Correspondence

Letter by Chin et al Regarding Article, “Efficacy and Safety of Dabigatran Compared With Warfarin in Relation to Baseline Renal Function in Patients With Atrial Fibrillation: A RE-LY (Randomized Evaluation of Long-Term Anticoagulation Therapy) Trial Analysis”

To the Editor:

We read with interest the article by Hijazi et al1 about the clinical outcomes of dabigatran compared with warfarin for atrial fibrillation in relation to estimates of renal function. The authors suggest that the Chronic Kidney Disease Epidemiology (CKD-EPI) equation may provide a better guide for dosing dabigatran compared with other renal function equations, at least in patients enrolled in the RE-LY trial with good kidney function.2 We believe there are several aspects of the article deserving of clarification and further consideration.

It is unclear whether the compensated Jaffe assay that was used to measure creatinine was standardized to the isotope dilution mass spectrometry (IDMS) method. This is important because the CKD-EPI equation was developed using creatinine measured by IDMS-aligned assays, and is not necessarily applicable to creatinine concentrations measured using assays that are not IDMS-aligned.2,3 In addition, the ‘186’ version of the Modification of Diet in Renal Disease (MDRD) Study equation was used in this study, instead of the ‘175’ version that was specifically derived for use with IDMS-aligned assays.1 It is difficult to gauge whether the results reported by Hijazi et al will have any bearing on current dabigatran dosing practice until this aspect of the analytical methods is clarified.

It is unclear what units were used in the data analysis for the estimated glomerular filtration rate (eGFR) calculated by the CKD-EPI equation. In the Abstract and Discussion section of the article, the units are stated as mL/min, whereas in the Results section the CKD-EPI eGFR was expressed as mL/min per 1.73 m2 of body surface area. Although the latter units are consistent with those used by international guidelines for defining categories of renal impairment, they are expected to be inferior to values of eGFR expressed as mL/min in the setting of drug dosing.1 A body surface area of 1.73 m2 reflects an individual with a height and weight of 170 cm and 64 kg, respectively. Although heights were not reported by Hijazi et al, the median (25th, 75th percentiles) weight was around 81 kg (70, 93), which suggests that most individuals had body surface areas greater than 1.73 m2. We have shown in a cohort of patients with a median (25th, 75th percentiles) body surface area of 1.94 m2 (1.73, 2.09) that estimates of gentamicin clearance using the CKD-EPI equation were significantly improved by converting the eGFR values from mL/min/1.73m2 to mL/min using individual body surface area.4 Others have reported similar improvements in relation to carboplatin, which is renally cleared, like dabigatran and gentamicin. If Hijazi et al used the CKD-EPI equation with units of mL/min/1.73 m2, it would be critical to know whether their findings are significantly altered with the use of CKD-EPI values adjusted for individual body surface area.

Choice of GFR equation may ultimately be important only for guiding the selection of the initial doses of dabigatran etexilate in the individual patient. In the future, subsequent doses may be adjusted according to targets based on either plasma dabigatran concentrations or clotting tests.5

Disclosures

None.

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References


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