Author's response to reviews

Title: The Top Tertile of Hematocrit Change During Hospitalization is Associated with Lower Risk of Mortality in Acute Heart Failure Patients

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Author’s response to reviews:

1. Line 216 cox --> Cox

Response: Thank you for pointing out this flaw. We have corrected it.

2. Table 2

There is no need to present analysis of all 3 states of Hematocrit as the referent group, as this is essentially presenting the same data from the viewpoint of the different referent groups, repetition that is unnecessary; and is not what was suggested by the reviewer. Using the Hemodilution group only as referent would fit best with the main message of the manuscript, as the reviewer suggested.

Response: Thank you for your suggestion. As is presented in revised table 2, we deleted unnecessary parts and used the hemodilution group as referent only in the Cox regression analysis.

3. As requested in Point 5 from Reviewer 2 the the authors should perform a formal sample size calculation for inclusion in the Statistical Analysis section, based on the effect sizes estimated
from analyses reported in the similar studies reported in the manuscript and extrapolated to the current study.

Statements such as "For cox regression, sample size should ≥ 15 times the number of variables. We were able to satisfy these standards." if included in the revised manuscript, should be supported by suitable citations.

Response:

1) We performed a sample size calculation with the consultation of the Department of Statistics, Southern Medical University. All analyses were performed using PASS version 11.0. Cox regression was selected.

Parameter settings: Power: 80%, Significance level: 0.025, R-squared of X1 with other X’s: 0.00, Standard deviation of X1: 0.50.

Hemoconcentration vs. hemodilution:

Overall event rate: we estimate the overall event rate to be 35% during the median follow-up of 20 months according to similar studies (Van der Meer, 180 days, 18.2% of patients died), (S.J. Greene, 9.9 months, 24.4% of patients died), (Davila, 15.4 months, 26.7% of patients died).

Log hazard ratio: Referring to other similar studies comparing patients hospitalized for HF with hemoconcentration to those without: (Van der Meer, HR=0.66), (J. Oh, HR=0.485), (Testani, HR=0.16), we estimate the HR to be 0.40.

The calculated sample size was 130.

NC vs. hemodilution:

With reference to the same research cited above, we estimate the overall event rate to be 45% and the HR to be 0.60. The calculated sample size was 324.

Finally, we choose a relatively larger value of 324. We estimate that every group include identical samples. The calculated sample size: (324/2)×3 = 486

2) However, calculation of sample size is imprecise, we should view the calculated sample size as an approximation to the necessary size. We have added sample size information to the Statistical Analysis section.