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Dual antiplatelet therapy (DAPT) after percutaneous coronary intervention (PCI) in patients with chronic coronary artery disease (CAD) - current state of knowledge and perspective for further research

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Abstract

Introduction and purpose: aa Chronic coronary artery disease (CAD) is a prevalent condition affecting millions of people worldwide, significantly reducing quality of life and increasing the risk of myocardial infarction (MI). Percutaneous coronary intervention (PCI), often combined with stent implantation, is a cornerstone of CAD treatment. However, it induces a prothrombotic state, necessitating dual antiplatelet therapy (DAPT) to mitigate the risk of thrombosis and MI. Despite its established role, the optimal duration and specific composition of DAPT still remain under investigation. This article aims to summarise current knowledge on DAPT and highlight gaps requiring further research.

Description of the state of knowledge: DAPT typically involves acetylsalicylic acid (ASA) 75 mg and clopidogrel 75 mg for 6 months after PCI. While this is effective in reducing thrombotic events, it also increases bleeding risk. Current European Society of Cardiology (ESC) guidelines recommend tailoring DAPT duration and composition based on individual patient risk factors for bleeding and ischemia. Alternatives include shortening DAPT to 1–3 months for patients with high bleeding risk or intensifying it with stronger antiplatelet agents

like ticagrelor or prasugrel for those at high ischemic risk. However, evidence supporting these alternatives remains limited, and require further investigation. Emerging options, such as vorapaxar, present additional potential, but also require further validation.

Summary: CAD management through PCI relies heavily on effective DAPT. Current strategies emphasize balancing ischemic and bleeding risks in optimising treatment. Although significant progress has been made, optimal DAPT regimens for specific patient groups remain uncertain, particularly in cases of shortened or intensified therapy. Continued research is crucial to refine treatment protocols and improve patient outcomes.

Key words: Chronic Coronary Artery Disease (CAD), Dual Antiplatelet Therapy (DAPT), Percutaneous Coronary Intervention (PCI), Antiplatelet Medications

INTRODUCTION

Chronic coronary disease is a widespread pathology common all over the world. It is estimated that 2 million people in Poland and 16.8 million people in the United States suffer from it. [1] CAD is a disease that decreases the quality of life, mostly by causing lower physical efficiency, fatigue and chest pain on exertion. Moreover, CAD is a state that highly increases the risk of myocardial infarction (MI), which is one of the most common causes of death (about 20 thousand people in Poland every year). [2] Therefore, prevention and therapeutic methods for CAD are still developed. One of the therapeutic methods that has a well established and important place in CAD treatment is percutaneous coronary intervention (PCI), often combined with stent implantation. [3] This method allows to enter an occluded coronary artery with a thin catheter and widen it, often leaving in that place a stent that prevents future reocclusion. However, manipulations inside coronary arteries and leaving a stent, which is a foreign body, generate a prothrombotic state in the coronary vessels and raise a risk of thrombosis and MI. [4] Therefore, after PCI procedure a specific antiplatelet treatment is introduced. It has a proven effect on lowering the risk of MI. [5] It is called dual antiplatelet therapy (DAPT). Although applying DAPT to the patients with CAD that underwent PCI is a standard, the optimal time of treatment and set of antiplatelet medications are still researched.

DESCRIPTION OF THE STATE OF KNOWLEDGE

Basic information on DAPT

DAPT is a treatment applied to all patients after a PCI procedure. Its role is to prevent thrombotic events in the operated artery, because the risk of thrombosis is elevated in this

vessel and may lead to MI and event death. [4] The risk of thrombosis is highest directly after the procedure and decreases with time. [6] The basic model of DAPT after PCI in CAD is an administration of 75mg acetylsalicylic acid (ASA) and 75mg of clopidogrel for 6 months after the PCI procedure. [7] However, the actual length of DAPT and set of antiplatelet drugs may vary and should fit the patient's specific risk factors. DAPT prevents thrombotic events, but also increases the risk of bleeding, which is its most important adverse effect [8, 9]. Therefore, in patients with important bleeding risk factors standard DAPT may cause net harm. In such situations it seems reasonable to deescalate a scheme of treatment. However, there are also some patients that have high ischaemic risk factors and may benefit from extensifying the basic pattern. Then, introducing a specific scheme of DAPT is based mainly on the balance between the patient's individual risk of both bleeding and thrombosis and ishaemia. [10, 11]

Current guidelines and state of knowledge

The European Society of Cardiology (ESC) regularly publishes guidelines of CAD treatment that also include recommendations about using DAPT in patients after PCI. The latest edition of the guidelines was published in August 2024 and includes a summary of a lot of research conducted in recent years. It is a basic and fundamental document that should be considered by every cardiologist in Europe in choosing a specific treatment for their patients. According to these guidelines, specific DAPT treatment should be based on the presence or absence of high bleeding risk factors and high ischaemic risk factors in specific patients. The criteria of these states are presented in Table 1. [7]

High bleeding risk criteria	High ischaemic risk criteria
For high bleeding risk at least 1 major criterium or at least 2 minor criteria must be present	For high ischaemic risk at least 1 criterium must be present
Major criteria • Expected long-term oral anticoagulant therapy • Chronic kidney diesease (eGFR <30 ml/min/1,73m²)	General criteria • Diabetes requiring treatment • Recurrent MI • Atherosclerosis of multiple vascular beds (e.g., CAD and PAD)

• Hemoglobin <11 g/dL • Thrombocytes < 100 x 1000/µL • Serious operation or injury in 30 days pre-PCI • Moderate or severe ischemic stroke in 6 months • Spontaneous bleeding requiring transfusion or hospitalization in 6 months or at any time, if recurrent • Active neoplastic disease in 12 months • Post-traumatic intracranial hemorrhage in 12 months • History of spontaneous intracranial hemorrhage • Intracerebral arteriovenous malformation (AVM) • Chronic bleeding diathesis • Cirrhosis with portal hypertension • Major non-deferrable surgery in a patient receiving two antiplatelet drugs Minor criteria • Age >= 75 • Chronic kidney disease (eGFR 30-59 ml/min/1,73m²) • Hemoglobin <11-12,9 g/dL male or <11-11,9 g/dL female • Chronic use of NSAIDs or glucocorticoids • Spontaneous bleeding requiring hospitalization and/or blood transfusion in the last 12 months	• Multivessel coronary artery disease • Premature (age <45) or accelerated (new lesions within 2 years) coronary artery disease • Concomitant systemic inflammatory and/or prothrombotic disease (e.g.HIV, systemic lupus erythematosus, chronic arthritis, antiphospholipid syndrome) Procedural criteria • At least 3 stents or treatment of at least 3 atherosclerotic lesions • Total stent length > 60 mm • Complex revascularization i.e. PCI (left main coronary artery, bifurcation with double stenting technique, chronic total occlusion, single patent vessel) • History of stent thrombosis during antiplatelet therapy

(not meeting the major criterion) • Any ischemic stroke ever experienced (not meeting the major criterion)	

Table 1. The European Society of Cardiology (ESC) criteria for high bleeding risk and high ischaemic risk in patients with coronary artery disease (CAD) undergoing percutaneous coronary intervention (PCI).

According to the recommendations, patients without any risk factors mentioned above should get basic DAPT containing ASA 75mg and clopidogrel 75mg for 6 months (class I/A). [12-16] However, there is also a possibility to administer ASA 75mg and clopidogrel 75mg for a shorter period of time, that is 1-3 months, in patients with confirmed low ischaemic risk. [17-20] Nevertheless, these recommendations are weak (IIb/B) and need conducting more research in the context of efficacy and safety.

Patients with no high bleeding risk, but with high ischaemic risk are recommended to get typical DAPT of ASA 75mg and clopidogrel 75mg for 6 months. [12-16] However, there is also a possibility to administer ASA 75mg and ticagrelor 60mg or prasugrel 10mg in this group of patients for 1 - 6 months (class IIb/C). [21-26] Ticagrelor and prasugrel are stronger antiplatelet drugs comparing to clopidogrel and are routinely used in the treatment of acute coronary syndromes like MI. It is believed that in this group of patients stronger antiplatelet activity may bring more benefit, as the initial risk of bleeding is low. Nevertheless, the quality of evidence is still low and this strategy needs further evaluation.

In patients that are assessed as high bleeding risk patients DAPT containing ASA 75mg and clopidogrel 75mg should be shortened and last for 1-3 months (class I/A). This treatment is recommended regardless of the presence of high ischaemic risk. This strategy allows to significantly decrease a risk of major or life-threatening bleeding and brings positive net outcomes for the patient. [27, 28]

The summary of present ESC guidelines are presented in Table 2.

	No high bleeding risk	High bleeding risk
No ischaemic risk	ASA 75mg + clopidogrel 75mg, 6 months (class I/A) Alternative: ASA 75mg + clopidogrel 75mg, 1 - 3 months (class IIb/B)	ASA 75mg + clopidogrel 75mg, 1 - 3 months (class I/A)
Ischaemic risk	ASA 75mg + clopidogrel 75mg, 6 months Alternative: ASA 75mg + ticagrelor 60mg or prasugrel 10mg, 1 - 6 months (class IIb/C)	

Table 2. Summary of the European Society of Cardiology (ESC) guidelines on dual antiplatelet therapy (DAPT) in patients with coronary artery disease (CAD) after percutaneous coronary intervention (PCI).

Gaps in knowledge and future perspective

Although there is already a lot of research and data on the optimal DAPT in patients with CAD after PCI, there are still many gaps in evidence and knowledge that need future examination and evaluation.

One of the main research area is shortening DAPT in patients with neither high bleeding risk nor high ischaemic risk. Now such treatment modification possibility is included in the guidelines, but only as an alternative and in class IIb/B. The research conducted in this area suggests that such treatment scheme is non-inferior compared to standard treatment lasting 6 months. [17-20] Nevertheless, the trials had some limitations, for example different stent models in two groups of patients or different treatment time. Therefore more well projected trials should be performed to confirm the value of such treatment.

There also comes a question if escalating DAPT in patients with high thrombotic risk and without high bleeding risk is legitimate. The guidelines allow the use of ticagrelor or

prasugrel instead of clopidogrel in such patients, however the class of these recommendations is only IIb/C. ALPHEUS and SASSAICA trials that compared intensified treatment with the standard variant showed the use of ticagrelor or prasugrel was not superior to clopidogrel in preventing ischemic events. However, bleeding risk was also comparable. Therefore the net effect of intensive antiplatelet treatment was similar to the standard one. [21-25] In the PATH-PCI trial patients were tested for platelet activity before introducing the treatment. An analysis of the trial showed that intensification of antiplatelet treatment may be beneficial in a subgroup of patients that had increased initial platelet activity compared to the lower platelet activity group. [26] Therefore, whether use of ticagrelor or prasugrel can be beneficial in patients undergoing PCI for CAD with a high thrombotic and low bleeding risk warrants further study.

An additional antiplatelet treatment option that was not included in the 2024 European guidelines but appears in the 2023 American guidelines (IIb) is vorapaxar. [29] This medication belongs to the class of inhibitors of the PAR-1 receptor for thrombin present on platelets. Vorapaxar is also available in Europe, including Poland, and may be added to ASA (acetylsalicylic acid) or clopidogrel in patients with a history of MI, but without a history of stroke, transient ischemic attack (TIA) or intracranial bleeding. However, data on the efficacy and safety of its use remain limited, and the American guidelines emphasize that the benefits of using vorapaxar remain unclear. [30-33] Therefore, the possibility of using this agent in patients after PCI requires further studies.

CONCLUSIONS

CAD is a very common disease that affects the quality and duration of life of many million people among the whole world. Therefore, the effort to prevent and treat this disease remains a very important aim for global health. One of the well-established treatment methods is PCI. However, the efficacy of this way of treatment is strongly dependent on the antiplatelet treatment following the procedure called DAPT. There are several DAPT schemes differing in both length of treatment and antiplatelet medications that are administered. An optimal DAPT pattern is still a subject of intensive research, however according to the current evidence, it is crucial to assess initial ischaemic and bleeding risk of the patient before making a decision about the best treatment. Although an optimal treatment in some clinical situations is already well established and based on extensive and high quality research, there are still many situations in which an optimal pattern is unclear and further research is essential in these areas.

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