5 Antiplatelet and Antithrombotic Therapy in Percutaneous Coronary Interventions

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Introduction

Dual antiplatelet therapy (DAPT) is the cornerstone of pharmacological therapy preventing atherothrombotic complications. Advances in drug-eluting stent technology, antiplatelet pharmacotherapy, and novel parenteral and oral anticoagulants (OAC) have led to constant evolution in periprocedural antithrombotic strategy. The following chapter outlines our cardiac catheterization laboratory's current approach to antiplatelet and anticoagulation therapy in various clinical settings based on current guidelines and expert opinion.

Oral Antiplatelet Therapy

Aspirin: All Patients

- For elective patients, with or without known stable CAD, aspirin 162 mg should be given at the time of obtaining consent.
- For ACS (acute coronary syndrome) patients, non-enteric aspirin 325 mg should be given as early as possible before PCI [1].
- Post-PCI, aspirin 81 mg daily should be continued indefinitely.

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Dual Antiplatelet Therapy

- All patients should be counseled on the necessity and concomitant risk associated with dual antiplatelet therapy (DAPT) before placement of intracoronary stents.
- For patients unable or unwilling to comply with the recommended duration of DAPT, alternative revascularization (bypass) or bare-metal stents (BMS) should be considered.

P2Y12 Antagonist Therapy

- Pre/intra-procedural loading doses for patients *not previously taking the same* $P2Y_{12}$ receptor inhibitor for ≥5 days:
  - Clopidogrel 600 mg.
  - Prasugrel 60 mg.
  - Ticagrelor 180 mg.
- Loading doses for patients *already taking the same* $P2Y_{12}$ receptor inhibitor for ≥5 days:
  - Clopidogrel 300 mg.
  - Prasugrel 30 mg.
  - Ticagrelor 90 mg.
- Platelet Reactivity Unit (PRU) should be checked in patients presenting with stent thrombosis. For clopidogrel *nonresponders* (with confirmed compliance), defined as PRU >230, load with prasugrel 60 mg or ticagrelor 180 mg.

Parenteral $P2Y_{12}$ Inhibitor – Cangrelor [2, 3]

- Only parenteral P2Y12 inhibitor.
- Onset-2 mins, offset of action-1 hour.
- Current Indications for IV Cangrelor use.
  - Bridge for elective non-cardiac surgery in a patient requiring DAPT (1-3 M or 6 M of DES, Table 5.1).
  - MI/ACS with hemodynamic instability and poor absorption status; Cardiogenic shock, Intubated.
  - ACS and SIHD PCI with multiple high-risk angio features (bifurcation, thrombus, 3+ stents, Ca+).
  - MI/ACS patient awaiting cardiac surgery or urgent non-cardiac surgery (hip fracture, GI surgery).
  - ACS patient with clinical presentation suggestive of CABG (marked ST-segment depression, known extensive CAD).

Table 5.1 Recommendation for bridging DAPT before surgery in recent PCI/stent, 0–1 M post stent placement, or 1–6 M from high-risk stent[a]

P2Y12 inhibitor	Surgery to be performed on ASA	Surgery to be performed on no antiplatelet
Clopidogrel or Ticagrelor	Stop P2Y12 inhibitor 5 days prior to surgery	Stop ASA 5 days prior to surgery.
		Stop P2Y12 inhibitor 10 days prior to surgery
	Start cangrelor[b] 3 days prior to surgery	Start cangrelor 7 days prior to surgery
Prasugrel	Stop P2Y12 inhibitor 7 days prior to surgery	Stop ASA 5 days prior to surgery.
		Stop P2Y12 inhibitor 14 days prior to surgery
	Start cangrelor 3 days prior to surgery	Start cangrelor 10 days prior to surgery

[a]LM, bifurcation with 2 stents, multivessel, long/diffuse disease
[b]Cangrelor dose: 0.75 μg/kg/min infusion without a bolus

Table 5.2 Switching to oral P2Y12 inhibitor in high-risk PCI patients on IV Cangrelor

Patient condition	Cangrelor dose	Antiplatelet to be restarted one pt. condition resolves: FOLLOW-ON ORAL DRUG
Patient unable to take PO or acute intracoronary thrombosis or cardiogenic shock or hemodynamic compromise with active consideration for LVAD escalation	30 μg/kg bolus and 4 μg/kg^{-1}/min^{-1} infusion for at least 2 h or duration PCI. Continue cangrelor at a rate of 0.75 μg/kg^{-1}/min^{-1} until patient can take PO or until shock resolves	Clopidogrel: 600 mg immediately after discontinuation of cangrelor
		Ticagrelor: 180 mg at any time during cangrelor infusion or immediately after discontinuation of cangrelor
		Prasugrel: 60 mg immediately after discontinuation of cangrelor

- Recommended dose: 30 mcg/kg IV bolus followed by 4 mcg/kg/min IV infusion, continue for at least 2 hours or the duration of the procedure, whichever is longer.
- Transition to oral P2Y12 inhibitor (Table 5.2):
  - Ticagrelor 180 mg at any time during cangrelor infusion or immediately after discontinuation.
  - Clopidogrel 600 mg or prasugrel 60 mg after cangrelor discontinuation as their antiplatelet effect will be attenuated due to competitive inhibition.

Special Considerations

- Clopidogrel is considered the default P2Y12 inhibitor of choice in patients with [4, 5]:
  - SIHD treated with PCI.
  - Concomitant OAC.
  - ACS patients in whom ticagrelor or prasugrel are contraindicated.
  - Drug intolerance/adverse effects to other P2Y12 inhibitors.
  - High bleeding risk.
- Prasugrel (contraindicated in patients with a history of TIA/CVA and avoided in patients weighing <60 kg or ≥ 75 years of age) should be preferred in the following clinical situations:
  - STEMI undergoing PCI.
  - High-risk coronary anatomy.
  - Clopidogrel allergy.
  - Clopidogrel nonresponder (PRU >230 on maintenance dose of clopidogrel).
  - Stent thrombosis on clopidogrel.
- In patients >75 years old or with history of TIA/CVA, or weighing <60 kg, ticagrelor should be preferred in the following clinical situations:
  - ACS (STEMI/NSTEMI) patients irrespective of PCI.
  - Complex PCI.
  - Clopidogrel allergy.
  - Clopidogrel nonresponder (PRU >230 on maintenance dose of clopidogrel).
  - Stent thrombosis on clopidogrel.
- For pre-liver or renal transplant patients, DES is preferred with a shorter duration of DAPT [5].
- Ticagrelor can be used as a monotherapy in selected patients with aspirin allergy or intolerance.

Duration and Switching of DAPT

- All ACS patients should receive 12 months of DAPT (Fig. 5.1).
- Non-ACS patients receiving DES should receive a minimum of 6 months of DAPT.
- Prolonged DAPT beyond 12 months may be considered in patients tolerating therapy without bleeding issues, with a complex disease requiring multiple stents, and/or significant residual CAD. Ticagrelor in a dose of 60 mg BID is the preferred P2Y12 inhibitor [6].
- Shorter DAPT <6 months should be considered in patients who are at HBR or had significant overt bleeding (Table. 5.3).
- Multiple studies with newer-generation DES have shown a shift towards shorter standard DAPT post-PCI in HBR individuals. 1–3 months of DAPT may ensure sufficient protection from stent thrombosis reducing the risk of bleeding [7, 8].

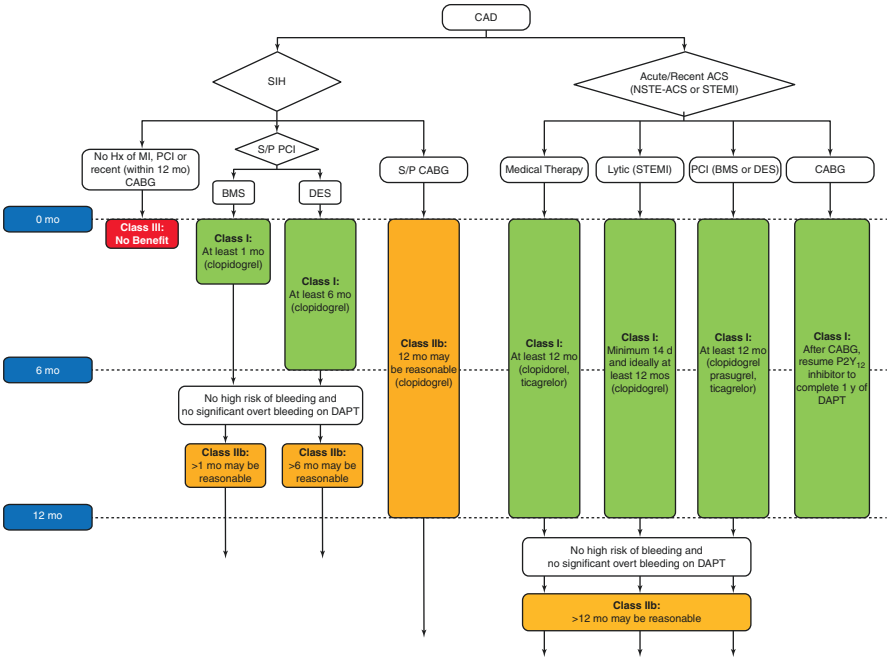


Fig. 5.1 Algorithm for current recommendations for the duration of DAPT. (Adapted from the 2016 ACC/AHA Guideline Focused Update on DAPT [4])

Table 5.3 Factors to consider when deciding the duration of DAPT

Favoring prolong DAPT	Favoring short DAPT/ HBR
Prior stent thrombosis on adequate Antiplatelet therapy	Any intracerebral bleed
Chronic kidney disease (CrCl <60 ml/min)	Clinical indication for anticoagulation
Multivessel disease in diabetics	Steroid use >30 days after PCI
≥3 stents implanted	Hospital admission for bleeding during the prior 12 months
Bifurcation with 2 stents implanted	Blood dyscrasia
Total stent length > 60 mm	History of bleeding diathesis
In-stent restenosis	Hgb <11 g/dl (or transfusion in <1 month prior)
Stenting of the last remaining patent coronary artery	Thrombocytopenia (Plt <100 K)
Multiple prior MIs	Ongoing malignancy with high bleeding Potential
CTO	Chronic alcohol abuse
	Low body weight
	ESRD
	Advanced age

Adapted from Capodanno et al. [9]

- DAPT and PRECISE-DAPT scores are helpful in decision making regarding the duration of DAPT beyond 12 months. DAPT score ≥ 2 points and PRECISE-DAPT score < 25 favors a standard or long DAPT duration and vice versa [5].
- Combined dosing for P2Y12 antagonists with aspirin 81 mg daily:
  - Clopidogrel 75 mg orally once daily.
  - Prasugrel 5 mg orally once daily (10 mg daily in patients >100 kg).
  - Ticagrelor 90 mg orally twice daily.
- Switching among different P2Y12 inhibitors, see Fig. 5.2.

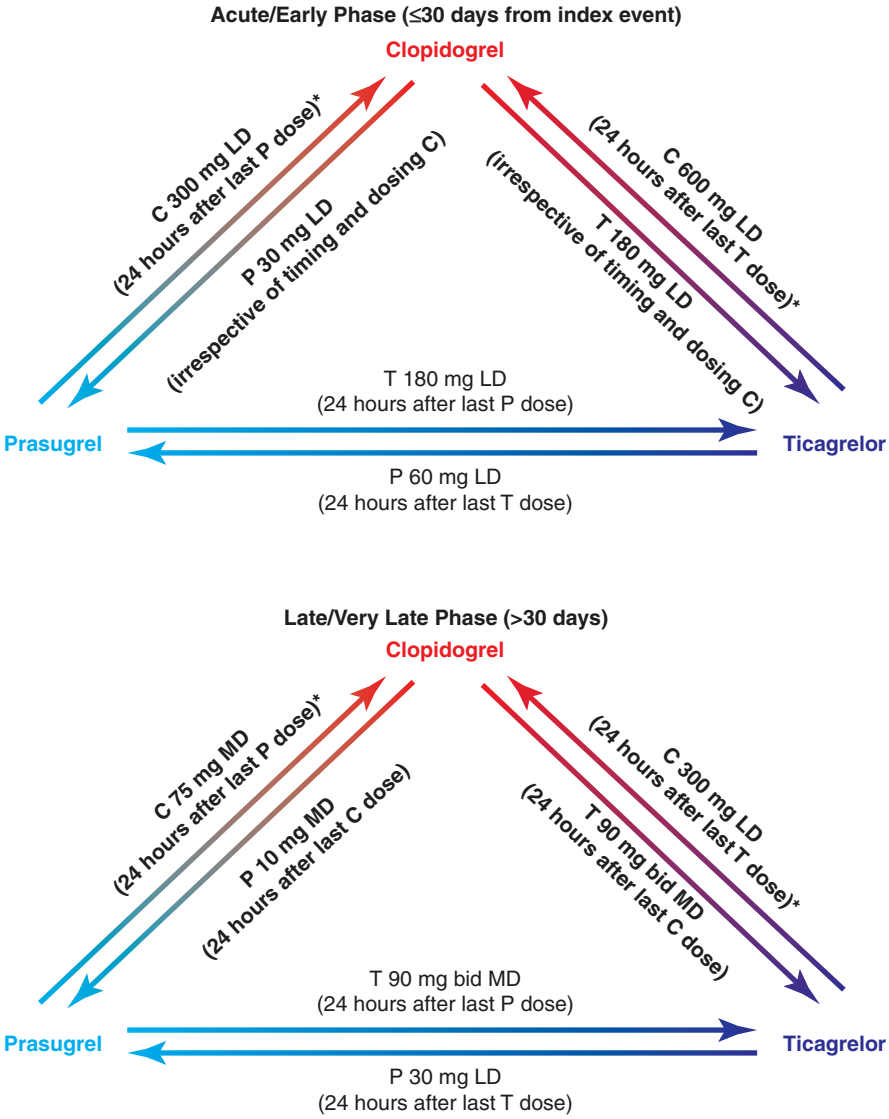


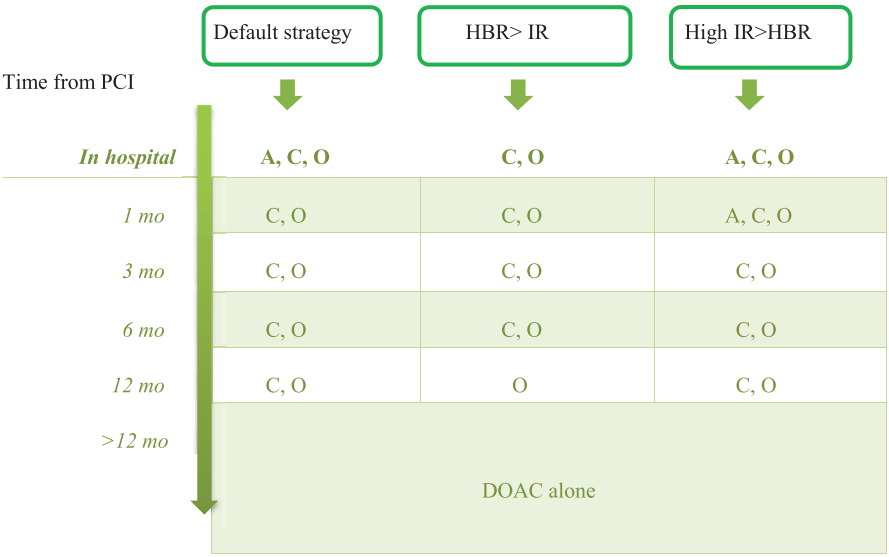
Fig. 5.2 Switching among different P2Y12 inhibitors. (Adapted from International Expert Consensus on Switching Platelet P2Y12 Receptor-Inhibiting Therapies [10])

Antiplatelet Therapy in PCI Patients Requiring Oral Anticoagulation

- Managing optimal antithrombotic therapy is a clinical conundrum. Numerous studies have shown single antiplatelet therapy (SAPT) preferably, clopidogrel in combination with DOACs provides better safety compared with a regimen with VKA and is the mainstay of therapy. Triple antithrombotic therapy (TAT) is associated with high bleeding risk and should be avoided except in rare patients at higher risk of ischemic events.
- DOACs should be preferred to VKA.
- No need to hold OAC in urgent or emergent procedures.
- Withhold DOAC 24 hours before an elective procedure, 48 hours if a patient has renal dysfunction.
- Recommended doses of DOACs:
  - Rivaroxaban 15 mg OD, 10 mg od in renal dysfunction.
  - Dabigatran 150 mg BID, 110 mg BID in age > 70 yrs.
  - Apixaban 2.5 mg BID.
- VKA (Coumadin) is indicated only in patients with [9]:
  - Moderate to severe mitral stenosis.
  - Mechanical prosthetic heart valves.
- All patients are loaded with aspirin and P2Y12 antagonist, regardless of the long-term anticoagulant requirement.
- In patients at higher risk for bleeding, clopidogrel is preferred as the initial P2Y12 antagonist of choice. If the patient is a clopidogrel nonresponder, ticagrelor is the next preferred option. Prasugrel is not recommended [9].
- For the duration of antiplatelet therapy in the setting of long-term anticoagulation, see Fig. 5.3.
- Post-PCI resumption of anticoagulant therapy:
  - Warfarin should be dosed the same day/evening due to an expected delay in achieving therapeutic INR (2–2.5).
  - DOACs should be dosed the following day unless there is a compelling indication for immediate resumption (Fig. 5.3) [11].
  - In patients with compelling indications requiring immediate anticoagulation (or re-bridge to oral anticoagulation) post-PCI, such as acute venous/pulmonary thromboembolism or mechanical valve, a heparin drip may be started without bolus 2 hours post-PCI with successful hemostasis using a closure device or 6 hours after sheath pull with successful hemostasis using manual compression or after a radial procedure.

Anticoagulation for PCI

- Administer bivalirudin bolus (0.75 mg/kg) via the intra-arterial sheath and begin continuous infusion (1.75 mg/kg/h).
- Check activated clotting time (ACT) 3 min after bolus:
  - For ACT <270, administer an additional 1/2 bolus of bivalirudin.



IR= Ischemic risk, HBR= High bleeding risk, A= Aspirin, C= Clopidogrel, O= Oral anticoagulation

Fig. 5.3 Current recommendations for the management of OAC and Antiplatelet Therapy in Patients with AF undergoing PCI. (Adapted from Capodanno et al. JACC 2019 [11])

  - For ACT 270–299, administer an additional 1/3 bolus of bivalirudin.
  - The guiding catheter may be inserted once ACT>200.
  - Intracoronary guidewire/equipment may be inserted once ACT >300.
- Post-PCI:
  - For patients naïve to clopidogrel (on therapy <1 week or receiving the first time load of 600 mg <2 hours before PCI), bivalirudin infusion should be continued for 2 hours from the time of stent implantation.
  - For patients receiving prasugrel or ticagrelor (on maintenance therapy or receiving the first time load on the table), bivalirudin infusion can be discontinued as soon as the PCI is completed.
  - For patients requiring a periprocedural glycoprotein (GP) IIb/IIIa inhibitor bolus, bivalirudin infusion can be stopped after administration of the GP IIb/IIIa bolus.

Elective Non-cardiac Surgery after PCI [5]

- Defer elective surgeries requiring discontinuation of the P2Y12 inhibitor for at least 1–3 months.
- Continue Aspirin perioperatively.
- Surgical procedures mandating interruption of DAPT perioperatively, a bridging strategy with cangrelor or GP IIb/IIIa may be considered, especially if performed within 1 month of PCI.

Role of Glycoprotein (GP) IIb/IIIa Inhibitors [13]

- GP IIb/IIIa antagonist administration for bailout purposes only.
- At the discretion of the operator, single (or double) bolus eptifibatide (single = 180 mcg/kg) may be administered in cases of edge dissection, side branch closure, slow flow, no-reflow, embolization, and large thrombus.
- For patients receiving abciximab, the platelet count should be checked 3 hours post-procedure and the following morning.
- For patients receiving eptifibatide, the platelet count should be checked 6 hours post-procedure and the following morning.
- GPIIb/IIIa infusion should be discontinued if significant thrombocytopenia develops (platelets <100 K).

Managing Thrombocytopenia Post-PCI

Platelets <20 K

- Discontinue all antiplatelet therapies.
- Transfuse 5 or more units of platelets until platelet count >20 K.
- Aspirin 81 mg and clopidogrel 75 mg can be resumed once platelet count >50 K.
- Platelet count should be checked daily until >70 K.

Platelets 20–50 K

- Discontinue GP IIb/IIIa inhibitor.
- Transfuse platelets only for active bleeding.
- Aspirin 81 mg and clopidogrel 75 mg can be resumed once platelet count >50 K.

Platelets 50–100 K

- Discontinue GP IIb/IIIa inhibitor.
- Aspirin 81 mg and clopidogrel 75 mg can be continued as long as platelet count remains >50 K.

Future Directions

Aspirin free-strategies 1–3 months post-PCI have shown encouraging results in several studies, thereby significantly reducing the incidence of bleeding events, without altering the ischemic risk [12]. Individualization of DAPT duration particularly in HBR patients appears therefore mandatory, making aspirin not necessary in several cases. Ongoing studies may potentially shift the paradigm of antiplatelet therapy after PCI in the near future.

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