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Title

Authors Have Incorrectly Calculated Need for Renal Dose Adjustments for NOACs

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To the Editor:

Yao, *et al.* report on NOAC dosing patterns in patients with atrial fibrillation and outcomes with under and overdosing. (1) A major concern is that in this study that investigates correct or incorrect dosing and the consequences—the authors have not correctly defined the need for adjustments based on renal function for two of the three NOACs studied (rivaroxaban and dabigatran). The recommendations for dosage reductions based on renal function for rivaroxaban are for patients with creatinine clearance as estimated by Cockcroft and Gault formula of <50 ml/min and for dabigatran if creatinine clearance is below 30 ml/min. The authors classified renal indications for dose reduction on eGFR in ml/min/1.73M² and not creatinine clearance as in FDA-approved dosing recommendations and as dosed in the randomized clinical trials that led to marketing approval and define the risk benefit ratios. (2, 3) Importantly, it has been shown that estimated glomerular filtration rate (eGFR) produces higher values than measured or Cockcroft and Gault-estimated CrCL at older ages (4) and may fail to identify 20-50% of patients for whom reduced dabigatran and rivaroxaban doses are recommended. (5) In the Figure, this is demonstrated with recent data from patients receiving NOACs at our institution. The investigators likely used eGFR since body weight is necessary to estimate CrCL and was not in the database as they note when acknowledging they did not consider weight that is 1 of 3 recommended criteria to be considered for reductions of apixaban dosing. (1) The results of Yao, *et.al.* as presented (1) likely underestimate higher than recommended dosing of rivaroxaban and dabigatran and further promote dosing errors in adjusting for renal function during use of rivaroxaban and dabigatran by suggesting eGFR and creatinine clearance are interchangeable in assessing the need for renal dose adjustment of these medications.

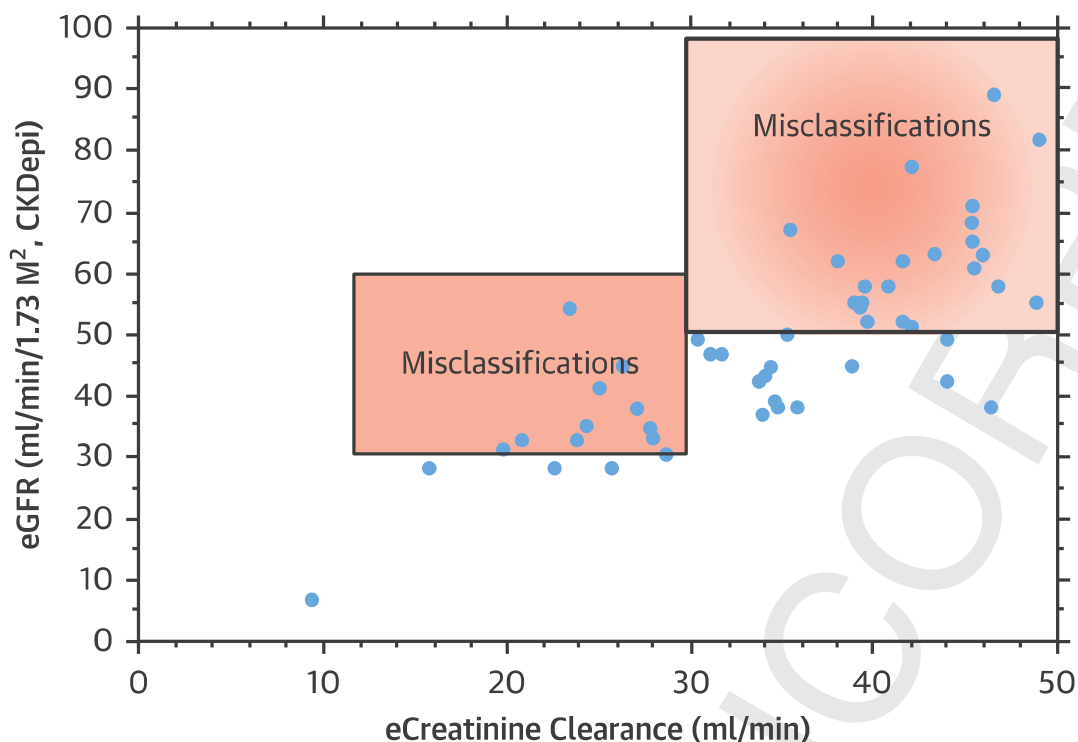
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Figure Legend

Estimated glomerular filtration rate (CKD-Epi) is presented on the vertical axis and estimated creatinine clearance (CrCL) on the horizontal axis for patients receiving NOACs. Estimates are numerically higher for eGFR. The shaded areas demonstrate differences that would result in failure to recognize the need for dosage reductions based on FDA recommendations if eGFR values were substituted for creatinine clearance (for rivaroxaban for CrCL below 50 ml/min or for dabigatran for CrCL below 30 ml/min).

FIGURE 1 ~~Estimated Glomerular Filtration Rate~~

Estimated glomerular filtration rate (eGFR) (Chronic Kidney Disease Epidemiology Collaboration formula [CKDepi]) is presented on the vertical axis and estimated creatinine clearance (eCreatinine Clearance) on the horizontal axis for patients receiving novel anticoagulants. Estimates are numerically higher for eGFR. The **shaded areas** demonstrate differences that would result in failure to recognize the need for dosage reductions based on recommendations from the U.S. Food and Drug Administration if eGFR values were substituted for creatinine clearance (for rivaroxaban for a creatinine clearance of <50 ml/min or for dabigatran for a creatinine clearance of <30 ml/min).