

Evolving clinical practice in atrial fibrillation

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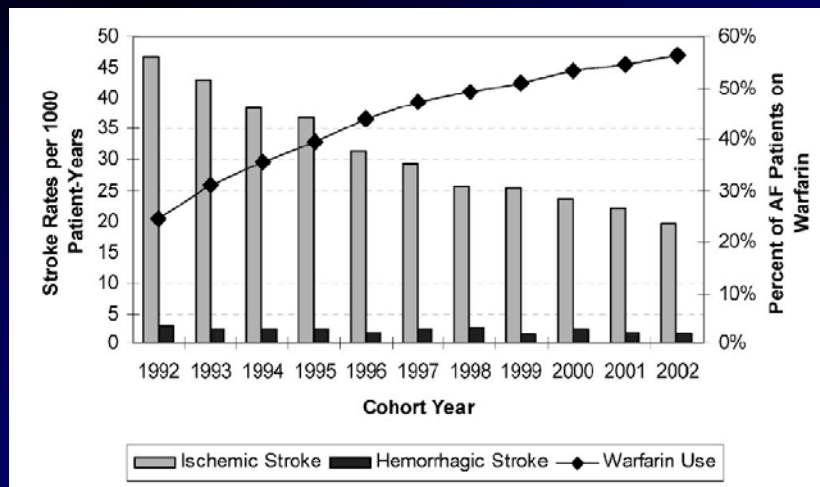
City Hospital

Birmingham B18 7QH

England UK

Trends in warfarin use and overall ischemic and hemorrhagic strokes among prevalent patients with AF

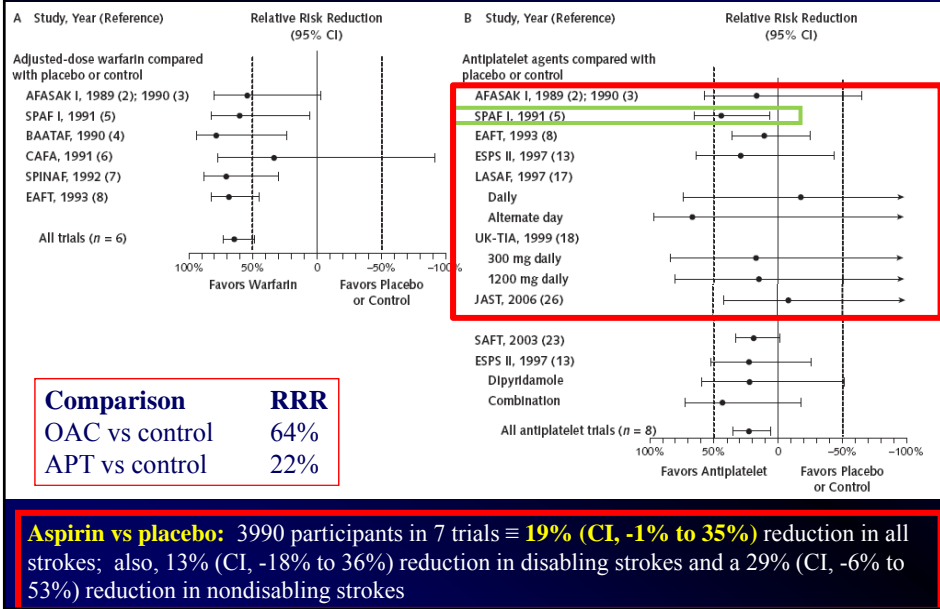
Lakshminarayan et al Stroke.2006;37:1969-1974.



Medicare patients aged ≥ 65 years

Antithrombotic Therapy to Prevent Stroke in Patients Who Have Nonvalvular AF

Hart et al Ann Intern Med. 2007;146:857-867.

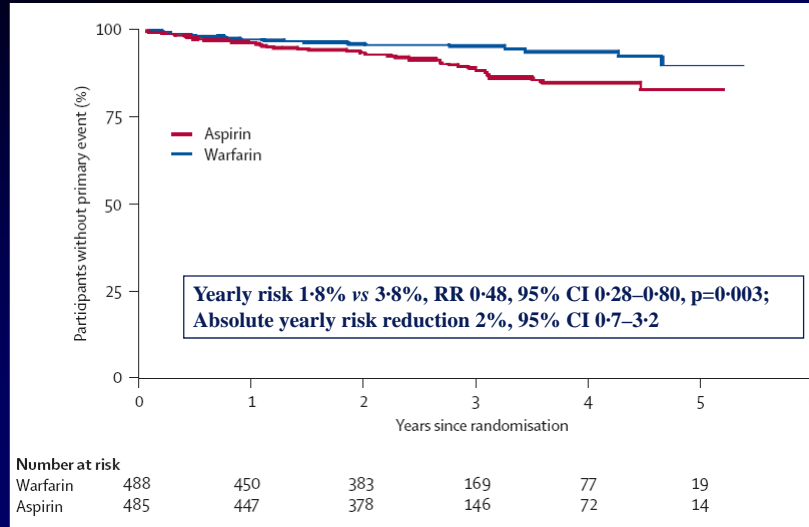


New data since the 2006 ACC/AHA/ESC guidelines Implications for new guidelines

Some examples		Evidence
Something better than warfarin	<i>Effectiveness and safety of new oral anticoagulant drug</i>	RE-LY trial, with dabigatran
The elderly	<i>Effectiveness and safety of warfarin vs aspirin, in elderly</i>	BAFTA, WASPO, van Walraven et al metaanalysis ;
	<i>Importance of age ≥ 75 as single risk factor</i>	<i>Gorin et al Thromb Haemostat 2010;103(4):833-40.</i>
CHADS ₂ =1	<i>Effectiveness of warfarin > aspirin</i>	ACTIVE-W, Lee et al, Gorin et al
Low risk patients	<i>Aspirin no better than control for reducing thromboembolism, with greater risk of bleeding</i>	Japan AF Stroke Trial <i>Sato et al Stroke. 2006;37:447-451</i>
Aspirin for CV prevention	<i>Aspirin no better than placebo for primary prevention, with more bleeds</i>	POPADAD, JPAD, AAA, etc
Greater evidence with some risk factors	<i>Female, vascular disease, age 65-74 Balancing stroke and bleeding risk</i>	Limitations of CHADS ₂ score

Warfarin vs aspirin for stroke prevention in an elderly community population with AF: the Birmingham Atrial Fibrillation Treatment of the Aged Study, BAFTA

Mant et al Lancet 2007; 370: 493–503



Antithrombotic treatment and risk of stroke and death in patients with AF at intermediate risk [CHADS2 score=1]

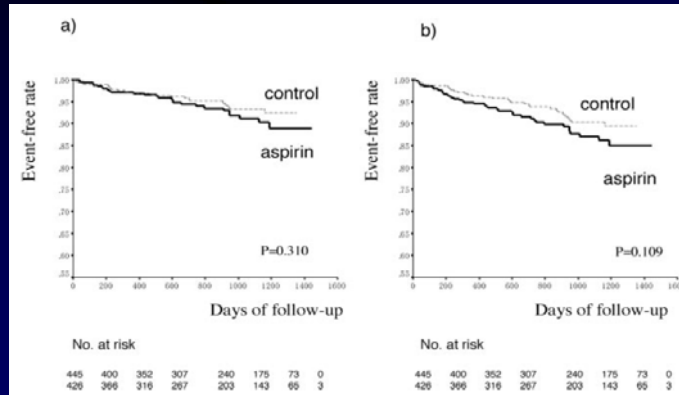
Gorin et al Thromb Haemostat 2010 March issue

vs. no anticoagulation	Anticoagulation alone		Antiplatelet agent alone		Anticoagulation plus antiplatelet agent	
	Hazard ratio (95% CI)	P-value	Hazard ratio (95% CI)	P-value	Hazard ratio (95% CI)	P-value
Stroke (n=19)	0.575 (0.168–1.966)	0.38	1.429 (0.403–5.070)	0.58	1.082 (0.198–5.194)	0.93
Death (n=108)	0.333 (0.208–0.532)	<0.0001	0.814 (0.502–1.321)	0.40	0.366 (0.154–0.871)	0.02
Death or stroke (n=124)	0.357 (0.231–0.552)	<0.0001	0.802 (0.506–1.271)	0.34	0.439 (0.205–0.940)	0.03
Net clinical benefit (death or stroke or major bleeding) (n=126)	0.374 (0.243–0.576)	<0.0001	0.803 (0.507–1.272)	0.35	0.439 (0.205–0.940)	0.03

The hazard ratio for major bleeding alone (n=4) was not calculable since no such event was recorded in patients not receiving anticoagulation. CI, confidence interval.

Hazard ratio of events in atrial fibrillation and a CHADS2 score =1 in patients treated with anticoagulation alone, antiplatelet agent alone or anticoagulation plus antiplatelet agent (vs. those receiving neither anticoagulation nor antiplatelet agent).

Low-Dose Aspirin for Prevention of Stroke in Low-Risk Patients With AF: Japan AF Stroke Trial *Sato et al Stroke. 2006;37:447-451*



Primary end points included cardiovascular death, symptomatic brain infarction, or TIA, whereas the secondary end points included noncardiovascular death, intracranial hemorrhage, major bleeding, and peripheral embolization.

Kaplan-Meier survival curves for primary end points (a) and for primary plus secondary end points (b). **Treatment with aspirin 150-200mg/day was not superior to treatment without aspirin for primary end points (log-rank; $P=0.310$) and secondary end points (log-rank; $P=0.109$)**

2010 ESC Guidelines for the management of atrial fibrillation

Camm, Kirchhof, Lip et al Eur Heart J 2010

European Heart Journal (2010) doi: 10.1093/eurheartj/ehq278

Clinical flowchart for the use of oral anticoagulation for stroke prevention in AF

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graph TD
    Start[CHADS2 score ≥ 2†] -- No --> Consider[Consider other risk factors*]
    Start -- Yes --> OAC[OAC]
    Consider --> Age[Age ≥ 75 years]
    Age -- No --> Risk2[≥ 2 other risk factors*]
    Age -- Yes --> OAC
    Risk2 -- No --> Risk1[1 other risk factor*]
    Risk2 -- Yes --> OAC
    Risk1 -- No --> Nothing[Nothing (or aspirin)]
    Risk1 -- Yes --> OACAsp[OAC (or aspirin)]
    
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†Congestive heart failure, Hypertension, Age ≥ 75 years, Diabetes, Stroke/TIA/thromboembolism (doubled)


*Other clinically relevant non-major risk factors: age 65-74, female sex, vascular disease

Guidelines for the management of atrial fibrillation

The Task Force for the Management of Atrial Fibrillation of the European Society of Cardiology (ESC)

Developed with the special contribution of the European Heart Rhythm Association (EHRA)
Endorsed by the European Association for Cardio-Thoracic Surgery (EACTS)

Authors/Task Force Members: A. John Camm (Chairperson) (UK), Paulus Kirchhof (Germany), Gregory Y. H. Lip (UK), Ulrich Schotten (Netherlands), Irene Savelieva (UK), Sabine Ernst (UK), Isabelle C. Van Gelder (Netherlands), Nawwar Al-Attar (France), Gerhard Hindricks (Germany), Bernard Prendergast (UK), Hein



European Heart Journal (2010)
doi:10.1093/eurheartj/ehs278

a) Risk factors for stroke and thromboembolism in non-valvular AF

'Major' risk factors	'Clinically relevant non-major' risk factors
Previous stroke, TIA or systemic embolism Age ≥ 75 years	Heart failure or moderate to severe LV systolic dysfunction [e.g. LV EF $\leq 40\%$] Hypertension - Diabetes mellitus Female sex - Age 65-74 years Vascular disease*

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Approach to thromboprophylaxis in patients with AF

Risk category	CHA ₂ DS ₂ -VASc score	Recommended antithrombotic therapy
One 'major' risk factor or ≥ 2 'clinically relevant non-major' risk factors	≥ 2	OAC
One 'clinically relevant non-major' risk factor	1	Either OAC or aspirin 75-325 mg daily. Preferred: OAC rather than aspirin.
No risk factors	0	Either Aspirin 75-325 mg daily or no antithrombotic therapy. Preferred: no antithrombotic therapy rather than aspirin.

CHA₂DS₂-VASc: Cardiac failure, Hypertension, Age ≥ 75 [Doubled], Diabetes, Stroke [Doubled] - Vascular disease, Age 65-74 and Sex category [Female]; OAC = oral anticoagulation, such as a vitamin K antagonist [VKA] adjusted to an intensity range of INR 2.0-3.0 (target 2.5).
New oral anticoagulants, which may be viable alternatives to a VKA, may ultimately be considered.

Evolving clinical practice in atrial fibrillation

- Anticoagulation is the best option for stroke prevention in AF
 - Aspirin has a minor role
- Stroke risk stratification artificially divides patients into low/moderate/high risk strata in view of the dis-utility of warfarin
 - 'High risk' category can be targeted for warfarin
 - New data suggest that even 'moderate' risk patients benefit from warfarin
- If we can identify 'truly low risk' patients with AF, no antithrombotic therapy is an option – all other patients with ≥ 1 risk factor should be considered for oral anticoagulation
 - The availability of new oral anticoagulants (eg dabigatran) that overcome the inconvenience of warfarin would enable wider use of anticoagulation and improve stroke prevention in AF