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REPLY

Warfarin in patients on haemodialysis with atrial fibrillation—friend or foe?

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We would like to thank G. Schlieper and J. Floege for their comments on our News & Views article (Anticoagulation therapy: Balancing the risks of stroke and bleeding in CKD. *Nat. Rev. Nephrol.* **11**, 200–202; 2015),[1] in which relevant concerns pertaining to the use of warfarin to prevent ischaemic stroke and systemic thromboembolism in patients with atrial fibrillation undergoing haemodialysis are raised (Challenging the use of warfarin in patients on dialysis with atrial fibrillation. *Nat. Rev. Nephrol.* 7 July 2015; doi:10.1038/nrneph.2015.87).[2] The authors discussed four observational studies[3–6] that caution against the use of warfarin in patients with atrial fibrillation undergoing haemodialysis, as well as the study published by Bonde *et al.*[7] We consider these studies to have several limitations, such that the reported associations might not be causal due to residual confounding. Importantly, the international normalized ratios (INR) at the time of stroke were largely unknown, and the cause of stroke in these patients could have been inadequate or excessive anticoagulation.[8]

Nevertheless, we agree that use of warfarin in patients with atrial fibrillation undergoing dialysis confers additional risk beyond what is seen in the general atrial fibrillation population, including excess risk of intracranial and access site bleeding.[9] Furthermore, warfarin might be associated with other adverse effects in patients on dialysis, including an increased risk of vascular calcification and calciphylaxis.[10]

The lack of randomized controlled trials evaluating the role of warfarin in preventing stroke and systemic thromboembolism in patients with atrial fibrillation undergoing haemodialysis has led to uncertainty regarding its safety and efficacy, as these patients are known to be at high risk of both thromboembolism and bleeding. Novel oral anticoagulants (NOACs) could provide an alternative to warfarin, but more data are needed regarding their safety and efficacy as most trials have excluded patients with severe renal impairment. An analysis of 29,977 US patients with atrial fibrillation on haemodialysis found that 5.9% of anticoagulated patients were administered either dabigatran or rivaroxaban, even though their use is contraindicated in patients receiving dialysis.[11] Anticoagulation with dabigatran or rivaroxaban was associated with increased risk of hospitalization or death from bleeding as compared to warfarin.

We agree with Schlieper and Floege that the overall data on warfarin in patients undergoing dialysis are conflicting[2] and we support the need for a large randomized controlled trial to test the efficacy and safety of warfarin versus a NOAC, potentially with monitoring of anticoagulant effects in both treatment groups. Until then, clinicians should be aware of the risks associated with warfarin in this patient population, and the decision to prescribe warfarin should involve an individualized approach that weighs the risk of stroke or thromboembolism against the risk of bleeding. Careful monitoring of the degree of anticoagulation and judicious use of heparin during haemodialysis could minimize the risk of bleeding complications with warfarin in these patients. In most cases, a considered approach will lead to a decision to prescribe warfarin.

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Competing interests
D.L.B. is on the advisory boards of Cardax, Elsevier Practice Update Cardiology, Medscape Cardiology, and Regado Biosciences; on the board of directors for Boston VA Research Institute and the Society of Cardiovascular Patient Care; Chair of the American Heart Association Get With The Guidelines Steering Committee; a member of the Data Monitoring Committees for the Duke Clinical Research Institute, Harvard Clinical Research Institute, Mayo Clinic, and the Population Health Research Institute; has honoraria from the American College of Cardiology (Senior Associate Editor, *Clinical Trials and News*, ACC.org), Belvoir Publications (Editor in Chief, *Harvard Heart Letter*), Duke Clinical Research Institute (clinical trial steering committees), Harvard Clinical Research Institute (clinical trial steering committee), HMP Communications (Editor in Chief, *Journal of Invasive Cardiology*), *Journal of the American College of Cardiology* (Associate Editor), Population Health Research Institute (clinical trial steering committee), and Slack Publications (Chief Medical Editor, *Cardiology Today's Intervention*), WebMD (CME steering committees); and is a deputy editor of *Clinical Cardiology*. He has received research funding from Amarin, AstraZeneca, Biotronik, Bristol-Myers Squibb, Eisai, Ethicon, Forest Laboratories, Ischemix, Medtronic, Pfizer, Roche, Sanofi Aventis, St. Jude Medical, and The Medicines Company, and has performed unfunded research for FlowCo, PLx Pharma, and Takeda. He is a trustee of the American College of Cardiology. A.Q. declares no competing interests.

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