Author’s response to reviews

Title: Long-term predictive value of acute kidney injury classification in diffuse proliferative lupus nephritis with acute kidney injury

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Dear editor and Reviewers:

Please find a manuscript number BNEP-D-19-00903,“Long-term predictive value of acute kidney injury classification in diffuse proliferative lupus nephritis with acute kidney injury”by Tianxin Chen, Ying Zhou, Jianna Zhang, Chaosheng Chen, Jingye Pan. Thank you for considering my article for publication in BMC Nephrology. I am grateful to you and the reviewers for the valuable suggestions provided. Those comments are all valuable and very helpful for revising and improving our paper, as well as the important guiding significance to our researches. We have studied the comments carefully and have correction which we hope meet with your approval. We would be happy to make any further changes that may be required. Revised portion are marked red in the paper.

The main corrections in the paper and the responds to the reviewers comments are as following:

1,Reply to Reviewer 1:

1) Please consider a Table to help readers remember AKI stages.
Response : We have added the table of KDIGO AKI classification to the paper to explain the definition of AKI stage.
3) Why did you decide on using the AKI stage on day of admission instead of highest AKI stage reached during the initial hospitalization?
Response: Diffuse proliferative lupus nephritis (DPLN) can manifest as endocapillary proliferative glomerular nephritis, mesangial proliferative glomerular nephritis, membranoproliferative glomerular nephritis or crescentic nephritis in renal biopsy. Glomerular proliferation can cause AKI. After admission, DPLN patients usually receive diuretics due to edema and ACEI/ARB due to proteinuria or hypertension. Some patients also complicate with infections. Medications and complications after admission can cause renal function decline. The causes of highest AKI stage reached during the initial hospitalization includes glomerular proliferation, medications and complications. We think the AKI stage on day of admission is better to reveal renal function impairment caused by DPLN than the highest AKI stage reached after admission.

4) Did many patients worsen AKI stage during initial hospitalization?
Response: Most DPLN patients during initial hospitalization didn’t progress to worsen AKI stage after immunosuppressive drugs. About 10% AKI patients had worsening AKI stage during initial hospitalization. The common factors making renal function worse are diuretics and infections. Rarely, one patient with AKI 2 stage progressed to AKI 3 stage due to hemorrhagic shock after renal biopsy. Some patients had Scr increase but didn’t fit the criteria of higher stage of AKI.

5) Page 8 of 24, Line 35 have category. Response: Done

6) Table 2: make font size in caption the same. Response: Done

7) Page 9, Line 45 needs spacing between words. Response: Done. We also put HR, HR 95%CI,P value into this sentence.

8) Page 9, Line 54. It doesn't make sense that there could be 'advances' in treatment if the outcomes have not improved. There may be more options for treatments, but the efficacy does not appear to be improved.
Response: The first sentence of discussion was replaced by “There are more options for treatments in recent years, but the efficacy does not appear to be improved obviously in DPLN patients.” which was accurately express my ideas. Thank reviewer giving me instruction on how to express the ideas.

9) Page 10, Line 38: However, the outcome of DPLN with AKI hasn't been improved obviously although intravenous MP pulse therapy. ?'although treated with intravenous MP pulse therapy."
Response: This sentence has syntax errors and can’t express my ideas clearly. It was replace by sentence--“More than 60% DPLN patients with AKI-2 and AKI-3 stage received intravenous MP pulse therapy, but the renal survival rate can’t be improved effectively.”

10) Page 11, Line 34: put the active RR value into your discussion sentences. Relative risks were particularly high in DPLN with AKI patients who had heavy proteinuria (24-hour urine protein>3.0g). Place values also: Besides, the multivariate Cox regression analysis revealed that anemia (Hb<8.0g/dl) and crescents (more than 30%) were independent risk factors for ESRD...
Response: we have put HR into the discussion sentences and put HR, HR 95%CI,P value into the results.

11) Page 12; patients' allocation. Response: Done
12) Page 12, Line 1: This sentence needs to be rewritten as it is not clear in its meaning. It was not easy to be affected artificially because this study was not a clinical trial to evaluate therapeutic effect of drug intervention.
Response: We want to express our ideas that” this study was not a clinical trial to evaluate therapeutic effect of drug intervention, so our doctors were not biased against certain groups of patients during follow-up.” It have been rewritten.

13) Page 12, Line 7: they may produce false-positive results, or they over-estimated the magnitude of an association. This sentence needs to be rewritten for both grammar and clarity.
Response: It have been rewritten and replaced by “our small size study may over-estimated the magnitude of an association between risk factors and renal outcomes.”

14) Page 12, line 12: These sentences need to be rewritten for grammar and clarity. However, estimated required sample size to get any kind of meaningful result was 122 based on power(1-β=0.8),α(5%) and overall probability of events. sample size in our study was 167 patients, which was sufficient to Cox regression analysis.
Response: The required sample size was 122 patients based on statistic power of a test(80%) and type I error (5%), so 167 patients in our study were sufficient to prognostic analysis of renal outcome using Cox regression model.

15) Figure 1: There appears to be no difference with censored lines of data. Are the censored lines necessary?
Response: no censored lines makes the figure more clear. Figure 1 has been revised.
We are very sorry for our negligence and having taken your precious time to correct our writing errors. Special thanks to you for your good comments.

Reply to Reviewer 2:
1) Comment 1: I am unclear if these patients presented as AKI, with prior normal kidney functions and biopsy post admission showed DPLN.
Response: Some patients had prior normal kidney functions (they had normal serum creatinine before admission); others didn’t have the records of serum creatinie, so the diagnosis of AKI was based on the clinical condition and renal biopsy (no chronic changes in renal pathology).

2) Comment 2: Or were they DPLN patients who were readmitted with AKI? If it is the latter, we need baseline and delta creatinine.
Response: AKI stages of DPLN patients were based on serum creatinine level at the day of initial admission. If the patient was readmitted with AKI-3, who would still be classified according the AKI stage of the first admission. During follow-up, we found some patients were readmitted with AKI due to complications such as sepsis shock and medications. So we think the AKI of initial admission is better to reveal renal function impairment caused by DPLN than the AKI after treatments. We assumed AKI caused by DPLN would predict the long-term outcome of DPLN patients.

3) Comment 3: Kindly check the formatting and the language throughout the paper please. There are many sentences in the article that would benefit from language correction.
Response: We are very sorry for our incorrect writing and now check the formatting and the language throughout the paper carefully. Revised portion are marked red in the paper.