Reviewer’s report

Title: Epidemiology and health outcomes associated with hyperkalemia in a primary care setting in England

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Reviewer: Mariana Murea

Reviewer's report:

In their study "Observations on hyperkalemia incidence, severity, recurrence, and clinical consequences in the general population in England: a population-based analysis," Horne and colleagues used a large electronic database to describe the incidence of hyperkalemia and the associated factors and clinical outcomes over a period of 5 years in English population. The authors captured events of hyperkalemia from inpatient and outpatient medical settings and had a comprehensive phenotyping of comorbidities and medications present at the time of incident hyperkalemia. Overall, this is a well done study and the most striking finding is the lack of repeat serum potassium testing in a large proportion of individuals even when the index serum potassium level was >6.0 mmol/L.

Few comments and questions:

1. Did this cohort include individuals who had index hyperkalemia during a hospitalization? If yes, it would be important to compare the outcome of serum potassium retesting between those who had index hyperkalemia diagnosed in an inpatient versus outpatient basis.

2. The authors analyzed the incidence of various outcomes (Table 5: Cardiac arrhythmia, All-cause hospitalization, Death) following the episode of index hyperkalemia. It is unclear what timeframe was used (after the date of index hyperkalemia) to include these outcomes in the study.

3. An event of death could have competed with the outcome of repeat serum K level. This was not addressed in the current analyses and it would be important to adjust the analyses in order to include this aspect.

4. Factors associated with adverse clinical outcomes following an initial hyperkalemic event were analyzed with stepwise adjustment (Table 6). However, it is unclear what variables were included in the adjustment. For example, serum K level during the index event was associated with cardiac arrhythmia, all-cause hospitalization and death. Were these associations independent on eGFR or lack of use of other medications (ACE inhibitor, ARB, MRA)?
Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

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