Hybrid Procedures: Adverse Events and Procedural Characteristics—Results of a Multi-institutional Registry

Ralf Holzer, MD,* Audrey Marshall, MD,† Jackie Kreutzer, MD,‡ Russel Hirsch, MD,§ Joanne Chisolm, RN,* Sharon Hill, ACNP,* Mark Galantowicz, MD,* Alistair Phillips, MD,† John Cheatham, MD,* and Lisa Bergerson, MD†

*Department of Cardiology, Nationwide Children's Hospital, Columbus, Ohio, §Department of Cardiology, Cincinnati Children's Hospital, Cincinnati, Ohio, †Department of Cardiology, Children's Hospital Boston, Boston, Mass, and ‡Department of Cardiology, Children's Hospital of Pittsburgh Pittsburgh, Pa, USA

ABSTRACT

Introduction. Procedural cooperation between cardiac surgeon and interventional cardiologist to facilitate interventions such as device delivery or angioplasty (hybrid procedure) has become increasingly common in the management of patients with congenital heart disease.

Design. Data were prospectively collected using a multicenter registry (C3PO). Between February 2007 and December 2008, seven institutions submitted data regarding 7019 cardiac catheterization procedures. Procedural data and adverse events (AEs) of 128 hybrid procedures were evaluated.

Results. There was significant variability in the number of hybrid procedures per center, ranging from one to 89 with a median of eight. A total of 60% of interventional (vs. strictly diagnostic) hybrid procedures were performed by one center. The median weight was 3.7 kg (0.7–86 kg). Single-ventricle circulation was present in 60% of the procedures. Hybrid procedures included: patent ductus arteriosus (PDA) stent placement (n = 55), vascular rehabilitation (n = 25), ventricular septal defect (VSD) device closure (n = 7), valvotomy (n = 3), and diagnostic hybrid procedures (n = 38). Sixteen AEs occurred in 15/128 (12%) procedures. These included minor or trivial AEs (n = 9), moderate AEs (n = 5), major AEs (n = 1), and catastrophic AEs (n = 1). The type of AE documented included arrhythmias (n = 6), hypoxia or hypotension (n = 3), vessel or cardiac trauma (n = 2), and other events (n = 5). Of documented AEs, 9/16 (56%) were classified as not preventable, 6/16 (38%) as possibly preventable, and 1/16 (6%) as preventable. The incidence of AE related to PDA stent placement with surgical exposure (5/50, 10%) was significantly lower when compared with PDA stent placement performed percutaneously (4/5, 80%, $P = .002$).

Conclusion. Hybrid procedures appear to have a low incidence of associated major AEs. PDA stent placement performed as a palliation of hypoplastic left heart syndrome (HLHS) or complex single/two ventricle patients may have a lower incidence of AEs if performed using a direct approach with surgical exposure rather than a percutaneous approach. Accurate definitions of these innovative procedures are required to facilitate prospective data collection.

Key Words. Hybrid Procedures; Cardiac Catheterization; Adverse Events

Background

Intraprocedural cooperation between cardiac surgeon and interventional cardiologist is not new in pediatric cardiology. Indeed, multiple reports can be found in the literature on such interventions (device closure of ventricular septal defects [VSDs] in the operating room, intraoperative stenting of vascular stenosis, or other interventional therapies performed in direct collaboration with the cardiac surgical team). Over the past few years, hybrid treatment strategies have become increasingly common in the management of patients with congenital heart disease and evolved as an important hybrid treatment strategy for selected patients.[1–7] Most studies reported are retrospective single-center experiences focusing predominantly on technical aspects of these hybrid procedures. Comparing procedural data and the incidence of adverse events (AEs) is difficult because of a lack of clear definitions relating to AE severity and overall capture of these events. Bergersen and colleagues recently reported on the "Congenital Cardiac Catheterizations Outcome

Project (C3PO),"[8] which is a multicenter registry devoted to prospectively collecting outcome data on a variety of cardiac catheterization procedures, enabling an adjustment for center-specific variations in patient case mix as well as using a comprehensive set of definitions for procedure-related AEs and efficacy. This study reports procedural data as well as AEs for hybrid procedures captured within this registry.

Methods

Data were prospectively collected using the "Congenital Cardiac Catheterization Outcomes Project" (C3PO), a multi-institutional interventional registry with seven participating institutions. Details pertaining to registry design and initial evaluation of AEs were recently reported by Bergersen and colleagues.[8] AEs captured in the C3PO registry occurred immediately before, during, or soon after the procedure with a direct relationship to the hybrid procedure. Adverse events occurring late and/or during a prolonged hospital stay not related to the hybrid procedure were not captured in this registry. Each AE was assigned a severity (Table 1) and preventability score (Table 2), which were independently reviewed for each documented AE. C3PO uses a web-based application for data entry and captures data on all cardiac catheterization procedures performed by the participating centers and operators. The completeness of case capture, data entry, and outcome classification were further validated using an independent audit of a random 10% of cases. Where data was entered incompletely, or the type of hybrid procedure was unclear, the relevant centers were contacted individually and asked to correct or clarify the data entered.

Inclusion and Exclusion Criteria

Included were all procedures that were classified within C3PO as hybrid procedures by the participating institution and where both cardiothoracic surgeon and interventional cardiologist participated directly in the same procedure at the same time and setting. Furthermore, the procedural component performed by the interventional cardiologist had to be facilitated by the cardiothoracic surgeon and/or vice versa, such as, for example, providing surgical access for a transcatheter intervention. Bailout surgical procedures, surgical procedures resulting from unsuccessful attempts at transcatheter therapy, and surgical procedures performed directly before or after transcatheter therapy with both components being technically independent from each other, were excluded from the analysis. The only exceptions were patients that underwent palliation of hypoplastic left heart

Table 1. Severity Level of Adverse Events

Severity Level of Adverse Events	
Severity level 1—none	No harm, no change in condition, may have required monitoring to assess for potential change in condition with no intervention indicated.
Severity level 2—minor	Transient change in condition, not life threatening, condition returns to baseline, required monitoring, required minor intervention such as holding a medication, obtaining lab test(s).
Severity level 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 intensive care unit for monitoring, or moderate transcatheter intervention to correct condition.
Severity level 4—major	Change in condition, life threatening if not treated, change in condition may be permanent, may have required intensive care unit admit or emergent readmit to hospital, may have required invasive monitoring, required interventions such as electrical cardioversion or unanticipated intubation or required major invasive procedures or transcatheter interventions to correct condition.
Severity level 5—catastrophic	Any death and emergent surgery or heart lung bypass support (extracorporeal membrane oxygenation [ECMO]) to prevent death with failure to wean from bypass support.

Table 2. Preventability of Adverse Events

Preventability of Adverse Events	
Category I: preventable	Events where definite breech of standard technique was identified; necessary precautions were not taken; event was preventable by modification of technique or care.
Category II: possibly preventable	Events where definite breech of standard technique was not identified but may have occurred; necessary precautions may not have been taken; event may have been preventable by modification of technique or care.
Category III: not preventable	Events where no obvious breech of standard technique occurred; necessary precautions were taken; no clearly known alteration in method or care exists to prevent the event.

syndrome (HLHS) or complex single-/two-ventricle physiology using a combination of patent ductus arteriosus (PDA) stent placement and surgical banding of the branch pulmonary arteries, where the two components of the procedure were performed individually at separate times, rather than in the same setting.

Between February 2007 and December 2008, 7019 cardiac catheterization procedures were entered into the C3PO registry by the participating institutions. One of the seven institutions joined the registry in 2007, and as such data do not include procedures performed at this institution prior to joining the registry. Only 2% (145/7019) of procedures were classified as Hybrid Procedures in C3PO. After applying inclusion and exclusion criteria, 128 procedures were included in this analysis. Excluding diagnostic exit angiographies, this represents 90/7019 (1%) procedures collected within the C3PO registry. The median age was 1.5 months (range 1 day–31 years), and the median weight was 3.7 kg (range 0.7–86 kg). The procedures were separated into five procedural groups, based on the main therapeutic strategy:

1. PDA stent placement performed as part of a treatment strategy that also included bilateral pulmonary artery banding for patient with HLHS or complex single-/two-ventricle physiology (n = 55), with PDA stent placement being performed either at the time of surgical pulmonary artery (PA) banding (usually using surgical exposure), or at a separate time from PA banding (usually percutaneously).
2. Vascular rehabilitation, which included any stent placement and/or balloon angioplasty of blood vessel other than PDA of group 1 (n = 25). This included procedures where the surgeon solely provided surgical access without any additional cardiothoracic surgical procedure, such as carotid cutdown for aortic stent placement in a small infant, usually performed in the catheterization laboratory as well as procedures that were performed using surgical access during concomitant cardiothoracic surgical procedures, such as pulmonary artery stent placement during surgical pulmonary valve replacement, usually performed in the operating room.
3. VSD closure (n = 7).
4. Diagnostic procedures without intervention (n = 38) mainly made up of completion angiograms performed in the operating room. These procedures were inconsistently captured in the database and therefore mainly reflect the experience of a single institution (35/38, 92%).
5. Pulmonary and aortic valvotomy (n = 3). This group was not analyzed separately because of the small number of patients.

Statistical Analysis

For all procedural and patient characteristics, median, range, and interquartile range were calculated for continuous variables and frequency with percentage for categorical variables. In addition to providing descriptive data for all hybrid procedures, most procedural and patient characteristics were further evaluated independently for individual procedural groups. StatsDirect software (StatsDirect Ltd., Cheshire, UK) was used for all statistical calculations. Procedures times were compared across types of hybrid procedures using the Kruskal–Wallis test. Adverse event rates were compared between PDA stent placement with and without surgical exposure as well as between hybrid procedures performed in the catheterization laboratory and operating room using Fisher's exact test. The same test was used to compare the incidence of AEs in the single largest center with all other centers in the study. The incidence of purely diagnostic procedures was compared between procedures performed in the catheterization laboratory and operating room using Fisher's exact test. All tests were performed at alpha = 5%.

Results

Demographic, Clinical, and Procedural Data

Out of the 128 hybrid procedures included in this study, 69 (54%) of the procedures were performed within the environment of a cardiac catheterization laboratory, while the remainder (46%) were performed in the operating room. Basic demographic and clinical characteristics are listed in Table 3. Sixty percent of the procedures were performed in the patients with single-ventricle physiology. Forty-seven percent of the patients were below 1 month of age. The majority of procedures were classified as nonelective or emergent procedures (Table 4). Many of the patients were on inotropic support prior to starting the procedure (23/128, 18%), especially in the group of PDA stent placement (25%) and VSD closure (57%). Two procedures were performed on extracorporeal membrane oxygenation (ECMO) support. General anesthesia with a secured airway was used in all of the procedures.

Table 3. Basic Demographic and Clinical Characteristics

	Total (n = 128) (%)	PDA Stent (n = 55) (%)	Vascular Rehab (n = 25) (%)	VSD Closure (n = 7) (%)	Diagnostic (n = 38) (%)
Age (months)					
<1 month	60 (47)	49 (89)	2 (8)	2 (29)	5 (13)
1 to 11 months	40 (31)	6 (11)	8 (32)	5 (71)	20 (53)
1 to 10 years	16 (13)	—	8 (32)	—	8 (21)
≥11 years	12 (9)	—	7 (28)	—	5 (13)
Weight (kg)	3.7	3	10.9	6.4	5.6
	0.7–86	1.4–4.1	2.5–86	3.4–8.7	2.4–79
	2.8–7.1	2.5–3.4	5.9–41.3	5.4–8.7	4.8–12.2
Diagnosis					
No structural heart disease	1 (1)	—	1 (4)	—	—
Transplanted heart	1 (1)	—	—	—	1 (3)
Isolated defects	8 (6)	—	—	2 (29)	4 (11)
Complex defect (2V)	41 (32)	2 (4)	18 (72)	5 (71)	15 (39)
Single ventricle	77 (60)	53 (96)	6 (24)	—	18 (47)

The total may be higher than the sum of all columns, as it also included few procedures that do not fall into any of the given subcategories; n (%) is provided for categorical variables, and median, range, and interquartile range (in separate rows) for continuous variables. PDA, patent ductus arteriosus; VSD, ventricular septal defect.

Table 4. Basic Procedural Characteristics

	Total (n = 128) (%)	PDA Stent (n = 55) (%)	Vascular Rehab (n = 25) (%)	VSD Closure (n = 7) (%)	Diagnostic (n = 38) (%)
Nonelective procedure	63 (49)	51 (93)	3 (12)	2 (29)	5 (13)
Emergent procedure	3 (2)	—	2 (8)	—	1 (3)
Transferred on ECMO support	2 (2)	—	—	—	2 (5)
Airway management					
Transferred ventilated	30 (23)	21 (38)	3 (12)	3 (43)	3 (8)
Intubated in cath lab/OR	98 (77)	34 (62)	22 (88)	4 (57)	35 (92)
Inotropic support at start	23 (18)	14 (25)	2 (8)	4 (57)	3 (8)
Case duration (minutes)	37	29	92	75	30
	5–326	16–242	30–209	15–326	5–179
	25–326	25–76	37–163	15–205	18–57
Fluoroscopy time (minutes)	3	4	11	1	3
	0–100	1–100	0–66	0–86	1–20
	2–11	2–8	3–21	0–38	1–3
Contrast dose (mL/kg)	2.2	2	2.8	1.8	2.1
	0–14.8	0.6–14.8	0–8.6	0–7	0.6–11.3
	1.2–4	1.2–4.6	1–4.9	0–4	1.3–3.1

The total may be higher than the sum of all columns, as it also included few procedures that do not fall into any of the given subcategories; n (%) is provided for categorical variables, and median, range, and interquartile range (in separate rows) for continuous variables. ECMO, extracorporeal membrane oxygenation, PDA, patent ductus arteriosus; VSD, ventricular septal defect.

The procedure time was defined from sheath entry to sheath removal and was accurately provided for 67/69 (97%) of the procedures performed in the catheterization laboratory. However, because of the lack of specifically assigned monitoring personnel, only 11/59 (19%) of the procedures performed in the operating room had its procedure time documented in the C3PO database. Fluoroscopy time was more readily available from the fluoroscopic equipment used and as such, was provided for 127/128 (99%) of the procedures. Using the limited data available, the median procedure time was 37 minutes (range 5–326 minutes), and the median fluoroscopy time was 3 minutes (range 0–100 minutes). Very short procedure times of as little as 5 minutes were seen with some diagnostic procedures (postoperative completion angiograms), with the duration of diagnostic procedure performed in the operating room ranging from 5 to 30 minutes. There was a significant difference in the overall procedure time between the four groups ($P = .0387$), with vascular rehabilitation having the longest procedure times (median 92 minutes) and PDA stent placement the shortest procedure times (median 29 minutes). Four VSD closures and four vascular rehabilitations, all in the operating room, were performed without the use of any fluoroscopy.

Typical vascular access routes reflected the type of procedure performed (Table 5). In seven patients, PDA stent placement was performed at

Table 5. Vascular Access with Surgical Exposure

Access with Surgical Exposure	Total (n = 128) (%)	PDA Stent (n = 55) (%)	Vascular Rehab (n = 25) (%)	VSD Closure (n = 7) (%)	Diagnostic (n = 38) (%)
Direct carotid entry	7 (5)	—	4 (16)	—	1 (3)
Direct aortic entry	11 (9)	—	1 (4)	—	10 (26)
Direct MPA entry	65 (51)	48 (87)	14 (56)	—	3 (8)
Direct cardiac entry (atria)	1 (1)	—	—	—	1 (3)
Direct cardiac entry (ventricle)	13 (10)	1 (2)	—	5 (71)	6 (16)
Other/unspecified direct entry	21 (16)	1 (2)	3 (12)	—	17 (45)

The total may be higher than the sum of all columns, as it also included few procedures that do not fall into any of the given subcategories; n (%) is provided for categorical variables. This table does not include vascular access without surgical exposure (such as percutaneous PDA stent placement in hybrid patients). The surgical entry site was not provided for two VSD closures and three vascular rehabilitations. MPA, main pulmonary artery; PDA, patent ductus arteriosus; VSD, ventricular septal defect.

Table 6. Hybrid Procedures Performed

Hybrid Procedures Performed	Total (n = 128) (%)	Cath Lab (n = 69)	OR (n = 59)
PDA stent (HLHS/complex single/two ventricle)	55 (43)	50	5
At time of PA banding	48 (38)	43	5
PDA stent	45 (35)	40	5
PDA stent + ASD stent	1 (1)	1	—
PDA stent + atrial septostomy	2 (2)	2	—
Separate setting from PA banding	7 (6)	7	—
PDA stent	3 (2)	3	—
PDA stent + atrial septostomy	2 (2)	2	—
PDA stent + LPA balloon	2 (2)	2	—
Vascular rehabilitation	25 (20)	10	15
Stent placement	15 (12)	4	11
Aorta	2 (2)	1	1
Pulmonary artery	10 (8)	—	10
Other	3 (2)	3	—
Balloon angioplasty	7 (5)	5	2
Aorta	1 (1)	1	—
Pulmonary artery	3 (2)	1	2
Other	3 (2)	3	—
Balloon angioplasty + stent placement	3 (2)	1	2
Pulmonary	2 (2)	—	2
Pulmonary + aortic	1 (1)	1	—
Valvotomy	3 (2)	3	—
Pulmonary	1 (1)	1	—
Aortic	2 (2)	2	—
VSD device closure	7 (5)	3	4
No intervention/diagnostic procedures	38 (30)	3	35

n (%) is provided for categorical variables. hypoplastic left heart syndrome; LPA, left pulmonary artery; PA, pulmonary artery; PDA, patent ductus arteriosus; VSD, ventricular septal defect.

a time different from PA banding, five of which had a femoral venous approach while two underwent stent placement using direct surgical exposure via median sternotomy and direct main pulmonary artery (MPA) entry. Direct MPA entry with surgical exposure was the most common form of vascular access for both vascular rehabilitation as well as PDA stent placement. In contrast, the chosen form of vascular entry was much wore variable for diagnostic hybrid procedures.

The most common hybrid intervention was PDA stent placement accounting for 55/128 (43%) procedures, the majority of which (87%) were performed at the same time as surgical banding of the branch pulmonary arteries (Table 6). Only in 5/55 (9%) procedures were atrial septal interventions performed at the same time as PDA stent placement. Pulmonary artery stent placement or balloon angioplasty was performed in 64% of the vascular rehabilitations and 38/128 (30%) of the hybrid procedures were of purely diagnostic nature. While the majority of the PDA stent placements were performed in the catheterization laboratory (91%), the majority of vascular rehabilitations (60%) and diagnostic procedures (92%) were performed in the operating room.

Adverse Events

Sixteen AEs occurred in 15/128 (12%) hybrid procedures and 15/90 (17%) interventional hybrid procedures (Table 7). The majority of AEs (12/16, 75%) occurred during the procedure itself, while three AEs occurred in the catheterization laboratory after sheath removal and one event occurred in the cardiac intensive care unit. The majority of AEs were either of minor or moderate severity, 14/16 (88%). Major or catastrophic AEs were documented in two cases. One was a major neurologic event leading to death in a 3-month-old infant who underwent balloon angioplasty of middle aortic syndrome using an approach via left carotid cutdown (in the presence of a very small right carotid artery). The other was a 7-day-old infant with HLHS who required multiple cardioversions for atrial flutter and supraventricular tachycardia (SVT) during the procedure. Adverse events by the highest recorded severity category per procedure are shown in Table 8. Types of AEs recorded in the database included arrhythmias (n = 6), hypoxia or hypotension (n = 3), as well as vessel or cardiac trauma (n = 2). Adverse events documented only once were stent malposition, nonspecific ST-T wave changes, local bleeding with line removal, systemic air embolus (no sequelea), as well as a central nervous system event with seizures (Table 7). Based on the definitions of preventability used for this study (Table 2), more than half of the AEs (9/16, 56%) were classified as not preventable, while 6/16 (38%) were classified as possibly preventable (Table 9). Only one AE was classified as preventable (bleeding with line removal).

Table 7. Adverse Events

Adverse Event Details	Severity	Preventability	Type Procedure
Arrhythmias			
Atrial Arrhythmia	4	3	PDA stent
Atrial Arrhythmia	3	3	PDA Stent
Atrial Arrhythmia	2	3	PDA Stent
Heart Block, resolved	3	3	Muscular VSD occlusion
Bradycardia (sinus)	3	3	Aortic valvotomy
Bradycardia (sinus)	2	3	Muscular VSD occlusion
Hypotension and hypoxia			
Hypotension*	2	3	PDA stent + LPA balloon
Hypotension needing inotropes	3	3	PDA stent + LPA balloon
Hypoxia	2	3	Pulmonary valvotomy
Vascular/cardiac trauma			
Perforation RVOT with wire	2	2	RVOT stent
Vessel trauma	2	2	PDA stent
Technical AEs			
Stent Malposition	3	2	PDA stent
CNS Events			
CNS event with seizure	5	2	Balloon aorta
Other AEs			
Nonspecific ST-T wave changes	2	2	PDA stent
Bleeding with line removal	2	1	PDA stent
Air embolus, systemic*	1	2	PDA stent + LPA balloon

*These two adverse events occurred during the same procedure.
Severity Level 1 to level 5 (Table 1), preventability category 1 to 3 (Table 2). AE, adverse event; CNS, central nervous system; LPA, left pulmonary artery; PDA, patent ductus arteriosus; RVOT, right ventricular outflow tract; VSD, ventricular septal defect.

Table 8. Procedures with Adverse Events by Highest Recorded Severity per Procedure

	Total (n = 128) n (%) or Med (RG, IQR)	PDA Stent (n = 55) n or Med (RG, IQR)	Vascular Rehab (n = 25) n or Med (RG, IQR)	VSD Closure (n = 7) n or Med (RG, IQR)	Diagnostic (n = 38) n or Med (RG, IQR)
Total procedures with AE					
Level 1—none	—	—	—	—	—
Level 2—minor	8 (6)	5	1	1	—
Level 3—moderate	5 (4)	3	—	1	—
Level 4—major	1 (1)	1	—	—	—
Level 5—death	1 (1)	—	1	—	—

If a procedure included more than one adverse event, the procedure would be listed under the highest severity category. The total number of procedures with adverse events may be higher than the sum of all columns, as it also included few patients that do not fall into any of the given subcategories; n (%) is provided for categorical variables. AE, adverse event; PDA, patent ductus arteriosus; VSD, ventricular septal defect.

Table 9. Adverse Events by Preventability

Adverse Event Rate Preventability	Total (n = 128) n (%) or Med (RG, IQR)	PDA Stent (n = 55) n or Med (RG, IQR)	Vascular Rehab (n = 25) n or Med (RG, IQR)	VSD Closure (n = 7) n or Med (RG, IQR)	Diagnostic (n = 38) n or Med (RG, IQR)
Not preventable	9 (7)	5	—	2	—
Possibly preventable	6 (5)	4	2	—	—
Preventable	1 (1)	1	—	—	—
Total	16 (13)	10	2	2	—

The total number of adverse events may be higher than the sum of all columns as it also included few patients that do not fall into any of the given subcategories; n (%) is provided for categorical variables. PDA, patent ductus arteriosus; VSD, ventricular septal defect.

Table 10. Hybrid Procedures per Center

Procedures per Center (N)	No 1	No 2	No 3	No 4	No 5	No 6	No 7
All hybrid procedures	5	8	11	89	10	1	4
Diagnostic hybrid proc.	—	—	3	35	—	—	—
Nondiag. hybrid proc.*	5	8	8	54	10	1	4
Stent PDA	—	7	1	35	10	—	2
Vascular rehab	1	1	6	17	—	—	—
VSD	4	—	1	1	—	—	1
Hybrid: OR	3	—	—	55	—	—	1
Hybrid: cath labs	2	8	11	34	10	1	3
All AEs	3	5	1	5	1	1	
Cat 3–5 AEs	2	3	—	1	—	1	

*The total may be higher than the sum of all three procedures, as it also included procedures that do not fall into any of the given subcategories. AE, adverse event; PDA, patent ductus arteriosus; VSD, ventricular septal defect.

Sixty-three percent (10/16) of AEs occurred during PDA stent placement. The incidence of AEs related to PDA stent placement with surgical exposure (5/50, 10%) was significantly lower when compared with PDA stent placement performed percutaneously (4/5, 80%, $P = .002$).

Even though the incidence of AEs was higher in the catheterization laboratory when compared with the operating room (19% vs. 3%, $P = .0065$), this datum has to be interpreted on the background of a significantly higher incidence of purely diagnostic procedures, such as exit angiographies, performed in the operating room (59% vs. 5%, $P < .0001$). The median time that the management of AEs added to the overall procedure time was 2 minutes (2–5 minutes).

Institutional Variability

Excluding diagnostic hybrid procedures, the median number of hybrid interventions performed per center was eight (one to 54), with 55/90 (60%) hybrid interventions being performed by a single institution (Table 10). Only three centers performed hybrid procedures in the operating room. The hybrid procedure frequency and type varied considerably by institution (Table 10). Vascular rehabilitation was performed in 4/7 (57%) centers, VSD closure in 4/7 (57%) centers, and PDA stenting in 5/7 (71%) centers. Only two centers performed all three types of hybrid interventions during the study period. The number of reported AEs and procedures per center was too small to compare between all the participating institutions. However, when evaluating hybrid interventions (excluding exit angiography), the incidence of AEs in one center that performed 60% of all the hybrid interventions in this study was significantly lower than the incidence of AEs in the remaining center (9% vs. 31%, $P = .0131$). The overall number of hybrid procedures increased during the study period from 55 in the first 11 months of data collection to 73 in the second half of the study period.

Discussion

The data collected in the C3PO registry on hybrid procedures demonstrate institutional variability not only in the overall number of hybrid procedures but also in the spectrum of hybrid procedures performed. While hybrid procedures appeared to become a more frequently chosen therapeutic strategy, as documented by a 33% increase between the first half and the second half of the study period, there was a considerable concomitant increase in (mainly diagnostic) surgical hybrid procedures in the second half of the study period (from 22 to 38). The increase in overall

hybrid procedures may therefore just reflect an increasing reporting of diagnostic hybrid procedures performed by a single institution, which introduced a fixed ceiling mounted c-arm in the surgical operating room halfway through the study period rather than being a genuine increase in the frequency of hybrid interventions performed.

This registry datum shows that five of the seven centers are pursuing a hybrid strategy in select patients for palliation of hypoplastic left heart syndrome and/or other complex single- or two-ventricle physiology, accounting for 61% of all interventional hybrid procedures. The majority of hybrid PDA stents were placed in the catheterization laboratory, which is likely related to the often more superior imaging equipment when compared with the operating room. Interestingly, this study documented a reduced incidence of AEs when performing hybrid PDA stent placement using direct surgical exposure when compared with percutaneous PDA stent placement. While this is conceivable, because of the ability to avoid the use of long (intracardiac) sheaths and guide wires, the overall number of procedures is too small to draw any more stringent conclusions.

Only in five procedures was PDA stent placement combined with an atrial septal intervention (stent or septostomy). This is expected and reflects an approach taken in many of the larger centers where patients undergo hybrid palliation and are then allowed to recover, with balloon atrial septostomy being performed semielectively prior to discharge.[7] The exceptions are patients with severely restrictive or intact atrial septum that are treated prior or at the time of hybrid stage I palliation.[7]

The overall incidence of level 3–5 AEs (moderate, major, catastrophic) was 8% for interventional hybrid procedures. However, interpreting this number is difficult because of the variable subset of patients, procedures, and diagnoses, as well as the small number of hybrid procedures when compared with overall catheterization procedures collected within the C3PO registry. Patients requiring hybrid procedures may represent a sicker population than those undergoing elective cardiac catheterization, as reflected in the high percentage of procedures performed nonelectively or emergently, on inotropic or on ECMO support. To evaluate and compare the result of complex hybrid strategies, such as, for example, hybrid stage I palliation of HLHS, which includes PA banding, PDA stent placement, and balloon atrial septostomy, one has to evaluate the overall composite outcome data, including median and long-term survival as well as neurodevelopmental outcome after bidirectional Glenn, comprehensive Stage II, or Fontan completion.[5,9] This appears to be beyond the capabilities of this registry.

With only a small number of AEs, it is difficult to draw any conclusion from the type of AEs encountered. While one would expect a reduced incidence of certain "technical" complications, relating to the use of long sheaths and wires, this has not been reflected in the current registry data. Arrhythmias were the most commonly encountered AEs, which is similar to what has been reported for the overall C3PO registry.[8] Hybrid VSD closure had no associated AE of major or catastrophic severity, which is similar to what has been reported in a multicenter experience by Bacha and colleagues.[4] Similar to percutaneous cardiac catheterization procedures, the incidence of preventable or possibly preventable AEs was as high as 44%, which highlights the need to modify techniques and approach to further reduce this number. The overall incidence of level 3–5 AEs (moderate, major, catastrophic) of 5% appeared to be comparable or slightly lower than the 6% incidence of level 3–5 AEs reported for all cardiac catheterization procedures within the C3PO registry.[8] However, comparisons are difficult because of the variable subset of patients, procedures, and diagnoses, as well as the small number of hybrid procedures when compared with overall catheterization procedures collected within the C3PO registry. Patients who require hybrid procedures likely represent a sicker population than those undergoing elective cardiac catheterization as seen in the high percentage of procedures performed nonelectively or emergently, on inotropic or on ECMO support.

Limitations

This study has several important limitations. First and foremost, the capture of hybrid procedures was incomplete because of the differences in definitions of hybrid procedures used by the various centers. In analyzing the data, it became clear that the ambiguity of the "hybrid" designation resulted in inconsistent inclusion of patients and procedures. This required additional retrospective data inquiries and resulted in some procedures being excluded from analysis, while for others, the prospectively collected procedural data had to be expanded to facilitate analysis within procedural groups, such as hybrid palliation for HLHS or complex single-/two-ventricle circulation.

To facilitate more consistent future prospective data collection that could enable a more detailed analysis of AEs, it would be helpful to categorize hybrid procedures into procedural groups as suggested in this document. These should include hybrid palliation for HLHS or complex single-/two-ventricle circulation either using a percutaneous approach for PDA stenting or an approach facilitated by surgical exposure through median sternotomy, usually at the same time as surgical PA banding. While percutaneous PDA stent placement following or preceding surgical PA banding is technically an isolated transcatheter procedure, the close relationship with surgical PA banding and the uniqueness of the overall approach justifies the inclusion as part of an alternative hybrid approach to the classical Norwood-type palliation. Procedural hybrid categories should further include specific transcatheter interventions (vascular rehabilitation or valvotomy) where the surgeon either provides surgical access without any additional cardiothoracic surgical procedure, such as carotid cutdown for aortic valvotomy or stent placement in an infant, or which were performed using surgical access during concomitant cardiothoracic surgical procedures, such as pulmonary artery stent placement during surgical pulmonary valve replacement. A final category should include diagnostic angiography or hemodynamic evaluation performed either intraoperatively (such as exit angiography) or in the catheterization laboratory with the surgeon providing vascular access due to the lack of suitable percutaneous access routes.

This study is also limited by the small number of individual procedures and related AEs, which does not allow a meaningful comparison between institutions, operators, and different individual hybrid procedures. Preventability of AEs is, to a degree, subjective, and while each event was independently reviewed, the classification is still likely to reflect some degree of operator bias. Some data, such as procedure time, were only inconsistently captured, and therefore, conclusions that can be drawn are limited.

The comparably low incidence of AEs for hybrid procedures performed in the operating room may not only be a result of an increased percentage of diagnostic hybrid procedures, but also be an underrepresentation of the true incidence of AEs. Adjudicating an AE to the hybrid procedures itself may be difficult, which applies particular to short diagnostic intraoperative angiograms, which may be better considered as supplemental imaging rather than a hybrid procedure. As an example, renal dysfunction is a recognized complication after cardiopulmonary bypass surgery. However, it is conceivable that the additional use of contrast during even a purely diagnostic intraoperative angiography may further increase the incidence of postoperative renal dysfunction, which may not necessarily be captured within the C3PO registry. These are important factors that have to be taken into consideration when evaluating the risks and potential benefits of not only therapeutic hybrid interventions but also diagnostic hybrid procedures such as completion angiograms.[10]

The overall incidence of category I AEs was surprisingly low compared with other AE categories. This may suggest that operators, while more consistently entering higher grade AEs, may be less consistent in entering these lower severity AEs. After a long complicated procedure, it may be difficult to recall a small CO2 leak of a wedge catheter compared with more serious AEs. Therefore, these lower grade AEs may be underrepresented in this study.

Overall, this study represents, to a large extent, the experience of one center that accounted for about 60% of all the hybrid interventions, even when excluding exit angiographies. This was particularly notable for intraoperative stent placement and more importantly, hybrid stage I palliation of patients with HLHS. The latter represents a fairly new and novel concept, and at this point, it is unclear how the long-term outcome will compare with conventional Norwood-type palliation. The largest center in this study has pioneered the foundations for this novel approach, and as such, it was not surprising to see the much higher usage of this approach by this center. Other centers use a different approach, either selecting solely high-risk patients or only very occasionally embarking on hybrid therapy without any set institutional policy. Interestingly, the largest center in this series had a lower incidence of AEs, which is not surprising considering that a significant learning curve is associated with hybrid therapy of patients with HLHS.[5] Overall, while Hybrid interventions do have their place in the management of patients with congenital heart disease, it is important to emphasize that the vast majority of centers only occasionally embark on hybrid therapies.

Conclusions

Overall, this study has highlighted for the first time the variety and types of hybrid procedures

performed at different larger tertiary referral centers for patients with congenital hearts disease. While the overall incidence of AEs was 12%, comparisons between individual procedures and centers were not possible because of the limited number of procedures performed. However, the incidence of major AEs was low for all procedure types: PDA stent placement, VSD closure, and vascular rehabilitation. The registry data suggest that PDA stent placement performed as a palliation of HLHS or complex single-/two-ventricle patients may have a lower incidence of AEs if performed using a direct approach with surgical exposure rather than a percutaneous approach. Hybrid procedures require uniform definitions as suggested in this document, and future prospective data collection is required to facilitate a comparison with other surgical or percutaneous techniques.

Acknowledgements

We would like to recognize the study coordinators and personnel that have made this project feasible: Gary Piercey, Denise Norton, Anniece Woods-Brown, Terri Mclees-Palinkas, and Cyndi Murphy. C3PO received grant support from the American Heart Association Physicians Roundtable Award.

Corresponding Author: Ralf Holzer, MD, Heart Center, Nationwide Children's Hospital, 700 Children's Drive, Columbus, OH 43205, USA. Tel: 614-722-2537; Fax: 614-722-5030; E-mail: ralf.holzer@nationwidechildrens.org

Conflict of interest: None.

Accepted in final form: February 11, 2010.

References

1 Hjortdal VE, Redington AN, de Leval MR, Tsang VT. Hybrid approaches to complex congenital cardiac surgery. *Eur J Cardiothorac Surg*. 2002;22:885–890.
2 Bacha EA, Marshall AC, McElhinney DB, del Nido PJ. Expanding the hybrid concept in congenital heart surgery. *Semin Thorac Cardiovasc Surg Pediatr Card Surg Annu*. 2007;146–150.
3 Akintuerk H, Michel-Behnke I, Valeske K, et al. Stenting of the arterial duct and banding of the pulmonary arteries: basis for combined Norwood stage I and II repair in hypoplastic left heart. *Circulation*. 2002;105:1099–1103.
4 Bacha EA, Cao QL, Galantowicz ME, et al. Multicenter experience with perventricular device closure of muscular ventricular septal defects. *Pediatr Cardiol*. 2005;26:169–175.
5 Galantowicz M, Cheatham JP, Phillips A, et al. Hybrid approach for hypoplastic left heart syndrome: intermediate results after the learning curve. *Ann Thorac Surg*. 2008;85:2063–2070.
6 Holzer R, Sisk M, Phillips A. Hybrid balloon pulmonary valvuloplasty in a 700 g infant: thinking outside the box. *Catheter Cardiovasc Interv*. 2008;72:93–96.
7 Holzer RJ, Wood A, Chisolm JL, et al. Atrial septal interventions in patients with hypoplastic left heart syndrome. *Catheter Cardiovasc Interv*. 2008;72:696–704.
8 Bergersen L, Marshall A, Gauvreau K, et al. Adverse event rates in congenital cardiac catheterization—a multi-center experience. *Catheter Cardiovasc Interv*. 2010;75:389–400.
9 Galantowicz M, Cheatham JP. Lessons learned from the development of a new hybrid strategy for the management of hypoplastic left heart syndrome. *Pediatr Cardiol*. 2005;26:190–199. [Republished from *Pediatr Cardiol*. 2005 Mar–Apr; 26:190–199; PMID: 15906023].
10 Holzer R, Hill SL, Chisolm JL, Phillips A, Galantowicz M, Cheatham JP. Exit angiography in a dedicated "Hybrid OR Suite"—initial experience. *Catheter Cardiovasc Interv*. 2008;71:O21–O21.