Atrial Fibrillation and the Risk of Stroke

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Atrial Fibrillation and Stroke: Epidemiology

- ~ 20 – 30% of strokes are thought to be cardioembolic in origin
- Most cardioembolic strokes are due to atrial fibrillation: 15 - 20% of all strokes are due to A Fib
- A Fib increases the risk of stroke 5-fold
- Incidence of A Fib increases with age
- Current prevalence of A Fib in US is 5.1 million; by 2050 it may be 16 million

Atrial Fibrillation and Stroke: Epidemiology

- But although 20 – 30% of strokes are thought to be cardioembolic in origin, not all of these are proven to be so
- Up to 20 - 30 % of strokes are cryptogenic - many of these could be of occult cardioembolic origin - in particular, due to unrecognized atrial fibrillation

Etiology of Strokes

Other
4%

Hemorrhagic
12%

Cryptogenic
26%

Cardioembolic
18%

Small Vessel
22%

Large Vessel
18%
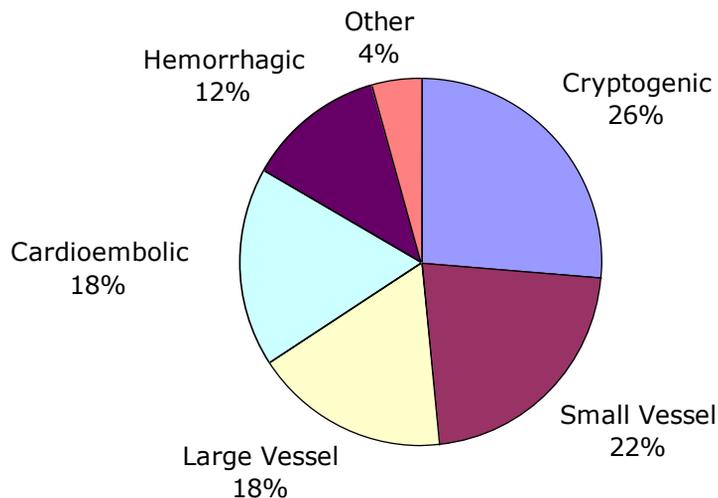
Albers et al Chest 2004; 126 (3 Suppl): 486S-512S
Thom et al AHA Circulation 2006; 113: e85-e151

CRYSTAL AF:
CRYptogenic STroke And underLying AF

- 441 patients randomized to either insertable cardiac monitor (ICM) or conventional follow-up
- Index event: cryptogenic ischemic stroke or TIA within 90 days
- No previous A Fib or flutter, no indication or contraindication for oral anticoagulation, no indication for pacemaker or difibrillator
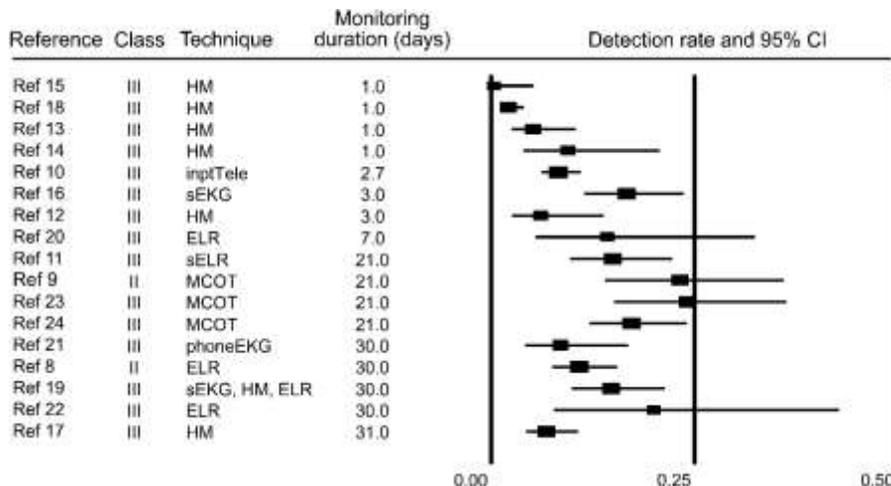- 40 years of age or older

Tommaso Sanna et al NEJM 2014

CRYSTAL AF:
Percentage of patients in whom A Fib was detected
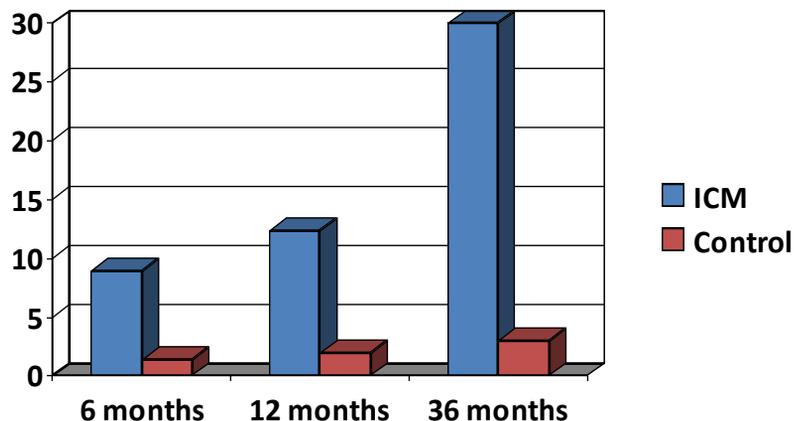
Tommaso Sanna et al NEJM 2014

Summary of evidence-based guidelines: Prevention of Stroke in Non-Valvular Atrial Fibrillation

Proportion of patients with ischemic stroke identified with non-valvular atrial fibrillation

| Reference	Class	Technique	Monitoring duration (days)	Detection rate and 95% CI
Ref 15	III	HM	1.0	
Ref 18	III	HM	1.0	
Ref 13	III	HM	1.0	
Ref 14	III	HM	1.0	
Ref 10	III	inptTele	2.7	
Ref 16	III	sEKG	3.0	
Ref 12	III	HM	3.0	
Ref 20	III	ELR	7.0	
Ref 11	III	sELR	21.0	
Ref 9	II	MCOT	21.0	
Ref 23	III	MCOT	21.0	
Ref 24	III	MCOT	21.0	
Ref 21	III	phoneEKG	30.0	
Ref 8	II	ELR	30.0	
Ref 19	III	sEKG, HM, ELR	30.0	
Ref 22	III	ELR	30.0	
Ref 17	III	HM	31.0	

ELR = Event Loop Recorder
HM = Holter Monitor
MCOT = Mobile Cardiac Outpatient Telemetry

Culebras A et al. Neurology 2014;82:716-724

Relative risk reductions of various outcomes in patients with nonvalvular atrial fibrillation receiving various antithrombotic regimens as compared with warfarin or its derivatives

Culebras A et al. Neurology 2014;82:716-724
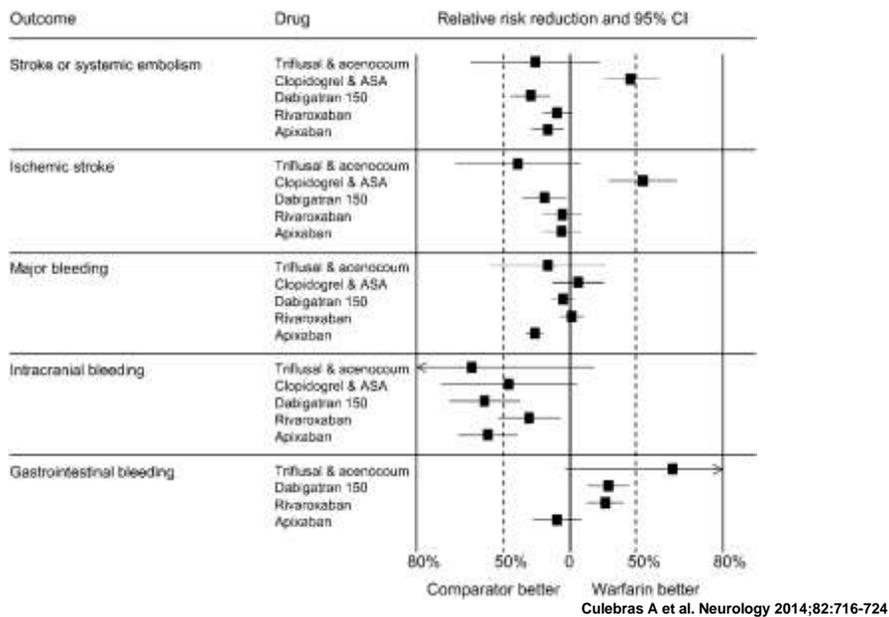
Identification of patients with occult NVAF

- Clinicians might obtain outpatient cardiac rhythm studies in patients with cryptogenic stroke without known NVAF, to identify patients with occult NVAF (Level C).

- Clinicians might obtain cardiac rhythm studies for prolonged periods (e.g., for 1 or more weeks) instead of shorter periods (e.g., 24 hours) in patients with cryptogenic stroke without known NVAF, to increase the yield of identification of patients with occult NVAF (Level C).

Selection of patients for antithrombotic therapy

- Clinicians should inform patients with NVAF that these patients have an increased stroke risk and that this risk can potentially be reduced by antithrombotic use. Patients should also be informed that antithrombotic use increases their risk of major bleeding (Level B).
- Clinicians should counsel all patients with NVAF that the decision to use antithrombotics must be made only after the potential benefit from the stroke risk reduction has been weighed against the potential harm from the increased risk of major bleeding. Clinicians should also emphasize the important role of judgment and preferences in this decision (Level B).

Selection of patients for antithrombotic therapy

- Routinely offer anticoagulation to patients with NVAF and a history of TIA or stroke, to reduce these patients' subsequent risk of ischemic stroke (Level B).
- Might not offer anticoagulation to patients with NVAF who lack additional risk factors ("lone" NVAF patients). Might reasonably offer antithrombotic therapy with aspirin to such patients or might not offer antithrombotic therapy at all (Level C).
- To judge which patients with NVAF might benefit from anticoagulation, use a risk stratification scheme to help identify patients with NVAF who are at higher risk for stroke or at no clinically significant risk. However, one should not rigidly interpret anticoagulation thresholds suggested by these tools as being definitive indicators of which patients require anticoagulation (Level B).

Selection of a specific oral anticoagulant

- To reduce the risk of stroke or subsequent stroke in patients with NVAF judged to require oral anticoagulants, choose one of the following options (Level B):
  - Warfarin, target INR 2.0–3.0
  - Dabigatran 150 mg twice daily (if creatinine clearance [CrCl] >30 mL/min)
  - Rivaroxaban 15 mg/d (if CrCl 30–49 mL/min) or 20 mg/d
  - Apixaban 5 mg twice daily (if serum creatinine <1.5 mg/dL) or 2.5 mg twice daily (if serum creatinine >1.5 and <2.5 mg/dL, and body weight <60 kg or age at least 80 years [or both])

Selection of a specific oral anticoagulant

- Patients taking warfarin whose condition is well-controlled should continue warfarin treatment rather than switch to treatment with a new oral anticoagulant (Level C).
- Administer dabigatran, rivaroxaban, or apixaban (rather than warfarin) to patients who have NVAF requiring anticoagulant medication and are at higher risk of intracranial bleeding (Level B).

Selection of a specific oral anticoagulant

- Offer apixaban to patients with NVAF and GI bleeding risk who require anticoagulant medication (Level C).
- Offer dabigatran, rivaroxaban, or apixaban to patients unwilling or unable to submit to frequent periodic testing of INR levels (Level B).

Selection of a specific oral anticoagulant

- Offer apixaban to patients unsuitable for being treated, or unwilling to be treated, with warfarin (Level B).
- Where apixaban is unavailable, consider dabigatran or rivaroxaban (Level C).
- Where oral anticoagulants are unavailable, consider a combination of aspirin and clopidogrel (Level C).

Selection of a specific oral anticoagulant for Special Populations

- Offer oral anticoagulants to elderly patients (aged >75 years) with NVAF if there is no history of recent unprovoked bleeding or intracranial hemorrhage (Level B).
- Clinicians might offer oral anticoagulation to patients with NVAF who have dementia or occasional falls. However, clinicians should counsel patients or their families that the risk–benefit ratio of oral anticoagulants is uncertain in patients with NVAF who have moderate to severe dementia or very frequent falls (Level B).
- Because the risk–benefit ratio of oral anticoagulants in patients with NVAF and end-stage renal disease is unknown, there is insufficient evidence for making practice recommendations (Level U).

And now to throw a wrench into the works . . .

What if stroke causes atrial fibrillation instead of atrial fibrillation causing stroke?

A Fib causing Stroke or Vice Versa?

- There is a well known circadian variation in the occurrence of both stroke and A Fib:
  - There are 49% more strokes between midnight and 6 am than would be expected if no circadian variation were present
  - 14 - 28 % strokes are "wake up strokes"
  - The frequency of paroxysmal A Fib peaks during the night and early morning hours
  - Odds of detecting newly diagnosed atrial fibrillation are 3-fold higher in wake up stroke/TIA than non-wake up stroke/TIA
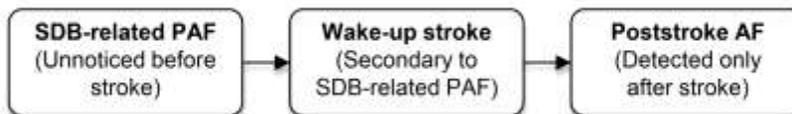
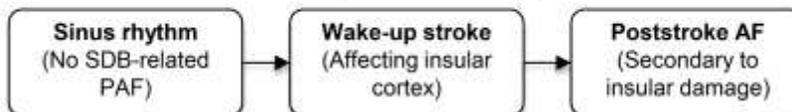# Proposed neurogenic mechanisms causing poststroke atrial fibrillation
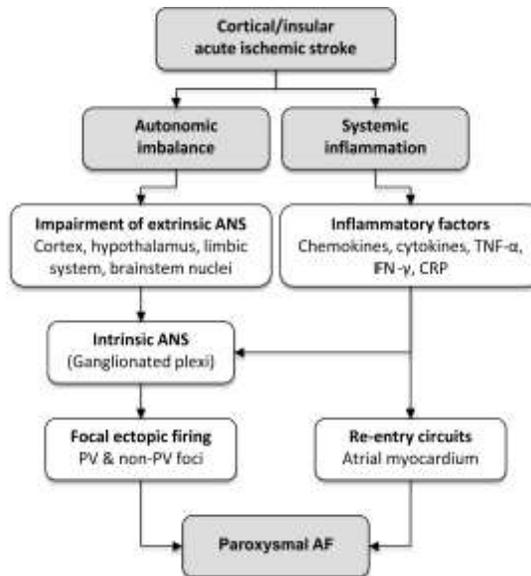
Sposato L A et al. Neurology 2014;82:1180-1186

Possible pathophysiologic pathways relating sleep-disordered breathing, wake-up stroke, and poststroke atrial fibrillation

Sposato L A et al. Neurology 2014;82:1180-1186

Does stroke-induced A Fib need permanent anticoagulation?

- Up to 1 in 4 instances of A Fib found in association with stroke may be the ***consequence*** of the 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"

References

- Antonio Culebras, MD, FAAN, FAHA, Steven R. Messé, MD, FAAN, FAHA, Seemant Chaturvedi, MD, FAAN, FAHA, Carlos S. Kase, MD, FAAN, FAHA and Gary Gronseth, MD, FAAN. 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(8): 716-724.
- William J. Elliott, MD, PhD. Circadian variation in the time o f stroke onset: A meta-analysis. Stroke 1998; 29:992-996.
- Tommaso Sanna MD, Diener HC, Passman RS, Di Lazzaro V, Bernstein RA, Morillo CA, Rymer MM, Thijs V, Rogers T, Beckers F, Lindborg K, Brachmann J; Cryptogenic stroke and underlying atrial fibrillation. **CRYSTAL AF** Investigators.N Engl J Med. 2014; 370(26):2478-86.
- Luciano A. Sposato, MD, MBA, FAHA, Patricia M. Riccio, MD and Vladimir Hachinski, CM, MD, FRCPC, DSc. Poststroke atrial fibrillation: Cause or consequence? Critical review of current views. Neurology **2014**; 82(13): 1180-1186.