Cureus
Part of SPRINGER NATURE

Open Access Editorial

A Clinical Framework for Antithrombotic Review in Anticoagulated Patients With Stable Coronary Artery Disease: When Should Aspirin Be Stopped?

Review began 10/07/2026
Review ended 10/15/2026
Published 10/17/2026

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DOI: 10.7759/cureus.118087

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Abstract

Patients receiving oral anticoagulation (OAC) for atrial fibrillation frequently have concomitant coronary artery disease (CAD), raising questions about the duration of additional antiplatelet therapy. Triple antithrombotic therapy combines OAC with aspirin and a $P2Y_{12}$ inhibitor, usually clopidogrel, whereas dual antithrombotic therapy combines OAC with a single antiplatelet agent. Early aspirin withdrawal from triple therapy and subsequent withdrawal of the remaining antiplatelet are separate decisions requiring assessment of the coronary timeline and current treatment indications. This narrative editorial examines randomized evidence and proposes a structured medication review framework. The evidence generally supports OAC monotherapy in appropriately selected patients with stable CAD, with reduced bleeding and favourable net clinical outcomes compared with combined treatment. However, aspirin-specific findings require distinction from comparisons involving clopidogrel or mixed antiplatelet regimens. Overall trial results do not establish identical benefits or harms across patients with previous myocardial infarction, multivessel disease, or complex coronary intervention. Differences in eligibility and composite endpoints, geographic concentration, open-label designs, early termination in some trials, and limited precision for uncommon ischemic events constrain interpretation and generalizability. The proposed framework comprises verification of the OAC indication and regimen, establishment of the coronary timeline, assessment of any current antiplatelet indication, review of bleeding risks and drug interactions, and documentation of the decision, responsible clinician, and reassessment date. Extrapolation requires particular caution in patients with previous stent thrombosis, mechanical valves, or OAC prescribed for venous thromboembolism. Continued combination therapy requires a current, documented justification. The framework remains unvalidated, and its reproducibility, feasibility, and effects on prescribing, bleeding, and ischemic outcomes require prospective evaluation.

Categories: Cardiology, Internal Medicine, Cardiac/Thoracic/Vascular Surgery
Keywords: antithrombotic therapy, aspirin, atrial fibrillation, oral anticoagulation, percutaneous coronary intervention, stable coronary artery disease

Editorial

Introduction

Consider a patient with atrial fibrillation (AF) who underwent percutaneous coronary intervention (PCI) for an acute coronary syndrome (ACS) three years previously and remains on oral anticoagulation (OAC) plus aspirin. OAC was prescribed for AF-related stroke prevention, whereas aspirin was initiated as part of antiplatelet treatment for the coronary event and intervention. These treatments originally addressed different thrombotic risks. At follow-up, however, the initial indication for aspirin requires distinction from a current indication for its continuation.

Combining antiplatelet therapy with OAC may be appropriate during the indicated treatment period after ACS or PCI, but the regimen and duration depend on the patient's coronary and bleeding risks. Reassessment considers the original coronary presentation, time since intervention, recurrent ACS or repeat revascularization, previous stent thrombosis, procedural complexity, and any unresolved coronary concern. Previous bleeding, anemia, renal impairment, and concomitant medicines also influence the treatment balance. In a patient without intervening coronary events who has completed the appropriate period of combined treatment, contemporary guidance generally favours OAC monotherapy [1].

Recent randomized evidence reinforces the importance of this individualized review. The Assessment of Quitting Versus Using Aspirin Therapy in Patients With Stabilized Coronary Artery Disease After Stenting Who Require Long-Term Oral Anticoagulation (AQUATIC) trial found that adding aspirin increased major bleeding and the primary cardiovascular composite in a selected population of previously stented patients with high atherothrombotic risk [2]. These findings challenge routine aspirin continuation based solely on a historical coronary diagnosis, without establishing an identical treatment effect in every high-risk subgroup. This editorial examines the evidence informing antiplatelet withdrawal in anticoagulated patients with

stable coronary artery disease and proposes a structured review process to identify ongoing indications and circumstances requiring specialist assessment.

Establish the coronary timeline

The first step is to confirm the indication for OAC and establish when the last ACS or PCI occurred. The choice, dose, and duration of anticoagulation depend on the underlying clinical condition, while the coronary timeline helps determine whether additional antiplatelet therapy remains indicated. Recent ACS or PCI may justify combined treatment, but the regimen and duration require assessment of the coronary presentation, procedural findings, and individual ischemic and bleeding risks [1].

Two treatment transitions must be distinguished. The first is withdrawal of aspirin from triple therapy, leaving OAC plus a $P2Y_{12}$ inhibitor, usually clopidogrel. The second is subsequent withdrawal of the remaining antiplatelet, leaving OAC alone if anticoagulation remains indicated. Specifically, for patients requiring OAC who undergo PCI for chronic coronary syndrome, European Society of Cardiology (ESC) guidance limits aspirin to an initial period, with continuation for up to 30 days in selected patients whose ischemic risk outweighs bleeding risk. OAC plus clopidogrel then generally continues for up to six months in patients without high ischemic risk or up to twelve months in those with high ischemic risk, before transition to OAC monotherapy [1]. These intervals concern the additional antiplatelet treatment, not the duration of anticoagulation, and should not be applied as a uniform schedule across acute and chronic coronary presentations.

This editorial primarily concerns patients with AF receiving indicated OAC who have medically managed stable coronary artery disease (CAD) or have completed the appropriate combined-treatment period after revascularization. Stability requires assessment of intervening events and current coronary concerns, rather than elapsed time alone. Evidence supporting antiplatelet withdrawal is less direct when OAC is prescribed for venous thromboembolism or mechanical valves; these patients require indication-specific assessment before extrapolation from AF populations [1].

What the randomized evidence changes

Randomized evidence supports reassessing the incremental value of antiplatelet therapy once CAD is stable in patients requiring OAC. The Atrial Fibrillation and Ischemic Events With Rivaroxaban in Patients With Stable Coronary Artery Disease (AFIRE) trial, published in 2019, randomized 2,236 patients with AF and CAD managed medically or revascularized more than one year previously. The primary efficacy composite comprised stroke, systemic embolism, myocardial infarction, unstable angina requiring revascularization, or death from any cause. Rivaroxaban monotherapy was noninferior to rivaroxaban plus a single antiplatelet, with rates of 4.14% versus 5.75% per patient-year (HR: 0.72; 95% CI: 0.55-0.95; $p < 0.001$ for noninferiority). Major bleeding, defined using International Society on Thrombosis and Haemostasis criteria, was lower with monotherapy: 1.62% versus 2.76% per patient-year (HR: 0.59; 95% CI: 0.39-0.89; $p = 0.01$). The trial stopped early because of excess mortality in the combination-therapy group [3].

Edoxaban Versus Edoxaban Plus Antiplatelet Agent in Patients With Atrial Fibrillation and Stable Coronary Artery Disease (EPIC-CAD) extended the evidence to edoxaban in 1,040 patients with AF and stable CAD. Monotherapy reduced the composite of death, ischemic events, and major or clinically relevant nonmajor bleeding compared with edoxaban plus an antiplatelet (HR: 0.44; 95% CI: 0.30-0.65). Major ischemic events appeared similar between groups, while bleeding was substantially lower [4]. Endpoint composition is important: AFIRE included all-cause death, whereas EPIC-CAD combined ischemic events and bleeding. Their results support the overall benefit-risk balance of monotherapy in the populations studied but do not establish superior prevention of individual coronary ischemic outcomes. Moreover, both trials evaluated withdrawal of a single antiplatelet that could be aspirin or a $P2Y_{12}$ inhibitor, limiting aspirin-specific conclusions [3,4].

AQUATIC provides more direct evidence concerning aspirin. This double-blind, placebo-controlled trial enrolled 872 patients receiving long-term OAC who had undergone coronary stenting more than six months previously and had high atherothrombotic risk. Adding aspirin increased the primary composite of cardiovascular death, myocardial infarction, stroke, systemic embolism, coronary revascularization, or acute limb ischemia (16.9% versus 12.1%; adjusted HR: 1.53; 95% CI: 1.07-2.18). Major bleeding was also increased (10.2% versus 3.4%; adjusted HR: 3.35; 95% CI: 1.87-6.00), and the trial stopped early because of excess all-cause mortality with aspirin [2]. Unlike the EPIC-CAD primary endpoint, AQUATIC's efficacy composite did not include bleeding. Nevertheless, its composite result does not establish that aspirin increased each individual ischemic outcome, and early termination limits confidence in the magnitude of benefit or harm and subgroup estimates. These findings challenge routine aspirin continuation in patients resembling the trial population; they do not demonstrate harm across all stable CAD populations.

Antithrombotic Dual Therapy After Drug-Eluting Stent Implantation in Patients With Atrial Fibrillation (ADAPT AF-DES) addressed the separate question of continued clopidogrel use. Among 960 patients with AF at least one year after drug-eluting stent implantation, OAC monotherapy reduced net adverse clinical events compared with OAC plus clopidogrel (HR: 0.54; 95.2% CI: 0.37-0.77) [5]. This supports avoiding

routine substitution of clopidogrel for aspirin once antiplatelet therapy is no longer indicated. However, the net clinical endpoint should not be interpreted as proof of superior protection against individual ischemic events.

Collectively, these trials support OAC monotherapy in appropriately selected patients who require anticoagulation and have completed the indicated period of combined treatment. Applicability depends on the OAC indication, coronary timeline, intervening events, and trial eligibility. Differences in populations, comparators, and endpoints limit direct comparisons, while uncommon events such as stent thrombosis remain imprecisely estimated. The clinical implication is therefore reassessment of the continuing antiplatelet indication, with a documented justification for combination therapy, rather than a universal conclusion that aspirin is harmful in stable CAD [2-5].

Does high coronary risk justify continued aspirin?

Previous myocardial infarction, multivessel disease, and complex PCI represent different clinical circumstances and should not be treated as interchangeable indications for continued aspirin. These features inform assessment of coronary risk, but their presence alone does not establish that adding aspirin to therapeutic OAC improves outcomes. Their relevance depends on the coronary timeline, procedural findings, intervening events, and competing bleeding risks [1].

AQUATIC provides direct evidence concerning aspirin in previously stented patients receiving long-term OAC who have high atherothrombotic risk. Its findings challenge routine aspirin continuation in patients resembling the trial population [2]. However, the overall result does not establish an identical treatment effect in every subgroup defined by previous myocardial infarction, multivessel disease, or complex PCI. AFIRE and EPIC-CAD support OAC monotherapy in appropriately selected patients with AF and stable CAD, but their combination-treatment groups included aspirin or a $P2Y_{12}$ inhibitor [3,4]. ADAPT AF-DES evaluated continued clopidogrel rather than aspirin [5]. Consequently, these comparisons do not establish an aspirin-specific benefit or harm separately for each coronary-risk phenotype. Limited precision for uncommon ischemic events also prevents firm conclusions about protection against individual coronary outcomes [2-5].

Coronary complexity therefore warrants review of the original procedure and subsequent clinical course. Relevant considerations include a new ACS, repeat intervention, previous stent thrombosis, or an unresolved procedural concern. Recent events may place the patient outside the stable-disease framework. Previous stent thrombosis requires specialist assessment because such patients were excluded from AFIRE [3]. These circumstances justify individualized review but do not independently establish a benefit from indefinite aspirin. If combination therapy is retained, its indication, intended duration, and reassessment date should be documented. Table *1* summarizes four principal randomized trials, including their geographic settings, populations, treatment comparisons, findings, and limitations.

Trial; publication year; country	Design and population	Treatment comparison	Principal findings	Important limitations
AQUATIC; 2025; France [2]	Double-blind, placebo-controlled trial; 872 patients receiving long-term OAC, with coronary stenting more than six months previously and high atherothrombotic risk.	Existing OAC plus aspirin 100 mg daily versus existing OAC plus placebo.	During median follow-up of 2.2 years, aspirin increased the cardiovascular composite (adjusted HR: 1.53; 95% CI: 1.07-2.18) and major bleeding (adjusted HR: 3.35; 95% CI: 1.87-6.00).	Stopped early because of excess all-cause mortality with aspirin. Selected high-risk, previously stented population; limited precision for individual outcomes and subgroups.
AFIRE; 2019; Japan [3]	Open-label noninferiority trial; 2,236 randomized; AF with PCI/CABG more than one year previously or CAD not requiring revascularization.	Rivaroxaban alone versus rivaroxaban plus aspirin or a $P2Y_{12}$ inhibitor.	Monotherapy was noninferior for the efficacy composite (HR, 0.72; 95% CI, 0.55–0.95) and superior for major bleeding (HR, 0.59; 95% CI, 0.39–0.89).	Stopped early because of excess mortality with combination therapy. Efficacy composite included all-cause death; comparator was not exclusively aspirin. Previous stent thrombosis was excluded.
EPIC-CAD; 2024; South Korea [4]	Open-label randomized trial; 1,040 patients with AF and stable revascularized or medically managed CAD.	Edoxaban alone versus edoxaban plus a single antiplatelet.	At 12 months, the composite of death, ischemic events, and clinically important bleeding occurred in 6.8% versus 16.2% (HR: 0.44; 95% CI: 0.30-0.65). Major ischemic events appeared similar.	Twelve-month follow-up; primary endpoint combined ischemic events and bleeding. Findings do not establish superiority for individual ischemic outcomes or an exclusively aspirin-related effect.
ADAPT AF-DES; online 2025, issue 2026; South Korea [5]	Open-label noninferiority trial; 960 patients with AF at least one year after drug-eluting stent implantation.	DOAC alone versus DOAC plus clopidogrel.	At 12 months, net adverse clinical events occurred in 9.6% versus 17.2% (HR: 0.54; 95.2% CI: 0.37-0.77), meeting noninferiority and superiority criteria.	Twelve-month follow-up; net clinical endpoint combines efficacy and safety. Limited precision for uncommon ischemic events; evaluates clopidogrel rather than aspirin.

TABLE 1: Four principal randomized trials comparing oral anticoagulant monotherapy with combined anticoagulant and antiplatelet therapy in stable coronary artery disease.

Abbreviations: AF, atrial fibrillation; CABG, coronary artery bypass grafting; CAD, coronary artery disease; CI, confidence interval; DOAC, direct oral anticoagulant; HR, hazard ratio; OAC, oral anticoagulation; PCI, percutaneous coronary intervention

An explicit framework for medication review

Medication review should produce an explicit antithrombotic decision rather than reproduce the previous prescription. The following five-component framework organizes the evidence discussed above into a proposed clinical review process. It is intended as a documentation and reassessment aid, rather than a validated decision rule. Although its components reflect established prescribing considerations, their integration into this framework has not been evaluated for reproducibility, implementation feasibility, or effects on patient outcomes.

The first component concerns the indication for anticoagulation and the appropriateness of the regimen. Assessment includes the indication, intended duration, adherence, renal function, and dose in relation to relevant prescribing criteria. OAC monotherapy presupposes an appropriate regimen. Aspirin should not compensate for uncertain adherence or inappropriate anticoagulant dosing. Patients with mechanical valves or OAC prescribed for venous thromboembolism require separate consideration because the supporting evidence is predominantly derived from AF populations [1,3-5].

The second component establishes the coronary timeline. The dates and indications for ACS, PCI, or coronary surgery, together with intervening events, determine the relevant treatment phase. Discharge plans and procedural records may clarify the intended regimen and duration. This assessment distinguishes an ongoing, indicated course of combined therapy from treatment continued beyond its intended duration [1].

The third component addresses the current indication for antiplatelet therapy and its intended duration. Remote stenting alone should prompt reassessment rather than automatic renewal. Previous stent thrombosis, recent intervention, or unresolved procedural concerns warrant discussion with the treating cardiologist before the decision is finalized [1,3].

The fourth component concerns bleeding risks and drug interactions. Relevant factors include previous bleeding, anemia, renal impairment, uncontrolled blood pressure, and concomitant medicines, including nonsteroidal anti-inflammatory drugs and nonprescription aspirin. Gastrointestinal protection may be appropriate when combined therapy remains necessary. Bleeding risk should prompt correction of modifiable factors and treatment review rather than automatic discontinuation of indicated OAC [1].

The final component concerns documentation, communication, and responsibility for reassessment. When aspirin is discontinued, documentation includes the rationale, communication of the updated regimen to the patient and other prescribers, and reconciliation of medication lists. When combination therapy continues, the record specifies the indication, intended duration, responsible clinician, and review date. Patient counselling reinforces the continuing importance of lipid lowering, blood pressure control, smoking cessation, and symptom assessment after aspirin withdrawal. A new coronary event, bleeding episode, or change in the OAC indication warrants reassessment [1].

Evaluation would require assessment of both reproducibility and clinical impact. Reproducibility could initially be examined by having independent clinicians apply standardized component definitions to the same clinical cases, measuring agreement on whether antiplatelet therapy should continue, be discontinued, or undergo specialist review. A subsequent prospective controlled evaluation could compare framework-supported review with usual care, assessing documentation completeness, concordance with applicable guideline recommendations, feasibility, and antiplatelet continuation without a documented indication. Clinical outcomes would include major bleeding, ischemic events, and unintended interruption of indicated OAC. Adequate sample size and follow-up would be necessary to assess uncommon outcomes such as stent thrombosis. Until such evaluation is available, the framework's reproducibility and effect on patient outcomes remain unestablished.

Strengths, limitations, and remaining uncertainties

A strength of this editorial is its distinction between early aspirin withdrawal after ACS or PCI and subsequent withdrawal of the remaining antiplatelet once coronary disease is stable. It also distinguishes aspirin-specific evidence from comparisons involving other antiplatelet agents and acknowledges the limits of applying overall trial findings to individual coronary-risk subgroups. The proposed five-component framework organizes these considerations into a structured process for medication review, documentation, and reassessment.

Several limitations require acknowledgment. This is a narrative editorial rather than a systematic review; evidence selection and interpretation may therefore be subject to selection bias, and no formal pooled analysis was undertaken. The underlying trials differ in eligibility criteria, anticoagulant regimens, antiplatelet comparators, and endpoint definitions, limiting direct comparisons. Several were open-label, follow-up duration varied, and uncommon ischemic outcomes, particularly stent thrombosis, remain imprecisely estimated. Early termination in AFIRE and AQUATIC warrants caution when interpreting effect magnitude [2-5]. Overall trial findings do not establish identical benefits or harms across patients with previous myocardial infarction, multivessel disease, or complex PCI [2-5]. Extrapolation also requires care in patients with previous stent thrombosis, mechanical valves, or OAC prescribed for venous thromboembolism [1,3].

Finally, the proposed review framework has not been evaluated for reproducibility, feasibility, or clinical effectiveness. Evidence supporting OAC monotherapy does not itself establish that implementing this review process improves outcomes. Prospective evaluation would be needed to determine whether it improves prescribing and documentation while reducing bleeding without increasing ischemic events or unintended interruption of indicated OAC.

Conclusion

In patients with AF receiving indicated OAC who have concomitant stable CAD, continued aspirin requires a current indication that is reassessed as clinical circumstances evolve. Randomized evidence generally supports OAC monotherapy in appropriately selected patients after completion of the indicated combined-treatment period. However, differences in trial populations, antiplatelet comparators, and endpoints limit aspirin-specific and subgroup conclusions. Clinical review should verify the anticoagulation indication and regimen, establish the coronary timeline, and determine whether an antiplatelet remains necessary. Continued combination therapy requires a documented rationale, responsible clinician, and reassessment plan. The proposed five-component framework offers a structured approach to this review, but its reproducibility and effects on patient outcomes remain unestablished and require prospective evaluation.

Additional Information

Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

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Disclosures

Conflicts of interest: In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

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