Summary of the European Society of Cardiology guidelines on dual antiplatelet therapy in patients after percutaneous coronary interventions

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ABSTRACT

This review is a summary of the European Society of Cardiology (ESC) guidelines focused on dual antiplatelet therapy in patients after percutaneous coronary interventions (PCI). Given a large number of recommendations concerning antiplatelet therapy published in various ESC guidelines, the main goal of this paper was to compile these separate recommendations into one document. In addition, we set out to present the current state of knowledge and create an algorithm that would be based on all of these guidelines in hope that it would allow quick navigation when selecting the type and duration of dual antiplatelet therapy (DAPT) depending on the clinical scenario with a special emphasis on evaluating both ischemic and bleeding risks.

The review is based on the ESC guidelines on the diagnosis and management of chronic coronary syndromes (2019), revascularization (2018), acute myocardial infarction in patients presenting with ST-segment elevation myocardial infarction (STEMI) (2017), DAPT (2017), and acute coronary syndromes in patients presenting without persistent ST-segment elevation (NSTE-ACS) (2020). The review also provides brief information on the most important studies and meta-analyses in this area, as well as practical pointers for management in the case of bleeding complications and before urgent surgery in patients on DAPT.

Key words: clopidogrel, dual antiplatelet therapy, percutaneous coronary intervention, prasugrel, ticagrelor

INTRODUCTION

Recently, a new generation of antiplatelet drugs has emerged that can be used in patients undergoing percutaneous coronary interventions (PCI). These more potent antiplatelet drugs have improved outcomes of both conservative and interventional treatments of patients with acute coronary syndrome (ACS). With technological progress and wide availability of secondand third-generation drug-eluting stents (DES) with improved design and drug delivery (biodegradable polymers, cobalt-chromium or platinum-chromium platforms, ultra-thin struts design), the recommended duration of dual antiplatelet therapy (DAPT) has also substantially evolved. Prolonged DAPT duration was associated with a reduced incidence of ischemic events but resulted in a significant increase in bleeding risk. Therefore, the debate on the optimization and individualization of antiplatelet therapy in patients after ACS and/or PCI remains open. Prevention of bleeding complications while maintaining effective protection against ischemic events is one of the main goals of medical treatment of patients after ACS and/or

PCI. The European Society of Cardiology (ESC) guidelines encourage clinicians to tailor DAPT duration and intensity according to the patients' individual bleeding and ischemic event risk.

In view of scientific and technological progress, expert recommendations regarding the DAPT strategy are constantly evolving. Our guide aims to compile these recommendations into one document so it would be readily available for quickly navigating the principles of selecting the type and duration of DAPT depending on the clinical scenario, including the bleeding and ischemic risk.

The need to make the correct decision regarding antiplatelet treatment may be challenging not only for cardiologists, but often for general practitioners, surgeons, or dentists alike [1]. Given the wide variety of recommendations concerning antiplatelet therapy algorithms, we set out to gather these recommendations in one document to facilitate an informed decision-making process in everyday clinical practice. It should be emphasized that this document presents only official recommendations without commenting on their content. Therefore, this review is based on the following ESC guidelines: the 2019 ESC guidelines on the diagnosis and management of chronic coronary syndromes (CCS), revascularization (2018), acute myocardial infarction in patients presenting with ST-segment elevation myocardial infarction (STEMI) (2017), dual antiplatelet therapy (2017), and acute coronary syndromes in patients presenting without persistent ST-segment elevation (NSTE-ACS) (2020).

CHOICE OF ANTIPLATELET THERAPY

A brief overview of antiplatelet drugs is included in the Supplementary material.

Acute coronary syndromes

The 2020 NSTE-ACS guidelines introduce significant changes to antiplatelet therapy, both in terms of the choice of $P2Y_{12}$ inhibitors, the time of initiation of therapy, and its duration. For the first time, there is a preference for prasugrel over ticagrelor in NSTE-ACS, making a significant difference in guiding antiplatelet management of STEMI and NSTE-ACS patients. Previous recommendations did not favor any of the more potent $P2Y_{12}$ inhibitors. The discrepancies in recommendations for prasugrel or ticagrelor use arise also from specific clinical scenarios and contraindications to their use. The 2017 STEMI guidelines allow the initiation of therapy with a potent $P2Y_{12}$ inhibitor at the time of diagnosis [2]. In turn, in the 2015 NSTE-ACS guidelines, initiation of treatment at diagnosis was possible only in the case of ticagrelor; the starting of prasugrel therapy had to be postponed until coronary angiography was performed and a decision on further invasive treatment was made. The recent 2020 NSTE-ACS guidelines recommend pretreatment only with acetylsalicylic acid (ASA). It is not recommended to apply routine pretreatment with a $P2Y_{12}$ inhibitor in patients in whom coronary anatomy is not known and early invasive management is planned (IIIA). Pretreatment with a $P2Y_{12}$ inhibitor may be considered in patients with NSTE-ACS who are not planned to undergo an early invasive strategy and do not have a high bleeding risk (HBR) (IIbC). These recommendations were based primarily on the results of the ACCOAST trial, which showed no reduction in ischemic events after pretreatment with $P2Y_{12}$ inhibitor, with a significant increase in bleeding complications with prasugrel [3]. Similar observations for all $P2Y_{12}$ inhibitors were made based on the analysis of the Swedish SCAAR registry [4]. In turn, the ISAR-REACT 5 trial did not demonstrate a benefit of pretreatment with ticagrelor [5]. A meta-analysis of 60 907 patients who underwent PCI has shown that the timing of ticagrelor or prasugrel loading dose had no effects on ischemic events in the acute setting; however, pretreatment with prasugrel in NSTE-ACS was associated with an increased risk of major bleeding events [6]. Postponing the addition of a $P2Y_{12}$ inhibitor to the therapy until coronary angiography is performed may result in multiple benefits, in particular reducing the risk of bleeding and avoiding unnecessary delay of coronary artery bypass surgery. Notably, a routine pretreatment strategy may be deleterious for a relevant proportion of patients with diagnoses other than NSTE-ACS (e.g. aortic dissection or bleeding complications including intracranial bleeding).

Another change concerns the position of prasugrel. Although both prasugrel and ticagrelor have retained their position (IB) as drugs that should be used with ASA for 12 months after PCI in patients with acute coronary syndrome if there are no contraindications to dual antiplatelet therapy, the 2020 NSTE-ACS guidelines recommend that prasugrel should be considered in preference to ticagrelor for NSTE-ACS patients who proceed to PCI [IIaB]. These recommendations are based on the results of the ISAR-REACT 5 trial [5], the first multicenter randomized trial comparing head-to-head prasugrel with ticagrelor in patients with acute coronary syndrome. This study generated a lot of controversies, mainly related to the study methodology. The obtained results, contrary to the hypothesis of the study, support the use of prasugrel (greater reduction in the composite endpoint at 12 months with no statistically significant difference in the incidence of bleeding complications). The primary endpoint event (death, myocardial infarction, or stroke at 1 year) occurred in 9.3% of patients in the ticagrelor group and 6.9% of patients in the prasugrel group (hazard ratio [HR], 1.36; 95% confidence interval [CI], 1.09–1.70; $P = 0.006$). The incidence rates of the individual components of the primary endpoint in the ticagrelor group and the prasugrel group were as follows: death 4.5% and 3.7% (HR, 1.23; 95% CI, 0.91–1.68); myocardial infarction 4.8% and 3.0% (HR, 1.63; 95% CI, 1.18–2.25); and stroke 1.1% and 1.0% (HR, 1.17; 95% CI, 0.63–2.15) [5]. Thus, the advantage of prasugrel over ticagrelor was driven exclusively by the excess of myocardial infarctions in the ticagrelor group.

Nevertheless, these data should be interpreted in light of their limitations, including (1) an open study plan; (2) a high percentage of patients who discontinued the assigned medication; (3) 83% of patient follow-up was done by telephone as opposed to face-to-face contact; (4) a lack of information on long-term bleeding complications (11.6% in the prasugrel arm vs. 1.1% in the ticagrelor arm), and (5) difficulties in interpreting the results in patients with different clinical settings (STEMI/non-ST-segment elevation myocardial infarction [NSTEMI]/unstable angina [UA]) with different timing strategies for $P2Y_{12}$ initiation.

Recently, Navarese et al. [7] published a network meta-analysis of twelve randomized controlled trials of 52 816 ACS patients. Compared to clopidogrel, ticagrelor significantly reduced cardiovascular mortality (HR, 0.82; 95% CI, 0.72–0.92) and all-cause mortality (HR, 0.83; 95% CI, 0.75–0.92), whereas there was no statistically significant mortality reduction with prasugrel (HR, 0.90; 95% CI, 0.80–1.01 and HR, 0.92; 95% CI, 0.84–1.02, respectively). When comparing ticagrelor and prasugrel to each other, there were no significant differences in mortality (HR prasugrel vs. ticagrelor 1.10 [95% CI, 0.94–1.29] and 1.12 [95% CI, 0.98–1.28]). In comparison with clopidogrel, prasugrel reduced myocardial infarction (HR, 0.81; 95% CI, 0.67–0.98), whereas ticagrelor showed no risk reduction (HR, 0.97; 95% CI, 0.78–1.22). Differences between prasugrel and ticagrelor with respect to myocardial infarction were not statistically significant. Compared with clopidogrel, both prasugrel (HR, 0.50; 95% CI, 0.38–0.64) and ticagrelor (HR, 0.72; 95% CI, 0.58–0.90) were associated with a significant reduction in definite or probable stent thrombosis. When compared to each other, prasugrel was linked to a significantly greater risk reduction of stent thrombosis than was ticagrelor (HR, 0.68; 95% CI, 0.50–0.90). In comparison with clopidogrel, both prasugrel (HR, 1.26 [95% CI, 1.01–1.56]) and ticagrelor (HR, 1.27 [95% CI, 1.04–1.55]) significantly increased major bleeding. However, the risk of major bleeding was similar when comparing ticagrelor to prasugrel (HR, 0.99; 95% CI 0.79–1.24) [7].

Recently, an expert opinion of the Association of Cardiovascular Interventions and the Working Group on Cardiovascular Pharmacotherapy of the Polish Cardiac Society on the place of prasugrel in the prevention of cardiovascular events in patients with acute coronary syndromes has been published. The document provides detailed characteristics of patients who can get the most benefit from prasugrel therapy. The experts concluded that prasugrel should be used in patients with ACS undergoing primary or delayed PCI. Compared to ticagrelor, prasugrel should be preferred in patients at increased risk of stent thrombosis. In patients with NSTEMI, the choice of a $P2Y_{12}$ inhibitor should be made after coronary angiography [8].

Chronic coronary syndromes

In patients with chronic coronary syndromes undergoing PCI, clopidogrel remains the preferred $P2Y_{12}$ inhibitor in addition to ASA. The recommendations for more potent $P2Y_{12}$ inhibitors are limited to patients at high risk of ischemic events — prasugrel or ticagrelor may be considered, at least as initial therapy, in specific high-risk situations of elective stenting (e.g. suboptimal stent deployment or other procedural characteristics associated with high risk of stent thrombosis, complex left main stem, or multivessel stenting) or if DAPT cannot be used because of ASA intolerance (IIbC) [9]. Similarly, if oral anticoagulation is needed (e.g., for stroke prevention in atrial fibrillation [AF]) in patients with chronic coronary syndrome, dual therapy with an oral anticoagulant (OAC) and either ticagrelor or prasugrel may be considered as an alternative to triple therapy with an OAC, ASA, and clopidogrel in patients with a moderate or high risk of stent thrombosis, irrespective of the type of stent used (IIbC) [9]. Notably, the use of ticagrelor or prasugrel is not recommended as part of triple antithrombotic therapy with ASA and an OAC (IIIC) [9].

BLEEDING RISK ASSESSMENT TOOLS

The use of DAPT, especially with a potent $P2Y_{12}$ inhibitor, is associated with an increased risk of bleeding complications which increases with longer duration of DAPT [10]. In the TRITON-TIMI 38 trial, the use of prasugrel compared to clopidogrel was associated with more major bleeding (2.4% vs. 1.8%; $P = 0.03$) and life-threatening bleeding (1.4% vs. 0.9%; $P = 0.01$), including fatal bleeding (0.4% vs. 0.1%; $P = 0.002$) [11]. For ticagrelor, there was no statistically significant difference in the incidence of major bleeding (11.6% for ticagrelor, 11.2% for clopidogrel; $P = 0.43$), but the use of ticagrelor was associated with more major bleedings unrelated to coronary artery bypass surgery (4.5% vs. 3.8%; $P = 0.03$), including fatal intracranial hemorrhage (0.1% vs. 0.01%; $P = 0.02$) [12].

In patients at high risk of bleeding complications or significant anemia, special care should be taken in the selection of an antiplatelet regimen. Therefore, bleeding risk assessment is crucial in the management of these patients. The bleeding and ischemic risk assessments allow for individualization of antiplatelet therapy, but we need to keep in mind that most of them were designed to assess the in-hospital or the short-term risk. The risk of bleeding complications should be minimized by identifying risk factors and selecting the correct dose of an appropriate $P2Y_{12}$ inhibitor, as well as adding a proton pump inhibitor in selected patients.

One of the recommended tools for bleeding risk assessment is the PRECISE-DAPT score (Table 1), which allows evaluation of the outpatient bleeding risk after stent implantation and helps to modify DAPT duration. A score of $\geq$25 denotes a high bleeding risk and correlates with the clinical benefit of shortening DAPT duration (3–6 months).

The CRUSADE score (Supplementary material, *Table S1*) is recommended to assess the risk of bleeding complications after NSTE-ACS [13].

Table 1. PRECISE-DAPT score

	PRECISE-DAPT Score
Predictors	Hemoglobin, g/dl
	White blood cells count, $\times 10^3$ cells/μl
	Age, years
	Creatinine clearance, ml/min
	Prior bleeding
Score points from 0 to 100	
Score ≥25 → Short DAPT (increasing bleeding risk) Score <25 → Standard/long DAPT	
In the case of the PRECISE-DAPT score, it is necessary to use a scoring nomogram to determine the value for each of the five variables and to determine the number of points obtained for each clinical variable or to use a calculator: *www.precisedaptscore.com*.	

Abbreviation: DAPT, dual antiplatelet therapy

Table 2. List of clinical criteria to define patients at high bleeding risk according to the Academic Research Consortium for High Bleeding Risk (ARC-HBR)

High bleeding risk definition according to the ARC-HBR	
• Bleeding Academic Research Consortium (BARC) 3 or 5 bleeding ≥4% at 12 months after PCI • The risk of intracranial bleeding ≥1% at 12 months after PCI	
HBR = ≥1 major criteria or ≥2 minor criteria	
Minor criteria	• Age ≥75 years
	• Moderate CKD (eGFR, 30–59 ml/min/1.73 m^2)
	• Hemoglobin 11–12.9 g/dl for men or 11–11.9 g/dl for women
	• Spontaneous bleeding requiring hospitalization and/or transfusion within the past 12 months not meeting the major criterion
	• Any ischemic stroke at any time not meeting the major criterion
	• Chronic use of oral non-steroidal anti-inflammatory drugs or steroids
Major criteria	• Severe or end-stage CKD (eGFR <30 ml/min/1.73 m^2)
	• Liver cirrhosis with portal hypertension
	• Active malignancy (excluding non-melanoma skin cancer) within the past 12 months
	• Hemoglobin <11 g/dl
	• Moderate or severe baseline thrombocytopenia (platelet count $<100 \times 10^9$/l)
	• Previous spontaneous intracranial hemorrhage (at any time)
	• Previous traumatic intracranial hemorrhage within the past 12 months
	• Presence of a brain arteriovenous malformation
	• Moderate or severe ischemic stroke within the past 6 months
	• Chronic bleeding diathesis
	• Spontaneous bleeding requiring hospitalization and/or transfusion in the past 6 months or at any time, if recurrent
	• Anticipated use of long-term oral anticoagulant
	• Non-deferrable major surgery on DAPT
	• Recent major surgery or major trauma within 30 days before PCI

Abbreviations: CKD, chronic kidney disease; eGFR, estimated glomerular filtrated rate; HBR, high bleeding risk; PCI, percutaneous coronary intervention; other — see Table 1

Alternatively, the Academic Research Consortium High Bleeding Risk (ARC-HBR) [14] definition of high bleeding risk may be used (Table 2). The proposed ARC-HBR criteria are intended to standardize the previously used various high bleeding risk definitions for both clinical trials and everyday medical practice.

Table 3. Criteria for high bleeding risk according to the European Society of Cardiology guidelines on chronic coronary syndromes (2019)

Predictors of high bleeding risk
• Prior history of intracerebral hemorrhage or ischemic stroke • History of other intracranial pathology • Recent gastrointestinal bleeding or anemia due to possible gastrointestinal blood loss • Other gastrointestinal pathology associated with increased bleeding risk • Liver failure • Bleeding diathesis or coagulopathy • Extreme old age or frailty • Renal failure requiring dialysis or with eGFR <15 ml/min/1.73 m^2

Abbreviations: see Table 2

The ESC guidelines on CCS also list a set of criteria for high bleeding risk which are summarized in Table 3.

In the NSTE-ACS guidelines, DAPT duration and the selection of $P2Y_{12}$ inhibitor depend on the classification of the patient into one of three categories: low, high, and very high risk of bleeding using the above-mentioned risk scores (PRECISE-DAPT, ARC-HBR).

MANAGEMENT OF BLEEDING COMPLICATIONS

Bleeding complications are the major side effect of all antiplatelet drugs. In the case of overdose of antiplatelet agents, there is no specific antidote and, if necessary, transfusion of platelet concentrate (PC) may be considered. The use of PC for correction of platelet function in $P2Y_{12}$ inhibitors therapy is not as well documented as it is for the reversal of ASA. However, it seems that more units of PC need to be transfused to neutralize the effect of $P2Y_{12}$ inhibitors. When active metabolites in the blood are present or when reversible ticagrelor used, the transfused platelets will be blocked by the drug or active metabolite present in the patient's blood, thus reducing the effectiveness of the transfused PC. Following PC transfusion, in the case of clopidogrel a >40% rate of uninhibited platelet is considered a significant correction. In the case of prasugrel, the rate needs to be much higher (>60%), but achieving this level of correction only provides a partial reversal of the antiplatelet effect of prasugrel. If the time since the last dose of prasugrel and clopidogrel is less than 6 hours, PC transfusion may be ineffective. This period is significantly extended (up to 24 hours) when using ticagrelor due to the long half-life of the drug itself and its active metabolite. Even after the active drug is cleared from the circulation, large numbers of platelets may be needed within the first 48 hours to restore platelet function because transfused platelets do not correct the hemostatic defect in platelets inhibited by ticagrelor. The use of desmopressin may be considered in addition to PC transfusion; however, there is no clear evidence of the effectiveness of such an approach, which, given possible side effects, makes such a strategy questionable. If ticagrelor reversal is required, recombinant activated factor VII (rFVIIa) may decrease ticagrelor-induced

bleeding, but this approach is not supported by strong clinical evidence.

Given the potential rFVIIa-associated thrombosis risk, a careful assessment of the benefit-risk balance is warranted before using rFVIIa to reverse ticagrelor effects.

The treatment algorithm for bleeding patients receiving dual antiplatelet therapy is shown in Figure 1.

MANAGEMENT OF ANTIPLATELET THERAPY BEFORE URGENT SURGERY

Reversing the effects of antiplatelet therapy before urgent surgery remains an open topic. There is a possibility of continuing treatment with ASA or clopidogrel in monotherapy, which, however, may be associated with an increased risk of bleeding complications. An alternative may be the transfusion of PC 1–2 hours before surgery and then return to antiplatelet therapy 6–9 hours after the end of the surgical procedure in the case of ASA or 24–48 hours in the case of clopidogrel.

SHORTENING OF DUAL ANTIPLATELET THERAPY

Standard DAPT after PCI should be continued for 6 months in patients with CCS and for 12 months in patients with ACS. Depending on the ischemic-bleeding risk, as well as the presence of comorbid conditions, DAPT duration should be appropriately modified. Due to the risk of stent thrombosis, it can be shortened only in justified clinical scenarios. Most clinical trials are currently focused on evaluating the strategy of early withdrawal of ASA and continuation of treatment with a $P2Y_{12}$ inhibitor (GLOBAL LEADERS, STOP-DAPT-2, SMART-CHOICE, TWILIGHT — Table 4).

Ticagrelor in monotherapy is the most frequently considered regimen for modifying antiplatelet therapy. In the GLOBAL LEADERS trial among patients who underwent PCI with a biolimus-eluting stent, 1 month of DAPT followed by ticagrelor monotherapy for 23 months was noninferior, but not superior, to 12 months of DAPT followed by ASA monotherapy for 12 months. The composite outcome, components of the primary outcome, and major bleeding were similar between the treatment groups [15]. In turn, the TWILIGHT trial showed that short-duration DAPT (3 months) followed by ticagrelor monotherapy for 12 months resulted in less bleeding compared with longer-duration DAPT (additional 12 months) among patients undergoing PCI with DES and at high ischemic or bleeding risk; ischemic rates (risk of death, myocardial infarction, and stroke) met criteria for noninferiority [16]. There are also studies investigating the efficacy and safety of prasugrel in monotherapy (the ASET Pilot Study [17], Multivessel TALENT Study [18]).

Acute and chronic coronary syndromes

In patients with CCS, shortening DAPT duration to 3 months in the case of a higher risk of life-threatening bleeding should be considered (IIaA) [9]; however, in situations of a very high risk of life-threatening bleeding, shorter DAPT duration of 1 month may be considered (IIbC) [9].

In patients with ACS and stent implantation who are at high risk of bleeding (e.g. PRECISE-DAPT ≥25), discontinuation of $P2Y_{12}$ inhibitor therapy after 6 months should be considered (IIaB) [19].

The NSTE-ACS guidelines emphasize the need for a more personalized approach to choosing a DAPT strategy (duration and intensity). First and foremost, the patient should be appropriately classified into one of the three categories: low, high, or very high risk of bleeding. In patients with low bleeding risk, apart from standard DAPT for 12 months, in the presence of low ischemic risk, DAPT (ASA + ticagrelor) duration can be shortened to 3 months, followed by ticagrelor monotherapy. The guidelines do not precisely define the duration of ticagrelor monotherapy. In turn, in patients at high risk of bleeding (e.g. PRECISE-DAPT ≥25 or ARC-HBR criteria met), discontinuation of $P2Y_{12}$ inhibitor therapy after 3 months should be considered followed by long-term ASA monotherapy (IIaB) [20]. Finally, in patients deemed at very high bleeding risk, DAPT (ASA + clopidogrel) is indicated for only 1 month followed by clopidogrel monotherapy. A very high bleeding risk was defined as a bleeding event within the past month or scheduled surgery that is impossible to postpone in the near future. The above indications are presented in Figures 2 and 3.

The two recently published studies assessed the appropriate duration of DAPT in patients at high risk bleeding after PCI (MASTER DAPT [21] and TWILIGHT-HBR [22]) and confirmed the benefits of shortened DAPT duration. In the MASTER DAPT trial among patients with acute or chronic coronary artery disease who underwent PCI and were at increased bleeding risk, abbreviated DAPT was noninferior to standard DAPT regarding net adverse clinical events and major adverse cardiac or cerebral events. Abbreviated DAPT was superior to standard antiplatelet therapy regarding major or clinically relevant nonmajor bleeding [21]. These results are specific to patients who received biodegradable-polymer sirolimus-eluting stents. On the other hand, TWILIGHT-HBR showed that selected HBR patients who tolerated 3 months of DAPT with ticagrelor after PCI, withdrawing ASA, and continuing ticagrelor monotherapy for 1 year, had significantly decreased clinically relevant as well as major bleeding events without compromising their ischemic protection, as compared with ticagrelor plus ASA [22].

Indications for oral anticoagulation

In the case of uncomplicated PCI, early cessation (≤1 week) of ASA and continuation of dual therapy with an OAC and $P2Y_{12}$ inhibitor (preferably clopidogrel) for 6 months (CCS) or 12 months (ACS) is recommended if the risk of stent thrombosis is low or if concerns about bleeding risk prevail over concerns about the risk of stent thrombosis, irrespective of the type of stent used (class IIaB recommendation

Table 4. The most important clinical trials evaluating the strategy of early withdrawal of acetylsalicylic acid and continuation of treatment with $P2Y_{12}$ inhibitor[a]

	TWILIGHT [16]	STOPTDAPT-2 [50]	SMART-CHOICE [49]	GLOBAL LEADERS [15]
Study population	7119	3009	2993	15968
Follow-up duration, months	15	12	12	24
Short-term DAPT	ASA (81–100 mg) with ticagrelor 2 × 90mg for 3 months followed by ticagrelor alone	ASA (81–100 mg) with clopidogrel 1 × 75mg (or prasugrel 1× 3.75 mg — the study conducted in Japan) for 1 month followed by clopidogrel in monotherapy	ASA (81–100 mg) with $P2Y_{12}$ inhibitor (ticagrelor 2 × 90 mg, prasugrel 1 × 10 mg or clopidogrel 1 × 75 mg) for 3 months followed by ticagrelor, prasugrel or klopidogrel in monotherapy	ASA (81–100 mg) with ticagrelor 2 × 90 mg for 1 month followed by continuation of ticagrelor alone for 23 months
Standard DAPT	ASA + ticagrelor for 15 months	ASA + clopidogrel for 12 months	ASA + $P2Y_{12}$ inhibitor (ticagrelor, prasugrel or clopidogrel) for 12 months	ASA + clopidogrel or ASA + ticagrelor for 12 months
Acute coronary syndrome, %	63.9/65.7	37.7/38.6	58.2/58.2	47.0/46.8
STEMI, %	0/0	19.4/17.9	11.0/10.0	13.3/12.9
NSTEMI, %	28.8/30.8	5.4/6.6	16.0/15.4	21.1/21.1
UA, %	35.1/34.9	12.9/14.2	31.2/32.8	12.6/12.7
Chronic coronary syndrome, %	29.5/28.0	62.3/61.4	41.8/41.8	53.0/53.2
ASA, %	100/100	99.8/100	99.8/99.9	100/100
Clopidogrel, %	0/0	60.2/62.9	76.9/77.6	53.0/53.2
Prasugrel, %	0/0	39.6/37.0	4.1/4.5	0/0
Ticagrelor, %	100/100	0/0	19.0/17.9	47.0/46.8
MACCE (myocardial infarction, ischemic stroke, all-cause death)	HR, 0.99 (95% CI, 0.78–1.25)	NA	HR, 0.4 (95% CI, –∞ – 1.3)	HR, 0.83 (95% CI, 0.69–1.00)
All-cause death	HR, 0.75 (95% CI, 0.48–1.18)	HR, 1.18 (95% CI, 0.63–2.21)	HR, 1.18 (95% CI, 0.63–2.21)	HR, 0.82 (95% CI, 0.64–1.06)
Myocardial infarction	HR, 1.00 (95% CI, 0.75–1.33)	HR, 1.19 (95% CI, 0.54–2.67)	HR, 0.66 (95% CI, 0.31–1.40)	HR, 1.14 (95% CI, 0.92–1.41)
Stroke (ischemic or hemorrhagic)	HR, 2.00 (95% CI, 0.86–4.67)	HR, 0.50 (95% CI, 0.22–1.18)	HR, 2.23 (95% CI, 0.78–6.43)	HR, 1.07 (95% CI, 0.72–1.57)
Stent thrombosis (definite or probable)	HR, 0.74 (95% CI, 0.37–1.47)	HR, 4.03 (95% CI, 0.45–36.08)	HR, 1.51 (95% CI, 0.25–9.02)	HR, 1.30 (95% CI, 0.86–1.95)
Major bleeding (BARC, 3 or 5)	HR, 0.49 (95% CI, 0.33–0.74)	HR, 0.30 (95% CI, 0.13–0.65)	HR, 0.87 (95% CI, 0.40–1.88)	HR, 0.86 (95% CI, 0.67–1.11)

[a]The results presented in the table correspond to the published trial results [15, 16, 49, 50]

Abbreviations: ASA, acetylsalicylic acid; BARC, Bleeding Academic Research Consortium; CI, confidence interval; HR, hazard ratio; MACCE, major adverse cardiovascular and cerebrovascular events; NA, non-applicable; NSTEMI, non-ST-segment elevation myocardial infarction; STEMI, ST-segment elevation myocardial infarction; UA, unstable angina; other — see Table 1

in the 2019 CCS guidelines was upgraded to class IA in the 2020 AF guidelines) [9, 23]. This issue is discussed in more detail elsewhere [24–26]. However, triple therapy with ASA, clopidogrel, and an OAC for longer than 1 week should be considered when the risk of stent thrombosis outweighs the bleeding risk with the total duration (≤1 month) decided according to assessment of these risks, and the treatment plan should be clearly specified at hospital discharge (IIaC) [9, 23]. As shown in the AUGUSTUS study, ASA reduces the risk of ischemic events up to one month after PCI or an ACS event. Beyond this period, ASA further increases the bleeding rate without reducing the risk of ischemic events [27].

ISCHEMIC RSK ASSESSMENT

After PCI, especially with the use of secondor third-generation DES, it is important to assess the risk of thrombotic/ischemic events and select an appropriate antiplatelet strategy (Figures 2 and 3). Risk factors of ischemic events are listed in Tables 5 and 6. There have been few changes in the assessment of the ischemic risk in each of the following documents.

According to the ESC guidelines on DAPT, the use of risk scores designed to evaluate the benefits and risks of different DAPT durations may be considered (IIbA) [10]. Currently, only the DAPT and PRECISE-DAPT scores (for bleeding risk assessment) meet these requirements.

The DAPT score gives clinicians an opportunity to see how patients with particular characteristics fared when randomized to either 30 months or 12 months of dual antiplatelet therapy after receiving a stent (Supplementary material, *Table S2*). It includes 9 factors based on the results of the DAPT study [28]. Receiving ≥2 points indicates a high risk of ischemic events and may justify prolongation of DAPT duration. However, the DAPT score should be used to guide antiplatelet therapy duration in conjunction with clinical judgment and applied on an individualized basis. It is not a substitute for clinical judgment.

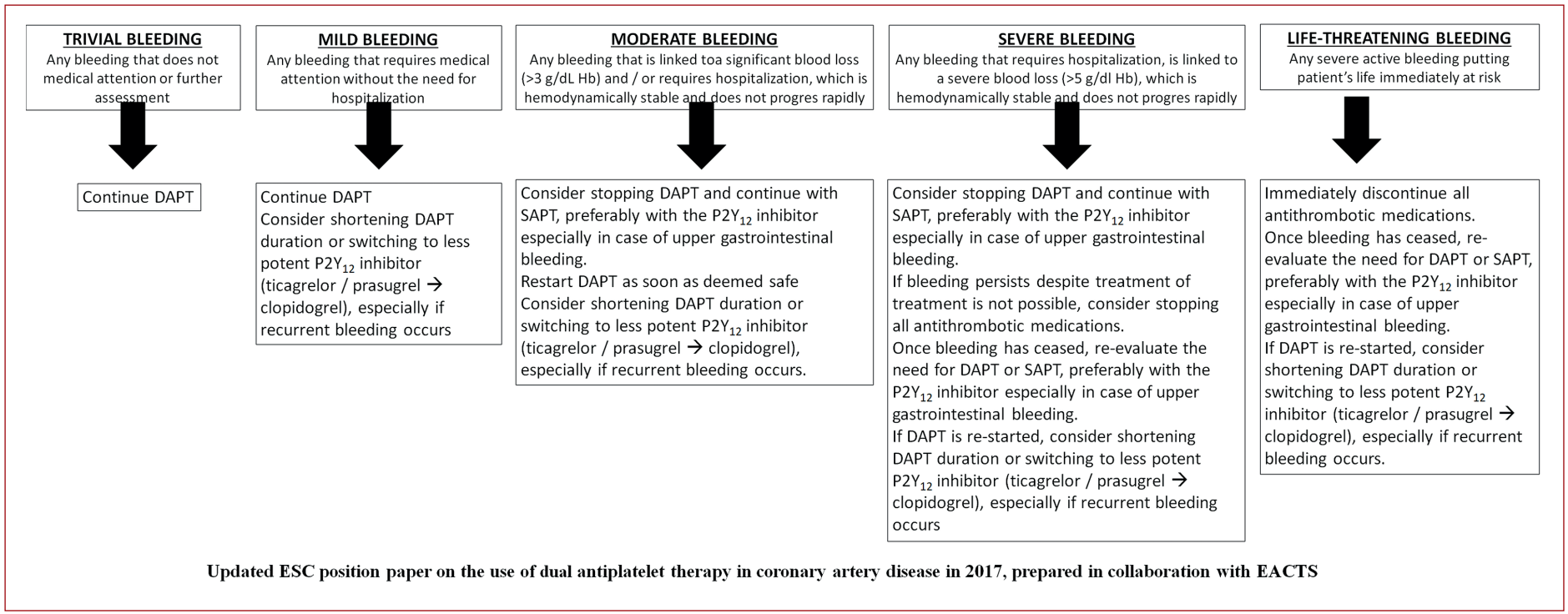


Figure 1. Algorithm for managing a bleeding patient on dual antiplatelet therapy (based on ESC-focused update on dual antiplatelet therapy in coronary artery disease developed in collaboration with EACTS [10])

Abbreviations: EACTS, European Association for Cardio-Thoracic Surgery; ESC, European Society of Cardiology; other — see Table 1

Table 5. Factors increasing the risk of recurrent ischemic events according to the ESC/EACTS guidelines on myocardial revascularization (2018)

High-risk features for ischemic events
• Prior stent thrombosis on adequate antiplatelet therapy
• Stenting of the last remaining patent coronary artery
• Diffuse multivessel disease, especially in diabetic patients
• Chronic kidney disease (i.e. creatinine clearance <60 ml/min/1.73 m^2)
• At least three stents implanted
• At least three lesions treated
• Bifurcation with two stents implanted
• Total stented length >60 mm
• Treatment of a chronic total occlusion
• History of STEMI

Abbreviations: see Figure 1 and Table 4

Table 6. Ischemic risk factors based on the ESC guidelines on chronic coronary syndromes (2019), modified in the ESC guidelines on NSTE-ACS (2020) **(bold)**

RISK STRATIFICATION OF STENT THROMBOSIS	
HIGH RISK: complex CAD[a] with at least one of the following:	
Clinical factors	• Diabetes mellitus requiring medication • History of recurrent MI • **Any multivessel CAD** • **Polyvascular disease (CAD + PAD)** • **Premature (<45 years old) or accelerated (new lesion within a 2-year time frame) CAD** • **Concomitant systematic inflammatory disease (e.g. HIV, systemic lupus erythematosus, chronic arthritis)** • CKD with eGFR 15–59 ml/min/1.73 m^2
Procedural factors	• At least three stents implanted • At least three lesions treated • Total stented length >60 mm • History of complex revascularization (i.e. stenting of the left main, proximal LAD, or last remaining patent artery; suboptimal stent deployment; bifurcation with at least two stents implanted; treatment of chronic total occlusion) • Previous stent thrombosis on adequate antiplatelet treatment
MODERATE RISK: non-complex CAD[a] and at least 1 criterion:	
Clinical factors	• Diabetes mellitus requiring medication • History of recurrent MI, • **Polyvascular disease (CAD + PAD)** • CKD with eGFR 15–59 ml/min/1.73 m^2

[a]Stratification of patients into complex vs. non-complex CAD is based on individual clinical judgment with knowledge of patients' cardiovascular history and/or coronary anatomy

Abbreviations: CAD, coronary artery disease; HIV, human immunodeficiency virus; MI, myocardial infarction; NSTE-ACS, non-ST-segment elevation acute coronary syndrome; PAD, peripheral artery disease; other — see Table 2

Prolonging antithrombotic treatment duration

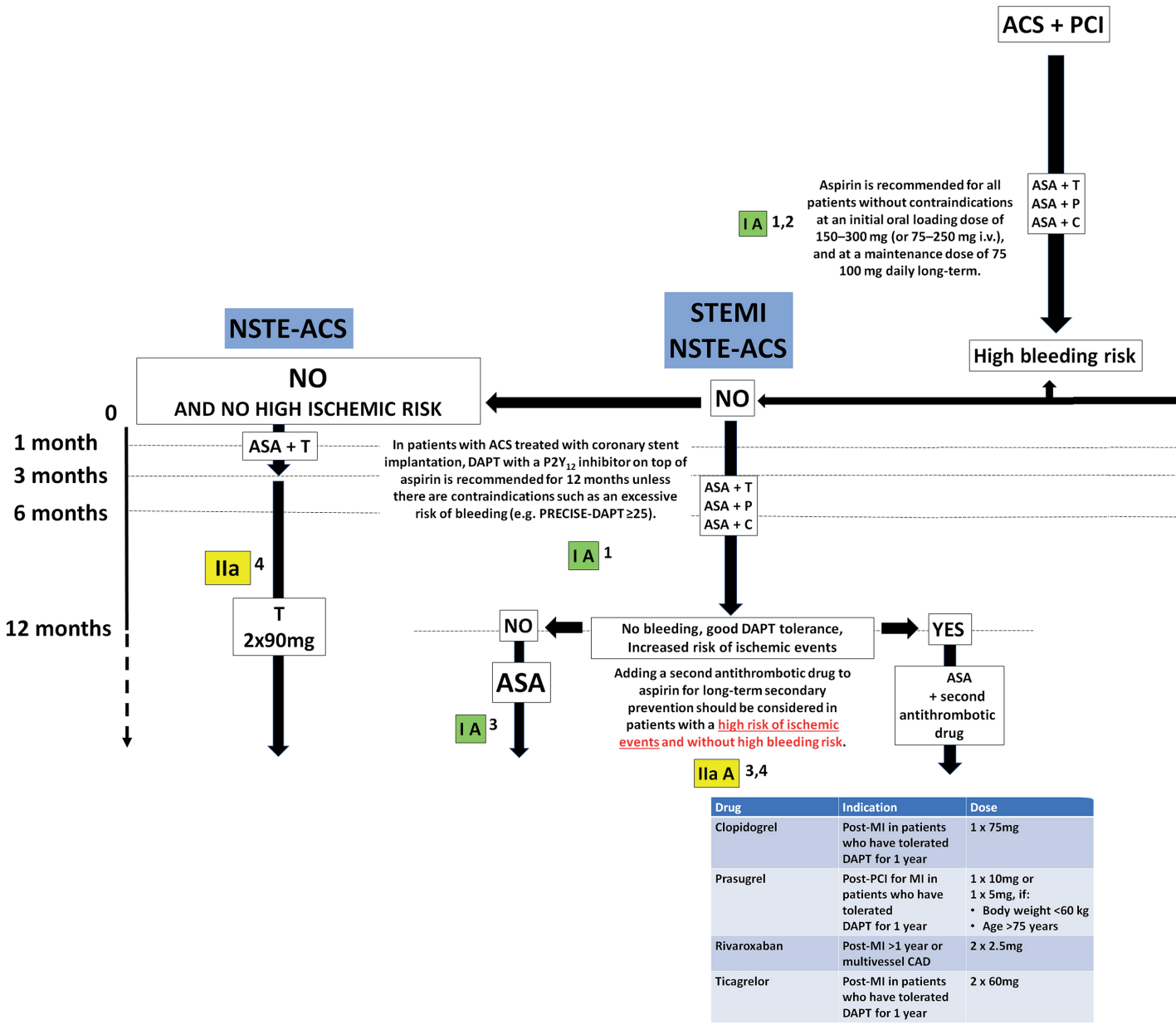
Adding a second antithrombotic agent ($P2Y_{12}$ inhibitor or low dose rivaroxaban) to ASA for extended long-term secondary prevention should be considered in patients with a high risk of ischemic events and without increased risk of major or life-threatening bleeding (IIaA) [9, 20]. In the case of a moderate risk of thrombotic events, such management may be considered (IIbA) [9, 20]. Treatment options for extended dual antithrombotic or antiplatelet therapies are summarized in Table 7.

The doses of antiplatelet agents remain the same as for standard therapy if treatment with clopidogrel or prasugrel is continued. These recommendations are based on the results of the DAPT study, in which continuation of DAPT beyond 12 months was associated with a reduced risk of stent thrombosis and major adverse cardiovascular and cerebrovascular events, with a simultaneous increase in bleeding complications and noncardiac mortality rate [23]. In turn, an increased risk of myocardial infarction and stent thrombosis was observed during the 3-month follow-up after discontinuation of thienopyridine therapy [28]. The positive effect of prolonging DAPT duration with a similar bleeding risk was more pronounced in the post-myocardial infarction (MI) group of patients [29]. However, in the case of ticagrelor, it is recommended to consider the continuation of treatment beyond one year at a reduced dose of 60 mg twice a day in patients after myocardial infarction who tolerated DAPT well for 12 months. In PEGASUS-TIMI 54, the use of both the standard dose (90 mg twice a day) and the reduced dose (60 mg twice a day) was associated with a reduction in thrombotic events and an increase in bleeding complications [30]; both doses showed a similar degree of platelet inhibition with a better safety profile of the reduced dose [30, 31]. A significant reduction in all-cause and cardiovascular mortality was achieved if the treatment with a lower dose of ticagrelor was initiated up to two years after the initial MI or within one year after stopping DAPT [32]. There is no evidence of significant benefits in prolonging DAPT in patients without a history of myocardial infarction [33]. In turn, based on the analysis of the RENAMI registry, the benefits of extending DAPT dura-

Table 7. Options for prolonged secondary antithrombotic regimens (including ASA, 75–100 mg/d)

Drug	Dose	Indication
Rivaroxaban (COMPASS trial)	2.5 mg BID	Patients with CAD or symptomatic PAD at high risk of ischemic events
Clopidogrel (DAPT trial)	75 mg/d	Post MI in patients who have tolerated DAPT for 1 year
Prasugrel (DAPT trial)	10 mg/d (5 mg/d if body weight <60 kg or age >75 years)	Post PCI for MI in patients who have tolerated DAPT for 1 year
Ticagrelor (PEGASUS-TIMI 54)	60 mg BID	Post MI in patients who have tolerated DAPT for 1 year

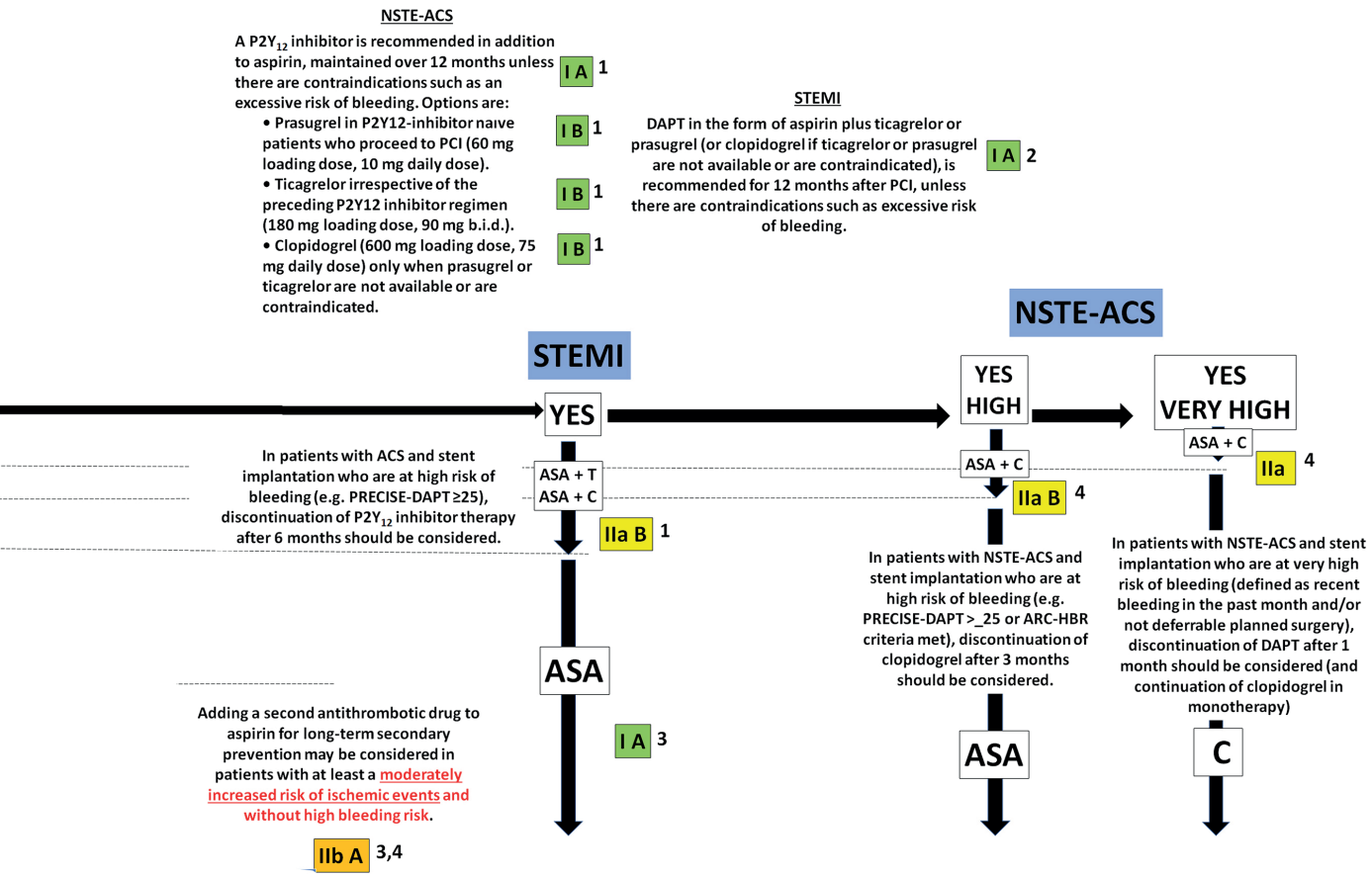
Abbreviations: BID, *bis in die* (twice a day); other — see Tables 1, 2 and 6



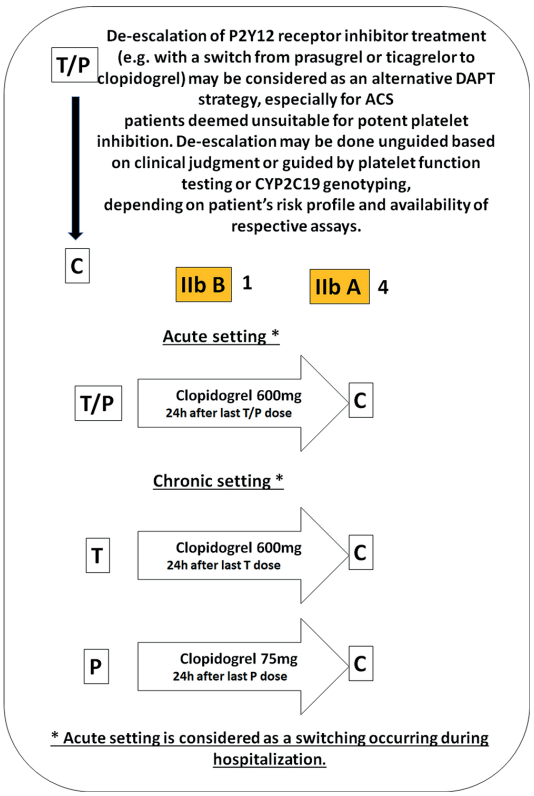
Drug	Indication	Dose
Clopidogrel	Post-MI in patients who have tolerated DAPT for 1 year	1 x 75mg
Prasugrel	Post-PCI for MI in patients who have tolerated DAPT for 1 year	1 x 10mg or 1 x 5mg, if: • Body weight <60 kg • Age >75 years
Rivaroxaban	Post-MI >1 year or multivessel CAD	2 x 2.5mg
Ticagrelor	Post-MI in patients who have tolerated DAPT for 1 year	2 x 60mg

Figure 2. Algorithm for dual antiplatelet therapy after PCI in patients with ACS (ESC/EACTS Guidelines on myocardial revascularization [19]; ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation [2]; ESC Guidelines for the diagnosis and management of chronic coronary syndromes [9]; ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation [20])

Abbreviations: ACS, acute coronary syndrome; other — see Figure 1 and Table 2



1 The ESC/EACTS guidelines on revascularization (2018)
2 The ESC guidelines on STEMI (2017)
3 The ESC guidelines on CCS (2019)
4 The ESC guidelines on NSTE-ACS (2020)



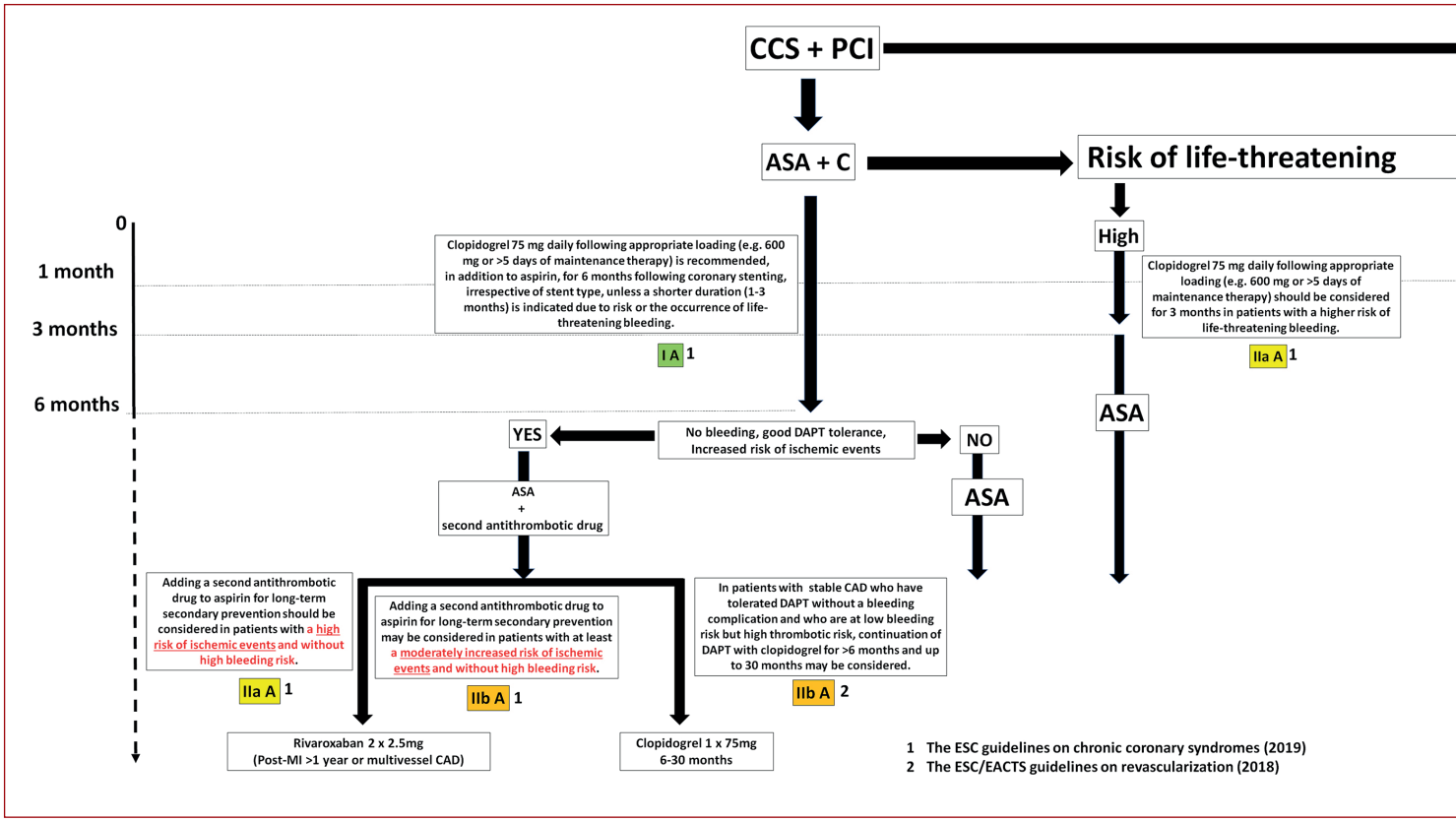
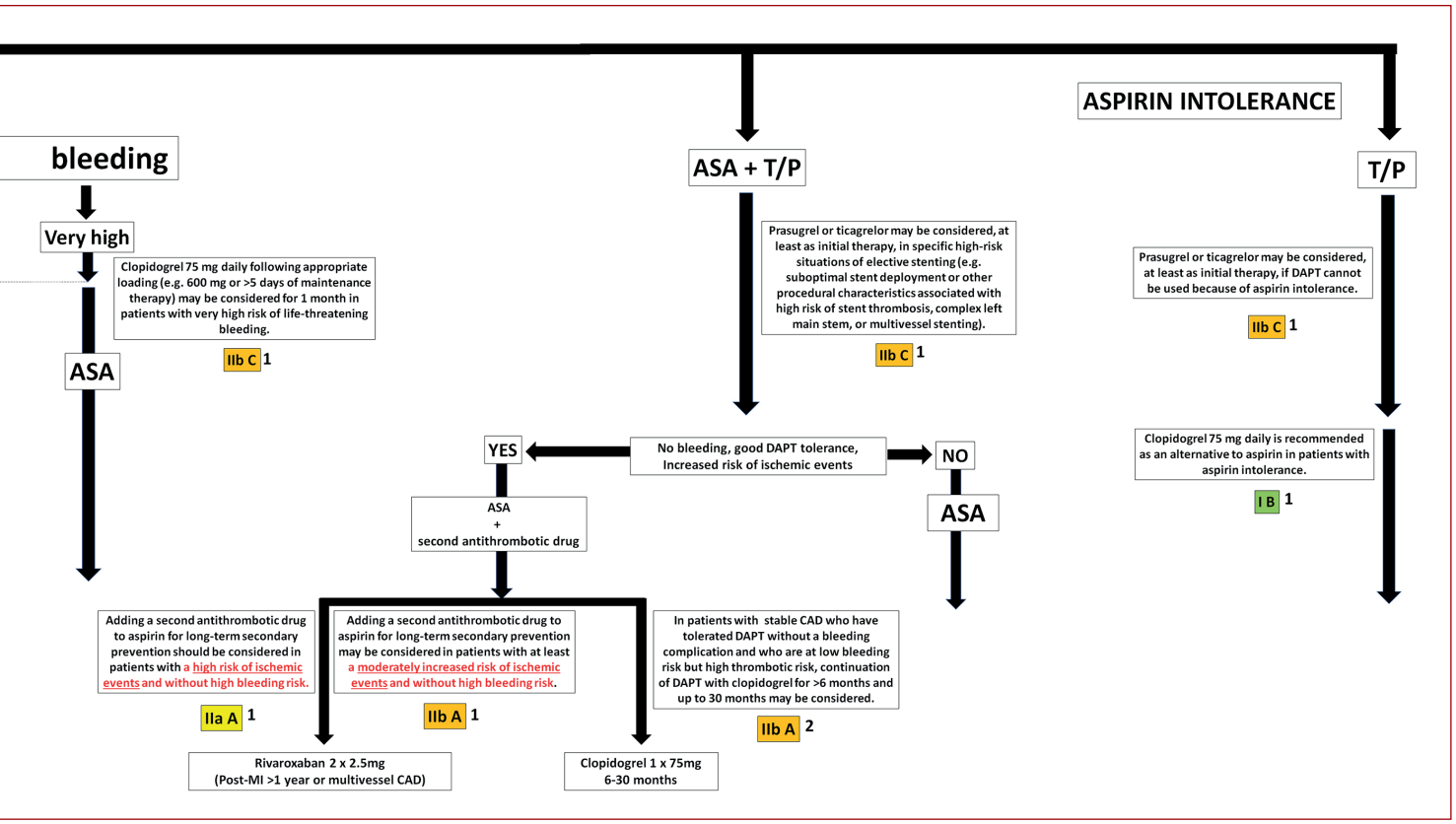


Figure 3. Algorithm for dual antiplatelet therapy after PCI in patients with CCS (ESC Guidelines for the diagnosis and management of chronic coronary syndromes [9]; ESC/EACTS Guidelines on myocardial revascularization [19])

Abbreviations: CCS, chronic coronary syndrome; other — see Figure 1 and Table 2


bleeding
Very high
Clopidogrel 75 mg daily following appropriate loading (e.g. 600 mg or >5 days of maintenance therapy) may be considered for 1 month in patients with very high risk of life-threatening bleeding.
IIb C 1
ASA
ASA + T/P
Prasugrel or ticagrelor may be considered, at least as initial therapy, in specific high-risk situations of elective stenting (e.g. suboptimal stent deployment or other procedural characteristics associated with high risk of stent thrombosis, complex left main stem, or multivessel stenting).
IIb C 1
ASPIRIN INTOLERANCE
T/P
Prasugrel or ticagrelor may be considered, at least as initial therapy, if DAPT cannot be used because of aspirin intolerance.
IIb C 1
Clopidogrel 75 mg daily is recommended as an alternative to aspirin in patients with aspirin intolerance.
I B 1
No bleeding, good DAPT tolerance, Increased risk of ischemic events
YES
NO
ASA
+
second antithrombotic drug
ASA
Adding a second antithrombotic drug to aspirin for long-term secondary prevention should be considered in patients with a high risk of ischemic events and without high bleeding risk.
IIa A 1
Adding a second antithrombotic drug to aspirin for long-term secondary prevention may be considered in patients with at least a moderately increased risk of ischemic events and without high bleeding risk.
IIb A 1
In patients with stable CAD who have tolerated DAPT without a bleeding complication and who are at low bleeding risk but high thrombotic risk, continuation of DAPT with clopidogrel for >6 months and up to 30 months may be considered.
IIb A 2
Rivaroxaban 2 x 2.5mg
(Post-MI >1 year or multivessel CAD)
Clopidogrel 1 x 75mg
6-30 months

tion beyond 12 months after ACS with the use of prasugrel or ticagrelor were associated with a reduction of ischemic events with an increased risk of bleeding, but positive effects of extending DAPT duration were less pronounced in women and patients over 75 years due to the increased risk of bleeding complications [34].

Data on a novel strategy of dual antithrombotic therapy (DAT) consisting of factor-Xa inhibition with a very low dose of rivaroxaban (2.5 mg twice a day) plus ASA has emerged in secondary prevention in patients with CAD or symptomatic peripheral artery disease at high risk or moderate risk of ischemic events, based on data from the COMPASS trial [35]. On the other hand, the 2018 guidelines on myocardial revascularization state that in ACS patients with no prior stroke/transient ischemic attack who are at high ischemic risk and low bleeding risk and are receiving ASA and clopidogrel, low-dose rivaroxaban (2.5 mg twice a day for approximately 1 year) may be considered. This recommendation was upheld in the 2020 NSTE-ACS guidelines (IIbB) [19, 20]. This recommendation was made based on the results of the ATLAS-ACS-2-TIMI-51 study [36].

In the presence of indications for anticoagulant treatment, ASA 75–100 mg daily (or clopidogrel 75 mg daily) may be considered in addition to long-term OAC therapy in patients with AF, history of MI, and at high risk of recurrent ischemic events who do not have a high bleeding risk (IIbB) [9].

In patients treated with bioresorbable scaffolds (BRS), DAPT should be considered for at least ≥12 months and up to the presumed full absorption of the BRS, based on an individual assessment of bleeding and ischemic risk (IIaC) [10, 19].

ASSESSMENT OF PLATELET ACTIVITY DURING ANTIPLATELET TREATMENT

Currently, routine platelet reactivity testing is not recommended and should be limited to selected clinical situations such as occurrence of stent thrombosis despite using recommended antiplatelet therapy, suspicion of malabsorption of oral medications, or selected cases of increased risk of cardiovascular events where there is a reasonable suspicion of inadequate inhibition of platelet function.

Insufficient platelet inhibition mainly concerns clopidogrel. Substantial inter-individual variability has been demonstrated in the ability of clopidogrel to inhibit ADP-induced platelet aggregation [37]. Genetic polymorphism in *CYP2C19* (presence of the loss of function *CYP2C19*2* and *CYP2C19*3* alleles) is essential for metabolic activation of clopidogrel in the liver and the development of clopidogrel resistance. These alleles are relatively common and observed in about 30% of the European population [38]. However, two large meta-analyses show divergent data on adverse effects of *CYP2C19* gene variants on the occurrence of major adverse cardiovascular events (MACE). One of them showed that the presence of even a heterozygote within the *CYP2C19* gene is associated with a significant risk of adverse cardiovascular events, especially stent thrombosis [39], but further studies did not confirm these results [40]. A higher incidence of MACE in the presence of loss-of-function *CYP2C19* alleles in patients who received clopidogrel has also been shown in an observational study in patients with stable coronary artery disease or ASC undergoing PCI [41]. The studies available so far have not demonstrated the superiority of genetic testing for clopidogrel resistance in patients requiring the use of a $P2Y_{12}$ inhibitor compared to standard treatment [42]. In the POPular Genetics Study, the strategy of performing genetic testing and using clopidogrel instead of prasugrel or ticagrelor in the absence of the specific alleles was not less effective than the traditional approach; however, it was associated with fewer bleeding complications in a 12-month follow-up (9.8% vs. 1.5%; $P = 0.04$) [43]. Nonetheless, current guidelines, both European and American, do not recommend routine genetic testing before treatment with clopidogrel. There is also no proven benefit in increasing the daily dose of clopidogrel to 150 mg to overcome resistance [44, 45]. It seems that *CYP2C19* polymorphism does not appear to affect the activity of prasugrel [46] and ticagrelor [47].

Approximately 10% to 15% of ACS patients will undergo coronary artery bypass grafting (CABG) surgery for index event, and current guidelines recommend stopping clopidogrel at least 5 days before CABG. This waiting time may have clinical implications. Nakashima et al. reported that a strategy that is guided by platelet reactivity is noninferior to the standard of care in patients with ACS awaiting CABG regarding peri-operative bleeding: it significantly shortens the waiting time to CABG and decreases hospital expenses [48].

SWITCHING ANTIPLATELET REGIMENS

Switching between $P2Y_{12}$ inhibitors may be dictated by economic considerations or individual clinical circumstances such as ineffectiveness of the current antiplatelet therapy — confirmed by the platelet reactivity test, the presence of at least one *CYP2C19* loss-of-function mutant allele, or occurrence of thrombosis during treatment with a given drug. Modification of pharmacotherapy may also result from drug intolerance.

The recommendations for switching between $P2Y_{12}$ inhibitors vary depending on the patient's clinical timing. In the acute phase of ACS, a loading dose of the $P2Y_{12}$ inhibitor is always mandated. In patients with ACS who were previously exposed to clopidogrel, switching from clopidogrel to ticagrelor is recommended early after hospital admission at a loading dose of 180 mg irrespective of timing and loading dose of clopidogrel, unless contraindications to ticagrelor exist (IB) [10]. This switching strategy has the strongest class of recommendation and has been confirmed in clinical trials. Other $P2Y_{12}$ inhibitor switching algorithms have a weaker recommendation class — additional switching between oral $P2Y_{12}$ inhibitors

may be considered in cases of side effects/drug intolerance according to the proposed algorithms (IIbC) [10]. When de-escalating treatment and switching from prasugrel or ticagrelor to clopidogrel or switching between prasugrel and ticagrelor, the standard loading dose of the new drug should be administered 24 hours after the last dose of the discontinued drug. The adopted management algorithms are based on the ESC 2017 DAPT guidelines. The ESC 2020 NSTE-ACS guidelines duplicate the previously proposed strategies [10, 20]. In the chronic setting, defined as a switching occurring following hospital discharge in patients with ACS, administration of a loading dose of the introduced antiplatelet drug is not required when switching from clopidogrel to ticagrelor, clopidogrel to prasugrel, prasugrel to clopidogrel, or prasugrel to ticagrelor. The maintenance dose of a new $P2Y_{12}$ inhibitor should be given 24 hours after the last dose of the drug is withdrawn. In the case of switching ticagrelor to clopidogrel or ticagrelor to prasugrel, a loading dose (600 mg of clopidogrel or 60 mg of prasugrel, respectively) is required even in chronic settings. The loading dose should be given 24 hours after the last ticagrelor dose [10].

RECENT STUDIES AND FUTURE PERSPECTIVES

The optimal duration of DAPT after PCI to prevent thrombotic events while minimizing the risk of bleeding events remains a broadly debated issue. This topic is particularly relevant nowadays. We have an aging population and an increasing number of comorbidities (both of which substantially enhance bleeding risk). On the other hand, we have secondand third-generation DES with improved design and drug delivery (biodegradable polymers, cobalt-chromium or platinum-chromium platforms, ultra-thin struts design), which have recently led to a significant reduction in the risk of stent thrombosis (translating to a lower risk of ischemic events).

Various preclinical studies have demonstrated the key role of $P2Y_{12}$ inhibitors versus ASA in inhibiting platelet activation. These observations led to the hypothesis about the benefit of early ASA discontinuation after PCI for a better balance of bleeding and thromboembolism risks. More recently, new evidence from randomized trials, meta-analyses, and registries has emerged, which is not yet included in the guidelines. The subject of these analyzes is the early discontinuation of ASA after 1 month or 3 months of using DAPT, followed by monotherapy with a $P2Y_{12}$ inhibitor. The most significant recently published randomized trials, i.e. GLOBAL LEADERS [15], SMART-CHOICE [49], STOPDAPT-2 [50], and TWILIGHT [16], aimed to fill this gap in the scientific evidence (Table 4).

A meta-analysis [51] of these four studies showed that the rates of adverse cardiac and cerebrovascular events (defined as myocardial infarction, ischemic stroke, and allcause death) were similar comparing the efficacy of shortterm DAPT, followed by a $P2Y_{12}$ inhibitor in monotherapy, compared to 12-month standard DAPT. Interestingly, this effect was also observed for the individual components of the composite endpoint: myocardial infarction, ischemic stroke, and all-cause death. Most importantly, the frequency of definite or probable stent thrombosis was comparable in the short-term DAPT group followed by $P2Y_{12}$ inhibitor monotherapy versus 12-month DAPT. On the other hand, the rate of major bleeding (Bleeding Academic Research Consortium [BARC], 3 or 5) was significantly lower in the short-term DAPT group, followed by the use of $P2Y_{12}$ inhibitor alone, compared to the traditional duration of DAPT.

However, the main question that still needs to be answered is the choice of a $P2Y_{12}$ inhibitor (clopidogrel, ticagrelor, prasugrel) that would provide the most favorable efficacy (low ischemic risk) and safety (low bleeding risk) profile. Given the high interpatient variability in pharmacodynamic response — especially for clopidogrel — genotyping or testing of platelet activation may be an option before early ASA discontinuation and maintaining the $P2Y_{12}$ inhibitor (clopidogrel) in monotherapy.

The current evidence provided by four randomized trials, as well as a meta-analysis of these studies, does not indicate that early discontinuation of ASA followed by $P2Y_{12}$ inhibitor monotherapy lead to an increase in adverse cardiac and cerebrovascular events while maintaining a very good safety profile. However, the STOPDAPT-2 ACS trial showed that 1-month DAPT followed by clopidogrel monotherapy for 11 months did not meet the criteria for noninferiority compared with standard 12-month duration DAPT for the composite ischemic/bleeding endpoint among ACS patients undergoing PCI with a cobalt-chromium (CoCr) DES. The primary outcome, cardiovascular death, MI, stroke, stent thrombosis, Thrombolysis In Myocardial Infarction [TIMI] major or minor bleeding, for 1–2 months vs. 12 months of DAPT, was 3.2% vs. 2.8% (HR, 1.14; 95% CI 0.80–1.62; *P* for noninferiority = 0.06). In fact, the composite ischemic endpoint trended towards harm in the short-duration DAPT arm, with a significant nearly 2-fold increase in the risk of MI (1.6% vs. 0.9% [HR, 1.91; 95% CI, 1.06–3.44; *P* <0.05]). Both major and minor bleeding events were lower with short-term DAPT [52].

The TALOS-AMI trial showed that among patients undergoing PCI for AMI and who had completed 1 month of DAPT with ASA and ticagrelor uneventfully, switching to ASA plus clopidogrel for the next 11 months met the criteria for noninferiority and superiority compared with continuing with ASA plus ticagrelor. The primary endpoint of cardiovascular death, MI, stroke, BARC bleeding 2, 3, or 5, for de-escalation vs. active control between 1 and 12 months post-PCI, was: 4.6% vs. 8.2% (*P* for noninferiority <0.001; *P* for superiority <0.001). This was primarily driven by a reduction in major bleeding, but ischemic events were also numerically lower with a de-escalation strategy. De-escalation was performed without genotype testing or reload [53].

The HOST-EXAM trial showed that clopidogrel monotherapy is superior to ASA monotherapy as chronic maintenance therapy among patients who have successfully completed the required duration of DAPT regimen post-DES PCI. The primary endpoint of all-cause mortality, MI, stroke, readmission due to ACS, major bleeding, for clopidogrel vs. ASA, was 5.7% vs. 7.7% (HR, 0.73; 95% CI, 0.59–0.90; $P = 0.003$). Secondary endpoints: thrombotic composite outcome (cardiovascular death, MI, stroke, ACS readmission, stent thrombosis): 3.7% vs. 5.5% ($P = 0.003$) and any bleeding: 2.3% vs. 3.3% ($P = 0.003$) were also lower in the clopidogrel group [54].

One limitation of the STOPDAPT-2 ACS, TALOS-MI, and HOST EXAM trials is that they included exclusively East Asian patients.

Surely, all of these studies will likely have a significant impact on antiplatelet treatment strategies in patients after PCI in the upcoming new guidelines.

In conclusion, selected patients at high risk of thrombotic and/or bleeding events may benefit from personalized antiplatelet therapy based on an individual assessment of thrombosis and bleeding risks. It should be remembered that these risk (especially of bleeding) are dynamic and change over time, and therefore they should be reassessed periodically (e.g. at subsequent follow-up visits).

Article information

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