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Review article

Dual antiplatelet therapy in coronary artery disease

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Abstract Coronary artery disease encompasses a spectrum of clinical presentations caused by underlying coronary atherosclerosis. Acute manifestations of atherosclerotic disease occur when rupture/erosion of atherosclerotic plaque becomes substrate for platelet activation and aggregation, which have a central role in the formation and propagation of intracoronary thrombi. Therefore, antiplatelet therapy represents a standard of care in the primary and secondary prevention of CAD.

Dual antiplatelet therapy (DAPT) typically refers to aspirin along with P2Y12 receptor inhibitor (clopidogrel, prasugrel or ticagrelor). Choice and duration of DAPT requires an individual approach and assessment of each patient, emphasizing the tailored antiplatelet treatment. This is largely driven by patient's clinical presentation (stable coronary artery disease or acute coronary syndrome), existing risk factors (ischemic vs. hemorrhagic risk), and following treatment plan (medical treatment, percutaneous coronary intervention, or coronary artery by-pass graft).

In this review, we present the evidence supporting DAPT administration and therapy duration in different subpopulations of patients with CAD. Also, we will review these data in the context of current 2017 ESC focused update on dual antiplatelet therapy in coronary artery disease, emphasizing the novelties from the present guidelines.

Key words dual antiplatelet therapy, aspirin, ticagrelor, prasugrel, coronary artery disease, acute coronary syndrome

Introduction

Coronary artery disease (CAD) can be presented with a variety of symptoms and different clinical presentations which are caused by underlying atherosclerotic disease. Acute manifestations of atherosclerotic disease occur when rupture/erosion of atherosclerotic plaque become substrate for platelet activation and aggregation, which is followed by the activation of clotting cascade[1]. Activation and aggregation of platelets has a central role in the formation and propagation of intracoronary thrombi. Therefore, antiplatelet therapy represents a standard of care in the primary and secondary prevention of CAD.

Numerous clinical trials have proven that antiplatelet therapy reduces recurrent major adverse cardiovascular events (MACE) in patients with acute coronary syndrome (ACS) or stable CAD[2,3]. Dual antiplatelet therapy (DAPT) results in more intense platelet inhibition than single antiplatelet therapy, with significant risk reduction of ischemic events after percutaneous coronary intervention (PCI) or ACS, but is accompanied by increased hemorrhagic risk.

Currently several antiplatelet drugs are available, each with their distinct pharmacokinetic and pharmacodynamic properties, which led to their specific indications. Although there are several possible combinations of antiplatelet regimen, DAPT typically refers to aspirin along with $P2Y_{12}$ receptor inhibitor (clopidogrel, prasugrel or ticagrelor). Choice and duration of DAPT requires an individual approach and assessment of each patient. This is largely driven by patient's clinical presentation (stable coronary artery disease or acute coronary syndrome), existing risk factors (ischemic vs. hemorrhagic risk), and following treatment plan (medical treatment, percutaneous coronary intervention, or coronary artery by-pass graft - CABG).

In this review, we will discuss the evidence supporting DAPT administration and therapy duration in different subpopulations of patients with CAD. Also, we will review these data in the context of current 2017 ESC focused update on dual antiplatelet therapy in coronary artery disease, emphasizing the novelties from the present guidelines[4].

Antiplatelet agents

In patients with CAD thrombus formation is generally driven by platelet aggregation. Therefore platelet inhibition plays a central role in the prevention and treatment of atherothrombotic ischemic events in patients with CAD. Oral antiplatelet agents for secondary prevention

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in patients with CAD include aspirin and $P2Y_{12}$ receptor inhibitors (clopidogrel, prasugrel and ticagrelor).

Aspirin (acetylsalicylic acid, ASA) has a mainstay role in DAPT. It acts by competitively inhibiting cyclooxygenase (COX) enzyme, reducing thromboxane A_2 formation and platelet aggregation, which is considered the main mechanism for the protection from thrombotic events[5]. The regular formulation of aspirin is rapidly absorbed from the stomach and small intestine, reaching its peak plasma concentration after 30-40 minutes. Contrary, enteric-coated formulations achieve antiplatelet effect after 2-3 hours upon administration. Aspirin use is associated with an increased risk of bleeding complications, mainly gastrointestinal origin, which is reduced by the introduction of buffered- and enteric-coated formulations. Daily doses of aspirin above 325 mg do not have any additional antithrombotic effect and are associated with increased toxicity. Therefore, the doses of aspirin from 75-150 mg are indicated for the long-term administration[6].

$P2Y_{12}$ receptor has an important role in thrombus formation and stabilization. Binding of ADP to the $P2Y_{12}$ receptor leads to glycoprotein IIb/IIIa receptor activation, which is necessary for strong, irreversible platelet aggregation. Therefore, $P2Y_{12}$ receptor inhibitors provide additional thrombotic protection accompanied by modest increase in bleeding risk[7]. The most frequently prescribed oral $P2Y_{12}$ antagonists are clopidogrel, ticagrelor and prasugrel. Thienopyridines (clopidogrel and prasugrel) irreversibly block the $P2Y_{12}$ receptor, while ticagrelor reversibly inhibits this receptor.

Clopidogrel is a second-generation thienopyridine irreversible $P2Y_{12}$ inhibitor, biologically inactive pro-drug that requires hepatic conversion to its active metabolite. Administration of this antiplatelet drug results is mean platelet inhibition of 40-60% within 2 to 6 hours. Clopidogrel has shown variable level of platelet inhibition between patients[8,9]. Response variability of clopidogrel is associated with numerous patients' characteristics and clinical factors (age, high body mass index, smoking, presence of diabetes mellitus, acute coronary syndrome, heart failure)[10,11], drug-drug interactions (calcium channel blockers, omeprazole and esomeprazole, ketoconazole)[11-13], and genetic polymorphism of CYP isoenzyme[14,15]. Many patients with inadequate platelet inhibition after clopidogrel administration may be at increased ischemic risk[16-18]. In CAPRIE (*The Clopidogrel versus Aspirin in Patients at Risk of Ischemic Events*) trial the efficacy of clopidogrel and aspirin was compared in 19,185 patients with recent MI, recent ischemic stroke or symptomatic peripheral arterial disease[19]. During the median follow-up of 1.91 years, clopidogrel was shown to reduce the risk of vascular death, MI or ischemic stroke by 8.7% (95% CI 0.3-16.5, p=0.043), while the overall safety of clopidogrel and aspirin was similar.

Clopidogrel response variability led to the development of more potent $P2Y_{12}$ inhibitors – ticagrelor and prasugrel. Their pharmacokinetic and pharmacodynamic profile provides more consistent, rapid and more potent platelet inhibition than clopidogrel. However, greater efficacy of ticagrelor and prasugrel translates into a greater hemorrhagic risk in patients[20].

Prasugrel is a third-generation thienopyridine, potent oral irreversible $P2Y_{12}$ receptor inhibitor. Similar to clopidogrel, prasugrel is also a pro-drug that requires hepatic activation upon administration, but with faster onset of action and less interindividual variability. Its superiority to clopidogrel, prasugrel has proven in TRITON-TIMI 38 trial (*Trial to Assess Improvement in Therapeutic Outcomes by Optimizing Platelet Inhibition with Prasugrel–Thrombolysis in Myocardial Infarction 38*) by reducing ischemic events by 19%[21].

Ticagrelor is a cyclopentyl-triazolo-pyrimidine, inhibitor of $P2Y_{12}$ platelet receptor. Different to previously described $P2Y_{12}$ inhibitors, ticagrelor is an active drug and does not require hepatic metabolism for its activity, and also binds to the receptor independently from ADP. In stable patients, maximum platelet inhibition with ticagrelor is achieved 1 hour after administration, while clopidogrel takes 6 – 12 hours for its maximal efficiency. Also, platelets regain their normal reactivity upon 3 days after cessation of ticagrelor therapy, which occurs after 5-7 days after clopidogrel cessation[22]. With faster onset of action and consistent reversible platelet inhibition, ticagrelor proved its superiority over clopidogrel in patients with ACS by significantly reducing ischemic risk by 16%, without increasing the risk of hemorrhage[23].

Stable coronary artery disease

Aspirin is the cornerstone for secondary prevention of patients with stable CAD, irrespective of the management strategy. Large meta-analysis which included 16 secondary prevention trials with 17,000 high-risk patients showed that aspirin administered in low doses (75–150 mg daily) was associated with a 20% relative risk reduction in major cardiovascular adverse events (MACE, RR 0.80, 95% CI 0.73 – 0.88), consisting of cardiovascular death or nonfatal myocardial infarction (MI)[24]. This meta-analysis also showed that aspirin administration was associated with a 31% relative risk reduction in MI (RR 0.69, 95% CI 0.60 - 0.80), 22% relative risk reduction in ischaemic stroke (RR 0.78, 95% CI 0.61 – 0. 99), and a 10% relative risk reduction in all-cause mortality (RR 0.90, 95% CI 0.82 - 0.99, p=0.02). This reduction was accompanied by an increased risk of major extracranial bleeding (RR 2,69, 95% CI 1.25 - 5.76). Therefore, current guidelines recommend long-term low dose (75-150 mg*)* aspirin in all patients with stable CAD (class I, level of evidence A)[6].

DAPT is not indicated in patients with stable CAD without prior MI or PCI. This recommendation is supported by the results of CHARISMA (*Clopidogrel or High Atherothrombotic Risk and Ischemic Stabilization, Management and Avoidance*) trial which enrolled more than 15,000 patients with stable cardiovascular disease or multiple risk factors[25]. Patients were randomly assigned to receive clopidogrel plus low-dose aspirin, or placebo plus low-dose aspirin. After a median follow-up of 28 months, clopidogrel plus aspirin was not significantly more effective in MACE reduction (composite of MI, stroke, or cardiovascular death) compared with aspirin alone (6.8% vs. 7.3%, RR 0.93, 95% CI, 0.83 – 1.05, p=0.22).

Percutaneous coronary intervention

The combination of aspirin and $P2Y_{12}$ receptor inhibitor therapy remains the standard of care for patients undergoing PCI with bare metal stents (BMS) or drug-eluting stents (DES). After stent implantation there is a general recommendation of 6-months DAPT consisting of aspirin and clopidogrel, regardless of the stent type (class I, level of evidence A).

In 2012 two randomized clinical trials were published comparing 6-months DAPT with at least 12-months DAPT in patients with coronary stent implantation. The first one is the EXCELLENT (*The Efficacy of Xience/Promus Versus Cypher to Reduce Late Loss After Stenting*) trial in which comparison of 6-months vs. 1-year DAPT (aspirin + clopidogrel) after DES implantation showed similar target vessel failure (composite of cardiac death, myocardial infarction, or ischemia-driven target vessel revascularization) in both groups (4.8% vs. 4.3% after 12 months)[26]. Additionally, there was a tendency towards lower bleeding risk with shorter DAPT duration. The second trial was the PRODIGY (*PROlonging Dual antiplatelet treatment after Grading stent induced intimal hYperplasia*) trial, comparing 6-months DAPT duration vs. 24-months DAPT (aspirin + clopidogrel) after BMS and three different DES[27]. There was no significant difference in 2-year primary endpoint (composite of all-cause death, MI, or cerebrovascular incident) between shorter (10.0%) and longer (10.1%) DAPT duration. The risk of major bleeding was significantly lower in patients receiving 6-months clopidogrel according to both the BARC and the TIMI bleeding criteria.

RESET (*Real Safety and Efficacy of 3-month dual antiplatelet Therapy following Endeavor zotarolimus-eluting stent implantation*) trial and OPTIMIZE (*Optimized Duration of Clopidogrel Therapy Following Treatment With the Endeavor*) trial showed that 3-month DAPT after DES implantation was noninferior to 12-month DAPT, without significantly increasing the risk of stent thrombosis[28,29]. Therefore, according to current guidelines, 3-month DAPT should be considered in patients with higher bleeding risk and stable CAD (class IIa, level of evidence B). Additionally, in certain patients with the risk of 3-month DAPT administration, 1 month of DAPT may be considered (class IIb, level of evidence C).

Several meta-analyses[30-32] supported the extension of DAPT beyond the 6 months in patients with stable CAD who previously well tolerated DAPT, particularly when there is a high thrombotic and low bleeding risk, which has class IIb, level of evidence A in current DAPT guidelines.

Although there are no data from clinical trials comparing DAPT duration after bioresorbable stents, present guidelines recommend considering at least 12 months DAPT administration (class IIa, level of evidence C). This was largely driven by the results of ABSORB III trial, where the efficacy and safety of everolimus-eluting bioresorbable vascular scaffold was compared to everolimus-eluting cobalt-chromium stent in patients with stable and unstable angina[33]. Also, recent trials pointed to very late bioresorbable scaffold thrombosis, suggesting an extended period of vulnerability for thrombotic events in these patients, and therefore supporting at least 12 months of DAPT administration[34,35].

Acute coronary syndrome

Antiplatelet therapy continues to be the cornerstone of pharmacological therapy for patients with ACS. Regardless of the implanted stent type (BMS or DES), patients with ACS require DAPT for 12 months unless contraindicated, egg. excessive bleeding risk (class I, level of evidence A). Along with aspirin, the first line $P2Y_{12}$ receptor inhibitor should be ticagrelor or prasugrel, while patients not eligible for ticagrelor or prasugrel should receive clopidogrel. PLATO (*PLATelet inhibition and patient Outcomes*) trial directly compared ticagrelor and clopidogrel in 18,624 patients with ACS[23]. Majority of these patients had non-ST elevation myocardial infarction (NSTEMI, 43%) about 38% of patients had ST-elevation myocardial infarction (STEMI), while 17% of patients had unstable angina. Ticagrelor reduced the risk of ischemic events (composite of death from vascular causes, myocardial infarction, or stroke) by 16% (HR 0.84, 95% CI 0.77-0.92, p<0.001), reduced the risk of MI by 16% (HR 0.84, 95% CI 0.75-0.95, p=0.001) and cardiovascular mortality by 21% (HR 0.79, 95% CI 0.69-0.91, p=0.001), without significant reduction of stroke risk when compared to clopidogrel. There was no significant difference in major bleeding between patients receiving ticagrelor (11.6%) and clopidogrel (11.2%, p=0.43), while ticagrelor showed increased rate of major bleeding not related to CABG (4.5% vs. 3.8%, p=0.03). Also, dyspnea and ventricular pauses were more frequently recorded in patients from ticagrelor group.

Prasugrel also proved superior to clopidogrel in TRITON-TIMI 38 trial[21]. In this trial more than 13,000 ACS patients scheduled for PCI randomly received prasugrel or clopidogrel for 6-15 months. The administration of prasugrel was associated with 19% lower MACE risk (composite of death from cardiovascular causes, nonfatal myocardial infarction, or nonfatal stroke, HR 0.81, 95% CI 0.73-0.90, p<0.001). Prasugrel also significantly reduced the rate of myocardial infarction by 24% (HR 0.76, 95% CI 0.67-0.85, p<0.001), urgent target-vessel revascularization by 34% (HR 0.66, 95% CI 0.54-0.81, p<0.001) and reduced the risk of stent thrombosis by 52% (HR 0,48, 95% CI 0.36-0.64, p<0.001) when compared to clopidogrel. However, the risk of major bleeding was significantly higher with prasugrel administration (HR 1.32, 95%CI 1.03-1.68, p=0.03), as well as life-threatening bleeding (HR 1.52, 95% CI 1.08-2.13, p=0.01).

According to current guidelines, in patients with ACS and stent implantation, accompanied by higher risk of hemorrhagic complications, cessation of DAPT after 6 months should be considered (class IIa, level of evidence B)[36-37].

PEGASUS-TIMI 54 (*Prevention of Cardiovascular Events in Patients with Prior Heart Attack Using Ticagrelor Compared to Placebo on a Background of Aspirin-Thrombolysis in Myocardial Infarction 54*) trial explored the efficacy of ticagrelor administration beyond 12 months after the myocardial infarction[38]. More than 21,000 patients were randomly assigned to receive ticagrelor (60 mg or 90 mg twice daily) or placebo. During 33 months of follow-up investigators recorded the occurrence of cardiovascular death, myocardial infarction, or stroke, showing significant risk reduction of these ischemic events with

ticagrelor treatment (ticagrelor 90 mg vs. placebo HR 0.85, 95% CI 0.75-0.96, p=0.008; ticagrelor 60 mg vs. placebo HR 0.84, 95% CI 0.74-0.95, p=0.004). However, ticagrelor administration in both doses significantly increased the risk of TIMI (*Thrombolysis in Myocardial Infarction*) major bleeding (2.60% in 90 mg-group, 2.30% in 60 mg-group vs. 1.06% in placebo-group).

Results from the DAPT (*Dual Antiplatelet Therapy*) study confirmed the efficacy of the extended DAPT duration in patients treated with everolimus-eluting stents (EES)[39]. Compared to placebo, continued thienopyridine therapy (clopidogrel or prasugrel) in EES-treated patients reduced the risk of stent thrombosis by 62% (HR 0.38, 95%CI 0.15-0.97, p=0.04) and MI by 37% (HR 0.63, 95% CI 0.44-0.91, p=0.01), without the reduction in composite of death, MI, and stroke. As expected, extended DAPT administration was accompanied by increase in moderate/severe bleeding (HR 1.79, 95% CI 1.15-2.80, p=0.01). Additional positive results for the extended DAPT duration came from meta-analysis that included 33,435 high-risk patients presented with MI or with a history of prior MI[3]. Extended DAPT treatment reduced MACE risk compared to aspirin-alone (6.4% vs. 7.5%, RR 0.78, 95% CI 0.67-0.90, p=0.001), along with the reduction of cardiovascular death, MI, stroke and stent thrombosis, with no significant change in non-cardiovascular death and all-cause mortality. Prolonged DAPT increased the risk of major bleeding by 73% (1.85% vs. 1.09%, RR 1.73, 95% CI 1.19-2.50, p=0.004), but had no effect on fatal bleeding.

Therefore, current guidelines recommend for patients with MI and high ischemic risk who previously well tolerated DAPT, to continue with DAPT beyond 12 months, with ticagrelor as preferred $P2Y_{12}$ inhibitor (over clopidogrel or prasugrel) (class IIb, level of evidence B).

For many years the first choice of $P2Y_{12}$ receptor inhibitor for STEMI patients after PCI was clopidogrel. But in the latest STEMI guidelines newer $P2Y_{12}$ inhibitors - ticagrelor or prasugrel, on top of aspirin, are now considered the first line DAPT treatment for 12 months of administration (class I, level of evidence A). In cases where ticagrelor or prasugrel are not available or contraindicated, clopidogrel should be administered. Ticagrelor (180 mg loading dose and 90 mg maintenance dose twice daily) and prasugrel (60 mg loading dose and 10 mg maintenance dose daily) are superior to clopidogrel in clinical outcomes, with more rapid onset of action and greater potency. This major change in $P2Y_{12}$ inhibitor recommendation came from positive results for prasugrel in TRITON-TIMI 38 trial[21] and positive results for ticagrelor in PLATO trial[23]. In the analysis of STEMI patients from PLATO study, MACE reduction (composite of myocardial infarction, stroke, or cardiovascular death) was observed similar to overall PLATO study (HR 0.87, 95% CI 0.75-1.01, p=0.07)[40]. It was noted that ticagrelor in STEMI patients reduced the risk of MI by 20 % (HR 0.80, 95% CI 0.65-0.98, p=0.03), total mortality by 18% (HR 0.82, 95% CI 0.67-1.00, p=0.05), and definite stent thrombosis by 34% (HR 0.66, 95% CI 0.45-0.95, p=0.03). However, there was increased risk of stroke in ticagrelor group compared to patients who received clopidogrel (HR 1.63, 95% CI 1.07-2.48, p=0.02).

New DAPT guidelines also underline switching between oral $P2Y_{12}$ inhibitors. In patients with ACS who previously received clopidogrel, it is now recommended to switch from clopidogrel to ticagrelor early after hospital admission at a loading dose of 180 mg irrespective of timing and loading dose of clopidogrel, unless ticagrelor is contraindicated (class I, level of evidence B). This „switch" is supported by the results of PLATO trial[23,41] where about 50% of patients were pre-treated mostly with loading dose of clopidogrel (300-600 mg), and afterwards randomly assigned to receive ticagrelor. Observed efficacy and safety of ticagrelor was not influenced by previous clopidogrel administration. Additionally, present guidelines recommend further switching between oral $P2Y_{12}$ inhibitors in cases of side effects or drug intolerance (class IIb, level of evidence C).

Coronary Artery Bypass Surgery

In patients with stable coronary artery disease undergoing CABG there is no evidence of a DAPT benefit, therefore DAPT is not recommended in this class of patients.

On the other hand, DAPT is indicated in patients with ACS treated with CABG, estimating the individual ischemic and hemorrhagic risk that will guide further antithrombotic management. It was shown that newer $P2Y_{12}$ inhibitors (ticagrelor and prasugrel) were more effective than clopidogrel when added to aspirin in this subpopulation of patients[42,43]. Therefore, when there is low bleeding risk in ACS patients undergoing CABG, administration of ticagrelor/prasugrel on top of aspirin therapy is recommended for 12 months, or clopidogrel if patient is not eligible for ticagrelor/prasugrel treatment (class I, level of evidence C). It may be considered to continue with DAPT for more than 12 months in patients with prior MI and high ischemic risk, who have tolerated DAPT without bleeding complications (class IIb, level of evidence B).

In patients receiving DAPT after PCI who are planned to undergo CABG, it is recommended to resume $P2Y_{12}$ therapy postoperatively as soon as evaluated safe until the recommended DAPT duration is completed (class I, level of evidence C). Similarly, patients with ACS already receiving DAPT and undergoing CABG are also advised to continue DAPT therapy up to 12 months as soon as is deemed safe after surgery (class I, level of evidence C).

Discontinuation of $P2Y_{12}$ inhibitor therapy prior to non-emergent CABG varies due to different properties of clopidogrel, ticagrelor and prasugrel. Ticagrelor administration should be discontinued at least 3 days prior to CABG (class IIa, level of evidence B). Recently published trial reported that discontinuing ticagrelor therapy 72-120 h or > 120 h before planned CABG did not show difference in major bleeding among these patients (OR 0.93, 95% CI 0.53-1.64, p=0.80), while stopping this therapy < 72h before surgery resulted in higher rate of major bleeding[44]. This finding was also supported by the results from PLATO trial, where patients discontinued ticagrelor treatment 24-72h prior the CABG[42]. Clopidogrel administration should be discontinued in longer period of time, at least 5 days prior to CABG (class IIa, level of evidence B), which is supported by the result of CURE trial[45]. Additionally, Swedish nationwide study confirmed these results, by

showing that quitting ticagrelor 72 h before CABG increases the risk of major bleeding compared with 72-120 h (OR 1.67, 95% CI 1.02-2.73, p=0.042) and >120 h (OR 2.85, 95% CI 1.98-4.10, p<0.0001). Due to its pharmacodynamic and pharmacokinetic properties, prasugrel should be discontinued at least 7 days before planned CABG (class IIa, level of evidence B), as reported by the results of TRITON-TIMI 38 trial[43,46]. Also, discontinuation of $P2Y_{12}$ inhibitor therapy should be considered after 6 months in patients with MI and higher bleeding risk undergoing CABG (class IIa, level of evidence C).

Medical Treatment Alone

In medically managed patients with stable CAD, DAPT is not indicated unless concomitant or prior indications exist[23,47]. However, in patients with ACS managed with medical treatment alone, it is recommended to continue with $P2Y_{12}$ inhibitor therapy for 12 months (class I, level of evidence A). Choice of $P2Y_{12}$ treatment should be either ticagrelor or clopidogrel, while negative results from TRILOGY ACS (*Targeted Platelet Inhibition to Clarify the Optimal Strategy to Medically Manage Acute Coronary Syndromes*) study indicate that prasugrel has no favor in medically managed patients with ACS[48].

Benefits from ticagrelor compared to clopidogrel in PLATO trial[23,49], and ticagrelor compared to placebo in PEGASUS trial[38] resulted in recommending ticagrelor over clopidogrel in medically managed patients with ACS, unless the bleeding risk is higher than potential ischemic benefit (class I, level of evidence B). In cases of higher hemorrhagic risk, 1 month DAPT administration should be considered (class IIa, level of evidence C).

Results from PEGASUS-TIMI 54 largely contributed that ticagrelor therapy along with aspirin may be considered in patients with prior MI at high ischemic risk for longer than 12 months up to 36 months, who are medically managed and previously well tolerated DAPT (class IIb, level of evidence B)[50]**.** Subgroup of these patients who are not eligible for ticagrelor treatment, may be considered for clopidogrel treatment for longer than 12 months (class IIb, level of evidence C).

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Sažetak

Dvojna antitrombocitna terapija u koronarnoj arterijskoj bolesti

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Koronarna arterijska bolest (CAD) obuhvata spektar kliničkih prezentacija uzrokovanih koronarnom aterosklerozom. Akutne manifestacije aterosklerotske bolesti javljaju se kada ruptura / erozija aterosklerotskog plaka postaje supstrat za aktivaciju i agregaciju trombocita, koji imaju centralnu ulogu u formiranju i širenju intakoronarnog tromba. Stoga, antitrombocitna terapija predstavlja standard u lečenju u primarnoj i sekundarnoj prevenciji koronarne arterijske bolesti. Dvojna antitrombocitna terapija (DAPT) tipično se odnosi na aspirin uz inhibitor P2Y12 receptora (klopidogrel, prasugrel ili tikagrelor). Izbor i trajanje DAPT-a zahteva individualni pristup i procenu kod svakog pacijenta, naglašavajući prilagođenu antitrombocitnu terapiju. Ovo u velikoj meri zavisi od kliničke prezentacije pacijenta (stabilna koronarna bolest ili akutni koronarni sindrom), postojećih faktora rizika (ishemijski ili hemoragijski rizik), i od pratećeg plana lečenja (medikamentozni tretman, perkutana koronarna intervencija ili koronarno arterijsko premošćavanje). U ovom radu predstavljamo dokaze koji podržavaju upotrebu DAPT-a i dužinu trajanje te terapije u različitim subpopulacijama bolesnika sa CAD. Isto tako ćemo razmotriti te podatke u kontekstu trenutnih 2017 ESC preporuka o dvojnoj antitrombocitnoj terapiji usmerenih na dvojnu antitrombocitnu terapiju u koronarnoj arterijskoj bolesti, naglašavajući novine iz ovih preporuka.

Ključne reči: *dvojna antitrombocitna terapija, aspirin, tikagrelor, prasugrel, koronarna arterijska bolest, akutni koronarni sindrom*