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LETTER

Machine Learning to Identify Patients at Risk of Inappropriate Dosing for Renal Risk Medications: A Critical Comment on Kaas-Hansen et al [Letter]

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Dear editor

Kaas-Hansen et al use machine learning to identify hospitalized patients at high risk of receiving a medication with inappropriate dose according to renal function.[1] Medication dosing during hospitalization is challenging, and we acknowledge the efforts by Kaas-Hansen to develop a prediction tool for prescribing errors. We have previously reported that at least 10% of older patients in our emergency department receive at least one medication at a dose higher than what would be recommended based on their renal function.[2] Ultimately, we believe machine learning could address this challenge by helping clinicians identify patients most likely to receive inappropriate medication doses. However, Kaas-Hansen et al do not assess the clinical applicability, implementation, or future improvement of their models, so it is difficult to comment on the impact of their study. We also have some methodological concerns with their study design.

One potential issue is the use of pro.medicin.dk for dosing recommendations. Pro.medicin.dk is used by many Danish clinicians but has several limitations. First, pro.medicin.dk does not provide any references, so it is impossible to validate its accuracy. Second, the recommendations in pro.medicin.dk are often ambiguous. For example, the recommendation for most opioids is "in patients with renal impairment dose reduction should be considered". In these cases, it is impossible to quantify the recommendation, which might explain why Kaas-Hansen studied only eight medications, none of which were opioids. Third, recommendations in pro.medicin.dk are based on GFR in body surface area (BSA)-normalized units (mL/min/1.73m^2), but dose recommendations from drug manufacturers are typically given in absolute units (mL/min).[3] Therefore, we believe it would have been more appropriate to calculate eGFR in absolute units and compare this to dose recommendations in the Summary of Product Characteristics for each medication.

The authors also do not consider the presence of acute kidney injury (AKI), which can affect the accuracy of GFR estimates and presents other challenges to medication dosing. In our own study of 339 older patients in the emergency department, we found that 33 patients (9.7%) met criteria for AKI within 48 hours of admission.[4] We would be interested to see a sensitivity analysis by Kaas-Hansen et al where patients with suspected AKI are excluded. A more general issue with this kind of study is that GFR can fluctuate during hospitalization. Even in the absence of AKI, patients with chronic kidney disease (CKD) can have up to 7% fluctuation in GFR due to biological variation alone.[5] Ideally, dosing of renal risk medications should be determined from the patient's baseline GFR, which is difficult to assess during hospitalization. Kaas-Hansen et al define their primary outcome as eGFR below 30 mL/min/1.73m^2 at any point during hospitalization, but temporary reclassification of CKD category is not necessarily clinically relevant. Dosing medications according the lowest GFR value during hospitalization could also lead to underdosing, which is itself problematic. For these reasons, it may be more useful to evaluate outcomes such as adverse drug events or rehospitalization.

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Disclosure

The authors declare no conflicts of interest in relation to this communication.

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