Procedural Risk in Congenital Cardiac Catheterization (PREDIC3T)

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BACKGROUND: Advancements in the field, including novel procedures and multiple interventions, require an updated approach to accurately assess patient risk. This study aims to modernize patient hemodynamic and procedural risk classification through the creation of risk assessment tools to be used in congenital cardiac catheterization.

METHODS AND RESULTS: Data were collected for all cases performed at sites participating in the C3PO (Congenital Cardiac Catheterization Project on Outcomes) multicenter registry. Between January 2014 and December 2017, 23,119 cases were recorded in 13 participating institutions, of which 88% of patients were <18 years of age and 25% <1 year of age; a high-severity adverse event occurred in 1193 (5.2%). Case types were defined by procedure(s) performed and grouped on the basis of association with the outcome, high-severity adverse event. Thirty-four unique case types were determined and stratified into 6 risk categories. Six hemodynamic indicator variables were empirically assessed, and a novel hemodynamic vulnerability score was determined by the frequency of high-severity adverse events. In a multivariable model, case-type risk category (odds ratios for category: 0=0.46, 1=1.00, 2=1.40, 3=2.68, 4=3.64, and 5=5.25; all P≤0.005) and hemodynamic vulnerability score (odds ratio for score: 0=1.00, 1=1.27, 2=1.89, and ≥3=2.03; all P≤0.006) remained independent predictors of patient risk.

CONCLUSIONS: These case-type risk categories and the weighted hemodynamic vulnerability score both serve as independent predictors of patient risk for high-severity adverse events. This contemporary procedure-type risk metric and weighted hemodynamic vulnerability score will improve our understanding of patient and procedural outcomes.

Key Words: comparative effectiveness/patient-centered outcomes research ■ congenital heart disease ■ pediatric intervention ■ pediatrics

Congenital cardiac catheterization is a constantly evolving field with novel interventions and new technology continuously introduced into standard practice. In these cases, the broad range of heterogeneous interventions, some infrequently performed, can limit meaningful comparisons.

To accurately adjust for case mix complexity, in 2011, the Congenital Cardiac Catheterization Project on Outcomes (C3PO), created 4 procedure-type risk categories to classify cases with similar expected risk for clinically relevant adverse events (AEs). Other procedure risk category methodologies have also been developed by the CCISC (Congenital Cardiac Interventional Study Consortium) and the IMPACT (Improving Pediatric and Adult Congenital Treatment) registries. The CCISC model, Catheterization Risk Score for Pediatrics (CRISP), which was developed in 2015, uses only 3 categories of procedure risk in their model, with 78% of cases in category 1, reducing the ability to differentiate risk among the 34 procedure types captured as category 1. Although the IMPACT procedure risk categories were broadened in 2017 to 6 categories and included some novel procedures, the historical data set spanned January 2011 to March 2017.
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Over the past decade, there have been numerous advancements in the field of congenital cardiac catheterization. The original C3PO procedure type risk groups do not account for advancements in technology and technique and the introduction of new interventions. Like the original C3PO categories, the CRISP categories, developed in 2015, do not account for novel interventions, such as transcatheter pulmonary valve replacement. Additionally, none of the existing procedure risk categories account changes in case-level risk when >1 intervention is performed, and instead classify a case only at the level of the highest individual intervention performed. Furthermore, the field has developed a broader understanding of patient and procedural determinants of risk, such as the relative importance of different hemodynamic indicators. Previous consideration of hemodynamic risk used in C3PO, CRISP, and IMPACT assign equal significance to all abnormal hemodynamic variables.

Given the evolution of congenital cardiac catheterization with the introduction of novel procedures and improved understanding of risk factors, contemporary risk assessment tools are warranted to allow for accurate AE outcome reporting for institutions performing these cases. The C3PO collaborative has expanded to include 20 institutions in the United States with a wide range of institution profiles, creating a rich data source for developing of novel outcome assessment tools to further congenital cardiac catheterization. The aim of this study was to improve upon and modernize available tools for assessment of procedural risk through the development of new case-type risk category designations and the addition of an improved measure for hemodynamic vulnerability using a modern C3PO data set.

METHODS

Data Source
Centers participating in the C3PO collaborative prospectively collected data on each pediatric or congenital cardiac catheterization case performed between January 1, 2014, and January 1, 2018. Institutional review board approval for this study was obtained at the sponsor site, Boston Children’s Hospital, and sought at local institutions in accordance with institutional requirements. Informed consent requirement was waived by the institutional review board given the quality improvement nature of the work. The data underlying this article will be shared on reasonable request to the corresponding author.

Data Collection
Patient characteristics included age, sex, ventricular circulation physiology (single-ventricle/biventricular circulation), any diagnosis of a genetic syndrome (yes/no) or an associated significant noncardiac comorbidity active at the time of the catheterization procedure (yes/no) with further specification for coagulation disorder, chronic lung disease, renal insufficiency, or other. Definitions for genetic syndrome and noncardiac
comorbidity were available in the C3PO User Manual. If a patient had a recent cardiac catheterization or surgery, the date of the procedure and procedure type were recorded.

Procedure baseline hemodynamic indicator variables collected included saturation measurements (systemic arterial saturation and mixed venous saturation), intracardiac and intravascular pressure measurements (end-diastolic pressure and pulmonary artery pressure), and calculated values of Qp:Qs and pulmonary vascular resistance.

Catheterizations were broadly captured as diagnostic only, biopsy in patients following heart transplant, or interventional. Using established nomenclature of the International Pediatric and Congenital Cardiac Code, each intervention performed as part of the procedure was recorded. Case types were used to summarize all interventions performed during a catheterization and defined on the basis of the primary and secondary intervention(s) performed to account for the increase in case complexity when multiple interventions are performed. Primary interventions were the most significant or intended intervention. Secondary interventions mostly included pulmonary artery angioplasty with or without stenting, systemic arterial or venous stenting, or aortopulmonary or venovenous collateral closure. Case types were further stratified on the basis of patient age to account for the significant differences in anticipated procedure risk profiles. Approximately 9% of cases did not meet a case-type definition and were not included because of the infrequency of these events, limiting the ability to accurately assign a risk category. Given the limited number of these cases and/or the heterogeneity in outcomes among procedures with the same recorded intervention, these cases were excluded from further analysis.

**Primary Outcome: Clinically Significant Adverse Events**

The primary outcome used to determine patient outcome was the occurrence of a clinically significant adverse event, or high-severity adverse event (HSAE), defined as a severity level 3, 4, or 5 event using established definitions for reporting of procedural complications, in harmony with the International Pediatric and Congenital Cardiac Code. Adverse events were defined as any anticipated or unanticipated event for which patient harm could have or did occur, potentially or definitely as a consequence of the procedure performed, and assigned a graded severity from 1 to 5 according to previously established definitions (Table 1).

All adverse events were independently reviewed by 2 fellowship-trained pediatric interventional cardiologists to ensure accuracy in AE reporting among institutions. Misapplication of AE severity definitions were appropriately adjusted to ensure standardized reporting of events on the basis of these established definitions.

**Statistical Analysis**

The outcome “adverse event” was defined at the case level, determined by the highest-severity AE occurring during a case and summarized for each case type. Continuous variables are summarized as median

| Severity level | Definition | Examples |
|----------------|------------|----------|
| Level 1: none  | No harm, no change in condition, may have required monitoring to assess for potential change in condition with no intervention indicated | • Balloon rupture  
• Equipment problem |
| Level 2: minor | Transient change in condition, not life threatening, condition returns to baseline, required monitoring, required minor intervention such as holding a medication, or obtaining laboratory test | • Groin hematoma  
• Self-resolving arrhythmia |
| Level 3: moderate | Transient change in condition may be life threatening if not treated, condition returns to baseline, required monitoring, required intervention such as reversal agent, additional medication, transfer to the intensive care unit for monitoring, or moderate transcatheter intervention to correct condition | • Unstable arrhythmia with preserved blood pressure requiring intervention  
• Vascular damage not life threatening but requiring intervention |
| Level 4: major | Change in the patient’s clinical condition that would be life threatening if not treated and require intense medical therapy and/or major invasive transcatheter or urgent/emergent surgical intervention to treat the condition. These conditions may also result in the need for unplanned cardiopulmonary support in the form of heart-lung bypass (extracorporeal membrane oxygenation) to prevent a catastrophic event from occurring | • Major life-threatening vascular injury that results in cardiopulmonary collapse, need for urgent blood product administration, and/or requires a major invasive procedure to successfully treat the condition  
• Any event requiring cardiopulmonary resuscitation  
• Emergent surgical intervention because of device or stent embolization; and unanticipated intubation or need for cardiopulmonary support in the setting of circulatory collapse or acute respiratory failure |
| Level 5: catastrophic | Any death, and emergent surgery or heart-lung bypass support (extracorporeal membrane oxygenation) to prevent death with failure to wean from bypass support | • Event resulting in death |
The discrimination of the hemodynamic vulnerability score categories and hemodynamic vulnerability score were tested in a stepwise-forward multivariable model. The model was generated starting with the newly developed PREDIC3T case-type risk categories, followed by the hemodynamic vulnerability score, and other clinical characteristics found to be important in univariate analysis were then tested for inclusion in the model, where $P<0.05$ was required for retention. Discrimination of the final model was evaluated using the c-statistic.

**Data Audit**
In July 2019, all participating centers underwent an independent audit, verifying complete case capture and accuracy of selected data elements in a random sample of 10% of cases (maximum, 50) at each site. Audited data elements included patient age, hemodynamic values, case type, and occurrence of an AE. The audits were executed using videoconferencing to ensure that sites confirmed data using institutional medical records. The provided answers were compared with database extracts. At the conclusion of each audit, sites were asked to confirm total annual case volume to compare with the C3PO registry to verify complete annual case capture.

**RESULTS**
From January 2014 through December 2017, a total of 23,119 cases met inclusion criteria and were recorded by 13 centers with average annualized case volume ranging from 195 to 1606 cases per year. Pediatric patients ≤18 years of age accounted for the majority of the cohort (88%), with ≈25% being <1 year of age (Table 2). Patients were classified as having single ventricle physiology in 20% of cases recorded. A genetic abnormality was identified in 9%, and the presence of an active noncardiac problem in 19%. Recent cardiac interventions within 90 days, either surgery or catheterization, had occurred in nearly 20% of the population. Of all catheterizations performed, 46% were defined as an interventional case, 23% as a biopsy, and 31% as a diagnostic or noninterventional case.

**Adverse Events**
Among all cases, an AE was recorded in 10.9% of cases (n=2528), with an HSAE in 5.2% of cases (n=1193), and 17 recorded deaths (level 5) in the cohort (0.07%). Age ≤30 days had a strong association with
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HSAE with an incidence of 11.1% compared with age >30 days to <1 year, 1 to 18 years, and >18 years at rates of 7.2%, 3.8%, and 5.9%, respectively (P<0.001; Table 3). Broadly, all interventional catheterizations as a group had a higher HSAE rate of 8.1% compared with diagnostic and biopsy catheterizations, 3.9% and 1.1%, respectively (P<0.001). Patients with single ventricle physiology had a higher HSAE rate at 6.5% compared with non–single-ventricle patients, 4.8% (P<0.001). Similarly, patients who had a recent cardiac surgery within 90 days of the index catheterization had an HSAE incidence of 6.0% compared with those who did not have a recent surgery (5.0%; P=0.017). There

Table 2. Patient and Procedural Characteristics

| Patient characteristics | Entire cohort (N=23,119) |
|-------------------------|--------------------------|
| Age                     |                           |
| ≤30 d                   | 1537 (7)                 |
| >30 d to <1 y           | 4417 (19)                |
| 1 to 18 y               | 14,492 (63)              |
| >18 y                   | 2673 (12)                |
| Sex, male (n=22,904)    | 12,590 (55)              |
| Single ventricle        | 4,608 (20)               |
| Genetic syndrome        | 2,153 (9)                |
| Any noncardiac problem  | 4,331 (19)               |
| Coagulation disorder    | 150 (1)                  |
| Chronic lung disease    | 1,291 (6)                |
| Renal insufficiency     | 473 (2)                  |
| Cardiac catheterization in past 90 d | 4,148 (18) |
| Cardiac surgery in past 90 d | 3,160 (14) |

Procedural characteristics

| Case type |                          |
|-----------|--------------------------|
| Biopsy (+/- coronary angiography) | 5,303 (23) |
| Diagnostic | 7,137 (31) |
| Interventional | 10,679 (46) |
| Duration of catheterization, h | 1.3 [0.8, 2.0] |

Abnormal hemodynamic indicator variables

| Low systemic arterial saturation | 6,502 (28) |
| BiV: <95%, SV: <78%              |            |
| Low mixed venous saturation      | 2,934 (13) |
| BiV: <80%, SV: <50%              |            |
| High pulmonary artery pressure   | 3,091 (13) |
| BiV: systolic ≥45 mm Hg; SV: mean ≥17 mm Hg |       |
| High systemic ventricle EDp      | 1,149 (5)  |
| ≥18 mm Hg                        |            |
| Qp:Qs >1.5                       | 2,243 (10) |
| Pulmonary vascular resistance    | 3,762 (16) |
| >3 iWU                           |            |

Adverse events

| Any adverse event | 2,528 (10.9) |
| Any level 3/4/5 adverse events | 1,193 (5.2) |
| Any level 4/5 adverse events    | 319 (1.4)   |
| Level 5 adverse events          | 17 (0.7)    |

Table 3. Univariate Analysis of Patient and Procedural Characteristics and Association With High Severity Adverse Events

| N (% of total) HSAE | 95% CI   | P value |
|---------------------|----------|---------|
| Age                 |          |         |
| ≤30 d               | 171 (11.1) | 9.6–12.8 | <0.001 |
| >30 d to <1 y       | 316 (7.2)  | 6.4–8.0  |         |
| 1 to 18 y           | 548 (3.8)  | 3.5–4.1  |         |
| >18 y               | 158 (5.9)  | 5.1–6.9  |         |
| Sex                 |          |         |
| Male                | 656 (5.2)  | 4.8–5.6  | 0.88    |
| Female              | 532 (5.2)  | 4.7–5.6  |         |
| Single ventricle    |          |         |
| Yes                 | 298 (6.5)  | 5.8–7.2  | <0.001  |
| No                  | 895 (4.8)  | 4.5–5.2  |         |
| Genetic syndrome    |          |         |
| Yes                 | 114 (5.3)  | 4.4–6.3  | 0.76    |
| No                  | 1,079 (5.2)| 4.9–5.5  |         |
| Any noncardiac problem |        |         |
| Yes                 | 191 (4.4)  | 3.8–5.1  | 0.013   |
| No                  | 1,002 (5.3)| 5.0–5.7  |         |
| Coagulation disorder|          |         |
| Yes                 | 10 (6.7)   | 3.2–11.9 | 0.36    |
| No                  | 1,183 (5.2)| 4.9–5.4  |         |
| Chronic lung disease |          |         |
| Yes                 | 64 (5.0)   | 3.8–6.3  | 0.80    |
| No                  | 1,129 (5.2)| 4.9–5.5  |         |
| Renal insufficiency |          |         |
| Yes                 | 14 (3.0)   | 1.6–4.9  | 0.027   |
| No                  | 1,179 (5.2)| 4.9–5.5  |         |
| Cardiac catheterization in past 90 d | 224 (5.4) | 4.7–6.1  | 0.44    |
| No                  | 969 (5.1)  | 4.8–5.4  |         |
| Cardiac surgery in past 90 d | 191 (6.0) | 5.2–6.9  | 0.017   |
| Yes                 | 1,002 (5.0)| 4.7–5.3  |         |
| No                  | 1,002 (5.0)| 4.7–5.3  |         |
| Procedural characteristics |      |         |
| Biopsy              | 56 (1.1)   | 0.8–1.4  | <0.001  |
| Diagnostic          | 275 (3.9)  | 3.4–4.3  |         |
| Interventional      | 862 (8.1)  | 7.6–8.6  |         |

HSAE indicates high-severity adverse event.
was no significant difference in incidence of HSAE in patients with a genetic syndrome or noncardiac problems such as a coagulation disorder and chronic lung disease. The most common events categorized into level 3 AEs and level 4/5 AEs are depicted in Table 4.

**Hemodynamic Vulnerability Score**

Hemodynamic indicators, stratified by single- or biventricular circulation, varied in their association with the outcome HSAE, ranging from 3.1% in patients with abnormal pulmonary vascular resistance and as high as 11.6% in all patients with high pulmonary artery pressure, with or without elevated vascular resistance (Table 5). Given this degree of heterogeneity in the strength of each hemodynamic variable, a hemodynamic vulnerability score was generated (0–6) on the basis of respective association with the outcome HSAE. Two points were assigned to the indicator variables with the highest HSAE rates: low systemic arterial saturation for single-ventricle circulation and high pulmonary artery pressure for both single- and biventricular circulations. More moderate risk indicators were given a value of 1 point, including low systemic arterial saturation in biventricular circulation, low mixed venous saturation, high systemic ventricle end-diastolic pressure, and high Qp:Qs. Abnormal pulmonary vascular resistance was not associated with increased HSAEs. Hemodynamic scores were generated for each case in the cohort and grouped according to a score of 0, 1, 2, and ≥3 with respective frequencies of HSAEs of 3.4%, 5%, 8.7%, and 9.5% (P < 0.001; Table 6).

**PREDICT Case-Type Risk Categories**

Case types with similar interventions and HSAE rates or case types in which additional interventions did not increase HSAE rates were combined into a single case

| Table 4. Common Adverse Events Summarized by Severity Levels |
|-------------------------------------------------------------|

| Level 3 adverse events | N  |
|------------------------|----|
| Vascular access–related complications including vessel thrombosis, vessel injury, and hemodynamically tolerated retroperitoneal hemorrhage | 161 |
| Atrial arrhythmias requiring medical and/or electrical cardioversion | 139 |
| Angioplasty–related complications including vascular tears or vessel injury needing moderate catheterization-based intervention such as stent placement | 111 |
| Device or stent related problem including embolization or malposition | 103 |
| Respiratory- or anesthesia-related events including airway obstruction, hypoxia, postoperative stridor, or apnea | 81 |
| Catheter-induced heart block requiring temporary intervention or observation | 63 |
| Hypotension requiring medical therapy or volume resuscitation | 46 |
| Pulmonary hemorrhage | 43 |
| Coil malposition or embolization requiring catheter retrieval or other minor catheterization-based intervention | 26 |
| Ventricular arrhythmia not requiring cardioversion/defibrillation | 18 |
| Nonspecific ST-T wave changes | 12 |
| Isolated central nervous system event not resulting in permanent injury | 12 |
| New valvar regurgitation not resulting in hemodynamic instability or requiring surgical intervention | 12 |
| Pulmonary edema and/or reperfusion injury | 11 |
| Bradycardia | 10 |

| Level 4 and 5 adverse events | N  |
|-----------------------------|----|
| Respiratory- or anesthesia-related event resulting in clinical decompensation and needing active resuscitation | 32 |
| Ventricular arrhythmia needing resuscitation or cardioversion/defibrillation | 30 |
| Cardiac arrest requiring cardiopulmonary resuscitation or extracorporeal membrane oxygenation | 29 |
| Device or stent embolization/malposition resulting in hemodynamic compromise and/or necessitating surgical repair | 29 |
| Vascular access related complications or vessel injuries which are deemed life threatening and/or requiring surgical intervention | 23 |
| Heart block requiring cardiopulmonary resuscitation or requiring placement of a permanent pacing device | 23 |
| Angioplasty-related complications resulting in significant vascular injury or hemodynamic instability | 18 |
| Heart perforation | 17 |
| Hypotension or depressed cardiac output deemed life threatening and requiring resuscitation | 10 |
| Central nervous system event resulting in stroke or permanent disability | 7 |
| Bradycardia deemed life threatening and requiring resuscitation | 6 |
| Pulmonary hemorrhage deemed life threatening | 5 |
Table 5. Hemodynamic Indicator Variables by Presence of HSAE

| Hemodynamic indicator variables | Presence of HSAE, n (%) | Weighted score value (0–2) |
|---------------------------------|-------------------------|---------------------------|
| Low systemic arterial saturation|                         |                           |
| BIV (<95%)                      | 107/2154 (5.0)          | 1                         |
| SV (<78%)                       | 43/479 (9.0)            | 2                         |
| Low mixed venous saturation     |                         |                           |
| BIV (<60%)                      | 18/303 (5.9)            | 1                         |
| SV (<50%)                       | 47/72 (5.6)             | 1                         |
| High pulmonary artery pressure  |                         |                           |
| BIV (>45 mm Hg)                 | 55/495 (11.1)           | 2                         |
| SV (mean ≥17 mm Hg)             | 24/189 (12.7)           | 2                         |
| High systemic ventricle         |                         |                           |
| EDp (≥18 mm Hg)                 | 20/431 (4.6)            | 1                         |
| High QpQs (>1.5)                | 48/1089 (4.2)           | 1                         |
| High PVR (>3 mU)                | 35/1140 (3.1)           | 0                         |

BIV indicates biventricular; EDp, end-diastolic pressure; HSAE, high-severity adverse event; IWU, indexed Wood units; PVR, pulmonary vascular resistance; and SV, single ventricle.

The percent HSAE listed for each hemodynamic indicator variable in Table 5 includes only cases with a single independent abnormal indicator variable.

type (Table 7). Thirty of 34 case types individually comprised ≤5% of the total cohort, 19 of which individually accounted for ≤1% of the cohort (Table 8). However, these 30 case types combined together accounted for 48.5% of the total cohort and 100% of all interventional cases. The frequency of reported HSAEs among all case types ranged from 0 recorded events out of 76 “Fontan fenestration or baffle leak device closure” cases to as high as 14 of 69 cases (20.3%) among “atretic valve perforation with or without valvotomy” cases. Differential HSAE rates for diagnostic cases stratified by age (<30 days, >30 days to <1 year, and ≥1 year) range from 2.8% to 9%. Six final case-type risk categories were created with HSAE rates of 1.1%, 2.7%, 4.2%, 7.7%, 10.8%, and 13.9% for categories 0 to 5, respectively (Table 8), with a univariate c-statistic of 0.72.

Multivariate Analysis of New Tools
PREDICT3T case-type risk categories, an important feature in univariate analysis, remained an independent predictor of the primary outcome, HSAE, when tested in a stepwise-forward modeling with the hemodynamic vulnerability score. Further addition of age categories added additional explanatory information about the risk of these important outcomes (c-statistic of 0.74; Table 9). Other patient and procedural characteristics were not statistically significant when added to this 3-feature model, indicating independent significance of the PREDICT3T case-type risk categories and the hemodynamic vulnerability score. Important variables included in the 3-feature model and their respective frequencies of HSAEs in relationship to categorical volume are depicted in the Figure.

Data Audit
All 13 centers participated in the audit, with a total of 650 cases randomly selected, not limited to cases with an AE. Case ascertainment and database recording was verified by matching case volume to institutional records with 97% to 99% agreement among the institutions. In these 650 cases, patient and procedural characteristics in the model were audited for accuracy in reporting. For case type and age, there was 100% agreement in the audited data set across centers. Among the 3900 hemodynamic indicator variables audited (6 per case), 57 were recorded incorrectly in a lower risk category, and 34 were recorded incorrectly in a higher risk category compared with the audit results. Thus, there was 97% (3809/3900) agreement in reported versus source document audited data. There was 96% accuracy in reporting 26 of 27 HSAEs, of which 6 AEs were designated as severity level 4/5. The single event not recorded in the database was a level 4 AE related to respiratory arrest in the recovery room following catheterization.

DISCUSSION
Using a robust multicenter data set with >20 000 prospectively gathered congenital catheterization cases, we were able to build upon previous methodology for risk assessment in congenital cardiac catheterization to meet the needs of an evolving and rapidly advancing field by modernizing procedural risk classification and developing a more robust predictive hemodynamic vulnerability scoring system. We have developed 6 procedural risk categories that identify patient risk at the case level rather than a focus on the individual interventions performed. Furthermore, the hemodynamic vulnerability scoring metric adds weighted value to each hemodynamic variable based on their relative strength at predicting the outcome, making this metric a more meaningful addition to further risk adjustment modeling. The case-type risk categories and hemodynamic vulnerability score developed from this
Table 7. **PREDICT** Case-Type Risk Categories

| Risk category 0 | Risk category 1 | Risk category 2 | Risk category 3 | Risk category 4 | Risk category 5 |
|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| Diagnostic case | Diagnostic ≥1 y | Diagnostic 1 mo to <1 y | Diagnostic ≤30 d | Pulmonary valvuloplasty +/− procedure, ≤30 d | Aortic valvuloplasty +/− procedure, ≤30 d |
| Valvuloplasty   | Pulmonary valvuloplasty >30 d | Pulmonary valvuloplasty + procedure >30 d | Pulmonary valvuloplasty +/− procedure ≤30 d | Aortic valvuloplasty +/− procedure, >30 d | Mitral valvuloplasty |
| Device or coil closure | Fontan fenestration or baffle leak device closure | ASD or PFO closure | Fontan fenestration or baffle leak device closure + procedure | ASD or PFO closure + procedure | VSD closure |
| Balloon angioplasty and/or stent placement | | Pulmonary artery (1 vessel) Pulmonary artery (1 vessel)+RVOT conduit dilation/stent Aorta (coarctation) dilation and/or stent | Pulmonary artery (1 vessel)+procedure Pulmonary artery (≥2 vessels) Pulmonary vein dilation and/or stent RVOT conduit dilation and/or stent PDA dilation and/or stent | Pulmonary artery (≥2 vessels)+RVOT +/− procedure Aorta (coarctation) dilation and/or stent + procedure |
| Other | Endomyocardial biopsy Endomyocardial biopsy with coronary angiography | Atrial septostomy | Atrial septostomy | Atrial septostomy + procedure TPV implantation +/− procedure Atrial septum static dilation and/or stent placement |

ASD indicates atrial septal defect; PDA, patent ductus arteriosus; PFO, patent foramen ovale; **PREDICT**, procedural risk in congenital cardiac catheterization; RVOT, right ventricular outflow tract; TPV, transcatheter pulmonary valve; and VSD, ventricular septal defect.

C-statistic 0.718, 95% bootstrapped CI (0.705–0.732).
Table 8. Case-Types by Frequency of HSAE

| Risk category | Number of cases in cohort | Frequency of HSAE |
|---------------|--------------------------|------------------|
| 0             | 5303 (23)                | 56 (1.1)         |
| Endomyocardial biopsy | 3190 (14)                | 17 (0.5)         |
| Endomyocardial biopsy with coronary angiography | 2113 (9) | 39 (1.9) |
| 1             | 5392 (23)                | 147 (2.7)        |
| Fontan fenestration or baffle leak device closure | 76 (<1) | 0 (0.0) |
| Pulmonary valvuloplasty, age >30 d | 463 (2) | 10 (2.2) |
| Diagnostic only, age ≥1 y | 4853 (21) | 137 (2.8) |
| 2             | 4362 (19)                | 184 (4.2)        |
| Pulmonary valvuloplasty+procedure, age >30 d | 62 (<1) | 2 (3.2) |
| ASD or PFO device closure | 944 (4) | 31 (3.3) |
| Venous collateral device or coil occlusion | 416 (2) | 15 (3.6) |
| PDA device or coil closure | 1189 (5) | 46 (3.9) |
| Diagnostic only, age >30 d to <1 y | 1751 (8) | 90 (5.1) |
| 3             | 3909 (17)                | 302 (7.7)        |
| Pulmonary artery dilation and/or stent (only 1 vessel) | 1006 (4) | 69 (6.9) |
| Fontan fenestration or baffle leak device closure+procedure | 84 (<1) | 6 (7.1) |
| Aorta (coarctation) dilation and/or stent | 564 (2) | 42 (7.5) |
| Systemic pulmonary collaterals or coil closure +/- procedure | 1024 (4) | 77 (7.5) |
| Pulmonary valvuloplasty +/- procedure age, age ≤30 d | 246 (1) | 21 (8.5) |
| Pulmonary artery dilation and/or stent (only 1 vessel)+RVOT conduit dilation and/or stent | 129 (1) | 11 (8.5) |
| Atrial septostomy | 323 (1) | 28 (8.7) |
| Diagnostic only, age ≤30 d | 533 (2) | 48 (9.0) |
| 4             | 2373 (10)                | 257 (10.8)       |
| Pulmonary artery dilation and/or stent (only 1 vessel)+procedure | 178 (1) | 18 (10.2) |
| ASD or PFO device closure+procedure | 39 (<1) | 4 (10.3) |
| Pulmonary vein dilation and/or stent | 660 (3) | 70 (10.6) |
| Pulmonary artery dilation and/or stent (≥2 vessels) | 903 (4) | 98 (10.9) |
| RVOT conduit dilation and/or stent | 409 (2) | 46 (11.3) |
| PDA dilation and/or stent | 186 (1) | 21 (11.3) |
| 5             | 1780 (8)                 | 247 (13.9)       |
| Aorta (coarctation) dilation and/or stent+procedure | 247 (1) | 30 (12.2) |
| Aortic valvuloplasty +/- procedure, age >30 d | 226 (1) | 29 (12.8) |
| Aortic valvuloplasty +/- procedure age ≤30 d | 100 (<1) | 13 (13.0) |
| Pulmonary artery dilation and/or stent (≥2 vessels)+RVOT and/or other procedure | 212 (1) | 28 (13.2) |
| VSD device closure | 45 (<1) | 6 (13.3) |
| Mitral valvuloplasty | 75 (<1) | 10 (13.3) |
| Atrial septostomy+procedure | 72 (<1) | 10 (13.9) |
| TPV implantation +/- procedure | 679 (3) | 98 (14.4) |
| Atrial septum static dilation and/or stent placement | 55 (<1) | 9 (16.4) |
| Atretic valve perforation +/- valvuloplasty | 69 (<1) | 14 (20.3) |

ASD indicates atrial septal defect; HSAE, high-severity adverse event; PDA, patent ductus arteriosus; PFO, patent foramen ovale; RVOT, right ventricular outflow tract; TPV, transcatheter pulmonary valve; and VSD, ventricular septal defect.

multi-institutional data set provide contemporary tools for outcome assessment, procedure planning, and risk adjustment.

Congenital cardiac catheterization cases are often heterogeneous procedures, especially when infrequently performed interventions occur in groupings with other interventions. The case types developed in this study improve upon previous intervention type classification schema1–3 and aim to identify HSAEs at the case level, yielding improved catheterization risk.
assessment by grouping like cases to maximize the strength of outcome analysis. Previously established methodology has been used to identify events at the intervention level, establishing case-level risk on the basis of the single most common and/or highest-risk intervention performed. However, this does not account for the added risk of performing multiple interventions, which is a significant improvement this model brings to the field or account for the novel interventions introduced over the past decade. The Catheterization for Congenital Heart Disease Adjustment for Risk Method procedure-type risk categories report a development cohort c-statistic of 0.72, yet when the Catheterization for Congenital Heart Disease Adjustment for Risk Method categories are applied to this data set, the c-statistic is 0.64. Additionally, by stratifying biopsy catheterizations into a unique risk category, centers that perform a disproportionate number of cardiac transplantation procedures will be more accurately assessed in future risk adjustment work. The PREDIC3T case-type risk categories, with a univariate c-statistic of 0.72, offer a generalizable tool that can be used to provide more meaningful outcome analysis and serve to more accurately reflect case mix complexity in a modern era of congenital interventional cardiology.

Hemodynamic vulnerability has previously been shown as a strong independent determinant of risk for patients undergoing congenital cardiac catheterization and remains an important consideration when assessing patient risk. These prior efforts have successfully identified important hemodynamic parameters, for both single- and biventricular circulations,

### Table 9. Multivariate Analysis of Predictors for Outcome High-Severity (Level 3/4/5) Adverse Events

|                   | OR (95% CI) | P value |
|-------------------|-------------|---------|
| PREDIC3T case type risk category |             |         |
| 0                 | 0.46 (0.33–0.62) | <0.001  |
| 1                 | 1.00        | ...     |
| 2                 | 1.40 (1.11–1.78) | 0.005   |
| 3                 | 2.68 (2.16–3.32) | <0.001  |
| 4                 | 3.64 (2.93–4.52) | <0.001  |
| 5                 | 5.25 (4.23–6.53) | <0.001  |
| Hemodynamic vulnerability score |             |         |
| 0                 | 1.00        | ...     |
| 1                 | 1.27 (1.07–1.50) | 0.006   |
| ≥2                | 1.89 (1.60–2.23) | <0.001  |
| ≥3                | 2.03 (1.71–2.42) | <0.001  |
| Age               |             |         |
| <1 mo             | 1.47 (1.21–1.79) | <0.001  |
| 1–11 mo           | 1.18 (1.01–1.39) | 0.041   |
| 1–18 y            | 1.00        | ...     |
| ≥19 y             | 1.51 (1.25–1.82) | <0.001  |

c-statistic 0.74. OR indicates odds ratio; and PREDIC3T, procedural risk in congenital cardiac catheterization.

**Figure 1.** Volume by risk feature and associated high-severity adverse event rates (severity 3/4/5). HSAE indicates high-severity adverse event; and PREDIC3T, procedural risk in congenital cardiac catheterization.
which are associated with higher risk for having a clinically important AE.3,5,16,17 This new methodology evolves the way hemodynamic vulnerability is scored by considering the relative risk of each individual hemodynamic variable and assigns a unique score calculating a cumulative risk score that more accurately reflects patient vulnerability.

The developed PREDIC3T case-type risk categories and hemodynamic vulnerability score will have a broad range of future applications and can be used to standardize outcome reporting and population comparisons among institutions and providers by defining case risk complexity. Additionally, it is important for institutions and operators to have a metric with which they can track population trends over time, highlighting changes in patient complexity and observed outcomes. Making these analyses with a readily available analytic tool grouping sometimes infrequently performed cases with cases of similar risk will allow for targeted risk mitigation strategies based on predicted risk complexity.

These risk categories can also assist in the development of novel outcome-based research such as current work being done to identify risk factors for failure to rescue.19 In the past decade, we have identified patient and procedural risk factors for experiencing an AE. However, we have yet to identify which events lead to patient harm or permanent injury, and when harm is attributable to a failure to rescue the patient from an AE. In the future, these risk categories can be paired with a metric that measures a change in a patient’s clinical status over the course of a cardiac catheterization to better understand the relationship between the case type and a change in the patient’s clinical status, evaluating both improvements as well as identifying harm. Ultimately, identification of system-level factors and programmatic quality, rather than just individual patient-level factors, will enable innovative strategies to mitigate risk and reduce both the occurrence of an AE and/or resulting harm, while improving clinical outcomes.

**Study Limitations**

Certain limitations should be considered when interpreting these findings. While C3PO is open to all institutions performing congenital cardiac catheterization, the registry does not include all centers performing cases, and outcomes may differ at nonparticipating centers. In addition, no centers with an annual volume of <200 catheterizations met inclusion criteria for this data set. C3PO is also based in the United States, which may limit the interpretability in international or low-resource settings.

Additionally, the primary outcome for this study was HSAEs, which includes severity levels 3, 4, and 5. Based on our data audit, there is high reliability across all centers in the accuracy of AE outcome reporting, particularly of the higher severity level 4/5 AE classifications. However, there may be variation in outcome reporting for lower severity level 3 AEs, which are not always life-threatening events. Furthermore, the 3-feature model used here was not tested against a validation data set and requires further model development. Another important factor to consider, particularly when comparing outcomes among sites and operators, is efficacy and how it relates to safety events. Further studies should focus on identifying efficacy measures for these various case types to identify when procedural success was achieved to carefully understand the balance between accepted risk and effective procedural outcome.

**CONCLUSIONS**

The refinement in procedural risk assessment developed in this robust multicenter study is an important step toward the development of a modernized risk adjustment methodology to allow accurate comparison of outcomes among institutions and operators performing congenital cardiac catheterization. We have created novel PREDIC3T case-type risk categories by stratifying case types with similar HSAE frequency. Defining procedural risk at the case level offers an enhanced ability to capture the overall complexity of each unique case rather than attributing risk to the highest risk intervention performed. Furthermore, with a better understanding of hemodynamic vulnerability we have provided an improved methodology to account for cumulative risk in patients with abnormal hemodynamic measurements, and therefore more accurately define a patient’s inherent risk to the case type being performed. We anticipate that these improvements in risk assessment tools along with the novel PREDIC3T case-type risk categories will allow for a generalizable process to evaluate and compare outcomes, plan for appropriate resources, and predict risk in congenital cardiac catheterization.

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REFERENCES

1. Bergersen L, Gauvreau K, Marshall A, Kreutzer J, Beekman R, Hirsch R, Foerster S, Balzer D, Vincent J, Hellenbrand W, et al. Procedure-type risk categories for pediatric and congenital cardiac catheterization. Circ Cardiovasc Inter. 2011;4:188–194. doi: 10.1161/CIRCINTERVENTIONS.111.959262

2. Nykanen DG, Forbes TJ, Du W, Divekar AA, Reeves JH, Hagler DJ, Fagan TE, Pedra CAC, Fleming GA, Khan DM, et al. CRISP: catheterization RISk score for pediatrics: a report from the Congenital Cardiac Interventional Study Consortium (CISC). Catheter Cardiovasc Inter. 2016;87:302–309. doi: 10.1002/ccd.26300

3. Jayaram N, Spertus JA, Kennedy KF, Vincent R, Martin GR, Curtis JP, Nykanen D, Moore PM, Bergersen L. Modeling major adverse outcomes of pediatric and adult patients with congenital heart disease undergoing cardiac catheterization: observations from the NCDR IMPACT registry (National Cardiovascular Data Registry Improving Pediatric and Adult Congenital Treatment). Circulation. 2017;136:2009–2019. doi: 10.1161/CIRCULATIONAHA.117.027714

4. Martin GR, Anderson JB, Vincent RN. IMPACT registry and national pediatric cardiology quality improvement collaborative: contributions to quality in congenital heart disease. World J Pediatr Congenit Heart Surg. 2019;10:72–80. doi: 10.1177/2151031318815059

5. Jayaram N, Beekman RH, Benson L, Holzer R, Jenkins K, Kennedy KF, Martin GR, Moore JW, Ringel R, Rome J, et al. Adjusting for risk associated with pediatric and congenital cardiac catheterization: a report from the NCDR IMPACT registry. Circulation. 2015;132:1863–1870. doi: 10.1161/CIRCULATIONAHA.114.005519

6. Taggart NW, Du W, Forbes TJ, Nykanen DG, Wax DF, Cabalka AK, Reeves JH, Du Y, Kobayashi D. A model for assessment of catheterization risk in adults with congenital heart disease. Am J Cardiol. 2019;123:1527–1531. doi: 10.1016/j.amjcard.2019.01.042

7. Hill KD, Du W, Fleming GA, Forbes TJ, Nykanen DG, Reeves J, Du Y, Kobayashi D. Validation and refinement of the catheterization RISk score for pediatrics (CRISP score): an analysis from the congenital cardiac interventional study consortium. Catheter Cardiovasc Inter. 2019;93:97–104. doi: 10.1002/ccd.27837

8. Goldstein BH, Bergersen L, Armstrong AK, Boe BA, El-Said H, Porras D, Shahanavaz S, Leahy RA, Kreutzer J, Zampi JD, et al. Adverse events, radiation exposure, and reinterventions following transcatheter pulmonary valve replacement. J Am Coll Cardiol. 2020;75:363–376. doi: 10.1016/j.jacc.2019.11.042

9. Quinn BP, Armstrong AK, Bauser-Heaton HD, Callahan R, El-Said HG, Foerster SR, Goldstein BH, Goodman AS, Gudausky TM, Kreutzer JN, et al. Radiation risk categories in cardiac catheterization for congenital heart disease: a tool to aid in the evaluation of radiation outcomes. Pediatr Cardiol. 2019;40:445–453. doi: 10.1007/s00246-018-2024-3

10. Ali F, Qasim Mehdi M, Akhtar S, Aslam N, Abbas R, Shah I, Abidi J, Arthur S, Nizar Z, Goodmann A, et al. Impact of congenital cardiac catheterization project on outcomes-quality improvement (CSPO-QI) in LMICs. Heart Asia. 2018;11:1–7. doi: 10.1136/heartsasia-2018-011050

11. Cevallos PC, Armstrong AK, Glatz AC, Goldstein BH, Gudausky TM, Leahy RA, Petit CJ, Shahanavaz S, Trucco SM, Bergersen LJ. Radiation dose benchmarks in pediatric cardiac catheterization: a prospective multi-center CSPO-QI study. Catheter Cardiovasc Inter. 2017;90:269–280. doi: 10.1002/ccd.26911

12. Cevallos PC, Rose MJ, Armsby LB, Armstrong AK, El-Said H, Foerster SR, Glatz AC, Goldstein BH, Hainstock MR, Kreutzer J, et al. Implementation of methodology for quality improvement in pediatric cardiac catheterization: a multi-center initiative by the Congenital Catheterization Project on Outcomes—Quality Improvement (CSPO-QI). Pediatr Cardiol. 2016;37:1436–1445. doi: 10.1007/s00246-016-1454-z

13. Bergersen L, Everett AD, Giroud JM, Martin GR, Franklin RCG, Béland MJ, Krogmann ON, Aiello VD, Colan SD, Elliott MJ, et al. Report from the international society for nomenclature of paediatric and congenital heart disease: cardiovascular catheterisation for congenital and paediatric cardiac disease (Part 1—procedural nomenclature). Cardiol Young. 2011;21:252–259. doi: 10.1017/S10479511100185X

14. Bergersen L, Giroud JM, Jacobs JP, Franklin RCG, Béland MJ, Krogmann ON, Aiello VD, Colan SD, Elliott MJ, Gaynor JW, et al. Report from the International Society for Nomenclature of Paediatric and Congenital Heart Disease: cardiovascular catheterisation for congenital and paediatric cardiac disease (Part 2—nomenclature of complications associated with interventional cardiology). Cardiol Young. 2011;21:260–265. doi: 10.1017/S104795111001861

15. Bergersen L, Marshall A, Gauvreau K, Beekmans R, Hirsch R, Foerster S, Balzer D, Vincent J, Hellenbrand W, Holzer R, et al. Adverse event rates in congenital cardiac catheterization—a multi-center experience. Catheter Cardiovasc Inter. 2010;75:389–400. doi: 10.1002/ccd.22286

16. Bergersen L, Gauvreau K, Foerster SR, Marshall AC, McElinney DB, Beekman RH, Hirsch R, Kreutzer J, Balzer D, Vincent J, et al. Catheterization for congenital heart disease adjustment for risk method (CHARM). JACC Cardiovasc Inter. 2011;4:1037–1046. doi: 10.1016/j.jcin.2011.05.021

17. Jenkins KJ, Beekman RH, Bergersen LJ, Everett AD, Forbes TJ, Franklin RCG, Kitzner TS, Krogman ON, Aiello VD, Colan SD, Elliott MJ, et al. Databases for assessing the outcomes of the treatment of patients with congenital and paediatric cardiac disease—the perspective of cardiology. Cardiol Young. 2008;18:116–123. doi: 10.1017/S1047951108002825

18. O’Byrne ML, Kennedy KF, Jayaram N, Bergersen LJ, Gillespie MJ, Dori Y, Silber JH, Kawut SM, Rome JJ, Glatz AC. Failure to rescue as an outcome metric for pediatric and congenital cardiac catheterization laboratory programs: analysis of data from the IMPACT Registry. J Am Heart Assoc. 2019;8:e013151. doi: 10.1161/JAHA.119.013151