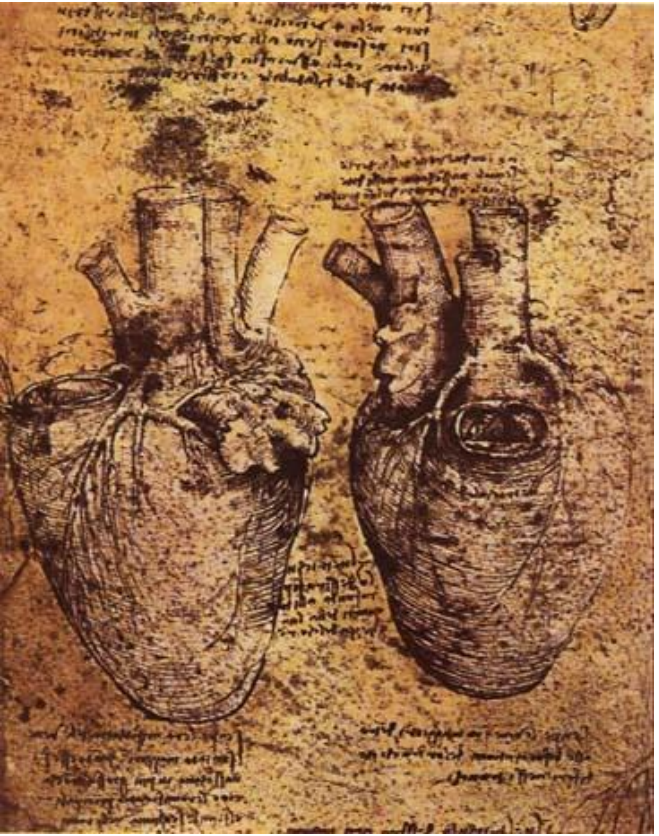
Sabato 25 Marzo 2023
HOTEL CASCINA FOSSATA
Via Ala di Stura 5 - Torino
IL PAZIENTE *FRAGILE* IN CARDIOLOGIA
VI Edizione

Terapia farmacologica del paziente con cardiopatia ischemica (CAD) e arteriopatia periferica (PAD)

Dott. Michele Boero – S.C. Chirurgia Vascolare, S.Giovanni Bosco



Anatomia particolare del paziente vascolare: anziano, comorbido, plurivasculopatico, FRAGILE

Cuore e vasi sanguigni, Leonardo Da Vinci, ca. 1500

PAZIENTI CON SINDROME CORONARICA ACUTA

Variable	PLATO	APPRAISE-2	TRA-CER	TRILOGY ACS
Intervention	Clopidogrel vs. Ticagrelor	Apixaban vs Placebo	Vorapaxar vs Placebo	Clopidogrel vs Prasugrel
Enrollment years	2006-2008	2009-2010	2007-2010	2008-2011
Number of patients	18,624	7,392	12,944	9,326

Variable	PLATO	APPRAISE-2	TRA-CER	TRILOGY ACS
Intervention	Clopidogrel vs. Ticagrelor	Apixaban vs Placebo	Vorapaxar vs Placebo	Clopidogrel vs Prasugrel
Prevalence of diabetes mellitus in the different arms %	Ticagrelor 24.9 Clopidogrel 25.1	Apixaban 48.7 Placebo 47.0	Vorapaxar 31.4 Placebo 31.5	Prasugrel 37.7 Clopidogrel 38.3
Definition of PAD	Peripheral Artery Disease IC with ABI <0.9 or LE revascularization	Peripheral Vascular Disease IC or ABI <0.9 or LE revascularization	Peripheral Vascular Disease IC with ABI <0.85 or LE revascularization or amputation	Peripheral Artery Disease LE revascularization or LE amputation
Prevalence of PAD in the different arms %	Ticagrelor 6.1 Clopidogrel 6.2	Apixaban 17.9 Placebo 18.3	All 7.2	Prasugrel 7.2 Clopidogrel 7.6

Randomized Controlled Trial > N Engl J Med. 2009 Sep 10;361(11):1045-57.
doi: 10.1056/NEJMoa0904327. Epub 2009 Aug 30.

PLATO

Ticagrelor versus clopidogrel in patients with acute coronary syndromes

Conclusions: In patients who have an acute coronary syndrome with or without ST-segment elevation, treatment with ticagrelor as compared with clopidogrel significantly reduced the rate of death from vascular causes, myocardial infarction, or stroke without an increase in the rate of overall major bleeding but with an increase in the rate of non-procedure-related bleeding. (ClinicalTrials.gov number, NCT00391872.)

Clinical Trial > N Engl J Med. 2011 Aug 25;365(8):699-708. doi: 10.1056/NEJMoa1105819. Epub 2011 Jul 24.

APPRAISE-2

Apixaban with antiplatelet therapy after acute coronary syndrome

EARLY TERMINATION FOR INCREASE IN BLEEDING

Conclusions: The addition of apixaban, at a dose of 5 mg twice daily, to antiplatelet therapy in high-risk patients after an acute coronary syndrome increased the number of major bleeding events without a significant reduction in recurrent ischemic events. (Funded by Bristol-Myers Squibb and Pfizer; APPRAISE-2 ClinicalTrials.gov number, NCT00831441.).

Randomized Controlled Trial > Eur Heart J. 2013 Jun;34(23):1723-31.
doi: 10.1093/eurheartj/eht104. Epub 2013 Mar 25.

Effect of vorapaxar on myocardial infarction in the thrombin receptor antagonist for clinical event reduction in acute coronary syndrome (TRA·CER) trial

Aims: The TRA·CER trial compared vorapaxar, a novel platelet protease-activated receptor (PAR)-1 antagonist, with placebo in 12 944 patients with high-risk non-ST-segment elevation acute coronary syndromes (NSTE ACS). In this analysis, we explored the effect of vorapaxar on myocardial infarction (MI).

Another failure, the study did not achieve its composite endpoint, but…

Randomized Controlled Trial > J Am Coll Cardiol. 2014 Mar 25;63(11):1048-57.
doi: 10.1016/j.jacc.2013.10.048. Epub 2013 Nov 21.

Vorapaxar in acute coronary syndrome patients undergoing coronary artery bypass graft surgery: subgroup analysis from the TRACER trial (Thrombin Receptor Antagonist for Clinical Event Reduction in Acute Coronary Syndrome)

Conclusions: In non-ST-segment elevation acute coronary syndrome patients undergoing CABG, vorapaxar was associated with a significant reduction in ischemic events and no significant increase in major CABG-related bleeding. These data show promise for protease-activated receptor 1 antagonism in patients undergoing CABG and warrant confirmatory evidence in randomized trials. (Trial to Assess the Effects of SCH 530348 in Preventing Heart Attack and Stroke in Patients With Acute Coronary Syndrome [TRA·CER] [Study P04736AM3]; NCT00527943).

Randomized Controlled Trial > N Engl J Med. 2012 Oct 4;367(14):1297-309.
doi: 10.1056/NEJMoa1205512. Epub 2012 Aug 25.

Prasugrel versus clopidogrel for acute coronary syndromes without revascularization

Conclusions: Among patients with unstable angina or myocardial infarction without ST-segment elevation, prasugrel did not significantly reduce the frequency of the primary end point, as compared with clopidogrel, and similar risks of bleeding were observed. (Funded by Eli Lilly and Daiichi Sankyo; TRILOGY ACS ClinicalTrials.gov number, NCT00699998.).

Am J Cardiol. 2022 Sep 1;178:11-17. doi: 10.1016/j.amjcard.2022.04.062. Epub 2022 Jul 11.

Outcomes After Acute Coronary Syndrome in Patients With Diabetes Mellitus and Peripheral Artery Disease (from the TRACER, TRILOGY-ACS, APPRAISE-2, and PLATO Clinical Trials)

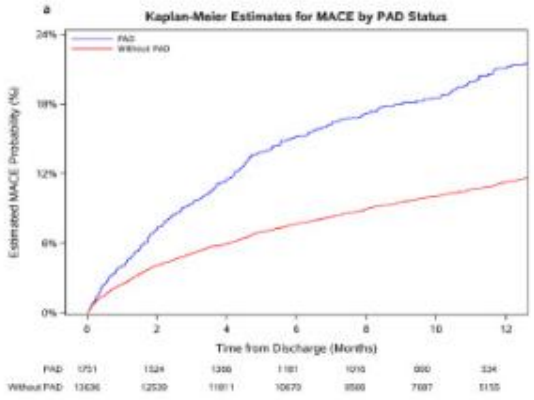
The American Journal of Cardiology
Volume 178, 1 September 2022, Pages 11-17

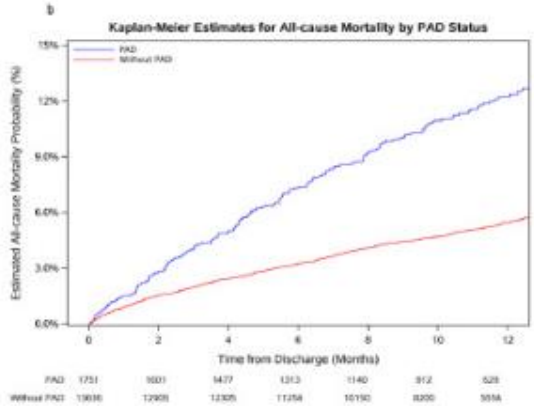
Sabato 25 Marzo 2023

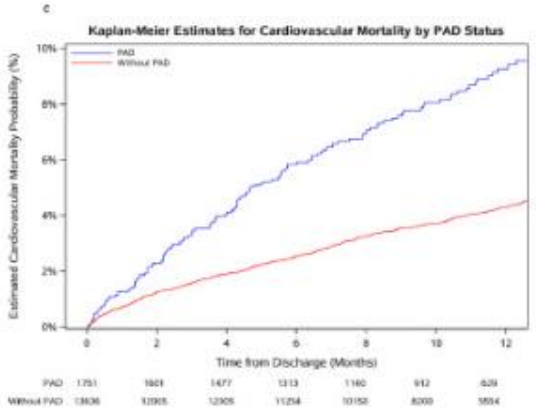
HOTEL CASCINA FOSSATA
Via Ala di Stura 5 - Torino

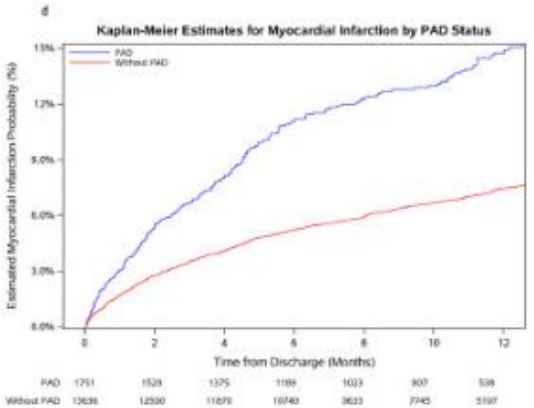
IL PAZIENTE *FRAGILE* IN CARDIOLOGIA

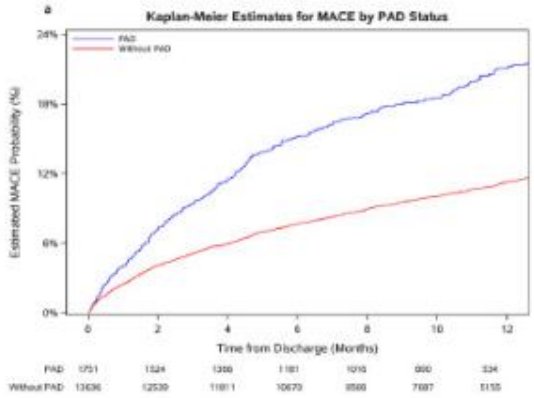
VI Edizione

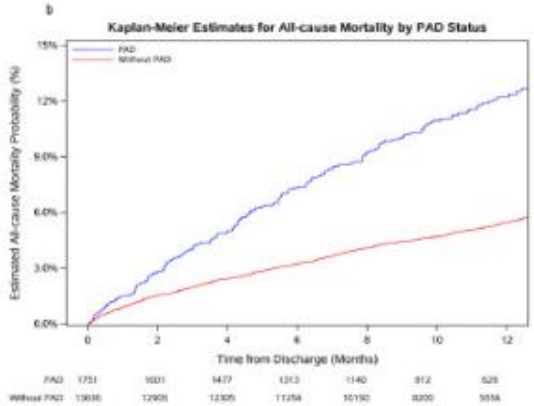


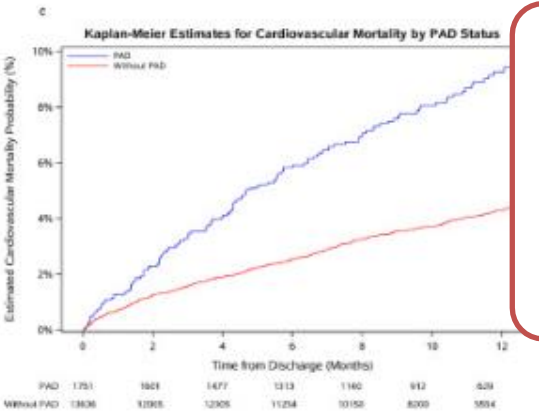












In conclusion, this analysis of 4 major post-ACS trials showed that patients with DM and PAD had a substantial higher risk for MACE, CV mortality, all-cause mortality, and myocardial infarction despite being optimally treated with guideline-based therapies. Future studies should focus on investigating the effects of therapies with novel agents on the adverse outcomes seen in this multimorbid population.

Review > Cardiovasc Ther. 2014 Oct;32(5):224-32. doi: 10.1111/1755-5922.12083.

The "dual-pathway" strategy after acute coronary syndrome: rivaroxaban and antiplatelet agents in the ATLAS ACS 2-TIMI 51 trial

Marc Cohen [1], Deepa Iyer

Conclusions: In patients with a recent acute coronary syndrome, rivaroxaban reduced the risk of the composite end point of death from cardiovascular causes, myocardial infarction, or stroke. Rivaroxaban increased the risk of major bleeding and intracranial hemorrhage but not the risk of fatal bleeding. (Funded by Johnson & Johnson and Bayer Healthcare; ATLAS ACS 2-TIMI 51 ClinicalTrials.gov number, NCT00809965.).

other adverse events. The twice-daily 2.5-mg dose resulted in fewer fatal bleeding events than the twice-daily 5-mg dose (0.1% vs. 0.4%, P=0.04).

Patients with recent ACS

- Rivaroxaban 2.5 mg twice daily
- Rivaroxaban 5 mg twice daily
- Placebo

All patients received standard antiplatelet therapy (usually DAPT)

COMPASS STUDY

Randomized Controlled Trial > Lancet. 2018 Jan 20;391(10117):219-229.
doi: 10.1016/S0140-6736(17)32409-1. Epub 2017 Nov 10.

Rivaroxaban with or without aspirin in patients with stable peripheral or carotid artery disease: an international, randomised, double-blind, placebo-controlled trial

Interpretation: Low-dose rivaroxaban taken twice a day plus aspirin once a day reduced major adverse cardiovascular and limb events when compared with aspirin alone. Although major bleeding was increased, fatal or critical organ bleeding was not. This combination therapy represents an important advance in the management of patients with peripheral artery disease. Rivaroxaban alone did not significantly reduce major adverse cardiovascular events compared with asprin alone, but reduced major adverse limb events and increased major bleeding.

Randomized Controlled Trial > Circulation. 2021 Oct 5;144(14):1104-1116.
doi: 10.1161/CIRCULATIONAHA.121.054835. Epub 2021 Aug 12.

Effect of Rivaroxaban and Aspirin in Patients With Peripheral Artery Disease Undergoing Surgical Revascularization: Insights From the VOYAGER PAD Trial

Background: Patients with peripheral artery disease requiring lower extremity revascularization (LER) are at high risk of adverse limb and cardiovascular events. The VOYAGER PAD trial (Vascular Outcomes Study of ASA [Acetylsalicylic Acid] Along With Rivaroxaban in Endovascular or Surgical Limb Revascularization for PAD) demonstrated that rivaroxaban significantly reduced this risk. The efficacy and safety of rivaroxaban has not been described in patients who underwent surgical LER.

Randomized Controlled Trial > Circulation. 2021 Oct 5;144(14):1104-1116.
doi: 10.1161/CIRCULATIONAHA.121.054835. Epub 2021 Aug 12.

Effect of Rivaroxaban and Aspirin in Patients With Peripheral Artery Disease Undergoing Surgical Revascularization: Insights From the VOYAGER PAD Trial

Conclusions: The efficacy of rivaroxaban is associated with a benefit in patients who underwent surgical LER. Although bleeding was increased with rivaroxaban plus aspirin, the incidence was low, with no significant increase in fatal bleeding, intracranial hemorrhage, or postprocedural bleeds requiring intervention. Registration: URL: http://www.clinicaltrials.gov; Unique Identifier:

THE LANCET

Volume 391, Issue 10117, 20–26 January 2018, Pages 183-184

Un utile riassunto…

Comment

Antithrombotic therapy in peripheral artery disease

Interpretation: Low-dose rivaroxaban taken twice a day plus aspirin once a day reduced major adverse cardiovascular and limb events when compared with aspirin alone. Although major bleeding was increased, fatal or critical organ bleeding was not. This combination therapy represents an important advance in the management of patients with peripheral artery disease. Rivaroxaban alone did not significantly reduce major adverse cardiovascular events compared with asprin alone, but reduced major adverse limb events and increased major bleeding.

several unresolved issues remain. First, COMPASS excluded patients taking dual antiplatelet therapy. Thus, the role of rivaroxaban plus aspirin in patients with peripheral artery disease requiring dual antiplatelet therapy is unknown. Second, clopidogrel monotherapy is an effective strategy in taking care of patients with peripheral artery disease.[4] The benefits of the use of rivaroxaban instead of, or in addition to, clopidogrel are uncertain. Third, a third of patients were on a proton-pump inhibitor (PPI) at baseline and the remaining two-thirds of patients were randomly assigned (1:1) to a PPI or no PPI. Thus, the risk of gastrointestinal bleeding with rivaroxaban might have been underestimated. Fourth, stopping the trial early might have overestimated the treatment effect and early stopping of this trial prevented a more robust analysis of the rivaroxaban alone group. Finally, patients without coronary artery disease and without peripheral artery disease symptoms who were diagnosed with peripheral artery disease via screening ankle–brachial index and receiving a score of less than 0·90 would not have been included in this trial and thus remain an unexplored population.

QUESTIONI APERTE:

- DAPT+RIVAROXABAN LOW DOSE?
- CLOPIDOGREL+RIVAROXABAN?
- PPI?
- LATE DATA?
- ASYMPTOMATIC PAD?

CLINICAL PRACTICE GUIDELINE DOCUMENT

esvs

Global Vascular Guidelines on the Management of Chronic Limb-Threatening Ischemia

4.3	Treat all patients with CLTI with an antiplatelet agent.	1 (Strong)	A (High)	Antithrombotic Trialists' Collaboration,[33] 2002 Antithrombotic Trialists' Collaboration,[34] 2009
4.4	Consider clopidogrel as the single antiplatelet agent of choice in patients with CLTI.	2 (Weak)	B (Moderate)	CAPRIE,[35] 1996 Hiatt,[36] 2017
4.5	Consider low-dose aspirin and rivaroxaban, 2.5 mg twice daily, to reduce adverse cardiovascular events and lower extremity ischemic events in patients with CLTI.	2 (Weak)	B (Moderate)	Anand,[37] 2018
4.6	Do not use systemic vitamin K antagonists for the treatment of lower extremity atherosclerosis in patients with CLTI.	1 (Strong)	B (Moderate)	Anand,[38] 2007
4.7	Use moderate- or high-intensity statin therapy to reduce all-cause and cardiovascular mortality in patients with CLTI.	1 (Strong)	A (High)	Leng,[39] 2000 Heart Protection Study Collaborative Group,[40] 2002 Meade,[41] 2002 Aung,[42] 2007 Mills,[43] 2011

CLINICAL PRACTICE GUIDELINE DOCUMENT

esvs

Global Vascular Guidelines on the Management of Chronic Limb-Threatening Ischemia

Dopo l'intervento:
(nota, dipende anche dal tipo di graft, i pazienti con bypass autologhi in vena beneficiano dell'anticoagulazione…)

10.3 Consider DAPT (aspirin plus clopidogrel) in patients who have undergone infrainguinal prosthetic bypass for CLTI for a period of 6 to 24 months to maintain graft patency.

Grade	Level of evidence	Key references
2 (Weak)	B (Moderate)	Brown,[127] 2008 Belch,[132] 2010 Gassman,[133] 2014 Bedenis,[128] 2015

10.4 Consider DAPT (aspirin plus clopidogrel) in patients who have undergone infrainguinal endovascular interventions for CLTI for a period of at least 1 month.

Grade	Level of evidence	Key references
2 (Weak)	C (Low)	Cassar,[134] 2005 Bhatt,[135] 2006 Tepe,[136] 2012 Strobl,137 2013

10.5 Consider DAPT for a period of 1 to 6 months in patients undergoing repeated catheter-based interventions if they are at low risk for bleeding.

Grade	Level of evidence	Key references
2 (Weak)	C (Low)	Cassar,[134] 2005 Tepe,[136] 2012 Strobl,[137] 2013

Terapia farmacologica del paziente con cardiopatia ischemica (CAD) e arteriopatia periferica (PAD)

Grazie per l'attenzione

Dott. Michele Boero – S.C. Chirurgia Vascolare, S.Giovanni Bosco
mpfboero@gmail.com