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綜合評述

使用抗血栓藥品病人於手術或侵入性處置前後之臨床因應策略

Perioperative and Periprocedural Management of Patients Receiving Antithrombotic Therapy

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摘要

手術或侵入性處置前後的抗血小板藥品及抗凝血藥品（統稱抗血栓藥品）之因應策略為重要的用藥安全議題，不適當停用抗血栓藥品可能增加病人栓塞風險或出血風險。術前應同時評估術式的出血風險、停藥的栓塞風險及其他個人風險因子（如年齡、肝腎功能、共病症、併用藥品等），並與開方醫師、術式相關醫師、麻醉醫師、藥師以及病人取得共識以擬訂個別化的停藥策略。除此之外，抗血栓藥品需依照藥物動力學特性及病人因素（如 international normalized ratio 數值、腎功能等）決定停用天數。而高栓塞風險病人可考慮在停用抗血栓藥品時使用銜接治療，緊急手術亦可考慮使用反轉劑，術後的復藥時機也是重要課題。

因此，完整的停藥策略應評估：(1) 是否停用抗血栓藥品、(2) 何時停用抗血栓藥品、(3) 是否使用銜接治療、(4) 是否使用反轉劑、(5) 何時復藥。本文回顧歐美各大學會指引，整理出血風險與栓塞風險之評估建議、進行常規手術前後抗血栓藥品之使用建議，以及進行緊急手術前抗血栓藥品之使用建議。期許藉由本文協助國內醫療團隊建立手術及侵入性處置前後使用抗血栓藥品的作業流程規範，以提升病人用藥安全。

關鍵字：抗血小板藥品、抗凝血藥品、手術、侵入性處置、周術期處置

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ABSTRACT

The use of perioperative and periprocedural antiplatelet and anticoagulant therapies (i.e., antithrombotic therapy) is a topic of critical concern. Inappropriate discontinuation of antithrombotic therapy may increase the risks of ischemic and bleeding events. Before an operation, clinical staff should evaluate the risk of surgical bleeding, the ischemic risk posed by drug discontinuation, and other personal risks (e.g., age, liver and kidney function, comorbidities, and concomitant medications) and establish an individualized perioperative and periprocedural antithrombotic strategy. In addition, antithrombotic agents should be discontinued in accordance with their pharmacokinetics and with patient-related factors (e.g., international normalized ratio and renal function). Clinical staff should consider the use of bridging therapy in patients at high ischemic risk when discontinuing antithrombotic therapy. Reversal agents can also be considered for emergency surgery. In addition, the timing of antithrombotic therapy resumption after an operation is crucial. Therefore, a complete perioperative and periprocedural antithrombotic therapy strategy should include the following details: (1) whether to stop antithrombotic therapy; (2) when to stop antithrombotic therapy; (3) whether to use bridging therapy; (4) whether to use a reversal agent; and (5) when to resume antithrombotic therapy. This article reviews the guidelines of major European and American medical societies. It summarizes the recommendations for assessing the risks of bleeding and ischemic events, antithrombotic therapy before and after routine surgery, and antithrombotic therapy before emergency surgery. This article provides evidence with which medical teams can establish perioperative and periprocedural management strategies for patients receiving antithrombotic agents to improve medication safety.

Key words: Anti-Platelet Agents, Anticoagulants, Surgery, Invasive Procedure, Perioperative Management

引言

手術或侵入性處置前後的抗血栓藥品因應策略為重要的用藥安全議題，抗血栓藥品的不當使用可能增加病人栓塞風險或出血風險，進而導致入院、延長住院時間、甚至死亡 [1-4]。依衛生福利部制定的 2022 年度醫療品質及病人安全工作目標，為提升病人用藥安全，應建立侵入性檢查及手術前後使用抗血栓藥品的作業流程規範，提供跨團隊溝通及諮詢機制，並定期檢討與回饋。完整的停藥策略應包含：一、是否停用抗血栓藥品、二、何時停用抗血栓藥品、三、是否使用銜接治療 (bridge therapy)、四、是否使用反轉劑 (reversal agent)、五、何時復藥。進行手術或侵入性處置前應同時評估出血風險及栓塞風險，出血風險包含了術式本身的出血風險以及病人相關的出血風險，例如年齡、共病症、肝腎功能、併用藥品等；而栓塞風險則需評估抗血栓藥品的使用目的以及使用期間；此外，高栓塞風險病人於停用抗血栓藥品期間如何進行銜接治療，以及術後復藥時機都是重要的課題。因此，執行手術或侵入性處置前務必由開方醫師（如心臟科醫師、神經科醫師等）、手術相關醫師（如外科醫師、腸胃科醫師、牙科醫師等）、麻醉醫師、藥師以及病人取得共識，擬定手術時間與完整的停藥計畫，並清楚指示醫療團隊成員與病人和家屬 [5,6]。

本文回顧歐美各大學會指引，整理出血風險與栓塞風險評估建議、進行常規手術前後抗血栓藥品之使用建議，以及進行緊急手術前抗血栓藥品之使用建議。本文整理之抗血栓藥品包含：口服抗凝血藥品 warfarin、非維他命 K 拮抗劑類口服抗凝血藥品 (non-vitamin K antagonist oral anticoagulant, NOAC)、注射型抗凝血藥品 unfractionated heparin (UFH) 和 low molecular weight heparin (LMWH)、抗血小板藥品以及雙重抗血小板藥品治療 (dual antiplatelet therapy, DAPT)。期許透過本文的回顧與整理，協助國內醫療團隊制定以實證醫學為依據的作業流程，提升病人照護品質。

壹、出血風險與栓塞風險評估建議

一、出血風險的評估

出血風險評估需考量手術本身出血風險和出血後併發症的嚴重程度，例如神經外科術式、心臟手術、大型腹腔手術、胸腔手術等術式，出血導致的併發症危險程度較高，因此歸類為高出血風險術式 [5,6]。針對不同手術的出血風險尚缺一致性的定義 (universal definition)，目前主要參考歐美治療指引、大型試驗以及學會分類等建議。依據 2021 年歐洲心律協會 (European Heart Rhythm Association, EHRA) 抗凝血藥品治療指引以及 2018 年發表於美國心臟病學會雜誌 (Journals of the American College of Cardiology, JACC) 與 2014 年義大利心臟學會、外科學會與麻醉學會共同擬定的針對抗血小板藥品使用的專家共識中 [2,5]， 將各種手術出血風險整理如 Table 1 [5] 及 Table 2 [2,7]。除此之外，病人的年齡、共病症（如肝腎功能不全）、併用藥物（如非類固醇類消炎止痛藥）、是否有出血病史等都會影響出血風險的評估 [8,9]。

二、栓塞風險的評估

栓塞風險的高低取決於病人使用抗血栓藥品的適應症、使用期間以及病人本身的風險因子。以心房顫動病人使用抗凝血藥品為例，如

Table 1. Type of surgery and hemorrhagic risk for anticoagulants by EHRA 2021 [5]

High risk	Low risk	Minor risk
• Cardiac surgery • Peripheral arterial revascularization surgery（e.g. aortic aneurysm repair, vascular bypass) • Complex invasive cardiological interventions, including lead extraction, (epicardial) VT ablation. Chronic total occlusion PCI etc. • Neurosurgery • Spinal or epidural anesthesia; lumbar diagnostic puncture • Complex endoscopy (multiple/ large polypectomy, ERCP with sphincterotomy etc.) • Abdominal surgery (including liver biopsy) • Thoracic surgery • Major urologic surgery/biopsy (including kidney) • Extracorporeal shockwave lithotripsy • Major orthopedic surgery	• Complex dental procedures • Endoscopy with simple biopsy • Small orthopedic surgery (foot, hand, arthroscopy.)	• Dental interventions (extraction 1–3 teeth, paradontal surgery, implant positioning, subgingival scalling/ cleaning) • Cataract or glaucoma intervention • Endoscopy without biopsy or resection • Superficial surgery (abscess incision, small dermatologic excisions, skin biopsy) • Pacemaker or ICD implantation (except complex procedures) • Electrophysiological study or catheter ablation (except complex procedures) • Routine elective coronary/peripheral artery intervention (except complex procedure) • Intramuscular injection (vaccination)

EHRA: European Heart Rhythm Association, VT: ventricular tachycardia, PCI: percutaneous coronary intervention, ERCP: endoscopic retrograde cholangiopancreatography, ICD: implantable cardioverter defibrillator.

Table 2. Type of surgery and hemorrhagic risk for anti-platelet agents by JACC and Italian cardiological/surgery/anaesthesiological societies [2,7]

Hemorrhagic Risk / Surgery	Low	Intermediate	High
General Surgery	• Hernioplasty • Plastic surgery of incisional hernias • Cholecystectomy • Appendectomy. colectomy • Gastric or intestinal resection • Breast surgery	• Hemorrhoidectomy • Splenectomy • Gastrectomy • Obesity surgery • Rectal resection • Thyroidectomy	• Hepatic resection • Duodenocefalopancreasectomy
Cardiac surgery	–	• Minithoracotomy • TAVI (apical approach) • OPCAB • CABG • Valve replacement	• Reintervention • Endocarditis • CABG in PCI failure • Aortic dissection, aortic surgery • Surgery with expected CEC time > 120 min
Vascular Surgery	• Carotid endarterectomy • Bypass or endarterectomy of lower extremity • EVAR、TEVAR • Limb amputations	• Open abdominal aorta surgery	• Open thoracic and thoracoabdominal surgery
Urology surgery	• Flexible cystoscopy • Ureteral catheterization • Ureteroscopy	• Prostate biopsy • Orchiectomy • Circumcision	• Radical and partial nephrectomy • Percutaneous nephrostomy • Percutaneous lithotripsy • Radical cystectomy • Prostatectomy • Endoscopic resection of prostate/endoscopic bladder surgery • Penectomy • Partial orchiectomy
Orthopedic surgery	• Hand surgery • Shoulder and knee arthroscopy • Minor spine surgery	• Prosthetic shoulder surgery • Major spine surgery • Knee surgery (anterior cruciate ligament, osteotomies) • Foot surgery	• Major prosthetic surgery (hip or knee) • Major traumatology (pelvis, long bones) • Fractures of the proximal femur in the elderly

Table 2. Type of surgery and hemorrhagic risk for anti-platelet agents by JACC and Italian cardiological/surgery/anaesthesiological societies [2,7] (continued)

Hemorrhagic Risk / Surgery	Low	Intermediate	High
Thoracic surgery	• Wedge resection • Diagnostic videothoracoscopy • Chest wall resection	• Lobectomy • Pneumonectomy • Mediastinoscopy • Sternotomy • Mediastinal mass excision	• Esophagectomy • Pleuropneumonectomy • Decortication of lung
Digestive endoscopy	• EGD or colonoscopy ± biopsy • Endoscopy without biopsy • Polypectomy/polyps < 1 cm • ERCP, stent, dilated papilla without sphincterotomy	• Endoscopy + FNA for solid lesions • Stenosis dilatation (esophageal, colorectal) • Gastroenteric stents • Argon plasma coagulation treatment • Polypectomy/polyps > 1 cm • PEG • Binding/variceal sclerosis • Binding/hemorrhoids sclerosis	• Dilatation in achalasia • Mucosectomy/submucosal resection • Echography with FNA biopsy of pancreatic cystic lesions • Ampullectomy of the ampulla of Vater
Dentistry	• Non-surgical periodontal therapy (including supragingival scaling); • Endodontic therapy; • Rubber dam positioning	• Surgical periodontal therapy (resective surgery, regenerative surgery, mucogingival surgery) • Oral surgery in general (teeth extractions, pre-prosthetic reconstructive surgery), implant surgery	
Ophthalmology	• Intravitreal injections • Cataract surgery • Peribulbar anesthesia	• Vitrectomy • Trabeculectomy	
Interventional pulmonology	• Bronchoscopic inspection • Bronchoaspiration • Bronchoalveolar lavage	• Bronchial biopsy • Transbronchial needle aspiration	• Lung and transbronchial biopsy • Rigid bronchoscopy • Medical thoracoscopy

Table 2. Type of surgery and hemorrhagic risk for anti-platelet agents by JACC and Italian cardiological/surgery/anaesthesiological societies [2,7] (continued)

Surgery \ Hemorrhagic Risk	Low	Intermediate	High
Neurosurgery	• Spinal neurosurgery: disc herniation, laminectomy (≤ 2 spaces) without arthrodesis • Cranial neurosurgery: external ventricular derivation, IVC placement for intracranial pressure monitoring, intraventricular reservoir placement	• Spinal neurosurgery: laminectomy > 2 spaces, spinal arthrodesis (any type) • Cranial neurosurgery: ventriculoperitoneal shunt, removal of extradural lesion	• Spinal and cranial neurosurgery: removal of intradural lesions (intracerebral tumors, intraparenchymal hemorrhage

JACC: Journals of the American College of Cardiology, TAVI: transcatheter aortic valve implantation, OPCAB: off-pump coronary artery bypass, CABG: coronary artery bypass graft, PCI: percutaneous coronary intervention, CEC: extracorporeal circulation, EVAR: endovascular repair for aortic aneurysm, TEVAR: thoracic endovascular aortic aneurysm repair, EGD: esophago-gastro-duodenoscopy, ERCP: endoscopic retrograde cholangiopancreatography, PEG: percutaneous endoscopic gastrostomy, FNA: fine needle aspiration biopsy, IVC: intraventricular catheter.

CHA_2DS_2-VASc score 7–9 分、三個月內曾發生缺血性中風事件、或風濕性瓣膜性心臟病，都屬於高栓塞族群 [6,10]；抗血小板藥品在冠心症的使用則需要評估經皮冠狀動脈介入治療的處置情況，包含適應症、採用氣球擴張或放置支架、金屬支架或是塗藥支架的置放時間以及冠狀動脈狹窄的程度等，而有不同的栓塞風險 [8,11]。栓塞風險越高，停用抗血栓藥品期間越可能發生栓塞事件，必要時，可能需要評估使用銜接治療 (bridge therapy)。停用抗凝血藥品造成血栓的風險評估整理如 Table 3 [6,10,12]，停用抗血小板藥品造成再栓塞的風險評估整理如 Table 4 [7,11]。

貳、進行術式前後抗凝血藥品之使用建議

一、常規手術前後抗凝血藥品之使用建議

常規手術經評估為輕微出血風險 (minor risk) 術式時，使用 NOAC 者可以於服藥 12–24 小時後進行手術，待手術完成止血 6 小時後加回 NOAC；例如青光眼或白內障、簡單的拔牙手術、心臟植入式電子裝置（如心律調節器、心臟除顫器）等，都可在 NOAC 濃度低谷（服藥 12–24 小時後）時執行，不需要停用 NOAC [5]。使用 warfarin 者，術前 international normalized ratio (INR) 於治療範圍內且病人本身沒有易出血因素時，可考慮不停用 warfarin；術後一旦止血，可於 12–24 小時加回 warfarin [6]。

進行低或高出血風險 (low or high risk) 術式前，使用 NOAC 者需要依照腎功能及手術高低風險決定預設的停藥時間，整理如 Table 5 [5,13]。停藥時，一般不需要使用 LMWH 或 UFH 作為銜接治療，因銜接治療可能增加出血風險 [5]。進行神經外科手術或心臟手術、嚴重腎功能不全者，或有任何因素可能導致 NOAC 濃度過高（如藥品交互作用）等情況時，可考慮監測 NOAC 血中濃度輔助決定停藥時機，但目前國內無常規監測 NOAC 濃度 [5]。一旦止血，手術醫師同意後可於術後 24 小時（低出血風險術式）及 48–72 小時（高出血風險術式）之下，考慮重新使用 NOAC [5]。

Table 3. Perioperative thromboembolism risk for anticoagulants [6,10,12]

	Mechanical heart valve	Atrial fibrillation	VTE
High Risk	• Any mitral valve prosthesis • Any caged-ball or tilting disc aortic valve prosthesis • Recent (< 6 month) stroke or TIA	• CHA_2DS_2-VASc score 7–9 • Recent (< 3 month) stroke or TIA • Rheumatic valvular heart disease	• Recent (< 3 month) VTE • Severe thrombophilia (eg. deficiency of protein C, protein S or antithrombin; antiphospholipid antibodies; multiple abnormalities)
Moderate Risk	• Bileaflet AVR with ≥1 risk factors	• CHA_2DS_2-VASc score 5–6	• VTE within the past 3 to 12 months • Non-severe thrombophilia (eg, heterozygous factor V Leiden or prothrombin gene mutation) • Recurrent VTE • Active cancer (treated within 6 months or palliative)
Low Risk	• Bileaflet AVR without AF and no other risk factors for stroke	• CHA_2DS_2-VASc score 1–4 and no prior stroke or TIA	• Single VTE > 12 months previous and no other risk factors

VTE: venous thromboembolism; TIA: transient ischemic attack; AF: atrial fibrillation; AVR: aortic valve replacement. High-risk patients may also include those with a prior stroke or transient ischemic attack occurring > 3 months before the planned surgery and a CHA2DS2-VASc score < 7, those with prior thromboembolism during temporary interruption of vitamin K antagonists, or those undergoing certain types of surgery associated with an increased risk for stroke or other thromboembolism (e.g, cardiac valve replacement, carotid endarterectomy, major vascular surgery).

Table 4. Perioperative ischemic risk for anti-platelet agents [7,11]

Perioperative ischemic risk	Coronary angiographic characteristics and PCI
High risk	• ≤ 2 weeks after PCI with POBA • ≤ 1 month after PCI with BMS • ≤ 6 months after PCI with DES • ≤ 12 months after complex PCI with DES (long stents, multiple stents, overlapping, small vessels, bifurcations, left main, last remaining vessel) • ≤ 6 months after PCI for MI • Previous stent thrombosis
Intermediate risk	• > 2 weeks and ≤ 4 weeks after PCI with POBA • > 1 month and ≤ 6 months after PCI with BMS • > 6 months and ≤ 12 months after PCI with DES • > 12 months after complex PCI with DES (long stents, multiple stents, overlapping, small vessels, bifurcations, left main, last remaining vessel)
Low risk	• > 4 weeks after PCI with POBA • > 6 months after PCI with BMS • > 12 months after PCI with DES

POBA: plain old balloon angioplasty; PCI: percutaneous coronary intervention; BMS: bare-metal stent; DES: drug-eluting stent; MI: myocardial infarction.

Table 5. Pharmacokinetics of NOAC and timing of last NOAC intake before an elective intervention [5,13]

NOAC	Dabigatran	Rivaroxaban	Apixaban	Edoxaban
Plasma peak	1.5–3.0 hr	2.0–4.0 hr	3–4 hr	1–2 hr
Clearance non-renal/renal	20%/80%	65%/35%	73%/27%	50%/50%
Half-life（hr）	CLcr > 80 mL/min: 12–17 CLcr 50–80 mL/min: ~17 CLcr 30–50 mL/min: ~19 CLcr 15–30 mL/min: ~ 28	CLcr > 80 mL/min: 5–9 (young), 11–13 (elderly) CLcr 50–80 mL/min: ~8.7 CLcr 30–50 mL/min: ~9 CLcr 15–30 mL/min: ~ 9.5	CLcr > 80 mL/min: 12 CLcr 50–80 mL/min: ~ 14.6 CLcr 30–50 mL/min: ~17.6 CLcr 15–30 mL/min: 17.3	CLcr > 80 mL/min: 10–14 CLcr 50–80 mL/min: ~8.6 CLcr 30–50 mL/min: ~9.4 CLcr 15–30 mL/min: ~16.9
Default timing of interruption				
	Dabigatran		Rivaroxaban/Apixaban/Edoxaban	
CLcr （mL/min）	≥ 80 mL/min	50–79 mL/min	0–49 mL/min	≥ 30 mL/min	15–29 mL/min
HBR procedure	≥ 48 hr	≥ 72 hr	≥ 96 hr	≥ 48 hr	≥ 48 hr
LBR procedure	≥ 24 hr	≥ 36 hr	≥ 48 hr	≥ 24 hr	≥ 36 hr
Default time for resume NOAC				
LBR procedure	24 hours after intervention			
HBR procedure	48–72 hours after intervention			

CLcr: creatinine clearance; NOAC: non-vitamin K antagonist oral anticoagulant; HBR: high bleeding risk; LBR: low bleeding risk.

針對進行輕微出血風險術式者，如果使用 warfarin 且病人相關出血風險低時，若 INR 在治療目標範圍內，可不需常規停用 warfarin [6]。針對進行低或高出血風險術式或是高出血風險族群者需要術前停用 warfarin 時，術前停用 warfarin 的天數依據停藥前 INR 數值而定，大約停用 3–5 天至 INR 恢復正常或 INR < 1.5 時進行手術，亦可於術前 24 小時監測 INR 以利手術進行 [6,12]。針對高栓塞風險族群，例如三個月內有栓塞事件者、曾因停藥發生栓塞事件者、或 CHA_2DS_2-VASc score 7–9 分者，可在停用 warfarin 後 INR 低於治療目標時，給予治療劑量的 LMWH 或 UFH 作為銜接治療，並於術前 12–24 小時停用 LMWH，或術前 4–6 小時停用 UFH [6]。術後如已完全止血且手術醫師同意，可於術後 12–24 小時加回 warfarin；高栓塞風險族群則考慮使用 warfarin 併用 UFH 或 LMWH 銜接至 INR 到達治療目標時，才停用注射型抗凝血藥品 [6]。針對低或中栓塞風險族群則不需要常規使用銜接治療 [9]。

二、緊急手術前抗凝血藥品之使用建議

進行高出血風險緊急手術時，如果 NOAC 最後服用時間為兩小時內，可考慮給予 activated charcoal 50 g；如果使用 dabigatran 者，確認最後服藥時間落於 3–5 個藥品半衰期內（約 42–140 小時，腎功能越差半衰期越長），可以給予反轉劑 idarucizumab。根據臨床試驗結果，給予 idarucizumab 後進行緊急手術的中位數時間為 1.6 小時，93.4% 受試者可於術中達到止血的效果 [14]。唯目前國內使用 Xa 抑制劑者，因尚未引進 Xa 抑制劑的反轉劑 andexanet alfa，故術前可考慮給予自費 prothrombin complex concentrate (PCC) 或 activated PCC，並且衡量血栓風險 [5,15]。Xa 抑制劑的反轉劑 andexanet alfa 有高低劑量兩種用法，在使用 rivaroxaban > 10 mg、apixaban > 5 mg 或是未知劑量時，給予高劑量 800 mg 靜脈輸注，前兩分鐘目標流速為 30 mg/min，接著以 8 mg/min 持續輸注兩小時；如果使用 rivaroxaban ≤ 10 mg、apixaban ≤ 5 mg 時則選擇低劑量用法，給予 400 mg 靜脈注射，前兩分鐘目標流速為 30 mg/min，接者以 4 mg/min 持續輸注兩小時 [5]。目前無大型臨床試驗研究在緊急手術前最合適的 PCC 及 activated PCC 劑量，專家建議可使用 25–50 IU/kg [16,17]。使用 warfarin 者可給予維生素 K 以及 PCC，無法使用 PCC 時亦可考慮 fresh frozen plasma (FFP) 反轉 warfarin 的作用。維生素 K 對於 warfarin 的反轉效果較慢，如果靜脈給予維生素 K，INR 約會在 1–2 小時開始下降，在 4–6 小時才達到最佳效果，而 PCC 作用時間快，可在 10–30 分鐘內使 INR 下降至小於 1.5，作用期間約 12–24 小時，可於緊急手術反轉 warfarin 效果；目前 PCC 的健保規定包含服用 coumarin 類抗凝血劑造成併發症引起的嚴重出血以及缺乏維生素 K 併發的嚴重出血或須緊急手術時 [6,18]。Protamine 為 UFH 的反轉劑，需依照 2–3 小時內使用的 UFH 總量決定 protamine 用量。Protamine 最多僅能中和 60%–75% LMWH 抑制凝血因子 Xa 的藥效。有關進行緊急手術前抗凝血藥品反轉劑的使用方式與劑量整理如 Table 6 [5,10,14,18]。

參、進行術式前後抗血小板藥品之使用建議

一、常規手術前後抗血小板藥品之使用建議

手術前應先確認病人使用抗血小板藥品之適應症、冠狀動脈支架置放時間、手術出血風險，再評估病人本身栓塞風險，包含冠狀動脈狹窄程度、腎功能、左心室收縮功能不全（左心室射出率 < 35%）、糖尿病、之前是否有支架栓塞病史或反覆心肌梗塞等因素考量，決定個人化的停藥策略 [2,8,11,19]。DAPT 的適應症及建議治療期間整理如 Table 7 [3,20,21]。依據術式的出血風險及停藥的栓塞風險，術前停用抗血小板藥品之建議於非心臟手術者可參考 Table 8 [19]，並與各科醫師取得共識後決定停藥時間。如需停用 P2Y12 抑制劑，則手術完成 24–72 小時後於手術醫師同意之下儘速加回 P2Y12 抑制劑；高栓塞風險者且術後已完全止血時，建議額外給予 P2Y12 抑制劑的速效劑量 [8]。

近期發生急性冠心症者、反覆發生心肌梗塞、複雜冠狀動脈疾病、近期支架置放者為相對高栓塞族群，其常規手術建議在完成指引或文獻所列之最短 DAPT 療程後進行，以減少發生栓

Table 6. Reversal agents for anticoagulants [5,10,14,18]

Anticoagulants	Reversal agents and dose
Dabigatran	Idarucizumab: 5 g IV in 2 divided doses within 15 min
Rivaroxaban, apixaban	Andexanet alf[a]: High dosea for rivaroxaban >10 mg, apixaban > 5 mg or unknown dose Low dose[b] for rivaroxaban ≤ 10 mg or apixaban ≤ 5 mg
Warfarin	Vitamin K: IV 2.5–10.0 mg, depending on INR and severity of bleeding. Prothrombin complex concentrate: 25–50 IU/kg Fresh frozen plasma: 10–15 mL/kg
UFH	For UFH use within 30 mins: protamine 1 mg for 100 U UFH For UFH use between 30–120 mins: protamine 0.5 mg for 100 U UFH For UFH use before 120 mins: protamine 0.250–0.375 mg for 100 U UFH
LMWH	For LMWH use within 8 hours: protamine 1 mg for 100 anti-Xa IU of LMWH For LMWH use during 8–12 hours: protamine 0.5 mg for 100 anti-Xa IU of LMWH For LMWH use before 12 hours: may not be required protamine

IV: intravenous; INR: international normalized ratio; UFH: unfractionated heparin; LMWH: low molecular weight heparin.
[a]High dose: 800 mg IV bolus administered at a rate of ~30 mg/min, followed within 2 mins by an IV infusion of 8 mg/min for up to 120 mins.
[b]Low dose: 400 mg IV bolus administered at a rate of ~30mg/min, followed within 2 mins by an IV infusion of 4 mg/min for up to 120 mins.

Table 7. Recommendation for DAPT treatment duration based on ACC/AHA and ESC guideline [3,20,21]

Indication		Patient bleeding risk	Treatment duration and class of evidence
Percutaneous coronary intervention	Stable CAD	No HBR	DAPT 6 months (class I, LOE A) DAPT > 6 months (class IIb, LOE A) If BMS: DAPT at least 1 month (class I, LOE A) DAPT 1–30 month (class IIb, LOE A)
		HBR	DAPT 1 month (class IIb, LOE C) DAPT 3 months (class IIa, LOE B) If BMS: DAPT at least month (class I, LOE A)
	Acute coronary syndrome	No HBR	DAPT 12 months (class I, LOE A) DAPT > 12 months (class IIb, LOE B)
		HBR	DAPT 6 months (class IIa, LOE B)
Coronary artery bypass grafting	Stable CAD		No DAPT
	Acute coronary syndrome	No HBR	DAPT 12 months (class I, LOE C) DAPT > 12 months (class IIb, LOE C)
		HBR	DAPT 6 month (class IIa, LOE C)
Medical therapy	Stable CAD		No DAPT
	Acute coronary syndrome	No HBR	DAPT 12 months (class I, LOE A) DAPT > 12 months (class IIb, LOE B)
		HBR	DAPT at least 1 month (class IIa, LOE C)

ACC/AHA: American College of Cardiology/American Heart Association; ESC: European Society of Cardiology; CAD: coronary artery disease; HBR: high bleeding risk; DAPT: dual antiplatelet therapy; BMS: bare-metal stent; LOE: level of evidence.

塞事件的風險 [11]。一般而言，不建議早期停用 DAPT。高出血及高栓塞族群如需早期進行手術，可於停用口服 P2Y12 抑制劑後，考慮給予靜脈抗血小板藥品銜接治療，如靜脈輸注 P2Y12 抑制劑或 GPIIb/IIIa 抑制劑。雖然尚無大型隨機試驗或明確的治療指引，但 2021 JACC 的系統

Table 8. Perioperative Management of DAPT in noncardiac surgery based on thrombotic and hemorrhagic risk [19]

		Hemorrhagic risk					
		Low		Intermediate		High	
Type of surgery	Thrombotic risk	Aspirin	P2Y12 inhibitor	Aspirin	P2Y12 inhibitor	Aspirin	P2Y12 inhibitor
Elective surgery	Low	Keep	Discontinued	Keep	Discontinued	discontinued	Discontinued
	Intermediate and high	Postpone surgery until DAPT completed					
Non-deferrable surgery	Intermediate	Keep	Keep	Keep	Discontinued	Keep	Discontinued
	High	Keep	Keep	Keep	Discontinued and consider bridge therapy	Keep	Discontinued and consider bridge therapy

文獻回顧指出 [8]，cangrelor 作為銜接治療時有明確的建議劑量，且藥效作用時間較短，可縮短停藥時間，以及經隨機臨床試驗證實 cangrelor 的出血與栓塞風險較低，因此 cangrelor 是比較建議的銜接治療選擇，但目前國內無引進此藥品。另外，因 GPIIb/IIIa 抑制劑缺乏銜接治療的建議劑量，過去文獻皆以急性冠心症的建議劑量進行銜接治療，且須依腎功能調整劑量，再加上文獻研究結果指出 GPIIb/IIIa 抑制劑的出血風險較高，且因藥效時間較長，需於術前 4–6 小時停用，因此 GPIIb/IIIa 抑制劑比起 cangrelor 較不建議用於銜接治療 [11,22]。

依照 2021 年英國腸胃學會 (British Society of Gastroenterology) 以及歐洲上消化內視鏡學會 (European Society of Gastrointestinal Endoscopy) 發表的治療指引，進行低出血風險術式，如診斷檢查或切片、腸胃道支架置放、沒有進行息肉切除術的內視鏡檢查等，術前皆不需停用 P2Y12 抑制劑 [23]。

進行常規性心臟手術時，一般建議不需停用 aspirin；如需停用 P2Y12 抑制劑，則建議 ticagrelor 停用 3–5 天、clopidogrel 停用 5 天、prasugrel 停用 7 天 [3] 。個別抗血小板藥品之作用時間可參考 Table 9 [3,24]，實際停藥時間則需與醫師討論後執行。

二、緊急手術前抗血小板藥品之使用建議

因抗血小板藥品目前無特定的反轉劑，進行緊急手術時，除了停用藥物之外，可考慮輸注血小板以恢復正常血小板功能，但血小板的輸注量目前尚無共識。考量 aspirin 半衰期約 15–20 分鐘，而口服 P2Y12 抑制劑半衰期較長（clopidogrel 約 30 分鐘、prasugrel 約 3.7 小時、ticagrelor 約 8.5–12.4 小時），因此建議血小板的輸注的時機為服用 clopidogrel 或 prasugrel 後的 4–6 小時，以及服用 ticagrelor 後的 10–12 小時，以避免輸注的血小板被體內殘存的抗血小板藥品抑制 [2,18,25]。除此之外，可考慮使用 desmopressin 促進血小板黏附 [2,18,25]。非特異性血小板功能檢測（如 Platelet function screen-100）也可作為參考依據，唯檢測敏感度不佳，仍以評估臨床狀況為主 [25]。

依照歐美冠心症治療指引，進行緊急冠狀動脈繞道手術時，可不需停用 aspirin，而 clopidogrel 及 ticagrelor 建議術前停用至少 24 小時，並於術後止血時加回 [3,26]。

結論

手術或侵入性處置前後抗血栓藥品的使用為用藥安全的重要課題，藥師應依據最新的實證文獻，協助醫療團隊擬定完整的停藥策略（是否停用、何時停用、是否使用銜接治療、是否使用反轉劑、何時復藥），以及協助建立相關作業流程規範，以確保手術前後的用藥安全，提升病人照護品質。

Table 9. Major characteristics of antiplatelet agents [3,24]

Drug	Mechanism of action	Half life	Time to recover PLT function after drug withdrawal	PLT inhibition	Duration of effect
Aspirin	COX-1 inhibition	15–20 min	30% at 48 hours	Irreversible	5–10 days
Clopidogrel	P2Y12 receptor inhibition	7–9 hours	40% at 3 days	Irreversible	5–7 days
Ticlopidine	P2Y12 receptor inhibition	12.6 hours	4-10 days	Irreversible	7–14 days
Ticagrelor	P2Y12 receptor inhibition	7–9 hours	57% at 24 hours	Reversible	3–7 days
Prasugrel	P2Y12 receptor inhibition	~7 hours	5–9 days	Irreversible	7–14 days
Dipyridamole	Phosphodiesterase inhibition	9–13 hours	NA	Reversible	2–3 days
Cilostazol	Phosphodiesterase inhibition	11–13 hours	96 hours	Reversible	2–3 days
Eptifibatide	Glycoprotein IIb/IIIa receptor inhibitor	2.5 hours	2–4 hours	Reversible	4 hours
Tirofiban	Glycoprotein IIb/IIIa receptor inhibitor	2 hours	2–4 hours	Reversible	4 hours
Pentoxifylline	Phosphodiesterase inhibition	0.5–1.6 hours	NA	NA	NA

PLT: platelet; NA: not available.

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