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PEDIATRIC AND CONGENITAL HEART DISEASE

Original Studies

Adverse Event Rates in Congenital Cardiac Catheterization – A Multi-Center Experience

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Objectives: To describe case mix variation among institutions, and report adverse event rates in congenital cardiac catheterization by case type. Background: Reported adverse event rates for patients with congenital heart disease undergoing cardiac catheterization vary considerably, due to non-comparable standards of data inclusion, and highly variable case mix. Methods: The Congenital Cardiac Catheterization Outcomes Project (C3PO) has been capturing case characteristics and adverse events (AE) for all cardiac catheterizations performed at six pediatric institutions. Validity and completeness of data were independently audited. Results: Between 2/1/07 and 4/30/

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Conflict of interest: Lisa Bergersen is PI on for the C3PO project which receives grant support from the AHA-PRA. She is also the co-investigator for a multi-center study evaluating the safety and efficacy of Cutting Balloon® to treat resistant pulmonary artery stenosis; Boston Scientific Corporation provides monetary support for this study and devices. Kathy Jenkins is the PI for the Cutting Balloon Study and Drs Marshall and Lock are collaborators. NMT Medical, Inc. provides monetary support for Kathy Jenkins to conduct the following two studies: long term follow-up study of STARFlex® device for ASD closure and a post-marketing study for VSD closure with the STARFlex® device. Kathy Jenkins coordinates the Data Coordinating Center for the COAST study evaluating bare metal and covered stents for the treatment of coarctation; John's Hopkins Provides funds to support the study and devices are provided by NuMED, Inc. The following authors participate in the COAST trial: Lisa Bergersen, Audrey C. Marshall, James E. Lock, William E. Hellenbrand. The following authors participate in the Medtronic, Inc. Melody® transcatheter valve implantation study: William E. Hellenbrand and James E. Lock. Children's Hospital Boston owns the STARFlex® device, which it licenses to NMT Medical, Inc.; Drs Jenkins and Lock receives royalty distributions according to institutional royalty sharing agreements. John Cheatham has a grant from AGA Medical Corporation to support the development of new devices for congenital heart disease. Biomedical companies have consultant or advisory board relationships with the following authors: TOSHIBA Medical Systems Corporation (John P. Cheatham) AGA Medical Corporation (John W. Moore, Russel Hirsch, Robert H. Beekman, John P. Cheatham, and William E. Hellenbrand), W.L. Gore & Associate, Inc. (Julie A. Vincent and John P. Cheatham), Medtronic, Inc. (John P. Cheatham and William E. Hellenbrand), Pfm Medical, Inc. (John W. Moore and wife), Phillips Medical (Russel Hirsch), and KARL STORZ GmbH & Co. (Russel Hirsch). The following authors have served as an expert witness in legal proceedings regarding catheterization complications: William Hellenbrand and John W. Moore. Funding Sources: A web-based application for data entry was developed in 2006 with funding support from the Children's Heart Foundation (Chicago, IL). The application was deployed on a Microsoft Internet Information Server (IIS) 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 (2006-2010).

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08, 3855 cases (670 biopsy, 1037 diagnostic, and 2148 interventional) were recorded, median number of cases per site 480 (308 to 1526). General anesthesia was used in 70% of cases (28 to 99%), and 22% of cases (15 to 26%) were non-electively or emergently performed. Three institutions performed a higher proportion of interventions during a case, 72 to 77% compared to 56 to 58%. The median rate of AE reported per institution was 16%, ranging from 5 to 18%. For interventional cases the median rate of AE reported per institution was 19% (7 to 25%) compared to 10% for diagnostic cases (6 to 16%). The incidence of AE was significantly higher for interventional compared to diagnostic cases (20% vs 10%, p<0.001), as was the incidence of higher severity AE (9% vs 5%, p<0.001). Adverse events in biopsy cases were uncommon. Conclusions: In this multi-institutional cohort, the incidence of AE is higher among interventional compared to diagnostic cases, and is very low among biopsy cases. Equitable comparisons among institutions will require the development and application of risk adjustment methods.

Key words: CATH - diagnostic cardiac catheterization; pCOMP - complications pediatric cath/intervention; PEDS - pediatric interventions

INTRODUCTION

Institutions have reported single center experiences and described case mix characteristics in pediatric and congenital cardiac catheterization [1–7]. In addition, collaborative efforts to investigate specific procedure types, such as angioplasty and site specific device placement have been undertaken [8–11]. The participants of the Congenital Cardiac Catheterization Outcomes Project (C3PO) are committed to understanding case mix variation and developing outcome measures, which adjust for these differences in patient populations. In 2006 the C3PO collaborative group was assembled, and in early 2007 data collection began that captured data on all cardiac catheterization cases (exclusive of purely electrophysiology studies) performed at the six institutions using uniform consensus based definitions to categorize case types, procedure types and immediate outcomes, including the occurrence of adverse events. In April 2008 the first phase of the project ended, the purpose of this report is to describe the methods for data collection, validation and review, describe case mix variation among institutions, and report adverse event rates in congenital cardiac catheterization by case type.

METHODS

Participating Institutions and IRB Approval

Children's Hospital Boston is the sponsor institution for the project. Based on funding, resources, and feasibility only five sites were initially invited to participate in the project. We focused our search on practitioners with a clinical role primarily defined by interventional catheterization and associated with an academic affiliated pediatric hospital. Five institutions representing diverse national locations were invited to participate. The institutions include dedicated pediatric cardiac interventionalists with an interest in evaluating contemporary outcomes in pediatric and congenital cardiac catheterization. The participants actively involved in data collection and contribute expertise and judgement at project meetings, Appendix I. The IRB at the sponsor institution, Children's Hospital Boston, approved the project with a waiver of patient consent.* Of the five other participating institutions, IRB waiver of consent was granted at four.

Practitioner involvement at the institutions was not mandatory, however, all physicians performing procedures at the six institutions agreed to participate. An IRB approved agreement between the practitioners and the principal investigator outlined the responsibilities of the physician to record data on all cases regardless of age, gender, race, or ethnicity, or the occurrence of adverse events among cases performed by the participating catheterization physician. The principal investigator and sponsor outlined plans for preserving the confidentiality of the physician's data. The sponsor obtained a certificate of confidentiality from the NIH in 2007 to further protect the data set from involuntary

*A waiver of patient consent was requested because the project goals include identifying crucial population characteristics for the development of outcome assessment tools. The loss of individual patient data due to failure to obtain consent would have compromised the validity of conclusions regarding the population of patients undergoing cardiac catheterization. Support for this waiver was granted based on the fact that patient identification data, as defined by the Health Information Protection Act, were not stored in the database. No additional testing or studies, not including routine clinical care, were performed on the patients undergoing procedures at the participating institutions.

TABLE I. Definitions for Adverse Event Severity

	Severity level	Definition
Low	1. None	No harm, no change in condition, may have required monitoring to assess for potential change in condition with no intervention indicated.
	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 lab test.
High	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 of a serious condition, or moderate trans-catheter intervention to correct condition.
	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 trans-catheter interventions to correct condition.
	5. Catastrophic	Any death, and emergent surgery or heart lung bypass support (ECMO) to prevent death with failure to wean from bypass support.

disclosure. In accordance with the investigator agreement, all interventional cardiologists who contributed to the data set presented in this manuscript reviewed and approved the document before peer review submission.

Population

The population includes all patients who underwent cardiac catheterization at the participating institutions between February 1st 2007 and April 30th 2008. For this analysis, we included data regarding only diagnostic, interventional, or biopsy cases, and excluded less common case types recorded in the database, such as hybrid procedures and combined diagnostic/electrophysiology procedures. Data on biopsy cases were not collected at one of the six institutions.

Web-Based Data Application and Security

A web-based application for data entry was created using Microsoft Visual Studio NET programming tools. The application was deployed on a Microsoft Internet Information Server (IIS) with secure Sockets Layer (SSL) encryption to protect all of the web data transactions. Programmed data interface modules accurately transferred data from Oracle tables into SAS (Cary, NC) data sets used for analyses. Role based security controlled by institution affiliation, provider identifiers, and password protected user authentication were built into the database to prevent access to any individual institution's data by any other participating institution.

Database Entry and Content

The principal investigator visited all the sites in December 2007 before the commencement of data collection. Each site received a project manual, which included all prospective data definitions to minimize misinterpretation or misapplication of data elements. Further, a system for reliable and complete data collection was formulated based on the workflow environment specific to each of the institutions. The principal investigator, programmer, and sponsor institution maintained ongoing on-line support with response to queries in a timely manner.

Data entry occurred at the time of the catheterization procedure, and was completed by the physician performing the procedure and/or designated data entry personnel. The recorded patient and procedural information included: case type, age, weight, gender, diagnosis, comorbidities, defined or suspected genetic syndromes, baseline hemodynamic data, method of airway management, access information, hemodynamic support information, such as transfusion administration and/or ECMO or inotropic support, interventions performed, procedure time (defined as time from first vessel accessed to last sheath removed), and fluoroscopy time.

Adverse events were defined as any anticipated or unanticipated event, for which avoidable injury could have occurred, or did occur, potentially or definitely as a consequence of performing the catheterization. Events were recorded at the time of identification, either at the time case or later if determined to be related to the procedure. Information regarding the adverse event included: event name and attributability, a brief narrative description, time of identification, symptoms, and interventions. We used previously established and tested definitions for adverse event severity ranging from severity level 1–5, Table I [7]. All AE data were entered in windows based pick lists with the exception of the narrative description. The attributability of the event was classified by picking one primary event from

TABLE II. Patient and Procedural Characteristics

Patient characteristics	Diagnostic $N = 1037$ N (%) or median [IQR]	Interventional $N = 2148$ N (%) or median [IQR]	Biopsy $N = 670$ N (%) or median [IQR]
Age			
Less than 1 month	93 (9%)	210 (10%)	1 (<1%)
1–11 months	286 (28%)	453 (21%)	54 (8%)
1–10 years	314 (30%)	900 (42%)	240 (36%)
Greater than 11 years	344 (33%)	585 (27%)	375 (56%)
Weight (kg)	14 [6, 48]	14 [7, 35]	36 [15, 59]
Diagnosis			
No structural heart disease (i.e., myopathy)	103 (10%)	33 (2%)	23 (3%)
Transplanted heart	8 (1%)	33 (2%)	644 (96%)
Pulmonary hypertension	82 (8%)	27 (1%)	–
Isolated defects	130 (13%)	730 (34%)	–
Complex defect with two ventricles	426 (41%)	761 (35%)	–
Complex defect with one ventricle	287 (28%)	562 (26%)	–
Baseline hemodynamic values			
Cardiac index L/min/M2	3.3 [2.7, 4.1]	3.5 [3.0, 4.4]	3.6 [3.0, 4.4]
RV systolic pressure	50 [33, 70]	45 [28, 71]	28 [24, 33]
LV (systemic ventricle) systolic pressure	85 [73, 100]	85 [75, 100]	98 [84, 116]
Ratio RV to LV pressure	0.6 [0.3, 0.9]	0.6 [0.3, 0.9]	0.3 [0.2, 0.3]
Systemic ventricle end diastolic pressure	10 [7, 13]	10 [7, 12]	10 [8, 13]
Main pulmonary artery systolic pressure	30 [21, 45]	27 [20, 40]	25 [21, 31]
Main pulmonary artery mean pressure	19 [15, 28]	17 [14, 24]	18 [14, 22]
Mixed venous saturation	66 [56, 73]	69 [62, 75]	71 [67, 76]
Systemic arterial saturation	93 [83, 97]	95 [86, 97]	98 [96, 99]
Admission source			
Elective discharged same day as case	457 (44%)	361 (17%)	515 (77%)
Elective inpatient for observation	310 (30%)	1282 (60%)	71 (11%)
Nonelective – case added from ICU or ward	254 (24%)	442 (21%)	77 (11%)
Emergent – direct transfer	16 (2%)	62 (3%)	7 (1%)
Transferred on ECMO support	18 (2%)	28 (1%)	4 (1%)
Method of airway management			
Spontaneous respirations	383 (37%)	553 (26%)	442 (66%)
Spontaneous with assisted BMV	5 (<1%)	4 (<%)	3 (<1%)
Intubated prior to transfer to lab	145 (14%)	283 (13%)	32 (5%)
Elective intubation prior to access	479 (46%)	1262 (59%)	139 (21%)
Intubated during case for intervention	0 (0%)	7 (<1%)	0 (0%)
Intubated for failed sedation	2 (<1%)	10 (<1%)	1 (<1%)
Intubated during the case for complication	1 (<1%)	5 (<1%)	0 (0%)
Laryngeal mask	5 (<1%)	6 (<1%)	46 (7%)
Existing tracheostomy tube	16 (2%)	18 (1%)	7 (1%)
Inotropic support during the case	150 (14%)	319 (15%)	36 (5%)
Case duration (minutes)	71 [51, 96]	103 [72, 147]	30 [19, 51]
Fluoroscopy (minutes)	17 [10, 28]	31 [17, 53]	8 [4, 14]
Contrast dose (cc/kg)	2.8 [1.3, 4.8]	3.7 [2.1, 5.9]	0 [0, 0.5]
Transfusion of PRBC	75 (7%)	294 (14%)	4 (1%)

a list within domains of attributability, such as sedation related, access related, dilation related, coil related, stent related, biopsy related, or general aspects of the catheterization case.

Data Exception Reports, AE review, and Audit

The sponsor provided an exception report to a designated person at each site every month to facilitate review of missing data or data out of range requiring validation. To assure complete data capture and entry all sites received a list of cases entered in the database to check against institutional records and were required to provide confirmation of complete case capture. One site identified a short period of time, in which one physician did not enter cases; these cases were added to the database. Two sites identified duplicate entries, thus, all sites were sent lists of potential duplicates to validate.

To prevent coding variations in the primary outcome, all adverse events were reviewed for proper application of seriousness and preventability definitions by the principal investigator and designee. Any misapplication of definitions was reported to the participant and disagreements resolved.

After 15 months of data collection an independent audit of a random 10% of cases was performed at each site by the sponsor. The accuracy and completeness of data entry was assessed by comparing information recorded in the database to the medical record, including the post-catheterization period, and the next admit to the hospital when present to screen for events identified after the case. Complete case capture was confirmed for all sites including the one site, which required consent. The independent auditor recognized a misapplication of the admission source variable; 23 hr admits (overnight admissions) had been classified as outpatient, so all the sites were sent a list of outpatient procedures to review and 23 hr admits were reclassified as same day admissions. In some cases biopsy cases were classified as diagnostic, therefore, any case not coded as biopsy with the diagnosis of heart transplant required validation of correct case type. Missing data was rare but occurred in some cases on the documentation of pre case hemoglobin or the use of ultrasound modalities, such as transthoracic or transesophageal echo. All interventions when performed were recorded correctly.

Among the 386 cases audited, 78 adverse events were identified on record review. Eighty six percent of the events were recorded in the database. All seven level 4 events were captured. For severity level 3 events, two events related to sedation and airway management, laryngospasm and hypotension with induction were not recorded, the remaining 16 level 3 events, including four related to sedation were captured in the database. A 92% event capture rate was observed among High severity (level 3, 4, and 5) events. Low severity (level 1 and 2 events) had less reliable reporting with a capture rate of 81%, 43 of 53. These lower severity events included transient hypotension, metabolic acidosis, rebleed, stridor, and pulmonary edema.

Statistical Analysis

The frequency and percent or median and interquartile range were calculated for patient and procedural characteristics and summarized according to case types: (1) biopsy, (2) diagnostic without intervention, or (3) interventional cases. Adverse event rates by case type were calculated based on the occurrence of at least one AE and according to highest severity AE recorded. Chi-square analysis was used to test differences in patient and procedural distributions and AE rates among cases types. To explore variation in practice and outcomes among institutions, the relative frequency of different case types, method of airway management (conscious sedation vs anesthesia), admission source, transfusion rates, and occurrence of adverse events were calculated and are presented anonymously by participating sites.

RESULTS

Patient and Procedure Characteristics

Between February 1st 2007 and April 30th 2008, 3,855 cases met inclusion criteria and were classified as a biopsy ($n = 670$), diagnostic ($n = 1037$), or interventional case ($n = 2148$). Cases classified as hybrid, combined electrophysiology and interventional, or only line, chest tube, or pericardiocentesis, were excluded ($n = 188$). Table II summarizes patient and procedural characteristics by case type. Among the 2148 interventional cases 31% included at least one angioplasty, and/or stent placement (27%), and/or device (27%) or coil placement (18%), and/or valvotomy (13%).

The majority of patients undergoing biopsy cases (77%) and nearly half of the diagnostic cases (44%) were discharged on the same day as the case. Fifty patients were transferred on ECMO support for catheterization, 2% of the interventional population and 1% of both diagnostic and biopsy cases. Most biopsy cases (66%) were performed while spontaneously breathing, in contrast to only 26% of interventional and 37% of diagnostic cases, $p < 0.001$. Interventional cases were longer, median 103 minutes, compared to both diagnostic (71 minutes) and biopsy cases (30 minutes), $p < 0.001$. The rate of transfusion administration was twice as high in interventional cases compared to diagnostic only (14% vs 7%, $p < 0.001$).

Adverse Events

The highest incidence of any AE was observed in interventional cases, 20% compared to 10% in diagnostic cases and only 4% in biopsy cases, $p < 0.001$. Many of the events were minor or of no clinical consequence to the patient, however, high severity (moderate level 3, major level 4, or catastrophic level 5) events occurred in 9% of interventional cases, 5% of diagnostic cases, and 1% of biopsy cases ($p < 0.001$), Table III. The majority of events occurred during the case (75%), but some occurred before catheters were inserted (6%) or after catheters were removed (7%), and the remaining (12%) were identified after the procedure on the ward or after discharge. Tables IV, V, and VI list all 675 AE recorded in the database by case type, severity, and attributability.

Eleven deaths occurred in the cohort (0.29%). Seven of these patients were newborns within 24 hr of birth including five premature infants (weight between 1.4 and 2.0 Kg). Two infants with cyanotic heart disease were transferred emergently from outside hospitals and

TABLE III. Adverse Event Details by Case Type

Characteristics	Diagnostic ($n = 1037$)	Interventional ($n = 2148$)	Biopsy ($n = 670$)
Any adverse event	109 (10%)	439 (20%)	29 (4%)
Highest severity AE			
1. none	5 (<1%)	31 (1%)	5 (1%)
2. minor	57 (6%)	225 (10%)	16 (2%)
3. moderate	34 (3%)	117 (5%)	7 (1%)
4. major	10 (1%)	58 (3%)	1 (<1%)
5. catastrophic	3 (<1%)	8 (<1%)	0 (0%)
	AE in Diagnostic cases ($n = 125$)	AE in Interventional cases ($n = 519$)	AE in Biopsy Cases ($n = 31$)
Timing of AE Identification			
Prior to catheter insertion	15 (12%)	21 (4%)	4 (13%)
After catheter insertion	68 (54%)	416 (80%)	21 (68%)
After catheters removed before transfer	17 (14%)	28 (5%)	3 (10%)
In recovery room	3 (2%)	10 (2%)	1 (3%)
In ICU or ward	18 (14%)	35 (7%)	1 (3%)
After discharge	4 (3%)	9 (2%)	1 (3%)

TABLE IV. Adverse Events Summarized by Severity – Biopsy Cases

	Number of adverse events by severity level						
	1	2	3	4	5	Total	AE rate (95% CI)
Access related AE							
Systemic arterial thrombosis	–	–	1	–	–	1	
Re-bleed	–	2	–	–	–	2	
Pain post procedure	–	1	–	–	–	1	
Sedation or airway related AE							
Anesthesia problem	–	2	–	–	–	2	
CNS event seizure sedation related	–	–	1	–	–	1	
Hypotension	–	2	–	1	–	3	
Lobar collapse	–	1	–	–	–	1	
Respiratory acidosis $PaCO_2 > 45$	–	–	1	–	–	1	
General catheterization related AE							
Atrial arrhythmia	–	4	2	–	–	6	
Bradycardia (sinus)	2	1	1	–	–	4	
Ventricular arrhythmia	1	–	1	–	–	2	
Heart block resolved	1	–	1	–	–	2	
Air embolus/venous	1	–	–	–	–	1	
Imaging equipment problem	1	–	–	–	–	1	
Coronary vasospasm	–	2	–	–	–	2	
Biopsy related AE							
Potential tricuspid valve damage	–	1	–	–	–	1	
Total	**6**	**16**	**8**	**1**	**–**	**31/670**	**4.6% (3.2%, 6.5%)**

were in low output with an arterial blood gas PH of less than 7.0 on arrival. Following an uncomplicated aortic valvotomy a 6 month infant died from a retroperitoneal bleed. A very ill 10 month old lung transplant patient died while trying to palliate pulmonary vein stenosis causing pulmonary hypertension. A 12 year old patient with severe restrictive cardiomyopathy arrested in the catheterization lab after the sheaths were removed. The oldest patient was a 39 year old with pulmonary hypertension. During attempted brockenbrough procedure the sheath was advance outside the heart and she developed a pericardial effusion with resulting clinical deterioration and cardiac arrest, from which the patient could not be resuscitated.

Case Mix and Event Rate Differences by Institution

The average number of cases performed at each institution in a 3 month period ranged from 62 to 305, median 98. Excluding biopsies, interventional cases comprised between 72 and 77% of the caseload for three sites compared to 56 to 58% at the remaining sites. General anesthesia utilization was observed in a median 70% of cases, varying from 28 to 99% across institutions (Fig. 1). In 22% of cases (range 15–26%) the procedure was not previously scheduled and performed non-electively, as an add-on case from the ward or intensive care unit, or emergently transferred.

TABLE V. Adverse Events Summarized by Severity Level and Attributability – Diagnostic Cases

	Number of Adverse Events by Severity Level						
	1	2	3	4	5	Total	AE rate (95% CI)
Access related AE							
Local hematoma groin	–	7	1	–	–	8	
Pulse loss (requiring intervention)	1	15	1	–	–	17	
Re-bleed	–	2	–	–	–	2	
Bleeding with line removal	–	–	1	–	–	1	
Sheath intended for vein placed in artery	–	1	–	–	–	1	
Intramural femoral vessel stain	–	1	–	–	–	1	
Total access related	**1**	**26**	**3**	**–**	**–**	**30**	**30/1037 2.9% (2.0%, 4.1%)**
Sedation or airway related AE							
Airway obstruction	–	1	–	–	–	1	
Anesthesia problem	–	2	2	–	–	4	
Apnea	–	1	4	–	–	5	
Hypotension	–	10	1	–	–	11	
Hypoxia	–	–	1	–	–	1	
Laryngospasm	–	1	–	–	–	1	
Post extubation stridor	–	2	1	–	–	3	
Respiratory acidosis $PaCO_2 > 45$	–	2	1	–	–	3	
Unplanned extubation resulting in arrest	–	–	–	1	–	1	
Total sedation related	**0**	**19**	**10**	**1**	**–**	**30**	**30/1037 2.9% (2.0%, 4.1%)**
General catheterization related AE							
Arrhythmia							
Asystole (cardiac arrest)	–	–	–	1	3	4	
Atrial arrhythmia	–	9	8	2	–	19	
Heart block resolved	2	7	1	3	–	13	
ST-T wave changes	–	1	2	–	–	3	
Tachycardia (sinus)	–	1	–	–	–	1	
Ventricular arrhythmia	1	1	1	1	–	4	
Bleeding via ETT	1	–	–	–	–	1	
Blood stream infection	–	–	1	–	–	1	
Broken end hole balloon	–	1	–	–	–	1	
Coronary vasospasm	–	–	2	–	–	2	
Hypercyanotic spell during case	–	–	–	1	–	1	
Hypotension (intervention = ionotropes)	–	1	1	1	–	3	
Hypoxia	–	–	1	–	–	1	
Pleural effusion	–	–	1	–	–	1	
Imaging equipment problem	1	–	–	–	–	1	
Metabolic acidosis	–	1	–	–	–	1	
Renal insufficiency or failure	–	1	–	–	–	1	
Re-catheterization for suspected thrombosis	–	–	1	–	–	1	
Vessel trauma	–	2	1	–	–	3	
Vessel stain with angiography	–	1	–	–	–	1	
Medication error	–	1	1	–	–	2	
Total catheterization related	**5**	**27**	**21**	**9**	**3**	**65**	**65/10376.3% (4.9%, 7.9%)**

The median rate of AE reported by institution was 16%, ranging from 5 to 18%. For interventional cases the median rate of AE reported by institution was 19% (range 7–25%) and 10% for diagnostic cases (range 6–16%).

DISCUSSION

In data obtained prospectively in this congenital cardiac catheterization cohort, we report the incidence of adverse event rates as a multi-institutional experience rather than a single center experience. We also sought to understand the characteristics of the populations undergoing different case types, and the associated hazards. Similar to others, we observed higher AE rates among interventional cases as compared to both diagnostic or biopsy cases, with exceedingly low event rates among biopsy cases [1–7,12]. We found an overall event rate among interventional cases of 20% as compared to 10% in diagnostic cases. Further, high severity events were more common in 9% of interventional cases as compared to diagnostic cases (5%). Fortunately, death is uncommon in this series (0.29% overall), consistent with other recent reports, and is

TABLE VI. Adverse Events Summarized by Severity Level and Attributability – Interventional Cases

	Number of adverse events by severity level						
	1	2	3	4	5	Total	AE rate (95% CI)
Access related AE							
Bleeding with line removal	1	1	–	–	–	2	
Blood loss from open stop cock on sheath	–	2	2	–	–	4	
Hemothorax	–	1	3	1	–	5	
Inadvertent sheath removal	–	2	–	–	–	2	
Inadvertent arterial puncture	1	–	–	–	–	1	
Local hematoma groin	1	7	1	–	–	9	
Local hematoma IJV	–	1	–	–	–	1	
Local groin infection	–	1	–	–	–	1	
Pulse loss (requiring intervention)	–	22	–	–	–	22	
Re-bleed	1	6	–	–	–	7	
Retroperitoneal hematoma	–	–	1	–	–	1	
Sheath intended for vein placed in artery	1	–	–	–	–	1	
Systemic venous thrombosis	1	–	1	–	–	2	
Systemic artery intimal dissection	–	2	–	–	–	2	
Total access related	**6**	**45**	**8**	**1**	**–**	**60**	**60/2148 2.8% (2.1%, 3.6%)**
Sedation or airway related AE							
Airway obstruction	–	4	2	1	–	7	
Anesthesia problem	–	–	2	–	–	2	
Apnea	–	4	1	–	–	5	
Bleeding via ETT	1	2	1	–	–	4	
Esophageal hematoma	–	1	2	–	–	3	
Hypotension	–	14	1	–	–	15	
Hypoxia	–	1	–	–	–	1	
Laryngospasm	–	–	1	–	–	1	
Post extubation stridor	–	–	1	–	–	1	
Respiratory acidosis PaCO2 $>$ 45	–	4	2	–	–	6	
Respiratory distress	–	1	1	–	–	2	
Unplanned extubation	–	1	–	–	–	1	
Total sedation or airway related	**1**	**32**	**14**	**1**	**–**	**48**	**48/2148 2.2% (1.7%, 3.0%)**
General catheterization related AE							
Air embolus other	1	2	–	1	–	4	
Air embolus systemic	1	3	1	1	–	6	
Air embolus venous/PA	1	–	–	–	–	1	
Allergic reaction	–	1	1	–	–	2	
Asystole (cardiac arrest)	–	–	–	2	4	6	
Atrial arrhythmia	–	34	19	2	–	55	
Bradycardia (sinus)	–	4	7	1	–	12	
Heart block resolved	6	20	8	8	–	42	
ST-T wave changes	1	6	3	–	–	10	
Ventricular arrhythmia	1	7	1	5	–	14	
Bleeding via ETT	1	2	–	–	–	3	
Broken guide wire	–	1	–	–	–	1	
Chest pain	–	1	–	–	–	1	
CNS event stroke	–	–	–	1	–	1	
Coronary vasospasm	–	1	–	1	–	2	
Depressed cardiac output	–	1	–	–	–	1	
Fever	1	–	–	–	–	1	
Heart stain with angiography	1	–	–	–	–	1	
Heart perforation	–	2	1	1	3	7	
Hypotension (intervention = ionotropes)	–	20	9	2	–	31	
Hypotension (intervention = volume resuscitation)	–	2	–	–	–	2	
Hypoxia	–	2	–	2	–	4	
Imaging equipment problem	4	–	–	–	–	4	
Infection	–	–	1	–	–	1	
Medication error	–	1	–	–	–	1	
Metabolic acidosis	–	–	–	1	–	1	
Mental status change	–	1	–	–	–	1	

(Continued)

Table VI. Adverse Events Summarized by Severity Level and Attributability – Interventional Cases (continued)

	Number of adverse events by severity level						
	1	2	3	4	5	Total	AE rate (95% CI)
Peripheral nerve injury	–	1	–	–	–	1	
Pulmonary edema	–	2	2	–	–	4	
Pulmonary hemorrhage	–	1	–	–	–	1	
Pulmonary hypertensive crisis	–	–	1	–	–	1	
Renal insufficiency or failure	–	1	–	–	–	1	
Retroperitoneal hematoma	–	–	–	–	1	1	
Transducer problem	1	–	–	–	–	1	
Thrombosis-vessel or conduit	–	–	1	1	–	2	
Urinary catheter trauma	–	–	1	–	–	1	
Vessel trauma	1	7	3	–	–	11	
Total catheterization related	**20**	**123**	**59**	**29**	**8**	**239**	**239/2148 11.1% (9.8%, 12.5%)**
Coil related AE							
Coil embolization	–	6	–	–	–	6	
Coil malposition	1	21	3	–	–	25	
Coil trapped in catheter	2	–	–	–	–	2	
Total coil related	**3**	**27**	**3**	**–**	**–**	**33**	**33/395 8.4% (5.8%, 11.5%)**
Device related AE							
Air emboli	–	1	–	–	–	1	
Atrial arrhythmia	–	1	–	–	–	1	
Device embolization	–	1	4	2	–	7	
Device erosion	–	–	–	2	–	2	
Device malposition	–	1	2	2	–	5	
Device mechanism failure	1	–	1	–	–	2	
Heart block resolved	–	2	–	–	–	2	
Heart block not resolved	–	–	1	–	–	1	
Intracardiac thrombi resolved	–	1	–	–	–	1	
Severe tricuspid valve regurgitation	–	–	–	1	–	1	
Total device related	**1**	**7**	**8**	**7**	**–**	**23**	**23/585 3.9% (2.5%, 5.8%)**
Angioplasty related AE							
Atrial arrhythmia	–	1	–	–	–	1	
Abdominal pain	–	1	–	–	–	1	
Balloon rupture	4	2	–	–	–	6	
Bleeding via ETT	–	–	–	1	–	1	
Bradycardia (sinus)	1	–	1	–	–	2	
Circumferential balloon rupture	6	2	1	–	–	9	
Confined vascular tear	–	12	5	–	–	17	
Heart block resolved	–	1	–	–	–	1	
Hypotension	–	1	–	–	–	1	
Intravascular tear with flow obstruction	–	–	4	–	–	4	
Intravascular tear without flow obstruction	–	1	–	–	–	1	
ST-T wave changes	–	1	–	–	–	1	
Pulmonary edema	–	5	3	2	–	10	
Pulmonary hemorrhage	–	–	–	1	–	1	
Sheath damaged by balloon	2	2	–	–	–	4	
Unconfined vascular tear	–	–	1	3	–	4	
Vessel aneurysm	–	3	1	1	–	5	
Other	2	7	–	–	–	9	
Total angioplasty related	**15**	**39**	**16**	**8**	**–**	**78**	**78/662 11.8% (9.4%, 14.5%)**
Valvotomy related AE							
Aortic regurgitation	–	1	1	1	–	3	
Balloon rupture with air embolus	1	–	–	–	–	1	
Confined vascular tear	–	1	–	–	–	1	
Heart block resolved	–	2	–	–	–	2	
Mitral regurgitation	–	–	–	2	–	2	
ST-T wave changes	–	1	–	–	–	1	
Unconfined vascular tear	–	–	–	1	–	1	
Ventricular arrhythmia	–	–	1	3	–	4	
Other	–	1	–	–	–	1	

(Continued)

Table VI. Adverse Events Summarized by Severity Level and Attributability – Interventional Cases (continued)

	Number of adverse events by severity level						
	1	2	3	4	5	Total	AE rate (95% CI)
Total valvotomy related	**1**	**6**	**2**	**7**	**–**	**16**	**16/274 5.8% (3.4%, 9.3%)**
Stent related AE							
Asystole (cardiac arrest)	–	–	–	1	–	1	
Balloon rupture	1	1	–	–	–	2	
Heart block resolved	–	1	–	–	–	1	
Hypotension	–	–	1	–	–	1	
Stent compression	–	–	1	–	–	1	
Stent embolization/migration	–	1	5	2	–	8	
Stent fragment embolization	–	1	–	–	–	1	
Stent malposition	–	4	3	1	–	8	
Stent related problem	–	2	4	2	–	8	
Vessel thrombosis	–	–	–	1	–	1	
Total stent related	**1**	**10**	**14**	**7**	**–**	**32**	**32/584 5.5% (3.8%, 7.6%)**

usually associated with severe illness before starting the case [6,7].

We found that the populations of patients undergoing diagnostic and interventional cases were similar with respect to baseline characteristics such as age, comorbidities, and hemodynamic characteristics. In contrast, patients undergoing biopsy procedures were generally older and had normal hemodynamics. Further, the AE rate among biopsy cases (4%) was much lower than either diagnostic (10%) or interventional (20%) cases and serious adverse consequences were exceedingly unusual (<1%). The future development of outcome assessment methods will need to account for the much lower expected event rate in biopsy cases.

All of the participating institutions are large cardiac catheterization programs associated with a Children's Hospital, and considered a referral base for congenital heart surgical intervention. Despite these similarities, variations in patient populations and practices were evident. The data revealed two distinct catheterization lab practices, with three institutions performing a higher frequency of interventions (excluding biopsies) during a case: 72–77% compared to 56–58% at the other institutions. Further, it is unlikely that only

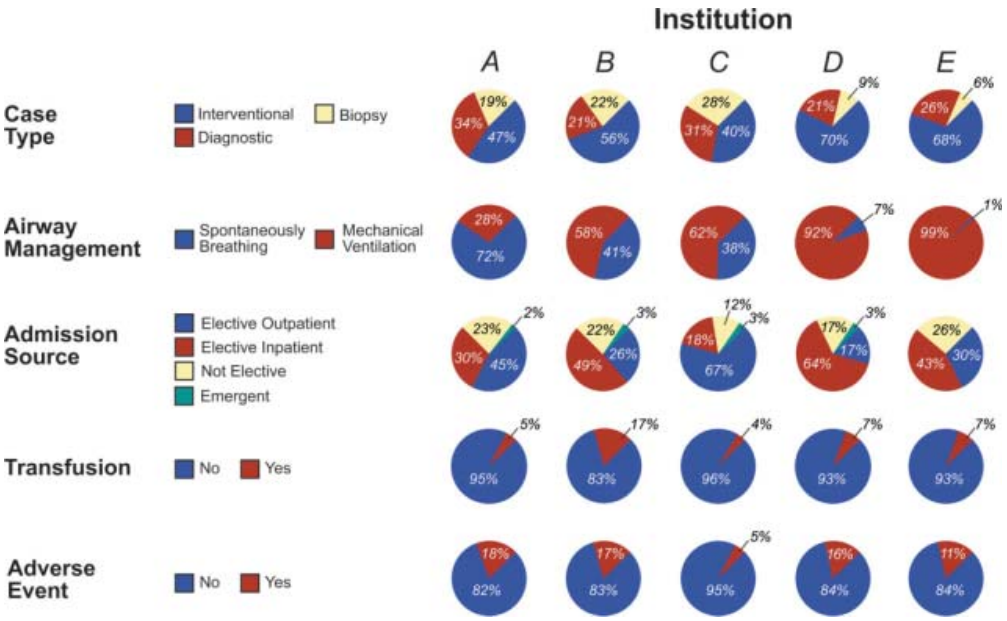

Fig. 1. Case characteristics and adverse events expressed as a percentage of the total cases performed by institution. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

differences in case mix can account for the wide variation in the use of general anesthesia from 28 to 99% of cases among the sites. Finally, the median rate of AE reported by institution was 16%, ranging from 5 to 18%. It is likely that case mix diversity affects institutional AE rates, and equitable comparisons in the future will undoubtedly require case mix adjustment methods.

Currently, C3PO participants benefit from the ability to use online report generation for internal quality assessment and event review. Participants have also been intrigued by the opportunity to review a blinded comparison of individual and institutional practices and outcomes. Nevertheless, there are weaknesses in our database, such as the requirement for manual data entry at most centers. Future efforts to collect and share data in our specialty should consider cooperation between software vendors, as well as integration and cross talk between applications to limit the burden of data entry. Finally, larger databases will likely benefit from improved programming and faster interfaces.

Participants, for the most part, have found the amount of data being collected to be reasonable and pertinent to our objectives. However, as our understanding of risk predictors and relevant outcomes becomes clearer, we may be able to streamline the collection of data elements for outcome assessment in the field of congenital cardiac catheterization. At the same time, our current methods for data collection will also need to be appropriately expanded to accommodate new procedures, and allow proper assessment of outcomes for novel techniques.

Despite site initiations and manuals of operation with database item definitions, we still experienced non random misclassification of certain data elements. These were identified in the audit and corrected, but highlight one of the difficulties in operating a multi-institutional registry and the importance of precise definitions for data collection elements. Nevertheless, capture of case characteristics and the occurrence of adverse events were strong due to the efforts of physicians and data coordinators dedicating time and a commitment to a complete, transparent, and accurate data set.

This cohort represents the cooperative effort of six institutions, and has involved the recording of patient and procedural characteristics, as well as the occurrence of adverse events using common nomenclature for case characteristics and outcomes. Important differences in institutional practices and the occurrence of adverse events are evident. As part of our commitment to outcomes assessment in congenital cardiac catheterization, we will continue to share the C3PO experience with the medical community. Currently, we are developing tools and assessing methods for risk stratification, which will allow equitable comparisons of outcomes among institutions and individual practitioners.

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APPENDIX: C3PO PARTICIPATING INTERVENTIONAL CARDIOLOGISTS AND INSTITUTIONS

Children's Hospital Boston

- Lisa Bergersen, M.D.
- Michael Landzberg, M.D.
- Peter Lang, M.D.
- James Lock, M.D.
- Audrey Marshall, M.D.
- Doff McElhinney, M.D.

Cincinnati Children's Hospital Medical Center

- Robert H. Beekman, III, M.D
- Russel Hirsch, M.D.
- Robert L. Spicer, M.D.

Morgan Stanley Children's Hospital of New York Presbyterian

- William Hellenbrand, M.D.
- Julie Vincent, M.D.
- Christine Donnelly, M.D.
- Alejandro Torres, M.D.

Nationwide Children's Hospital

- John Cheatham, M.D.
- Curt Daniels, M.D.
- Timothy Hoffman, M.D.
- Ralf Holzer, M.D.

St. Louis Children's Hospital

- David Balzer, M.D.
- Susan Foerster, M.D.
- Ramzi Nicolas, M.D.

Rady Children's Hospital — San Diego

- John Moore, M.D.
- Howaida El-Said, M.D.

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