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Diagnostic value of chest CT combined with x-ray for premature infants with bronchopulmonary dysplasia

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Abstract

Bronchopulmonary dysplasia (BPD) is a common chronic lung disease in the newborns. Staging of BPD severity does not have a high predictive value for the outcomes. This study was aimed to assess the diagnostic value of chest computed tomography (CT) combined with x-ray for premature infants with BPD.

Twenty-five premature infants with mild BPD and 20 premature infants with moderate to severe BPD treated at our hospital from January 2015 to December 2015 were randomly selected. The imaging features were compared between premature infants with different severity of BPD.

In mild BPD group, the incidence of increased lung opacity (at 3–10 and 29 days) were significantly higher than those in infants with moderate to severe BPD ($P = .034$, $P = .003$, respectively). However, the incidences of stage III BPD (3–10 days) and stage IV BPD (11–27 days) were significantly lower in infants with mild BPD than those in infants with moderate to severe BPD ($P = .013$, $P = .033$, respectively). The chest x-ray score in the mild BPD group was significantly lower than that in moderate to severe BPD group [3.0 (1.0) vs 5.0 (1.0), $P < .001$]. Spearman rank correlation analysis indicated that chest x-ray score had significant correlation ($r = 0.787$, $P < .001$) with the clinical severity. In the mild BPD group, the chest CT scan score was 11.52 ± 3.49, which was considerably lower than that in the moderate to severe BPD group (24.70 ± 4.32) ($P < .001$). Moreover, the severity of BPD in the premature infants was significantly correlated to the chest CT scan score ($r = 0.855$, $P < .001$).

Chest CT combined with x-ray is an effective method for predicting the severity of BPD in premature infants.

Abbreviations: BPD = bronchopulmonary dysplasia, CT = computed tomography, FiO_2 = fraction of inspired oxygen, NRDS = neonatal respiratory distress syndrome.

Keywords: bronchopulmonary dysplasia, chest CT, chest x-ray, premature infants

1. Introduction

Bronchopulmonary dysplasia (BPD) is a common chronic lung disease in the newborns. Histologic chorioamnionitis is associated with an increased risk of BPD.[1] The survival of extremely underweight premature infants has been improved along with the advance in medical technology, though the incidence of BPD increases correspondingly.[2,3] New-type BPD caused by retarded lung development, rather than by neonatal respiratory distress syndrome (NRDS), has become the dominant type of BPD.[4] BPD caused by NRDS is considered as the typical type, and the staging criteria for typical BPD no longer apply. New diagnostic criteria for BPD were proposed jointly by several public health research institutions in the United States in 2010: First, BPD is diagnosed for the newborns who have a need for oxygen supplementation for over 28 days after birth with abnormal imaging findings of the lung; Second, chest x-ray is not used as a tool for predicting the severity of BPD.[5] However, the staging criteria for BPD are absent in this new criteria. Recent studies demonstrated that staging of BPD severity did not have a high predictive value for the outcomes.[6,7]

It is now technically feasible to acquire high-resolution chest computed tomography (CT) images under a low radiation dose, which promotes the use of chest CT for assessing the severity of BPD in premature infants. This study retrospectively analyzed the clinical value of chest CT combined with x-ray for assessing the severity of BPD in mild and moderate to severe cases.

2. Patients and methods

2.1. Patients

The clinical data of 45 premature infants with varied severity of BPD were collected in the First People's Hospital of Jining City (China) from January 2015 to December 2015. According to the US grading criteria for BPD severity (2010) in premature infants (<32 weeks gestation),[8] the included infants were divided into mild BPD group and moderate to severe BPD group. Mild cases were those who had no need for oxygen supplementation or fraction of inspired oxygen (FiO_2) < 21% upon discharge or at a

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corrected gestational age of 36 weeks; moderate to severe cases were those who had FiO_2 >21% or a need for mechanical ventilation upon discharge or at a corrected gestational age of 36 weeks. This research was approved by the Ethics Committee of the First People's Hospital of Jining City (China).

All cases received chest CT scan within 10 days after birth as well as chest x-ray at 1, 3–10, 11–27, and 29 days after birth. Infants with congenital heart disease, pulmonary hypertension, chromosomal abnormality and incomplete data were excluded.

2.2. Chest x-ray and diagnostic criteria

Chest x-rays were performed at 1, 3–10, 11–27, and 29 days after birth using digital radiography. The anteroposterior chest radiographs were taken in the supine position. X-ray images for each infant were reviewed by 3 associate chief physicians (or physicians with professional title above associate chief physician). The chest x-ray score was assigned according to the scoring criteria by Toce et al.[9] In this study, the x-ray image obtained at 29 days after birth was used to score.

2.3. Chest CT scan and scoring criteria

All 45 cases received chest CT scan within 10 days after birth using the 16-slice spiral CT scanner at a low radiation dose. Other scan parameters were as follows: tube voltage 100 to 120 kV, tube current 70 to 100 mAs, reconstructed slice thickness and slice interval 5 mm, and pitch 1.5:1. CT images of each infant were reviewed by 3 associate chief physicians (or physicians with professional title above associate chief physician), and the CT score was assigned according to the scoring criteria by Ochiai et al.[10,11] First, whether there was pulmonary hyperinflation (for 18 pulmonary segments, the presence of pulmonary hyperinflation was given 1 point, and the absence 0 point); Second, whether there were pulmonary parenchymal lesions (for 18 pulmonary segments, the presence of pulmonary parenchymal lesions was given 1 point, and the absence 0 point); Third, the chest CT scan score was the sum of the above 2 scores.

2.4. Statistical analysis

Statistical analyses were performed using SPSS 19.0 software. Gestational age, body weight, Apgar score, clinical parameters of treatment, as well as time, radiation dose, and score of chest CT scan were reported as mean ± standard deviation. Independent samples *t*-test was used for intergroup comparison, and $P < .05$ indicated significant difference. Data distributed non-normally were presented as median with interquartile range and analyzed by the Mann–Whitney *U* test. Other baseline information was reported in terms of number of cases and percentages, and chi-square test or the Fisher's exact test was used for intergroup comparison, with $P < .05$ indicating significant difference. Spearman rank correlation analysis was performed to evaluate the correlation between the clinical severity of the patients and the chest x-ray score or CT score.

3. Results

3.1. Baseline information

No significant differences were found in gestational age, body weight, gender, Agar score at 1 and 5 minutes after birth, mode of delivery, and other baseline information between groups ($P > .05$). However, premature infants with mild BPD had a significantly reduced time of intravenous nutrition, time of antibiotics use, duration of invasive and non-invasive ventilation, and the time of oxygen supplementation as compared with the moderate to severe cases ($P < .001$, Table 1).

3.2. Findings of chest x-ray

In mild BPD group, the incidence of increased lung opacity (at 3–10 and 29 days) were significantly higher than those in infants with moderate to severe BPD ($P = .034$, $P = .003$, respectively). However, the incidences of stage III BPD (3–10 days) and stage IV BPD (11–27 days) were significantly lower in infants with mild BPD than those in infants with moderate to severe BPD ($P = .013$, $P = .033$, respectively) (see Table 2). Figure 1 shows the number of cases with increased lung opacity, grade I RDS, stage III BPD

Table 1

Comparison of the baseline information of the patients between groups.

Item	Mild BPD group (n = 25)	Moderate to severe BPD group (n = 20)	t/χ^2	*P*
Gestational age, weeks	28.78 ± 1.21	28.04 ± 1.18	2.068	.450
Body weight, g	1281.04 ± 134.13	1219.65 ± 123.64	1.579	.122
Male (n/%)	17/68.00	14/70.00	0.021	.885
Apgar 1min score	6.20 ± 0.76	6.40 ± 0.60	0.959	.343
5 min	7.40 ± 0.71	7.05 ± 0.83	1.532	.133
Retinopathy of prematurity (cases /%)	11/44.00	9/45.00	0.005	.947
Pulmonary hemorrhage (cases /%)	4/16.00	4/20.00	–	.513*
Natural childbirth—planning of the uterus (case)	21-4	18-2	–	.447*
The symptoms of PDA (cases/%)	11/44.00	13/65.00	1.969	.161
Parenteral nutrition, days	32.48 ± 3.58	41.40 ± 3.82	8.061	<.001
Antibiotic treatment, days	28.20 ± 2.71	37.75 ± 2.92	11.358	<.001
Invasive ventilation time, days	10.84 ± 2.43	24.30 ± 3.43	15.388	<.001
Noninvasive ventilation time, days	18.24 ± 4.15	24.90 ± 4.15	5.350	<.001
Oxygen therapy time, days	39.64 ± 4.51	64.45 ± 4.99	17.496	<.001

BPD = bronchopulmonary dysplasia.

* Fisher's exact test.

Table 2

Findings of chest x-ray in the 2 groups.

Time and results of chest x-ray examination		Mild BPD Group (n/%)	Moderate to severe BPD Group (n/%)	χ^2 or *Z*	*P*
1 days	RDS I	7/28.0	1/5.00	–	.050*
	RDS II	8/32.0	8/40.0	0.310	.577
	RDS III	7/28.0	5/25.0	0.051	.821
	RDS IV	3/12.0	6/30.0	–	.131*
3–10 days	Hypolucency of lungs	20/80.0	10/50.0	4.500	.034
	BPD III	2/8.0	8/40.0	–	.013*
	Hypolucency with lung atelectasis	1/4.0	1/5.00	–	.697*
	BPD III with atelectasis	2/8.0	1/5.00	–	.585*
11–27 days	Hypolucency of lungs	13/52.0	9/45.0	0.218	.641
	BPD III	7/28.0	4/20.0	–	.396*
	BPD III with atelectasis	5/20.0	3/15.0	–	.487*
	BPD IV	0/0.00	4/20.0	–	.033*
29 days	Increased lung texture	1/4.00	0/0.00	–	.556*
	Hypolucency of lungs	13/52.0	2/10.0	8.820	.003
	BPD III	9/36.0	6/30.0	0.180	.671
	BPD IV	2/8.00	12/60.0	14.018	<.001
Chest x-ray score					
Median (interquartile range)		3.0 (1.0)	5.0 (1.0)	–5.220	<.001†

BPD = bronchopulmonary dysplasia, RDS = respiratory distress syndrome.

* Fisher's exact test.

† Mann–Whitney *U* test.

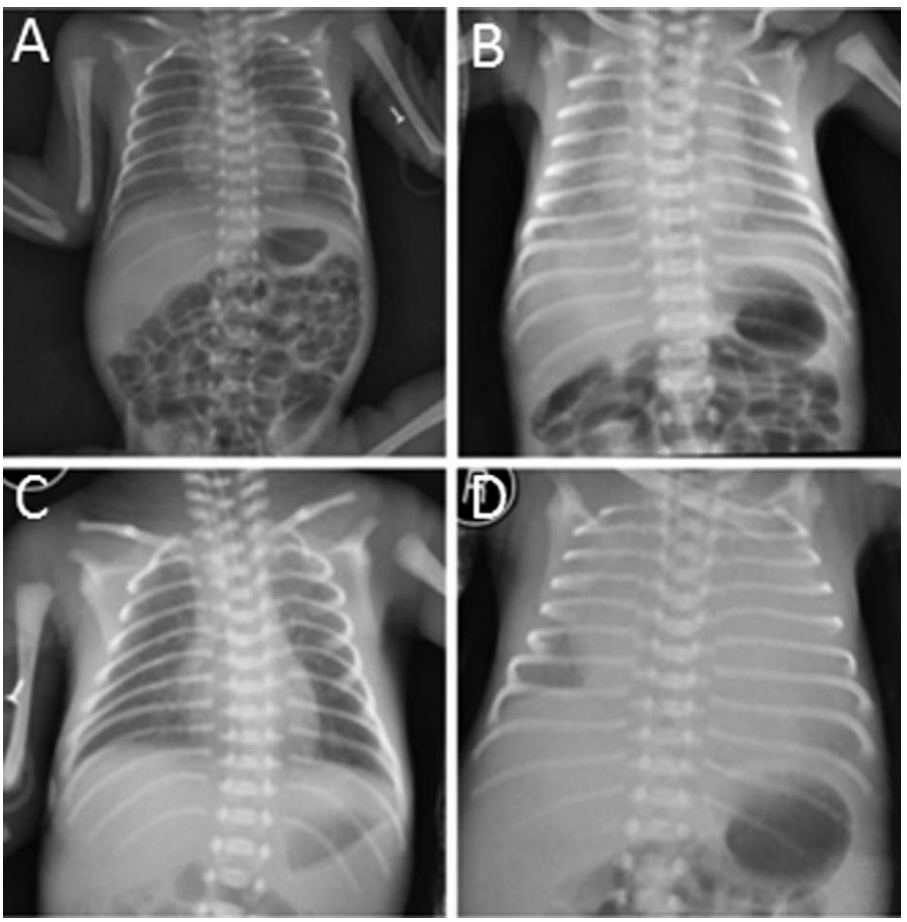

Figure 1. Chest radiographic manifestations in premature infants with BPD. (A) Increased lung opacity; (B) Grade I RDS; (C) Stage III BPD; (D) Stage IV BPD. BPD = bronchopulmonary dysplasia, RDS = respiratory distress syndrome.

Table 3

Comparison of chest CT scan parameters of the patients between groups.

Parameters	Mild BPD group (n=25)	Moderate to severe BPD group (n=20)	*t*	*P*
Time of the scan, weeks	5.36±3.33	5.45±2.80	0.097	.923
Radiation dose, mGy cm	87.64±6.17	86.95±6.61	0.361	.720
Chest CT scan score	11.52±3.49	24.70±4.32	11.331	<.001

BPD= bronchopulmonary dysplasia, CT=computed tomography.

and stage IV BPD. The chest x-ray score in the mild BPD group was significantly lower than that in moderate to severe BPD group [3.0 (1.0) vs 5.0 (1.0), $P<.001$, Table 2]. Spearman rank correlation analysis indicated that chest x-ray score had significant correlation ($r=0.787$, $P<0.001$) with the clinical severity.

3.3. Chest CT scan

Patients in 2 groups had no significant differences in the time of chest CT scan and the radiation dose ($P>0.05$). However, the chest CT scan score in the mild BPD group was significantly lower than that in moderate to severe BPD group (11.52±3.49 vs 24.70±4.32, $P<.001$, Table 3). Spearman rank correlation analysis indicated that the severity of BPD was significantly correlated to the chest CT scan score ($r=0.855$, $P<.001$). Figure 2 shows the chest CT images of 2 cases, who had mild and moderate BPD, respectively.

4. Discussion

BPD is a chronic lung disease involving the alveoli and pulmonary vessels due to neonatal pulmonary underdevelopment, oxygen therapy after birth and infection.[12] Northway first described BPD in 1967 as a chronic lung disease associated with NRDS. Clinically, typical BPD is diagnosed if the newborns need oxygen supplementation at 28 days after birth and has the characteristic features on chest x-ray at the corrected gestational age of 36 weeks. Typical BPD is divided into stages I–IV according to the characteristic features on chest x-ray: Stage I (1–3 days) is featured by similar findings on chest x-ray with NRDS; Stage II (4–10 days), complete opacification in the 2 lungs; Stage III (11–30 days), nonuniform density of bilateral lung fields, with strip or patchy shadows upon chest x-ray; Stage IV (30 days), increased opacity in bilateral lungs with pulmonary hyperinflation, atelectasis, scattered linear, or patchy shadows.

The survival of extremely preterm infants and extremely underweight premature infants has been constantly improved due to the use of pulmonary surfactant and various protective ventilation techniques. Stroustrup and Trasande[13] found that the incidence of BPD among newborns from 1996 to 2006 in the United States was 4.3%, and the incidence was inversely correlated to the birth weight. As many as 42% of the newborns weighing below 750 g have BPD, while only 4% of the newborns weighing 1251 to 1500 g have BPD. According to a collaborative investigation for BPD in premature infants,[14] the overall incidence of BPD among China's premature infants was about 1.28% in 2011, as opposed to 19.3% among extremely preterm infants (<28 gestational weeks). Li et al[15] analyzed the influence factors of BPD severity among premature infants and demonstrated that birth weight and gestational age were not only related to the incidence of BPD, but also to the severity of BPD; Low birth weight (<1000 g) and low gestational age (<28 weeks) were associated with a higher incidence and higher severity of BPD. For preterm infants the pulmonary development is usually retarded due to intrauterine hypoxia or infection, which further contributes to poor development of alveoli and pulmonary capillaries. BPD associated with obstructive ventilation impairment and pulmonary emphysema as the final outcome is a new type of BPD, which is significantly different from the typical BPD in terms of clinical and pathological features and outcomes. Therefore, the conventional 4-stage radiographic classification for typical BPD does not apply to the new-type BPD. However, the radiographic staging criteria are not yet available for the

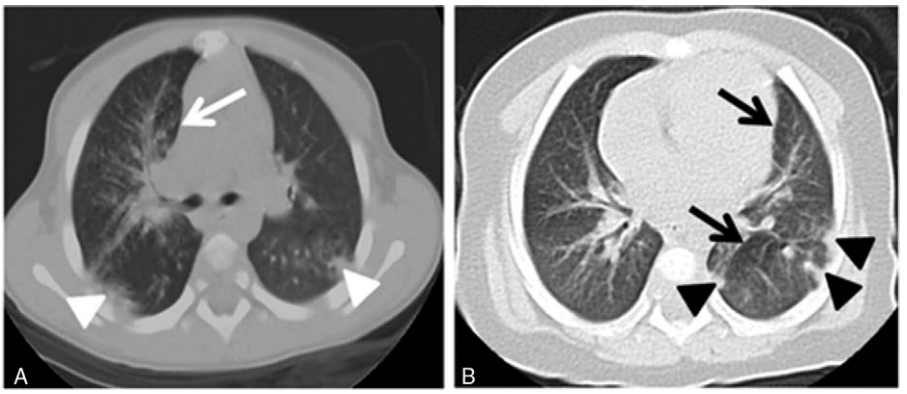

Figure 2. CT images of 2 premature infants with BPD. (A) In case 1, pulmonary hyperinflation was found in the anterior segment of the right upper lobe (arrow) and pulmonary parenchymal lesions were observed in the anterior-posterior segment of the right lobe and the left lobe (triangle), with CT score of 12 (pulmonary hyperinflation and parenchymal lesions in 6 segments); (B) In case 2, pulmonary hyperinflation was found in the lateral basal segment and posterior basal segment of the left lower lobe (arrow) and parenchymal lesions were observed in the lateral left lower lobe and posterior basal segment (triangle), with CT score of 24 (pulmonary hyperinflation in 13 segments and parenchymal lesions in 11 segments). CT=computed tomography.

new-type BPD, and chest x-ray is still used clinically for severity assessment.

In this study, we compared the chest x-ray images between mild cases and moderate to severe cases of BPD. The incidences of increased lung opacity (at 3–10 and 29 days) were significantly higher in mild BPD group than those in infants with moderate to severe BPD. However, the proportions of infants with stage III BPD (3–10 days) and stage IV BPD (11–27 days) were significantly lower than those in infants with moderate to severe BPD. Although chest x-ray is not a qualified tool for assessing the severity of BPD, it has a certain predictive value. The more severe the BPD, the earlier the characteristic changes upon chest x-ray will appear. The chest x-ray score in the mild BPD group was significantly lower than that in moderate to severe BPD group, and the x-ray score had significant correlation ($r = 0.787$, $P < .001$) with the clinical severity. It should be noted, however, that chest x-ray has a low diagnostic specificity for BPD in the premature infants. Because of this limitation, chest x-ray is better used as an auxiliary tool for BPD diagnosis and staging.

Chest CT scan can provide a good quantitative evaluation of lung morphology with high sensitivity. Spiral chest CT scan is much more sensitive to pulmonary parenchymal damage and hyperinflation.[16,17] Brody et al[18] pointed out in 2006 that chest CT scan is a qualified tool for assessing cystic fibrosis of the lung. In 2008 Ochiai et al[10] established a set of scoring criteria for chest CT scan in BPD based on the discovery of pulmonary parenchymal damage and hyperinflation. Sarria E et al.[19] reported in 2011 that the chest CT scan score of infants with BPD was significantly higher than that of the healthy newborns; moreover, the chest CT scan score was correlated to the concentration and duration of oxygen supplementation and severity of BPD.

We applied the scoring criteria for chest CT scan in BPD established by Ochiai et al[10] to the premature infants with varied degree of BPD and analyzed the correlation with the severity of BPD. It was found that the chest CT scan score was 11.52 ± 3.49 in infants with mild BPD versus 24.70 ± 4.32 in infants with moderate to severe BPD; there was significant difference in the chest CT scan score and the severity was significantly correlated to the chest CT scan score ($r = 0.855$, $P < .001$).

Compared with CT-only examination, a combined use of CT and x-ray in this study increases the radiation exposure of the infants. It is especially critical to reduce the radiation dose in children because the radio-sensitivity for organs is significantly higher in children compared with that in adults.[20,21] One-year-old patients receiving a chest CT scan are exposed to a radiation-effective dose ranging from 1.05 to 11.9 mSv,[22,23] which is 200 times of the radiation dose when they receives a chest x-ray examination.[24] Thus, 4 more x-ray examinations did not significantly increase a radiation exposure for the patients in this study. Because the radiation dose of CT scan is significantly higher than that in x-ray, optimal low-dose CT protocol for infants and the refinement of imaging procedures should be explored in future studies. Azithromycin, a macrolide antibiotic, was used in both groups along with parenteral nutrition, ventilation and oxygen therapy. Ballard et al[25] reported that the incidence of BPD was 76% in the infants less than 1250 g after treatment with azithromycin, which was not significantly different from that in placebo group (84%, $P = .2$). Thus, routine use of azithromycin treatment was not recommended to prevent BPD. In this study, chest x-rays were performed at 1, 3–10, 11–27, and 29 days after birth according to the diagnostic criteria established by multiple public health research institutions of United States in 2001.[26] All 45 cases received chest CT scan within 10 days after birth. During these days, infants in both groups received similar dose of azithromycin. Therefore, the influence of azithromycin on the results of x-ray and CT scan could be excluded.

There are some limitations in this study. First, the small sample size is the major drawback in the present study, which restricts an in-depth analysis of the constituent ratio of different pathological changes on the findings of chest x-ray at varied time points between groups. Second, a combined use of CT scan and chest x-ray may potentially increase the risk of radiation exposure, and we did not explore a lower tube voltage to reduce radiation dose in this study. Third, the time points of the second and third chest x-ray are not fixed (at 3–10 days and 11–27 days, respectively), which influence the comparison of the x-ray findings between groups. A larger sample size is needed to eliminate this bias.

5. Conclusion

Despite these study limitations, we clearly demonstrate for the first time that a combined use of chest CT scan and x-ray is an effective method for an early prediction of severity for premature infants with BPD. Our results provide insight into clinical practice in diagnosis of BPD using imaging tools.

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