2017 Essential Messages from ESC Guidelines

Committee for Practice Guidelines

DAPT

Focused Update on Dual Antiplatelet Therapy in Coronary Artery Disease

ESC
European Society of Cardiology

Essential Messages

2017 ESC focused update on dual antiplatelet therapy in coronary artery disease developed in collaboration with EACTS*

The Task Force for dual antiplatelet therapy in coronary artery disease of the European Society of Cardiology (ESC) and of the European Association for Cardio-Thoracic Surgery (EACTS)

Chairperson

Marco Valgimigli
Swiss Cardiovascular Center - Inselspital,
University of Bern
CH-3010, Bern, Switzerland
Tel: **+41 31 632 3077**
Fax: **+41 10 7035258**
Email: **marco.valgimigli@insel.ch**

Task Force Members

Héctor Bueno (Spain), Robert Byrne (Germany), Jean-Philippe Collet (France), Francesco Costa (Italy), Anders Jeppsson (Sweden), Peter Jüni (Switzerland), Adnan Kastrati (Germany), Philippe Kolh (Belgium), Laura Mauri (USA), Gilles Montalescot (France), Franz-Josef Neumann (Germany), Mate Petricevic (Croatia), Marco Roffi (Switzerland), Philippe Gabriel Steg (France), Stephan Windecker (Switzerland), Jose Luis Zamorano (Spain)

Additional Contributor: Glenn Levine (USA)

ESC entities having participated in the development of this document:

Associations: *Acute Cardiovascular Care Association (ACCA), European Association for Preventive cardiology (EAPC), European Association of Percutaneous Cardiovascular Interventions (EAPCI).*

Working Groups: *Cardiovascular Pharmacotherapy, Cardiovascular Surgery, Coronary Pathophysiology and Microcirculation, Peripheral Circulation, Pulmonary Circulation and Right Ventricular Function, Thrombosis, Valvular Heart Disease.*

*Adapted from the ESC Focused Update on Dual Antiplatelet Therapy in Coronary Artery Disease (European Heart Journal 2018;39:213-254 - doi:10.1093/eurheartj/ehx419).

ESSENTIAL MESSAGES FROM THE 2017 ESC FOCUSED UPDATE ON DUAL ANTIPLATELET THERAPY IN CORONARY ARTERY DISEASE DEVELOPED IN COLLABORATION WITH EACTS

Table of contents

European Heart Journal 2018;39:213-254 - doi:10.1093/eurheartj/ehx419

Key messages

1. **Benefits and risks of DAPT**

   DAPT reduces the risk of stent thrombosis across the entire spectrum of events, from acute to very late occurrences. However, treatment with DAPT beyond 1 year after MI, or after PCI, exerts the majority of its benefit by reducing the rate of spontaneous MI. The risk of bleeding in patients on DAPT is proportionally related to its duration both within and beyond 1 year of treatment duration. Since the benefits of prolonged DAPT, especially for mortality endpoints, appear highly dependent on prior cardiovascular history (such as prior ACS/MI vs. stable CAD), and prediction models to estimate on-DAPT bleeding risk have been developed, an individualized approach based on ischaemic vs. bleeding risk assessment is warranted.

2. **Bleeding mitigation strategy**

   Every effort should be pursued to mitigate the risk of bleeding complications while the patient is on DAPT, including access site selection, modulation of modifiable risk factors for bleeding, low dose aspirin, low dose of $P2Y_{12}$ inhibitor as appropriate, and routine use of PPI.

3. **$P2Y_{12}$ inhibitor selection**

   Clopidogrel is considered the default $P2Y_{12}$ inhibitor in patients with stable CAD treated with PCI, those with indication to concomitant oral anticoagulation, as well as in ACS patients in whom ticagrelor or prasugrel are contraindicated. Ticagrelor or prasugrel is recommended in ACS patients unless drug-specific contraindications exist.

4. **Timing of $P2Y_{12}$ inhibitor initiation**

   The timing of initiation of a $P2Y_{12}$ inhibitor is both drug- (i.e. ticagrelor or clopidogrel vs. prasugrel) and disease-specific (i.e. SCAD vs. ACS and type thereof).

5. **Stable CAD patients treated with PCI**

   Irrespective of the type of metallic stent implanted, the duration of DAPT is 1–6 month(s) depending on the bleeding risk. For patients in whom the ischaemic risk prevails over the risk of bleeding, a longer DAPT duration may be considered.

6. **Metallic stent type and DAPT duration**

   The need for a short DAPT regimen should no longer justify the use of BMS instead of newer-generation DES. DAPT duration in each individual patient should be guided by an individualized approach based on ischaemic vs. bleeding risk assessment and not by the stent type.

7. **Stable CAD patients treated with CABG**

   There is insufficient data to recommend DAPT in this patient population.

Key messages

8. ACS patients

Irrespective of the final revascularization strategy (e.g. medical therapy, PCI, or CABG), the default DAPT duration in these patients is 12 months. Six-month therapy duration should be considered in high bleeding risk patients, whereas >12-month therapy may be considered in ACS patients who have tolerated DAPT without a bleeding complication.

9. Patients with indication for oral anticoagulation

Compared with OAC therapy alone, the addition of DAPT to OAC therapy results in at least a two- to three-fold increase in bleeding complications. Therefore, these patients should be considered at high risk of bleeding and the indication for OAC should be reassessed and treatment continued only if a compelling indication exists. The duration of triple therapy should be limited up to a maximum of 6 months or omitted after hospital discharge, taking into account the ischaemic (e.g. complexity of treated CAD, amount of disease left untreated, technical considerations regarding stent implantation techniques, and results) as well as the bleeding risk. The use of ticagrelor or prasugrel in this setting is not recommended.

10. Patients undergoing elective non-cardiac surgery after coronary stent implantation

A multidisciplinary expert team should be considered for pre-operative evaluation of patients with an indication for DAPT before elective surgery. Scheduled surgery requiring discontinuation of the $P2Y_{12}$ inhibitor should be considered after at least 1 month, irrespective of the stent type, if aspirin can be maintained throughout the perioperative period. If both oral antiplatelet agents have to be discontinued perioperatively, a bridging strategy with cangrelor, tirofiban, or eptifibatide may be considered, especially if surgery has to be performed within 1 month after stent implantation.

11. Gender consideration and special populations

Similar type and duration of DAPT are recommended in male and female patients, as well as in patients with and without diabetes mellitus. Patients with prior stent thrombosis, especially in the absence of correctable causes, should receive prolonged DAPT. A prolonged DAPT regimen may also be considered in patients with LEAD or who have undergone complex PCI. It is recommended to reassess the type, dose, and duration of DAPT in patients with actionable bleeding complications while on treatment. In patients with active bleeding while on DAPT, the decision to stop both antiplatelet agents, especially if shortly after PCI, should be taken only if the bleeding is life-threatening and the source has not been or cannot be treated. In such a rare case scenario, the patient should be transferred to a primary PCI facility centre.

Gaps in evidence

Dual antiplatelet therapy and percutaneous coronary intervention

With a marginal overall benefit-to-risk ratio of extended DAPT beyond 1 year after DES placement, tools to identify ideal candidates for long-term or even indefinite DAPT duration are critically needed. The DAPT score as well as the subgroup analyses of PEGASUS are important steps forward, but prospective validation in contemporary cohorts of newer-generation DES patients is needed.

The optimal level of platelet inhibition during the various stages of CAD remains an open question. The risk of ischaemic complication is highest immediately after PCI and then gradually declines. The same is true for patients managed for ACS, although the risk remains elevated above that of patients who never experienced an acute exacerbation for years. Thus, it is intuitive that during the chronic phase after stabilization the level of platelet inhibition may be reduced as compared with the acute phase. Until recently, there were only limited data addressing this issue from beyond the periprocedural phase to 1 year. By now, two studies addressing such a step-down concept have finished recruitment: Testing Responsiveness to Platelet Inhibition on Chronic Antiplatelet Treatment For Acute Coronary Syndromes Trial (TROPICAL-ACS) (NCT01959451) with a step-down from prasugrel to clopidogrel after the peri-interventional phase in acute MI; and GLOBAL-LEADERS (NCT01813435) with a step-down from DAPT to single antiplatelet therapy with ticagrelor beyond the first month after PCI in an all-comers cohort with DES.

The risks and benefits of shortening DAPT to 3 months or even shorter is another area with limited evidence. There are only two randomized studies with a total of 5236 patients. Both studies used the first-generation ZES that, due to its limited efficacy in suppressing neointima formation, has been largely replaced by a newer generation. Thus, in most cases with high bleeding risk, the decision to shorten DAPT below 6 months needs to rely on circumstantial evidence suggesting comparable safety of different stent types.

As outlined in section 4.1 (Dual antiplatelet therapy after percutaneous coronary intervention for stable coronary artery disease), there are no dedicated studies on the optimal duration of DAPT after the application of drug-eluting balloons or after implantation of a bioresorbable scaffold. It is also unclear whether, early after placement of a bioresorbable stent, patients may benefit from the more potent $P2Y_{12}$ inhibition achieved by prasugrel or ticagrelor as compared with the current practice of clopidogrel administration.

Gaps in evidence

DUAL ANTIPLATELET THERAPY AND CARDIAC SURGERY

There are several gaps in the evidence that pertain to the use of DAPT in cardiac surgery. Clear gaps in evidence related to DAPT in cardiac surgery patients include the question of whether DAPT should be started after CABG in patients with stable CAD. Also, the exact timing of post-operative DAPT restart remains unclear, and it remains uncertain for how long the post-operative DAPT should last. Further gaps in the evidence relate to: the optimal time point for discontinuation of the different $P2Y_{12}$ inhibitors; the optimal use of platelet function testing in patients awaiting cardiac surgery; how to manage perioperative bleeding complications in cardiac surgery patients caused by DAPT; and whether and how an incomplete response or inadequate antiplatelet effect of aspirin after CABG should be addressed.

The following material was adapted from the 2017 ESC focused Update on Dual Antiplatelet Therapy in Coronary Artery Disease in collaboration with EACTS (European Heart Journal 2012018;39:213-254 - doi:10.1093/eurheartj/ehx419).

To read the full report as published by the European Society of Cardiology, visit our Web Site at:
www.escardio.org/guidelines

European Society of Cardiology
Les Templiers - 2035, Route des Colles
CS 80179 Biot
06903 Sophia Antipolis Cedex - France

Phone: +33 (0)4 92 94 76 00
Fax: +33 (0)4 92 94 76 01
Email: guidelines@escardio.org

www.escardio.org/guidelines