Occurrence and severity of bronchopulmonary dysplasia and respiratory distress syndrome after a preterm birth

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BACKGROUND: Despite notable advances in neonatal care, bronchopulmonary dysplasia (BPD) remains an important complication of preterm birth, frequently resulting in prolonged hospital stay and long-term morbidity.

METHODS: A historical cohort study of all preterm infants (gestational age younger than 37 weeks) admitted to the Montreal Children's Hospital (Montreal, Quebec) between January 1, 1980, and December 31, 1992, was conducted. Information collected included demographic data, maternal and perinatal history, and main neonatal outcomes. Independent risk factors associated with BPD were identified by univariate analysis using one-way ANOVA, *t* tests or Mantel-Haenszel χ^2 testing. Severity of disease was studied using an ordinal multinomial logistic regression model.

RESULTS: In total, 1192 preterm infants were admitted, of whom 551 developed respiratory distress syndrome and 322 developed BPD. For each additional week of prematurity, the risk of developing BPD increased by 54% (adjusted OR 1.54/week [95% CI 1.45 to 1.64]). For each point subtracted on the 1 min Apgar score, the risk of developing BPD was increased by 16% (OR 1.16 [95% CI 1.1 to 1.3]). BPD was also associated with the presence of patent ductus arteriosus (OR 3.5 [95% CI 2.1 to 6.0]), pneumothorax in the first 48 h (OR 9.4 [95% CI 3.6 to 24.8]) or neonatal pneumonia/sepsis in the neonatal period (OR 1.9 [95% CI 1.1 to 3.2]). Severity of BPD was associated with gestational age, 1 min Apgar score, very low birth weight and the presence of neonatal pneumonia/sepsis.

CONCLUSION: Factors associated with BPD following a preterm birth were the degree of prematurity, birth weight, Apgar score at 1 min, and the presence of patent ductus arteriosus, pneumothorax or neonatal pneumonia/sepsis.

Key Words: *Bronchopulmonary dysplasia; Infant; Newborn; Premature; Respiratory distress syndrome*

L'occurrence et la gravité de la dysplasie bronchopulmonaire et du syndrome de détresse respiratoire après une naissance prématurée

HISTORIQUE : Malgré les progrès remarquables des soins néonatals, la dysplasie bronchopulmonaire (DBP) demeure une complication importante de la prématurité et entraîne souvent une hospitalisation prolongée et une morbidité à long terme.

MÉTHODOLOGIE : Les chercheurs ont procédé à une étude de cohorte historique de tous les nourrissons prématurés (de moins de 37 semaines d'âge gestationnel) hospitalisés à L'Hôpital de Montréal pour enfants, au Québec, entre le 1er janvier 1980 et le 31 décembre 1992. L'information colligée incluait les données démographiques, les antécédents maternels et périnatals et les principales issues néonatales. Les chercheurs ont repéré les facteurs de risque indépendants associés à la DBP au moyen d'une analyse univariée faisant appel à l'ANOVA unidirectionnel, aux tests *t* ou au test χ^2 de Mantel-Haenszel. Ils ont étudié la gravité de la maladie au moyen d'un modèle ordinal de régression logistique multinomiale.

RÉSULTATS : Au total, 1 192 nourrissons prématurés ont été hospitalisés, dont 551 ont présenté un syndrome de détresse respiratoire et 322, une DBP. À chaque semaine supplémentaire de prématurité, le risque de DBP augmentait de 54 % (RRA 1,54/semaine [95 % IC 1,45 à 1,64]). À chaque point soustrait de l'indice d'Apgar à une minute de vie, le risque de DPB augmentait de 16 % (RR 1,16 [95 % IC 1,1 à 1,3]). La DBP s'associait également à une persistance du canal artériel (RR 3,5 [95 % IC 2,1 à 6,0]), à un pneumothorax au cours des 48 premières heures de vie (RR 9,4 [95 % IC 3,6 à 24,8]) ou à une pneumonie ou une septicémie néonatale pendant la période néonatale (RR 1,9 [95 % IC 1,1 à 3,2]). La gravité de la DBP s'associait à l'âge gestationnel, à l'indice d'Apgar à une minute de vie, à un très faible poids de naissance et à la présence d'une pneumonie ou d'une septicémie néonatale.

CONCLUSIONS : Les facteurs associés à la DPB après une naissance prématurée étaient le degré de prématurité, le poids de naissance, l'indice d'Apgar à une minute de vie et une persistance du canal artériel, un pneumothorax ou une pneumonie ou une septicémie néonatale.

Despite notable advances in prenatal and neonatal care, respiratory distress syndrome (RDS) and bronchopulmonary dysplasia (BPD) remain important complications of preterm births, frequently resulting in mortality as well as short-term and long-term morbidity.

BPD, as originally described by Northway et al (1), is less common today, but it has been replaced by a 'new' disease that typically follows mild to moderate RDS in small preterm infants who respond quickly to surfactant therapy but require prolonged ventilation for apnea and poor respiratory efforts (2). The accurate prediction of the development and severity of lung disease in preterm infants could assist clinicians in making critical decisions quickly (3) and could provide a better idea of the short-term prognosis to the treating team and family members. Identifying factors associated with preventing the onset of BPD is also an important facet of neonatology research.

The present study of a large cohort of preterm infants had three objectives: to examine factors associated with the development of RDS and BPD, to examine factors associated with BPD severity and to develop a predictive equation for the occurrence of BPD following a preterm birth.

METHODS

Subjects

The study population included all preterm infants (defined as a gestational age of younger than 37 weeks) who were admitted to the Montreal Children's Hospital (Montreal, Quebec) between January 1, 1980, and December 31, 1992. The Montreal Children's Hospital is a tertiary paediatric hospital with a specialized neonatal care department that serves as a referral centre for the province of Quebec. No infants are born at the Montreal Children's Hospital, and all study subjects were transferred to this institution following

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TABLE 1
Characteristics of the study population

	Premature with no lung disease	RDS without subsequent BPD	BPD	P*
Perinatal characteristics				
n (% of total)	319 (26.8)	551 (46.2)	322 (27.0)	–
Birth weight, kg	1.82±0.63	2.02±0.70	1.11±0.46	<0.0001
Gestational age, days	229.1±20.5	228.6±22.5	195.7±21.0	<0.0001
Male sex, n (%)	178 (55.8)	347 (62.3)	190 (59.0)	0.16
1 min Apgar score	5.85±2.4	5.82±2.6	4.06±2.4	<0.0001
5 min Apgar score	7.72±2.0	7.49±2.2	6.35±2.0	<0.0001
Mortality, n (%)	36 (11.3)	76 (13.8)	53 (16.7)	0.25
Length of hospital stay, days	42.4±63.9	28.5±40.2	139.8±114.8	<0.0001
Maternal or antenatal characteristics				
Maternal age, years	26.0±5.2	26.7±5.8	27.1±5.6	0.11
Twin or multiple births, n (%)	61 (19.1)	72 (13.1)	42 (13.0)	0.38
Antenatal steroids, n (%)	60 (18.8)	64 (11.6)	95 (29.5)	<0.0001
Vaginal delivery, n (%)	166 (53.7)	275 (58.6)	147 (53.1)	0.47
Prolonged rupture of membrane, n (%)	31 (13.1)	54 (12.7)	35 (14.6)	0.57
Premature labour, n (%)	129 (54.7)	218 (51.1)	103 (42.9)	0.07
Gestational diabetes, n (%)	5 (2.63)	15 (4.14)	8 (3.83)	0.35
Secondary diagnoses, n (%)				
Intraventricular hemorrhage	17 (5.4)	46 (8.4)	75 (23.4)	<0.0001
Retinopathy of prematurity	9 (2.8)	9 (1.6)	72 (22.4)	<0.0001
Neonatal pneumonia/sepsis	69 (21.6)	82 (14.9)	121 (37.6)	<0.0001
Patent ductus arteriosus	46 (14.4)	87 (15.8)	172 (53.6)	<0.0001
Apnea of prematurity	85 (26.7)	134 (24.3)	119 (36.9)	0.0001
Pneumothorax	7 (2.2)	76 (13.8)	61 (19.1)	0.17
Necrotizing enterocolitis	42 (13.2)	32 (5.8)	50 (15.6)	<0.0001
Seizure	20 (6.3)	21 (3.8)	52 (16.2)	<0.0001
Anemia	40 (12.5)	46 (8.4)	71 (24.0)	<0.0001

*Data presented as mean ± SD unless otherwise indicated. *P value comparing the means between categories was obtained by ANOVA testing for continuous variables. The Mantel-Haenszel χ^2 test was used to determine whether a relationship existed among categorical variables across the three groups. BPD Bronchopulmonary dysplasia; RDS Respiratory distress syndrome*

a premature birth. The study was approved by the Research Ethics Board of the McGill University Health Centre in Montreal.

Data collection

Data were abstracted from hospital records using a standardized data collection sheet. Information collected included demographic data, maternal and prenatal history, and delivery and main neonatal outcomes.

Definitions

BPD: BPD is a chronic lung disorder that is common among premature infants. It is defined clinically as the need for supplemental oxygen for at least 28 days, according to the National Institutes of Health (NIH) consensus criteria (4,5). BPD severity was graded based on an assessment performed at 36 weeks' postmenstrual age (or 56 days of life if born after 32 weeks). Mild disease was defined as breathing room air; moderate disease as requiring supplemental oxygen, but a fraction of inspired oxygen (FiO_2) of less than 0.30; and severe disease as requiring an FiO_2 of 0.30 or greater, or requiring positive pressure ventilation in infants with BPD, who died of respiratory causes before the assessment date.

Antenatal steroids: A partial or complete course of antenatal costicosteroid given to the mother for fetal maturation.

Intraventricular hemorrhage: Grade I to IV intraventricular hemorrhage detected using cranial ultrasound.

Necrotizing enterocolitis: Confirmed cases of necrotizing enterocolitis (stage 2 and above), as defined using Bell's criteria (6).

Patent ductus arteriosus: Clinically significant patent ductus arteriosus as documented by the presence of clinical signs (systolic murmur, wide pulse and hyperdynamic precordium).

Retinopathy of prematurity: Stage 1 to 5 retinopathy as seen on ophthalmoscopic examination.

Pneumothorax: Because the present study focused on clinical factors that predicted pulmonary complications, only pneumothoraces that occurred within the first 48 h of life were tabulated to minimize the confounding effect of mechanical ventilation on the incidence of pneumothorax.

Neonatal pneumonia/sepsis: The presence of pneumonia or sepsis that occurred in the first 28 days of life (7). Because of interest in the prediction of BPD, the episode of sepsis or pneumonia had to occur before the assessment date to establish the diagnosis of BPD.

The variable "premature labour" used in Tables 1 and 2 was defined as an uncomplicated pregnancy resulting in a preterm delivery.

Statistical analyses

To assess neonatal, maternal and perinatal characteristics associated with the development of RDS or BPD, all preterm infants were grouped into three categories: preterm with no lung disease; preterm with RDS and no subsequent diagnosis of BPD; and preterm with BPD (with or without preceding RDS). Using univariate and multivariable approaches, risk factors associated with RDS and BPD were examined by comparing each group with the group of infants who did not develop any respiratory problems. To assess factors associated with the severity of BPD, infants with BPD were categorized as mild, moderate or severe by using the NIH consensus criteria. To assess potential predictive factors for the subsequent development of BPD and its ensuing severity, clinical variables present in the first 28 days of life and the maternal and neonatal variables were studied.

Differences between groups were tested using one-way ANOVA or *t* tests for continuous variables (eg, birth weight, gestational age, Apgar score, length of stay and maternal age), and Mantel-Haenszel χ^2 tests (8) were used for ordinal variables. P≤0.05 was considered to be statistically significant.

For multivariable analysis, variables that were significantly associated with the outcome in univariate analyses were initially included. Variables were then selected using a stepwise forward method, with the cut-off for significance set at P≤0.05 (8,9). An ordinal multinomial logistic regression using the CATMOD procedure (9) was used to determine the association of clinical factors and outcomes with disease severity among infants with BPD (severe and moderate versus mild BPD).

The variables gestational age and Apgar score at 1 min were then dichotomized using a gestational age of younger than 30 weeks and a 1 min Apgar score of lower than 5 to enable calculation of probabilities. Both cut-offs were previously shown to be significant (10). A multiple logistic model was selected for one-half of the total study sample selected randomly, representing the derivation subset. The model was retested on the remainder of the study population (the validation subset) to confirm its predictive value. The model was calibrated using the Hosmer-Lemeshow test by means of the goodness-of-fit statistic (11), with the aim of describing the precision of predicted and observed results as a whole. Statistical analyses were conducted using SAS version 9.1 (SAS Institute Inc, USA).

RESULTS

Population characteristics

From discharge records, 1402 subjects who were admitted to the Montreal Children's Hospital between January 1, 1980, and December 31, 1992, with a diagnosis of preterm birth were identified; of these, 79 were excluded because their charts could not be found. An additional 131 subjects were excluded because they were born at a gestational age of older than 37 weeks. This left a study population of 1192 subjects. The perinatal characteristics of the population are summarized in Table 1.

Factors associated with BPD or RDS

As demonstrated in Table 1, birth weight was significantly lower in patients with BPD than in patients with RDS or without lung disease. The Apgar score at 1 min and 5 min, and the gestational age were also significantly different. Male sex was more frequent in all three groups. The infants who developed RDS were found to have a significantly higher birth weight than both the BPD subjects and the preterm infants without lung disease. This observation was not solely attributable to maternal or gestational diabetes because only 2.7% of pregnancies were complicated by diabetes in the RDS group. The rate of gestational diabetes did not significantly differ among the three groups.

Table 1 shows that infants who developed BPD were more likely to have been given antenatal steroids, likely reflecting their shorter gestational age at the time of the onset of labour or delivery. All other characteristics were similar in the three groups.

The incidences of common complications of preterm birth are also shown in Table 1. Most complications were significantly more frequent in the BPD group, which was also the most premature and had the lowest birth weight. A total of 215 infants (67%) who developed BPD were also diagnosed with RDS.

Table 2 summarizes the associations between perinatal and maternal factors, secondary diagnoses and the development of RDS or BPD after a preterm birth. Male sex, although usually associated with prematurity and RDS, was not found to be associated with the subsequent development of pulmonary complications such as RDS or BPD. No maternal or antenatal factors, such as age, multiple pregnancies or gestational diabetes, were found to be associated with the development of subsequent pulmonary complications, except for prolonged rupture of membranes.

TABLE 2
Association of perinatal and maternal factors with respiratory distress syndrome (RDS) and bronchopulmonary dysplasia (BPD) after premature birth

	BPD		RDS without subsequent BPD	
Variables	**OR**	**95% CI**	**OR**	**95% CI**
Perinatal factors				
Birth weight	1.23/100 g	1.2–1.3	0.95/100 g	0.93–0.98
Gestational age	1.54/week	1.47–1.64	1.00/week	0.93–1.07
Male sex	1.1	0.8–1.5	1.4	1.0–1.8
1 min Apgar score	1.35/point	1.25–1.45	1.01/point	0.94–1.06
5 min Apgar score	1.39/point	1.27–1.54	1.05/point	1.0–1.14
Maternal and antenatal factors				
Maternal age	1.04/year	1.0–1.08	1.02/year	0.99–1.05
Twin or multiple births	0.6	0.4–0.9	0.6	0.4–0.9
Antenatal steroids	1.2	0.6–2.3	0.48	0.3–0.9
Prolonged rupture of membrane	1.4	1.0–2.0	1.04	0.8–1.4
Premature labour	0.4	0.2–1.1	0.7	0.3–1.7
Gestational diabetes	1.6	0.5–4.9	2.5	0.9–7.3
Secondary diagnoses				
Intraventricular hemorrhage	5.4	3.1–9.3	1.6	0.9–2.9
Retinopathy of prematurity	9.9	4.9–20.2	0.6	0.2–1.5
Neonatal pneumonia/ sepsis	2.2	1.5–3.1	0.6	0.5–0.9
Patent ductus arteriosus	6.9	4.7–10.0	1.1	0.8–1.6
Apnea of prematurity	1.6	1.2–2.3	0.9	0.7–1.2
Pneumothorax	10.5	4.7–23.3	7.1	3.3–15.7
Necrotizing enterocolitis	1.2	0.8–1.9	0.4	0.3–0.7
Seizures	2.9	1.7–5.0	0.6	0.3–1.1
Anemia	2.2	1.4–3.4	0.6	0.4–1.0

As shown in Table 2, BPD was very strongly associated with several conditions commonly observed among preterm infants such as intraventricular hemorrhage, retinopathy and necrotizing enterocolitis. These complications were less frequently seen in the RDS group, partly due to their greater gestational age and weight at birth. Only the presence of a pneumothorax within the first 48 h of life was associated with RDS.

In a multiple logistic regression analysis, BPD was significantly associated with a lower gestational age, a lower Apgar score at 1 min, the presence of patent ductus arteriosus, neonatal pneumonia/sepsis and the occurrence of pneumothorax in the first few days of life (Table 3). For each additional week of prematurity, the risk of developing BPD increased by 54% (OR 1.54/week [95% CI 1.45 to 1.64]). For each point subtracted on the 1 min Apgar score, the risk of developing BPD was increased by 16%. The c-statistic associated with this model was 0.899.

Factors associated with the severity of bronchopulmonary dysplasia

Among the subjects confirmed to have BPD (n=322), 18.6% had mild disease, 38.2% had moderate disease and 33.2% developed severe disease. Thirteen patients fulfilling the NIH consensus criteria for BPD and who died of respiratory causes before the assessment date for severity were included in the severe disease group.

TABLE 3
Association of clinical factors with bronchopulmonary dysplasia (BPD) and respiratory distress syndrome (RDS) (from multivariable logistic regression) among infants with a premature birth

	BPD		RDS	
	Adjusted		Adjusted	
Variables	OR	95% CI	OR	95% CI
Gestational age	1.54/week	1.45–1.64	1.00/week	1.00–1.07
Birth weight*	1.22/100g	1.16–1.28	0.94/100g	0.92–0.97
1 min Apgar score	1.16/point	1.05–1.28	1.12/point	1.02–1.2
Patent ductus arteriosus	3.5	2.1–6.0	–	–
Pneumothorax	9.4	3.6–24.8	5.8	2.5–13.7
Neonatal pneumonia/sepsis	1.9	1.1–3.2	–	–

**The adjusted OR for birth weight was obtained by running the model a second time in parallel with all the other variables, with the exception of gestational age, to avoid collinearity between the two variables. Patent ductus arteriosus and neonatal pneumonia/sepsis were not included in the RDS model because both diagnoses were made during or after the development of the RDS*

TABLE 4
Association of perinatal factors with bronchopulmonary dysplasia (BPD) severity

	Severe versus mild BPD		Moderate versus mild BPD	
Variables	OR	95% CI	OR	95% CI
Birth weight	1.23/100g	1.19–1.28	1.04/100g	1.02–1.06
Gestational age	1.54/week	1.43–1.67	1.08/week	0.93–1.09
Male sex	1.1	0.9–1.3	1.2	1.0–1.3
1 min Apgar score	1.32/point	1.22–1.41	1.01/point	0.94–1.06
5 min Apgar score	1.33/point	1.23–1.45	1.06/point	0.98–1.15

The severity of BPD was not assessed in 32 subjects with confirmed BPD; the most frequent reason for this was a transfer to another institution before the NIH-defined assessment date. These were excluded from the analysis.

A lower Apgar score at 1 min was a predictor of greater disease severity (P=0.002), but birth weight, gestational age and male sex were not. Higher mortality and longer hospital stay were associated with greater BPD severity (P<0.0001). Maternal or antenatal factors, such as maternal age, multiple pregnancies or gestational diabetes, were not found to be associated with the severity of BPD.

RDS was not found to be associated with the resulting severity of BPD, whereas the presence of intraventricular hemorrhage, neonatal pneumonia/sepsis and seizures were associated (P<0.008). Seizures and the occurrence of neonatal pneumonia or sepsis were associated with more severe BPD.

In Table 4, perinatal variables are studied for a possible association with more severe disease (severe or moderate BPD versus mild BPD) following a preterm birth. A lower birth weight, a younger gestational age, and a lower Apgar score at 1 min and 5 min were all significantly associated with severe BPD.

Several conditions were significantly more frequent in infants with severe BPD. Among the conditions consistently (or by definition) diagnosed before the diagnosis of BPD was made, it was observed that pneumothorax (OR 3.2 [95% CI 2.2 to 4.8]), patent ductus arteriosus (OR 2.6 [95% CI 2.2 to 3.2]) and neonatal sepsis/pneumonia (OR 1.5 [95% CI 1.2 to 1.8]) were associated with the development of more severe disease. Among conditions diagnosed at the same time as BPD or after the diagnosis of BPD had been established, intraventricular hemorrhage (OR 2.3 [95% CI 1.8 to 3.1]), anemia (OR 1.5 [95% CI 1.2 to 1.8]), anoxic encephalopathy (OR 2.6 [95% CI 1.2 to 5.5]), retinopathy of prematurity (OR 3.2 [95% CI 2.2 to 4.5]) and seizure (OR 1.7 [95% CI 1.3 to 2.2]) were

TABLE 5
Association of clinical factors with bronchopulmonary dysplasia (BPD) severity (from ordinal multinomial logistic regression) among infants with BPD

	Severe BPD		Moderate BPD	
	Adjusted		Adjusted	
Variables	OR	95% CI	OR	95% CI
Gestational age	1.45/week	1.23–1.67	1.08/week	0.93–1.33
Very low birth weight	2.3	1.3–4.6	0.9	0.5–1.6
1 min Apgar score	1.32/point	1.14–1.54	1.28/point	1.1–1.5
Neonatal pneumonia/sepsis	1.5	1.1–2.1	0.9	0.6–1.3

significantly associated with more severe disease. In a multivariable analysis, a smaller gestational age, the presence of extreme low birth weight, a lower Apgar score at 1 min, and the presence of neonatal pneumonia or sepsis were found to be associated with greater disease severity (P<0.005) (Table 5).

Prediction of BPD after a preterm birth

Use of the ORs estimated in multivariable regression for gestational age of younger than 30 weeks, Apgar score at 1 min and less than 5 min, and the presence of secondary diagnoses occurring shortly after birth (patent ductus arteriosus and pneumothorax) or in the neonatal period before the diagnosis of BPD is made (neonatal pneumonia/sepsis) resulted in the following formula to estimate the probability of development of BPD after a preterm birth:

$$P(\text{BPD}) = \frac{e^{-2.27+2.23(\text{GA}<30\text{ weeks})+0.6(1\text{ min Apgar score}<5)+1.54(\text{PDA})+2.89(\text{PTX})+0.57(\text{Pneum/sepsis})}}{1+e^{-2.27+2.23(\text{GA}<30\text{ weeks})+0.6(1\text{ min Apgar score}<5)+1.54(\text{PDA})+2.89(\text{PTX})+0.57(\text{Pneum/sepsis})}}$$

The tested model had a sensitivity of 82% and a specificity of 84% when applied to the validation dataset. The c-statistic associated with this model was 0.871.

DISCUSSION

Of the 1192 subjects included in the historical cohort study of preterm infants, 27% developed BPD and 46% developed RDS; this is comparable with previously published data (12). Among all preterm infants, 25.6% suffered from patent ductus arteriosus, 10.4% from necrotizing enterocolitis and 11.6% from intraventricular hemorrhage. These frequencies of neonatal morbidities are comparable with those found in previously published literature (13,14).

In the present study, we found that the OR for developing BPD was 1.54 for each additional week below 37 weeks' gestational age (95% CI 1.45 to 1.64). Many authors reported similar results, with ORs ranging from 4.76 (95% CI 1.97 to 11.51) for gestational age younger than 30 weeks (15), to 2.4 per lower week of gestational age for the development of chronic lung disease in infants with a birth weight of less than 1501 g (16), to 2.0 per lower week of gestational age for developing BPD (10) and a near doubling of the odds for BPD in extreme preterm birth (2).

An earlier study estimated that for each lower point on the Apgar scoring system, the likelihood of chronic lung disease in very low birth weight infants increased by 26% (16). This is comparable with our estimate of a 16% increase for each lower point in our subjects with a very low birth weight. In another study of BPD in very low birth weight infants (14), the Apgar score was predictive of adverse developmental outcomes. Use of an Apgar score of lower than 9 to predict the occurrence of BPD was associated with a higher false-positive rate (17). The observation of a lower Apgar score at 1 min, and the finding that a pneumothorax occurring in the first 48 h are both associated with a greater probability of developing BPD when adjusted for gestational age and birth weight, points to the importance of using gentle resuscitation techniques for premature infants in the delivery room.

In agreement with our findings, the presence of patent ductus arteriosus has been recognized by other studies as an additional risk factor for lung disease in infants with a very low birth weight (16) and extreme prematurity (18). Secondary surgical closure of patent ductus arteriosus after failure of medical management was found to have a negative impact on neurological development (18) and was associated with the development of BPD.

Prediction of BPD

Three other probabilistic models have been developed to predict BPD. Using various cut-off points for birth weight and gestational age, as well as including the presence of secondary diagnoses, such as patent ductus arteriosus or use of supplemental oxygen and mechanical ventilation, their maximal predictive probabilities were 75%, 85% and 93.7%, respectively, which was comparable with our model (15,16,19). The sensitivity and specificity of our model on the validation subset (82% and 84%, respectively) was much better than a recently published model of BPD using variables present at seven days (16), which had a positive predictive value of only 22%, although the negative predictive value was 98% (compared with a positive predictive value of 82% and a negative predictive value of 84% for our model).

Strengths and limitations

Findings of the present study were derived from a study population that included all preterm births, regardless of their birth weight and degree of prematurity. This is likely to result in a model that is more useful in predicting BPD in a nonselected population of all preterm infants. The model predicting BPD used variables that are easily identified, making it easy to use in the clinical setting. Furthermore, the predictive equation derived from part of the study cohort demonstrated good accuracy when internally validated using a separate subset of the study cohort.

However, the present study had several important limitations including its retrospective design. Severity could not be assessed for 32 BPD subjects, mainly because of transfer to other institutions. This might have led to an overestimate of the severity in patients with BPD in that those patients may have been transferred back to the referring hospital because they had already recovered – reflecting milder disease.

Temporality of the associations between variables and the outcomes of RDS or BPD were also an issue because of the retrospective study design. This was addressed by choosing variables that were easy to measure and clearly preceded the diagnoses of RDS or BPD. Hence, the present study was able to explore the temporal nature of the observations, although inferences should be made with caution, and considered primarily useful for formulating hypotheses (20).

All subjects included in our cohort were infants who were transferred to the Montreal Children's Hospital following a preterm birth elsewhere. This introduces the possibility of selection for more severe cases requiring tertiary care. However, 97% of these infants were transferred within the first 24 h following their birth. This means that the transfer occurred long before the development of BPD and that the reason motivating the transfer was simply preterm birth or the presence of RDS (67% of BPD subjects had a preceding diagnosis of RDS). Selection bias for subsequent BPD severity appears to have been minimal (or at least similar to other studies) because the proportion of BPD subjects in each severity category was comparable with other published cohorts (5,14,15) including the cohort used to validate the NIH consensus definition of BPD (5).

A final important limitation was that the study population was composed of 'old' BPD cases; only 29.5% of all infants received antenatal corticosteroids and only 9.3% of BPD cases were treated with exogenous surfactants. This limits the generalizability of findings, especially with regard to factors associated with BPD severity and the usefulness of the equation predicting BPD.

CONCLUSION

Development of BPD was associated with gestational age, birth weight, Apgar score at 1 min, pneumothorax, patent ductus arteriosus and neonatal pneumonia/sepsis. BPD severity was associated with gestational age, extreme low birth weight, Apgar score at 1 min and the presence of neonatal pneumonia/sepsis. Also, a simple predictive equation was designed for calculating the likelihood of developing BPD, which may prove to be useful for clinicians in caring for preterm infants, and in discussing their care and prognosis with their families.

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