Author's response to reviews

Title: Risk Factors and Outcomes Associated with Acute Kidney Injury following Ruptured Abdominal Aortic Aneurysm

Authors:

Ilana Kopolovic (kopolovi@ualberta.ca)
Kim Simmonds (mksimmonds@gmail.com)
Shelley Duggan (sduggan@sedmnepr.ca)
Mark Ewanchuk (m.ewanchuk@gmail.com)
Daniel E. Stollery (dstoller@gpu.srv.ualberta.ca)
Sean M Bagshaw (bagshaw@ualberta.ca)

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Author's response to reviews: see over
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Authors:

Ilana Kopolovic (kopolovi@ualberta.ca)
Kim Simmonds (mksimmonds@gmail.com)
Shelley Duggan (sduggan@sedmeph.ca)
Mark Ewanchuk (m.ewanchuk@gmail.com)
Daniel E. Stollery (dstoller@gpu.srv.ualberta.ca)
Sean M Bagshaw (bagshaw@ualberta.ca)

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Author's response to reviews: see over
Dear Prof. Henderson,

Re: M S: 7609631499020601 – “Risk Factors and Outcomes Associated with Acute Kidney Injury following Ruptured Abdominal Aortic Aneurysm”

Thank you for the opportunity to revise and resubmit our manuscript to *BM C Nephrology*. We have reviewed your letter dated March 31, 2013 and have provided itemized responds to the Reviewer’s comments below. We appreciate your suggestions and believe the manuscript has now been strengthened.

Response to Reviewer1 Comments:

Methods: Missing baseline creatinine. Although methods are well described, it may be interesting to mention if any of the included patients had missing baseline creatinine as expected. If so, how these missing variables were handled. *Baseline creatinine values were available for all included patients. We have clarified this in the Methods section.*

Results, Crude mortality. Crude ICU and hospital mortality in patients without AKI being null, reporting OR for these events in patients with AKI seem unreliable. *We agree with the reviewer. We have omitted the OR for mortality.*

Results, recovery. The chosen definition is likely to have underestimated rate of partial or absence of renal recovery. Indeed, definition of renal recovery is based on return to baseline serum creatinine. As consequences of the hospital length of stay, weight and muscles loss, “normal” discharge creatinine in patients without persistent renal dysfunction should be lower than baseline creatinine. Hence, discharge serum creatinine in patients with AKI was 6 µmol/L lower than baseline creatinine. This limit probably deserves to be mentioned more clearly in discussion section. *This is a thoughtful comment by the Reviewer. We agree with the Reviewer that our definition could indeed overestimate the rate of complete recovery and misclassify certainly partial recovery. We doubt we would significantly misclassify non-recovery given this represents less than 10% decline from peak SCr. We have included comment on this issue in the discussion section. Ideally, to enable careful quantification of discharge kidney function, this would require measurement of kidney function (and with inulin clearance instead of time urine collection for creatinine). We added comment regarding this to the Limitations section.*

Was any information regarding the type of surgery (open vs. endo-vascular repair), delay between diagnosis and surgery or existence of shock at time of the surgery available? In addition, location of the AAA (infra renal vs. supra or pararenal AAA) is likely to have influenced post-operative renal function.
Of the 140 patients with rAAA, 96.4% (n=135/140) received open repair. We have included this data in the results section. We unfortunately do not have available the duration of time between diagnosis and surgical intervention. We recognize this maybe a confounding factor for the risk of post-operative AKI along with mortality. We have commented on this in the Limitations section. Of the 140 patients, 83.3% had infra-renal AAA and cross-clamping while the remaining were documented as supra-renal. In our study, we did not find statistical association between cross-clamp site and post-operative AKI (75.5% vs. 77.3%, p=1.0). We have included this data in Table 1.

Response to Reviewer 2 Comments: Major Compulsory Revisions

1. Figure 1. If data was extracted 1 year postdischarge from mortality, how are there 1500 post-operative days in the x-axis. If data was extracted for patients beyond 1 yr, then it needs to be mentioned in the methods.

   This was a retrospective study over an 8 year period and data was extracted in 2011-2012 for admissions with rAAA ending at December 31, 2009. To ensure at minimum 1-year follow-up for all enrolled patients, we extracted data up to Dec 31, 2010. Accordingly, some patients who presented at the beginning of the data collection period (i.e., 2001-2005) may have available up to 5 years of follow-up for survival. While we could truncate the survival time at 1-year, we felt it was more informative to include the longer time-to-event where relevant for patients still alive at the time of data extraction.

Minor Essential Revisions

1. In Operational Definitions: need to say how information on pre-op medications obtained.

   We have clarified that this was extracted from the patient's medical record. This is a provincial electronic medical record that links to pharmacy data on all prescription medications.

2. In Operational Definitions: need to say what was a positive troponin, was it any detectable troponin or a specific value.

   We have now clarified this in the Methods section.

3. Operational definitions: Need to more specifically define AKI. Was the initial creatinine the baseline creatinine 6 months prior? Was the AKI-defining creatinine at the time of hospital presentation, post-operative creatinine or creatinine anytime during the hospitalization.

   As stated in the Methods section, baseline creatinine was any outpatient creatinine available within 6 months of acute hospitalization. We have now better clarified the definition we utilized for ascertaining the diagnosis of AKI and severity stage following presentation.

4. Operational definitions. The term post-operative AKI needs to be defined, and which creatinine was the post-op creatinine compared to, was it the baseline creatinine or the creatinine at presentation.

   See above comment.

5. In Epidemiology and patient characteristics: Please specify if there were any patients with missing baseline data on Creatinine or other missing variables of baseline characteristics.

   There were no missing data for creatinine or other baseline characteristics.
6. In Epidemiology and patient characteristics: Please specify if there were any exclusions for ESRD.

As stated in the Methods section “Design, Setting, and Participants”, those with ESKD were excluded.

7. Incidence and peri-operative factors associated with AKI: In the end of para 1, the table referenced should be table 1, not table 2.

This has been clarified.

8. Hospital Outcomes: Table referenced should be Table 2, not Table 1.

This has been clarified.

9. Long-term outcomes: please mention if anyone had missing 1 year data for mortality.

We had complete ascertainment of vital status for all patients at 1-year. This has been clarified.

10. Table 2. Row 1. Baseline SCr needs units.

This has been corrected.

11. Table 2. Rows 2,3. Units for GFR should be ml/m in/1.73m², not cm². Also it should say baseline eGFR rather than just GFR.

These have been corrected.

12. Table 2. Row 6. Delta SCr needs units and need to put SD or IQR at the end.

This has been corrected.

13. Table 2. Column 6. Need to know if p is for trend of AKI stages or for comparison between AKI and no AKI.

P-value is comparison across all groups. This has been clarified.

14. Table 3. Rows 11,12. Same as point 9 above.

These have been corrected.

15. Table 3. Column 5. Need to know if p is for trend or for comparison between recovery and non recovery.

P-value is comparison across all groups. This has been clarified.

16. Figure 1. y axis needs Survival, % as an axis legend.

This has been corrected.

17. Figure 2. y axis needs the units of eGFR in the axis legend.

This has been corrected.

18. Figure 2. x axis should say Complete Recovery and Partial Recovery rather than just Complete or Partial.

This has been corrected.

Discretionary Revisions
1. Epidemiology and patient characteristics: I think the increase in incidence of
rAAA should say 6.9% per million per year.  
*This has been corrected.*

2. Key findings: same points as above.  
*This has been corrected.*

3. Figure legend for figure 2. Maybe it should say, Renal recovery status at hospital discharge or in-hospital mortality stratified by baseline estimated glomerular filtration rate.  
*This has been corrected.*

4. Table 2, Row 4. Due to large variability in urine output among patients the mean output does not convey much. It may be better to say number of patients that had oliguria, for example. Please say in methods, when the mean urine output data is from during the hospitalization.  
*We have defined the variable oliguria in the Methods section and added it to Table 2.*

The manuscript has been reviewed and approved by all authors. The authors have no conflicts of interest to declare.

If you require any additional information, please contact us as necessary. We appreciate your consideration of our manuscript for possible publication in *BMJ Nephrology* and look forward to your review.

Sincerely,

Ilana Kopolovic  
Kim Simmonds  
Shelley Duggan  
Mark Ewanchuk  
Daniel E. Stollery  
Sean M. Bagshaw