in the dual antithrombotic therapy group received clopidogrel. Clopidogrel might be less effective in reducing the rate of cardiovascular events in people who carry loss-of-function *CYP2C19* alleles that are associated with reduced conversion of clopidogrel to its active metabolite.[2-4] Clopidogrel non-responsiveness or hyporesponsiveness has been shown to occur in up to 40% of patients with stent thrombosis and in up to 25% of patients who have undergone PCI.[5] Edoxaban and a P2Y12 inhibitor probably have little antiplatelet effect early after PCI in patients who carry loss-of-function *CYP2C19* alleles, which might result in a higher risk of stent thrombosis, myocardial infarction, and death. In their meta-analysis including all non-vitamin K antagonist oral anticoagulant atrial fibrillation PCI studies, Vranckx and colleagues[1] reported a risk ratio of 1·55 (95% CI 0·99–2·41) for stent thrombosis in patients assigned to an aspirin-free therapy early after PCI. Thus, despite a lower bleeding risk with very early reduction of the intensity of antiplatelet therapy, concerns regarding efficacy still remain.

We declare no competing interests.

*Johann Auer, Robert Berent, Franz Gurtner
johann.auer@khbr.at

Department of Cardiology, St Josef Hospital, Braunau 5280, Austria (JA, FG); and HerzReha, Bad Ischl, Austria (RB)

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See **Online** for appendix

In the ENTRUST-AF PCI trial[1] published by Pascal Vranckx and colleagues, an edoxaban-based antithrombotic strategy was non-inferior for bleeding compared with a vitamin K antagonist-based regimen in patients with atrial fibrillation who had undergone percutaneous coronary intervention (PCI). These results are consistent with those observed in other similar trials; however, unlike other non-vitamin K antagonist oral anticoagulants (NOACs), edoxaban did not show superiority over vitamin K antagonists in terms of safety.[1]

Edoxaban is approved for the thromboprophylaxis of atrial fibrillation. However, the US Food and Drug Administration recommend against the use of edoxaban in patients with creatinine clearance equal to or more than 95 mL/min because of the potential for decreased effectiveness.[2] The European Heart Rhythm Association's practical guide on the use of NOACs in atrial fibrillation recommends cautionary use of edoxaban in the case of supranormal renal function.[3]

In the ENGAGE AF-TIMI 48 trial,[4] patients with high creatinine clearances showed the highest reduction in bleeding events. Among coagulation factor Xa inhibitors, edoxaban is consistently the most affected by renal excretion (50% elimination for edoxaban *vs* 27% for apixaban and 35% for rivaroxaban).[3]

In the ENTRUST-AF PCI trial, patients with a creatinine clearance equal to and more than 95 mL/min were included. Unlike the ENGAGE AF-TIMI 48 study, those with a creatinine clearance between 15 mL/min and 30 mL/min were also included.[1] Patients at the extremes of creatinine clearance (high and low) might have a different risk–benefit profile, with an imbalance between thrombotic and bleeding risk.

Do Vranckx and colleagues think that the inclusion of patients with extreme creatinine clearance values might have affected their results, in terms of both safety and efficacy? Do the authors endorse the clinical application of these findings in this set of patients?

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*Giulio Francesco Romiti, Stefania Basili, Marco Proietti
giuliofrancesco.romiti@uniroma1.it

Department of Internal Medicine and Medical Specialties (GFR) and Department of Translational and Precision Medicine (SB), Sapienza-University of Rome, Rome 00161, Italy; and Department of Clinical Sciences and Community Health, University of Milan, Milan, Italy (MP)

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Clinical trials, such as the one published by Pascal Vranckx and colleagues, have shown that dual antithrombotic therapy (non-vitamin K antagonist oral anticoagulant [NOAC] and a P2Y12 inhibitor) results in less bleeding than does triple therapy (vitamin K antagonist, P2Y12 inhibitor, and aspirin) in patients with atrial fibrillation who have received percutaneous coronary intervention.[1–4] Based on the results from these clinical trials (appendix), guidelines recommend standard dose NOAC in combination with antiplatelet therapy for these patients.[3] However, dual therapy with NOACs increases the risk of thrombotic events (eg, myocardial infarction or stent thrombosis) compared with triple therapy, which suggests that patients at high risk of thrombotic events might benefit from the addition of aspirin to