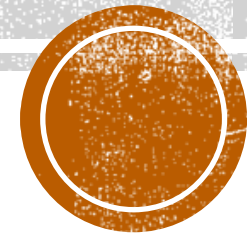


DENTAL EXTRACTIONS IN PATIENTS ON ANTICOAGULATION THERAPY



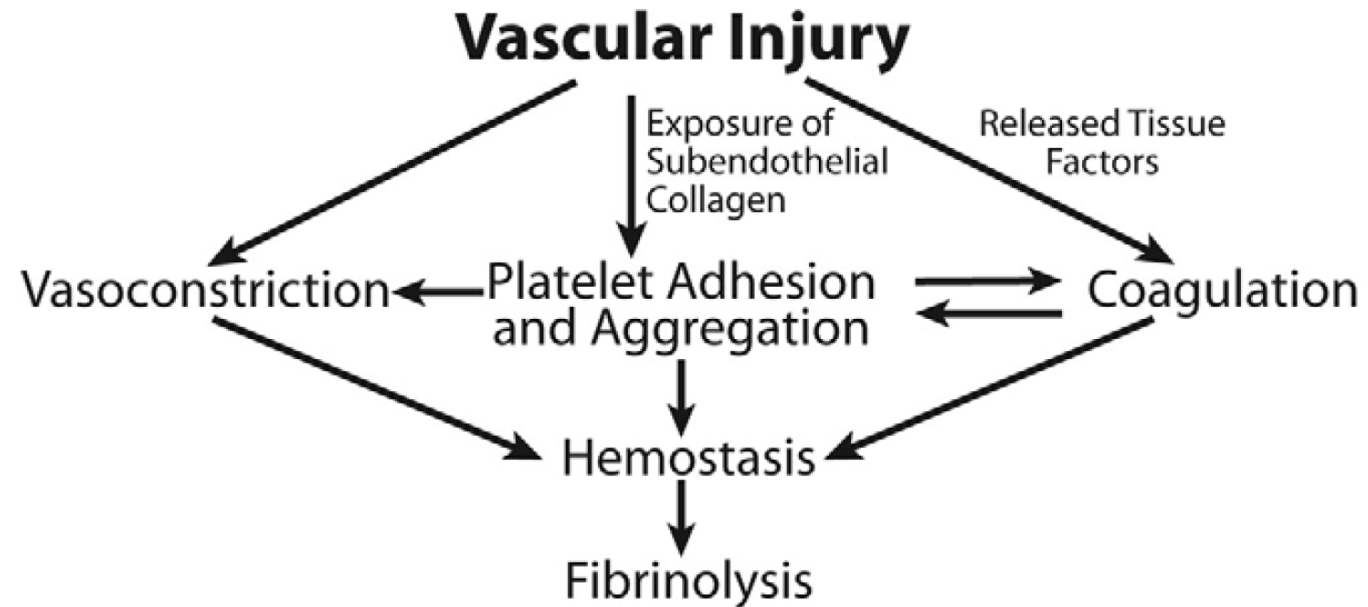
*Dr. Andrea Bordoy, DDS
Assistant Professor
Oral and Maxillofacial Surgery Department
School of Dentistry*

OBJECTIVES

- To understand the principles of anticoagulation therapy and its impact on dental procedures.
- To identify the common anticoagulant medications and their management during dental extractions.
- To learn about the precautions, techniques, and protocols for safe dental extractions in patients on anticoagulation therapy.
- To discuss case studies and best practices in managing bleeding and complications in such patients during and after dental extraction

HEMOSTASIS

Simplified View of the Hemostasis Process



HEMOSTASIS

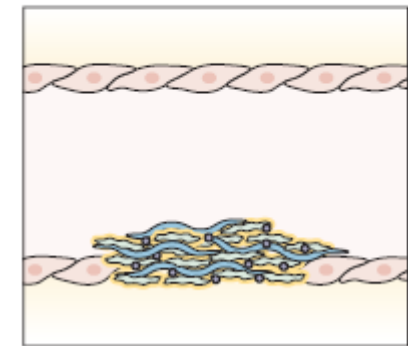
PRIMARY HEMOSTASIS



BOX 24-2 Normal Control of Bleeding

1. Vascular phase
 - a. Vasoconstriction occurs in area of injury.
 - b. Begins immediately after injury.
2. Platelet phase
 - a. Platelets and vessel wall become "sticky."
 - b. Mechanical plug of platelets seals off openings of cut vessels.
 - c. Begins seconds after injury.
3. Coagulation phase
 - a. Blood lost into surrounding area coagulates through extrinsic and common pathways.
 - b. Blood in vessels in area of injury coagulates through intrinsic and common pathways.
 - c. Takes place more slowly than other phases.
4. Fibrinolytic phase
 - a. Release of antithrombotic agents
 - b. Destruction of antithrombotic agents by spleen and liver

SECONDARY HEMOSTASIS



COAGULATION CASCADE

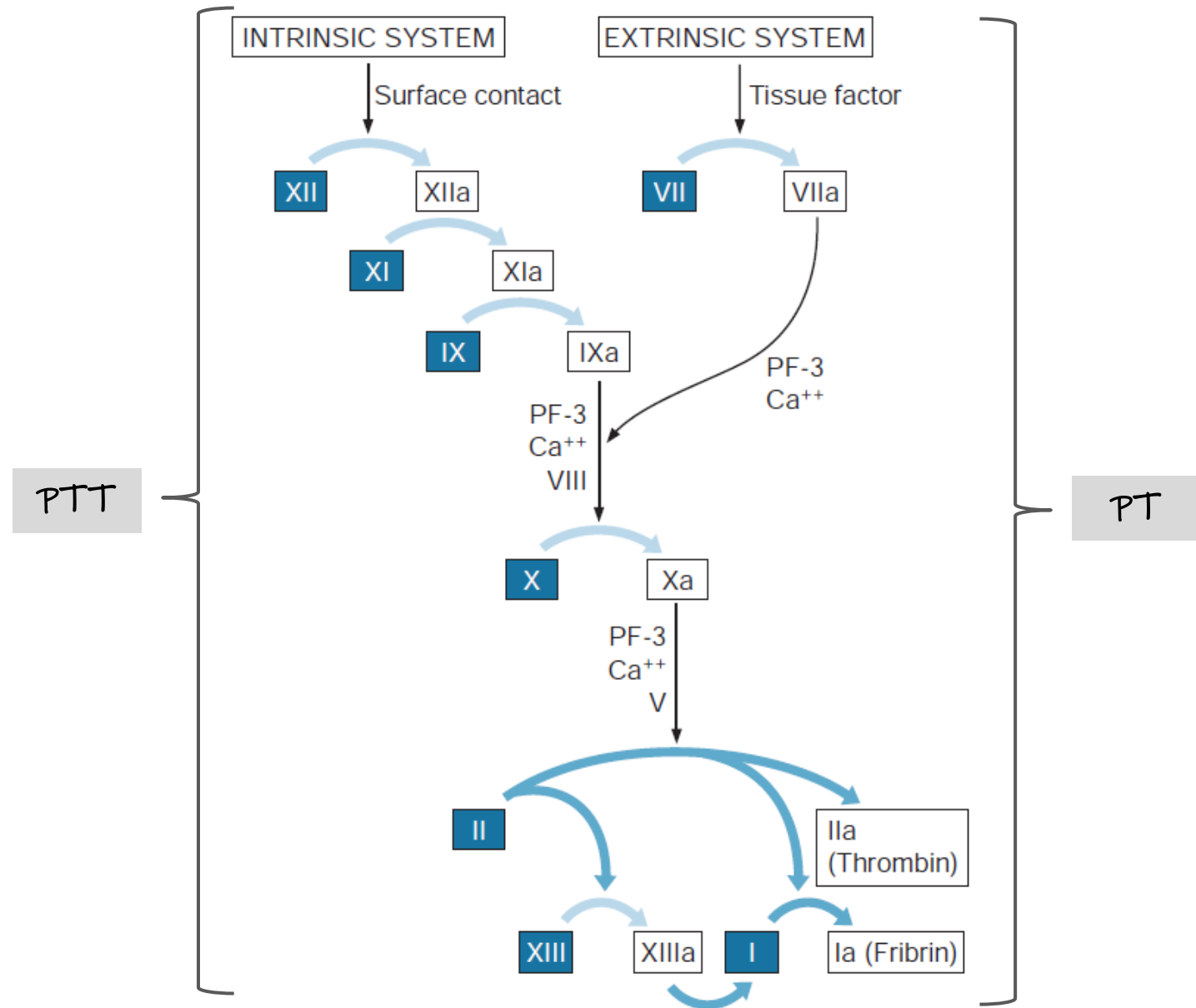


Table. Common anticoagulants, their indications, and potential interactions with dental medications.

DRUG CLASS	USUAL INDICATION	NEED FOR ROUTINE MONITORING	DRUG INTERACTIONS WITH COMMON DENTAL MEDICATIONS*
Vitamin K Antagonists Warfarin (Coumadin) Acenocoumarol (Sintrom)	Rheumatic atrial fibrillation Mechanical heart valve Thrombosis with anti-phospholipid antibodies Contraindication to alternative agents	Yes (international normalized ratio)	Antibiotics ^{†,10,11} Clindamycin Amoxicillin Amoxicillin clavulanate Cephalexin Doxycycline Metronidazole Macrolides Azole antifungals ¹⁰ Analgesics ¹²⁻¹⁴ Carbamazepine Oxcarbazepine NSAIDs [‡]
Direct Oral Anticoagulants Apixaban (Eliquis) Rivaroxaban (Xarelto) Dabigatran (Pradaxa) Edoxaban (Savaysa, Lixiana)	Nonvalvular atrial fibrillation Venous thrombosis without cancer or severe thrombophilia	No [§]	Antibiotics ¹⁵ Clarithromycin Erythromycin [¶] Azole antifungals ¹⁵ Analgesics ¹⁵ Carbamazepine NSAIDs
Low-Molecular-Weight Heparins Tinzaparin (Innohep) Dalteparin (Fragmin) Enoxaparin (Lovenox)	Thrombosis or prophylaxis in pregnancy Thrombosis in cancer	No [§]	Analgesics ¹⁶ NSAIDs

* This list is not exhaustive. † Single doses of antibiotics are unlikely to alter anticoagulation effect in a clinically significant manner. Consider increased monitoring for 2 or more days of therapy. ‡ NSAID: Nonsteroidal anti-inflammatory drug. § Direct drug levels or surrogate markers (factor Xa, dilute thrombin time) are used in rare circumstances. ¶ Erythromycin predominantly interacts with dabigatran and edoxaban.

INDICATIONS

ANTITHROMBOTIC DRUGS

TABLE 24-5 Current Antithrombotic Agents: Antiplatelet Drugs

Agent	Indication(s)	Dosage	Monitoring	Complications
Aspirin	Prevention: recurrent MI, stroke, coronary thrombosis	Oral; 75-325 mg once daily	Usually none	GI bleeding Tinnitus Urticaria Bronchospasm
Aspirin plus dipyridamole (Aggrenox)	Stroke prevention (history of TIA)	Oral; <i>aspirin</i> : 50 mg bid; <i>dipyridamole</i> : 200 mg	Usually none	GI bleeding GI ulceration Urticaria Bronchospasm
NSAIDs Ibuprofen (Advil, Motrin)	Prevention: recurrent MI, stroke, coronary thrombosis.	Oral; 400 mg once daily	Usually none	GI bleeding GI ulceration Rash, urticaria Tinnitus
ADP inhibitors Clopidogrel (Plavix) Ticlopidine (Ticlid)	TIA, stroke, and MI prevention	Oral; <i>clopidogrel</i> : 75 mg once daily; <i>ticlopidine</i> : 250 mg bid	Usually none CBC q2wk	GI bleeding Thrombocytopenia Diarrhea
Fibrinogen receptor inhibitors (GP IIb/IIIa) Tirofiban (Aggrastat) Abciximab (ReoPro) Eptifibatid (Integrilin)	Prevention: recurrent MI, stroke, TIA	<i>Tirofiban</i> : IV 0.4 µg/kg/min for 30 minutes, then 0.1 µg/kg/min until steady state achieved	Usually none	GI bleeding GI ulceration Rash Neutropenia Thrombocytopenia

Antiplatelets

ADP, Adenosine diphosphate; CBC, Complete blood count; GI, Gastrointestinal; GP, Glycoprotein; IV, Intravenously; MI, Myocardial infarction; NSAIDs, Nonsteroidal antiinflammatory drugs; Rx, Prescription; TIA, Transient ischemic attack.

ANTICOAGULANTS

ANTITHROMBOTIC DRUGS

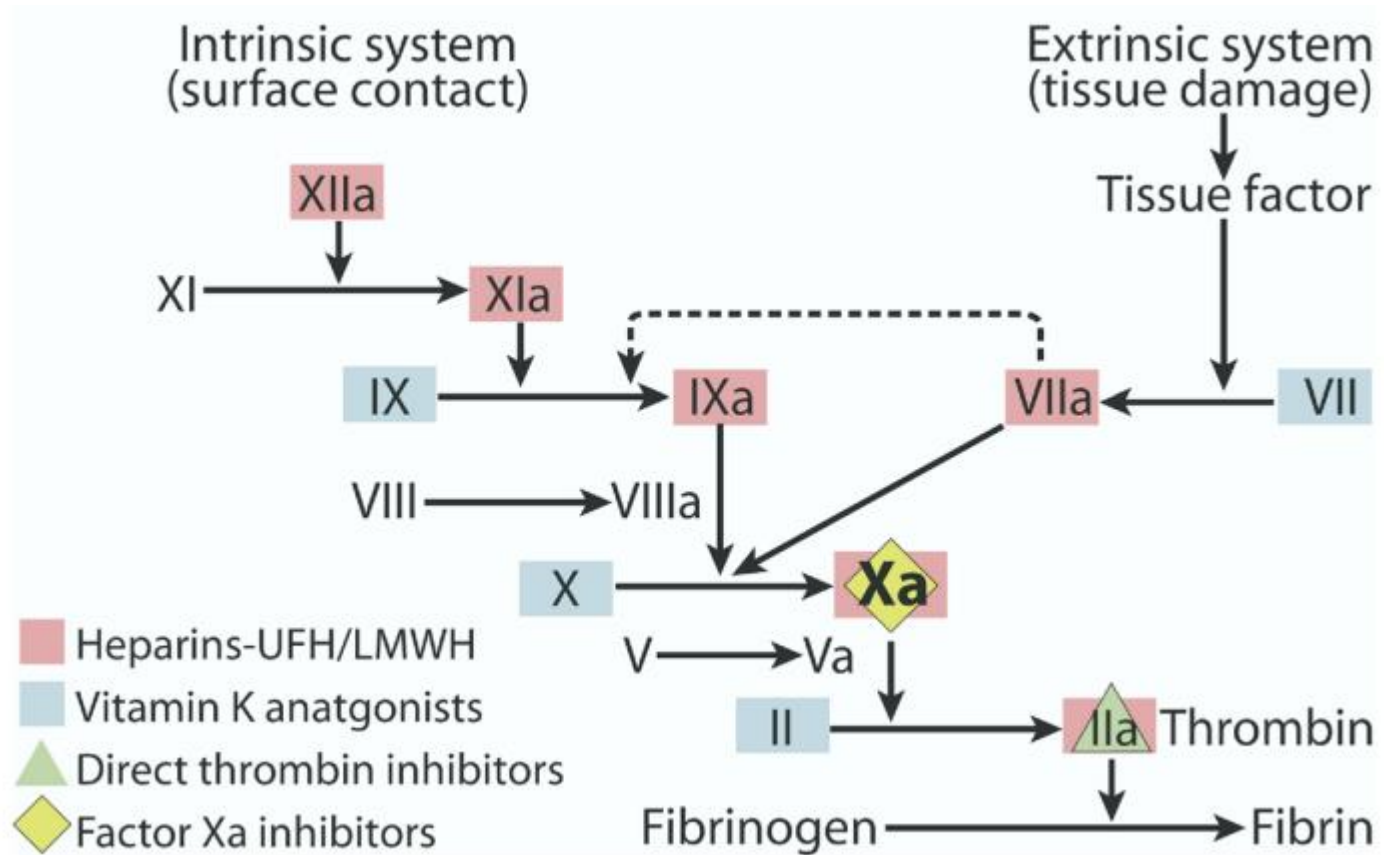
TABLE 24-4 Current Antithrombotic Agents: Anticoagulants

Agent	Indications	Dosage	Monitoring	Complications
Standard heparin, high-dose	Treatment of DVT Treatment of PE Prevention of DVT	IV bolus 5000-10,000 units, IV infusion at rate of 1300 U/hr over 5-10 days	aPTT 1.5-2.5 times the mean laboratory control value	Bleeding Thrombocytopenia
Standard heparin, low-dose	Prevention of DVT	SC; 5000 units 2 hr before surgery and q8-12h until ambulatory	None	Bleeding Thrombocytopenia
Warfarin (Coumadin)	Treatment of DVT, PE Prevention of DVT, or thrombosis in AF: MPHV Prevention of recurrent MI	Oral, 5-7 mg/day for 3 to 6 months Oral, 7-10 mg/day, long term	INR: 2.0 to 3.0 INR: 2.5 to 3.5	Bleeding intolerance Alopecia GI discomfort Rash, skin necrosis
LMWHs Enoxaparin (Lovenox)	Prevention of DVT Prevention of PE Treatment of DVT	<i>Enoxaparin</i> : 30 mg SC every 12 hours for up to 14 days (knee or hip) 40 mg SC once daily, with first dose 2 hours before abdominal surgery 1 mg/kg SC q12h up to 5 days	None Oral warfarin started within 72 hr	Bleeding Thrombocytopenia Anemia Fever Peripheral edema
Ardeparin (Normiflo) Dalteparin (Fragmin) Nadroparin (Fraxiparine) Reviparin (Clivarin) Tinzaparin (Innohep)				
Synthetic heparins Fondaparinux (Arixtra) Idraparinix	Prevention and treatment of DVT, PE Idraparinix in phase III trials	Given SC, 2.5 mg to 10 mg per day	None	Bleeding
Direct thrombin inhibitors Lepirudin (Refludan) Desirudin (Revasc) Argatroban (Acova) Bivalirudin (Angiox) Dabigatran (Pradaxa)	Used in patients with history of HIT; prevention or treatment of DVT FDA approval for preventing stroke in patients with atrial fibrillation	<i>Lepirudin</i> : IV 0.4 mg/kg bolus, with IV infusion 0.15 mg/ kg Given orally, 110 mg or 150 mg twice per day	aPTT: 1.5-2.5 times laboratory normal test time None	Bleeding Allergy Anaphylaxis Bleeding Dyspepsia Hypersensitivity Gastritis-like symptoms
Direct factor Xa inhibitors Rivaroxaban (Xarelto) Apixaban (Eliquis)	Rivaroxaban gained FDA approval in July of 2011 for prevention of DVT in orthopedic patients, and approval for Apixaban is expected by the end of 2011	Rivaroxaban given orally, 10 mg/day for 13 days for knee replacement surgery and for 35 days for hip replacements	None	Bleeding Nausea, vomiting Anemia Xerostomia Increase in liver transaminases

Anticoagulants

AF, Atrial fibrillation; DVT, Deep venous thrombosis; HIT, Heparin-induced thrombocytopenia; IV, Intravenously; MI, Myocardial infarction; MPHV, Mechanical prosthetic heart valve; PE, Pulmonary embolus; SC, Subcutaneously; TIA, Transient ischemic attack; FDA, Federal Drug Administration.

ANTICOAGULATION DRUGS-TARGET



UNFRACTIONATED HEPARIN (UFH) & LOW MOLECULAR WEIGHT HEPARIN (LMWH)

- Binding to antithrombin III, which *increases the ability of antithrombin III to inactivate factor Xa and factor II*
- They are *indirect inhibitors of thrombin*
- Treatment and prevention of DVT, treatment of PE
- **PTT** is used to monitor anticoagulation with *heparin* (UFH)



WARFARIN (COUMADIN®)

- Vitamin K antagonist (VKAs): *block the function of the vitamin K epoxide reductase enzyme in the liver.*
- The half-life of warfarin is generally 20 to 60 hours (mean: 40 hours)
- *PT (INR)* is used to monitor warfarin therapy because it *measures three of the vitamin K-dependent coagulation proteins: factors VII and X and prothrombin.*

TABLE 24-3 Recommended Therapeutic Range for Warfarin Therapy

INR 2.0 to 3.0 With Target of 2.5

Prophylaxis of venous thrombosis (high-risk surgery)
Treatment of venous thrombosis
Treatment of pulmonary embolism
Prevention of systemic embolism
Tissue heart valves in aortic or mitral position for first 3 months
Tissue heart valves with history of pulmonary embolism
Tissue heart valves with atrial fibrillation
Acute myocardial infarction
Atrial fibrillation
Valvular heart disease
Mitral valve prolapse with history of atrial fibrillation or embolism

INR 2.5 to 3.5 With Target of 3.0

Mechanical prosthetic heart valves
Prevention of recurrent myocardial infarction
Treatment of thrombosis associated with antiphospholipid antibodies

DIRECT ORAL ANTICOAGULANTS (DOACs)

○ Factor Xa inhibitors



1. No routine monitoring
2. Are considered safer and more predictable because of their direct effect on the coagulation cascade (targeting 1 specific factor)
3. The shortened half-life



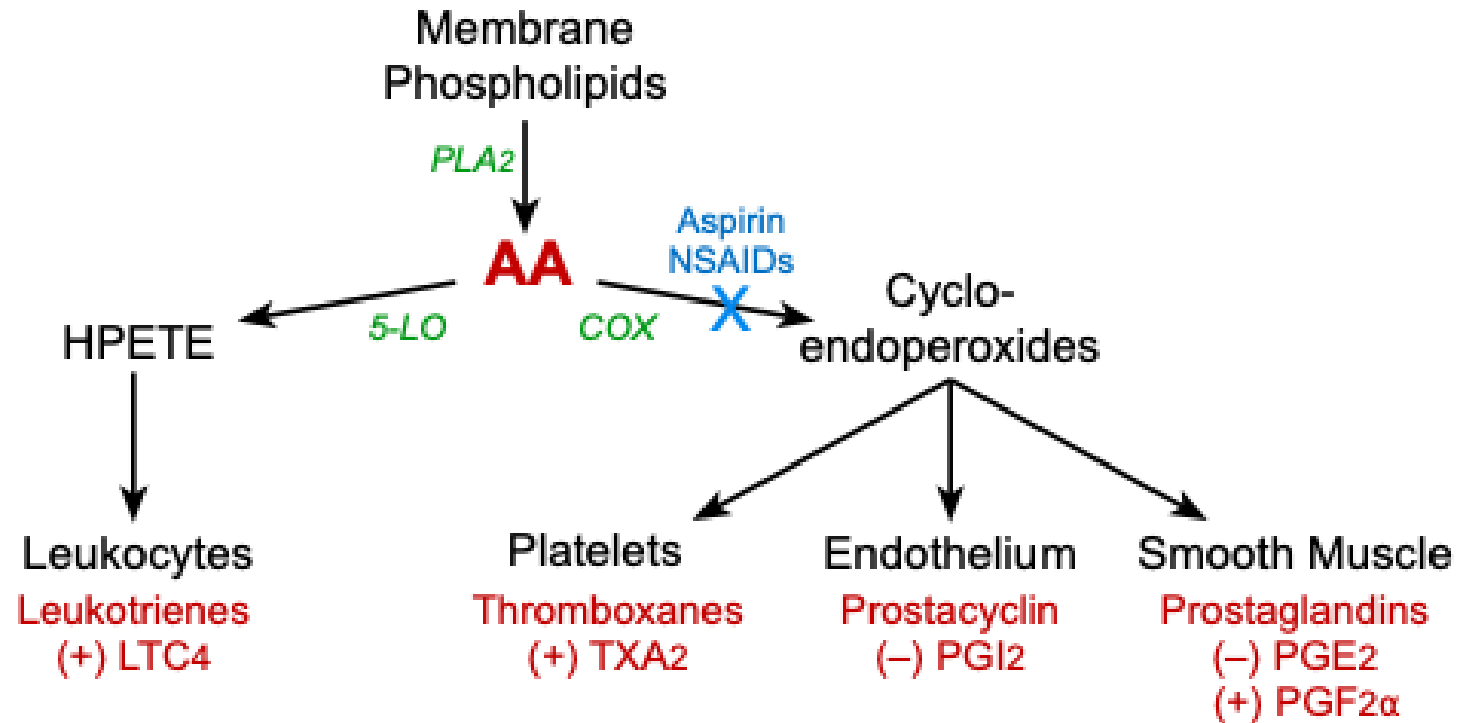
DIRECT ORAL ANTICOAGULANTS (DOACs)

- **Factor Xa inhibitors** Rivaroxaban (Xarelto), Apixaban (Eliquis), and Edoxaban which have renal excretion rates of 25 to 35% and half-lives of 5 to 9, 8 to 15, and 10 to 14 hours, respectively.
- Dabigatran, a **direct thrombin inhibitor** that has an 80 to 85% renal excretion rate and a half-life of 12 to 17 hours



ANTIPLATELETS

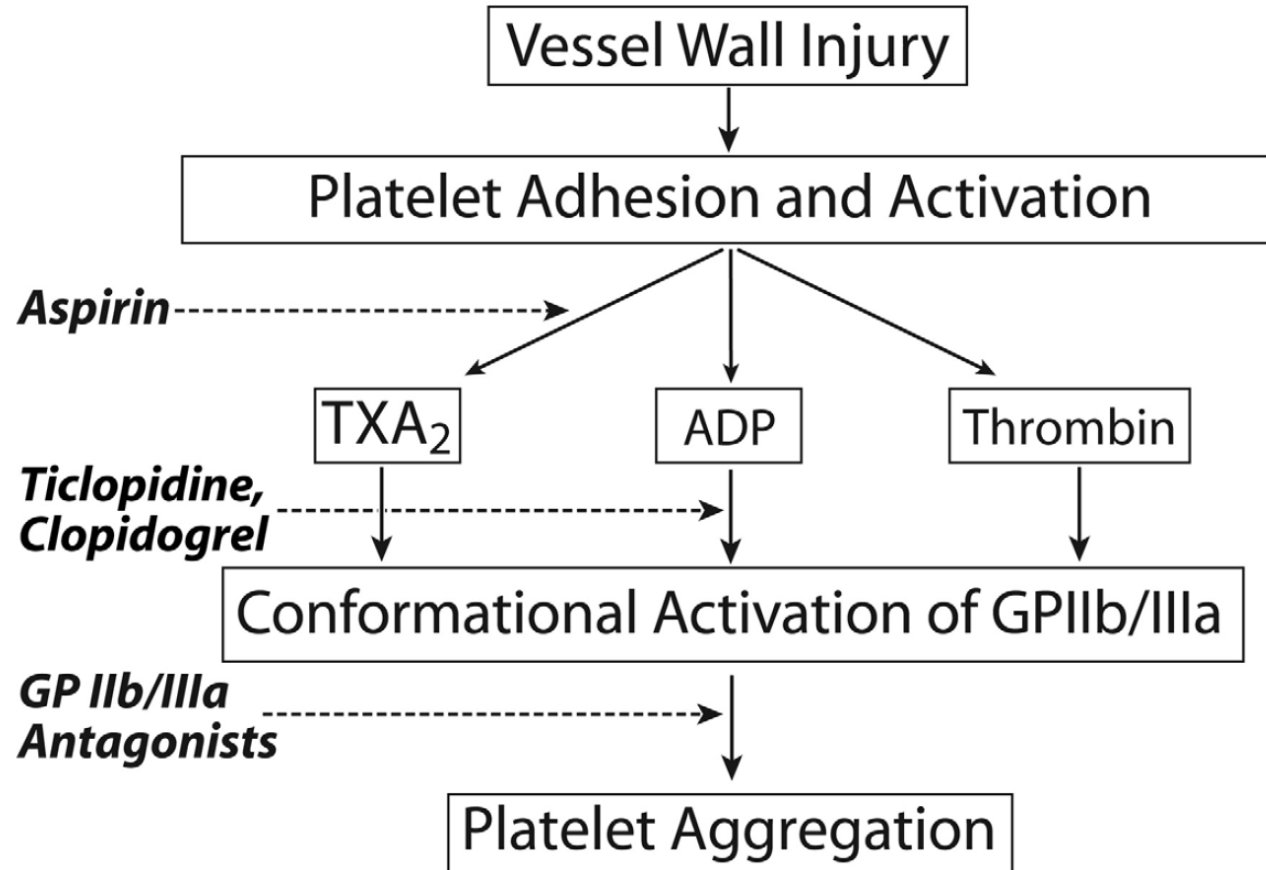
ANTIPLATELET DRUGS-TARGET



Abbreviations: AA, arachidonic acid; PLA2, phospholipase A2; COX, cyclooxygenase; NSAIDs, non-steroidal anti-inflammatory drugs; HPETE, hydroxyperoxy-eicosatetraenoic acid.

RK '22

ANTIPLATELET DRUGS-TARGET



THROMBOXANE A₂ INHIBITORS

- Acetylsalicylic acid (ASA) irreversibly acetylates and **inactivates platelet cyclooxygenase (Cox-1)**, a crucial enzyme in the Prostaglandin synthesis of Thromboxane A₂ and Prostacyclin.
- This leads to **permanent inhibition of Thromboxane A₂ production** for the lifespan of the platelet.
- The plasma half-life of aspirin is only **20 minutes**; however, because platelets cannot generate new COX, the effects of aspirin last for the duration of the life of the platelet (≈10 days)



ADP RECEPTOR ANTAGONISTS

- Ticlopidine and clopidogrel are thienopyridine derivatives that irreversibly block the binding of ADP to the platelet receptor P2Y₁₂, thus inhibiting platelet aggregation responses by various platelet agonists: thrombin, collagen, ADP, and epinephrine.
- Half life of is 6-8 hours but the effect of clopidogrel on the platelets may last for up to five days.



GP IIB-IIIa RECEPTOR ANTAGONISTS

- They block GP IIB-IIIa receptors on activated platelets, preventing fibrinogen and vWF binding, the final common pathway of platelet aggregation.
- This blockage results in more than 80% inhibition of platelet aggregation, irrespective of the platelet agonist(s).

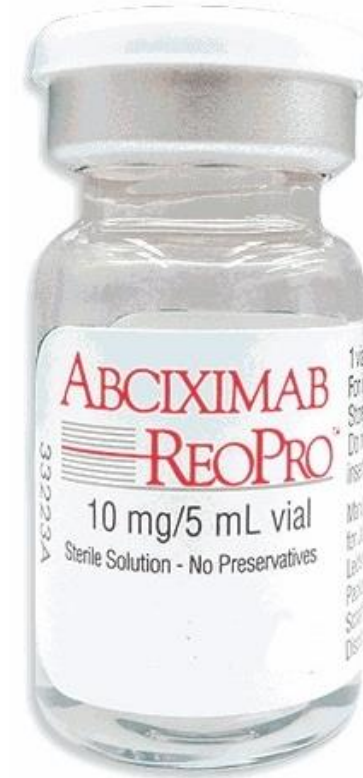


Table 1 Pharmacokinetic parameters

Drug (references)	Onset of action	Metabolism/elimination	Mean half-life*	Reversal of effect
Anti-platelet drugs				
ASA ⁹⁻¹¹	Formulation dependent, maximum effect within 0.25-12 hrs	Hydrolyzed in GI mucosa, liver, and plasma. Metabolites excreted renally.	0.4 hrs	2-4 days
Ticlopidine ¹²⁻¹³	2-4 days (maximum effect in 8-11 days)	Renal (60%) and biliary/fecal (23%)	4-5 days after repeated doses	14 days
Clopidogrel ¹⁴⁻¹⁶	Dose dependent, as early as 2 hrs	Extensively metabolized by liver	Active metabolite 8 hrs	5-7 days
Abciximab ¹⁷⁻¹⁹	10 mins following IV bolus and infusion	Unknown, probably catabolized similar to other natural proteins	Initial half life 10 mins. Then a second phase half life of 30 mins	24-48 hrs
Eptifibatide ²⁰⁻²²	15 mins	Renal (50%) and non-renal	3 hrs	4 hrs
Tirofiban ²³⁻²⁴	5 mins following IV bolus	Renal (66%), feces (23%), limited metabolism	2 hrs	4-8 hrs
Anticoagulants				
Warfarin ²⁵⁻²⁷	24 hrs, maximum effect in 2-7 days	Metabolized to inactive metabolites in liver	Variable, average of 40 hrs	2-5 days following single dose
Unfractionated heparin ²⁹⁻³⁰	Immediate following IV, 20-60 mins, following SC	Removed by the reticuloendothelial system and liver. Small fraction is excreted in urine	Route/dose dependent, average of 1-2 hrs	Variable, generally within several hrs
Low molecular weight heparin ³¹⁻³⁶	2-3 hours, maximum in 4-5 hrs	Renal excretion. Partially metabolized by liver	Drug dependent 3-5 hrs following SC	Dose- and drug-dependent, up to 24 hrs
Fondaparinux ³⁷⁻⁴⁰	30 min	Majority is excreted unchanged in urine	17-21 hrs	2-4 days
Danaparoid ⁴¹⁻⁴⁴	2-5 hrs	Renal	24 hrs	2-3 days
Direct thrombin inhibitors				
Lepirudin ⁴⁵	Rapid	Catabolic hydrolysis, renal excretion	1.3 hrs	Estimated at 5-7 hrs
Bivalirudin ⁴⁷	Immediate	Partial renal, liver metabolism, proteolysis	25 mins	1-2 hrs
Argatroban ⁴⁸	Immediate	Metabolized in liver	40-50 mins	Within 1-2 hrs

*Not known for an individual patient.

Drug (references)	Onset of action	Metabolism/elimination	Mean half-life*	Reversal of effect
Anticoagulants				Vit K
Warfarin ²⁵⁻²⁷	24 hrs, maximum effect in 2-7 days	Metabolized to inactive metabolites in liver	Variable, average of 40 hrs	2-5 days following single dose
Unfractionated heparin ²⁹⁻³⁰	Immediate following IV, 20-60 mins, following SC	Removed by the reticuloendothelial system and liver. Small fraction is excreted in urine	Route/dose dependent, average of 1-2 hrs	Variable, generally within several hrs
Low molecular weight heparin ³¹⁻³⁶	2-3 hours, maximum in 4-5 hrs	Renal excretion Partially metabolized by liver	Drug dependent 3-5 hrs following SC	Dose- and drug-dependent, up to 24 hrs

Vit K

Protamine

Drug (references)	Onset of action	Metabolism/elimination	Mean half-life*	Reversal of effect	
Direct thrombin inhibitors Lepirudin ⁴⁵	Rapid	Catabolic hydrolysis, renal excretion	1.3 hrs	Estimated at 5–7 hrs	
Bivalirudin ⁴⁷	Immediate	Partial renal, liver metabolism, proteolysis	25 mins	1–2 hrs	No specific antidote
Argatroban ⁴⁸	Immediate	Metabolized in liver	40–50 mins	Within 1–2 hrs	

*Not known for an individual patient.

Table 1 Pharmacokinetic parameters

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Anti-platelet drugs				
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Abciximab ¹⁷⁻¹⁹	10 mins following IV bolus and infusion	Unknown, probably catabolized similar to other natural proteins	Initial half life 10 mins. Then a second phase half life of 30 mins	24–48 hrs
Eptifibatide ²⁰⁻²²	15 mins	Renal (50%) and non-renal	3 hrs	4 hrs
Tirofiban ²³⁻²⁴	5 mins following IV bolus	Renal (66%), feces (23%), limited metabolism	2 hrs	4–8 hrs

No specific antidote

PREOPERATIVE EVALUATION

PREOPERATIVE EVALUATION

- *Comprehensive medical history*
- *Patient's individual bleeding risk:* past and current usage and dosage of medications, including vitamins, herbal remedies, over-the-counter drugs, and prescription medications
- *Assess bleeding risk* (intra-op and post-op) based on medical conditions, medications, previous surgical history or complications, screening labs (as needed), and the type of surgery planned
- *Medical consult?*



Box. Low-risk dental procedures not requiring anticoagulation therapy interruption.*

Dental scaling

Dental restorations that involve soft-tissue manipulation

Dental extractions that are not surgically complex

 Fewer than 3 teeth

Soft-tissue biopsy

Endodontic procedures

Implant placement

Prosthodontic procedures

 Fixed and removable dentures

 Crowns

 Bridges

* If a vitamin K antagonist is the anticoagulant used, international normalized ratio values should be within the therapeutic range whenever possible.

SCREENING LABS

BOX 24-8

Selection of Screening Laboratory Tests for Clinical Recognition of the Patient with a Potential Bleeding Problem Based on History and Examination Findings

1. No clinical or historical clues to cause of bleeding problem: excessive bleeding occurs after surgery
2. History or clinical findings or both suggest possible bleeding problem but no clues to the cause: PT, aPTT, TT, platelet count
3. Aspirin therapy: PFA-100 if available
4. Warfarin (Coumadin) therapy: INR; low-molecular-weight heparin: aPPT
5. Possible liver disease: platelet count, PT
6. Chronic leukemia: platelet count
7. Malabsorption syndrome or long-term antibiotic therapy: PT
8. Renal dialysis (heparin): aPTT
9. Vascular wall alteration: BT (results often inconsistent)
10. Primary fibrinolysis (active plasmin in circulation), cancers (lung, prostate): TT

aPTT, Activated partial thromboplastin time; *BT*, Bleeding time; *INR*, International normalized ratio; *PT*, Prothrombin time; *TT*, Thrombin time.

GUIDELINES AND RECOMMENDATIONS

TABLE 2] Suggested Risk Stratification for Procedural Bleed Risk, Based on ISTH Guidance Statements²⁵

<p>High-bleed-risk surgery/procedure^a (30-d risk of major bleed \geq 2%)</p>	<p>Major surgery with extensive tissue injury Cancer surgery, especially solid tumor resection (lung, esophagus, gastric, colon, hepatobiliary, pancreatic) Major orthopedic surgery, including shoulder replacement surgery Reconstructive plastic surgery Major thoracic surgery Urologic or GI surgery, especially anastomosis surgery Transurethral prostate resection, bladder resection, or tumor ablation Nephrectomy, kidney biopsy Colonic polyp resection Bowel resection Percutaneous endoscopic gastrostomy placement, endoscopic retrograde cholangiopancreatography Surgery in highly vascular organs (kidneys, liver, spleen) Cardiac, intracranial, or spinal surgery Any major operation (procedure duration > 45 min) Neuraxial anesthesia^b Epidural injections</p>
<p>Low-to-moderate-bleed-risk surgery/procedure^c (30-d risk of major bleed 0%-2%)</p>	<p>Arthroscopy Cutaneous/lymph node biopsies Foot/hand surgery Coronary angiography^d GI endoscopy \pm biopsy Colonoscopy \pm biopsy Abdominal hysterectomy Laparoscopic cholecystectomy Abdominal hernia repair Hemorrhoidal surgery Bronchoscopy \pm biopsy</p>
<p>Minimal-bleed-risk surgery/procedure^e (30-d risk of major bleed approximately 0%)</p>	<p>Minor dermatologic procedures (excision of basal and squamous cell skin cancers, actinic keratoses, and premalignant or cancerous skin nevi) Ophthalmologic (cataract) procedures Minor dental procedures (dental extractions, restorations, prosthetics, endodontics), dental cleanings, fillings Pacemaker or cardioverter-defibrillator device implantation</p>

Perioperative Management of Antithrombotic Therapy

 Check for updates

An American College of Chest Physicians Clinical Practice Guideline

James D. Douketis, MD, FCCP; Alex C. Spyropoulos, MD, FCCP; M. Hassan Murad, MD, MPH; Juan I. Arcelus, MD; William E. Dager, PharmD; Andrew S. Dunn, MD, MPH; Ramiz A. Fargo, MD, FCCP; Jerrold H. Levy, MD; C. Marc Samama, MD; Sahrish H. Shah, MBBS; Matthew W. Sherwood, MD; Alfonso J. Tafur, MD; Liang V. Tang, MD; and Lisa K. Moores, MD, FCCP

CHEST 2022; 162(5):e207-e243

VKA (WARFARIN)

VKA (WARFARIN)

Perioperative Management of Antithrombotic Therapy

 Check for updates

An American College of Chest Physicians Clinical Practice Guideline

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CHEST 2022; 162(5):e207-e243

- Among four randomized trials comparing VKA continuation vs interruption, **none showed a significant increase in bleeding with VKA continuation**
- One meta-analysis comparing continuing vs interrupting VKAs found **no significant increased intra-procedural bleeding or post-procedural bleeding with VKA continuation**

Continuing VKAs is associated with a low (approximately 5%) risk for any bleeding



VKA (WARFARIN)

Management of anticoagulated patients in dentoalveolar surgery: a clinical comparative study

CM Schmitt^{1,2} · B Rusche^{1,3} · R Clemm^{1,4} · FW Neukam¹ · M Buchbender¹

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Management of patients with vitamin K inhibitors	Patients		Bleeding events	Severity of postoperative bleeding						
	#	%		#	1	2	3	4	5	
Total	80	100	9							
Continued	64	80	6	9.4	4	6.2	0	0	2	3.1
Bridged with LMWH	12	15	3	25	1	8.3	0	0	2	16.7
Reduced	4	5	0	0	0	0	0	0	0	0

No statistically significant differences for any of the comparisons concerning anticoagulation management (continued, bridged with LMWH or reduced) were detected.

INR value: 1.09 to 2.84 with a group average of 1.97.

Management recommendations for invasive dental treatment in patients using oral antithrombotic medication, including novel oral anticoagulants

Denise E. van Diermen, MD, PhD,^a Isaïc van der Waal, DDS, PhD,^b and Johan Hoogstraten, PhD^c
Academic Centre for Dentistry Amsterdam, Amsterdam, the Netherlands

Oral Surg Oral Med Oral Pathol Oral Radiol 2013;116:709-716

Table III. Definition of the levels of evidence as described by other clinical practice guidelines

Levels of evidence used by Aframian et al.¹⁹:

- Level A: Based on multiple randomized controlled trials
- Level B: Based on data from a single randomized trial or nonrandomized studies
- Level C: Expert opinion

Classification of evidence levels used by Perry et al.¹⁸:

- Ia Evidence obtained from meta-analysis of randomized controlled trials
- Ib Evidence obtained from at least one randomized controlled trial
- IIa Evidence obtained from at least one well-designed controlled study without randomization
- IIb Evidence obtained from at least one other type of well-designed quasiexperimental study
- III Evidence obtained from well-designed nonexperimental descriptive studies, such as comparative studies, correlation studies, and case studies
- IV Evidence obtained from expert committee reports or opinions or from clinical experiences of respected authorities

Levels of evidence of the Brazilian Society of Cardiology²¹

- A. Evidence in several populations from multiple randomized clinical trials or meta-analyses
 - B. Evidence in a limited group of populations from a single randomized clinical trial or from nonrandomized clinical studies
 - C. Evidence in a very limited group of populations from consensus and experts' opinions, case reports, and series
-

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Table IV. Definition of the grades of recommendations

Classes of recommendations used by Aframian et al.¹⁹:

Class I: Benefit to patients clearly outweighs any risks; procedure **SHOULD** be performed

Class II: Conflicting evidence or a divergence of opinion about the usefulness of a procedure or treatment

IIa: Benefit seems to outweigh the risk; weight of evidence is in favor of usefulness. **IT IS REASONABLE** to perform the procedure

IIb: Benefit seems to outweigh the risk; usefulness is less well established. **IT IS NOT UNREASONABLE** to perform the procedure

Class III: Risk outweighs the benefit; **IT MAY BE HARMFUL AND IS UNHELPFUL**. Procedure should **NOT** be performed

Classification of grades of recommendations used by Perry et al.¹⁸:

A. Requires at least one randomized controlled trial as part of a body of literature of overall good quality and consistency addressing specific recommendation. (Evidence levels Ia, Ib)

B. Requires the availability of well conducted clinical studies but no randomized clinical trials on the topic of recommendation. (Evidence levels IIa, IIb, III)

C. Requires evidence obtained from expert committee reports or opinions or from clinical experiences of respected authorities. Indicates an absence of directly applicable clinical studies of good quality. (Evidence level IV)

Classification of degree of recommendations used by Brazilian Society of Cardiology²¹:

Degree of Recommendation I—Benefit >>> Risk; the treatment/procedure must be indicated/administered;

Degree of Recommendation IIa—Benefit >> Risk; the choice for the treatment/procedure may help the patient;

Degree of Recommendation IIb—Benefit > Risk; it is not defined if the treatment/procedure can help the patient;

Degree of Recommendation III—Risk > Benefit; the treatment/procedure must not be performed because it does not help and may be harmful for the patient.

Classification of grades of recommendation used by Douketis et al.²⁰:

1A. Strong recommendation, high-quality evidence

1B. Strong recommendation, moderate-quality evidence

1C. Strong recommendation, low- or very-low-quality evidence

2A. Weak recommendation, high-quality evidence

2B. Weak recommendation, moderate-quality evidence

2C. Weak recommendation, low- or very-low-quality evidence

Management recommendations for invasive dental treatment in patients using oral antithrombotic medication, including novel oral anticoagulants

Denise E. van Diermen, MD, PhD,^a Isaïc van der Waal, DDS, PhD,^b and Johan Hoogstraten, PhD^c
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VKA

Oral Surg Oral Med Oral Pathol Oral Radiol 2013;116:709-716

Table V. Review of the recommendations from guidelines and systematic reviews on patients undergoing dental surgery using oral antithrombotic drugs (aspirin, clopidogrel, warfarin, and novel oral anticoagulants, such as dabigatran and rivaroxaban)

	<i>Level of evidence*</i>	<i>Recommendation class, grade, or degree†</i>
b. Oral anticoagulants (warfarin)		
Oral anticoagulants should not be discontinued in the majority of patients requiring outpatient dental surgery, including extraction. ¹⁸	Level Ib	Grade A
When the INR is less than 3.5, do not modify or discontinue warfarin therapy for simple single dental extractions. ¹⁹	Level A	Class I
When the INR is 3.5 or more and complicated or invasive oral surgery procedures are planned, discuss with physician. ¹⁹	Level A	Class I
Continue VKAs with an oral prohemostatic agent in patients who require a minor dental procedure. ²⁰		Grade 2C
Do not discontinue OAM before simple surgeries (e.g., extraction of ≤ 3 teeth, gingival surgery, periodontal scaling) in patients with INR < 3.0 . ²¹	Level C	
Do not discontinue or modify the regular dose of warfarin for patients undergoing minor dental procedures (up to 5 dental extractions or 6 dental implants). ²¹	Level 1A	Class I

Management of dental extraction in patients undergoing anticoagulant oral direct treatment: a pilot study



Cédric Mauprivez, DDS, PhD,^a Roman Hossein Khonsari, MD, PhD,^b Omar Razouk, DDS,^b Patrick Goudot, MD, PhD,^b Philippe Lesclous, DDS, PhD,^c and Vianney Descroix, DDS, PhD^d

VKA (WARFARIN) VS. DOACS

(Oral Surg Oral Med Oral Pathol Oral Radiol 2016;122:e146-e155)

- No significant difference in number of post-extraction bleeding events (defined as hemorrhage lasting longer than 20 minutes) between the 2 groups.
- 91.7% of the bleeding events were mild and could be controlled by applying pressure to the bleeding site with gauze. The remaining 8.3% required re-approximating the wound margins, applying a fibrin sealant and then re-suturing.

Dental extractions and less-invasive procedures may be safely performed using local hemostatic measures, if necessary, without modifying or interrupting ongoing oral anticoagulant therapy

DOACs (DIRECT ORAL ANTICOAGULANTS)

DOACs

22. In patients receiving apixaban who require an elective surgery/procedure, we suggest stopping apixaban for 1 to 2 days before the surgery/procedure over apixaban continuation (Conditional Recommendation, Very Low Certainty of Evidence).

23. In patients receiving dabigatran who require an elective surgery/procedure, we suggest stopping dabigatran for 1 to 4 days before the surgery/procedure over dabigatran continuation (Conditional Recommendation, Very Low Certainty of Evidence).

24. In patients receiving edoxaban who require an elective surgery/procedure, we suggest stopping edoxaban for 1 to 2 days before the surgery/procedure over edoxaban continuation (Conditional Recommendation, Very Low Certainty of Evidence).

25. In patients receiving rivaroxaban who require an elective surgery/procedure, we suggest stopping rivaroxaban for 1 to 2 days before the surgery/procedure over rivaroxaban continuation (Conditional Recommendation, Very Low Certainty of Evidence).

Perioperative Management of Antithrombotic Therapy

An American College of Chest Physicians Clinical Practice Guideline

 Check for updates

James D. Douketis, MD, FCCP; Alex C. Spyropoulos, MD, FCCP; M. Hassan Murad, MD, MPH; Juan I. Arcelus, MD; William E. Dager, PharmD; Andrew S. Dunn, MD, MPH; Ramiz A. Fargo, MD, FCCP; Jerrold H. Levy, MD; C. Marc Samama, MD; Sahrish H. Shah, MBBS; Matthew W. Sherwood, MD; Alfonso J. Tafur, MD; Liang V. Tang, MD; and Lisa K. Moores, MD, FCCP

CHEST 2022; 162(5):e207-e243

26. In patients who require DOAC interruption for an elective surgery/procedure, we suggest against perioperative heparin bridging (Conditional Recommendation, Very Low Certainty of Evidence).

27. In patients who had DOAC interruption for an elective surgery/procedure, we suggest resuming DOACs > 24 hours after a surgery/procedure over resuming DOACs within 24 hours (Conditional Recommendation, Very Low Certainty of Evidence).

28. In patients who had DOAC interruption for an elective surgery/procedure, we suggest against routine DOAC coagulation function testing to guide perioperative DOAC management (Conditional Recommendation, Very Low Certainty of Evidence).

DOACs

Bleeding related to dental treatment in patients taking novel oral anticoagulants (NOACs): a retrospective study

Eun-Jung Kwak¹ · Sangook Nam¹ · Kyeong-mee Park¹ · Seo-yul Kim¹ · Jisun Huh¹ · Wonse Park¹



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- The administration of *NOACs does not need to be interrupted in most dental treatments*, and the application of a *hemostatic agent is normally sufficient to achieve hemostasis* when postoperative bleeding events do occur.
- The authors recommend at least *1 day of discontinuance in cases of the first stage of implant surgery, multiple tooth extraction and deep scaling* with local inflammation, based on consideration of the medication half-life and the renal clearance rate.

Direct Oral Anticoagulants and Medical Comorbidities in Patients Needing Dental Extractions: Management of the Risk of Bleeding

Nadia Cocero, DDS, Michele Basso, DDS,†
 Simona Grosso, DDS,‡ and Stefano Carossa, MD§*

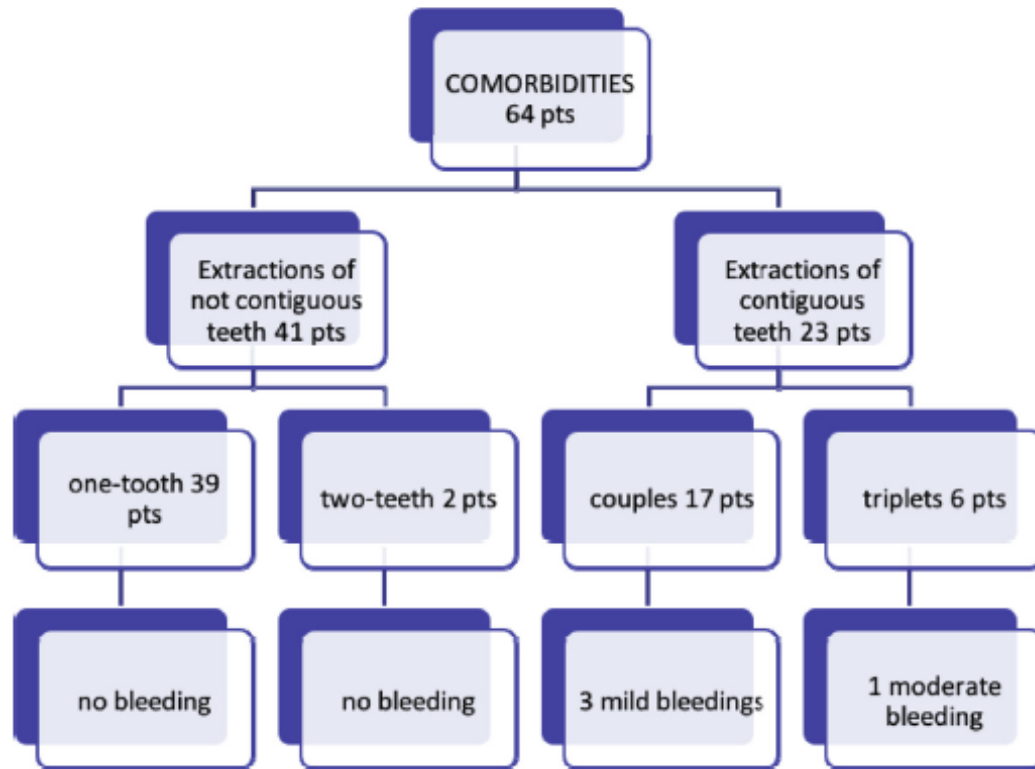


FIGURE 1. Details of extractions in comorbidity group of patients (pts).

- Patients taking DOACs **can be safely managed**, even when affected by comorbidities.
- The **2 causes possibly favoring excessive bleeding can in fact be controlled by the dentist**. The first is the timing of the extraction, which must respect an interval of at least 4 hours after the last DOAC intake. The second is the extraction of 2 or 3 contiguous premolars and molars, which should be avoided by scheduling more than 1 session.
- **If 1 or both of these precautions cannot be satisfied**, the collaboration of the **patient's cardiologist needs to be sought**.

Cocero et al. Direct Oral Anticoagulants. J Oral Maxillofac Surg 2019.

DOACs

Perioperative Management of Antithrombotic Therapy


An American College of Chest Physicians Clinical Practice Guideline

 Check for updates

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CHEST 2022; 162(5):e207-e243

Direct Oral Anticoagulant	Procedure Bleeding Risk	Pre-Procedure DOAC Interruption						Surgery/Procedure (Day 0)	Post-Procedure Resumption*			
		Day -6	Day -5	Day -4	Day -3	Day -2	Day -1		Day +1	Day +2	Day +3	Day +4
Apixaban	High	[Red arrow from Day -6 to Day -3]						Surgery/Procedure (Day 0)	[Red bar from Day +2 to Day +3]			
	Low/Mod	[Red arrow from Day -6 to Day -2]							[Red arrow from Day +1 to Day +4]			
Dabigatran (CrCl ≥ 50 ml/min)	High	[Blue arrow from Day -6 to Day -3]							[Blue bar from Day +2 to Day +3]			
	Low/Mod	[Blue arrow from Day -6 to Day -2]							[Blue arrow from Day +1 to Day +4]			
Dabigatran (CrCl < 50 ml/min)	High	[Grey arrow from Day -6 to Day -4]							[Grey bar from Day +2 to Day +3]			
	Low/Mod	[Grey arrow from Day -6 to Day -3]							[Grey arrow from Day +1 to Day +4]			
Edoxaban	High	[Orange arrow from Day -6 to Day -3]							[Orange bar from Day +2 to Day +3]			
	Low/Mod	[Orange arrow from Day -6 to Day -2]							[Orange arrow from Day +1 to Day +4]			
Rivaroxaban	High	[Cyan arrow from Day -6 to Day -3]							[Cyan bar from Day +2 to Day +3]			
	Low/Mod	[Cyan arrow from Day -6 to Day -2]							[Cyan arrow from Day +1 to Day +4]			

 No DOAC administered that day

*DOAC can be resumed ~24 hours after low/moderate-bleed-risk procedures, and 48-72 hours after high-bleed-risk procedures. In selected patients at high risk for VTE, low-dose anticoagulants (i.e., enoxaparin, 40 mg daily or dalteparin, 5,000 IU daily) can be given for the first 48-72 hours post-procedure.

Figure 2 – Perioperative management of direct oral anticoagulants (DOACs). CrCl = creatinine clearance.

ANTIPLATELETS

ANTIPLATELET DRUGS

Perioperative Management of Antithrombotic Therapy

 Check for updates

An American College of Chest Physicians Clinical Practice Guideline

James D. Douketis, MD, FCCP; Alex C. Spyropoulos, MD, FCCP; M. Hassan Murad, MD, MPH; Juan I. Arcelus, MD; William E. Dager, PharmD; Andrew S. Dunn, MD, MPH; Ramiz A. Fargo, MD, FCCP; Jerrold H. Levy, MD; C. Marc Samama, MD; Sahrish H. Shah, MBBS; Matthew W. Sherwood, MD; Alfonso J. Tafur, MD; Liang V. Tang, MD; and Lisa K. Moores, MD, FCCP

CHEST 2022; 162(5):e207-e243

In patients receiving an antiplatelet drug (ASA or P2Y₁₂ inhibitor) who are undergoing a **minor dental procedure**, we suggest continuing the antiplatelet drug (ASA or the P2Y₁₂ inhibitor) over stopping the antiplatelet agent before the procedure


Conditional Recommendation, Very Low Certainty of Evidence

Guideline Implementation Considerations: Patients who are receiving dual antiplatelet therapy with ASA and a P2Y₁₂ inhibitor can continue ASA and interrupt the P2Y₁₂ inhibitor





Dental management of patient with dual antiplatelet therapy: a meta-analysis

Lin Li¹ · Wenyi Zhang² · Yun Yang¹ · Liyuan Zhao¹ · Xinyao Zhou¹ · Jian Zhang³ 

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ANTIPLATELET DRUGS

- Dental extractions can be performed while patients continue the DAPT.
- Although local factors such as periodontal disease or periapical lesions may lead post-extraction bleeding increasing, but local hemostasis measures are effective.
- There is no need to interrupt antiplatelet therapy before extraction because the risk is significantly greater than its benefit.

Management recommendations for invasive dental treatment in patients using oral antithrombotic medication, including novel oral anticoagulants

Denise E. van Diermen, MD, PhD,^a Isaïc van der Waal, DDS, PhD,^b and Johan Hoogstraten, PhD^c
Academic Centre for Dentistry Amsterdam, Amsterdam, the Netherlands

Oral Surg Oral Med Oral Pathol Oral Radiol 2013;116:709-716

ANTIPLATELET DRUGS

Table V. Review of the recommendations from guidelines and systematic reviews on patients undergoing dental surgery using oral antithrombotic drugs (aspirin, clopidogrel, warfarin, and novel oral anticoagulants, such as dabigatran and rivaroxaban)

	<i>Level of evidence</i> [*]	<i>Recommendation class, grade, or degree</i> [†]
1. Continuation of antithrombotic drugs		
a. Antiplatelet medications		
Do not interrupt low-dose aspirin therapy (100 mg or less) for outpatient dental procedures. ^{19,21}	Level B	Class I
Continue ASA around the time of minor dental procedures in patients who are receiving ASA for the secondary prevention of cardiovascular disease. ²⁰		Grade 2C
Do not alter or stop single or dual antiplatelet therapy for invasive dental treatment (single or multiple tooth extractions, deep scaling and probing, biopsies, flap surgery, gingivectomy, alveoloplasty). ¹⁹	Level 1A	Class I

PRE-OP, INTRA-OP AND POST-OP MEASURES

Management recommendations for invasive dental treatment in patients using oral antithrombotic medication, including novel oral anticoagulants

Denise E. van Diermen, MD, PhD,^a Isaïc van der Waal, DDS, PhD,^b and Johan Hoogstraten, PhD^c
Academic Centre for Dentistry Amsterdam, Amsterdam, the Netherlands

PREOPERATIVE MEASURES

3. Preoperative measures

Check INR 72 hours before dental surgery in patients that have stable[‡] INRs.¹⁸

Check INR at least 24 hours before the dental procedure.²¹

Evaluation of INR 72 hours before the procedure is acceptable in stable[‡] patients.²¹

Discuss with physician in charge when $INR \geq 3.0$ and the planned procedures are more extensive.²¹

Assess the patient's complete medical history.²¹

Schedule a larger number of visits when there is extraction of more than 3 teeth.²¹

Plan the surgeries earlier in the day and in the beginning of the week.²¹

Level Ib	Grade A
Level IC	Degree I
Level C	Degree I
Level C	Degree I
Level C	Degree I
Level C	Degree I
Level C	Degree I

Management recommendations for invasive dental treatment in patients using oral antithrombotic medication, including novel oral anticoagulants

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OPERATIVE MEASURES

4. Operative measures

Inform the patients that minor bleeding or oozing from gingival mucosa may be more common when not interrupting VKAs during dental procedures.²⁰

Minimize surgical trauma.²¹

Reduce areas of periodontal surgery and scaling and root planing (per quadrant).²¹

Grade 2C

Level C


Degree I

Level C

Degree I



Management of anticoagulated patients in dentoalveolar surgery: a clinical comparative study

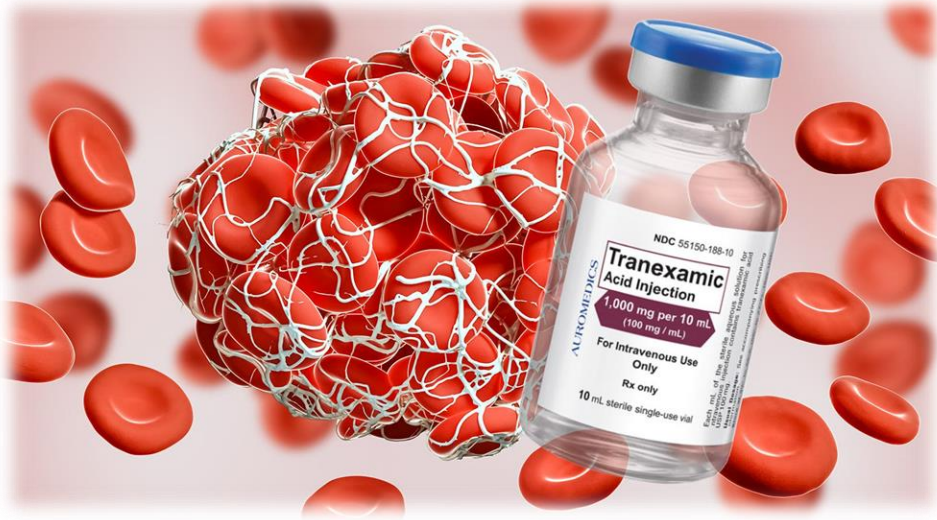
CM Schmitt^{1,2}  • B Rusche^{1,3} • R Clemm^{1,4} • FW Neukam¹ • M Buchbender¹

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OPERATIVE MEASURES

Table 2 AT group and applied local hemostatic measures. Applied local hemostatic measures in the AT group and the resulting postoperative bleeding (in parenthesis). *AT*, anticoagulation therapy; *LMWH*, low molecular weight heparin; *DOACs*, direct oral anticoagulants; *PAIs*, platelet aggregation inhibitors; #, number of patients

Applied local hemostatic measures	AT groups			
	Vitamin K inhibitors (<i>n</i> = 80) #	PAIs (<i>n</i> = 121) #	LMWH (<i>n</i> = 6) #	DOACs (<i>n</i> = 28) #
Bite swab	1	5	0	0
Suturing and bite swab	22 (2)	81 (1)	5	16 (1)
Hemostyptic filler, suturing and bite swab	33 (6)	14	1	
Suturing and bite swab with tranexamic acid	10 (1)	11	0	6
Hemostyptic filler, suturing and bite swab with tranexamic acid	12	6	0	1
Bipolar electrocoagulation and suturing	2	4	0	0



Antifibrinolytic effects by blocking lysine binding sites on plasminogen molecules, inhibiting the interaction of plasminogen with formed plasmin and fibrin.



Resorbable oxidized cellulose



Absorbable Gelatin Sponge
Porcine Gelatin

Management recommendations for invasive dental treatment in patients using oral antithrombotic medication, including novel oral anticoagulants

Denise E. van Diermen, MD, PhD,^a Isaïc van der Waal, DDS, PhD,^b and Johan Hoogstraten, PhD^c
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POSTOPERATIVE MEASURES

5. Postoperative pain control

Do not prescribe NSAIDs and COX-2 inhibitors as analgesics.¹⁸

Level III Grade B

Consider using gelatin sponges, fibrin glue, fibrin adhesive dressing, oxidized cellulose, or ε-aminocaproic acid mouthwash.¹⁹

Level B Class I

Give patients on OAC a 2-day regimen of postoperative 4.8% tranexamic acid mouthwash.¹⁹

Level A Class I

Give patients who do not interrupt VKAs a 5-mL oral dose of tranexamic acid, 5 to 10 min before the dental procedure and 3 to 4 times daily for 1 to 2 days after the procedure.²⁰

Grade 2C

Remove nonabsorbable sutures after 4 to 7 days.²¹

Level C Degree I

Compress with gauze for 15 to 30 minutes after the surgical procedure.²⁰

Level C Degree I

Use coagulating agents, such as gelatin sponges, oxidized regenerated cellulose, synthetic collagen, or tranexamic acid mouthwash in 4.8% aqueous solution during and 7 days after the surgery, using 10 mL, 4 times a day for 2 minutes.²¹

Level C Degree I

6. Referral

Refer patients whose INR is unstable.^{‡,18}

Level Ib Grade A

OAC, oral anticoagulation; OAM, oral antithrombotic medication; TAR, thrombocyte aggregation inhibitor; ASA, acetylsalicylic acid; VKA, vitamin K antagonist; INR, international normalized ratio; NOAC, novel oral anticoagulant; NSAID, nonsteroidal anti-inflammatory drug; COX-2, cyclooxygenase-2.

MANAGEMENT ALGORITHMS



Treatment in the dental practice of the patient receiving anticoagulation therapy

Eric Kaplovitch, MD, FRCPC; Vera Dounaevskaia, MD, FRCPC

ABSTRACT

JADA 2019;150(7):602-608

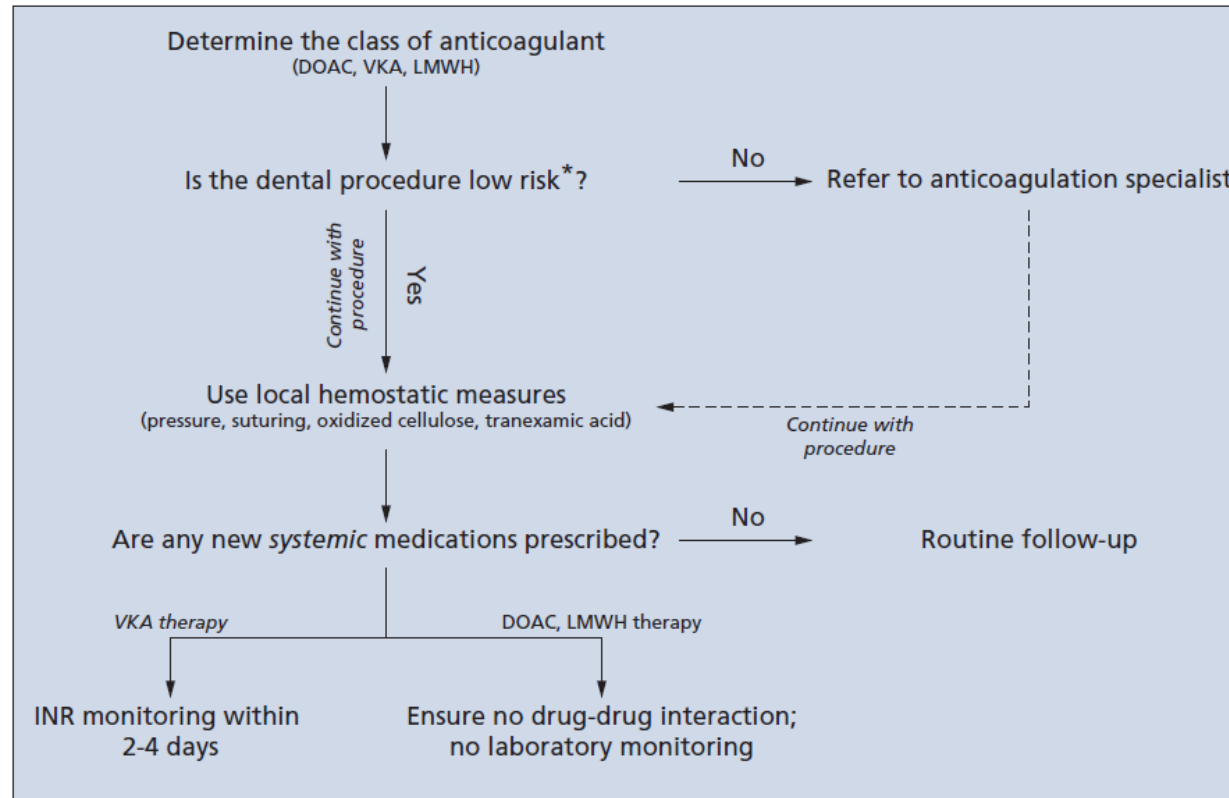


Figure. Algorithm for performing dental procedures in patients receiving systemic anticoagulation therapy. * Low-risk dental procedures include dental scaling, dental restorations that involve soft-tissue manipulation, dental extractions that are not surgically complex (< 3 teeth), soft-tissue biopsies, endodontic procedures, implant placements, and prosthodontic procedures (fixed and removable dentures, crowns, and bridges). DOAC: Direct oral anticoagulant. INR: International normalized ratio. LMWH: Low-molecular-weight heparin. VKA: Vitamin K antagonist.

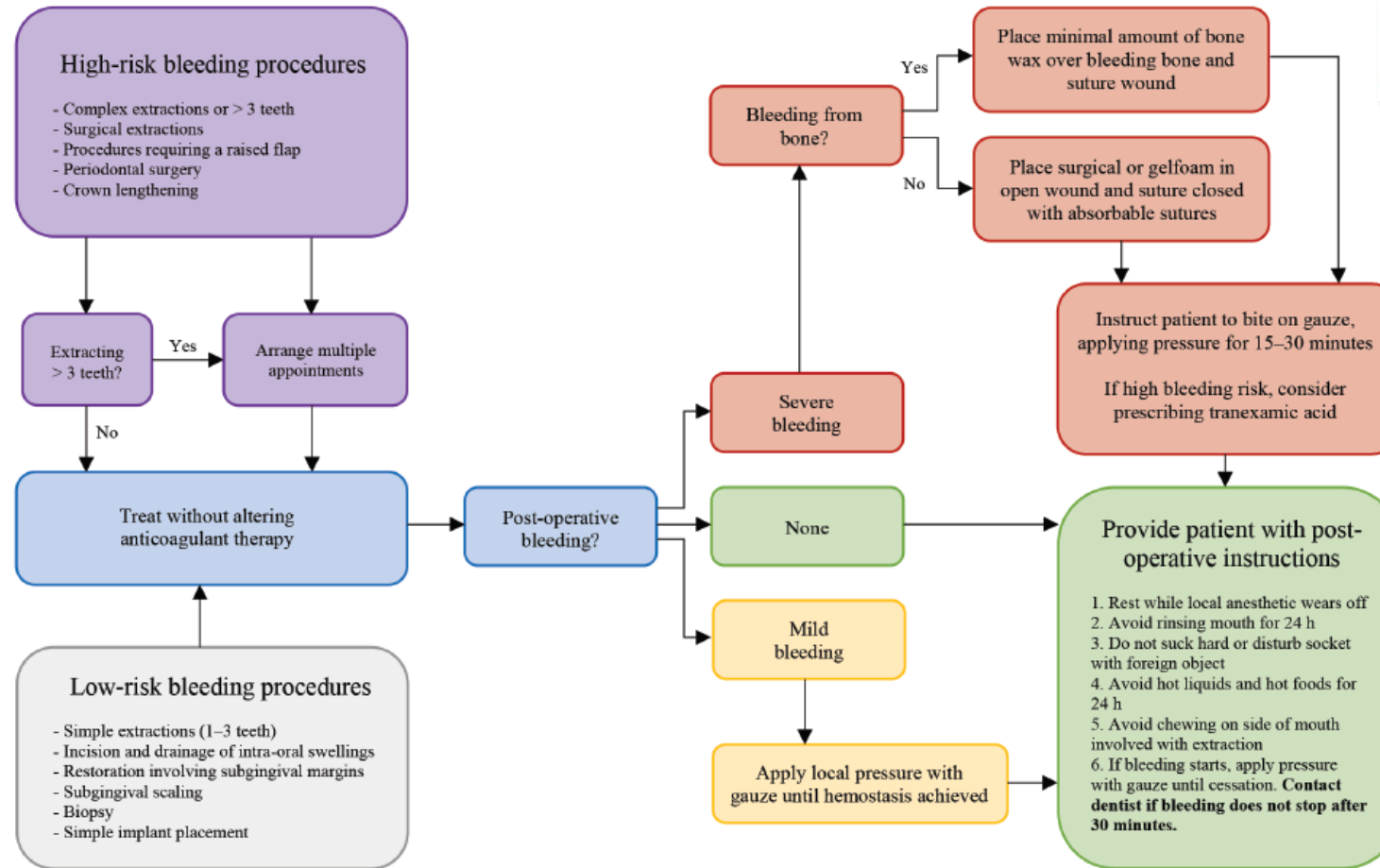


Dental Management of Patients Undergoing Antithrombotic Therapy

Justin Felix, DDS; Peter Chaban, DDS; Aviv Ouanounou, MSc, DDS, FICO

Cite this as: J Can Dent Assoc. 2020;86:i17

Figure 2: Treatment management for patients undergoing antithrombotic therapy.





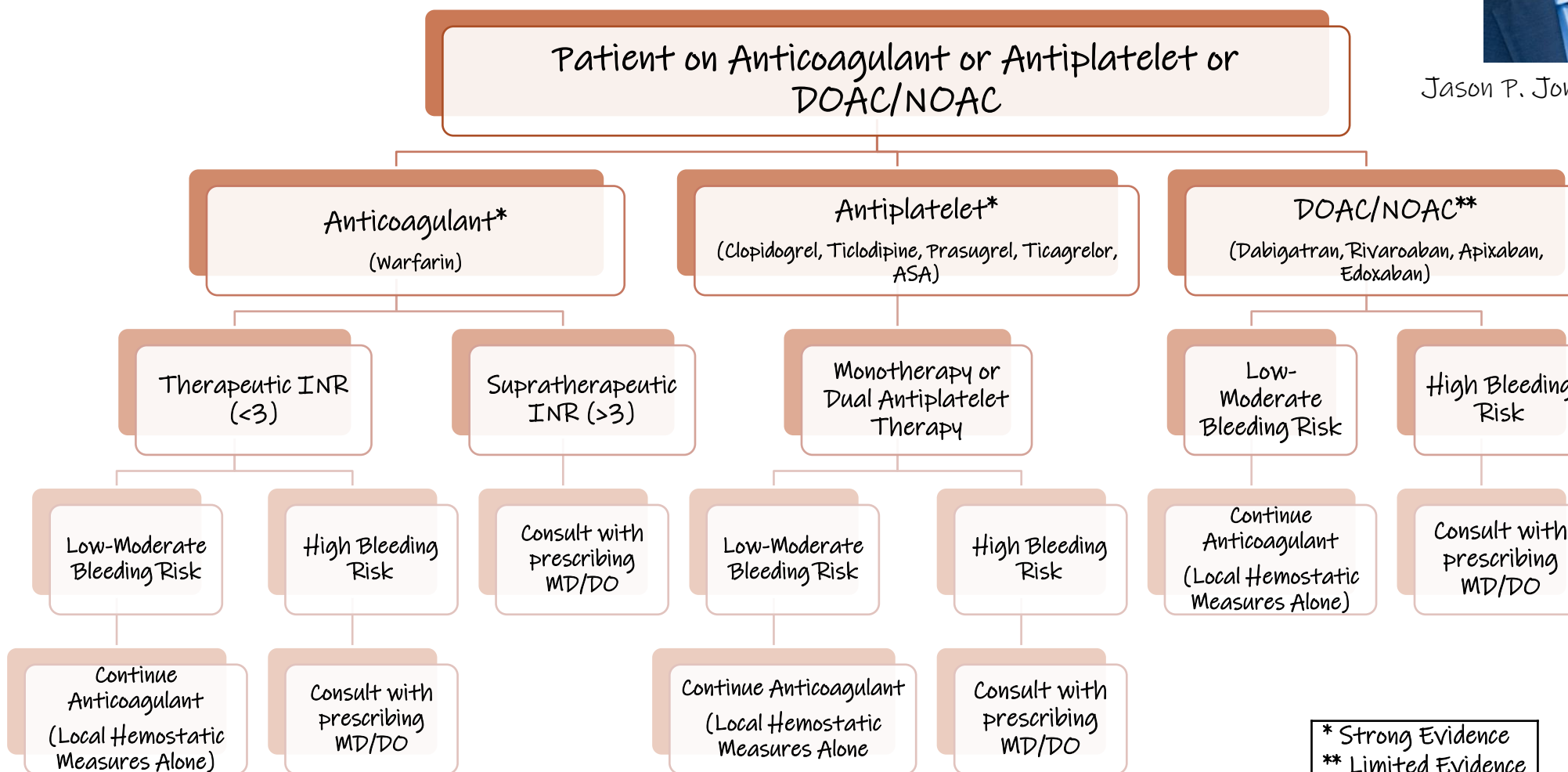
Jason P. Jones, D.D.S., M.D.

Drug Class	Drug Names
Anticoagulant*	Warfarin (Coumadin®)
Antiplatelet Agents*	Clopidogrel (Plavix®) Ticlopidine (Ticlid®) Prasugrel (Effient®) Ticagrelor (Brilinta®) Aspirin
Direct-acting (or novel-acting) oral anticoagulants** (Direct Thrombin Inhibitor)	Dabigatran (Pradaxa®)
Direct-acting (or novel-acting) oral anticoagulants** (Factor Xa inhibitors)	Rivaroxaban (Xarelto®) Apixaban (Eliquis®) Edoxana (Savays® in US, Lixiana® in Europe, Japan, elsewhere)

Low Bleeding Risk	Moderate bleeding Risk	High bleeding Risk
Local anesthetic administration Supragingival scaling Single tooth extraction Simple restorations	Extractions of 2-4 teeth Gingival surgery of ≤5 teeth Dental implants ≤ 3 sites Abscess incision Apex Resection	Extractions of ≥4 teeth Gingival surgery ≥5 teeth Dental implants ≥4 sites *Determined by provider*



Jason P. Jones, D.D.S., M.D.



* Strong Evidence
 ** Limited Evidence

TAKE HOME POINTS

- Acquiring a patient's past medical history, including a list of medications, is the initial step to assess whether a treatment is feasible or if clearance is required.
- It is crucial to evaluate the risk of bleeding associated with planned procedures (#teeth extractions, contiguous teeth, alveoloplasty, etc.) to determine the necessity of clearance for a drug holiday.
- If the potential risks of discontinuing antithrombotic medications outweigh the benefits, it is advisable to stage dental procedures taking appropriate intraoperative and postoperative precautions.

TAKE HOME POINTS



- For patients on Vitamin K antagonists, *minor dental procedures with minimal bleeding risk* can proceed without modifying medication if the INR is <3 .
- For patients on DOACs or dual antiplatelet therapy, *minor dental procedures with minimal bleeding risk* can generally be performed without discontinuing medication.



THANK YOU

Los Roques, Venezuela