Author’s response to reviews

Title: Risk factors for community-acquired Acute Kidney Injury in patients with and without chronic kidney injury and impact of its initial management on prognosis: a prospective observational study

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Point by point answers to the referees:

Referee one.

We thank the referee for his helpful review and comments.

Point 1 Not entirely clear why author’s chose to use 'the lowest creatinine value within the next 28 days after AKI' for patients who has no recent or previous creatinine values. I do not believe this assumption is standard practice and has likely confounded some of the results. Wouldn't the preferred method be to censor patients who did not have baseline values from those calculations?
Regarding baseline “reference” serum creatinine, as one fifth of our patients did not have a baseline creatinine prior to the onset of AKI (and to censor them would have excluded too many data), the reference serum creatinine was estimated from the nadir serum creatinine value if patient recovers from AKI (according to the clinical practice guidelines of the UK renal association). The 28-days limit was arbitrarily decided by ourselves as the great majority of reversible AKI recovered in our study within this time limit during their hospital stay.

Manuscript change: see modifications in the methods and results section

Point 2: Recommend creating one more abbreviation for patients with CKD and AKI (page 10, line 20): CA-ACKI (Community Acquired-Acute on chronic kidney injury)

New abbreviation added in manuscript as suggested. CKD replaced by CKI and AKI/CKD by CA-ACKI

Point 3: Please reword line 31 on page 11.

Could the reviewer be more specific, we do not really understand what we have to reword?

Point 4: Recommendations are generally not appropriate in the concluding paragraph of a manuscript (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3626472/). Suggest shortening the conclusion.

Conclusion shortened as suggested. Last paragraph suppressed

Manuscript change: see modifications in the discussion section

Referee two.

Point 1: Patients with an eGFR less than 60 mL/min/1.73 upon admission to the emergency department were screened for changes in creatinine levels. Why only patients at eGFR below 60 mL/min? A drop in eGFR from 120 to 60 mL/min would signify serious AKI, but appears to be ignored?
The enrollment was based on the availability of the eGFR provided automatically by the laboratory using MDRD equation at the time of the study, and displaying directly eGFR < 60ml/min/1.73m2. We agree that we probably have missed some cases by not using the cut-off estimated by the CKD-EPI equation, not available at this time. We also agree that we have probably missed significant drop of eGFR in those having higher eGFR, but the idea was also to identify those with CK injury. We added this information in the methodology section and discuss this limitation in the discussion.

Manuscript change: see modifications in the methods and discussion sections

Point 2. Although the authors claim to have performed a prospective study in patients presenting at the ED and report mortality data after one and three years, the outcome data were not derived from prospective follow-up, but from community registry data. Please provide more data to define data quality. There must be some migration and thus loss of follow-up. How was this taken care of?

Geneva is a very dense urban community with only one public hospital and the information about follow-up can be retrieved quite easily in our database as well as from general practitioners, with whom there is close contact. There was no loss of follow-up (as mentioned in our discussion)

Point 3. Causes of AKI were adjudicated as renal/prerenal/postrenal. Only a minority of cases appear to be adjudicated as renal AKI. Please clarify adjudication rules.

They were adjudicated as renal/prerenal/postrenal according to classical diagnostic criteria. Our results do not differ significantly from other studies (see ref 4,7) which also have a predominance of prenal etiology in their population.

Manuscript change: see modifications in the methods section

Point 4. In general, please describe the workings of the group of nephrologists responsible for case review. How many nephrologists in total, how many nephrologists reviewed individual cases, what was the procedure in case of disagreement between nephrologists.
We have detailed the involvement of our nephrologists in the cases’ reviewing process

Manuscript change: see modifications in the methods and Authors’ contributions sections

Point 5. Did the authors explore outcomes as a function of severity of AKI?

We have analyzed the impact of AKI severity on mortality and renal recovery at 3 years, but due to the likely lack of power of our study, the results in the multivariate analysis are not contributive and we decided not to include them in our paper.

3yr-Mortality stage II: HR (95% CI): 1.59 (1.08-2.35); stage III: HR (95% CI): 1.24 (0.66-2.31)
Renal recovery: stage II: HR (95% CI): 1.60 (0.78-3.28); stage III: HR (95% CI): 0.77 (0.21-2.91)

Point 6. In the introduction, the authors refer to a study stating that AKI is a frequent disorder with an incidence of 400 cases per 100000 persons (or 0.4%). In their study on the ED of the Geneva university hospital, a tertiary reference center, the observed incidence is 4%. Please elaborate on this quite discrepant incidence rates. Does this point to selection bias?.

Likely due to different types of populations studied as in the study by Wonnacott and colleagues; their patients had a lower socio-economic profile and more severe AKI (57% stage II-III versus 24 % in our study). Wonnacott’s restrospective study focused on hospitalized patients and collected with a time study of 6 months and we were studying prospectively patients sent to the ED of our hospital within a 6-week period.

Manuscript change: see modifications in the discussion section

Point 7. The authors used modified KDIGO criteria. Why not use the original KDIGO criteria? Please clarify the interested reader to the exact modifications.
We suppressed “modified “ in this definition. This term was referring to the definition of our reference baseline serum creatinine. Manuscript change: see modifications in the methods section.

Point 8. The authors looked at changes in serum creatinine and urinary output to diagnose AKI. What percentage of diagnoses were made based on serum creatinine values and what percentage based on urinary output data. What was the delay between presentation at the ED and the diagnosis of AKI based on serum creatinine vs. urinary output data?

10 percent of our patients (31/325 patients) had their urine output recorded and the diagnosis was therefore based exclusively on a rise in serum creatinine. Laboratory results are usually available within less than one hour.

Manuscript change: see modifications in the methods section

Point 9. Patient characteristics are reported as mean ± standard deviation (see Table 1). When assuming a normal distribution, a mean age of 79.5 and a SD of 12.8 in patients having acute of chronic kidney injury, this would imply that about 2.5% of cases were 105 or older at time of presentation at the ED. Unless one in forty patients belongs to the extremely old, it seems wise to provide median plus interquartile range.

Although SD is, we believe, a valid measure of variability regardless of the shape of the distribution. we have added the median + IQR in table 1