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υπό

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"ANTITHROMBOTIC TREATMENT AFTER COMPLEX ENDOVASCULAR REPAIR FOR THORACOABDOMINAL ANEURYSMS"

by

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To my children Apostolos and Iokasti who give meaning to everything I do.

To my father and mother, for their endless love and support.

And to my wife, for standing by me every step of the way.

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1. ABSTRACT

Introduction:

Complex endovascular aortic repair (F/BEVAR and ChEVAR) has become an established treatment option for thoracoabdominal and juxtarenal aneurysms. Despite the increasing number of procedures, evidence guiding optimal postoperative antithrombotic therapy for maintaining target vessel patency and reducing thrombotic events remains limited. Current practice varies widely, and concerns persist regarding both the efficacy of antiplatelet or anticoagulant regimens and the associated bleeding risk.

Materials & Methods:

This systematic review was conducted in accordance with PRISMA 2020 guidelines. A structured search of PubMed, SCOPUS, and CENTRAL databases was performed until March 1st, 2025. Eligible studies included patients undergoing elective FEVAR, BEVAR, or ChEVAR in which postoperative antithrombotic therapy and outcomes on target vessel patency, occlusion, reintervention, and bleeding complications were reported. Case reports, non-English publications, and studies without specific reference to antithrombotic regimens were excluded. Given the limited number of studies and heterogeneity of protocols, a descriptive synthesis of the available data was performed.

Results:

Four observational studies met the inclusion criteria, encompassing a total of 3,138 patients and more than 6,200 target vessels. Antithrombotic regimens varied, including single antiplatelet therapy (SAPT), dual antiplatelet therapy (DAPT), oral anticoagulation (OAC), and combinations thereof. DAPT was associated with improved short- to mid-term target vessel patency in two multicenter analyses, without a corresponding increase in major bleeding events. One large registry study suggested a protective effect of DAPT on branch vessel outcomes compared with SAPT, while another demonstrated increased cardiovascular ischemic event prevention with DAPT, particularly in BEVAR patients. However, two single-center retrospective studies did not confirm a statistically significant benefit of DAPT over SAPT, and none

demonstrated superiority of OAC. The incidence of bridging stent occlusion remained low overall (<6%), with higher occlusion rates observed in renal arteries compared with visceral branches.

Conclusions:

The current evidence does not provide definitive guidance on the optimal antithrombotic regimen after complex EVAR. DAPT appears to confer advantages in maintaining target vessel patency and reducing ischemic complications, particularly in BEVAR cases, while not significantly increasing early bleeding events. Nevertheless, the available data remain limited, heterogeneous, and observational in nature. Further randomized controlled trials are needed to validate these findings and establish standardized recommendations for antithrombotic therapy after complex aortic repair.

Keywords: complex endovascular repair, FEVAR, BEVAR, ChEVAR, antithrombotic therapy, SAPT, DAPT, DOAC, patency, target vessel, occlusion

2.ΠΕΡΙΛΗΨΗ

Εισαγωγή:

Η ενδοαγγειακή αποκατάσταση σύνθετων ανευρυσμάτων (F/BEVAR και ChEVAR) έχει καθιερωθεί τα τελευταία χρόνια ως θεραπευτική επιλογή για θωρακοκοιλιακά και παρανεφρικά ανευρύσματα. Παρά τη διευρυμένη εφαρμογή των σύνθετων ενδοαγγειακών επεμβάσεων, τα διαθέσιμα δεδομένα σχετικά με τη βέλτιστη μετεγχειρητική αντιθρομβωτική αγωγή για τη διατήρηση της βατότητας των αγγείων στόχων και την αποφυγή θρομβωτικών επιπλοκών παραμένουν περιορισμένα. Η πρακτική διαφέρει σημαντικά μεταξύ των διαφόρων κέντρων, ενώ εξακολουθούν να υπάρχουν προβληματισμοί σχετικά με την αποτελεσματικότητα και τον αιμορραγικό κίνδυνο των αντιαιμοπεταλιακών και αντιπηκτικών φαρμάκων και του χρόνου χορήγησής τους.

Υλικά & Μέθοδοι:

Η παρούσα συστηματική ανασκόπηση πραγματοποιήθηκε σύμφωνα με τις κατευθυντήριες οδηγίες PRISMA 2020. Η αναζήτηση πραγματοποιήθηκε στις βάσεις δεδομένων PubMed, SCOPUS και CENTRAL με καταληκτική ημερομηνία την 1η Μαρτίου 2025. Συμπεριλήφθηκαν μελέτες σε ασθενείς που υπεβλήθησαν σε FEVAR, BEVAR ή ChEVAR, όπου καταγράφονταν η μετεγχειρητική αντιθρομβωτική αγωγή και τα αποτελέσματα σχετικά με τη βατότητα των αγγείων στόχων, την βατότητα αυτών, τις επανεπεμβάσεις και τις αιμορραγικές επιπλοκές. Εξαιρέθηκαν αναφορές περιστατικών, μη αγγλόφωνες δημοσιεύσεις και άρθρα χωρίς συγκεκριμένη αναφορά στην αντιθρομβωτική αγωγή. Λόγω της ετερογένειας των δεδομένων και του περιορισμένου αριθμού μελετών, πραγματοποιήθηκε περιγραφή των αποτελεσμάτων των μελετών.

Αποτελέσματα:

Συνολικά τέσσερις παρατηρητικές μελέτες πληρούσαν τα κριτήρια ένταξης, περιλαμβάνοντας 3.138 ασθενείς και περισσότερα από 6.200 αγγεία στόχους. Οι χρησιμοποιούμενες αντιθρομβωτικές αγωγές περιλάμβαναν μονή αντιαιμοπεταλιακή αγωγή (SAPT), διπλή αντιαιμοπεταλιακή αγωγή (DAPT), από του στόματος αντιπηκτικά (OAC) και συνδυασμούς τους. Η διπλή

αντιαιμοπεταλιακή αγωγή, συσχετίστηκε με βελτιωμένα ποσοστά βατότητας βραχυπρόθεσμα και μεσοπρόθεσμα σε δύο πολυκεντρικές μελέτες, χωρίς αντίστοιχη αύξηση μείζονων αιμορραγικών επεισοδίων. Μία μεγάλη μελέτη κατέδειξε προστατευτικό όφελος της διπλής αντιαιμοπεταλιακής αγωγής όσων αφορά την βατότητα των αγγείων στόχων σε ασθενείς που υπεβλήθησαν σε BEVAR έναντι της μονής αντιαιμοπεταλιακής αγωγής, ενώ άλλη ανέδειξε μείωση ισχαιμικών καρδιαγγειακών συμβαμάτων, ιδίως σε ασθενείς που υπεβλήθησαν σε BEVAR. Ωστόσο, δύο μονοκεντρικές αναδρομικές μελέτες δεν επιβεβαίωσαν στατιστικά σημαντική υπεροχή της διπλής έναντι της μονής αντιαιμοπεταλιακής αγωγής, ενώ καμία δεν τεκμηρίωσε υπεροχή των από του στόματος αντιπηκτικών. Το συνολικό ποσοστό απόφραξης των ενδοναρθήκων ήταν χαμηλό (<6%), με υψηλότερα ποσοστά απόφραξης των νεφρικών αρτηριών έναντι των σπλαχνικών αγγείων.

Συμπεράσματα:

Τα διαθέσιμα δεδομένα δεν επαρκούν για την εξαγωγή σαφών οδηγιών σχετικά με τη βέλτιστη μετεγχειρητική αντιθρομβωτική αγωγή μετά από σύνθετη ενδοαγγειακή αποκατάσταση ανευρυσμάτων. Η διπλή αντιαιμοπεταλιακή αγωγή φαίνεται να προσφέρει οφέλη στη διατήρηση της βατότητας των αγγείων στόχων και στη μείωση των ισχαιμικών επιπλοκών, κυρίως σε επεμβάσεις BEVAR, χωρίς να αυξάνει σημαντικά τον αιμορραγικό κίνδυνο. Ωστόσο, τα διαθέσιμα στοιχεία είναι περιορισμένα, ετερογενή και από αναδρομικές μελέτες παρατήρησης. Απαιτούνται τυχαιοποιημένες κλινικές μελέτες για να επιβεβαιωθούν τα αποτελέσματα αυτά και να καθοριστούν τεκμηριωμένες κατευθυντήριες οδηγίες για την αντιθρομβωτική αγωγή μετά από F/BEVAR και ChEVAR.

3. ABBREVIATIONS

*In order of appearance

EVAR; Endovascular Aneurysm Repair

FEVAR; Fenestrated Endovascular Aneurysm Repair

BEVAR; Branched Endovascular Aneurysm Repair

ChEVAR; Chimney Endovascular Aneurysm Repair

SAPT; Single Antiplatelet Therapy

DAPT; Dual Antiplatelet Therapy

OAC; Oral Anticoagulation

DOAC; Direct Oral Anticoagulant

PRISMA; Preferred Reporting Items for Systematic Reviews and Meta-Analyses

RCT; Randomized Controlled Trial

CTA; Computed Tomography Angiography

OSR; Open Surgical Repair

TAAA; Thoracoabdominal Aortic Aneurysm

SMA; Superior Mesenteric Artery

RAA; Renal Artery Aneurysm

IVUS; Intravascular Ultrasound

ESVS; European Society for Vascular Surgery

SVS; Society for Vascular Surgery

NICE; National Institute for Health and Care Excellence

VKA; Vitamin K Antagonist

US-ARC; US-Aortic Research Consortium

ROBINS-I; Risk of Bias in Non-Randomized Studies of Interventions

HR; Hazard Ratio

4. INTRODUCTION

4.1 Background on Aneurysmal Disease

Aneurysmal disease, particularly of the aorta, represents a significant global health burden due to its silent progression and potentially fatal outcomes. Aneurysms are defined as permanent dilatations of an artery, with an increase in diameter of at least 50% compared to the expected normal size for a given segment. In the case of the abdominal aorta, this generally refers to a diameter exceeding 3 cm, while thoracic aneurysms are typically diagnosed when the diameter exceeds 4.5 cm in the ascending segment or 6.0 cm in the descending aorta [1]. Aortic aneurysms are broadly classified into thoracic, abdominal, or thoracoabdominal based on anatomical location. They may occur as isolated findings or as part of systemic conditions like connective tissue disorders or inflammatory syndromes. The pathophysiology involves complex interactions between genetic predisposition, inflammation, proteolytic degradation of extracellular matrix components (mainly elastin and collagen), and biomechanical wall stress [2]. Atherosclerosis, hypertension, smoking, and male sex are the strongest established risk factors, particularly for abdominal aortic aneurysms (AAAs) [3].

The prevalence of AAAs in men over 65 years is approximately 4-8%, while thoracic and thoracoabdominal aneurysms are less common but often more complex to manage [4]. Thoracoabdominal aortic aneurysms (TAAAs), which involve both thoracic and abdominal segments, are especially challenging due to the inclusion of vital visceral arteries, such as the celiac trunk, superior mesenteric artery (SMA), and renal arteries [5]. Left untreated, aneurysms may continue to enlarge, ultimately leading to rupture-a catastrophic event associated with mortality rates exceeding 80% in most series [6]. Over the past two decades, the natural history of aneurysmal disease has been reshaped by advances in screening, surveillance, and especially treatment strategies. While open surgical repair (OSR) was historically the standard approach, endovascular aneurysm repair (EVAR) has become the preferred option for many patients due to its reduced perioperative morbidity and mortality [7]. However, conventional EVAR is not feasible in

many patients with complex anatomy—particularly those with aneurysms involving branch vessels—which has led to the development of more advanced techniques such as fenestrated EVAR (FEVAR), branched EVAR (BEVAR), and chimney EVAR (ChEVAR). Despite these advancements, the optimal management of aneurysmal disease remains complex and individualized. Patient-specific factors such as age, comorbidities, life expectancy, and anatomic suitability heavily influence treatment choice. Furthermore, long-term durability and prevention of complications such as endoleak, graft migration, or thrombosis remain central concerns, especially in complex cases [8]. In parallel with the evolution of surgical techniques, there is growing interest in understanding the role of antithrombotic therapies in preventing thrombotic graft complications, preserving stent patency, and improving long-term outcomes after endovascular repair. This area, however, remains underexplored in the context of complex thoracoabdominal interventions and represents a key focus of this thesis.

4.2 Types of aneurysms involving renal arteries and thoracoabdominal aorta

Aneurysms involving the renal arteries and thoracoabdominal aorta are classified as complex aortic aneurysms, primarily due to their anatomical proximity to or involvement of vital visceral branches. These aneurysms pose unique technical and clinical challenges, requiring advanced planning and individualized treatment strategies.

4.2.1 Renal Artery Involvement

Aneurysms that extend to or originate near the renal arteries are considered juxtarenal, pararenal, or suprarenal, depending on their precise relationship to the renal arteries.

- **Juxtarenal aneurysms** are located immediately adjacent to the renal arteries without involving them directly.

- **Pararenal aneurysms** involve the renal arteries but not the superior mesenteric artery (SMA).
- **Suprarenal aneurysms** extend above the renal arteries and may involve both renal and visceral branches [1].

These distinctions are not just anatomical but carry implications for procedural planning. For example, infrarenal aneurysms are typically suitable for standard EVAR, whereas aneurysms involving the renal arteries require advanced techniques such as fenestrated or branched endografts, or chimney grafts, to maintain renal perfusion during repair [9].

In rare instances, isolated renal artery aneurysms (RAAs) can occur. These are generally saccular and may be congenital, traumatic, or related to connective tissue disorders. While uncommon, their management may necessitate endovascular or open intervention, particularly if symptomatic, enlarging, or discovered in women of childbearing age [10].

4.2.2. Thoracoabdominal Aneurysms (TAAAs)

Thoracoabdominal aortic aneurysms (TAAAs) represent a more extensive form of aneurysmal disease that spans both the thoracic and abdominal portions of the aorta. These aneurysms often involve multiple visceral branches including the celiac trunk, SMA, and both renal arteries, making them particularly hazardous and technically demanding to treat.

The Crawford classification, first introduced in 1986 and later refined by Safi et al., remains the most widely used system for categorizing TAAAs **(Figure 1)**. It divides TAAAs into five main types based on the extent of aortic involvement:

- **Type I**: Involves: The distal half or more of the descending thoracic aorta and most or all of the abdominal aorta above the renal arteries and does not extend to the aortoiliac bifurcation.
- **Type II**: Involves: Most of the descending thoracic aorta and entire abdominal aorta, from the left subclavian artery to the aortoiliac bifurcation. This is the most extensive form and carries the highest risk of spinal cord ischemia.

- **Type III**: Involves: Distal thoracic aorta (below T6) and abdominal aorta, usually beginning mid-thoracic and extending to the aortoiliac bifurcation. Spares the upper thoracic aorta.
- **Type IV**: Involves: Most or all of the abdominal aorta, starting at or just below the diaphragm, and extending to the aortoiliac bifurcation.
- **Type V**: Involves the distal thoracic aorta and upper abdominal aorta but spares the infrarenal segment [11].

This classification system helps predict both technical complexity and risk of spinal cord ischemia, renal failure, and paraplegia following intervention. Notably, Type II TAAAs carry the highest operative risk due to the extensive replacement needed and the frequent involvement of intercostal arteries supplying the spinal cord [12]. Aneurysms in these regions may also be complicated by aortic dissections, which can alter the aortic architecture and complicate endovascular planning. In chronic dissections, true and false lumens may persist and challenge the seal and fixation zones needed for successful graft deployment [13]. The presence of visceral malperfusion, branch vessel occlusion, or involvement of the renal arteries in dissection-related aneurysms often necessitate advanced techniques and individualized stent configurations.

Aneurysms involving the renal arteries and thoracoabdominal aorta are anatomically and functionally complex. Their classification not only informs the surgical approach but also predicts complication risk and long-term outcomes. These aneurysms fall outside the scope of traditional EVAR and require tailored solutions such as FEVAR, BEVAR, and ChEVAR. Understanding the precise type and extent of aortic involvement is essential for determining the appropriate interventional strategy and postoperative management plan.

4.3 Complex Aneurysm Repair Techniques

Management of complex aortic aneurysms has evolved significantly in the past two decades, with endovascular techniques increasingly replacing

open surgery for high-risk anatomies and patients. Complex aneurysm repair refers to the treatment of aortic aneurysms that involve or are adjacent to vital branch vessels—most notably, the visceral arteries such as the celiac trunk, superior mesenteric artery (SMA), and renal arteries. These cases are not suitable for standard endovascular aneurysm repair (EVAR) due to inadequate proximal or distal sealing zones. Consequently, several advanced endovascular techniques have been developed: fenestrated EVAR (FEVAR), branched EVAR (BEVAR), and chimney EVAR (ChEVAR) [9].

4.3.1. Evolution from Open Repair to Complex EVAR

Historically, open surgical repair (OSR) was the standard for thoracoabdominal aneurysms, involving extensive exposure, aortic cross-clamping, and reimplantation of visceral arteries. Although durable, this approach is associated with substantial perioperative morbidity and mortality—especially in elderly or comorbid patients [12]. The development of endovascular options has enabled less invasive treatment, decreasing perioperative risk while offering comparable mid-term outcomes for select anatomies [16].

4.3.2. Fenestrated Endovascular Aneurysm Repair (FEVAR)

FEVAR utilizes custom-made or off-the-shelf endografts with carefully designed fenestrations or scallops in the graft fabric that align with the visceral arteries. These fenestrations allow for targeted cannulation and stenting of arteries such as the renal arteries, SMA, or celiac trunk [17]. The key advantage of FEVAR is its anatomical precision, but it demands meticulous preoperative planning using high-resolution CTA and three-dimensional reconstruction to ensure accurate alignment and graft fit. Indications for FEVAR include juxtarenal, pararenal, suprarenal, and certain thoracoabdominal aneurysms where visceral preservation is essential. FEVAR offers high technical success rates, with reported 30-day mortality rates under 5% in experienced centers and low rates of endoleak or reintervention in the short term [18].

4.3.3. Branched Endovascular Aneurysm Repair (BEVAR)

BEVAR employs modular or single-body stent grafts that include side branches or inner branches to facilitate perfusion of visceral arteries. Unlike fenestrations, which are flush with the graft surface, branches provide a more stable conduit for target vessel stenting—especially valuable in longer or tortuous aortas [19].

BEVAR is often used for extensive Type II and III TAAAs, especially in cases of chronic dissections, post-surgical recurrence, or where FEVAR is not technically feasible due to anatomy. Challenges include increased procedure time, contrast load, and a higher learning curve. Nonetheless, early and mid-term results are encouraging, with primary target vessel patency exceeding 90% in most large series [20].

4.3.4. Chimney EVAR (ChEVAR)

ChEVAR, involves placement of parallel covered stents (chimneys) in the visceral arteries that extend alongside the aortic main graft to maintain branch perfusion. This approach allows off-the-shelf availability and rapid deployment, making it valuable in urgent or bailout settings, such as in ruptured aneurysms [21]. However, ChEVAR is associated with a higher risk of gutter-related type I endoleaks, which occur due to incomplete sealing between the parallel stents and the main graft. Meticulous technique and selection of appropriately oversizing the graft are essential to reduce these risks [22]. Despite these limitations, ChEVAR remains a valid option in high-risk or unfit patients, with several meta-analyses demonstrating acceptable patency rates and low 30-day mortality [23].

4.3.5. Considerations for Dissections and Reinterventions

Chronic dissections that evolve into aneurysmal degeneration present unique challenges due to the presence of a false lumen and altered branch origins. Both FEVAR and BEVAR may be employed in such settings, though

preoperative imaging must confirm adequate seal zones and re-entry tears. Visceral vessels originating from the false lumen may require additional stenting or fenestration techniques [24]. In addition, reinterventions after failed or complicated open or endovascular procedures may necessitate approaches that involving combinations of FEVAR/BEVAR or open surgical bypasses. The increased complexity in these cases also affects antithrombotic strategy, as discussed later in the thesis.

4.4 Indications and Definitions of FEVAR, BEVAR, and ChEVAR Including Use in Dissections

The choice of endovascular technique for complex aortic aneurysm repair depends on anatomical considerations, patient risk profile, device availability, and urgency of the procedure. FEVAR, BEVAR, and ChEVAR each offer distinct advantages in specific clinical contexts, and their definitions have evolved as evidence has accumulated over the past two decades. In addition to aneurysmal degeneration, these techniques are increasingly being adapted for the treatment of chronic aortic dissections, especially when the dissection results in aneurysmal enlargement and branch vessel involvement.

4.4.1. Definitions and Device Concepts

- **FEVAR (Fenestrated Endovascular Aneurysm Repair)**

FEVAR involves custom-made or off-the-shelf endografts that have fenestrations or scallops corresponding to the visceral arteries (celiac trunk, SMA, renal arteries). These openings allow for precise alignment and subsequent stenting of the target vessels through the graft fabric. FEVAR is typically indicated for juxtarenal, pararenal, suprarenal, and some Type IV thoracoabdominal aneurysms, particularly when the proximal sealing zone is insufficient for standard EVAR [9,17].

- **BEVAR (Branched Endovascular Aneurysm Repair)**

BEVAR uses stent grafts with preloaded branches or inner directional cuffs designed to connect with visceral arteries. These branches provide more robust and stable access to target vessels, especially in Type II or III TAAAs, where the aorta is long, tortuous, or affected by prior dissection. BEVAR is suitable for high-risk patients, redo operations, or those with aneurysmal degeneration following dissection [19,20,24].

- **ChEVAR (Chimney EVAR)**

ChEVAR involves the placement of covered stents in visceral arteries parallel to the main endograft, preserving perfusion while extending the sealing zone of the main graft. It is mostly used in emergent or salvage settings, such as ruptures or hostile anatomies where patient-specific fenestrated or branched grafts are not available. The technique is known for its off-the-shelf feasibility but carries a risk of type Ia endoleaks from the gutters between the parallel grafts [21,22].

4.4.2. Clinical Indications

The selection of techniques depends on several anatomical and clinical variables **(Table 1):**

Table 1. Technique Selection by Aneurysm Type

Aneurysm Type	Preferred Technique	Notes
Juxtarenal or Pararenal AAA	FEVAR	When proximal sealing is <15 mm below the renal arteries
Type IV TAAA	FEVAR or BEVAR	FEVAR for less extensive disease; BEVAR when renal arteries are highly angulated or difficult to cannulate
Type II–III TAAA	BEVAR	For extensive thoracoabdominal aneurysms involving multiple visceral arteries
Ruptured or emergent aneurysms	ChEVAR	Fast deployment; may be used as a bridging or bailout procedure
Chronic aortic dissection with aneurysmal degeneration	BEVAR or FEVAR	Selection depends on true lumen size, location of visceral arteries, and seal zone quality

Footnote: AAA; Abdominal Aortic Aneurysm, TAAA; Thoracoabdominal Aortic Aneurysm, FEVAR; Fenestrated Endovascular Aneurysm Repair, BEVAR; Branched Endovascular Aneurysm Repair, ChEVAR; Chimney Endovascular Aneurysm Repair

4.4.3. Application in Aortic Dissections

Aortic dissections can complicate aneurysm repair because of the presence of a false lumen, which may continue to perfuse the aneurysm sac even after repair, leading to persistent pressurization and expansion. Furthermore, visceral arteries may arise from either the true or false lumen, or even from both, increasing procedural complexity [24,25].

In such cases:

- FEVAR may be chosen when the true lumen provides sufficient diameter for seal and branch access.
- BEVAR is often necessary when visceral arteries originate from the false lumen or when more complex reconstruction is required.
- Careful imaging using CTA or intravascular ultrasound (IVUS) is crucial for procedural planning and determining the suitability of branch cannulation.

Some centers have also reported success with hybrid techniques, combining open visceral bypasses with endografts, though these are typically reserved for reinterventions or complex dissection cases with no clear endovascular solution [26].

4.5 Current Guideline Recommendations for Antithrombotic Therapy After Aneurysm Repair

Antithrombotic therapy is an established component of postoperative management following endovascular aneurysm repair (EVAR), primarily aimed at reducing thromboembolic complications, preserving endograft and branch vessel patency, and improving long-term durability of the repair. However, while guidance on antithrombotic regimens exists for standard infrarenal EVAR, there is a notable lack of procedure-specific recommendations for complex repairs involving fenestrated (FEVAR), branched (BEVAR), or chimney (ChEVAR) techniques. The European Society for Vascular Surgery (ESVS) 2019 Clinical Practice Guidelines on abdominal aorto-iliac artery aneurysms recommend single antiplatelet therapy (SAPT), typically aspirin, for patients undergoing EVAR. Specifically, they state:

"*In patients undergoing EVAR, single antiplatelet therapy (SAPT), usually aspirin, is recommended in the absence of other indications for anticoagulation or dual antiplatelet therapy (DAPT).*"

This recommendation holds a Class I strength with Level C evidence, reflecting strong expert consensus in the absence of randomized controlled trial data [27]. However, these guidelines address only standard infrarenal EVAR, with no reference to FEVAR, BEVAR, or ChEVAR, nor any consideration of the specific anatomical or technical complexities they entail.

Similarly, the Society for Vascular Surgery (SVS) 2018 guidelines recommend aspirin following EVAR in patients who do not require anticoagulation for other reasons, supported by a Grade 1B recommendation (strong recommendation, moderate-quality evidence). Again, these recommendations are based on data from standard EVAR and do not extend to complex aneurysm repair [1].

More recently, the ESVS 2022 and 2023 guidance documents on thoracoabdominal aortic pathology have addressed technical aspects of branched and fenestrated repairs. These publications emphasize spinal cord protection, visceral revascularization, and imaging follow-up but stop short of

issuing recommendations on antiplatelet or anticoagulant therapy in the postoperative period [29]. The authors acknowledge the heterogeneity of current practice and the lack of comparative studies that would allow formulation of specific pharmacological guidance.

In parallel, the National Institute for Health and Care Excellence (NICE) NG156 guidelines for abdominal aortic aneurysm management also provide no dedicated recommendations on antithrombotic therapy following either standard or complex EVAR. NICE emphasizes perioperative optimization and long-term surveillance but defers decisions on pharmacologic prophylaxis to clinician judgment [30].

As a result, vascular specialists are left to develop institutional or operator-specific protocols, often extrapolating from other endovascular disciplines such as coronary or peripheral arterial interventions. These may include lifelong aspirin monotherapy, time-limited DAPT (e.g., 1 to 6 months), or in selected cases, full-dose anticoagulation with warfarin or direct oral anticoagulants (DOACs). However, there is significant variation in these practices, both between and within centers [31,32].

It is thus evident that none of the major international vascular guidelines provide formal, evidence-based recommendations for antithrombotic therapy following complex EVAR (Table 2). This gap is clinically significant given the higher thrombotic risk associated with complex repairs—due to bridging stents, small-caliber target vessels, increased turbulence, and the modular architecture of the endografts. The lack of standardized guidance not only contributes to variability in patient care but also impedes comparative research and outcome evaluation. This lack of specificity underscores the importance of the current thesis, which aims to explore the impact of antithrombotic regimens specifically in the setting of complex endovascular aneurysm repair. In the following section, we will critically examine whether the principles guiding antithrombotic therapy after standard EVAR can be validly applied to the more intricate setting of FEVAR, BEVAR, and ChEVAR.

Table 2. Comparison of Antithrombotic Therapy Recommendations in Major Guidelines

Guideline	Scope	Recommendation	Strength of Recommendation	Application to Complex EVAR
ESVS 2019	Management of abdominal aorto-iliac aneurysms, standard EVAR	SAPT (aspirin) recommended post-EVAR in patients without other indications for anticoagulation or DAPT	Class I, Level C	Not addressed
SVS 2018	Care of patients with abdominal aortic aneurysm (AAA), standard EVAR	Aspirin recommended post-EVAR if no indication for anticoagulation	Grade 1B	Not addressed
NICE NG156 (2020)	Diagnosis and management of AAA in England and Wales	No specific recommendation on antithrombotic therapy post-EVAR	Not specified	Not addressed

Wanhainen et al. (2019) [27], Chaikof et al. (2018) [1], NICE NG156 (2020) [30]

4.6 Limitations of Extrapolating Antithrombotic Protocols from Standard to Complex EVAR

In the absence of dedicated guidelines for antithrombotic therapy following complex endovascular aneurysm repair, many clinicians default to applying recommendations established for standard infrarenal EVAR. While this approach may offer a convenient interim solution, it fails to consider the significant anatomical, procedural, and biomechanical differences that distinguish complex repairs from conventional ones. Consequently, the validity of such extrapolation remains highly questionable. Standard EVAR typically involves the placement of a bifurcated stent graft within a relatively straight segment of the infrarenal abdominal aorta, with minimal involvement of branch vessels and limited modular overlap. The risk of thrombosis in these cases is generally low, and thus single antiplatelet therapy—most often aspirin—is deemed sufficient for maintaining graft patency [1,27]. However, complex procedures such as FEVAR, BEVAR, and ChEVAR introduce a vastly different risk profile. One of the most important distinctions is the incorporation of

multiple visceral branches using bridging stents. These stents are frequently narrow in diameter, sometimes less than 6 mm, and often subject to difficult cannulation angles, tortuosity, or kinking. In the case of BEVAR, side branches may be long and subject to sharp curvatures, increasing resistance and stagnation zones that predispose to thrombus formation [33]. Similarly, in ChEVAR, the presence of parallel stents adjacent to the main graft creates “gutter” spaces, which have been associated with type Ia endoleaks and may promote flow disturbances that further raise the thrombotic risk [34].

The issue is further compounded by the modular design of complex endografts. FEVAR and BEVAR devices are typically composed of several components joined together, creating multiple junctions where incomplete sealing, turbulence, or stent migration may occur. These junctions may act as niduses for thrombus development, especially in the early postoperative period when endothelialization is incomplete [35]. Additionally, many patients undergoing complex EVAR are at higher baseline risk for thrombosis due to advanced age, chronic kidney disease, atrial fibrillation, or a history of prior interventions. Despite these known differences, there is a surprising lack of evidence evaluating whether the antithrombotic strategies proven effective in standard EVAR provide the same benefits—or safety—in the context of complex repairs. Retrospective series and small observational studies have suggested that limb thrombosis and target vessel occlusion rates may be higher after complex EVAR, particularly in the absence of dual antiplatelet therapy or anticoagulation [36]. Yet there are no randomized controlled trials comparing different pharmacological regimens in this setting. Another concern is that aggressive antithrombotic regimens may increase the risk of hemorrhagic complications, especially in elderly patients or those with impaired renal function. Bleeding risk is further amplified when antiplatelets or anticoagulants are administered in conjunction with spinal cord protection strategies, such as cerebrospinal fluid drainage or permissive hypertension [37]. Therefore, the assumption that more intensive therapy equates to better outcomes may not be universally applicable and requires careful patient selection. Moreover, differences in postoperative surveillance also impact the interpretation of outcomes. While standard EVAR patients are often followed with duplex

ultrasonography or annual CTA, complex EVAR patients require more intensive imaging protocols to monitor branch patency and detect early complications. This higher surveillance burden reflects not only the anatomical complexity but also the uncertainty regarding the long-term performance of adjunctive stents under suboptimal pharmacologic protection [38].

In summary, although current clinical practice often involves extrapolating antithrombotic protocols from standard to complex EVAR, this approach is inherently limited by significant anatomical, mechanical, and patient-related differences. The lack of high-quality evidence specific to complex repair strategies undermines the validity of this extrapolation. Until prospective data are available, treatment decisions should be guided by an individualized risk-benefit assessment that incorporates procedural complexity, patient comorbidities, and institutional experience.

4.7 Clinical Relevance

The management of thoracoabdominal aortic aneurysms has undergone a paradigm shift with the development and increasing use of complex endovascular techniques such as fenestrated (FEVAR), branched (BEVAR), and chimney (ChEVAR) endografts. These approaches offer life-saving, minimally invasive options for patients with anatomically complex or high-risk aneurysms that would otherwise require extensive open surgery. Despite their growing adoption and technical refinement, the postoperative management of these patients - especially regarding antithrombotic therapy - remains largely empirical. Stent graft and target vessel patency are critical determinants of long-term success in complex EVAR. Target vessels, particularly the renal arteries, superior mesenteric artery, and celiac trunk, are essential for organ perfusion and graft stability. Thrombosis or occlusion of these branches can lead to renal failure, bowel ischemia, or need for urgent reintervention. Moreover, occlusion of graft limbs or modular junctions in branched or fenestrated devices may compromise overall graft integrity, risking sac pressurization, endoleak, or rupture [39]. Although the thrombotic risk in complex EVAR is intuitively higher due to the use of multiple bridging stents and the presence of narrow-caliber, tortuous target vessels, the absence of evidence-based antithrombotic

protocols introduces significant variability in clinical practice. Some centers adopt a conservative approach with single antiplatelet therapy alone, while others routinely employ dual antiplatelet therapy or systemic anticoagulation based on perceived risk. This lack of standardization contributes to heterogeneity in outcomes and complicates efforts to interpret the efficacy of various treatment strategies.

Furthermore, current international guidelines from ESVS, SVS, and NICE do not provide specific recommendations for antithrombotic therapy after complex EVAR. Instead, they focus on standard infrarenal EVAR or open repair, leaving a substantial clinical and evidence gap for more advanced interventions. This has direct implications for patient safety, as inappropriate or inadequate pharmacologic management may increase the likelihood of graft thrombosis or bleeding complications. The clinical significance of this issue is heightened by the growing number of patients undergoing complex EVAR worldwide. As these procedures become more common in both elective and emergent settings, ensuring long-term graft and limb patency becomes paramount. In this context, the development of standardized antithrombotic regimens tailored to procedural complexity and individual patient risk is not only necessary but urgent. Additionally, as newer-generation devices and techniques continue to evolve, with lower-profile delivery systems and off-the-shelf branched designs, the pool of eligible patients is expected to increase. Consequently, the need for reproducible, evidence-based postoperative management protocols including antithrombotic strategies will only grow. This underscores the importance of research efforts focused specifically on the interaction between antithrombotic therapy and graft outcomes in complex aortic repairs.

Ultimately, improving patency rates and reducing thrombotic complications through optimized pharmacologic strategies has the potential to directly influence patient morbidity, mortality, healthcare resource use, and reintervention rates. This thesis aims to contribute to this area by synthesizing the available evidence and evaluating the role of antithrombotic treatment on endograft and limb patency following complex endovascular aneurysm repair.

4.8 Aim and Objectives of the Thesis

This thesis aims to investigate the role of antithrombotic therapy in maintaining stent graft and target vessel patency following complex endovascular repair of thoracoabdominal aortic aneurysms using fenestrated (FEVAR), branched (BEVAR), and chimney (ChEVAR) techniques. As these advanced procedures are increasingly adopted for anatomically challenging aortic pathologies, the lack of standardized postoperative pharmacological protocols represents a significant clinical gap. This study reviews the pathophysiological and anatomical considerations that define complex aneurysms, describes the indications and technical aspects of modern endovascular solutions, and examines how these differ from standard EVAR. It analyzes current guideline recommendations from major vascular societies (ESVS, SVS, NICE) regarding antithrombotic therapy and critically evaluates their applicability to complex repairs. Furthermore, it explores the evidence on the impact of antithrombotic regimens on graft and limb patency, highlighting the limitations of current practices and the heterogeneity of available data. By synthesizing this information, the thesis aims to support the need for dedicated, evidence-based guidelines for antithrombotic therapy following complex aortic aneurysm repair.

5. MATERIALS & METHODS

5.1 Study aim

The aim of the current study was to systematically evaluate the existing clinical evidence regarding the effect of antithrombotic therapy on stent graft and target vessel patency following complex endovascular repair (FEVAR, BEVAR, and ChEVAR) for thoracoabdominal aortic aneurysms. The primary outcomes of interest include the type, duration, and impact of antiplatelet and/or anticoagulant regimens on the prevention of thrombotic complications, particularly graft limb occlusion and target vessel stent thrombosis, in the postoperative period

5.2 Study Protocol

The PRISMA 2020 guidelines (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) were strictly followed in the design and conduct of this systematic review. Both randomized controlled trials and non-randomized observational studies that reported outcomes on stent graft and target vessel patency following complex endovascular repair (FEVAR, BEVAR, or ChEVAR) in relation to postoperative antithrombotic therapy were considered eligible. Studies that were excluded included case reports, case series, non-English publications, studies involving deceased subjects, and those focused on experimental or investigational therapies. Additionally, studies published before the year 2000 were excluded. Importantly, only studies that explicitly evaluated stent patency in the context of antithrombotic therapy were included. Publications presenting patency outcomes without any reference to the antithrombotic regimen were excluded from analysis. Due to the nature of this literature-based review, approval from an ethics committee or institutional review board was not required. A systematic search of the literature was independently carried out by two reviewers (A.B. and M.D.B.), adhering to the methodological recommendations of the Cochrane Handbook for Systematic Reviews of Interventions. To enhance accuracy and minimize selection bias, a third reviewer (G.K.) verified and cross-checked the eligibility and extraction process. Data extraction and quality assessment of the included studies were also performed independently by two reviewers (A.B. and M.D.B.),

with disagreements resolved through discussion or arbitration by the third investigator (G.K.).

Full-text screening of all potentially relevant studies was conducted based on pre-defined inclusion and exclusion criteria. The search included peer-reviewed, English-language medical publications with a cut-off date of March 1st, 2025. The electronic databases searched were PubMed (MEDLINE), SCOPUS, and CENTRAL (Cochrane Central Register of Controlled Trials). The search strategy was constructed around focused clinical questions developed using the PICO framework (Population, Intervention, Comparator, Outcome), which are detailed in Table 3.

Table 3. P.I.C.O. Model

P	**Patient, population or problem**	**Patients who have undergone complex endovascular repair for thoracoabdominal aneurysms.**
I	Intervention, prognostic factor or exposure	Antithrombotic treatment (antiplatelets, anticoagulants).
C	Comparison of intervention	No antithrombotic (antiplatelet, anticoagulant) treatment.
O	Outcome you would like to measure or achieve	Postoperative complications (stent graft occlusion, graft patency, target vessel patency, bleeding events, thromboembolic events)
	What type of question are you asking?	What are the best available antithrombotic strategy for patients who underwent complex endovascular repair for thoracoabdominal aneurysms?
	Type of study you want to find	Observational studies (Randomized, Non-randomized), Clinical Trials, Randomized control trials.

Footnote: P.I.C.O. (patient; intervention; comparison; outcome) model was used to define the clinical questions and clinically relevant evidence in the literature.

5.3. Search Strategy

The terms “endovascular repair for thoracoabdominal aneurysms”, “complex endovascular repair for pararenal aneurysms”, “complex endovascular aneurysm repair”, “branched endovascular aneurysm repair”, “fenestrated endovascular aneurysm repair”, “BEVAR”, “FEVAR”, “antiplatelet complex aneurysm repair”, “anticoagulant complex aneurysm repair”, “antithrombotic complex aneurysm repair”, “antiplatelets thoracoabdominal aneurysms”, “anticoagulants thoracoabdominal aneurysms”, “antithrombotics thoracoabdominal aneurysms”, “antiplatelets BEVAR”, “anticoagulants BEVAR”, “antithrombotics BEVAR”, “antiplatelets FEVAR”, “anticoagulants FEVAR”, “antithrombotics FEVAR”, “target vessel patency”, “target vessel occlusion”, “target vessel instability”, “target vessel thrombosis”, “bleeding events”, “hemorrhage”, “thromboembolic events”, were used in various combinations, both as specific items as well as in MeSH Terms, as proposed by the Cochrane Handbook for Systematic Review and Interventions. The complete search strategy and combinations of terms used based on each database’s structured format is shown on Table 4.

Table 4. Search strategy algorithm by database

PUBMED	(((((((((endovascular repair for thoracoabdominal aneurysms) OR (endovascular repair for thoracoabdominal aneurysms[MeSH Terms])) OR ((complex endovascular repair for pararenal aneurysms) OR (complex endovascular repair for pararenal aneurysms[MeSH Terms]))) OR ((complex endovascular aneurysm repair) OR (complex endovascular aneurysm repair[MeSH Terms]))) OR ((branched endovascular aneurysm repair) OR (complex endovascular aneurysm repair[MeSH Terms]))) OR ((fenestrated endovascular aneurysm repair) OR (fenestrated endovascular aneurysm repair[MeSH Terms]))) OR ((BEVAR) OR (BEVAR[MeSH Terms]))) OR ((FEVAR) OR (FEVAR[MeSH Terms]))) AND ((((((((((((antiplatelet complex aneurysm

	repair) OR (antiplatelet complex aneurysm repair[MeSH Terms])) OR ((anticoagulant complex aneurysm repair) OR (anticoagulant complex aneurysm repair[MeSH Terms]))) OR ((antithrombotic complex aneurysm repair) OR (antithrombotic complex aneurysm repair[MeSH Terms]))) OR ((antiplatelets thoracoabdominal aneurysms) OR (antiplatelets thoracoabdominal aneurysms[MeSH Terms]))) OR ((anticoagulants thoracoabdominal aneurysms) OR (anticoagulants thoracoabdominal aneurysms[MeSH Terms]))) OR ((antithrombotics thoracoabdominal aneurysms) OR (antithrombotics thoracoabdominal aneurysms[MeSH Terms]))) OR ((antiplatelets BEVAR) OR (antiplatelets BEVAR[MeSH Terms]))) OR ((anticoagulants BEVAR) OR (anticoagulants BEVAR[MeSH Terms]))) OR ((antithrombotics BEVAR) OR (antithrombotics BEVAR[MeSH Terms]))) OR ((antiplatelets FEVAR) OR (antiplatelets FEVAR[MeSH Terms]))) OR ((anticoagulants FEVAR) OR (anticoagulants FEVAR[MeSH Terms]))) OR ((antithrombotics FEVAR) OR (antithrombotics FEVAR[MeSH Terms])))) AND (((((((target vessel patency) OR (target vessel patency[MeSH Terms])) OR ((target vessel occlusion) OR (target vessel patency[MeSH Terms]))) OR ((target vessel instability) OR (target vessel instability[MeSH Terms]))) OR ((target vessel thrombosis) OR (target vessel thrombosis[MeSH Terms]))) OR ((bleeding events) OR (bleeding events[MeSH Terms]))) OR ((hemorrhage) OR (hemorrhage[MeSH Terms]))) OR ((thromboembolic events) OR (thromboembolic events[MeSH Terms]))))
SCOPUS	("carotid near total occlusion" OR "carotid artery near total occlusion" OR "stroke" OR "carotid artery stenosis" OR "symptomatic carotid artery stenosis" OR "asymptomatic carotid artery stenosis" OR "TIA" OR "amaurosis fugax" OR "conservative management") AND ("carotid endarterectomy"

	OR "CEA" OR "carotid artery stenting" OR "CAS") AND ("perioperative stroke" OR "perioperative death" OR "mortality")
CENTRAL	#1 endovascular repair for thoracoabdominal aneurysms #2 [mh "endovascular repair for thoracoabdominal aneurysms"] #3 complex endovascular repair for pararenal aneurysms #4 [mh "complex endovascular repair for pararenal aneurysms"] #5 complex endovascular aneurysm repair #6 [mh "complex endovascular aneurysm repair"] #7 branched endovascular aneurysm repair #8 [mh "branched endovascular aneurysm repair"] #9 fenestrated endovascular aneurysm repair #10 [mh "fenestrated endovascular aneurysm repair"] #11 BEVAR #12 [mh "BEVAR"] #13 FEVAR #14 [mh "FEVAR"] #15 antiplatelet complex aneurysm repair #16 [mh "antiplatelet complex aneurysm repair"] #17 anticoagulant complex aneurysm repair #18 [mh "anticoagulant complex aneurysm repair"] #19 antithrombotic complex aneurysm repair #20 [mh "antithrombotic complex aneurysm repair"] #21 antiplatelets thoracoabdominal aneurysms #22 [mh "antiplatelets thoracoabdominal aneurysms"] #23 anticoagulants thoracoabdominal aneurysms #24 [mh "anticoagulants thoracoabdominal aneurysms"] #25 antithrombotics thoracoabdominal aneurysms #26 [mh "antithrombotics thoracoabdominal aneurysms"] #27 antiplatelets BEVAR #28 [mh "antiplatelets BEVAR"]

	#29	anticoagulants BEVAR
	#30	[mh "anticoagulants BEVAR"]
	#31	antithrombotics BEVAR
	#32	[mh "antithrombotics BEVAR"]
	#33	antiplatelets FEVAR
	#34	[mh "antiplatelets FEVAR"]
	#35	anticoagulants FEVAR
	#36	[mh "anticoagulants FEVAR"]
	#37	antithrombotics FEVAR
	#38	[mh "antithrombotics FEVAR"]
	#39	target vessel patency
	#40	[mh "target vessel patency"]
	#41	target vessel occlusion
	#42	[mh "target vessel occlusion"]
	#43	target vessel instability
	#44	[mh "target vessel instability"]
	#45	target vessel thrombosis
	#46	[mh "target vessel thrombosis"]
	#47	bleeding events
	#48	[mh "bleeding events"]
	#49	hemorrhage
	#50	[mh "hemorrhage"]
	#51	thromboembolic events
	#52	[mh "thromboembolic events"]
	#53	{OR #1-#14}
	#54	{OR #15-#38}
	#55	{OR #39-#52}
	#56	{AND #53-#55}

Footnote: EVAR; endovascular aneurysm repair, US; ultrasound, CTA; computed tomography angiography.

Duplicate records were first removed using automated reference management software (EndNote version 20.2.1 X9, Clarivate), followed by a

manual screening process conducted independently by two reviewers (A.B. and M.D.B.). Final inclusion of studies for data extraction was determined after a comprehensive secondary review of the full-text articles, including relevant data presented in tables and figures.

5.4. Data Extraction

Data extraction and documentation were carried out using a standardized Microsoft Excel spreadsheet. The extracted data included general study characteristics such as author names, study title, journal of publication, year of publication, study design, number of participating centers, study objectives, and the definitions of the outcomes reported. Patient demographic and clinical parameters were also collected, including age, sex, and relevant comorbidities. Furthermore, procedural and treatment-related variables were recorded, including the number of patients undergoing FEVAR, BEVAR, or ChEVAR, the type of endografts used, and the anatomic extent of aortic involvement. Detailed information regarding the postoperative antithrombotic regimens was documented, such as the type of therapy (antiplatelet or anticoagulant), dosage, duration, and whether the protocol was standardized or individualized. Reported outcomes focused on stent graft and target vessel patency, occurrence of thrombotic events, and any related reinterventions.

5.5. Data Analysis

When numerical data are available for primary or secondary outcomes, appropriate statistical analyses will be conducted. If significant heterogeneity among the included studies prevents meaningful comparison, the findings will instead be presented in a descriptive format.

5.6. Definitions

Patency was defined as the continued presence of blood flow through the endograft and its branches (including target vessels and graft limbs). Occlusion was defined as the complete absence of blood flow within a segment

of the stent graft (main body, limb, or target vessel), caused by thrombosis, kinking, or device-related failure.

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6. RESULTS

The initial search across PubMed, Scopus, and CENTRAL retrieved 273 records. After removal of duplicates using automated reference management software (EndNote version 20.2.1 X9, Clarivate) and manual verification, 216 studies remained for screening. Title and abstract screening resulted in the exclusion of 177 studies, leaving 39 articles for full-text evaluation. Among these, 35 studies were excluded during detailed assessment for reasons including lack of specific data on antithrombotic therapy after complex endovascular repair, outcomes not stratified for FEVAR/BEVAR/ChEVAR, insufficient detail in case reports or small case series, and non-English language publications. Ultimately, 4 studies fulfilled the inclusion criteria and were incorporated into the final analysis. The process of study selection is illustrated in **Figure 2** (PRISMA 2020 flow diagram).

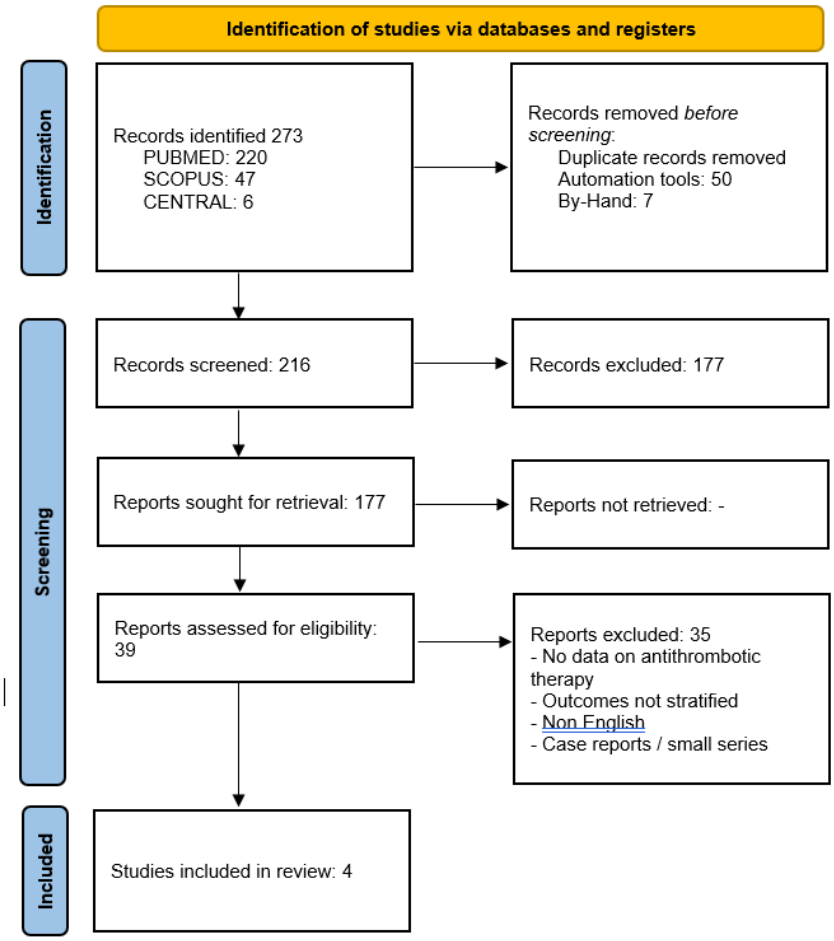

Figure 2: Prisma 2020 Flow Diagram for Systematic Reviews and Registries[40]

6.1. Types of Studies – Time Span – Procedures

The final 4 studies included in this review were published between 2023 and 2025, reflecting contemporary practice in complex endovascular repair. Patient recruitment occurred between approximately 2012 and 2023, ensuring inclusion of modern device designs and perioperative protocols. All studies were non-randomized observational cohorts, with either retrospective or prospective data collection. Two were multicenter series (Dabravolskaite et al. [43]; Nana et al. [44]), while the remaining two were registry-based or single-center analyses (Fan et al. [41]; Wagenhäuser et al. [42]).

With respect to procedural type, BEVAR was evaluated in a dedicated cohort [43] and in subgroup analyses of a multicenter study Nana [44]. Combined FEVAR and BEVAR outcomes were reported in three studies [41],[42],[44]. None of the included studies provided separate analyses for ChEVAR, and thus this subgroup could not be evaluated. Across all reports, the principal endpoints were target vessel and endograft patency, stent occlusion, and thrombotic reintervention, with limited information available on major bleeding events (**Table 5**).

Table 5. Study characteristics and type of procedure

Author	Year	Journal	Study Type	Study Period	Center	Type of Procedure
Fan et al. [41]	2023	*J Vasc Surg*	Registry-based observational	2015–2020	Multicenter (registry)	FEVAR & BEVAR
Wagenhäuser et al. [42]	2025	*J Surg Res*	Retrospective	2017–2023	Multicenter (2 European centers)	FEVAR & BEVAR
Dabravolskaite et al. [43]	2024	*J Endovasc Ther*	Retrospective	2014–2022	Multicenter (4 European centers)	BEVAR
Nana et al. [44]	2025	*Eur J Vasc Endovasc Surg*	Retrospective	2018-2022	Multicenter (15 European centers)	FEVAR & BEVAR

Footnotes: FEVAR; fenestrated endovascular aneurysm repair, BEVAR; branched endovascular aneurysm repair

6.2. Aim of Studies – Antithrombotic Regimens – Primary & Secondary Patency Rates

All four included studies reported on target vessel patency as their primary outcome, although the specific definitions of patency and occlusion varied slightly. Fan et al. [41] focused on early target vessel patency at one year across different international practice patterns. Wagenhäuser et al. [42] compared single versus dual antiplatelet therapy and reported outcomes on overall survival, freedom from reintervention, incidence of endoleaks, and both primary and secondary patency rates during follow-up. Dabravolskaite et al. [43] presented detailed outcomes on primary branch occlusion in BEVAR, highlighting differences between renal and visceral branches and reporting cumulative patency estimates during mid-term follow-up. Nana et al. [44] analyzed both primary and secondary patency rates in patients treated with FEVAR or BEVAR, demonstrating higher mid-term patency in patients receiving dual compared to single antiplatelet therapy (**Table 6**).

Aspirin was the most prescribed antithrombotic agent, either as single antiplatelet therapy (SAPT) or in combination with clopidogrel as dual antiplatelet therapy (DAPT) [41–44]. Clopidogrel was consistently evaluated as the second antiplatelet drug in DAPT protocols across all four studies. Oral anticoagulants were variably reported, either as monotherapy or in combination with SAPT, although the numbers of patients in these subgroups were limited [41,43]. None of the included studies evaluated other agents such as ticagrelor, dipyridamole, or fish-oil derivatives. Placebo or untreated control arms were not included, although in the multicenter analysis by Dabravolskaite et al. [43], a small proportion of patients discharged without any antithrombotic therapy served as a natural comparator, and this subgroup demonstrated the highest occlusion rates (**Table 6**).

Table 6. Characteristics of Included Studies and Target Vessel Distribution

Author (Year)	N Patients	N Target Vessels	BEVAR / FEVAR (%)	Device Type (%)	Follow-up (m)	Pre-op Therapy n, (%)	Post-op Therapy n, (%)	Target Vessel Distribution n, (%)
Fan et al. (2024) [41]	1525	5791	BEVAR (55%), FEVAR (45%)	Cook CMD (87.4%), T-branch (11.4%), P-branch (0.3%), physician-modified (0.9%)	12	SAPT 840 (55.1%), No therapy 227 (14.9%), DAPT 209 (13.7%), SAPT+OAC 151 (9.9%), OAC 84 (5.5%), TT 12 (0.8%)	DAPT 756 (49.6%), SAPT 439 (28.8%), SAPT+OAC 151 (9.9%), TT 49 (3.2%), OAC 40 (2.6%), No therapy 34 (2.2%)	CT1365 (23.6%), SMA 1483 (25.6%), Renal 2836 (49%), Other 107 (1.8%)
Wagenhäuser et al. (2025) [42]	63	210	BEVAR 33 (52.4%), FEVAR 30 (47.6%)	Cook + other	15	SAPT 48 (76.2%)	SAPT 19 (30%), DAPT 44 (70%)	CT 32 (15.2%), SMA ~32 (15.2%), Renal ~146 (69.5%)
Dabravolskaite et al. (2024) [43]	120	416	BEVAR 100%	Cook CMD, T-branch; Jotec E-nside, E-Xtra	21	ASA 66 (55%), Clopidogrel 16 (13%), OAC 26 (21.7%)	ASA 44 (36.7%), Clopidogrel 8 (6.7%), DAPT 57 (47.5%), OAC 31 (25.8%)	LRA 97 (23.3%), RRA 101 (24.3%), SMA 116 (27.9%), CT 102 (24.5%)
Nana et al. (2024) [44]	1430	-	BEVAR + FEVAR (not separated)	Cook Zenith custom + off-the-shelf	22	All patients on SAPT (ASA or clopidogrel)	SAPT 955 (66.8%), DAPT 475 (33.2%)	-

Footnotes: FEVAR; fenestrated endovascular aneurysm repair, BEVAR; branched endovascular aneurysm repair, CMD; custom-made devices, SAPT; single antiplatelet therapy, DAPT; dual antiplatelet therapy, OAC; oral anticoagulant therapy, ASA; acetylosalicylic acid, CT; celiac trunk, SMA; superior mesenteric artery, RRA; right renal artery, LRA; left renal artery, TT; triple therapy

6.3. Observational studies

All four included studies [41–44] were observational in design and, according to the ROBINS-I assessment, were judged to carry an overall “Serious” risk of bias. The predominant source of bias was confounding, as none of the studies implemented randomization or robust adjustment for baseline characteristics, anatomic complexity, or clinical comorbidities that could influence the choice of antithrombotic regimen. Additional concerns related to the classification of interventions, particularly in registry-based data where details on drug exposure, timing, and duration were incompletely verified. Further domains of potential bias included the selection of participants,

where multicenter cohorts may have applied variable inclusion criteria without comprehensive reporting of excluded patients, and the presence of missing data, largely due to heterogeneity in follow-up protocols and loss to follow-up across centers. While outcome measurement was generally considered low risk, as target vessel patency and occlusion were objectively assessed using imaging, the selection of reported results introduced uncertainty, given the retrospective nature of data analysis and the lack of pre-specified protocols.

Importantly, none of the included studies was graded as “Critical” risk of bias; however, the consistent “Serious” overall ratings emphasize the methodological constraints and the need for higher-quality prospective trials to better define optimal antithrombotic regimens following complex endovascular repair.

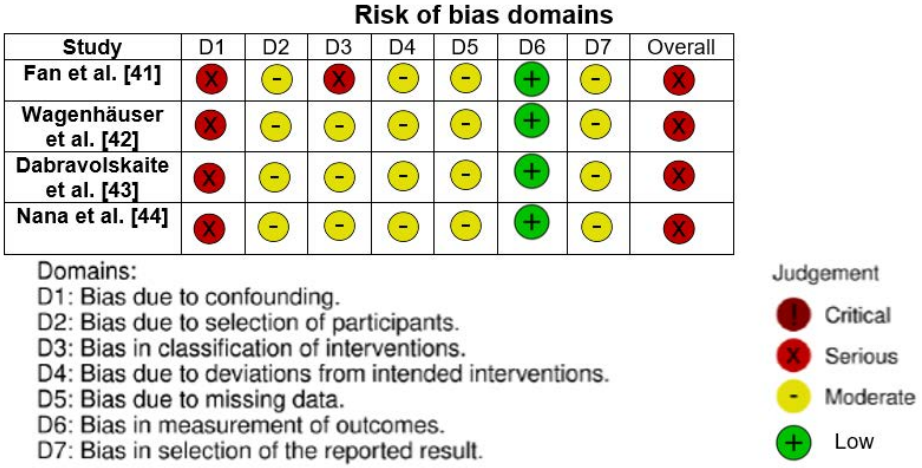

Figure VII. ROBINS-I evaluation for observational studies.

6.4. Outcomes of the included studies

The available evidence on antithrombotic therapy following complex endovascular aneurysm repair (F/BEVAR) is limited to four contemporary observational studies, each addressing different aspects of patency and clinical outcomes. The largest dataset comes from Fan et al. [41], who analyzed 1,525 patients across 10 investigational device exemption studies within the US-

Aortic Research Consortium (US-ARC) between 2012 and 2023. Procedures involved custom-made Cook devices, T-branch, P-branch, and physician-modified endografts, incorporating a total of 5,791 target arteries (mean 3.8 per case). At discharge, patients received diverse antithrombotic regimens: DAPT in 49.6%, SAPT in 28.8%, SAPT + anticoagulant in 9.9%, anticoagulant alone in 2.6%, triple therapy in 3.2%, and no therapy in 2.2%. At one year, overall survival was 91%, with a target artery primary patency rate of 95%. Kaplan–Meier analysis demonstrated significantly different patency rates across regimens ($p = 0.043$): anticoagulant-only patients had 100% patency, DAPT 95%, SAPT + anticoagulant 94%, triple therapy 94%, SAPT 89%, and no therapy 86%. On multivariable analysis, DAPT was associated with a reduced hazard of target artery occlusion compared to SAPT (HR 0.48, 95% CI 0.27–0.84; $p = 0.01$), although this protective effect did not persist in subgroup analyses of renal or visceral arteries. Importantly, renal arteries accounted for 74% of all occlusions, reinforcing their higher vulnerability. No differences in bleeding complications, survival, or reintervention rates were identified, and the duration of DAPT (1 month, 6 months, or 1 year) did not influence outcomes.

Complementary evidence was provided by Wagenhäuser et al. [42], who retrospectively reviewed 63 patients undergoing FEVAR (n = 30) or BEVAR (n = 33) at two German centers between 2012 and 2020. Endovascular repair was performed using branched and fenestrated stent grafts from two manufacturers. Patients were stratified into SAPT (n = 19) and DAPT (n = 44) groups. Notably, most patients in the DAPT group received aspirin + clopidogrel for 6 months (45.5%) or lifelong therapy (29.5%), reflecting variability in local practice. Technical success was achieved in all cases. Approximately 20% of patients were treated in urgent or emergency settings, but this did not significantly influence target vessel patency. Overall, 210 target vessels were treated (120 branches and 90 fenestrations). At 36 months, overall survival was 95% in SAPT vs. 88% in DAPT, and target vessel patency across celiac, SMA, and renal arteries did not differ significantly between regimens. Freedom from endoleak was also similar (SAPT 35% vs. DAPT 30%). Logistic regression confirmed that neither the antiplatelet regimen nor anatomical parameters predicted occlusion. Rates of perioperative bleeding, wound complications, and

limb occlusions were similar, suggesting anatomical complexity and patient-specific factors may outweigh pharmacological influence.

Focusing exclusively on BEVAR, Dabravolskaite et al. [43] analyzed 120 patients treated electively between 2014 and 2022 with Cook (CMD, T-branch) and Jotec/Artivion (E-nside, E-Xtra) devices, incorporating 416 target vessels. Preoperative therapy consisted of aspirin (55%), clopidogrel (13%), and oral anticoagulation (22%). Postoperatively, 36.7% received aspirin alone, 6.7% clopidogrel alone, 47.5% DAPT, and 25.8% OAC. After a median follow-up of 21 months, 24 bridging stent occlusions (5.8%) occurred, more frequently in renal arteries compared with visceral arteries ($p = 0.013$). Occlusion rates at 1 year were 7.8% for renal vs. 1.5% for visceral arteries, increasing to 10.6% vs. 3.7% at 5 years. Importantly, absence of any antithrombotic therapy was strongly associated with occlusion (HR 10.7, 95% CI 1.12–102; $p = 0.039$), while greater stent length independently predicted occlusion (HR 1.03 per mm, 95% CI 1.01–1.06; $p = 0.015$). Sixteen occlusions involved outer branches (5.5%), and eight inner branches (6.2%). Many occlusions occurred after patients were stepped down from DAPT to aspirin monotherapy, though this trend did not reach statistical significance. No clear difference was found between SAPT and DAPT regarding long-term patency.

Finally, Nana et al. [44] provided multicentre evidence from 15 European centers, analyzing 1,430 patients treated between 2018 and 2022 with custom-made or off-the-shelf Cook Zenith devices for thoraco-abdominal, pararenal, juxtarenal aneurysms, or chronic dissections. Importantly, all patients were already on at least one antiplatelet agent preoperatively, while those on anticoagulation (VKA or DOACs), ticagrelor, prasugrel, or with cancer/hematologic disease were excluded. Patients were discharged on SAPT ($n = 955$) or DAPT ($n = 475$), maintained for 1–6 months. At 30 days, mortality was low (SAPT 2.1% vs. DAPT 1.5%), and major bleeding events were comparable (SAPT 7.5% vs. DAPT 6.3%). Cardiovascular ischemic events were significantly lower in the DAPT group (8.2% vs. 11.9%; $p = 0.040$), particularly acute mesenteric ischemia (0.2% vs. 1.9%; $p = 0.009$) and limb ischemia (0.6% vs. 2.7%; $p = 0.008$). During a mean follow-up of 22 months, 36-month target vessel patency was significantly higher with DAPT (97.0% vs.

93.4%; p = 0.007). Sub-analyses showed this advantage persisted in both BEVAR and FEVAR, with patency rates of 94.9% vs. 87.2% in BEVAR, and 97.2% vs. 93.0% in FEVAR (all favoring DAPT). Among 163 target vessel occlusion events, ~32% required secondary intervention, highlighting the clinical burden of loss of patency despite antiplatelet therapy.

Taken together, these four studies highlight the heterogeneity of current practice in postoperative antithrombotic therapy after F/BEVAR. DAPT consistently trends toward improved target vessel patency and reduced ischemic complications, particularly in large multicenter cohorts, while smaller studies with shorter follow-up have not demonstrated statistically significant differences. Absence of antithrombotic therapy is consistently linked with poor outcomes, while anticoagulant-only regimens achieved excellent patency in the limited patients reported. Importantly, none of the studies reported a significant excess of bleeding with DAPT, suggesting a favorable safety profile in complex endovascular repair.

7. DISCUSSION

Fenestrated and branched endovascular aneurysm repair (F/B-EVAR) has become the preferred modality for the treatment of thoracoabdominal and pararenal aortic aneurysms in many high-volume centers, accounting for more than half of repairs in recent years [23,24]. This evolution has been driven by lower perioperative morbidity and mortality compared with open repair, particularly in patients with significant comorbidity [1,25–27]. However, concerns remain regarding long-term durability, reintervention rates, and target vessel (TV) occlusion [1,29]. The role of postoperative antithrombotic therapy is therefore of paramount importance, yet current evidence is scarce, heterogeneous, and often conflicting.

In this systematic review, four studies examining postoperative antithrombotic regimens following F/B-EVAR were included. The largest, a multicenter registry analysis by Fan et al. [41], demonstrated that patients discharged on dual antiplatelet therapy (DAPT) had significantly higher one-year TV patency compared with those on single antiplatelet therapy (SAPT), without an increase in major bleeding. Notably, more than 1500 patients and almost 6000 target vessels were included, providing a degree of statistical robustness. However, the retrospective design, variability in device types, and lack of standardized follow-up imaging protocols limit the certainty of these findings.

A similarly large multicenter European analysis by Nana et al. [44] corroborated these findings, showing improved TV patency with DAPT at 36 months, particularly in BEVAR cases. Importantly, DAPT was also associated with reduced early cardiovascular ischemic events, including acute mesenteric and limb ischemia, without an observed increase in major bleeding events. These data reinforce the hypothesis that DAPT may offer an advantage in maintaining branch patency, especially in more technically demanding repairs.

Smaller studies, including Dabravolskaite et al. [43] and Wagenhäuser et al. [42], did not identify statistically significant differences between SAPT and DAPT. Dabravolskaite and colleagues, in 120 patients with 416 target vessels undergoing elective BEVAR, observed a trend towards higher renal artery

occlusion rates compared with visceral arteries, but no clear superiority of any antithrombotic strategy except for an increased risk of occlusion in patients discharged without any therapy. Similarly, Wagenhäuser et al. reported no significant differences in survival, endoleak, or TV patency between SAPT and DAPT in their smaller cohort of 63 patients. Both studies underline the limitations imposed by sample size, heterogeneity in patient selection, and differences in device use and follow-up strategies.

The PRINCE2SS Delphi consensus [45] highlighted anatomical risk factors for bridging stent occlusion, including vessel diameter <6 mm, high tortuosity, and long stent configurations, and recommended the use of DAPT for 1–6 months postoperatively in patients deemed at increased risk. This consensus aligns with the observed trends in Fan et al. and Nana et al., suggesting that patient-specific anatomy and stent configuration may be as important as the pharmacological regimen in determining outcomes. The review by Oliveira-Pinto and Twine (2025) [46] also emphasized the absence of randomized controlled data and the need for individualized treatment strategies, warning against extrapolation from other vascular territories where DAPT has clearer benefit.

Another challenge in interpreting the available evidence lies in the variability of therapy duration**.** While some centers prescribe DAPT for one month, others extend therapy to six months or indefinitely. Fan et al. found no significant difference in patency according to DAPT duration, though the lack of standardized protocols raises questions regarding real-world adherence and the potential impact of clopidogrel resistance, a phenomenon affecting up to 30% of patients [45]. Moreover, bleeding outcomes were inconsistently reported. While no increase in major bleeding was observed in the larger cohorts [41,44], smaller studies may have been underpowered to detect clinically meaningful differences.

Taken together, the current literature supports the hypothesis that DAPT is associated with improved target vessel patency, particularly in BEVAR, without a consistent increase in bleeding risk. However, all available studies are retrospective observational analyses, prone to confounding and selection

bias. No study provided randomized allocation of therapy, standardized imaging surveillance, or systematic reporting of bleeding complications. Importantly, anticoagulation therapy was rarely studied and is not supported by the available data, consistent with existing guidelines [30].

The key implication of this review is that, while DAPT may be advantageous, the strength of evidence remains insufficient to support strong recommendations. Current international guidelines, including ESVS (2024) [30], NICE, and SVS, provide no specific directives for F/B-EVAR, reflecting the uncertainty of the field. The limited evidence base underscores the urgent need for prospective multicenter randomized controlled trials to evaluate the efficacy and safety of antithrombotic strategies in this patient population.

8. CONCLUSION

The incidence of target vessel occlusion following complex endovascular aortic repair (F/B-EVAR and ChEVAR) remains relatively low, though renal arteries consistently demonstrate higher rates of loss of patency compared to visceral branches. Across the current evidence base, no antithrombotic regimen (SAPT, DAPT, or OAC) has shown definitive superiority in preventing bridging stent occlusion. While DAPT appears to provide a signal of improved target vessel patency in some cohorts, this has not translated into consistent survival benefit, reduced reintervention, or lower bleeding risk. Conversely, the absence of any antithrombotic therapy was consistently associated with increased stent occlusion. Current recommendations, such as those from the PRINCE2SS consensus and recent commentaries, remain based on expert opinion rather than high-level evidence. Larger, prospective, randomized trials are needed to define the optimal antithrombotic strategy in this growing population, with attention to balancing thrombotic and hemorrhagic risks.

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10. SUPPLEMENTARY MATERIAL

Supplementary Table 1. Outcomes of Antithrombotic Strategies after F/BEVAR

Author (Year)	TV Patency SAPT	TV Patency DAPT	TV Patency OAC	TV Patency No Therapy	Survival	Reintervention	Bleeding Events	Ischemic Events	Comments
Fan et al. (2024) [41]	89%	95% (p=0.01)	100%	86%	91%	NS difference	4.5%	NS difference	Renal arteries 74% of occlusions; SAPT + OAC 94%, TT 94%
Wagenhäuser et al. (2025) [42]	CT 100%, SMA 86%, LRA 92%, RRA 72%	CT 87%, SMA 100%, LRA 95%, RRA 81%	–	–	SAPT 95%, DAPT 88%	NS	NS	NS	DAPT duration: 45.5% 6 mo, 29.5% lifelong; 20% urgent/emergency cases
Dabravolskaite et al. (2024) [43]	Higher occlusion risk on ASA alone	47.5% of patients; not statistically different from SAPT	25.8% patients; not worse	HR 10.7 for occlusion risk	–	Many occlusions required secondary intervention	NS	NS	24 occlusions (5.8%); renal branches worse than visceral; occlusions often after DAPT→SAPT step-down
Nana et al. (2024) [44]	93.4%	97% (p=0.007)	Excluded	Excluded	84–85%	32% of occlusion events reintervened	SAPT 7.5%, DAPT 6.3%	SAPT 11.9%, DAPT 8.2% (p=0.04)	DAPT protective in BEVAR (94.9% vs 87.2%) and FEVAR (97.2% vs 93%)

Footnotes: FEVAR; fenestrated endovascular aneurysm repair, BEVAR; branched endovascular aneurysm repair, CMD; custom-made devices, SAPT; single antiplatelet therapy, DAPT; dual antiplatelet therapy, OAC; oral anticoagulant therapy, ASA; acetylosalicylic acid, CT; celiac trunk, SMA; superior mesenteric artery, RRA; right renal artery, LRA; left renal artery, TT; triple therapy, TV; target vessels