**Supplementary Material**

Supplementary Table 1: Demographics and Clinical Characteristics of External Validation Cohort

Supplementary Table 2*:* Comparison of Developmental and External Validation Cohorts

Supplementary Table 3: Summary of Genetic Conditions

Supplementary Table 4: Summary of Candidate Variables

Supplementary Table 1: Demographics and Clinical Characteristics of External Validation Cohort

|  |  |  |
| --- | --- | --- |
|  | **No Chylothorax****(n = 114)** | **Chylothorax****(n = 57)** |
| Malea  | 64 (56%) | 32 (56%) |
| Genetic conditiona | 36 (32%) | 18 (32%) |
| Surgical weight (kg, median) | 8.2(IQR 5.0, 19.7) | 5.2(IQR 3.3, 8.0) |
| Age at surgery(years, median) | 0.9(IQR 0.3, 5.9) | 0.4(IQR 0.1, 1.0) |
| DSC  | 10 (9%) | 20 (35%) |
| CPB time (minutes, median) | 176(IQR 109, 248) | 173(IQR 0, 285) |
| STAT category 1, 2, 3 | 62 (54%) | 25 (44%) |
| STAT category 4, 5 | 52 (46%) | 32 (56%) |
| CTO on PCD 1(mL/kg/day, median) | 11.3(IQR 4.9, 17.5) | 21.6(IQR 16.6, 35.4) |
| PCD at chylothorax diagnosis(day, median) |  | 9.7(IQR 4.7, 15.3) |

aMatched variables in the cohort

CPB: cardiopulmonary bypass, CTO: chest tube output, DSC: delayed sternal closure, PCD: post-closure day, STAT: The Society of Thoracic Surgeons-European Association for Cardio-Thoracic Surgery

Missing values: None

Supplementary Table 2: Comparison of Developmental and External Validation Cohorts

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Utah**(n = 763) | **Stanforda**(n = 171) | P-value |
| Age at surgery(years, median) | 0.5(IQR 0.1, 3.4) | 0.7(IQR 0.2, 3.8) | **0.026** |
| Race | Caucasian | 697 (91%) | 73 (43%) | **<0.001** |
| Non-Caucasian | 66 (9%) | 98 (57%) |
| CPB time (minutes, median) | 100(IQR 62.5, 136) | 173(IQR 104.5, 275.5) | **<0.001** |
| CTO on PCD 1(mL/kg/day, median) | 7.9(IQR 3, 16.9) | 13.2(IQR 5.7, 20.3) | **<0.001** |

a Stanford cohort with each chylothorax encounter matched 1:2 to a non-chylothorax encounter based on gender and presence of genetic condition with 1:2 ratio of patients with chylothorax

CPB: cardiopulmonary bypass, CTO: chest tube output, PCD: post-closure day

Missing values: None

Supplementary Table 3: Summary of Genetic Conditions

|  |  |  |  |
| --- | --- | --- | --- |
|  | **No Chylothorax (n=185)** | **Chylothorax** **(n=21)** | **Total (n=206)** |
| **Genetic Syndromes** |  |  |  |
| Trisomy 21 | 73 (39%) | 11 (52%) | 84 (41%) |
| 22q11 Deletion | 31 (17%) | 0 (0%) | 31 (15%) |
| Heterotaxy Syndrome | 14 (8%) | 4 (19%) | 18 (9%) |
| Chromosome 15 Microdeletion | 4 (2%) | 0 (0%) | 4 (2%) |
| Turner Syndrome | 2 (1%) | 0 (0%) | 2 (1%) |
| Williams Syndrome | 2 (1%) | 0 (0%) | 2 (1%) |
| Noonan Syndrome | 1 (0.5%) | 1 (5%) | 2 (1%) |
| Apert Syndrome | 1 (0.5%) | 0 (0%) | 1 (0.5%) |
| Cornelia de Lange Syndrome | 1 (0.5%) | 0 (0%) | 1 (0.5%) |
| G6PD Deficiency | 1 (0.5%) | 0 (0%) | 1 (0.5%) |
| Holt Oram Syndrome | 1 (0.5%) | 0 (0%) | 1 (0.5%) |
| Hurler-Scheie syndrome | 1 (0.5%) | 0 (0%) | 1 (0.5%) |
| Marfan Syndrome | 1 (0.5%) | 0 (0%) | 1 (0.5%) |
| Trisomy 12 | 1 (0.5%) | 0 (0%) | 1 (0.5%) |
| Trisomy 13 | 1 (0.5%) | 0 (0%) | 1 (0.5%) |
| Wolf-Hirschhorn syndrome | 1 (0.5%) | 0 (0%) | 1 (0.5%) |
| **Extracardiac Anomalies** |  |  |  |
| Cleft Lip/Palate | 3 (2%) | 1 (5%) | 4 (2%) |
| Major Abnormality of the Spine | 3 (2%) | 0 (0%) | 3 (1%) |
| Major Abnormality of the Kidney | 2 (1%) | 0 (0%) | 2 (1%) |
| CHARGE | 1 (0.5%) | 1 (5%) | 2 (1%) |
| VACTERL | 1 (0.5%) | 1 (5%) | 2 (1%) |
| Alagille Syndrome | 1 (0.5%) | 0 (0%) | 1 (0.5%) |
| CAM | 1 (0.5%) | 0 (0%) | 1 (0.5%) |
|  |  |  |  |
| **Other** | 37 (20%) | 2 (10%) | 39 (19%) |

CAM: cystic congenital adenomatous malformation of the lung; CHARGE: coloboma, heart defect, atresia choanae, restricted growth and development, genital abnormality, and ear abnormality; G6PD Deficiency: glucose -6-phospate dehydrogenase deficiency; VACTERL: vertebral abnormalities, anal atresia, cardiac defects, tracheal anomalies, esophageal atresia, renal and radial abnormalities, limb abnormalities

Supplementary Table 4: Univariable Analysis Candidate Variables

|  |  |  |
| --- | --- | --- |
| **Candidate Variables** | **OR (95% CI)**a | **p-value**a |
| Age (yr) | 0.82 (0.71,0.91) | 0.001 |
| Weight (kg) | 0.93 (0.88,0.97) | 0.002 |
| Race (caucasian) | 0.87 (0.4,2.15) | 0.73 |
| Gender (male) | 1.12 (0.68,1.85) | 0.66 |
| Genetic Condition | 1.13 (0.65,1.9) | 0.66 |
| STAT Categories 4 & 5 | 3.08 (1.86,5.22 | <0.001 |
| **Surgical Procedure** |
|  One ventricle without arch | 0.33 (0.13,0.85) | 0.021 |
|  Two ventricles with arch | 0.26 (0.1,0.65) | 0.004 |
|  Two ventricles without arch | 0.25 (0.12,0.55) | <0.001 |
| CPB time (min) | 1.01 (1,1.01) | <0.001 |
| Delayed sternal closure | 4.65 (2.71,7.87) | <0.001 |
| **Prior cardiothoracic surgery** |
|  One | 1.05 (0.57,1.89) | 0.87 |
|  Two | 1.09 (0.6,1.93) | 0.77 |
| **Chest Tube Output on Post-Closure Day 1** |
|  Less than 15.6ml/kg/day | 1.12 (1.09,1.14) | <0.001 |
|  Greater than 15.6ml/kg/day | 13.53 (7.71,25.04) | <0.001 |

aAnalysis of all 763 subjects

Supplementary Figure 1: Flowchart of Patient Selection

Supplementary Figure 2: Goodness of fit plot with external validation data set with Model A (left) and Model B (right)

Supplementary Figure 3: Model B Receiver Operating Characteristic (ROC) Curve