

Peri-Procedural Management ◆ of Antithrombotic Agents

*An Integrated Care Pathway of the
Collaborative Care Network*

Subject Matter Experts:

Will Maxted, MD

Veronica Kerner, PharmD

Pathway Custodian: Pat Czapp, MD

First, a Friendly Reminder. . .

This Integrated Care Pathway was developed by and for members of the AAMC CCN.

These materials will refer to some resources available **only** to CCN members and their patients.

Not a CCN member?

We invite you to join the CCN! Membership is free. Contact the CCN at AAMCCollaborativeCareNetwork@aaahs.org

Learning Objectives

This CME material will help you to:

- Provide evidence-based instructions to your patients on how to manage antithrombotic agents in the peri-procedural period;
- Reduce procedure-related risks of bleeding and thrombotic events for your patients;
- Use efficient communication tools to facilitate collaborative decision-making among members of our patients' care teams

Intended Audience and Scope

- **Intended Audience for this Pathway**
 - Primary care clinicians, who frequently provide preoperative “clearance” and advice
 - Hospitalists who are managing inpatient care that involves a procedure
- **Scope of Pathway**
 - Patients chronically taking antithrombotic agents (antiplatelet and anticoagulant drugs) who will be undergoing procedures that incur varying risks of bleeding

Antithrombotic Agents Include:

- **Antiplatelet Agents**

- Aspirin, clopidogrel, prasugrel, ticagrelor, others
- Used to prevent and treat arterial thrombosis

- **Anticoagulant Agents**

- Warfarin, the DOACs, LMWH, UFH
- Used to prevent and treat venous thromboembolism and prevent cardioembolic events in patients with atrial fibrillation
 - DOAC: direct oral anticoagulant
 - LMWH: low molecular weight heparin
 - UFH: unfractionated heparin

The WHY of this Integrated Care Pathway

- Clinicians asked us to digest evidence-based guidelines and provide a simplified methodology for decision-making.
- They also asked for go-to subject matter experts if they still weren't sure what to do.

Those resources are supplied here.

Three Big Questions

This CME program will provide you with evidence-based guidelines to help you answer these 3 questions:

1. Does my patient's planned procedure require that we stop his antithrombotic agent(s)?
2. If so, for how long prior to and after the procedure?
3. Is bridging with a parental anticoagulant necessary prior to and after the procedure?

A Handy Tool Will Pull It All Together

Relax. All CCN members for whom this Integrated Care Pathway is relevant will receive a digested version of this material from CCN Field Support

- Laminated version (one page, 2 sides)
- Accessible, on-line version of same

Let's get started

Think About It This Way

My patient who is on chronic antithrombotic therapy is going to have a procedure



1. What is the risk that my patient will have a thrombotic event if antithrombotic therapy is interrupted for the procedure?
2. What is the risk that my patient will have a bleeding event if antithrombotic therapy is continued for the procedure?



There are evidence-based tools to help guide the decision on whether to stop, continue, or bridge antithrombotic therapy in the peri-procedural timeframe.

REMEMBER:

- 1) You Are Not Working Alone
- 2) Not All Procedures Have to Be Done Right Now

In cases where recommendations are not clear cut, *always* discuss the potential bleeding and clotting risks directly with your colleagues:

- Surgeon
 - Cardiologist
 - Anesthesiologist
- . . . And your patient, *well before the planned procedure.*

What's *Clear Cut*?

Some General Guidelines

1. Postponing Procedures

If at all possible, postpone elective procedures (particularly major surgery) for those patients who have within the past 12 WEEKS experienced a venous thromboembolism (VTE) or ischemic event (TIA/STROKE).

They are at very high risk for another thromboembolic event in this time period.

More On Postponing Procedures

What about patients who've had a RECENT myocardial infarction (MI) or percutaneous coronary intervention (PCI) with bare or drug-eluting stent? How long to wait before surgery?

Recommendations are evolving, due to better understanding of variables and also newer drugs and stents - **always confer with your patient's cardiologist.**

Another General Guideline

2. Patients with coronary artery disease (CAD) should ALWAYS remain on aspirin, except for procedures for which even a small amount of bleeding is dangerous, e.g. intracranial, posterior eye, intramedullary spine procedures.

How to Approach Cases That Aren't Clear Cut

Balancing Two Dangers

When managing antithrombotic agents in the peri-procedural period, the primary consideration for any patient is determining both:

1. An individual's risk of thrombosis
2. An individual's risk of bleeding

FIRST: Determine Risk of Thrombosis

Which Patients Are At **Highest Risk** for a Thromboembolic Event?

“Highest risk” means a 10% or higher annual risk for VTE or ischemic stroke if on no antithrombotic therapy. Individuals with the following risk factors meet that definition:

- Acute VTE or TIA/stroke within the past 12 weeks
- Previous VTE during interruption of chronic anticoagulation
- Active malignancy
- Severe thrombophilia
 - Protein C or S deficiency, antithrombin deficiency, antiphospholipid antibody syndrome
- Atrial fib with CHA₂DS₂-VASc score of ≥ 7 (see next few slides)
- Mechanical heart valves
 - Any mechanical MITRAL valve
 - Older, caged ball or tilting disk valves

Additional Risk Factors That Confer Thromboembolic Risk

Factor these into your consideration

- **Personal:**
 - OCP and ERT use, pregnancy
 - Leg or hip fractures, immobility, spinal cord injury
 - Obesity
- **Inherent Thrombotic Risks of the Procedure:**
 - Knee and hip arthroplasty, hip fracture repair, major trauma, spinal cord surgery (VTE risk)
 - Coronary bypass, heart valve replacement, carotid endarterectomy (ischemic stroke risk)

Atrial Fibrillation: Its Own Considerations, Particularly for Those Patients on Warfarin.

The CHA₂DS₂VASc scoring tool estimates annual thrombosis risk based on the presence of risk factors.

The scoring tool is helpful not just for deciding whether to start anticoagulation; it also helps to determine which atrial fib patients on warfarin would benefit from bridging therapy when their warfarin is held for a procedure.

Bridging therapy is the provision of a low-molecular weight heparin (LMWH) or unfractionated heparin (UFH) to those patients on chronic warfarin who are undergoing an elective invasive procedure.

Atrial Fib Patients Undergoing Surgery: *To Bridge or Not to Bridge?*

The 2017 guidelines from the American College of Cardiology recommend using the $\text{CHA}_2\text{DS}_2\text{-VASc}$ tool to determine whether to bridge.

- ***Score of ≥ 7 : Bridging is recommended for those procedures with a high risk of bleeding that require interruption of warfarin therapy (more on those procedures in a minute). In patients who've had a stroke or TIA in the past 6 months, consider bridging when the score is ≥ 5 , as long there is no significant bleeding risk.***

CHA₂DS₂-VASc

Risk Factor	Score
CHF	1
Hypertension	1
Age > 75	2
Diabetes Mellitus	1
History of ischemic stroke or TIA	2
History of vascular disease	1
Age 65-74	1
Female sex	1

Balancing Two Dangers

When managing antithrombotic agents in the peri-procedural period, the primary consideration for any patient is determining both:

1. An individual's risk of thrombosis (prior slides)
2. An individual's risk of bleeding (*what we'll cover now*)

Bleeding:

Personal and Procedure-related Risks

Let's consider PERSONAL risks first. These include:

- A bleeding event in the last 12 weeks
- A supra-therapeutic INR at time of procedure
- A history of bleeding from previous bridging
- A history of bleeding from similar procedure
- A HAS-BLED score ≥ 3

HAS-BLED

This scoring tool has been validated for atrial fib patients taking warfarin and it is commonly also used to estimate bleeding risk.

Score of ≥ 3 predicts $\geq 4\%$ risk of surgical and nonsurgical MAJOR bleeding.

HAS-BLED helps you determine who might benefit from interruption OR reduced dosing of antithrombotic therapy for procedures.

HAS-BLED

Risk Factor (see laminated tool for definitions)	Score
Uncontrolled hypertension	1
Severely abnormal liver or renal function	1
History of stroke	1
Bleeding history or predisposition	1
Labile INR	1
Age > 65	1
Drugs that increase bleeding risk (antiplatelet agents, NSAIDs, corticosteroids) or heavy alcohol use	1

Bleeding Risks: Procedure-Related

Different procedures pose different risks of bleeding, fairly predictably.

In the next few slides, we'll group procedures into minimal, low, and high-risk for bleeding.

When in doubt, discuss the perceived bleeding and clotting risks directly with the person performing the procedure.

Remember: if a patient has had a VTE or ischemic event (stroke/TIA/MI) within the past 3 months, consider postponing the procedure, if possible, so that needed antithrombotic therapy is not interrupted.

Now Let's Look at Procedure-Specific Risks of Bleeding

- The lists are not exhaustive, and are meant to serve simply as a general guide.
- Consult your surgeon colleague when in doubt regarding bleeding risk of the specific procedure being planned

MINIMAL BLEEDING RISK PROCEDURES

For these procedures, don't stop* antithrombotic therapy.

- Minor derm procedures, including abscess incision, small excisions
- Dental procedures including extraction of 1-2 teeth, periodontal surgery, incision of abscess, implant positioning
- Endoscopy WITHOUT plan for biopsy
- Cataract or glaucoma procedures
- Central venous catheter removal

* Check INR if on warfarin to make sure it is not supratherapeutic.

LOW (not minimal) Bleeding Risk

- Abdominal hernia repair
- Axillary node dissection
- Certain biopsies: skin/bladder/prostate/thyroid/breast/lymph node
- Bronchoscopy
- Cardiac electrophysiology studies and/or ablation
- Carpal tunnel release
- ERCP without sphincterotomy
- Biliary/pancreatic stent
- Endosonography withOUT fine needle aspiration
- Hemorrhoidal surgery
- Hydrocele repair
- Noncoronary angiography

HIGH Bleeding Risk, Slide 1 of 3

- Any surgery lasting > 45 minutes
- AAA repair
- Biliary sphincterotomy
- Bladder resection
- Bowel resection
- Cancer surgery
- Cardiac surgery: bypass, valve replacement, device implantation
- Endoscopic fine needle aspiration
- Head and neck surgery

HIGH Bleeding Risk, Slide 2 of 3

- Liver biopsy or surgery
- Intracranial surgery
- Joint arthroplasty
- Laser ablation and coagulation
- Kidney biopsy
- Laminectomy
- Nephrectomy
- Neurosurgery
- PEG placement
- Polypectomy
- Pneumatic dilation

HIGH Bleeding Risk, Slide 3 of 3

- Reconstructive plastic surgery
- Retina surgery
- Operations in highly vascular organs
- Spinal surgery
- Splenic surgery
- TURP/TURBT
- Lithotripsy
- Sinus surgery
- Variceal treatment
- Vascular surgery

So Now You Know About the Relative Risks of Bleeding and Thrombosis for Your Patient

Now what? We go back to the THREE big questions

1. Does my patient's planned procedure require that we stop his antithrombotic agent(s)?
2. If so, for how long prior to and after the procedure?
3. Is bridging with a parental anticoagulant necessary prior to and after the procedure?

Let's Talk First about Patients on Anti-Platelet Agents

- These include
 - Aspirin
 - Clopidogrel (Plavix)
 - Prasugrel (Effient)
 - Ticagrelor (Brilinta)
 - Others
- When aspirin and another agent in the class are taken together, that constitutes Dual Anti-Platelet Therapy. More on that special case in a moment.

Patients On Aspirin Alone

- On Aspirin for Primary Prevention
 - No diagnosis of CAD
 - No stroke or TIA history
 - OK to stop aspirin 5-7 days prior to procedure with more than minimal bleeding risk
- On Aspirin for Secondary or Tertiary Prevention
 - **DO NOT STOP** the ASPIRIN without talking to surgeon, cardiologist, or anesthesiologist

Dual Anti-Platelet Therapy (DAPT)

- Aspirin plus another antiplatelet agent are commonly used together, particularly after acute coronary syndrome and/or percutaneous coronary intervention
- DAPT should be continued for at least six months following placement of drug-eluting stents and at least one month following placement of bare stents.

DAPT and Surgery

- Generally speaking, aspirin should never be stopped.
- As for the second agent, **there are many nuances and insufficient firm evidence regarding how to manage these patients in the peri-procedural period. Therefore, consider each case individually, involving the patient, cardiologist, anesthesiologist, surgeon in the decision-making process.**

Patients on WARFARIN

Warfarin is still commonly used as a low-cost anticoagulant for atrial fibrillation, particularly valvular atrial fibrillation.

Because it has a half-life of about 36 hours, it can be stopped 5 days prior to a procedure, *if needed*.

There is NO need to stop warfarin for procedures with MINIMAL bleeding risk.

How to Think About Patients on Warfarin

	Patient with HIGH risk of thromboembolism	Patient with LOW risk of thromboembolism
Procedure with HIGH risk of bleed	HOLD warfarin for 5 days prior and BRIDGE with LMWH or UFH	Hold warfarin for 5 days prior, DO NOT BRIDGE
Procedure with MINIMAL risk of bleed	DO NOT STOP WARFARIN	DO NOT STOP WARFARIN

WARFARIN and BRIDGING

- Warfarin should be stopped 5 days prior to procedures with a high bleeding risk.
- AND, if the patient is at high thromboembolic risk, e.g. some mechanical heart valves, then BRIDGING with LMWH before and after the procedure should be considered
- If patient has creatinine clearance < 30 ml/min, then UFH is the preferred agent for bridging (inpatient) OR use LOWER doses of LMWH. (Recipe is in next slide)
- The decision to use bridging therapy needs to carefully weigh the benefits against potential risks of bleeding.

How To Bridge Warfarin with LMWH BEFORE the Procedure

Does My Patient Need Bridging AFTER the Procedure?

If your patient is at high risk for clotting, and you bridged BEFORE the procedure, you should bridge AFTER the procedure, as well.

See next slide

(Relax, this is all on the handy tool you'll get)

How to Bridge Warfarin with LMWH AFTER the Procedure

1. Resume warfarin immediately if hemostasis is secure.
2. Resume LMWH or UFH at a therapeutic dose (no bolus) 24-48 hours after procedure. Wait 72 hours if patient has undergone endoscopic sphincterotomy or has additional bleeding risk factors, e.g. HAS-BLED score >3)
3. Discontinue LMWH or UFH when INR is in the therapeutic range.

ALWAYS CONSULT WITH PROCEDURALIST/SURGEON ABOUT TIMING OF RESUMING ANTICOAGULATION REGARDING SURGERY.

What About Heparin? (UFH)

Some inpatients may be on heparin rather than enoxaparin, for any number of reasons (e.g. stage IV or V kidney disease).

STOP heparin 4-5 hours prior to a high bleed risk procedure.

RESUME heparin 1-3 hours after the procedure.

Now Let's Talk About DOACs

Direct oral anticoagulants are commonly used nowadays instead of warfarin, particularly for reducing embolic risk from non-valvular atrial fibrillation.

They have a shorter half-life than warfarin and quicker onset of action, conferring two advantages:

1. Bridging is unnecessary
2. They can be withheld prior to surgery for shorter periods of time, but the amount of time is dependent on the patient's renal function.

Impaired renal function prolongs the half-life of these agents.

DOACs, continued. When to Stop?

MINIMAL bleeding risk procedures: Don't stop the DOAC. Note: it is ideal to time the procedure when the DOAC is at trough concentration, i.e. just before the next dose is due.

OTHER PROCEDURES:

DOACs generally should be stopped 24 hours prior to procedures with LOW bleeding risk, and 48 hours prior to procedures with HIGH bleeding risk. BUT they need to be withheld for an additional 1-2 days in patients with acute kidney injury or stage IV kidney disease.

SEE NEXT SLIDE. (Relax, this is all on the handy tool too!)

How Many DOAC Doses to Hold Prior to Procedures With More Than Minimal Bleeding Risk

		Hold this NUMBER OF DOSES prior to procedure	
DOAC	Creatinine Clearance (mL/min)	Procedures with LOW bleeding risk	Procedures with HIGH bleeding risk
Apixaban (Eliquis)	≥30	2	4
	15-29	4	6
Rivaroxaban (Xarelto) and Edoxaban (Savaysa)	≥30	1	2
	15-29	2	3
Dabigatran (Pradaxa)	≥80	2	6
	30-79	4	6 to 8
	15-29	6 to 8	10 to 12

Resuming DOACs After Procedures

Resume these agents 1-3 days post-procedure, depending on bleeding risk (consult surgeon, and use HAS-BLED score).

Curbside Consulting

Should you need a quick curbside pharmacologic consultation on peri-procedural management of antithrombotic agents, call the Anticoagulation Center at 443 481 5826. They will also see your patient for a consultation and education, if needed.

Secure Texting

- Your CCN colleagues (e.g. surgeons, cardiologists, anesthesiologists, primary care clinicians, hospitalists) are using secure texting to communicate efficiently with one another.
- If you are not using secure texting and would like to do so, contact the CCN at AAMCCollaborativeCareNetwork@aaahs.org

What This Material Was Designed to Help You Achieve

- Provide evidence-based instructions to your patients on how to manage antithrombotic agents in the peri-procedural period;
- Reduce procedure-related risks of bleeding and thrombotic events for your patients;
- Use efficient communication tools to facilitate collaborative decision-making among members of our patients' care teams

How Did We Do?

Please move on to the test module so that we can gather your feedback and you can get CME credit.

Thank you!