JACC: CARDIOVASCULAR INTERVENTIONS VOL. 4, NO. 9, 2011
© 2011 BY THE AMERICAN COLLEGE OF CARDIOLOGY FOUNDATION
ISSN 1936-8798/$36.00
PUBLISHED BY ELSEVIER INC. DOI: 10.1016/j.jcin.2011.05.021

Catheterization for Congenital Heart Disease Adjustment for Risk Method (CHARM)

Lisa Bergersen, MD, MPH,* Kimberlee Gauvreau, ScD,* Susan R. Foerster, MD,† Audrey C. Marshall, MD,* Doff B. McElhinney, MD,* Robert H. Beekman III, MD,‡ Russel Hirsch, MD,‡ Jacqueline Kreutzer, MD,§ David Balzer, MD,† Julie Vincent, MD,‖ William E. Hellenbrand, MD,‖ Ralf Holzer, MD,¶ John P. Cheatham, MD,¶ John W. Moore, MD,# Grant Burch, MD,** Laurie Armsby, MD,** James E. Lock, MD,* Kathy J. Jenkins, MD, MPH*

Boston, Massachusetts; St. Louis, Missouri; Cincinnati and Columbus, Ohio; Pittsburgh, Pennsylvania; New York, New York; San Diego, California; and Portland, Oregon

Objectives This study sought to develop a method to adjust for case mix complexity in catheterization for congenital heart disease to allow equitable comparisons of adverse event (AE) rates.

Background The C3PO (Congenital Cardiac Catheterization Project on Outcomes) has been prospectively collecting data using a Web-based data entry tool on all catheterization cases at 8 pediatric institutions since 2007.

Methods A multivariable logistic regression model with high-severity AE outcome was built using a random sample of 75% of cases in the multicenter cohort; the models were assessed in the remaining 25%. Model discrimination was assessed by the C-statistic and calibration with Hosmer-Lemeshow test. The final models were used to calculate standardized AE ratios.

Results Between August 2007 and December 2009, 9,362 cases were recorded at 8 pediatric institutions of which high-severity events occurred in 454 cases (5%). Assessment of empirical data yielded 4 independent indicators of hemodynamic vulnerability. Final multivariable models included procedure type risk category (odds ratios [OR] for category: 2 = 2.4, 3 = 4.9, 4 = 7.6, all $p < 0.001$), number of hemodynamic indicators (OR for 1 indicator = 1.5, ≥2 = 1.8, $p = 0.005$ and $p < 0.001$), and age <1 year (OR: 1.3, $p = 0.04$), C-statistic 0.737, and Hosmer-Lemeshow test $p = 0.74$. Models performed well in the validation dataset, C-statistic 0.734. Institutional event rates ranged from 1.91% to 7.37% and standardized AE ratios ranged from 0.61 to 1.41.

Conclusions Using CHARM (Catheterization for Congenital Heart Disease Adjustment for Risk Method) to adjust for case mix complexity should allow comparisons of AE among institutions performing catheterization for congenital heart disease. (J Am Coll Cardiol Intv 2011;4:1037–46)
© 2011 by the American College of Cardiology Foundation

From the *Department of Cardiology, The Children's Hospital, Boston, Massachusetts; †Washington University, St. Louis, Missouri; ‡Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio; §Children's Hospital of Pittsburgh, Pittsburgh, Pennsylvania; ‖Morgan Stanley Children's Hospital of New York Presbyterian, New York, New York; ¶Nationwide Children's Hospital, Columbus, Ohio; #Rady Children's Hospital, San Diego, California; and the **Oregon Health Sciences University, Portland, Oregon. A Web-based application for data entry was developed in 2006 with funding support from the Children's Heart Foundation (Chicago, Illinois). The application was deployed on a Microsoft Internet Information Server obtained with funding support from the American Heart Association. The American Heart Association Physicians Roundtable Award (AHA-PRA) provides support for the project and career development plan for Dr. Bergersen (2006 to 2010). The Keane Operating Fund at The Children's Hospital in Boston provided the resources necessary to perform site visits and independent audits. Drs. McElhinney and Vincent are consultants and proctors for Medtronic. Drs. Beekman and Balzer are proctors for AGA Medical Inc. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

Manuscript received April 12, 2011; revised manuscript received May 9, 2011, accepted May 14, 2011.

Until recently, the field of pediatric cardiac catheterization has lacked standardized nomenclature and definitions for adverse events (AE). This, in turn, led to different arbitrary definitions for adverse events being used by different institutions and inhibited the ability to establish benchmarks or expected outcomes in this specialty (1–7). Comparisons between and within institutions were further limited by the lack of ability to adjust for case mix differences. The C3PO (Congenital Cardiac Catheterization Project on Outcomes) was developed and executed to overcome these limitations in our ability to assess and compare outcomes in the field. Specifically, we sought to collect data in a uniform manner on all catheterization procedures performed at multiple institutions, including patient and procedural characteristics and the occurrence of AE (8). After 1 year of planning and development of a Web-based data entry tool, data collection commenced in 2007, and has resulted in the creation of a large multicenter dataset of congenital cardiac catheterization cases.

Abbreviations and Acronyms

AE = adverse event(s)
CI = confidence interval
EDP = end-diastolic pressure
MPAmp = main pulmonary artery mean pressure
MPAsp = main pulmonary artery systolic pressure
MVsat = mixed venous saturation
nonSV = 2-ventricle physiology
OR = odds ratio
RV = right ventricle
SAER = standardized adverse event ratio(s)
SAsat = systemic arterial saturation
SV = single-ventricle physiology

Cardiac catheterization in pediatrics and for adults with congenital heart disease encompasses a broad range of procedures, some of which occur infrequently, precluding assessment of risk for individual procedure types. Further, there is variation in the frequency of different procedures between centers and practitioners and a wide variety of adverse outcomes can occur in different interventions. To account for procedural diversity, we developed procedure type risk categories using both consensus and empirical methods (9). Although the procedure type risk categories have a strong relationship with AEs, other patient and/or procedural factors may also influence outcome. Thus, we sought to develop a method of case mix adjustment that would include the most important patient and procedural determinants of risk for clinically important AE in a multivariable model. The population analyzed included the entire cohort of patients undergoing catheterization for congenital heart disease, with a secondary cohort consisting of children <18 years of age. This was necessary to develop a risk adjustment method focused on pediatrics in parallel with the broader goal of developing a method for practitioners and institutions caring for both children and adults with congenital heart disease.

Methods

Data source. After institutional review board approval was obtained, 6 participating centers collected patient and procedural information and the occurrence of adverse events on all diagnostic and interventional catheterization procedures starting in February 2007. One of the 6 institutions did not start collecting data on biopsy cases until March 2009. Two additional sites became participants in April 2008 and June 2009, respectively. Thus, 8 sites contributed data to the registry (Online Appendix). Primary electrophysiology cases were not included. This analysis is limited to cases entered after August 1, 2007, because additional hemodynamic variables were added to the database and prospectively collected only after this date.

The methods for data collection and validation were previously published (8,9). Patient and procedural characteristics as well as the occurrence and type of adverse events were prospectively recorded. The following patient and procedural characteristics were recorded: type of case (diagnostic, interventional, or biopsy), center, admission status (elective, nonelective, emergent), age, sex, diagnosis, noncardiac problem, known or suspected genetic abnormality, airway management during catheterization (spontaneous respiration or mechanical support), types of interventions, case duration, and hemodynamic variables.

Because cardiac catheterization for congenital heart disease encompasses such a broad range of therapeutic and diagnostic procedures, we previously developed procedure type risk categories (Table 1). These categories were developed using both consensus and empirical methods. The categories represent procedure types with similar risk of adverse outcomes during cardiac catheterization procedures for congenital heart disease (9). As previously described, cases with multiple procedures were assigned to the category corresponding to the highest risk procedure.

AE were defined as any anticipated or unanticipated event from which injury could have occurred or did occur, potentially or definitely because of performing the catheterization. Events were recorded at the time of identification, either at the time of the case or later if determined to be related to the procedure. We used previously established and tested definitions for AE severity ranging from levels 1 to 5 (Table 2) (1,8). For this analysis, clinically important higher severity AE were defined as levels 3 and 4, or 5 AE. All AE were reviewed for proper application of seriousness definitions by the principal investigator and a designee. Any misapplication of definitions was reported to the participant and disagreements were resolved.

Hemodynamic vulnerability. It was our supposition that a patient with abnormal hemodynamics would be at increased risk for clinically important AE. In previous work at The Children's Hospital in Boston, we defined abnormal hemodynamics using judgment and consensus and were able to show an association with AE (1). However, the thresholds were

Table 1. Procedure Type Risk Categories

	Risk Category 1	Risk Category 2	Risk Category 3	Risk Category 4
Diagnostic case	Age ≥1 yr	Age ≥1 month <1 yr	Age <1 month	
Valvuloplasty		Pulmonary valve ≥1 month	Aortic valve ≥1 month Pulmonary valve <1 month Tricuspid valve	Mitral valve Aortic valve <1 month
Device or coil closure	Venous collateral LSVC	PDA ASD or PFO Fontan fenestration Systemic to pulmonary artery collaterals	Systemic surgical shunt Baffle leak Coronary fistula	VSD Perivalvular leak
Balloon angioplasty		RVOT Aorta dilation <8 atm	Pulmonary artery <4 vessels Pulmonary artery ≥4 vessels all <8 atm Aorta >8 atm or CB Systemic artery (not aorta) Systemic surgical shunt Systemic to pulmonary collaterals Systemic vein	Pulmonary artery ≥4 vessels Pulmonary vein
Stent placement		Systemic vein	RVOT Aorta Systemic artery (not aorta)	Ventricular septum Pulmonary artery Pulmonary vein Systemic surgical shunt Systemic pulmonary collateral
Stent redilation		RVOT Atrial septum Aorta Systemic artery (not aorta) Systemic vein	Pulmonary artery Pulmonary vein	Ventricular septum
Other	Myocardial biopsy	Snare foreign body Transseptal puncture	Atrial septostomy Recanalization of jailed vessel in stent Recanalization of occluded vessel	Atrial septum dilation and stent Any catheterization <4 days after surgery Atretic valve perforation

ASD = atrial septal defect; CB = cutting balloon; LSVC = left superior vena cava; PDA = patent ductus arteriosus; PFO = patent foramen ovale; RVOT = right ventricular outflow tract (RVOT includes right ventricle to pulmonary artery conduit or status post-RVOT surgery with no conduit); VSD = ventricular septal defect.

arbitrarily defined and not based on data. In this study, we sought to use empirical data to develop a single composite indicator of hemodynamic vulnerability based on the hemodynamic factors with the greatest ability to predict high-severity AE, while eliminating collinear variables with less explanatory value. The following 8 hemodynamic variables were assessed for inclusion in this composite measure: cardiac index, right ventricular (RV) systolic pressure, RV to systemic pressure ratio (RV ratio), systemic ventricle end-diastolic pressure (EDP), mixed venous saturation (MVsat), systemic arterial saturation (SAsat), main pulmonary artery systolic pressure (MPAsp), and main pulmonary artery mean pressure (MPAmp).

Table 2. Definitions for Adverse Event Severity

Severity Level	Definition	Examples
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
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
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
4–Major	Change in condition, life-threatening if not treated, change in condition may be permanent, may have required an intensive care unit admission or emergent readmit to hospital, may have required invasive monitoring, required interventions such as electrical cardioversion or unanticipated intubation or required major invasive procedures or transcatheter interventions to correct condition.	Event requiring cardiopulmonary resuscitation Event leading to surgery or repeat catheterization Stroke
5–Catastrophic	Any death, and emergent surgery or heart lung bypass support (ECMO) to prevent death with failure to wean from bypass support.	Event resulting in death

Statistical methods. Frequency with percentage or median with interquartile range (25th and 75th percentiles) were calculated for patient and procedural characteristics of the entire cohort and for the subgroup of patients <18 years of age. Using a random sample of 75% of the cases collected between August 1, 2007, and December 31, 2009, the composite indicator of hemodynamic vulnerability was derived and multivariable models for predicting the outcome of high severity AE were developed. Model performance was then assessed both in this dataset as well as in the remaining 25% of cases.

HEMODYNAMIC VULNERABILITY INDICATOR. Before any analyses were conducted, correlations among the 8 hemodynamic variables were explored using Pearson and Spearman correlation coefficients. For each individual variable, a receiver-operator characteristic curve was used to identify the threshold value that maximized discrimination for predicting a high-severity AE. A binary variable was then created based on this cutpoint. The entire cohort was used to derive single threshold values for cardiac index and EDP. For other variables, such as MVsat, SAsat, and MPAmp the cohort was divided into patients with single-ventricle (SV) and 2-ventricle (nonSV) physiologies. Threshold values for RV, RV ratio, and MPAsp were only assessed in the nonSV subset of the cohort.

Once the best threshold value had been determined for each of the 8 individual hemodynamic variables, the resulting binary variables were used to create a composite hemodynamic vulnerability indicator. Multivariable logistic regression with backward elimination was used to identify the subgroup of hemodynamic variables with the greatest ability to predict a high-severity AE. We started with a model containing all 8 hemodynamic variables, and removed them 1 at a time. If the area under the receiver-operator characteristic curve improved when a variable was removed, that variable was eliminated and the process repeated until eliminating an additional variable no longer improved the discrimination of the model. Once the most important hemodynamic variables were identified, we considered different methods of combining them to quantify hemodynamic vulnerability. This included using each hemodynamic risk factor as a simple binary variable indicating whether a case had any of the hemodynamic risk factors, taking the total number of hemodynamic risk factors present, and combining the number of risk factors into a score. Factors were weighted according to whether they were more or less predictive of the outcome. The simplest model with the highest discrimination was chosen as the final composite indicator of hemodynamic vulnerability.

RISK ADJUSTMENT MODEL. The random sample of 75% of the cases collected between August 1, 2007, and December 31, 2009, was used to create a multivariable logistic regression model for the outcome severity levels 3 and 4, or 5 AE in the entire cohort, as well as in the secondary cohort of children <18 years of age. Forward selection was used. The patient characteristic with the highest statistically significant improvement in the area under the receiver-operator characteristic curve (C-statistic), as assessed by the likelihood-ratio test, was retained in the model, and the remaining variables were reassessed. This process was repeated until there was no significant contribution to outcome prediction for any of the remaining variables.

The following patient and procedural characteristics were considered to develop the model: procedure risk category, diagnosis, age, noncardiac problem, known or suspected genetic abnormality, and hemodynamic vulnerability. Odds ratio (OR) with 95% confidence intervals (CIs) are presented for the final risk adjustment models. The Hosmer-Lemeshow goodness of fit test was used to assess calibration (10,11). Discrimination and calibration were also assessed in the validation datasets.

CHARM. The final CHARM (Catheterization for Congenital Heart Disease Adjustment for Risk Method) model was used to determine risk-adjusted AE rates for severity levels 3 and 4, or 5 AE by institution for the entire cohort as well as for children <18 years of age. Standardized adverse event ratios (SAER) were calculated by dividing the observed AE rate within each institution by the expected AE rate accounting for the institution's case mix. To calculate the expected AE rate, the expected number of events was counted for each institution by summing the predicted probabilities of the outcome—generated from the final logistic regression model—for each case within that institution. The expected number of events was then divided by the total number of cases at that institution to calculate the expected rate. A SAER of 1.0 indicates that the observed event rate is equal to the expected rate given the institution's case mix complexity. If the SAER is >1.0, the institution has more events than would have been expected. If the SAER is <1.0, the institution has fewer events than expected. The 95% CIs were calculated for each SAER; if a CI does not contain the value 1.0, then the AE rate for that institution is significantly different from average ($p < 0.05$).

Results

Population. Between August 1, 2007, and December 31, 2009, 9,362 diagnostic and interventional cardiac catheterization cases were recorded in the database, 85% of which were performed in children <18 years of age (Table 3). One-half the population was composed of patients with SV circulation or complex 2-ventricle anatomy with outflow tract obstruction and/or intracardiac shunts due to septal defects. Twenty percent of the population had isolated lesions such as an atrial septal defect, patent ductus arteriosus, or valve abnormality. Genetic abnormalities were present in 12% of the cohort and noncardiac problems in 27%. Most of the procedures were performed electively (81%). When the population was limited to pediatric patients, there was a lower prevalence of spontaneous respirations as the

Table 3. Patient and Procedural Characteristics August 1, 2007, to December 31, 2009

	Entire Cohort (N = 9,362)	<18 Years of Age (n = 7,970)
Patient characteristics		
Age		
<1 month	637 (7)	637 (8)
1–11 months	1,699 (18)	1,699 (21)
1–9 yrs	3,598 (38)	3,598 (45)
≥10 yrs	3,425 (37)	2,036 (26)
Male	4,909 (52)	4,224 (53)
Diagnosis		
No structural heart disease*	2,571 (27)	2,114 (27)
Pulmonary hypertension	262 (3)	220 (3)
Isolated defects	1,933 (21)	1,612 (20)
Complex defect with 2 ventricles	2,847 (30)	2,402 (30)
Complex defect with 1 ventricle	1,746 (19)	1,621 (20)
Genetic syndrome	1,091 (12)	996 (13)
Noncardiac problem	2,475 (27)	1,975 (25)
Procedural characteristics		
Case type		
Diagnostic	2,561 (27)	2,127 (27)
Interventional	4,589 (49)	4,037 (51)
Biopsy	2,212 (24)	1,806 (23)
Admission type		
Elective	7,537 (81)	6,261 (79)
Nonelective	1,661 (18)	1,553 (19)
Emergent	162 (2)	154 (2)
Spontaneous respirations	2,864 (31)	2,024 (25)
Types of interventions		
Any balloon angioplasty	1,480 (16)	1,339 (17)
Any valvotomy	590 (6)	557 (7)
Any stent placement	1,275 (14)	1,073 (13)
Any device placement	1,298 (14)	1,065 (13)
Any coil placement	850 (9)	811 (10)
Procedure type risk categories		
Category 1	3,934 (42)	3,092 (39)
Category 2	2,698 (29)	2,402 (30)
Category 3	1,751 (19)	1,582 (20)
Category 4	979 (10)	894 (11)
Case duration		
<1 h	3,362 (36)	2,830 (36)
≥1 h, <2 h	3,860 (41)	3,345 (42)
≥2 h, <3 h	1,469 (16)	1,252 (16)
≥3 h	652 (7)	527 (7)
Any level 3, 4, or 5 severity AE	454 (5)	407 (5)

Values are n (%). *Examples include patients with cardiomyopathy or after heart transplantation. AE = adverse events.

method of airway management (25% vs. 31%). Patient and procedural characteristics were otherwise similar. The lowest procedure type risk category comprised the largest proportion of the procedures, with 42% in category 1, 29% in category 2, 19% in category 3, and 10% in category 4. The outcome for the risk adjustment model, high-severity AE, occurred in 5% of the entire cohort and at a similar rate in the secondary cohort of patients <18 years of age.

Hemodynamic vulnerability. The following correlations were found among the hemodynamic variables: 1) higher cardiac index and higher MVsat; 2) higher MVsat, higher SAsat, and lower RV ratio; and 3) higher RV ratio, higher RV, higher MPAsp, and MPAmp. None of the other hemodynamic variables were associated with EDP (Fig. 1). We assigned threshold values empirically for each of the 8 hemodynamic variables (Table 4, Fig. 2). Multivariable modeling yielded 4 indicators of hemodynamic vulnerability independently associated with the occurrence of a high severity AE: EDP ≥18 mm Hg; SAsat <95% if nonSV or <78% if SV; MVsat <60% if nonSV or <50% if SV; and MPAsp ≥45 mm Hg if nonSV or MPAmp ≥17 mm Hg if SV. The number of hemodynamic variables present among these 4 categorized as 0, 1, 2, or more was the simplest composite indicator of hemodynamic vulnerability for predicting the outcome any severity levels 3 and 4, or 5 AE (C-statistic: 0.632) (Table 5).

Multivariable risk adjustment model: CHARM. The final multivariable model for the overall cohort included procedure type risk category, number of hemodynamic indicators, and age <1 year, with a C-statistic of 0.737 and Hosmer-Lemeshow test p value 0.74 (Table 6). For the age variable, we started with 5 categories (age <1 month, 1 month to <1 year, 1 to 10 years, 11 to 17 years, ≥18 years) but then collapsed categories with OR that were not significantly different from each other. In the secondary cohort of patients <18 years of age, the same 3 variables were identified; the model showed similar predictive performance and calibration, C-statistic: 0.734, and Hosmer-Lemeshow

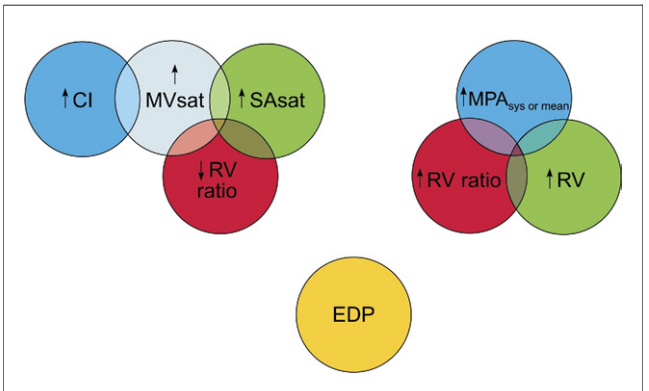

Figure 1. Correlations Among Hemodynamic Variables

The hemodynamic variables assessed were found to be correlated as depicted in the bubble diagram. Higher cardiac index (CI) was related to higher mixed venous saturation (MVsat). Higher MVsat was also related to higher systemic arterial saturation (SAsat) and lower right ventricular to systemic pressure ratio (RV ratio). Higher RV, pulmonary artery (MPA), and RV ratio were correlated. Differences in end-diastolic pressure (EDP) in the systemic ventricle were not related to the other hemodynamic variables assessed.

JACC: CARDIOVASCULAR INTERVENTIONS, VOL. 4, NO. 9, 2011
SEPTEMBER 2011:1037–46

Table 4. Potential Indicators of Hemodynamic Vulnerability and Empirically Derived Threshold Values for the Outcome High Severity AE

	Sample Size, N	Cutpoint	Patients, n (%)	Odds Ratio	95% CI	p Value	Area Under ROC
Cardiac index	6,160	<2.8	1,190 (19%)	1.5	1.1–1.9	0.009	0.532
Systemic ventricle EDP	4,909	≥18	355 (7%)	1.8	1.2–2.6	0.005	0.523
MVsat	6,619	<60 nonSV <50 SV	905 (14%)	2.6	2.0–3.4	<0.001	0.576
SAsat	6,322	<95 nonSV <78 SV	1,827 (29%)	1.9	1.5–2.4	<0.001	0.573
MPAmp	6,214	≥26 nonSV ≥17 SV	1,412 (23%)	2.0	1.6–2.6	<0.001	0.573
MPAsp	6,501	≥45 nonSV	854 (13%)	2.7	1.9–3.6	<0.001	0.618
Systolic RV	6,546	≥45 nonSV	1,865 (28%)	2.7	2.0–3.5	<0.001	0.634
RV ratio	4,923	≥0.4 nonSV	1,953 (40%)	2.0	1.4–2.8	<0.001	0.598

AE = adverse event; CI = confidence interval; EDP = end-diastolic pressure; MPAmp = main pulmonary artery mean pressure; MPAsp = main pulmonary artery systolic pressure; MVsat = mixed venous saturation; nonSV = 2-ventricle physiology; ROC = receiver-operator characteristic; RV = right ventricle; SV = single ventricle physiology.

test p = 0.52. Models also performed well in the validation dataset, C-statistic: 0.734 for the entire cohort (Hosmer-Lemeshow p = 0.20) and 0.728 (Hosmer-Lemeshow p = 0.10) when limited to patients <18 years of age.

The observed adverse event rates among the 8 institutions ranged from 1.91% to 7.37% for the entire cohort (Table 7). Similarly, for patients <18 years of age, there was a wide range of observed AE rates among institutions, 1.71% to 7.86%. The CHARM model was used to determine an expected AE rate based on the case mix for each of the institutions, and SAERs were determined. For all institutions, SAER ranged from 0.61 to 1.41 in the entire cohort and 0.51 to 1.39 in patients <18 years of age (Fig. 3). Institutions C and G had lower AE rates than would be expected given their case mix, whereas institution E had a higher rate than would be expected.

Discussion

The C3PO collaborative group has been accruing data on all congenital catheterizations at several U.S. centers over the course of more than 3 years, with data from nearly 10,000 cases available for this analysis. The investigative group previously was able to stratify catheterization procedure types based upon the risk for adverse outcomes, initially using expert consensus, then modifying the procedure type categories based on empirical methods (9). The risk categories were validated through comparison to a separate cohort of prospectively collected patients. In this analysis, we have identified 4 important hemodynamic variables associated with adverse outcomes including: systemic ventricular EDP ≥18 mm Hg, a SAsat <95% (or <78% if SV), MVsat <60% (or <50% if SV), and pulmonary artery systolic pressure ≥45 mm Hg (or mean ≥17 if SV). These easily and commonly measured factors of hemodynamic vulnerability, when combined with the previously validated procedure type risk categories and patient age, can be applied to make comparisons of the outcome of high-severity AE by adjusting for some of the case mix differences at different centers.

Risk adjustment. Risk adjustment has been successfully employed for many years in the fields of adult cardiology coronary intervention and pediatric cardiac surgery (12–14). This is a much more difficult process in pediatric cardiology, given the wide heterogeneity of diagnoses and types of interventions, as well as the relatively limited sample size of patients as a whole. However, despite this heterogeneity, risk adjustment models, including the RACHS-1 (Risk Adjustment in Congenital Heart Surgery) score and the Aristotle system, have been developed and have been included in the Society of Thoracic Surgeons and European Association for Cardio-Thoracic Surgery databases for congenital cardiac surgery for many years; the data have been useful in improving the ability to compare institutional outcomes adjusted for case mix and certain patient variables (15–20).

There is a comparative deficit in outcomes assessment in the realm of pediatric interventional cardiology, which has lagged behind in the development of a broadly collected, inclusive, and prospective database with sufficient anatomic and physiological information to allow for substantive interrogation. Currently, there are several groups gathering this type of data, including C3PO, the MAGIC (Mid-Atlantic Group of Interventional Cardiology), and the CCISC (Congenital Cardiovascular Interventional Study Consortium), but these efforts have been relatively recent and there is limited ability to cross-communicate between the systems (8,21–23). There is an effort to make a more widely used outcomes registry through the American College of Cardiology IMPACT (Improving Pediatric Adult Congenital Treatments) registry, which began in 2011 (24). Once the data are available, there will be a need for one or more methods allowing comparison between centers and interventionalists, given the wide variation in case type, referral patterns, and approaches to care between these groups. Physicians are understandably concerned that they be fairly compared when sensitive topics such as outcomes and adverse event rates are being critically evaluated and used for compensation and accreditation. In some states, these will also be available in the public record.

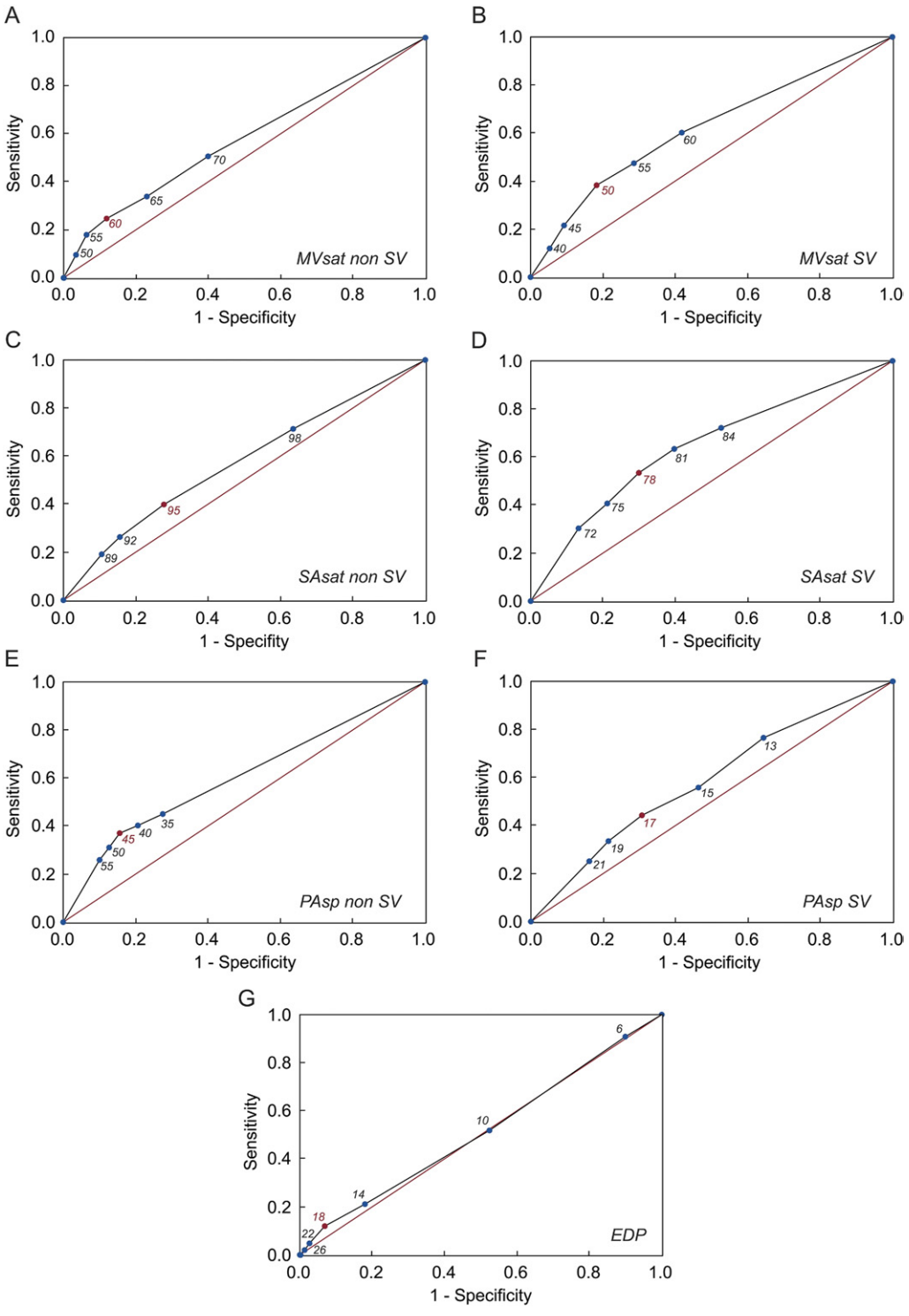

Figure 2. ROC Curves for the Final Hemodynamic Variables

Receiver-operator characteristic (ROC) curves were assessed for all the hemodynamic variables to determine threshold values with the most predictive performance. In this figure, the curves for the final variables are shown with the threshold value in **red**. **(A)** Mixed venous saturation in nonsingle-ventricle physiology (MVsat nonSV). **(B)** Mixed venous saturation in single ventricle-physiology (MVsat SV). **(C)** Systemic arterial saturation in nonsingle-ventricle physiology (SAsat nonSV). **(D)** Systemic arterial saturation in single-ventricle physiology (SAsat SV). **(E)** Pulmonary artery systolic pressure in nonsingle-ventricle physiology (PAsp nonSV). **(F)** Pulmonary artery mean pressure in single-ventricle physiology (PAmp SV). **(G)** Systemic ventricle end-diastolic pressure (EDP).

Table 5. Final Indicator of Hemodynamic Vulnerability for the Outcome High-Severity AE

AE Rates					
Hemodynamic			Any 3/4/5 AE		
Variables (n of 4)*	Sample Size	Any 3/4/5 AE (%)	OR	95% CI	p Value
0	4,212	3.0	1.0	—	—
1	1669	6.4	2.2	1.7–2.8	<0.001
≥2	1,141	8.8	3.1	2.3–4.0	<0.001

*Hemodynamic variables: EDP ≥18 mm Hg, SAsat <95% if nonSV or <78% if SV, MVsat <60% if nonSV or <50% if SV, and MPAsp ≥45 mm Hg if nonSV or MPAmp ≥17 mm Hg if SV.
OR = odds ratio; SAsat = systemic arterial saturation; other abbreviations as in Table 4.

The hope is that interventionalists will be able to use these data to improve patient care and outcomes, not just to satisfy outside agencies. For a tool to be useful, it must be able to collect data in a standardized fashion, with easily understandable terminology that will be uniformly employed by the myriad of physicians and administrators who will ultimately use the system. The data must be stringently acquired and are likely to be improved by intermittent auditing for completeness and accuracy. The tool must be generalizable to the entire population and have demonstrated reliability in multiple settings. Although similar methods were used previously to derive a risk adjustment method at Children's Hospital in Boston, it was always considered preliminary because it was derived using only a single institutional dataset (25).

Hemodynamic vulnerability indicator. Empirical data informed the development of the indicator of hemodynamic vulnerability. Based on our experience, the 4 hemodynamic risk factors incorporated in the composite indicator variables also have significant face validity. However, there are some limitations with the indicator of hemodynamic vulnerability. Because of nonlinear relationships between hemodynamic values and risk of AE, we chose to use binary rather than continuous variables that meant threshold values were required. Although based on data, we admit that the thresholds may not be an important distinction for an individual patient, for example, an

Table 6. Multivariable Models for Risk Adjusting High-Severity AE Rates

Outcome: Any Level 3/4/5 AE						
	Derivation Dataset			Validation Dataset		
All Ages*	OR	95% CI	p Value	OR	95% CI	p Value
Risk category						
2	2.4	1.6–3.6	<0.001	2.0	1.0–3.8	0.04
3	4.9	3.4–7.2	<0.001	4.9	2.7–9.0	<0.001
4	7.6	5.2–11.2	<0.001	4.8	2.5–9.2	<0.001
Hemodynamic variables, n (of 4)						
1	1.5	1.1–2.0	0.005	1.8	1.2–2.8	0.01
≥2	1.8	1.3–2.4	<0.001	2.0	1.2–3.3	0.008
Age <1 yr	1.3	1.1–1.6	0.04	1.5	1.0–2.2	0.05
Area under ROC curve	0.737			0.734		
Hosmer-Lemeshow test p value	0.74			0.20		
Age <18 yrs*						
Risk category						
2	2.1	1.4–3.2	<0.001	1.7	0.9–3.5	0.12
3	4.5	3.0–6.8	<0.001	4.6	2.4–8.9	<0.001
4	7.0	4.6–10.6	<0.001	4.4	2.2–8.9	<0.001
Hemodynamic variables, n (of 4)						
1	1.6	1.2–2.1	0.003	1.9	1.2–3.1	0.007
≥2	1.9	1.4–2.6	<0.001	1.8	1.0–2.3	0.03
Age <1 yr	1.3	1.0–1.7	0.05	1.5	1.0–2.3	0.05
Area under ROC curve	0.734			0.728		
Hosmer-Lemeshow test p value	0.52			0.10		

Sample calculation of predicted probability of a high-severity AE used in computation of expected AE rate: for a patient in risk category 2 with 1 hemodynamic risk factor and age <1 year, $\ln[p/1-p] = -4.3588 + (0.8831 \times 1) + (1.5972 \times 0) + (2.0345 \times 0) + (0.3960 \times 1) + (0.5803 \times 0) + (0.2366 \times 1) = -2.8431$, and the predicted probability of a high-severity AE is p = 0.055. *Results from generalized estimating equation models that account for the correlation among cases from the same institution were similar to those presented. Model coefficients for all ages: intercept −4.3588, risk2 0.8831, risk3 1.5972, risk4 2.0345, hemodynamic1 0.3960, hemodynamic2 0.5803, age 0.2366. Model coefficients for age <18 years: intercept −4.3034, risk2 0.7478, risk3 1.5137, risk4 1.9424, hemodynamic1 0.4409, hemodynamic2 0.6434, age 0.2380.
ROC = receiver-operator characteristic; other abbreviations as in Tables 3, 4, and 5.

Table 7. SAER for C3PO Participant Institutions

Institution	Number of Cases	Observed Event Rate	Expected Event Rate	SAER	95% CI
All ages					
A	1356	4.65	4.94	0.94	0.72–1.20
B	3,078	5.88	5.66	1.04	0.89–1.20
C	931	2.58	4.13	0.62	0.40–0.93
D	805	6.58	5.59	1.18	0.88–1.54
E	828	7.37	5.22	1.41	1.08–1.81
F	1,186	3.71	3.96	0.94	0.68–1.26
G	1,048	1.91	3.14	0.61	0.37–0.94
H	130	6.15	4.91	1.25	0.54–2.47
<18 yrs of age					
A	1,265	4.90	5.04	0.97	0.75–1.25
B	2,533	6.12	6.04	1.01	0.86–1.19
C	839	2.74	4.26	0.64	0.41–0.97
D	636	7.86	6.01	1.31	0.97–1.72
E	778	7.33	5.29	1.39	1.05–1.79
F	947	4.01	4.26	0.94	0.67–1.29
G	879	1.71	3.36	0.51	0.28–0.84
H	93	7.53	5.60	1.34	0.54–2.77

CI = confidence interval; C3PO = Congenital Cardiac Catheterization Project on Outcomes; SAER = standardized adverse event ratio.

EDP of 17 mm Hg versus 18 mm Hg. Also, because they were empirically derived, different thresholds may have been chosen in a different dataset. Another limitation pertains to the measurement of these factors. Limited hemodynamic data may be obtained in a very ill or otherwise high risk patient resulting in the inability to account for risk due to lack of measurement. But by combining multiple variables in our final composite indicator of vulnerability variable (0, 1, or 2 or more), we sought to overcome this limitation in most cases.

Institutional variation. It is important to consider the wide variation in observed AE rates by institution, ranging from 1.9% to 7.4%, and the narrower range of expected rates (3.1% to 5.7%) as supporting evidence of the need for a risk adjustment method to make equitable comparisons. Our analysis did show statistically significant variation in SAER at different institutions, even after risk adjustment, with 1 high and 2 low outliers. However, a number of factors potentially influencing the SAER must be considered before interpretation. First, one must consider the reliability of event reporting at different institutions, especially those with SAER <1.0. In the C3PO dataset, an independent record review and monitoring of a 10% sample revealed a 91% capture of high-severity events (9), but differential reporting remains a possibility. Second, and perhaps most importantly, we have not made any adjustment or consideration of efficacy as it relates to safety. Are institutions with lower than expected event rates avoiding taking on risk at the expense of completing all the objectives of the procedure? This must be considered carefully in the future as we try to understand what risk we must accept to achieve the best outcomes (26). Institutional comparisons cannot be regarded as definitive unless comparisons of both efficacy and safety are included. Alternatively, on the other extreme, does the 1 institution with lower 95% CI of 1.08 represent a performance outlier? Perhaps, but there may be unmeasured factors not accounted for, or optimized, in these models that are associated with higher event rates, but not associated with the quality of care. For example, although the models were developed using both pediatric and adult data, there may be factors unique to the adult congenital population that may be important to consider in a model for an isolated adult population, such as comorbidities not as common in the pediatric population. Despite the large size of the cohort used to derive and test our models, only 15% of the data was from adults >18 years of age. Finally, there may be differences in physician performance such as procedural duration, which was found to be independently associated with higher event rates in previous

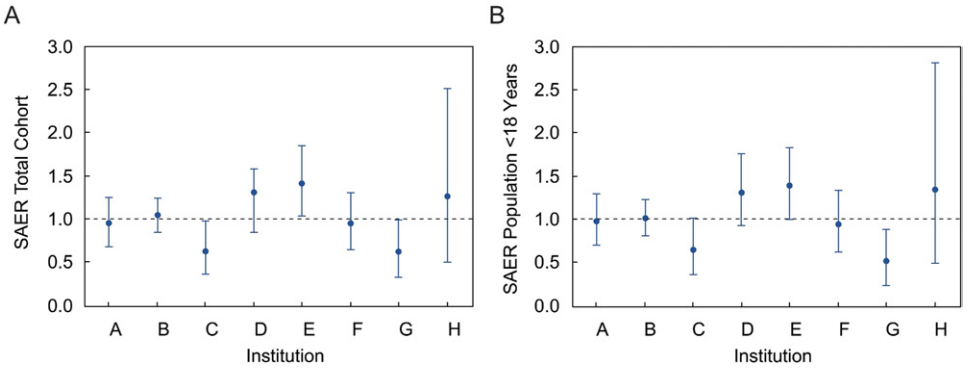

Figure 3. SAER by Institution

Standardized adverse event ratio (SAER) by institution for the entire cohort **(A)** and population <18 years of age **(B)** are shown with bars representing the 95% confidence interval for each of the 8 participating institutions. SAER were calculated by dividing the observed AE rate by the expected rate calculated by summing the predicted probabilities of the outcome, generated from the logistic regression model, for all cases performed at the institution.

work (1). At present, taking into account these issues, we believe the CHARM model can be used to make comparisons of AE rates after pediatric cardiac catheterizations and can be regarded as a preliminary way to make similar comparisons for adult congenital heart procedures. As additional data for adult congenital procedures accrues, the performance of the CHARM model can be assessed further and refined if necessary.

Conclusions

The CHARM model to adjust for case mix complexity, based on procedure type, hemodynamic features, and age allows for equitable comparisons of adverse event rates among the institutions performing catheterization for congenital heart disease.

Acknowledgments

The authors would like to recognize the study coordinators and personnel that have made this project feasible: Gary Piercey, BS; Stephanie Valcourt, BA; Anniece Woods-Brown, RN, BSN; Joanne Chisolm, RN; Sharon Hill, MSN, ACNP-BC; Terri Mclees-Palinkas, MS, CCRC; Cyndi Murphy, RN, BSN; Rebecca Raic, MSN, RN, CPNP–PC; Holly Pfreim, RN, MSN, CNP; and Janene Allen, RN, CNP.

Reprint requests and correspondence: Dr. Lisa Bergersen, Department of Cardiology, The Children's Hospital, Longwood Avenue, Boston, Massachusetts. E-mail: lisa.bergersen@cardio.chboston.org.

REFERENCES

1. 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.
2. Vitiello R, McCrindle BW, Nykanen D, Freedom RM, Benson LN. Complications associated with pediatric cardiac catheterization. J Am Coll Cardiol 1998;32:1433–40.
3. Zeevi B, Berant M, Fogelman R, Galit BM, Blieden LC. Acute complications in the current era of therapeutic cardiac catheterization for congenital heart disease. Cardiol Young 1999;9:266–72.
4. Tavli V, Kayhan B, Okur FF, Kirman M, Tekdoğan M. Complications of pediatric cardiac catheterization: 18-month study. Turk J Pediatr 2000;42:294–7.
5. Agnoletti G, Bonnet C, Boudjemline Y, et al. Complications of paediatric interventional catheterisation: an analysis of risk factors. Cardiol Young 2005;15:402–8.
6. Mehta R, Lee KJ, Chaturvedi R, Benson L. Complications of pediatric cardiac catheterization: a review in the current era. Catheter Cardiovasc Interv 2008;72:278–85.
7. Phillips BL, Cabalka AK, Hagler DJ, Bailey KR, Cetta F. Procedural complications during congenital cardiac catheterization. Congenit Heart Dis 2010;5:118–23.
8. Bergersen L, Marshall A, Gauvreau K, et al. Adverse event rates in congenital cardiac catheterization—a multi-center experience. Catheter Cardiovasc Interv 2010;75:389–400.
9. Bergersen L, Gauvreau K, Marshall A, et al. Procedure type risk groups for pediatric and congenital cardiac catheterization. Circ Cardiovasc Interv 2011;4:188–94.
10. Lemeshow S, Hosmer DW. A review of goodness of fit statistics for use in the development of logistic regression models. Am J Epidemiol 1982;115:92–106.
11. Hosmer D, Lemeshow S. Applied Logistic Regression. 2nd edition. New York, NY: John Wiley & Sons, 2000.
12. Peterson ED, Dai D, DeLong ER, et al., for the NCDR Participants. Contemporary mortality risk prediction for percutaneous coronary intervention: results from 588,398 procedures in the National Cardiovascular Data Registry. J Am Coll Cardiol 2010;55:1923–32.
13. Mavroudis C, Gevitz M, Ring WS, McIntosh CL, Schwartz M. The Society of Thoracic Surgeons National Congenital Heart Surgery Database Report: analysis of the first harvest (1994–1997). Ann Thorac Surg 1999;68:601–24.
14. Jacobs J, Maruszewski B, European Association for Cardio-Thoracic Surgery–Society of Thoracic Surgeons Joint Congenital Heart Surgery Nomenclature and Database Committee. Computerized outcomes analysis for congenital heart disease. Curr Opin Pediatr 2005;17:586–91.
15. Jenkins KJ, Gauvreau K, Newburger JW, Spray TL, Moller JH, Iezzoni LI. Consensus-based method for risk adjustment for surgery for congenital heart disease. J Thorac Cardiovasc Surg 2002;123:110–8.
16. Jenkins KJ, Gauvreau K. Center-specific differences in mortality: preliminary analyses using the Risk Adjustment in Congenital Heart Surgery (RACHS-1) method. J Thorac Cardiovasc Surg 2002;124:97–104.
17. Benavidez OJ , Gauvreau K, Del Nido P , Bacha E, Jenkins KJ. Complications and risk factors for mortality during congenital heart surgery admissions. Ann Thorac Surg 2007;84:147–55.
18. Lacour-Gayet F, Clarke D, Jacobs J, et al., for the Aristotle Committee. The Aristotle score: a complexity-adjusted method to evaluate surgical results. Eur J Cardiothorac Surg 2004;25:911–24.
19. O'Brien SM, Clarke DR, Jacobs JP, et al. An empirically based tool for analyzing mortality associated with congenital heart surgery. J Thorac Cardiovasc Surg 2009;138:1139–53.
20. Jacobs JP, Jacobs ML, Lacour-Gayet FG, et al. Stratification of complexity improves the utility and accuracy of outcomes analysis in a Multi-Institutional Congenital Heart Surgery Database: application of the Risk Adjustment in Congenital Heart Surgery (RACHS-1) and Aristotle Systems in the Society of Thoracic Surgeons (STS) Congenital Heart Surgery Database. Pediatr Cardiol 2009;30:1117–30.
21. Jenkins KJ , Beekman III RH, Bergersen LJ, 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;18:116–23.
22. Everett AD, Ringel R, Rhodes JF, et al. Development of the MAGIC congenital heart disease catheterization database for interventional outcome studies. J Interv Cardiol 2006;19:173–7.
23. Forbes TJ, Garekar S, Amin Z, et al., for the Congenital Cardiovascular Interventional Study Consortium (CCISC). Procedural results and acute complications in stenting native and recurrent coarctation of the aorta in patients over 4 years of age: a multi-institutional study. Catheter Cardiovasc Interv 2007;70:276–85.
24. Martin GR, Beekman RH, Ing FF, et al. The IMPACT Registry: IMproving Pediatric and Adult Congenital Treatments. Semin Thorac Cardiovasc Surg Pediatr Card Surg Annu 2010;13:20–5.
25. 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;3:230–40.
26. Lee TH, Torchiana DF, Lock JE. Is zero the ideal death rate? N Engl J Med 2007;357:111–3.

Key Words: cardiac catheterization ■ cardiovascular interventions ■ complications ■ heart defects congenital ■ outcome.

APPENDIX

For a list of the expert panel and participating centers, please see the online version of this paper.