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ORIGINAL ARTICLE

Importance of Prevention and Early Intervention of Adverse Events in Pediatric Cardiac Catheterization: A Review of Three Years of Experience

Yu-Chih Huang[1], Jeng-Sheng Chang[1]*, Yung-Chang Lai[1], Ping-Chun Li[2]

[1]*Division of Pediatric Cardiology, Department of Pediatrics, China Medical University Hospital, Taichung, Taiwan*
[2]*Division of Cardiovascular Surgery, Department of Surgery, China Medical University Hospital, Taichung, Taiwan*

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Background: In spite of advances in many noninvasive instruments for studying cardiac anomalies in children, cardiac catheterization (CC) is still an essential method for the precise calculation of cardiovascular hemodynamic status and for performing therapeutic interventions. Accordingly, all adverse events (AE) related to CC are a major concern to pediatric cardiologists.
Patients and Methods: A total of 220 children with congenital heart disease (CHD) who received cardiac catheterization in our tertiary care hospital between the period of January 2000 and December 2002 were studied. One hundred and thirty-eight patients were non-cyanotic CHD, 71 were cyanotic CHD and 11 were complex CHD. Diagnostic CC was performed in 138 patients and therapeutic CC in 82 patients. All AEs that occurred during the CC procedures were identified, recorded and managed at the scene. The severities of AE were further classified into minor, obvious and severe.
Results: AEs were observed in 41 patients, including 22 (10%) minor, 16 (7.27%) obvious and 3 (1.36%) severe AEs. The three severe AEs were cardiac tamponade, severe ventricular tachycardia and marked hypoxia-and-bradycardia. None of the patients died. Therapeutic CC did not present a higher incidence of AE occurrence than diagnostic CC. However, a young age ($p<0.0001$), low body weight ($p<0.0001$) and cyanotic or complex CHD ($p=0.01$) appeared to be risk factors for obvious and severe AE.
Conclusion: Although the complication of severe AE during CC may not be totally preventable, it is important to be aware of every early sign of AE and to initiate an effective intervention by a well trained resuscitation team.

1. Introduction

With improvements in echocardiography, the role of cardiac catheterization (CC) in investigating congenital heart disease (CHD) has been re-directed to either making a precise hemodynamic study, or implement some interventional procedures. However, CC-associated complications including arrhythmia, massive bleeding, heart perforation, cardiac tamponade, thromboembolism, shock,

*Corresponding author. Division of Pediatric Cardiology, Department of Pediatrics, China Medical University Hospital, 2 Yuh-Der Road, Taichung 40443, Taiwan.
E-mail: d0669@mail.cmuh.org.tw

hypoxemia and vessel occlusion remain a major concern for performing the procedure.

The complication rate of diagnostic CC is approximately 0.8%, and those serious complications requiring emergent surgical interventions are only 0.08%–0.6%.[1–4] However, the complication rate can be as high as 4% to 8% in children's interventional CC.[4–11] This finding is well documented in Vitiello et al's series of 4,500 pediatric CCs in 10 years (2.1% major complications, 9.3% minor complications and 0.14% CC-related mortality).[8]

It is occasionally difficult to distinguish an unexpected CC-related adverse reaction from a true complication. In this study, we attempted to enroll patients with all types of unexpected events identified during CC for analysis regardless of the severity of the adverse event (AE). Therefore, we choose to use the term "adverse event" rather than "complication", to better reflect and to describe all CC-related events.

2. Methods and Patients

A total of 220 children with CHD who received cardiac catheterization in our tertiary care hospital between the period of January 2000 and December 2002 were studied. Among those patients, 138 patients received diagnostic CC and 82 patients received therapeutic CC. Their median age was 15-months-old and their median body weight was 9.5 kg. All CCs were performed by one pediatric cardiologist and one in-training cardiologic fellow doctor. All of the relevant medical records, CC reports, medications and interventions were reviewed by one pediatric cardiologist.

2.1. Catheterization technique

For diagnostic CC, patients were sedated by intravenous infusion of combined drugs of midazolam (0.1 mg/kg/dose), demerol (0.5–1 mg/kg/dose) and ketamine (1 mg/kg/dose). For therapeutic CC, patients were put under general anesthesia. Heparin sodium at doses of 50–100 U/kg were administered intravenously at the beginning of interventional CC, and followed with bolus heparin injections to maintain the patient's hourly activated clotting time above 200 seconds. Carbon dioxide inflated balloon catheters (Berman Angiographic Balloon Catheter; Arrow International Inc., Reading, PA, USA) were used in most diagnostic CCs. Dilatation balloon catheters with inflation pressures of 3 to 8 atmospheres were used to dilate the obstructed valves or vessels. Gianturco coils were used to embolize small-to-medium size patent ductus arteriosus. An Amplatzer septal occluder or CardioSEAL (NMT Medical, Inc., Boston, MA, USA) device was used to occlude atrial septal defects. Non-ionized contrast media was used for each cineangiogram and the dosage was kept between 0.8 to 1.3 mL/kg with the total dosage not exceeding 6 mL/kg. Cefazolin (40 mg/kg) was administered intravenously as prophylactic antibiotics both before and after the CC procedures. Fluoroscopic time of each examination was recorded automatically by the CC system. Procedure time was defined as the period between entering and leaving the CC laboratory.

2.2. Demographic data

According to their cardiac anomalies, the 220 patients were grouped into three groups: non-cyanotic CHD (138 patients, 64.5%, including ventricular septal defects, coarctation of the aorta, atrial septal defects, etc.), cyanotic CHD (71 patients, 30.5%, including tetralogy of Fallot, transposition of the great arteries, double outlet right ventricle, etc.) and complex CHD (11 patients, 5%, mainly asplenia syndrome).

2.3. Definition of AEs

CC procedures were completed uneventfully in 179 patients and were defined as the non-AE group. The remaining 41 patients suffered different severities of AEs and were defined as the AE group.

The severities of AE were classified into three groups: (1) minor AE (unexpected but displayed transient hypoxia or arrhythmia, which reverted to normal spontaneously without any intervention); (2) obvious AE (significant hypoxia, hypotension or paleness prompting intervention such as drug infusion, O_2 inhalation, mask-and-ambu bagging or blood transfusion); (3) severe AE (life threatening events requiring cardiopulmonary resuscitation and/or emergent surgical interventions).

Age, body weight, cardiac defects (non-cyanotic, cyanotic or complex heart disease), and modes of CC procedure (diagnostic or therapeutic) were compared between the AE and the non-AE groups, as well as between the pooled groups of obvious or severe AE groups and the non-AE or minor AE groups to further elucidate the risk factors associated with different severities of AE.

3. Results

The underlying three categories of cardiac anomalies of the 138 patients who received diagnostic CC were non-cyanotic CHD (88 patients; 63.8%), cyanotic CHD (39 patients; 28.3%) and complex CHD (11 patients; 8.0%). The underlying cardiac

anomalies of the 82 patients who received therapeutic CC were non-cyanotic CHD (50 patients; 60.9%) and cyanotic CHD (32 patients; 39.1%).

Therapeutic CC procedures performed on the 82 patients consisted of six different procedures as follows: (1) 29 (35.4%) patients had coil embolizations for patent ductus arteriosus, major aortopulmonary collateral arteries and Blalock-Thomas-Taussig shunt, (2) 11 (13.4%) patients received septal occluder procedures for atrial septal defect, (3) 36 (43.9%) patients received balloon valvuloplasty procedures for valvular pulmonary stenosis or aortic stenosis, (4) 4 (4.9%) patients who had transposition of the great arteries received balloon atrioseptostomy procedures, (5) 1 (1.2%) patient had temporary pacing lead insertion for complete heart block, and (6) 1 (1.2%) patient had an endomyocardial biopsy procedure.

AEs occurred in 41 of the total 220 patients (18.6%), including 25 out of 138 diagnostic CC (18.1%) and 16 out of 82 therapeutic CC (19.5%, Table 1). These AEs were further classified into three categories (minor, obvious and severe) according to the severities of AE. In the diagnostic CC group, the distributions of cases in the minor, obvious and severe categories were 15, 9 and 1, respectively, while the therapeutic CC group cases had a distribution of 7, 7 and 2, respectively. Obvious AE occurred in 7.2% of cases among the total 220 CC procedures, while severe AE occurred in 1.4% of the cases.

All different kinds of AE were categorized into four groups as follows. Group 1—arrhythmias: 20 patients (9.1%) with symptoms including transient bradycardia, 1st to 3rd degree of atrioventricular block, atrial flutter, paroxysmal supraventricular tachycardia and ventricular tachycardia. Group 2—hypoxia: 10 patients (4.6%) with symptoms ranging from transient oxygen desaturation to remarkable apnea and bradycardia requiring cardiopulmonary resuscitation and even endotracheal intubation. Group 3—bleeding: Five patients (2.3%) who suffered significant bleeding at the puncture sites and required blood transfusion. Group 4—miscellaneous: Six patients (2.8%) with symptoms including hypothermia, carbon dioxide retention and cardiac tamponade.

3.1 Three cases who suffered from severe AE

The first case was a 17-day-old, 2.5 kg male newborn with severe pulmonary valvular stenosis whose right ventricle outflow tract was accidentally perforated by a guide wire. Cardiac tamponade then occurred and was managed emergently with needle pericardiocentesis. The bleeding stopped spontaneously. The newborn received a right ventricular outflow tract reconstruction the next day.

The second case was a 2-month-old, 3.6 kg infant with pulmonary atresia with an intact ventricular septum whose atretic pulmonary valve was perforated and dilated by a radiofrequency wire and a dilatation balloon catheter a few days after birth. This 2nd CC was placed to re-dilate residual pulmonary stenosis of a moderate degree. Unexpectedly, a severe ventricular tachycardia with shock occurred when we attempted to place a JR catheter across the stenotic pulmonary valve. The arrhythmia was finally converted by electric cardioversion and lidocaine infusion.

The third case was a 12-month-old, 9.8 kg infant with a large ventricular septal defect and severe pulmonary hypertension. She appeared very resistant to the usual dose of sedatives and eventually she received two doses of midazolam (0.1 mg/kg), ketamine (1 mg/kg) and demerol (0.5 mg/kg) injections. Apnea, cyanosis and bradycardia rapidly occurred and cardiopulmonary resuscitation was started; she was then revived after 1 minute of cardiac massage.

3.2 Risk factors for AE

The mean age and body weight of the 41 AE-suffering patients and 179 non-AE patients are presented in Table 1, respectively.

Furthermore, those with obvious AE and those with severe AE, together termed significant AE, showed significantly different mean age and body weight from the rest of the patients (Table 2).

Table 1 Risk factors associated with adverse events (AE)

	AE (n=41)	Non-AE (n=179)	p	OR	CI
Age (mo)	14.26±20.35	43.82±56.44	<0.0001	0.97	0.96, 0.99
Body weight (kg)	7.72±6.00	14.95±12.91	<0.0001	0.91	0.85, 0.96
Procedure time (min)	164.88±80.24	118.73±66.57	<0.0001	1.01	1.004, 1.01
Fluoroscopic time (min)	30.37±23.29	23.37±19.58	0.035	1.02	1.00, 1.03
Diagnostic CC	25	113	0.7971	0.91	0.45, 1.83
Therapeutic CC	16	66			

OR=odds ratio; CI=confidence interval; CC=cardiac catherterization.

AE patients also required a significantly longer procedure time than non-AE patients (164.9±80.2 *vs.* 118.7±66.6 minutes, $p<0.0001$, Table 1), and this difference was still significant when those with significant AE were pooled together to compare with the minor and non-AE patients (172.6±86.4 *vs.* 123.1±68.6 minutes, $p=0.008$, Table 2). Fluoroscopic time was slightly longer in the AE group as compared to the non-AE group (30.4±23.3 *vs.* 23.4±19.6 minutes, $p=0.035$, Table 1).

When occurrence of AE was compared between the different categories of cardiac anomalies including non-cyanotic, cyanotic and complex CHD, both the cyanotic and complex CHD groups were found to have a higher incidence of AE (26.8% and 36.4%) than the non-cyanotic group (13%, $p=0.02$, odds ratio 2.4 and 3.8, respectively, Table 3).The occurrences of AE for the combined group of cyanotic and complex CHD patients were still significantly higher than those of the non-cyanotic patients (28% *vs.* 13%, $p=0.01$, odds ratio 2.6, Table 3).

Patients with either cyanotic or complex CHD also presented a higher risk for the occurrences of significant AEs (12.7% and 27.3%, respectively) than those with non-cyanotic CHD (5.1%, $p=0.01$, odds ratio 2.7 and 7.0, respectively, Table 4). The occurrences of significant AEs for the combined group of cyanotic and complex CHD patients were still significantly higher than those of the non-cyanotic patients (14.6% *vs.* 5.1%, $p=0.03$, odds ratio 3.2, Table 4).

4. Discussion

This 3-year study of pediatric CC found that there was an 18.6% incidence of all types of AE, including

Table 2 Risk factors associated with obvious and severe adverse events (AEs)

	Obvious+severe AE ($n=19$)	Minor+non-AE ($n=201$)	p	OR	CI
Age (mo)	8.16±10.93	41.17±54.4	<0.001	0.94	0.90, 0.99
Body weight (kg)	6.21±4.40	14.31±12.52	<0.001	0.85	0.75, 0.96
Procedure time (min)	172.63±86.42	123.05±68.57	0.008	1.01	1.002, 1.01
Fluoroscopic time (min)	31.70±23.11	24.03±20.12	0.12	1.02	0.996, 1.04
Diagnostic CC	10	128	0.48	0.65	0.25, 1.63
Therapeutic CC	9	73			

OR=odds ratio; CI=confidence interval; CC=cardiac catherization.

Table 3 Risk for adverse event (AE) occurrences in cyanotic and complex coronary heart disease (CHD) as compare to the non-cyanotic CHD

	AE	Non-AE	OR	95% Wald CL	p
Non-cyanotic	18 (13.0%)	120 (87.0%)	1.00	–	–
Cyanotic	19 (26.8%)	52 (73.2%)	2.44	1.18–5.02	0.02
Complex	4 (36.4%)	7 (63.6%)	3.81	1.01–14.33	0.02
Cyanotic+complex	23 (28.0%)	59 (72.0%)	2.60	1.30–5.19	0.01

OR=odds ratio; CL=confidence limits.

Table 4 Risk for obvious and severe adverse event (AE) occurrences in cyanotic or complex coronary heart disease (CHD) as compare to non-cyanotic CHD

	Obvious+Severe AE	Minor AE+Non-AE	OR	95% Wald CL	p
Non-cyanotic	7 (5.1%)	131 (94.9%)	1.00	–	–
Cyanotic	9 (12.7%)	62 (87.3%)	2.72	0.97–7.63	0.01
Complex	3 (27.3%)	8 (72.7%)	7.02	1.52–32.39	0.01
Cyanotic+complex	12 (14.6%)	70 (85.4%)	3.21	1.21–8.52	0.03

OR = odds ratio; CL = confidence limits.

8.6% of obvious and severe AE. These data are consistent with previous reports in pediatric CC.[4,8–11] In addition, patients who received therapeutic CC in this study had a higher risk for occurrence of AE than those who received diagnostic CC, for all severities of AE (Tables 1 and 2). Moreover, young age, low body weight and cyanotic or complex CHD (26.8%, 36.4% *vs*. 13%, $p=0.02$) are major risk factors for AE occurrence (Tables 1 and 3). Our results showed that the more severe the AE, the longer the procedure time is required (Tables 1 and 2). However, the cause-and-effect relationship is not clear.

Since all minor AE events revert to normal spontaneously, it seems reasonable to consider only the obvious and severe AE as significant AE and the patients who have non-AE and minor AE as controls (Table 4). We showed that cyanotic or complex CHD is a risk factor for the occurrence of significant AE, as compared to the patients with simple CHD, for all degrees of AE severity (Tables 3 and 4).

Fortunately, in spite of the 8.6% occurrence rate of obvious or severe AE in this study, no deaths occurred. This emphasizes the importance of an efficient resuscitation team be set up in the catheterization laboratory and this team should be capable of detecting all types of AE at the earliest stage, as well as be able to implement necessary interventions in patients without delay. In addition, a backup team of cardiac surgeons needs to be prepared for emergent interventions when required.

Severe AE requiring resuscitation occurred in three patients in this study; 2 in therapeutic CC and one in diagnostic CC. These results illustrate that not only therapeutic CC, but a young-age for diagnostic CC, are risk factors for occurrence of severe AE. In order for the members of the catheter laboratory team to be familiar with the common AE, we have described their presenting signs and symptoms and specific managing strategies as follows. Arrhythmias ranked the highest incidence of AE in this study, which is consistent with other reports.[12,13] They include sinus bradycardia, various degrees of atrioventricular block, atrial flutter, paroxysmal supraventricular tachycardia and ventricular tachycardia. Most arrhythmias are associated with inadvertently probing or compressing on the myocardium or conduction tissue, so it is more prudent and safer to use as much balloon-tipped soft catheters as possible rather than the stiff-end catheters in most CC procedures. It is advisable to be very cautious to not probe the areas of conduction tissue, such as the lower superior vena cava and the atrioventricular node, and areas involved in the arrhythmia pathways, such as the pulmonary venous orifices. Moreover, patients with l- or d-transposition of the great arteries, tetralogy of Fallot and pre-existing bifascicular block are also high-risk for complete atrioventricular block.

Hypoventilation, apnea, oxygen desaturation or even bradycardia requiring cardiopulmonary resuscitation and/or endotracheal intubation occurred in 10 of our 220 CC patients (4.6%). Hypoxemia was documented by pulse oximeters in all cases. Risk factors for hypoventilation are sedative drugs, physical restraint, congenital airway anomalies, gastroesophageal reflux, high pulmonary vascular resistance, jugular or subclavian venous puncture, Down's syndrome with a short chin and large tongue, and newborns undergoing prostaglandin infusion. Although most diagnostic CCs can be performed safely under proper intravenous sedation, high-risk patients should have pre-catheter consultations and thorough communication with the anesthesiologist to be well prepared.

Blue spells or hypoxic spells can appear in patients with tetralogy of Fallot and can be a life threatening event, which occurred in one of our CC patients during the procedure. In addition to reducing all kinds of stimulations in the patient as much as possible, we also make it routine practice to give the patient another dose of oral propranolol 4–6 hours before the CC.

Paroxysmal pulmonary artery hypertension crisis (PPHC), which occurs in patients with long term pulmonary arterial hypertension, can be another life-threatening complication during CC; this occurred in two of our patients. When it occurs, the patient may be overtaken by a cascade of cyanosis, hypotension and bradycardia in minutes, and it is crucially important to reduce all types of stimulations in high-risk patients; there may even be a need to have someone on standby when tracheal intubation is necessary. Furthermore, inhalation nitric oxide is the only specific therapy for PPHC attacks and it should always be available in the catheterization laboratory.[14–18]

Cardiac perforation with cardiac tamponade is the worst situation for all interventional cardiologists. This complication is always the first one to be ruled out whenever hypotension suddenly occurs during CC. The diagnosis can be confirmed by either fluoroscope or echocardiography. In addition, an emergent needle pericardiocentesis to drain off bloody pericardial fluid should be performed by the operating cardiologist without delay, as well as cardiopulmonary resuscitation. In the case of a large volume of bleeding, the cardiac surgeon needs to be summoned urgently to create a pericardial window.

When hypothermia ($\leq$35°C) occurs in a small infant for long time, it may cause low cardiac output. Three of our patients showed hypothermia during CC.

Fortunately their cardiac outputs were well maintained. Therefore, a small infant should be kept warm throughout CC with a heating lamp or blanket if a prolonged CC is unavoidable.

Femoral vessel injury was documented in three of our patients by angiograms or CT scans. The first patient was a 4-day-old newborn who received femoral arterial cut-down for performing a balloon angioplasty of the coarctation of aorta. The femoral artery occlusion was documented by 2nd CC at 11 months of age. The other two patients, 7 months and 4 years of age, were thought to have their femoral veins injured during device retrieving procedures when an 8 mm Gianturco coil and a 28 mm CardioSEAL device, respectively, were pulled out forcefully from their femoral veins. Femoral arterial injuries after pediatric CC include bleeding, hematoma, pseudoaneurysm, arteriovenous fistula, thrombosis and occlusion. The incidence of femoral arterial injuries can be as high as 40% in young patients less than 10-years-old. Its risk factors include young age, surgical cut down, use of large bore catheters, interventional catheterization, low cardiac output, dehydration and polycythemia.[20] Femoral anterial injuries should be suspected whenever a leg becomes cool and pulseless after a CC. It has been recommended that high dose (50 units/kg) heparin be given to patients younger than 10 years of age prior to CC as a preventive measure. In case of a femoral artery injury, it should be managed with continuous infusion of heparin and thrombolytic agents such as streptokinase or urokinase. A surgical embolectomy may even be required to save the ischemic limb.[19,20]

5. Conclusion

AE can occur throughout the entire course of CC procedures, from premedication for sedation, vessel puncture, and diagnostic catheterizations to therapeutic interventions. The catheterization team needs to be familiar with all types of AE and their specific management protocols so that early recognition and early intervention can be accomplished. This study showed that a young age, lower body weight and cyanotic or complex CHD are risk factors for occurrence of AE. Although therapeutic CC appears to have a higher risk for AE than that of diagnostic CC, the difference is not statistically significant in pediatric CC.

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