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Predictive factors for longer length of hospital stay in patients with heart failure

To the Editor,

I have read the article by Kato et al. (1) entitled "Higher diuretic dosing within the first 72 h is predictive of longer length of stay in patients with acute heart failure" which was published in Anatol J Cardiol 2018; 20: 110-6, with great interest. In their study, authors reported that higher diuretic dosing in the first 72 h of hospitalization was an independent predictor of longer length of hospital stay in patients with acute heart failure. In addition, they concluded that there could be important predictors of the length of hospital stay that were not included in their study. Beside this, they reported that laboratory data of patients, including serum sodium level and cardiac troponin values, were recorded on admission and during the first 72 h of hospitalization (1). I would like to emphasize some important points about this well-written study.

It has been demonstrated that cardiac troponin is an important marker for the prognosis of acute heart failure. In previous studies, it has been shown that an elevated cardiac troponin level on admission has been associated with increased length of hospital stay (2, 3). Moreover, hyponatremia is a common electrolyte disorder in patients with heart failure. It has been reported that patients admitted with hyponatremia show increased hospital mortality and rates of longer hospital stay (4). Therefore, I wish to ask the authors why they did not mention about serum sodium levels and cardiac troponin values of patients in baseline characteristics and did not use these parameters in the statistical evaluation, although they possessed the data for these parameters.

Further, the presence of edema at admission and the change in weight during hospitalization are major factors influencing the length of hospital stay in patients with heart failure (5). I believe that the aforementioned factors should be considered to verify the predictive value of higher diuretic dosing within the first 72 h on hospital stay in patients with acute heart failure.

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Length of hospital stay, diuretic dosing, and regression strategies

To the Editor,

In previous issues of the journal, we read with great interest the article by Kato et al. (1) entitled "Higher diuretic dosing within the first 72 h is predictive of longer length of stay in patients with acute heart failure" published in Anatol J Cardiol 2018; 20: 110-6.

The study included 333 patients with acute heart failure, and the authors demonstrated that higher diuretic dosing in the first 72 h of hospitalization was an independent predictor for a longer length of stay. However, we have major concerns regarding the methodology and statistical design of the study.

First, it is well known that the “length of stay” has a right skewed distribution (2, 3). Accordingly, the mean length of stay was 7.9±6.4 days, which was found to be not distributed normally [large standard deviation (SD)]. In this case, it is possible to have incorrect results if an ordinary least square (OLS) is performed for a prediction model. It is more reasonable to perform a Poisson regression or negative binomial regression analysis instead of OLS for evaluating the length of stay data. In addition, the percentage of patients was discharged from hospital is not known because a histogram for length of stay was not provided by the authors. Thus, it is not possible to extrapolate the data used for analysis regarding the percentage of patients discharged from the hospital and the diuretic dosing of the patients in the first 72 h.

Second, the authors stated that a stepwise regression model was performed by using every variable except creatinine (Cr), hematocrit (Hct), and mean arterial pressure (MAP) on presentation (there are 30 variables in Table 1). The variables were not included into the stepwise regression model because of the presence of significant multicollinearity and correlation between Cr, Hct, and MAP on presentation with blood urea nitrogen (BUN), ∆Hct and ∆MAP. The major drawback for this method is to ignore the possibility that a variable and its delta or change-percent relationship can have a significant correlation. In addition, change and/or delta variables of a parameter are not considered statistically powerful compared to those obtained directly from a patient. As an example, Hct and MAP on presentation are always statistically more powerful than ∆Hct and ∆MAP.

Third, it is known that the stepwise regression analysis may lead to biased and incorrect results particularly in cases of significant overfitting (4). The authors performed logistic regression analysis for 30 day readmission and in-hospital mortality. In the best scenario, there should be either 250–300 readmission and/or 250–300 in-hospital mortality outcomes to reduce the risk of overfitting (a rule of thumb at least 10). The presence of both performing stepwise regression and significant overfitting generally lead to biased/incorrect estimation of regression coefficients (as examples, diabetes mellitus reduced the risk of in-hospital mortality by 9–10 fold and brain natriuretic peptide had odds ratio=1.00, 95% confidence interval=1.00–1.00, and p=0.001 for in-hospital mortality).

Fourth, the authors performed mediation analysis to evaluate the relationship between diuretic dosing, length of stay, and worsening renal function (WRF). In fact, mediation analysis was performed by adding only one covariate to the simple regression model that included dependent and independent variables. This model had a trivial contribution to statistical analysis.

Lastly, we think it would be more appropriate to perform Poisson or negative binomial regression analysis for length of stay predictors, linear regression or quantile regression in case of violation of OLS assumption for WRF predictors, and binary logistic regression analysis for readmission and in-hospital mortality outcomes. The number of variables included in statistical models should be limited to prevent overfitting (reduce the number of candidate predictor or dimension reduction methods) or preferably use penalized regression methods. In addition, biologically plausible and other prognostically important variables should be included in the statistical models instead of choosing variables from stepwise analysis and univariable significance. The model should be improved after the imputation of missing data, and performance measures (calibration and discrimination etc.) of the model should be provided.

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Author`s Reply

To the Editor,

We appreciate insightful comments regarding our study demonstrating the predictive value of higher diuretic dosing in the first 72 h of hospitalization on the length of hospital stay (1). We are happy to provide further clarification and data to address their concerns in our statistical approaches.