Reviewer's report

Title: B-type natriuretic peptide and mortality in extremely low birth weight infants with pulmonary hypertension: a retrospective cohort analysis

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Reviewer: Kathryn Farrow

Reviewer's report:

In this retrospective cohort study, the authors examined the utility of serum BNP levels as a predictor of outcome in preterm infants with bronchopulmonary dysplasia-associated pulmonary hypertension (BPD-associated PH). The authors demonstrate that the peak BNP level was significantly lower among infants who survived than among those that died. Statistical analysis revealed that a BNP level of 220 pg/mL had a 90% sensitivity and 65% specificity in predicting mortality.

Major Compulsory Revisions:

1. The authors report that in their population there is no difference in SGA status between the survivors and non-survivors. However, there is a significant body of data in the literature that SGA infants are at increased risk for BPD-associated pulmonary hypertension versus AGA infants (Bhat, et al. Pediatrics 2012; Check, et al. J Perinatol 2013). The present data would suggest that once these SGA infants develop the disease, they are at no greater risk to die than AGA infants. This is an important and novel concept that should be emphasized in the discussion.

2. The authors performed all of their analysis using the peak BNP levels, but as shown in Figure 1, there is a large amount of overlap between the levels in survivors vs. non-survivors. For those survivors with levels above the identified threshold of 220 pg/mL, did serial levels return to “normal” levels more quickly than the elevated levels in non-survivors? The authors themselves state that: “Serial BNP measurements may be helpful in identifying those infants at high and low risk for mortality.” It would seem from the methods that the authors already have some of this data from this population. Perhaps they could provide some insight in the discussion about trends, if the data are not yet statistically significant due to small sample size.

3. In the discussion, the authors state, “An important limitation is the lack of follow-up data on survivors, including rehospitalization and post-discharge mortality.” However, in Figure 3, the authors present survival data for the patients with elevated BNP out to 600 days. Does that mean 20% of the patients with elevated BNP (approximately 3 patients) were in the hospital for almost 2 years before their initial discharge? Furthermore, Figure 3 would suggest that some late mortality for those with low BNP levels as the survival curve drops...
precipitously from 100% survival to 40% survival at 400 days. This is very confusing and needs clarification.

Minor Issues Not for Publication:

1. There is a typographical error in the last sentence of the discussion. It should be “BNP levels will lead to decreased morbidity and mortality.”

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

I declare that I have no competing interests.