Chapter

Dual Antiplatelet Therapy after PCI: When Could We Go Shorter?

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Abstract

The optimal duration of dual antiplatelet therapy (DAPT) after percutaneous coronary intervention (PCI) remains an important clinical question in interventional cardiology. Several clinical and angiographic variables are associated with an increased risk for thrombotic events, and prolonged DAPT duration may improve long term clinical outcome. However, some patients also present high bleeding risk (HBR) characteristics and may require a shorter DAPT duration. The guidelines recommendations consider the data from randomized clinical trials, however numerous exclusion criteria may create gaps in the evidence leading to uncertainties, the need for expert opinion and patient level decision making. Furthermore, the stent platforms have evolved in such way that opportunities now exist to shorten duration of DAPT. This chapter will review the variables associated with ischemic and bleeding risks as well as different stent platforms to help clinicians optimize DAPT duration in patients undergoing PCI.

Keywords: percutaneous coronary intervention, stents, acute coronary syndrome, high bleeding risk, duration of antiplatelet therapy

1. Introduction

The optimal antiplatelet therapy after percutaneous coronary intervention (PCI) remains an unanswered clinical question. The last 25 years of clinical investigations has mainly been focused on the choice of P2Y12 agents and on treatment duration. Initially, the observation that bare metal stents (BMS) implantation could be associated with thrombosis, and, subsequently, the observation that first-generation drug eluting stents (DES) were associated with very-late thrombosis risk led to studies evaluating prolonged duration regimens of DAPT after PCI, but also to innovations in stent technology. However, the newer, more potent drugs (prasugrel and ticagrelor) and the advent and evolution of modern second- and third-generation DES dramatically dwindled the incidence of late and very late thrombotic complications. Thus, interest has shifted in trying to find the optimal, shortened DAPT treatment to prevent the early thrombotic complications while avoiding the late hemorrhagic events, the latter being associated with a similar risk of all-cause mortality than post-PCI recurrent myocardial infarctions [1].

Numerous trials attempted to answer these important questions, sometimes leading to discrepant results. This chapter will focus on the current evidence listed on the guidelines of main scientific societies for three groups of patients: elective PCI,
PCI in the setting of acute coronary syndromes (ACS), and PCI for patients with a coexisting indication of oral anticoagulation (OAC). For each of them we will highlight the standard recommendations for DAPT duration, as well as the main clinical, angiographic and stent-derived variables that should be used in the decision-making process to tailor a shortened DAPT therapy reflecting each patient need.

2. Latest guidelines on the topic

This document will include the latest recommendations of Canadian, American and European guidelines. Canadian scientific societies published two documents in 2018 addressing antithrombotic treatment: The Canadian Cardiovascular Society (CCS)/Canadian Association of Interventional Cardiology focused update for the use of antiplatelet therapy [2] and the CCS focused update for the management of atrial fibrillation [3]. The American College of Cardiology/American Heart Association (ACC/AHA) published a focused update on the duration of DAPT in patients with coronary artery disease (CAD) in 2016, [4] while a recent AHA/ACC/Heart Rhythm Society (HRS) focused update in the management of patients with atrial fibrillation was published in 2019 [5]. Lastly, the European Society of Cardiology (ESC) and European Association for Cardio-Thoracic Surgery (EACTS) published a focused update on DAPT in 2017 [6]. However, the most recent 2020 ESC guidelines for management of ACS in patients presenting without persistent ST-segment elevation [7] and 2020 ESC/EACTS guidelines for the management of atrial fibrillation [8] will also be reviewed. A dedicated, critical comparison of the available guidelines on DAPT was published previously this year [9].

3. Evaluation of bleeding and thrombotic risk

In order to tailor optimal DAPT duration, many variables must be taken into account to ensure adequate thrombotic protection while avoiding hemorrhagic complications. To that extent, different risk scores have been derived and validated. The PARIS risk score was one of the first tools intended to predict risks for out-of-hospital events directly modified by prolonging DAPT beyond one year (i.e. coronary thrombosis and bleeding) [10]. The aim of the DAPT score is to identify patients expected to derive benefit or harm from continuing P2Y₁₂ beyond 1 year. To that extent, data was gathered among patients that had not experienced any major ischemic or bleeding event 12 months after the index procedure [11]. Similarly, the CALIBER score includes patients surviving 12 months after a MI, including those not treated with PCI [12]. Hence, these three risk scores help establishing the security of long term DAPT duration.

In contrast, the PRECISE-DAPT score [13] assesses the benefit of a short (3–6 month) versus a long (12–24 month) DAPT duration. Furthermore, it allows clinicians to select DAPT duration upfront instead of at another point in time during follow-up. Of note, patients with the need of OAC were excluded from the derivation cohort. Patients undergoing elective, urgent and emergent PCI were all included in the analysis. At the time of the index PCI, an additive score is calculated by means of the presence of five clinical and biochemical variables (age, creatinine clearance, hemoglobin, white blood cell count and prior spontaneous bleeding), ranging 0 to 100 points. Patients ≥25 points were considered high bleeding risk (HBR), while <25 points were defined as non-HBR. Among HBR patients based on this score, prolonged DAPT contributed to no significant ischemic benefit, while, on the other hand, led to an increased risk of bleeding (number to harm
(NNH) = 38). In parallel, non-HBR patients benefited of a longer DAPT regimen in the form of a significant reduction in the composite endpoint of myocardial infarction (MI), definite stent thrombosis, stroke and target vessel revascularization (NNT for benefit of 68), with no significant increase in bleeding risk [13]. Results were consistent across the full spectrum of indications for PCI.

Some works have compared the accuracy of these scores head-to-head, in general showing little to no difference in their ability to predict bleeding [14–16].

More recently, the new ARC-HBR criteria have been validated at identifying patients at high bleeding risk, being more sensitive than the PRECISE-DAPT and PARIS risk scores (at the expense of specificity) [17]. Trials where these criteria are used to compare different antiplatelet durations are awaited.

It is worth noting, however, that no prediction model has been prospectively tested in the setting of a RCT.

On the other side of the coin, clinicians should be aware of certain clinical and angiographic features associated with a higher thrombotic risk in some patients, thus making it unadvisable to shorten their antiplatelet regimens. These characteristics are summarized in Table 2.

4. Evidence for DAPT duration after PCI in non-ACS setting

Many trials have demonstrated the non-inferiority of 6-month versus longer treatment duration amid “all-comer” patients undergoing PCI for stable and ACS settings, [18–22] and so the recommendations for elective PCI are extrapolated for the aggregated results. The ACC and ESC guidelines give strong recommendations on a standard 6-month duration of DAPT in stable patients. As for the CCS, it places greater emphasis on reduction of major CV thrombotic events vs. an increase in bleeding complications, by recommending DAPT duration from 6 up to 12 months. (Table 1) This is due to some metaanalysis showing increased risk of ischemic outcomes with shorter DAPT durations in certain groups with high risk angiographic features (Table 2) [24–26].

All three guidelines suggest considering a 3-month DAPT course in patients at HBR. This comes from the experience of two trials where a zotarolimus-eluting stent was tested [27, 28]. However, due to the fact that this platform is no longer available, the recommendation stands at a weak level of evidence. The ESC guidelines also include the possibility of a 1-month period of DAPT in patients in whom 3-month DAPT poses safety concerns. This recommendation comes from two trials in which a zotarolimus-eluting Endeavor sprint stent or Biofreedom drug-coated stent reduced ischemic endpoints compared to bare-metal stent under similar DAPT duration [29, 30].

Since their publication, some new evidence supports aspirin-free strategies early after PCI: the TWILIGHT trial included high risk patients who had not had an ischemic or bleeding event after a three-month course of aspirin plus ticagrelor and randomized them to aspirin or placebo for one year. Patients with ticagrelor monotherapy had a lower clinically relevant bleeding incidence while providing no higher death or ischemic endpoints [31]. The SMART-CHOICE randomized patients to receive aspirin plus a P2Y12 inhibitor for 3 months and thereafter a P2Y12 inhibitor alone or DAPT por 12 months. The monotherapy arm resulted in noninferior rates of major adverse cardiac events [32].

The GLOBAL LEADERS trial assessed the combination of ticagrelor and aspirin for one month followed by ticagrelor alone for 23 month versus 12 months of standard DAPT followed by 12 month of aspirin alone, with neutral results [33]. Later, its ancillary substudy (GLASSY) showed the non-inferiority, but not superiority,
### DES-PCI for stable patients

| DAPT duration | Grade of recommendation | ACC/AHA – 2016 | CCS – 2017 [3] | ESC – 2017 [6] | ACC/AHA – 2016 | CCS – 2017 [3] | ESC – 2020 [7] |
|---------------|-------------------------|----------------|----------------|----------------|----------------|----------------|----------------|
| Standard duration | 6–12 months | Strong recommendation, moderate-quality evidence | 6 months | Class I, level B-R | 6 months | Class I, level B-R |
| Minimal duration (HBR) | 3 months | Weak recommendation, low-quality evidence | Class IIb, level C-LD | 3 months (HBR) | Class IIa, level B |
|                | 1 month (if bleeding safety concern with 3-month DAPT) |                      |                     | 1 month (if bleeding safety concern with 3-month DAPT) |                     |

### DES-PCI for ACS

| DAPT duration | Grade of recommendation | ACC/AHA – 2016 | CCS – 2017 [3] | ESC – 2020 [7] | ACC/AHA – 2016 | CCS – 2017 [3] | ESC – 2020 [7] |
|---------------|-------------------------|----------------|----------------|----------------|----------------|----------------|----------------|
| Standard duration | 12 months | Strong recommendation, high-quality evidence | 12 months | Class I, level B-R | 12 months | Class I, level B-R |
| Minimal duration | 12 months | Strong recommendation, high-quality evidence | Class IIb, level C-LD | 3 months (HBR) | Class IIa, level B |
|                | 3–6 months, depending on ischemic/bleeding risk balance |                      |                     | 3–6 months, depending on ischemic/bleeding risk balance |                     |

**Table 1.**  
Standard and shortened DAPT duration according to different guidelines. Adapted and updated from [9].
of shortened DAPT arm in a selected subpopulation of the 20 highest recruiting sites of the main trial [34]. On the other hand, the STOPDAPT-2 trial showed the benefit of 1 month of aspirin plus clopidogrel followed by clopidogrel monotherapy vs. 12 month of standard DAPT, meeting the criteria for both noninferiority and superiority [35].

5. Evidence for DAPT duration after PCI in ACS setting

The three sets of guidelines provide strong recommendation for a standard 12-month DAPT treatment after an ACS, based on the CURE trial and the PCI-CURE substudy published nearly two decades ago, in which DAPT with aspirin and clopidogrel was prescribed for 3 to 12 months after PCI [36, 37]. More recently, the pivotal prasugrel and ticagrelor trials, conducted in patients with ACS, used a 12-month default DAPT duration, furthermore establishing this approach as the standard of practice (Table 1) [38, 39].

5.1 Scenarios for shortened DAPT

Due to the time gap between the latest ESC guidelines on this topic and its American and Canadian counterparts, recommendations on minimal DAPT duration differ between the former and the latter (Table 1). The scarce evidence available at the time of the last ACC/AHA and CCS guidelines led to only weak recommendation for a 6-month DAPT on the former, while the latter holds at a 12-month recommendation. This year’s ESC guidelines on the management of ACS in patients presenting without persisting ST-segment elevation includes various guidance on short DAPT.

As discussed previously, the insight from the PRECISE-DAPT study led to consider a shortened 3-month DAPT duration in patients at HBR (PRECISE-DAPT score ≥ 25) (Recommendation IIa B) [13]. What is probably more interesting, however, is the evidence gathered recently on patients at low-to-intermediate ischemic risk and low bleeding risk. The previously described TWILIGHT and SMART-CHOICE trials included a high proportion of patients presenting with ACS (64.8% and 58.2%, respectively), with the benefits of antiplatelet monotherapy

| Clinical [23] |
|-----------------|
| Previous myocardial infarction |
| Diabetes mellitus |
| Chronic kidney disease (creatinine clearance <60 mL/min) |
| Previous stent thrombosis |
| Current smoker |

| Angiographic |
|-----------------|
| Implantation of ≥3 stents [24] |
| Stented length (>60 mm) [24] |
| Complex lesions (bifurcation, chronic total occlusion) [24] |
| Left main or left anterior descending stenting [25] |
| Multivessel stenting [26] |

Table 2. High risk features associated with thrombotic events. Adapted from [3].
being consistent between subgroups. On the other hand, the SMART-DATE trial [40] specifically assessed 6 versus 12-month DAPT in patients with ACS. Although mortality, stroke and BARC type 2–5 bleeding did not differ between the two groups, the rate of myocardial infarction was higher in the short DAPT group. Combining the information of these three trials, the ESC guidelines suggest a 3 to 6-month DAPT therapy depending on the balance of ischemic and hemorrhagic risk in a Class IIa, level A recommendation. The recent TICO trial evaluated another aspirin-free strategy, specifically among patients undergoing PCI for an ACS [41]. Ticagrelor monotherapy after 3 months of DAPT resulted in a slight, significant reduction of the composite outcome of major bleeding and cardiovascular events at one year, compared with a ticagrelor-based 12-month DAPT.

6. Evidence of shortened DAPT duration in patients after PCI requiring lifelong oral anticoagulation

The landscape of evidence for the treatment of patients requiring lifelong oral anticoagulation after PCI has expanded notably in the last years, the main landmarks being (1) the ISAR-TRIPLE trial, where no significant difference was found in the primary endpoint of “net clinical benefit” (which included ischemic and bleeding outcomes) between 6 weeks and six months of triple therapy; [42] (2) the WOEST trial, where a dual pathway strategy (warfarin and clopidogrel) versus standard triple therapy (warfarin, clopidogrel and ASA) reduced bleeding while not increasing thrombotic events; [43] and (3) the advent of the new four direct oral anticoagulants (DOAC) and their specific trials for patients undergoing PCI.

| AF patients with ACS/PCI | Clinical setting | Therapy regimen | Recommendation |
|--------------------------|------------------|-----------------|---------------|
|                          | Uncomplicated or bleeding\(>\) ischemic\(>\) risk | • TT < 1 week | I B |
|                          |                   | • OAC + P2Y12 (preferably clopidogrel) up to 12 months |
|                          | Ischemic\(>\) bleeding\(>\) risk | • TT > 1 week and ≤ 1 month | IIa C |
|                          |                   | • OAC + P2Y12 (preferably clopidogrel) up to 12 months |

| AF patients with CCS undergoing PCI | Clinical setting | Therapy regimen | Recommendation |
|-----------------------------------|------------------|-----------------|---------------|
|                                   | Uncomplicated or bleeding\(>\) ischemic\(>\) risk | • TT ≤ 1 week | I B |
|                                   |                   | • OAC + P2Y12 (preferably clopidogrel) up to 6 months |
|                                   | Ischemic\(>\) bleeding\(>\) risk | • TT > 1 week and ≤ 1 month | IIa C |
|                                   |                   | • OAC + clopidogrel up to 12 months |

\(a\) Evaluation based on HAS-BLED score: Hypertension, Abnormal renal or liver function, Stroke or ICH history, Bleeding history or bleeding diathesis, Labile INR, Elderly (>65 years), Drugs (concomitant OAC and antiplatelet therapy, NSAIDs).

\(b\) Evaluation based on (1) clinical factors: diabetes, prior ACS, multivessel CAD, concomitant peripheral artery disease, premature or accelerated CAD, chronic kidney disease, ACS as clinical presentation; (2) anatomical factors: multivessel stenting, complex stenting (left main or last patent vessel stenting, chronic total occlusion intervention), prior stent thrombosis on antiplatelet treatment.

TT: Triple therapy; CCS: chronic coronary syndrome.

Table 3.
Recommendations for antithrombotic patients of AF patients undergoing PCI. Adapted from the 2020 ESC ESC/EACTS guidelines for the management of atrial fibrillation [8].
[dabigatran/RE-DUAL PCI [44]; rivaroxaban/PIioneer AF-PCI [45]; apixaban/ AUGUSTUS [46]; edoxaban/ENTRUST-AF PCI [47]. The new 2020 ESC ESC/ EACTS guidelines for the management of atrial fibrillation is the latest consensus document on the subject, and the only one after the publication of the four DOAC trials for AF patients undergoing PCI [8].

As a whole, these trials evaluated dual (DOAC + P2Y_{12}) vs. triple (VKA + P2Y_{12} + aspirin) therapy. They included a notable proportion of ACS (37–52%), although the highest risk patients were underrepresented (i.e., culprit lesions in a previously stented segment). Moreover, they all used triple therapy during PCI until randomization (1–14 days post PCI) and the most commonly P2Y_{12} inhibitor used was clopidogrel, as neither prasugrel or ticagrelor have evidence supporting their safety in combination with an OAC. As per outcomes, they reported a significant reduction of major/clinically significant bleeding, comparable rates of ischemic stroke, similar or non-significantly higher rates of myocardial infarction and stent thrombosis and a neutral effect on major adverse cardiac events and all-cause mortality [48]. Also, it is worth emphasizing that the AUGUSTUS trial is the only one that studied whether the advantages of dual pathway (vs. triple therapy) is independent of the type of OAC.

The ESC guidelines include four recommendations, according to the clinical presentation and the ischemic/bleeding risk balance (Table 3). Due to the under-representation of high ischemic risk patients on the trials, the recommendations for this population have a weak level of evidence. The evaluation of the ischemic risk is based on the presence of variables known to pose higher risk in the general population (also previously described in Table 2). Regarding the bleeding risk, evaluation with the AF-specific HAS-BLED risk score is recommended. This bleeding risk score has proven to be more useful at predicting bleeding risk in AF patients [49].

7. Beyond guidelines: tailored shortened DAPT durations according to stent platforms

Current guidelines include DAPT length recommendations irrespective of the DES type, encompassing the evidence of the multiple platforms in various trials. It is worth mentioning, however, some recent trials in which specific platforms have been tested in two main scenarios: one stent tested at short vs. longer DAPT durations; and two different stents compared in a short DAPT duration for patients not deemed amenable for prolonged DAPT duration. While acknowledging the limited value of a single trial, they may still be useful for tailored antiplatelet regimens. Table 4 summarizes the current knowledge of some specific DES platforms in these two scenarios.

8. Conclusions

As new antiplatelet and anticoagulant drugs have entered the therapeutic arsenal, and as stent platforms continue to be refined through the years, established dogmas of the treatment of patients with ischemic heart disease should be reassessed. Most notably, current evidence strongly supports that for a considerable number of patients, shorter antithrombotic, aspirin-free treatment is associated not only with fewer bleeding complications, but with comparable rates of hard ischemic endpoints. Hence, a paradigm shift is underway, in which the concern should not be to find reasons to reduce the classical 12 months of DAPT. Rather, patients should be evaluated for causes not to receive an abbreviated aspirin-free antithrombotic
| Trial                          | Stent platform          | Population study | Study arms and DAPT therapy                                                                 | Outcomes                                                                 |
|-------------------------------|-------------------------|------------------|--------------------------------------------------------------------------------------------|--------------------------------------------------------------------------|
| **Trials testing short vs. long DAPT durations in patients treated with new stent platforms** |
| GLOBAL LEADERS [33]           | BioMatrix (Biosensors Europe) | All comers       | Biomatrix stent 1 month DAPT ASA + ticagrelor followed by ticagrelor 12 months vs. DAPT ASA + clopidogrel (stable patients) or ASA/ticagrelor (ACS) followed by ASA (1:1) | No superiority of the ticagrelor arm for efficacy                         |
| COBRA-REDUCE [50]             | Cobra PzF (CeloNova Biosciences) | Patients taking OAC | Cobra stent vs. standard DES Cobra: DAPT 14 days, then OAC + ASA until 6 months. Control stent: DAPT 3–6 months. After 6 months, all received OAC + ASA | Cobra PzF stents did not achieve bleeding reduction and did not meet non-inferiority criteria with respect to thrombotic events |
| XIENCE 90/28 [51]             | Xience (Abbott Vascular)   | High bleeding risk | Xience stent DAPT 1 month and DAPT 3 months, compared to historical cohort DAPT 12 months | Non-inferior ischemic outcomes, similar rates of clinically relevant and reduction in major bleeding |
| EVOLVE Short DAPT [52]        | Synergy (Boston Scientific) | High bleeding risk | Synergy stent 3 month DAPT vs. 12 month historical cohort | Non inferior ischemic outcomes |
| TICO [41]                     | Orsiro (Biotronik AG)      | Acute coronary syndromes | Orsiro stent 3 month DAPT followed by ticagrelor monotherapy vs standard 12 month DAPT | Modest reduction of bleeding and cardiovascular events. |
| **Trials testing different stent technologies in patients deemed for short DAPT** |
| LEADERS FREE [30]             | Biofreedom (Biosensors Europe) | High bleeding risk | Biofreedom vs. similar BMS (1:1) 1 month DAPT ASA + clopidogrel followed by clopidogrel | Superiority of the Biofreedom stent in safety and efficacy |
| ONYX ONE [53]                 | Resolute Onyx (Medtronic)  | High bleeding risk | Resolute Onyx vs. Biofreedom (1:1) 1 month DAPT followed by SAPT | Resolute Onyx non-inferior to Biofreedom in safety and effectiveness |
| ZEUS [29]                     | Endeavor (Medtronic)       | High bleeding risk | Endeavor stent vs. ultra-thin BMS (1:1) 1 month DAPT | Low risk of 1-year MACE in Endeavor patients |
| SENIOR [54]                   | Synergy (Boston Scientific) | Elderly patients (>75 yo) undergoing PCI | Synergy stent vs. ultra-thin BMS 1 month or 6 months DAPT, according to stable or unstable presentation | Low risk of ischemic endpoints in the Synergy arm |

Table 4. Recent trials on the performance of different stent platforms on shortened DAPT scenarios.
regimen. In order to provide the most accurate treatment regimens, a careful evaluation should be made by taking into account the clinical presentation, coexisting conditions that are prone to a higher ischemic or bleeding risk and awareness of the stent platform used.

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References

[1] Marquis-Gravel G, Dalgaard F, Jones AD, et al. Post-Discharge Bleeding and Mortality Following Acute Coronary Syndromes With or Without PCI. J. Am. Coll. Cardiol. 2020;76:162-171.

[2] Mehta SR, Bainey KR, Cantor WJ, et al. 2018 Canadian Cardiovascular Society/Canadian Association of Interventional Cardiology Focused Update of the Guidelines for the Use of Antiplatelet Therapy. Can. J. Cardiol. 2018;34:214-233.

[3] Andrade JG, Verma A, Mitchell LB, et al. 2018 Focused Update of the Canadian Cardiovascular Society Guidelines for the Management of Atrial Fibrillation. Can. J. Cardiol. 2018;34:1371-1392.

[4] Levine GN, Bates ER, Bittl JA, et al. 2016 ACC/AHA guideline focused update on duration of dual antiplatelet therapy in patients with coronary artery disease. J. Thorac. Cardiovasc. Surg. 2016;152:1243-1275.

[5] January CT, Wann LS, Calkins H, et al. 2019 AHA/ACC/HRS focused update of the 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation. Hear. Rhythm 2019;16:e66-e93.

[6] Valgimigli M, Bueno H, Byrne RA, et al. 2017 ESC focused update on dual antiplatelet therapy in coronary artery disease developed in collaboration with the European Association of Cardio-Thoracic Surgery (EACTS). Eur. Heart J. 2020:1-126.

[7] Collet J-P, Thiele H, Barbato E, et al. 2020 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation. Eur. Heart J. 2020:1-79.

[8] Hindricks G, Potpara T, Dagres N, et al. 2020 ESC Guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association of Cardio-Thoracic Surgery (EACTS). Eur. Heart J. 2020:1-126.

[9] Marquis-Gravel G, Mehta SR, Valgimigli M, et al. A Critical Comparison of Canadian and International Guidelines Recommendations for Antiplatelet Therapy in Coronary Artery Disease. Can. J. Cardiol. 2020;36:1298-1307. Available at: http://www.ncbi.nlm.nih.gov/pubmed/32553812.

[10] Baber U, Mehran R, Giustino G, et al. Coronary Thrombosis and Major Bleeding after PCI with Drug-Eluting Stents Risk Scores from Paris. J. Am. Coll. Cardiol. 2016;67:2224-2234.

[11] Yeh RW, Secemsky EA, Kereiakes DJ, et al. Development and validation of a prediction rule for benefit and harm of Dual antiplatelet therapy beyond 1 year after percutaneous coronary intervention. JAMA - J. Am. Med. Assoc. 2016;315:1735-1749.

[12] Pasea L, Chung SC, Pujades-Rodriguez M, et al. Personalising the decision for prolonged dual antiplatelet therapy: Development, validation and potential impact of prognostic models for cardiovascular events and bleeding in myocardial infarction survivors. Eur. Heart J. 2017;38:1048-1055.

[13] Costa F, van Klaveren D, James S, et al. Derivation and validation of the predicting bleeding complications in patients undergoing stent implantation and subsequent dual antiplatelet therapy (PRECISE-DAPT) score: a pooled analysis of individual-patient datasets from clinical trials. Lancet 2017;389:1025-1034.

[14] Bianco M, D’ascenzo F, Raposeiras Roubin S, et al. Comparative external validation of the PRECISE-DAPT and PARIS risk scores in 4424 acute
coronary syndrome patients treated with prasugrel or ticagrelor. Int. J. Cardiol. 2020;301:200-206. Available at: https://linkinghub.elsevier.com/retrieve/pii/S0167527319309891.

[15] Marquis-Gravel G, Neely ML, Valgimigli M, et al. Long-Term Bleeding Risk Prediction with Dual Antiplatelet Therapy after Acute Coronary Syndromes Treated without Revascularization. Circ. Cardiovasc. Qual. Outcomes 2020;6:267-268.

[16] Abu-Assi E, Raposeiras-Roubin S, Cobas-Paz R, et al. Assessing the performance of the PRECISE-DAPT and Paris risk scores for predicting one-year out-of-hospital bleeding in acute coronary syndrome patients. EuroIntervention 2018;13:1914-1922.

[17] Ueki Y, Bär S, Losdat S, et al. Validation of the Academic Research Consortium for High Bleeding Risk (ARC-HBR) criteria in patients undergoing percutaneous coronary intervention and comparison with contemporary bleeding risk scores. EuroIntervention 2020;16:371-379.

[18] Bertrand ME, Legrand V, Boland J, et al. Randomized multicenter comparison of conventional anticoagulation versus antiplatelet therapy in unplanned and elective coronary stenting. The full anticoagulation versus aspirin and ticlopidine (FANTASTIC) study. Circulation 1998;98:1597-1603.

[19] Colombo A, Chieffo A, Frascheri A, et al. Second-generation drug-eluting stent implantation followed by 6- versus 12-month dual antiplatelet therapy: the SECURITY randomized clinical trial. J. Am. Coll. Cardiol. 64:2086-97. Available at: http://www.ncbi.nlm.nih.gov/pubmed/25236346.

[20] Gwon H-C, Hahn J-Y, Park KW, et al. Six-month versus 12-month dual antiplatelet therapy after implantation of drug-eluting stents: the Efficacy of Xience/Promus Versus Cypher to Reduce Late Loss After Stenting (EXCELLENT) randomized, multicenter study. Circulation 2012;125:505-13. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22179532.

[21] Schulz-Schüpke S, Byrne RA, Ten Berg JM, et al. ISAR-SAFE: A randomized, double-blind, placebo-controlled trial of 6 vs. 12 months of clopidogrel therapy after drug-eluting stenting. Eur. Heart J. 2015;36:1252-1263.

[22] Valgimigli M, Campo G, Monti M, et al. Short-versus long-term duration of dual-antiplatelet therapy after coronary stenting: A randomized multicenter trial. Circulation 2012;125:2015-2026.

[23] Bonaca MP, Bhatt DL, Cohen M, et al. Long-Term Use of Ticagrelor in Patients with Prior Myocardial Infarction. N. Engl. J. Med. 2015;372:1791-1800.

[24] Giustino G, Chieffo A, Palmerini T, et al. Efficacy and Safety of Dual Antiplatelet Therapy After Complex PCI. J. Am. Coll. Cardiol. 2016;68:1851-1864.

[25] Costa F, Adamo M, Ariotti S, et al. Left main or proximal left anterior descending coronary artery disease location identifies high-risk patients deriving potentially greater benefit from prolonged dual antiplatelet therapy duration. EuroIntervention 2016;11:e1222–e1230.

[26] Lee SY, Hong MK, Shin DH, et al. Association between Duration of Dual Antiplatelet Therapy and Angiographic Multivessel Disease on Outcomes in Patients Treated with Newer-Generation Drug-Eluting Stents. Circ. Cardiovasc. Interv. 2016;9.

[27] Kim B-K, Hong M-K, Shin D-H, et al. A New Strategy for Discontinuation of Dual Antiplatelet Therapy. J. Am. Coll. Cardiol. 2012;60:1340-1348.
[28] Feres F, Costa RA, Abizaid A, et al. Three vs twelve months of dual antiplatelet therapy after zotarolimus-eluting stents: The OPTIMIZE randomized trial. JAMA - J. Am. Med. Assoc. 2013;310:2510-2522.

[29] Valgimigli M, Patialiakas A, Thury A, et al. Zotarolimus-eluting versus bare-metal stents in uncertain drug-eluting stent candidates. J. Am. Coll. Cardiol. 2015;65:805-815.

[30] Urban P, Meredith IT, Abizaid A, et al. Polymer-free Drug-Coated Coronary Stents in Patients at High Bleeding Risk. N. Engl. J. Med. 2015;373:2038-2047.

[31] Mehran R, Baber U, Sharma SK, et al. Ticagrelor with or without aspirin in high-risk patients after PCI. N. Engl. J. Med. 2019;381:2032-2042.

[32] Hahn JY, Song Y Bin, Oh JH, et al. Effect of P2Y12 Inhibitor Monotherapy vs Dual Antiplatelet Therapy on Cardiovascular Events in Patients Undergoing Percutaneous Coronary Intervention: The SMART-CHOICE Randomized Clinical Trial. JAMA - J. Am. Med. Assoc. 2019;321:2428-2437.

[33] Vranckx P, Valgimigli M, Jüni P, et al. Ticagrelor plus aspirin for 1 month, followed by ticagrelor monotherapy for 23 months vs aspirin plus clopidogrel or ticagrelor for 12 months, followed by aspirin monotherapy for 12 months after implantation of a drug-eluting stent: a multicentre, open-la. Lancet 2018;392:940-949.

[34] Franzone A, McFadden E, Leonardi S, et al. Ticagrelor Alone Versus Dual Antiplatelet Therapy From 1 Month After Drug-Eluting Coronary Stenting. J. Am. Coll. Cardiol. 2019;74:2223-2234.

[35] Watanabe H, Domei T, Morimoto T, et al. Effect of 1-Month Dual Antiplatelet Therapy Followed by Clopidogrel vs 12-Month Dual Antiplatelet Therapy on Cardiovascular and Bleeding Events in Patients Receiving PCI: The STOPDAPT-2 Randomized Clinical Trial. JAMA - J. Am. Med. Assoc. 2019;321:2414-2427.

[36] Yusuf S, Zhao F, Mehta SR, Chrolavicius S, Tognoni G, Fox KK. Effects of clopidogrel in addition to aspirin in patients with acute coronary syndromes without ST-segment elevation. N. Engl. J. Med. 2001;345:494-502.

[37] Mehta SR, Yusuf S, Peters RJG, 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;358:527-533.

[38] Wiviott SD, Braunwald E, McCabe CH, et al. Prasugrel versus clopidogrel in patients with acute coronary syndromes. N. Engl. J. Med. 2007;357:2001-15. Available at: http://www.ncbi.nlm.nih.gov/pubmed/17982182.

[39] Wallentin L, Becker RC, Budaj A, et al. Ticagrelor versus clopidogrel in patients with acute coronary syndromes. N. Engl. J. Med. 2009;361:1045-1057. Available at: http://www.nejm.org/doi/abs/10.1056/NEJMoa0904327.

[40] Hahn JY, Song Y Bin, Oh JH, et al. 6-month versus 12-month or longer dual antiplatelet therapy after percutaneous coronary intervention in patients with acute coronary syndrome (SMART-DATE): a randomised, open-label, non-inferiority trial. Lancet 2018;391:1274-1284.

[41] Kim BK, Hong SJ, Cho YH, et al. Effect of Ticagrelor Monotherapy vs Ticagrelor with Aspirin on Major Bleeding and Cardiovascular Events in Patients with Acute Coronary Syndrome: The TICO Randomized Clinical Trial. JAMA - J. Am. Med. Assoc. 2020;323:2407-2416.
[42] Fiedler KA, Maeng M, Mehilli J, et al. Duration of Triple Therapy in Patients Requiring Oral Anticoagulation After Drug-Eluting Stent Implantation: The ISAR-TRIPLE Trial. J. Am. Coll. Cardiol. 2015;65:1619-1629. Available at: http://www.ncbi.nlm.nih.gov/pubmed/25908066.

[43] Dewilde WJM, Oirbans T, Verheugt FWA, et al. Use of clopidogrel with or without aspirin in patients taking oral anticoagulant therapy and undergoing percutaneous coronary intervention: An open-label, randomised, controlled trial. Lancet 2013;381:1107-1115.

[44] Cannon CP, Bhatt DL, Oldgren J, et al. Dual Antithrombotic Therapy with Dabigatran after PCI in Atrial Fibrillation. N. Engl. J. Med. 2017;377:1513-1524.

[45] Gibson CM, Mehran R, Bode C, et al. Prevention of Bleeding in Patients with Atrial Fibrillation Undergoing PCI. N. Engl. J. Med. 2016;375:2423-2434.

[46] Lopes RD, Heizer G, Aronson R, et al. Antithrombotic Therapy after Acute Coronary Syndrome or PCI in Atrial Fibrillation. N. Engl. J. Med. 2019;380:1509-1524.

[47] Vranckx P, Valgimigli M, Eckardt L, et al. Edoxaban-based versus vitamin K antagonist-based antithrombotic regimen after successful coronary stenting in patients with atrial fibrillation (ENTRUST-AF PCI): a randomised, open-label, phase 3b trial. Lancet 2019;394:1335-1343.

[48] Gargiulo G, Goette A, Tijssen J, et al. Safety and efficacy outcomes of double vs. triple antithrombotic therapy in patients with atrial fibrillation following percutaneous coronary intervention: A systematic review and meta-analysis of non-Vitamin K antagonist oral anticoagulant-based randomized clinical trials. Eur. Heart J. 2019;40:3757-3767.

[49] Borre ED, Goode A, Raitz G, et al. Predicting Thromboembolic and Bleeding Event Risk in Patients with Non-Valvular Atrial Fibrillation: A Systematic Review. Thromb. Haemost. 2018;118:2171-2187.

[50] Byrne RA. Randomized Trial of COBRA PzF Stenting to REDUCE Duration of Triple Therapy (COBRA-REDUCE). In: Presented at TCT 2020.

[51] Mehran R. The XIENCE Short DAPT Program: XIENCE 90/28 - Evaluating the Safety of 3-month and 1-month DAPT in HBR Patients. In: Presented at TCT 2020.

[52] Kirtane AJ. EVOLVE Short DAPT: A Single Arm Study of 3-Month DAPT in Patients at High Bleeding Risk Treated with a Bioabsorbable Polymer- Based Everolimus-Eluting Stent. In: Presented at TCT 2019.

[53] Windecker S, Latib A, Kedhi E, et al. Polymer-based or polymer-free stents in patients at high bleeding risk. N. Engl. J. Med. 2020;382:1208-1218.

[54] Varenne O, Cook S, Sideris G, et al. Drug-eluting stents in elderly patients with coronary artery disease (SENIOR): a randomised single-blind trial. Lancet 2018;391:41-50.