



# 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%.



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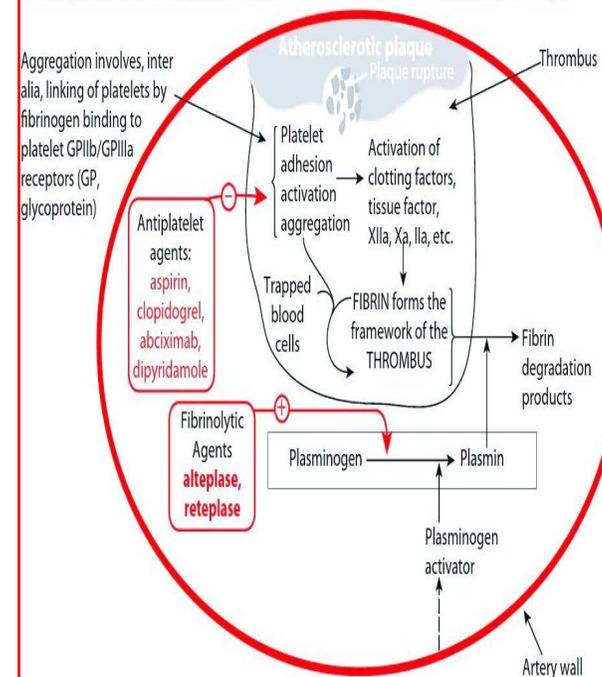
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# Common Antithrombotic Drugs

## Antiplatelet Drugs

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

The basic processes involved in the formation of a thrombus and its dissolution by fibrinolysis



## 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

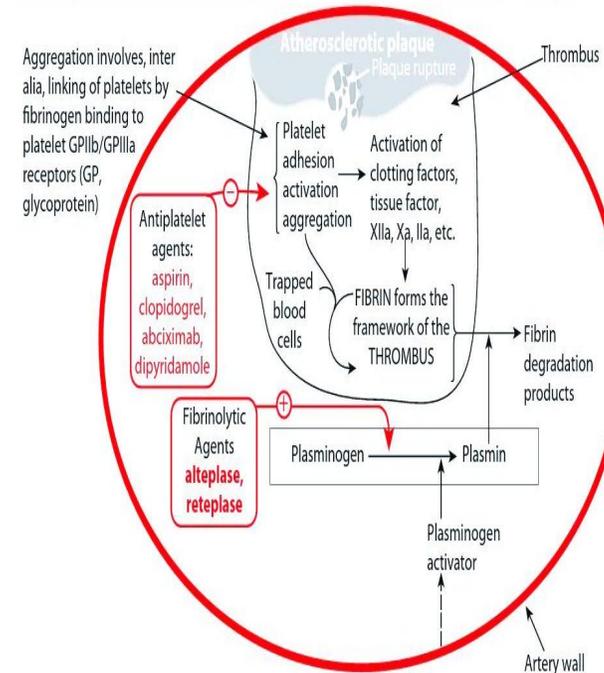
Characteristics	Aspirin	ADP P <sub>2</sub> Y <sub>12</sub> Receptor Antagonists			GPIIb/IIIa Receptor Inhibitors
		Clopidogrel	Prasugrel	Ticagrelor	Tirofiban
MOA	Irreversible inhibition of cox1&2	Irreversible P <sub>2</sub> Y <sub>12</sub> inhibitor	Irreversible P <sub>2</sub> Y <sub>12</sub> inhibitor	Reversible, noncompetitive P <sub>2</sub> Y <sub>12</sub> 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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The basic processes involved in the formation of a thrombus and its dissolution by fibrinolysis

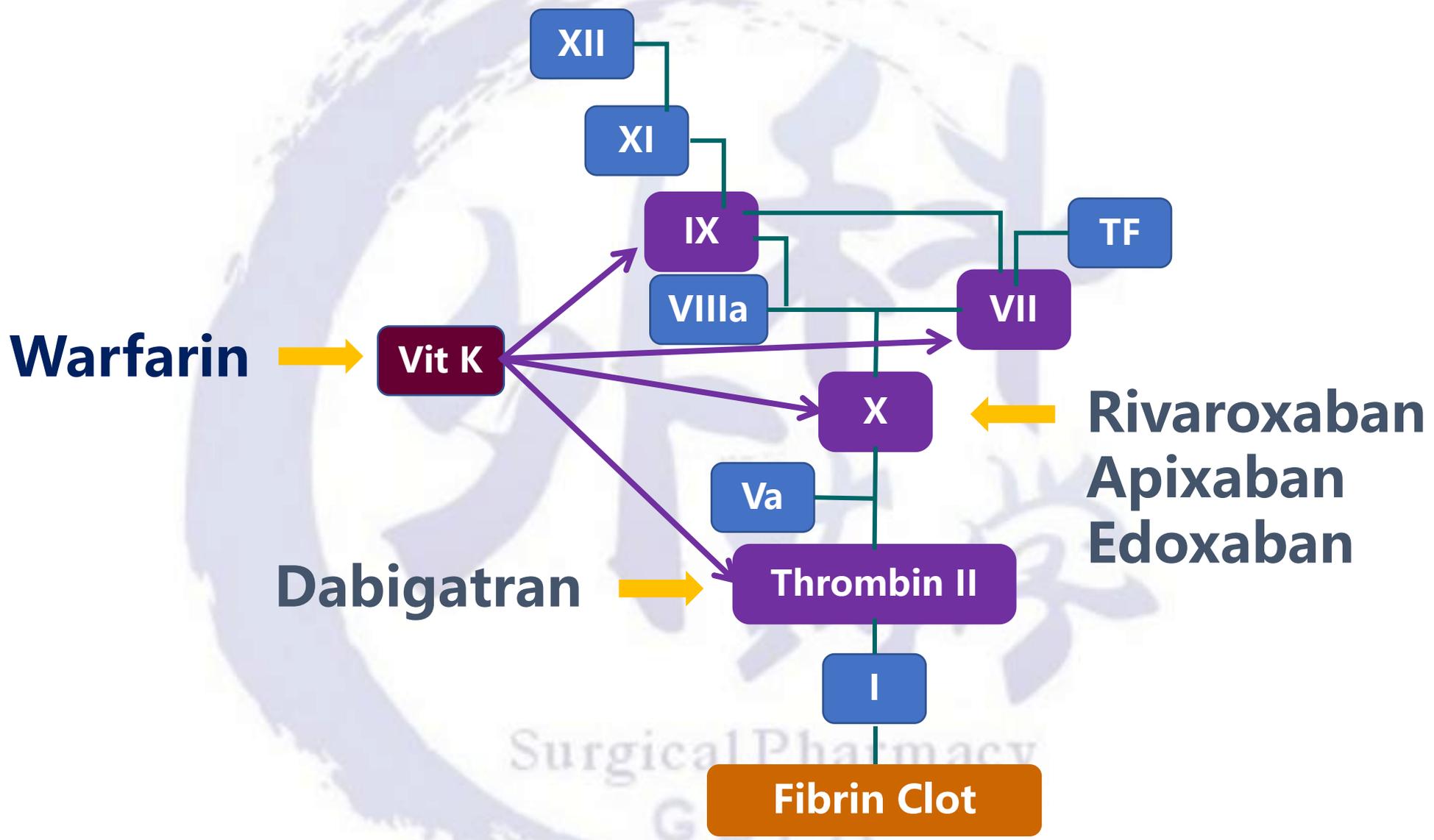


## anticoagulant drugs

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

# Intrinsic Pathway

# Extrinsic Pathway



# Anticoagulant drugs

## Warfarin

Characteristics	Warfarin
MOA	Vitamin K antagonist
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

Characteristics	Dabigatran	Rivaroxaban	Apixaban	Edoxaban
<b>MOA</b>	<b>Factor IIa inhibitor</b>	<b>Factor Xa inhibitor</b>	<b>Factor Xa inhibitor</b>	<b>Factor Xa inhibitor</b>
<b>Peak Effect</b>	<b>2-3 hours</b>	<b>2-4 hours</b>	<b>1-3 hours</b>	<b>1-2 hours</b>
<b>Half-life</b>	<b>12-17 hours</b>	<b>5-9 hours</b>	<b>9-14 hours</b>	<b>9-11 hours</b>
<b>Reversal agents</b>	<b>Idarucizumab</b>	<b>Andexanet alfa or PCC</b>	<b>Andexanet alfa or PCC</b>	<b>Andexanet alfa or PCC</b>



# Anticoagulant drugs

## Heparin

Characteristics	Low Molecular Weight Heparin	Unfractionated Heparin	Fondaparinux
MOA	Indirect factor Xa/IIa inhibitor via AT	Indirect factor Xa/IIa 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



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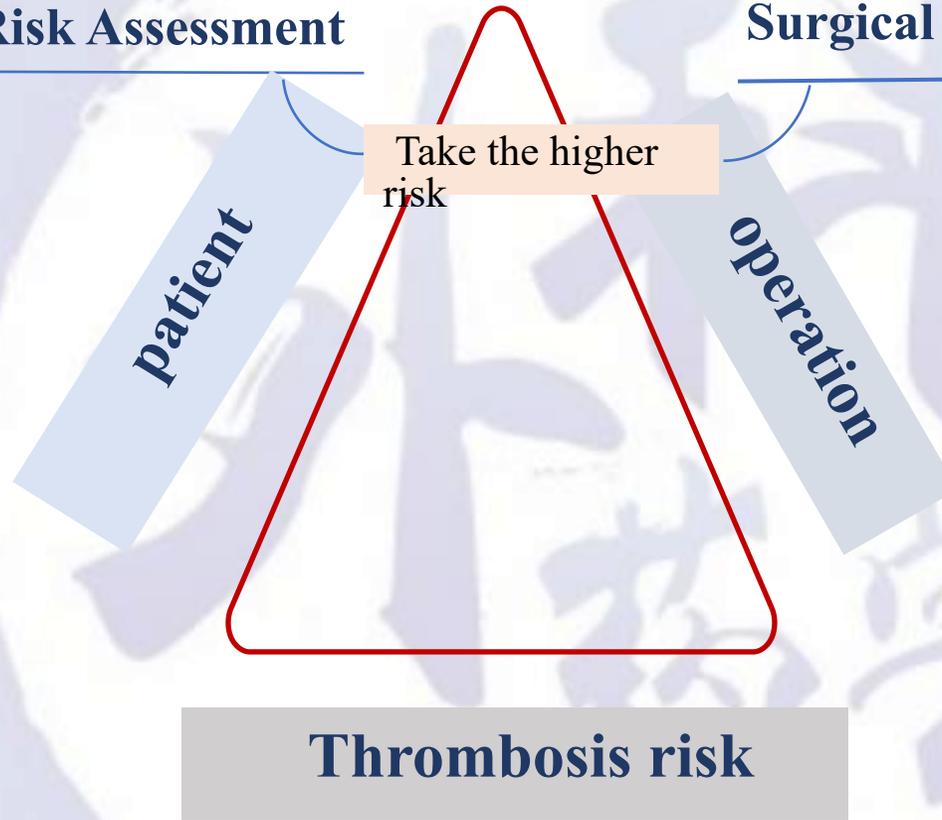
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# Bleeding & Thrombosis Risk Assessment

Individual Bleeding Risk Assessment

Surgical Bleeding Risk Assessment



Thromboembolism risk assessment

# Bleeding Associated with Antithrombotic Agents

## Bleeding scoring system

**ATRIA**

**HEMORR2HAGES**

**ORBIT**

**HAS-BLED**

**ABH**

	ATRIA[11]	HEMORR2HAGES[12]	ORBIT[13]	HAS-BLED[14]	ABH[17]
Prior bleeding	1	2	2	1	2
Older age		1	1		
Age>75	2			1	
Age>65				1	1
Age 65-75					2
Age<65					0
Renal disease	3	1	1	1	
Hypertension	1	1		1	
Anemia	3	1	2		
Non-bleeding-related hospitalization in the last 12 months					1
Alcohol		1		1	
Liver disease		1		1	
Stroke		1		1	
Platelet abnormality		1			
Antiplatelet agents			1		
Aspirin				1	
INR				1	
Malignancy		1			
Genetic factor		1			
Excessive fall risk		1			
<b>Maximum score</b>	<b>10</b>	<b>12</b>	<b>7</b>	<b>9</b>	<b>5</b>
<b>High-risk cut-off</b>	<b>5</b>	<b>4</b>	<b>4</b>	<b>5</b>	<b>4</b>



# Surgical Bleeding Risk Assessment

High bleeding risk procedures (30-day risk of major bleed >2%)	Low/moderate bleeding risk procedures (30-day risk of major bleed 0%-2%)	Minimal bleeding risk procedures (30-day risk of major bleed 0%)
Any major operation procedure duration >45min) Major surgery with extensive tissue injury Major orthopedic surgery Urological or gastrointestinal surgery Reconstructive plastic surgery Kidney biopsy Colonic polyp resection PEG placement ERCP Surgery in highly vascular organs Cardiac, intracranial, or spinal surgery Neuronal anesthesia	Arthroscopy Cutaneous/lymph node biopsies Forehand surgery Coronary angiography GIT endoscopy +1-biopsy Abdominal hysterectomy Laparoscopic cholecystectomy Abdominal hernia repair Hemorrhoidal surgery Bronchoscopy +/- biopsy Epidural injections	Minor dermatologic procedures Ophthalmological procedures Minor dental procedures Pacemaker or cardioverter defibrillator 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

Bleeding risk	Type of surgery
<b>Very Low Risk</b>	Tooth extraction Skin biopsy or excision of skin tumors Cataract surgery
<b>Low Risk</b>	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
<b>Moderate-High Risk</b>	Other abdominal/thoracic/orthopedic/vascular surgeries Colon polypectomy Prostate or cervical biopsy
<b>High Risk</b>	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-VASc score
Prosthetic heart valve	Stratify risk according to valve type,location,and individual thromboembolic 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	Symptomatic patients should be managed in dose consultation with a vascular specialist or vascular surgeon.

**Indication**  
↓  
**Stroke risk**

Condition	CHA <sub>2</sub> DS <sub>2</sub> -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 (i.e. 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"



# Embolism Risk Assessment--VTE

	Provoked		Unprovoked
	Transient	Permanent	
Major: within the last 3 months	Minor: within the last two months		
Surgery with general anesthesia for > 30 min. <i>or</i> Confined to bed in hospital for at least 3 days <i>or</i> Caesarean section	Surgery with general anesthesia for < 30 min. <i>or</i> Admission to hospital for < 3 days with an acute illness <i>or</i> Pregnancy or puerperium <i>or</i> Estrogen therapy <i>or</i> Confined to bed out of hospital for at least 3 days with an acute illness <i>or</i> Leg injury with reduced mobility for at least 3 days	Active cancer with ongoing treatment <i>or</i> Inflammatory bowel diseases	Not exposed to any of these risk factors
>10-fold 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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# 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 $\leq 1.5$ )	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 $\geq 30$ 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**

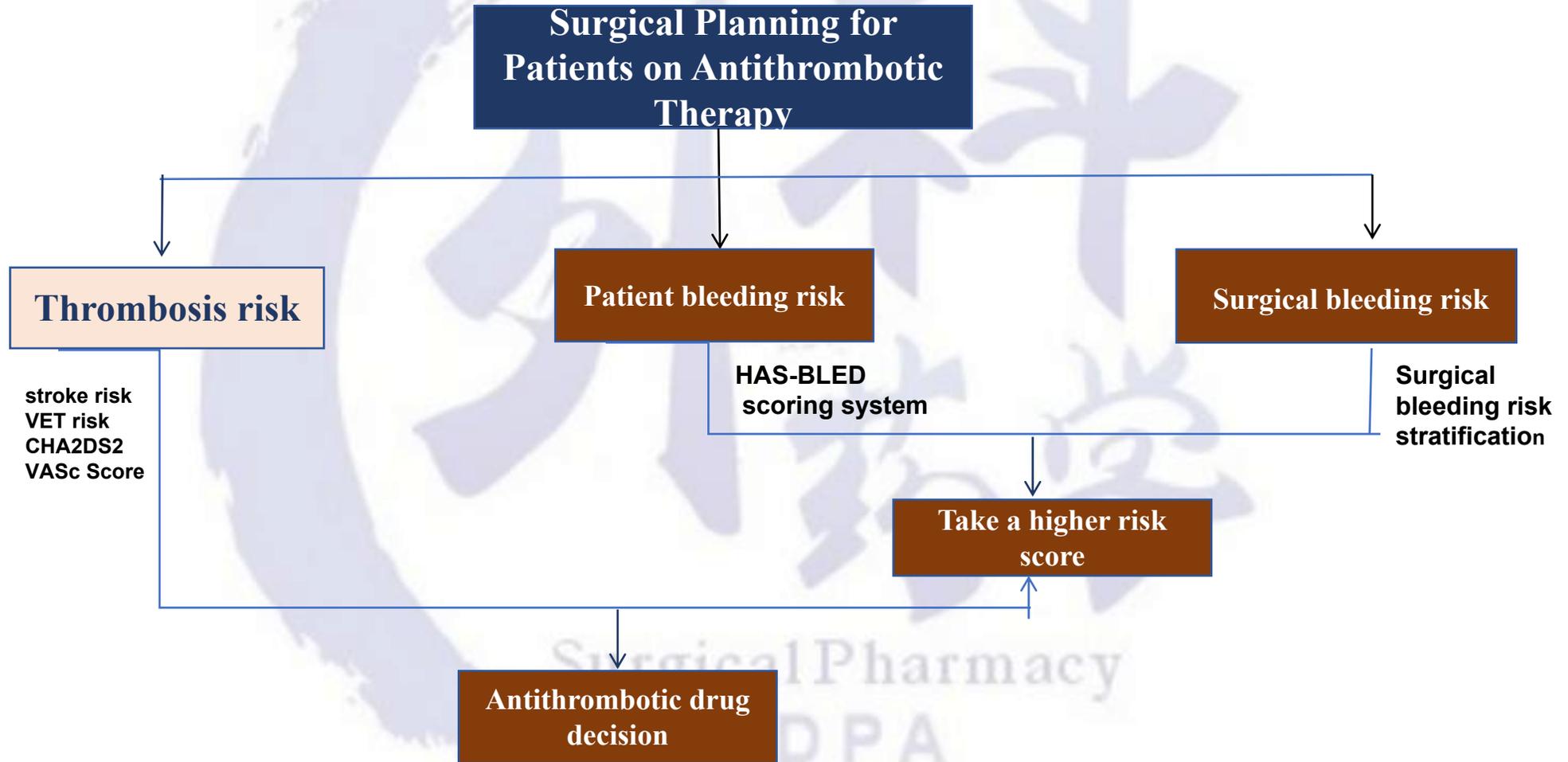
**Drug onset time**



**Timing of postoperative resumption**

G D P A

# Withdrawal and bridging strategies of antithrombotic drugs



# Bridging strategies for anticoagulant drugs

## ➤ Bridging drug selection

LMWH

## ➤ Bridging contraindications

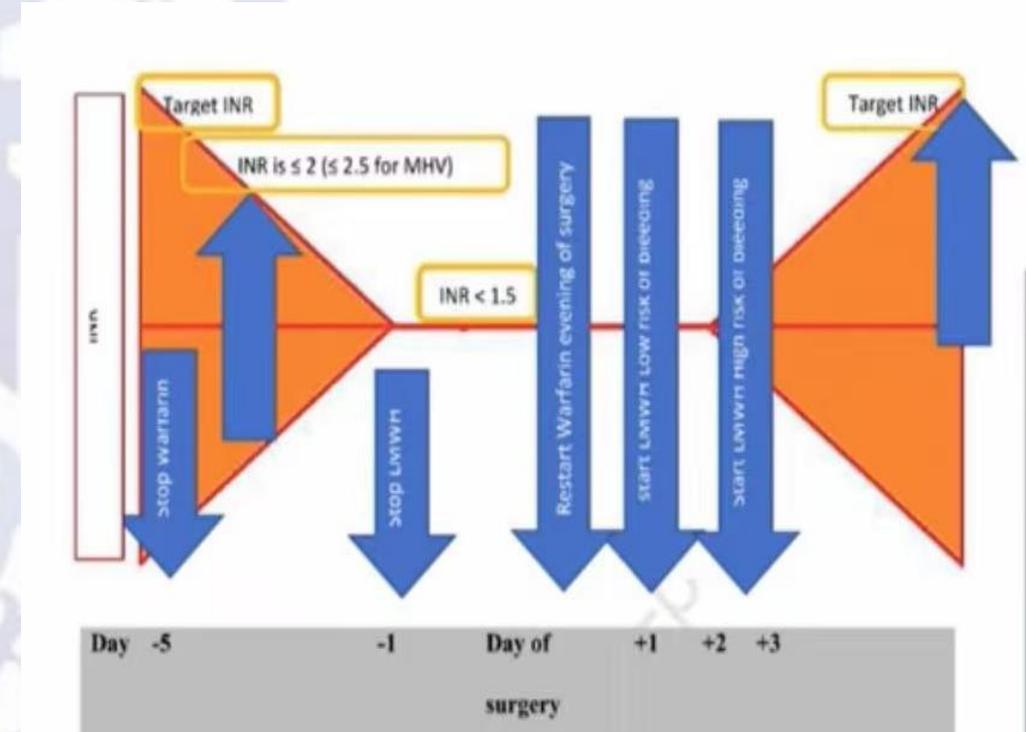
- Severe renal damage
- Immediate reversal indicated (UFH preferred)

## ➤ Creatinine clearance correction dose

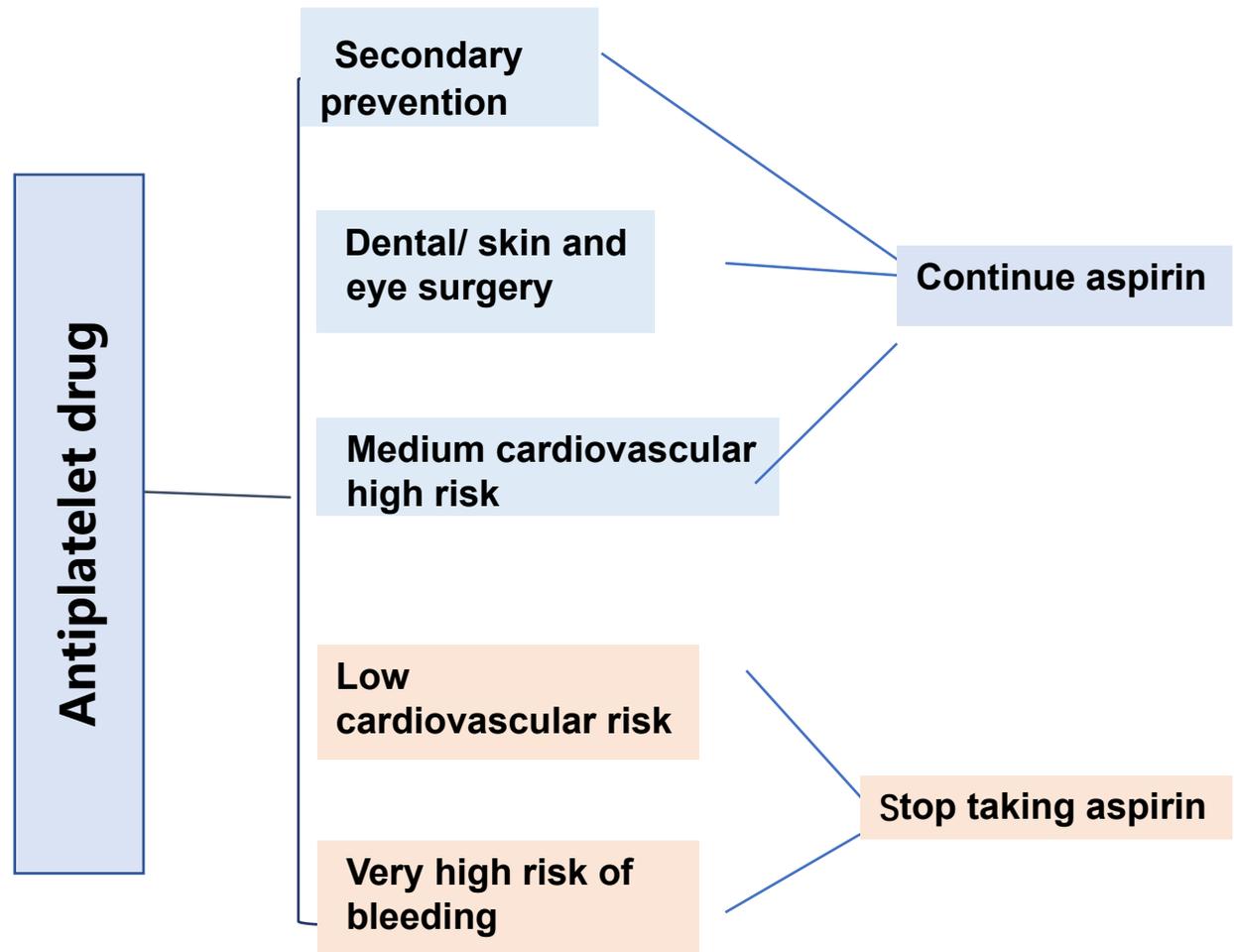
- Crd < 30, 1mg/kg qd
- Crd ≥ 30, 1mg/kg or 1.5mg/kg bid

## ➤ 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 Idarucizumab, 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.**





# 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.



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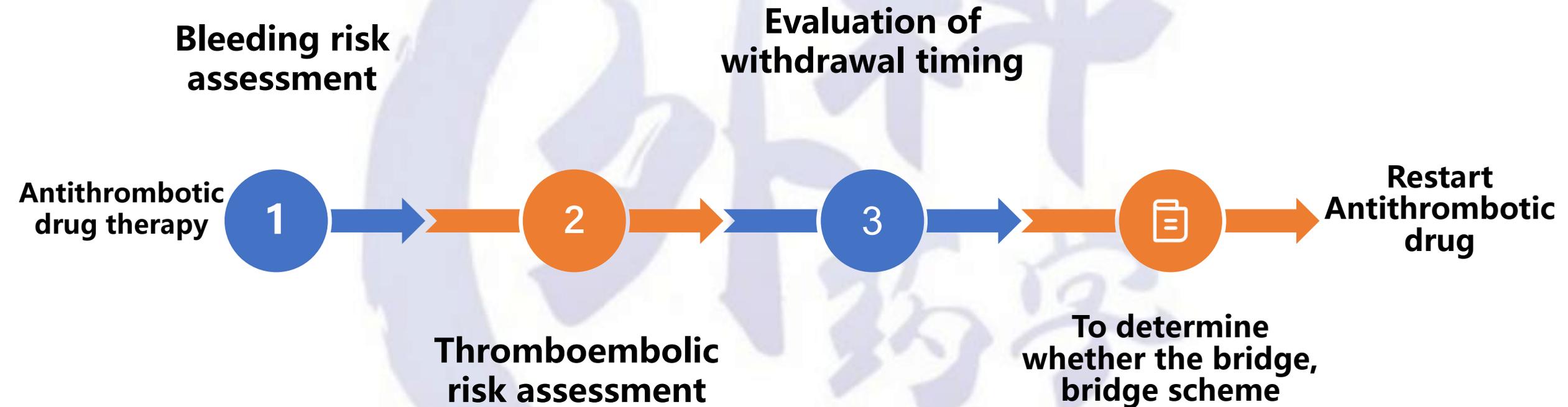
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# Perioperative Antithrombotic drug Management Process





# 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**

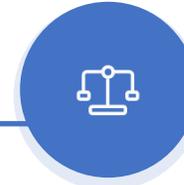
# Perioperative pharmaceutical care of antithrombotic therapy



- 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**

