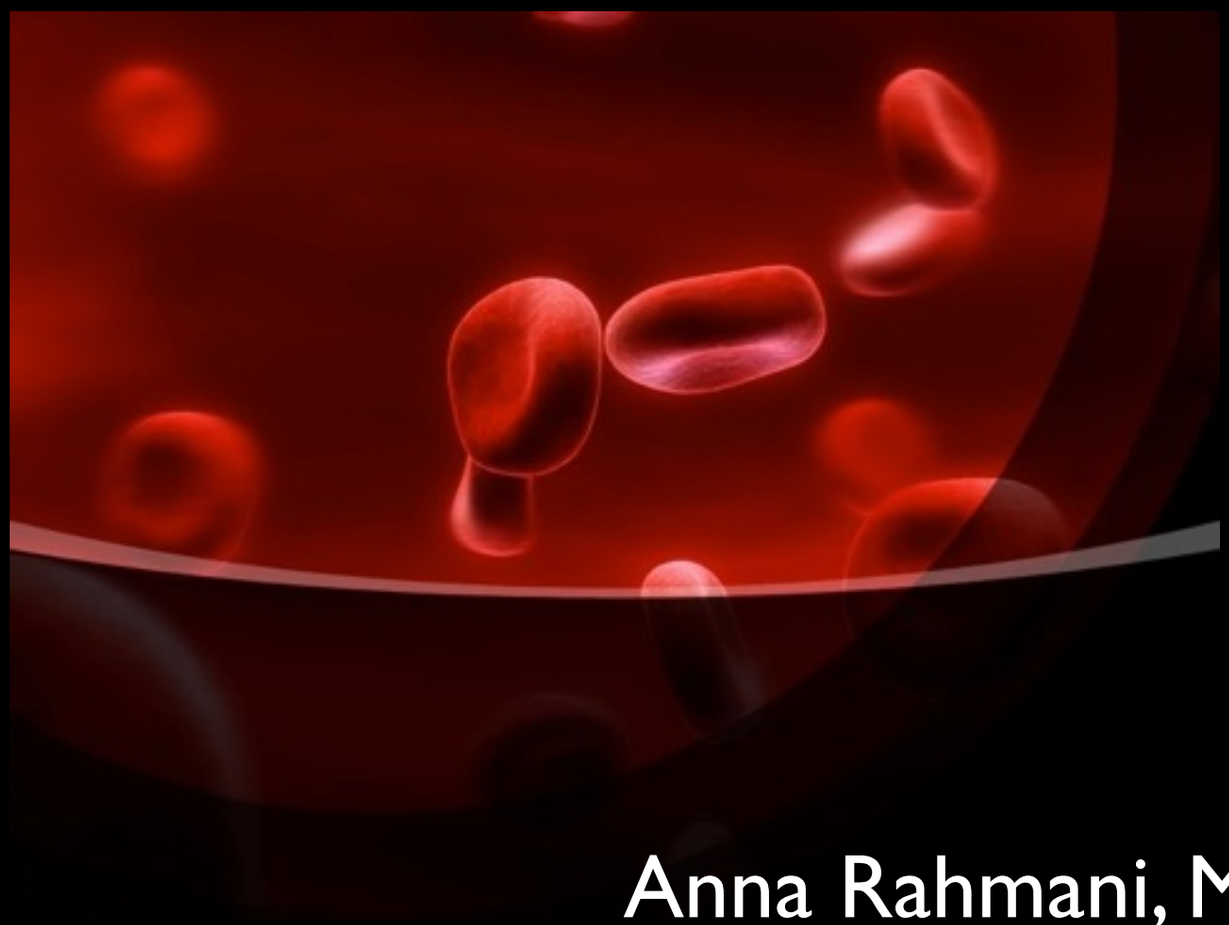
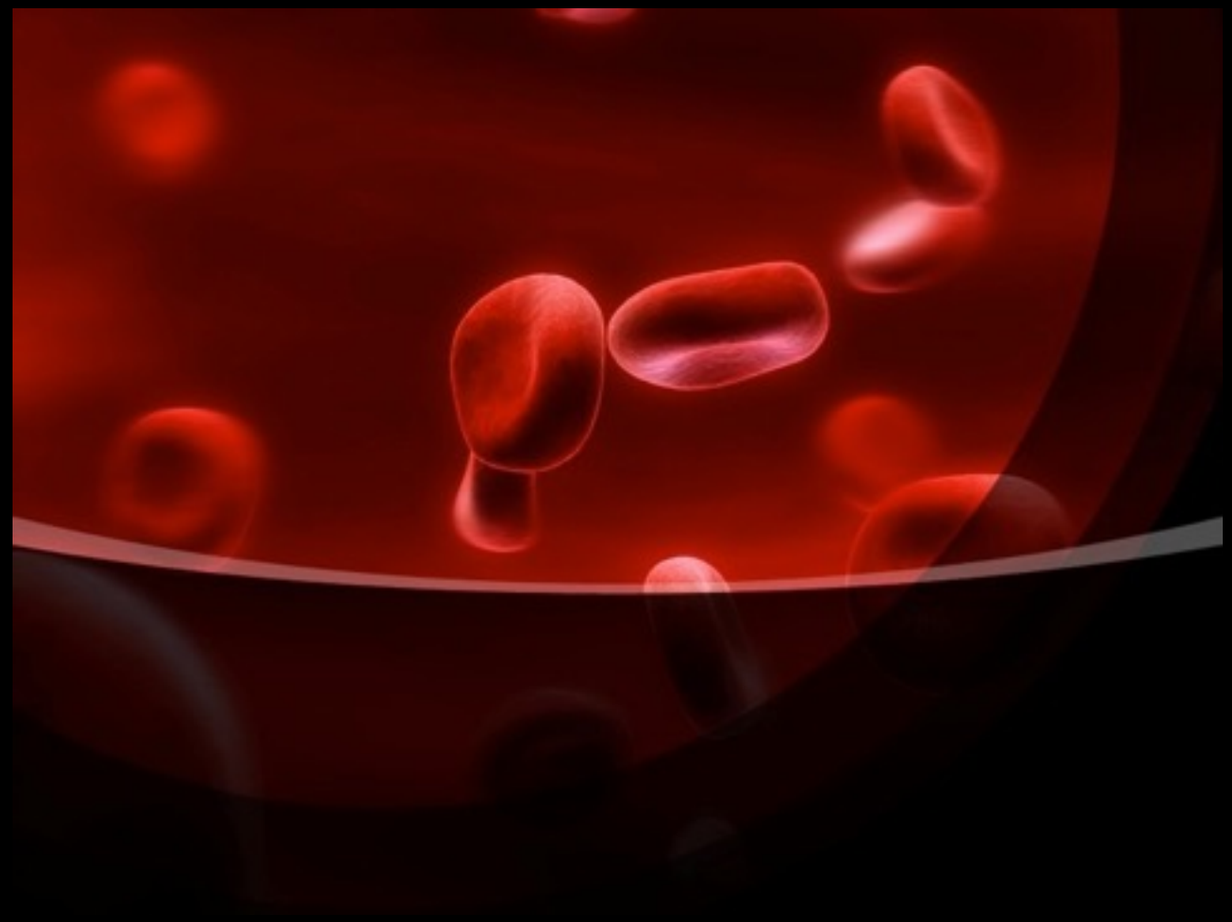
Anti-thrombotics and Colonoscopy

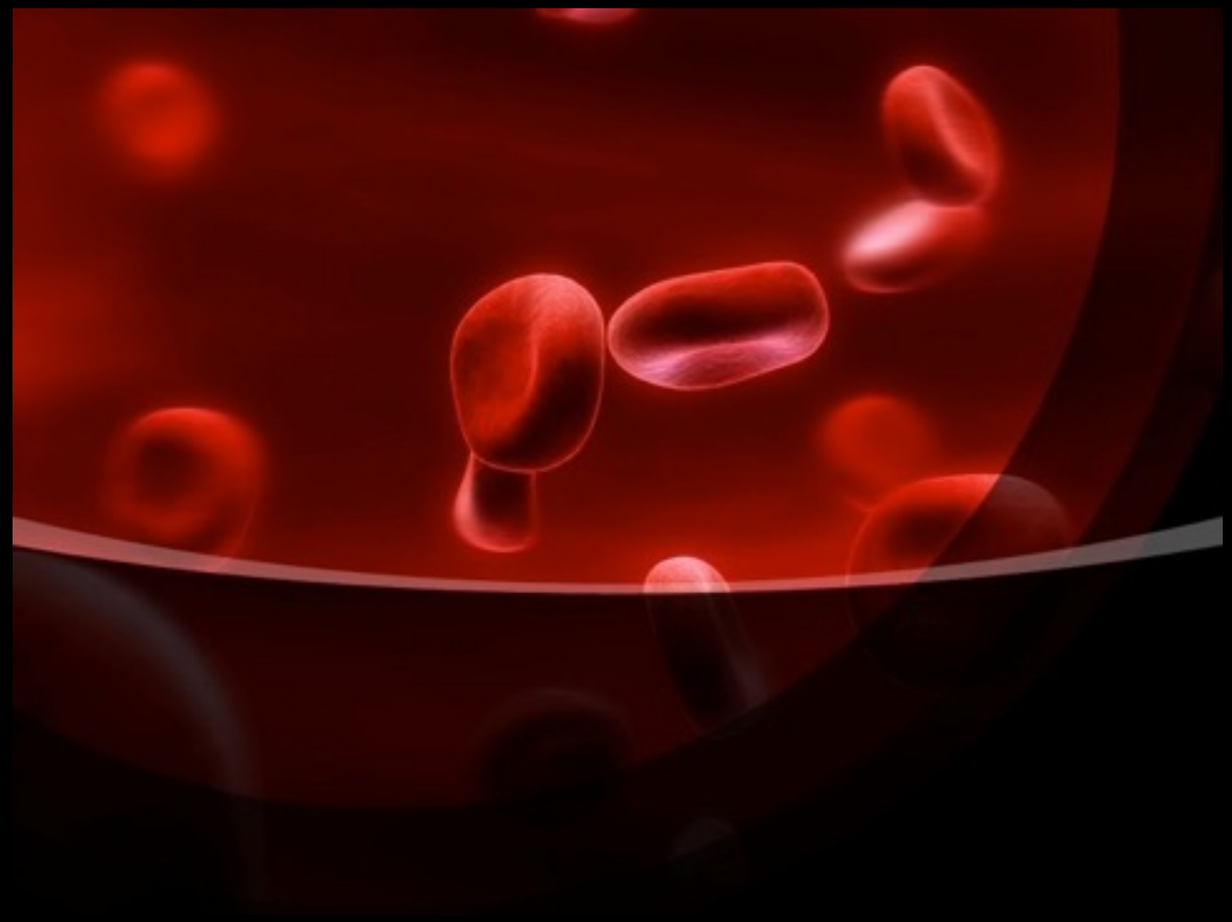


Anna Rahmani, MD. Ph.D. FRCPC



DICLOSURES:

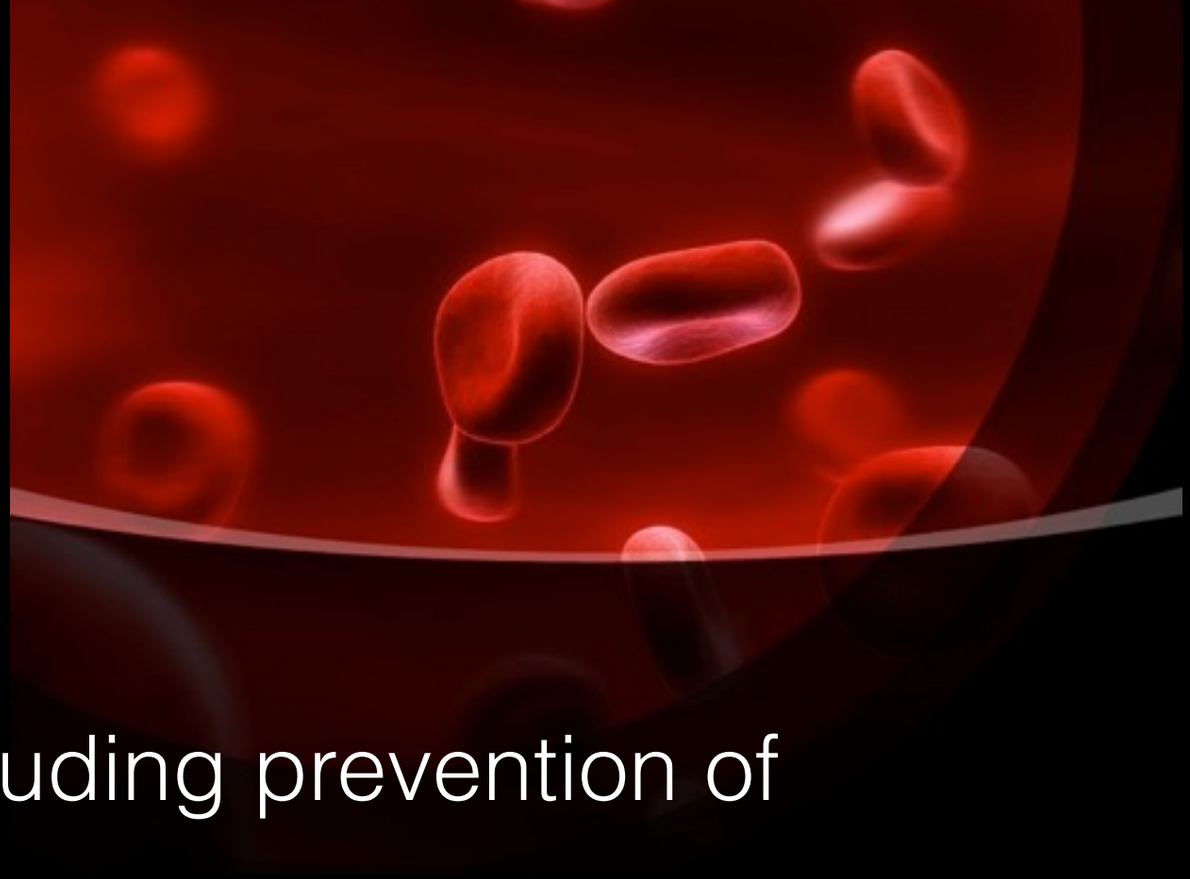
- consultations fees: Servier and Sanofi Pharmaceuticals
- Thrombosis Clinic Educational Fund: Servier



CONFLICT OF INTEREST:
NONE

Overview and Objectives:

- Indication and modes of anti-platelet and anticoagulation therapy.
- Risk of bleeding and thrombotic events with each treatment mode after polypectomy.
- Indication for bridging anticoagulation
- Peri-procedural management of anticoagulation in era of Direct Oral Anticoagulants (DOACs).

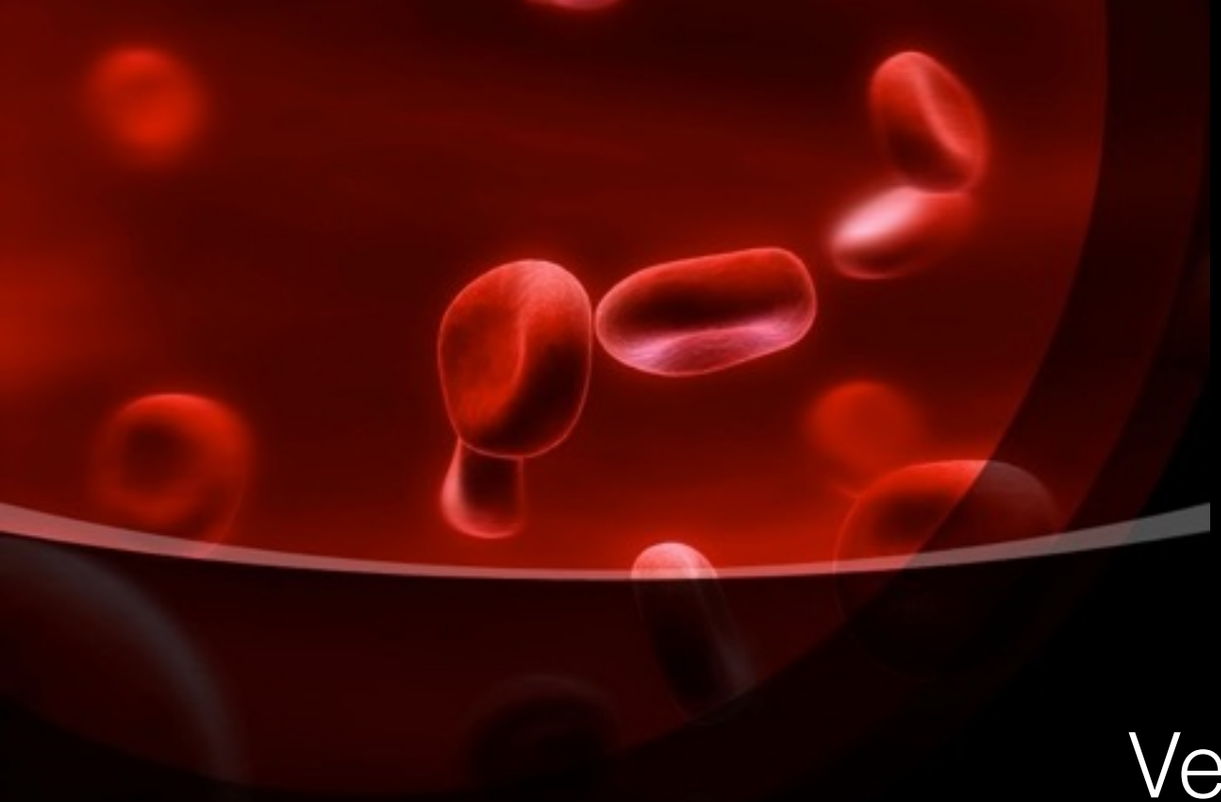


Arterial:

- **<u>Antiplatelet:</u>**
  - Coronary artery disease including prevention of stent thrombosis
  - peripheral vascular disease
  - cerebrovascular disease

<u>Anticoagulation:</u>

- Atrial Fibrillation/ Flutter
- Mechanical valves
- Hypercoagulable state such as antiphospholipid antibody syndrome.



Venous:

- **<u>Antiplatelet:</u>**
  - rarely used, unless as prophylaxis for DVT/PE

<u>Anticoagulation:</u>

- Deep vein thrombosis and pulmonary embolism
- Hypercoagulable state: Antiphospholipid antibody syndrome or high risk thrombophilia such as protein C, protein S and anti-thrombin III deficiency.

Antiplatelet Therapy

Antiplatelet Agents	Mechanism	Indications	Examples	Recommended Time of Stopping Drug Preprocedure, if Indicated
Aspirin	Irreversibly acetylates and inactivates cyclooxygenase	Primary and secondary cardiovascular protection; cerebrovascular protection	Oral: aspirin (Bayer, Ecotrin)	7-10 d, not recommended to stop if high risk for cardiovascular disease
NSAIDs	Reversibly block cyclooxygenase; can be selective (blocking cyclooxygenase-2) or nonselective (blocking both COX-1 and COX-2)	Pain, osteoarthritis, rheumatoid arthritis, inflammatory arthritis, dysmenorrhea, fever, anti-inflammatory	Oral: ibuprofen (Advil, Motrin), naproxen (Naprosyn), celecoxib (Celebrex), diclofenac, ketoprofen, indomethacin, sulindac, meloxicam, piroxicam	Short-half life: ibuprofen, diclofenac, ketoprofen, indomethacin (1 d) Intermediate half life: naproxen, sulindac, celecoxib (2-3 d) Long half life: meloxicam, piroxicam (10 d)
Dipyridamole	Inhibits uptake of adenosine into platelets leading to inhibition of platelet aggregation	Thrombotic stroke prevention	Oral: dipyridamole (Persantine), aspirin/ dipyridamole (Aggrenox)	2 d (7-10 d if being given as Aggrenox, the combination of aspirin and dipyridamole)
Thienopyridines	Irreversibly inhibits platelets by blocking their ADP receptors	Acute coronary syndrome, thrombotic event prevention	Oral: clopidogrel (Plavix), prasugrel (Effient), ticlopidine (Ticlid), ticagrelor (Brilinta)	5-7 d for clopidogrel, 7-9 d for prasugrel, 3-5 d for ticagrelor, 10-14 d for ticlopidine

Antiplatelet Therapy

Bleeding Risk

Based on several retrospective studies, guidelines agree that aspirin can be safely continued during colonoscopy with polypectomy without concern for a significant increase in bleeding.

Veitch AM, Baglin TP, Gershlick AH, et al. Guidelines for the man- agement of anticoagulant and antiplatelet therapy in patients undergoing endoscopic procedures. Gut. 2008;57(9):1322-1329.

Becker RC, Scheiman J, Dauerman HL, et al. Management of platelet- directed pharmacotherapy in patients with atherosclerotic coronary artery disease undergoing elective endoscopic gastrointestinal proced- ures. Am J Gastroenterol. 2009;104(12):2903-2917.

ASGE Standards of Practice Committee; Anderson MA, Ben-Menachem T, Gan SI, et al. Management of antithrombotic agents for endoscopic procedures. Gastrointest Endosc. 2009;70(6):1060-1070.

Antiplatelet Therapy

Bleeding Risk

Anti-inflammatory drugs (NSAIDs) have short-acting effects on bleeding.

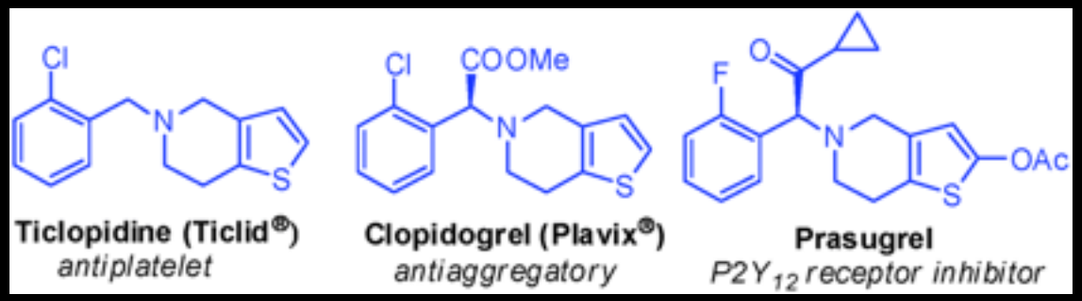
Guidelines agree that stopping NSAIDs prior to diagnostic or therapeutic endoscopic procedures is not mandatory.

Veitch AM, Vanbiervliet G, Gershlick AH, et al. Endoscopy in patients on antiplatelet or anticoagulant therapy, including direct oral anticoagulants: British Society of Gastroenterology (BSG) and European Society of Gastrointestinal Endoscopy (ESGE) guidelines. Gut. 2016;65(3):374-389

ASGE Standards of Practice Committee; Acosta RD, Abraham NS, Chandrasekhara V, et al. The management of antithrombotic agents for patients undergoing GI endoscopy. Gastrointest Endosc. 2016;83(1): 3-16

Antiplatelet Therapy

Bleeding Risk



- In patients with coronary artery disease, especially in the setting of coronary stents, thienopyridines are frequently given in combination with aspirin (dual antiplatelet therapy).
- For patients who are continued on thienopyridines during polypectomy, retrospective studies have estimated the risk of clinically important postpolypectomy bleeding to be 0.9-2.1%.
- Required treatment in bleeding patients, in a prospective study included: pRBC transfusion and repeat colonoscopy. There were no angiography, surgery or mortality.

Feagins LA, Uddin FS, Davila RE, Harford WV, Spechler SJ. The rate of post-polypectomy bleeding for patients on uninterrupted clopidogrel therapy during elective colonoscopy is acceptably low. Dig Dis Sci. 2011;56(9):2631-2638

Singh M, Mehta N, Murthy UK, Kaul V, Arif A, Newman N. Post- polypectomy bleeding in patients undergoing colonoscopy on unin- terrupted clopidogrel therapy. Gastrointest Endosc. 2010;71(6): 998-1005

Feagins LA, Iqbal R, Harford WV, et al. Low rate of postpolypectomy bleeding among patients who continue thienopyridine therapy during colonoscopy. Clin Gastroenterol Hepatol.

2013;11(10):1325-1332

Thromboembolic risk of interrupting antiplatelet agents

- Aspirin
  - cardiovascular risk associated with stopping aspirin is high in patients with prior history of CAD.
  - Most adverse events are identified within one month of stopping aspirin.
  - Cessation of antiplatelet therapy for elective procedure, in patients with previous history of ACS, was associated with higher 30-day rates of death or MI.

Collet JP, Montalescot G, Blanchet B, et al. Impact of prior use or recent withdrawal of oral antiplatelet agents on acute coronary syn- dromes. Circulation. 2004;110(16):2361-2367

Thromboembolic risk of interrupting antiplatelet agents

Cardiovascular risks of interrupting thienopyridines include:

- stent thrombosis,
- myocardial infarction,
- stroke
- death

Iakovou I, Schmidt T, Bonizzoni E, et al. Incidence, predictors, and outcome of thrombosis after successful implantation of drug-eluting stents. JAMA. 2005;293(17):2126-2130

Thromboembolic risk of interrupting antiplatelet agents

Discontinuing aspirin or clopidogrel for noncardiac surgery within 2-4 weeks of stent placement is associated with a high rate (30%) of major cardiovascular events.

Kaluza GL, Joseph J, Lee JR, Raizner ME, Raizner AE. Catastrophic outcomes of noncardiac surgery soon after coronary stenting. J Am Coll Cardiol. 2000;35(5):1288-1294

Wilson SH, Fasseas P, Orford JL, et al. Clinical outcome of patients undergoing non-cardiac surgery in the two months following coronary stenting. J Am Coll Cardiol. 2003;42(2):234-240

Thromboembolic risk of interrupting antiplatelet agents

The joint guidelines published by the American College of Gastroenterology (ACG) and the American College of Cardiology (ACC) recommend against interruption of platelet antagonists for elective procedures, particularly for patients at high risk for deadly stent thrombosis

Becker RC, Scheiman J, Dauerman HL, et al. Management of platelet- directed pharmacotherapy in patients with atherosclerotic coronary artery disease undergoing elective endoscopic gastrointestinal proced- ures. Am J Gastroenterol. 2009;104(12):2903-2917

When should elective noncardiac surgery be done?

- Canadian Cardiovascular Society recommendations:
    - Bare Metal Stents (BMS): delay procedure or surgery for at least 6 weeks (Class I, level B).
    - Drug Eluting Stent (DES): delay surgery for at least 12 months (Class I, level B).

Bell AD , Roussin A , Cartier R , et al ; Canadian Cardiovascular Society . The use of antiplatelet therapy in the outpatient setting: Canadian Cardiovascular Society guidelines . Can J Cardiol .2011 ; 27 (suppl A): S1 - S59 .

Which Antiplatelet Agents Should Be Stopped or Continued Around the Time of Procedure?

- If urgent surgery needed within 6 wk of BMS or 1 yr of DES implantation, continue DAPT if possible during perioperative period (class 1, level B)
- For elective procedures, if the risk for cardiovascular events is high, continue ASA (class IIa, level C) but discontinue clopidogrel (class IIb, level C).

Bell AD , Roussin A , Cartier R , et al ; Canadian Cardiovascular Society . The use of antiplatelet therapy in the outpatient setting: Canadian Cardiovascular Society guidelines . Can J Cardiol .2011 ; 27 (suppl A): S1 - S59 .

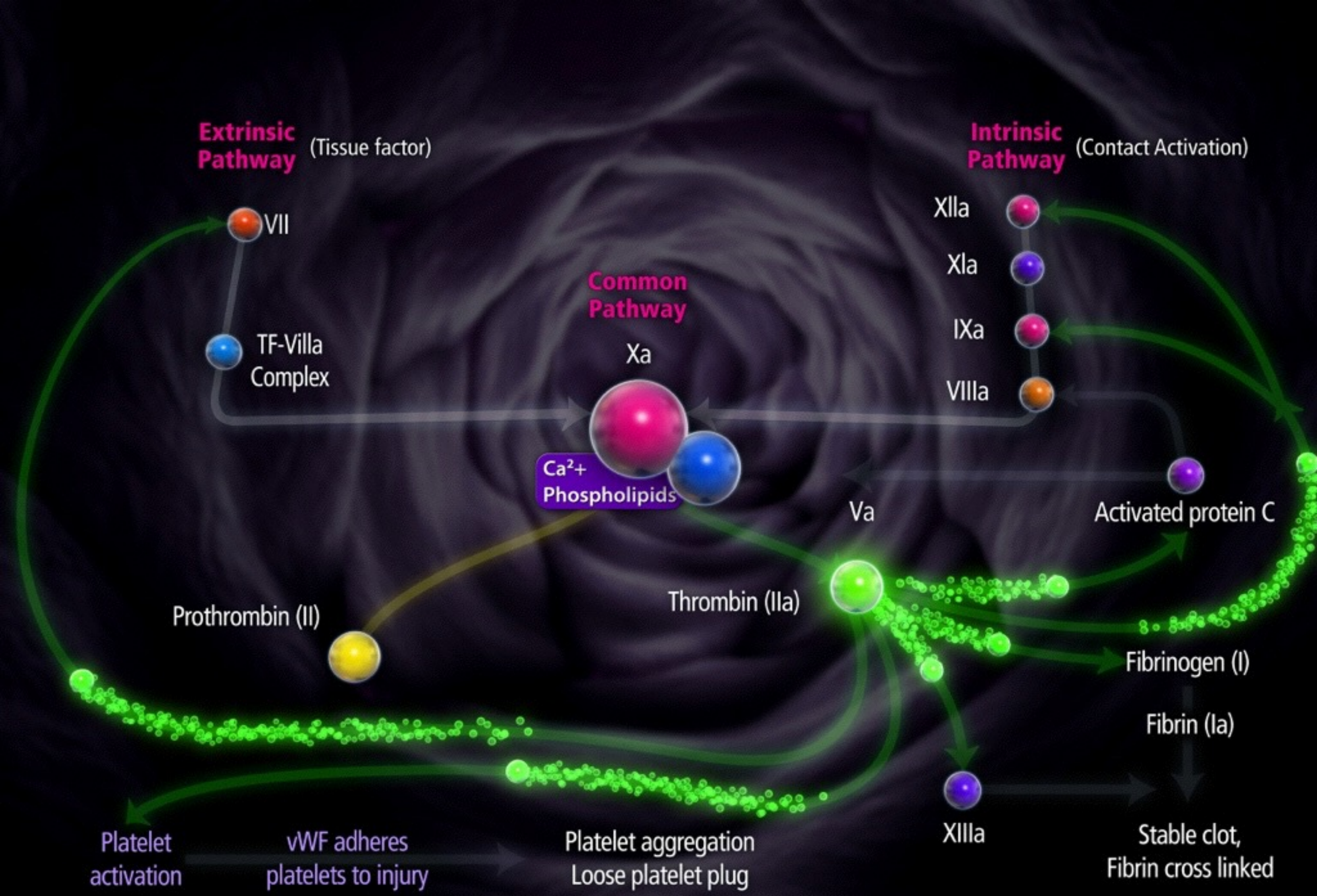
Indication for Anticoagulation

<u>Arterial:</u>

- Atrial Fibrillation/ Flutter
- Mechanical valves
- Hypercoagulable state such as antiphospholipid antibody syndrome.

<u>Venous:</u>

- Deep vein thrombosis and pulmonary embolism
- Hypercoagulable state: Antiphospholipid antibody syndrome or high risk thrombophilia such as protein C, protein S and anti-thrombin III deficiency.


Extrinsic Pathway
(Tissue factor)
VII
TF-VIIa Complex
Intrinsic Pathway
(Contact Activation)
XIIa
XIa
IXa
VIIIa
Common Pathway
Xa
Ca2+ Phospholipids
Va
Activated protein C
Prothrombin (II)
Thrombin (IIa)
Fibrinogen (I)
Fibrin (Ia)
XIIIa
Platelet activation
vWF adheres platelets to injury
Platelet aggregation
Loose platelet plug
Stable clot,
Fibrin cross linked

Rivaroxaban
Apixaban
Edoxaban
Betrixaban

Extrinsic Pathway (Tissue factor)

VII warfarin

TF-Villa Complex

Intrinsic Pathway (Contact Activation)

XIIa

XIa

IXa warfarin

VIIIa

Common Pathway

Xa

warfarin

Ca^{2+} Phospholipids

Va

Activated protein C

warfarin

Prothrombin (II)

Thrombin (IIa)

Dabigatran

Fibrinogen (I)

Fibrin (Ia)

Platelet activation

vWF adheres platelets to injury

Platelet aggregation
Loose platelet plug

XIIIa

Stable clot,
Fibrin cross linked

Warfarin

A retrospective cohort study focused on the use of periprocedural anticoagulation found that delayed postpolypectomy bleeding occurred in 2.6% of patients who discontinued warfarin prior to colonoscopy, compared with 0.2% of patients who are not anticoagulated.

The risk of bleeding with heparin bridging during warfarin interruption is higher (20%) than no bridging (1.4%)

Witt DM, Delate T, McCool KH, et al. Incidence and predictors of bleeding or thrombosis after polypectomy in patients receiving and not receiving anticoagulation therapy. J Thromb Haemost. 2009;7(12): 1982-1989

Inoue T, Nishida T, Maekawa A, et al. Clinical features of post-polypectomy bleeding associated with heparin bridge therapy. Dig Endosc. 2014;26(2):243-249

Warfarin

- Current guidelines recommend discontinuing warfarin for high risk procedures like polypectomy.
- In high risk patients, bridging anticoagulation is recommended.

Indications for Bridging Anticoagulation

Table 1—*[Introduction] Suggested Risk Stratification for Perioperative Thromboembolism*

Risk Stratum	Indication for VKA Therapy		
	Mechanical Heart Valve	Atrial Fibrillation	VTE
High[a]	• Any mitral valve prosthesis • Any caged-ball or tilting disc aortic valve prosthesis • Recent (within 6 mo) stroke or transient ischemic attack	• $CHADS_2$ score of 5 or 6 • Recent (within 3 mo) stroke or transient ischemic attack • Rheumatic valvular heart disease	• Recent (within 3 mo) VTE • Severe thrombophilia (eg, deficiency of protein C, protein S, or antithrombin; antiphospholipid antibodies; multiple abnormalities)
Moderate	• Bileaflet aortic valve prosthesis and one or more of the of following risk factors: atrial fibrillation, prior stroke or transient ischemic attack, hypertension, diabetes, congestive heart failure, age > 75 y	• $CHADS_2$ score of 3 or 4	• VTE within the past 3-12 mo • Nonsevere thrombophilia (eg, heterozygous factor V Leiden or prothrombin gene mutation) • Recurrent VTE • Active cancer (treated within 6 mo or palliative)
Low	• Bileaflet aortic valve prosthesis without atrial fibrillation and no other risk factors for stroke	• $CHADS_2$ score of 0 to 2 (assuming no prior stroke or transient ischemic attack)	• VTE > 12 mo previous and no other risk factors

$CHADS_2$ = congestive heart failure, hypertension, age ≥ 75 years, diabetes mellitus, and stroke or transient ischemic attack; VKA = vitamin K antagonist.
[a]High-risk patients may also include those with a prior stroke or transient ischemic attack occurring > 3 mo before the planned surgery and a $CHADS_2$ score < 5, those with prior thromboembolism during temporary interruption of VKAs, or those undergoing certain types of surgery associated with an increased risk for stroke or other thromboembolism (eg, cardiac valve replacement, carotid endarterectomy, major vascular surgery).

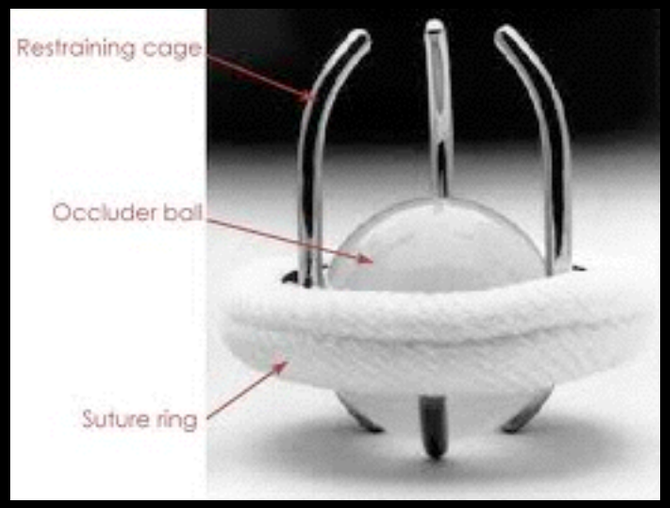
- individual patient factors need to be considered when using this risk stratification table.
  - ex. PE more than one year ago, associated with severe pulmonary hypertension.
- **High risk**: >10% risk of thromboembolism per year
- **moderate risk:** 5 - 10% risk of thromboembolism per year
- **low risk:** <5% risk of thromboembolism per year

Table 1—*[Introduction] Suggested Risk Stratification for Perioperative Thromboembolism*

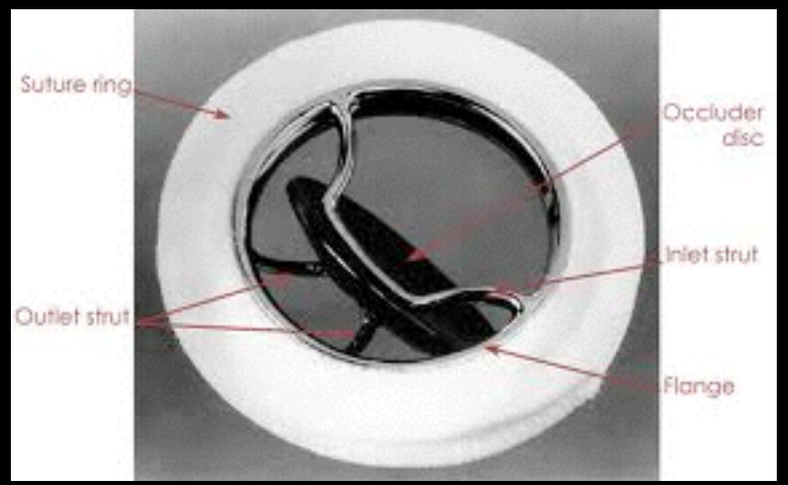
Risk Stratum	Indication for VKA Therapy		
	Mechanical Heart Valve	Atrial Fibrillation	VTE
High[a]	• Any mitral valve prosthesis • Any caged-ball or tilting disc aortic valve prosthesis • Recent (within 6 mo) stroke or transient ischemic attack	• $CHADS_2$ score of 5 or 6 • Recent (within 3 mo) stroke or transient ischemic attack • Rheumatic valvular heart disease	• Recent (within 3 mo) VTE • Severe thrombophilia (eg, deficiency of protein C, protein S, or antithrombin; antiphospholipid antibodies; multiple abnormalities)
Moderate	• Bileaflet aortic valve prosthesis and one or more of the of following risk factors: atrial fibrillation, prior stroke or transient ischemic attack, hypertension, diabetes, congestive heart failure, age > 75 y	• $CHADS_2$ score of 3 or 4	• VTE within the past 3-12 mo • Nonsevere thrombophilia (eg, heterozygous factor V Leiden or prothrombin gene mutation) • Recurrent VTE • Active cancer (treated within 6 mo or palliative)
Low	• Bileaflet aortic valve prosthesis without atrial fibrillation and no other risk factors for stroke	• $CHADS_2$ score of 0 to 2 (assuming no prior stroke or transient ischemic attack)	• VTE > 12 mo previous and no other risk factors

$CHADS_2$ = congestive heart failure, hypertension, age ≥ 75 years, diabetes mellitus, and stroke or transient ischemic attack; VKA = vitamin K antagonist.
[a]High-risk patients may also include those with a prior stroke or transient ischemic attack occurring > 3 mo before the planned surgery and a $CHADS_2$ score < 5, those with prior thromboembolism during temporary interruption of VKAs, or those undergoing certain types of surgery associated with an increased risk for stroke or other thromboembolism (eg, cardiac valve replacement, carotid endarterectomy, major vascular surgery).

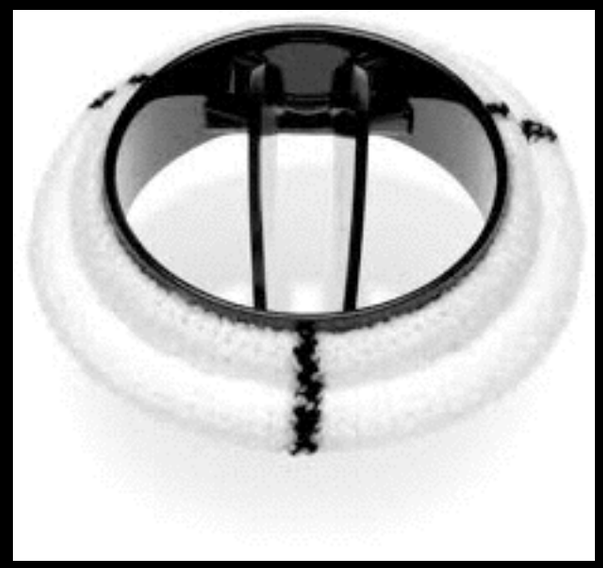
Risk Stratum	Mechanical Heart Valve
High[a]	• Any mitral valve prosthesis • Any caged-ball or tilting disc aortic valve prosthesis • Recent (within 6 mo) stroke or transient ischemic attack
Moderate	• Bileaflet aortic valve prosthesis and one or more of the of following risk factors: atrial fibrillation, prior stroke or transient ischemic attack, hypertension, diabetes, congestive heart failure, age > 75 y
Low	• Bileaflet aortic valve prosthesis without atrial fibrillation and no other risk factors for stroke



Starr-Edwards
Ball-in-Cage



SingleTilting leaflet
Medtronic Hall



St. Jude Bileaflet

Table 1—*[Introduction] Suggested Risk Stratification for Perioperative Thromboembolism*

Risk Stratum	Indication for VKA Therapy		
	Mechanical Heart Valve	Atrial Fibrillation	VTE
High[a]	• Any mitral valve prosthesis • Any caged-ball or tilting disc aortic valve prosthesis • Recent (within 6 mo) stroke or transient ischemic attack	• $CHADS_2$ score of 5 or 6 • Recent (within 3 mo) stroke or transient ischemic attack • Rheumatic valvular heart disease	• Recent (within 3 mo) VTE • Severe thrombophilia (eg, deficiency of protein C, protein S, or antithrombin; antiphospholipid antibodies; multiple abnormalities)
Moderate	• Bileaflet aortic valve prosthesis and one or more of the of following risk factors: atrial fibrillation, prior stroke or transient ischemic attack, hypertension, diabetes, congestive heart failure, age > 75 y	• $CHADS_2$ score of 3 or 4	• VTE within the past 3-12 mo • Nonsevere thrombophilia (eg, heterozygous factor V Leiden or prothrombin gene mutation) • Recurrent VTE • Active cancer (treated within 6 mo or palliative)
Low	• Bileaflet aortic valve prosthesis without atrial fibrillation and no other risk factors for stroke	• $CHADS_2$ score of 0 to 2 (assuming no prior stroke or transient ischemic attack)	• VTE > 12 mo previous and no other risk factors

$CHADS_2$ = congestive heart failure, hypertension, age ≥ 75 years, diabetes mellitus, and stroke or transient ischemic attack; VKA = vitamin K antagonist.

[a]High-risk patients may also include those with a prior stroke or transient ischemic attack occurring > 3 mo before the planned surgery and a $CHADS_2$ score < 5, those with prior thromboembolism during temporary interruption of VKAs, or those undergoing certain types of surgery associated with an increased risk for stroke or other thromboembolism (eg, cardiac valve replacement, carotid endarterectomy, major vascular surgery).

Table 1—*[Introduction] Suggested Risk Stratification for Perioperative Thromboembolism*

Risk Stratum	Indication for VKA Therapy		
	Mechanical Heart Valve	Atrial Fibrillation	VTE
High[a]	• Any mitral valve prosthesis • Any caged-ball or tilting disc aortic valve prosthesis • Recent (within 6 mo) stroke or transient ischemic attack	• $CHADS_2$ score of 5 or 6 • Recent (within 3 mo) stroke or transient ischemic attack • Rheumatic valvular heart disease	• Recent (within 3 mo) VTE • Severe thrombophilia (eg, deficiency of protein C, protein S, or antithrombin; antiphospholipid antibodies; multiple abnormalities)
Moderate	• Bileaflet aortic valve prosthesis and one or more of the of following risk factors: atrial fibrillation, prior stroke or transient ischemic attack, hypertension, diabetes, congestive heart failure, age > 75 y	• $CHADS_2$ score of 3 or 4	• VTE within the past 3-12 mo • Nonsevere thrombophilia (eg, heterozygous factor V Leiden or prothrombin gene mutation) • Recurrent VTE • Active cancer (treated within 6 mo or palliative)
Low	• Bileaflet aortic valve prosthesis without atrial fibrillation and no other risk factors for stroke	• $CHADS_2$ score of 0 to 2 (assuming no prior stroke or transient ischemic attack)	• VTE > 12 mo previous and no other risk factors

$CHADS_2$ = congestive heart failure, hypertension, age ≥ 75 years, diabetes mellitus, and stroke or transient ischemic attack; VKA = vitamin K antagonist.
[a]High-risk patients may also include those with a prior stroke or transient ischemic attack occurring > 3 mo before the planned surgery and a $CHADS_2$ score < 5, those with prior thromboembolism during temporary interruption of VKAs, or those undergoing certain types of surgery associated with an increased risk for stroke or other thromboembolism (eg, cardiac valve replacement, carotid endarterectomy, major vascular surgery).

Risk Stratum	Atrial Fibrillation
High[a]	• $CHADS_2$ score of 5 or 6 • Recent (within 3 mo) stroke or transient ischemic attack • Rheumatic valvular heart disease
Moderate	• $CHADS_2$ score of 3 or 4
Low	• $CHADS_2$ score of 0 to 2 (assuming no prior stroke or transient ischemic attack)

Table 1—*[Introduction] Suggested Risk Stratification for Perioperative Thromboembolism*

Risk Stratum	Indication for VKA Therapy		
	Mechanical Heart Valve	Atrial Fibrillation	VTE
High[a]	• Any mitral valve prosthesis • Any caged-ball or tilting disc aortic valve prosthesis • Recent (within 6 mo) stroke or transient ischemic attack	• $CHADS_2$ score of 5 or 6 • Recent (within 3 mo) stroke or transient ischemic attack • Rheumatic valvular heart disease	• Recent (within 3 mo) VTE • Severe thrombophilia (eg, deficiency of protein C, protein S, or antithrombin; antiphospholipid antibodies; multiple abnormalities)
Moderate	• Bileaflet aortic valve prosthesis and one or more of the of following risk factors: atrial fibrillation, prior stroke or transient ischemic attack, hypertension, diabetes, congestive heart failure, age > 75 y	• $CHADS_2$ score of 3 or 4	• VTE within the past 3-12 mo • Nonsevere thrombophilia (eg, heterozygous factor V Leiden or prothrombin gene mutation) • Recurrent VTE • Active cancer (treated within 6 mo or palliative)
Low	• Bileaflet aortic valve prosthesis without atrial fibrillation and no other risk factors for stroke	• $CHADS_2$ score of 0 to 2 (assuming no prior stroke or transient ischemic attack)	• VTE > 12 mo previous and no other risk factors

$CHADS_2$ = congestive heart failure, hypertension, age ≥ 75 years, diabetes mellitus, and stroke or transient ischemic attack; VKA = vitamin K antagonist.

[a]High-risk patients may also include those with a prior stroke or transient ischemic attack occurring > 3 mo before the planned surgery and a $CHADS_2$ score < 5, those with prior thromboembolism during temporary interruption of VKAs, or those undergoing certain types of surgery associated with an increased risk for stroke or other thromboembolism (eg, cardiac valve replacement, carotid endarterectomy, major vascular surgery).

Table 1—*[Introduction] Suggested Risk Stratification for Perioperative Thromboembolism*

Risk Stratum	Indication for VKA Therapy		
	Mechanical Heart Valve	Atrial Fibrillation	VTE
High[a]	• Any mitral valve prosthesis • Any caged-ball or tilting disc aortic valve prosthesis • Recent (within 6 mo) stroke or transient ischemic attack	• $CHADS_2$ score of 5 or 6 • Recent (within 3 mo) stroke or transient ischemic attack • Rheumatic valvular heart disease	• Recent (within 3 mo) VTE • Severe thrombophilia (eg, deficiency of protein C, protein S, or antithrombin; antiphospholipid antibodies; multiple abnormalities)
Moderate	• Bileaflet aortic valve prosthesis and one or more of the of following risk factors: atrial fibrillation, prior stroke or transient ischemic attack, hypertension, diabetes, congestive heart failure, age > 75 y	• $CHADS_2$ score of 3 or 4	• VTE within the past 3-12 mo • Nonsevere thrombophilia (eg, heterozygous factor V Leiden or prothrombin gene mutation) • Recurrent VTE • Active cancer (treated within 6 mo or palliative)
Low	• Bileaflet aortic valve prosthesis without atrial fibrillation and no other risk factors for stroke	• $CHADS_2$ score of 0 to 2 (assuming no prior stroke or transient ischemic attack)	• VTE > 12 mo previous and no other risk factors

$CHADS_2$ = congestive heart failure, hypertension, age ≥ 75 years, diabetes mellitus, and stroke or transient ischemic attack; VKA = vitamin K antagonist.
[a]High-risk patients may also include those with a prior stroke or transient ischemic attack occurring > 3 mo before the planned surgery and a $CHADS_2$ score < 5, those with prior thromboembolism during temporary interruption of VKAs, or those undergoing certain types of surgery associated with an increased risk for stroke or other thromboembolism (eg, cardiac valve replacement, carotid endarterectomy, major vascular surgery).

Risk Stratum	VTE
High[a]	• Recent (within 3 mo) VTE • Severe thrombophilia (eg, deficiency of protein C, protein S, or antithrombin; antiphospholipid antibodies; multiple abnormalities)
Moderate	• VTE within the past 3-12 mo • Nonsevere thrombophilia (eg, heterozygous factor V Leiden or prothrombin gene mutation) • Recurrent VTE • Active cancer (treated within 6 mo or palliative)
Low	• VTE > 12 mo previous and no other risk factors

Table 1—*[Introduction] Suggested Risk Stratification for Perioperative Thromboembolism*

Risk Stratum	Indication for VKA Therapy		
	Mechanical Heart Valve	Atrial Fibrillation	VTE
High[a]	• Any mitral valve prosthesis • Any caged-ball or tilting disc aortic valve prosthesis • Recent (within 6 mo) stroke or transient ischemic attack	• $CHADS_2$ score of 5 or 6 • Recent (within 3 mo) stroke or transient ischemic attack • Rheumatic valvular heart disease	• Recent (within 3 mo) VTE • Severe thrombophilia (eg, deficiency of protein C, protein S, or antithrombin; antiphospholipid antibodies; multiple abnormalities)
Moderate	• Bileaflet aortic valve prosthesis and one or more of the of following risk factors: atrial fibrillation, prior stroke or transient ischemic attack, hypertension, diabetes, congestive heart failure, age > 75 y	• $CHADS_2$ score of 3 or 4	• VTE within the past 3-12 mo • Nonsevere thrombophilia (eg, heterozygous factor V Leiden or prothrombin gene mutation) • Recurrent VTE • Active cancer (treated within 6 mo or palliative)
Low	• Bileaflet aortic valve prosthesis without atrial fibrillation and no other risk factors for stroke	• $CHADS_2$ score of 0 to 2 (assuming no prior stroke or transient ischemic attack)	• VTE > 12 mo previous and no other risk factors

$CHADS_2$ = congestive heart failure, hypertension, age ≥ 75 years, diabetes mellitus, and stroke or transient ischemic attack; VKA = vitamin K antagonist.
[a]High-risk patients may also include those with a prior stroke or transient ischemic attack occurring > 3 mo before the planned surgery and a $CHADS_2$ score < 5, those with prior thromboembolism during temporary interruption of VKAs, or those undergoing certain types of surgery associated with an increased risk for stroke or other thromboembolism (eg, cardiac valve replacement, carotid endarterectomy, major vascular surgery).

Two patients with A. Fib:
CHADS2 score: 3 (stroke, DM)
CHADS2 score: 3 (HTN, DM, age)

Patient with >1 year ago VTE associated with pulmonary hypertension

Indications for Bridging Anticoagulation

- Complex decision
- often associated with increase morbidity (bleeding/thrombosis)
- Different comfort zones for different health care providers.
- Patient health literacy plays a significant role in reducing morbidity around bridging anticoagulation.

	Rivaroxaban	Edoxaban	Apixaban	Dabigatran
Mechanism of Action	Direct factor Xa inhibitor			Direct thrombin inhibitor
Bioavailability	80%	62%	50%	6.5%
Renal Excretion	30%	50%	25%	80%
Peak Serum concentration	2.5 - 4 hrs	1-2 hrs	1 -2 hrs	1 - 2 hrs
Half-life	5 - 9 hrs	9 - 11 hrs	12 hrs	12 -17 hrs

Bleeding and Thrombotic Risk associated with DOACs

- Currently no clear data available

- published data are retrospective and based on the pivotal trials which introduced these drugs

Preoperative Interruption of DOACs

	Low Bleeding Risk		High Bleeding Risk	
Renal Function:	CrCl >50 ml/min	CrCl 30-49 ml/min	CrCl >50 ml/min	CrCl 30-49 ml/min
Dabigatran	**24 hrs**	**48 -72 hrs**	**48-72hrs**	**96 hrs**
Rivaroxaban	**24 hrs**	**48 hrs**	**48-72 hrs**	**72 hrs**
Apixaban	**24 hrs**	**48 hrs**	**48-72 hrs**	**72 hrs**

Postoperative Resumption of DOACs

	Low Bleeding Risk	High Bleeding Risk
Dabigatran	**resume 24 hr after surgery**	**Resume 48-72 hrs after surgery***
Rivaroxaban	**resume 24 hr after surgery**	**Resume 48-72 hrs after surgery***
Apixaban	**resume 24 hr after surgery**	**Resume 48-72 hrs after surgery***

* Consider DVT prophylaxis and/or alternatives such as IV heparin

Thank you.