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Low Weight as an Independent Risk Factor for Adverse Events During Cardiac Catheterization of Infants

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Background: Studies have documented the importance of procedure type and hemodynamic variables on the incidence of procedure related adverse events (AE) after cardiac catheterization. However, little is known about the impact of low weight on the incidence and severity of AE. Methods: Data were prospectively collected using a multicenter registry (C3PO). Infants <1 year were divided into four weight categories: <2 kg, 2–3 kg, 3–5 kg, ≥5 kg. AE severity was classified as level 1–5 (none, minor, moderate, major, death). Results: Eight centers submitted details on 3,679 cases (34% diagnostic) performed in infants <1 year from 2/07 to 6/10: <2 kg: 57 (1.5%), 2–3 kg: 403 (11%), 3–5 kg: 1,527 (41.5%), ≥5 kg: 1,692 (46%). AE occurred in 20% of cases (<2 kg: 28%, 2–3 kg: 25%, 3–5 kg: 23%, ≥5 kg: 16%) with 41% of all AE being level 3–5 AE. Death occurred more frequently in the <2 kg group (12%), 71% of which were interventional cases. The case-related mortality in all other weight groups was <1%. By multivariable analysis, weight <2 kg, 2–3 kg, and 3–5 kg were independent risk factors for high severity (level 3–5) AE (<2 kg: OR 2, 95%CI 1.1–3.6; 2–3 kg: OR 1.4, 95%CI 1–1.8; 3–5 kg: OR 1.3, 95%CI 1.1–1.5), with similar findings for all AE. Blood transfusions were more common in lower weight categories (<2 kg: 42%, 2–3 kg: 29%, 3–5 kg: 25%, ≥5 kg: 15%, p<0.001). Conclusions: The risk of AE during cardiac catheterization of infants increases with lower weight. Infants who weigh less than 2 kg have a significantly higher risk of adverse events (most notably death) even after correcting for hemodynamic vulnerability and procedure type risk group. © 2013 Wiley Periodicals, Inc.

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

INTRODUCTION

Advances in perinatal medicine have led to dramatic improvements in survival among low weight infants [1]. This has resulted in increasing numbers of low and often very low weight infants with complex congenital heart disease requiring therapy. Historically, cardiac catheterizations performed in low weight infants were reported to be associated with increased mortality and vascular compromise [2]. However, significant progress has been made with regards to miniaturization of catheterization laboratory equipment, and more recent data suggest that procedural success and complications may be similar to procedures performed in larger infants [3].

Interpreting these data is difficult without adjusting for procedure and patient-specific risk factors. Bergersen *et al*. recently reported on the "Catheterization for Congenital Heart Disease Adjustment for Risk Method" (CHARM) [4], which includes procedure type risk group (diagnostic and therapeutic) [5], age less than 1 year, and hemodynamic vulnerability criteria to risk adjust and facilitate comparison of adverse event rates between operators and institutions. Young age (<1 year) was found to be a risk factor for adverse events, both as an independent component of CHARM (age < 1 year) [4], as well as being integral to procedure type

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Additional Supporting Information may be found in the online version of this article.

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risk categories [5], where diagnostic catheterization, as well as balloon aortic or pulmonary valvuloplasty within the first month of life had higher associated risks when compared with the same procedure performed in older infants. However, it is unclear whether low weight infants experience a risk above and beyond that adjusted for infants 1 year of age or lower and, if so, which low weight groups may be at particularly increased risk. This study presents the largest experience of low weight infants undergoing cardiac catheterization.

SPECIFIC AIMS AND OBJECTIVES

The overall objective of this study was to evaluate the effect of low patient weight on procedural outcome.

Primary Aim

1. To evaluate the effect of patient weight on incidence of (risk adjusted) adverse events in infants undergoing cardiac catheterization

Secondary Aims

2. For infants undergoing cardiac catheterization (and differentiated by weight groups):
   a. To describe case and patient characteristics
   b. To describe types and severity level of adverse events

METHODS

Data were prospectively collected by the "Congenital Cardiac Catheterization Outcomes Project" (C3PO), a multicenter registry with eight participating pediatric cardiac catheterization programs. Details pertaining to registry design, data submission and completeness have been reported by Bergersen and colleagues [6]. All physicians participating in the C3PO registry reviewed and approved the content of this manuscript.

Inclusion and Exclusion Criteria

All cases in the registry performed in infants below one year of age between 02/2007 and 06/2010 were eligible for inclusion. Cases were not eligible if the weight was not recorded.

Data Collected

Patient and procedural characteristics reported in this study included the procedure(s) performed, baseline hemodynamic data, case duration, fluoroscopy time, contrast volume, blood transfusion, vascular access routes, the occurrence of an adverse event, presence of a genetic abnormality diagnostic category, and basic case types (e.g., diagnostic, interventional, Hybrid). Hybrid cases were defined as procedures where both the interventional cardiologist and cardiothoracic surgeon both participated in the same procedure at the same time and setting. In addition, the procedural component performed by the interventional cardiologist in the hybrid case had to be facilitated by the cardiothoracic surgeon and/or vice versa. C3PO captured data on any adverse event occurring during the procedure, or later, if determined to be related to the procedure. C3PO was not designed as a longitudinal registry and as such does not include long-term outcome data. Adverse events included not only direct procedure related adverse events, such as technical adverse events, arrhythmias, vascular trauma, or cardiac trauma, but also sedation, anesthesia, or airway related adverse events and other adverse events. Each adverse event was assigned a severity category from 1–5 (none, minor, moderate, major, catastrophic), as defined in the International Pediatric Congenital Cardiology Code nomenclature [7] (Supplemental table S1). All level 3–5 adverse events were defined as high severity adverse events (HSAE). All AE were independently reviewed in a non-blinded fashion by two interventional cardiologists for appropriate and consistent application of seriousness and preventability criteria and where necessary adjusted.

To facilitate risk adjustment, parameters that have previously been identified within the "catheterization for congenital heart disease adjustment for risk method (CHARM)" [4] were included in the data collection. These variables were procedure type risk group [5], as well as hemodynamic vulnerability score [4]. According to CHARM, all patients in this study were by definition within the higher risk category of age below one year. The hemodynamic vulnerability score was calculated based on the number of hemodynamic risk factors present (0, 1, or >=2), as described in the CHARM method, which included threshold values for SVEDP, PA pressures, systemic arterial oxygen saturations and mixed venous saturations [4].

Statistical Analysis

To define weight groups, unadjusted adverse event rates for any as well as higher severity (level 3–5) AE were examined for predefined weight categories. Initially, weight categories were chosen with a very fine granularity (200 g increments). Weight categories with similar adverse event rates were then combined, leading to weight groups of <2 kg, 2–3 kg, 3–5 kg, and ≥ 5 kg which were used in the analysis (Table 1). Patient and case characteristics were summarized for all cases, and were stratified by weight groups. Median,

TABLE I. Unadjusted Adverse Event Rates by Different Weight Groups

		Any AE		Any Level 3/4/5 AE	
	n	Number	Percent	Number	Percent
Total < 1 Year	3679	736	20.0%	329	8.9%
< 1.8 kg	36	9	25.0%	5	13.9%
≥ 1.8 kg, < 2.0 kg	21	7	33.3%	6	28.6%
≥ 2.0 kg, < 2.2 kg	36	8	22.2%	4	11.1%
≥ 2.2 kg, < 2.4 kg	48	10	20.8%	5	10.4%
≥ 2.4 kg, < 2.6 kg	83	24	28.9%	11	13.3%
≥ 2.6 kg, < 2.8 kg	108	28	25.9%	12	11.1%
≥ 2.8 kg, < 3.0 kg	128	31	24.2%	17	13.3%
≥ 3.0 kg, < 4.0 kg	918	217	23.6%	101	11.0%
≥ 4.0 kg, < 5.0 kg	609	128	21.0%	59	9.7%
≥ 5.0 kg, < 6.0 kg	612	106	17.3%	46	7.5%
≥ 6.0 kg, < 7.0 kg	505	89	17.6%	31	6.1%
≥ 7.0 kg, < 8.0 kg	269	33	12.3%	14	5.2%
≥ 8.0 kg, < 9.0 kg	183	30	16.4%	10	5.5%
≥ 9.0 kg, <10.0 kg	68	8	11.8%	3	4.4%
≥ 10.0 kg	55	8	14.5%	5	9.1%
< 2.0 kg	57	16	28.1%	11	19.3%
≥ 2.0 kg, < 3.0 kg	403	101	25.1%	49	12.2%
≥ 3.0 kg, < 5.0 kg	1,527	345	22.6%	160	10.5%
≥ 5.0 kg	1,692	274	16.2%	109	6.4%

range, and interquartile range were calculated for all continuous variables and frequency with percentages for categorical variables. Patient and case characteristics were compared among the different weight groups using the Kruskal-Wallis test for continuous variables and the Fisher's exact test for categorical variables. Weight group, presence of a genetic abnormality, procedure type risk group, and hemodynamic vulnerability were assessed in univariate logistic regression analysis for a relationship with any AE as well as any high severity AE. All predictors with $p<0.05$ by the likelihood ratio test were retained in the final multivariable models. Odds ratios (OR) and 95% confidence intervals were provided. SAS 9.2 was used for statistical calculations.

RESULTS

Demographic, Clinical, and Procedural Data

Case and demographic data are listed in Table 2. The study cohort included 3,679 cases performed in infants less than 1 year of age. The weight was documented for all cases and therefore no case was excluded from analysis. Within the study cohort 57 (1.5%) of patients had a weight below 2 kg, 403 (11%) had a weight between 2 and 3 kg, 1527 (41.5%) had a weight between 3 and 5 kg, while 1,692 (46%) had a weight equal to or greater than 5 kg. The weight distribution is displayed in Fig. 1. Three cases were performed in patients <1 kg, 12 between 1 and 1.5 kg, and 42 between 1.5 and 2 kg.

Only 420 (11%) of cases were performed in infants breathing spontaneously, with the proportion being highest in larger patients (<2 kg: 2%, 2–3 kg: 5%, 3–5 kg: 9%, ≥5 kg: 15%, $P < 0.001$) (Table 2). Inotropic support at the start of the procedure was required in 891 (24%) of infants, more commonly in patients below 5 kg (<2 kg: 33%, 2–3 kg: 37%, 3–5 kg: 33%, ≥5 kg: 14%, $P < 0.001$). One third of cases were performed in infants with single ventricle physiology. The incidence of blood transfusions was highest for patients with a weight below 2 kg (<2 kg: 42%, 2–3 kg: 29%, 3–5 kg: 25%, ≥5 kg: 15%, $P < 0.001$).

Case Types and Interventions Performed

Patients with a weight below 2 kg had a lower proportion of purely diagnostic cases, a higher incidence of Hybrid cases, and a higher incidence of isolated balloon atrial septostomy ($P < 0.001$, Supporting Information Table S2). There was also a significant difference in the relative frequency of specific interventions that were performed ($P < 0.001$, Supporting Information Table S3). Creating, maintaining, or enlarging an atrial septal defect accounted for just 2% in the ≥5 kg group, but as much as 21% in the <2 kg group, and 25% in the 2–3 kg group. Valvuloplasty, both aortic and pulmonary, accounted for a higher percentage of the interventions performed in smaller patients. In contrast, occlusion of a PDA was performed in only a single patient below 3 kg, but accounted for 6% of interventions performed in infants ≥5 kg.

Vascular Access

The most common sheath sizes used for arterial and venous vascular access (excluding monitoring lines)

TABLE II. Case Characteristics

	Total <1 year (n = 3,679) N (%) or median [IQR] (range)	<2.0 kg (n = 57) N (%) or median [IQR] (range)	≥2.0, <3.0 kg (n = 403) N (%) or median [IQR] (range)	≥3.0, <5.0 kg (n = 1,527) N (%) or median [IQR] (range)	≥5.0 kg (n = 1,692) N (%) or median [IQR] (range)	P value
Weight (kg)	4.7 [3.4, 6.2] (0.7–19.7)	1.6 [1.4, 1.8] (0.7–1.9)	2.6 [2.4, 2.8] (2.0–2.9)	3.7 [3.3, 4.3] (3.0–4.9)	6.4 [5.6, 7.5] (5.0–19.7)	<0.001
Spontaneous Respiration (n=57, 403, 1527, 1691)	420 (11)	1 (2)	22 (5)	139 (9)	258 (15)	<0.001
Inotropic Support at Start (n=57, 397, 1512, 1673)	891 (24)	19 (33)	146 (37)	492 (33)	234 (14)	<0.001
Diagnostic Category						
Isolated lesions	636 (17)	12 (21)	52 (13)	269 (18)	303 (18)	<0.001
Complex 2V	1460 (40)	27 (47)	185 (46)	612 (40)	636 (38)	
Single V	1207 (33)	13 (23)	145 (36)	503 (33)	546 (32)	
Other	375 (10)	5 (9)	20 (5)	143 (9)	207 (12)	
Case Duration (min) (n = 54, 395, 1,482, 1,637)	82 [56, 117] (10–524)	48 [25, 80] (16–185)	73 [46, 104] (10–282)	82 [55, 114] (10–390)	87 [61, 124] (11–524)	<0.001
Case Duration						
<1 hr	1000 (28)	33 (61)	146 (37)	431 (29)	390 (24)	<0.001
1–1.9 hr	1718 (48)	16 (30)	175 (44)	721 (49)	806 (49)	
2–2.9 hr	599 (17)	3 (5)	58 (15)	235 (16)	303 (18)	
≥3 hr	251 (7)	2 (4)	16 (4)	95 (6)	138 (8)	
Fluoroscopy Time (min) (n = 57, 400, 1,519, 1,688)	22 [12, 37] (0–204)	15 [7, 25] (1–136)	20 [11, 33] (0–162)	22 [12, 38] (0–204)	22 [12, 38] (0–165)	<0.001
Contrast Dose (ml/kg) (n = 57, 401, 1,526, 1,692)	4.3 [2.6, 6.2] (0–18.4)	3.6 [1.7, 5.1] (0–15.6)	4.4 [2.6, 6.6] (0–16.1)	4.3 [2.6, 6.3] (0–16.9)	4.3 [2.6, 6.0] (0–18.4)	0.04
Transfusion (n = 57, 395, 1,513, 1,668)	765 (21)	24 (42)	116 (29)	372 (25)	253 (15)	<0.001

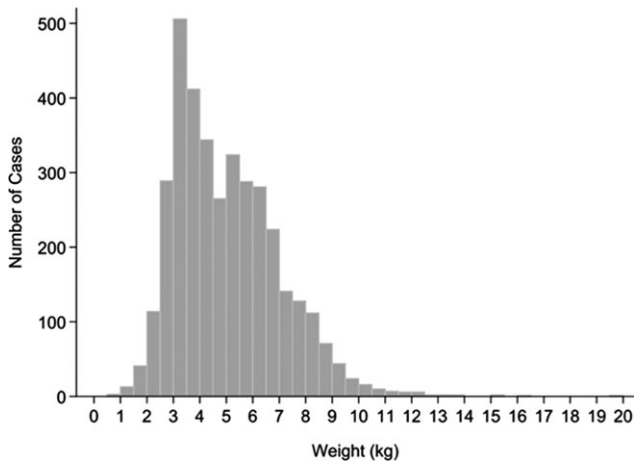

Fig. 1. Weight distribution of infants (< 1 year) undergoing cardiac catheterization.

are shown in Supporting Information Table 4. Arterial access was less commonly used in smaller patients (<2 kg: 35%, 2–3 kg: 57%, 3–5 kg: 69%, ≥5 kg: 79%, $P < 0.001$). In those patients who required placement of an arterial sheath, a 3Fr sheath size was used in 60% in the <2 kg group, 62% in the 2–3 kg group, 46% in the 3–5 kg group, and 18% in the ≥5 kg group ($P < 0.001$). The maximum arterial sheath size used was 4Fr for the <2 kg group, and 6Fr or larger for all other weight groups. The maximum venous sheath size used was 7Fr for the <2 kg and 2–3 kg group, and 8Fr or greater for larger patients.

Procedural Risk Assessment

There was a significant difference in distribution of procedure type risk groups between the four weight groups ($P < 0.001$) (Supporting Information Table S5). Lower procedure type risk groups accounted for a significantly higher percentage of cases in the 3–5 kg and ≥5 kg groups, when compared with the <2 kg and 2–3 kg groups (Fig. 2).

There was also a significant difference in hemodynamic vulnerability between weight groups ($P = 0.004$)(Supporting Information Table S5). Where documented, two or more parameters of hemodynamic vulnerability were present in 13% for the <2 kg group, 28% for the 2–3 kg group, 34% for the 3–5 kg group, and 33% for the ≥5 kg group (Fig. 3). This difference between weight groups was similar to differences in the number of patients with low mixed venous saturations, as well as increased pulmonary artery pressures.

Adverse Events

There were a total of 849 adverse events, 346 (41%) of which were high severity adverse events (Table 3).

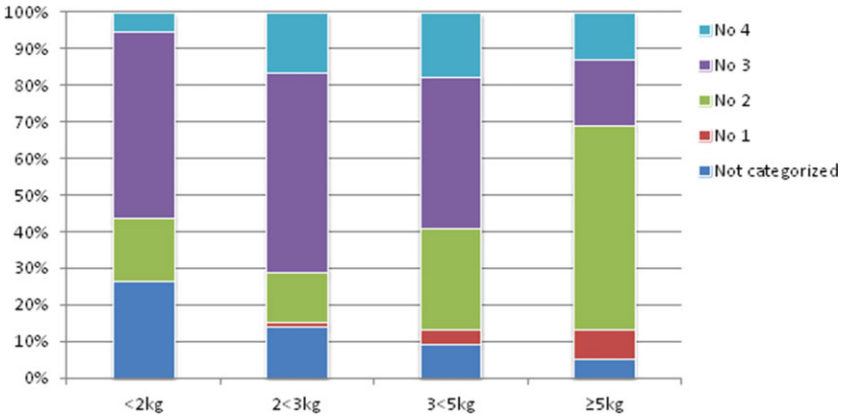

Fig. 2. Procedure type risk groups for different weight groups.

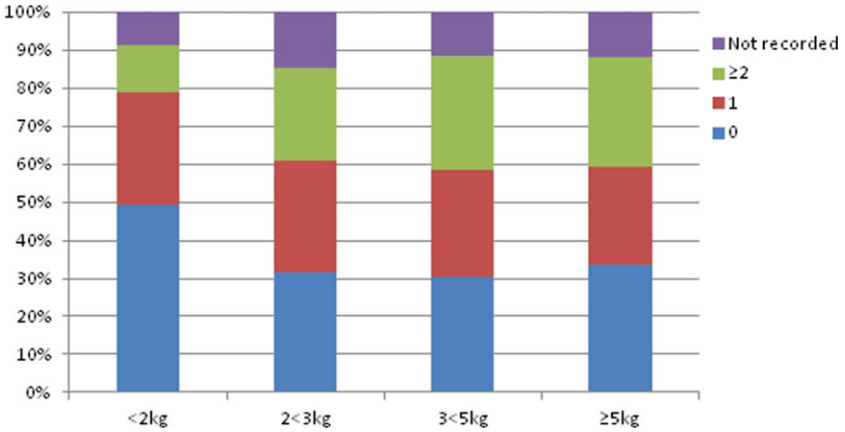

Fig. 3. Hemodynamic vulnerability for different weight groups.

TABLE III. Total Adverse Events by Severity

	Total <1 year (n = 849) N (%)	<2.0 kg (n = 22) N (%)	≥2.0, <3.0 kg (n = 119) N (%)	≥3.0, <5.0 kg (n = 399) N (%)	≥5.0 kg (n = 309) N (%)	P Value
Severity						<0.001
1 – None	75 (9)	1 (5)	14 (12)	31 (8)	29 (9)	
2 – Minor	428 (50)	9 (41)	54 (45)	201 (50)	164 (53)	
3 – Moderate	226 (27)	3 (14)	33 (28)	119 (30)	71 (23)	
4 – Major	99 (12)	2 (9)	15 (13)	42 (11)	40 (13)	
5 – Catastrophic	21 (2)	7 (32)	3 (3)	6 (2)	5 (2)	

Figure 4 demonstrates adverse events by highest severity adverse event per case for the four different weight groups. There was a significant difference in the highest severity level adverse events between weight groups ($P < 0.001$), with level 5 adverse events (death) occurring in 12% of cases <2 kg, while all other weight groups had incidences of level 5 adverse events of less than 1%. (Supporting Information Table S6).

Overall, the most common type of adverse event seen were arrhythmias (28%) and hemodynamic adverse events (19%) (Supporting Information Table S7). There was no statistically significant difference in the distribution of types of advents between the four weight groups.

Level 5 Adverse Events

In total, 21 level 5 (catastrophic) adverse events were encountered, with the <2 kg group having the highest incidence of these events, occurring in 7/57 (12%) of cases. Causes of death in the <2 kg group were cardiac perforation (n = 3), as well as

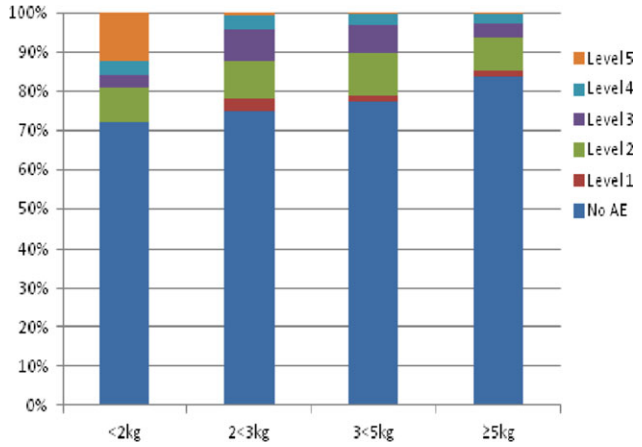

Fig. 4. Adverse events by highest severity adverse event per patient for different weight groups.

hypotension, bradycardia, and heart block leading to cardiac arrest ($n = 4$). The underlying diagnostic category was single ventricle in 5/7 (71%) patients, and complex 2–ventricle anatomy in 2/7 (19%) patients. All patients in this group who died were on inotropic support on arrival to the cardiac catheterization laboratory. Furthermore, three of these seven patients arrived in the cardiac catheterization laboratory in critical condition with pH values less than 7.0 and were noted to be "critically ill on arrival." Two of the deaths occurred in patients undergoing hemodynamic catheterization, while four deaths occurred in single ventricle patients with intact atrial septum who were undergoing attempted emergent atrial decompression—three of these four patients had cardiac perforation during these attempts, while one patient was found technically not to be suitable for atrial decompression. One patient with single ventricle died after a failed transcatheter attempt of PDA stent placement to facilitate right to left shunting via the PDA that was converted to a Hybrid approach via median sternotomy.

Three deaths occurred in patients with a weight between $2 < 3$ kg (0.7%). One patient with complex 2–ventricle anatomy died from cardiac perforation during attempts at atrial septoplasty. Another patient was severely hypoxic while recannalizing an obstructed BT shunt and subsequently died from an intracranial bleed. A third patient was profoundly cyanotic during a diagnostic catheterization and eventually arrested, requiring ECMO support but never recovered. All three patients were on inotropic support at the start of the procedure.

Eleven patients with a weight equal to or above 3 kg died (0.3%), out of which 4 had single ventricle physiology, while 7 had complex 2-ventricle anatomy. Diagnostic catheterization was performed in 1 patient, while interventions were performed in 10 patients. The interventions performed were attempts at rehabilitating an occluded or severely stenotic shunt or previously stented PDA ($n = 3$), angioplasty of the aorta ($n = 2$), attempts at opening an intact atrial septum ($n = 2$), and one each for pulmonary artery rehabilitation, pulmonary vein rehabilitation, and PDA coil occlusion (which resulted in coil embolization to the superior mesenteric artery). The type of adverse events included cardiac perforation during atrial septostomy attempts in the face of an intact atrial septum ($n = 2$), severe gut ischemia as a result of coil embolization to a mesenteric vessel ($n = 1$), retroperitoneal hematoma ($n = 1$), severe hypoxia while attempting to open an occluded or severely stenosed BT shunt ($n = 2$), a devastating neurological event after carotid cutdown to treat middle aortic syndrome ($n = 1$), and hypotension, bradycardia, and heart block leading to cardiac arrest ($n = 4$). Death occurred in 3/3 (100%) of patients in the <2 kg group who underwent either RF or needle perforation of an atrial septum, compared to 3/132 (2%) in all other weight groups combined.

Predictors of Adverse Events

By univariate analysis, procedure type risk group 3 or 4, weights below 5 kg, as well as 1 or more parameter of hemodynamic vulnerability were associated with a significantly higher incidence of any adverse event, while presence of a genetic syndrome did not appear to have any significant impact (Table 4A). In risk-adjusted multivariate analysis independent risk factors for any adverse event were procedure type risk group 3 or 4, one or more parameters of hemodynamic vulnerability, as well as weight below 5 kg. Similar results were also found for high severity (level 3–5) adverse events in the univariate and multivariate analysis, applying to procedure type risk group 3 or 4), one or more parameters of hemodynamic vulnerability, as well as weight below 5 kg (Table 4B).

Institutional Variations

Among the eight participating institutions, the <2 kg group accounted for 1% (1–3%) of the overall institutional case volume, the 2–3 kg group accounted for 11% (6–15%), the 3–5 kg group accounted for 41.5% (34–48%), and the ≥5 kg group for 46% (41–49%) of the infant cardiac catheterization case volume (Supporting Information Table S 8). Due to the small number of cases in the <2 kg and 2–3 kg categories per center, more detailed analysis and comparison of adverse events between institutions was not feasible.

TABLE IV. (A) Risk Factors for Any Adverse Event in Patients < 1 Year of Age; (B) Risk Factors for Level 3/4/5 Adverse Event in Patients < 1 Year of Age

	Total procedures *N*	Procedures with any AE (A) /3/4/5 AE (B) *N* (%)	Univariate analysis		Multivariable analysis	
			Odds ratio (95% CI)	*P* value	Odds ratio (95% CI)	*P* value
A						
Weight						
≥ 5.0 kg	1692	274 (16%)	1	–	1	–
≥ 3.0, < 5.0 kg	1527	345 (23%)	1.51 (1.27, 1.80)	<0.001	1.26 (1.05, 1.52)	0.02
≥ 2.0, < 3.0 kg	403	101 (25%)	1.73 (1.34, 2.24)	<0.001	1.37 (1.04, 1.80)	0.03
< 2.0 kg	57	16 (28%)	2.02 (1.12, 3.65)	0.02	1.97 (1.07, 3.63)	0.03
Genetic Syndrome					–	–
Yes	526	113 (21%)	1.11 (0.89, 1.39)	0.37		
No	3148	623 (20%)	1	–		
Procedure Type Risk Group						
1	201	21 (10%)	1	–	1	–
2	1429	207 (14%)	1.45 (0.90, 2.34)	0.12	1.33 (0.83, 2.15)	0.24
3	1186	293 (25%)	2.81 (1.76, 4.50)	<0.001	2.36 (1.46, 3.81)	<0.001
4	560	173 (31%)	3.83 (2.36, 6.23)	<0.001	3.24 (1.98, 5.31)	<0.001
Not categorized	303	42 (14%)	1.38 (0.79, 2.41)	0.26	1.29 (0.73, 2.27)	0.38
Hemodynamic Vulnerability						
0	1191	183 (15%)	1.0	–	1.0	–
1	991	202 (20%)	1.41 (1.13, 1.76)	0.002	1.31 (1.04, 1.65)	0.02
2+	1052	246 (23%)	1.68 (1.36, 2.08)	<0.001	1.56 (1.25, 1.95)	<0.001
Not recorded	445	105 (24%)	1.70 (1.30, 2.23)	<0.001	1.62 (1.23, 2.13)	<0.001
B						
Weight						
≥ 5.0 kg	1692	109 (6%)	1.0	–	1.0	–
≥ 3.0, < 5.0 kg	1527	160 (10%)	1.70 (1.32, 2.19)	<0.001	1.35 (1.04, 1.77)	0.03
≥ 2.0, < 3.0 kg	403	49 (12%)	2.01 (1.41, 2.87)	<0.001	1.47 (1.01, 2.14)	0.04
< 2.0 kg	57	11 (19%)	3.47 (1.75, 6.90)	<0.001	3.03 (1.49, 6.14)	0.002
Genetic Syndrome					–	–.
Yes	526	49 (9%)	1.05 (0.77, 1.45)	0.75		
No	3148	280 (9%)	1.0	–		
Procedure Type Risk Group						
1	201	6 (3%)	1.0	–	1.0	–
2	1429	74 (5%)	1.78 (0.76, 4.13)	0.18	1.62 (0.69, 3.79)	0.26
3	1186	127 (11%)	3.90 (1.69, 8.97)	0.001	3.13 (1.35, 7.26)	0.008
4	560	92 (16%)	6.39 (2.75, 14.8)	<0.001	5.30 (2.27, 12.4)	<0.001
Not categorized	303	30 (10%)	3.57 (1.46, 8.75)	0.005	3.21 (1.30, 7.94)	0.02
Hemodynamic Vulnerability						
0	1191	80 (7%)	1.0	–	1.0	–
1	991	91 (9%)	1.40 (1.03, 1.92)	0.03	1.41 (1.02, 1.95)	0.04
2+	1052	108 (10%)	1.59 (1.18, 2.15)	0.003	1.58 (1.15, 2.16)	0.005
Not recorded	445	50 (11%)	1.76 (1.21, 2.55)	0.003	1.76 (1.20, 2.57)	0.004

DISCUSSION

This study found that infants undergoing cardiac catheterization with weight groups below 5 kg had significantly higher odds of any or a high severity adverse event when compared to larger patients, even when adjusting for procedure type risk group and hemodynamic vulnerability. The highest relative risk was found in infants with a weight below 2 kg. Despite representing just 1.5% of the overall population in this study, infants with a weight below 2 kg accounted for 33% (7/21) of the catheterizations resulting in death. To that end, while there was more than a ten-fold increase in mortality among infants <2 kg when compared to all other weight groups, there was no significant difference in mortality between the other three (heavier) weight groups (mortality rate all <1%). Half of all deaths (4/8 level 5 AE) in the <2 kg and 2–3 kg groups occurred in infants with a single ventricle who underwent RF or needle perforation of an intact atrial septum.

This study has also confirmed procedure type risk group and hemodynamic vulnerability to be associated with an increased risk of clinically significant adverse events among infants less than one year of age undergoing cardiac catheterization. This is consistent with previous reports from the entire C3PO dataset for high severity adverse events [6].

This study documented increasing odds for any adverse event, as well as high severity adverse events, for lower weight groups (adjusted for procedure type risk group and hemodynamic vulnerability), findings which are consistent with previous studies showing that low weight is associated with increased rates of catheterization-related complications [8,9]. However, in contrast to the <2 kg group, the difference in odds between the 2–3 kg and the 3–5 kg groups was very small, as was the difference to larger patients above 5 kg. Empirical analysis of the data in a continuous fashion, while advantageous, was not feasible due to the small number of patients in the important weight group <2 kg. However, the data can be interpreted as a fairly even and slow increase in the incidence of adverse events with decreasing weight, with the incidence of adverse events then increasing substantially with weights below 2 kg. From a practical standpoint, most procedures performed in infants with a very low weight are performed as life- saving measures in critically ill infants and cannot and should not be delayed.

While there are risks in any cardiac catheterization, certain technical challenges may be exaggerated in very small patients. For example, this study identified high mortality risk associated with RF or needle perforation of an intact atrial septum, when performed in infants with a single ventricle who are under 2 kg. Nevertheless, therapeutic options in this group of patients are very limited and alternative strategies to reduce the incidence of these high severity adverse events are often lacking.

The unique vulnerability of infants <2 kg was reflected in the higher utilization of general anesthesia (98%), need for inotropic support (33%), and blood transfusions (42%). This is consistent with previous experience of Rhodes *et al*. who found that low weight infants are more than 4 times as likely to require a blood transfusion during cardiac catheterization than normal weight counterparts of similar gestation [8]. The optimal hemoglobin concentration for critically ill infants, particularly in those with congenital heart disease, remains unknown. As such, marked variability exists among clinicians in terms of both hemoglobin thresholds for transfusions and the volume of transfusions ordered [10].

Limitations

This study has a variety of limitations. While care has been taken to capture all adverse events, there is a strong likelihood of underreporting of particularly low-severity adverse events. An initial audit of 10% of cases entered into C3PO, revealed a 92% capture of high severity adverse events, and a 81% capture of level 1 or level 2 adverse events [6]. Furthermore, even though this study represents a large cohort of infants undergoing cardiac catheterization, the overall number of patients within the lower weight groups was fairly small. As such, distinct weight categories were chosen rather than trying to establish a continuous relationship between lower weight and incidence of adverse events. However, operators need to be aware that these were arbitrary thresholds, and that risks likely don't suddenly decrease because of a weight increase from 1.9 to 2.0 kg, but rather follow a more continuous decrease with increasing weight.

This study did not capture gestational age and premature birth, which may have an important impact on procedural morbidity and mortality. Furthermore, most participating institutions represent tertiary referral centers, and as such this study does not represent current practice at smaller institutions, which may have a higher number of patients offered supportive care at lower weights. Therefore, the general applicability of our findings to all pediatric hospitals with cardiac catheterization programs is unknown.

CONCLUSIONS

The risk of adverse events during cardiac catheterization increases for infants with a weight below 5 kg. Risks are highest in infants with a weight <2 kg, who have a significantly higher risk of severe adverse events, most notably death (as high as 12%) even after correcting for hemodynamic vulnerability and procedure type risk group. This relationship is likely a continuous relationship, and should not be understood as a threshold above/below which catheterizations should be considered safe or unsafe. The inherent risks of catheter procedures in these patients have to be weighed against those associated with alternative surgical and medical management options, which may themselves carry higher risks of adverse patient outcome.

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