Asemptomatik Atriyal Fibrilasyon Kriptojenik İnmelerden Sorumlu mudur?

Dr. Sinan Aydoğdu

Türkiye Yüksek İhtisas Hastanesi

Kardiyoloji Kliniği

Kriptojenik inme

- Tanım
  - Kapsamlı vasküler, kardiyak ve serolojik değerlendirmelere rağmen net sebebi saptanamamış iskemik inme
- Sıklık
  - Tüm iskemik inmelerin yaklaşık % 25'i

- MR veya CT
- 12-lead EKG
- 24-saat Holter
- TEE
- < 55 yaş ise protrombotik durum değerlendirmesi
- Baş-boyun bölgesi için CTA, MRA veya konv anjiyo

Sessiz AF

- Sık
  - % 90'a varan oranlar
- Klasik bilgi
  - AF'daki inme riski klinik tezahür tipinden bağımsız
  - Dolayısıyla sessiz de olsa, AF iskemik inmeye yol açabilir

SPECIAL ARTICLE

AMERICAN ACADEMY OF NEUROLOGY.

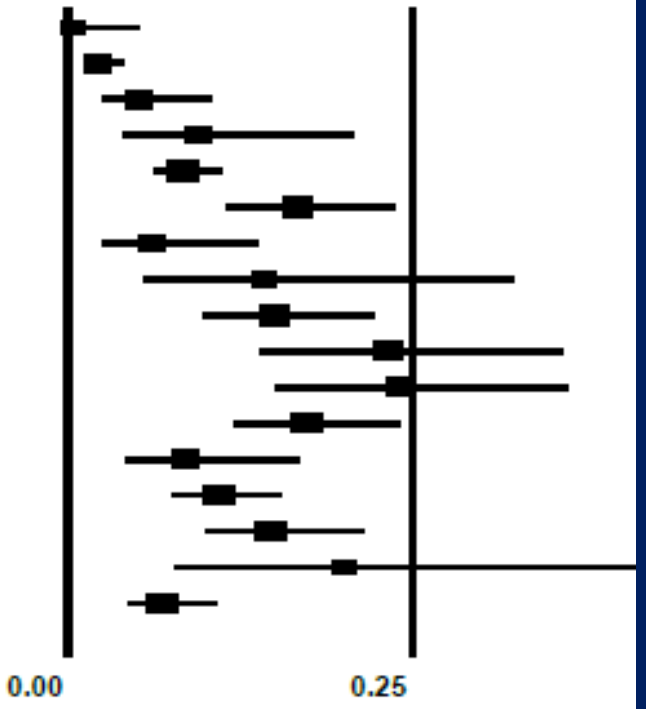
Summary of evidence-based guideline update: Prevention of stroke in nonvalvular atrial fibrillation

Report of the Guideline Development Subcommittee of the American Academy of Neurology

Neurology® 2014;82:716–724

Figure e-1 Proportion of ischemic stroke patients identified with NVAF, by study

Author, year	Class	Technique	Monitoring duration (days)
Douen 2007[e23]	III	HM	1.0
Schaer 2004[e26]	III	HM	1.0
Vandenbroucke 2004[e21]	III	HM	1.0
Lazzaro 2012[e22]	III	HM	1.0
Rizos 2012[e18]	III	inptTele	2.7
Douen 2008[e24]	III	sEKG	3.0
Schuchert 1999[e20]	III	HM	3.0
Barthelemy 2003[e28]	III	ELR	7.0
Wallmann 2007[e19]	III	sELR	21.0
Tayal 2008[e17]	II	MCOT	21.0
Bhatt 2011[e31]	III	MCOT	21.0
Miller 2013[e32]	III	MCOT	21.0
Gaillard 2010[e29]	III	phoneEKG	30.0
Flint 2012[e16]	II	ELR	30.0
Jabaudon 2004[e27]	III	sEKG, HM, ELR	30.0
Elijovich 2009[e30]	III	ELR	30.0
Doliwa 2012[e25]	III	HM	31.0



NVAF at a rate ranging from 0% to 23% (weighted average of 10.7%)

Prolonged Ambulatory Cardiac Monitoring Improves the Detection and Treatment of Atrial Fibrillation in Patients with Cryptogenic Stroke: Primary Results from the EMBRACE Multicenter Randomized Trial

Background: Detecting atrial fibrillation (AF) in stroke/TIA patients can result in therapy to prevent recurrent strokes. However, standard short duration monitoring (24-48 h) for atrial fibrillation may not detect AF.

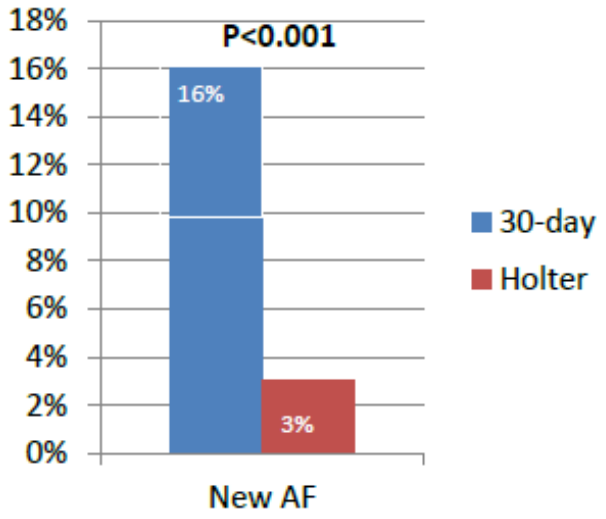
Purpose: This study is the first randomized trial to evaluate whether longer non-invasive ECG monitoring after stroke/TIA would produce beneficial results.

Methods: n=572 (age 73±9yrs;); recent ischemic stroke/TIA, no known AF; 16 stroke centers; Randomized to wear either an event-triggered cardiac monitor up to 30 days or a repeat 24 h Holter. AF events automatically recorded.

Primary Outcome: ≥1 episodes of AF of at least 30 seconds within 90 days of randomization

Secondary Outcomes: monitoring adherence ; anticoagulation status

Results: New AF detected among 16% of 30-day monitoring group, vs. 3% in the Holter group (p<0.001). In the 30 day group three quarters of AF events occurred within the first 2 weeks. 71% of all patients were anticoagulated; anticoagulant use at 90 days > 30 day group (49/280; 18%) vs. Holter group (28/279; 10%; p=0.01).



Conclusion: Paroxysmal AF is undiagnosed and untreated in many stroke/TIA patients ; in the post-stroke setting it is under-detected by the Holter monitor. Prolonged continuous monitoring for 30 days is "feasible, more effective, and leads to clinically meaningful changes in patient management. "

Presented by: Gladstone DJ, International Stroke Conference, Honolulu, HI

CRYSTAL AF

Study of Continuous Cardiac Monitoring to Assess Atrial Fibrillation After Cryptogenic Stroke

Phase 3, randomized, prospective study in patients with cryptogenic stroke
Sample size ~ 450 patients

- Inclusion criteria
  - Recent cryptogenic symptomatic transient ischemic attack (TIA) or cryptogenic ischemic stroke

Continuous cardiac monitoring:
Reveal XT™ insertable cardiac monitor

Control arm:
Follow-up at the same frequency, but with no insertable cardiac monitor

Primary outcome: Time to first documented episode of AF within 6 mo after stroke

Secondary outcomes: Time to first documented episode of AF by 12 mo of CRM; incidence of stroke and transient ischemic attack (TIA); cardiovascular drug changes (oral anticoagulation and antiarrhythmic drugs); quality of life; clinical disease burden and care pathway; patient assistant impact on AF diagnosis

ClinicalTrials.gov website.[11]

Methods

- AF defined as an episode of irregular heart rhythm, without detectable p waves, greater than 30 seconds
- AF episodes were identified by patient's physician and adjudicated by an independent committee

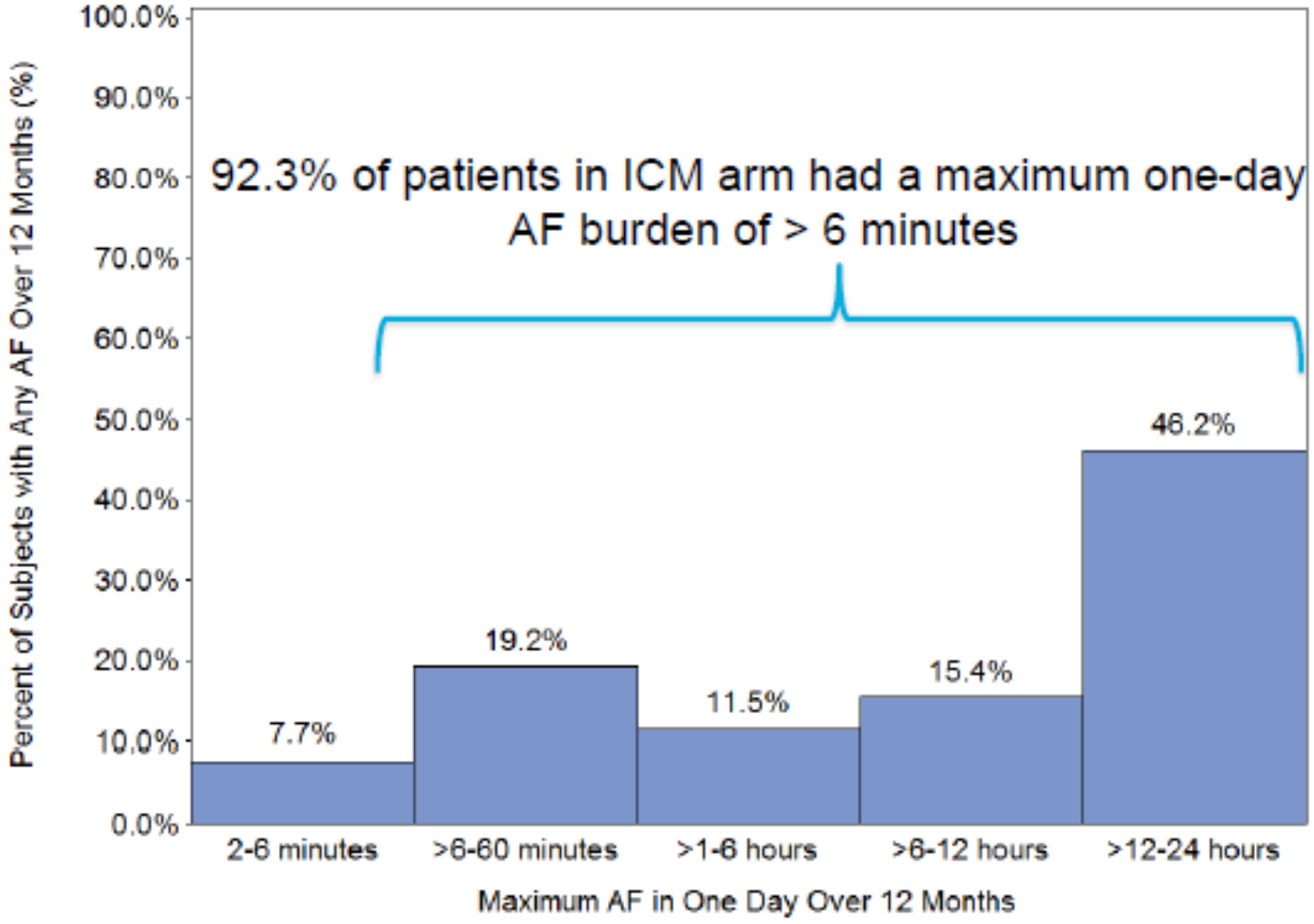
CRYSTAL AF

Detection of AF With Insertable Cardiac Monitor

Time, mo	ICM, %	Control, %	HR	*P* Value
6	8.9	1.4	6.43	.0006
12	12.4	2.0	7.32	.0001
36	30.0	3.0	8.78	.0001

Bernstein RA, et al. International Stroke Conference 2014. Abstract LB11.[12]

Atrial Fibrillation Duration in ICM Arm at 12 months (N=29)



Sessiz AF – inme ilişkisi ?

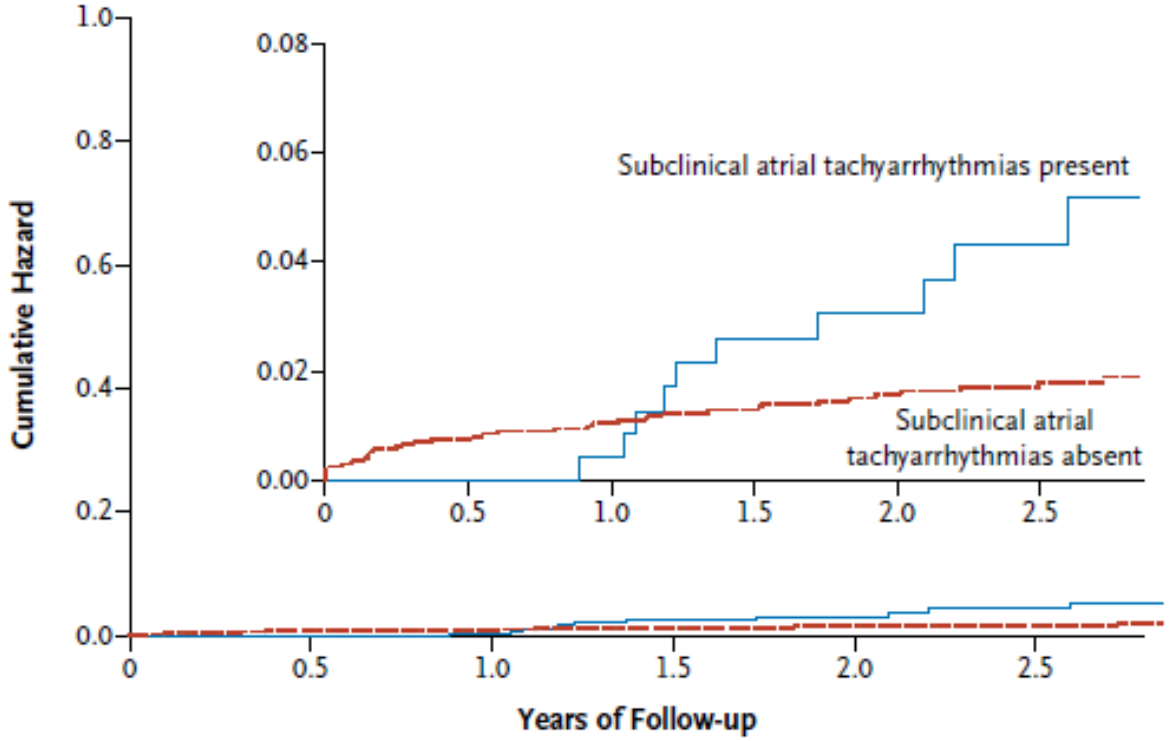
Subclinical Atrial Fibrillation and the Risk of Stroke

Jeff S. Healey, M.D., Stuart J. Connolly, M.D., Michael R. Gold, M.D., Carsten W. Israel, M.D., Isabelle C. Van Gelder, M.D., Alessandro Capucci, M.D., C.P. Lau, M.D., Eric Fain, M.D., Sean Yang, M.Sc., Christophe Bailleul, M.D., Carlos A. Morillo, M.D., Mark Carlson, M.D., Ellison Themeles, M.Sc., Elizabeth S. Kaufman, M.D., and Stefan H. Hohnloser, M.D., for the ASSERT Investigators*

- Pil veya ICD taşıyan 2580 olgu
- 65 yaş ve üstü
- AF öyküsü yok
- 2.5 yıl takip

NEJM 2012;366:120

B Risk of Ischemic Stroke or Systemic Embolism



No. at Risk

Subclinical atrial tachyarrhythmias present	261	249	238	218	178	122
Subclinical atrial tachyarrhythmias absent	2319	2145	2070	1922	1556	1197

Figure 1. The Risk of Clinical Atrial Tachyarrhythmias and of Ischemic Stroke or Systemic Embolism, According to the Presence or Absence of Subclinical Atrial Tachyarrhythmias.

Table 3. Risk of Ischemic Stroke or Systemic Embolism after the 3-Month Visit, According to Baseline $CHADS_2$ Score and According to Whether Subclinical Atrial Tachyarrhythmias Were or Were Not Detected between Enrollment and the 3-Month Visit.

$CHADS_2$ Score	No. of Patients	Subclinical Atrial Tachyarrhythmias between Enrollment and 3 Months						Hazard Ratio for Ischemic Stroke or Systemic Embolism with Subclinical Atrial Tachyarrhythmias (95% CI)*
		Present			Absent			
		no. of patients	*no. of events*	%/yr	*no. of patients*	*no. of events*	%/yr	
1	600	68	1	0.56	532	4	0.28	2.11 (0.23–18.9)
2	1129	119	4	1.29	1010	18	0.70	1.83 (0.62–5.40)
>2	848	72	6	3.78	776	18	0.97	3.93 (1.55–9.95)

* The P value for trend is 0.35.

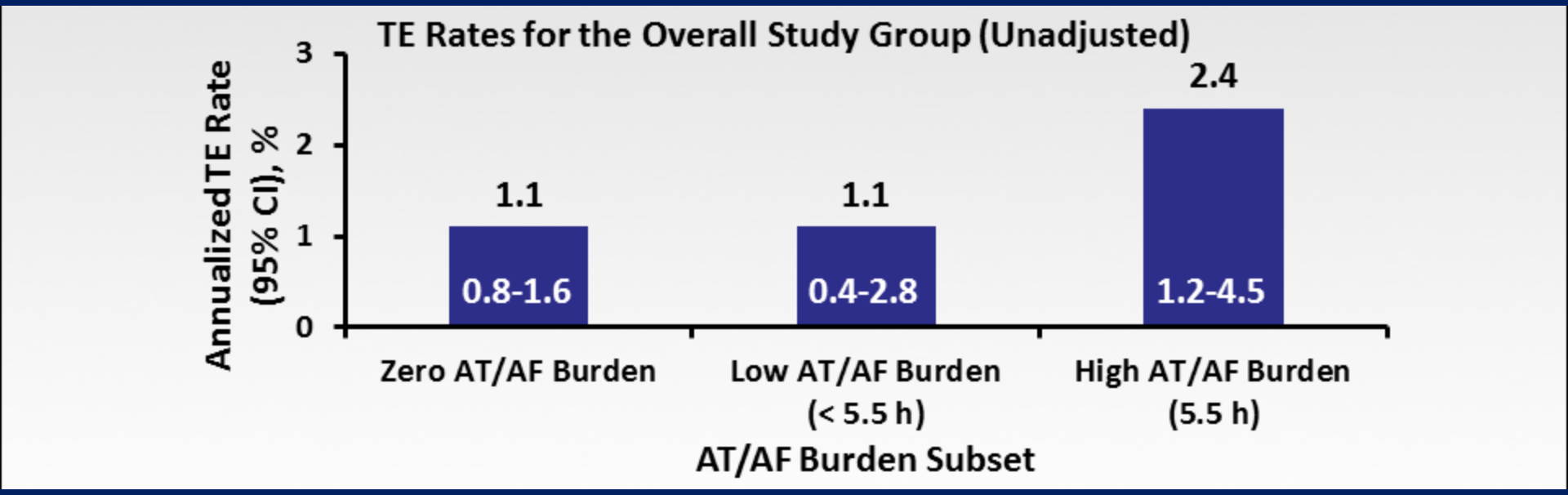
AF’nin süresi önemsiz mi ?

AF epizod süresi	İnme/emboli sıklığı (%/yıl)
≤ 0.86 saat	1.23
0.87-3.63 saat	0
3.64-17.72 saat	1.18
> 17.72 saat	4.89

Original Articles

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

The TRENDS Study



Circ Arrhythmia Electrophysiol. 2009;2:474-480.

European Heart Journal
doi:10.1093/eurheartj/eht491

Device-detected atrial fibrillation and risk for stroke: an analysis of >10 000 patients from the SOS AF project (Stroke preventiOn Strategies based on Atrial Fibrillation information from implanted devices)

Objective The aim of this study was to assess the association between maximum daily atrial fibrillation (AF) burden and risk of ischaemic stroke.

Background Cardiac implanted electronic devices (CIEDs) enhance detection of AF, providing a comprehensive measure of AF burden.

Design, setting, and patients A pooled analysis of individual patient data from five prospective studies was performed. Patients without permanent AF, previously implanted with CIEDs, were included if they had at least 3 months of follow-up. A total of 10 016 patients (median age 70 years) met these criteria. The risk of ischaemic stroke associated with pre-specified cut-off points of AF burden (5 min, 1, 6, 12, and 23 h, respectively) was assessed.

Results During a median follow-up of 24 months, 43% of 10 016 patients experienced at least 1 day with at least 5 min of AF burden and for them the median time to the maximum AF burden was 6 months (inter-quartile range: 1.3–14). A Cox regression analysis adjusted for the $CHADS_2$ score and anticoagulants at baseline demonstrated that AF burden was an independent predictor of ischaemic stroke. Among the thresholds of AF burden that we evaluated, 1 h was associated with the highest hazard ratio (HR) for ischaemic stroke, i.e. 2.11 (95% CI: 1.22–3.64, $P = 0.008$).

Conclusions Device-detected AF burden is associated with an increased risk of ischaemic stroke in a relatively unselected population of CIEDs patients. This finding may add to the basis for timely and clinically appropriate decision-making on anticoagulation treatment.

AF yükünün önemi

$CHADS_2$	ASSERT YILLIK İNME %	KLİNİK AF ÇALIŞMALARI YILLIK İNME %
1	*0.56*	2.8
2	*1.29*	4.0
≥3	*3.78*	6.4

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

*From *Ohio State University Medical Center, Ross Heart Hospital, Columbus, Ohio, †Hackensack University Medical Center, Hackensack, New Jersey, ‡Libin Cardiovascular Institute of Alberta, Calgary, Alberta, Canada, and ¶Lankenau Institute for Medical Research, Philadelphia, PA; §Medtronic Inc., Minneapolis, Minnesota.*

TRENDS çalışması

- Embolik olaydan 30 gün öncesinde AF % 27 olguda var
- Embolik olay olduğunda olguların % 15'inde AF mevcut

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

*From *Ohio State University Medical Center, Ross Heart Hospital, Columbus, Ohio, †Hackensack University Medical Center, Hackensack, New Jersey, ‡Libin Cardiovascular Institute of Alberta, Calgary, Alberta, Canada, and ¶Lankenau Institute for Medical Research, Philadelphia, PA; §Medtronic Inc., Minneapolis, Minnesota.*

BACKGROUND The temporal relationship between atrial tachyarrhythmias (atrial tachycardia [AT] and atrial fibrillation [AF]) and cerebrovascular events/systemic emboli (CVE/SE) is unknown.

OBJECTIVE The purpose of this study was to evaluate this relationship using stored AT/AF diagnostic data from implanted devices in patients with and those without AF.

METHODS The TRENDS study enrolled 2,486 patients with an indication for an implantable device, at least one stroke risk factor, and available device data. The current study includes the subgroup of 40 (1.6%) patients enrolled in TRENDS who experienced CVE/SE.

RESULTS AT/AF was detected *prior* to CVE/SE in 20 (50%) of 40 patients. Other than average and maximum daily AT/AF burden and duration of device monitoring prior to CVE/SE, no statistically significant differences were found between patients with and those without AT/AF prior to CVE/SE. For the 20 patients with AT/AF detected prior to CVE/SE, 9 (45%) did not have any AT/AF in the 30 days prior to CVE/SE. Therefore, 29 (73%) of 40 patients with CVE/SE had zero AT/AF burden within 30 days prior to CVE/SE. Fourteen (70%) of the 20 patients with AT/AF detected prior to CVE/SE were not in AT/AF at diagnosis of CVE/SE. The last episode of AT/AF in these 14 patients was 168 ± 199 days (range 3–642 days) before CVE/SE.

CONCLUSION The majority of CVE/SE in this population did not occur proximal to recent AT/AF episodes. These data imply that the mechanisms of CVE/SE in patients with implantable devices may importantly involve mechanisms other than cardioembolism due to atrial tachyarrhythmias.

KEYWORDS Atrial fibrillation; Atrial tachyarrhythmia; Implantable cardiac device; Stroke

ABBREVIATIONS **AF** = atrial fibrillation; **AT** = atrial tachycardia; **CVE** = cerebrovascular event; **SE** = systemic embolus; **TIA** = transient ischemic attack

(Heart Rhythm 2011;8:1416–1423)

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

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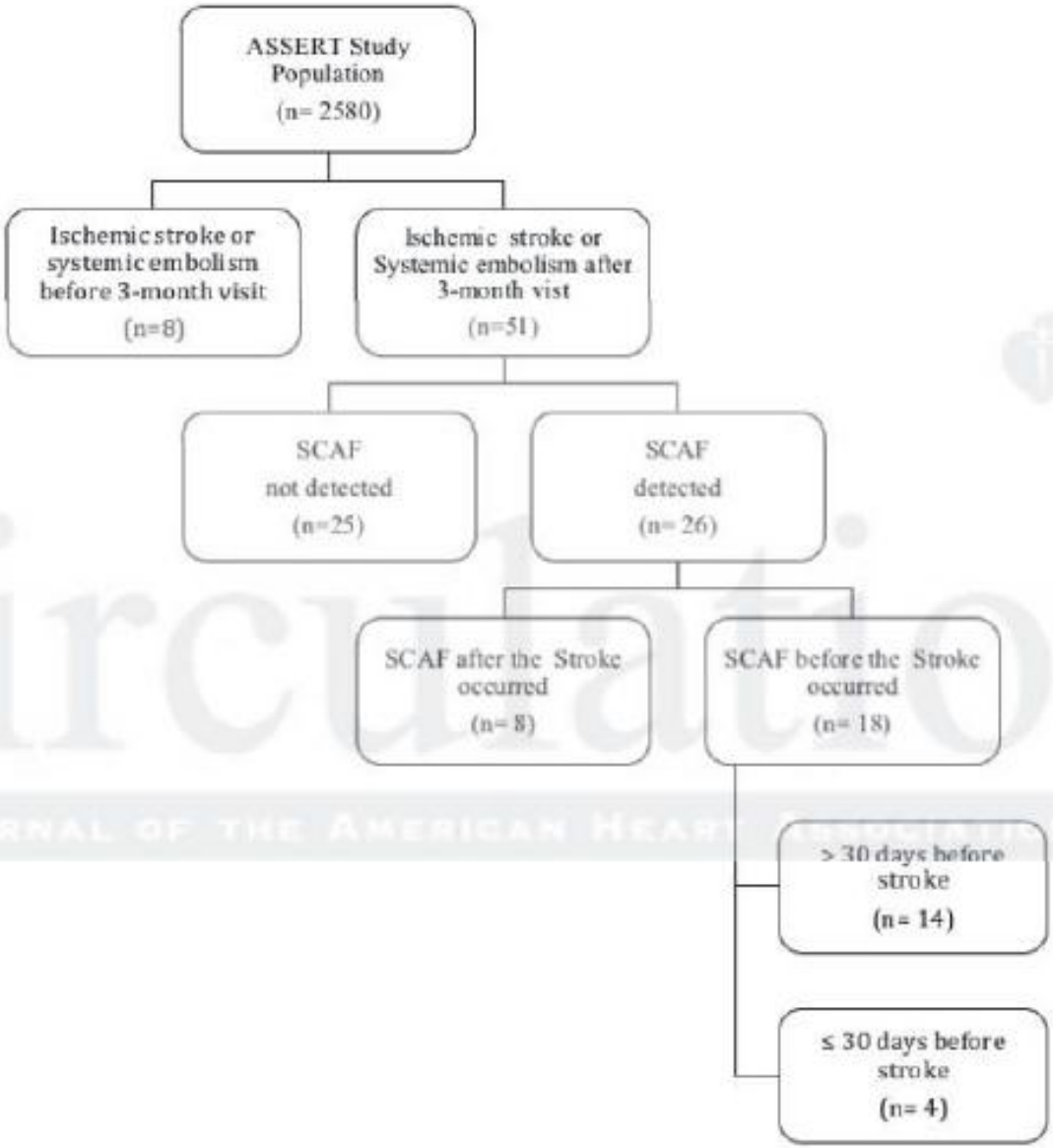

Median İnterval
339 gün

Poststroke atrial fibrillation: Cause or consequence?

Critical review of current views

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Patricia M. Riccio, MD
Vladimir Hachinski, CM, MD, FRCPC, DSc

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ABSTRACT

Poststroke atrial fibrillation (AF) represents up to 1 of 4 overall AF cases in acute ischemic stroke. Current guidelines recommend oral anticoagulation for every ischemic stroke patient in whom AF is diagnosed. However, in some cases, AF detected after acute ischemic stroke may be short-lasting and perhaps a nonrecurrent autonomic and inflammatory epiphenomena of stroke. The autonomic regulation of cardiac rhythm constitutes an integrated relay system. The highest level of control is exerted by the cerebral cortex, particularly the insula. The onset of AF may be associated with an imbalance of sympathetic and parasympathetic activity, a common consequence of insular infarctions. This autonomic imbalance and an interruption in the cerebral regulation of the intrinsic cardiac autonomic system constitute the most likely mechanisms responsible for the autonomic pathway. The role of inflammation in the genesis of AF within the first few days after ischemic stroke may occur through inflammatory mediators stimulating the intrinsic autonomic system and by direct damage to atrial myocardium. To what extent poststroke AF is the cause or a consequence remains uncertain. *Neurology*® 2014;82:1180–1186

GLOSSARY

AF = atrial fibrillation; **CABG** = coronary artery bypass graft; **CI** = confidence interval; **CRP** = C-reactive protein; **IL-6** = interleukin-6; **OR** = odds ratio; **SDB** = sleep-disordered breathing; **TNFα** = tumor necrosis factor α.

"Do not fear to be eccentric in opinion, for every opinion now accepted was once eccentric."

—Bertrand Russell

Guidelines for the Prevention of Stroke in Patients With Stroke and Transient Ischemic Attack: A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association

Walter N. Kernan, Bruce Ovbiagele, Henry R. Black, Dawn M. Bravata, Marc I. Chimowitz, Michael D. Ezekowitz, Margaret C. Fang, Marc Fisher, Karen L. Furie, Donald V. Heck, S. Claiborne (Clay) Johnston, Scott E. Kasner, Steven J. Kittner, Pamela H. Mitchell, Michael W. Rich, DeJuran Richardson, Lee H. Schwamm and John A. Wilson

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AF Recommendations

1. **For patients who have experienced an acute ischemic stroke or TIA with no other apparent cause, prolonged rhythm monitoring (≈30 days) for AF is reasonable within 6 months of the index event *(Class IIa; Level of Evidence C)*.** (New recommendation)

- KS demeden önce :
  - EKG
  - Hastane içi devamlı monitor
  - TTE
  - TEE
  - Uzun süreli EKG kaydı
    - Ne süre ile ?
    - Nasıl ?
      - ILR ?
      - ELR ?

ILR – kime ?

- > 65 yaş
- Yüksek CHADSVASc skoru
- Ağır inme tablosu
- Sık APS
- TTE'da geniş sol atriyum

KS – AF saptandı ne yapalım ?

- Hayat boyu antikoagülan

KS – AF arandı, bulunamadı ne yapalım ?

- Nasıl arandı ?
  - 1 günlük Holter ?
  - ILR ?
  - ELR ?
- CHADSVASc skoru kaç ?

Stroke
Journal of the American Heart Association

American Heart Association | American Stroke Association

Prolonged Cardiac Monitoring for Detection of Paroxysmal Atrial Fibrillation After Cerebral Ischemia

Alejandro A. Rabinstein

Stroke. 2014;45:1208-1214; originally published online March 11, 2014;

Table 1. Main Characteristics of Available Methods for Prolonged Ambulatory Cardiac Rhythm Monitoring

Device	Location	Duration	Minimal Threshold	Limitations
Holter	Skin surface	Usually 1–2 d	Few seconds	Short duration
External loop recorder	Skin surface	≤30 d	Few seconds	Requires patient action
Ambulatory telemetry	Skin surface	≤30 d	Few seconds	Patient compliance Skin irritation Cost
Implantable loop recorder	Subcutaneous	≤3 y	2 min	Invasiveness (minimal) Does not detect PAF<2 min Cost
Dual-chamber pacemaker and defibrillator	Intracardiac	Many years	Seconds	Only indicated for life-threatening arrhythmias

PAF indicates paroxysmal atrial fibrillation.

Table 3. Risk Factors for Paroxysmal Atrial Fibrillation Detection

Older age
Cryptogenic stroke/TIA
Documented vascular disease
Vascular risk factors (higher $CHADS_2$ or CHA_2DS_2-VASc score)
Greater stroke severity
Frequent PACs on ECG or Holter
Left atrial dilatation on TTE
Left atrial appendage dysfunction on TEE
Multiterritorial or single corticosubcortical DWI lesions