

Perioperative Management of VTE

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GuangDong Pharmaceutical Association

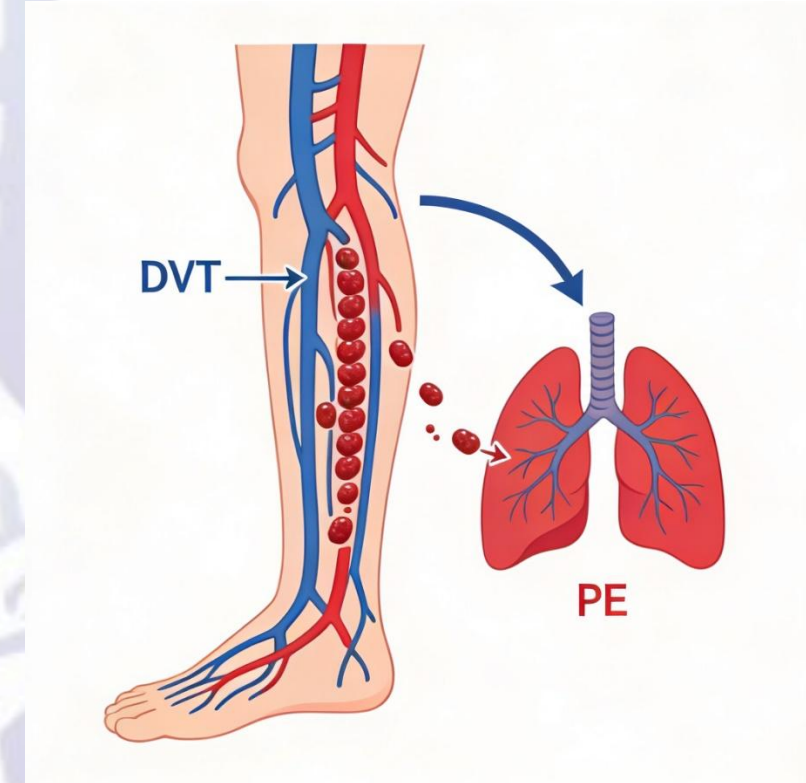
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Background Introduction

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- VTE refers to the abnormal coagulation of blood within veins, resulting in partial or complete obstruction of the venous lumen. It includes deep vein thrombosis (DVT) and pulmonary embolism (PE). DVT and PE represent different stages of VTE.
- Worldwide, nearly 10 million people are diagnosed with VTE each year, with an annual incidence ranging from 41.7 to 269 per 100,000 population. The incidence of VTE continues to rise annually.
- Following ischemic heart disease and stroke, VTE ranks as the third leading cause of death among cardiovascular diseases worldwide.





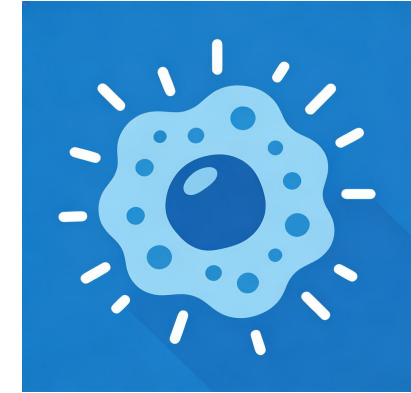
Vascular Wall Damage

Factors such as surgical trauma, inflammatory stimulation, and central venous catheterization can directly damage the vascular endothelium, creating the initial conditions for thrombosis.



Stasis

Stagnant blood flow leads to local accumulation of coagulation factors, increasing the risk of thrombosis. Common in patients with prolonged bed rest, surgery, long-distance travel, or heart failure.



Hypercoagulability

Surgical stress, anesthetic agents, advanced age, obesity, tumors and other factors predispose the blood to a hypercoagulable state.



Basic Prophylaxis

- Elevate the affected limb postoperatively.
- Provide patient education on venous thrombosis; encourage frequent repositioning, early ambulation, early functional exercise, as well as deep breathing and coughing exercises.
- Maintain adequate fluid intake and hydration to prevent postoperative dehydration.
- Promote healthy lifestyle modifications, including smoking cessation, alcohol restriction, and control of blood glucose and lipid levels.



Mechanical Prophylaxis

- By mechanical principles to accelerate venous blood flow in the lower extremities, reduce venous stasis, and lower the risk of postoperative DVT.
- Mechanical modalities include plantar venous pumps, intermittent pneumatic compression devices, and graduated compression elastic stockings.



Pharmacological Prophylaxis

- Medications should be selected and adjusted according to the patient's disease condition, surgical type, drug contraindications, and other relevant factors.



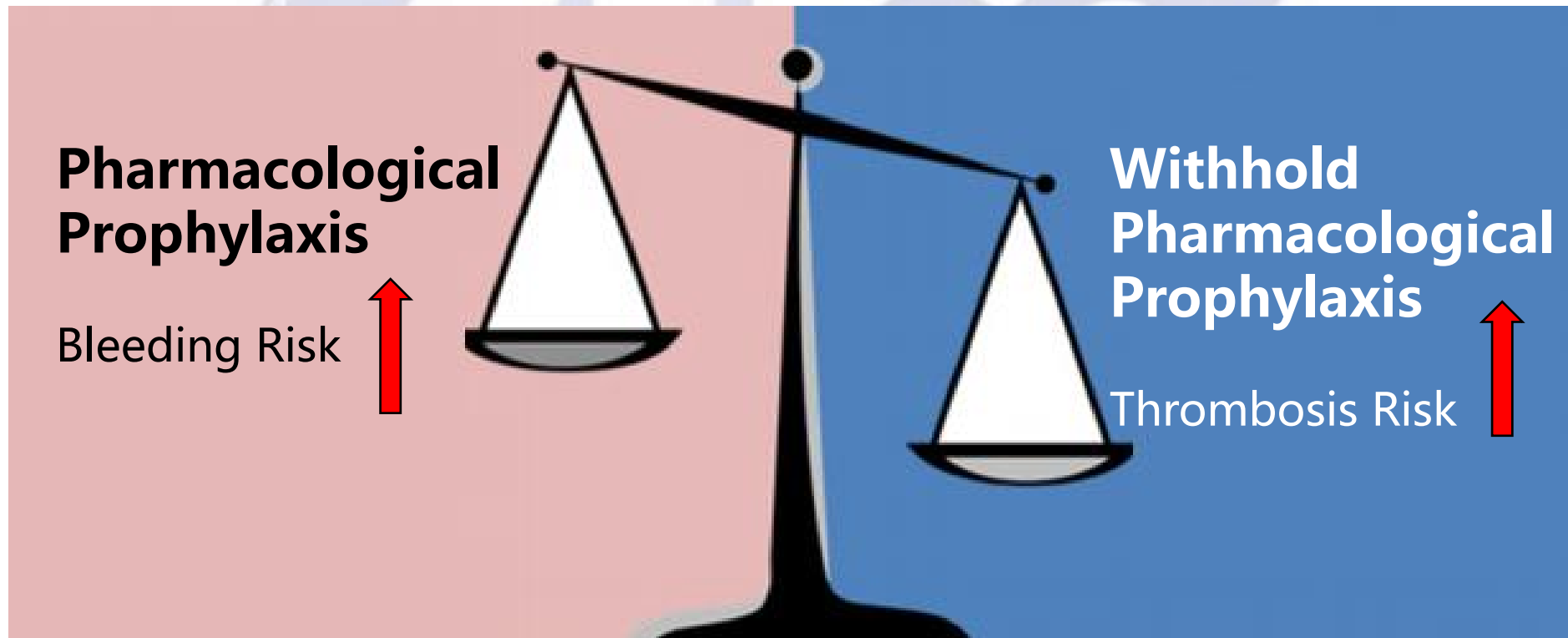
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Medication management

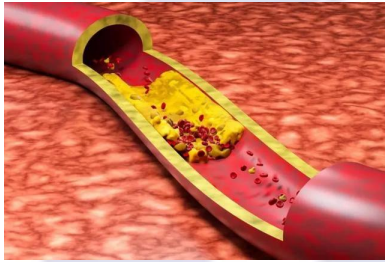
- **Perioperative VTE Management Strategy**
- Perioperative Commonly Used Anticoagulants and Pharmaceutical Monitoring

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Perioperative VTE Pharmacological Prophylaxis: The Dilemma of Bleeding vs. Thrombosis



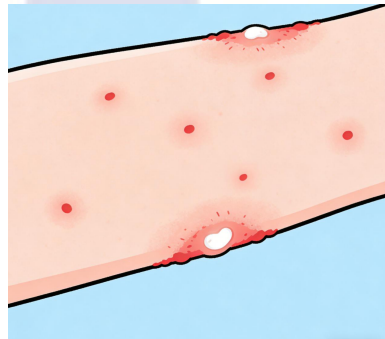
Determine Perioperative VTE Management Strategy Based on Risk Stratification



1-Assess VTE risk



2-Evaluate bleeding risk



3-Screen for contraindications to relevant preventive measures



4-Determine the optimal VTE prophylaxis strategy



VTE risk assessment

Disease-related factors:
Malignant neoplasms, immobilization due to various causes, infection, trauma, and fractures.

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Patient-related factors:

Advanced age, obesity, thrombophilia, and history of previous VTE.

03

Surgical and procedural factors:

Surgery (duration, type, location, approach), estrogen therapy, central venous catheterization.



VTE risk assessment

Caprini

A simple and comprehensive tool for thrombus risk assessment;
Recommended for risk assessment in surgical patients.

Padua

Primarily used for assessing hospitalized medical patients;
Includes 11 risk factors.

Wells

Used for the assessment of patients with suspected acute PTE and for early warning of deep vein thrombosis.

RAPT

Primarily used to assess the risk of VTE in trauma patients.

Autar

Mainly applied to patients with one of the three major risk factors (venous stasis, hypercoagulability, vascular endothelial injury) and patients on long-term bed rest or absolute bed rest during the acute phase of illness.

Khorana

Adopted by the ASCO as part of its guidelines for the management of venous thromboembolism.



VTE risk assessment (Caprini)



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Thrombosis Risk Factor Assessment

Patient's Name: _____ Age: ___ Sex: ___ Wgt: ___ lbs

Choose All That Apply

- Each Risk Factor Represents 1 Point**
- Age 41-60 years
 - Minor surgery planned
 - History of prior major surgery (< 1 month)
 - Varicose veins
 - History of inflammatory bowel disease
 - Swollen legs (current)
 - Obesity (BMI > 25)
 - Acute myocardial infarction
 - Congestive heart failure (< 1 month)
 - Sepsis (< 1 month)
 - Serious lung disease incl. pneumonia (< 1 month)
 - Abnormal pulmonary function (COPD)
 - Medical patient currently at bed rest
 - Other risk factors _____

- Each Risk Factor Represents 2 Points**
- Age 60-74 years
 - Arthroscopic surgery
 - Malignancy (present or previous)
 - Major surgery (> 45 minutes)
 - Laparoscopic surgery (> 45 minutes)
 - Patient confined to bed (> 72 hours)
 - Immobilizing plaster cast (< 1 month)
 - Central venous access

- Each Risk Factor Represents 5 Points**
- Elective major lower extremity arthroplasty
 - Hip, pelvis or leg fracture (< 1 month)
 - Stroke (< 1 month)
 - Multiple trauma (< 1 month)
 - Acute spinal cord injury (paralysis)(< 1 month)

- Each Risk Factor Represents 3 Points**
- Age over 75 years
 - History of DVT/PE
 - Family history of thrombosis***
 - Positive Factor V Leiden
 - Positive Prothrombin 20210A
 - Elevated serum homocysteine
 - Positive lupus anticoagulant
 - Elevated anticardiolipin antibodies
 - Heparin-induced thrombocytopenia (HIT)
 - Other congenital or acquired thrombophilia
- If yes:
Type _____
*most frequently missed risk factor

- For Women Only (Each Represents 1 Point)**
- Oral contraceptives or hormone replacement therapy
 - Pregnancy or postpartum (<1 month)
 - History of unexplained stillborn infant, recurrent spontaneous abortion (≥ 3), premature birth with toxemia or growth-restricted infant

Total Risk Factor Score

TABLE 2. Prophylaxis regimen

Total Risk Factor Score	Incidence of DVT	Risk Level	Prophylaxis Regimen
0-1	<10%	Low	No specific measures; early ambulation
2	10-20%	Moderate	ES or IPC or LDUH, or LMWH
3-4	20-40%	High	IPC or LDUH, or LMWH alone or in combination with ES or IPC
5 or more	40-80% 1-5% mortality	Highest	Pharmacological: LDUH, LMWH,* Warfarin,* or Fac Xa* alone or in combination with ES or IPC



Bleeding risk assessment

High-bleed-risk surgery/procedure† (30-day risk of major bleed ≥2%)

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 gastrointestinal 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 minutes)
 Neuraxial anaesthesia¶
 Epidural injections

Low/moderate-bleed-risk surgery/procedure‡ (30-day risk of major bleed 0%–2%)

Arthroscopy
 Cutaneous/lymph node biopsies
 Foot/hand surgery
 Coronary angiography by femoral artery approach
 Gastrointestinal endoscopy ± biopsy§
 Colonoscopy ± biopsy§
 Abdominal hysterectomy
 Laparoscopic cholecystectomy
 Abdominal hernia repair
 Hemorrhoidal surgery
 Bronchoscopy ± biopsy

Minimal-bleed-risk surgery/procedure§ (30-day risk of major bleed ~0%)

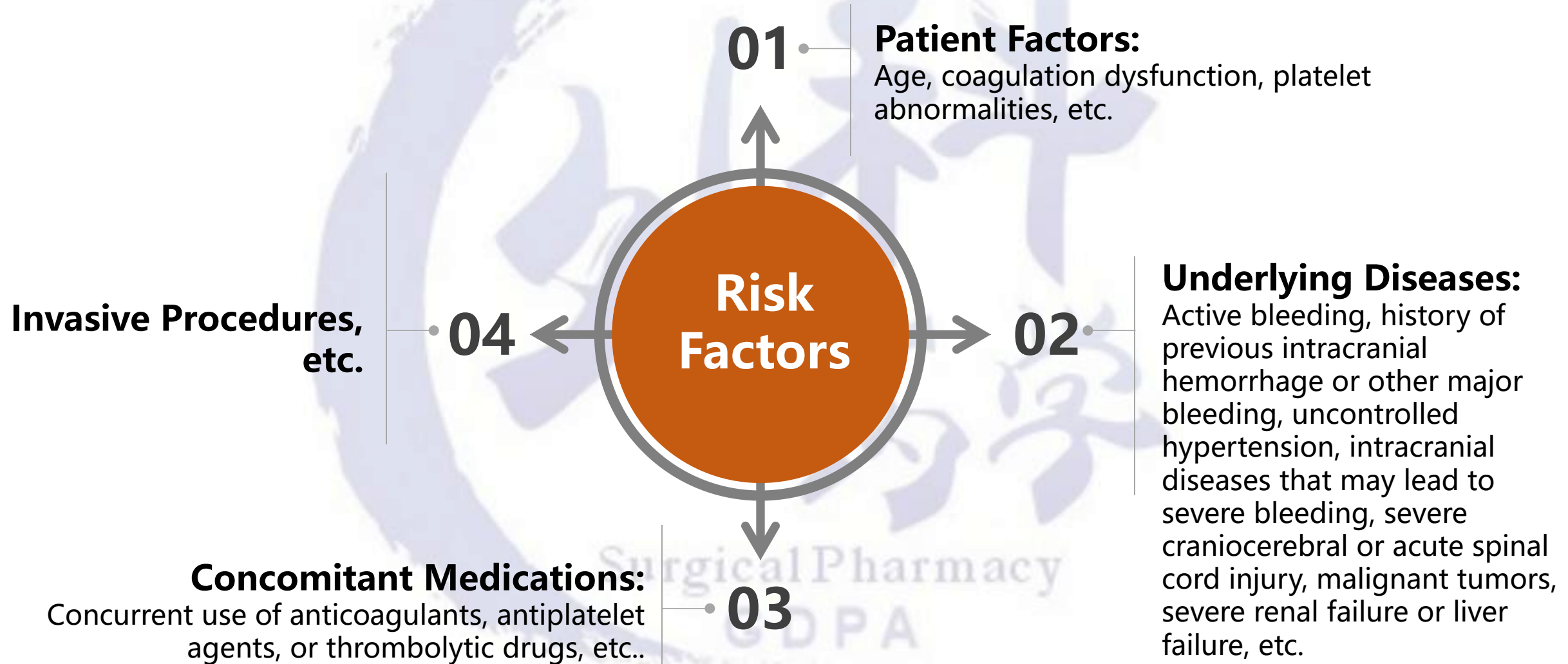
Minor dermatologic procedures (excision of basal and squamous cell skin cancers, actinic keratoses, and premalignant or cancerous skin nevi)
 Ophthalmological (cataract) procedures
 Minor dental procedures (dental extractions, restorations, prosthetics, endodontics), dental cleanings, fillings
 Pacemaker or cardioverter-defibrillator device implantation
 Coronary angiography by radial artery approach
 Selected patients requiring screening gastrointestinal endoscopy and colonoscopy ± biopsy||

HAS-BLED Score

Variable	Score
Age ≥ 65 years	1
Hypertension (Systolic Blood Pressure ≥ 160mmHg)	1
Abnormal renal function	1
Abnormal liver function	1
Stroke in past	1
Bleeding	1
Labile INRs	1
Taking other drugs as well	1
Alcohol intake at the same time	1



Bleeding risk assessment



Determine the optimal VTE prophylaxis strategy


VTE Risk Level (Caprini Score)	Bleeding Risk	Prophylaxis Measures
Very Low Risk (Caprini 0)	–	Early ambulation; no mechanical or pharmacological anticoagulation required
Low Risk (Caprini 1–2)	–	Mechanical prophylaxis; intermittent pneumatic compression (IPC) is recommended
Moderate Risk (Caprini 3–4)	No high bleeding risk	LMWH, UFH, or IPC
	High bleeding risk	IPC
High Risk (Caprini ≥ 5)	No high bleeding risk	LMWH, UFH; combined mechanical prophylaxis (e.g., compression stockings or IPC) is recommended
	High bleeding risk	IPC; pharmacological prophylaxis may be initiated qd bleeding risk resolves

Non-ambulatory orthopaedic surgery



Preoperative

Pre-operative evaluation of the risk of VTE and bleeding according to the type of procedure and the planned post-operative course (fast-track or standard post-operative procedure) *Grade 2B*

Postoperative

 Routine fast-track procedures (including early ambulation and joint mobilization) over timing of procedures based on convenience *Grade 1B*

	LOW THROMBOSIS RISK		HIGH THROMBOSIS RISK	
	LOW BLEEDING RISK	HIGH BLEEDING RISK	LOW BLEEDING RISK	HIGH BLEEDING RISK
No patient-related risk factors	No pharmacological prophylaxis (2B)		Pharmacological prophylaxis with LMWH or DOACs over no VTE prophylaxis (2B)	
Patient-related risk factors	Pharmacological prophylaxis with LMWH or DOACs over no prophylaxis (2B)	Mechanical prophylaxis over no VTE prophylaxis (2B)	Pharmacological prophylaxis with LMWH or DOACs over no VTE prophylaxis (2B)	Mechanical VTE prophylaxis over pharmacological prophylaxis (2C)

- Previous or family history of venous thromboembolism
- Major thrombophilia
- Age > 70 years
- Obesity
- Hypoalbuminemia
- Active cancer
- Estrogenic oral contraception and oral hormone therapy for menopause
- Renal insufficiency

- Surgery on the lower limb
 - pelvic, hip, knee
- Long duration surgery
- Cast immobilization
- Allogenic blood transfusion
- Use of tourniquet

THA
TKA
Hip fractures

Pharmacological prophylaxis over no prophylaxis *Grade 1A*

LMWH or DOACs over no prophylaxis *Grade 1A*

Fast-track THA, TKA, hip fracture











Pharmacological VTE prophylaxis with either

LMWH	<i>Grade 1B</i>
DOACs	<i>Grade 1B</i>
Aspirin	<i>Grade 1C</i>

over no prophylaxis

THA: Total Hip Arthroplasty
TKA: Total Knee Arthroplasty

Cardiovascular Surgery

	 Incidence of VTE	 Risk factors	 Recommendations
Coronary artery bypass grafting surgery 	1.3-1.75 % mortality 6.8%	 <ul style="list-style-type: none"> • History of VTE • Obesity • Heart failure • Prolonged bed rest • Mechanical ventilation 	 6h-24h post-surgery Early initiation (between 6h-24h) post-surgery of pharmacological VTE prophylaxis in the absence of significant bleeding risk <i>Grade 1C</i>
Vascular surgery 	0.7 %	 <ul style="list-style-type: none"> • Obesity • Postoperative pneumonia • Prolonged ventilation (>48 h) 	 <24h post-surgery Early initiation (<24h) of pharmacological VTE prophylaxis should be considered in patients with an increased procedural risk <ul style="list-style-type: none"> • Open Thoracoabdominal aortic aneurysm repair • Abdominal aortic aneurysm repair • Thoracic Endovascular Aortic Repair • Patients with increased VTE risk factors <i>Grade 2C</i>
	Low Molecular Weight Heparin should be considered as a first-line therapy over Unfractionated Heparin in view of the increased risk of heparin-induced thrombocytopenia in cardiac and vascular surgery		<i>Grade 2B</i>

Surgery during pregnancy and the immediate postpartum period

Personalized evaluation of VTE risk factors *Grade 1C*

- ✓ Multidisciplinary scores
- ✓ Personal and family history of thrombosis
- ✓ Bed rest, obesity, other clinical conditions
- ✓ Preeclampsia, postpartum haemorrhage



Adapt the scores to the local epidemiology



Update in the postpartum period regardless of the mode of delivery *Grade 1C*

Rationale

VTE is rare but potentially fatal during pregnancy and postpartum



0.21%



Within a year following delivery

Caesarean surgery

Postoperative prophylaxis is recommended except for elective low-risk patients *Grade 1C*



At least 6 weeks for high-risk patients

At least 7 days for the other patients requiring anticoagulation *Grade 1C*

Non-obstetric surgery

Prophylaxis following surgery during pregnancy or the postpartum period when they imply, as a consequence, bed rest until full mobility is recovered *Grade 1C*

No change compared to the 2018 guideline

Pharmacological prevention

Adjust LMWH dosing to weight if the BMI > 40kg/m²




Grade 2C

Personal history of VTE for surgery during pregnancy and postpartum: thromboprophylaxis with either a low dose or an intermediate dose of LMWH *Grade 2B*



Grade 2B

Compression stockings can be used, although there is no evidence that they prevent perioperative VTE 



Other Surgical Procedures

Surgery	Recommendation
Thoracic oncology surgery	<ul style="list-style-type: none">◆ Conditional recommendations for use of parenteral anticoagulation for VTE prevention, in combination with mechanical methods, over no prophylaxis for cancer patients undergoing lobectomy, segmentectomy, pneumonectomy, or oesophagectomy.◆ For patients at high risk of VTE, pharmacological prophylaxis should be initiated preoperatively, withheld 12 h prior to surgery, and resumed as soon as possible postoperatively◆ Conditional recommendation for using extended prophylaxis for 28 to 35 days over in-hospital prophylaxis only for patients at moderate or high risk of thrombosis.
Neurosurgery	<ul style="list-style-type: none">◆ In patients at high risk of thrombosis, a combination of mechanical and pharmacological prophylaxis is suggested, starting LMWH or UFH in the first 24 h postoperatively and no later than 72 h, provided that the risk of bleeding is ruled out and haemostasis is correct.◆ After nontraumatic intracerebral haemorrhage, provided the volume of intracranial blood is not expanding and haemostasis is correct, it is suggested to start pharmacological prophylaxis 2 to 4 days after the bleeding.
Urologic Surgery	<ul style="list-style-type: none">◆ In all patients undergoing ambulatory day surgery (e.g. circumcision, vasectomy, hydrocoelectomy and ureteroscopy), the use of pharmacological prophylaxis or mechanical prophylaxis is not recommended.◆ In all patients undergoing open radical cystectomy, or open radical prostatectomy with extended lymphadenectomy, the use of pharmacological prophylaxis is recommended.◆ Starting thromboprophylaxis (LMWH or DOACs) on post-operative day 1. Continuing thromboprophylaxis for 2-4 weeks when pharmacological thromboprophylaxis is used.



Other Surgical Procedures

Surgery	Recommendation
Gynaecological Surgery	<ul style="list-style-type: none"> ◆ Either LMWH or low-dose UFH is recommended as the first choice for pharmacological thromboprophylaxis in most cases. ◆ For patients undergoing gynaecological surgery for benign disease, postoperative low-dose UFH should be administered every 12 h. For patients undergoing gynaecological surgery for malignant disease, postoperative low-dose UFH should be administered every 8 h. ◆ For patients at high risk for VTE, continued dosing for 4 weeks postoperatively is recommended
Bariatric surgery	<ul style="list-style-type: none"> ◆ VTE prophylaxis with LMWH, UFH or fondaparinux over no prophylaxis in patients with high VTE risk and low risk for bleeding is recommended. ◆ For patients at high risk of VTE, extending pharmacological prophylaxis with LMWH, UFH, or fondaparinux for at least 10 days is recommended over prophylaxis limited to the hospital stay.
Oral and maxillofacial surgery	<ul style="list-style-type: none"> ◆ Pharmacological prophylaxis is not routinely recommended for patients undergoing minor to moderate procedures, fracture fixation, orthognathic surgery, treatment of space infections, or pedicled flap surgery.

Guideline No. 417: Prevention of Venous Thromboembolic Disease in Gynaecological Surgery. J Obstet Gynaecol Can. 2022, 44(1):82-96.e1.

The American Society for Metabolic and Bariatric Surgery (ASMBS) updated position statement on perioperative venous thromboembolism prophylaxis in bariatric surgery. Surg Obes Relat Dis. 2022, 18(2):165-174.

European guidelines on peri-operative venous thromboembolism prophylaxis: first update.: Chapter 10: Surgery in the obese patient. Eur J Anaesthesiol. 2024, 41(8):607-611.

Expert Consensus on Perioperative Strategies of VTE Prevention and Treatment, and Pharmaceutical Care. Herald of Medicine. 2025, 44(11): 1717-1735.



Perioperative VTE treatment strategies

- ◆ For patients with acute perioperative VTE, anticoagulant therapy should be initiated immediately. Commonly used agents include LMWH, fondaparinux, rivaroxaban, or apixaban, with selection individualized based on the patient's clinical condition.
- ◆ Anticoagulation therapy should be administered for at least 3 months. For VTE patients with unprovoked events or persistent thrombotic risk, extended anticoagulation therapy is required to reduce the recurrence rate.
- ◆ For isolated distal DVT: If severe symptoms or risk factors for thrombus progression are present, immediate initiation of routine anticoagulation therapy is recommended. If no severe symptoms or risk factors for thrombus progression are present, serial imaging surveillance for 2 weeks is recommended. If there is no progression of thrombosis, routine anticoagulation therapy is not recommended.



Chapter Summary

- 📍 Evaluate VTE and bleeding risk for surgical inpatients based on surgical type, patient comorbidities, and clinical conditions.
- 📍 Exclude patients with contraindications to mechanical prophylaxis and pharmacological prophylaxis.
- 📍 Develop a personalized VTE prevention plan in accordance with relevant clinical guidelines, based on the above assessments.
- 📍 For patients with acute perioperative VTE, timely anticoagulation therapy is indicated, except in those with isolated distal DVT.





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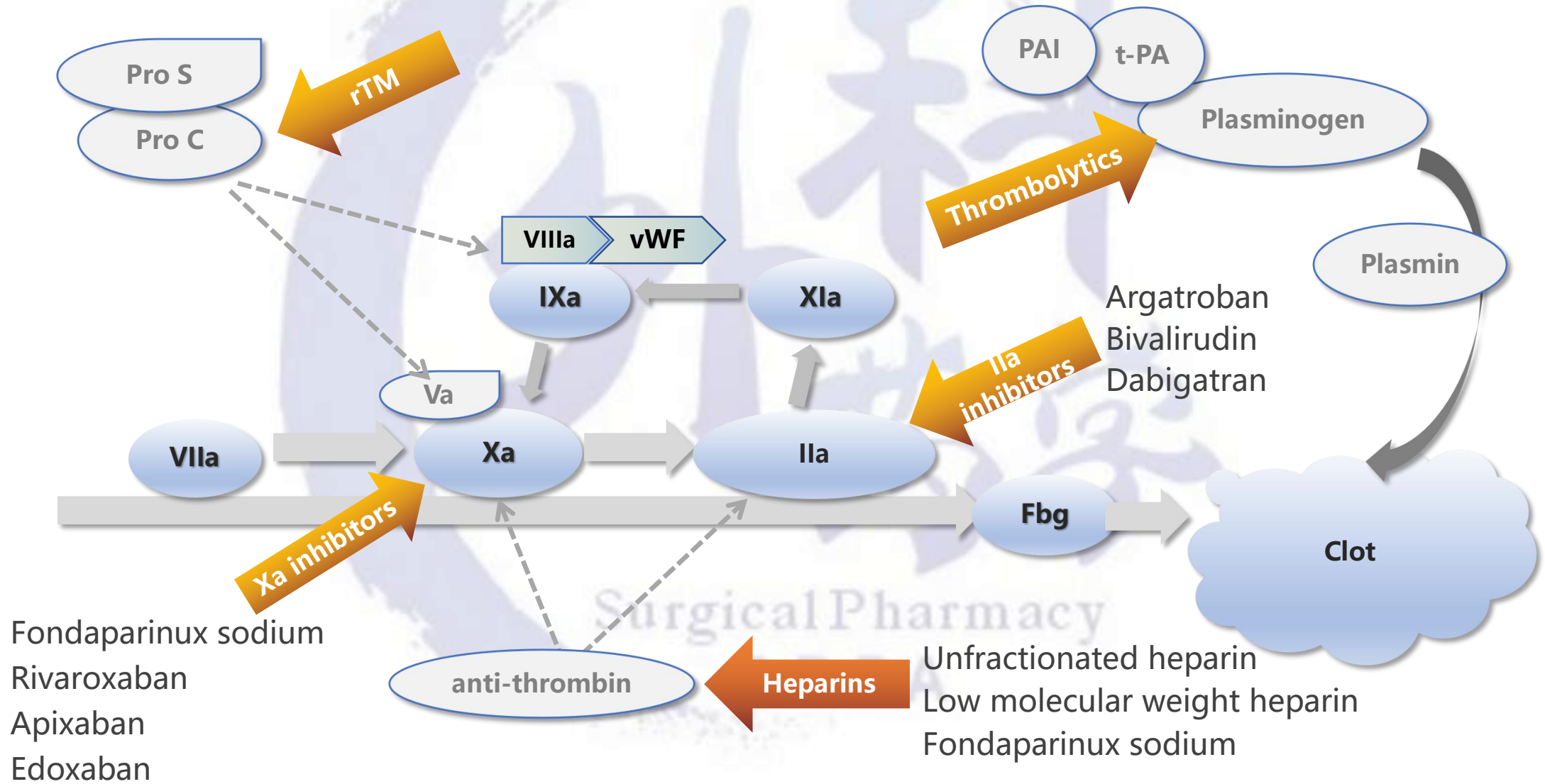
Medication management

- Perioperative VTE Management Strategy
- **Perioperative Commonly Used Anticoagulants and Pharmaceutical Monitoring**

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Anticoagulants, thrombolytics, and hemostatic agents act on their respective targets



Anticoagulant Drugs for VTE Prophylaxis: Dosage & Monitoring

Agent	Prophylaxis Dosage & Administration	Therapeutic Dosage & Administration	Monitoring Parameters
UFH	5000 U, q12h	Initial: 80 U·kg ⁻¹ iv, followed by 18 U·kg ⁻¹ ·h ⁻¹ ivgtt	APTT: 1.5–2.5 ULN
Nadroparin	2850 U, ih, qd	85 U·kg ⁻¹ , ih, q12h	Anti-Xa activity: 0.5–1.0 U·ml ⁻¹
Enoxaparin	2000 or 4000 U, ih, qd	1 mg·kg ⁻¹ , ih, q12h	Anti-Xa activity: 0.6–1.0 U·ml ⁻¹
Dalteparin	2500 or 5000 U, ih, qd	100 U·kg ⁻¹ , ih, bid or 200 U·kg ⁻¹ , ih, qd	Anti-Xa activity: 0.5–1.0 U·ml ⁻¹
Fondaparinux Sodium	2.5 mg, ih, qd	5–10 mg, ih, qd	Anti-Xa activity: 0.46–0.62 U·ml ⁻¹
Warfarin	Initial dose: 1–3 mg, qd	Initial dose: 1–3 mg, qd; overlap with parenteral anticoagulants until INR is therapeutic	INR 2.0–3.0
Rivaroxaban	10 mg, qd	15 mg, bid for the first 3 weeks, then 20 mg, qd	-
Apixaban	2.5 mg, bid	10 mg, bid for 7 days, then 5 mg, bid	-
Edoxaban	60 mg, qd	Initiate after at least 5 days of initial parenteral anticoagulation; 60 mg, qd	-
Dabigatran	150 mg, bid	Initiate after at least 5 days of initial parenteral anticoagulation; 150 mg, bid	-



Anticoagulant Drugs for VTE Prophylaxis: Dosage & Monitoring

- For prophylactic medication, except for warfarin with a target INR range of 2.0-3.0, routine monitoring is not required for other drugs;
- LNWH, rivaroxaban, apixaban, and edoxaban generally do not require routine coagulation monitoring. However, anti-Xa monitoring may be performed for special patients such as those with renal insufficiency, obesity, or pregnancy. Anti-Xa activity is typically measured 3~4 h after administration;
- During the use of UFH, APTT should be monitored every 4-6 h;
- Rivaroxaban is only used for VTE prophylaxis in patients undergoing elective hip or knee replacement surgery, as well as in patients with persistent VTE risk after completing at least 6 months of standard anticoagulation therapy;
- Apixaban is only used for VTE prophylaxis in patients undergoing elective hip or knee replacement surgery;
- The dose of edoxaban should be adjusted to 30 mg qd in the following situations: moderate to severe renal impairment (Cr_{cl} 15- 50 ml/min), low body weight (60 kg), or concomitant use with P-gp inhibitors;
- The dose of dabigaran should be adjusted to 110 mg bid in the following situations: age ≥ 80 years old or concurrent use with verapamil.

Dose adjustment of anticoagulants for perioperative patients with liver dysfunction

Anticoagulant	Child-Pugh Class	Dosage Adjustment	Anticoagulant	Child-Pugh Class	Dosage Adjustment
LMWH	A	Preferred agent; no dosage adjustment required	Dabigatran	A	No dosage adjustment required; not recommended if AST/ALT >2× ULN or liver disease
	B				
	C			Contraindicated	
Fondaparinux Sodium	A	No dosage adjustment required	Apixaban	A	No dosage adjustment required; use with caution if AST/ALT >2× ULN or TBIL ≥1.5× ULN
	B			Not recommended	
	C			Contraindicated	
Warfarin	A	No dosage adjustment required	Edoxaban	A	No dosage adjustment required; use with caution if AST/ALT >2× ULN or TBIL ≥1.5× ULN
	B	Not recommended		B	Not recommended
	C			Contraindicated	
			Rivaroxaban	A	No dosage adjustment required
				B	Contraindicated
				C	

Dose adjustment of anticoagulants for perioperative patients with renal dysfunction

Anticoagulant	Indication	$50 \text{ ml}\cdot\text{min}^{-1} \leq \text{CrCl} \leq 70 \text{ ml}\cdot\text{min}^{-1}$	$30 \text{ ml}\cdot\text{min}^{-1} \leq \text{CrCl} < 50 \text{ ml}\cdot\text{min}^{-1}$	$15 \text{ ml}\cdot\text{min}^{-1} \leq \text{CrCl} < 30 \text{ ml}\cdot\text{min}^{-1}$	$\text{CrCl} < 15 \text{ ml}\cdot\text{min}^{-1}$	Monitoring Parameters & Target Range
UFH	VTE Prophylaxis	5000 U, bid-tid, ih	No dosage adjustment required			—
	VTE Treatment	Initial: $80 \text{ U}\cdot\text{kg}^{-1}$ iv, then $18 \text{ U}\cdot\text{kg}^{-1}\cdot\text{h}^{-1}$ ivgtt	Adjust dose based on APTT or anti-Xa activity		Loading dose: $60 \text{ U}\cdot\text{kg}^{-1}$; maintenance: $12 \text{ U}\cdot\text{kg}^{-1}\cdot\text{h}^{-1}$, then adjust based on APTT	APTT: 1.5–2.5× ULN
Nadroparin	VTE Prophylaxis	2850–5700 U (0.3–0.6 ml), qd, ih	Reduce by 25–33%	Not recommended		—
	VTE Treatment	$85 \text{ U}\cdot\text{kg}^{-1}$, q12h, ih	Reduce by 25–33%	Not recommended		Anti-Xa activity: $0.5\text{--}1.0 \text{ U}\cdot\text{ml}^{-1}$
Enoxaparin	VTE Prophylaxis	2000–4000 U, qd, ih	2000 U, qd, ih	Not recommended		—
	VTE Treatment	$1 \text{ mg}\cdot\text{kg}^{-1}$, q12h, ih	$1 \text{ mg}\cdot\text{kg}^{-1}$, q12h, ih; adjust based on anti-Xa activity	$1 \text{ mg}\cdot\text{kg}^{-1}$, qd, adjust based on anti-Xa activity	Not recommended; if necessary, $1 \text{ mg}\cdot\text{kg}^{-1}$, qd, adjust based on anti-Xa activity	Anti-Xa activity: $0.6\text{--}1.0 \text{ U}\cdot\text{ml}^{-1}$
Dalteparin	VTE Prophylaxis	2500–5000 U, qd, ih	No dosage adjustment required	Monitor anti-Xa levels		Anti-Xa activity: $0.2\text{--}0.4 \text{ U}\cdot\text{ml}^{-1}$
	VTE Treatment	$100 \text{ U}\cdot\text{kg}^{-1}$, q12h, ih or $200 \text{ U}\cdot\text{kg}^{-1}$, qd, ih	No dosage adjustment required	Use with caution; reduce dose, adjust based on anti-Xa activity		Anti-Xa activity: $0.5\text{--}1.0 \text{ U}\cdot\text{ml}^{-1}$
Fondaparinux Sodium	VTE Prophylaxis	2.5 mg, qd, ih	1.5 mg, qd, ih	Not recommended if $\text{CrCl} < 20 \text{ ml}\cdot\text{min}^{-1}$	Not recommended	Anti-Xa activity: $0.2\text{--}0.3 \text{ U}\cdot\text{ml}^{-1}$
Argatroban	HIT/Heparin Resistance	$1.2\text{--}2.0 \mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$; adjust based on APTT		$0.8 \mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$; adjust based on APTT		APTT: 1.5–3.0× ULN
Bivalirudin	HIT/Heparin Resistance	$1.75 \text{ mg}\cdot\text{kg}^{-1}\cdot\text{h}^{-1}$; adjust based on APTT		$1 \text{ mg}\cdot\text{kg}^{-1}\cdot\text{h}^{-1}$; adjust based on APTT		APTT: 1.5–2.0× ULN

Dose adjustment of anticoagulants for perioperative patients with renal dysfunction

Anticoagulant	Indication	$50 \text{ ml}\cdot\text{min}^{-1} \leq \text{CrCl} \leq 70 \text{ ml}\cdot\text{min}^{-1}$	$30 \text{ ml}\cdot\text{min}^{-1} \leq \text{CrCl} < 50 \text{ ml}\cdot\text{min}^{-1}$	$15 \text{ ml}\cdot\text{min}^{-1} \leq \text{CrCl} < 30 \text{ ml}\cdot\text{min}^{-1}$	$\text{CrCl} < 15 \text{ ml}\cdot\text{min}^{-1}$
Warfarin	VTE Prophylaxis/Treatment	Adjust dose based on INR			
Dabigatran	VTE Prophylaxis	110 mg 1d, then 220 mg qd, po (administered on the day of surgery); or 220 mg qd, po (if not used on the day of surgery)	No dosage adjustment required	Not recommended	
	VTE Treatment	150 mg, bid, po	110 mg, bid, po	Not recommended	
Rivaroxaban	VTE Prophylaxis	10 mg, qd, po	No dosage adjustment required	Not recommended	
	VTE Treatment	15 mg, bid, po for 21 d; then 20 mg, qd, po	15 mg, bid, po for 21 d; then 15 mg, qd, po	Use with caution, 15 mg qd, monitor anti-Xa activity or drug concentration	Not recommended (dialysis patients: 10 mg, qd, po)
Apixaban	VTE Prophylaxis	2.5 mg, bid, po	No dosage adjustment required		
	VTE Treatment	10 mg, bid, po for 5 d; then 5 mg, bid, po	No dosage adjustment required	2.5 mg, bid, po	Not recommended (dialysis patients: 2.5 mg, bid, po)
Edoxaban	VTE Treatment	60 mg, qd, po	30 mg, qd, po		



Pharmaceutical care for anticoagulant drugs



Embolism

Bleeding

Liver Function

Drug Interactions

Renal Function

INR Level

HIT

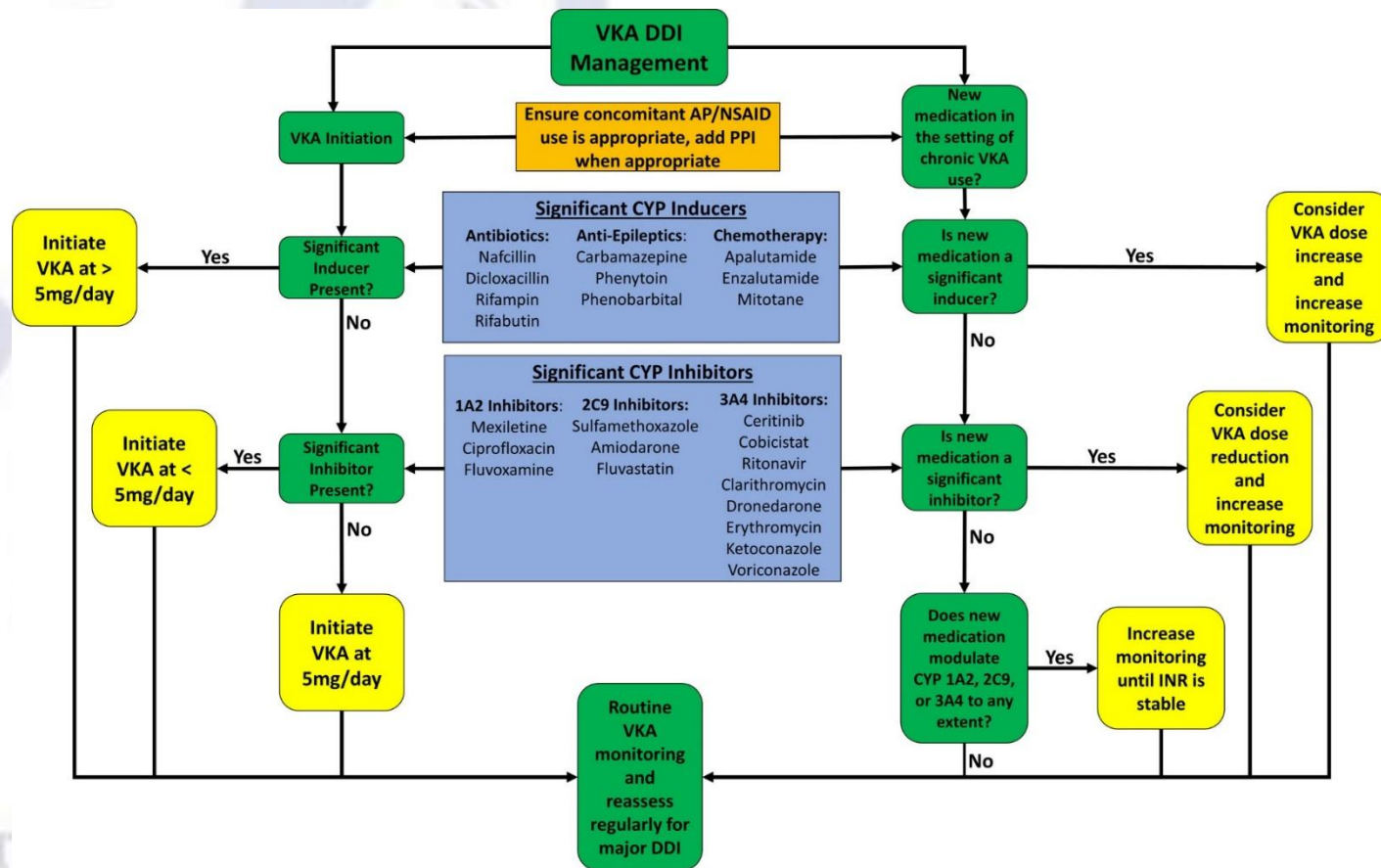
Etc.

Pharmaceutical care for anticoagulant drugs

Anticoagulant	Pharmacological Monitoring Points					Specific Antidote
	Bleeding	Liver Function	Renal Function	HIT	Drug Interactions (CYP3A4/P-gp Inhibitors)	
UFH	✓	✓		✓		Protamine
LMWH	✓	✓	✓	✓		Protamine
Fondaparinux Sodium	✓	✓	✓			—
Warfarin	✓	✓			✓	Vitamin K
Rivaroxaban	✓	✓	✓		✓	Andexanet alfa
Apixaban	✓	✓	✓		✓	Andexanet alfa
Edoxaban	✓	✓	✓		✓	Andexanet alfa
Dabigatran	✓	✓	✓		✓	Idarucizumab

Pharmaceutical care for anticoagulant drugs

- All anticoagulant drugs can be nonspecifically antagonized by prothrombin complex concentrate, fresh frozen plasma or recombinant coagulation factor VIIa;
- Rivaroxaban 10 mg can be taken with or without food, while rivaroxaban 15 mg or 20 mg tablets should be taken with food ;
- Dabigatran should be taken orally with water, swallowed whole, and can be administered during or after meals;
- Warfarin has numerous drug interactions (strong inducer/inhibitor of CYP, etc.)





Chapter Summary

- 📍 Pharmacists should provide personalized monitoring for patients on anticoagulants, considering their clinical condition, drug type, and dosage regimen.
- 📍 The content of pharmaceutical care encompasses the occurrence of bleeding or thromboembolic events, the hepatic and renal function, etc.
- 📍 Special attention must be paid to drug–drug interactions, especially for patients taking warfarin.





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03

Case Analysis

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Case Introduction

Chief Complaint

Left knee joint pain with limited movement for over 5 years, worsened in the past 2 months.

Previous History

CKD began 3 years ago but has not taken medication regularly (CrCl: 33.5 ml/min) . Denies any other significant medical history.

01

Patient

Female, 68 years old

02

Current Medical History

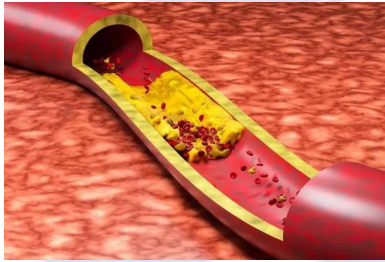
Left knee pain with restricted movement for over 5 years. Has undergone multiple intra-articular injections of hyaluronic acid at local hospitals, the most recent one a year ago. Symptoms persisted, with limited left knee movement, a limping gait while walking, and was admitted for "knee osteoarthritis" .

03

04

**The patient is scheduled for knee replacement surgery.
Consult the Department of Pharmacy for perioperative VTE management.**

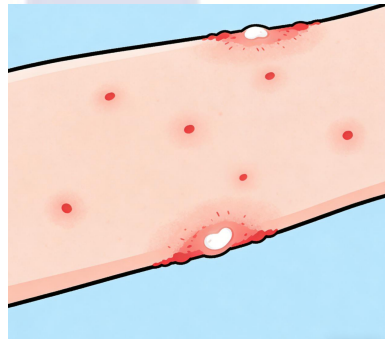
Determine Perioperative VTE Management Strategy Based on Risk Stratification



1-Assess VTE risk



2-Evaluate bleeding risk



3-Screen for contraindications to relevant preventive measures



4-Determine the optimal VTE prophylaxis strategy



Assess VTE risk



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Thrombosis Risk Factor Assessment

Patient's Name: _____ Age: ____ Sex: ____ Wgt: ____ lbs

Choose All That Apply

Each Risk Factor Represents 1 Point

- Age 41-60 years
- Minor surgery planned
- History of prior major surgery (< 1 month)
- Varicose veins
- History of inflammatory bowel disease
- Swollen legs (current)
- Obesity (BMI > 25)
- Acute myocardial infarction
- Congestive heart failure (< 1 month)
- Sepsis (< 1 month)
- Serious lung disease incl. pneumonia (< 1 month)
- Abnormal pulmonary function (COPD)
- Medical patient currently at bed rest
- Other risk factors _____

Each Risk Factor Represents 3 Points

- Age over 75 years
 - History of DVT/PE
 - Family history of thrombosis***
 - Positive Factor V Leiden
 - Positive Prothrombin 20210A
 - Elevated serum homocysteine
 - Positive lupus anticoagulant
 - Elevated anticardiolipin antibodies
 - Heparin-induced thrombocytopenia (HIT)
 - Other congenital or acquired thrombophilia
- If yes:

Type _____

*most frequently missed risk factor

Each Risk Factor Represents 2 Points

- Age 60-74 years**
- Arthroscopic surgery
- Malignancy (present or previous)
- Major surgery (> 45 minutes)
- Laparoscopic surgery (> 45 minutes)
- Patient confined to bed (> 72 hours)
- Immobilizing plaster cast (< 1 month)
- Central venous access

Each Risk Factor Represents 5 Points

- Elective major lower extremity arthroplasty**
- Hip, pelvis or leg fracture (< 1 month)
- Stroke (< 1 month)
- Multiple trauma (< 1 month)
- Acute spinal cord injury (paralysis)(< 1 month)

For Women Only (Each Represents 1 Point)

- Oral contraceptives or hormone replacement therapy
- Pregnancy or postpartum (<1 month)
- History of unexplained stillborn infant, recurrent spontaneous abortion (≥ 3), premature birth with toxemia or growth-restricted infant

Total Risk Factor Score



**7 points
high risk**

Patient-related VTE risk factors include (but are not limited to):

- previous or family history of venous thromboembolism^{1,2}
- major thrombophilia³
- age >70 years⁴
- obesity⁵
- hypoalbuminaemia⁶
- active cancer⁷
- oestrogenic oral contraception and oral hormone therapy for the menopause⁸
- renal insufficiency⁹**

Patient-related risks can increase the risk of bleeding

HAS-BLED Score

Variable	Score
Age ≥ 65 years	1
Hypertension (Systolic Blood Pressure ≥ 160mmHg)	1
Abnormal renal function	1
Abnormal liver function	1
Stroke in past	1
Bleeding	1
Labile INRs	1
Taking other drugs as well	1
Alcohol intake at the same time	1



2 points
Low bleeding risk

Patient-related bleeding risk factors include (but are not limited to):

- coagulopathy¹⁵
- anticoagulant medication¹⁶

Bleeding risk factors related to the procedure performed are (but are not limited to):

- duration of procedure¹⁷
- length of skin incision¹⁸
- use of drains¹⁹



Perioperative VTE Management Strategy

(3) High VTE risk surgery:

- (a) No high risk of bleeding: We suggest VTE prophylaxis with either LMWH or DOAC rather than no VTE prophylaxis for procedures with high VTE risk without high risk of bleeding (Grade 2B). We are unable to make a recommendation for or against the use of aspirin.
- (b) High risk of bleeding: We suggest mechanical VTE prophylaxis rather than pharmacological prophylaxis for procedures with high VTE risk with high risk of bleeding (Grade 2C).

2.2. For patients undergoing major orthopedic surgery (THA, TKA, HFS) and receiving LMWH as thromboprophylaxis, we recommend starting either 12 h or more preoperatively or 12 h or more postoperatively rather than within 4 h or less preoperatively or 4 h or less postoperatively (Grade 1B).



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Periprocedural Management of Patients on Direct Oral Anticoagulants

Anticoagulant	Indication	$50 \text{ ml}\cdot\text{min}^{-1} \leq \text{CrCl} \leq 70 \text{ ml}\cdot\text{min}^{-1}$	$30 \text{ ml}\cdot\text{min}^{-1} \leq \text{CrCl} < 50 \text{ ml}\cdot\text{min}^{-1}$	$15 \text{ ml}\cdot\text{min}^{-1} \leq \text{CrCl} < 30 \text{ ml}\cdot\text{min}^{-1}$	$\text{CrCl} < 15 \text{ ml}\cdot\text{min}^{-1}$	Monitoring Parameters & Target Range
UFH	VTE Prophylaxis	5,000 U, bid-tid, ih	No dosage adjustment required			—
	VTE Treatment	Initial: $80 \text{ U}\cdot\text{kg}^{-1}$ IV bolus, then $18 \text{ U}\cdot\text{kg}^{-1}\cdot\text{h}^{-1}$ IV infusion	Adjust dose based on APTT or anti-Xa activity		Loading dose: $60 \text{ U}\cdot\text{kg}^{-1}$; maintenance: $12 \text{ U}\cdot\text{kg}^{-1}\cdot\text{h}^{-1}$, then adjust based on APTT	APTT: 1.5–2.5× ULN
Nadroparin	VTE Prophylaxis	2,850–5,700 U (0.3–0.6 ml), qd, ih	Reduce by 25–33%	Not recommended		—
	VTE Treatment	$85 \text{ U}\cdot\text{kg}^{-1}$, q12h, ih	Reduce by 25–33%	Not recommended		Anti-Xa activity: 0.5–1.0 $\text{U}\cdot\text{ml}^{-1}$
Enoxaparin	VTE Prophylaxis	2,000–4,000 U, qd, ih	2,000 U, qd, ih	Not recommended		—
	VTE Treatment	$1 \text{ mg}\cdot\text{kg}^{-1}$, q12h, ih	$1 \text{ mg}\cdot\text{kg}^{-1}$, q12h, ih; adjust based on anti-Xa activity	$1 \text{ mg}\cdot\text{kg}^{-1}$, qd, adjust based on anti-Xa activity	Not recommended; if necessary, $1 \text{ mg}\cdot\text{kg}^{-1}$, qd, adjust based on anti-Xa activity	Anti-Xa activity: 0.6–1.0 $\text{U}\cdot\text{ml}^{-1}$
Dalteparin	VTE Prophylaxis	2,500–5,000 U, qd, ih	No dosage adjustment required	Monitor anti-Xa levels		Anti-Xa activity: 0.2–0.4 $\text{U}\cdot\text{ml}^{-1}$
	VTE Treatment	$100 \text{ U}\cdot\text{kg}^{-1}$, q12h, ih or $200 \text{ U}\cdot\text{kg}^{-1}$, qd, ih	No dosage adjustment required	Use with caution; reduce dose, adjust based on anti-Xa activity		Anti-Xa activity: 0.5–1.0 $\text{U}\cdot\text{ml}^{-1}$
Fondaparinux Sodium	VTE Prophylaxis	2.5 mg, qd, ih	1.5 mg, qd, ih	Not recommended if $\text{CrCl} < 20 \text{ ml}\cdot\text{min}^{-1}$	Not recommended	Anti-Xa activity: 0.2–0.3 $\text{U}\cdot\text{ml}^{-1}$



Summary

Risk Stratification as Decision Basis

- VTE risk ; Bleeding risk.

Comprehensive Consideration

- The formulation of a perioperative VTE prevention strategy requires comprehensive consideration of surgical type, patient condition, drug characteristics, and evidence-based medicine.

Multidisciplinary Collaboration & Monitoring Focus

- Dynamic hepatic/renal function monitoring; Drug-drug interactions; bleeding/thromboembolic events, etc.



Q1: (single choice) For patients with a $\text{CrCl} < 15 \text{ ml}\cdot\text{min}^{-1}$, which anticoagulant can be selected for perioperative VTE prophylaxis?

- A. Warfarin
- B. Apixaban
- C. Enoxaparin
- D. Nadroparin



Q2: (single choice) For patients undergoing cardiac and vascular surgery, which anticoagulant is recommended for VTE prophylaxis?

- A. UFH
- B. LMWH
- C. Apixaban
- D. Warfarin



Q3: (multiple choice) 1. When formulating perioperative VTE management strategies for patients, we need to consider?

- A. Assessing the risk of VTE
- B. Assessing the risk of bleeding
- C. Hepatic function of patient
- D. Drug interactions
- E. Renal function of patient



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**Your constructive criticism and guidance
are greatly appreciated!**

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