**Online Supplement**

**Detailed Methods**

The current study analyses a prospective cohort of pediatric patients who underwent congenital heart surgery at Johns Hopkins Hospital between 2010 to 2014 (n=244). Children were excluded if they did not have preoperative biomarker information collected, immediately prior to skin incision, during their index cardiac surgery operation (n=70). Children were also excluded if they were older than 18 years of age (n=9), weighted 2.5 kg or less at the time of birth (n=1), or had an unknown prematurity status (n=2). The final analytic cohort consisted of 162 pediatric congenital heart surgery patients at risk for hospital readmission (Figure 1).

Patient, clinical, and outcome data were collected using a software platform that is approved by The Society of Thoracic Surgeons as being suitable for submission of data to the Society of Thoracic Surgeons Congenital Heart Surgery Database.  Blood samples were collected immediately prior to surgery and at the end of bypass. Biomarkers were measured using Meso Scale Discovery. The Committee for the Protection of Human Subjects at Dartmouth College Institutional Review Board approved this study for the prospective cohort with child/parental consent.

*Assays*

A custom made robotically spotted multiplex chemoelectrolumiscent ELISA for sST2 and Gal3 (Meso Scale Discovery, Gaithersburg, MD) was developed using commercial capture, detection and standards (R&D systems). Interplate (N=10) percent coefficient of variation for low and high internal controls for sST2 and Gal 3 was a mean of 11.2 and 14.9 and 13 and 18.3 respectively. The GFAP assay has been described previously and had an interplate percent coefficient of variation of 12.2 for an internal control.18,21-26

*Outcome*

The composite study endpoint was unplanned readmission or mortality within 30 days following discharge from the index surgical admission. These outcomes were verified via data linkage between state all-payers claims data, hospital chart review, and the National Death Index using Social Security numbers and date of birth. Mortality included both in-hospital mortality during the index surgical admission or mortality at any location within 30 days after discharge from the surgical admission. Readmissions to Johns Hopkins Hospital between 2010 and 2015 were included. Readmissions were defined as the first unplanned admission within 30 days of an index hospitalization where the congenital heart surgery occurred. Planned readmissions were assessed via pediatric-specific measure specifications developed by the Boston Children’s Hospital Center of Excellence for Pediatric Quality Measurement (CEPQM).27 The cardiologist responsible for data collection in the current study served as an expert reviewer to identify planned readmissions via CEPQM specified International Classification of Diseases, Ninth and Tenth Revision, Clinical Modification procedure codes. These specifications are endorsed by the National Quality Forum (NQF) and Agency for Healthcare Research and Quality (AHRQ). In the study’s final cohort (n=162) no child experienced planned readmission within thirty days after discharge from index hospitalization.

*Predictive models*

We developed three predictive models. The first was a clinical risk model developed to characterize risk of post-discharge hospital readmissions or mortality after pediatric congenital heart surgery. This model was adapted from the Society of Thoracic Surgeons Congenital Heart Surgery Database mortality risk model.28 Variables in this backwards stepwise model were based on key risk factors associated with pediatric congenital heart surgery. Variables included in the initial backwards stepwise regression included: STAT mortality category,29 cardiopulmonary bypass time, any preoperative factor, acute kidney injury, ICU length of stay, hospital length of stay and presence or absence of (i) any preoperative risk factor, (ii) and major complication and (iii) acute kidney injury. “Any preoperative risk factor” was considered to be present if the child experienced preoperative mechanical circulatory support, shock persistent at time of operation, renal dysfunction, mechanical ventilation to treat cardiorespiratory failure, preoperative neurological deficit, or any other preoperative factor. The final backwards stepwise regression model included cardiopulmonary bypass time, any preoperative risk factor and any major complication.

The second model was an augmented clinical risk model with the addition of our novel preoperative biomarker panel. This biomarker panel includes preoperative Galectin-3, sST2, NT-ProBNP, and GFAP.

The third model was an augmented clinical risk model with the addition of a pre-and postoperative biomarker panel. The biomarker panel includes pre-and postoperative Galectin-3, sST2, NT-proBNP and GFAP. Pre-and postoperative biomarker ranges are outlined in Table 1.

*Statistical Analysis*

Descriptive statistics and univariate analyses were used to describe the sample and compare patient and clinical characteristics by 30-day readmission or mortality status. Univariate and multivariable logistic regression was used to examine the relationship between preoperative biomarker values and 30-day readmission or mortality. Backwards stepwise logistic regression (p-values < 0.1) and the area under the receiver operating characteristics curve (AUROC), were utilized to explore variables to be included in the models. The two models were evaluated via AUROC, net reclassification improvement (NRI) and integrated discrimination improvement (IDI) analyses. The discriminating ability of the regression model was determined by the AUROC and bootstrap to calculate 95% CI’s around the ROC-curve.30,31

The AUROC measures the model’s ability to distinguish between subjects with and without the outcome of interest.32 The IDI and NRI quantify the added value of additional predictors (i.e., a biomarker panel) to the original model (i.e., clinical model), in terms of difference in precision gains and the probability of providing a correct reclassification of risk.33 These three measures offer complementary information on the assessment of incremental predictive value and therefore are reported together.34,35