Perioperative Management of Antithrombotic Drugs

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Translated the American Pharmacists Association (APhA) Medication Therapy Management Services (MTMs) textbook into Chinese and led the drafting of China's first standard for Medication Therapy Management (MTM) Pharmacy Clinic Services.

Perioperative risk of bleeding and thrombosis

Bleeding related risk

- The incidence of major bleeding in patients receiving vit K antagonist therapy ranges from 1~ 3%.
- The gastrointestinal bleeding rate during antithrombotic therapy for AMI with PCI is 16.6%
- Approximately 25% of intracranial hemorrhage cases are associated with oral anticoagulant therapy.

Thrombosis related risk

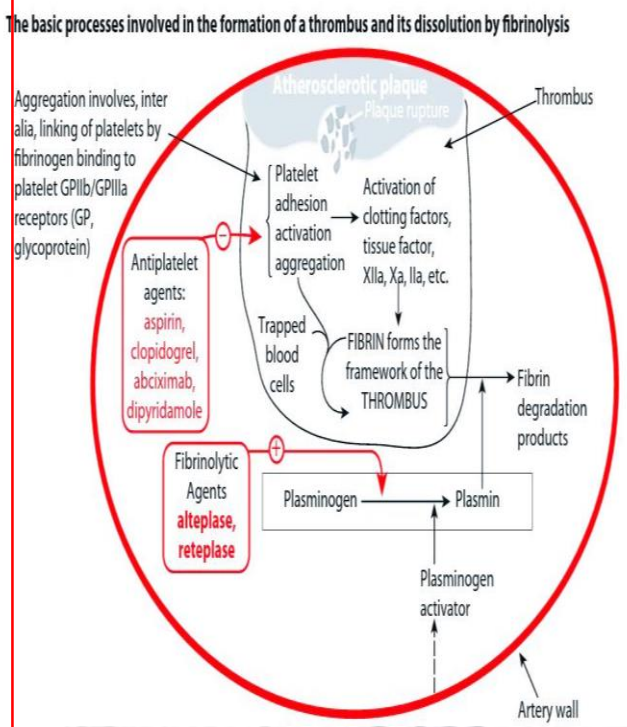
- Stroke and other thromboembolic events are the leading causes of death and disability in atrial fibrillation.
- The annual stroke incidence after mechanical valve replacement with anticoagulation is 5-10%.
- If antithrombotic drugs are stopped within 1 month after venous thrombosis, the monthly recurrence rate can be as high as 40%.

CONTENT

Common Antithrombotic Drugs

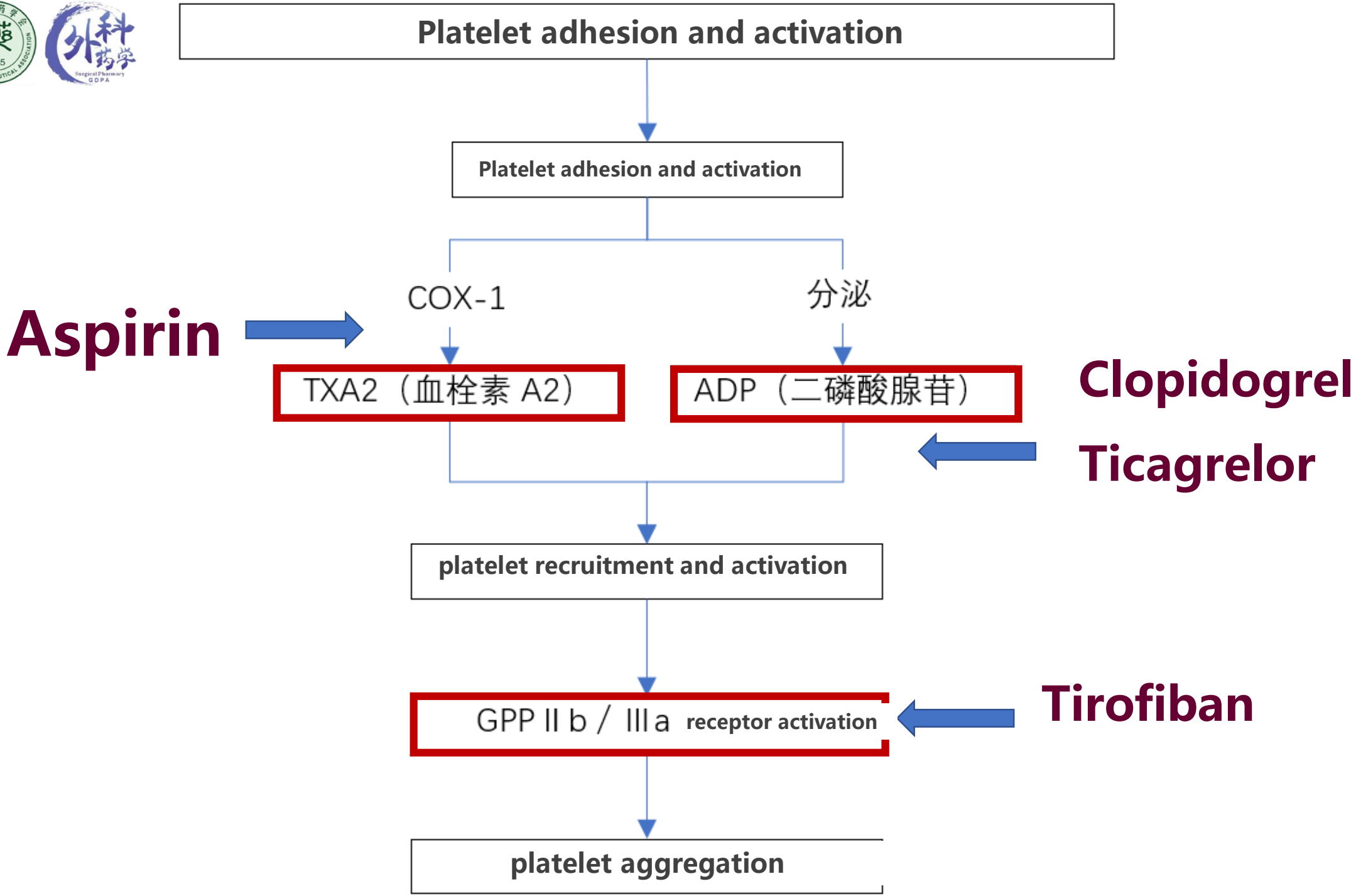
Antiplatelet Drugs

- Thromboxane A2 inhibitors
- ADP P2Y12 receptor antagonists
- GPIIb/IIIa receptor inhibitors



Anticoagulant Drugs

- Vitamin K antagonists
- Indirect thrombin inhibitors
- Direct thrombin inhibitors
- Factor Xa inhibitors


Platelet adhesion and activation
Platelet adhesion and activation
COX-1
分泌
Aspirin
TXA2（血栓素 A2）
ADP（二磷酸腺苷）
Clopidogrel
Ticagrelor
platelet recruitment and activation
GPP II b / III a receptor activation
Tirofiban
platelet aggregation

Antiplatelet Drugs

Characteristics	Aspirin	ADP P2Y12 Receptor Antagonists			GPIIb/IIIa Receptor Inhibitors
		Clopidogrel	Prasugrel	Ticagrelor	Tirofiban
MOA	Irreversible inhibition of cox1&2	Irreversible P_2Y_{12} inhibitor	Irreversible P_2Y_{12} inhibitor	Reversible, noncompetitive P_2Y_{12} inhibitor	GPIIb/IIIa eceptor inhibitors
Peak Effect	N/A	6-8 hours	2-4 hours	2 hours	30 mins
Half-life	3~6 hours	~6 hours	~7 hours	7~9 hours	1.5~ 2 hours

Common Antithrombotic Drugs

Antiplatelet drugs

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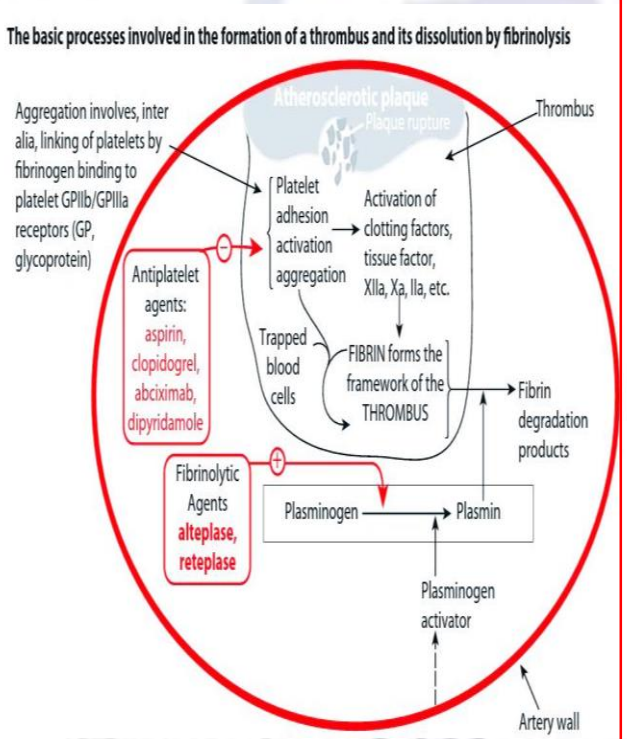

anticoagulant drugs

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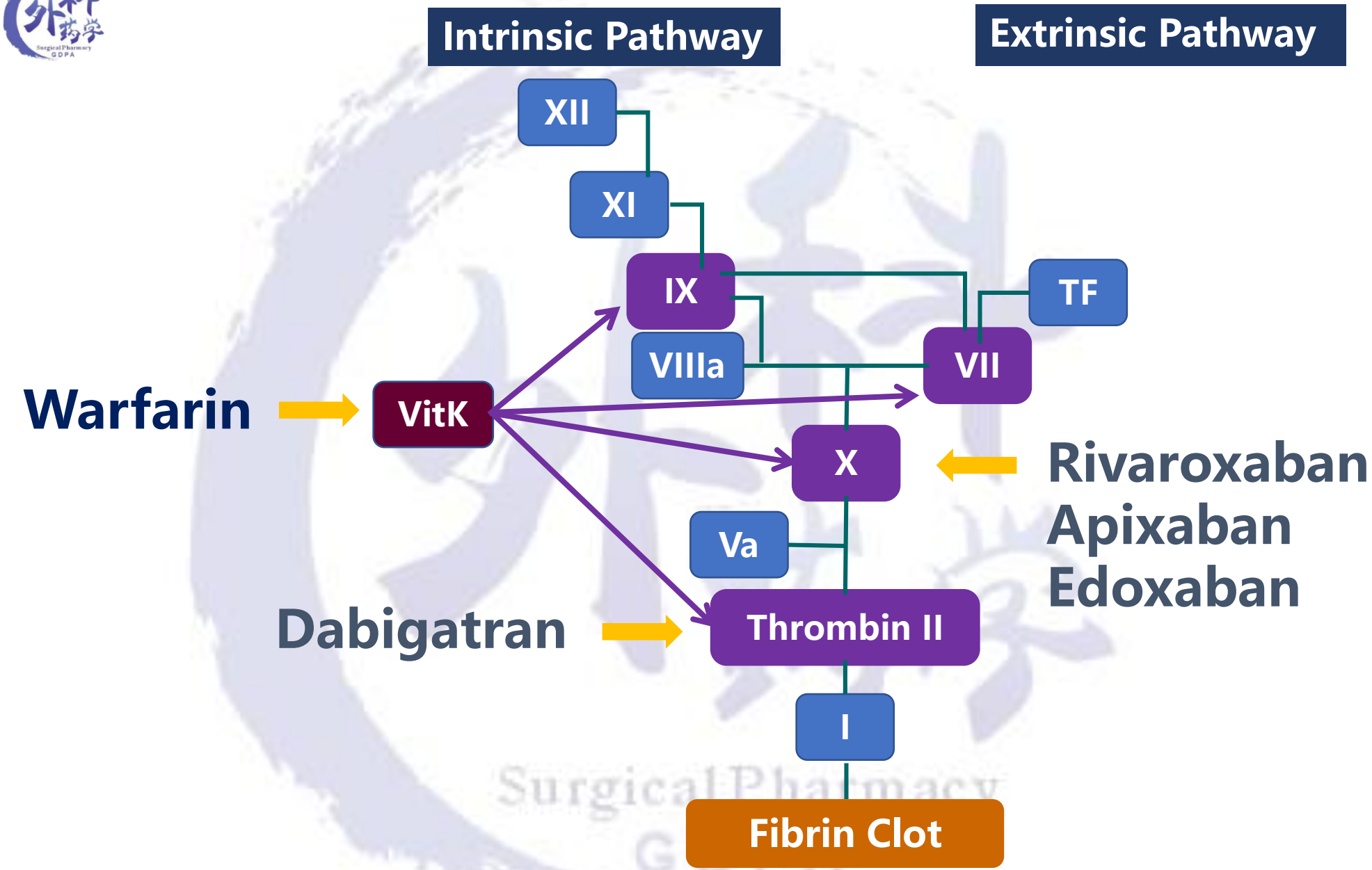

Intrinsic Pathway
Extrinsic Pathway
XII
XI
IX
VIIIa
TF
VII
Warfarin
VitK
X
Rivaroxaban
Apixaban
Edoxaban
Va
Dabigatran
Thrombin II
I
Fibrin Clot

Anticoagulant drugs

wafarin

Characteristics	Warfarin
MOA	Vitamin Kantagonist
Peak Effect	5 days
Half-life	40 hours
Reversal agents	Vitamin K or prothrombin complex concentrate (PCC)

- Target factors: II, VII, IX, X
- Anticoagulant efficacy can be monitored by INR (generally target 2.0-3.0)
- Onset of action in 2-3 days, reaching steady state in about one week
- Numerous drug/food interactions
- Rapid reversal: PCC+IV vitamin k

Anticoagulant drugs

DOACs

Characterristics	Dabigatran	Rivaroxaban	Apixaban	Edoxaban
MOA	Factor lla inhibitor	Factor Xa inhibitor	Factor Xa inhibitor	Factor Xa inhibitor
Peak Effect	2-3 hours	2-4 hours	1-3 hours	1-2 hours
Half-life	12-17 hours	5-9 hours	9-14 hours	9-11 hours
Reversal agents	Idarucizumab	Andexanet alfa or PCC	Andexanet alfa or PCC	Andexanet alfa or PCC

Anticoagulant drugs

Heparin

Characteristics	Low Molecular Weight Heparin	Unfractionated Heparin	Fondaparinux
MOA	Indirect factor Xa/lla inhibitor via AT	Indirect factor Xa/lla inhibitor via AT	Selective factor Xa inhibitor via AT
Peak Effect	20-30 minutes	Instantaneous	2-3 hours
Half-life	3-5 hours	45-60 minutes	17-21 hours
Reversal agents	Protamine (70%)	Protamine(100%)	No approved agent

Main Detection indicators of Antithrombotic Drugs

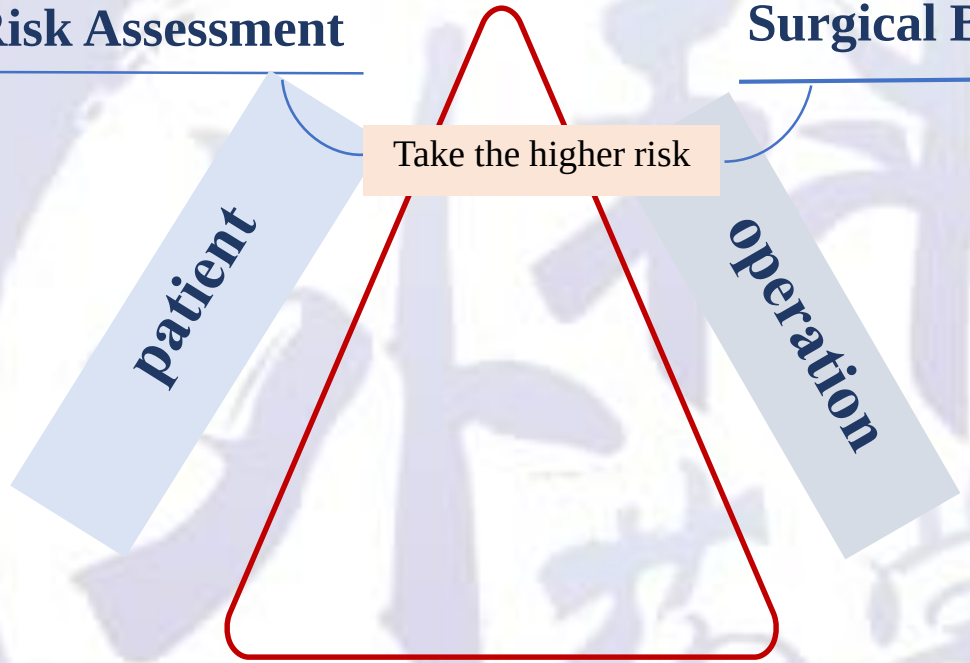
Antithrombotic Agent	Main Detection Index
Antiplatelet Drugs	TEG-AA(Aspirin) TEG-ADP(Clopidogrel) LTA-AA(Aspirin) LTA-ADP(Clopidogrel)
warfarin	PT/INR
Heparin	APTT Anti-Xa color development method
LMWH	Anti-Xa color development method
Factor Xa inhibitor	golden standard：LC-MS/MS quantitative test：Anti-Xa color development method qualitative test：PT
Oral direct thrombin inhibitors	golden standar：LC-MS/MS法： uantitative test： ECA法； qualitative test：TT
Intravenous direct thrombin inhibitors	APTT

CONTENT

Bleeding & Thrombosis Risk Assessment

Individual Bleeding Risk Assessment

Surgical Bleeding Risk Assessment



Thrombosis risk

Thromboembolism risk assessment

Bleeding Associated with Antithrombotic Agents

Bleeding scoring system

- ATRIA
- HEMORR2HAGES
- ORBIT
- HAS-BLED
- ABH

	ATRIA[11]	HEMORRaHAGES[12]	ORBIT[13]	HAS-BLED[14]	ABH[17]
Mior bleding					2
Olderage					
Age>75					
Ae>65					1
Age 65-75					
ge65					0
Renal disease	3		1		
Hypertenslon					
Aoemi	3	1	2		
Nom bleeding-relatedHospitaliration in the lat iamonths					
Aleohol					
Lher disease					
Stroke					
Hatdt abnormality					
Aatiplutelet agents					
Aspirin					
INR					
Malignancy					
Genetk tator					
Excesveflik					
Maxdmum score	10	12	7	9	5
Hgbrisk cut-of	5	4 4	5	4	

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Surgical Bleeding Bisk Assessment

High bleedng nsk procoduros(30-day risk of major boed >2%)	Low/moderate bleeding nisk proceduros(30-dayk of major bleed 0%-2%)	Minimal bleeding risk procedures(30-day isk of major bieod-0%)
Any major operaton procedure duration >45min) Major surgery with exlensive tissue injury Major orthopedic surgery Urological or gastrointestina sungory Roconstructive plastic surgory Kdney biopsy Colonic polyp resection PEGplacement ERCP Surgery in highiy vascular organs Cardiec,intracranial,o spinal surgery Neuranal anesthesa	AthrosC0py Cutaneous/ymph node biopsios Foovhand surgery Coronary angiography GIT endoscopy +1-biopsy Abdominal hystereclormy Laparoscopic cholocystocomy Abdominal hemia repair Homorhoidal suroery Bronchoscopy+/-biopsy Epidural injocfions	Minor dermatologic procedures Ophthalmological procedures Minor dental procedures Pacemaker or cardoverter defbilator device implantation

Risk Stratification Based on Surgical Type

- High bleeding risk: >2%
- Low to moderate risk: 0–2%
- Minimal risk: ~0%

Surgical bleeding risk assessment

出血风险	手术类别
Very Low Risk	Tooth extraction Skin biopsy or excision of skin tumors Cataract surgery
Low Risk	Laparoscopic cholecystectomy Laparoscopic hernia repair Non-cataract ophthalmic surgery Coronary angiography Gastrointestinal endoscopy (with or without biopsy) Bone marrow or lymph node biopsy Pericardial, pleural, abdominal, or joint cavity puncture
Moderate -High Risk	Other abdominal/thoracic/orthopedic/vascular surgeries Colon polypectomy Prostate or cervical biopsy
High Risk	Craniotomy or spinal surgery Major vascular surgery Pneumonectomy Major orthopedic surgery (e.g., hip replacement) Oral and maxillofacial surgery Small bowel anastomosis Kidney biopsy / Multi-site colon biopsy Large colon polypectomy Permanent pacemaker/implantable cardioverter-defibrillator (ICD) placement Endoscopic retrograde cholangiopancreatography (ERCP) with sphincterotomy Major urological surgery (e.g., prostatectomy, bladder tumor resection) Major hepatic surgery (e.g., hepatectomy, liver transplantation, portosystemic shunt or devascularization) Major abdominal surgery (e.g., pancreaticoduodenectomy, biliary tract tumor resection)

- **When the patient's bleeding risk level and the surgical bleeding risk level differ, the higher risk level should be applied.**

Embolism Risk Assessment--Stroke

Clinical Area	Guidelines
Non valvular AF	Stratify risk using the CHA2DS2-VASe score
Prosthetie heart valve	Stratify risk according to valve type,location,and individual thromboembolie risk factors(AF,history of thromboembolism).
VTE	Stratify based on time elapsed since VTEdiagnosis and individual risk factors(cancer,thrombophilia) Elective operation should be deferred for3months after VTE diagnosis.
CAD	Elective operation should be deferred for214d for ballon angioplasty,30 days for bare metal stent placement,and iyear for drug-eluting stent placement
Stroke	Elective operation should be deferred for 29 months after an ischemic stroke
Peripheral arterial disease	Symptomatie patients should be managed in dose consultation with a vascular specialist or vascular surgeon.

Indication

↓

Stroke risk

Condition	CHA_2DS_2-VASc score	Points
C	Congestive heart failure(or left ventricular systolic dysfunction)	1
H	Hypertension	1
A2	Age≥75years	2
D	Diabetes mellitus	1
S2	Prior stroke or TIA or thromboembolism	2
V	Vascular disease	1
A	Age 65-74years	1
Se	Sex category(iLe. female sex)	1

Stroke prediction in patients with atrial fibrillation

↓

Normal sinus rhythm? Other blood clots?

0 points: No anticoagulation needed or only aspirin

1 point: Preferred oral anticoagulant or aspirin

≥2 points: Oral anticoagulant"

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Embolism Risk Assessment--VTE

Provoked			Unprovoked
Transient		Permanent	
Major:within the last 3months	Minor:within the last two months		
Surgery with general anesthesia for >30 min or Confined to bed in hospital for at least 3 days or Caesarean section	Surgery with general anesthesia for<30 min or Admission to hospita for<3 days with an acute illness or Pregnancy or puerperium or Estrogen therapy or Confined to bed out of hospital for at least 3 days with an acute illness orLeg injury with reduced mobility for at least 3 days dd	Active cancer with ongoing treatment or Inflammatory bowel diseases	Not exposed to any of these risk factors
>10-old increased risk of recurrent VTE	3-10-fold increased risk of recurrent VTE	2-fold increased risk of recurrent VTE	

The risk of VTE in high-risk years is >10%

The risk of VTE in moderate risk years is 5-10%

The risk of VTE in low-risk years is <5%

Additional risk factors(cancer)need.to be considered as well

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CONTENT

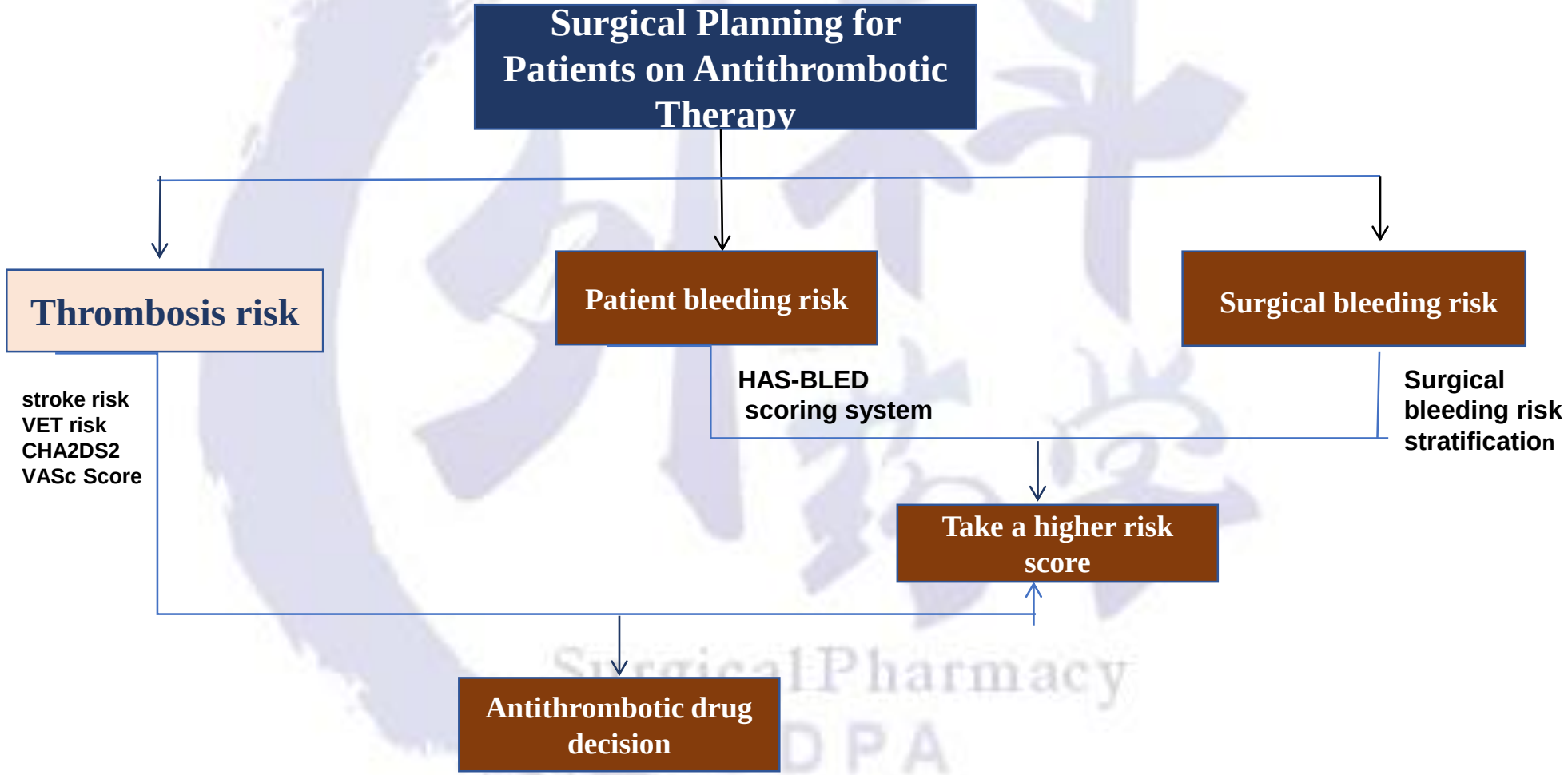
Withdrawal and bridging strategies of antithrombotic drugs

Drug	Preoperative Discontinuation	Postoperative Resumption
Vitamin K Antagonists (e.g., Warfarin)	Discontinue 5 days pre-op (target INR ≤1.5)	24-72 hours post-op (after hemostasis, often with heparin bridging)
Aspirin	Low-bleeding-risk surgery: Continue; High-bleeding-risk surgery: Discontinue 7 days pre-op	24 hours post-op (if no active bleeding)
Clopidogrel/Ticagrelor	Discontinue 5-7 days pre-op	24 hours post-op (early reassessment for coronary stent patients)
NOACs (Rivaroxaban, Apixaban, Dabigatran)	Based on renal function: - Low-bleeding-risk surgery: 24-48 hours pre-op; - High-bleeding-risk surgery: 3-5 days pre-op (CrCl ≥30 ml/min)	48-72 hours post-op (after confirmed hemostasis)
Unfractionated Heparin	IV infusion: Stop 4-6 hours pre-op; Subcutaneous: Stop 12 hours pre-op	6-12 hours post-op (depending on bleeding risk)
LMWH (e.g., Enoxaparin)	Prophylactic dose: Stop 12 hours pre-op; Therapeutic dose: Stop 24 hours pre-op	24-72 hours post-op (based on surgical bleeding risk)

Antithrombotic drug decision

Bleeding risk Thromboembolic risk	→	Whether to discontinue medication before surgery
Drug half-life Creatinine clearance rate	⇒	Timing of medication discontinuation before surgery
Drug onset time	→	Timing of postoperative resumption

Withdrawal and bridging strategies of antithrombotic drugs



Bridging strategies for anticoagulant drugs

➢ Bridging drug selection

LMWH

➢ Bridging contraindications

· Severe renal damage

· Immediate reversal indicated (UFH preferred)

➢Creatinine clearance correction dose

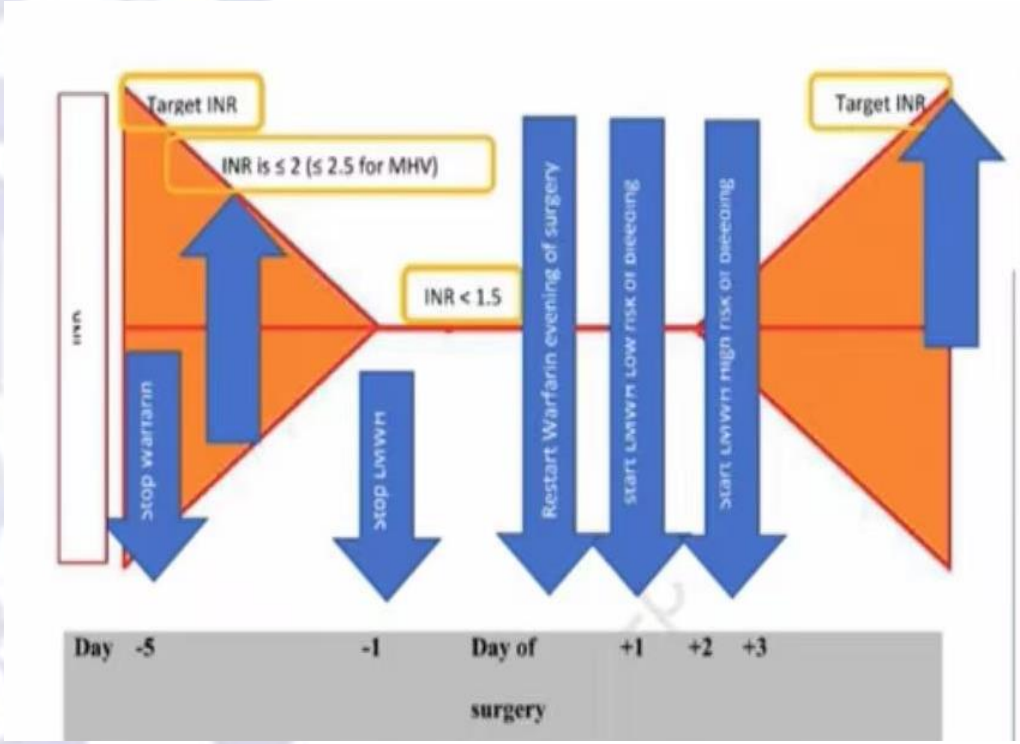
· Crd<30,1mg/kg qd

· Crd≥30,1mg/kg or 1.5mg/kg bid

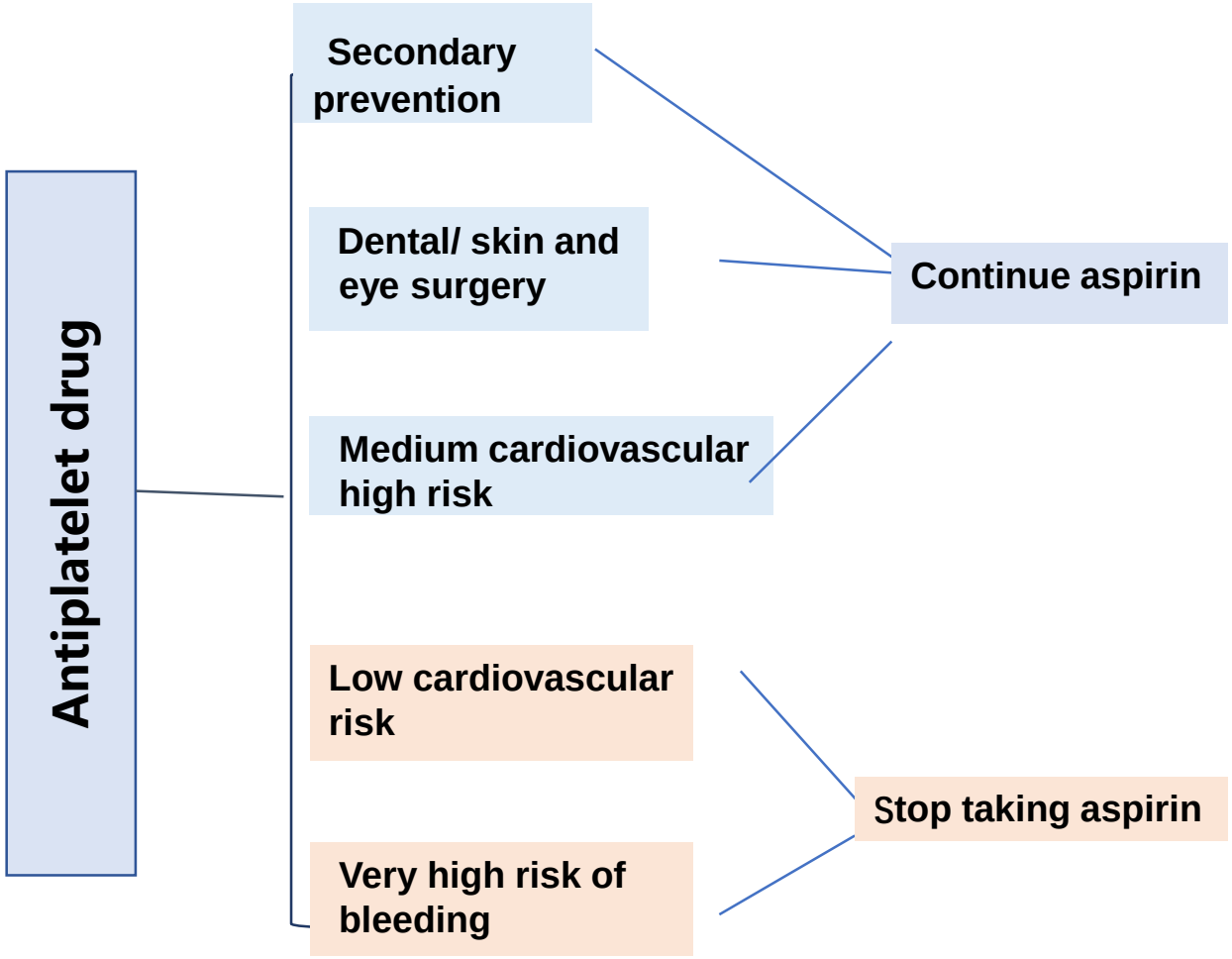
➢ Withdrawal and resume timing

· 5 days before surgery;Patients with moderate risk of bleeding 3d

· Time of onset of hemostasis Risk of sufficient bleeding (12-24h after surgery)



Bridging strategy for antiplatelet agents



Bridging drug selection

- Short-acting - No evidence to support
- Long-acting - Not recommended (UFH, LMWH, NSAIDs)
- ·Intravenous antiplatelet agents

Post-PCI 1 month + time-sensitive surgery + high bleeding risk

- Multidisciplinary consultation
- Bridging with intravenous antiplatelet agents
- Intensive care unit + close monitoring

Postoperative recovery

- Clopidogrel 600mg loading dose recommended

Urgent Surgical Management for Patients on Antithrombotics

Vitamin K(1-10mg>30min)
Prothrombin complex concentrate(PCC)(25-50U/kg)
Fresh frozen plasma (FFP)(10-15ml/kg)

UFH- Protamine(1mg vs 80-120U)
LMWH- Protamine (0.5-1mg vs 1mg)
LMWH-Aripazine Under study

Consider platelet transfusion (1 apheresis unit or 10 mg/kg) preoperatively in DAPT patients if platelet function testing is feasible

Clearance is usually 48-72 hours
The dabigatrate-specific antagonist: 5g Edacezumab, can be cleared by dialysis

Urgent Surgical Management for Patients on Antithrombotics

Reversal of bleeding associated with antithrombotic drugs →

- Use PCC + vitamin K for warfarin-induced bleeding.
- Protamine is preferred for hepan reversal.
- Use specific antidotes or hemodialysis for direct thrombin inhibitor bleeding.
- Use specific reversal agents or PCC for factor Xa inhibitor bleeding.
- Give fibrinogen + antifibrinolytics for thrombolytic-related bleeding.
- Reverse antiplatelet bleeding guided by platelet function tests.
- Urgent reversal is needed for surgery-requiring bleeding on antithrombotics.

Clarify present illness history/Past medical and medication history → Bleeding Severity Assessment → Discontinue antithrombotic agents Emergency reversal → Hemostasis Maintain hemodynamic stability

Perioperative Management of Antithrombotic drug

■ Oral antiplatelet agents

If discontinuation is required, stop 5–10 days in advance.

■ Anticoagulants

Warfarin: Discontinue 5 days prior, until INR <1.5.
NOACs (DOACs): Generally stop 1–2 days before (earlier if renal impairment).

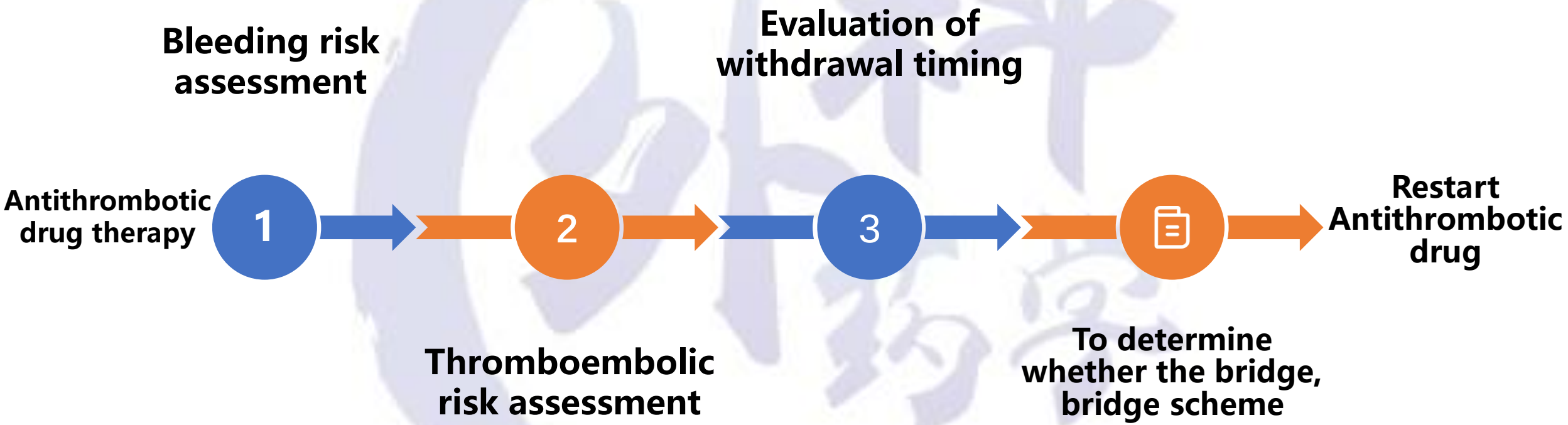
■ High thrombotic risk patients(Consider bridging therapy during discontinuation)

Warfarin → Low-molecular-weight heparin (LMWH)
Antiplatelet drugs → Tirofiban

The management of antithrombotic drugs in perioperative patients should involve a careful balance of benefits and risks, with individualized drug administration.

CONTENT

Perioperative Antithrombotic drug Management Process



Perioperative pharmaceutical care of antithrombotic therapy

一、Bleeding Risk Assessment

- **Patient-specific factors:**

  General condition, age, body weight, hepatic/renal function, coagulation status, etc.

- **Primary disease status**

- **Comorbidities:** Uncontrolled hypertension, active bleeding, etc.

- **Surgical factors:** Procedure type, operative site, duration of surgery

- **Concurrent medications:** Antiplatelet agents, anticoagulants, hemostatics, hormonal drugs, etc.

Perioperative pharmaceutical care of antithrombotic therapy

二、Thrombosis Risk Assessment

- **Patient-specific factors**: General condition, age, body weight, hepatic/renal function, coagulation status, smoking history, etc.
- **Primary disease status**: Based on indications for antithrombotic therapy and relevant risk stratification scores
- **Comorbidities:** Diabetes mellitus, coronary artery disease, stroke, peripheral vascular disease, hyperlipidemia, etc.
- **Hemostatic agents used during surgery**
- **Postoperative immobilization:** Bed rest, restricted turning, indwelling invasive catheters, and other factors contributing to VTE risk

Perioperative pharmaceutical care of antithrombotic therapy

三、Indicators that require monitoring

- **Efficacy evaluation:** Symptoms related to thrombotic events， Diagnostic tests: ECG, color Doppler ultrasound, CTA, MRI
- **Safety evaluation:** Bleeding-related symptoms, allergic reactions, adverse drug reactions (ADRs)， Postoperative drainage volume, blood tests (hemoglobin, platelet count), coagulation parameters, hepatic/renal function tests
- **Assessment of medical order adherence and patient compliance**

Perioperative pharmaceutical care of antithrombotic therapy

- Discontinue antithrombotic drug at the appropriate time before surgery

- Achieve effective hemostasis postoperatively

- Restart antithrombotic therapy at the optimal postoperative timing

Thanks for your attention