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Preterm Infants With Congenital Heart Disease and Bronchopulmonary Dysplasia: Postoperative Course and Outcome After Cardiac Surgery

Colin J. McMahon, MRCPI*; Daniel J. Penny, MD¶; David P. Nelson, MD, PhD#; Anne M. Ades, MD**;
Salim Al Maskary, MRCP¶; Michael Speer, MD‡; Julie Katkin, MD§; E. Dean McKenzie, MD||;
Charles D. Fraser, Jr, MD||; and Anthony C. Chang, MD*

ABSTRACT. *Objective.* Success in treatment of premature infants has resulted in increased numbers of neonates who have bronchopulmonary dysplasia (BPD) and require surgical palliation or repair of congenital heart disease (CHD). We sought to investigate the impact of BPD on children with CHD after heart surgery.

Methods. This was a retrospective, multicenter study of patients who had BPD, defined as being oxygen dependent at 28 days of age with radiographic changes, and CHD and had cardiac surgery (excluding arterial duct ligation) between January 1991 and January 2002. Forty-three infants underwent a total of 52 cardiac operations. The median gestational age at birth was 28 weeks (range: 23–35 weeks), birth weight was 1460 g (range: 431–2500 g), and age at surgery was 2.7 months (range: 1.0–11.6 months). Diagnoses included left-to-right shunts ($n = 15$), conotruncal abnormalities ($n = 13$), arch obstruction ($n = 6$), univentricular hearts ($n = 4$), semilunar valve obstruction ($n = 3$), Shone syndrome ($n = 1$), and cor triatriatum ($n = 1$).

Results. Thirty-day survival was 84% with 6 early and 6 late postoperative deaths. Survival to hospital discharge was 68%. There was 50% mortality for patients with univentricular hearts and severe BPD. The median duration of preoperative ventilation was 76 days (range: 2–244 days) and of postoperative ventilation was 15 days (range: 1–141 days). The median duration of cardiac ICU stay was 7.5 days (range: 1–30 days) and of hospital stay was 115 days (range: 35–475 days). Current pulmonary status includes on room air ($n = 14$), O₂ at home ($n = 4$), and ventilated at home ($n = 4$) or in hospital ($n = 4$), and 5 patients were lost to follow-up.

Conclusions. BPD has significant implications for children who have CHD and undergo cardiac surgery, leading to prolonged ICU and hospital stays, although most survivors are not O₂ dependent. Postoperative mortality was highest among patients with univentricular hearts and severe BPD. Optimal timing of surgery and strategies to improve outcome remains to be delineated. *Pediatrics* 2005;116:423–430; *bronchopulmonary dysplasia*, *congenital heart disease/defects*, *cardiac surgery*, *low birth weight*.

Abbreviations. BPD, bronchopulmonary dysplasia; HMD, hyaline membrane disease; NHLBI, National Heart, Lung, and Blood Institute; VLBW, very low birth weight; CHD, congenital heart disease; PCR, pulmonary vascular resistance; MOSF, multiorgan system failure; PA, pulmonary artery; VSD, ventricular septal defect; iNO, inhaled nitric oxide; NEC, necrotizing enterocolitis; BCPA, bicavopulmonary anastomosis; HLHS, hypoplastic left heart syndrome; CICU, cardiac ICU.

ABBREVIATIONS. BPD, bronchopulmonary dysplasia; HMD, hyaline membrane disease; NHLBI, National Heart, Lung, and Blood Institute; VLBW, very low birth weight; CHD, congenital heart disease; PCR, pulmonary vascular resistance; MOSF, multiorgan system failure; PA, pulmonary artery; VSD, ventricular septal defect; iNO, inhaled nitric oxide; NEC, necrotizing enterocolitis; BCPA, bicavopulmonary anastomosis; HLHS, hypoplastic left heart syndrome; CICU, cardiac ICU.

Bronchopulmonary dysplasia (BPD) was first reported by Northway in 1967 because before that era, most premature neonates succumbed from hyaline membrane disease (HMD) or other complications of prematurity.¹ Subsequently, a classification of BPD was formulated by the National Heart, Lung, and Blood Institute (NHLBI) in 1978 with additional refinement by Jobe et al in 2001.^{2,3} Improvements in ventilator management strategies, widespread use of surfactant, and prenatal administration of glucocorticoids have improved survival of premature infants and hence the prevalence of BPD.^{4,5} Although BPD is rare among infants who are >30 weeks' gestation and have a birth weight >2500 g, its development cannot always be predicted on the basis of initial severity of HMD. Very low birth weight (VLBW) infants with mild or even no obvious HMD may progress to develop increased oxygen and ventilation requirements.⁶ Preterm infants with BPD, in the absence of congenital heart disease (CHD), often have involvement of extrapulmonary organ systems.^{7–10} The long-term outcome has been well defined in such children^{11–13}; however, the coexistence of CHD has been shown to result in a slower rate of recovery of pulmonary function.¹⁴ Furthermore, the excessive pulmonary blood flow that accompanies many types of CHD is likely to exacerbate respiratory abnormalities.¹⁵

Although there are several reports of cardiac surgery in low birth weight children,^{16–22} there are no data regarding outcomes after surgical interventions in children with BPD. Children with BPD would be expected to have a worse clinical course after surgery as a result of elevations in pulmonary vascular resistance (PVR) and adverse inflammatory effects on a previously damaged lung.²³ In addition, such children may have limited defenses to free radical damage sustained during cardiopulmonary bypass.²⁴

From the Divisions of *Pediatric Cardiology, †Neonatology, §Pulmonology, and ||Congenital Heart Surgery, Texas Children's Hospital, Houston, Texas; ¶Department of Pediatric Cardiology, Royal Children's Hospital, Melbourne, Australia; #Department of Pediatric Cardiology, Cincinnati Children's Hospital, Cincinnati, Ohio; and **Division of Neonatology, Children's Hospital of Philadelphia, Philadelphia, Pennsylvania.

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Reprint requests to (C.J.M.) Department of Pediatric Cardiology, Our Lady's Hospital for Sick Children, Crumlin, Dublin 12, Ireland. E-mail: colin.mcmahon@olhsc.ie

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This multicenter study was undertaken to elucidate the clinical outcomes after cardiac surgery in such children.

METHODS

This was a retrospective, multicenter study involving 4 cardiac centers (3 US, 1 Australian) that investigated all children who had BPD and underwent cardiac surgery, excluding ligation of a patent ductus arteriosus, between January 1991 and January 2002. Patients who had BPD and CHD and underwent surgical procedures were identified from echocardiography and surgical databases of each institution. The study was approved by the Institutional Review Board of each participating institution. The following data were collected for each patient: (1) pregnancy profile of the mother, including maternal age, gestation, and multiple pregnancies; (2) delivery history, including mode of delivery, Apgar scores, and birth weight; (3) preoperative status, including chromosomal aberrations, congenital anomalies, and systemic illness including intraventricular hemorrhage (IVH), sepsis, retinopathy of prematurity, and necrotizing enterocolitis; (4) pulmonary airway issues, including results of bronchoscopy when performed; (5) cardiac diagnosis derived from echocardiographic and/or cardiac catheterization studies; (6) cardiac surgical intervention and postoperative clinical course, including mortality and morbidity, the latter including ventilatory support before and after intervention; (7) duration of hospitalization, ICU stay, and current status of pulmonary support; and (8) resource utilization for total hospital stay for each patient at 2003 cost levels.

We compared morbidity and mortality (duration of ICU and hospital stay, complication rate) between the study group and an age- and lesion-matched control group without BPD. The clinical course (duration of ventilation and hospitalization, rate of weight gain) of a subgroup of patients who had protracted ventilation and underwent tracheostomy was compared with a similar number of patients who continued on mechanical ventilation alone. We compared morbidity (complication rate) and mortality between BPD patients who were operated on during 2 periods, January 1991 to December 1995 (group 1) and January 1996 to January 2002 (group 2), to evaluate evolution in clinical outcomes.

Definitions

BPD was defined as patients who required oxygen at 28 days of age with characteristic radiographic changes and further classified into mild, moderate, and severe on the basis of the most recent criteria for BPD from the NHLBI, as outlined in Table 1. Low birth weight was defined as a birth weight ≤ 2500 g and VLBW as ≤ 1500 g. Prematurity was defined as < 37 weeks' gestation. Infants with a birth weight < 10 th percentile for gestational age were defined as small for gestational age. Multiorgan system failure (MOSF) was defined as patients who developed a combination of ≥ 3 of the following: renal (serum creatinine > 1.2 mg/dL associated with decreased urine output), hepatic (elevation in transaminases), cardiac, or respiratory failure. Surgical interventions were

classified as palliative (systemic-pulmonary artery [PA] shunt, PA band, Glenn shunt) or corrective (repair of ventricular septal defect [VSD], complete atrioventricular canal, coarctation, tetralogy of Fallot, or arterial switch operation). Early intervention was classified as occurring before 3 months of age; late intervention was classified as occurring at > 3 months of age. Protracted ventilation and hospitalization was defined as ventilation and hospitalization lasting longer than 100 days after cardiac surgery. Sepsis was defined as a positive blood culture or acute clinical deterioration (hypotensive episode, increase in ventilatory requirements, labile glucose homeostasis, or poor perfusion with mottled appearance). Pulmonary hypertension was based on the following criteria: an acute drop in systemic oxygen saturation accompanied by systemic hypotension, which resolved with hyperventilation, 100% O₂, or inhaled nitric oxide (iNO) therapy in combination with echocardiographic evidence of elevated right ventricular pressure by tricuspid regurgitation jet velocity or right-to-left shunting at the atrial level. Necrotizing enterocolitis (NEC) was defined as a clinical deterioration in association with obvious intramural bowel gas pattern, intrahepatic air, or frank intestinal perforation. Pregnancy-induced hypertension was defined as newly elevated maternal blood pressure $\geq 140/100$ mm Hg during pregnancy. PA band constituted surgical placement of a band around the main pulmonary artery to control pulmonary blood flow. Biventricular anastomosis (BCPA) or Glenn shunt constituted connecting 1 or both superior caval veins to the pulmonary arteries.

Statistics

Data are presented as mean (SD) or median (range) depending on distribution. A 1:1 matched control group from 1 institution consisted of full-term infants who did not have BPD and were randomly selected and matched for cardiac lesions, cardiac surgeries, and year of surgical procedure. Data were compared between groups using the *t* test when normally distributed or the Mann-Whitney rank sum test when abnormally distributed. *P* $< .05$ was considered significant.

RESULTS

Pregnancy and Delivery

Of the 43 patients, all were premature, 22 were VLBW, and 6 were small for gestational age. Three infants were born to young mothers (< 18 years), and 12 infants were born to older mothers (> 32 years). There were 4 twin pregnancies and 3 triplet pregnancies. Four mothers had gestational diabetes, 1 mother had type 2 diabetes, and 6 mothers had pregnancy-induced hypertension. Twenty-nine infants were delivered by cesarean section, and 14 infants were delivered vaginally. In 13 infants, the Apgar score was

TABLE 1. Classification and Severity of BPD in 43 Children Who Underwent Cardiac Surgical Intervention

	Gestational Age	
	< 32 Weeks	> 32 wk
Time of assessment	36 wk PMA or discharge home, whichever is first All patients are treated with oxygen $> 21\%$ for at least 28 days PLUS	> 28 d but < 56 d postnatal age, or discharge home, whichever is first
Mild BPD (<i>N</i> = 3)	Breathing room air at 36 wk PMA or discharge home, whichever is first	Breathes room air by 56 d postnatal or discharge home, whichever is first
Moderate BPD (<i>N</i> = 20)	Need for $< 30\%$ O ₂ at 36 wk PMA or discharge home, whichever is first	*Need for $< 30\%$ O ₂ at 56 d postnatal or discharge home, whichever is first
Severe BPD (<i>N</i> = 20)	Need for $\geq 30\%$ O ₂ and/or positive pressure (PPV or NCPAP) at 36 wk PMA or discharge home, whichever is first	Need for $\geq 30\%$ O ₂ and/or positive pressure (PPV or NCPAP) at 56 d postnatal age or discharge home, whichever is first

PMA indicates postmenstrual age; PPV, positive pressure ventilation; NCPAP, nasal continuous positive airway pressure. The clinical features of BPD and radiographic features have not been included in this definition. It is taken for granted that most infants have tachypnea, rales, retractions, etc. The oxygen requirement must be for at least 12 hours of the day and reflect a chronic state that the infant is in, not an "acute event" that happened to occur on day 56 of life. In other words, such oxygen requirement should be baseline for the infant.

* These criteria were modified from the criteria presented by Jobe and Bancalari E.³

≤5 at 1 minute, and in 3 infants, the Apgar score was ≤5 at 5 minutes and required resuscitation. The mothers of 33 (77%) children were treated with antenatal glucocorticoids to augment fetal lung development. Thirty-eight (88%) children received endotracheal surfactant therapy (median: 2 doses) after delivery. There were 25 male and 18 female patients with a median gestational age of 28 weeks (range: 23–35 weeks) and birth weight of 1460 g (range: 431–2500 g).

Preoperative Neonatal Morbidity

The severity of BPD was classified as mild in 3 patients, moderate in 20 patients, and severe in 20 patients using modified criteria for severity of BPD (Table 1).³ Tracheo/bronchomalacia was determined by bronchoscopy in 10 (23%) patients. Sepsis was the most common preoperative morbidity in 19 patients (*Staphylococcus epidermidis* in 8, *Staphylococcus aureus* in 5, *Pseudomonas* in 4, and *Enterococcus* and *Escherichia coli* in 1 patient each). Thirteen (87%) of these patients were on corticosteroids at some point during their preoperative course. Ten patients experienced intraventricular hemorrhage diagnosed on transcranial ultrasound (3 patients grade 1 and 7 patients grade 2). Fifteen patients had retinopathy of prematurity determined by ophthalmologic evaluation at some stage during their clinical course; 5 patients requiring surgery. NEC occurred in 6 patients; 4 patients underwent laparotomy. Five patients had a genetic disorder: trisomy 21 ($n = 3$) and Turner's syndrome ($n = 1$), and 1 patient received a diagnosis of trisomy 18 after surgery.

Diagnosis of Congenital Heart Lesions

Cardiac diagnoses are presented in Table 2. Fifteen patients had ductus-dependent lesions and were treated for a median of 43 days with prostaglandin infusion until surgical intervention. The median age at diagnosis was 9 days (range: 0–51 days). Diagnosis was delayed until >30 days in 5 patients: tetralogy of Fallot in 2 patients and coarctation, VSD, and cor triatriatum in 1 patient each. Unsuspected heart disease was present in 3 patients (tetralogy of Fallot and coarctation) who presented with systemic desaturation that was initially attributed to their lung disease. In 2 patients (both early 1990s), poor echocardiographic windows failed to detect the cardiac lesion (VSD and cor triatriatum).

Cross-sectional echocardiography ± color Doppler

was the diagnostic modality in 41 patients, Cardiac catheterization diagnosed cor triatriatum in 1 patient and delineated intracardiac anatomy in another patient with heterotaxy, asplenia, isomeric right atria, single right ventricular, d-malposition of the great vessels, and pulmonary stenosis. Concentric ventricular hypertrophy with impaired diastolic relaxation was found in 4 neonates who were treated with corticosteroids; 2 mothers had gestational diabetes. In the catheterization laboratory, septostomy was performed in 2 patients, and balloon valvuloplasty was performed in 3 patients with semilunar valve stenosis (pulmonary stenosis in 2 patients, aortic stenosis in 1 patient) with no mortality. Two patients who underwent catheterization sustained vascular trauma: unilateral femoral venous obstruction in 1 patient and bilateral venous injury in a second, requiring fasciotomy.

Surgical Interventions in BPD Patients

There were 52 surgeries in the 43 patients, which are listed in Table 3.

Palliative Procedures

Palliative procedures were performed in 18 patients. The most common procedure was creation of a systemic-PA shunt ($n = 9$) followed by placement of a PA band ($n = 6$). Median systemic O₂ saturation increased from 65% (range: 55–76%) to 79% (45–89%) in patients after placement of a systemic-PA shunt. The median age at the time of all surgical interventions was 85 days (range: 34–356 days). Palliative procedures were performed earlier than corrective procedures at a median age of 77 days versus 123 days, respectively ($P < .001$). The median weight at time of palliative procedure was 2.5 kg (range: 1.5–5.2 kg) compared with 3.1 kg (range: 1.5–11.2 kg) at the time of corrective surgical intervention. Postoperative duration of ventilation was significantly lower for patients who underwent palliative procedures (7 vs 17 days; $P < .001$), but the mortality was comparable to those who underwent corrective procedures (17% vs 26%; nonsignificant).

Corrective Procedures

Corrective procedures were performed in 34 patients. The most frequent corrective procedure was closure of a VSD ($n = 7$), followed by aortic arch repair ($n = 6$) and repair of tetralogy of Fallot ($n = 6$). With the exception of aortic arch repair, cardiopul-

TABLE 2. Cardiac Diagnoses and Timing of Palliative or Corrective Surgical Procedures in 43 Children Who Had BPD and Underwent 52 Cardiac Surgeries

Anatomy	Total Patients	Total No. of Procedures	Procedures			
			Palliative		Corrective	
			Early	Late	Early	Late
Left-to-right shunt	15	18	2	4	3	9
Conotruncal abnormality	12	18	5	5	1	7
Aortic arch obstruction	6	6	0	0	6	0
Univentricular heart	4	4	3	1	0	0
Semilunar valve stenosis	3	3	0	0	1	2
Shone syndrome	1	2	0	1	1	0
Cor triatriatum	1	1	0	0	0	1

TABLE 3. Palliative and Corrective Surgical Interventions in 43 Children With BPD and CHD

Surgical Procedure	No. of Patients
Palliative procedures, CPB–	
Blalock-Taussig shunt	8
PA band	6
Aortopulmonary (Waterson) shunt	1
Palliative procedures, CPB+	
Glenn (bicavopulmonary) shunt	3
Corrective procedures, CPB+	
VSD closure	7
TOF repair	6
Aortic arch/interruption repair	3
Arterial switch operation	2
Mitral valve repair	2
Pulmonary valvotomy	2
Atrial septal defect closure	2
Aortic valvotomy	1
Ross-Konno procedure	1
Tricuspid valve repair	1
Aortopulmonary window repair	1
Cor triatriatum repair	1
Truncus repair	1
CAVC + TOF	1
Corrective procedures, CPB–	
Aortic arch repair	3

CPB indicates cardiopulmonary bypass; CAVC, complete atrioventricular canal; TOF, tetralogy of Fallot.

monary bypass was required for surgical intervention in this group.

Second Operations

Eight patients underwent a second surgical procedure at a median age of 7 months (range: 2–18 months). These included tetralogy of Fallot repair in 4 patients and PA band, mitral valve repair, tricuspid valve repair, and BCPA in 1 patient each.

Late Redo Surgical-Catheter Procedures (>18 Months After Surgery)

One patient with tetralogy of Fallot underwent replacement of a right ventricular to pulmonary artery conduit for severe pulmonary regurgitation 3 years after repair. A second patient with recoarctation was brought to the catheterization laboratory for balloon dilation 20 months after repair. Two patients with repaired tetralogy of Fallot each underwent placement of stents in the branch PAs.

Preoperative Support of BPD Patients

All patients were intubated and mechanically ventilated at some stage during their clinical course. Data for ventilatory support in the preoperative and postoperative period are presented in Table 4.

Fourteen patients required ventilation immediately before surgical intervention, and 16 patients were treated with pressure support only (eg, nasal continuous positive airway pressure). Two patients were supported with high-frequency oscillators during their preoperative clinical course. One patient developed pulmonary interstitial emphysema with pulmonary hypertension for 14 days, and a second patient who had severe HMD and required peak inspiratory pressure >55 and 100% fraction of inspired oxygen to maintain satisfactory oxygenation and acid-base status was supported using high-frequency

TABLE 4. Preoperative and Postoperative Ventilation Requirements in 43 Children With BPD and CHD

Variable	Preoperative Period	Postoperative Period
No. of patients ventilated	40	40
No. of patients on PS/CPAP	16	21
Median PIP (range)	23 (18–40)	25 (18–66)
Median PEEP (range)	5 (2–7)	5 (3–10)
Median F_{iO_2} , % (range)	50 (30–100)	55 (25–100)
Duration ventilated, d (range)	76 (2–244)	15 (1–141)
Duration PS/CPAP, d (range)	12 (1–123)	11 (3–57)

CPAP, continuous positive airway pressure; F_{iO_2} , percentage fractional inspired oxygen; PEEP, peak end-expiratory pressure; PIP, peak inspiratory pressure; PS, pressure support. Values are expressed for the maximum ventilatory requirement for >24 hours.

quency oscillatory ventilation for 9 days. Nine patients required intravenous inotropic support for congestive heart failure (excluding septic shock) in the preoperative period.

Postoperative Support

The median duration of mechanical ventilation after surgery was 15 days (range: 1–141 days) for the BPD group compared with 2 days for the control group (range: 0.1–7 days; $P < .01$). The median ventilatory requirements for the BPD group are presented in Table 4. Ventilation requirement was higher in the postoperative than in the preoperative period for 7 patients. Comparing patients who had a protracted hospital stay and underwent tracheostomy with those who were treated with conventional mechanical ventilation, the median weekly weight gain was 83 g compared with 51 g for the groups, respectively ($P = .10$). Time to discharge in the tracheostomy group was 48 days compared with 67 days for the ventilated group ($P = .20$).

Thirty-seven patients required inotropic support (dopamine, dobutamine, or milrinone) after surgery for a median duration of 2 days (range: 1–12 days). Delayed sternal closure was used in 5 patients (3 corrective procedures, 2 palliative). No patient was placed on extracorporeal membrane oxygenation during the study period. Of the 4 patients with steroid cardiomyopathy, 2 were treated with an esmolol infusion in the perioperative period.

Postoperative Complications

In the BPD group, 42 postoperative complications occurred in 32 (74%) patients compared with 5 (11%) complications in the control group ($P < .05$). These included sepsis ($n = 14$); MOSF ($n = 6$); pulmonary hypertension ($n = 5$); arrhythmia ($n = 5$); failed extubation ($n = 4$); chylothorax ($n = 3$); postoperative bleeding ($n = 2$), 1 of whom required mediastinal reexploration; endotracheal tube obstruction ($n = 1$); pneumothorax ($n = 1$); and *Staphylococcus aureus* mediastinitis ($n = 1$). Five patients had evidence of pulmonary hypertension that required treatment with iNO; the starting dose was 40 parts per million (ppm) in 4 patients and 80 ppm in the fifth patient. Two patients had hypoxia in the absence of hypotension, which responded to iNO (20 ppm). Arrhythmias included complete atrioventricular block in 1

patient and high-grade second-degree arteriovenous block in a second patient; both required placement of a pacemaker. Junctional ectopic tachycardia, junctional escape rhythm, and ventricular tachycardia occurred in 1 patient each.

Mortality

Kaplan-Meier curve for survival is presented in Fig 1. Thirty-day postoperative survival for the BPD group was 84%, and total survival was 68% (excluding patients who were lost to follow-up) for the study cohort compared with 95% 30-day survival (2 deaths) and 93% total survival (3 total deaths) for the control group ($P < .05$). In the BPD group, 6 patients died within 30 days of surgical intervention and 6 patients died after 30 days. Three deaths were among patients who underwent palliative procedures, and 9 deaths occurred after corrective procedures. Causes of death in the first postoperative week included failure to wean from cardiopulmonary bypass in 2 patients and a combination of MOSF, disseminated intravascular coagulation, and sepsis in a third patient. Between 7 and 30 days after surgery, 2 patients died from pulmonary hypertension crises despite institution of iNO, and 1 patient died from MOSF and sepsis.

There were 6 late deaths (>30 days) in the BPD group. Causes of late death included MOSF ($n = 2$), pulmonary hypertension ($n = 1$), respiratory failure ($n = 1$), withdrawal of care in a patient with trisomy 18 ($n = 1$), and massive pulmonary hemorrhage ($n = 1$). The patient who developed pulmonary hemorrhage and respiratory failure had developed respiratory syncytial virus infection during his postoperative course.

Mortality for children with BPD and univentricular hearts was 50% (2 of 4 infants): 1 child with hypoplastic left heart syndrome (HLHS) after Glenn shunt and a second child with heterotaxy syndrome, pulmonary atresia, isomeric right atria, and asplenia after modified Blalock-Taussig shunt. Both died from MOSF; the patient with HLHS died 80 days after surgery (complicated by disseminated intravascular coagulation), and the child with heterotaxy syndrome died 79 days after surgery from pulmonary hypertension. The other 2 children with univentricular hearts had significantly protracted hospital courses (>100 days) with high morbidity. One patient with severe BPD (preoperative pulmonary venous saturation of 73%) had persistent systemic desaturation of 40% to 50% for several weeks after BCPA with gradual improvement in systemic saturation to 65%. On most recent follow-up, he is doing well with systemic oxygen saturations of 65% to 70% on room air.

Changes in Mortality and Morbidity Over the Decade

Fifteen patients with BPD were operated on between January 1991 and December 1995 (group 1) compared with 27 (group 2) between January 1996 and 2002. Mortality for the 2 groups was 40% and 22%, respectively ($P < .05$). Complications occurred in 13 (80%) patients in the first group compared with 19 (74%) patients in the second group (nonsignificant).

Current Status of BPD Patients

Follow-up data were available in 38 (88%) patients with BPD; 5 patients were lost to follow-up. Twenty-two patients are at home and 4 patients remain hos-

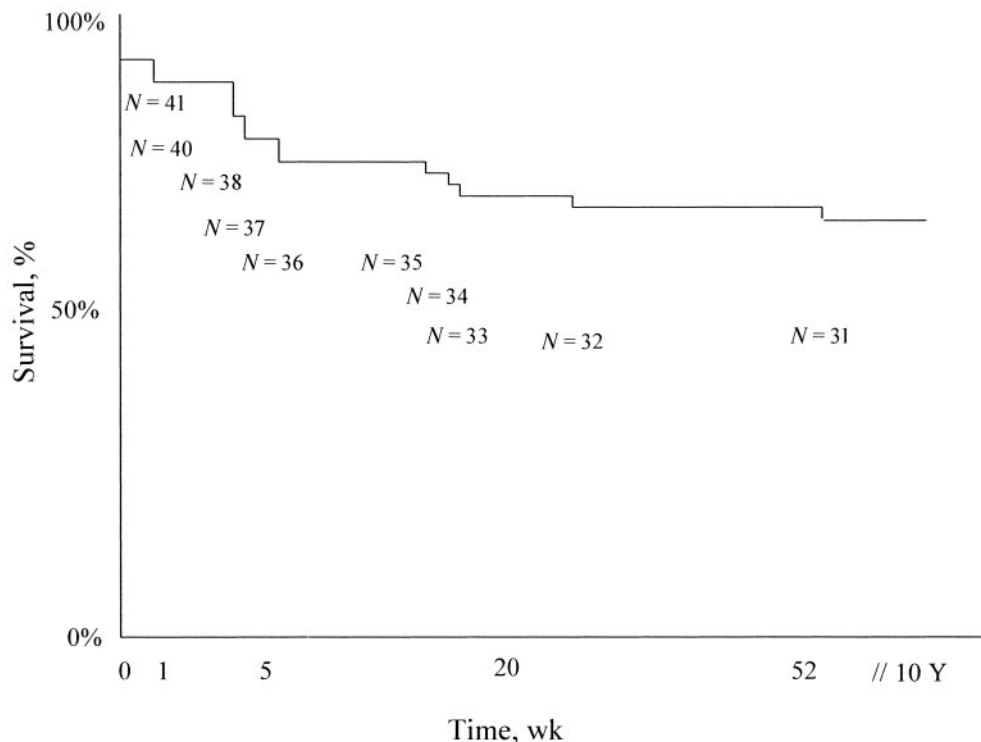


Fig 1. Kaplan-Meier survival curve for children who had BPD and underwent cardiac surgery.

pitalized at a median of 4 months after surgery (Table 5). The current pulmonary status of patients included 14 on room air (55%), 4 at home on oxygen therapy (15%), 4 tracheostomy-dependent or ventilated at home (15%), and 4 ventilated in hospital (15%). Eleven (26%) patients were treated with a tracheostomy at one point during their postoperative course. The median duration of home oxygen therapy was 4.2 months (range: 1.5–8.9 months).

Resource Utilization of BPD Patients

The median duration of stay in the cardiac ICU (CICU) was 7.5 days (range: 1–30 days) for the BPD group compared with 3 days (range: 1–10 days) for the control group ($P < .05$). Total median hospital stay was 115 days (range: 35–475 days) for the BPD group compared with 8 days (range: 4–28 days) for the control group ($P < .05$). The median cost (\$2003–\$2004 US) of hospital stay for a single patient with BPD was estimated at \$930 000 (range: \$425 000–\$2 750 000) based on a median CICU stay of 7.5 days and total hospital stay of 115 days (including surgery, medicines, and radiologic procedures).

DISCUSSION

Patients with CHD and BPD have significant morbidity and mortality compared with patients with isolated heart disease as demonstrated by the findings of this study. This may be partly accounted for by abnormalities in pulmonary compliance, elevation in airway resistance as a result of bronchial vessel compression, bronchial compression by enlarged pulmonary arteries, abnormal perfusion of segments of the trachea, and a predisposition to pulmonary hypertension.^{23,25,26,27,28–33}

Mortality and Current Status in BPD Patients

The 30-day postoperative survival of 84% was not unexpected given the high preoperative and postoperative morbidity of the study cohort, although this was significantly increased compared with children without BPD. However, the high in-hospital attrition among BPD patients was reflected by a 68% survival to hospital discharge. Evolution in trends over the past decade show an increasing number of patients undergoing surgery and, more important, reduced

mortality over the decade. This may be secondary to improved patient selection despite the increased number of surgeries. Increasing experience in postoperative management, including better nutritional support, early tracheostomy in chronic respiratory failure, and appropriate use of inhaled steroids and diuretics, all may be factors.

In group 1, 2 mortalities occurred secondary to failure to wean from cardiopulmonary bypass; extracorporeal membrane oxygenation in the postsurgical setting was still in its infancy, and appropriate-sized ventricular assist devices were unavailable, which may have significantly affected outcome.^{34–36} Despite availability of these modalities, there was no case of postcardiopulmonary bypass pump failure among group 2 patients, perhaps indicating improvements in cardiopulmonary bypass.

Late mortality in both groups was most commonly attributed to respiratory failure and sepsis. Pulmonary hemorrhage and respiratory failure were responsible for 1 late death in group 2 in a chronically hospitalized neonate who acquired severe respiratory syncytial virus pneumonia during his postoperative course. This highlights the importance of Palivizumab prophylaxis for all CHD patients who have BPD and are ≤ 24 months of age.³⁷ Mortality was greatest among patients with univentricular hearts (50%; both patients in group 2). From these data, subjecting children with a univentricular heart and pulmonary venous hypoxemia to a cavo-pulmonary connection resulting in protracted desaturation seems to carry a high risk for mortality. Only 1 patient with HLHS and severe BPD underwent Glenn and eventually died from MOSF. Abnormal capillary distribution and the presence of aortopulmonary collaterals in children with BPD may also have significant implications for regulating pulmonary blood flow in palliated univentricular hearts. Surgical intervention for patients with severe BPD and HLHS or complex heterotaxy syndrome is an aggressive strategy, although more data on outcomes in these groups are required to validate this finding.

The postoperative duration of mechanical ventilation and morbidity was significantly less in patients who underwent a palliative procedure compared with intracardiac repair. Whether palliating high-risk patients (borderline PVR, severe BPD) in the early postnatal period until their pulmonary arterial and alveolar function has had an opportunity to recover is preferable to an early corrective procedure is an important question. However, palliation, including banding of the pulmonary trunk or shunting the PA in the face of labile pulmonary vasculature, can pose serious problems in regulating pulmonary blood flow.

Postoperative Management and Morbidity

The postoperative complication rate was comparable for patients who were operated on in the first half of the last decade compared with the second half (80% vs 74%, respectively), despite improved surgical techniques, cardiopulmonary bypass, increased experience in postoperative care, and heightened awareness of the specific needs of infants with BPD.

TABLE 5. Current Status of 43 Postoperative Cardiac Patients with BPD

Status	No. of Patients
Hospitalized	4
Ventilated	4
On O ₂	—
Room air	—
At home	22
Ventilated	4
On O ₂	4
Room air	14
Lost to follow-up	5
Deceased	12
Total	43
Tracheostomy in hospital	3
Tracheostomy at home	4
Tracheostomy at one time	11
Duration O ₂ therapy, mo	4.2 (1.5–8.9)

Prolonged stay in the CICU was primarily the result of prolonged ventilatory support, with a median duration of 15 days. Weaning such children off the ventilator was slow using either pressure support ventilation or slow weaning of synchronized intermittent mandatory ventilation.

A small subgroup analysis of patients with protracted ventilation for >100 days showed that performing a tracheostomy accelerated patient growth and facilitated earlier discharge home, although this did not reach statistical significance. The optimum timing for placement of a tracheostomy remains contentious and at the physician's discretion. Prolonged conventional mechanical ventilation may potentially increase risk for iatrogenic infection, increase energy expenditure, and contribute to failure to thrive.^{38,39}

Fluid restriction and diuretic therapy is of vital importance in the treatment of infants with BPD in both the postoperative and the preoperative periods. Brion et al⁴⁰ reviewed the Cochrane Neonatal Database and showed for preterm infants who are >3 weeks' postnatal age and have chronic lung disease that acute and chronic administration of diuretics improves pulmonary mechanics, although it is uncertain whether diuretics improved mortality, duration of oxygen therapy, and long-term outcome for patients who were already receiving steroids and bronchodilators. Another randomized study demonstrated improved pulmonary function and decreased oxygen requirements in the group on long-term diuretic therapy.⁴¹ Studies are still required to determine the efficacy and benefits of aerosolized furosemide.⁴² The importance of adequate nutritional intake, despite fluid restriction, is vital as meta-analyses show that infants with CHD have a 35% increase in total daily energy expenditure and require substantially higher energy intake (at least an additional 100 kJ/kg/day).⁴³ This should be managed in consultation with a pediatric nutritionist.

Sepsis proved a prominent postoperative complication in this study. Chronic colonization of the skin and upper airways often with *Pseudomonas* and other organisms may have contributed, and although this was not studied, the majority of patients had been treated previously with steroids, which may increase risk for infection. Although there was only 1 case of mediastinitis requiring sternal resection and placement of a skin flap in a patient who had a tracheostomy before surgery, early preoperative decannulation of tracheostomy and meticulous care of old tracheostomy sites are required.

NEC in this study was significantly associated with ductal-dependent lesions in 4 of the 6 cases, which has been reported previously.⁴⁴ Other reported risk factors for development of NEC include congenital heart lesions with significant "steal syndrome," including truncus arteriosus, and episodes of poor systemic perfusion or shock.

PVR

Preoperative planning in select patients should include calculation of pulmonary arterial pressures and PVR in the catheterization laboratory.^{45,46} It is vital to determine the degree of vasoreactivity using

nitric oxide, 100% oxygen, sildenafil, or a combination of these therapies.^{47,48} Patients with univentricular circulations should be evaluated before Norwood or Glenn procedures, in which postoperative pulmonary blood flow may be significantly compromised in the face of elevated PVR.⁴⁹ One quarter of patients who died had pulmonary hypertension, underscoring the importance of this evaluation. Patients with borderline elevation in PVR (4–6 Wood units, U/m²) may provide a therapeutic dilemma depending on the surgical procedure, although deferral of surgery may be optimal in cases with significant and irreversible elevation in PVR.

Given the extensive resource utilization involved in managing such cases, centers with limited resources may have difficult choices in patient selection. Resource utilization is considerable, and depriving other children with critical cardiac lesions of surgery because of prolonged CICU bed occupation may have serious consequences.

Limitations

Our study was limited by its retrospective design. Our classification of severity of BPD was also arbitrary. The outcomes in this study cohort may be biased for a number of reasons. Each center is a tertiary cardiac center with a minimum of ~300 surgical cardiopulmonary bypass procedures per year, which may confer a better prognosis than smaller cardiac centers.⁵⁰ There also may have been selection bias in the patients who were chosen to undergo surgery, with poor candidates from a cardiopulmonary standpoint not being offered surgical treatment or undergoing attrition before surgery was considered or feasible. This study also failed to take into account patients who died before surgery and those who avoided surgery after successful management in the catheterization laboratory.

CONCLUSIONS

The mortality for children who have BPD and undergo cardiac surgery has improved over the past decade, although this still represents a high-risk population when compared with a control group of children without BPD. Certain groups, particularly patients with univentricular hearts and severe BPD, have a very high mortality. Resource utilization is extensive in caring for such children. Optimal timing of surgery and strategies to improve outcome remain to be delineated.

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