Supplemental Material). Additional validation on non-European cohorts, using our online tool (https://rejectclass.pythonanywhere.com), would be very valuable to further strengthen confidence in the utility of our algorithm for reclassification of kidney transplant rejection.

DISCLOSURES

M. Naesens reports serving as an advisor for the European Medicines Agency and on the editorial boards of several journals. O. Thaunat reports receiving research funding from bioMérieux, Bristol Myers Squibb, Immucor, and Novartis; receiving honoraria from Biotest and Novartis; serving as a scientific advisor for, or member of, the European Society for Organ Transplantation; and having consultancy agreements with Novartis. The remaining author has nothing to disclose.

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REFERENCES


Addressing Transplant Candidacy When Evaluating Safety of Direct Oral Anticoagulant Agents in Patients on Hemodialysis

In their analysis of the subgroup of patients on hemodialysis in the Valkyrie study, De Vriese et al. do not directly address the risks and benefits of rivaroxaban in patients on dialysis who are candidates for kidney transplantation. Direct oral anticoagulant agents (DOACs) may affect transplantation because some surgeons will not proceed with transplant due to the risk of bleeding.

Although the timely discontinuation of DOACs is easily arranged before living-donor kidney transplantation, transplants from deceased donors, which account for two thirds of transplants in the United States, are nonelective procedures that do not accommodate advanced planning. The optimal time of DOAC discontinuation before surgery has not been established, particularly in patients with kidney failure. Reversal agents for DOACs remain expensive and rare and, as with DOACs, the safety and efficacy of these agents in the kidney failure population is lacking. Although table 2 of the De Vriese et al. manuscript notes one trial participant who discontinued rivaroxaban prematurely due to “registration on the transplant list,” the authors do not report how many other subjects were already on a transplant waiting list. In some transplant programs, patients may be inactivated on the waiting list when a DOAC is initiated, or sent home in the event they are called in unexpectedly for a deceased-donor kidney. The risk of a patient on DOACs being turned away for transplant increases if the organ offer comes late after recovery, when further delay in transplant would add unacceptably to the cold ischemia time. Organ offers made early, before deceased-donor organ recovery, may allow for discontinuation of the DOACs in sufficient time for the transplantation to proceed. A recent survey of transplant pharmacists emphasized the lack of evidence-based data and the variability in practice across centers and organ programs.

Patients on dialysis who have atrial fibrillation face many competing risks. Over the 18 months of follow-up in the Valkyrie study, 15 of 46 (32%) and 13 of 42 (31%) patients in the two respective rivaroxaban arms died (figure 1). Although no optimal treatment strategy exists for these complex patients, kidney transplantation is generally associated with lower

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mortality and higher quality of life compared with remaining on dialysis. Thus, a full discussion with patients of the risks and benefits of DOACs should include the effect on the patient’s transplant listing status and their ability to receive an organ if offered.

DISCLOSURES

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REFERENCES


See related reply on pages 2390–2391, and original article “Safety and Efficacy of Vitamin K Antagonists versus Rivaroxaban in Hemodialysis Patients with Atrial Fibrillation: A Multicenter Randomized Controlled Trial” in Vol. 32, Iss. 6, pages 1474–1483.

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Authors’ Reply

Reliable data on reversal of oral factor Xa inhibitors at the time of transplant surgery are lacking. Andexanet alfa, a recombinant variant of human factor Xa, efficiently reduced anti-factor Xa activity in patients with acute major bleeding,1 but no data exist in the setting of urgent transplant surgery. Alternatively, prothrombin complex concentrates can be used, despite not being specific reversal therapy agents, but published experience at the time of emergency surgery is limited to case reports.2 A survey of reversal practices among adult transplant programs in the United States indeed revealed that, although 64% of kidney transplant programs allow patients to remain on direct oral anticoagulants (DOAC) while on the transplant waiting list, only 7.8% reported routine use of DOAC reversal agents.3 This large practice variability calls for more guidance by professional societies, pending reliable research in this context. Taken together, we agree with Heher and Elias that the patient’s transplant listing status should be borne in mind when assessing the risk-benefit ratio of oral anticoagulation in the individual patient receiving hemodialysis.

However, patients with atrial fibrillation who are on hemodialysis are generally old and have a high burden of cardiovascular disease, as reflected by the median CHA2DS2-VASc score of five in our study population.4 As such, the large majority of these patients will not qualify for registration on the transplant waiting list. A small proportion of patients on hemodialysis with atrial fibrillation but less comorbid disease may be considered for kidney transplantation. In these patients, physicians face the dilemma advocated by Heher and Elias and may prefer vitamin K antagonists rather than DOAC. Oral anticoagulation is officially recommended when patients with atrial fibrillation have CHA2DS2-VASc scores of two or more for men and three or more for women. However, indirect evidence suggests that the CHA2DS2-VASc score overestimates stroke risk in patients on hemodialysis and that anticoagulation initiation should probably be more restrictive than is currently advocated.5 As such, many of these patients may be better treated without anticoagulation. Therefore, we believe the issue raised by Heher and Elias, although important and valid, applies only to a small minority of patients on dialysis and should not detract from the main message of our paper. We found that rivaroxaban significantly reduced the composite outcome of fatal and nonfatal cardiovascular events and major bleeding complications compared with vitamin K antagonists, and, therefore, submit that DOAC are the anticoagulants of choice in the hemodialysis population.

DISCLOSURES

A.S. De Vriese reports serving as a scientific advisor for, or member of, Ablync, Alexion, Amgen, Catenion, and Navigant; having consultancy agreements with Amgen; receiving honoraria from Amgen and Baxter; serving on a speakers bureau for Amgen and Baxter; and receiving research funding from Amgen, Kaydence Pharma, and NattoPharma.

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