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Risk of cardiac catheterization under anaesthesia in children with pulmonary hypertension

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Background. Children with primary pulmonary hypertension (PHT) are a high-risk group who require assessment by cardiac catheterization under anaesthesia. Complications, including death, have occurred during anaesthesia in these patients, but the true risk has not been quantified.

Methods. The clinical records of children with PHT undergoing general anaesthesia for pulmonary vascular resistance studies were reviewed retrospectively. Data collected included pre-catheter measures of severity of disease, details of clinical management, and complications occurring within 24 h of the start of anaesthesia.

Results. During the past 5 yr, 75 consecutive patients were catheterized and usable records were available in 70. The age range was 0.1–18 yr (mean 7.1). Four children required external cardiac massage [6% (95% confident limits 1–11%)] and one of these died. Of the four, two had an arrhythmia related to the mechanical effects of catheterization, one was hypotensive during anaesthesia and the other had fatal cardiac failure in recovery. All four had severe PHT as judged by echocardiographic estimation of tricuspid regurgitant jet velocity > 4 m s^{-1}.

Conclusions. Resuscitation or death occurred in 6% of cases. Any associated risk factors could not be determined because the number of complications was too small. Risks may be highest in children with severe idiopathic PHT and symptoms of chest pain, syncope, or dizziness.

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Children with primary pulmonary hypertension (PHT) are a high-risk group who, untreated, have a median survival rate of approximately 10 months.[1] If they are carefully investigated and treated with appropriate medication, their median survival can be increased to 8 yr or more, without transplantation.[2] Investigation includes cardiac catheterization to measure directly the pulmonary artery pressure and cardiac output (CO) for calculation of pulmonary vascular resistance (PVR). This is undertaken while the child breathes air and then repeated to test the pulmonary vasodilatation effects of hyperoxia and nitric oxide. General anaesthesia is used for practical reasons to ensure physiological stability and to enable the control of inspired oxygen and nitric oxide. Complications, including death, have occurred during anaesthesia in these patients, but the risk has not been quantified. Data exist for adults with PHT undergoing these procedures under local anaesthesia.[3] Although there are data published about the rate of complications occurring in children undergoing cardiac catheterization, these are not specific to children with PHT.[4] We have reviewed our own data in children with both primary and secondary disease to estimate the risk of cardiac catheterization under general anaesthesia and to identify any features associated with complications.

Methods

The clinical records of children with PHT undergoing general anaesthesia for PVR studies over a 5-yr period,

between July 1999 and November 2004, were reviewed retrospectively. The project was registered with the Research and Development office and the Chairman of the Local Research Ethics Committee considered that parental (or patient) consent was unnecessary for this retrospective study.

We collected data from 94 consecutive anaesthesia records from 75 patients, as some patients had more than one anaesthetic for procedures in addition to cardiac catheterization. A standard data collection form was used and data included patient details, measures of severity of disease from the pre-anaesthetic clinical history, examination and investigations, the pre-anaesthesia echocardiographic examination (echo), drug therapy, anaesthesia management, cardiovascular measurements from the PVR study, and complications during both the procedure itself and over the following 24 h. Electrocardiographs were examined for signs of right ventricular strain, including ST depression in leads V1-3, aVR, or III, and any other abnormalities. Radiologists' chest X-ray reports were noted. Echocardiographic assessment was performed by trained technicians and from their reports, the following were recorded; (i) right ventricular function (classified as good, moderate, or poor), (ii) the presence of dilatation or hypertrophy of the right ventricle, (iii) any restriction of the left ventricle due to the size of right ventricle, and (iv) estimation of the systolic pulmonary artery pressure (sPAP) in mm Hg based on the velocity of the regurgitant systolic jet through the tricuspid valve utilizing a modified 'Bernoulli equation' (see the appendix).[4–7]

During the audit period, anaesthesia management for cardiac catheterization involved muscle relaxation, tracheal intubation with a cuffed tracheal tube, and mechanical pulmonary ventilation with oxygen, air, and a volatile agent. The inspired concentration of isoflurane was adjusted to achieve steady heart rate, arterial pressure, and end-tidal concentrations of isoflurane and carbon dioxide. Local anaesthesia skin infiltration was used to minimize stimulation.

A volume generator ventilator (Siemens Servo 900C, Solna, Sweden) delivered a mixture of oxygen and air to the patient from which all exhaled gas was collected into a mixing chamber. End-tidal carbon dioxide was measured with a capnograph (Hewlett Packard, Palo Alto, CA, USA), and exhaust from this instrument was directed into the expiratory mixing chamber. A mass spectrometer (Amis2000, Innovision, Denmark) measured inhaled and exhaled gas fractions and calculated minute ventilation oxygen consumption and carbon dioxide production.

The cardiac catheterization technique depended on cardiac anatomy but most often involved femoral vascular access. Catheters were inserted to measure both the pulmonary arterial and pulmonary venous pressures and oxygen content. In the presence of an intra-cardiac shunt, catheters were manipulated into the left atrium or pulmonary vein to determine pulmonary venous saturation and pressure. When no intra-cardiac shunt existed, systemic arterial blood samples and pulmonary capillary wedge pressures were measured instead. Intravascular pressures were measured using strain gauge pressure transducers and stored by a haemodynamic recording system (Siemens Sensis, Sweden). Total blood oxygen content was calculated from haemoglobin oxygen saturation measured by an oximeter (Radiometer, Copenhagen), and dissolved oxygen from blood gas analysis. CO was derived by the Fick principle and PVR was calculated from Ohms law. Cardiac index (CI) was calculated by dividing CO by body surface area. PVR was indexed (PVRI) using CI in the calculation, expressed in Woods units m^2 (see the Appendix). Surface area was estimated from the crown to heel length and body weight using a nomogram. Measurements were recorded during two conditions; first, a baseline, with low inspired oxygen concentration ($<25\%$) and second, attempted pulmonary vasodilatation using oxygen enrichment (60%) together with inhaled nitric oxide (20 parts per million).

Major complications were defined as hypotension, hypoxia or arrhythmia occurring during or within 24 h of anaesthesia that required resuscitation either by external cardiac massage, direct current electrical shock, rapid i.v. fluid bolus greater than 20 ml kg^{-1}, inotrope or anti-arrhythmic drug administration, unplanned tracheal intubation or mechanical ventilation. Minor complications were defined as transient self-limiting disturbances in blood pressure, oxygenation, or cardiac rhythm that required either minimal therapy (e.g. oxygen or fluid only) or no treatment at all.

The number and percentage of children with clinically important symptoms, physical signs, or results of investigations present before anaesthesia was calculated in the groups of children with and without complications (Table 2). To determine whether or not pulmonary artery pressure or resistance was related to important complications or clinical features, we compared the distributions of pressures and resistances between children who did and did not have complications or selected important clinical features.

Only data from 'first anaesthetics' were analysed and are presented with descriptive statistics. The frequencies of important features of disease in children with and without complications were compared by assessing using multiple Fisher's exact tests. *T*-tests were used to compare pulmonary artery pressures and resistances. $P < 0.01$ were considered significant because of the multiplicity of statistical comparisons.

Results

Of 75 consecutive patients catheterized over 5 yr, records were missing in four cases, insufficient in one and consequently only the remaining 70 were studied. Some patients

Table 1 Demographic details of all children. PHT was considered secondary if there had been communication, either closed or unclosed, between systemic and pulmonary circulations (ASD, VSD, AVSD = atrial, ventricular and atrioventicular septal defects, respectively; PDA = patent ductus arteriosus)

Sample size (n)	70
Male/female	27/43
Age range (mean) (yr)	0.1–18 (7.1)
Weight range (mean) (kg)	3.5–77 (24.7)
Type of PHT (*n*)	
Idiopathic	23
Secondary	47
Unclosed circulation communications (*n*)	
ASD (alone)	10
VSD (including AVSD)	12
PDA	3
Treatment with home oxygen (*n*)	24
Treatment with specific pulmonary vasodilators (*n*)	12

had more than one anaesthetic and therefore 'first' and 'subsequent' anaesthetics were considered separately. Of the 70, 23 had primary idiopathic PHT and the remainder had disease secondary to anomalies causing increased pulmonary artery pressure and flow (Table 1).

Complications occurred in 6 out of 70 patients; two had minor transient self-limiting arrhythmias, four had a major complication, one of whom died. These figures represent an overall major complication of approximately 6% for all cases and 13% (3 in 23) if primary disease is considered separately.

Table 2 Number (%) of children with pre-catheter features (aetiology, symptoms, physical signs, and results of investigations) who did and did not have major complications. Features are those that were noted in at least one child who had a major complication. See text and the Appendix for abbreviations

Features	**No major complications *n* = 66**	**Major complications *n* = 4**	***P*-value of Fisher's exact test**
Aetiology: idiopathic	20 (30)	3 (75)	0.09
Symptoms major			
Syncope or dizziness	5 (8)	2 (50)	0.05
Chest pain	4 (7)	0	1
Signs			
Hepatomegaly	16 (26)	2 (50)	0.3
Distended neck veins	5 (8)	1 (25)	0.3
ECG			
RV strain	13 (21)	1 (25)	1
CXR			
Oligaemic lungs	10 (16)	1 (25)	0.5
Large pulmonary vessels	33 (53)	2 (50)	1
Right atrial or ventricular dilatation			
Right ventricular echocardiography	30 (48)	3 (75)	0.6
Reduced contractility	31 (50)	3 (75)	0.6
Dilatation	55 (89)	4 (100)	1
Septal bulging	10 (16)	1 (25)	0.53
Hypertrophy	42 (70)	2 (50)	0.6
TR jet ≥ 4 m s^{-1}	40 (65)	4 (100)	0.3
ASD present	12 (19)	0	1

Table 3 Distributions (mean and SD) of cardiovascular variables related to pulmonary hypertension in children who did not have major complications compared with the four children who did. See text and the appendix for abbreviations

	TR jet	**mPAP**	**mPAP/ mSAP**	**PVRI**
Children without complications ($n = 62$)	4.17 (0.76)	51.1 (20.3)	0.86 (0.34)	17.5 (14.7)
Individuals with complications				
Child 1	4.6	68	1.03	31
Child 2	>6	31	0.47	Not done
Child 3	4.1	43	0.74	8
Child 4	5.3	60	1.18	43

There were 24 'subsequent' PVR studies; 16 patients had a second study and four patients had a third for atrial septostomy. Two patients had transient arrhythmias that were self-limiting. One major complication occurred in a 2-yr-old girl who had had syncopal attacks; she was catheterized in order to perform an atrial septostomy.

There was no statistic difference in the incidence of important pre-catheterization features, including symptoms, physical signs, and results of investigations, that were present in at least one child who had a major complication (Table 2). However, the power to detect any was low because of the size of the groups. There was no obvious link between anaesthesia management and any major complication. Of the 70 'first anaesthetics', echo assessments identified a TR jet in 66 patients; four did not have tricuspid regurgitation. Four had a TR jet velocity of <3 m s^{-1}, 25 had a jet velocity of 3–4 m s^{-1} and $37 >$ 4 m s^{-1}. All four patients with major complications had a TR jet greater than 4 m s^{-1} (Table 3). In those who had TR jet greater than 4 m s^{-1} and right ventricular dilatation, the rate of major complications was 12% and the death rate was 1 in 33 or 3%. In children without complications, there was a wide range of pulmonary artery pressures and resistances (Table 3). Pulmonary artery pressures and resistances tended to be higher in children with major symptoms (Table 4).

Discussion

In this series of cardiac catheterization, the overall risk of requiring cardiac massage was 5.7% (binomial 95% confidence limits 1.6–14%). The risk increased to 13% in children with primary PHT. Risk may also be increased if there are major symptoms, such as syncope, dizziness, and chest pain, or if the TR jet >4 m s^{-1}. However, firm conclusions cannot be made because the number of children with complications was too small. We believe that cardiac arrest was related to the mechanical effects of

Table 4 Mean (SD) of pulmonary artery pressures and resistances in children who did and did not have major symptoms of PHT (either dizziness, syncope or chest pain). See text and the Appendix for abbreviations

	TR jet	mPAP	mPAP/ mSAP	PVRI
Without major symptoms ($n = 59$)	4.15 (0.77)	49.6 (21.2)	0.84 (0.36)	16.4 (15.2)
With major symptoms ($n = 7$)	4.42 (0.69)	58.4 (10.7)	0.94 (0.19)	23.8 (12.3)
T-test, *P*-value	0.27	0.05	0.18	0.1

catheterization in two of the four cases. The overall complication rate of cardiac catheterization in children under general anaesthesia has been described,[4] but there are no data published specific to investigation of pulmonary hypertension. The rate of major complications in a series of adults having PVR studies under local anaesthesia was 4 out of 202 (2%), of whom three died.[3] Intensive care is necessary when there is a major complication and we always make sure that it is available before a PVR study. If the procedure has been uneventful, our policy is to monitor the child in a high dependency area for at least 4 h before transfer to the ward.

It is widely believed that cardiac decompensation follows an acute rise in PVR and that this can be prevented by maximum oxygenation, hypocarbia, alkalosis, and opioid administration.[8] In many of our patients, PVR may have been fixed and, therefore, a strained pulmonary ventricle is more likely to fail due to ischaemia, or depression by anaesthesia agents, than due to a rising PVR. Furthermore, the systemic ventricle can be compressed by the dilated pulmonary ventricle which reduces its stroke volume.[9 10] The inevitable reduction in CO could reduce crucial coronary artery blood flow.[10–12] An atrial septal defect (ASD) may be protective during a pulmonary hypertensive crisis because it allows a right to left shunt that maintains systemic ventricular filling. This causes a degree of systemic desaturation but tissue oxygen delivery is maintained because CO increases.[13 14]

We try to avoid any triggers of PHT but do not use high-dose opioid routinely. Instead, our priority is to maintain the systemic pressure. Anaesthesia is maintained by adjusting isoflurane concentrations to maintain a steady heart rate and arterial pressure. Recently, we have begun to use a BIS monitor to guide the use of isoflurane, not only to help avoid potentially dangerous doses of anaesthetic agent, but also minimize explicit recall.

The World Health Organization have classified PHT, based on invasive measurements.[15] Non-invasive estimation of the PAP can be made using echocardiography. The velocity of blood through an incompetent tricuspid valve relates to the pressure difference according to the modified Bernoulli equation, although there are several limitations, for example, where there is pulmonary stenosis or heart failure the right atrial pressure is often elevated.[16] TR jet measurement is not always possible and for this and other echocardiographic measurements there is appreciable inter-observer error, even with experienced technicians.

Determination of direct vascular and intra-cardiac pressures by catheterization is still the gold standard of assessment. This is much easier in young children when they are in a stable haemodynamic state under general anaesthesia rather than sedation, which may have a variable effect. Also, CO measurements rely upon collection of expired gas which may be less accurate without tracheal intubation.

Catheter assessment of pulmonary vascular disease allows selection of drug treatment, prognosis, assessment for transplantation and, if necessary, the creation of an atrial septostomy. This retrospective audit has allowed us to provide better information to parents and children so that they, and we, can achieve the right balance between risk and benefit.

This retrospective audit describes the risk of major complications in 70 children with PHT having a general anaesthetic for cardiac catheterization. We found that resuscitation by external cardiac massage was required in 5.7% of patients (95% CI 1.6–14%) and one child died. The risks may be higher in children with severe idiopathic pulmonary artery hypertension causing recurrent syncope or dizziness.

Appendix

Definitions and abbreviations of cardiovascular variables

Direct measurement of pulmonary artery pressure

$$\text{mPAP} = \text{mean systolic pulmonary artery pressure } (\text{mm Hg}).$$

$$\text{mSAP} = \text{mean systolic systemic artery pressure } (\text{mm Hg}).$$

Indirect estimation of pulmonary artery pressure

$$\text{TR jet} = \text{velocity of tricuspid regurgitation } (\text{m s}^{-1}).$$

The pressure gradient between the right ventricle and pulmonary artery was estimated by the following calculation based on a modification of the Bernoulli equation. Pulmonary artery pressure (mm Hg) = 4 (TR jet velocity).[2] For example, if velocity = 4 m s^{-1}, pressure = 64 mm Hg.

Cardiac output

$$\text{Cardiac index (CI)} = \text{Cardiac output/body surface area}$$

By the Fick principle, cardiac output = oxygen consumption/(difference in arterial − venous oxygen content).

Pulmonary vascular resistance

PVRI = pulmonary vascular resistance index;

international units are 'Woods units m^2'

$$\text{PVRI} = \frac{\text{mean pulmonary artery pressure} - \text{mean pulmonary vein pressure}}{\text{cardiac index}}$$

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