Incidence of chronic kidney disease in patients with atrial fibrillation and its relevance for prescribing new oral antithrombotic drugs

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Atrial fibrillation (AF) is one of the major indications for therapy with direct thrombin (dabigatran etexilate) or factor Xa inhibitors (rivaroxaban). Both Dabigatran (80%) and Rivaroxaban (65%) are primarily excreted via the kidney [1]. Therefore, prescribing these drugs in patients with chronic kidney disease (CKD) could lead to accumulation and hence potentially to more bleeding complications [2]. Importantly, patients with an estimated glomerular filtration rate (eGFR) of < 30 mL min^{-1} have been excluded from trials with new antithrombotics [2–4]. However, patients with severe CKD are at increased risk of AF due to structural and electrical atrial remodeling [5,6]. Dabigatran has been approved by the Food and Drug Administration in an oral dose of 150 mg twice daily in AF patients with eGFR > 30 mL min^{-1} and in a dose of 75 mg twice daily in patients with eGFR 15–30 mL min^{-1} [7].

The National Kidney Foundation [8] has created guidelines to indicate stages of chronic kidney disease. Stage 1 incorporates patients with eGFR > 90 mL min^{-1} per 1.73 m^2 with structural abnormalities or genetic trait points. Patients with eGFR 60–90 mL min^{-1} per 1.73 m^2 fall into stage 2, those with eGFR 30–60 mL min^{-1} per 1.73 m^2 into stage 3, those with eGFR 15–30 mL min^{-1} per 1.73 m^2 into stage 4 and finally those with eGFR < 15 mL min^{-1} per 1.73 m^2 into stage 5. The incidence of AF in patients with CKD stage 5 is well known (about 7–13%). However, the different stages of CKD are not well studied in patients with AF [9]. Therefore, we evaluated the incidence of CKD stages 3–5 in patients with AF.

In a multicenter retrospective cohort study the medical charts of AF patients from the Leiden anticoagulation clinic starting anticoagulant therapy between January 1997 and April 2005 were scrutinized for creatinine levels. Patients were included if serum creatinine values were available within 6 months before or after the diagnosis of AF. The eGFR was calculated using the abbreviated MDRD formula because our study population was comprised of elderly patients, in whom the MDRD is more accurate in estimating the GFR in the lower ranges than the Cockroft–Gault formula [10,11].

During the inclusion period of our study, a total of 6933 new patients with AF visited the Leiden anticoagulation clinic. We excluded 1894 (27%) patients due to missing creatinine values, leaving 5039 (73%) patients for inclusion in our study. Fifty-nine per cent of patients were male and the mean age was 69.9 years (SD 12.4). The mean number of days between the first visit to the Leiden anticoagulant clinic and serum creatinine measurement was 2.2 days.

In 65.8% of all AF patients no renal impairment was found (i.e. eGFR > 60 mL min^{-1} per 1.73 m^2); 30.9% of patients had stage 3 CKD (eGFR 30–60 mL min^{-1} per 1.73 m^2), 2.5% had stage 4 CKD (eGFR 15–30 mL min^{-1} per 1.73 m^2) and 0.8% had end-stage kidney disease stage 5 (eGFR < 15 mL min^{-1}; see Fig. 1). In total 3.3% (95% CI, 2.8–3.8) of patients had an eGFR of < 30 mL min^{-1} per 1.73 m^2. According to

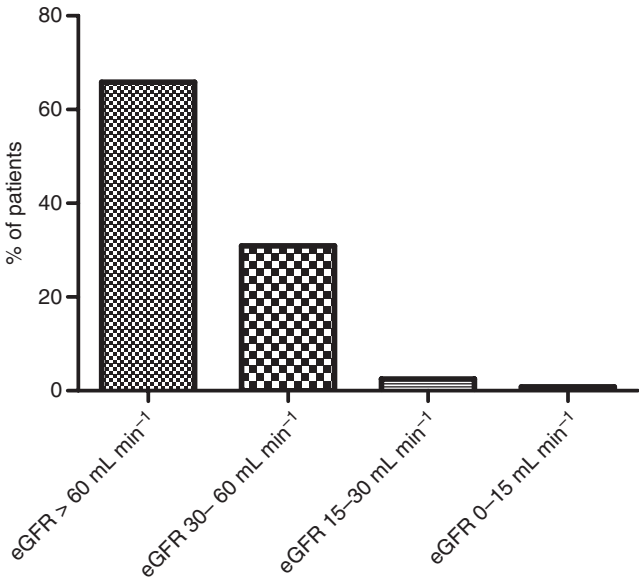

Fig. 1. Renal function in patients with atrial fibrillation.

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the criteria these patients would have been excluded from the RE-LY and Rocket AF studies [3,4].

The incidence of CKD in AF patients of 34.2% is comparable with the scarce literature [12]. Moreover, creatinine measurements were performed close to the diagnosis of AF, within a mean of 3 days.

Our study has limitations. First, we performed a retrospective analysis, which can be subject to various biases: the protocol for evaluating renal function in patients was not prespecified, leading to a variation in time between creatinine levels and diagnosis of AF. Second, creatinine levels were missing in 27% of patients. This might have affected our analysis. Third, due to missing values for bodyweight in our cohort, we were unable to compare the incidences of the different stages of CKD verified by both the MDRD and the Cockcroft–Gault formula. Fourth, there might be a small group of patients with CKD stage 5 for whom the physician decided not to prescribe VKA treatment because it could be anticipated that the risk of bleeding on VKA treatment would outweigh the benefit of the expected decreased risk of stroke. As a result, it might be possible that the incidence of CKD stage 5 in patients with AF is actually slightly higher than was reported in our analyses.

In conclusion, our study has potentially important implications for clinical practise. Prior to starting dabigatran or rivaroxaban, proper evaluation of kidney function is mandatory because 3.3% of patients with AF have an eGFR < 30 mL min^{-1} per 1.73 m^2 and cannot be treated with these drugs.

Disclosures and Conflict of Interests

The authors state that they have no conflict of interest.

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