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Impact of Access Site on Bleeding and Ischemic Events in Patients With Non–ST-Segment Elevation Myocardial Infarction Treated With Prasugrel

The ACCOAST Access Substudy

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ABSTRACT

OBJECTIVES This study assessed whether the choice of vascular access site influenced outcomes among non-ST-segment elevation myocardial infarction (NSTEMI) patients enrolled in the ACCOAST (A Comparison of prasugrel at the time of percutaneous Coronary intervention Or as pre-treatment At the time of diagnosis in patients with non-ST-segment elevation myocardial infarction NCT01015287).

BACKGROUND Transfemoral access (TFA) has been associated with the risk of bleeding and increased mortality that is elevated compared to transradial access (TRA) in acute coronary syndromes, although less consistently in NSTE acute coronary syndrome (NSTE-ACS) than in STE-ACS.

METHODS The ACCOAST study evaluated a prasugrel loading dose of 60 mg given at the start of percutaneous coronary intervention (PCI) versus a split loading dose of 30 mg given at the time of diagnosis of NSTE-ACS (prior to coronary angiography), followed by 30 mg given at the start of PCI. In the study, choice of access site was at the investigator's discretion. We compared ischemic and bleeding outcomes with TFA versus those with TRA, using propensity score correction.

RESULTS Of 4,033 patients, 1,711 (42%) underwent TRA. Use of TRA varied widely by country. TFA was not associated with significant increases in noncoronary bypass graft (CABG)-related thrombolysis in myocardial infarction (TIMI) (hazard ratio [HR] for TFA = 1.46; 95% confidence interval [CI]: 0.59 to 3.62; p = 0.42), nor in GUSTO (Global Utilization Of Streptokinase and Tpa for Occluded arteries) or STEEPLE (Safety and Efficacy of Enoxaparin in PCI) major bleeding after propensity score correction. TFA, however, increased combined non-CABG TIMI major or minor bleeding (HR for TFA = 2.34; 95% CI: 1.17 to 4.69; p = 0.017). Primary ischemic outcomes did not differ by access site, albeit individual endpoint analysis suggested an association between TFA with an increase in urgent revascularizations and reduced risk of procedure-related stroke.

CONCLUSIONS In the ACCOAST trial, TFA did not significantly increase TIMI major bleeding, although TRA was associated with a reduction in TIMI major or minor bleeding. Further study is needed to determine whether wider application of radial approach to NSTE-ACS patients at high risk for bleeding improves overall outcomes.
(A Comparison of Prasugrel at PCI or Time of Diagnosis of Non-ST Elevation Myocardial Infarction [ACCOAST]; NCT01015287)
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ABBREVIATIONS AND ACRONYMS

ACS = acute coronary syndrome(s)

HR = hazard ratio

MI = myocardial infarction

NST-ACS = non-ST-segment elevation ACS

PCI = percutaneous coronary intervention

TRA = transradial access

TFA = transfemoral access

Bleeding related to either access site or non-access site is an important adverse event in patients with acute coronary syndromes (ACS) undergoing cardiac catheterization and percutaneous coronary intervention (PCI) (1–3). Whereas non-access site-related hemorrhages carries an independent prognostic value, there is more controversy over the relevance of access site-related bleeding and on the role of transradial access (TRA), a strategy associated with a marked decrease in access site-related bleeding and vascular complications compared to transfemoral access (TFA) (2,4–6). In particular, there is relative agreement on the benefits of TRA in ST-segment elevation-ACS (STE-ACS) (7–10), whereas no clear picture emerges in the field of non-STE-ACS (NSTE-ACS). Indeed, in NSTE-ACS, the available randomized data do not show a beneficial impact of TRA on ischemic and hemorrhagic major endpoints (11), whereas registry derived publications (12,13) and subanalysis of randomized trials (14–17) are limited in their conclusions by the tendency of operators to adopt TRA in patients at lower bleeding risk and by the small size of the TRA group (as many of these trials were conducted mainly in the United States where TRA has only recently become popular) (18,19).

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The ACCOAST (A Comparison of prasugrel at the time of percutaneous Coronary intervention Or as pre-treatment At the time of diagnosis in patients with non-ST-segment elevation myocardial infarction) study was a multicenter, randomized trial conducted to appraise the efficacy (using ischemic endpoints) and safety (using bleeding endpoints) of pre-treatment with prasugrel, a potent P2Y12 inhibitor, in NSTE-ACS patients (20). Main results of the trial (21) and outcomes in the patients who underwent PCI (22) were published previously.

In a pre-specified subanalysis, we took advantage of the ACCOAST database to analyze ischemic and bleeding outcomes according to the access site used, with the aim of clarifying the role of TFA versus that of TRA in modern treatment of NSTE-ACS patients.

METHODS

PATIENT POPULATION. The ACCOAST trial was a prospective, randomized trial involving 4,033 patients with a diagnosis of NSTE-ACS and an elevated troponin level, who were randomized to receive either

University Hospital, Paris, France. This trial was sponsored by Daiichi-Sankyo Company, Ltd., and Eli Lilly and Co. The coordinating center was the ACTION Study Group, Institute of Cardiology of Pitié-Salpêtrière Hospital. ACCOAST trial data from the primary study were collected, managed, and analyzed by a clinical research organization contracted by the sponsors according to the protocol and a pre-defined statistical analysis plan. Dr. Porto has received consulting and lecture fees from AstraZeneca, Boston Scientific, St. Jude Medical, Terumo, and Volcano. Dr. Bolognese has received fees for board membership from Daiichi-Sankyo and Eli Lilly; consulting fees from Daiichi-Sankyo; and lecture fees from Daiichi-Sankyo, Eli Lilly, Menarini, Abbott, AstraZeneca, and Iroko Cardio International. Dr. Dudek has received consulting and lecture fees from Abbott, Adamed, Adyton Medical Polska, Abiomed Europe, AstraZeneca, Biotronik, Balton, Bayer, Braun, BioMatrix, Boston Scientific, Boehringer Ingelheim, Bracco, Bristol-Myers Squibb, Comesa Polska, Cordis, Cook, Covidien Polska, DRG MedTek, Eli Lilly, EuroCor, Hammermed, GE Healthcare, GlaxoSmithKline, Inspire-MD, Iroko Cardio International, Medianet, Medtronic, The Medicines Company, Meril Life Sciences, Merck Sharp & Dohme, Orbus-Neich, Pfizer, Possis, ProCardia Medical, Promed, REVA Medical, Sanofi, Siemens, Solvay, Stentys, St. Jude Medical, Terumo, Tyco, and Volcano. Dr. Goldstein has received fees for board membership from Boehringer Ingelheim, The Medicines Company, Daiichi-Sankyo, and Eli Lilly; consulting fees from Boehringer Ingelheim, Bayer, Sanofi, and AstraZeneca; lecture fees from Boehringer Ingelheim, The Medicines Company, Daiichi-Sankyo, Bayer, Sanofi, AstraZeneca, and Eli Lilly; payment for the development of educational presentations from Boehringer Ingleheim and AstraZeneca; and travel support from AstraZeneca, Bayer, Boehringer Ingelheim, Daiichi-Sankyo, The Medicines Company, and Sanofi. Dr. Hamm has received payment for board membership from AstraZeneca, Medtronic, and Boehringer Ingelheim; consulting and lecture fees from Medtronic, Boehringer Ingelheim, Eli Lilly, The Medicines Company, Abbott Vascular, Bayer, Sanofi, Boston Scientific, Correvio, Roche Diagnostics, Pfizer, Cordis, Daiichi-Sankyo, and GlaxoSmithKline; and lecture fees from AstraZeneca and Merck. Dr. Tanguay has received consulting fees from Eli Lilly, AstraZeneca, Abbott Vascular, Roche, and GlaxoSmithKline; lecture fees from Bayer, Sanofi, Eli Lilly, AstraZeneca, Abbott Vascular, Pfizer, and Bristol-Myers Squibb; and grant support from Eli Lilly, AstraZeneca, Roche, Hexacath, Ikaria, Abbott Vascular, GlaxoSmithKline, Roche, and Sanofi. Dr. ten Berg has received fees for board membership from AstraZeneca; consulting fees from AstraZeneca, Eli Lilly, and Merck; and lecture fees from AstraZeneca, Eli Lilly, and The Medicines Company. Dr. Widimsky has received consulting and lecture fees from Eli Lilly and Daiichi-Sankyo. Mr. Le Gall is an employee of inVentiv Health Company, whose work is funded by Eli Lilly. Mr. Zagar, Dr. LeNarz, and Ms. Miller are employees and shareholders of Eli Lilly and Company. Dr. Montalescot has received consulting fees from Bayer, Boehringer Ingelheim, Cardiovascular Research Foundation, Europa Organisation, the Gerson Lehrman Group, Iroko Cardio International, Lead-Up, Luminex, McKinsey & Company, Inc., Remedica, Servier, TIMI Study Group, WebMD, Wolters Kluwer Health, Bristol-Myers Squibb, AstraZeneca, Biotronik, Eli Lilly, The Medicines Company, Menarini Group, Roche, Sanofi, Pfizer, Daiichi-Sankyo, and Medtronic; and grant support from Bristol-Myers Squibb, AstraZeneca, Biotronik, Eli Lilly, The Medicines Company, Menarini Group, Sanofi, Pfizer, Roche, Accumetrics, Medtronic, Abbott Laboratories, Daiichi-Sankyo, Nanosphere Inc., and Stentys.

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