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Perioperative Antithrombotic Management in Major Vascular Surgery: A Narrative Review of Competing Thrombotic and Haemorrhagic Risks

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Abstract

Objective: To critically synthesize the available evidence on perioperative antithrombotic strategies across major vascular surgical procedures, with emphasis on study design, level of evidence, and clinical applicability, and to identify persistent evidence gaps.

Methods: A narrative review of the literature was performed, focusing on randomized controlled trials, large observational studies, and major registry datasets evaluating perioperative antithrombotic strategies in vascular surgery. Evidence was stratified according to procedure type, data source, and geographic origin.

Results: The evidence base is overwhelmingly observational, with predominant reliance on North American registry data, particularly the Vascular Quality Initiative (VQI). No procedure-specific randomized controlled trial has directly evaluated perioperative antithrombotic strategies in major vascular surgery. Carotid endarterectomy (CEA) remains the most extensively studied procedure, although the effect of dual antiplatelet therapy (DAPT) on ischaemic outcomes is inconsistent across large datasets (e.g., VQI RR 0.80 in 125,469 patients; pooled international analyses OR 0.87 in 47,411 patients), while an increased bleeding risk is consistently reported across studies. For infrageniculate prosthetic bypass, observational data suggest a potential association between direct oral anticoagulants and improved outcomes compared with warfarin; however, this signal lacks randomized or externally validated confirmation. The WAVE trial, the only large randomized study in peripheral arterial disease evaluating antithrombotic intensification, demonstrated increased bleeding without reduction in major cardiovascular events. Across vascular procedures, no randomized evidence supports routine escalation of perioperative antithrombotic therapy.

Conclusion: Current evidence does not support definitive, procedure-specific recommendations for perioperative antithrombotic management in vascular surgery and should be considered hypothesis-generating. The absence of randomized, procedure-targeted trials represents a major limitation in the field. Future research should prioritize high-quality prospective studies to better define risk–benefit

balance, particularly in high-risk procedures such as major amputation. A structured framework incorporating thrombotic risk, bleeding risk, and procedural factors may support individualized decision-making but requires formal validation.

Keywords: perioperative; antithrombotic; vascular surgery; antiplatelet; anticoagulation; competing risks; dual antiplatelet therapy; haemorrhage; thrombosis; DOAC; confounding by indication.

Highlights

- Vascular surgery patients simultaneously face elevated thrombotic and haemorrhagic risks in the perioperative period. This competing risks scenario is not well-served by uniform protocols and generally requires individualized antithrombotic decision-making.
- The available evidence base is driven almost entirely by observational registry data, predominantly from the North American Vascular Quality Initiative (VQI). No procedure-specific randomized controlled trial has addressed the perioperative antithrombotic question in vascular surgery, and causal inference cannot be drawn from the primary data reviewed.
- For carotid endarterectomy (CEA), the stroke benefit of dual antiplatelet therapy (DAPT) appears inconsistent across studies (VQI registry: RR 0.80; international systematic review: non-significant OR 0.87). The haemorrhagic risk signal is directionally consistent across all datasets and all geographies.
- For prosthetic infrageniculate bypass, VQI registry data suggest DOACs may be associated with better outcomes than warfarin; this signal is hypothesis-generating and has not been confirmed by any randomized trial or European cohort.
- Major amputation represents the most critical evidence gap: the population carries the highest dual-risk profile, yet prospective antithrombotic data are absent.

- A conceptual three-variable decision framework (procedure urgency, intrinsic haemorrhagic risk, individual thrombotic profile) is proposed to structure perioperative antithrombotic reasoning; prospective validation is required before clinical adoption.

Introduction

Patients presenting for major vascular surgery occupy one of the most demanding positions in perioperative medicine. They simultaneously carry some of the highest thrombotic risks encountered in clinical practice and face substantial haemorrhagic risk from the surgery itself. This concurrent dual-risk profile, a competing risks scenario, is particularly pronounced in vascular surgery, where the near-universal coexistence of advanced systemic atherosclerosis with surgical procedures carrying intrinsic bleeding hazard from calcified tissue planes, arteriotomy, systemic heparinisation, and anastomotic suturing defines the perioperative antithrombotic challenge.

Approximately 10–20% of all patients chronically receiving antithrombotic therapy require a surgical procedure each year [1,2]. Among patients presenting for vascular surgery, the vast majority are already on at least one antithrombotic agent, and a growing proportion are on combination therapy [3]. Continuing these agents risks perioperative haemorrhage; interrupting them risks acute thrombosis, stroke, or limb loss. This pharmacological dilemma remains unresolved across every major vascular procedure type.

Methods

This narrative review synthesizes the available evidence on perioperative antithrombotic strategies in vascular surgery, with a targeted focus on major procedure types, study design, and geographic origin. The evidence base is derived almost entirely from observational registry studies, predominantly the Vascular Quality Initiative (VQI), which represents the largest contemporary source of perioperative antithrombotic outcome data in vascular surgery [4–7]. These data are inherently limited by confounding by indication, as patients receiving more intensive antithrombotic regimens are systematically at higher baseline thrombotic risk, precluding causal inference from observed associations. Randomized controlled trial (RCT) evidence specifically addressing perioperative

antithrombotic strategies in vascular surgical populations is essentially absent. The few available randomized trials in peripheral arterial disease populations, including WAVE, CHARISMA, and VOYAGER PAD, were not designed to address perioperative surgical decision-making and therefore provide only indirect contextual evidence [8–10]. Accordingly, the current literature should be interpreted as hypothesis-generating rather than practice-defining.

Interpretation of the evidence is further complicated by substantial geographic asymmetry. The VQI primarily reflects North American practice patterns, where clopidogrel is the dominant antiplatelet agent, whereas ticagrelor use is more prevalent in Europe, particularly following acute coronary syndromes. Additional systematic differences exist in renal impairment prevalence, anticoagulation monitoring practices, and platelet function testing strategies. These differences limit direct transferability of effect estimates across healthcare systems. Furthermore, major guideline frameworks, including the 2023 European Society for Vascular Surgery (ESVS) Antithrombotic Guidelines [1], the 2024 ESVS abdominal aortic aneurysm (AAA) Guidelines [11], the 2026 ESVS Guidelines on Descending Thoracic and Thoraco-Abdominal Aortic Diseases [12], the 2022 American College of Chest Physicians (ACCP) perioperative guideline [2], and the 2024 American Heart Association/American College of Cardiology (AHA/ACC) perioperative cardiovascular guideline [3], reflect differing methodological approaches and interpretative thresholds. Real-world practice variability is further demonstrated by a national survey of 169 German vascular surgery centres, which reported 75% non-compliance with ESVS recommendations and a complete absence of standardized institutional protocols [13]. This variability is not confined to a single healthcare system: the International ACTION survey, conducted by the European Vascular Research Collaborative and the ACTION-1 Research Collaborative among 436 vascular specialists across 45 countries, similarly documented substantial heterogeneity in peri-procedural antithrombotic management — including wide variation in heparin dosing, monitoring, and reversal strategies — together with considerable dissatisfaction with existing protocols [14]. Together, these data likely reflect both clinical uncertainty and the limited robustness of the underlying evidence base.

The literature was identified through a targeted, non-systematic search of MEDLINE, EMBASE, and the Cochrane Library from 2010 to April 2025, including landmark trials irrespective of publication date. Priority was given to randomized controlled trials, large registry-based studies, clinical practice guidelines, and high-quality systematic reviews relevant to perioperative antithrombotic management in vascular surgery. Study selection was based on clinical relevance and interpretative value rather than predefined systematic review eligibility criteria. The search and study selection were performed independently by two reviewers (L.G. and F.F.): titles and abstracts were screened against these criteria, and potentially relevant full-text articles were subsequently assessed in duplicate. Disagreements regarding study inclusion were resolved by discussion between the two reviewers and, where consensus could not be reached, adjudicated by a third senior author (M.L.R.). Studies focusing exclusively on stable outpatient peripheral arterial disease, non-vascular surgical populations, or non-perioperative contexts were excluded. Given the narrative design and heterogeneity of the available evidence, no formal meta-analysis or quantitative synthesis was performed, and no standardized risk-of-bias tool was applied; however, confounding by indication, selection bias, and geographic variability were qualitatively considered throughout interpretation. The objective of this methodological approach is to provide a clinically oriented critical synthesis of the literature rather than a comprehensive systematic review of all available evidence.

Definitions and Terminology

Because key terms in this field are used inconsistently across studies, the following operational definitions are applied throughout this review.

Perioperative. The interval extending from preoperative planning and any antithrombotic interruption, through the intraoperative period, to the early postoperative phase, conventionally up to 30 days after surgery or until the index antithrombotic regimen is resumed, consistent with the time frame adopted in the ACCP and ESVS guidelines [1,2].

Major vascular surgery. Open or endovascular arterial reconstructive procedures, together with major lower-limb amputation, that carry substantial perioperative cardiovascular and/or haemorrhagic risk.

The procedures considered here comprise carotid endarterectomy (CEA), endovascular and thoracic endovascular aortic repair (EVAR and TEVAR), open aortic surgery, infrainguinal (peripheral) bypass, major (above- or below-knee) amputation, and urgent interventions for acute limb ischaemia (ALI). Major amputation is grouped with reconstructive procedures because, although it is not itself a revascularisation, it is performed predominantly in the same end-stage peripheral arterial disease population, shares the same dual thrombotic and haemorrhagic risk profile, frequently follows or coexists with prior vascular reconstruction (including amputation of a limb with a patent proximal bypass), and is routinely captured within vascular surgical registries; excluding it would omit one of the highest-risk and least-studied perioperative antithrombotic scenarios in the specialty.

Major bleeding. In keeping with International Society on Thrombosis and Haemostasis (ISTH) and Bleeding Academic Research Consortium (BARC) criteria, fatal bleeding; symptomatic bleeding in a critical site or organ (for example intracranial haemorrhage, or a neck haematoma compromising the airway after CEA); bleeding causing a fall in haemoglobin of at least 2 g/dL or requiring transfusion of two or more units of red cells; or bleeding requiring reoperation. The primary studies cited in this review apply heterogeneous bleeding definitions, ranging from reoperation for haemorrhage to broader composite clinical endpoints, which limits their direct comparison.

Thrombotic complications. Procedure-relevant arterial thrombotic and thromboembolic events, encompassing perioperative ischaemic stroke or transient ischaemic attack (TIA), myocardial infarction (MI), graft or endograft thrombosis, ALI, and the composite endpoints of major adverse cardiovascular events (MACE) and major adverse limb events (MALE).

Pathophysiology of the Competing Risks Scenario

Thrombotic Risk in the Vascular Patient

Patients requiring major vascular surgery are almost by definition affected by advanced, systemic atherosclerosis. The underlying pathophysiology involves chronic endothelial dysfunction, subintimal lipid accumulation, platelet hyperreactivity, and persistent activation of the coagulation cascade [15,16].

Surgical manipulation, vascular clamping, and reperfusion amplify this prothrombotic state through tissue factor release, complement cascade activation, and platelet aggregation at sites of vessel injury.

Thrombotic risk is not homogeneous across procedures. In CEA, the primary threat is cerebral embolism from unstable plaque or perioperative thrombus formation, with reported stroke rates of 1.5–3% in experienced centres [4]. In peripheral bypass surgery, early graft thrombosis, particularly in prosthetic conduits with poor distal runoff, drives meaningful failure rates in high-risk anatomical configurations, particularly below the knee [17]. In endovascular aortic repair, endograft thrombosis and type I/III endoleaks represent the dominant flow-related complications [18]. Acute limb ischaemia carries mortality rates of 15–20% and amputation rates up to 30% if revascularisation is substantially delayed [19].

Haemorrhagic Risk in the Perioperative Setting

Major vascular surgery is intrinsically haemorrhagic. Dissection through calcified fibrotic tissue planes, systemic heparinisation, and arteriotomy with anastomotic suturing create substantial blood loss potential. When superimposed on ongoing antithrombotic therapy, these factors may produce life-threatening haemorrhage. Return to theatre for bleeding after major vascular surgery has been associated with a two- to four-fold increase in 30-day mortality, prolonged intensive care unit (ICU) stay, and coagulopathy from massive transfusion in observational data [20].

The consequences of haemorrhagic complications extend beyond the immediate postoperative period in procedure-specific ways. Neck haematoma after CEA may compromise airway patency, a uniquely dangerous local consequence. Wound dehiscence following amputation through ischaemic tissue may precipitate stump revision to a higher level. Postoperative haematoma after peripheral bypass may compress and occlude the graft. These procedure-specific haemorrhagic endpoints carry clinical consequences comparable to thrombotic outcomes and merit symmetrical consideration in any evidence evaluation.

The Competing Risks Concept and Its Clinical Implications

Vascular surgery occupies a high-risk zone in both dimensions simultaneously, distinguishing it from other high-stakes perioperative settings. In elective orthopaedic surgery, haemorrhagic risk is high but thrombotic risk from interrupting antithrombotic therapy is often modest. In the early post-coronary stenting period, thrombotic risk from interruption is very high but the procedure itself may carry lower haemorrhagic risk. The simultaneous elevation of both risks, combined with procedural diversity, a full urgency spectrum, and the near-total absence of procedure-specific RCT data, makes protocol-driven uniformity inadequate and individualized decision-making necessary.

Three clinical subgroups carry the highest complexity and most difficult competing risk balance in this population: patients with recent coronary stenting or acute coronary syndrome (peak thrombotic risk from DAPT interruption), patients with atrial fibrillation requiring therapeutic anticoagulation (continuous anticoagulant requirement versus procedural bleeding risk), and patients with advanced renal impairment (uraemic platelet dysfunction compounding haemostatic impairment alongside direct oral anticoagulant (DOAC) accumulation risk). These subgroups are addressed explicitly in the conceptual decision-making framework and represent the clinical scenarios where the absence of RCT data is most consequential.

Results: Evidence by Procedure Type

Carotid Endarterectomy

Carotid endarterectomy is the most extensively studied vascular procedure regarding perioperative antithrombotic management. Despite this, the evidence remains conflicting and derives almost entirely from observational data. The central tension is between two datasets that point in different directions for stroke benefit while agreeing on the direction of haemorrhagic harm.

The Stroke Benefit Signal: Divergent and Uncertain

The two principal evidence sources offer incompatible stroke signals. The largest available dataset, a VQI registry analysis of 125,469 CEA procedures (2010–2021) [4], found DAPT associated with a 20% relative reduction in in-hospital stroke compared with aspirin monotherapy. An earlier VQI cohort

covering 2003–2014 reported an even larger apparent stroke reduction of approximately 40%, though accompanied by nearly doubling of reoperation for bleeding [21]. By contrast, a 2022 EJVES international systematic review and meta-analysis (n=47,411; 11 studies; lead institution University of Toronto, Canada) found no statistically significant stroke reduction with DAPT [22]. A German national statutory quality assurance registry analysis of 117,973 CEA procedures similarly found no significant additional stroke benefit from DAPT [23].

This divergence between North American and international datasets is not straightforwardly resolved by pooling. VQI cohorts include a larger proportion of patients with recent coronary stenting or acutely symptomatic carotid disease, the subgroup where DAPT benefit may be genuine; European datasets may include more elective, lower-risk patients where the incremental benefit of DAPT over aspirin monotherapy appears less evident. Antiplatelet agent differences (ticagrelor versus clopidogrel) may also modify observed effects. The appropriate interpretation is that the stroke benefit of DAPT for CEA is uncertain overall and likely heterogeneous across patient subgroups.

The Haemorrhagic Risk Signal: Consistent and Directional

Unlike the stroke signal, the haemorrhagic risk signal is directionally consistent across all available analyses and across both European and North American data. The large VQI registry analysis reported a 60% relative increase in bleeding complications with DAPT (RR 1.6, 95% CI 1.4–1.8) [4]. The international systematic review found significantly higher reoperation for haemorrhage (OR 1.98, 95% CI 1.77–2.23) and neck haematoma (OR 2.79, 95% CI 1.87–4.18) with DAPT [22]. The Dutch DACI national registry analysis found no statistically significant overall difference between DAPT and single antiplatelet therapy (SAPT) in this population, though numerically higher bleeding rates were observed with DAPT; the authors recommended SAPT at the time of CEA with DAPT reserved for the post-acute stroke period, a direction consistent with the haemorrhagic signal from other datasets [24]. A single-centre European cohort identified DAPT as an independent risk factor for perioperative haemorrhage on multivariate analysis [25]. A large VQI registry-derived risk score analysis (n=192,547) confirmed DAPT as independently associated with reoperation for bleeding (adjusted OR

1.51) and found that patients returning to theatre for bleeding experienced significantly higher rates of 30-day mortality and other adverse events [26].

The asymmetry between evidence quality for the two endpoints, uncertain and inconsistent for stroke benefit; directionally consistent and robust for haemorrhagic harm, represents the most clinically important finding from the CEA antithrombotic literature. This asymmetry supports restricting DAPT to the highest-risk thrombotic subgroups, where the potential thrombotic benefit may more plausibly outweigh the consistent haemorrhagic cost.

Pragmatic Approaches, Long-Term Effects, and Guideline Position

A sequential antithrombotic strategy, consisting of aspirin monotherapy in the preoperative period followed by early postoperative transition to dual antiplatelet therapy (DAPT), has been evaluated in a multicenter cohort of 821 patients and was associated with a combined stroke/death rate of 1.6% with an acceptable haemorrhagic profile, although this remains non-randomized and requires prospective validation before routine adoption [27]. In addition, a retrospective cohort study reported that DAPT was associated with significantly reduced late restenosis after carotid endarterectomy (adjusted OR 0.48, 95% CI 0.30–0.76), without a corresponding reduction in reintervention rates, suggesting a potential morphological effect that has not translated into clear clinical benefit [28]. Current European Society for Vascular Surgery (ESVS) 2023 Guidelines recommend continuation of aspirin monotherapy in most patients undergoing carotid endarterectomy, reserving DAPT for patients with recent coronary stenting or acutely symptomatic carotid disease within two weeks of presentation [1]. This strategy appropriately concentrates intensified antiplatelet therapy in the subgroup with the highest thrombotic risk, where haemorrhagic trade-offs may be more acceptable, while reflecting the consistent safety signal observed across observational datasets.

Overall, the evidence base remains entirely observational, with no randomized controlled trials specifically addressing perioperative antiplatelet strategies in carotid endarterectomy. The available data demonstrate an inconsistent effect of DAPT on stroke prevention across large studies, including a VQI registry analysis of 125,469 patients reporting a relative risk reduction in stroke (RR 0.80),

contrasted with an international systematic review including 47,411 patients showing no statistically significant effect (OR 0.87). By contrast, the haemorrhagic risk associated with DAPT is consistently observed across all major datasets and analytical approaches, including increased bleeding in the VQI registry (RR 1.6), higher reoperation for bleeding (OR 1.98), increased neck haematoma (OR 2.79) in pooled analyses, and an independent association with reoperation in a large VQI-derived risk score cohort (n=192,547; adjusted OR 1.51) [4,22,26]. Across geographies and study designs, the haemorrhagic signal is more stable and reproducible than the thrombotic benefit signal, and all available evidence is subject to confounding by indication inherent to observational data. As a result, the overall interpretation is that DAPT may confer a subgroup-dependent and context-specific stroke benefit, but this remains uncertain, whereas the bleeding risk signal is consistent and likely generalizable across populations.

EVAR and TEVAR

EVAR: Postoperative Antithrombotic Therapy

Endovascular aortic repair presents a distinct antithrombotic challenge: the procedure is less haemorrhagic than open aortic surgery, but the implanted endograft creates a thrombogenic surface and may coexist with underlying atrial fibrillation or other anticoagulation indications.

A retrospective cohort of 616 consecutive EVAR patients found no significant difference in major adverse cardiovascular events between SAPT, anticoagulation, or DAPT at approximately four years [29], suggesting limited incremental benefit from antithrombotic intensification in unselected patients. A separate retrospective cohort found chronic anticoagulation post-EVAR associated with higher incidence of endoleak and reintervention at five years [30]. A 2022 EJVES systematic review and meta-analysis concluded that the overall certainty of evidence is very low; neither antiplatelet therapy nor anticoagulation has demonstrated meaningful clinical benefit in unselected EVAR patients, and anticoagulants may be associated with higher mortality [31]. These findings are hypothesis-generating. SAPT with aspirin remains the pragmatic default for unselected EVAR patients, though it is not evidence-validated. For patients with concurrent atrial fibrillation (AF), anticoagulation for the AF

indication should not be withdrawn on the basis of these observational data without individualized assessment.

TEVAR: Specific Considerations

Thoracic endovascular aortic repair introduces specific complexity: endograft proximity to spinal cord arteries creates a competing risk between antithrombotic therapy and spinal cord ischaemia management. The 2026 ESVS Guidelines on Descending Thoracic and Thoraco-Abdominal Aortic Diseases recommend individualized perioperative anticoagulation management with explicit integration of spinal cord protection protocols [12]. Evidence for TEVAR-specific antithrombotic protocols is limited to expert consensus, and individualized clinical judgment is correspondingly prominent in this procedure type.

Ruptured AAA

In ruptured AAA, haemorrhagic control is the overriding priority. The ESVS 2024 Guidelines recommend deferring systemic heparin until after repair has achieved haemostasis, with postoperative deep vein thrombosis (DVT) prophylaxis initiated once coagulopathy has resolved [11]. When ruptured AAA presents in a patient anticoagulated with warfarin, reversal with 4-factor prothrombin complex concentrate (4F-PCC; 25–50 IU/kg INR-guided, target INR <1.5) is recommended; vitamin K 10 mg IV should be co-administered for sustained effect, with reversal onset within 15–30 minutes.

Peripheral Bypass Surgery

The question of optimal anticoagulation for peripheral bypass has been reshaped by the introduction of DOACs, but the available evidence must be assessed with rigorous geographic and methodological contextualization. Conduit type, prosthetic versus autologous vein, is an important modifier that the evidence does not yet adequately address.

Landmark RCT Evidence: The Cautionary Context

Before reviewing registry-derived DOAC data, the foundational RCT evidence provides an important cautionary context against antithrombotic intensification without clear benefit.

The WAVE trial (n=2,161 PAD patients) demonstrated that adding warfarin to antiplatelet therapy did not reduce the composite of cardiovascular death, MI, or stroke compared with antiplatelet therapy alone, while significantly increasing life-threatening bleeding, an absolute increase of 2.8 percentage points (4.0% versus 1.2%; RR 3.41, p<0.001) [8]. The CHARISMA trial (n=15,603) found that long-term DAPT did not reduce MACE compared with aspirin alone in a PAD and atherothrombosis population, while significantly increasing clinically significant bleeding [9]. Together, these trials suggest that antithrombotic intensification in unselected PAD populations consistently increases haemorrhagic risk without demonstrating clear thrombotic benefit.

The COMPASS PAD substudy (n=7,470 PAD patients) [32] and VOYAGER PAD trial (n=6,564 patients after lower extremity revascularization) [10] demonstrated that low-dose rivaroxaban (2.5 mg twice daily) plus aspirin reduced ischaemic limb and cardiovascular events compared with aspirin alone, at the cost of increased major bleeding without a significant increase in fatal or critical organ bleeding. VOYAGER PAD is the most directly analogous RCT to the post-bypass perioperative context. These findings suggest that low-dose rivaroxaban plus aspirin may be associated with net benefit in carefully selected patients after revascularization, though the balance between ischaemic benefit and haemorrhagic risk must be considered individually.

DOACs vs. Warfarin: VQI Registry Evidence and Historical Context

Three VQI registry analyses constitute the principal contemporary evidence comparing DOACs with warfarin in patients undergoing infrainguinal bypass surgery, and should be interpreted as hypothesis-generating given their observational design and absence of randomization. In a large VQI analysis of infrageniculate bypass procedures (n=2,786; 2007–2020), discharge prescription of DOACs was associated with improved overall survival and graft patency compared with warfarin [5]. A subsequent analysis focusing on prosthetic conduits (n=1,571) reported associations between DOAC use and lower risk of mortality (HR 0.61), loss of patency (HR 0.70), and major amputation (HR 0.71) [6]. A further observational study suggested shorter hospital length of stay and reduced transfusion requirements in patients discharged on DOACs [7]. Historically, a Cochrane systematic review of 14 randomized trials in infrainguinal arterial bypass suggested better vein graft patency with vitamin K antagonists compared

with antiplatelet therapy; however, these studies pre-date the DOAC era and are of variable methodological quality [33]. By contrast, a European retrospective cohort of below-knee autologous vein bypasses found no significant differences in graft patency between DOAC- and warfarin-treated patients, indicating limited external generalizability of the North American registry signals across conduit types and healthcare systems [34].

These associations are likely driven in part by residual confounding and treatment selection bias, as patients receiving DOACs may represent a lower-risk, more contemporary population treated in higher-volume centres with standardized perioperative pathways, with prescribing patterns potentially reflecting institutional practice quality rather than pharmacologic superiority. Randomized controlled trial evidence specific to the perioperative bypass setting is lacking. In peripheral arterial disease populations, the WAVE trial demonstrated that anticoagulation intensification increases life-threatening bleeding without reduction in major cardiovascular events [8], whereas the VOYAGER PAD trial showed that low-dose rivaroxaban plus aspirin reduces ischaemic limb and cardiovascular events after lower extremity revascularization, at the cost of increased bleeding [10]. These trials provide important contextual evidence for antithrombotic intensity but do not directly address bypass-specific perioperative management. Taken together, the available data suggest a possible benefit signal for DOACs in prosthetic bypass grafts that remains unconfirmed in randomized or European studies, with conduit type, indication for anticoagulation, and baseline patient risk likely acting as key modifiers of observed effects.

Major Amputation

Major amputation represents the final stage of peripheral arterial disease and is paradoxically both one of the most common major vascular surgery procedures and one of the most poorly studied from an antithrombotic perspective. Patients arriving for major amputation are systematically underrepresented in most vascular surgery registries.

Patient Profile and High-Risk Subgroup Complexity

Patients presenting for major amputation typically represent the most medically complex subgroup within vascular surgery: residual antithrombotic therapy from multiple prior interventions, frequently impaired renal function, compromised nutritional status, and ischaemic wound beds with poor healing capacity. Three subgroups carry particularly complex competing risk profiles.

Patients with atrial fibrillation, highly prevalent in this elderly, multi-morbid population, require continuous therapeutic anticoagulation while facing substantial wound-level haemorrhagic risk from amputation. The timing and dose of anticoagulation resumption after amputation in this subgroup is entirely unanswered by prospective data.

Patients with residual patent bypasses proximal to the amputation level require continued anticoagulation for graft patency while simultaneously facing amputation wound haemorrhagic risk. How to balance these competing requirements in the immediate post-amputation period is a clinically important and unanswered question.

Patients with significant renal impairment (estimated glomerular filtration rate [eGFR] <30 mL/min) present uraemic platelet dysfunction compounding haemostatic impairment, alongside DOAC accumulation risk requiring dosing adjustment or avoidance of renally eliminated agents.

Procedure-Specific Haemorrhagic Risks

Major amputation involves wide-field soft tissue dissection through ischaemic, poorly vascularized tissue. Wound dehiscence and stump haematoma are common and carry disproportionate consequences: in a limb with impaired healing capacity, a wound complication may delay prosthetic fitting, expose underlying bone to infection, and require revision to a higher amputation level. These outcomes represent a dimension of haemorrhagic risk not captured in standard composite bleeding endpoints used in most vascular surgery registries.

Current Evidence and Practice

There are no prospective randomized or controlled studies specifically addressing perioperative antithrombotic management in major amputation, and the available literature is entirely observational

or consensus-driven. Practice survey data indicate that management is largely empirical: aspirin is generally continued perioperatively, clopidogrel is typically discontinued approximately five days before surgery in most centres, and anticoagulants are managed according to the underlying indication rather than any amputation-specific protocol [13]. A single prospective registry-based cohort has begun to characterize postoperative cardiac risk following major amputation [35], representing the only prospective dataset in this population, although its focus is on risk stratification rather than antithrombotic strategy. In this context, major amputation emerges as the most under-investigated procedure in vascular surgery with respect to perioperative antithrombotic management.

This absence of evidence is particularly relevant given that the population undergoing major amputation concentrates the highest competing-risk burden in vascular surgery. Patients with atrial fibrillation requiring therapeutic anticoagulation, those with residual proximal bypass grafts dependent on anticoagulation for patency, and those with advanced renal impairment represent three clinically important subgroups in whom antithrombotic decision-making is especially complex, yet none are specifically addressed by existing prospective data. As a result, perioperative strategies in these patients remain entirely extrapolated from non-amputation populations and general perioperative principles. This represents a critical evidence gap in the field, as no targeted prospective cohorts, randomized studies, or registry substudies have yet been designed to evaluate antithrombotic interruption, continuation, or resumption strategies in the context of major amputation.

Vascular Emergencies: Acute Limb Ischaemia and Reversal Agent Considerations

Acute Limb Ischaemia: Initial Antithrombotic Management

Acute limb ischaemia requires antithrombotic decisions under time pressure, often with incomplete information about the patient's baseline therapy. ALI is caused by arterial embolism (30–46% of cases), in-situ thrombosis (24–40%), graft thrombosis (approximately 20%), or popliteal aneurysm thrombosis (approximately 5%) [36]. The recently published PROMOTE-ALI study, a prospective multicentre observational cohort conducted by the European Vascular Research Collaborative, has further characterized contemporary ALI presentation, management, and outcomes, underscoring persistently

high rates of death and major amputation and identifying factors associated with loss of amputation-free survival [37]. Intravenous unfractionated heparin (UFH) is the cornerstone of initial management, recommended by ESVS 2023 Guidelines for all patients with suspected ALI planned for urgent intervention, pending formal Rutherford staging [1]. UFH is generally preferred over low molecular weight heparin (LMWH) in the acute setting because it allows rapid reversal with protamine and dose titration via activated partial thromboplastin time (APTT) monitoring.

Reversal Agents in Vascular Emergencies

Three specific reversal agents are clinically relevant in vascular emergencies and must feature in institutional preparedness protocols, as their availability varies substantially across European hospitals.

Idarucizumab (5 g IV in two sequential vials) provides dabigatran reversal within minutes, with a duration of approximately 24 hours; re-heparinisation is immediately possible following reversal.

Andexanet alfa reverses Factor Xa inhibitors (rivaroxaban, apixaban) via weight- and dose-dependent IV bolus/infusion. European Medicines Agency (EMA) approval has not translated into universal formulary availability across European hospitals due to acquisition cost. A clinically important post-reversal thrombotic rebound risk warrants monitoring.

4-Factor Prothrombin Complex Concentrate (4F-PCC; 25–50 IU/kg INR-guided) is the standard for warfarin reversal, with target INR <1.5; onset within 15–30 minutes; vitamin K 10 mg IV co-administered for sustained effect.

In life-threatening vascular emergencies, surgery without full reversal may be preferable to delays awaiting unavailable agents. No prospective data exist on the optimal DOAC–UFH interaction sequence in ALI; post-intervention antithrombotic regimen following ALI revascularisation is entirely consensus-based.

Geographic Asymmetry of the Evidence Base and Real-World Practice Variability

Two features of the current evidence base bear directly on its interpretation. First, most high-volume perioperative antithrombotic datasets originate from North American registries, particularly the VQI,

whereas European antiplatelet selection and perioperative pathways differ, so registry-derived effect estimates may not transfer directly across healthcare systems. Second, real-world implementation is highly variable: surveys of both German centres and the wider international vascular community document frequent deviation from guideline recommendations and an absence of standardized institutional protocols [13,14], while VQI analyses of infrainguinal bypass reveal centre-level heterogeneity in antithrombotic prescribing that is only partially explained by patient or conduit characteristics [5–7]. Taken together, these observations indicate that registry-derived estimates should be regarded as context-dependent rather than universally generalisable.

Evidence Summary

The evidence base for perioperative antithrombotic management in vascular surgery is characterized by three consistent structural features across procedures.

First, the literature is dominated by observational registry data, primarily from North American sources, with very limited randomized controlled trial evidence directly addressing perioperative surgical contexts. As a result, all reported associations should be interpreted as hypothesis-generating rather than causal.

Second, across all vascular procedures, a consistent asymmetry is observed between thrombotic and haemorrhagic endpoints. While estimates of thrombotic benefit vary substantially across studies and populations, bleeding risk signals associated with intensified antithrombotic therapy are more consistently directionally concordant across datasets and geographic settings.

Third, evidence certainty declines systematically with procedural urgency and complexity. Elective carotid and infrainguinal procedures are supported by the largest observational datasets, whereas endovascular aortic interventions rely on lower-certainty evidence, and major amputation and vascular emergencies are largely informed by consensus-based practice.

These patterns are synthesized in Figure 1, which illustrates the procedural hierarchy of evidentiary certainty, and in Table 1, which summarizes procedure-specific findings and gaps. Together, these

elements define a structured interpretive framework used throughout this review and highlight the progressive shift from data-informed to consensus-driven decision-making in vascular surgery.

A Conceptual Framework for Perioperative Antithrombotic Decision-Making

Perioperative antithrombotic management in vascular surgery cannot be standardized across procedures or patient groups. The available evidence supports a structured, risk-stratified approach based on three interacting determinants: procedure urgency, intrinsic haemorrhagic risk, and individual thrombotic risk profile.

Procedure urgency defines the time window available for modification of antithrombotic therapy, ranging from elective surgery, where planned interruption or bridging strategies can be implemented, to emergency vascular scenarios in which immediate haemostatic control supersedes pharmacological optimization [1–3].

Intrinsic haemorrhagic risk is primarily procedure-dependent. Endovascular interventions generally confer lower bleeding risk, whereas open aortic surgery, major amputation, and ruptured vascular emergencies carry substantially higher haemorrhagic burden [11,12].

Individual thrombotic risk is driven by patient-level factors, including recent coronary stenting, acute limb ischaemia, mechanical heart valves, atrial fibrillation, and advanced peripheral arterial disease [8–10,32].

Within this three-axis framework, perioperative decisions should be individualized and multidisciplinary, particularly in patients with competing high-risk features. The model is intended to formalize risk visibility rather than prescribe fixed therapeutic pathways.

Discussion

The principal finding of this review is the marked limitation of the current evidence base, which is dominated by observational registry data and lacks procedure-specific randomized controlled trials. Within this context, observed associations should be interpreted as descriptive rather than causal. The

527 divergence seen in carotid endarterectomy between studies suggesting potential stroke reduction with
528 dual antiplatelet therapy and those showing no benefit likely reflects differences in case selection,
529 procedural urgency, and regional practice patterns rather than true biological disagreement. Importantly,
530 the haemorrhagic risk signal associated with dual antiplatelet therapy is more consistent across datasets
531 and populations [4,22–26].

532 In peripheral arterial disease and infrainguinal bypass, randomized evidence from unselected PAD
533 populations demonstrates that intensification of antithrombotic therapy increases bleeding risk without
534 clear overall cardiovascular benefit [8,9]. Registry-based signals suggesting improved outcomes with
535 direct oral anticoagulants in selected bypass populations [5–7] remain unconfirmed in randomized
536 settings and should be interpreted cautiously in light of inherent selection effects.

537 Overall, the evidence supports the concept that the net benefit of antithrombotic intensification is highly
538 context-dependent, varying according to procedure type and patient risk profile, and cannot be
539 generalized across vascular surgical populations.

540 **The Role of Survey and Secondary Data**

541 This review has included practice survey data and has limited their interpretive weight to characterizing
542 practice heterogeneity and guideline non-compliance. Survey data describe prescribing patterns; they
543 do not constitute clinical evidence supporting or refuting antithrombotic strategies. Similarly, secondary
544 sources including narrative reviews and expert consensus documents have been used as contextual
545 sources, not as primary evidence for clinical effect estimates.

546 **Future Research Priorities**

547 **Randomized controlled trials.** No procedure-specific RCT addresses the perioperative antithrombotic
548 question in vascular surgery. Adaptive platform or Bayesian adaptive designs may address reluctance
549 to randomize when one arm involves interrupting protective therapy. Priority populations include CEA
550 patients on DAPT for recent acute coronary syndrome (ACS), prosthetic bypass patients comparing
551 DOAC versus warfarin, and major amputation patients on DOACs or dual antithrombotic therapy.

Prospective international registries. Coordinated ESVS–SVS (Society for Vascular Surgery) prospective registry collaboration, with standardized data collection on antithrombotic agent, dose, timing of last preoperative administration, intraoperative anticoagulation, reversal agent use, and resumption timing, would substantially advance this field. Specific substudies should target major amputation populations.

Prospective validation of the decision framework. The three-variable framework proposed in this review requires prospective validation: apply the framework at preoperative decision-making, document actual decisions and deviations, record 30-day and one-year thrombotic and haemorrhagic outcomes, and assess interrater reliability of variable classification.

Point-of-care biomarker panels. Standard risk scores (HAS-BLED, CHA_2DS_2-VASc) were developed in non-surgical populations. Multicenter validation of point-of-care panels incorporating thromboelastography (TEG/ROTEM), platelet function assays (VerifyNow), and thrombin generation assays may enable real-time individualized assessment of the competing risks profile.

Limitations

This review has several limitations that should be acknowledged. The underlying literature is highly heterogeneous with respect to study design, patient populations, definitions of antithrombotic exposure, and outcome reporting, particularly for bleeding endpoints, which vary from reoperation to composite clinical measures [4,22–26]. The evidence base is dominated by retrospective observational studies, primarily derived from large registries [4–7], and is therefore subject to confounding by indication and residual confounding despite multivariable adjustment. A substantial proportion of available data originates from a single North American registry [4], which may limit generalizability to European and other healthcare systems due to differences in antithrombotic practice patterns, perioperative pathways, and patient characteristics [13]. In addition, important perioperative variables such as timing of drug interruption and resumption, intraoperative anticoagulation management, and use of reversal agents are inconsistently reported or absent [11,12], limiting interpretability and clinical translation. Finally, the narrative design of this review introduces the potential for selection and interpretive bias, as study

inclusion was based on clinical relevance rather than formal systematic review methodology. These limitations reinforce the observational and hypothesis-generating nature of the available evidence.

Conclusions

Perioperative antithrombotic management in vascular surgery remains an area of substantial evidence uncertainty, dominated by observational data and lacking procedure-specific randomized trials. As a result, causal inference is not currently possible, and clinical recommendations must rely on contextual risk interpretation rather than standardized protocols.

Across procedures, the effect of antithrombotic intensification is inconsistent or unproven, while bleeding risk signals are more stable and reproducible. In carotid endarterectomy, dual antiplatelet therapy shows a consistent increase in bleeding without a clearly established stroke benefit. In peripheral arterial disease, randomized trials show harm in unselected populations, while registry signals for direct oral anticoagulants remain hypothesis-generating. Major amputation represents the most significant evidence gap in the field.

Clinical decision-making should therefore remain individualized, explicitly risk-balanced, and procedure-specific until randomized evidence becomes available.

TAKE-HOME MESSAGES

◆ **Carotid Endarterectomy**

- *Dual antiplatelet therapy (DAPT) is associated with a consistent increase in bleeding complications, while stroke benefit remains inconsistent and likely subgroup-dependent.*
- *Aspirin monotherapy remains the default perioperative regimen for most patients undergoing CEA.*
- *DAPT should be restricted to high thrombotic risk scenarios (e.g., recent coronary stenting or acute cerebrovascular presentation).*

◆ **EVAR / TEVAR**

- *For unselected EVAR patients, no antithrombotic intensification strategy has demonstrated clear clinical benefit in observational or RCT-derived evidence.*
- *Single antiplatelet therapy is a pragmatic default approach, unless a separate systemic indication for anticoagulation exists (e.g., atrial fibrillation).*
- *In TEVAR, antithrombotic management must be individualized and integrated with spinal cord protection strategies, given the absence of procedure-specific evidence.*

◆ **Peripheral Bypass Surgery**

- *RCT evidence in PAD does not support routine antithrombotic intensification due to increased bleeding without consistent cardiovascular benefit (WAVE, CHARISMA).*
- *Low-dose rivaroxaban plus aspirin (VOYAGER PAD regimen) may be beneficial after revascularization in selected patients, but perioperative applicability remains uncertain.*
- *Observational signals suggesting DOAC superiority over warfarin in bypass surgery are hypothesis-generating only and not practice-defining.*

◆ **Major Amputation**

- *There is a complete absence of procedure-specific prospective evidence guiding perioperative antithrombotic management in major amputation.*
- *Antithrombotic therapy should generally be managed according to the underlying indication (AF, graft patency, PAD stage) rather than the amputation procedure itself.*
- *Patients with combined AF, prosthetic grafts, or severe renal impairment represent the highest-risk and least-evidence-supported subgroup.*

◆ **Acute Limb Ischaemia & Emergencies**

- *Intravenous unfractionated heparin remains the standard initial therapy for ALI prior to revascularization, unless contraindicated.*
- *DOAC reversal (idarucizumab, andexanet alfa, PCC) should be protocol-driven and immediately available in vascular emergency pathways.*

- *In life-threatening vascular emergencies, delaying surgery for full anticoagulation reversal may be harmful; rapid intervention often takes precedence.*

◆ **Global Principle**

- *Across all vascular procedures, the net clinical effect of antithrombotic intensification is highly context- and patient-dependent.*
- *Bleeding risk signals are generally more consistent and reproducible than thrombotic benefit signals across observational datasets.*
- *No procedure-specific randomized controlled trial currently exists; therefore, all strategies remain individualized and non-definitive.*

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Figure Legends

Figure 1. Evidence hierarchy across major vascular surgical procedures. Procedures are stratified according to evidence source, study design, and inferential certainty. Observational data dominate across all domains, with decreasing evidence strength from elective carotid and peripheral bypass surgery to endovascular aortic procedures and complete evidence gaps in major amputation and vascular emergencies. Bleeding risk signals are more consistent across datasets than thrombotic benefit signals. **Abbreviations: AAA, abdominal aortic aneurysm; EVAR, endovascular aortic repair; RCT, randomised controlled trial; SR, systematic review; TEVAR, thoracic endovascular aortic repair; VQI, Vascular Quality Initiative.**

Table Legends

Table 1. Evidence summary by procedure type. Evidence levels are assigned using an adapted CEBM framework for descriptive purposes only. All evidence is subject to the overarching interpretive position established in the introduction: available findings are hypothesis-generating rather than practice-defining in the absence of procedure-specific RCT data.

Table 2. Conceptual framework intended to structure perioperative antithrombotic reasoning. The table is not a treatment algorithm and should not be interpreted as a substitute for formal guideline recommendations or individualized multidisciplinary decision-making.

Table 1. Evidence summary by procedure type. Evidence levels are assigned using an adapted CEBM framework for descriptive purposes only. All evidence is subject to the overarching interpretive position established in the introduction: available findings are hypothesis-generating rather than practice-defining in the absence of procedure-specific RCT data.

Procedure	Evidence Level	Geographic Origin	Principal Findings	Evidence Gap
CEA	IIa–IIb (observational)	NA (VQI) + International systematic review	DAPT stroke benefit: inconsistent (VQI RR 0.80 vs. international systematic review non-significant OR 0.87). Haemorrhagic risk: directionally consistent (RR 1.6 bleeding; OR 1.98 reoperation; OR 2.79 neck haematoma). Dutch DACI: no significant DAPT vs. SAPT difference.	No RCT. Divergent stroke signal. DAPT benefit uncertain overall; may be subgroup-specific.
EVAR	IIb–III (observational, very low certainty)	Mixed (predominantly European)	SAPT likely sufficient for unselected patients. Anticoagulation may increase endoleak risk (low certainty, hypothesis-generating).	No RCT. Endoleak mechanism uncertain. Complex anatomy subgroups unstudied.
TEVAR	III–IV (expert consensus)	Expert consensus	Individualized approach required. Spinal cord protection protocols must be explicitly integrated.	No prospective data. Optimal agent, dose, and duration undefined.
Peripheral bypass (prosthetic)	IIb (observational, VQI) + RCT context (VOYAGER PAD)	NA (VQI) + International RCTs	DOACs may be associated with better outcomes than warfarin (VQI, n=1,571–2,786). WAVE trial: combination therapy substantially increases haemorrhagic risk without MACE benefit (RCT, n=2,161). VOYAGER PAD: rivaroxaban + aspirin reduces events after revascularization (RCT, n=6,564).	No perioperative-specific RCT. No European data confirming VQI DOAC advantage. Effect may be conduit-type specific.
Peripheral bypass (autologous vein)	IIb–III (limited observational)	Mixed	VKA historically associated with better venous graft patency (Cochrane, 14 RCTs). European cohort: no significant DOAC vs. warfarin patency difference.	Single European cohort. Cochrane data pre-date DOAC era.
Major amputation	IV (survey/empirical)	Survey only	All management is empirical. Aspirin typically continued; clopidogrel suspended 5 days preoperatively;	No prospective data. Highest dual-risk profile; most underrepresented in evidence base.

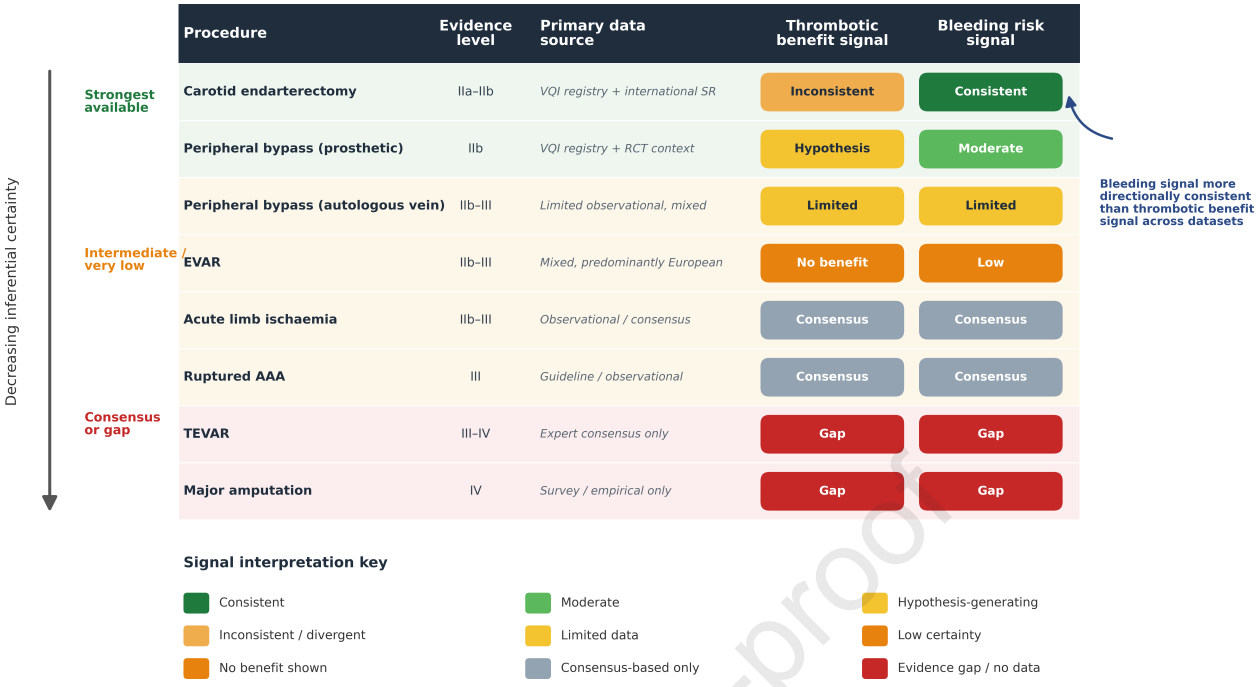
Procedure	Evidence Level	Geographic Origin	Principal Findings	Evidence Gap
			anticoagulants managed by underlying indication.	
Acute limb ischaemia	IIb–III (observational/consensus)	Mixed	UFH recommended for all patients planned for intervention. Reversal agents (idarucizumab, andexanet alfa) for DOAC-anticoagulated patients.	No prospective DOAC–UFH interaction data. Post-intervention antithrombotic regimen undefined.
Ruptured AAA	III (observational/guideline)	Mixed	Defer systemic anticoagulation until haemostasis achieved. Warfarin reversal with 4F-PCC (INR target <1.5).	Reversal agent availability variable. Optimal heparin protocols for EVAR of ruptured AAA undefined.

Abbreviations: 4F-PCC, four-factor prothrombin complex concentrate; AAA, abdominal aortic aneurysm; CEA, carotid endarterectomy; CEBM, Centre for Evidence-Based Medicine; DACI, Dutch Audit for Carotid Interventions; DAPT, dual antiplatelet therapy; DOAC, direct oral anticoagulant; EVAR, endovascular aortic repair; INR, international normalised ratio; MACE, major adverse cardiovascular events; NA, not applicable; OR, odds ratio; PAD, peripheral arterial disease; RCT, randomised controlled trial; RR, relative risk; SAPT, single antiplatelet therapy; TEVAR, thoracic endovascular aortic repair; UFH, unfractionated heparin; VKA, vitamin K antagonist; VQI, Vascular Quality Initiative; WAVE, Warfarin Antiplatelet Vascular Evaluation.

Table 2. Conceptual framework intended to structure perioperative antithrombotic reasoning. The table is not a treatment algorithm and should not be interpreted as a substitute for formal guideline recommendations or individualized multidisciplinary decision-making.

Variable	Lower Risk	Intermediate Risk	Higher Risk
Procedure urgency	Elective (>4 weeks planned)	Semi-urgent (1–4 weeks)	Emergency / Vascular emergency
Intrinsic haemorrhagic risk	EVAR (percutaneous access)	Open infrainguinal bypass	Open aortic repair / Major amputation / Ruptured AAA
Individual thrombotic profile	Stable PAD, SAPT only, no recent ACS/stent	Chronic AF on anticoagulation, CLTI on DAPT	Recent coronary stent (<3 months), active ALI, mechanical valve
Suggested approach	Continue SAPT. Hold anticoagulation per standard bridging (ACCP/ESVS protocol).	Individualized: weigh procedure haemorrhagic risk vs. interruption risk explicitly. Consider reduced-dose or abbreviated bridging. Document reasoning.	Minimize interruption or employ reversal agents where available. Document competing risk explicitly. Multidisciplinary input where feasible.
High-risk patient subgroup modifiers		Advanced renal impairment (eGFR <30): adjust DOAC dosing; assess uraemic platelet dysfunction; consider point-of-care platelet function testing.	AF on anticoagulation + major amputation: highest-complexity competing risk scenario; no data to guide resumption timing. Residual proximal bypass + amputation: simultaneous graft and wound haemorrhagic risk; no prospective data.

Abbreviations: AAA, abdominal aortic aneurysm; ACCP, American College of Chest Physicians; ACS, acute coronary syndrome; AF, atrial fibrillation; ALI, acute limb ischaemia; CLTI, chronic limb-threatening ischaemia; DAPT, dual antiplatelet therapy; DOAC, direct oral anticoagulant; eGFR, estimated glomerular filtration rate; ESVS, European Society for Vascular Surgery; EVAR, endovascular aortic repair; PAD, peripheral arterial disease; SAPT, single antiplatelet therapy.



Procedure	Evidence level	Primary data source	Thrombotic benefit signal	Bleeding risk signal
Carotid endarterectomy	IIa–IIb	*VQI registry + international SR*	**Inconsistent**	**Consistent**
Peripheral bypass (prosthetic)	IIb	*VQI registry + RCT context*	**Hypothesis**	**Moderate**
Peripheral bypass (autologous vein)	IIb–III	*Limited observational, mixed*	**Limited**	**Limited**
EVAR	IIb–III	*Mixed, predominantly European*	**No benefit**	**Low**
Acute limb ischaemia	IIb–III	*Observational / consensus*	**Consensus**	**Consensus**
Ruptured AAA	III	*Guideline / observational*	**Consensus**	**Consensus**
TEVAR	III–IV	*Expert consensus only*	**Gap**	**Gap**
Major amputation	IV	*Survey / empirical only*	**Gap**	**Gap**

Signal interpretation key

- Consistent
- Inconsistent / divergent
- No benefit shown
- Moderate
- Limited data
- Consensus-based only
- Hypothesis-generating
- Low certainty
- Evidence gap / no data