

Anticoagulanti e mono-antiaggregazione: a chi, quali e per quanto tempo

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Anticoagulazione: attualità cliniche, di laboratorio e aspetti sociali
Bologna, 21-22 Gennaio 2016

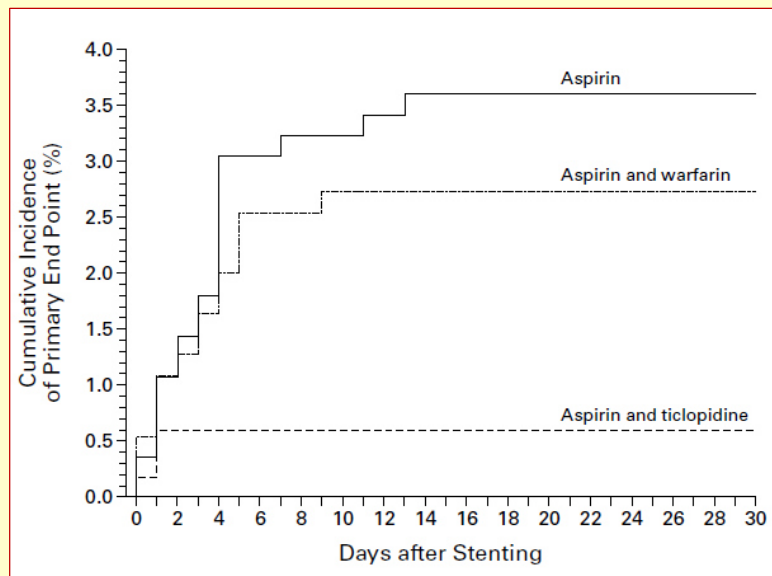
Indications to oral anticoagulation in patients with coronary artery disease

- 3 to 7% of patients admitted for an ACS are on OAC
- AF often occurs during ACS (6-21% of cases)
- AF patients have frequently other cardiac comorbidities (hypertensive heart disease, CAD, valvular heart disease, cardiomyopathy)
- 20-30% of patients with coronary artery disease present with AF

Rubboli A et al., Coronary Artery Dis 2007, 18: 193
Oudot A et al., Heart 2006, 92: 1077
Aggarwal A et al., Am J Cardiol 2008, 101: 1413
Boutsikov M et al., Cardio Hematol Agent Med Chem 2014, 12: 16

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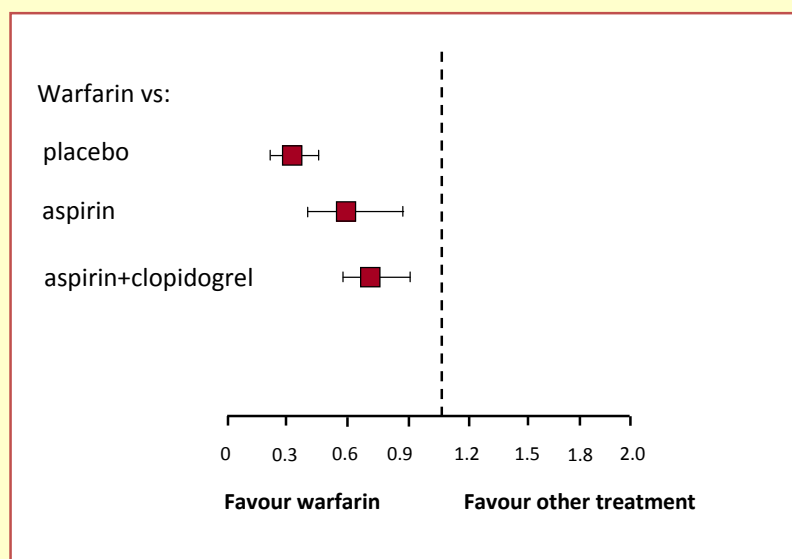
Dual antiplatelet therapy is better than aspirin or aspirin and warfarin in patients undergoing PCI



Leon MB et al., NEJM 1998;339:1665

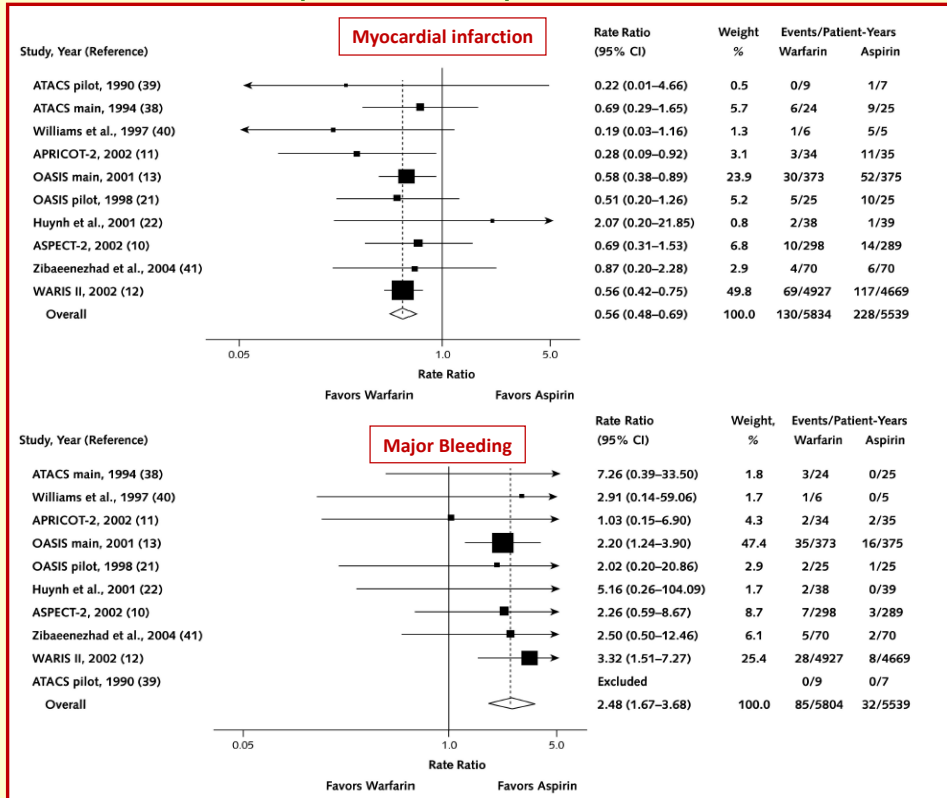
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Antithrombotic Treatments vs Warfarin in Atrial Fibrillation



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Warfarin+aspirin vs aspirin after MI or ACS

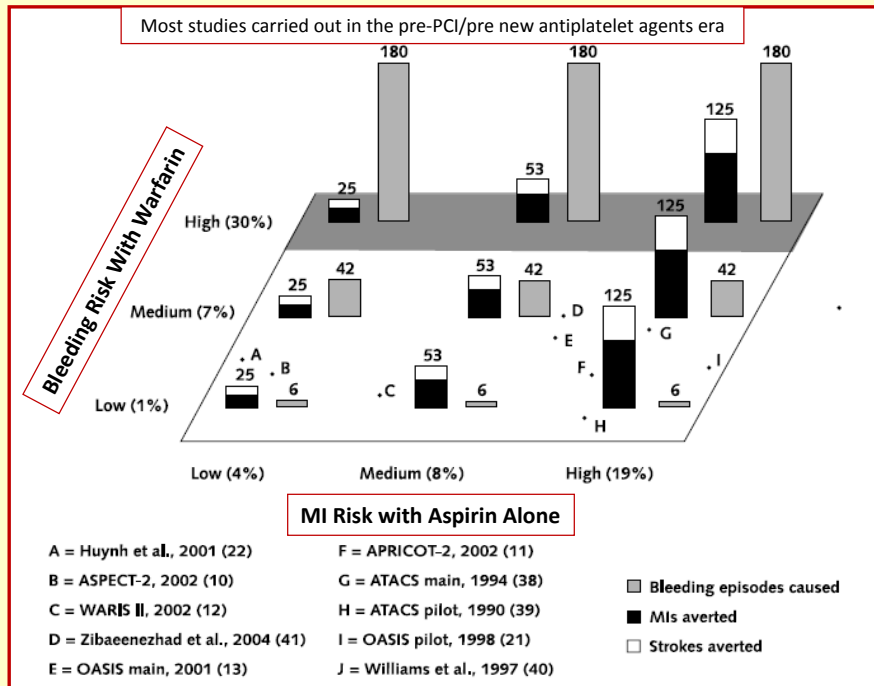


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10 trials
5938 patients, 11334 patient-years

Rothberg MB et al., Ann Intern Med 2005;143:241

Absolute benefit and harm caused by adding warfarin to aspirin for 1 year in 1000 patients stratified by bleeding and MI risk



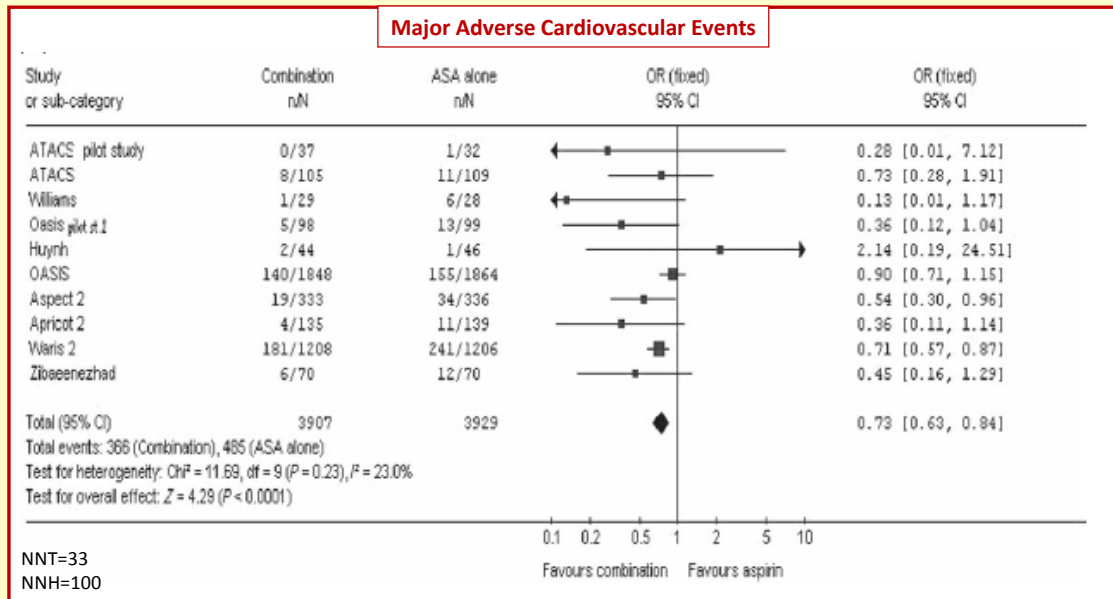
«... for patients with ACS at low or intermediate risk for bleeding the cardiovascular benefit or warfarin outweighs the bleeding risk...»

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Rothberg MB et al., Ann Intern Med 2005;143:241

Metaanalysis of trials of aspirin + AVK vs aspirin alone after ACS

only studies with INR values between 2 and 3

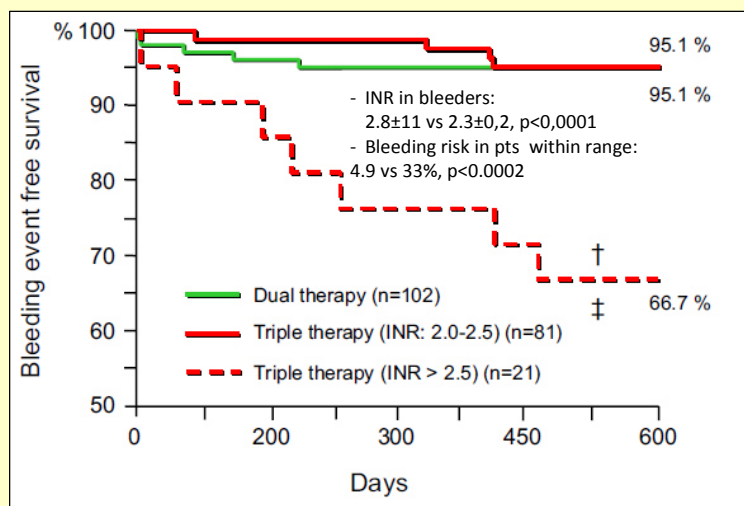


No significant increase in ICH

Andreotti F et al., EHJ 2006;27:519

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Bleeding in patients on triple therapy depending on INR values



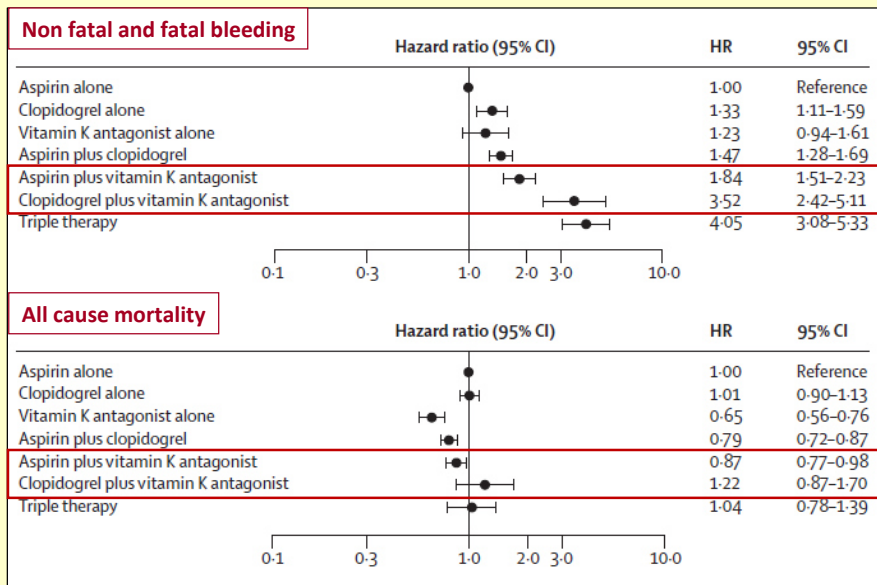
- 102 patients on TT vs 102 on DAPT
 - Follow-up: 18 months, duration TT: 157±134 d

Rossini R et al., Am J Cardiol 2008;102:1618

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Major events in patients treated with different antithrombotic regimens after first myocardial infarction

Retrospective nationwide Denmark registry



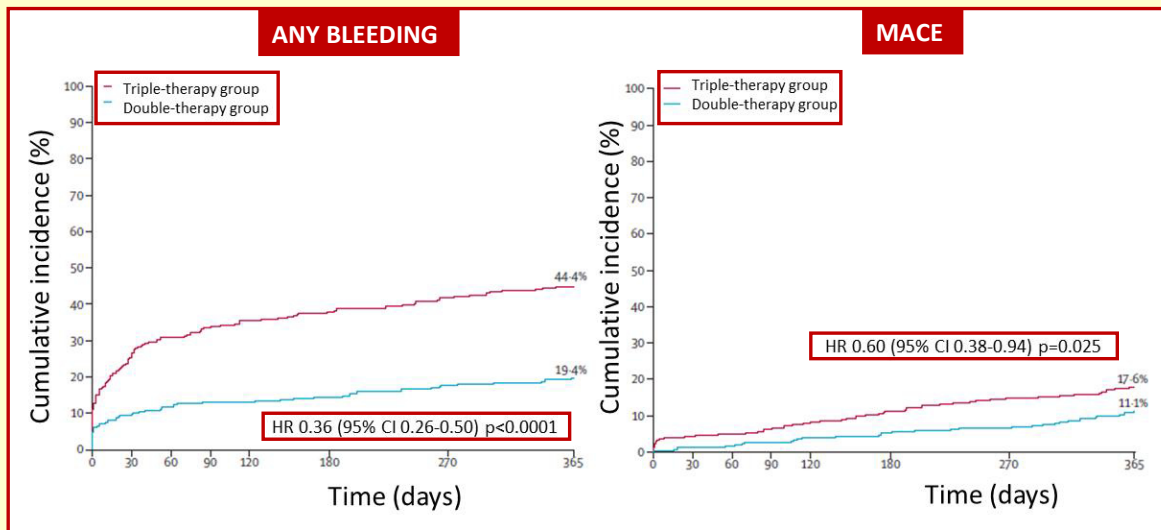
- 40,812 patients with first time AMI
- Mean follow-up 476 days
- NNT vs aspirin alone: ASA+CLOP: 81; ASA+AVK:45; CLOP+AVK: 15; Triple Ther:12.

Sorensen R, Lancet 2009; 374: 1967

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AVK + clopidogrel vs AVK + DAPT in patients on oral anticoagulant undergoing PCI

The WOEST Trial

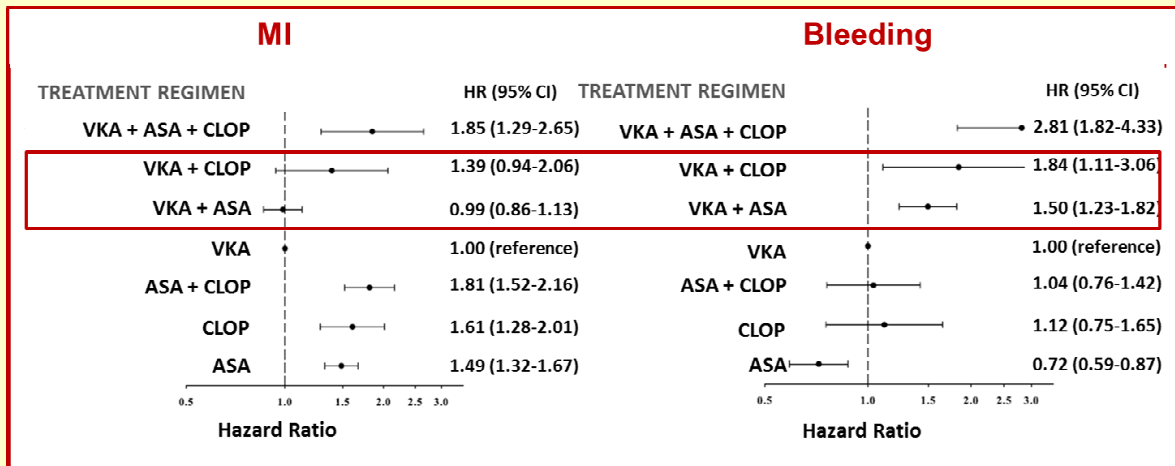


- Prospective, open-label, randomised
- 573 patients, 1 year follow-up

Dewilde WJM et al., Lancet 2013;381:1107

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Incidence rates of MI/coronary death after MI or coronary intervention in AF patients

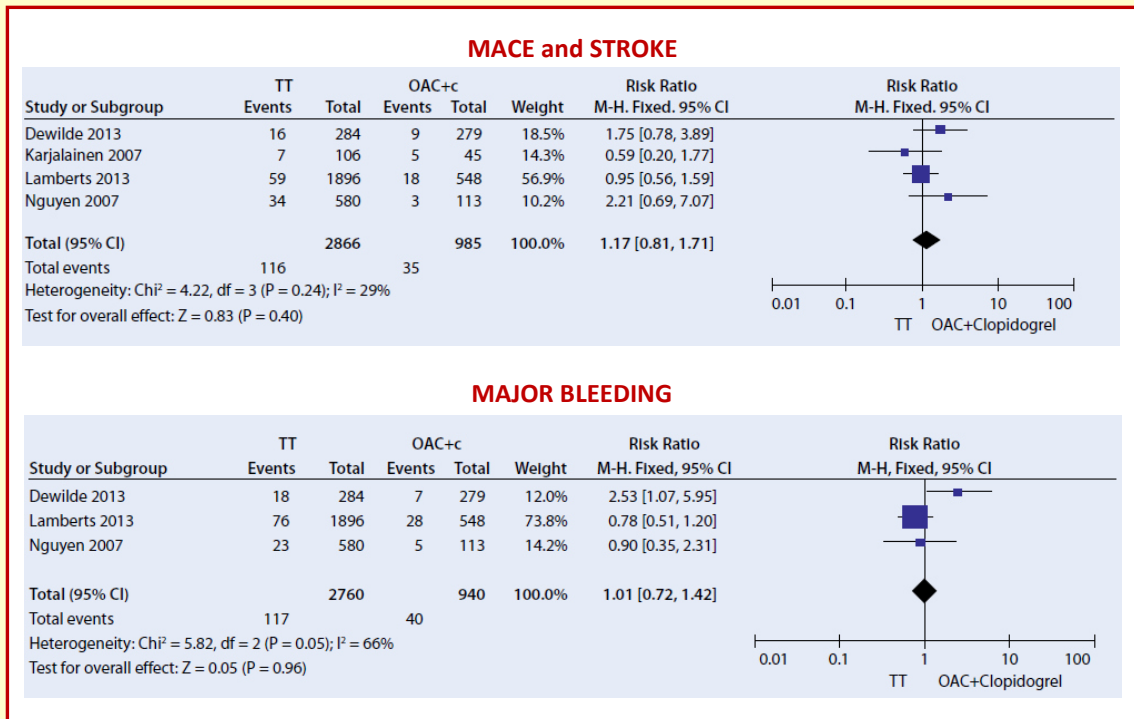


-Cohort study 8700 patients with AF and stable CAD
-Mean follow up: 3.3 years

Lambert M et al., Circulation 2014;129:1577

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Triple antithrombotic therapy (TT) vs AVK+clopidogrel: a metaanalysis

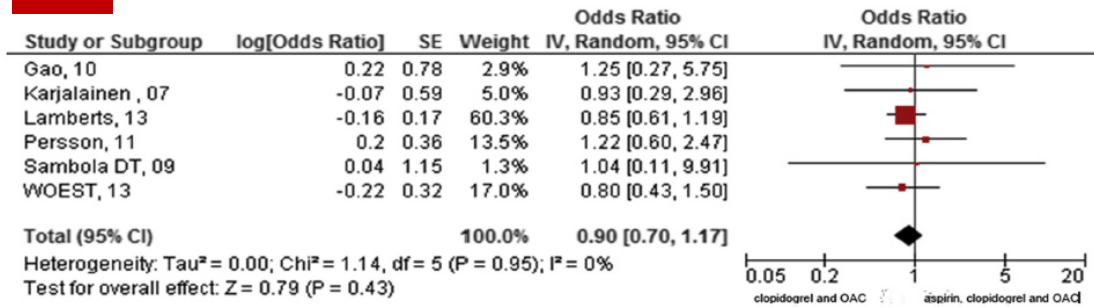


Chen FC et al., Herz 2015, 40:1070

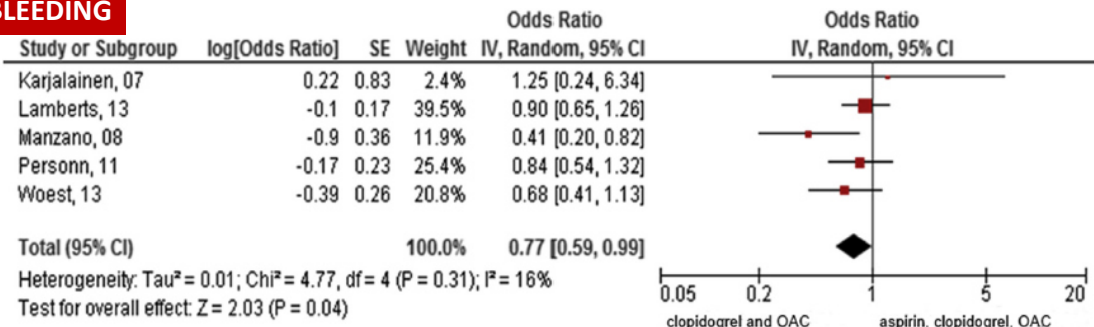
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Rates of MACE and bleeding in patients treated with clop+AVK vs triple therapy

MACE



BLEEDING



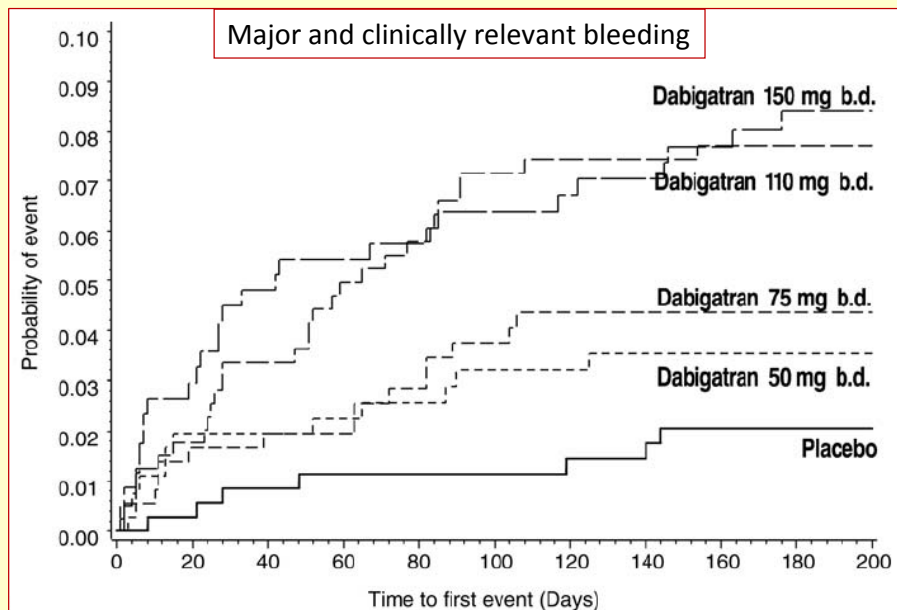
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D'Ascenzo F et al., Am J Cardiol 2015;115:1185

Dabigatran vs placebo in patients with ACS

The RE-DEEM study

A phase II, dose-escalation trial



1861 patients; 7.5 d after ACS (100% ASA, 99% DAPT) for 6 mo
 No difference in CV event rates

Oldgren J et al., EHJ 2011;32:2781

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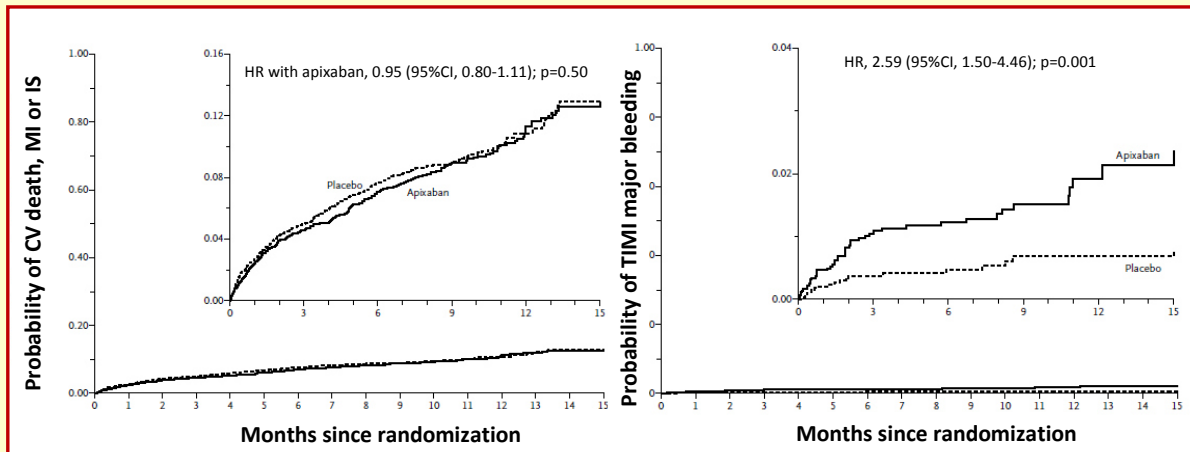
ANTICOAGULAZIONE:

attualità cliniche, di laboratorio e aspetti sociali

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Apixaban with antiplatelet therapy after ACS

The APPRAISE-2 trial



- 7392 patients with recent ACS (6 days) and 2 additional risk factor
- Randomized to apixaban 5mg x 2/d or placebo
- 97% aspirin, 81% DAPT
- Median follow-up 241 days

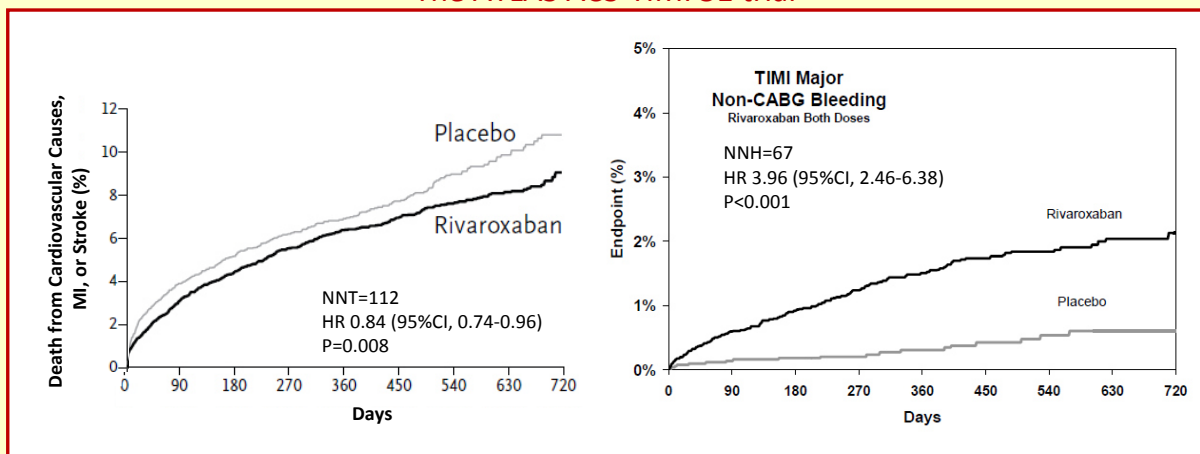
Terminated prematurely because of increase in major bleeding

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Alexander JH et al., NEJM 2011;365:699

Rivaroxaban in patients with a recent acute coronary syndrome

The ATLAS ACS-TIMI 51 trial



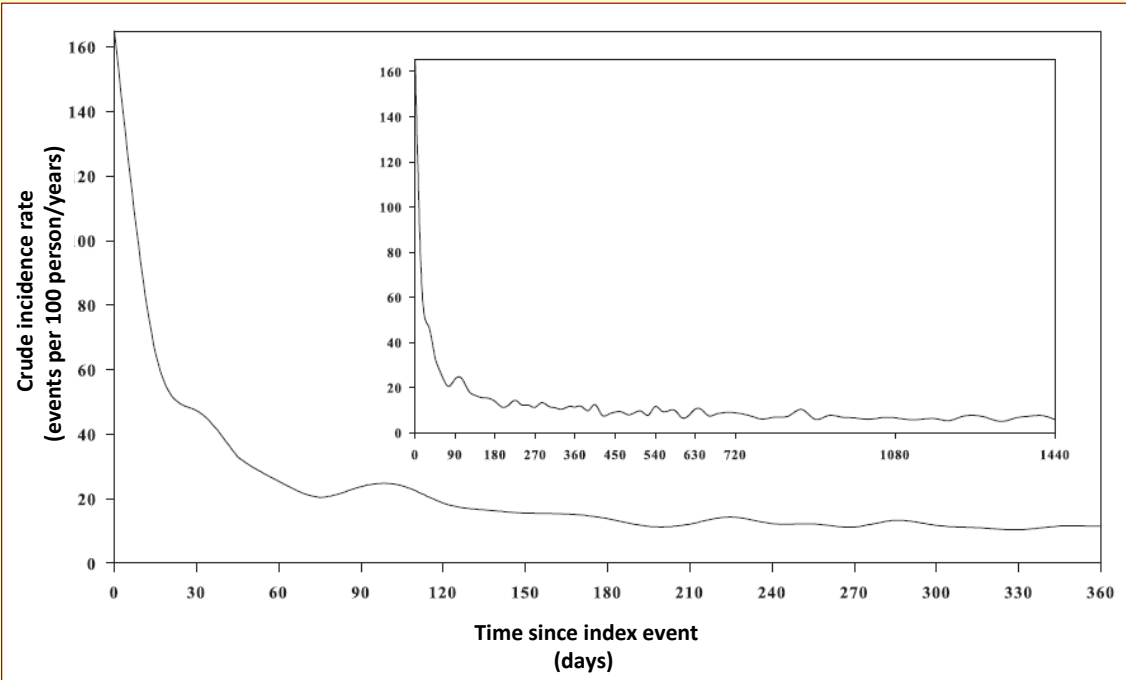
- 15526 patients with recent ACS
- Randomized to rivaroxaban 2.5mg x 2, 5mg x 2, placebo
- 98.6% aspirin, 92.8% DAPT
- Average follow-up: 13 months

Mega JL et al., NEJM 2012;366:9

FDA public meeting: unanticipated high rate of missing data
 -1294 patients withdrew consent (8.3%); for 1117 of these vital status not reported
 -Imbalance in missing MACE data (11% placebo, 12.4% rivaroxaban)
 -Higher bleeding rates in patients with incomplete follow-up

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Incidence rates of MI/coronary death after MI or coronary intervention in AF patients

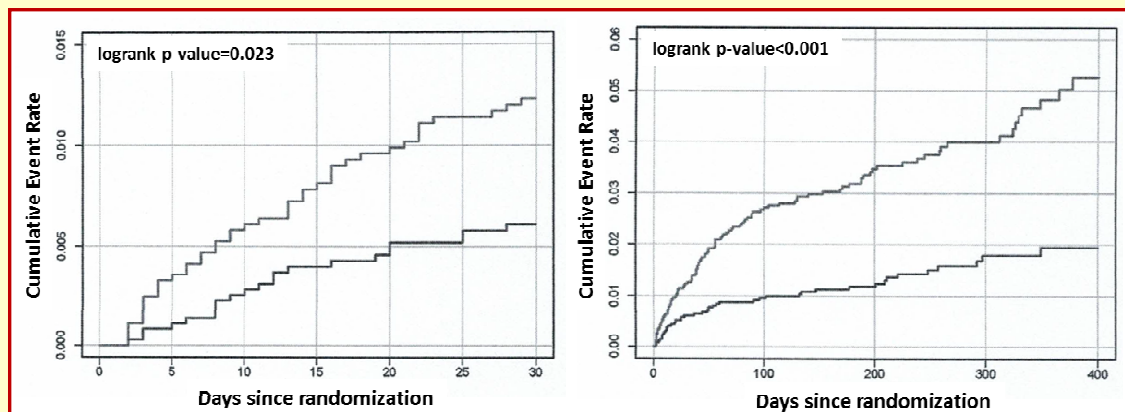


- Cohort study in 8700 patients
- Mean follow-up 3.3 years

Lambert M et al., Circulation 2014;129:1577

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Short and long term bleeding events in the APPRAISE-2 trial

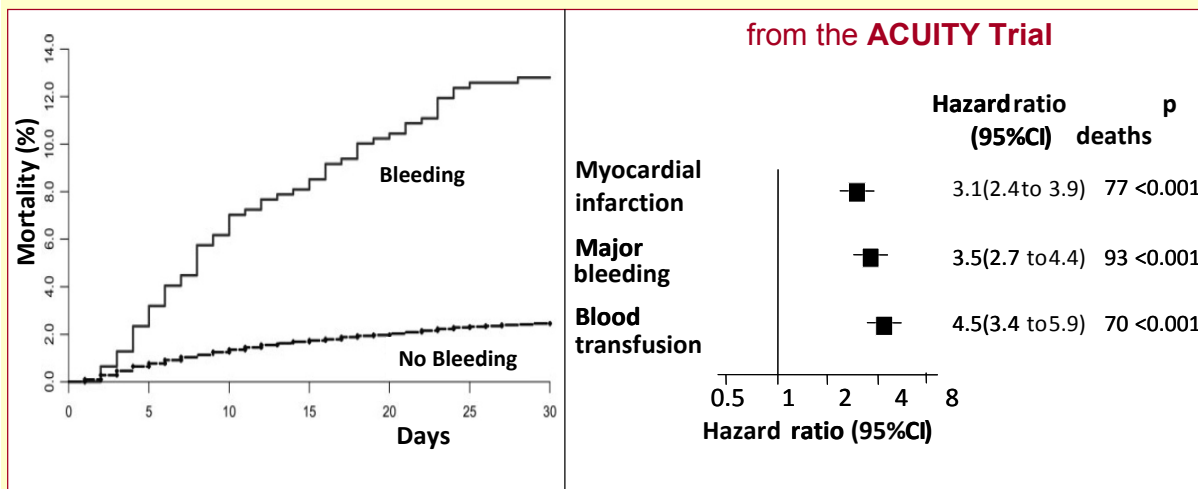


End point	0-30 days		30 days to end of study		Total number of bleeds
	Count, n (%)	Events per 12 patient-months	Count, n (%)	Events per 12 patient-months	
ISTH major/CRNM	64 (39.5)	0.11	98 (60.5)	0.03	162
TIMImajor/minor	42 (38.5)	0.08	67 (61.5)	0.02	109
Any bleeding	478 (48.6)	0.88	506 (51.4)	0.14	984

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Khan R et al., Heart 2015;101:1475

Major bleeding predicts mortality in patients with ACS



34,146 pts with ACS enrolled in OASIS registry, OASIS-2, CURE

Analysis of independent predictors to 1-year mortality for 13,819 pts with ACS from the ACUTY Trial

Eikelboom JW et al., Circulation 2006, 114: 774-782.
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Mehran R et al., Eur Heart J 2009, 30:1457

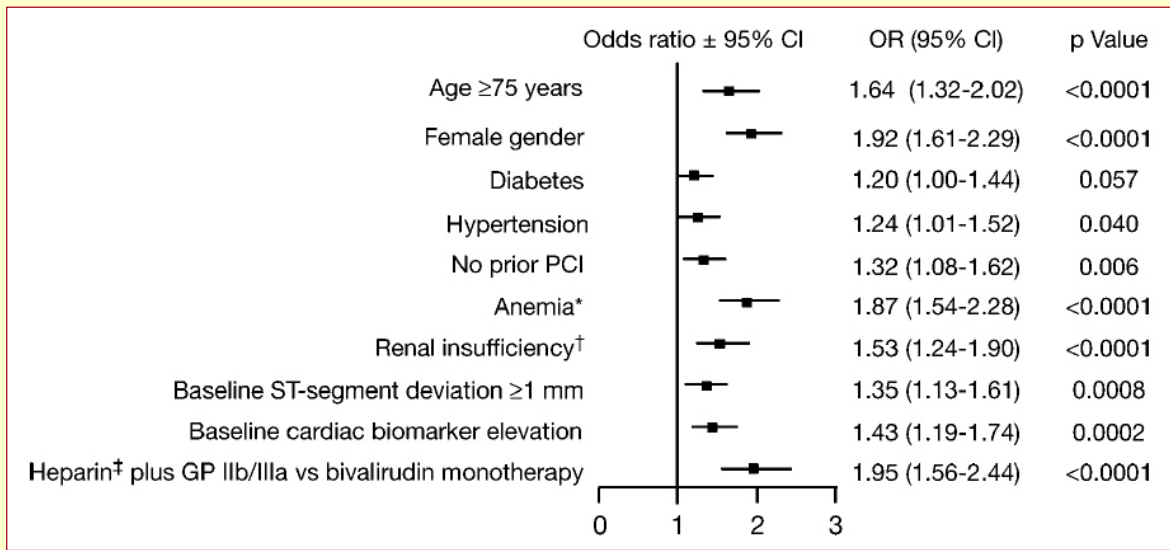
Predictive model of bleeding events in the APPRAISE-2 trial

	HR (95% CI)	p value
Age (per 10-year increase)	1.25 (1.17 to 1.33)	<0.001
Dual antiplatelet therapy	2.05 (1.65 to 2.54)	<0.001
Bleed during index ACS events	2.36 (1.79 to 3.12)	<0.001
Diastolic BP>80 mm Hg (per 10 mm Hg increase)	1.26 (1.07 to 1.49)	<0.001
Prasugrel	1.81 (1.30 to 2.53)	<0.001

Khan R et al., Heart 2015;101:1475

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Independent predictors of major bleeding in patients with ACS from the **ACUITY** Trial

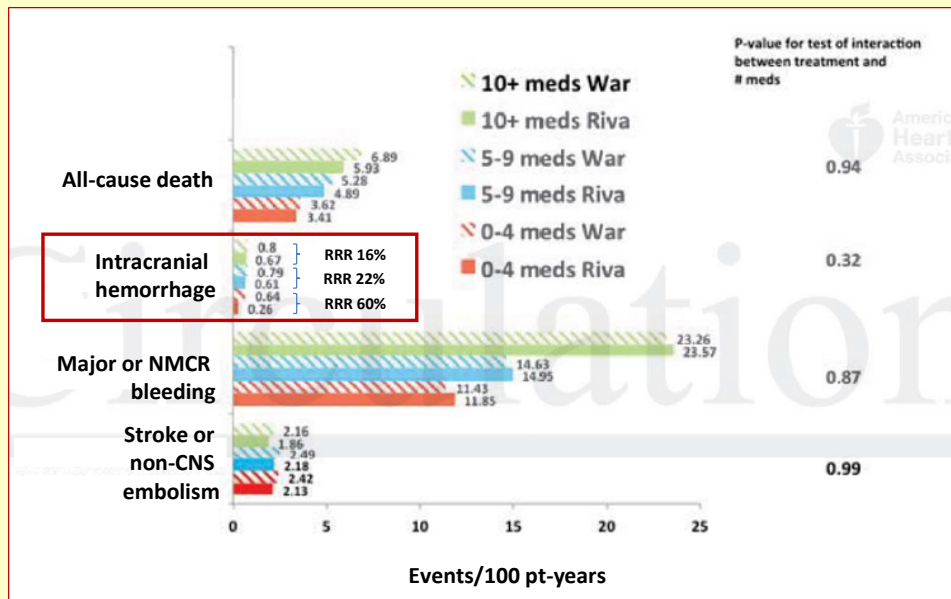


-history of bleeding
-prior vascular disease (stroke)
-lower body weight

Manoukian SV et al., Clin Cardiol 2007;30:11-24

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Number of concomitant medication determines bleeding events with rivaroxaban or warfarin from the **ROCKET AF** Trial



Piccini JP et al., Circulation 2016, epub

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CONCLUSIONS

- Management of patients with indications to both antiplatelet and anticoagulant therapy is challenging
- The association of a DOAC (anti Xa), at reduced dosage, or an aVK (INR 2-2.5), to aspirin (or/and clopidogrel) may be considered after an ACS in patients with a favourable risk/safety profile
- A careful evaluation of the bleeding/thrombotic risk balance must guide treatment decisions
- Precautions, like lower target and tight control of aVK, lowest active aspirin dose (75 mg), gastric protection, avoidance of NSAIDs, radial access/use of BMS for PCI, and shortest possible duration of combined therapy may limit complications.
- The association of DOACs or aVK to the new/more potent antiplatelet agents (prasugrel, ticagrelor, cangrelor, vorapaxar) is likely to greatly increase bleeding
- There is no strong evidence that DOACs provide significant advantage in combined therapy with antiplatelet drugs as compared with AVK

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