Trattamento delle arteriopatie periferiche: AVK versus antiaggregante

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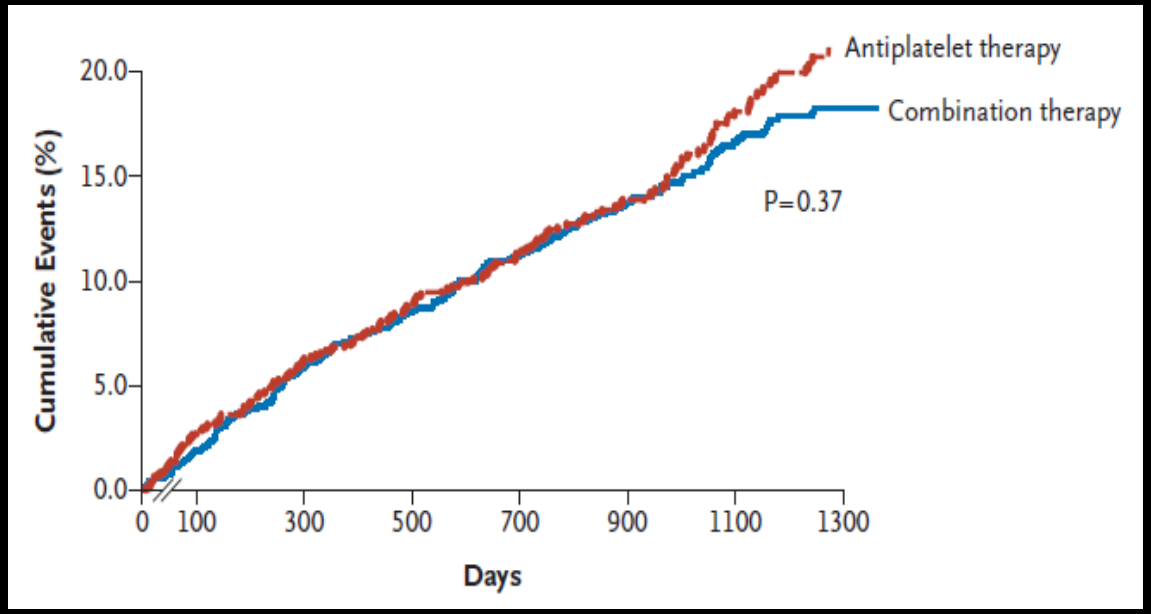
Oral Anticoagulant and Antiplatelet Therapy and Peripheral Arterial Disease

The Warfarin Antiplatelet Vascular Evaluation Trial Investigators*

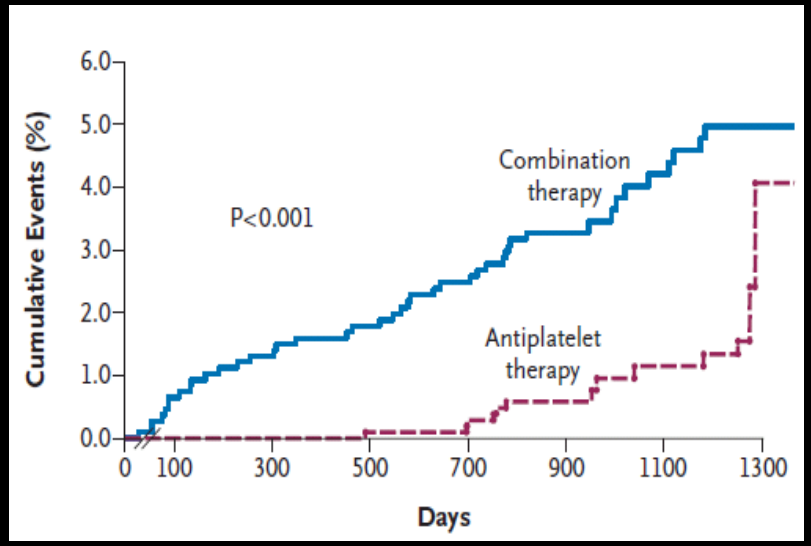
Table 1. Baseline Characteristics of the Patients.*

Characteristic	Oral Anticoagulant plus Antiplatelet Therapy (N=1080)	Antiplatelet Therapy Alone (N=1081)	P Value
Age — yr	63.9±9.4	63.8±9.5	0.88
Male sex — no. (%)	796 (73.7)	795 (73.5)	0.93



The WAVE Study NEJM 2007

Cumulative Incidence of the Coprimary End Points



Cumulative Incidence of Life-Threatening Bleeding

Wave study: conclusions

Combination of VKAs and ASA in patients with PAD

- **No more effective** than ASA alone in preventing major cardiovascular complications
- Associated with an **increase in life-threatening bleeding**

Anticoagulants: heparin, LMWH and VKAs for intermittent claudication

Cochrane Database of Systematic Reviews 2001, Issue 2. Art.
Publication status and date: (No change to conclusions), published in Issue 1, 2009.

- No significant effect on overall mortality or cardiovascular events
- No benefit for intermittent claudication
- Increased risk of major bleeding, especially with VKAs

Use of anticoagulants for intermittent claudication is not recommended

B. Cosmi, E. Conti, S. Coccheri

- *Warfarin added to antiplatelet therapy is of no benefit and potentially harmful*

✓We recommend against the use of warfarin plus aspirin in patients with symptomatic PAD (Grade 1B). ***Antithrombotic Therapy in PAD. ACCP guidelines. CHEST 2012***

Antithrombotics for preventing thrombosis after infrainguinal arterial bypass surgery (Review)

Conclusions

- Patients undergoing infrainguinal **venous graft** *are more likely to benefit* from treatment with VKAs than platelet inhibitors
- Patients receiving an **artificial graft** benefit from platelet inhibitors (aspirin)
- However, the evidence is not conclusive
- Randomised controlled trials with larger patient numbers are needed in the future to compare antithrombotic therapies with either placebo or antiplatelet therapies.

Geraghty AJ, Welch K, 2011

Targets of therapy in patients with Peripheral Artery Disease (PAD)

- **To lower the rate of cardovascular complications**
- To hinder the worsening of the disease
- To avoid thrombosis after revascularization
- To improve walking capacity

Indications for VKA in PAD

Patients already on AVK, or with a “new” indication for:

- Prosthetic heart valves
- Atrial fibrillation
- Venous thromboembolism

VKA + ASA: in quali pazienti?

- Una metanalisi evidenzia che:
  - il vantaggio clinico riguarda i pazienti con protesi valvolari meccaniche
  - non vi sono vantaggi per i pazienti con sola FA (OR 0.99, 95% CI 0.47-2.07)
  - VKA+ASA determina un aumentato rischio emorragico (OR 1.43, 95% CI 1.00-2.02)

Dentali F et al. Arch Intern Med 2007;167:117-124

Antiplatelet and anticoagulation for patients with prosthetic heart valves

Massel DR & Little SH, Cochrane Syst Rev. 2013

- In total, 4122 patients, 13 studies (published between 1971 and 2011)
- The addition of an antiplatelet agent:
  - reduced thromboembolic events (OR 0.43, CI 0.32-0.59; P < 0.00001) and total mortality (OR 0.57, CI 0.42-0.78; P = 0.0004)
  - increased major bleeding (OR 1.58, 95% CI 1.14 to 2.18; P = 0.006)

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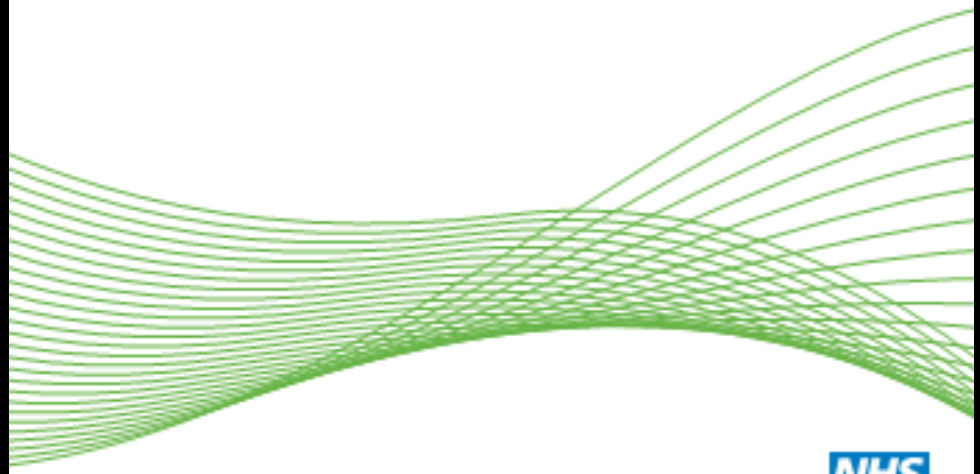
Combined anticoagulation and antiplatelet therapy for high-risk patients with atrial fibrillation: a systematic review

DA Lane, S Raichand, D Moore, M Connock, A Fry-Smith and DA Fitzmaurice on behalf of the Steering Committee



NHS
National Institute for Health Research

DOI 10.3310/hta17300

208 pagine !

Conclusions

- There are not sufficient data from the 5 randomised comparisons and 18 non-randomised comparisons to conclude whether or not there are patients with AF who would benefit from combined ACT and APT compared with ACT alone

Terapia combinata nei pazienti con FA

- Nonostante non vi sia dimostrazione di una migliore efficacia, rispetto alla sola anticoagulazione, si assiste ad un progressivo aumento del numero di pazienti con FA trattati con VKA+ASA

Trials con i DOAC nella FA: % di pazienti trattati con ASA (ache nel braccio di controllo)

DOAC	Studio, anno	% ASA +
ximelagatran	SPORTIF III, 2003	10
ximelagatran	SPORTIF V, 2005	15
idraparinux	Amadeus, 2008	20
dabigatran	RE-LY, 2009	21
rivaroxaban	ROCKET, 2011	18
apixaban	ARISTOTLE, 2011	31
edoxaban	Engage AF, 2013	29

Risk of bleeding in patients with acute myocardial infarction treated with different combinations of aspirin, clopidogrel, and vitamin K antagonists in Denmark: a retrospective analysis of nationwide registry data

Rikke Sørensen, Morten L Hansen, Steen Z Abildstrom, Anders Hvelplund, Charlotte Andersson, Casper Jørgensen, Jan K Madsen, Peter R Hansen, Lars Køber, Christian Torp-Pedersen, Gunnar H Gislason

Lancet 2009; 374: 1967–74

	Incidence (% per person-year)	Unadjusted risk ratio (95% CI)	Number needed to harm§	
			Unadjusted	Adjusted¶
Monotherapy				
Aspirin alone	2·6%	Reference	Reference	Reference
Clopidogrel alone	4·6%	1·75 (1·75–1·76)	50·8	115·7
Vitamin K antagonist alone	4·3%	1·63 (1·62–1·65)	60·2	165·9
Dual therapy				
Aspirin plus clopidogrel	3·7%	1·43 (1·43–1·43)	89·3	81·2
Aspirin plus vitamin K antagonist	5·1%	1·94 (1·94–1·95)	40·5	45·4
Clopidogrel plus vitamin K antagonist	12·3%	4·68 (4·64–4·74)	10·4	15·2
Triple therapy				
Aspirin, clopidogrel, and vitamin K antagonist	12·0%	4·57 (4·55–4·61)	10·7	12·5

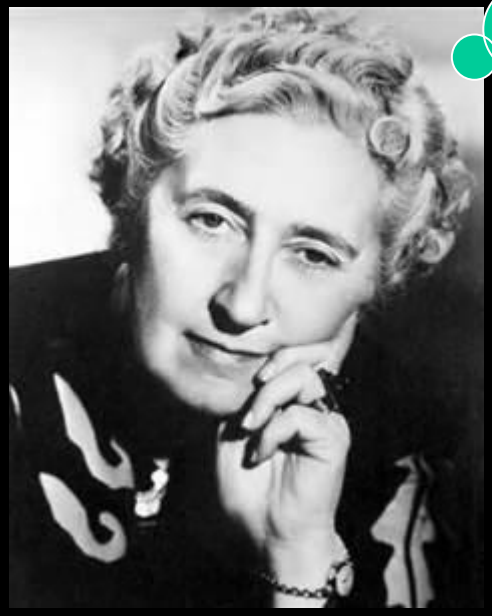
Antithrombotic regimens in patients with indication for long-term anticoagulation undergoing coronary interventions-systematic analysis, review of literature, and implications on management.

Deshmukh A et al, Am J Ther 2013;20:654-63

- Ten retrospective studies, 1 post hoc analysis of a major registry, and 2 prospective studies

- Major bleeding at 1 year:
  - Triple antithrombotic therapy: 5,2 %
  - Dual antiplatelet therapy: 2,4 %

*un **indizio** è un **indizio**,*
***due indizi** sono una*
coincidenza, ma
tre indizi fanno una
prova



Agatha Christie

Dual or single antiplatelet therapy with anticoagulation?

- Clinicians are becoming increasingly aware of the importance of reducing bleeding risk
- "More potent is not always better"

Keith A A Fox

Centre for Cardiovascular Science,

University of Edinburgh, UK

Lancet, 2013