INBRIEF | Summarizing the Evidence

Standard-Duration Versus Extended-Duration Dual Antiplatelet Therapy Following Percutaneous Coronary Intervention: A Review

Key Messages

- The Canadian Drug Expert Committee (CDEC) recommends that a P2Y12 inhibitor (clopidogrel, prasugrel, or ticagrelor) be reimbursed for use beyond 12 months in combination with ASA in patients who have undergone PCI with drug-eluting stent insertion. The decision to extend DAPT should account for whether the potential benefits (i.e., reduced risk of blood clots post-PCI) outweigh the risks (i.e., bleeding risks) based on individual patient characteristics.
- As evidence comparing the different P2Y12 inhibitors was limited, CDEC further recommends that the selection of which P2Y12 inhibitor (clopidogrel, prasugrel, or ticagrelor) be made at the discretion of the treating physician, based on the individual characteristics and risk profile of each patient.

Context

Percutaneous coronary intervention (PCI) is a treatment frequently given to patients following a myocardial infarction (heart attack), or for the treatment of angina. Its purpose is to alleviate the narrowing or blockage in the affected coronary artery (coronary arteries deliver blood to the heart) in order to restore blood flow and oxygenation. The procedure involves inserting a catheter into the patient's groin or arm, and then threading the catheter through the patient's blood vessels until it reaches the narrowed or blocked artery. A balloon is then inflated to help re-open the affected artery, and a stent may be inserted.

Following PCI with stent insertion, it is routine to administer dual antiplatelet therapy (DAPT) — the combination of a P2Y12 inhibitor (e.g., clopidogrel, prasugrel, or ticagrelor) with acetylsalicylic acid (ASA, or aspirin) — for six to 12 months. However, there is ongoing debate about the optimal duration of treatment, and whether treatment should be extended beyond 12 months. There is also uncertainty about which drug (clopidogrel versus prasugrel versus ticagrelor) is most appropriate in which setting.

Of note, the preferred management strategy for patients who have undergone PCI with stenting varies based on the individual characteristics and risk profile of each patient. As a result, it is important to consider clinically relevant subgroups (i.e., patients who have had a prior heart attack, those with acute coronary syndrome at presentation, those with diabetes, those who smoke, and those younger or older than 75) in order to more fully characterize which patients may benefit most from different treatment strategies (including different durations of treatment and different drug choices).

Technology

DAPT consists of administering two different types of antiplatelet drugs — a P2Y12 inhibitor (e.g., clopidogrel, prasugrel, or ticagrelor) in combination with ASA. DAPT helps to reduce the risk of clot formation in patients who have undergone PCI with stent insertion (thus reducing the risk of a subsequent heart attack, stroke, clot at the site of the stent, need for repeat PCI, etc.); however, it also results in an increased bleeding risk. Therefore, the benefits must be weighed against the risks.

CADTH considered three P2Y12 inhibitors in this report: clopidogrel, prasugrel, and ticagrelor. All three drugs function by inhibiting platelet aggregation and thus reducing clot formation. The newer drugs, prasugrel and ticagrelor, have proposed advantages such as a faster onset of action and reduced inter-person variability compared with clopidogrel. However, uncertainty remains as to which drug is most appropriate in which setting.

Issue

Synthesizing the evidence regarding the clinical benefits and risks, as well as the cost-effectiveness of different DAPT durations (standard duration [six to 12 months] versus extended duration [beyond 12 months]) and drug choices (clopidogrel versus prasugrel versus ticagrelor) will help to guide treatment decisions for clinically relevant subgroups of patients who recently underwent PCI with stenting. It will also inform reimbursement decisions by publicly funded drug plans.

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Methods

CADTH undertook a systematic review of randomized clinical trials (RCTs) in addition to a cost-utility analysis comparing standard-duration DAPT with extended-duration DAPT following PCI with stent insertion. Three different P2Y12 inhibitors were considered: clopidogrel, prasugrel, and ticagrelor. Key outcomes were evaluated for all patients who received PCI with stent insertion, as well as for clinically relevant subgroups (i.e., patients who have had a prior heart attack, those with acute coronary syndrome at presentation, those with diabetes, those who smoke, and those older or younger than 75). The Canadian Drug Expert Committee (CDEC) then developed recommendations based on the findings from CADTH's report in addition to consultations with clinical experts and other stakeholder groups.

Results

The clinical review included seven RCTs. Overall, extending DAPT beyond 12 months after PCI was found to be predominantly beneficial in reducing heart attack and probable or definite stent thrombosis (clotting at the site of the stent). However, this benefit was accompanied by an increased risk of bleeding. No significant differences were found for the other outcomes of interest.

Subgroup analyses suggested that patients who have had a prior heart attack, those with acute coronary syndrome at presentation, those without diabetes, or those younger than 75 may derive the most benefit from extended DAPT. However, the results of the subgroup analyses should be interpreted with caution due to limitations. As a result, CDEC did not make subgroup-level prescribing or reimbursement recommendations and instead noted that patient selection needs to be highly individualized.

The economic analyses found that, when projecting the effect over a lifetime, extended-duration DAPT is likely to be more effective and less costly compared with standard-duration DAPT.

In terms of the choice of P2Y12 inhibitor, there was limited evidence comparing different P2Y12 inhibitors for extended-duration DAPT. (Note that the majority of patients in the included RCTs received clopidogrel.) As a result, no conclusions were able to be drawn regarding the comparative clinical- or cost-effectiveness of clopidogrel versus prasugrel versus ticagrelor. Therefore, CDEC recommended that all three drugs be reimbursed beyond 12 months and that the choice of P2Y12 inhibitor be left to the discretion of the treating physician, based on the individual characteristics and risk profile of each patient.

Lastly, the majority of the patients in the included RCTs had drug-eluting stents rather than bare-metal stents. As a result, CDEC's recommendations were specific to patients with drug-eluting stents. However, CDEC noted that this should not preclude the reimbursement of extended DAPT for patients with bare-metal stents if this is recommended by the treating physician based on individual patient assessment.

Read more about CADTH and its review of dual antiplatelet therapy following percutaneous coronary intervention:

https://cadth.info/standard-vs-extended-DAPT

ABOUT CADTH

CADTH is an independent, not-for-profit organization responsible for providing Canada's health care decision-makers with objective evidence to help make informed decisions about the optimal use of drugs and medical devices in our health care system.

CADTH receives funding from Canada's federal, provincial, and territorial governments, with the exception of Quebec.

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