Perioperative Bleeding and Coagulation Management and Pharmaceutical Care

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Academic positions include: Member of the Clinical Pharmacy Quality Control Working Group of the National Medical Quality Control Center for Pharmacy Administration, Member of the Hospital Pharmacy Committee of the Chinese Pharmaceutical Association, Member of the Drug Clinical Evaluation Research Committee of the Chinese Pharmaceutical Association, Vice Chair of the Pharmacy Administration and Therapeutics Committee of the Guangdong Provincial Health Commission, Chair of the Drug Vigilance Committee of the Guangdong Pharmaceutical Association, and Chair-elect of the Clinical Pharmacy Branch of the Guangdong Medical Association, among others.

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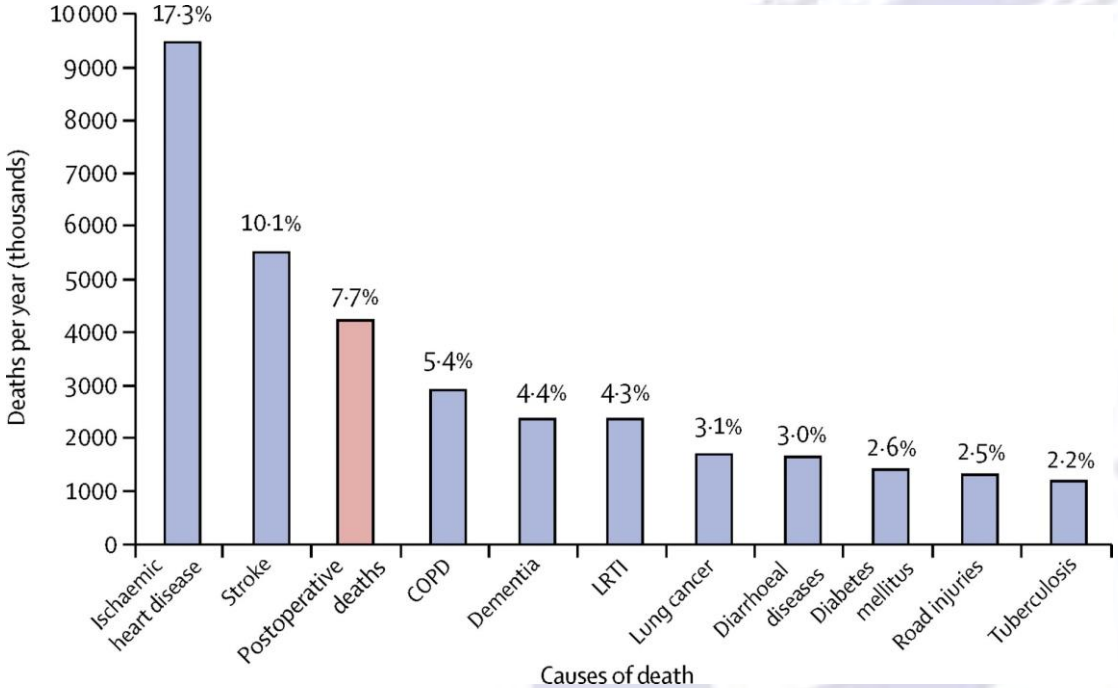
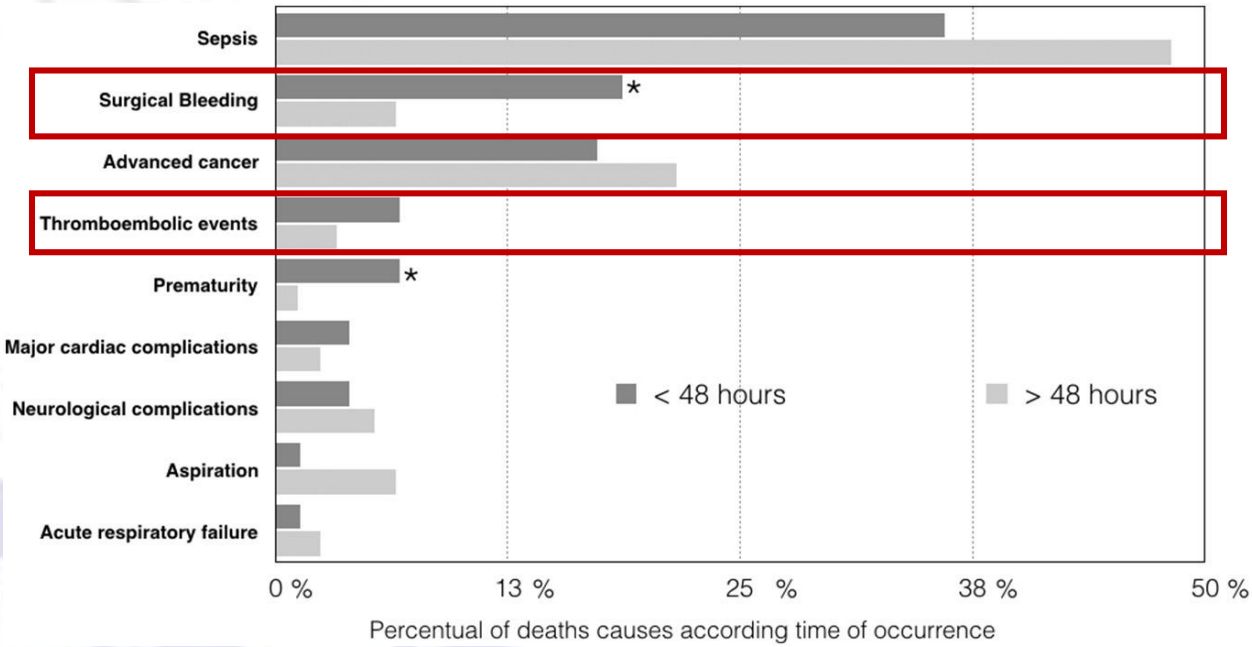
01 Background Introduction





- Each year, there are 313 million surgeries worldwide, with more than 4.2 million (1.34%) all-cause deaths occurring within 30 days postoperatively. **Postoperative deaths** account for 7.7% of total global deaths, making it **the third leading cause of death**.
- Common causes of postoperative death include sepsis, **bleeding**, malignancies, and **embolism**, with bleeding being the second most common cause of early postoperative death after sepsis.
- Managing bleeding and embolic events in perioperative patients is critically important.

Nepogodiev D, et al. Lancet. 2019, 393(10170):401.
Stefani LC, et al. J Clin Anesth. 2018, 49:79-86.

Management of severe peri-operative bleeding: Guidelines from the European Society of Anaesthesiology and Intensive Care (ESAIC)

Update to the Clinical Practice Guidelines on Patient Blood Management (STS/SCA/AmSECT/SABM)

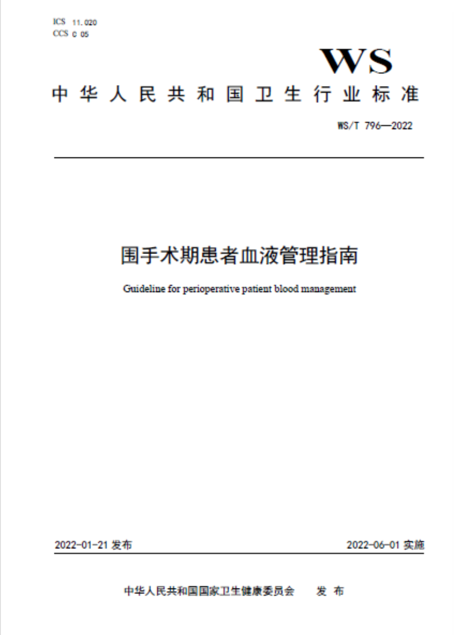
Guideline for perioperative patient blood management (National Health Commission of the People's Republic of China)

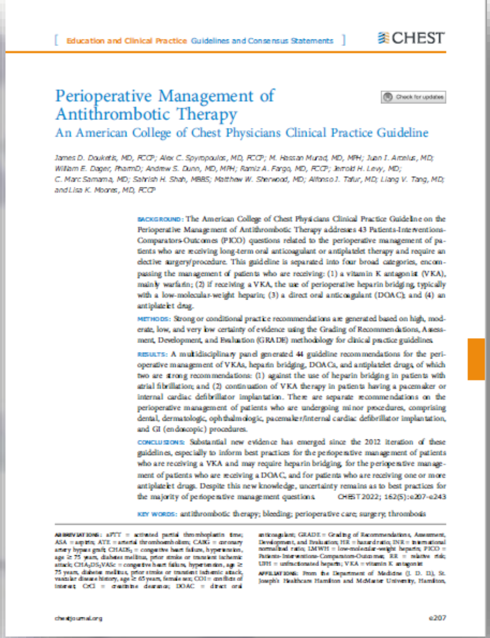
Perioperative Management of Antithrombotic Therapy (ACCP)

American College of Surgeons' Guidelines for the Perioperative Management of Antithrombotic Medication (ACS)


EJA
Eur J Anaesthesiol 2023; 40:226–304
GUIDELINES
Management of severe peri-operative bleeding: Guidelines from the European Society of Anaesthesiology and Intensive Care
Second update 2022


Journal of Cardiothoracic and Vascular Anesthesia
Special Article
STS/SCA/AmSECT/SABM Update to the Clinical Practice Guidelines on Patient Blood Management


WS
中华人民共和国卫生行业标准
WS/T 796—2022
围手术期患者血液管理指南
Guideline for perioperative patient blood management
2022-01-21 发布
2022-06-01 实施
中华人民共和国国家卫生健康委员会 发布


CHEST
Perioperative Management of Antithrombotic Therapy
An American College of Chest Physicians Clinical Practice Guideline


COLLECTIVE REVIEW
American College of Surgeons' Guidelines for the Perioperative Management of Antithrombotic Medication

Several guidelines have been published on the management of perioperative bleeding and coagulation:

- Perioperative Bleeding Management: The European Society of Anesthesiology and Intensive Care (ESAIC), the Society of Thoracic Surgeons (STS), and other organizations have released relevant guidelines. In China, industry standards for perioperative blood management, as well as guidelines specific to different types of surgeries, have also been published.

- Perioperative Antithrombotic Therapy Management: The American College of Chest Physicians (ACCP) and the American College of Surgeons (ACS) have successively issued relevant guidelines.

02

Medication Management

Medication Management

01 Medication Management Consensus

02 Drug Evaluation and Selection

1. Medication Management-Hemostatic Drugs

中国医院药学杂志 2024 年 3 月第 44 卷第 5 期 Chin J Hosp Pharm, Mar 2024, Vol 44, No. 5 · 485 ·

·指南·共识·规范·

围手术期非血液制品止血药物应用管理专家共识(广东)

广东省药学会药物警戒专业委员会

[摘要] 围手术期使用止血药物是减少手术失血,促进患者术后康复的一项重要措施。同时,止血药物使用不当,有可能增加发生血栓栓塞性疾病和血管内弥漫性凝血的风险。为规范围手术期止血药物的合理使用,特制定本共识。该共识基于最新的循证医学证据,并广泛征求了药学和临床专家建议,主要对围手术期常用非血液制品止血药物的作用机制、临床应用建议以及药学监护等方面进行了陈述,旨在为临床医生和外科药师在围手术期合理使用止血药物提供一定的参考。

[关键词] 围手术期;止血药物;合理用药;药学监护;专家共识
[中图分类号] R969.3 [文献标识码] A [文章编号] 1001-5213(2024)05-0485-11 DOI:10.13286/j.1001-5213.2024.05.01

Expert consensus on the management of non-blood hemostatic drugs during peri-operative period (Guangdong)

Pharmacovigilance Professional Committee of Guangdong Pharmaceutical Association

ABSTRACT: The use of hemostatic drugs during peri-operative period is an important measure to reduce blood loss and promote postoperative rehabilitation. Meanwhile, the improper use of hemostatic drugs may increase the risk of thromboembolic disease and disseminated intravascular coagulation. This consensus is aim to regulate the rational use of hemostatic drugs during peri-operative period. Based on the latest evidence of evidence-based medicine and suggestions from pharmaceutical and clinical experts, this consensus states the mechanism, clinical application suggestions and pharmaceutical care of commonly used non-blood hemostatic drugs during peri-operative period, which doesn't contain blood products. The purpose of this work is to provide reference for clinicians and surgical pharmacists to rationally use hemostatic drugs during peri-operative period.

KEY WORDS: peri-operative period; hemostatic drugs; rational drug use; pharmaceutical monitoring; expert consensus

围手术期出血是手术的主要风险之一,与术后高死亡率、术后并发症等相关[1-2]。围手术期使用止血药物是减少手术失血、促进患者术后康复的一项重要措施[3-4]。同时,止血药使用不当,有可能增加发生血栓栓塞性疾病和血管内弥漫性凝血(disseminated intravascular coagulation, DIC)的风险。因此,围手术期使用止血药物时,需评估患者出血风险,选择合适的止血药物,严格把握止血药物使用时机和用法用量,并注意监测不良反应。

2015 年起,广东省药学会提出设立"外科药师",构建外科药学,让药师参与到围手术期的用药管理中,提高围手术期用药的合理性和安全性[5]。作为减少围手术期失血的主要措施之一,止血药物的合理使用需要医、药等多学科共同管理。本专家共识旨在通过医师、药师的共同讨论,为临床医生和外科药师在围手术期合理使用止血药物提供一定的参考。本共识强调,对于特殊患者,应根据临床具体情况,必要时由医生、麻醉师和临床药师等共同商榷决定止血药物的使用。

本共识的制定步骤及方法:(1)成立共识编写专家组。(2)文献检索,检索数据库包括 PubMed、Cochrane Library、中国知网、万方等。(3)对文献进行总结分析,并结合临床经验,初步拟定推荐建议。由于本共识不是基于系统评价的循证指南,故不作证据质量分级。(4)对初拟的推荐建议进行专家调研和投票,每次调查结束后,根据专家的反馈意见对推荐建议进行修改或增补。最终投票设置同意、不同意、不确定 3 个选项。若投票同意率(即选择"同意"的专家人数比例)≥75%,则认为该条推荐建议达成共识,同意率>90% 为强推荐,同意率 75%~90% 为弱推荐。

1 围手术期应用的止血药物及作用机制

机体正常的止血机制有赖于凝血系统、纤溶系统、血管壁和血小板等结构与功能的完整性,以及它们之间的生理性调节和相互平衡。止血药物是指作用于上述一个或多个环节,能促进止血的药

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fip

About FIP Structures What we do Get involve

FIP in China

FIP is active in China supported by the FIP China Envoy Snr Col. Chen Zheng-Yu and through FIP's membership organisation the Chinese Pharmaceutical Association.

Snr Col Chen works with the GuangDong Pharmaceutical Association, including on the development of

Chinese Expert Consensus on the Management of Non-Blood Hemostatic Drugs During Perioperative Period

The Pharmacovigilance Committee of GuangDong Pharmaceutical Association

ABSTRACT: The use of hemostatic drugs during perioperative period is an important measure to reduce blood loss and promote postoperative rehabilitation. Meanwhile, the improper use of hemostatic drugs may increase the risk of thromboembolic disease and disseminated intravascular coagulation. This consensus aims to regulate the use of hemostatic drugs during perioperative period. Based on the latest evidence of evidence-based medicine and suggestions from pharmaceutical and clinical experts, this consensus states the mechanism, clinical application suggestions and pharmaceutical care of commonly used non-blood hemostatic drugs during perioperative period, which contain no blood products. The purpose of this work is to provide reference for clinicians and surgical pharmacists to rationally use hemostatic drugs during perioperative period.

KEY WORDS: perioperative period; hemostatic drugs; rational drug use; pharmaceutical monitoring; expert consensus

- Clinical pharmacists' pharmaceutical care for postoperative pain in Guangdong Province
- Guidelines on integrated surgical pharmaceutical managements for immune checkpoint inhibitor therapy in malignancy
- Long-term management of immunosuppressants in Chinese renal transplant recipients
- Management of non-blood haemostatic drugs during perioperative period
- Perioperative medication therapy management within enhanced recovery after surgery programmes
- Physician-pharmacist co-management of perioperative airway
- Physician-pharmacist co-management of perioperative blood glucose
- Precision medicine by surgical pharmacists for oncology in the perioperative period
- Surgical pharmacy practice of parenteral and enteral nutrition

- **Includes commonly used non-blood product hemostatic drugs.**
- **Jointly developed by pharmacy and clinical medical experts.**
- **It provides a detailed introduction to the pharmaceutical care of hemostatic drugs, including drug interactions, adverse reactions, etc.**

Chinese Expert Consensus on the Management of Non-Blood Hemostatic Drugs During Perioperative Period

1. Hemostatic drugs used in perioperative period and their mechanism of action

Antifibrinolytic drugs, Hemocoagulase from snake venom, Vitamin K. Desmopressin, Ethamsylate, Carbazochrome sodium sulfonate

2. Suggestions on the application of hemostatic drugs in perioperative period

Bleed risk assessment; Clinical application of hemostatic drugs

3. Pharmaceutical Care

Precautions for use; Key monitoring points

Chinese Expert Consensus on the Management of Non-Blood Hemostatic Drugs During Perioperative Period

Bleeding Risk Assessment — Patient Factors/Drug Factors

In addition to surgical factors, it is recommended to comprehensively and systematically assess the patient for other potential bleeding risk factors before surgery, including patient-specific factors and drug-related factors.

- **Physical Examination Focus**: Include the patient's general nutritional status and signs related to bleeding disorders.
- **Assessment for Abnormal Bleeding**: Check for the presence of abnormal bleeding, spontaneous bleeding, or significant bleeding after minor trauma.
- **Medical History Assessment**: History of previous surgeries or trauma; Presence of significant postoperative bleeding, whether immediate or delayed; History of blood transfusions; For female patients, inquire about any history of menorrhagia (heavy menstrual bleeding).
- **Medication History Assessment:** Determine whether the patient has a history of taking oral antiplatelet or anticoagulant drugs, whether they have discontinued the medication, and if so, how long it has been since they stopped.
- **Coagulation Function Tests**

Chinese Expert Consensus on the Management of Non-Blood Hemostatic Drugs During Perioperative Period

Clinical Application Recommendations for Hemostatic Drugs

1. Before operation, it is necessary to systematically evaluate whether the patient has any risk factors that cause bleeding, and intervene accordingly according to the risk factors. If necessary, hemostatic drugs should be used preventively to reduce the risk of bleeding during and after operation. **(Recommendation level: Strong recommendation)**
2. For patients undergoing CPB heart surgery, major orthopedic surgery, partial gynecological surgery and other operations with estimated blood loss of >500 mL or moderate blood loss (such as liver transplantation, hepatectomy, trauma surgery and some neurosurgical operations, etc.), it is suggested to prevent the use of tranexamic acid before operation (unless contraindicated) to reduce the amount of blood loss and blood transfusion requiremen. **(Recommendation level: Strong recommendation)**
3. For surgical patients with high bleed risk, especially those who are undergoing heparin or low molecular weight heparin and need emergency surgery, low-dose of hemocoagulase can be used before and during surgery, and if necessary, it can be used after surgery. **(Recommendation level: Weak recommendation)**
4. For patients with decreased synthesis of coagulation factors II, VII, IX and X caused by liver dysfunction, vitamin K can be supplemented to enhance coagulation function; For patients who have been using VKA for anticoagulant therapy for a long time, it is suggested to be stopped 5 days before operation, and INR should be detected before operation. If INR is > 1.5, vitamin K should be supplemented to restore INR to normal. **(Recommendation level: Strong recommendation)**
5. For patients with platelet dysfunction (such as patients with von Willebrand, mild hemophilia A or uremia without contraindications) and those who used antiplatelet drugs before operation, it is recommended to prevent the use of DDAVP to reduce bleeding during invasive operation; DDAVP is recommended for patients with bleeding caused by abnormal platelet function after CPB heart surgery. **(Recommendation level: Strong recommendation)**

Chinese Expert Consensus on the Management of Non-Blood Hemostatic Drugs During Perioperative Period

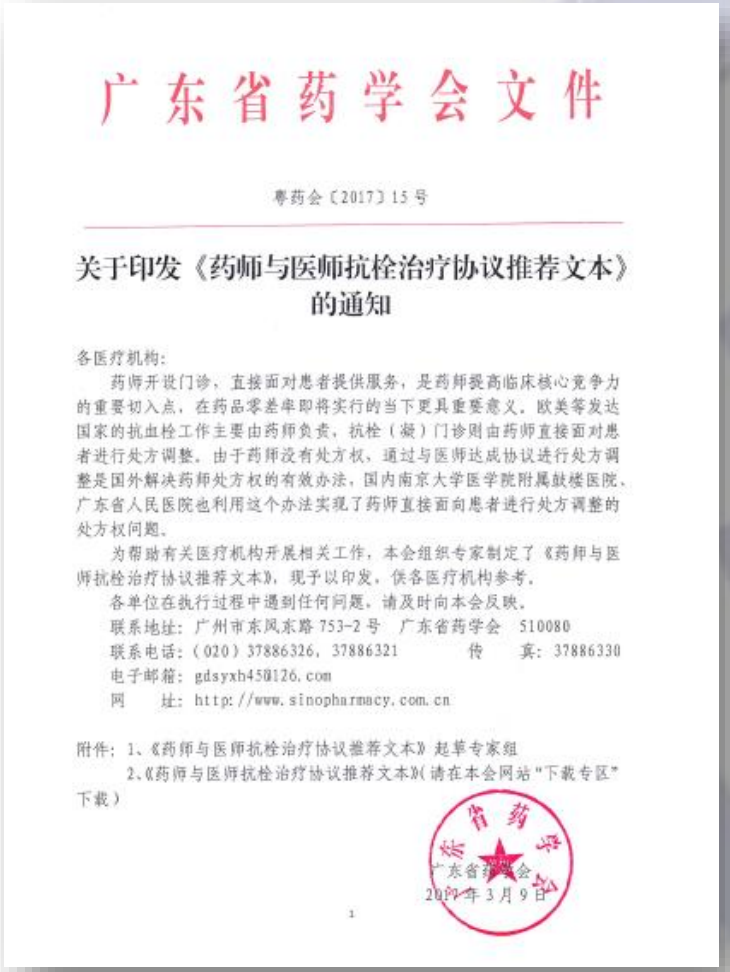
3.1 Precautions for the use of hemostatic drugs

Table 5 Precautions for the use of hemostatic drugs

Drug name	Contraindications	Drug interactions	Incompatibility	Medication for special population	Adverse reaction	Others
Tranexamic acid	Forbidden for patients with acquired color vision deficiency, subarachnoid hemorrhage, and active intravascular coagulation or those allergic to tranexamic acid or any component.	(1) It may increase the risk of thrombosis of human prothrombin complex concentrate, human anticoagulant complex and human factor VII complex, and it is forbidden to use them together. (2) Estrogen derivatives may enhance the thrombogenic effect of tranexamic acid, and their combination is prohibited. (3) The combined use of thrombolytic drugs (alteplase, streptokinase, urokinase, etc.) and tranexamic acid can affect each other, and their combined use is prohibited.	Incompatibility with penicillin or blood transfusion.	The excretion of tranexamic acid is highly dependent on renal function. For patients with renal insufficiency, the administration interval should be obviously prolonged or the dosage should be reduced.	Compared with aminocaproic acid, its adverse reactions are rare, and the main adverse reactions include nausea, vomiting and loss of appetite.	(1) Patients with thrombosis (cerebral thrombosis, myocardial infarction, thrombophlebitis, etc.) and those who may cause thrombosis and those with wasting coagulation disorders should be carefully administered. (2) As this medicine can lead to secondary pyelonephritis and obstruction of ureteral blood clots, it should be used with caution when hemophilia or renal pelvis parenchymal lesions cause massive hematuria. (3) It is generally not used alone for secondary fibrinolytic bleeding caused by DIC. If necessary, this medicine should be used on the basis of heparinization. (4) Heparin is safer than this medicine in the treatment of low fibrinogen bleeding caused by intrauterine stillbirth. (5) Tranexamic acid may induce epilepsy, and the risk of epilepsy may be greater in patients with end-stage renal disease or moderate to severe renal insufficiency. (6) If the injection speed is too fast, there can be occasional symptoms of nausea, chest discomfort, palpitation and blood pressure drop. So when in use, intravenous injection should be slow for 2-5 min, or slow to 5-10 min according to clinical needs.
Aminocaproic acid	Forbidden for patients with thrombosis tendency or past history of vascular embolism.	(1) It may increase the risk of thrombosis of drugs such as human prothrombin complex concentrate, and their combined use is prohibited. (2) Its combined use with oral contraceptives and estrogen can increase the risk of thrombosis.	Incompatibility with phenethylamine.	It is easy to form thrombus and damage heart, liver and kidney function, so pregnant women should use it with caution (grade C); Forbidden for lactating women (L4 level); Use with caution in patients with renal insufficiency; This medicine contains benzyl alcohol, and giving drugs containing benzyl alcohol as preservative to premature infants is related to fatal wheezing syndrome.	Adverse reactions are common, mainly including nausea, vomiting and diarrhea, followed by dizziness, itching, dizziness, tinnitus, general malaise, nasal congestion, rash, erythema, non-ejaculation, etc., especially when the daily dose exceeds 16g. Rapid intravenous injection can cause hypotension, tachycardia and arrhythmia, and a few people can have convulsions and heart or liver damage. High dose or course of treatment for more than four weeks can cause myalgia, weakness, fatigue, myoglobinuria, and even renal failure, which can be relieved and recovered after stopping taking the medicine.	(1) It is excreted quickly, so continuous administration is needed, otherwise it is difficult to maintain a stable effective blood concentration. (2) Its effect of immediate hemostasis is poor, and it should be used in combination with other hemostatic drugs for acute massive hemorrhage. (3) It cannot prevent arteriole bleeding. Ligation is needed to if there is active arterial bleeding during operation. (4) In the absence of heparin, it should not be used in the presence of DIC. (5) It should not be injected too fast, otherwise it will cause obvious blood pressure reduction, tachycardia and arrhythmia.
Hemocoagulase	Forbidden for patients with a history of thrombosis and those who are allergic to this kind of drugs.	—	—	Not for pregnant women unless there is an emergency.	The incidence of adverse reactions is low. It does not increase the risk of thrombosis, and occasionally allergic reactions occur. If allergic reactions occur, antihistamines or/and glucocorticoids can be given timely	(1) It is not suitable for bleeding caused by DIC and hematological diseases. (2) It has no compensatory effect if blood lacks platelets or some coagulation factors (such as prothrombin), so it should be applied on the basis of supplementing platelets or the lack of coagulation factors or transfusion of

- The usage precautions for tranexamic acid, aminocaproic acid, hemocoagulase from snake venom,, vitamin K, desmopressin, etamsylate, and carbazochrome sodium sulfonate have been summarized.
- This includes contraindications, drug interactions, incompatibility with other drugs, considerations for special populations, adverse reactions, and other precautions.
- This summary can provide a reference for the pharmaceutical care provided by surgeons and pharmacists.

1. Medication Management – Antithrombotic Drugs



广东省药学会文件

粤药会〔2017〕15号

关于印发《药师与医师抗栓治疗协议推荐文本》的通知

各医疗机构：

药师开设门诊，直接面对患者提供服务，是药师提高临床核心竞争力的重要切入点，在药品零差率即将实行的当下更具重要意义。欧美等发达国家的抗血栓工作主要由药师负责，抗栓（凝）门诊则由药师直接面对患者进行处方调整。由于药师没有处方权，通过与医师达成协议进行处方调整是国外解决药师处方权的有效办法，国内南京大学医学院附属鼓楼医院、广东省人民医院也利用这个办法实现了药师直接面向患者进行处方调整的处方权问题。

为帮助有关医疗机构开展相关工作，本会组织专家制定了《药师与医师抗栓治疗协议推荐文本》，现予以印发，供各医疗机构参考。

各单位在执行过程中遇到任何问题，请及时向本会反映。

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附件：1、《药师与医师抗栓治疗协议推荐文本》起草专家组

2、《药师与医师抗栓治疗协议推荐文本》（请在本会网站"下载专区"下载）

广东省药学会

2017年3月9日

1

Recommendation for Antithrombotic Treatment Agreement between Pharmacists and Physicians

① Postoperative Anticoagulation Therapy Protocol for Cardiothoracic and Cardiovascular Surgery

② Warfarin Anticoagulation Dose Adjustment Protocol

③ Antithrombotic Therapy Protocol for Atrial Fibrillation

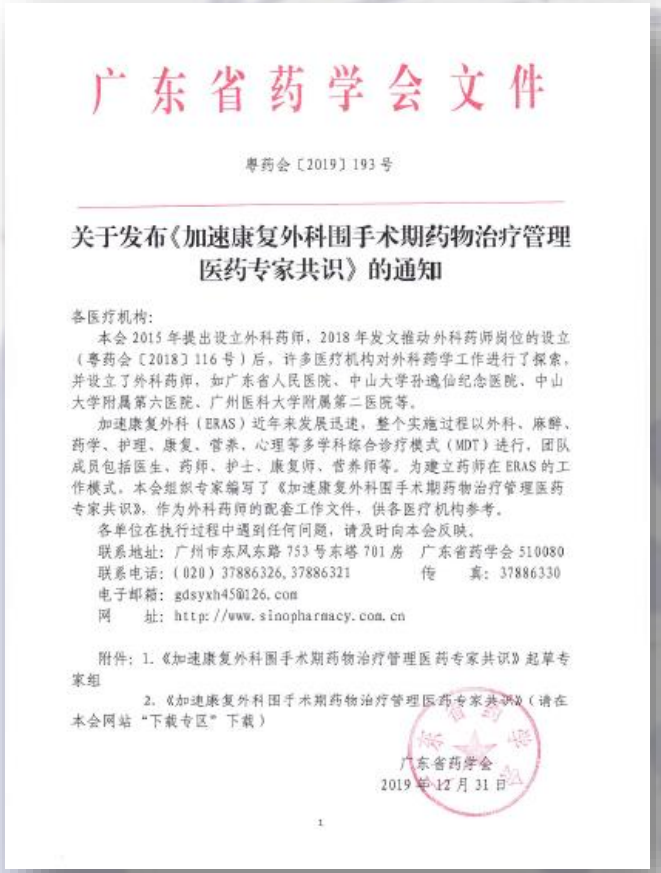
④ CABG Perioperative Antiplatelet Therapy Protocol

⑤ Antithrombotic Therapy Protocol for Acute Ischemic Stroke

⑥ Antithrombotic Therapy Protocol for Acute Pulmonary Embolism (PE)

⑦ Antithrombotic Therapy Protocol for Deep Vein Thrombosis (DVT)

Expert Consensus on Perioperative Medication Management in Enhanced Recovery after Surgery



广东省药学会文件

粤药会〔2019〕193号

关于发布《加速康复外科围手术期药物治疗管理医药专家共识》的通知

各医疗机构：

本会2015年提出设立外科药师，2018年发文推动外科药师岗位的设立（粤药会〔2018〕116号）后，许多医疗机构对外科药学工作进行了探索，并设立了外科药师，如广东省人民医院、中山大学孙逸仙纪念医院、中山大学附属第六医院、广州医科大学附属第二医院等。

加速康复外科（ERAS）近年来发展迅速，整个实施过程以外科、麻醉、药学、护理、康复、营养、心理等多学科综合诊疗模式（MDT）进行，团队成员包括医生、药师、护士、康复师、营养师等。为建立药师在ERAS的工作模式，本会组织专家编写了《加速康复外科围手术期药物治疗管理医药专家共识》，作为外科药师的配套工作文件，供各医疗机构参考。

各单位在执行过程中遇到任何问题，请及时向本会反映。

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电子邮箱：gdsyxh450126.com
网　　址：http://www.sinopharmacy.com.cn

附件：1.《加速康复外科围手术期药物治疗管理医药专家共识》起草专家组

2.《加速康复外科围手术期药物治疗管理医药专家共识》（请在本会网站"下载专区"下载）

广东省药学会
2019年12月31日

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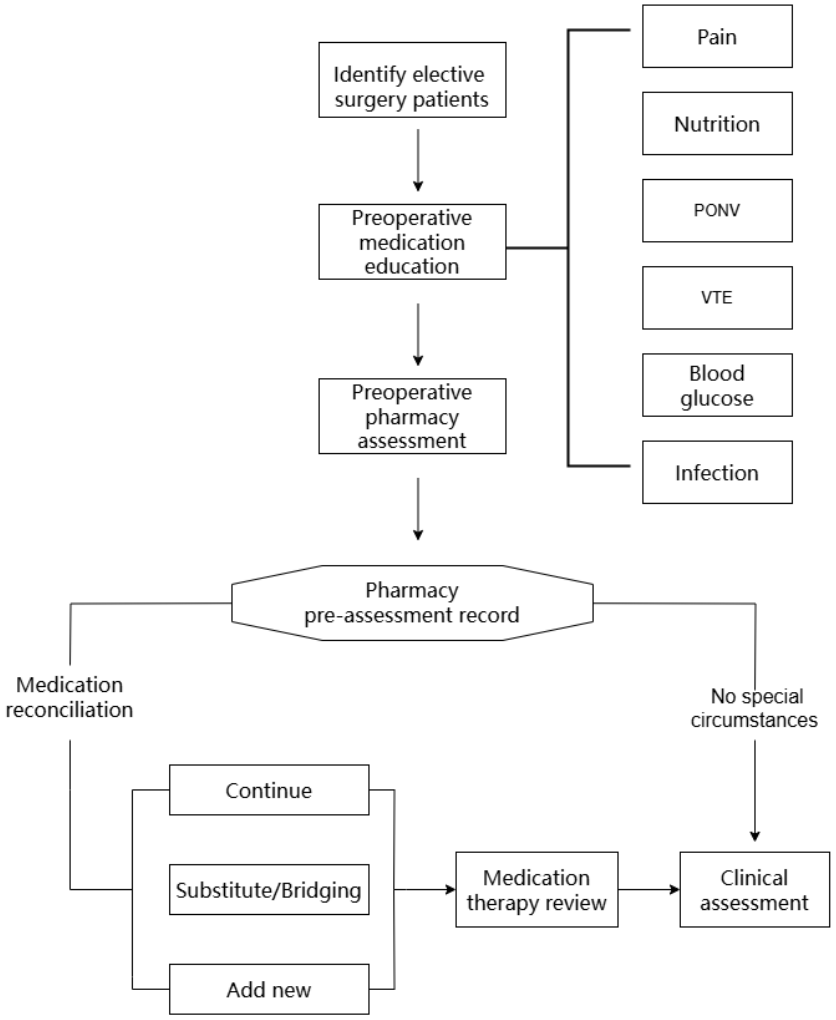


- The consensus focuses on the dimensions through which pharmacists can fully participate in perioperative medication management within the Enhanced Recovery After Surgery (ERAS) team, collaborating in comprehensive multidisciplinary diagnosis and treatment practices to optimize related medication therapy pathways.
- The emphasis on antithrombotic drug management lies in the prevention of perioperative venous thromboembolism (VTE) and the management of antithrombotic therapy in patients already receiving such treatment prior to surgery.

Authored by experts from the Sixth Affiliated Hospital of Sun Yat-sen University.

2. Medication Evaluation and Selection

Target Medications：

Same-class drugs with identical mechanisms of action;
Same drugs from different manufacturers.

Evaluation Rationale：

Although these drugs share the same mechanism of action, differences in pharmaceutical properties and cost-effectiveness make clinical selection challenging.

Evaluation Significance：

Conducting multidimensional evaluations provides a reference for hospitals in drug selection and promotes rational clinical drug use.

Scoring Criteria

Pharmaceutical Properties	
Indications	Clinically necessary, first choice Clinically needed, second choice Multiple optional drugs available
Pharmacological Action	Clinically effective with a clear mechanism of action Clinically effective, mechanism of action not fully clear Moderate clinical efficacy, unclear mechanism of action
In vivo Process	In vivo process clear, pharmacokinetic parameters complete In vivo process mostly clear, pharmacokinetic parameters incomplete In vivo process unclear, no pharmacokinetic studies
Pharmaceutics and Usage Methods (multiple selections possible)	Main components and excipients defined Suitable dosage form Manageable dosage Appropriate frequency of administration Convenient to use
Consistency Evaluation	Original brand/reference drug Generic drugs that have passed the consistency evaluation Non-original brand or generics that have not passed the consistency evaluation
Efficacy	
	Recommended by treatment guidelines (National Health Administrative Department) Guideline Level I recommendation (Evidence Grade A 18, Grade B 17, Grade C 16, Others 15) Guideline Level II and below recommendation (Evidence Grade A 14, Grade B 13, Grade C 12, Others 11) Expert consensus recommendation No recommendations above

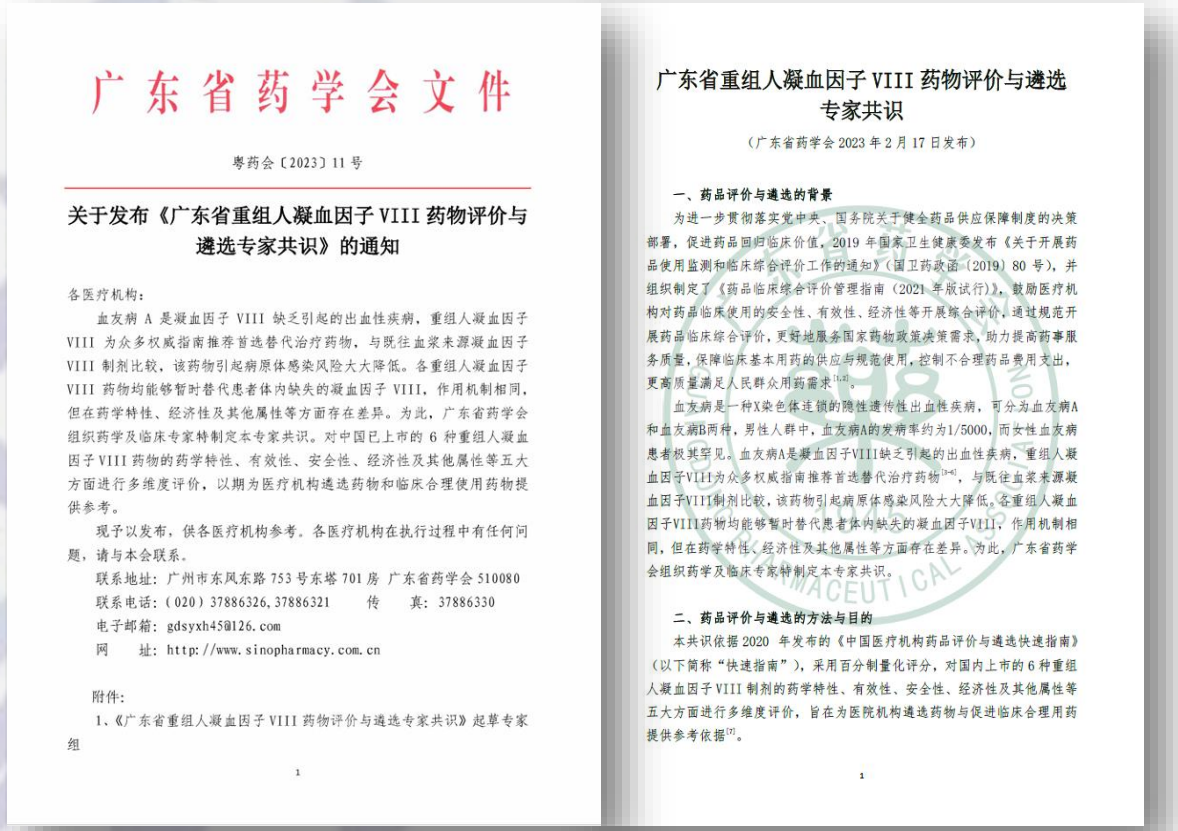
Safety	
Adverse Reaction Conditions	Symptoms minor, no treatment needed or CTC grade 1 Symptoms mild, intervention required or CTC grade 2 Symptoms noticeable, intervention required or CTC grade 3 Symptoms severe, life-threatening or CTC grades 4-5, incidence <0.1% Symptoms severe, life-threatening or CTC grades 4-5, incidence 0.1%-1% Symptoms severe, life-threatening or CTC grades 4-5, incidence >0.1%-10% Symptoms severe, life-threatening or CTC grades 4-5, incidence > 10%
Special Populations (multiple selections possible)	Suitable for children Suitable for elderly Suitable for pregnant women Suitable for breastfeeding women Suitable for those with abnormal liver function Suitable for those with abnormal kidney function
Drug Interaction Induced Adverse Reactions	Mild to moderate; generally no need to adjust dosage Severe; dosage adjustment needed Contraindicated; prohibited from concurrent use
Other (multiple selections possible)	All adverse reactions are reversible No teratogenic or carcinogenic effects No special medication warnings required

Cost-Effectiveness	
Average Daily Treatment Cost of the Evaluated Medication (percentage, single choice)	Lowest P20% P20%~40% Range P40%~60% Range P60%~80% Range P80%~100% Range
Other Attributes	
National Health Insurance	National health insurance class A, no payment restrictions National health insurance class A, with payment restrictions National health insurance class B/negotiated drugs, no payment restrictions National health insurance class B/negotiated drugs, with payment restrictions Not included in the national health insurance catalog
Essential Medicines	Included in the “National Essential Medicines List”, no requirements Included in the “National Essential Medicines List”, with requirements Not included in the “National Essential Medicines List”
Storage Conditions	Store at room temperature Store at room temperature, protected from light Store in a cool place Store in a cool place, protected from light Refrigerated/frozen storage
Shelf Life of Medication	More than 36 months 24~36months Less than 24 months
Global Usage	Available in the USA, Europe, and Japan Available in either the USA, Europe, or Japan Not available in the USA, Europe, and Japan
Producer Information	Manufacturer is among the top 50 pharmaceutical companies in global sales (American Pharma Managers) Manufacturer listed in the top 100 pharmaceutical companies by the Ministry of Industry and Information Technology Other

Drug Evaluation and Selection- Recombinant Human Coagulation Factor VIII

Evaluation Dimension	百因止 ADVATE	任捷 Xyntha	绿茵芷 GreenGene F	诺易 NovoEight	科跃奇 Kovaltry	安佳因 Omfilocto cog alfa
Drug Characteristics	18	17.8	18	18	18	18
Efficacy	20	20	20	20	20	20
Safety	17	16	15	15.5	17.5	15
Economic Aspects	8	11	8	11	8	11
Other Attributes	12	11	8.5	12.5	12.5	8
Total Score	**75**	**75.8**	**69.5**	**77**	**76**	**72**

Evaluation score results for 6 types of recombinant human coagulation factor VIII Column



广东省药学会文件

粤药会〔2023〕11号

关于发布《广东省重组人凝血因子VIII药物评价与遴选专家共识》的通知

各医疗机构：

血友病A是凝血因子VIII缺乏引起的出血性疾病，重组人凝血因子VIII为众多权威指南推荐首选替代治疗药物，与既往血浆来源凝血因子VIII制剂比较，该药物引起病原体感染风险大大降低。各重组人凝血因子VIII药物均能够暂时替代患者体内缺失的凝血因子VIII，作用机制相同，但在药学特性、经济性及其他属性等方面存在差异。为此，广东省药学会组织药学及临床专家特制定本专家共识。对中国已上市的6种重组人凝血因子VIII药物的药学特性、有效性、安全性、经济性及其他属性等五大方面进行多维度评价，以期为医疗机构遴选药物和临床合理使用药物提供参考。

现予以发布，供各医疗机构参考。各医疗机构在执行过程中有任何问题，请与本会联系。

联系地址：广州市东风东路753号东塔701房 广东省药学会 510080

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附件：

1、《广东省重组人凝血因子VIII药物评价与遴选专家共识》起草专家组

1

广东省重组人凝血因子VIII药物评价与遴选专家共识

（广东省药学会2023年2月17日发布）

一、药品评价与遴选的背景

为进一步贯彻落实党中央、国务院关于健全药品供应保障制度的决策部署，促进药品回归临床价值，2019年国家卫生健康委发布《关于开展药品使用监测和临床综合评价工作的通知》（国卫药政函〔2019〕80号），并组织制定了《药品临床综合评价管理指南（2021年版试行）》，鼓励医疗机构对药品临床使用的安全性、有效性、经济性等开展综合评价，通过规范开展药品临床综合评价，更好地服务国家药物政策决策需求，助力提高药事服务质量，保障临床基本用药的供应与规范使用，控制不合理药品费用支出，更高质量满足人民群众用药需求[1,2]。

血友病是一种X染色体连锁的隐性遗传性出血性疾病，可分为血友病A和血友病B两种，男性人群中，血友病A的发病率约为1/5000，而女性血友病患者极其罕见。血友病A是凝血因子VIII缺乏引起的出血性疾病，重组人凝血因子VIII为众多权威指南推荐首选替代治疗药物[3-6]，与既往血浆来源凝血因子VIII制剂比较，该药物引起病原体感染风险大大降低。各重组人凝血因子VIII药物均能够暂时替代患者体内缺失的凝血因子VIII，作用机制相同，但在药学特性、经济性及其他属性等方面存在差异。为此，广东省药学会组织药学及临床专家特制定本专家共识。

二、药品评价与遴选的方法与目的

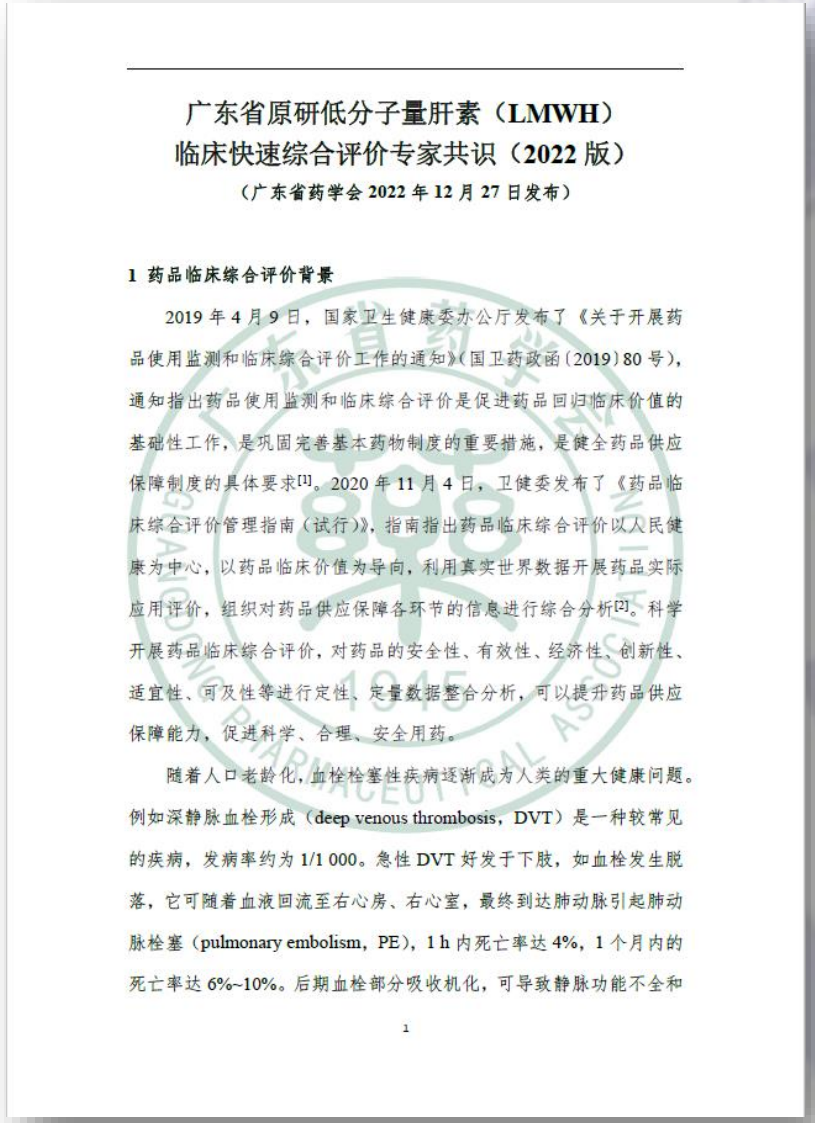
本共识依据2020年发布的《中国医疗机构药品评价与遴选快速指南》（以下简称“快速指南”），采用百分制量化评分，对国内上市的6种重组人凝血因子VIII制剂的药学特性、有效性、安全性、经济性及其他属性等五大方面进行多维度评价，旨在为医院机构遴选药物与促进临床合理用药提供参考依据[7]。

1

Expert Consensus on the Evaluation and Selection of Recombinant Human Coagulation Factor VIII Drugs

- All recombinant human coagulation factor VIII drugs can temporarily replace the missing factor VIII in patients, sharing the same mechanism of action. However, they differ in **pharmaceutical properties**, **cost-effectiveness, and other attributes**.
- After evaluation, the drugs were ranked based on their scores, serving as a reference for drug selection.

Drug Evaluation and Selection – Low Molecular Weight Heparin



广东省原研低分子量肝素（LMWH）
临床快速综合评价专家共识（2022 版）

（广东省药学会 2022 年 12 月 27 日发布）

1 药品临床综合评价背景

2019 年 4 月 9 日，国家卫生健康委办公厅发布了《关于开展药品使用监测和临床综合评价工作的通知》（国卫药政函〔2019〕80 号），通知指出药品使用监测和临床综合评价是促进药品回归临床价值的基础性工作，是巩固完善基本药物制度的重要措施，是健全药品供应保障制度的具体要求[1]。2020 年 11 月 4 日，卫健委发布了《药品临床综合评价管理指南（试行）》，指南指出药品临床综合评价以人民健康为中心，以药品临床价值为导向，利用真实世界数据开展药品实际应用评价，组织对药品供应保障各环节的信息进行综合分析[2]。科学开展药品临床综合评价，对药品的安全性、有效性、经济性、创新性、适宜性、可及性等进行定性、定量数据整合分析，可以提升药品供应保障能力，促进科学、合理、安全用药。

随着人口老龄化，血栓栓塞性疾病逐渐成为人类的重大健康问题。例如深静脉血栓形成（deep venous thrombosis，DVT）是一种较常见的疾病，发病率约为 1/1 000。急性 DVT 好发于下肢，如血栓发生脱落，它可随着血液回流至右心房、右心室，最终到达肺动脉引起肺动脉栓塞（pulmonary embolism，PE），1 h 内死亡率达 4%，1 个月内的死亡率达 6%~10%。后期血栓部分吸收机化，可导致静脉功能不全和

1

Expert Consensus on the Rapid Clinical Comprehensive Evaluation of Original Low Molecular Weight Heparin

- A clinical evaluation was conducted on different low molecular weight heparin (LMWH), including bemiparin, dalteparin, enoxaparin, nadroparin, and heparin.
- Due to the varying daily costs of LMWHs for different indications, the final evaluation results were summarized according to the specific indications.

Evaluation score results for LMWH class drugs in the prevention of thromboembolic diseases

Evaluation Dimension	Sodium Low Molecular Weight Heparin	Enoxaparin Sodium	Nadroparin Calcium Injection	Dalteparin Sodium Injection	Bemiparin Sodium Injection
Drug Characteristics	18.6	19.8	17.8	18.8	16.8
Efficacy	16	17.8	16	16	16
Safety	10	10.5	9	9.5	10
Economic Aspects	17	14	14	17	8
Other Attributes	13	16.5	16	17	10.5
Total Score	**74.6**	**78.6**	**72.8**	**78.3**	**61.3**

Evaluation score results for LMWH class drugs in the treatment of thromboembolic diseases

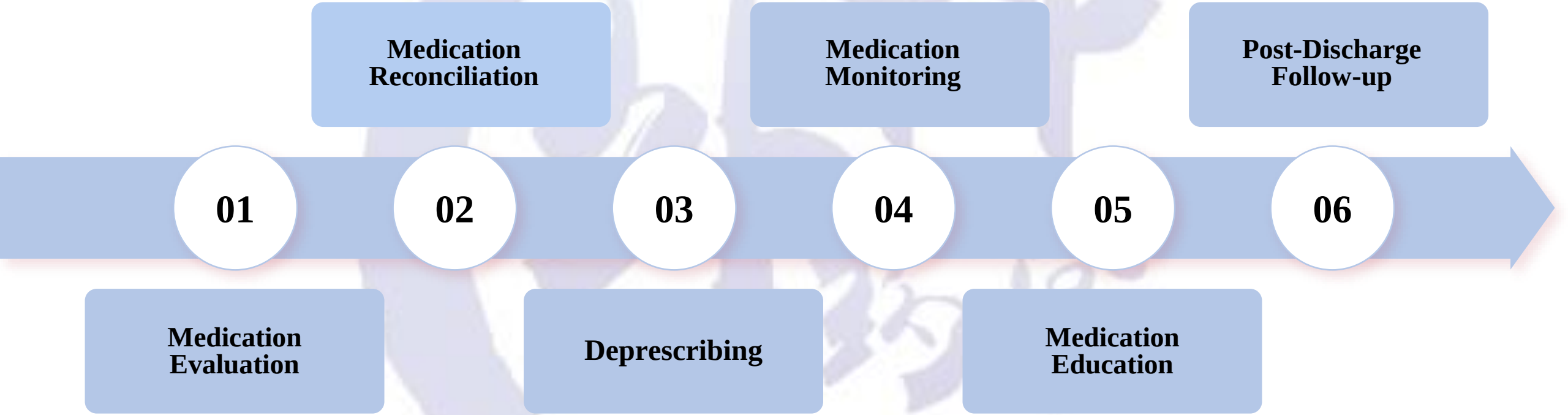
Evaluation Dimension	Sodium Low Molecular Weight Heparin	Enoxaparin Sodium	Nadroparin Calcium Injection	Dalteparin Sodium Injection	Bemiparin Sodium Injection
Drug Characteristics	18.6	19.65	18	19	14.8
Efficacy	14	17.7	14.5	14.5	0
Safety	10	10.5	9	9.5	10
Economic Aspects	8	8	11	14	0
Other Attributes	13	16.5	16	17	10.5
Total Score	**63.6**	**72.35**	**68.5**	**74**	**35.3**

Authored by experts from the General Hospital of Southern Theatre Command of PLA.

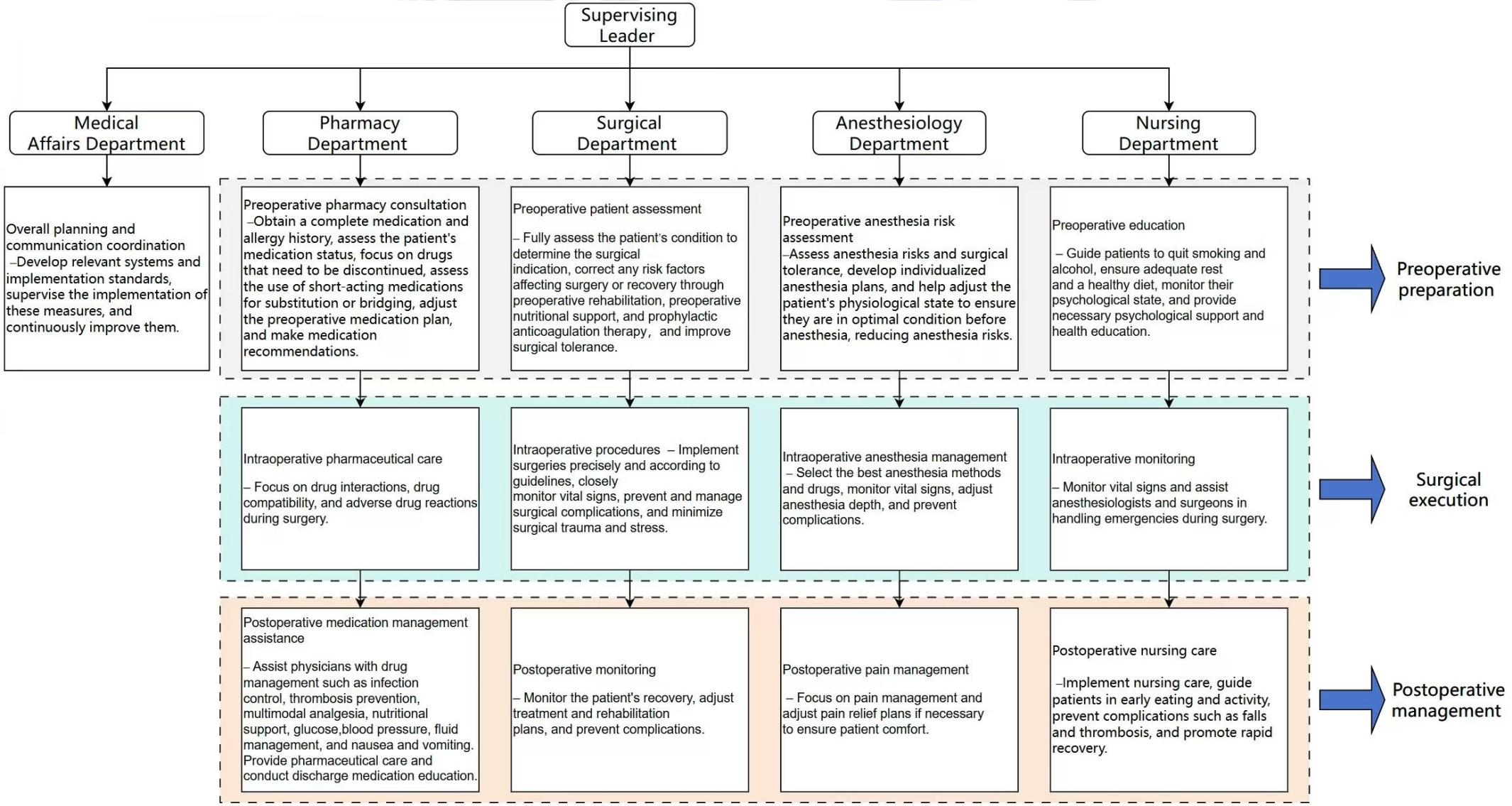
03

Pharmaceutical Care

Workflow of Surgical Pharmacists



Multidisciplinary Integrated Collaboration



Key Focus Areas in Management Tasks

Surgical pharmacists manage perioperative bleeding or coagulation patients primarily by evaluating multiple aspects such as patient conditions, drug characteristics, and precautions to ensure rational use of hemostatic and antithrombotic drugs during the perioperative period. They also assess the effectiveness of these medications based on the occurrence of bleeding and thrombosis. Additionally, they monitor for adverse drug reactions in patients, make assessments, provide essential treatment when reactions occur, and offer medication education based on the patient's condition during this process.

Patient Condition

When choosing a hemostatic or antithrombotic drug regimen, thoroughly assess the patient's bleeding and thrombotic risks, along with their medical history.

Drug Properties

1. Manage perioperative antithrombotic drugs considering their characteristics, including discontinuation, timing, and bridging.
2. Select appropriate hemostatic drugs based on their properties.

Precautions

Contraindications, drug interactions, incompatibilities, special populations, etc.

Rational Use

Clinical pharmacists need to assess from multiple aspects such as patient conditions, drug characteristics, and precautions.

Effectiveness Evlaution

Clinical pharmacists assess by observing intraoperative bleeding, postoperative bleeding, and thrombotic conditions; they must also pay attention to adverse drug reactions.

Workflow

1. **Medication Reconciliation and Deprescribing:**
   - Review medical history; Review medication orders; Identify drug-related problems.
2. **Formulating Hemostasis/ Antithrombotic Treatment Plan:**
   - Assessment of bleeding/embolism risk; Confirming patient's medication needs; Medication recommendations.
3. **Pharmaceutical Care After Treatment:**
   - Evaluation of treatment effectiveness; Assessment of treatment risks; Pharmacotherapy intervention.
4. **Management of Long-term Medication Patients**
   - Medication education; Post-discharge follow-up.

Comprehensive Management

Home-based patients

↓

Local hospital testing

↓

Test results or issues uploaded

↓

Pharmacist provides answers

↓

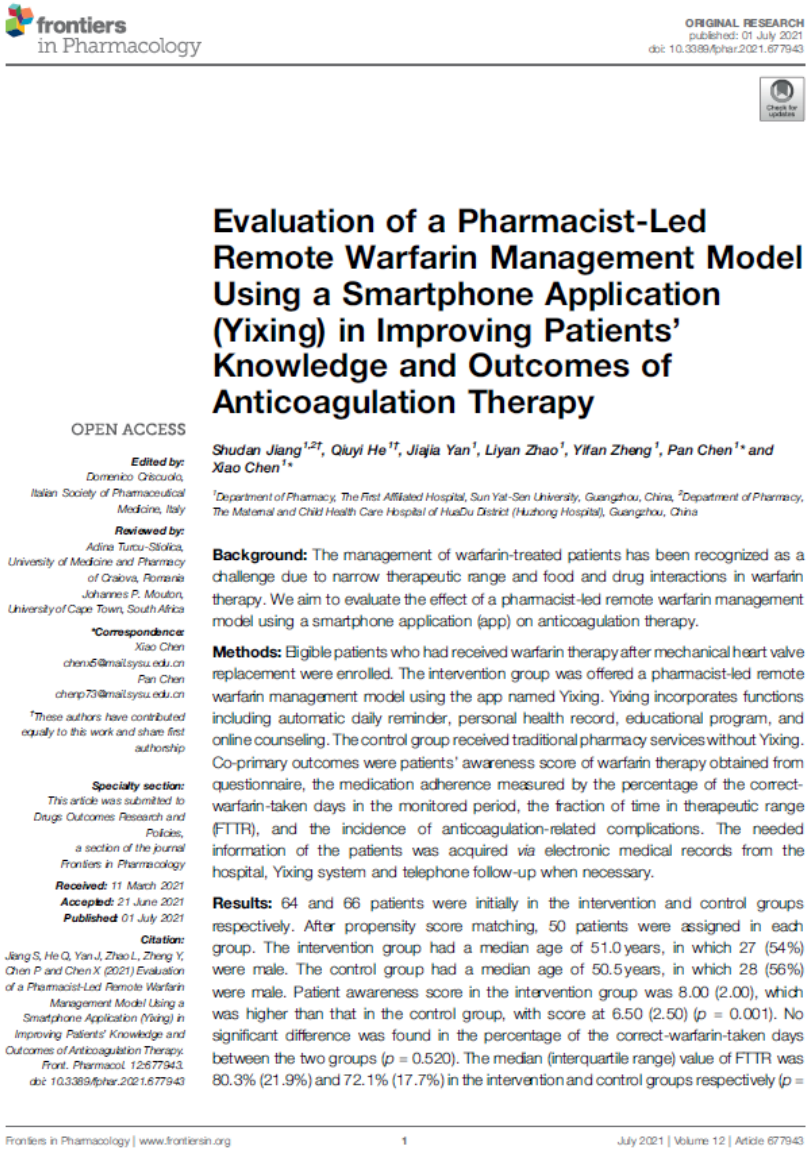
Dosage adjustments or answers to questions

Internet Hospital

04

Clinical Research

Impact of Smartphone Applications on the Management of Anticoagulation Therapy



frontiers in Pharmacology

ORIGINAL RESEARCH
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Evaluation of a Pharmacist-Led Remote Warfarin Management Model Using a Smartphone Application (Yixing) in Improving Patients' Knowledge and Outcomes of Anticoagulation Therapy

OPEN ACCESS

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Background: The management of warfarin-treated patients has been recognized as a challenge due to narrow therapeutic range and food and drug interactions in warfarin therapy. We aim to evaluate the effect of a pharmacist-led remote warfarin management model using a smartphone application (app) on anticoagulation therapy.

Methods: Eligible patients who had received warfarin therapy after mechanical heart valve replacement were enrolled. The intervention group was offered a pharmacist-led remote warfarin management model using the app named Yixing. Yixing incorporates functions including automatic daily reminder, personal health record, educational program, and online counseling. The control group received traditional pharmacy services without Yixing. Co-primary outcomes were patients' awareness score of warfarin therapy obtained from questionnaire, the medication adherence measured by the percentage of the correct-warfarin-taken days in the monitored period, the fraction of time in therapeutic range (FTTR), and the incidence of anticoagulation-related complications. The needed information of the patients was acquired *via* electronic medical records from the hospital, Yixing system and telephone follow-up when necessary.

Results: 64 and 66 patients were initially in the intervention and control groups respectively. After propensity score matching, 50 patients were assigned in each group. The intervention group had a median age of 51.0 years, in which 27 (54%) were male. The control group had a median age of 50.5 years, in which 28 (56%) were male. Patient awareness score in the intervention group was 8.00 (2.00), which was higher than that in the control group, with score at 6.50 (2.50) ($p = 0.001$). No significant difference was found in the percentage of the correct-warfarin-taken days between the two groups ($p = 0.520$). The median (interquartile range) value of FTTR was 80.3% (21.9%) and 72.1% (17.7%) in the intervention and control groups respectively ($p =$

TABLE 4 | Patients' distribution in the FTTR.

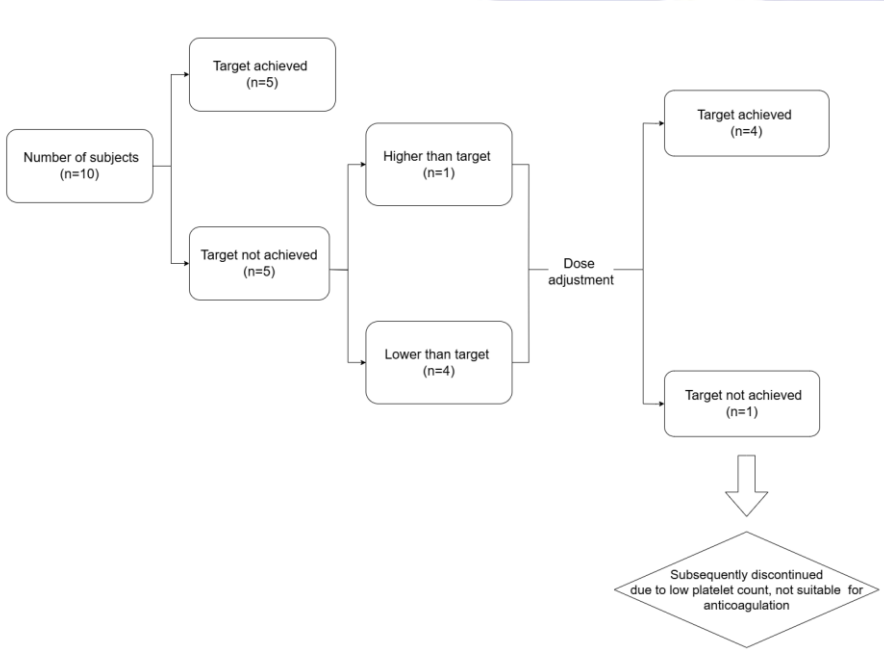
FTTR	Intervention	Control
(10, 30%]	1 (2%)	1 (2%)
(30%, 50%]	4 (8%)	6 (12%)
(50%, 70%]	11 (22%)	16 (32%)
(70%, 90%]	25 (50%)	23 (46%)
(90%, 100%]	9 (18%)	4 (8%)
	50 (100%)	50 (100%)

- Evaluating the impact of pharmacist-led remote management of warfarin using smartphone applications on anticoagulation therapy
- The pharmacist-led remote warfarin management model improved patients' understanding of warfarin therapy and increased the time in the therapeutic range (TTR).
- There was no significant difference in medication adherence and safety compared to traditional pharmacy services.
- The application established a communication platform for patients and pharmacists, facilitating timely warfarin management and improving efficiency.

Jiang S, et al. Evaluation of a Pharmacist-Led Remote Warfarin Management Model Using a Smartphone Application (Yixing) in Improving Patients' Knowledge and Outcomes of Anticoagulation Therapy. Front Pharmacol. 2021, 12:677943.

Exploring Therapeutic Drug Monitoring of Anticoagulants Based on Real-world Data from Pharmaceutical Care

- A retrospective analysis of anticoagulation treatment outcomes in patients with liver cirrhosis complicated by portal vein thrombosis at our hospital showed that the complete recanalization rate in the anticoagulation group was significantly different compared to the non-anticoagulation group.
- A prospective study used therapeutic drug monitoring (TDM) to guide rivaroxaban dosage adjustments in such patients. Ten patients were initially enrolled, five of whom did not reach the target blood concentration of rivaroxaban. After dosage adjustments, four patients reached the target. More patients will be included, and follow-up studies will continue to explore the impact of TDM on treatment outcomes in this patient population.



PMC 精准医学中心 PRECISION MEDICINE CENTER

南方医科大学南方医院精准医学中心检验报告单

姓　名：		ID　号：		样本类型： 血清	样本编号：
年　龄：		送检科室：肝脏中心		接收日期： 2024-07-16	报告日期： 2024-07-19
性　别： 男		送检医生：		检测方法： LC-MS/MS	仪器型号： Waters Xevo TQD
检测项目： 心血管药物浓度		备　注：		临床诊断： 肝衰竭	

编　号	项目名称	检测结果		参考范围	单位
1	利伐沙班	4.51	↓	6-87（谷浓度） 189-419（峰浓度，一天一次）	ng/mL

No.	Item Name	Test Result	Reference Range
1	Rivaroxaban	4.51	6–87 (trough) 189–419 (peak, once daily)

Clinical Pharmacist's Recommendations and Explanations:
Rivaroxaban must be taken continuously for at least 2.5 days to achieve a steady-state concentration. The patient started taking rivaroxaban 10 mg qd on May 21, 2024, and has reached a steady-state concentration. The current blood concentration is the trough concentration.
Plasma trough concentration for rivaroxaban VTE treatment should be 6–87 ng/mL, and the patient's current concentration is lower than the lower therapeutic concentration threshold
The patient's GFR is 55.01 mL/min/1.73m².
Recommendation: based on the patient's current coagulation markers, it is recommended to increase rivaroxaban dose to 15 mg qd for treatment.
If there are changes in liver or kidney function, bleeding, poor anticoagulation efficacy, the patient undergoes surgery or invasive interventions, trauma, gastrointestinal malabsorption, or the use of drugs that interact with rivaroxaban, the blood concentration of rivaroxaban should be monitored again when thrombolytic therapy is required.

IRB Approval

SOP017/05.04

南方医科大学南方医院
Medical Ethics committee of NanFang Hospital of Southern Medical University
伦理审查批件 Approval Letter

批件号 No.	NFEC-2023-146		
研究项目名称 Protocol Title	利伐沙班在肝硬化合并门静脉血栓患者中的药代动力学及剂量优化研究		
项目来源 Submitter	南方医科大学南方医院		
研究科室 Research department	药剂科		
主要研究者 Principal Investigator	郑萍		
审查类别 Scope of review	复审 临床研究		
审查方式 Review mode	■会议审查 Full board review　□快速审查 Expedited review		
审查日期 Review Date	2023 年 03 月 23 日	审查地点 Review Place	伦理委员会会议室
审查委员 Review members	高方，刘世霞，尹红蕾，张玉珍，陈冰娜，姜耀东，李娟，汤明芳，严金海，陈安乔，薛莲		
审查文件 Documents	1. 行政管理部门受理表 2. 临床研究立项申请学术审查意见表 3. 初始审查申请表 4. 项目负责人履历 5. 项目负责人资质证明材料 6. 项目负责人责任声明 7. 研究团队职责分工表 8. 研究团队相关培训证书 9. 项目风险预评估及处置预案 10. 试验方案（版本号：5.0，版本日期：2023-03-10） 11. 知情同意书（版本号：4.0，版本日期：2023-03-10） 12. 药品说明书 13. 复审申请		
审查意见 Comments	同意，跟踪审查频率为 12 个月，批件有效期一年。		
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Analysis of Factors Affecting Platelet Function After Discontinuation of Ticagrelor

frontiers in Pharmacology

ORIGINAL RESEARCH
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Pharmacokinetic and Pharmacogenetic Factors Contributing to Platelet Function Recovery After Single Dose of Ticagrelor in Healthy Subjects

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Objectives: This study aimed to elucidate the contribution of candidate single nucleotide polymorphisms (SNPs) related to pharmacokinetics on the recovery of platelet function after single dose of ticagrelor was orally administered to healthy Chinese subjects.

Methods: The pharmacokinetic profiles of ticagrelor and its metabolite AR-C124910XX (M8), and the platelet aggregation (PA), were assessed after 180 mg of single-dose ticagrelor was orally administered to 51 healthy Chinese subjects. Effects of *CYP2C19*2*, *CYP2C19*3*, *CYP3A5*3*, *UGT1A1*6*, *UGT1A1*28*, *UGT2B7*2*, *UGT2B7*3*, *SLCO1B1* 388A>G, and *SLCO1B1* 521T>C, on the pharmacokinetics of ticagrelor and M8, and platelet function recovery were investigated.

Results: The time to recover 50% of the maximum drug effect (RT_{50}) ranging from 36 to 126 h with 46.9% CV had a remarkable individual difference and was positively associated with the half-life ($t_{1/2}$) of M8 ($r = 0.3901$, $P = 0.0067$). The time of peak concentration (T_{max}) of ticagrelor for CYP2C19*3 GG homozygotes was significantly higher than that of GA heterozygotes ($P = 0.0027$, $FDR = 0.0243$). Decreased peak concentration (C_{max}) of M8 was significantly associated with *SLCO1B1* 388A>G A allele ($P = 0.0152$, $FDR = 0.1368$). *CYP2C19*2* A was significantly related to decreased C_{max} of M8 ($P = 0.0455$, $FDR = 0.2048$). While, the influence of these nine SNPs on the recovery of platelet function was not significant.

Conclusion: Our study suggests that the elimination of M8 is an important factor in determining the recovery of platelet function. Although CYP2C19 and SLCO1B1 genetic variants were related to the pharmacokinetics of ticagrelor or M8, they did not show a significant effect on the platelet function recovery in this study.

Clinical Trial Registration: https://clinicaltrials.gov/ct2/show/NCT03092076, identifier: NCT03092076

Keywords: genetic variants, healthy subjects, pharmacokinetics, recovery of platelet function, ticagrelor

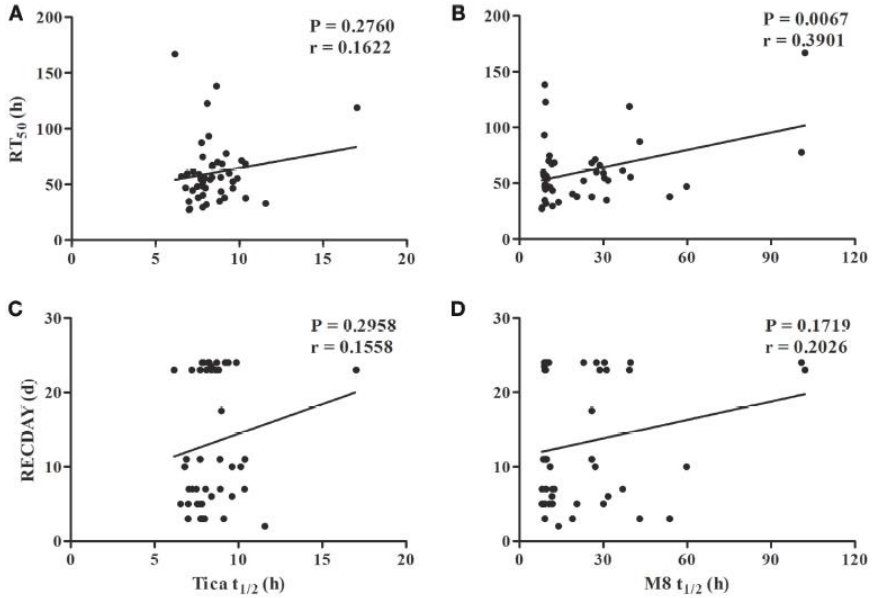


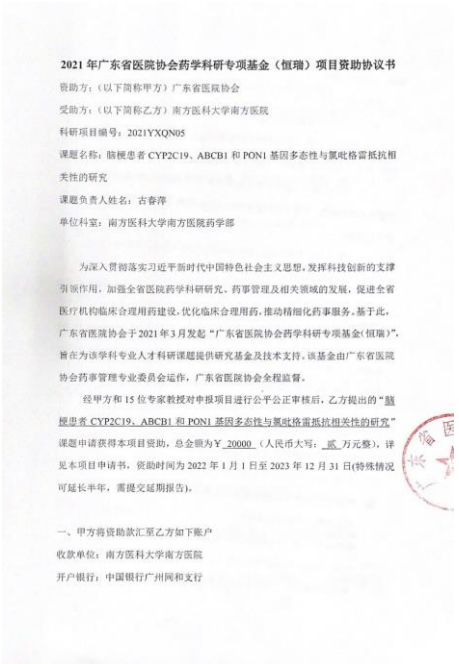
FIGURE 4 | Association of half-life of ticagrelor and M8 with recovery of platelet function. **(A)** Association of half-life ($t_{1/2}$) of ticagrelor with the time to recover 50% of the maximum drug effect (RT_{50}); **(B)** association of $t_{1/2}$ of M8 with RT_{50}; **(C)** association of $t_{1/2}$ of ticagrelor with the recovery day to the baseline platelet aggregation (RECDAY); **(D)** association of $t_{1/2}$ of M8 with the RECDAY.

- The elimination of M8 (the metabolite of ticagrelor) is an important factor in determining the recovery of platelet function.
- Although CYP2C19 and SLCO1B1 gene variations are related to the pharmacokinetics of ticagrelor or M8, they did not have a significant impact on platelet function recovery in this study.

Zhu Q, et al. Pharmacokinetic and Pharmacogenetic Factors Contributing to Platelet Function Recovery After Single Dose of Ticagrelor in Healthy Subjects. Front Pharmacol. 2019, 10:209.

Using pharmacogenetic Guidance for Clopidogrel Administration Reduces the Risk of Resistance or Bleeding Events

- ABCB1, CYP2C19, and PON1 all play important roles in the activation of clopidogrel.
- The data indicate that the CYP2C19*2 variant is associated with clopidogrel resistance, and this association is statistically significant.
- Stratified by NIHSS score greater than 3, the risk of clopidogrel resistance is related to changes in the antiplatelet therapy regimen.



2021 年广东省医院协会药学科研专项基金（恒瑞）项目资助协议书

资助方：（以下简称甲方）广东省医院协会

受助方：（以下简称乙方）南方医科大学南方医院

科研项目编号：2021YXQN05

课题名称：脑梗患者 CYP2C19、ABCB1 和 PON1 基因多态性与氯吡格雷抵抗相关性的研究

课题负责人姓名：古春萍

单位科室：南方医科大学南方医院药学部

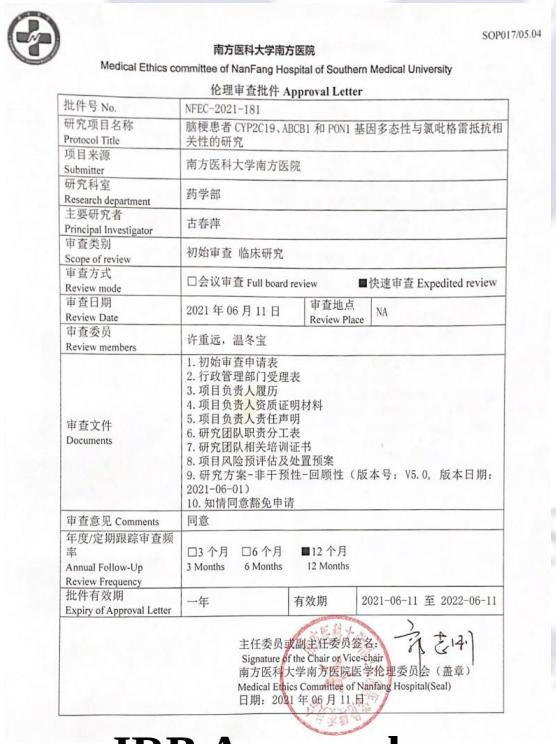
为深入贯彻落实习近平新时代中国特色社会主义思想，发挥科技创新的支撑引领作用，加强全省医院药学科研研究、药事管理及相关领域的发展，促进全省医疗机构临床合理用药建设，优化临床合理用药，推动精细化药事服务，基于此，广东省医院协会于 2021 年 3 月发起“广东省医院协会药学科研专项基金(恒瑞)”，旨在为该学科专业人才科研课题提供研究基金及技术支持，该基金由广东省医院协会药事管理专业委员会运作，广东省医院协会全程监督。

经甲方和 15 位专家教授对申报项目进行公平公正审核后，乙方提出的“脑梗患者 CYP2C19、ABCB1 和 PON1 基因多态性与氯吡格雷抵抗相关性的研究”课题申请获得本项目资助，总金额为￥ 20000 （人民币大写：贰 万元整），详见本项目申请书。资助时间为 2022 年 1 月 1 日至 2023 年 12 月 31 日(特殊情况可延长半年，需提交延期报告)。

一、甲方将资助款汇至乙方如下账户

收款单位：南方医科大学南方医院

开户银行：中国银行广州同和支行



SOP017/05.04

南方医科大学南方医院

Medical Ethics committee of NanFang Hospital of Southern Medical University

伦理审查批件 Approval Letter

批件号 No.	NFEC-2021-181		
研究项目名称 Protocol Title	脑梗患者 CYP2C19、ABCB1 和 PON1 基因多态性与氯吡格雷抵抗相关性的研究		
项目来源 Submitter	南方医科大学南方医院		
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主要研究者 Principal Investigator	古春萍		
审查类别 Scope of review	初始审查 临床研究		
审查方式 Review mode	□会议审查 Full board review	■快速审查 Expedited review	
审查日期 Review Date	2021 年 06 月 11 日	审查地点 Review Place	NA
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审查意见 Comments	同意		
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批件有效期 Expiry of Approval Letter	一年	有效期	2021-06-11 至 2022-06-11

主任委员或副主任委员签名：
Signature of the Chair or Vice-chair
南方医科大学南方医院医学伦理委员会（盖章）
Medical Ethics Committee of Nanfang Hospital(Seal)
日期：2021 年 06 月 11 日

IRB Approval

Table Modification of antiplatelet drugs associated with CPGR risk level.

Antiplatelet drugs	genotypes					CPGR risk level	P value
	CYP2C19*2	CYP2C19*3	CYP2C19*17	ABCB1	PON1		
Aspirin plus Clopidogrel	AG	GA	CC	CT	AA	4	0.005
Aspirin plus Clopidogrel→Aspirin plus Cilostazol	AG	GG	CC	TT	AA	3	
Clopidogrel	AA	GG	CC	CC	GA	3	
Clopidogrel→Aspirin	AA	GG	CC	CT	GG	3	
Clopidogrel→Aspirin plus Cilostazol	GG	GG	CC	CC	AA	3	

unpublished data

05

Case Analysis

Case 1

Patient Information	Female，63 years old，61 kg.
Chief Complaint	Left knee joint pain with limited movement for over 5 years, worsened in the past 2 months.
Present 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”.
Past Medical History	Chronic kidney disease (CKD) began 3 years ago but has not taken medication regularly. Denies any other significant medical history.
Auxiliary Examinations	Routine blood tests, coagulation function, liver function, and urinalysis: No significant abnormalities. Estimated glomerular filtration rate (eGFR): 29.1 mL/min/1.73 m ²(Stage 4 CKD). X-ray Findings: Bilateral degenerative knee osteoarthritis.
Diagnosis	Degenerative knee osteoarthritis.
Clinical Question	Plan for knee replacement surgery (**High bleeding risk and risk of VTE prevention**) in a patient with Stage 4 CKD. **How should hemostatic and anticoagulant medications be managed during the perioperative period?**

Bleeding Management

Knee replacement surgery is a **high-bleeding-risk** procedure.

Guideline: **For major orthopedic surgeries, it is recommended to use tranexamic acid prophylactically before surgery to reduce blood loss and the need for transfusions**.

1. Research reports suggest that during the perioperative period of knee replacement surgery, intravenous infusion combined with local application of tranexamic acid is more effective in reducing blood loss and transfusion rates than intravenous or local application alone. **Pharmacist's Recommendation**: Use a **combination of intravenous infusion and local application** of tranexamic acid.

2. Tranexamic acid elimination is highly dependent on renal function. The dosage interval should be significantly extended or the dose reduced in patients with renal insufficiency. **Pharmacist's Recommendation**: For this patient with Stage 4 CKD, use a **low dose** of tranexamic acid.

Coagulation Management

The patient's Caprini score is 7, indicating **an extremely high risk of VTE** (≥5).

Guideline: To balance antifibrinolytic and anticoagulant drugs, **anticoagulants should be started 6–8 h postoperatively or after bleeding has stopped**.

1. Considering the patient's **adherence**, **oral anticoagulants** should be used.

2. **Pharmacist's Recommendation**: For this patient with severe renal insufficiency, it is recommended to use **apixaban** 2.5 mg twice daily to prevent VTE.

The physician followed the clinical pharmacist's recommendations. During the surgery, the patient lost approximately 100 mL of blood, and there were no adverse events such as VTE or seizures.

Case 2

Patient Information	Male, 61 years old, 62 kg.
Chief Complaint	Intermittent palpitations for 1 year, worsened over the past month.
Present Medical History	Palpitations began 1 year ago without an obvious trigger, accompanied by shortness of breath after activity. No chest tightness, chest pain, dizziness, or blackouts, and without seeking medical attention. Symptoms worsened 1 month ago.
Past Medical History	Denies history of hypertension, diabetes, coronary heart disease, or cerebrovascular disease.
Auxiliary Examinations	Electrocardiogram: atrial fibrillation, frequent ventricular premature beats. Echocardiogram: mild aortic regurgitation, enlarged left atrium, severe mitral regurgitation, left atrial thrombus formation (approximately 22 mm x 76 mm), mild tricuspid regurgitation, LVEF 63%. No significant abnormalities in kidney function.
Diagnosis	Severe mitral regurgitation, atrial fibrillation, left atrial thrombus.
Clinical Question	**The patient meets the criteria for surgical intervention, planned to occur in 5 d later.** **Management of antithrombotic drugs during the perioperative period? (Balancing the risk of surgical bleeding with the need for anticoagulation due to atrial thrombus)**

The echocardiogram indicates the formation of a large thrombus in the left atrium, necessitating the immediate initiation of anticoagulation therapy.

1. During the perioperative period, the temporary discontinuation of anticoagulant medication must be considered.
2. Issues on the onset and cessation times of oral anticoagulants.

Pharmacist's recommendation: 1. For the thrombus already present, therapeutic doses of low-molecular-weight heparin should be used preoperatively. **2.** Determine the appropriate dosage of LMWH based on the patient's weight and discontinue it 1 d before surgery.

One week after admission, the patient underwent 'mechanical mitral valve replacement + left atrial thrombus removal surgery' under general anesthesia with cardiopulmonary bypass. The procedure went smoothly, and the patient was safely returned to the ICU postoperatively.

Pharmacist Recommendation: 1. After mechanical mitral valve replacement surgery, and in conjunction with atrial fibrillation, warfarin anticoagulation is administered postoperatively, with doses adjusted based on INR levels, and should be taken for life. **2.** Cardiac surgery is a high risk for bleeding; if hemostasis is good, start warfarin 24 h postoperatively. **3.** The patient has a high risk of thrombosis; warfarin is slow to act. You can co-administer LMWH at least 2-3 d after surgery, starting 48 h postoperatively, recheck INR, and discontinue low-molecular-weight heparin when INR is within the target range.

Case 3

Patient Information	Male，69 years old，67 kg.
Chief Complaint	Intermittent discomfort in the precordial region for one month, 2 d post-PCI (Percutaneous Coronary Intervention).
Present Medical History	The patient suddenly fell without any apparent cause, landing on the right side of the body and head, accompanied by unconsciousness. The patient reported gradually regaining consciousness after about 15 min and sought treatment at a local hospital, where an acute inferior myocardial infarction was diagnosed. Emergency coronary angiography + IVUS + PCI was performed, with a stent implanted in the distal circumflex artery. Postoperatively, the patient was given enteric-coated aspirin 100 mg and clopidogrel 75 mg for antiplatelet therapy. On the second day after the surgery, the patient experienced fluctuations in blood pressure, mild headaches, nausea, and vomiting. A head CT scan showed subarachnoid hemorrhage (SAH), and dual-antiplatelet therapy (DAPT) was immediately discontinued.
Previous Medical History	Denies history of hypertension, diabetes, or cerebrovascular disease.
Auxiliary Examination	Cerebral angiography: 1) Occlusion of the left vertebral artery; 2) Mild stenosis at the origin of the right vertebral artery; 3) Cerebral arteriosclerosis, no intracranial aneurysms detected. Head CT scan: 1) SAH, small amounts of subdural effusion bilaterally at the frontal and parietal regions; 2) Bilateral internal carotid arteries and multiple calcified plaques in the intracranial segment of the left vertebral artery.
Diagnosis	Coronary atherosclerotic heart disease (inferior myocardial infarction, post-PCI, mild tricuspid regurgitation, cardiac function Class I); SAH.
Clinical Question	The patient experienced a sudden SAH less than one week after PCI. **When should antiplatelet therapy be resumed?**

1. Embolic Risk Assessment

- The patient, post-acute myocardial infarction PCI, belongs to a **very high-risk group**.
- The patient has a history of smoking and alcohol consumption. Cerebral angiography indicated left vertebral artery occlusion, mild stenosis at the origin of the right vertebral artery, and cerebral arteriosclerosis.
- **Restarting antiplatelet therapy is essential for the patient's prognosis**.

2. Bleeding Risk Assessment

- The CRUSADE bleeding risk score is 23, indicating **low bleeding risk** (21–30 points); PRECISE-DAPT score < 25.
- The likelihood of spontaneous SAH is low. Comprehensive analysis suggests that **the SAH was likely traumatic, caused by cardiogenic syncope**, while perioperative dual-antiplatelet therapy for PCI exacerbated the bleeding.
- A history of subarachnoid hemorrhage is not a contraindication for antiplatelet therapy.

3. Multidisciplinary Comprehensive Assessment

- Considering the stable condition of the SAH and the scores indicating high embolic risk and low bleeding risk, a **multidisciplinary consultation involving neurosurgery, cardiology, and clinical pharmacists** concluded to restart DAPT 5 d after discontinuation.

During hospitalization, clinical pharmacists strengthened pharmaceutical care and monitored the patient for bleeding tendencies. Subsequent follow-up head CT scans showed significant improvement in the SAH compared to previous findings.

Summary

- Well perioperative bleeding and coagulation management is significance to ensuring medical safety, shorting hospital stays and reducing medical costs.
- The management of bleeding and coagulation in perioperative requires joint efforts from medical, pharmaceutical, and nursing teams.
- Individualized hemostasis and antithrombotic treatment plans should be formulated according to the type of surgery and the specific conditions of the patient.
- Perioperative bleeding and coagulation management is an integral part of surgical pharmacy.

Your constructive criticism and guidance are greatly appreciated!