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ORIGINAL ARTICLE

Sedation and Anesthesia in Pediatric and Congenital Cardiac Catheterization: A Prospective Multicenter Experience

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Abstract Sedation/anesthesia is critical to cardiac catheterization in the pediatric/congenital heart patient. We sought to identify current sedation/anesthesia practices, the serious adverse event rate related to airway, sedation, or anesthesia, and the rate of intra-procedural conversion from procedural sedation to the use of assisted ventilation or an artificial airway. Data from 13,611 patients who underwent catheterization at eight institutions were prospectively collected from 2007 to 2010. Ninety-four (0.69 %) serious sedation/airway-related adverse events occurred; events were more likely to occur in smaller patients (<4 kg, OR 4.4, 95 % CI 2.3–8.2, $p < 0.001$), patients with non-cardiac comorbidities (OR 1.7, 95 % CI 1.1–26, $p < 0.01$), and patients with low mixed venous oxygen saturation (OR 2.3, 95 % CI 1.4–3.6, $p < 0.001$). Nine thousand three hundred and seventy-nine (69 %) patients were initially managed with general endotracheal anesthesia, LMA, or tracheostomy, whereas 4232 (31 %) were managed with procedural sedation without an artificial airway, of which 75 (1.77 %) patients were converted to assisted ventilation/general anesthesia. Young age (<12 months, OR 5.2, 95 % CI 2.3–11.4, $p < 0.001$), higher-risk procedure (category 4, OR 10.1, 95 % CI 6.5–15.6, $p < 0.001$), and continuous pressor/inotrope requirement (OR 11.0, 95 % CI 8.6–14.0, $p < 0.001$) were independently associated with conversion. Cardiac catheterization in pediatric/congenital patients was associated with a low rate of serious sedation/airway-related adverse events. Smaller patients with non-cardiac comorbidities or low mixed venous oxygen saturation may be at higher risk. Patients under 1 year of age, undergoing high-risk procedures, or requiring continuous pressor/inotrope support may be at higher risk of requiring conversion from procedural sedation to assisted ventilation/general anesthesia.

Keywords Anesthesia · Heart defects · Congenital · Pediatrics · Catheterization · Angioplasty

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Introduction

Safe and effective sedation or anesthesia is challenging but essential to cardiac catheterization in pediatric and congenital heart disease patients [13]. Although guidelines from the American Society of Anesthesiology (ASA) and American Academy of Pediatrics (AAP) have been established for sedation of pediatric patients outside of the operating room setting [6], guidelines specific to the unique environment of the cardiac catheterization laboratory have

not been proposed. Different modes of sedation and airway management directly impact measurements of cardiopulmonary physiology and additional challenges derived from significant heterogeneity in patients and complexity of transcatheter procedures [4]. This heterogeneity has resulted in significant differences in the approach to sedation and airway management for pediatric and congenital cardiac catheterizations between and within institutions.

The purpose of this study was to use data collected prospectively from the multi-center Congenital Cardiac Catheterization Project on Outcomes (C3PO) to answer the following questions: What adverse events related to airway and sedation management occur during catheterization? What patient and procedural variables are associated with these adverse events or conversion of strategy from procedural sedation to managed airway? What are institutional practices for use of sedation versus general endotracheal anesthesia? Are there patient or procedural characteristics that favor better outcomes with anesthesia and managed airway versus natural airway?

While this dataset is limited as it was designed primarily to study catheterization-related complications, we present the first prospectively collected multicenter study of sedation-, anesthesia-, and airway-related adverse events during congenital and pediatric cardiac catheterization and patient/procedural characteristics related to these adverse events.

Methods

Data were prospectively collected as part of a multi-institutional collaborative, C3PO, in which participating centers recorded patient and procedural characteristics and the occurrence of adverse events in a web-based data entry tool. Children's Hospital Boston was the sponsor and data coordinating center for the project. Data collection started on February 1, 2007 by six centers; two more centers joined in May 2008 and July 2009. Data collection, validation, and auditing methods have previously been reported [3]. IRB approvals were obtained at each of the institutions. All interventional cardiologists who contributed cases to this database reviewed and approved the document before peer review submission.

Population, Patient, and Procedural Characteristics

Patients who underwent cardiac catheterization at the participating institutions between February 1, 2007, and June 31, 2010, were included in the study. Demographic variables recorded include age, weight, gender, non-cardiac diagnoses, genetic syndrome, cardiac diagnoses, and admission source (elective or non-elective). Procedural variables included method of airway management, case time defined by sheath insertion to removal, procedure performed, and adverse events (Supplemental Table 1A). Hemodynamic data included cardiac index, systemic ventricular end diastolic pressure, systemic arterial saturation, and pulmonary artery (PA) pressure. In addition, need for continuous supportive intravenous (IV) medications (including vasoactive and inotropic medications) and/or mechanical circulatory support including extracorporeal membrane oxygenation (ECMO) was also recorded. Indicators of hemodynamic vulnerability were developed previously by this group [4] and include low cardiac index, elevated systemic ventricle end diastolic pressure, low systemic arterial saturation, and elevated main PA systolic pressure (Supplemental Table 1B). Airway management for the procedure was recorded by the attending interventionalist as "spontaneous respirations" (natural airway with spontaneous ventilation), endotracheal intubation, laryngeal mask airway (LMA), or tracheostomy.

Sedation-, Anesthesia-, or Airway-Related Adverse Events

All adverse events [5] were recorded at the time of identification, either at the time of the procedure or later if determined to be related to the procedure. Information regarding the adverse event included: event name and attributability, a brief narrative description, when the event occurred, symptoms, and interventions. Adverse event severity was ranked according to a five-level severity scale (Supplemental Table 1A) and further grouped according to low (severity level 1—none/very mild and level 2—minor) and high (severity level 3—moderate, level 4—major, and level 5—catastrophic). Attribution of the adverse event to sedation, anesthesia, or airway was determined by the attending interventionalist during or immediately following the adverse event. Events in the database underwent independent review by two overseeing interventional cardiologists for appropriate categorization of severity level.

Statistical Analysis

Categorical variables were summarized with frequencies and percentages, and continuous variables with medians and interquartile ranges. Comparisons between groups were made using the Chi-square test for categorical variables and the Wilcoxon rank sum test for continuous variables. Adverse events are tabulated by type and severity. Logistic regression analysis was used to identify patient and procedural characteristics associated with high-severity (level 3–5) sedation- and/or airway-related adverse events and also conversion of spontaneous respirations to intubation; odds ratios and 95 % confidence intervals are presented. Multivariable models were built using forward selection among factors significant at $p < 0.1$ in univariate

analyses. A p value of <0.05 was necessary for a variable to be retained in the final model. Frequencies and percentages of sedation- and/or airway-related adverse events were calculated by institution and mode of airway management at the start of the case.

CHARM Risk Adjustment

The Congenital Heart Disease Adjustment for Risk Model (CHARM) [4] was applied to examine the risk-adjusted relationship between management via intubation and the occurrence of any high-severity adverse events using logistic regression. In addition, the coefficients of each variable in the CHARM model were used to assign point values to each risk factor (procedure type risk category, number of hemodynamic indicators, age group, see Supplemental Table 1B and C); points were summed to obtain a risk score ranging from 0 to 8 for each subject, based on the patient's risk profile. Rates of high-severity adverse events were then calculated by the presence of artificial airway and CHARM risk score.

Propensity Score Analysis

A logistic regression model with outcome variable management via intubation and risk factors consisting of all patient and procedural characteristics considered to be potentially related to this outcome was used to generate a propensity score for each subject in the study cohort. Propensity score was categorized into quintiles and used as a covariate in a logistic regression model relating the outcome any high-severity adverse event to the risk factor management via intubation.

Results

Between February 1, 2007, and June 31, 2010, 13,611 patients in the C3PO cohort underwent catheterization. During this period, 252 sedation- or airway-related adverse events were reported in 249 cases (1.83 %),[1] of which 94 (0.69 %) events were categorized as high severity (category 3–5) (Fig. 1, Supplemental Table 1A). There were nineteen (0.14 %) major (category 4—life-threatening if not treated) sedation/anesthesia- or airway-related adverse events (described below). Two (0.015 %) catastrophic (category 5—resulting in death) events occurred: One patient had sudden unexplained respiratory arrest followed by cardiopulmonary arrest after the case was completed. A second patient came to the catheterization laboratory hypoxemic and hypotensive, progressing to bradycardia, and ultimately arrested during attempted access. Both of these patients were managed with artificial airway during the procedure.

Sedation- and Anesthesia-Related Adverse Events

The most commonly reported adverse event was hypotension which occurred in 93 cases (0.68 %); sedation, anesthesia, and airway events as reported by the attending interventionalist in each case are reported in Supplemental Table 2.

In order to better understand these events, we performed detailed review of these cases and found that 70 events occurred specifically on initiation/induction of anesthesia: 66 cases were described as minor-to-moderate severity (category 1–3, data not shown in tables). These cases were managed with a combination of volume infusion and/or low-dose vasopressors or inotropes which were weaned by the end of the case. Four events, however, were considered major (category 4) and required cardiopulmonary resuscitation (CPR) and epinephrine for management, one of which required temporary ECMO until a central shunt was successfully dilated at which point ECMO was weaned.

In addition to the above cases, one event resulted in severe hemodynamic compromise after the conclusion of the case following a bolus dose of propofol while transferring the patient from the table to stretcher; the patient required CPR, transvenous pacing, and ultimately was initiated on ECMO (category 4 event). Another patient remained persistently hypotensive at the end of the case, and on transfer to the ICU required fluids, CPR, and ultimately temporary ECMO.

Airway- and Ventilation-Related Events

Forty (0.3 %) primary airway and 65 (0.5 %) ventilation adverse events occurred (Supplemental Table 2). Specific post-extubation hypoxia, hypoventilation, or other airway obstruction was the primary adverse event in 20 cases, six of which were category 4 events, requiring CPR, bag mask ventilation, and/or re-intubation. Difficult intubation resulted in four clinically significant adverse events, with one category 4 event requiring temporary use of a laryngeal mask airway (LMA), CPR, and vasopressors. In addition, seven unplanned extubations occurred; one developed into a major adverse event (category 4) as the patient became hemodynamically unstable prior to recognition of dislodgement of the endotracheal tube (ETT) and required transient CPR and vasopressors. Four clinically significant occurrences of right mainstem bronchus intubation were reported; one patient became hypotensive and bradycardic (category 4 adverse event), requiring epinephrine, CPR,

[1] Three cases had two adverse events each such that 252 events occurred in 249 cases. To avoid double-counting, 249 events were used for subsequent statistics.

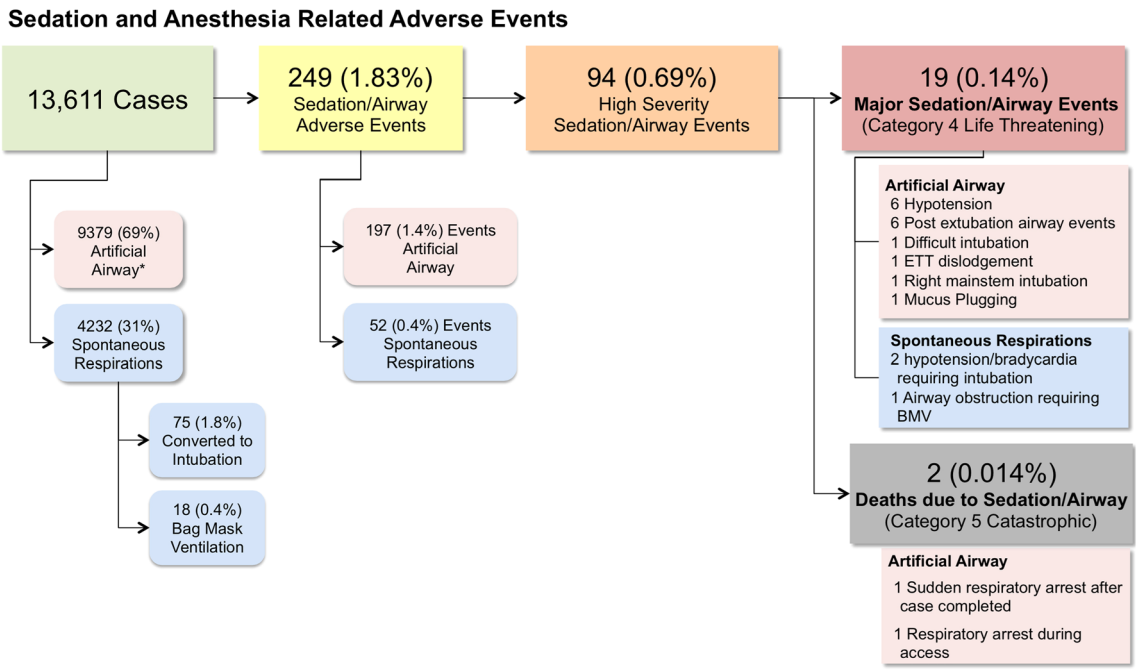

Fig. 1 Sedation-, anesthesia-, and airway-related events. Data from 13,611 cases were prospectively collected, and adverse events are delineated by severity and association with airway management strategy

and then ECMO. Finally, one event was related to severe mucus plugging at the end of the case under general anesthesia which became hemodynamically significant, requiring transient CPR with rapid stabilization following adequate pulmonary toilet.

Predictors of High-Severity Sedation, Anesthesia, and Airway Adverse Events

The role of patient and procedural characteristics in high-severity sedation- and airway-related adverse events (category 3, 4, and 5) was evaluated using univariate and multivariable analysis (Table 1). In the multivariable model, low patient weight (weight <4 kg, OR 4.4, 95 % CI 2.3–8.2; weight 4–19 kg, OR 2.1, 95 % CI 1.3–3.6), presence of a non-cardiac comorbidity (OR 1.7, 95 % CI 1.1–2.6), and low mixed venous oxygen saturation (single ventricle <50 % or two ventricles <60 %, OR 2.3, 95 % CI 1.4–3.6) were independent predictors of high-severity sedation- and airway-related adverse events.

Differences in Airway and Anesthesia Practice Between Institutions

Nine thousand three hundred and seventy-nine patients were managed by endotracheal intubation, laryngeal mask airway, or other artificial airway (e.g., tracheostomy), whereas 4232 patients were managed with a natural airway with spontaneous ventilation during cardiac catheterization (Table 2). Institutional preference for airway and sedation management was highly variable. Institutions B, C, D, E, F, and G showed a preference for airway management by intubation, LMA, or other artificial airway: institutions D and G with 10:1 preference and E with nearly 100:1 preference for management by artificial airway (Fig. 2). Only institutions A and H demonstrated preference for spontaneous respirations/natural airway with 58 and 70 % of cases starting with a natural airway, respectively.

Specific data regarding provider expertise (e.g., cath laboratory nurse or pediatric cardiac anesthesiologist) or how sedation/anesthesia strategy was chosen were not collected prospectively as part of C3PO, and we were not able to acquire meaningful retrospective data by survey of C3PO institutions. Instead, an informal survey of *current* practice demonstrated that procedural sedation versus general anesthesia strategy is decided by the attending interventionalist at five institutions and by anesthesia staff at three institutions, highlighting an additional source of heterogeneity. At all eight institutions, a pediatric cardiac anesthesiologist is responsible for administration of general anesthesia for these patients; however, general anesthesiologists also provide services for patients at two of these institutions. Finally, procedural sedation is administered predominantly by an attending anesthesiologist at half the institutions, certified nurse anesthetist (CRNA) at two

Table 1 Predictors of high-severity sedation- and/or airway-related adverse events and multivariable analysis

	Number	Univariate analysis		Multivariable analysis	
		N (%)	Odds ratio (95 % CI)	Odds ratio (95 % CI)	*p* value
High-severity sedation- and/or airway-related adverse events					
Age					
<1 month	890	12 (1.4 %)	2.9 (1.2, 6.6)		
≥1, <12 months	2467	32 (1.3 %)	2.8 (1.3, 5.6)		
1–9 years	5212	34 (0.7 %)	1.4 (0.7, 2.8)		
10–17 years	2939	6 (0.2 %)	0.4 (0.2, 1.2)		
≥18 years	2103	10 (0.5 %)	1.0		
Weight (kg)					
<4	1161	22 (1.9 %)	5.7 (3.1, 10.4)	4.4 (2.3, 8.2)	<0.001
4–9	2944	28 (1.0 %)	2.8 (1.6, 5.0)	2.1 (1.3, 3.6)	0.005
10–19	3267	23 (0.7 %)	2.1 (1.2, 3.8)		
≥20	6234	21 (0.3 %)	1.0	1.0	–
Gender					
Male	7189	48 (0.7 %)	1.0		
Female	6422	46 (0.7 %)	1.1 (0.7, 1.6)		
Diagnosis					
Isolated defect or structurally normal	6891	29 (0.4 %)	1.0		
Complex defect with 2 V physiology	4103	40 (1.0 %)	2.3 (1.4, 3.8)		
Complex defect with 1 V physiology	2614	25 (1.0 %)	2.3 (1.3, 3.9)		
Genetic syndrome					
Yes	1655	19 (1.2 %)	1.8 (1.1, 3.0)		
No	11,945	75 (0.6 %)	1.0		
Non-cardiac problem					
Yes	3707	37 (1.0 %)	1.7 (1.1, 2.6)	1.7 (1.1, 2.6)	0.01
No	9868	57 (0.6 %)	1.0	1.0	–
Surgery within 30 days of cath					
Yes	809	9 (1.1 %)	1.7 (0.8, 3.4)		
No	12,802	85 (0.7 %)	1.0		
Admission source					
Elective outpatient	10,943	50 (0.5 %)	1.0		
Non-elective	2426	39 (1.6 %)	3.6 (2.3, 5.4)		
Emergent or add-on ICU	241	4 (1.7 %)	3.7 (1.3, 10.3)		
Hemodynamic indicators of vulnerability					
MV (<60 2 V or <50 single V)					
Yes	1784	31 (1.7 %)	3.3 (2.1, 5.1)	2.3 (1.4, 3.6)	<0.001
No	11,827	63 (0.5 %)	1.0	1.0	–
Systemic ventricle end diastolic pressure ≥18					
Yes	699	6 (0.9 %)	1.3 (0.6, 2.9)		
No	12,912	88 (0.7 %)	1.0		
Systemic arterial saturation (<95 2 V or <78 single V)					
Yes	3538	42 (1.2 %)	2.3 (1.5, 3.5)		
No	10,073	52 (0.5 %)	1.0		
Main pulmonary artery pressure (≥45 2 V or ≥17 single V)					
Yes	1953	21 (1.1 %)	1.7 (1.0, 2.7)		
No	10,120	66 (0.7 %)	1.0		

Table 1 continued

	Number	Univariate analysis		Multivariable analysis	
		N (%)	Odds ratio (95 % CI)	Odds ratio (95 % CI)	*p* value
Number of hemodynamic indicators					
0	7311	34 (0.5 %)	1.0		
1	2812	21 (0.8 %)	1.6 (0.9, 2.8)		
2+	1950	32 (1.6 %)	3.6 (2.2, 5.8)		
Not entered	1538	7 (0.5 %)	1.0 (0.4, 2.2)		
Case type					
Diagnostic	3596	28 (0.8 %)	2.8 (1.3, 5.9)		
Interventional	6802	57 (0.8 %)	3.0 (1.5, 6.1)		
Biopsy	3213	9 (0.3 %)	1.0		
Procedure type risk category					
1	5603	21 (0.4 %)	1.0		
2	3835	26 (0.7 %)	1.8 (1.0, 3.2)		
3	2442	26 (1.1 %)	2.9 (1.6, 5.1)		
4	1362	18 (1.3 %)	3.6 (1.9, 6.7)		
Not assigned	369	3 (0.8 %)	2.2 (0.6, 7.3)		
Continuous pressor or inotrope support					
Yes	1520	35 (2.3 %)	4.8 (3.1, 7.3)		
No	11,986	59 (0.5 %)	1.0		
Case duration (h)					
<1	4850	20 (0.4 %)	1.0		
1–1.9	5539	44 (0.8 %)	1.9 (1.1, 3.3)		
2–2.9	2193	17 (0.8 %)	1.9 (1.0, 3.6)		
≥3	991	13 (1.3 %)	3.2 (1.6, 6.5)		
Contrast dose (cc/Kg)	–	–	1.1 (1.0, 1.2)		

institutions, and nurse with interventionalist at two institutions.

Spontaneous Respirations and Conversion to Intubation

Of the 4232 cases conducted with spontaneous respirations, however, 75 (1.8 %) required conversion to intubation (Fig. 1). Patients who were converted to intubation had a higher rate of all high-severity adverse events during cardiac catheterization (27 vs. 2 %, $p < 0.001$). While the majority of sedation- and airway-related adverse events related to conversion to intubation were clinically minor, two patients had major adverse events (category 4) and became bradycardic, requiring CPR, vasopressors, and intubation due to hemodynamic instability. In addition to the cases requiring intubation, 18 additional cases initially managed with spontaneous respirations required bag mask ventilation (BMV) or noninvasive positive pressure ventilation; one case experienced a major adverse event (category 4) due to hypoxia and bradycardia requiring BMV, CPR, but stabilized without further intervention.

Multivariable analysis demonstrated that younger patients (e.g., age 1–11 months, OR 5.2, 95 % CI 2.3–11.4), patients undergoing high-risk procedures (category 3, OR 5.0, 95 % CI 3.1–8.2; category 4, OR 10.1, 95 % CI 6.5–15.6), and patients who required inotropic support during the case (OR 11.0, 95 % CI 8.6–14.0) were likely to require conversion to intubation (Table 3). Other patient characteristics such as weight, non-cardiac diagnosis, genetic syndrome, and hemodynamic indicators of vulnerability were not associated with an increased likelihood of conversion to intubation after adjusting for these factors.

Effect of Choice of Sedation and Airway Management

In order to determine whether choice of sedation and airway management had an effect on all high-severity adverse events (sedation/airway-related and non-sedation/airway-related), we compared outcomes in patients who underwent procedures with spontaneous respirations/natural airway management versus patients with artificial airway. Patients who underwent procedures with spontaneous airway

Table 2 Choice of airway management strategy: patient and procedural characteristics for cases managed by spontaneous respiration versus artificial airway

	Spontaneous respirations ($n = 4232$) *N* (%) or median [IQR]	Intubation, LMA, tracheostomy ($n = 9379$) *N* (%) or median [IQR]	*p* value
Patient characteristics			
Age			<0.001
<1 month	82 (2 %)	808 (9 %)	
≥1, <12 months	344 (8 %)	2123 (23 %)	
1–9 years	1171 (28 %)	4041 (43 %)	
10–17 years	1394 (33 %)	1545 (16 %)	
≥18 years	1241 (29 %)	862 (9 %)	
Weight (kg)			<0.001
<4	99 (2 %)	1062 (11 %)	
4–9	453 (11 %)	2491 (27 %)	
10–19	682 (16 %)	2585 (28 %)	
≥20	2995 (71 %)	3239 (35 %)	
Not entered	3	2	
Gender			0.37
Male	2211 (52 %)	4978 (53 %)	
Female	2021 (48 %)	4401 (47 %)	
Diagnosis ($n = 4230,9378$)			<0.001
Isolated defect or structurally normal	2795 (66 %)	4096 (44 %)	
Complex defect with 2 V physiology	885 (21 %)	3218 (34 %)	
Complex defect with 1 V physiology	550 (13 %)	2064 (22 %)	
Genetic syndrome ($n = 4230,9370$)	308 (7 %)	1347 (14 %)	<0.001
Non-cardiac problem ($n = 4220,9355$)	1019 (24 %)	2688 (29 %)	<0.001
Surgery within 30 days of cath	133 (3 %)	676 (7 %)	<0.001
Admission source ($n = 4231,9379$)			<0.001
Elective outpatient	3827 (90 %)	7116 (76 %)	
Non-elective	395 (9 %)	2031 (22 %)	
Emergent	9 (<1 %)	232 (2 %)	
Hemodynamic indicators of vulnerability			
MVO2 saturation (<60 % 2 V or <50 % 1 V)	353 (8 %)	1431 (15 %)	<0.001
Systemic ventricle end diastolic pressure ≥18	262 (6 %)	437 (5 %)	<0.001
Systemic arterial saturation (<95 % 2 V or <78 % 1 V)	848 (20 %)	2690 (29 %)	<0.001
Main pulmonary artery pressure (≥45 mmHg 2 V or ≥17 mmHg 1 V) ($n = 3652, 8421$)	473 (13 %)	1480 (18 %)	<0.001
Number of hemodynamic indicators			<0.001
0	2462 (58 %)	4849 (52 %)	
1	776 (18 %)	2036 (22 %)	
2+	414 (10 %)	1536 (16 %)	
Not entered	580 (14 %)	958 (10 %)	
Procedure characteristics			
Case type			<0.001
Diagnostic	1098 (26 %)	2498 (27 %)	
Interventional	1499 (35 %)	5303 (57 %)	
Biopsy	1635 (39 %)	1578 (17 %)	
Procedure type risk category			<0.001
1	2547 (60 %)	3056 (33 %)	
2	929 (22 %)	2906 (31 %)	

Table 2 continued

	Spontaneous respirations ($n = 4232$) *N* (%) or median [IQR]	Intubation, LMA, tracheostomy ($n = 9379$) *N* (%) or median [IQR]	*p* value
3	495 (12 %)	1947 (21 %)	
4	173 (4 %)	1189 (13 %)	
Not assigned	88 (2 %)	281 (3 %)	
Continuous pressor or inotrope support ($n = 4212,9294$)	121 (3 %)	1399 (15 %)	<0.001
Case duration (h) ($n = 4216,9357$)			<0.001
<1	2067 (49 %)	2783 (30 %)	
1–1.9	1527 (36 %)	4012 (43 %)	
2–2.9	453 (11 %)	1740 (19 %)	
≥3	169 (4 %)	822 (9 %)	
Contrast dose (cc/Kg) ($n = 4227, 9371$)	1.07 [0, 2.81]	3.13 [1.05, 5.21]	<0.001
Any adverse event	354 (8 %)	1352 (14 %)	<0.001
Any high-severity adverse event	100 (2 %)	578 (6 %)	<0.001
Any sedation/airway-related adverse event	52 (1 %)	197 (2 %)	<0.001
Any high-severity sedation/airway-related adverse event	21 (<1 %)	73 (1 %)	0.07
Institution			<0.001
A	1127 (27 %)	817 (9 %)	
B	1711 (40 %)	2751 (29 %)	
C	410 (10 %)	928 (10 %)	
D	95 (2 %)	1101 (12 %)	
E	10 (<1 %)	1156 (12 %)	
F	545 (13 %)	1308 (14 %)	
G	134 (3 %)	1231 (13 %)	
H	200 (5 %)	87 (1 %)	

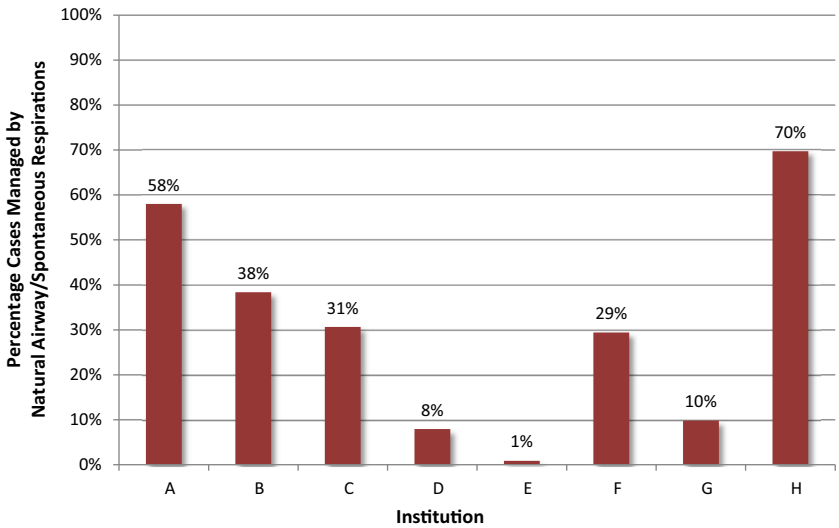

Fig. 2 Percentage of pediatric and congenital cardiac catheterization cases initially managed by spontaneous respirations (rather than artificial airway) by institution

management had fewer high-severity adverse events (100 events, 2 %) than patients who were managed with artificial airway (578 events, 6 %).

We could not, however, rule out the presence of confounders (higher complexity patients and procedures) associated with use of artificial airway strategy. Therefore, using factors that compose the CHARM model [4]: age, hemodynamic vulnerability (Supplemental Table 1B), and procedural complexity (Supplemental Table 1C), we developed a risk score to adjust for these factors and

Table 3 Multivariable analysis of factors related to conversion of spontaneous respirations to intubation

	Odds ratio	95 % CI	*p* value
Age			
<1 month	3.0	(1.9, 4.9)	<0.001
≥1, <12 months	5.2	(2.3, 11.4)	<0.001
1–9 years	2.6	(0.9, 6.8)	0.06
10–17 years	1.8	(1.1, 3.0)	0.01
≥18 years	1.0	–	
Procedure type risk category			
1	1.0	–	
2	1.6	(1.1, 2.2)	0.005
3	5.0	(3.1, 8.2)	<0.001
4	10.1	(6.5, 15.6)	<0.001
Not assigned	6.7	(3.3, 13.2)	<0.001
Continuous pressor or inotrope support			
Yes	11.0	(8.6, 14.0)	<0.001
No/not reported	1.0	–	

Table 4 Stratified analysis by CHARM score for high-severity adverse events (category 3, 4, 5) in cases managed with spontaneous respiration versus artificial airway

Risk predictor		CHARM score
(a) CHARM score definition		
Procedure type risk category	1	0 point
	2	2 points
	3	4 points
	4	5 points
Number of hemodynamic indicators	0	0 point
	1	1 point
	2+	2 points
Age (years)	≥1	0 point
	<1	1 point

	Rate of high-severity adverse events		
CHARM score	Total (%)	Spontaneous respiration (%)	Artificial airway (%)
(b) Stratified analysis by CHARM score			
0–1	1.3	0.8	1.7
2–3	3.3	1.7	4.0
4–5	7.1	5.6	7.4
6	10.5	7.2	11.1
7–8	14.9	10.1	15.4

Rate of high-severity adverse events by airway management strategy

performed a stratified analysis by risk quantiles; this demonstrated that even in similar CHARM risk strata, there were a greater number of events in patients who underwent management by artificial airway (Table 4). Further, in multivariable analysis adjusting for the variables included in the CHARM risk adjustment model, use of artificial airway remained a predictor for high-severity adverse events (Supplemental Table 3).

Similarly, we performed propensity-stratified analysis (Supplemental Table 4) to adjust for confounders associated with patient assignment to artificial airway, and artificial airway was associated with a higher odds ratio for serious adverse events compared to spontaneous respirations. In contrast, more than half of the procedures performed under spontaneous respirations were low-risk procedures performed in low-risk patients (CHARM score of 0 or 1) with a very low rate of events (1.5 % with spontaneous respirations, 1.4 % with artificial airway, Table 5). Consequently, high-severity adverse event rates were low in low-risk patients undergoing catheterization using a strategy of spontaneous respirations with the caveat of the above predictors of conversion to intubation. Furthermore, high-risk patients and procedures were associated with higher adverse event rates, irrespective of airway management strategy chosen.

Discussion

Sedation, anesthesia, and airway management are essential, but underexamined components of congenital and pediatric cardiac catheterization and interventions. We report the first large-scale, multicenter study investigating the effects of sedation, general anesthesia, and airway management on outcomes during congenital and pediatric catheterization. High-severity sedation-, anesthesia-, and airway-related adverse events were infrequent (0.69 %), with a very low mortality rate (0.015 %), in the context of overall mortality rate of 0.28 % in pediatric and congenital catheterization [11]. Independent predictors for high-severity sedation- and airway-related adverse events included low patient weight, presence of a non-cardiac comorbidity, and low mixed venous oxygen saturation. Choice of procedural airway management (spontaneous respirations vs. artificial airway) was heterogeneous between institutions, with one institution favoring artificial airway by nearly 100:1. Overall, spontaneous respirations were selected as an initial airway management strategy in approximately one-third of the cases; however, a small fraction of these cases required conversion to intubation (1.8 %) during the case. Younger patients, those requiring inotropic support or undergoing high-risk procedures, were more likely to undergo conversion to intubation. Finally, use of spontaneous respiration as an airway management strategy in low-risk procedures in low-risk patients was safe and effective with a very low risk of events, whereas high-risk patients undergoing high-risk procedures were at risk of high-severity

Table 5 Low-risk procedures and rate of high-severity events by airway management strategy

		Total		Spontaneous respirations		Artificial airway	
	Case type	Cases	Adverse events (%)	Cases	Adverse events (%)	Cases	Adverse events (%)
(a) Adverse events for CHARM score 0 (Procedure risk = 1, Hemodynamic indicator = 0, Age ≥ 1 year)							
CHARM score 0	Biopsy	2363	24 (1.0 %)	1202	10 (0.8 %)	1161	14 (1.2 %)
	Diagnostic	1100	16 (1.5 %)	394	1 (0.3 %)	706	15 (2.1 %)
	Interventional	73	3 (4.1 %)	14	0 (0.0 %)	59	3 (5.1 %)
	Total	3536	43 (1.2 %)	1610	11 (0.7 %)	1926	32 (1.7 %)
		Total		Spontaneous respirations		Artificial airway	
	Case type	Cases	Adverse events (%)	Cases	Adverse events (%)	Cases	Adverse events (%)
(b) Adverse events for CHARM score 1 (Procedure risk = 1, Hemodynamic indicator = 1, Age ≥ 1 year)							
CHARM score 1	Biopsy	333	2 (0.6 %)	185	1 (0.5 %)	148	1 (0.7 %)
	Diagnostic	541	10 (1.9 %)	215	5 (2.3 %)	326	5 (1.5 %)
	Interventional	27	1 (3.7 %)	6	0 (0.0 %)	21	1 (4.8 %)
	Total	901	13 (1.4 %)	406	6 (1.5 %)	495	7 (1.4 %)

events irrespective of airway management strategy. In summary, this study has identified factors to consider when tailoring airway and sedation strategies for cardiac catheterization in congenital and pediatric patients.

By nature, however, this study has specific limitations as the C3PO collaborative was designed by interventional cardiologists with the intent to study patient and procedural risk during specific cardiac catheterization and intervention procedures rather than specific details of airway, sedation, and anesthesia strategies. As such, we are unable to address questions regarding the effects of specific sedation and anesthetic agents, the role of specific expertise of the practitioner administering anesthesia (e.g., cardiac anesthesia, general anesthesia, CRNA, cath laboratory nurse, or interventional cardiologist), the utility of pre-procedural American Society of Anesthesiology and Mallampati classification, the degree of sedation required for successful case completion, and patient awareness and comfort/discomfort. While we attempted to examine some of these specific questions by surveying C3PO members, the retrospective nature of the data precluded meaningful analysis, and these issues will be important to study in future studies. Despite these limitations, this study is an important first step toward answering these complex and critical questions with a number of key findings.

Choice of Sedation and Airway Management

Choice of procedural sedation with spontaneous respiration versus general anesthesia and managed airway was heavily institution dependent and extremely heterogeneous across institutions, in part related to the availability of anesthesia support based on an informal survey of participating centers. This finding further emphasized the need for data-driven guidance for sedation and airway management strategies. To this end, one of the major objectives of this study was to determine the risk of adverse events associated with strategy of procedural sedation with spontaneous respiration versus general anesthesia and managed airway. In comparing strategies, we employed CHARM [4] as a method to normalize risk in order to control for confounding factors associated with choice of airway management (i.e., "sicker patients" undergoing higher-risk procedures may be assigned artificial airway); however, artificial airway remained an independent predictor of high-severity adverse events and had a higher odds ratio for adverse events when compared with the same risk strata of patients managed by spontaneous respirations, findings further confirmed by propensity analyses. This higher rate of serious adverse events associated with artificial airway must be interpreted with caution, however, as we cannot exclude the possibility of unmeasured patient and procedural confounding characteristics or factors not accounted for by CHARM or propensity analysis.

Furthermore, a subset of patients managed initially with spontaneous respirations and procedural sedation required conversion to intubation and had a significantly higher rate of overall serious adverse events. Indeed, a few patients had hemodynamic compromise requiring CPR prior to stabilization. Similarly, additional patients required BMV or positive pressure for ventilation with at least one patient who became hemodynamically unstable as a result of the airway issue. Findings suggest that procedural sedation should be used with caution in younger patients, those requiring (or likely to require) continuous pressor and/or inotrope support (in this context, we interpreted the need for inotropic support as an additional surrogate for tenuous hemodynamic status) or those undergoing a high-risk procedure. In addition, the significance of specific anesthesia

staff supporting procedural sedation in these cases will be an important area of future study. In contrast, the "typical cohort" of low-risk patients undergoing low-risk procedures had a very low rate of events when managed by spontaneous respirations, suggesting that anesthesia resources may be conserved in these procedures.

Taken together, while natural airway with spontaneous respirations can be safe in low-risk patients undergoing low-risk procedures, younger patients with evidence of hemodynamic vulnerabilities (and potentially requiring inotropic support) undergoing high-risk procedures are at higher risk of serious adverse events irrespective of airway and sedation strategies. In this study, these higher-risk patients/procedures were more likely to have been managed with artificial airway and general anesthesia. Lastly, adult patients made up 15 % of the study population, and as such additional studies are required to further define the risk of airway and anesthesia strategies during cardiac catheterization in adults with congenital heart disease especially in the context of coronary disease, renal failure, and diabetes. Indeed, a number of studies have advocated the use of procedural sedation in procedures as complex as transcatheter aortic valve implantation [7] and carotid endarterectomy [10] in adult patients.

Sedation- and Anesthesia-Related Adverse Events During Cardiac Catheterization

One of the most common sedation- and anesthesia-related adverse events reported was hypotension associated with anesthesia (0.68 %), but the majority of these events were low risk, self-resolved, without durable consequences. Patients with congenital heart disease, however, frequently have exquisitely sensitive hemodynamics [13, 14]. Patients with shunt or duct-dependent circulation are vulnerable to fluctuations in systemic and pulmonary vascular resistance with narcotics or inhaled anesthetics, and positive pressure ventilation can be detrimental in single-ventricle physiology dependent on passive pulmonary circulation [15, 17, 18]. As such, prior efforts have been made to quantify the hemodynamic effects of anesthetics [1, 16, 19], anxiolytics [9], and analgesics [8]. Fentanyl/midazolam combination induced a decrease in mean arterial pressure (MAP 10 mmHg). Halothane, removed from the US market, induced significant depression of ejection fraction (EF, mean decrease 13 %) as well as MAP (mean decrease of 28 mmHg) [16]. Newer agents were associated with less hemodynamic depression: Sevoflurane was associated with mean decrease in EF 10 % and MAP 9 mmHg and isoflurane with no change in EF and 19 mmHg in MAP. As such, the use of anesthetic, analgesic, and anxiolytic agents during procedural sedation or general anesthesia requires a continuous risk-benefit analysis before, during, and after the procedure. While adjunctive monitoring techniques such as bispectral index and near-infrared spectroscopy seem intuitively appealing to this end, use at C3PO institutions was widely heterogeneous (data not shown), and additional studies are required to define their utility in cardiac catheterization of congenital and pediatric patients [2, 12].

Airway-Related Adverse Events

Sedation or anesthesia also requires vigilant monitoring of airway and ventilation, and while rare, airway-related events were morbid. First, right mainstem intubation resulting in an overt adverse event occurred in only four cases; this low rate of adverse events is likely a result of the unique advantage of continuous fluoroscopy in the cath laboratory. Indeed, a consistent and systematic protocol of endotracheal tube evaluation under fluoroscopy should eliminate future events. Similarly, while unplanned extubation was rare, even these events may be prevented by vigilant and systematic examination under fluoroscopy; in at least one case, hemodynamic compromise resulted from delayed recognition of extubation. Third, difficult airway was reported as an adverse event in four cases, two of which required assistance by otolaryngology consultants due to anatomic abnormalities and a third requiring fiberoptic bronchoscopy. While no catastrophic events occurred, adjunctive techniques such as fiberoptic intubation could be routinely considered during intubation of high-risk patients. Fourth, post-extubation hypoventilation or airway obstruction was reported in 20 cases, and while some patients were managed with stimulation or bronchodilator therapy, others required re-intubation and observation. Finally, a number of cases reported airway obstruction during the case in the form of upper or distal airway obstruction and/or mucus plugging, during spontaneous respiration as well as artificial airway cases. In sum, airway and pulmonary risks are a critical component in pre-procedural evaluation and risk stratification prior to cardiac catheterization, especially in the decision for management by procedural sedation versus general endotracheal anesthesia.

Limitations

As described above, our study is subject to a number of inherent limitations. In addition, present analyses were performed in data that were prospectively acquired but retrospectively analyzed. As such, comparison of artificial airway versus spontaneous respiration strategy must be considered in light of potential unmeasured confounders as discussed above. Second, an important limitation was our inability to distinguish levels of sedation, such that patients managed with spontaneous respirations were considered to

have received "procedural sedation," irrespective of the specific sedation strategy. Similarly, patients managed with artificial airway were analyzed as "general anesthesia," such that subjects treated with a large spectrum of agents ranging from narcotics, propofol, and benzodiazepines to paralytics and inhaled agents and dexmedetomidine and varying depths of sedation were all considered as a homogeneous group for analysis, likely degrading our ability to evaluate the role of depth of anesthesia/sedation and the specific safety issues related to specific sedation/anesthesia strategy. Likewise, we acknowledge that the distinction between procedural sedation and general anesthesia with managed airway can often be very minimal, even with shared agents. Third, our data rely on self-reporting, and adverse events may be underreported. As well, we had no data regarding under-sedation and patient discomfort or awareness and how this may impact serious adverse events or successful completion of a case. Fourth, conclusions regarding predictors for conversion to intubation may be influenced by the individual operator's threshold and comfort level for continuing the procedure without mechanical ventilation. Likewise, the cognitive ability of the patient to comprehend and cooperate with catheterization using procedural sedation was not evaluated or taken into account. In summary, these results highlight the limitations of a study designed by interventional cardiologists, focused on capturing procedure-related adverse events, which may not be the best approach to evaluate sedation/anesthesia outcomes in the cath laboratory; however, present findings provide important pathophysiological data for the design of future prospective studies to address the role of these in the cardiac catheterization laboratory [13].

Conclusions

This study is the first to examine sedation/anesthesia- and airway-related adverse events in a large multicenter group of cardiac catheterization of pediatric and congenital heart patients and the effects of airway management strategy on high-severity adverse events. Pre-procedural risk stratification of patients and procedures may aid in the decision toward airway management, conserving anesthesia resources, and may potentially decrease the risk of anesthesia-related and non-anesthesia-related adverse events during cardiac catheterization. Conversely, high-risk patients undergoing procedures which may require conversion to intubation may be identified in advance and airway strategy amended accordingly. Additional studies are required to examine the impact of different sedation/airway strategies on cardiopulmonary physiology measured at catheterization which are critical to guiding medical, transcatheter, and surgical decisions and examine the role of specialized anesthesia care (i.e., cardiac anesthesia) in high-risk patients and high-risk procedures, patient cognitive maturity, and post-procedural anesthesia/analgesia management. Furthermore, future efforts will require multidisciplinary effort to create such a multicenter dataset to inform with evidence based on well-thought out outcome measures.

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