

Incorporating Comorbidity Within Risk Adjustment for UK Pediatric Cardiac Surgery

Katherine L. Brown, MPH, MD, Libby Rogers, MMath, David J. Barron, FRCS, MD, Victor Tsang, MS, FRCS, David Anderson, MD, Shane Tibby, MBChB, MSc, Thomas Witter, RN, John Stickley, BS, Sonya Crowe, PhD, Kate English, MRCP, MBChB, Rodney C. Franklin, MD, FRCP, and Christina Pagel, PhD

Great Ormond Street Hospital NHS Foundation Trust, London; Clinical Operational Research Unit, University College London, London; Department of Cardiac Surgery, Birmingham Children's Hospital, Birmingham; Department of Paediatric Cardiology and Cardiac Surgery, Evelina London Children's Hospital, London; Department of Cardiology, Leeds General Infirmary, Leeds; and Paediatric Cardiology Department, Royal Brompton and Harefield NHS Foundation Trust, London, United Kingdom

Background. When considering early survival rates after pediatric cardiac surgery it is essential to adjust for risk linked to case complexity. An important but previously less well understood component of case mix complexity is comorbidity.

Methods. The National Congenital Heart Disease Audit data representing all pediatric cardiac surgery procedures undertaken in the United Kingdom and Ireland between 2009 and 2014 was used to develop and test groupings for comorbidity and additional non-procedure-based risk factors within a risk adjustment model for 30-day mortality. A mixture of expert consensus based opinion and empiric statistical analyses were used to define and test the new comorbidity groups.

Results. The study dataset consisted of 21,838 pediatric cardiac surgical procedure episodes in 18,834 patients with 539 deaths (raw 30-day mortality rate, 2.5%). In addition to surgical procedure type, primary cardiac diagnosis, univentricular status, age, weight, procedure

type (bypass, nonbypass, or hybrid), and era, the new risk factor groups of non-Down congenital anomalies, acquired comorbidities, increased severity of illness indicators (eg, preoperative mechanical ventilation or circulatory support) and additional cardiac risk factors (eg, heart muscle conditions and raised pulmonary arterial pressure) all independently increased the risk of operative mortality.

Conclusions. In an era of low mortality rates across a wide range of operations, non-procedure-based risk factors form a vital element of risk adjustment and their presence leads to wide variations in the predicted risk of a given operation.

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Case mix adjustment for pediatric cardiac surgery incorporates operative complexity as well as the severity and type of the heart defect, patient age, size, and further noncardiac aspects of the patient's health or condition referred to as comorbidity [1-3]. The Partial Risk Adjustment in Surgery 1 (PRAiS1) risk model was developed and validated in 2011 to 2012, based on 10 years of National Congenital Heart Disease Audit (NCHDA) data from the United Kingdom [2]. Although the UK national audit data quality involved was in general excellent, the 1 area where data quality was poor was in respect of comorbidity information. For this reason, although a provisional categorization scheme was

developed (consisting of 4 main groups: Down syndrome, congenital conditions other than Down syndrome, acquired comorbidity, and prematurity) [2], it was only feasible to include a simple single factor indicating the presence/absence of a non-Down comorbidity within the PRAiS1 risk model. We note that Down syndrome was not associated with 30-day mortality and hence was not included in the PRAiS1 risk model [4]. Given the importance attributed to comorbidity in determining case mix complexity by stakeholders, it was hoped that inclusion of comorbidity within the PRAiS1 risk model would result in more comprehensive capture of comorbidity information within the national audit dataset and indeed this did turn out to be the case: the proportion of patients that had a documented non-Down comorbidity doubled in the NCHDA dataset from 15% to 30% between 2010 and 2013 [5]. Figure 1 shows the changing proportion of individual procedure records where specific reference was made to comorbidity (presence or absence) over time in the

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Address correspondence to Dr Brown, Great Ormond Street Hospital NHS Foundation Trust, Great Ormond St, London, WC1N 3JH, United Kingdom; email: katherine.brown@gosh.nhs.uk.

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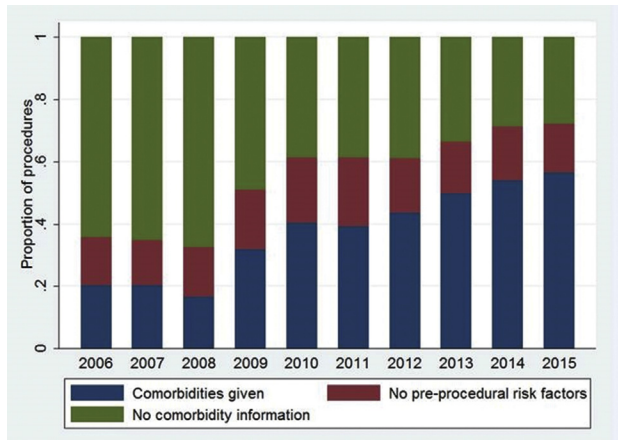


Fig 1. The changing proportion of comorbidity information (any code in a European Pediatric Cardiac Code [EPCC] comorbidity group) based on individual procedure records over time in the National Congenital Heart Disease Audit. Note that there is a specific EPCC code for no preprocedural risk factors.

NCHDA. Alongside this increase in data completeness, concerns were expressed by stakeholders about the large range of severity within the conditions included within the single comorbidity factor in the PRAiS1 risk model, and further it was noted that certain comorbid conditions were poorly defined within the NCHDA dataset and hence potentially a source of systematic bias or what has been referred to as gaming.

The aim of this study was to review the potential comorbidity conditions captured within recent NCHDA data and to explore options for better incorporating comorbidity within an updated version of the risk model referred to as the PRAiS2 risk model (described by Rogers and colleagues) [6], including consideration of how to address inclusion of conditions that were viewed as open to variable interpretation.

Patients and Methods

Dataset

The NCHDA is a mandatory and comprehensive audit of all pediatric cardiac surgery procedures undertaken in the United Kingdom and Ireland, with centers subjected to a continuous and completely inclusive system of validation that includes the review of a sample of case notes by external auditors to ensure coding accuracy [7]. Further information about the study dataset, which consisted of 21,838 pediatric cardiac surgical procedure episodes undertaken in 18,834 patients between 2009 and 2014, with 539 deaths (raw 30-day mortality rate, 2.5%), is available Rogers and colleagues [6]. The unit of analysis in the study was a 30-day episode of surgical management and the outcome was vital status at 30-days following the first surgery in such an episode. The NCHDA dataset uses the European Pediatric Cardiac Code (EPCC) system [8] and each procedure can have several different comorbidity codes recorded.

Expert Panel

A clinical expert panel was convened, which included 2 data managers (T.W., J.S.), 3 pediatric cardiac surgeons (D.A., D.J.B., and V.T.), 2 cardiologists (R.C.F., K.E.), and 2 pediatric cardiac intensive care specialists (K.L.B., S.T.) representing a range of large and smaller UK centers. The clinical expert panel and the analytical team worked iteratively to improve the scope, relevance, and validity of the comorbidity information included in the risk adjustment model.

Aims of the Expert Panel

The expert panel held 2 face-to-face meetings over the course of a year and took part in iterative discussion between these meetings, with the following aims:

- 1) To explore options for incorporating comorbidity within the PRAiS2 risk model—options included a list of individual conditions, a simple count of conditions, and modified groupings of comorbidity conditions building on the previous categories formed during the development of the PRAiS1 model [2].
- 2) To identify and exclude comorbidities represented in the NCHDA dataset that may be difficult to define consistently such as where existing definitions are not available and conditions that are very rare within the context of pediatric cardiac surgery or are otherwise not clinically relevant.

Context in Terms of the Wider Risk Adjustment Model

In addition to comorbidity risk factors, which are the subject of this report, the PRAiS2 risk model is a logistic regression model including: surgical procedure type (16 distinct risk groups of individual specific cardiac procedures), primary cardiac diagnosis (11 risk groups of individual primary cardiac conditions), age, weight, uni-ventricular status, procedure type (bypass or nonbypass), and an era indicator variable showing whether the procedure episode happened before or after 2013 [6]. Given the low raw mortality rate and overall number of deaths (539) there was a limit to the number of free parameters that could reasonably be included in the risk model and therefore the analysts advised the expert panel to limit the number of free parameters related to comorbidity and additional nonprocedural risk factors to less than 10.

Analyses

The expert panel qualitatively reviewed the entire list of 1,357 EPCC codes with focus on the 776 nonprocedural codes grouped as shown in Figure 2. The expert panel considered relevant literature, in particular recent publications regarding the Society of Thoracic Surgeons Congenital Heart Surgery Database (STS-CHSD) and current STS Risk Model to explore how comorbidity information was used within this risk score [3, 9, 10]. Based on consensus, a list of comorbid conditions that were considered to represent potential operative risk and to be clearly definable was identified based on specific EPCC codes.

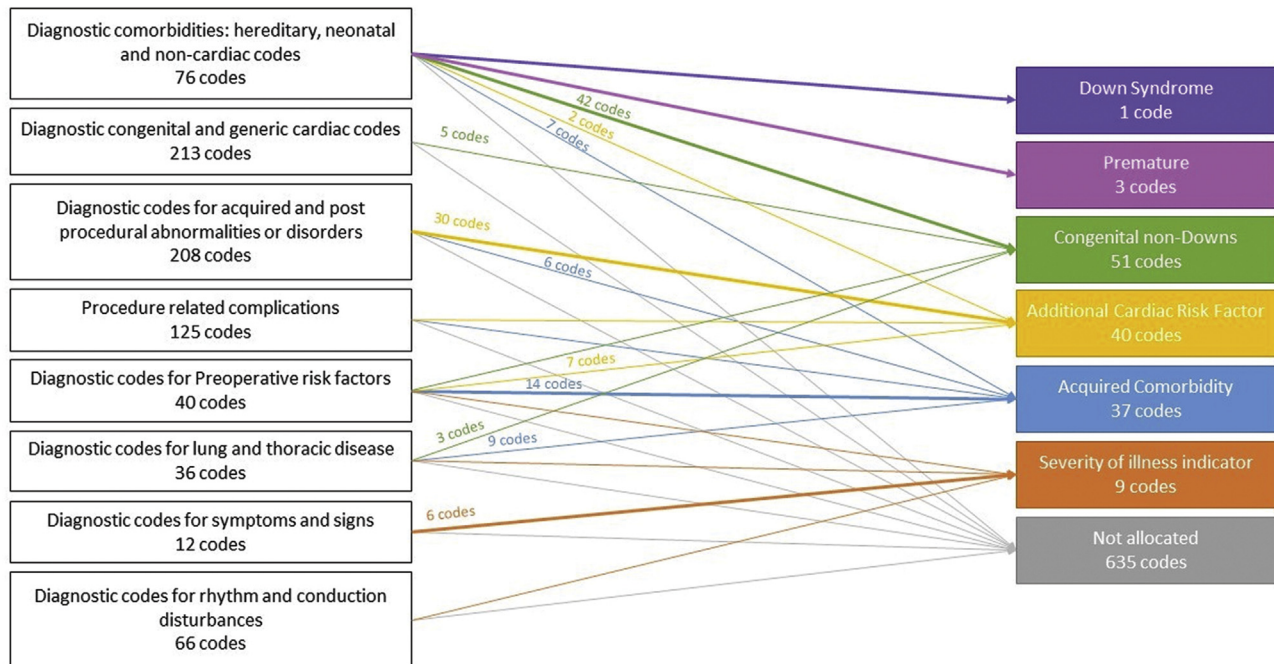


Fig 2. How individual conditions within European Pediatric Cardiac Code groups mapped to preoperative factors.

Conditions selected by the expert panel for inclusion were placed into groups linked by common distinct etiology.

Once preliminary comorbidity groups had been defined, univariate and multivariate logistic regression were used to explore the association with mortality of each of the candidate comorbidity groups in turn and when incorporating all statistically significant factors in the wider PRAiS2 model (see Rogers and colleagues) [6]. With a view to better understanding first the face validity of proposed comorbidity groupings (the extent to which the proposed comorbidity groups subjectively encapsulated the concept of comorbidity related to pediatric cardiac surgery) and second the added value within the risk adjustment model of individual conditions within each group, the expert panel considered the frequency and outcomes, based on 30-day surgical episodes, of individual conditions and comorbidity groups. This was augmented by review of frequencies of comorbidity groups in combination and of comorbidity groups based on age and univentricular status (both important risk factors included within the risk adjustment model). Associations between higher risk comorbidity groups and age or univentricular status were evaluated based on the chi-square test. In the final stages of the process the expert panel reviewed examples of risk predictions for individual patients to explore the face validity of the risk model in respect of the new comorbidity groupings.

Results

Preoperative Patient-Specific Factor Groups

Based on consensus and in consideration of the grouping options, relevant EPCC codes, and review of relevant

literature [4, 9, 10] the expert panel suggested 6 comorbidity groups. Figure 2 displays the EPCC code categories, from which the individual EPCC codes comprising each of the 6 comorbidity groups originate.

- 1) Down syndrome.
- 2) Congenital comorbidities excluding Down syndrome (all genetic syndromes, clinical constellations of features that constitute a recognized syndrome, and congenital structural defects of organs other than the heart) [11].
- 3) Acquired comorbidities, (preoperative comorbidities acquired as a result of heart disease or its treatments, such as renal failure or necrotizing enterocolitis) [12].
- 4) Prematurity (birth at a gestational age of less than 37 weeks).
- 5) Conditions indicating increased severity of illness in surgical candidates such as preoperative mechanical ventilation and preoperative mechanical circulatory support as feature in the current STS Risk Model [9, 13].

The panel noted evidence that additional or acquired cardiac specific conditions, in particular elevated pulmonary vascular resistance and impaired ventricular function, may place surgical candidates at increased risk [14–16], and therefore proposed the formation of a further category.

- 6) Additional cardiac risk factors, as is shown in Figure 2, conditions within the diagnostic codes for acquired and postprocedural abnormalities or disorders category (acquired cardiac conditions) [17] were predominant in this group. Codes were only put forward for inclusion where they were considered to have an unambiguously negative impact in any surgical candidate whatever the primary cardiac

diagnosis was (eg, cardiomyopathy, suprasystemic pulmonary arterial pressure) [18], and codes were ruled out where it was considered that clinically the impact of the condition under consideration might be variable from one patient to another and might even be the primary indication for surgery (for example pulmonary regurgitation) [19] or where a code was highly specific to a given primary diagnosis that was already a factor in the risk model (eg, intramural coronary in transposition of the great arteries) [20].

The wider risk model includes the risk factors of primary diagnosis and univentricular status, hence the expert panel elected not to consider prior cardiac surgery as a preoperative factor given its overlap with these features.

The expert panel considered that a simple count of comorbidities could lead to inflated predicted risk if several comorbidity codes for similar conditions were used, when the actual additional risk from the extra codes would be minimal. For this reason it was decided not to include an overall count of comorbidities, or a count within different categories. A yes or no indicator for each different category of additional risk meant that predicted risk would be increased if a surgical procedure episode contained different types of comorbidities or additional risk factors, while meaning records with several similar additional risk factors from the same group did not have any additional weighting for predicted risk.

Statistical Analyses

The frequency with which the preoperative factors were found within the study dataset are shown in Table 1 alongside the mortality rate for surgical episodes with the stated factor, whether other preoperative factors were also present within individual surgical episodes. The unadjusted odds ratios indicate that the univariate risk of postoperative death was significantly higher for congenital comorbidity, acquired comorbidity, severity of illness indicator, additional cardiac risk factors, and prematurity. Conversely, univariate risk of postoperative death was significantly lower in surgical episodes with Down syndrome. When multivariate risk of postoperative mortality was considered, there was no longer evidence for increased risk of postoperative death with prematurity,

most likely because weight and age, which are included in the PRAiS2 risk adjustment model, were more important and no longer evidence of significantly reduced risk of death with Down syndrome, most likely because Down tends to be associated with certain, low-risk diagnoses and procedures already included in the PRAiS2 model. The other 4 factors (comorbidity groups) remained individually statistically significant.

Risk Factor Combinations

There were 16,093 (73.7%) surgical episodes with no additional risk factors in terms of comorbidity and only 10 surgical episodes (<0.1%) with all 4 comorbidity risk factors present. The most common risk factor as a single condition was congenital comorbidity in 1,881 (8.6%), then severity of illness indicator in 1,538 (7.0%), then additional cardiac risk factors in 656 (3%), and last acquired comorbidity in 575 (2.6%). The most common combination of 2 risk factor groups was acquired comorbidity and severity of illness indicator in 274 (1.3%) which most likely reflects the clinical evolution of end organ dysfunction (conditions such as necrotizing enterocolitis or renal failure) in preoperative candidates that are more unstable and thus requiring preoperative intensive care supports (Table 2).

Distribution of Risk Factor Variables Within the Study Population

Based on the chi-square test, the only comorbidity risk factor that was evenly distributed between age groups and between functionally univentricular and biventricular hearts was acquired comorbidity. The other 3 risk factors all had statistically significant differences of proportion by age group and by number of functional ventricles ($p < 0.01$ for all differences, as follows). There was an increased proportion of surgical episodes with a severity of illness risk factor in the first year of life (when emergency procedures are more common) as compared to older children. Congenital comorbidity was more commonly noted with increasing age at surgical episode, most likely because certain conditions may take time for identification, and was more common in surgical episodes for biventricular hearts as compared with functionally univentricular hearts, reflecting the distribution

Table 1. Preoperative Patient Specific Factors and Outcome

Risk Factor	Number of Episodes With Risk Factor (%)	Mortality With Risk Factor (%)	Mortality Without Risk Factor (%)	Unadjusted Odds Ratio (95% CI)	Adjusted Odds Ratio (95% CI) (PRAiS2 ^a)
Acquired comorbidity	1,254 (5.7)	6.5	2.2	3.03 (2.38–3.87)	1.99 (1.52–2.61)
Additional cardiac risk factors	1,053 (4.8)	5.3	2.3	2.36 (1.78–3.14)	2.20 (1.61–3.03)
Congenital comorbidity	2,445 (11.2)	3.7	2.3	1.61 (1.28–2.03)	1.52 (1.18–1.95)
Down syndrome ^a	1,690 (7.7)	1.5	2.6	0.60 (0.40–0.89)	1.17 (0.72–1.91)
Prematurity ^a	2,664 (12.2)	4.0	2.3	1.82 (1.46–2.25)	0.87 (0.62–1.20)
Severity of illness indicator	2,260 (10.3)	7.5	1.9	4.23 (3.51–5.11)	1.75 (1.40–2.18)

^a Prematurity and Down syndrome were not significant on multivariate logistic regression, and hence are not included in the final Partial Risk Adjustment in Surgery 2 (PRAiS2) risk model, but were included in the adjusted odds ratios for this table.

Table 2. Combinations of Comorbidities and Additional Risk Factors

		No Additional Cardiac Risk		Additional Cardiac Risk Present	
		No Congenital Comorbidity	Congenital Comorbidity Present	No Congenital Comorbidity	Congenital Comorbidity Present
No acquired comorbidity	No severity of illness indicator	16,093 (73.7)	1,881 (8.6)	656 (3.0)	91 (0.4)
	Severity of illness indicator Present	1,538 (7.0)	161 (0.7)	143 (0.7)	21 (0.1)
Acquired comorbidity present	No severity of illness indicator	575 (2.6)	213 (1.0)	51 (0.2)	18 (0.1)
	Severity of illness indicator Present	274 (1.3)	50 (0.2)	63 (0.3)	10 (0.0)

Values are n (%).

of particular specific known combinations of cardiac and congenital comorbidity (eg, 22q11 deletion). There was a significantly lower proportion in the dataset with additional cardiac risk factors undergoing surgery in childhood than in infancy and with functionally univentricular as compared to biventricular circulation. This aspect requires further research into long term outcomes based on underlying primary cardiac diagnosis since it may reflect an adverse effect of acquired cardiac risk factors on survival over childhood and with certain more high risk CHD types (Table 3).

Risk Factors and Risk Prediction for Individual Patients

Table 4 displays a series of individual patients A to C, D to F, and G and H that have similar characteristics in respect of specific procedure, weight, age, and primary cardiac diagnosis. There are differences shown in terms of the individual additional risk factors (congenital comorbidity, acquired comorbidity, severity of illness, and additional cardiac risk factors), and the calculated risk predictions based on the PRAiS1 and PRAiS2 risk models show how dramatically predicted risk may change based on the way that these variables are dealt with in the risk adjustment model. Patients A, B, and C are all children with hypoplastic left heart syndrome that have undergone a Fontan operation, which is a low-risk procedure. Patient A has an additional cardiac risk factor and his risk is higher based on the PRAiS2 model than the PRAiS1 model, because the PRAiS1 model did not include consideration of additional cardiac risk factors. Patient B has no additional risk factors and his risk is almost identical between the PRAiS1

and PRAiS2 models. Patient C has a congenital comorbidity and hence within the PRAiS2 model has a specific additional risk linked to this risk factor, whereas based on the PRAiS1 model the additional risk is a broad non-procedure-based factor risk that incorporates the combined influence of a range of different comorbidities that were all grouped together as non-Down comorbidity risk factor in the PRAiS1 model.

Comment

Nonprocedural risk factors are important components of multivariate risk for 30-day outcome of pediatric cardiac surgery. The average risk associated with pediatric cardiac surgery is now very low (in this national dataset related to pediatric cardiac surgery between 2009 and 2014, the raw 30-day mortality rate was 2.5%), and specific procedures may be banded together into groups with similar (and in the majority of cases, low) risk: the discrimination of risk within such surgical procedure risk bands may vary considerably based on additional risk factors and comorbidities. The 4 broad clinical groups of congenital comorbidity, acquired comorbidity, severity of illness indicators, and additional cardiac risk factors as defined based on selected EPCC codes were each independently associated with increased risk of 30-day mortality. Consistent definition and case ascertainment for such preprocedural risk factors is of key importance when utilizing them within a risk adjustment model for research and for driving quality improvement in the care of pediatric cardiac surgery patients.

Table 3. Preoperative Risk Factors or Comorbidities in Relation to Age and Number of Functional Ventricles at Surgical Episode

Risk Factor	Neonatal Episodes	Infant Episodes	Childhood Episodes	Univentricular Episodes	Biventricular Episodes
Congenital comorbidity	387 (8.2)	1,005 (11.6)	1,053 (12.5)	310 (8.3)	2,135 (11.8)
Acquired comorbidity	298 (6.3)	491 (5.7)	465 (5.5)	214 (5.7)	1,040 (5.7)
Severity of illness indicator	1,102 (23.4)	996 (23.4)	162 (1.9)	325 (8.7)	1,935 (10.7)
Additional cardiac risk factors	197 (4.2)	590 (4.2)	266 (3.2)	126 (3.4)	927 (5.1)
Total	4,709	8,685	8,444	3,737	18,101

Values are n (%). There were statistically significant differences ($p < 0.01$) in terms of the proportion of surgical episodes with the preoperative risk factor by age and by number of functional ventricles for congenital comorbidities, severity of illness indicators, and additional cardiac risk factors based on chi-square test.

Table 4. Individual Patient Type Risk Profiles in the PRAiS1 and PRAiS2 Risk Models

Characteristic	Patient A	Patient B	Patient C	Patient D	Patient E	Patient F	Patient G	Patient H
Age	4 years, 7.4 months	4 years, 7.6 months	4 years, 7.8 months	5 days	6 days	9 days	5.3 months	5.4 months
Weight, kg	15.7	16.0	16.0	3.3	3.3	3.3	5.9	6.0
Specific procedure	Fontan ^a	Fontan	Fontan	Truncus and interruption repair ^b	Truncus and interruption repair	Truncus and interruption repair	Glenn ^c	Glenn
Diagnosis	HLHS	HLHS	HLHS	Common arterial trunk	Common arterial trunk	Common arterial trunk	HLHS	HLHS
Congenital comorbidity	No	No	Yes	No	No	No	Yes	Yes
Acquired comorbidity	No	No	No	Yes	No	No	No	No
Severity of illness indicator	No	No	No	Yes	Yes	No	Yes	No
Additional cardiac risk factor	Yes	No	No	Yes	No	No	No	Yes
PRAiS1 non-Down comorbidity	No	No	Yes	Yes	Yes	No	Yes	Yes
PRAiS2 calculated risk, %	2.17	0.96	1.44	33.30	10.16	6.15	4.06	5.04
PRAiS1 calculated risk, %	1.03	0.99	1.98	17.72	17.74	9.76	2.99	3.00

^a Completion of total cavopulmonary connection.^b Common arterial trunk and interrupted aortic arch repair.^c Unilateral or bilateral superior cavopulmonary anastomosis(es).

HLHS = hypoplastic left heart syndrome;

PRAiS = Partial Risk Adjustment in Surgery.

Findings in Context

The use of preoperative factors that go beyond procedure type, primary cardiac diagnosis, age, and weight has previously been limited by the availability of accurate registry-based data, with earlier risk adjustment efforts focused more narrowly [1]. In 2014 and based on recent data on 25,476 procedures, the STS-CHSD reported increased mortality rates associated with individual specific preoperative risk factors of mechanical circulatory support, renal dysfunction, shock, and mechanical ventilation [13]. These variables have since been included in the current empiric risk adjustment model supported by STS-CHSD for use in research and quality assurance [3], the variables represent important components of operative risk and vary widely in frequency across congenital heart programs [21]. We note that although the treatment of these additional preprocedural risk factors in terms of groupings differs between the PRAiS2 model and the current STS Risk Model, the factors or conditions included have much in common between the 2 risk adjustment methods.

Strengths and Weaknesses

One of the strengths of our study is that a consensus-based approach among clinical experts was deployed alongside empirical data analyses, with the specific aim of informing the creation of non-procedure-based risk groups. This process incorporated a review of every individual EPCC code by a multidisciplinary panel that aimed to achieve consistency and to include clinically important but also crucially readily definable conditions. That said, the project deliverables will inevitably reflect the views of the judging panel involved. A weakness of our methodology is that it is infeasible to pull out the relative importance of individual conditions that are grouped together, for example the magnitude of the risk linked individually to mechanical circulatory support, shock, mechanical ventilation, severe acidosis and cardiac arrest may differ. Although it might be clinically interesting to know this, there are limitations in terms of the absolute number of episodes with certain conditions present (problems of small numbers and lack of power), and furthermore there are limitations in terms of the degrees of freedom for a risk adjustment model (all important descriptors need to be included while limiting the number of parameters to avoid overfitting).

Conclusions and Future Directions

Although it is recognized that 30-day mortality has more limited scope as an outcome measure than it did 10 to 20 years ago, and progress has been made to develop other outcome metrics such as postprocedural morbidities, 30-day mortality remains the most widely used and accepted benchmark among stakeholders. The new PRAiS2 risk model, which includes the 4 nonprocedural risk factor or comorbidity groups, has been validated in an independent test dataset, as reported in Rogers and colleagues [6] and has already being used for center-specific risk adjustment of 30-day mortality rates in the

United Kingdom for audit and benchmarking of pediatric cardiac surgery outcomes. Future analyses of morbidity outcomes for pediatric cardiac surgery will certainly need to take account of case complexity in terms of the non-procedural risk factors and comorbidities.

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