

Letter to the Editor

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Response by Izzy et al to Letter Regarding Article, “Cerebrovascular Accidents During Mechanical Circulatory Support: New Predictors of Ischemic and Hemorrhagic Stroke and Outcome”

In Response:

We thank Drs Zheng and Niu for their interest in our study. The first question concerns the results of multivariable logistic regression and more specifically the odds ratios and their corresponding 95% CIs of post-LVAD ischemic stroke and post-LVAD hemorrhagic stroke. In our multivariable regression model to predict mortality, we included post-LVAD ischemic stroke and hemorrhagic strokes as 2 independent variables. The reference population for both of these outcomes is the group of patients who underwent LVAD implantation but did not experience either ischemic or hemorrhagic stroke. Consequently, these odds ratios and 95% CIs reflect the risk of each type of stroke relative to an outcome of no stroke. Our intention was to assess the effect of stroke on mortality, not to compare the mortality of ischemic to hemorrhagic stroke. The odds ratio of hemorrhagic stroke was higher than that of ischemic stroke, which is suggestive but not statistically conclusive of a higher magnitude of association with mortality. We agree with your criticism that the abstract should not suggest such a comparison. The finding is correctly stated in the Results of the article: post-LVAD ischemic stroke and hemorrhagic stroke were both predictors of mortality independent of each other as compared with post-LVAD patients who did not develop stroke.¹

To address the question of bimodal risk over time, we estimated hazard functions of post-LVAD overall stroke, ischemic stroke, and hemorrhagic stroke over time in our cohort. This analysis showed that the risks of both overall stroke and ischemic stroke, but not hemorrhagic stroke, were higher early and late in the post-LVAD implantation period, suggesting that our cohort also demonstrates a bimodal distribution. We were unable to assess the association of risk factors for ischemic and hemorrhagic stroke in the immediate postoperative period compared with the postdischarge period using the same timeline criteria as Frontera et al² because of the small sample size (pre-discharge post-LVAD censored and post-LVAD stroke patients n=11) in the early timeline, which limited our analysis and did not allow our model to converge.

We agree that incorporating many variables into the prediction model may result in collinearity and make it challenging to interpret the results. Though stepwise selection can address the issue of collinearity, one of the limitations of the stepwise approach is that it fails to account for clinical and physiological significance. As a consequence, it may eliminate potential predictors of survival, such as, age, dialysis dependence, or history of prior

stroke, for which one has a good a priori justification to anticipate relevance. A solution to this problem is to force such covariates into the model even though their *P* values are not significant to account for their potential confounding effect and obtain adjusted measures of association. For mortality, we think that all of the variables included in the regression model are highly supported by evidence-based literature to be likely significant predictors of life span and survival; thus we included them in the final model. This statistical approach of force inclusion of a large number of covariates in the regression model is not unique to this study and has been adapted by other published studies in the literature.³ This trade-off in the choice of analysis captures information lost by step-wise selection, while accepting the ambiguities because of possible collinearity.

Disclosures

None.

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Stroke. published online July 5, 2018;

Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231

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Print ISSN: 0039-2499. Online ISSN: 1524-4628

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