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Brief Reviews

Managing Anticoagulation and Dual Antiplatelet Therapy in Patients with Active Bleed or Upcoming Procedure: A Scoping Review

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Introduction: The aim of this paper is to provide primary care providers and hospitalists with up-to-date guidance surrounding the management of anticoagulation and antiplatelet agents in periprocedural settings and when unexpected bleeding complications arise. **Methods:** We searched PubMed, Cochrane CENTRAL, and Web of Science using applicable MeSH terms and keywords. No date limits or filters were applied. Articles cited by recent cardiovascular guidelines were also utilized. **Results:** For direct oral anticoagulants (DOACs) and vitamin K agonists (VKAs), a patient's risk for clot and procedural risk of bleeding should be assessed. Generally, patients considered at high risk for venous thromboembolism (VTE) should be bridged, patients at low risk should forgo bridging therapy, and patients in the intermediate range should be evaluated on a case-by-case basis. Emergent anticoagulation reversal treatment is available for both warfarin (i.e., prothrombin complex concentrate, phytonadione) and DOACs (i.e., idarucizumab for dabigatran reversal; andexanet alfa for apixaban and rivaroxaban reversal). DAPT does not need to be held for paracentesis or thoracentesis and is low risk for those needing urgent lumbar punctures. In patients with clinically significant bleeding, those with percutaneous coronary intervention (PCI) performed in the last three months should resume DAPT as soon as the patient is hemodynamically stable, while patients greater than three months out from PCI at high risk of bleed can be de-escalated to single antiplatelet therapy. **Conclusions:** Appropriate management of anticoagulation and antiplatelet agents in the periprocedural setting and patients with active bleed remains critical in inpatient management.

PERIPROCEDURAL MANAGEMENT OF PATIENTS ON ORAL ANTICOAGULATION

The periprocedural management of patients receiving chronic therapy with oral anticoagulants (ACs) is a common clinical problem. The most common indications for oral ACs are atrial fibrillation (AF), the presence of a mechanical heart valve, and venous thromboembolism.[1] When to hold oral ACs and whether to utilize a bridging AC therapy to shorten the period a patient is not receiving therapeutic anticoagulation to minimize the risk of thromboembolic events and bleeding are challenging decisions often faced by clinicians. Patient-related risk factors for thrombosis and procedural risks for bleeding should be risk-stratified to determine a patient's periprocedural anticoagulation management plan.

PATIENT RISK-STRATIFICATION

A summary of patient risk stratification can be seen in **Table 1**. In general, patients considered at high risk for venous thromboembolism (VTE) should be bridged, patients at low risk of VTE should forgo bridging therapy, and patients with intermediate-risk should be evaluated on a case-by-case basis. Patients at the highest risk of thromboembolism who would benefit from bridging therapy are those with a CHA2DS2Vasc risk score ⩾7, patients with recent stroke or transient ischemic attack (TIA (<3 months prior), rheumatic valvular heart disease and AF, mechanical mitral valve, those with known prothrombotic conditions, and active malignancies with high VTE risk.[2]

PATIENTS WITH ATRIAL FIBRILLATION

AF is the most common indication for long-term anticoagulation and often does not require bridging therapy. The

Table 1. Patient thromboembolic risk stratification.

Risk Category	Atrial Fibrillation	Mechanical Heart Valve	Venous Thromboembolism
High	CHA_2DS_2Vasc score ≥7 Recent (< 3 months) stroke or TIA Rheumatic valvular heart disease	Mechanical mitral valve (particularly with recurrent stroke, perioperative stroke, or valvular thrombosis)	Recent (< 3 months) VTE Deficiency of protein C, protein S, or antithrombin Antiphospholipid antibodies High thrombotic risk cancer (pancreatic, brain, gastric, esophageal cancer or myeloproliferative disorder) Apical LV thrombus
Intermediate	CHA_2DS_2Vasc score = 5–6	Bileaflet mechanical aortic valve with major risk factors for stroke	VTE within the past 3-12 months Recurrent VTE Active cancer or recent history of cancer Non-severe thrombophilia (Heterozygous factor V Leiden, heterozygous prothrombin gene mutation)
Low	CHA_2DS_2Vasc = 1–4 (and no prior stroke or TIA)	Bileaflet mechanical aortic valve without major risk factors for stroke	VTE more than 12 months ago

Abbreviations: TIA – transient ischemic attack; VTE – venous thromboembolism
Note: CHA_2DS_2Vasc – congestive heart failure (1), hypertension (1), age >75yo (2), diabetes mellitus (1), stroke (2), vascular disease (1), age > 65 yo (1), female gender (1)

BRIDGE trial showed that in patients on warfarin for either valvular or non-valvular AF who needed treatment interruption for an elective procedure, there was no difference in the rate of acute thromboembolism between bridging and no-bridging strategy. Not bridging was associated with a significantly lower risk of major bleeding. Notably, this study excluded patients with mechanical heart valves, stroke, embolism, TIA, or major bleeding within 12 weeks of the study.[3] Similarly, a meta-analysis of 34 studies on periprocedural anticoagulation management showed no significant difference in the rate of periprocedural thromboembolism between patients who received bridging and those who did not. However, bridging significantly increased the risk of major bleeding.[4]

The CHA2DS2-VASc score is widely used to assess stroke risk in patients with AF, and the CHEST guidelines recommend its use.[5,6] Patients with a CHADS2-VASC score of 5 or 6, recent stroke or transient ischemic attack (TIA), or rheumatic valve disease are considered high risk for thromboembolic events. Patients considered moderate risk are those with a CHADS2-VASC score of 3 or 4. Those considered low risk have a score of 0-2 without a history of stroke or TIA.[7] Selection of AC therapy should be based on the risk of thromboembolism irrespective of the pattern of AF (paroxysmal, persistent, or permanent).[8,9]

Percutaneous left atrial appendage occlusion (LAAO) has been compared with warfarin in patients with non-valvular AF in two randomized control trials (PROTECT AF and PREVAIL), demonstrating fewer hemorrhagic strokes. Patients with a history of intracranial hemorrhage who are at high risk of recurrent bleeding (i.e., cerebral amyloid angiopathy) should undergo left atrial appendage occlusion with WATCHMAN (Boston Scientific, Boston, MA) or Amulet (Amplatzer Abbott, Chicago, IL) rather than using anticoagulation.[10] A clinical trial directly compared the two devices and found similar clinical outcomes at 45 days. However, AMULET was associated with more periprocedural complications.[11] LAAO may also be considered in patients with AF at increased risk of stroke but contraindication to anticoagulation due to a history of major bleed.[12]

AC management for stroke and thromboembolism in patients with AF must be adjusted for patients who become pregnant. Warfarin and other vitamin K antagonists cross the placenta and are teratogenic; therefore, they should be avoided if possible. Low molecular weight heparin is generally the preferred AC during the early stages of pregnancy. It is replaced by unfractionated heparin during weeks 26 to 38 to minimize the risk of going into labor while on a longer-acting AC.[10]

PATIENTS WITH MECHANICAL HEART VALVES

Patients with mechanical heart valves (MHV) often require bridging to avoid thrombosis, stroke, and arterial embolization. Direct oral anticoagulants (DOACs) are not currently approved or recommended for use with mechanical heart valves.[13,14] The RE-ALIGN study assessed the efficacy and safety of dabigatran relative to warfarin for stroke prevention in patients with MHV and AF. It was terminated early due to higher rates of ischemic stroke with dabigatran.[15]

Mechanical valves in the aortic position are at lower risk for thromboembolism due to the high flow environment, while mechanical mitral, tricuspid, or pulmonary valves are considered higher risk. One study found that a prosthesis in the mitral position had almost double the risk of throm-

boembolism compared with the aortic position.[16] Right-sided mechanical valves have a nearly 20 times greater thrombosis rate than left-sided mechanical values, likely due to lower flow rates.[17] The American College of Chest Physicians Guidelines recommend long-term vitamin K antagonist (VKA) therapy for all mechanical valves with a target international normalized ratio (INR) of 2.5 for aortic and 3.0 for mitral valves.[18] The American College of Cardiology and the American Heart Association (ACC/AHA) 2020 Guidelines also recommend an INR goal of 3.0 for mechanical mitral valves as well as for patients with mechanical aortic valve replacement (AVR) with additional risk factors for thromboembolism (AF, prior thromboembolism, left ventricular dysfunction, hypercoagulable state) an INR goal of 3.0 is recommended.[19]

There is no unified consensus on the perioperative management of mechanical valves; hence bridging strategies may vary by institution.[20] The 2020 ACC/AHA Guidelines for Management of Patients with Valvular Heart Disease states patients with mechanical heart valves undergoing minor procedures (i.e., dental extraction or cataract removal), the continuation of VKA anticoagulation with a therapeutic INR is recommended. However, they recommend that patients with mechanical AVR plus any thromboembolic risk factor or a mechanical mitral valve replacement should receive bridging therapy during the preoperative interval if the INR is subtherapeutic. The risk of bleeding must be weighed against the benefits of thromboembolism prevention on an individual basis. Patients who require emergency noncardiac surgery or an invasive procedure can be given prothrombin complex concentrate.[21] In the postoperative period, the PERIOP2 trial found no significant benefit in patients with AF or mechanical heart valves on low molecular weight heparin bridging back to warfarin in reduction of the incidence of VTE.[22]

PATIENTS WITH DEEP VEIN THROMBOSIS AND VENOUS THROMBOEMBOLISM

Venous thromboembolism (VTE), including deep vein thrombosis (DVT) and pulmonary embolism (PE), occurs in 1 to 2 individuals per 1000 each year. The American Society of Hematology 2020 guidelines recommend home treatment over hospital treatment for uncomplicated DVT and PE with a low risk of complications based on the Pulmonary Embolism Severity Index (PESI) score. DOACs are first-line treatment for venous thromboembolism due to a lower risk of bleeding than VKA and greater ease of use.[23,24]

AC treatment should be continued for at least three months to prevent early recurrences. Longer periods of anticoagulation should be considered for proximal DVTs if VTE was unprovoked or for secondary persistent risk factors.[25,26] The American Society of Hematology 2020 guidelines recommend indefinite anticoagulation in a patient with unprovoked DVT or PE.[25] Use of thrombolysis should be limited to pulmonary embolism associated with hemodynamic instability.[25,26] Instances of PE with positive cardiac biomarkers (serum troponin I, B-type natriuretic peptide) or echocardiographic evidence of right ventricular dysfunction without hemodynamic compromise (submassive PE), anticoagulation alone is recommended. The Society of Interventional Radiology outlines the indications of IVC filters to include documented VTE with contraindication to anticoagulation, complications of anticoagulation necessitating cessation, failure of anticoagulation, or progression of VTE during therapeutic anticoagulation.[27]

Patients with inherited or acquired thrombophilias and those with recurrent VTEs within three months will require bridging. Low-risk patients are those without thrombophilia and an episode of VTE more than 12 months ago.[7,28] Barnes et al. evaluated the use of periprocedural bridging anticoagulation based on recurrent VTE risk. They found that bridging anticoagulation was commonly overused among low-risk patients and underused among high-risk patients treated with warfarin for VTE.[29]

PATIENTS WITH ANTIPHOSPHOLIPID ANTIBODY SYNDROME AND HIGH-RISK PROTHROMBOTIC CONDITIONS

Several inherited thrombophilias increase the risk of thromboembolism, including antiphospholipid antibody syndrome, factor V Leiden, protein S deficiency, protein C deficiency, and antithrombin deficiency. Factor V Leiden does not change the recommended length of treatment in provoked DVT beyond three months, and indefinite anticoagulation is recommended for unprovoked VTE. Primary prophylaxis in carriers (heterozygotes and homozygotes) without symptoms is not recommended.[30]

The Annual European Congress of Rheumatology provides AC recommendations for managing antiphospholipid antibody syndrome. They include low-dose aspirin for primary prophylaxis in antiphospholipid antibody carriers and long-term treatment with VKA for an unprovoked VTE with an INR goal of 2-3.[31] The use of low-dose aspirin for primary thrombosis prevention is controversial, as DOACs are not recommended in these patients.[32,33] The RAPS trial showed that antiphospholipid antibody patients treated with rivaroxaban had a significant twofold-increased thrombin potential, suggesting a higher thrombotic risk when compared to warfarin users.[34] This finding was further supported by a meta-analysis of four open-label randomized control trials of patients with antiphospholipid antibody syndrome that showed those randomized to DOACs (versus warfarin) had higher thrombosis rates.[35]

For patients with protein C deficiency who develop VTE and decide to pursue warfarin for therapy, special attention must be made to prevent warfarin-induced skin necrosis caused by transient hypercoagulability during warfarin initiation. Suggestions include the utilization of a DOAC, a lower-than-average starting dose of warfarin, and a longer duration of overlapping heparin administration.[36,37]

DIRECT ORAL ANTICOAGULANTS (DOACS) VS. VITAMIN K ANTAGONIST (VKA)

Several studies that assessed the periprocedural risk of thromboembolism and bleeding in patients on DOACs vs. warfarin have found no significant difference. The RE-LY trial compared dabigatran to warfarin, the ROCKET AF trial compared rivaroxaban to warfarin, and the ARISTOTLE trial compared apixaban to warfarin.[4,38,39] One of the advantages of DOACs is the short preoperative time on subtherapeutic anticoagulation. Warfarin generally requires holding five days before a procedure. DOACs can be stopped one day before a low bleeding-risk procedure and two days before a high bleeding-risk procedure.[40] The PAUSE trial found no increased risk of thromboembolism or bleeding in patients with AF who had their DOAC therapy interrupted prior to an elective procedure.[41] This is also supported by the American Society of Regional Anesthesia guidelines.[42]

Per the AHA/ACC/HRS (Heart Rhythm Society) Guidelines for the Management of Patients with Atrial Fibrillation, DOACs are non-inferior or superior to warfarin in preventing stroke or thromboembolism. They note that apixaban has a lower risk of bleeding (including intracranial hemorrhage), and the risk of bleeding for rivaroxaban is comparable to warfarin.[12] CHEST guidelines favor DOACs over warfarin for non-valvular AF, but patient preferences and cost should be incorporated into clinical decision-making.[10] If warfarin is used for non-valvular AF, an INR goal of 2.0-3.0 should be used.

PROCEDURE RISK STRATIFICATION

High bleeding-risk procedures include those with extensive tissue injury, cancer surgery, orthopedic surgery, reconstructive plastic surgery, vascular surgery, urologic, GI surgery, surgery in highly vascular organs including kidneys, liver, spleen, cardiac surgery, intracranial or spine surgery.[43] Low bleeding-risk procedures include ophthalmologic, dental, and dermatological procedures, hernia repair or laparoscopic cholecystectomy, colonoscopy, or endoscopy.[44] Although standardized definitions for bleeding exist, they yet to be consistently applied to studies evaluating procedural risk, and thus most recommendations on procedural risk are based on expert consensus.[43,45] A summary of procedure risk-stratification can be seen in **Table 2**.

EMERGENT ANTICOAGULATION REVERSAL

In the event of a life-threatening bleed or urgent procedure, rapid reversal of warfarin can be performed with prothrombin complex concentrate (PCC), fresh frozen plasma (FFP), or IV Vitamin K1 (phytonadione). IV vitamin K1 has a time of onset of 1-2 hours, while oral vitamin K1 has a 6–10-hour delay before onset.[46] For patients with severe, life-threatening bleeding, PCC is recommended, as well as IV vitamin K1 for warfarin reversal. PCC is recommended for urgent surgery/procedures that need to be performed on the same day. Patients who can wait 24 hours prior to surgery are recommended to use vitamin K1.[47]

Idarucizumab is recommended to reverse dabigatran, and andexanet alpha has been used to reverse apixaban and rivaroxaban.[12] Both the ANNEXA-A and ANNEXA-R trials demonstrated thrombin generation of 100% and 96% after an andexanet bolus in patients taking apixaban and rivaroxaban, respectively, without adverse clinical effects.[48] If these specific DOAC reversal agents are unavailable, nonspecific agents such as PCC, FFP, or desmopressin can be given.[49]

DUAL ANTI-PLATELET THERAPY

MANAGING DAPT-ASSOCIATED BLEEDING

Patients who receive a coronary stent must be started on dual antiplatelet therapy (DAPT) for 6-12 months to prevent stent thrombosis. Approximately 1 in 20 post-percutaneous coronary intervention (PCI) patients are hospitalized for bleeding complications, with most cases occurring within the first 30 days.[50] Therefore, the safety of stopping versus continuing antiplatelet therapies while managing an acutely ill patient is a commonly faced dilemma.

ONE MONTH AFTER PCI

DAPT-associated bleeding is a challenging clinical scenario where clinical evidence guiding management is lacking. The PARIS registry showed that patients who were non-adherent with DAPT 30 days after PCI were approximately 2-3 times more likely to have a major adverse cardiac event or spontaneous myocardial infarction.[51] However, in a patient presenting with clinically significant bleeding, the risk versus benefit of antiplatelet therapy should be assessed with each clinical scenario. Resuming DAPT as soon as possible after bleeding is controlled in patients who have undergone PCI within three months is generally recommended. Recent advances in stent technology (Xience, Onyx) have allowed for only one month of DAPT.[52]

THREE MONTHS AFTER PCI

After three months post-PCI, emerging data suggest replacing DAPT with anti-platelet monotherapy in high-bleeding risk patients has favorable outcomes. The TWILIGHT trial assessed bleeding, death, and other adverse events in patients three months after PCI on ticagrelor monotherapy vs. ticagrelor and aspirin. Patients taking ticagrelor alone had a lower incidence of bleeding without a higher risk of myocardial infarction, stroke, or death.[53] The EVOLVE Short DAPT study further investigates patients who received 2nd generation SYNERGY everolimus-eluting stents and found that aspirin monotherapy had similar outcomes to those who continued DAPT for 12 months.[54] Therefore, high bleeding risk patients may benefit from anti-platelet therapy de-escalation three months post-PCI.

Table 2. Risk stratification of procedure-related bleeding risk

Low Bleeding Risk Procedures	High Bleeding Risk Procedures
Dental extraction/restoration/fillings	Cancer surgery
Cutaneous biopsies	Reconstructive plastic surgery
Lymph node biopsies	Major orthopedic surgery
Cataract, glaucoma surgery	Urologic or gastrointestinal surgery (ie. bowel resection)
Coronary angiography	Surgery on higher vascular organs (kidneys, liver, spleen, prostate) (i.e. nephrectomy, kidney or liver biopsy)
Pacemaker or cardioverter-defibrillator device implantation	Cardiac surgery, thoracic surgery, lung resection
Laparoscopic cholecystectomy	Intracranial or spinal surgery (including spinal epidural anesthesia)
Abdominal hernia repair, colon resection	Vascular surgery (ie. abdominal aortic aneurysm, vascular bypass)
Abdominal hysterectomy	
Colonoscopy and endoscopy	
Bronchoscopy	
Hemorrhoidal surgery	
Foot/hand surgery	
Breast surgery	

SIX TO TWELVE MONTHS AFTER PCI

In high-bleeding risk patients, reducing total DAPT duration has shown promising results. The American College of Cardiology and European Society of Cardiology recommend stratifying patients into low and high-bleeding risk categories. In patients who received a drug-eluting stent (DES) for ischemic heart disease without acute coronary syndrome, DAPT duration can be reduced to 3-6 months. This comes with the benefit of reduced clinically significant bleeding events (OR: 0.63 [95% CI: 0.52 to 0.75]; $p < 0.001$] but with a higher risk of ischemic events (OR: 1.54 [95% CI: 0.96 to 2.47]. Overall shorter duration of DAPT in high bleeding risk patients suggested a potential reduction in all-cause mortality (OR 0.87 [95% CI 0.74 to 1.01]; $p = 0.073$.[55] Patients who received a DES for acute coronary syndrome should ideally complete a minimum of twelve months of DAPT before transitioning to antiplatelet monotherapy. However, in high bleeding-risk patients or patients that develop a clinically significant bleeding event, the American College of Cardiology suggests six months of DAPT is acceptable before transitioning to antiplatelet monotherapy.[56] **(Figure 1)**

BEYOND TWELVE MONTHS AFTER PCI

Established practices have recommended DAPT for a minimum of twelve months after PCI. However, as stent technology has advanced beyond bare metal and first-generation drug-eluting stents, recommendations on total DAPT duration have evolved. A large clinical trial evaluated DAPT (aspirin + clopidogrel or prasugrel) beyond twelve months in patients that received a drug-eluting stent versus aspirin monotherapy alone. The authors found lower rates of stent thrombosis and major cardiovascular/cerebrovascular adverse events in the DAPT group. Prolonged DAPT, however, caused an increased risk of bleeding. Nevertheless, overall, the data suggests prolonging DAPT after DES PCI beyond one year if it is tolerated from a bleeding perspective.[57]

DAPT MANAGEMENT BASED ON BLEEDING SEVERITY

The European Society of Cardiology (ESC) guidelines aim to guide DAPT management based on the clinical significance of active bleeding. They define bleeding into the categories of: (1) Mild (2) Moderate (3) Severe (4) Life-threatening. An evidence-based management plan can be formed by understanding the recommended DAPT duration after PCI and de-escalation recommendations when complications arise.

MILD BLEEDING

Mild bleeding is defined as any bleeding that requires medical attention without the need for hospitalization. This most commonly includes gingival bleeding, epistaxis, or hematochezia. The ESC recommends continuing DAPT through the bleeding episode. However, clinicians can consider shortening the total duration of DAPT versus switching to a less potent $P2Y_{12}$ inhibitor such as clopidogrel.[58]

MODERATE BLEEDING

Moderate bleeding is defined as clinically significant blood loss (Hg decrease >3g/dL) that requires hospitalization but with the patient remaining hemodynamically stable. An

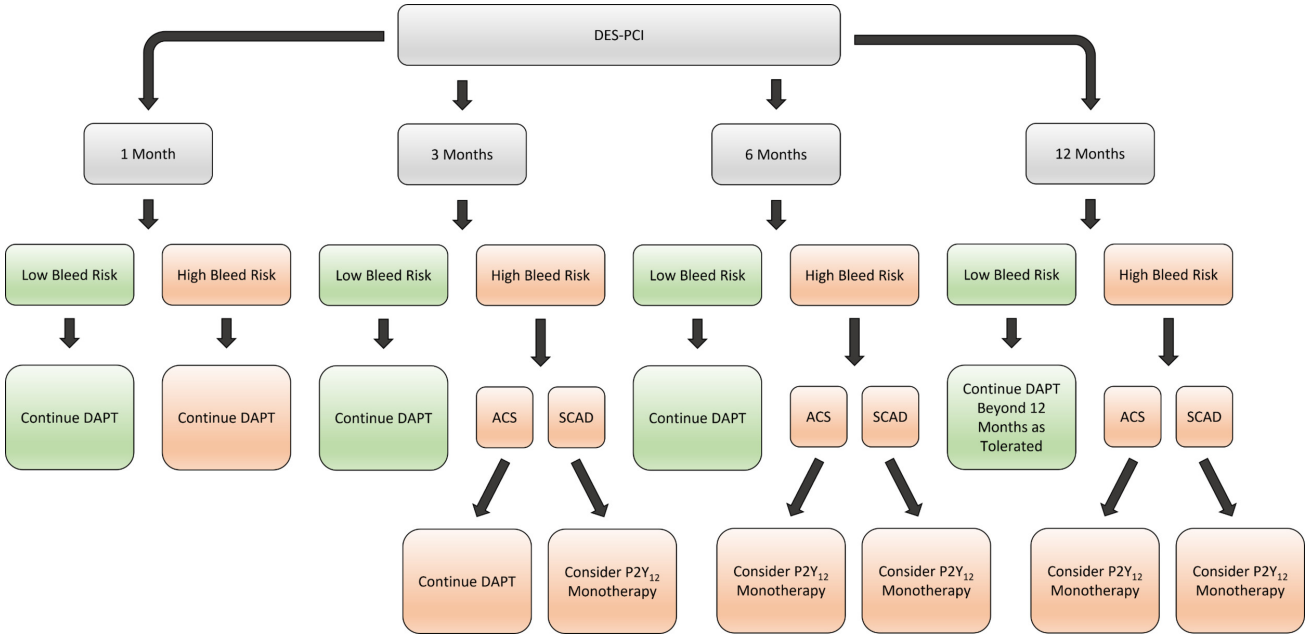

Figure 1. DAPT de-escalation guidelines after DES-PCI stratified into months after PCI and high versus low bleeding risk.

Abbreviations: ACS - acute coronary syndrome; DAPT =-dual antiplatelet therapy; DES-PCI - drug eluting stent–percutaneous coronary intervention; SCAD - stable coronary artery disease.

upper or lower gastrointestinal (GI) bleed is the most common example.[59] The ESC recommends temporarily discontinuing aspirin and continuing the $P2Y_{12}$ inhibitor.[58] Once the bleeding has resolved, DAPT should be resumed.

SEVERE BLEEDING

Severe bleeding is defined as bleeding that requires hospitalization (Hg decrease >5g/dL) with the patient maintaining hemodynamic stability. Examples include severe genitourinary or upper/lower GI bleeding. The ESC recommends de-escalating to a single anti-platelet agent, preferably a P2Y12 inhibitor. If the bleeding cannot be controlled, discontinuing all anti-platelet agents is reasonable until the bleeding has stopped. If anti-platelet therapy is restarted, it is reasonable to shorten the total DAPT duration or switch to a less potent P2Y12 inhibitor such as clopidogrel.[58]

LIFE-THREATENING BLEEDING

Life-threatening bleeding is defined as any bleeding with hemodynamic instability or otherwise putting the patient's life immediately at risk. When this occurs, it is recommended to discontinue all anti-platelet agents regardless of duration from PCI. Similar to the 'Severe Bleeding' recommendations, once the patient has stabilized, it is essential to reevaluate the need for DAPT, single anti-platelet therapy, or $P2Y_{12}$ de-escalation.[58] **(Figure 2)**

PROTON PUMP INHIBITOR CONSIDERATIONS WHILE ON DAPT

Patients on DAPT who develop a GI bleed should be started on a proton pump inhibitor (PPI). However, it is essential to note that the concomitant use of omeprazole and clopidogrel can lower the efficacy of clopidogrel by competing with CYP450 enzyme activity. The clinical significance of this interaction remains unclear. A subgroup analysis of the PLATO trial demonstrated higher adverse cardiovascular events in patients with acute coronary syndrome taking both omeprazole and clopidogrel.[60] This finding was further confirmed by a meta-analysis that showed patients taking both clopidogrel and a PPI after undergoing PCI had a higher incidence of major adverse cardiovascular events (MACE) (hazard ratio 1.28, 95% CI 1.24–1.32), myocardial infarction (hazard ratio 1.51, 95% CI 1.40–1.62) and stroke (hazard ratio 1.46, 95% CI 1.15–1.86). This meta-analysis did not investigate the effects of other individual PPIs on clopidogrel.[61] Alternatives include pantoprazole, which has minimal CYP450 activity and has an insignificant effect on the anti-platelet activity of clopidogrel.[62] Ticagrelor does not require hepatic conversion to an active form and has not shown an increased incidence of MACE when combined with omeprazole.[63]

BEDSIDE PROCEDURE SAFETY

The fear of complications while performing bedside procedures in patients on DAPT may cause a delay in clinically indicated interventions. After cessation of antiplatelet agents, platelet function recovery takes approximately [clopidogrel 5-7 days, prasugrel 7-10 days, ticagrelor 3-5 days, aspirin 4-10 days].[64,65] Acutely ill hospitalized patients often require diagnostic or therapeutic bedside procedures without delay. Patients taking a single antiplatelet agent such as aspirin or NSAIDs do not have a higher risk of bleeding complications with bedside procedures.[66] Patients

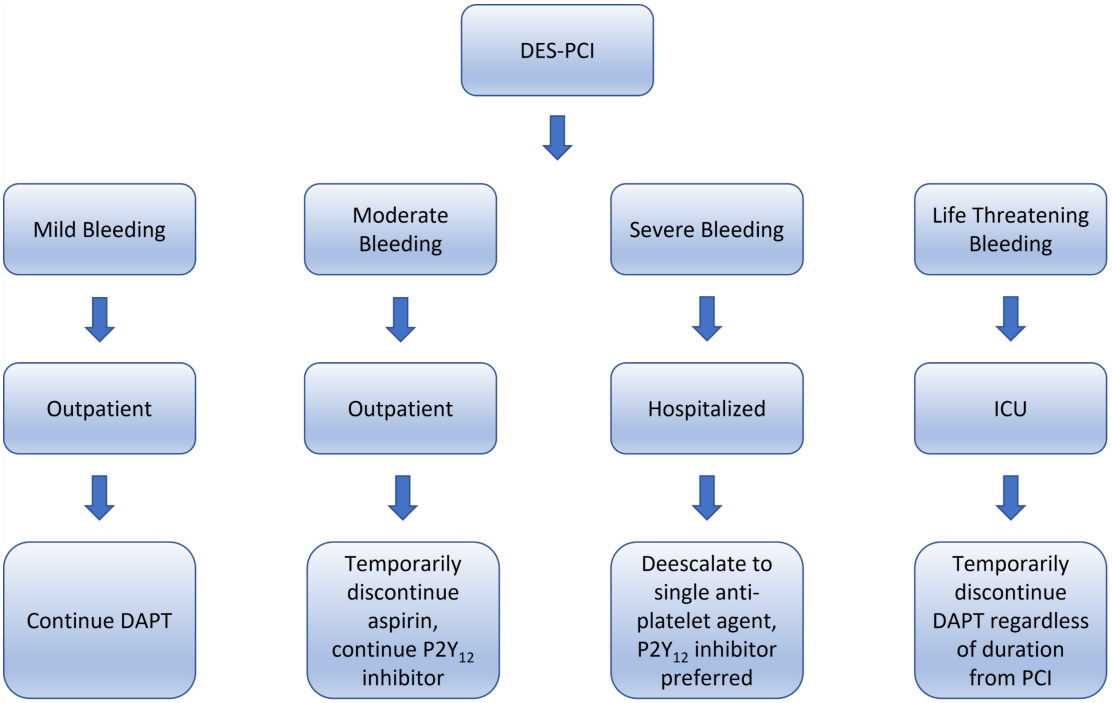

Figure 2. DAPT de-escalation after DES-PCI stratified into clinically significant bleeding severity.

Abbreviations: DAPT =-dual antiplatelet therapy; ICU – intensive care unit; PCI - percutaneous coronary intervention.

Table 3. An overview of safety guidelines regarding discontinuation of dual antiplatelet therapy after a coronary stent and before performing a bedside procedure

Discontinuing Dual Antiplatelet Therapy Overview	
One Month After PCI	If a stent was placed <3 months ago, antiplatelet therapy should be restarted as soon as possible once life-threatening bleeding is controlled.
Three Months After PCI	For stents placed >3 months ago, Cardiology consultation is warranted to consider de-escalation of anti-platelet agents in high bleeding risk patients.
Mild Bleeding	Continue DAPT through the bleeding episode.
Moderate Bleeding	Discontinue aspirin and continue the $P2Y_{12}$ inhibitor. Start pantoprazole if bleeding source is from the GI tract.
Severe Bleeding	Continuing $P2Y_{12}$ inhibitor is preferred, but also reasonable to stop all anti-platelet agents if bleeding is uncontrolled.
Life Threatening Bleeding	Discontinue all anti-platelet agents regardless of duration from PCI.
Lumbar Puncture	If lumbar puncture cannot be delayed, a lumbar puncture while on DAPT has a low risk of serious complications.
Paracentesis	Paracentesis can be safely performed while on DAPT.
Thoracentesis	Thoracentesis can be safely performed while on DAPT.

Abbreviations: PCI – percutaneous coronary intervention.

receiving DAPT after a coronary stent carry a substantially higher risk of bleeding that must be weighed against the potential benefit of the indicated procedure (**Table 3**). Generally, patients should have elective procedures delayed at least six months after implantation of a DES. DAPT should be continued in emergent procedures throughout the peri- and postoperative periods.[67]

LUMBAR PUNCTURE

Regional Anesthesia and Acute Pain guidelines recommend against lumbar puncture (LP) on patients until they can safely hold anti-platelet agents until platelet recovery.[68] In some cases, LP is necessary to diagnose a potentially life-threatening condition such as meningitis or subarachnoid hemorrhage. A retrospective analysis of 100 patients at Mayo Clinic who underwent an LP while on aspirin and clopidogrel found that no patients in their cohort had major complications (epidural hematoma, subsequent hospitalizations, or death) following the procedure.[69] These results align with a retrospective study of 300 patients who received epidural anesthesia while on clopidogrel showing no patients with neurologic complications resulting from the procedure.[70]

The standard of care dictates that following PCI, most patients will be placed on one of the more potent antiplatelet agents, ticagrelor or prasugrel. With these newer agents, it is reasonable to assume the bleeding risk from lumbar punctures is increased compared to clopidogrel. The Association of British Neurologists recommends holding ticagrelor and prasugrel for seven days before a lumbar puncture and holding the first dose until 6 hours after the procedure is completed. In cases where anti-platelet agents should not be held, they recommend performing a fluoroscopic guided lumbar puncture to avoid repeated traumatic attempts.[71]

PARACENTESIS AND THORACENTESIS

Both paracentesis and thoracentesis are considered low-bleeding-risk procedures that can provide a crucial diagnostic and therapeutic role in a hospitalized patient. According to the Society of Interventional Radiology consensus guidelines, DAPT does not need to be held before performing these procedures.[72]

CONCLUSION

Periprocedural management of patients on anticoagulation and DAPT is a frequent challenge managed by hospital-based and outpatient providers. For both DOACs and VKAs, a patient's risk for clot and procedural risk of bleed should be assessed. Generally, patients considered at high risk for VTE should receive bridging therapy, while patients at low risk of VTE should forgo bridging therapy. DAPT does not need to be held for paracentesis or thoracentesis and is likely low risk for those needing urgent lumbar punctures. In patients with active bleeding, patients with PCI performed in the previous three months should resume DAPT as soon as the patient is hemodynamically stable, while patients 3-6 months out from PCI at high risk of bleeding complications can be de-escalated to single antiplatelet therapy. More research is necessary into the safety profile of the newer antiplatelet agents such as ticagrelor and procedural bleeding complications.

AUTHOR CONTRIBUTIONS

All authors have reviewed the final manuscript prior to submission. All the authors have contributed significantly to the manuscript, per the International Committee of Medical Journal Editors criteria of authorship.

- Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; AND
- Drafting the work or revising it critically for important intellectual content; AND
- Final approval of the version to be published; AND
- Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

DISCLOSURES/CONFLICTS OF INTEREST

The authors declare they have no conflicts of interest.

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