Preventing Gastrointestinal Bleeds While Taking Dual Antiplatelet Therapy (DAPT)

Proton Pump Inhibitors (PPI) for Gastrointestinal Bleed Prophylaxis

When managing a patient on DAPT, prescribers may encounter difficulty when trying to control the risk of lower gastrointestinal bleeds (LGIB) and upper gastrointestinal bleeds (UGIB) associated with DAPT. In some situations, co-prescription of a PPI may be appropriate to manage the risk of gastrointestinal bleeds.

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REVIEW OF DUAL ANTIPLATELET THERAPY AND ASSOCIATED RISKS

DAPT is the use of aspirin and a $P2Y_{12}$ receptor inhibitor (clopidogrel, prasugrel, or ticagrelor).[1]
Duration of DAPT therapy varies by indication. The ischemic benefit and bleed risk should be assessed for every patient to ensure that DAPT is still appropriate. Drug regimens must be assessed for duration and appropriateness of therapy for every patient before initiating or continuing therapy.

The following table has been adapted from the 2016 ACC/AHA Guideline Focused Update on Duration of Dual Antiplatelet Therapy in Patients With Coronary Artery Disease[2]

INDICATION	DURATION OF DAPT
BARE METAL STENT PLACEMENT	AT LEAST 1 MONTH
DRUG ELUTING STENT PLACEMENT	AT LEAST 6 MONTHS
CORONARY ARTERY BYPASS GRAFT	AT LEAST 12 MONTHS
NON–ST-ELEVATION ACUTE CORONARY SYNDROME	AT LEAST 12 MONTHS
ST-ELEVATION MYOCARDIAL INFARCTION	AT LEAST 12 MONTHS

DAPT increases the risk of both Upper GI Bleed and Lower GI Bleed
Aspirin, even low dose, decreases mucus production along the GI tract. P2Y12 receptor inhibitors may promote bleeding in patients experiencing ulcers, hemorrhoids, diverticulosis, and other types of GI bleeds.

See Appendix 1. for the ACC DAPT Risk calculator, a tool for clinicians to weigh ischemic vs bleed risk for patients[3].

ROLE OF PPIS FOR PREVENTION OF GI BLEEDS

The following individuals may benefit from PPI use during DAPT[4]

- Anyone with a history of gastrointestinal bleeding
  OR
- Patients with multiple risk factors (2 or more of the following) for GI bleeds
  - Advanced age (>65 years)
  - Concomitant use of warfarin, steroids, and/or nonsteroidal anti-inflammatory drugs
  - Current *H. pylori* infection

PPIs do not reduce the risk of LGIB. The risk of LGIB should be weighed against the cardiovascular benefits in patients who have a history of LGIB.

PPI DURATION, ADMINISTRATION AND DISCONTINUATION

For patients receiving DAPT, who are at an increased risk of bleed, there are no specific dosing guidelines for PPI dosing and duration. Some general recommendations are below.

- PPIs should be used only for the duration of the DAPT and if the patient's bleeding risk continues to be high.
  - **Patient risk factors should be continuously re-evaluated to ensure appropriateness of PPI use. If risk factors are no longer present, discontinuation of the PPI may be appropriate.**
- Administration of PPI should be separated from $P2Y_{12}$ receptor inhibitor administration by at least 2 hours[1].
  - The plasma half-life of both drugs is less than 2 hours, so the risk of potential drug interactions will be minimized by separating the administration.
- Lansoprazole[5] and esomeprazole[6] are FDA approved for the primary prevention of nonsteroidal anti-inflammatory drugs (NSAIDs) (including aspirin)-induced ulcers in patients who are at an increased risk of GI bleeds.
  - This group includes patients taking DAPT (aspirin with a P2Y12 receptor inhibitor).
- A drug-drug interaction exists between omeprazole/esomeprazole and clopidogrel, avoid this medication combination[7].
  - Consider pantoprazole as an alternative therapy[8]

Appendix 1. *American College of Cardiology's* DAPT Risk Calculator[3]

Link to website: *https://tools.acc.org/daptriskapp/#!/content/calculator/*

The *American College of Cardiology*'s DAPT Risk Calculator is a tool used to assess the risk of bleeding for a patient compared to their ischemic risk.

The tool was created using patients who:

- Completed 12 months of DAPT
- Did not have any major bleeding or ischemic events
- Were not on chronic anticoagulation

The tool is recommended by the ACC to be used for guidance for DAPT, not as a recommendation for or against any medical treatment.

Using the calculator

The calculator will first ask you to input certain patient characteristics:

- Age
- Medical history
  - Diabetes mellitus
  - Prior myocardial infarction or percutaneous coronary intervention
  - Hypertension
  - Peripheral arterial disease
  - Cigarette smoking within the last two years
  - History of congestive heart failure or left ventricular ejection fraction of <30%
  - Renal insufficiency
- Procedure characteristics
  - Myocardial infarction at presentation
  - Stent diameter <3mm
  - Stenting of vein graft

After inputting the characteristics, the tool will then show results:

- Assigns patients a score from -2 through 9, representing the benefit-to-risk ratio of utilizing DAPT
  - -2 shows a higher bleeding risk.
    - **Lower scores suggest an unfavorable benefit/risk ratio.**
  - 9 shows a higher ischemic risk.
    - **Higher scores suggest a more favorable benefit/risk ratio of prolonged DAPT use**.
- Risk of the following events if DAPT is continued or if DAPT is discontinued
  - Stent thrombosis/myocardial infarction
  - Major adverse cardiovascular & cerebrovascular events (MACCE)
  - Moderate to severe bleeding based on GUSTO criteria
- The change in risk if DAPT is continued at 12-30 months minus discontinued treatment at 12-30 months

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