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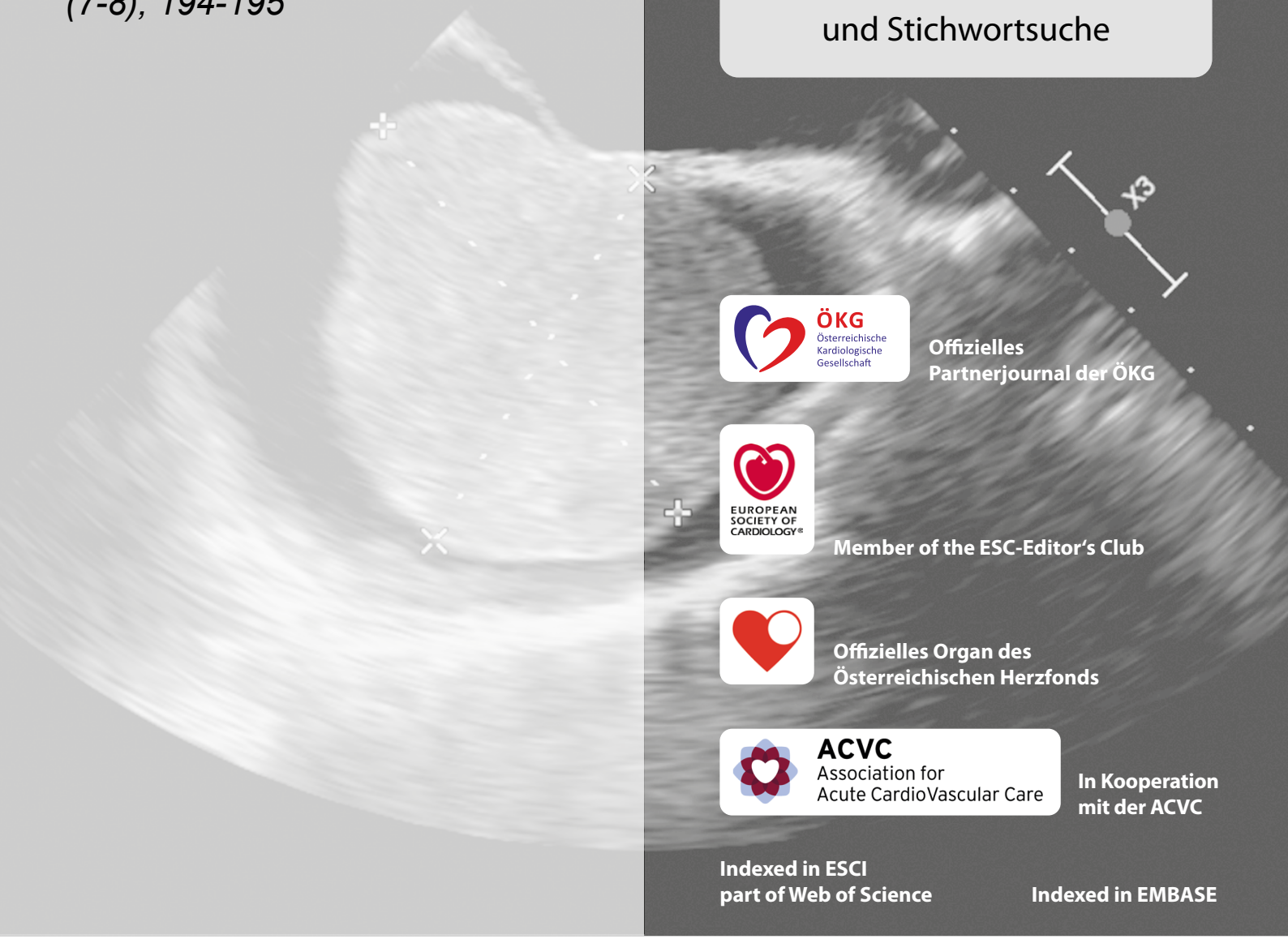

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The ACCOAST Trial – Is upstream DAPT in NSTEACS dead or alive?

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Although many clinicians have adopted a practice of pretreatment with dual antiplatelet therapy (DAPT) in patients with non-ST-segment-elevation acute coronary syndromes (NSTEMI ACS) and European and American guidelines [1, 2] recommend giving P2Y12inhibitors as soon as possible, the optimal timing of DAPT is a subject of continuing debate.

Much of this controversy stems from the fact that previous clinical trials have not been explicitly designed to inform clinical practice. Instead, contemporary management strategies are a patchwork of individualized interpretation of the evidence, which is far from robust.

Two studies, one post-hoc observational study of a larger trial involving patients with NSTEMI ACS [3] and one randomized involving patients undergoing elective percutaneous coronary intervention (PCI) [4], suggested that pretreatment with clopidogrel could reduce the rate of ischemic events at the cost of an increase in the rate of major bleeding.

PCI-CURE was a nonrandomized, *post hoc* observational study of a larger trial (CURE) designed to compare clopidogrel with placebo in patients with NSTEMI ACS with planned conservative treatment. Sites routinely practicing an early invasive strategy were excluded from the trial; patients receiving GP IIb/IIIa inhibitors within 3 days were excluded. PCI was performed on the basis of clinical indications, such as refractory ischemia. Patients randomized to clopidogrel were considered pretreated, whereas those who received placebo were not. The median period of pretreatment was 6 days. Thus, the study design is very far from current clinical practice.

In order to focus on the question of benefit of clopidogrel pre-treatment and reduction of PCI-related procedural complications, it is necessary to evaluate short-term treatment effects.

In the PCI-CURE 30-day trial data, the pre-treatment benefit with clopidogrel was limited to reduction of frequency of MI, with a trend toward benefit in need for urgent revascularization but no effect at all on cardiovascular death [3].

CREDO is the only randomized trial to date that provides partially relevant information on the pretreatment questions. Patients with symptomatic coronary artery disease and evidence of ischemia who were referred for PCI or were thought to be at a high likelihood for requiring PCI were randomized to receive clopidogrel (300 mg) or matching placebo 3 to 24 hours before PCI.

Thus, CREDO is really a comparison of administering a loading dose before PCI versus not administering a loading dose; however, there is no direct comparison of giving a loading dose before PCI versus at the time of PCI.

Nevertheless, there were no significant differences in outcome at 30 days. A prespecified subgroup analysis did, however, show a trend toward benefit in the patients who received the study drug 6 hours before PCI.

A subsequent *post hoc* analysis suggested that clopidogrel had to be ingested at least 15 hours before PCI to decrease 30-day clinical events.

Subsequent randomized studies did not confirm the benefit of clopidogrel pretreatment with respect to ischemic events among patients in stable condition who were undergoing elective PCI [5–7], and a recent metanalysis did not show a survival benefit of clopidogrel pretreatment among more than 37,000 patients undergoing PCI, while there was an excess of major bleeding and little impact on ischemic outcomes [8].

The ACCOAST study is the first randomized trial that specifically addressed the issue of pretreatment with P2Y12 inhibitors in NSTEMI. The results offer new insights and give rise up new questions:

For which patients groups does ACCOAST apply? The risk profile of ACCOAST population was similar to that in contemporary randomized clinical trials of patients with ACS who were undergoing PCI, but lower than that of the main registries on NSTEMI ACS. Furthermore, timing for coronary angiography was relatively short when compared to everyday clinical practice. Thus, ACCOAST findings are certainly applicable to most intermediate risk patients presenting with NSTE-ACS addressed to an early invasive strategy.

Do we need preloading in NSTEMI anymore? Times to PCI are now shrinking and the risk of an ischemic complication

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before coronary angiography is extremely low. Thus, the practical difference between upstream and downstream therapy is diminishing. In addition, a relevant percentage of NSTE-ACS population does not need pretreatment as they undergo to CABG or are medically managed. Finally, the rapid onset of action of the new oral P2Y12 inhibitors associated with the short delays to catheterization, suggest that a pretreatment strategy may be avoided in most patients as demonstrated in the ACCOAST trial.

Can the ACCOAST results be applied to other P2Y12inhibitors, such as clopidogrel and ticagrelor? For clopidogrel, as previously mentioned, the oldest studies suggest a potential benefit for pretreatment when there is a very long delay between randomization and PCI [3, 4]. More recent studies have not confirmed the benefit of pretreatment with shorter delays and higher doses of clopidogrel [5–8]. For ticagrelor, in the PLATO trial [9] all patients were pretreated with clopidogrel, ticagrelor or both before PCI; thus, the question of pretreatment has not been addressed for ticagrelor. One may speculate that similar result would be achieved when ticagrelor would be used within the same study design instead of prasugrel.

Conclusion

The new insights provided by the ACCOAST trials have important every-day practical implications: in patients with an intermediate risk and a short delay (< 24) from admission to angiography, pretreatment should be avoided; in high-risk patients with a delay from admission to angiography of > 24 hours, pretreatment with either clopidogrel (on the basis of old data) or ticagrelor (without data) may be considered.

References:

1. Hamm CW, Bassand JP, Agewall S, et al. ESC guidelines for the management of acute coronary syndromes in patients presenting without persistent STsegment elevation: the Task Force for the management of acute coronary syndromes (ACS) in patients presenting without persistent ST-segment elevation of the European Society of Cardiology (ESC). Eur Heart J 2011; 32: 2999–3054.

2. Jneid H, Anderson JL, Wright RS, et al. 2012 ACCF/AHA focused update of the guideline for the management of patients with unstable angina/non-ST-elevation myocardial infarction (updating the 2007 guideline and replacing the 2011 focused update): a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol 2012; 60: 645–81.

3. Mehta SR, Yusuf S, Peters RJ, et al. Effects of pretreatment with clopidogrel and aspirin followed by long-term therapy in patients undergoing percutaneous coronary intervention: the PCI-CURE study. Lancet 2001; 358: 527–33.

4. Steinhubl SR, Berger PB, Mann JT III, et al. Early and sustained dual oral antiplatelet therapy following percutaneous coronary intervention: a randomized controlled trial. JAMA 2002; 288: 2411–20.

5. Widimsky P, Motovsky Z, Simek S, et al. Clopidogrel pre-treatment in stable angina: for all patients > 6 h before elective coronary angiography or only for angiographically selected patients a few minutes before PCI? A randomized multicentre trial PRAGUE-8. Eur Heart J 2008; 29: 1495–503.

6. Di Sciascio G, Patti G, Pasceri V, et al. Effectiveness of in-laboratory high-dose clopidogrel loading versus routine pre-load in patients undergoing percutaneous coronary intervention: results of the ARMYDA-5 PRELOAD (Antiplatelet therapy for Reduction of MYocardial Damage during Angioplasty) randomized trial. J Am Coll Cardiol 2010; 56: 550–7.

7. Davlouros PA, Arseniou A, Hahalis G, et al. Timing of clopidogrel loading before percutaneous coronary intervention in clopidogrel-naive patients with stable or unstable angina: a comparison of two strategies. Am Heart J 2009; 158: 585–91.

8. Bellemain-Appaix A, O'Connor SA, Silvain J, et al. Association of clopidogrel pretreatment with mortality, cardiovascular events, and major bleeding among patients undergoing percutaneous coronary intervention: a systematic review and meta-analysis. JAMA 2012; 308: 2507–16.

9. Wallentin L, Becker RC, Budaj A, et al. Ticagrelor versus clopidogrel in patients with acute coronary syndromes. N Engl J Med 2009; 361: 1045–57.

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