EuroIntervention
2026;22:e417-e418
published online e-edition April 2026
DOI: 10.4244/EIJ-D-26-00300

EDITORIAL

Stable coronary patients with atrial fibrillation: when the kidneys tip the balance

Martine Gilard*, MD, PhD; Romain Didier, MD, PhD

Corresponding author: UMR1078, 22 Avenue Camille Desmoulins, 29238, Brest, France. E-mail: martine.gilard@gmail.com

The management of atrial fibrillation (AF) in patients with concomitant coronary artery disease (CAD) has progressively shifted from "more is safer" to "simpler is better", particularly once CAD is stable. Recent studies have shown that anticoagulation alone, as compared to anticoagulation plus antiaggregation, reduces bleeding risk without increasing ischaemic risk in these patients.[1-3] In surprising ways, the addition of aspirin to anticoagulation was even associated with excess mortality in the AQUATIC trial.[4] Yet a common clinical hesitation persists: when a patient is older, comorbid, and has a history of CAD, can clinicians truly step back from antiplatelet therapy?

Chronic kidney disease (CKD) is a widespread comorbidity that further complicates the choice of antithrombotic therapy. Renal dysfunction simultaneously increases thrombotic risk and amplifies bleeding liability, while also affecting the level of exposure to direct oral anticoagulation.

In this issue of EuroIntervention, Lee et al, the authors of the prespecified EPIC-CAD trial,[5] directly address the matter of whether kidney function modifies the net clinical benefit of edoxaban monotherapy compared with edoxaban plus a single antiplatelet agent in patients with AF and stable CAD. The authors should be congratulated for their insightful research.

Article, see page e432

EPIC-CAD was a multicentre, open-label, adjudicator-masked, randomised trial conducted at 18 hospitals in South Korea between May 2019 and September 2022. The trial enrolled 1,040 patients with high-risk AF (CHA_2DS_2-VASc score ≥2) and stable CAD, who were randomised 1:1 to edoxaban monotherapy or edoxaban combined with single antiplatelet therapy. Stable CAD was rigorously defined, and patients with severe renal dysfunction (creatinine clearance <15 mL/min) were excluded. The primary endpoint was net clinical adverse events (NACE) at 12 months, integrating death, myocardial infarction, stroke, systemic embolism, urgent revascularisation, and International Society on Thrombosis and Haemostasis major or clinically relevant non-major bleeding. The renal function stratification in this prespecified analysis is particularly pragmatic. Rather than relying solely on epidemiological estimated glomerular filtration rate categories, patients were grouped according to the edoxaban dose-reduction threshold (creatinine clearance 50 mL/min), a cutpoint that clinicians routinely use in practice. Of the 1,040 randomised patients, 252 (24.2%) had creatinine clearance <50 mL/min. As expected, this subgroup represented a higher-risk phenotype, with greater rates of NACE, bleeding, and ischaemic events compared with patients with better renal function.

The clinically decisive question is whether renal dysfunction modifies the relative advantage of monotherapy? It does not. Edoxaban monotherapy reduced NACE compared with dual therapy across both renal strata, with no signal of heterogeneity. Among patients with creatinine clearance <50 mL/min, NACE occurred in 12.1% of those receiving monotherapy versus 21.7% of those on dual therapy (hazard ratio [HR] 0.52, 95% confidence interval [CI]: 0.28-0.98; p=0.04). In patients with creatinine clearance ≥50 mL/min, NACE occurred in 5.2% versus 14.5% (HR 0.40, 95% CI: 0.25-0.65; p<0.001). Importantly, the treatment by renal function interaction was neutral (p-interaction=0.53). In other words, kidney disease identifies a higher baseline risk, but it does not invalidate the strategy of treatment simplification. The reduction in NACE was largely driven by bleeding, with a consistent effect size across renal strata. By contrast, major ischaemic events were infrequent and did not differ in terms of statistical significance between treatment strategies.

As with any subgroup analysis, the strengths of this work must be weighed against its limitations. The most persuasive feature is its prespecified design and the clinically meaningful renal categorisation anchored to dosing practice. The use of a composite endpoint such as NACE is also appropriate for the contemporary clinical question, recognising that bleeding outcomes are not secondary in this population. Conversely, ischaemic endpoints were relatively uncommon, limiting the statistical power of the study; the investigators appropriately acknowledge the exploratory nature of these comparisons. Multiplicity was not formally controlled, and renal function fluctuated across clinically relevant thresholds over a year. Finally, extrapolation beyond an East Asian population should be approached with caution, given potential differences in bleeding susceptibility.

The EPIC-CAD findings reinforce a recurring theme in the management of patients with both AF and CAD: beyond the acute coronary phase, adding antiplatelet therapy to anticoagulation tends to confer uncertain ischaemic benefit at a predictable cost in bleeding risk – an unfavourable tradeoff that becomes even more consequential in patients with CKD. Nevertheless, we should not forget that patients with CKD are vulnerable under any antithrombotic regimen and may therefore derive particular benefit from avoiding additional haemorrhagic exposure with marginal incremental efficacy.

In the opposite way, patients with very high renal clearance may experience reduced edoxaban exposure. This observation is not a reason to abandon monotherapy in patients with high clearance, but rather a signal that further investigation is warranted. Ultimately, there may not be a clear-cut distinction between black and white among patients with renal insufficiency. Could the varying degrees of renal insufficiency have an impact? Larger trials may help clarify whether renal function carries distinct efficacy implications in this subgroup.

Where does this leave practice? EPIC-CAD's renal analysis supports a clear and implementable principle: in patients with AF with truly stable CAD, anticoagulation monotherapy, whichever the anticoagulation type, should be the default strategy even in those with moderate renal impairment, while ongoing antiplatelet therapy should be reserved for patients with a persistent coronary indication that clearly outweighs the bleeding risk. This approach does not represent therapeutic minimalism; rather, it reflects risk-aligned precision.

In patients with AF and stable CAD, renal dysfunction increases baseline risk but does not diminish the net clinical advantage of simplifying treatment to anticoagulant monotherapy rather than combination therapy, largely through a reduction in clinically relevant bleeding without an evident ischaemic penalty.

Authors' affiliation

Department of Cardiology, Brest University Hospital, Brest, France, and Inserm, UMR 1304 (GETBO), Western Brittany Study Group, Brest, France

Conflict of interest statement

The authors have no conflicts of interest to declare.

References

1. Cho MS, Kang DY, Ahn JM, et al. Edoxaban Antithrombotic Therapy for Atrial Fibrillation and Stable Coronary Artery Disease. *N Engl J Med.* 2024;391:2075-86.

2. Matsumura-Nakano Y, Shizuta S, Komasa A, et al. Open-Label Randomized Trial Comparing Oral Anticoagulation With and Without Single Antiplatelet Therapy in Patients With Atrial Fibrillation and Stable Coronary Artery Disease Beyond 1 Year After Coronary Stent Implantation. *Circulation.* 2019;139:604-16.

3. Yasuda S, Kaikita K, Akao M, et al. Antithrombotic Therapy for Atrial Fibrillation with Stable Coronary Disease. *N Engl J Med.* 2019;381:1103-13.

4. Lemesle G, Didier R, Steg PG, et al. Aspirin in Patients with Chronic Coronary Syndrome Receiving Oral Anticoagulation. *N Engl J Med.* 2025;393:1578-88.

5. Lee JM, Cho MS, Kang DY, et al. Impact of renal function on edoxaban antithrombotic therapy in patients with atrial fibrillation and stable coronary artery disease: a prespecified analysis of the EPIC-CAD trial. *EuroIntervention.* 2026;22:e432-43.