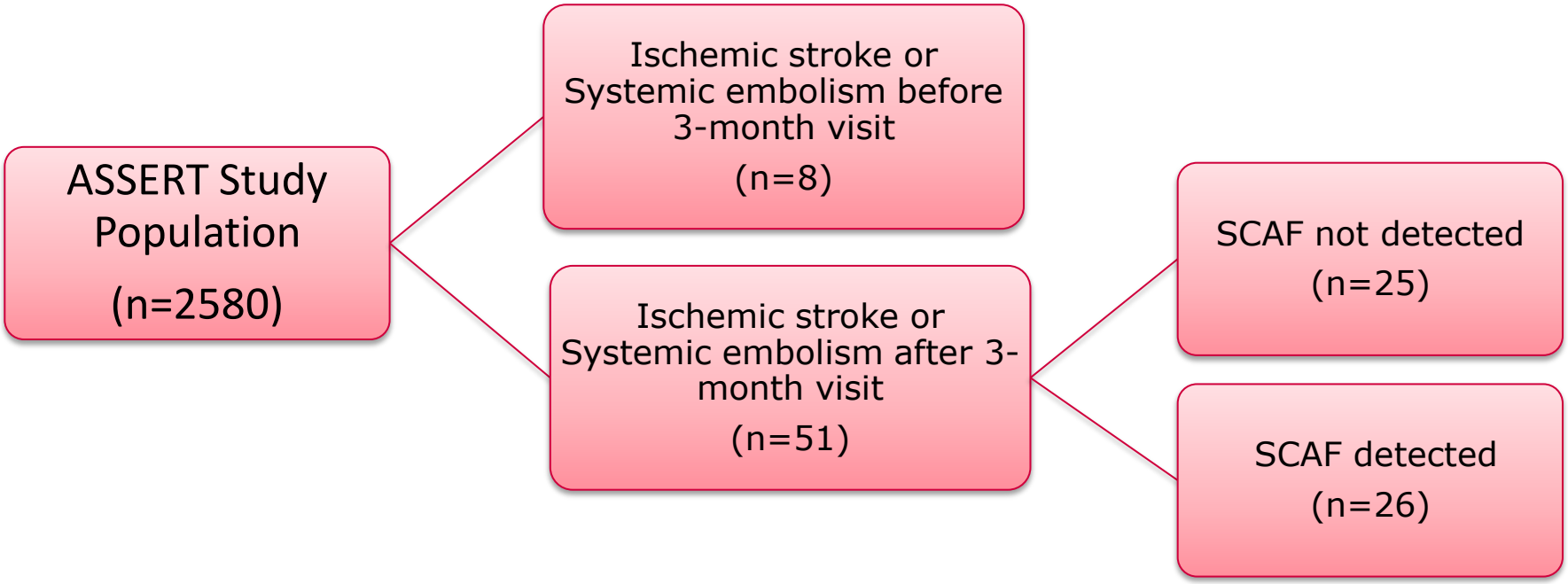
Stored Device Data (Date, Time of onset and duration*) of all SCAF events detected for the entire FU

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

Outcome

- Ischemic stroke or systemic embolism

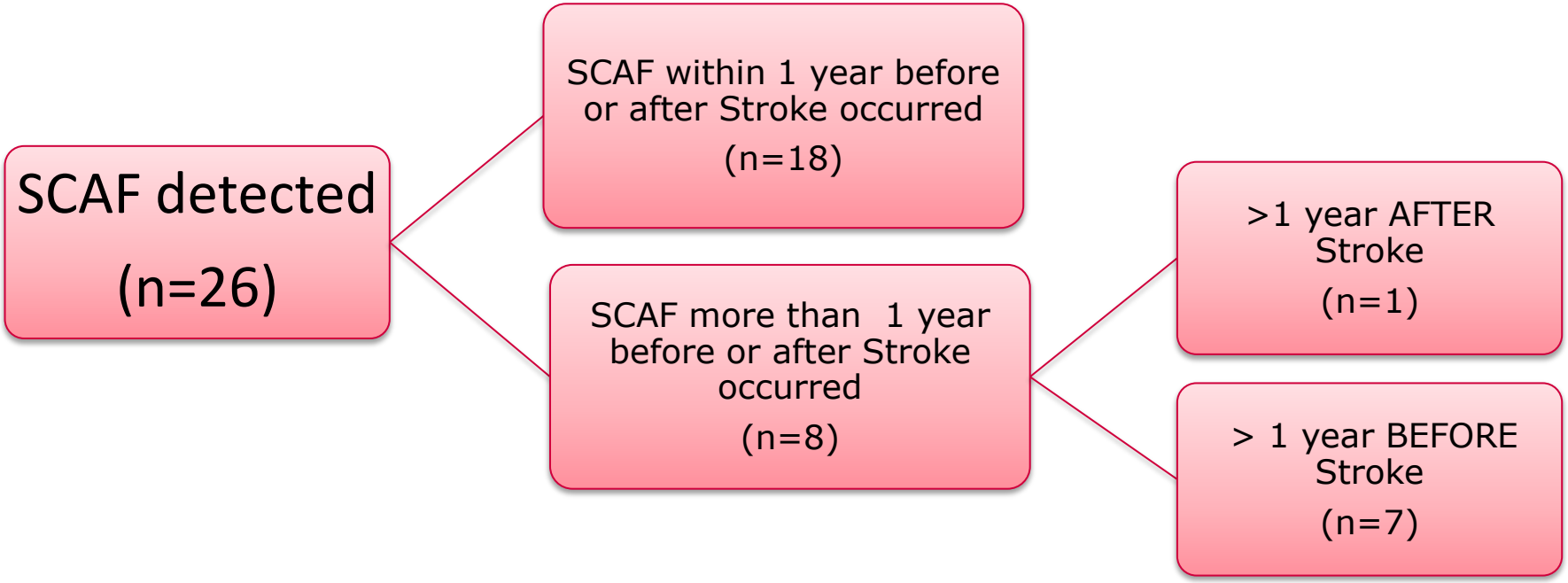
STUDY FLOW CHART



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)
Time from Device Implant to Stroke (days)	**Mean (SD)**	**580 ± 357**	**703 ± 394**	**643 ± 377**
	Median (P25-P75)	**570 (263-816)**	**670 (456-900)**	**612 (293-890)**
Time from Stroke to last follow up (days)	**Mean (SD)**	**477 ± 399**	**452 ± 480**	**464 ± 438**
	Median (P25-P75)	**404 (93-866)**	**350 (41-731)**	**398 (71-825)**

STUDY FLOW CHART

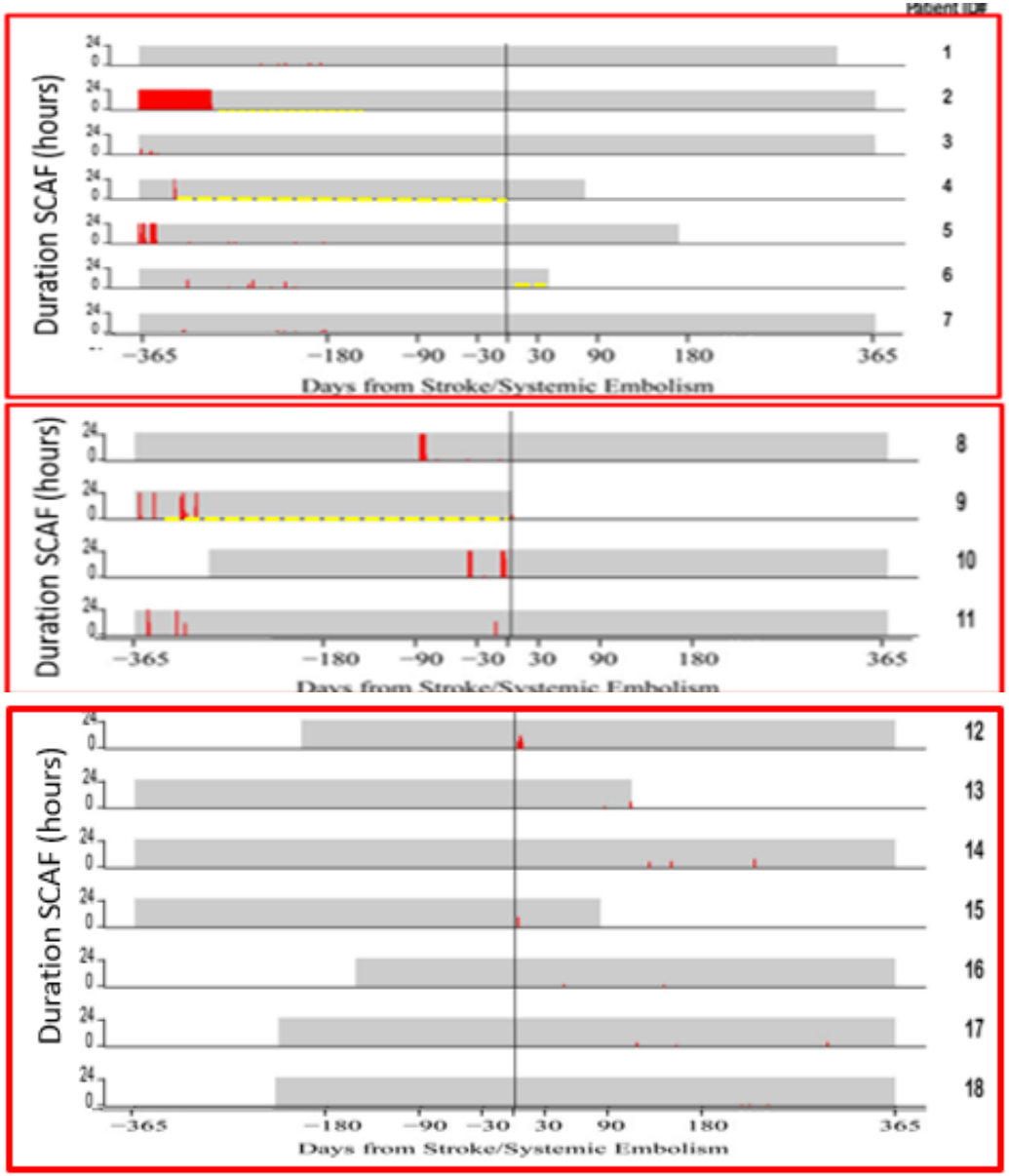


Results: SCAF occurring within 1 year before or after Stroke

SCAF detected
> 30 days BEFORE the Stroke

SCAF detected
< 30 days BEFORE the Stroke

SCAF detected AFTER Stroke



Brambatti M.

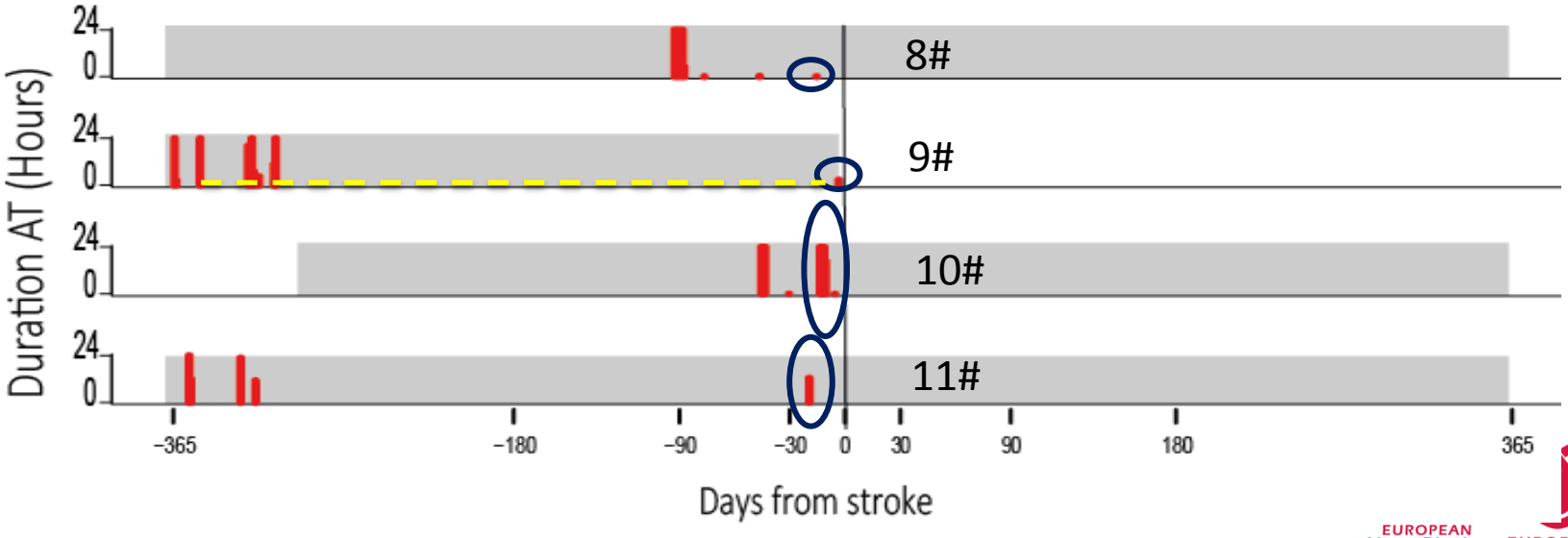
Results: SCAF occurring PRIOR to the Stroke

- **In <u>14 PATIENTS (27%)</u> 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 <u>4 PATIENTS (8%)</u> 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).

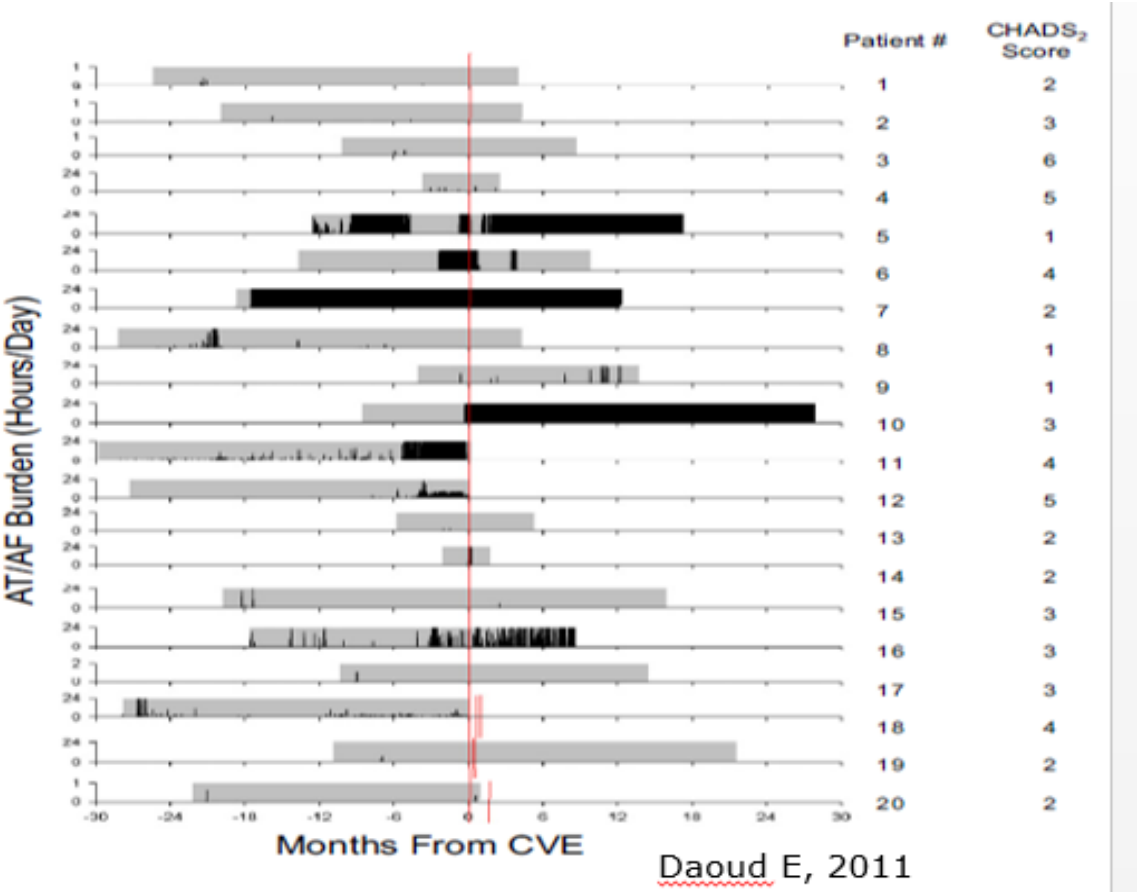
- The maximum median SCAF duration on a single day was 6.3 hours (P25-P75:1.9-10.3).

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



→ 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* Intensive°	285 286	75.1±38.6	90	3.2 16.1	11.1 18.6
CRYSTAL AF (NEMJ 2014)	Usual* Intensive§	220 221	38.1±27.6	180	1.4 8.9	4.6 10.1

*12-lead ECG and Holter ECG monitoring for 24-48 h. ° 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