Delivery room resuscitation and short-term outcomes of extremely preterm and extremely low birth weight infants: a multicenter survey in North China

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Abstract

Background: Delivery room resuscitation assists preterm infants, especially extremely preterm infants (EPI) and extremely low birth weight infants (ELBWI), in breathing support, while it potentially exerts a negative impact on the lungs and outcomes of preterm infants. This study aimed to assess delivery room resuscitation and discharge outcomes of EPI and ELBWI in China.

Methods: The clinical data of EPI (gestational age [GA] <28 weeks) and ELBWI (birth weight [BW] <1000 g), admitted within 72 h of birth in 33 neonatal intensive care units from five provinces and cities in North China between 2017 and 2018, were analyzed. The primary outcomes were delivery room resuscitation and risk factors for delivery room intubation (DRI). The secondary outcomes were survival rates, incidence of bronchopulmonary dysplasia (BPD), and risk factors for BPD.

Results: A cohort of 952 preterm infants were enrolled. The incidence of DRI, chest compressions, and administration of epinephrine was 55.9% (532/952), 12.5% (119/952), and 7.0% (67/952), respectively. Multivariate analysis revealed that the risk factors for DRI were GA <28 weeks (odds ratio [OR], 3.147; 95% confidence interval [CI], 2.082–4.755), BW <1000 g (OR, 2.240; 95% CI, 1.606–3.125), and antepartum infection (OR, 1.429; 95% CI, 1.044–1.956). The survival rate was 65.9% (627/952) and was dependent on GA. The rate of BPD was 29.3% (181/627). Multivariate analysis showed that the risk factors for BPD were male (OR, 1.603; 95% CI, 1.061–2.424), DRI (OR, 2.094; 95% CI, 1.328–3.303), respiratory distress syndrome exposed to ≥2 doses of pulmonary surfactants (PS; OR, 2.700; 95% CI, 1.679–4.343), and mechanical ventilation ≥7 days (OR, 4.358; 95% CI, 2.777–6.837). However, a larger BW (OR, 0.998; 95% CI, 0.996–0.999), antenatal steroid (OR, 0.577; 95% CI, 0.379–0.880), and PS use in the delivery room (OR, 0.273; 95% CI, 0.160–0.467) were preventive factors for BPD (all $P < 0.05$).

Conclusion: Improving delivery room resuscitation and management of respiratory complications are imperative during early management of the health of EPI and ELBWI.

Keywords: Extremely preterm; Extremely low birth weight infants; Delivery room resuscitation; Survival rate; BPD; Risk factors

Introduction

Extremely preterm infants (EPI, gestational age [GA] <28 weeks) and extremely low birth weight infants (ELBWI, birth weight [BW] <1000 g) are both high-risk neonates and pose challenges in perinatal medicine. Despite mechanical advances and the efforts of neonatologists over the last few decades, EPI and ELBWI have still been subjected to neonatal complications, death, and long-term neurodevelopmental impairments.[1-4] While delivery room intubation (DRI) effectively provides breathing assistance for preterm infants, the incidence of bronchopulmonary dysplasia (BPD) concomitantly increases,[5,6] resulting in neurological impairments.[6-8] Antenatal steroids (ANS)[9,10] and enhanced delivery room resuscitation strategies are associated with a reduction in the need for DRI [11-13] and incidence of BPD, thus improving the outcomes of preterm infants.[14,15]

Few studies from China regarding delivery room resuscitation of EPI and ELBWI have been reported. Thus, this multicenter study aimed to primarily evaluate the incidence, risk factors of DRI and secondarily assess rates of survival and BPD of EPI and ELBWI in China.

Methods

Ethical approval

The study was approved by the Ethics Committee of Peking University First Hospital.

Subjects

This study was conducted within the North China Neonatal Alliance, which comprised 44 centers. Clinical data of EPI (GA <28 weeks) and ELBWI (BW <1000 g) were analyzed from tertiary and secondary hospitals in Beijing, Tianjin, Hebei, Shanxi Province, and Inner Mongolia Autonomous Region in North China between January 1, 2017 and December 31, 2018. Inclusion criteria for the study were preterm infants with a GA <28 weeks or BW <1000 g, who were admitted within 72 h of birth with complete data. Exclusion criteria were infants with lethal congenital heart diseases, such as Tetralogy of Fallot and complete transposition of the great arteries; malformed digestive systems, such as intestinal stenosis and intestinal atresia; or central nervous system disorders, and inborn metabolic diseases.

This study was conceptualized and coordinated by the Pediatric Department of Peking University First Hospital as the host unit, and was reviewed by the collaborative hospitals. All collaborators agreed to sign a cooperation agreement. Data were collected by collaborators using a questionnaire designed with EpiData Software (The EpiData Association, Odense, Denmark). Collected data were stored, analyzed at the host unit reviewing the data. Collected data comprised infants' and mothers' demographics, delivery room resuscitation information, major respiratory complications, respiratory assistance, and outcomes at discharge regarding infants. The EPI and ELBWI were categorized by GA, BW, outcomes at discharge and whether or not have BPD.

Definitions

For consistency, the following criteria were defined and adopted: (1) small for gestational age (SGA) was defined as a newborn whose BW was <10th percentile for GA according to Fenton Growth Curves[16]; (2) ANS describes a completed drug course of a mother that received four consecutive intramuscular injections of dexamethasone before delivery; (3) ANS exposure was defined as a mother who received less than four intramuscular injections of dexamethasone before delivery; (4) respiratory assistance was presented as one form of non-invasive ventilation (NIV) that consisted of nasal continuous positive airway pressure, bi-level positive airway pressure, non-invasive positive pressure ventilation (NIPPV), or another form of mechanical ventilation (MV) referred to as endotracheal intubation; (5) antepartum infection was described as

premature rupture of the membranes ≥18 h or mothers with fever or contaminated amniotic fluid; (6) respiratory distress syndrome (RDS) was defined as a newborn who was diagnosed with progressive dyspnea with a chest radiograph showing homogeneous, diffuse fine-grained change in two lungs. Severe RDS was confirmed by a chest radiograph showing the heart margin, a diaphragmatic blurred shadow, or white lung; and (7) BPD was diagnosed if infants required oxygen at 36 weeks corrected GA.

Outcomes at discharge

There were three main outcomes at discharge: (1) discharge according to medical advice was described as infants who underwent complete care until vital signs were stable and could be discharged from the hospital according to the physicians' recommendation; (2) discharge against medical advice was defined as infants who did not require a ventilator but whose therapy was terminated by the parents before the physicians' recommendation to discharge, or infants who were transferred for surgery; and (3) death was referred to as infants that died despite receiving therapy or as a result of parents terminating treatment when infants were mechanically ventilated shortly after birth.

Statistical analysis

Continuous variables with a normal distribution were described as the mean ± standard deviation (SD) and compared by analysis of variance among the three groups and multiple comparisons were performed using Fisher least significant difference procedure. Continuous variables with a normal distribution in univariate analysis for BPD were described as the mean ± SD and compared between two groups using *t*-test. Data with skew distributions were shown as the median (interquartile range [IQR]) and compared using a Mann-Whitney *U* test between two groups and Kruskal-Wallis *H* test between three groups. Categorical variables were expressed as the counts and percentages and compared using χ^2tests or Fisher exact test, in which *P* value was adjusted with Bonferroni method for multiple comparisons and less than 0.017 was considered as statistically significant. We used multivariable logistic regression analysis to assess the association between DRI and the perinatal risk factors and potential confounders, identified as a priori on the basis of clinical importance. A similar logistic regression was fitted to assess the association between BPD and potential factors. *P* value < 0.05 was considered statistically significant. All statistical analyses were performed using SPSS 22.0 software (IBM, Armonk, NY, USA).

Results

Study centers

In total, 33 centers (30 tertiary hospitals and three secondary hospitals) from North China Neonatal Alliance participated in this study. Twelve, four, eight, three, and six centers were located in Beijing, Tianjin, Hebei Province, Shanxi Province, and Inner Mongolia Autonomous Region, respectively. Of the 34,179 preterm infants (GA <37 weeks) who were admitted to these institutions, between January 1, 2017 and December 31, 2018, 952 cases were EPI and ELBWI and eligibled for this study.

Infants' characteristics

A cohort of 952 infants (498 [52.3%] males) were enrolled for the study, of whom 152 infants were not born in the participated centers. The median (IQR) age of the admitted infants was 0.43 (0.25, 0.90) h. Infants were categorized into three groups according to GA and BW: <28 weeks and <1000 g (*n* = 380); <28 weeks and ≥1000 g (*n* = 273), and ≥28 weeks and <1000 g (*n* = 299). The mean (SD) GA was 27.7 (1.8) weeks. Infants with GA of <25, 25, 26, 27, and ≥28 weeks accounted for 4.3% (41/952), 7.2% (69/952), 18.1% (172/952), 39.0% (371/952), and 31.4% (299/952), respectively. The mean (SD) BW was 938 (162) g. Infants weighing <750, 750 to 899, 900 to 999, and ≥1000 g accounted for 9.6% (91/952), 26.8% (255/952), 35.0% (333/952), and 28.7% (273/952), respectively. Among the 679 ELBWI, infants born at <28 weeks accounted for 56.0% (380/679), and among the 653 EPI, infants weighing <1000 g accounted for 58.2% (380/653) [Table 1].

Maternal characteristics

The overall mean (SD) maternal age was 32.2 (4.7) years. The mean (SD) maternal age of <28 weeks and <1000 g,<28 weeks and ≥1000 g, ≥28 weeks and <1000 g group was 32.6 (4.4), 31.8 (4.6), 32.3 (5.1) years, respectively ($F = 2.4$, $P = 0.100$). It was noted that the mothers of the EPI group (GA <28 weeks) received additional assisted reproductive technology (30.3% [198/653] *vs.* 16.4% [49/299], $\chi^2 = 14.3$, $P < 0.001$), and experienced a higher proportion of antepartum infection (30.0% [196/653] *vs.*

Table 1: Characteristics of infants in three groups (*n* = 952).

Variables	Overall	<28 weeks and <1000 g	<28 weeks and ≥1000 g	≥28 weeks and <1000 g	*F*/χ^2	*P**
n (%)	952 (100.0)	380 (39.9)	273 (28.7)	299 (31.4)		
GA (weeks), mean ± SD	27.7 ± 1.8	26.4 ± 1.1	27.3 ± 0.5†	29.7 ± 1.5†,‡	765.5§	<0.001
BW (g), mean ± SD	938 ± 162	839 ± 119	1127 ± 109†	891 ± 90†,‡	608.1§	<0.001
Male, *n* (%)	498 (52.3)	197 (51.8)	176 (64.5)†	125 (41.8)†,‡	29.4	<0.001
SGA, *n* (%)	170 (17.9)	17 (4.5)	0 (0.0)	153 (51.2)†,‡	194.4	<0.001

BW: Birth weight; GA: Gestational age; SD: Standard deviation; SGA: Small for gestational age. *Comparison among the three groups. †Compared with <28 weeks and <1000 g group, $P < 0.01$. ‡Compared with <28 weeks and ≥1000 g group, $P < 0.01$. §*F* value.

Table 2: Delivery room resuscitation of infants in three groups ($n = 952$).

Variables	Total	<28 weeks and <1000 g	<28 weeks and ≥1000 g	≥28 weeks and <1000 g	χ^2	P^*
n (%)	952 (100.0)	380 (39.9)	273 (28.7)	299 (31.4)		
No positive pressure ventilation, *n* (%)	229 (24.1)	52 (13.7)	76 (27.8)†	101 (33.8)†	40.0	<0.001
Intubation, *n* (%)	532 (55.9)	264 (69.5)	139 (50.9)†	129 (43.1)†	50.9	<0.001
Chest compressions, *n* (%)	119 (12.5)	69 (18.2)	23 (8.4)†	27 (9.0)†	18.6	<0.001
Epinephrine, *n* (%)	67 (7.0)	41 (10.8)	11 (4.0)†	15 (5.0)†	27.3	<0.001
PS in DR, *n* (%)	257 (27.0)	129 (33.9)	83 (30.4)	45 (15.1)†,‡	32.6	<0.001
5-min Apgar score <5, *n* (%)	36 (3.9)	20 (5.3)	7 (2.6)	9 (3.0)	3.9	0.143

BW: Birth weight; DR: Delivery room; GA: Gestational age; PS: Pulmonary surfactant. *Comparison among the three groups. †Compared with <28 weeks and <1000 g group, $P < 0.01$. ‡Compared with <28 weeks and ≥1000 g group, $P < 0.01$.

Table 3: Multivariable logistic regression analysis of risk factors for DRI.

Variable	β	*P*	OR	95% CI
GA <28 weeks	1.146	<0.001	3.147	2.082–4.755
BW <1000 g	0.806	<0.001	2.240	1.606–3.125
Antepartum infection	0.357	0.026	1.429	1.044–1.956
Delivery mode*		0.011		
Forceps delivery	1.384	0.003	3.991	1.613–9.874
Constant	–1.346	<0.001	0.260	

BW: Birth weight; CI: Confidence interval; DRI: Delivery room intubation; GA: Gestational age; OR: Odds ratio. *Natural delivery as referrence, delivery mode included natural, cesarean, and forceps deliveries.

18.4% [55/299], $\chi^2 = 14.3$, $P < 0.001$) compared to the mothers of infants with ≥28 weeks and <1000 g. However, the mothers of infants with ≥28 weeks and <1000 g showed an increased incidence of hypertension (61.5% [184/299] *vs.* 18.2% [119/653], $\chi^2 = 177.3$, $P < 0.001$), higher occurrence of cesarean delivery (82.3% [246/299] *vs.* 26.3% [172/653], $\chi^2 = 260.5$, $P < 0.001$), and lower incidence of forceps delivery (1.3% [4/299] *vs.* 5.4% [35/653], $\chi^2 = 6.4$, $P < 0.05$) compared to the EPI group (GA <28 weeks). Mothers of the infants in the <28 weeks and ≥1000 g group had the lowest rate of hypertension ($P < 0.05$).

Delivery room resuscitation for EPI and ELBWI

The overall rate of DRI among infants was 55.9% (532/952). A 5-min Apgar score <5 was observed for 3.9% (36/952) of the total infants. Infants with a BW ≥1000 g or GA ≥28 weeks did not require positive pressure ventilation, with rates of 27.8% (76/273) and 31.4% (101/299), respectively. The infants with a GA <28 weeks and BW <1000 g had a higher rate of DRI (69.5% [264/380]), chest compression (18.2% [69/380]), and epinephrine use (10.8% [41/380]) compared with infants with a BW ≥1000 g or GA ≥28 weeks ($P < 0.001$). Overall, 27.0% of infants received pulmonary surfactants (PS) therapy during delivery room resuscitation of which infants with GA <28 weeks accounted for the rate of PS therapy (82.5% [212/257]) [Table 2].

We assessed the risk factors for DRI by multivariable logistic regression analysis. Independent variables for the analysis included GA <28 weeks (reference: ≥28 weeks), BW <1000 g (reference: ≥1000 g), male (reference: female), SGA at birth (reference: non-SGA), ANS (reference: no), antepartum infection (reference: no), multiple births (reference: single birth), delivery mode (natural, cesarean, and forceps deliveries [reference: natural]), and hypertension (reference: no). Overall, GA <28 weeks, BW <1000 g, antepartum infection, and forceps delivery were risk factors for DRI ($P < 0.05$) [Table 3].

Discharge outcomes

Overall, 65.9% (672/952), 25.3% (241/952), and 8.8% (84/952) of all EPI and ELBWI were discharged according to medical advice, died during hospitalization, and discharged against medical advice (whose outcomes remained unknown), respectively. The mean duration of hospitalization of infants discharged according to medical advice was 69.6 (18.0) days; for the dead infants, death occurred at a median age of 3.0 (1.7, 10.0) days after birth; for the infants discharged against medical advice, they were discharged at a median age of 12.0 (3.3, 31.8) days ($P < 0.05$). Overall, the infants between the three groups had a similar mean GA of 27.9 (1.7), 27.2 (1.9), and 27.9 (1.9) weeks, respectively; and a similar mean BW of 959 (153), 883 (174), and 941 (164) g, respectively ($P > 0.05$).

Perinatal factors and respiratory complications for infants with different outcomes

Non-survivors had a higher rate of DRI, MV, ≥2 doses of PS therapy, severe RDS, and pulmonary hemorrhage; however, they also had a lower rate of ANS exposure (all

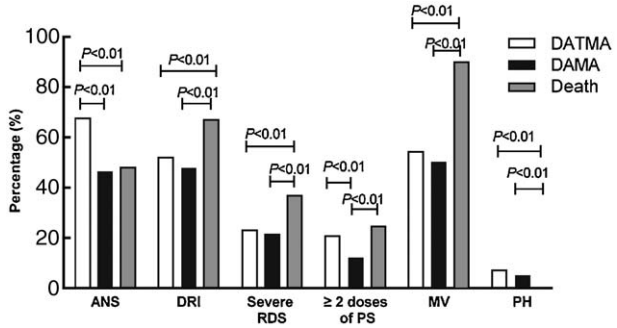

Figure 1: Perinatal factors and respiratory complications of infants with different outcomes. ANS: Antenatal steroid; DAMA: Discharge against medical advice; DATMA: Discharge according to medical advice; DRI: Delivery room intubation; MV: Mechanical ventilation; PH: Pulmonary hemorrhage; PS: Pulmonary surfactant; RDS: Respiratory distress syndrome.

$P < 0.05$). These infants also had a lower incidence of ≥1 complete course of ANS ($P > 0.05$) [Figure 1].

Infants discharged according to medical advice

Of the 627 infants that were discharged according to medical advice, 29.3% (181/627) were diagnosed with BPD. Univariate analysis revealed that preterm infants with BPD had a smaller GA and BW; higher rates of DRI, RDS, severe RDS, administration of ≥2 doses of PS therapy, and pulmonary hemorrhage; lower rate of ANS; and were more likely to be male, use MV, and have prolonged MV (all $P < 0.05$). Compared to the infants with non-BPD, infants with BPD had a lower rate of antepartum infection (21.5% [39/181] *vs.* 30.0% [134/446]) and a longer duration of hospitalization (77.1 ± 18.9 days *vs.* 66.6 ± 16.7 days, $P < 0.001$) [Table 4].

To assess the risk factors for BPD, independent variables included GA (weeks), BW (g), male (reference: female), SGA at birth (reference: non-SGA), hypertension (reference: non-hypertension), ANS (reference: no), antepartum infection (reference: no), DRI (reference: no), administration of PS in the delivery room (reference: no), RDS (reference: no), receiving ≥2 doses of PS therapy (reference: ≤1 doses of PS therapy), pulmonary hemorrhage (reference: no), and MV duration of ≥7 days (reference: <7 days). Multivariable logistic regression analysis confirmed that risk factors for BPD were male, DRI, RDS, requiring ≥2 doses of PS therapy, and MV duration of ≥7 days ($P < 0.05$). However, larger BW, ANS exposure, and administration of PS in the delivery room were preventive factors for BPD ($P < 0.05$). GA, SGA, hypertension, antepartum infection, and pulmonary hemorrhage were not associated with BPD ($P > 0.05$) [Table 5].

Discussion

This cohort of EPI and ELBWI admitted to neonatal intensive care units (NICUs) in North China were used to evaluate the outcomes of treating high-risk preterm infants. The survival rate of preterm infants was 65.9% at discharge, while the mortality rate was 25.3%. The remaining 8.8% were discharged against medical advice, and thus the outcomes are unknown. Of the total 952 infants, 61.3% and 55.9% were exposed to ANS and underwent DRI, respectively. Infants with BPD comprised 29.3% of the preterm infants discharged according to medical advice.

Respiratory support is the essence of delivery room resuscitation. In our study, 55.9% of infants were intubated, which is less than that reported by studies in 2015 from the United States[17] and Italy, respectively.[18] Studies concerning risk factors for DRI are limited. A multicenter study of premature infants (born at 29th–32nd weeks GA), reported that older GA, ANS exposure, and premature rupture of the membranes (>18 h) could reduce the degree of delivery room resuscitation, and maternal chorioamnionitis could decrease the risk of oxygenation or continuous positive airway pressure and intubation requirement, but SGA infants had an increased risk of DRI.[19] A previous study showed that intrauterine infection could accelerate fetal lung maturation, which would reduce the risk of intubation.[20] However, in the current study, prenatal infection was a risk factor for DRI, which does not correspond with previous research, as the infants in this study were more immature, and our definition of infection was non-histological chorioamnionitis. Additionally, in the current study, the number of SGA infants was high and rate of ANS exposure was lower. Therefore, these factors may aid in reducing the need for DRI and improve comprehensive management. Previous studies have shown that DRI is related to the premature death rate and rate of BPD.[5,21] Recent reports have indicated that increasing the peak inspiratory pressure,[11] positive-end expiratory pressure of NIV,[12] and application of nasal intermittent positive pressure ventilation[13] reduced the need for intubation in the delivery room, rate of intubation within 24 h after birth, and MV duration for preterm infants with a GA <29 weeks.[13] As there was a higher rate of DRI required for EPI and ELBWI, this study showed that suitable breathing support devices are imperative in the delivery room, and that practices of resuscitation should be improved with the focus during resuscitation being on long-term lung protection.

The survival rate of preterm infants was 65.9% in this study, which is lower than previous reports worldwide,[17,22,23] but higher than those reported by other studies in China.[24-26] In total, 8.8% of preterm infants were discharged against medical advice, with a median age of 14 days after birth. Thus, the outcomes of these infants were not determined. The median age of infants that died in this study was three days old. Among the infants that had died, high rates of DRI, serious RDS, administration of ≥2 doses of PS therapy, MV, and pulmonary hemorrhage were observed, indicating that early mortality was associated with vigorous resuscitation, the early onset of severe respiratory diseases, and comprehensive management of EPI and ELBWI. Similar results were reported in a multicenter study in Finland in 2019,[27] where the median age of mortality of EPI was within two days after birth and the causes of mortality were younger GA, RDS, and severe intracranial hemorrhage.

Table 4: Univariate analysis of risks for bronchopulmonary dysplasia among 627 infants discharged according to medical advice.

Variables	BPD	Non-BPD	t/χ^2	*P*
n (%)	181 (29.3)	446 (70.7)		
GA (weeks), mean (SD)	27.6 ± 1.4	28.0 ± 1.8	–3.2*	0.002
BW (g), mean (SD)	932 ± 155	970 ± 152	–2.8*	0.005
Male, *n* (%)	109 (60.2)	217 (48.7)	6.9	0.009
SGA, *n* (%)	23 (12.7)	85 (19.1)	3.6	0.056
Antepartum infection, *n* (%)	39 (21.5)	134 (30.0)	4.6	0.031
ANS, *n* (%)	108 (60.0)	320 (71.7)	8.7	0.003
Inborn birth, *n* (%)	155 (85.6)	378 (84.8)	0.1	0.779
DRI, *n* (%)	115 (63.5)	214 (48.0)	12.5	<0.001
RDS, *n* (%)	173 (95.6)	385 (86.3)	11.3	0.001
Severe RDS, *n* (%)	56 (30.9)	91 (20.4)	4.7	0.030
RDS receiving ≥2 doses of PS, *n* (%)	66 (36.5)	55 (12.3)	48.1	<0.001
Pulmonary hemorrhage, *n* (%)	21 (11.6)	27 (6.1)	417.1	<0.001
MV, *n* (%)	154 (85.1)	192 (43.0)	92.0	<0.001
MV duration (days), median (IQR)	8.0 (2.9, 18.0)	0.0 (0.0, 4.6)	–11.1	<0.001
MV duration ≥7 days, *n* (%)	99 (54.7)	81 (18.2)	49.3	<0.001
DOH (days), mean (SD)	77.1 ± 18.9	66.6 ± 16.7	6.9*	<0.001

ANS: Antenatal steroid; BPD: Bronchopulmonary dysplasia; BW: Birth weight; DOH: Duration of hospitalization; DRI: Delivery room intubation; GA: Gestational age; IQR: Interquartile range; MV: Mechanical ventilation; PS: Pulmonary surfactant; RDS: Respiratory distress syndrome; SD: Standard deviation; SGA: Small for gestational age. *t value.

Table 5: Multivariable logistic regression analysis of risk factors for BPD.

Variable	β	*P*	OR	95% CI
BW (g)	–0.002	0.008	0.998	0.996–0.999
Male	0.472	0.025	1.603	1.061–2.424
ANS	–0.549	0.011	0.577	0.379–0.880
DRI	0.739	0.001	2.094	1.328–3.303
Administration of PS in delivery room	–1.297	<0.001	0.273	0.160–0.467
RDS receiving ≥2 doses of PS	0.993	<0.001	2.700	1.679–4.343
MV duration ≥7 days	1.472	<0.001	4.358	2.777–6.837
Constant	1.510	0.547	4.525	

ANS: Antenatal steroid; CI: Confidence interval; BPD: Bronchopulmonary dysplasia; BW: Birth weight; DRI: Delivery room intubation; MV: Mechanical ventilation; OR: Odds ratio; PS: Pulmonary surfactant; RDS: Respiratory distress syndrome.

BPD remains one of the most common and important complications in preterm infants, which is associated with long-term outcomes.[15,28] In this study, the incidence of BPD was lower than that of similar preterm infants examined in previous studies.[17,22,23,25,29] This discrepancy may be because partial preterm infants were discharged against medical advice. BPD not only pre-disposes preterm infants to respiratory diseases, but also results in adverse effects on long-term cardiovascular health,[14] neurodevelopment,[28,30] mortality, and disability,[15] as well as other comorbidities due to the chronic hypoxia resultant from BPD and prematurity. Therefore, optimizing management strategies for infants susceptible to BPD and decreasing the overall incidence of BPD will be crucial in improving short and long-term prognoses. Immature lungs and RDS increase the occurrence rate of BPD. In the current study, while multivariate analysis established that RDS with ≥2 doses of PS therapy was a risk factor for BPD, larger BW, ANS exposure, and a single administration of PS therapy in the delivery room were associated with a reduction of BPD. These results are similar to those of Rutkowska *et al*[31] and Lapcharoensap *et al*.[32] In addition, no association between GA and BPD was observed in the current study, possibly because of the fewer preterm infants with a smaller and limited range of GA. Perinatal care exerts a critical effect on the outcomes of EPI and ELBWI. In addition to prolonging the gestational period and maintaining healthy intrauterine growth, ensuring ANS exposure to prevent gestational complications and RDS is essential in reducing the rate of BPD. Moreover, in addition to perinatal care, integrated management strategies for preterm infants susceptible to BPD in NICUs are crucial. Although respiratory assistance and PS therapy were provided for preterm infants with RDS, this study demonstrated that the occurrence of BPD was related to DRI and MV duration (≥7 days). Furthermore, administration of PS in the delivery room was a preventive factor for BPD. European Consensus Guidelines on the Management of RDS recommend that a GA <26 weeks is an indication of prophylactic PS treatment,[9] while PS usage is an indicator for DRI. Therefore, it is hypothesized that the higher incidence of

DRI and active administration of PS in the delivery room have a positive effect on decreasing the risk factors for BPD. In addition, improving the implementation of NIV, and thus a reduction in intubation, were beneficial in reducing the occurrence of BPD. To prevent prematurity, systematic usage of NIPPV, avoidance of hyperoxia exposure, PS use, caffeine, and vitamin A were associated with a reduction in the occurrence rate of BPD.[33] Raghuram *et al*[34] showed that PS therapy can aid in reducing the rate of BPD.

China is a vast country, with wide discrepancies in economy and medical care. Treatments for EPI and ELBWI in North China were assessed between 2017 and 2018. When compared with a multicenter study regarding EPI in the Guangdong Province in China between 2008 and 2017.[35] In our study, the use of complete courses of ANS and survival were higher, BPD morbidity and infant mortality were lower, and delivery room resuscitation data were more detailed. These discrepancies are importantly associated with different therapeutic practices and the different levels of hospitals of each study. Different studies from the Chinese mainland have shown that the number of critical preterm infants is increasing in different regions and that treatment practices are improving; however, a gap in treatment practices remains compared to other developed countries.

A major strength of the study was that enrolled infants included both EPI and ELBWI. Unlike previous studies, the data were collected and rigorously assessed in detail, especially delivery room resuscitation data that previous studies from China lacked. Thirty-three NICUs participated in this study, including 30 tertiary hospitals and three secondary hospitals, which are widely distributed in the northern areas of China. Characteristics and outcomes of EPI and ELBWI, grouped by GA and BW, are highlighted in the current study.

A limitation of the current study is that the mortality and incidences of BPD of the infants who were discharged against medical advice could not be determined.

Overall, these findings are conducive towards the improvement of treatment strategies and the outcomes of EPI and ELBWI. Multiple interventions are required for prenatal management, delivery room resuscitation, and treatment practices in NICUs to ensure positive outcomes for EPI and ELBWI.

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Conflicts of interest

None.

References

1. Institute of Medicine (US) Committee on Understanding Premature Birth and Assuring Healthy Outcomes. Preterm Birth: Causes, Consequences, and Prevention. Behrman RE, Butler AS, editors. Washington (DC): National Academies Press (US); 2007. PMID: 20669423.
2. Saigal S, Doyle LW. An overview of mortality and sequelae of preterm birth from infancy to adulthood. Lancet 2008;371:261–269. doi: 10.1016/S0140-6736(08)60136-1.
3. Johnson S, Marlow N. Early and long-term outcome of infants born extremely preterm. Arch Dis Child 2016;102:97–102. doi: 10.1136/archdischild-2015-309581.
4. Glass HC, Costarino AT, Stayer SA, Brett CM, Cladis F, Davis PJ. Outcomes for extremely premature infants. Anesth Analg 2015;120:1337–1351. doi: 10.1213/ANE.0000000000000705.
5. Schmolzer GM, Kumar M, Pichler G, Aziz K, O'Reilly M, Cheung PY. Non-invasive versus invasive respiratory support in preterm infants at birth: systematic review and meta-analysis. BMJ 2013;347:f5980. doi: 10.1136/bmj.f5980.
6. DeMauro SB, Roberts RS, Davis P, Alvaro R, Bairam A, Schmidt B. Impact of delivery room resuscitation on outcomes up to 18 months in very low birth weight infants. J Pediatr 2011;159:546–550.e1. doi: 10.1016/j.jpeds.2011.03.025.
7. Barton SK, Tolcos M, Miller SL, Christoph-Roehr C, Schmölzer GM, Moss TJ, *et al*. Ventilation-induced brain injury in preterm neonates:

a review of potential therapies. Neonatology 2016;110:155–162. doi: 10.1159/000444918.
8. Barton SK, Tolcos M, Miller SL, Roehr CC, Schmölzer GM, Davis PG, *et al*. Unraveling the links between the initiation of ventilation and brain injury in preterm infants. Front Pediatr 2015;3:97. doi: 10.3389/fped.2015.00097.
9. Sweet DG, Carnielli V, Greisen G, Hallman M, Ozek E, Te Pas A, *et al*. European consensus guidelines on the management of respiratory distress syndrome–2019 update. Neonatology 2019;115:432–450. doi: 10.1159/000499361.
10. Roberts D, Brown J, Medley N, Dalziel SR. Antenatal corticosteroids for accelerating fetal lung maturation for women at risk of preterm birth. Cochrane Database Syst Rev 2017;3:CD004454. doi: 10.1002/14651858.CD004454.pub2.
11. Kakkilaya V, Jubran I, Mashruwala V, Ramon E, Simcik VN, Marshall M, *et al*. Quality improvement project to decrease delivery room intubations in preterm infants. Pediatrics 2019;143: e20180201. doi: 10.1542/peds.2018-0201.
12. Petrillo F, Valenzano L, Franco C, Calò G, Dentico D, Manzoni P, *et al*. Pulmonary recruitment strategy in preterm neonates <29 weeks of gestational age to reduce the need for intubation in the delivery room. Am J Perinatol 2019;36 (S 02):S115–S119. doi: 10.1055/s-0039-1692134.
13. Biniwale M, Wertheimer F. Decrease in delivery room intubation rates after use of nasal intermittent positive pressure ventilation in the delivery room for resuscitation of very low birth weight infants. Resuscitation 2017;116:33–38. doi: 10.1016/j.resuscitation.2017.05.004.
14. Thébaud B, Goss KN, Laughon M, Whitsett JA, Abman SH, Steinhorn RH, *et al*. Bronchopulmonary dysplasia. Nat Rev Dis Primers 2019;5:78. doi: 10.1038/s41572-019-0127-7.
15. Schmidt B, Roberts RS, Davis PG, Doyle LW, Asztalos EV, Opie G, *et al*. Prediction of late death or disability at age 5 years using a count of 3 neonatal morbidities in very low birth weight infants. J Pediatr 2015;167:982–986.e2. doi: 10.1016/j.jpeds.2015.07.067.
16. Fenton TR, Kim JH. A systematic review and meta-analysis to revise the Fenton growth chart for preterm infants. BMC Pediatrics 2013;13:59–159. doi: 10.1186/1471-2431-13-59.
17. Stoll BJ, Hansen NI, Bell EF, Walsh MC, Carlo WA, Shankaran S, *et al*. Trends in care practices, morbidity, and mortality of extremely preterm neonates, 1993-2012. JAMA 2015;314:1039–1051. doi: 10.1001/jama.2015.10244.
18. Mardegan V, Satariano I, Doglioni N, Criscoli G, Cavallin F, Gizzi C, *et al*. Delivery room management of extremely low birth weight infants in Italy: comparison between academic and non-academic birth centres. J Matern Fetal Neonatal Med 2015;29:2592–2595. doi: 10.3109/14767058.2015.1094787.
19. Bajaj M, Natarajan G, Shankaran S, Wyckoff M, Laptook AR, Bell EF, *et al*. Delivery room resuscitation and short-term outcomes in moderately preterm infants. J Pediatr 2018;195:33–38.e2. doi: 10.1016/j.jpeds.2017.11.039.
20. Moss TJM, Westover AJ. Inflammation-induced preterm lung maturation: lessons from animal experimentation. Paediatr Respir Rev 2017;23:72–77. doi: 10.1016/j.prrv.2016.10.004.
21. Foglia EE, Jensen EA, Kirpalani H. Delivery room interventions to prevent bronchopulmonary dysplasia in extremely preterm infants. J Perinatol 2017;37:1171–1179. doi: 10.1038/jp.2017.74.
22. Lee JH, Noh OK, Chang YS. Neonatal outcomes of very low birth weight infants in Korean neonatal network from 2013 to 2016. J Korean Med Sci 2019;34:e40. doi: 10.3346/jkms.2019.34.e40.
23. Travers CP, Carlo WA, McDonald SA, Das A, Bell EF, Ambalavanan N, *et al*. Mortality and pulmonary outcomes of extremely preterm infants exposed to antenatal corticosteroids. Am J Obstet Gynecol 2018;218:130.e1–130.e13. doi: 10.1016/j.ajog.2017.11.554.
24. Collaborative Study Group for Extremely Preterm Infants and Extremely Low Birth Weight Infants. A study on clinical outcomes of extremely preterm infants and extremely low birth weight infants. Chin J Neonatal 2020;35:108–111. doi: 10.3760/cma.j.issn.2096-2932.2020.02.008.
25. Lin HJ, Du LZ, Ma XL, Shi LP, Pan JH, Tong XM, *et al*. Mortality and morbidity of extremely low birth weight infants in the mainland of China: a multi-center study. Chin Med J (Engl) 2015;128:2743–2750. doi: 10.4103/0366-6999.167312.
26. Jiang S, Yan W, Li S, Zhang L, Zhang Y, Shah PS, *et al*. Mortality and morbidity in infants <34 weeks' gestation in 25 NICUs in China: a prospective cohort study. Front Pediatr 2020;8:33. doi: 10.3389/fped.2020.00033.
27. Härkin P, Marttila R, Pokka T, Saarela T, Hallman M. Survival analysis of a cohort of extremely preterm infants born in Finland during 2005-2013. J Matern Fetal Neonatal Med 2019;1–7. doi: 10.1080/14767058.2019.1668925.
28. Brumbaugh JE, Bell EF, Grey SF, DeMauro SB, Vohr BR, Harmon HM, *et al*. Behavior profiles at 2 years for children born extremely preterm with bronchopulmonary dysplasia. J Pediatr 2020;219:152–159.e5. doi: 10.1016/j.jpeds.2019.12.028.
29. Collaborative Study Group for Extremely Preterm and Extremely Low Birth Weight Infants. Short-term outcomes and their related risk factors of extremely preterm and extremely low birth weight infants in Guangdong province. Chin J Pediatr 2019;57:934–942. doi: 10.3760/cma.j.issn.0578-1310.2019.12.008.
30. Lee J, Choi Y, Hong J, Kim NY, Kim EB, Lim J, *et al*. Bronchopulmonary dysplasia is associated with altered brain volumes and white matter microstructure in preterm infants. Neonatology 2019;116:163–170. doi: 10.1159/000499487.
31. Rutkowska M, Hożejowski R, Helwich E, Borszewska-Kornacka MK, Gadzinowski J. Severe bronchopulmonary dysplasia - incidence and predictive factors in a prospective, multicenter study in very preterm infants with respiratory distress syndrome. J Matern Fetal Neonatal Med 2019;32:1958–1964. doi: 10.1080/14767058.2017.1422711.
32. Lapcharoensap W, Gage SC, Kan P, Profit J, Shaw GM, Gould JB, *et al*. Hospital variation and risk factors for bronchopulmonary dysplasia in a population-based cohort. JAMA Pediatrics 2015;169: e143676. doi: 10.1001/jamapediatrics.2014.3676.
33. Principi N, Di Pietro GM, Esposito S. Bronchopulmonary dysplasia: clinical aspects and preventive and therapeutic strategies. J Transl Med 2018;16:36. doi: 10.1186/s12967-018-1417-7.
34. Raghuram K, Mukerji A, Young J, Yee W, Seshia M, Dow K, *et al*. Surfactant utilization and short-term outcomes in an era of non-invasive respiratory support in Canadian neonatal intensive care units. J Perinatol 2017;37:1017–1023. doi: 10.1038/jp.2017.98.
35. Wu F, Liu G, Feng Z, Tan X, Yang C, Ye X, *et al*. Short-term outcomes of extremely preterm infants at discharge: a multicenter study from Guangdong province during 2008-2017. BMC Pediatr 2019;19:405. doi: 10.1186/s12887-019-1736-8.

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