**A Complicated Glenn Procedure: risk factors and association with adverse long-term neurodevelopmental and functional outcomes**

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**Online Supplemental Text**

**1. Supplemental Methods Section**

**2. Supplemental Results Section**

**3. Supplemental Discussion Section**

**1. Supplemental Methods Section**

*Post-hoc statistical analyses*

For use of inhaled nitric oxide (iNO), we explored association with lowest PaO2 on day 1 and day 2-5 post-operatively, highest lactate on day 1 and day 2-5 post-operatively and time for lactate to fall to ≤2 mmol/L post-operatively; inotrope score on day 2-5 post-operatively (33); and number of transfusions on day 1 post-operatively. This was done using Pearson correlation coefficients with two-sided p-value.

For day 1 inotrope score, we explored association with lowest PaO2 on day 1 and day 2-5 post-operatively, highest lactate on day 1 and day 2-5 post-operatively and time for lactate to fall to ≤2 mmol/L post-operatively. This was done using univariate linear regression and presented as effect size with 95% CI and two-sided p-value.

These variables were chosen as variables that may reflect the cardiac output and pulmonary blood flow of the patient when iNO and inotropes were used. We also explored all pre- and post-operative echocardiographic and MRI/catheterization data for their association with iNO use and day 1 inotrope score using univariate logistic or linear regression respectively.

Finally, we also explored the association of highest CVP (i.e. Glenn Pressure) on day 1-5 post-operative and a surrogate for transpulmonary gradient, measure by d1-5 postoperative highest CVP minus d1-5 postoperative highest LA pressure (in the n=108 who had this measured), with having a cGP.

**2. Supplemental Results Section**

*Post-hoc exploratory associations*

We explored associations with the use of iNO post-operatively after the Glenn procedure as this was strongly associated with developing a cGP. Use of iNO was associated with: highest lactate post-operative day 1 (OR 1.55, 95% CI 1.16, 2.07; p=0.003) and day 2-5 (OR 1.37, 95% CI 1.09, 1.74; p=0.008) and time for lactate to fall to ≤2 mmol/L (OR 1.20, 95% CI 1.04, 1.37; p=0.01); lowest PaO2 post-operative day 1 (OR 0.89, 95% CI 0.82, 0.97; p=0.005) and day 2-5 (OR 0.93, 95% CI 0.87, ,0.99; p=0.03); highest inotrope score on post-operative day 2-5 (OR 1.30, 95% CI 1.17, 1.43; p<0.001); and with number of transfusions on post-operative day 1 (OR 3.01, 95% CI 1.52, 5.93; p=0.002).

We also explored associations with the inotrope score post-operative day 1, finding the following correlations with inotrope score: highest lactate post-operative day 1 (r=0.29, p<0.001) and day 2-5 (r=0.23, p=0.003) and time for lactate to fall to ≤2 mmol/L (r=0.34, p<0.001); and post-operative lowest PaO2 on day 1 (r=-0.27, p<0.001) and day 2-5 (r=-0.19, p=0.01).

The hemodynamic and anatomic variables we collected were analyzed for univariate associations with use of iNO, and post-operative day 1 inotrope score (eTable 4). Collateral vessels identified post-operatively, present in 5.9% of patients, was associated with less iNO use and higher inotrope score. Moderate ventricular dysfunction post-operatively, present in 15.4% of patients, was associated with a higher inotrope score.

We also explored the association of highest CVP (i.e. Glenn Pressure) on day 1-5 post-operative with a cGP, with HR 1.00 (95% CI 0.94, 1.06) p=0.99. We explored the association of a surrogate for transpulmonary gradient, measure by d1-5 postoperative highest CVP minus d1-5 postoperative highest LA pressure (in the n=108 who had this measured), with univariate HR 0.99 (95% CI 0.91, 1.09) p=0.91.

**3. Supplemental Discussion Section**

After multivariable logistic regression, DHCA used during the Glenn procedure was independently associated with higher Bayley-III Cognitive and Language scores. Our center routinely uses regional cerebral perfusion techniques during DHCA. While historically there was an association between length of DHCA and neurological morbidity (both short term and long term), a recent review emphasizes that there is no evidence to support one technique over another (specifically, DHCA vs low flow CPB or regional cerebral perfusion) (28). The lack of difference is likely attributed to improved intraoperative neuromonitoring and improved intraoperative techniques (29). In our series, 15 of 169 patients required DHCA for concomitant procedures at the time of the Glenn operation; 10 of these required an arch repair. As DHCA was used in only 8.9% of patients, and we explored many relationships, it is possible this association with neurodevelopmental outcomes was a false positive.

After multivariable logistic regression, the presence of pre-Glenn PA obstruction was independently associated with higher cognitive and motor scores on the Bayley-III. This might reflect pre-operative surgical planning to optimize repair of this PA obstruction, resulting in a drop in cerebral venous pressure postoperatively. This is consistent with the finding that post-operative PA obstruction was independently associated with adverse motor scores on the Bayley-III, likely due to persistent high cerebral venous pressures postoperatively. Nevertheless, pre-operative PA obstruction was not statistically associated with highest CVP d1-5 or highest TPG d1-5 post-operatively. Of patients with pre-operative PA obstruction, 28 (35%) had pulmonary artery plasty at the time of the Glenn; however, having this done for the PA obstruction was also not statistically associated with post-operative d1-5 highest CVP or TPG. These findings do not support our hypothesis but must be interpreted in light of the limitations of the CVP, LAP, and TPG not being recorded simultaneously nor continuously. The p-values for this finding can be considered only suggestive and confirmation is required in future studies.