A Model for Assessment of Catheterization Risk in Adults With Congenital Heart Disease

Nathaniel W. Taggart, MD[a,*], Wei Du, PhD[b], Thomas J. Forbes, MD[c], David G. Nykanen, MD[d], David F. Wax, MD[e], Allison K. Cabalka, MD[a], Jaxk H. Reeves, PhD[f], Yan Du, MS[f], and Daisuke Kobayashi, MD[c]

The purpose of this study was to define the risk for adults with congenital heart disease who underwent cardiac catheterization and to propose a precatheterization risk scoring system. Data were prospectively collected using a multicenter registry of the Congenital Cardiovascular Interventional Study Consortium. The occurrence of serious adverse events (SAE) was correlated with 12 predefined variables. Catheterization RISk in Adult patients (CRISA) score was derived using multivariate logistic regression with backward elimination model selection method. The CRISA score was compared with the American Society of Anesthesiology score and a consensus-derived, 20-point risk score based on their ability to predict SAE. From June 2008 to September 2017, 300 adjudicated SAE's occurred in 7317 catheterization procedures (overall SAE rate 4.1%) performed in adults over 18 years of age at 27 contributing centers. Nine of the 12 tested variables were ultimately included in the CRISA score. CRISA score positively correlated with risk of SAE, and was superior to American Society of Anesthesiology and the 20-point risk score in predicting SAE. Minimal (CRISA score 0 to 2), low (3 to 7), moderate (8 to 10) and high (≥11) risk categories were identified, corresponding to 0.5%, 3.2%, 7.9%, and 16.7% risk of SAE, respectfully. In conclusion, the CRISA score reliably predicts risk of SAE in adults with congenital heart disease who underwent cardiac catheterization and may be useful for preprocedural risk assessment. **(Am J Cardiol 2019;123:1527−1531)**

Improvements in the diagnosis and treatment of children with congenital heart disease (CHD) over the past 25 to 30 years have resulted in a significant increase in the average age of people living with CHD.[1] Most adults with CHD undergo cardiac catheterization in pediatric/congenital catheterization laboratories. Recent efforts by the Congenital Cardiac Interventional Study Consortium (CCISC) and others have sought to better define adverse events and risk adjustment in the current catheterization era through systematic, multicenter data acquisition and analysis.[2−8] These efforts have yielded valuable tools to better assess the risk factors for children who underwent cardiac catheterization, including the Catheterization Risk Score for Pediatrics (CRISP) in 2015.[9] The purpose of this study is to define the risk for adults with CHD who underwent cardiac catheterization and to propose a user friendly, multifactorial, and precatheterization risk scoring system for adults with CHD.

[a]Mayo Clinic, Rochester, Minnesota; [b]Wayne State University, Detroit, Michigan; [c]Children's Hospital of Michigan, Wayne State University, Detroit, Michigan; [d]The Heart Center at Arnold Palmer Hospital for Children, Orlando, Florida; [e]Division of Pediatric Cardiology, Ann & Robert H. Lurie Children's Hospital, Chicago, Illinois; and [f]University of Georgia, Athens, Georgia. Manuscript received November 20, 2018; revised manuscript received and accepted January 21, 2019.

Support/Grant Information: CCISC has received monetary donations from Festival of Trees (FOT), The DeSeranno Foundation, Cold Heading Foundation, David and Marie Quint Charitable Gift Fund as well as industry support from AGA/Abbott, Siemens, Gore, Cook, Medtronic, NuMED, Atrium, BBraun, Cordis, and Arrow. None of these donations to CCISC were directly related to this manuscript.

See page 1531 for disclosure information.

*Corresponding author: Tel: (507) 266-0676.

E-mail address: taggart.nathaniel@mayo.edu (N.W. Taggart).

Methods

A 20-point scoring system consisting of 10 discrete variables (Table 1) was developed based on consensus opinion of interventional cardiologists. For the purposes of this report this score is referred to as the original 20-point risk score. Each variable was classified into 3 levels of perceived increasing risk; each level was assigned a point value of 0, 1, or 2, respectively, for each of the 10 variables. Where multiple factors contribute to a variable, a threshold strategy was employed wherein only the highest scoring factor was used to assign the 0, 1, or 2 points. Anatomic diagnosis utilizing the STS/EACTS short list definitions, procedures, and physiologic parameters were similarly divided into 3 levels of perceived increasing risk (on-line Appendix 1) based upon consensus opinion. A serious adverse event (SAE) was defined as any adverse event causing mortality, permanent morbidity, need for further interventions, or extended length of stay (Appendix 2).

These 10 sub-scores as well as the total score (original 20-point risk score) were calculated and recorded in the CCISC open, unrestricted multi-institutional registry whose participating institutions consist of differing case volumes, practice locations, and academic affiliations in North America, Europe, and Latin America. Participation in the registry was entirely voluntary. Patient data were submitted by each site through a secure password-protected website. The server for the CCISC is housed and maintained at the Medical School Information System at Wayne State University School of Medicine. Data entry was deidentified and there was no way to electronically link specific patient data back to the site from the CCISC database application.

0002-9149/© 2019 Published by Elsevier Inc.
https://doi.org/10.1016/j.amjcard.2019.01.042

Table 1
The 12 risk assessment variables used in model

Assigned points	0	1	2
Patient status/timing (X_1)	Elective	Emergent/urgent	Postoperative
Age (X_2) (years)	<50	50−60	≥60
Weight (X_3)	Normal	overweight	underweight
Inotropic support (X_4)	None	Yes − Stable	Yes − Unstable or ECMO
Respiratory status (X_5)	Own Airway	Stable on ventilator or known difficult/unusual airway	Respiratory failure on mechanical ventilation
Other systemic illness/failure (X_6)	None	Medically controlled or 1 organ system failure	Uncontrolled or >1 organ system failure
ASA score (X_7)	1 or 2	3	4 or 5
Physiologic category (X_8)[a] (category)	1	2	3
Precatheterization diagnosis (X_9)[b] (category)	1	2	3
Procedure risk category (X_{10})[c] (category)	1	2	3
Procedure type (X_{11})	Diagnostic	Intervention	Hybrid
Sedation (X_{12})	None/mild	Moderate	General anesthesia

X_1-X_{10} comprised the 10 variables included in the original 20-point risk score.
ASA = American Society of Anesthesia; ECMO = Extracorporeal membrane oxygenation.
a−c = see Appendix 3 for classification of low, medium, and high risk categories

All local centers obtained approval for the project with their local Institutional Review Boards or Research Ethics Committees.

Univariate chi-square analysis was performed to correlate each of 12 variables with SAE occurrence (Table 2). These 12 variables include the 10 risk factors (scaled 0, 1, and 2) in the original 20-point risk score plus procedure type (diagnostic, interventional, or hybrid) and sedation level (none/mild, moderate, and general anesthesia). These 12 variables were entered into a multivariate logistic regression analysis to develop a mathematical model for predicting cardiac Catheterization RISk in Adult (CRISA) patients. A backward elimination stepwise model selection procedure was used to select the final subset of variables used in the CRISA risk score model.

To compare the newly developed CRISA score with the ASA score and the original 20-point risk score, we first fitted each of the 3 risk score models with a simple logistic regression model:

$$\ln(P/(1-P)) = \beta_0 + \beta_1 * (\text{riskscore})^{10},$$

where P is the probability of a patient developing an SAE significant complication using the respective risk score model. Thus,

$$P = \frac{e^{\beta 0 + \beta 1 * \text{riskscore}}}{1 + e^{\beta 0 + \beta 1 * \text{riskscore}}}$$

The 3 risk score models were then compared using 4 methods: (1) −2log Likelihood (N2LL), an assessment for model fit; (2) Akaike's Information Criteria, defined as N2LL+(2*k), which is a best model fit statistic that adjusts for the number of parameters (k)); (3) Schwarz's Bayes Information Criteria, defined as N2LL+(ln(N)*k), where N = sample size; and (4) Area under the receiver operator curve.[10]

Results

From June 2008 to September 2017, 7317 catheterization procedures were recorded into the CCISC complications database from 27 centers (Appendix 3). Mean and median ages of these patients were 34.8 years and 30.6 years (interquartile range [IQR], 21.7 to 43.8 years), respectively, and the mean and median weights were 74.7 kg and 76 kg, respectively (IQR, 60 to 85.9 kg). The gender distribution of patients was 49.9% male and 50.1% female.

A total of 300 procedures (4.1%) were complicated by SAEs (Appendix 4). Mean and median age of patients who experienced SAE were 38.1 years and 34.1 years (IQR, 23.7 to 51.0 years), and the mean and median weight were 74.4 kg and 70.0 kg, respectively (IQR, 58.0 to 88.0 kg). The gender distribution of patients was 50.5% male and 49.5% female. The most common SAEs were arrhythmia (n = 55; 0.75%), vascular injury (n = 44; 0.6%), and need for hemodynamic support (n = 42; 0.57%).

Table 2 shows the correlation of SAE incidence with each of the 10 variables (X_1-X_{10}) included in the original 20-point risk score, as well as the procedure type (X_{11}) and sedation method (X_{12}). All variables except inotropic support at time of catheterization significantly predicted SAE ($p < 0.050$), but not all variables were included in the final risk score model due to the intercorrelation of these variables. A backward model selection method yielded the following model with the regression coefficients rounded to the nearest integers:

$$\text{CRISA} = 2 * X_{2ab} + X_{6ab} + 2 * X_{7b} + 3 * X_{8b} + X_{9ab} + 2 * X_{10ab} + 3 * X_{11a} + 8 * X_{11b} + 3 * X12_b$$

Where

X_{2ab} = 1 if age score = 1 or 2; 0 if age score = 0

Table 2
Chi-square analysis of serious adverse events by patient/procedural characteristics

Characteristic	N	SAE (+)	p Value
Patient status/timing (X_1)			0.039
Elective	7172	4.03%	
Emergent/urgent	133	8.27%	
Postoperative	12	0%	
Patient age (X_2) (years)		< 0.001	
<50	6019	3.70%	
50-60	655	5.34%	
≥60	643	6.53%	
Patient weight (X_3)		0.011	
Normal	5376	3.72%	
Overweight	1363	4.77%	
Underweight	578	6.06%	
Inotropic support (X_4)			0.382
None	7148	4.07%	
Yes − Hemodynamically stable	149	4.70%	
Yes − Unstable or mechanical cardiopulmonary support	20	10.0%	
Respiratory status (X_5)			0.002
Own airway	7248	4.03%	
Stable on ventilator or known difficult/unusual airway	52	9.62%	
Respiratory failure on mechanical ventilation	17	17.65%	
Systemic illness/failure (X6)			< 0.001
None	4582	3.36%	
Medically controlled or 1 organ system failure	2423	4.87%	
Uncontrolled or >1 organ system failure	312	8.97%	
ASA score (X_7)			< 0.001
1 or 2	4890	3.35%	
3	2065	4.94%	
4 or 5	362	9.39%	
Physiologic score (X_8) (category)			< 0.001
1	5462	3.37%	
2	1422	5.70%	
3	433	8.08%	
Precatheterization diagnosis (X_9) (Category)			< 0.001
1	3617	2.96%	
2	3365	5.17%	
3	335	5.67%	
Procedure risk category (X_{10}) (category)			< 0.001
1	6004	2.98%	
2	714	9.38%	
3	599	9.02%	
Procedure type (X_{11})			< 0.001
Diagnostic	3134	2.23%	
Interventional	4174	5.46%	
Hybrid	9	22.22%	
Sedation (X_{12})			< 0.001
None	194	3.09%	
Moderate	3281	2.34%	
General anesthesia	3842	5.65%	

$X_{6ab} = 1$ if other systemic illness score = 1 or 2; if systemic illness score = 0

$X_{7b} = 1$ if ASA score ≥4; 0 if ASA score <4

$X_{8b} = 1$ if physiologic score = 2; 0 if physiologic score = 0 or 1

$X_{9ab} = 1$ if diagnosis score = 1 or 2; 0 if diagnosis score = 0

$X_{10ab} = 1$ if procedure score = 1 or 2, 0 if procedure score = 0

$X_{11a} = 1$ if procedure type = interventional only; 0 if procedure type = diagnostic or hybrid

$X_{11b} = 1$ if procedure type = hybrid; 0 if procedure type = interventional only or diagnostic

$X_{12b} = 1$ if sedation method = general anesthesia; 0 if sedation method = none/mild/moderate

(see Table 1 for the original 0-2 point definition)

The multivariable model selection procedure used to define the CRISA score model determined that timing (X_1), weight (X_3), inotrope support (X_4), and precatheterization airway status (X_5) did not significantly add to the predictive power of the model. Table 3 illustrates the point values assigned to each variable in the new CRISA risk score model, resulting in a total possible score ranging from 0 to 22. CRISA score was found to be superior to ASA score and the original 20-point risk model for predicting SAE in adults (Table 4).

Table 3
Adult risk assessment model

Patient clinical characteristics	Points assigned
Age (X_2) (years)	
<50	0
≥50	2
Systemic illness/organ failure (X_6)	
None	0
Medically controlled/1 organ failure, or uncontrolled/ >1 organ failure <2.5 kg	1
American Society of Anesthesia (ASA) Score (X_7)	
1-3	0
4-5	2
Physiologic score category (X_8)	
1 or 2	0
3	3
Precatheterization diagnosis category (X_9)	
1	0
2 or 3	1
Procedure risk category (X_{10})	
1	0
2 or 3	2
Procedure type (X_{11})	
Diagnostic	0
Interventional	3
Hybrid	8
Sedation (X_{12})	
None/mild/moderate	0
General anesthesia	3
Total risk score =	
Possible risk score =	0-22

Table 4
Comparison of risk score models in prediction of SAE

Risk model	N2LL	AIC	BIC	AUC
ASA (1-5)	2504	2506	2513	0.56
Original risk score (0-20)	2234	2236	2243	0.66
CRISA (0-22)	1781	1783	1790	0.68

AIC = Akaike's information criteria; AUC = area under the receiver operator curve; BIC = Schwarz's Bayes Information Criteria; N2LL = −2log likelihood (an assessment for model fit).

Not surprisingly, the incidence of SAE increased with increasing CRISA score (Figure 1). Of note, no patient received a score of 18 or above. There is also a progressive decrease in the absolute number of catheterizations represented as CRISA score increases. Due to the relatively low number of procedures for a score of ≥13, for practical purposes, we propose defining procedures as *minimal, low, moderate*, and *high* risk by CRISA score corresponding with observed SAE risks of 0.5%, 3.2%, 7.9%, and 16.7%, respectively.

Discussion

Despite an ongoing, system-wide emphasis on improving quality outcomes in the care of adults with congenital heart disease,[11] there is a relative lack of data regarding the safety and outcomes of performing cardiac catheterization on adults in the setting of a pediatric congenital cardiac catheterization laboratory. Previously published estimates of risk during congenital cardiac catheterization have often combined pediatric and adult patients into a single cohort, neglecting the potential risk factors unique to adults with congenital heart disease. CRISA, through CCISC, takes many of these factors into consideration. Herein, we identified several demographic, physiologic, and procedural factors that cumulatively predict the overall risk of SAE during cardiac catheterization of adults with congenital heart disease. Of these factors, general procedure type (diagnostic vs. interventional vs. hybrid), specific procedure type (e.g., type of intervention), and physiologic risk category (eg, systemic oxygen saturation, pulmonary hypertension) carried the greatest weight in predicting the risk of SAE in our model. Other purported risk factors, such as patient weight, respiratory status, and type of anesthesia, did not add predictive value to our model.

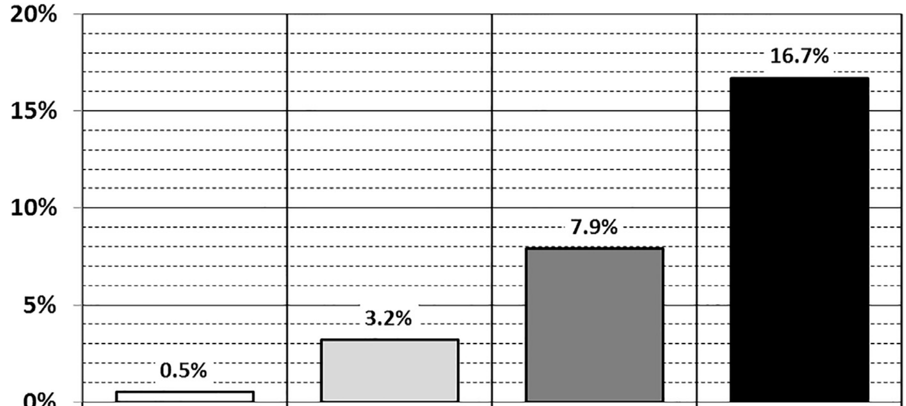
Previous reports have sought to define the risk and risk factors for adults with congenital heart disease who underwent cardiac catheterization. The Improving Pediatric and Adult Congenital Treatment (IMPACT) Registry reported a SAE rate of 2.5% in the entire cohort of 27,293 procedures in adolescents and adults, a rate lower than among our cohort.[12] However, >60% of procedures reported in the IMPACT study involved older children 10 to 17 years of age ("adolescents" by their definition), a population that was intentionally excluded from our study. As one might expect, this younger cohort had a significantly lower rate of SAE than older (≥18 years old) patients (2.2% vs. 3.1%) in their analysis. Furthermore, we accepted a broader definition of SAE that includes complications that would not have met criteria for inclusion in the IMPACT analysis, such as events that were not per se uniquely related to cardiac catheterization (e.g., airway compromise, bronchospasm). In addition, the general threshold to be counted as a nonmortality SAE in the IMPACT registry is a complication or physiologic change that necessitates potentially life-saving treatment or an additional procedure. By comparison, CCISC counts as SAE events that may have prolonged the hospital stay even if they did not lead to an unanticipated surgical or transcatheter intervention.

This discrepancy in study methodology raises an important question: how should we define SAE? CCISC has espoused the view that a procedural SAE should include any complication that occurs during a patient's time in the cardiac catheterization lab, irrespective of whether the root cause is the catheterization procedure (vascular access, manipulation of catheters or wires within the cardiovascular system, or transcatheter intervention) or to other aspects of the procedural episode of care (eg, anesthetic induction, airway management, etc.). Certainly a narrow definition of SAE can be helpful, particularly when identifying modifiable technical or systematic factors that may lead to SAE. By comparison, the advantage of a broader definition of SAE is that it facilitates a more informed and nuanced preprocedural discussion with patients about the risk of complications.

Previously reported risk assessment models have most often focused on reporting and comparing procedural outcomes. By comparison, CRISA is intended to be a *predictive* tool for use in preprocedural planning and consultation with patients and families. As a result, the score is derived primarily from demographic and other variables that are available before cardiac catheterization. We note that our model does include certain physiologic variables most often measured during cardiac catheterization, such as pulmonary vascular resistance, which may affect the CRISA score significantly. In most cases, these variables can be estimated before the procedure through a patient's clinical history and with the use of echocardiography and other noninvasive tests, thus maintaining the utility of CRISA score as a predictive model for preprocedural risk assessment.

We acknowledge that the CRISA risk score model has certain limitations. First, as discussed above the CRISA score considers certain physiologic variables that are typically measured during cardiac catheterization, such as pulmonary vascular resistance. Although in most cases these variables can be accurately estimated preprocedure, we recognized that such estimates may not always reflect reality. Second, the CRISA score model was based on a relatively small number of total SAE, which limits our ability to draw more precise conclusions about the influence of specific risk factors on the overall risk of SAE in general or the specific risk of a particular SAE. Lastly, although CRISA performed favorably relative to other risk prediction models, it has not yet been validated in a separate cohort of patients. Ongoing research involving larger cohorts of patients is needed to address the each of these limitations and to further refine our prediction and assessment of risk for adults with congenital heart disease who underwent cardiac catheterization.

In conclusion, the frequency of SAE in adults with congenital heart disease increases with increasing CRISA



	MINIMAL	LOW	MODERATE	HIGH
CRISA Score	0-2	3-7	8-10	≥ 11
Total procedures (#)	1360	4274	1401	282
SAE (#)	7	136	110	47

Figure 1. **CRISA risk score categories**. Bar graph comparing the 4 CRISA risk score categories by risk of serious adverse event, including numerical score for each category and observed rates of serious adverse event. CRISA = catheterization RISk score in adults; SAE = serious adverse event(s).

score. The CRISA score predicts risk of SAE more reliably than alternative risk score models and may be useful for preprocedural risk assessment.

Disclosures

The investigators have no conflicts of interest to disclose.

Supplementary materials

Supplementary material associated with this article can be found in the online version at https://doi.org/10.1016/j.amjcard.2019.01.042.

1. Marelli AJ, Mackie AS, Ionescu-Ittu R, Rahme E, Pilote L. Congenital heart disease in the general population: changing prevalence and age distribution. *Circulation* 2007;115:163–172.
2. Bergersen L, Gauvreau K, Foerster SR, Marshall AC, McElhinney DB, Beekman RH 3rd, Hirsch R, Kreutzer J, Balzer D, Vincent J, Hellenbrand WE, Holzer R, Cheatham JP, Moore JW, Burch G, Armsby L, Lock JE, Jenkins KJ. Catheterization for Congenital Heart Disease Adjustment for Risk Method (CHARM). *JACC Cardiovasc Interv* 2011;4:1037–1046.
3. Bergersen L, Gauvreau K, Jenkins KJ, Lock JE. Adverse event rates in congenital cardiac catheterization: a new understanding of risks. *Congenit Heart Dis* 2008;3:90–105.
4. Bergersen L, Gauvreau K, Lock JE, Jenkins KJ. A risk adjusted method for comparing adverse outcomes among practitioners in pediatric and congenital cardiac catheterization. *Congenit Heart Dis* 2008;3:230–240.
5. Bergersen L, Gauvreau K, Marshall A, Kreutzer J, Beekman R, Hirsch R, Foerster S, Balzer D, Vincent J, Hellenbrand W, Holzer R, Cheatham J, Moore J, Lock J, Jenkins K. Procedure-type risk categories for pediatric and congenital cardiac catheterization. *Circ Cardiovasc Interv* 2011;4:188–194.
6. Bergersen L, Marshall A, Gauvreau K, Beekman R, Hirsch R, Foerster S, Balzer D, Vincent J, Hellenbrand W, Holzer R, Cheatham J, Moore J, Lock J, Jenkins K. Adverse event rates in congenital cardiac catheterization − a multi-center experience. *Catheter Cardiovasc Interv* 2010;75:389–400.
7. Holzer RJ, Gauvreau K, Kreutzer J, Moore JW, McElhinney DB, Bergersen L. Relationship between procedural adverse events associated with cardiac catheterization for congenital heart disease and operator factors: results of a multi-institutional registry (C3PO). *Catheter Cardiovasc Interv* 2013;82:463–473.
8. Learn CP, Holzer RJ, Daniels CJ, Torres AJ, Vincent JA, Moore JW, Armsby LB, Landzberg MJ, Bergersen L. Adverse events rates and risk factors in adults undergoing cardiac catheterization at pediatric hospitals—results from the C3PO. *Catheter Cardiovasc Interv* 2013;81:997–1005.
9. Nykanen DG, Forbes TJ, Du W, Divekar AA, Reeves JH, Hagler DJ, Fagan TE, Pedra CA, Fleming GA, Khan DM, Javois AJ, Gruenstein DH, Qureshi SA, Moore PM, Wax DH. CRISP: Catheterization RISk score for Pediatrics: a report from the Congenital Cardiac Interventional Study Consortium (CCISC). *Catheter Cardiovasc Interv* 2016;87:302–309.
10. K.P. Burnbaum DRA. *Model Selection and Multimodal Inference: A Practical Information-Theoretic Approach*. (2nd Ed.) New York, NY: Springer-Verlag; 2002.
11. Gurvitz M, Marelli A, Mangione-Smith R, Jenkins K. Building quality indicators to improve care for adults with congenital heart disease. *J Am Coll Cardiol* 2013;62:2244–2253.
12. Stefanescu Schmidt AC, Armstrong A, Kennedy KF, Nykanen D, Aboulhosn J, Bhatt AB. Prediction of adverse events after catheter-based procedures in adolescents and adults with congenital heart disease in the IMPACT registry. *Eur Heart J* 2017;38:2070–2077.