How common is severe pulmonary hypertension after pediatric cardiac surgery?

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Background: Pulmonary hypertension may result in significant morbidity and mortality after pediatric cardiac surgery. The objective of this study was to determine the incidence and outcome of severe pulmonary hypertension, defined as a ratio of pulmonary to systemic arterial pressure equal to or greater than 1.0, after cardiac surgery in children.

Methods: Data from all children younger than 18 years who had undergone cardiothoracic surgery from January 1, 1994, to December 31, 1998, were examined. To find children with severe pulmonary hypertension, we reviewed intensive care unit charts from patients who had been monitored with a pulmonary artery catheter after the operation (n = 151), had received mechanical ventilation for more than 4 days after the operation (n = 124), or had died in the operating room or the intensive care unit (n = 22). Intraoperative and postoperative measurements of mean pulmonary arterial pressure and postoperative echocardiographic studies during the first 3 postoperative days were used to select the children.

Results: During the study period, 1349 children (including 164 neonates and 511 infants, median age 12 months) underwent cardiac operations with an overall perioperative mortality of 22 patients (1.6%). Twenty-seven children (2%, median age 4.2 months) had severe pulmonary hypertension. Of these, 2 (7.4%) died within 30 days of the operation, and 3 others (11%) died within a year (median follow-up 53 months). Nitric oxide inhalation was used in 5 of the 27 cases, and it probably saved the life of 1 patient, may have helped in 1 case, and had no discernible effect in 3 cases. Severe pulmonary hypertension was most common after correction of complete atrioventricular septal defects (14%, n = 12/85). Thirteen of 131 children with Down syndrome (9.9%) had severe pulmonary hypertension.

Conclusion: Severe postoperative pulmonary hypertension occurred after 2% of the cardiac procedures and in most cases was managed successfully with conventional treatment and had a favorable postoperative outcome. The low incidence relative to previous reports may reflect the benefits of early correction and improved intraoperative and postoperative care.

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Postoperative pulmonary hypertension (PH) is a feared complication after heart surgery in children in whom increased pulmonary blood flow, pulmonary venous obstruction, or both, have caused increased pulmonary vascular resistance (PVR) and reactivity.[1,2] The operative trauma (eg, the endothelial injury caused by cardiopulmonary bypass [CPB])[3] may further increase pulmonary vascular reactivity and create a situation in which moderate postoperative stress dramatically increases PVR. In

TABLE 1. Pediatric heart operations according to the risk classification used by the Swedish National Health Institute

Group 1	Group 2A	Group 2B	Group 2C	Group 3A	Group 3B	Group 3C
ASD secondary	TOF	AVSD	Switch	VSD plus conduit	Fontan or TCPC	Prematurity (< 1500 g)
ASD primary	VSD plus AS	TOF plus conduit	Mustard	Bidirectional Glenn	Septation	TAPVD plus UVH
VSD	VSD plus PS	Peripheral PS	Senning	PA plus VSD (conduit)	Complex Glenn plus (eg) VSD enlargement	AVSD plus LV hypoplasia
PS, age >1 mo	VSD plus coarctation	DORV		CTGA (conduit)	Complex switch plus (eg) VSD closure	AS plus LV hypoplasia
AS, age > 1 y	ASD plus PAPVD	Multiple VSDs		PA plus IVS	Complex DORV	HLHS
	Common atrium	CTGA: VSD closure		Critical PS	Taussig-Bing	
	AS, age 1-12 mo	AS, age <1 mo		Unifocalization	TAPVD, age <1 mo	
		MS, MR, age >1 y		Atrial septectomy	Rastelli	
		TOF plus LAD (Dx)		MR, MS, age <1 y	Aortic root reconstruction	
		Absent pulmonary valve		TAPVD, age >1 mo	Konno, Ross	
				AP window	Truncus arteriosus	
				ALCAPA	IAA	
				Cor triatriatum	Damus-Kaye-Stansel	
				Multiple sternotomies, if not 3B	AVSD plus TOF	

Both general conditions and specific corrective procedures are listed. *ASD*, atrial septal defect; *AVSD*, atrioventricular septal defect; *TOF*, tetralogy of Fallot; *VSD*, ventricular septal defect; *TCPC*, total cavopulmonary connection; *AS*, aortic stenosis; *TAPVD*, total anomalous pulmonary venous return; *UVH*, univentricular heart; *PS*, pulmonary stenosis; *PA*, pulmonary atresia; *LV*, left ventricular; *DORV*, double-outlet right ventricle; *CTGA*, congenital corrected transposition of the great arteries; *PAPVD*, partial anomalous pulmonary venous return; *IVS*, intact ventricular septum; *HLHS*, hypoplastic left heart syndrome; *MS*, mitral stenosis; *MR*, mitral regurgitation; *LAD (Dx)*, descent of left anterior descending coronary artery from right coronary artery; *AP*, aortopulmonary; *ALCAPA*, anomalous left coronary artery from pulmonary artery; *IAA*, interrupted aortic arch.

children with decreased right ventricular contractility, this may result in acute right ventricular dilation, circulatory collapse, and death.

It is probable that corrective surgery on younger children (as is currently common practice) and improvements in perfusion technology and perioperative care have both decreased the risk of PH and improved its outcome. Intraoperative ultrafiltration[4] and selective decrease of PVR by administration of inhaled nitric oxide (NO)[5,6] have shown promising results and are now routinely used in many institutions. The creation of larger pediatric surgery programs may also have promoted early recognition and treatment of PH, thus increasing the chances of a positive outcome.[7]

This study was designed to determine the incidence and clinical outcome of severe postoperative PH. This was defined as increase in mean pulmonary arterial pressure (PAP) to the level of systemic mean arterial pressure (MAP) or greater.

Patients and Methods

Data on all children younger than 18 years who underwent cardiac surgery in our institution during a 5-year period (January 1, 1994–December 31, 1998) were retrieved from an intensive care data base. The children were classified according to risk as recommended by the Swedish National Board of Health and Welfare (Table 1).[8] Several patients underwent more than one operation, but in the text and statistical assessment each operation is referred to as one individual when not otherwise indicated.

To select children with or at risk for clinically important PH, we studied all children who were monitored with pulmonary artery catheters after the operation (n = 151), who needed mechanical ventilation longer than 4 postoperative days (n = 124), or who died in the operating room or intensive care unit (ICU, n = 22). Inclusion of children who had PAP continuously monitored after the operation was likely to select most patients with severe PH, because pulmonary artery catheters were routinely placed in children deemed at risk for postoperative PH and in whom intraoperative, postbypass cardiac pressure recordings indicated such a risk. The pulmonary artery catheter was placed in the main pulmonary

artery through the right ventricular infundibulum by the surgeon. Recognizing that severe PH might also have occurred in children without PAP catheters, but believing that severe PH would influence the postoperative course, we added the second and third selection criteria. We thus reviewed 234 charts from which further information was obtained. Seventy-eight children could be excluded because they had cardiac anomalies or had undergone corrections not compatible with PH (eg, tetralogy of Fallot, pulmonary stenosis or atresia, cavopulmonary connections, and the Norwood procedure for hypoplastic left heart syndrome).

In the 156 children remaining after exclusions, the degree of PH was classified as follows: as none or mild when mean PAP was normal or only transiently elevated above 30 mm Hg, as moderate when mean PAP exceeded 30 mm Hg on more than 3 occasions after the operation but did not reach MAP levels, as severe when mean PAP was at least as great as MAP, and as a PH crisis when mean PAP equal to or greater than MAP was combined with a decrease in MAP. In the text, severe PH and PH crisis are collectively referred to as *severe PH.* In 122 of the 156 cases the classification was guided by recorded data obtained from continuous postoperative pulmonary arterial pressure monitoring. In the cases of the 34 children without a pulmonary artery catheter, the classification was based on pulmonary arterial or right ventricular pressure measurements done in the operating room directly after the surgical correction and on PAPs calculated from velocities of the tricuspid or pulmonary valve regurgitations obtained by echocardiographic Doppler studies in the ICU. It should be noted that our selection criteria would discriminate children with severe PH but give no information about the incidences of no PH, mild PH, and moderate PH. In addition, we reviewed charts of all children who had undergone correction of complete atrioventricular septal defects (AVSDs, n = 85) and children with Down syndrome (n = 131).

Perioperative or early mortality was defined as death occurring during the operation or within 30 days of the operation. ICU morbidity was expressed as duration of ventilatory support, duration of ICU stay, and number of registered complications. The latter were classified as follows: circulatory complications were noted when at least two inotropic drugs were used or a myocardial infarction was diagnosed in the postoperative period; respiratory complications were noted when stridor, obstruction, pulmonary secretion, pulmonary edema, respiratory bronchitis, pneumothorax, hemothorax, atelectasis, or pulmonary aspiration occurred and required specific treatment; infectious complications were noted when septicemia, wound infection, gastroenteritis, urinary tract infection, or upper airway infection was diagnosed; renal complications were noted when hemodialysis or peritoneal dialysis was used; and neurologic complications were noted when seizure, cerebral infarction, cerebral bleeding, peripheral nerve palsy, or clinical disturbance of consciousness or motor function was recognized.

To determine the risk of late death among children with severe PH, follow-up data were obtained from the Swedish Census Bureau and referring cardiology departments.

Intraoperative and Postoperative Routines

Anesthesia was induced with thiopental and maintained with low to moderate doses of fentanyl, pancuronium, halothane or isoflurane (inhaled concentration $\leq$1%), and nitrous oxide. All patients received antibiotics intravenously, and children weighing less than 10 kg were given dexamethasone (1 mg/kg intravenously) immediately after induction of anesthesia. CPB was managed with nonpulsatile perfusion, a membrane oxygenator (Cobe VPCML; Gambro AB, Stockholm, Sweden) and arterial line filters (Dideco D733 or D736; Dideco Scandinavia, Malmo, Sweden). The circuit was primed with crystalloids, mannitol, 20% albumin, buffer solution tris(hydroxymethyl)aminomethane, and erythrocyte concentrate as needed to keep the hemoglobin concentration around 70 g/L. Cold crystalloid cardioplegia was used for all procedures requiring aortic crossclamping. Ultrafiltration was introduced in 1996 and was used to decrease excessive fluid overload in the bypass circuit for 10 to 15 minutes during rewarming in 84 of the 812 children operated on between 1996 and 1998.

After the operation, all patients were monitored with arterial and central venous pressure catheters. Pulmonary artery catheters were placed during the operation as indicated by intraoperative measurements and preoperative studies. Arterial and central venous blood gas values were monitored as needed. Intraoperative transesophageal echocardiography was used only occasionally. Children with complex lesions or with hemodynamic instability had transthoracic or transesophageal echocardiographic studies done in the ICU.

All patients, including neonates and infants, were intubated with cuffed endotracheal tubes, and intraoperative and postoperative ventilation was maintained with volume- and pressure-controlled ventilation, respectively, with a Siemens 900 C ventilator (Siemens, Solna, Sweden). Patients for whom cardiac function prohibited immediate discontinuation of CPB were usually treated with low-flow CPB in the operating room until cardiac function had improved. During the study period, postoperative mechanical circulatory support was used for 1 patient with left ventricular failure.

Children at risk for or with signs of postoperative PH were sedated, received mechanical ventilatory support, and usually received inotropic support (dobutamine, dopamine, or both) and nitroglycerine infusion. PH crisis reactions were treated with manual hyperventilation with 100% oxygen and intravenously administered opiates (usually fentanyl at 5-10 μg/kg). NO inhalation is not an approved medical therapy in Sweden and was therefore only used when PH was considered life-threatening and other therapeutic measures were ineffective. For patients with PH, mechanical ventilation was continued until the PAP was well-controlled or echocardiographic studies and the clinical course indicated that myocardial function had recovered. After extubation and when there was no longer any need for invasive monitoring or vasoactive drugs, the child was transferred to the ward.

Statistical Analysis

Data were analyzed with the STATISTICA for Windows software package (StatSoft Inc, Tulsa, Okla). Descriptive statistics are expressed as median and range. The Mann-Whitney *U* test was used for comparisons of quantitative variables and followed by Bonferroni correction when multiple comparisons were done. Qualitative variables were compared with the χ^2 test.

TABLE 2. Cardiac surgery in Lund during the study period of January 1, 1994, through December 31, 1998

Group	Premature infants*		0-1 mo		1-12 mo		1-17 y		Total		Operative risk
	All	Deaths†	All	Deaths†	All	Deaths†	All	Deaths†	All	Deaths†	
1	0	0	0	0	130	0	256	1	386	1	0.3%
2A	0	0	3	0	91	0	74	0	168	0	0.0%
2B	0	0	13	0	123	2	34	0	170	2	1.2%
2C	1	0	47	1	2	0	1	0	51	1	2.0%
3A	1	0	16	0	84	4	120	0	221	4	1.8%
3B	3	0	44	2	54	2	163	0	264	4	1.5%
3C	4	0	32	5	27	4	20	1	83	10	12.0%
Transplantation	0	0	0	0	0	0	6	0	6	0	0.0%
Total	9	0 (0.0%)	155	8 (5.2%)	511	12 (2.3%)	674	2 (0.3%)	1349	22	1.6%

The patients are classified according to risk as recommended by the Swedish National Health Institute (see Table 1).
*Infants weighing less than 2500 g.
†Perioperative death, within 30 days after operation.

Results

During the study period, a total of 1349 patients underwent cardiac procedures. Twenty-two (1.6%) died within 30 days of surgery. The mortalities in different age and risk groups are shown in Table 2.

Severe PH was observed in 27 patients, for an overall incidence of 2.0% (n = 27/1349). PH crises occurred in 9 of these children (0.7%, n = 9/1349; Table 3). The PH classification was based on direct measurements of PAP in 26 cases and on intraoperative pressure measurements and postoperative Doppler measurements in 1 case. Two infants with severe PH died within 30 days (7.4%, n = 2/27). Both deaths occurred immediately after correction. The infants, a 5-week-old girl with a ventricular septal defect and bilateral pulmonary venous stenosis and a 3-month-old boy with an AVSD, had suprasystemic right ventricular pressure, tricuspid insufficiency, and severe right to left shunting with a transcutaneous oxygen saturation of 40% to 80%. At the end of the correction both infants had severe PH, and inotropic support and prolonged mechanical support with low-flow CPB were both ineffective. Postmortem examination showed advanced muscle hypertrophy in the small arteries and intimal proliferation and small vessel occlusion in the pulmonary circulation.

Children with severe PH were younger, needed longer postoperative ventilation, stayed longer in the ICU, and had more circulatory and renal complications than did the other children (Table 4). Inhalation of NO was used in 5 cases of severe PH. Inhaled NO was tried for the 2 children with PH crises who died during the operation after the surgical correction, but it had no effect on PAP. In 1 case NO inhalation was given before the operation, but the patient could easily be weaned during the operation. NO inhalation probably saved the life of 1 patient, may have helped in 1 case, and had no discernible effect in 3 cases.

The median follow-up for the 25 surviving children with severe PH was 53 months (range 13-70 months). Most patients (n = 17/27) had signs of residual PH on echocardiographic studies before discharge from our hospital (tricuspid insufficiency with a maximum velocity >2.5 m/s). Three children (n = 3/27, 11%) 4 months, 4 months, and 7 weeks old at operation died 205, 211, and 218 days after the operation, respectively. All 3 had been in need of long ICU treatment after the initial operation (24, 19, and 49 days, respectively). Two of these children had a hypoplastic left ventricle, a hypoplastic mitral valve, or mitral stenosis and persistent severe PH and needed prolonged and repeated hospitalizations for the remainder of life. One child had undergone correction with two-patch technique for an unbalanced AVSD and had normal PAP at discharge from the hospital (maximum velocity in tricuspid insufficiency of 2 m/s) but died suddenly 6 months later in what was interpreted as arrhythmia.

There was clear overrepresentation of children with AVSD (n = 12) and children with Down syndrome (n = 12) among those with severe PH. These two groups were therefore studied more closely (Tables 5 and 6). Of the 85 children with complete AVSD who underwent biventricular correction during the study period, records of 56 had been retrieved with the selection criteria, whereas those of 29, because of lack of pulmonary arterial catheter monitoring and an uncomplicated postoperative course, had not. The charts of the latter 29 patients were reviewed, and the patients were classified. None of these patients had signs of severe PH and were therefore classified as having none or moderate PH. Thus of the 85 children, 86% (n = 73/85) had no, mild, or moderate PH, 14% (n = 12/85) had severe PH, and 4.7% (n = 4/85) had PH crises. Children with AVSD who had severe PH had longer perfusion and aortic cross-clamp times, needed longer mechanical ventilation, and spent longer time in the ICU than did those who had no, mild, or moderate PH, but there was no difference in mor-

TABLE 3. Patients with PH crisis

Age at operation	Preoperative diagnosis	Operation	Postoperative course	Survival
5 wk	Bilateral pulmonary venous stenosis plus VSD	Resection of bilateral pulmonary vein stenosis plus suture of VSD	Died in operating room	Died d 0
7 wk	Hypoplastic LV plus hypoplastic mitral valve (MS) plus ASD plus Down syndrome	Exploration of mitral valve plus closure of ASD	Possibly too small LV, postoperative pneumonia	Died d 218
3 mo	Complete AVSD	Correction of AVSD with 2-patch technique	Died in operating room	Died d 0
3 mo	TGA plus VSD	Arterial switch operation plus closure of VSD with patch plus resuture of coronary artery	LV failure	
4 mo	Unbalanced AVSD plus Down syndrome	Correction of AVSD with 2-patch technique	Possibly arrhythmia	Died d 205
6 mo	Complete AVSD plus Down syndrome	Correction of AVSD with 2-patch technique	LV failure	
13 mo	Supravalvular MS plus parachute mitral valve plus previous VSD operation	Resection of supravalvular membrane plus commissurotomy	MR, reoperated, with no MR or PH afterward	
2 y	Unbalanced AVSD plus Down syndrome	Correction of AVSD with 2-patch technique		
3 y	Congenital MR plus left pulmonary vein stenosis	Revalvuloplasty of mitral valve	MR	

VSD, Ventricular septal defect; *AVSD*, atrioventricular septal defect; *LV*, left ventricle; *MS*, mitral stenosis; *ASD*, atrial septal defect; *TGA*, transposition of great arteries; *MR*, mitral regurgitation.

tality or age at operation between the two groups (Table 5). The early mortality among children with AVSD was 2.4% (n = 2/85).

Of the 12 children with AVSD who had severe PH, 10 also had Down syndrome. Down syndrome may, however, be an independent risk factor for severe PH. Of the 131 patients with this diagnosis, 59 had been identified as "at-risk patients." None of the other 71 patients had a postoperative course complicated by severe PH. The incidence of severe PH among children with Down syndrome was thus 9.9% (n = 13/131) and the early mortality was 0.8% (n = 1/131). As could be expected, children with Down syndrome who had severe PH needed longer mechanical ventilation and ICU treatment and had longer perfusion and aortic crossclamp times than did children with Down syndrome who had no, mild, or moderate PH, but the ages at operation were not different between the two subgroups (Table 6).

Discussion

In this retrospective study, we found a 2% incidence of severe PH and a 0.7% incidence of PH crisis after cardiac surgical procedures. These rates are lower than has been reported earlier. One obstacle when comparing the incidence of PH, however, is that the criteria for PH, most notably the criteria for clinically important or severe PH, vary in the literature. We chose to define severe PH as a mean PAP that rose to equal or exceed MAP, because we were interested in selecting patients with a PAP increase that had a clear impact on postoperative care and outcome. Because we did not measure postoperative PAP in all children, but only in those believed to be at risk for postoperative PH, we cannot exclude the possibility that some children with transient increases in PAP, even to suprasystemic levels, may have been missed. If this did occur, however, the clinical consequences were obviously not dramatic, because none of these children died or were in need of more

TABLE 4. Intraoperative and postoperative characteristics of the total study population and of children with severe PH

	All children	Severe PH	*P* value
No. of patients	1349	27	
Perioperative deaths (No.)	22 (1.6%)	2 (7.4%)	
Perfusion time (min, median and range)	81 (11-650)	124 (44-620)	<.001
Aortic crossclamp time (min, median and range)	35 (53-172)	71 (4-172)	<.001
Postoperative mechanical ventilation (d, median and range)	0.6 (0-86.6)	7.7 (0.7-45.6)	<.001
Time in ICU (d, median and range)	3.0 (1.0-87.0)	9.0 (0-48)	<.001
Age at operation (mo, median and range)	11.9 (0.03-219)	4.2 (0.03-59)	<.05
Complications			
Circulatory	12.8%	33.3%	<.001
Respiratory	14.1%	25.9%	.073
Renal	4.8%	18.5%	<.001
Infectious	3.2%	7.4%	.474
Neurologic	2.5%	0%	.031

TABLE 5. Clinical findings in children operated for complete AVSD

	No PH, mild PH, or moderate PH (*n* = 73)		Severe PH (*n* = 12)		
	Median	Range	Median	Range	*P* value
Time on ventilator (d)	0.9	0.1-63.7	7.3	0-36.3	<.001
Perfusion time (min)	109	70-333	138	101-540	.003
Aortic crossclamp time (min)	69	34-123	76	60-88	.028
Time in ICU (d)	3	2-64	9	1-42	<.001
Age at operation (mo)	4.2	0.6-81	4.2	3.3-26	.435

TABLE 6. Clinical findings in children with Down syndrome

	No PH, mild PH, or moderate PH (n = 118)		Severe PH (n = 13)		
	Median	Range	Median	Range	*P* value
Time on ventilator (d)	0.8	0-63.7	7.7	0.9-44.6	<.001
Perfusion time (min)	92	22-301	129	44-325	.01
Aortic crossclamp time (min)	49	0-117	76	4-88	.035
Time in ICU (d)	3	2-64	12	4-49	<.001
Age at operation (mo)	6.2	0.6-219	4.2	1.3-26	.197

than 96 hours of postoperative mechanical ventilation. We thus believe that our study design did select all children with clinically important PH. We also made a clear distinction between children with PH who had a sustained stable MAP and those who did not (PH crisis). In the literature critical or severe PH is usually defined as a PAP that is close to or exceeds MAP, although some have called this a "minor PH crisis" or a "PH event."[5,6,9-11] As was the case in this study, the designation *PH crisis* has mostly been reserved for situations in which PAP acutely exceeds MAP and is accompanied by a fall in MAP, a fall in arterial or venous oxygen saturation, or both.

Previous studies have thus reported both higher incidences of and higher mortalities associated with severe PH. In 1991, Hopkins and colleagues[12] prospectively investigated the incidence of PH crisis and observed a 10 times greater incidence (7.6%) than we did. Moreover, they found a mortality of 54.5% among children with PH crisis,[12] as compared with 22.2% (n = 2/9) among our patients. Our mortality among patients with severe PH—7.4% (n = 2/27) died during the first 30 days after the operation—is also lower than that observed by Bando and coworkers.[9] These authors used a more generous definition of severe PH (with a PH event defined as PH crisis *or* systolic PAP more than

50% of MAP continuing for >6 hours after repair) and found a mortality of 18.5% (n = 10/54) in 1980 through 1984 and a mortality of 35.5% (n = 11/31) in 1990 through 1994.[9]

Study Population and Incidence of Severe Pulmonary Hypertension

We think that it is unlikely that our lower incidence and mortality were due to the differences in study design. Rather, they may reflect the differences in the population of children admitted to surgery and possibly recent improvements in intraoperative and postoperative care. The two factors that are most likely to influence the incidence of severe PH are probably the diagnosis and the age of the patient at surgery. The diagnoses and age distribution of our patients (Tables 1 and 2) are probably representative of the situation in other Scandinavian and northern European centers, but the incidence would be expected to be higher in institutions that operate on a relatively larger number of patients with diagnoses associated with PH or in those with patients operated on later, with more advanced disease. In addition to AVSD, the diagnoses most commonly and traditionally associated with severe PH are transposition of the great arteries, truncus arteriosus, total anomalous pulmonary venous drainage, and ventricular septal defect.[9,12] Our study design did not allow a multiple regression risk analysis, but our findings suggest that the presence of pulmonary venous obstruction—as can be seen in patients with pulmonary venous stenosis, mitral stenosis or regurgitation, and elevated left atrial pressure as a result of left ventricular failure—was a more important predictor of severe PH than was the diagnosis itself. When we reviewed the other 20 perioperative deaths during the study period, we found that most of them were of neonates and infants with the most complex cardiac defects. An increased PVR may have played an important role in several of these deaths, making it clear that subsystemic increases in PAP are not harmless. Clearly, moderate increases in PVR and PAP may be life threatening in patients with a Fontan circulation or in patients with a failing right ventricle. In this study the median age of infants with severe PH was 4.2 months, and only 4 of the patients were more than 1 year old. This reflects the structure of the Swedish health system, which promotes early diagnosis and treatment, so that rather few patients are referred at a late stage of their disease.

Intraoperative and Postoperative Care

Early identification and treatment of PH and improvements in intraoperative and postoperative treatment may also have contributed to the lower incidence and more effective treatment of severe PH. One would like to believe that the increase in caseload and experience that occurred after the centralization of Swedish pediatric cardiac surgery in 1993, which increased the population of the Lund University Hospital referral area to approximately 5 million inhabitants, promoted early detection and improved outcome,[13] but the number of patients with severe PH was too small to detect any clear changes in the annual incidences or outcomes during the study period.

CPB induces pulmonary endothelial cell injury and pulmonary dysfunction, probably from hypoperfusion of the lung during CPB or activation of the systemic inflammatory response, which exacerbates the reactivity of the pulmonary vascular bed. This may result in inhibition of NO production[3] and increase in the production of endothelin 1 after CPB.[14,15] Several interventions, including dexamethasone, ultrafiltration, aprotinin, leukocyte depletion, antioxidants, and heparin-coated circuits,[4,16-19] may decrease the inflammatory response during CPB, but more studies are needed to clarify whether their use is really cost-effective. Of these, only dexamethasone and ultrafiltration were used in this study.

Treatment for PH can be regarded as a bridge until the increase in PVR has subsided or the right ventricle is able to cope with the increased PVR. In our study no patient with severe PH died in the ICU, indicating that treatment today is usually successful, albeit long and sometimes challenging. As is the case in most ICUs, our treatment (see the Methods section) is only partially based on scientific data. Rather, it reflects local tradition and our own experiences and biases. Inhalation of NO can selectively decrease mean PAP and improve arterial and venous oxygen saturation, and it is the preferred treatment for severe postoperative PH in many centers.[6,10,11] In Sweden, NO treatment is only allowed when conservative treatment is ineffective and the patient has life-threatening PH. In this study severe PH could usually be managed with conventional therapies. NO inhalation was only used for 5 patients with life-threatening PH. One patient was probably saved by the treatment, but neither of the 2 children with PH-associated death had any response. We can, of course, not exclude the possibility that a more liberal use of NO inhalation would have improved postoperative care and shortened the ICU stay. On the other hand, a more generous use of NO might have created a risk for overtreatment and prolonged ICU stay. We believe that the function of the right ventricle is an important guide for treatment and weaning from mechanical ventilation, and we usually do not await normalization of PAP before extubation. The failure of the operation to achieve a competent mitral valve is an important factor leading to postoperative PH and may be a predictor of outcome. Most children with mitral regurgitation could be weaned from the ventilator after improved medical treatment and in some cases after several trials of extubation.

All our children with PH crises had multiple episodes of high PAP. In other institutions, some of them would perhaps

have been candidates for extracorporeal membrane oxygenation. Again, it should be noted that conservative ICU treatment was successful; none of our patients with severe PH died in the ICU. Obviously we cannot exclude the possibility that extracorporeal membrane oxygenation would have saved the lives of the 2 infants who died in the operating room, but their responses during prolonged low-flow CPB make this unlikely. When it comes to other measures that may be helpful for patients with PH, Bando and coworkers[9] found that α-blockers and continuous monitoring of systemic venous saturation were both beneficial. Neither was used in our case series.

Although the immediate outcome of patients with severe PH were good, all had long ICU stays (Table 4). We thus expected significant late morbidity and mortality in the group. The rather low late mortality (n = 3/27) was therefore encouraging.

Incidence and Outcome Among Children with AVSD and with Down Syndrome

Complete AVSD was the most common diagnosis among children with severe PH. The high incidence of PH in this patient group may have been due to the combination of pulmonary overcirculation and increased pulmonary venous pressure seen with this anomaly. In addition, 10 of the 12 children with severe PH also had Down syndrome, which entails a higher incidence of airway obstruction and nocturnal hypoxia.[20,21] Children with complete AVSD who show clinically important PH have been reported to have a high mortality rate (55%).[9] This is in contrast to the 17% observed in this study. Only 1 of the 12 children with complete AVSD who had suprasystemic PAP (7.7%) died, and the total mortality in the AVSD group was only 2.4% (n = 2/85), indicating that further improvement in the treatment of this category of children has occurred.[22,23]

Down syndrome is often associated with congenital heart disease, and data suggest that children with Down syndrome have a propensity toward early development of severe damage to the pulmonary vascular bed.[24,25] In our study children with Down syndrome were equally distributed among the different grades of PH and had a mortality of 0.8% (n = 1/131). Thus children with Down syndrome who underwent cardiac surgery had a survival similar to that of a comparable group of children without Down syndrome. This was also true for children with AVSD; children with AVSD and Down syndrome did not have a higher mortality than did other children with AVSD. This differs from the findings of Reller and Morris,[26] who reported a 13% mortality for children with Down syndrome and complete AVSD but a mortality of only 5% for other children with AVSD. We believe that early correction of AVSD in children with Down syndrome is an important strategy to avoid postoperative PH. All children with AVSD now undergo correction before the age of 3 to 4 months.

In conclusion, the incidence of systemic or suprasystemic PAP was 2% in our patient population, and most children who had such reactions had favorable postoperative outcomes. Only 2 of the 22 deaths during the study period were related to PH crisis. Long-term survival was surprisingly good, and late deaths occurred in only 3 cases of ventricular imbalance. We believe that early surgery, the preoperative condition, and the local referral pattern are important contributing factors for the low incidence of severe PH and PH crisis.

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