Early pulmonary hypertension is a risk factor for bronchopulmonary dysplasia-associated late pulmonary hypertension in extremely preterm infants

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Supplemental Table 1. Diagnosis and echocardiographic findings of early and late PH

	Early PH (N=74)	Late PH (N=23)
SPAP>40, n (%)	9 (12.2%)	6 (26.1%)
SHUNT, n (%)	0 (0.0%)	0 (0.0%)
IVS, n (%)	49 (66.2%)	9 (39.1%)
SPAP>40 and SHUNT, n (%)	0 (0.0%)	0 (0.0%)
SPAP>40 and IVS, n (%)	13 (17.6%)	8 (37.8%)
SHUNT and IVS, n (%)	2 (2.7%)	0 (0.0%)
SPAP>40, SHUNT, and IVS, n (%)	1 (1.4%)	0 (0.0%)

PH, pulmonary hypertension; SPAP>40, systemic or suprasystemic pulmonary artery pressure >40 mmHg as estimated by peak Doppler velocity of tricuspid regurgitation; SHUNT; right-to-left or bidirectional shunting of blood through patent ductus arteriosus, patent foramen ovale, or atrial septal defect; IVS, flattened interventricular septum or D-shaped left ventricle at end systole. N(%) or mean (SD).

Supplement Table 2. Perinatal demographic characteristics among subgroup of moderate to severe BPD patients

	No BPD-PH (N=70)	BPD-PH (N=23)	*P* value
Neonatal characteristics			
Gestational age, (week)	25.0±1.2	25.1±1.3	0.61
22+0 to 23+6 weeks, n (%)	15 (21.4)	4 (17.4)	0.68
24+0 to 25+6 weeks, n (%)	40 (57.1)	12 (52.2)	0.68
26+0 to 27+6 weeks, n (%)	15 (21.4)	7 (30.4)	0.38
Birthweight (g)	709.7±124.5	663.0±178.1	0.17
400-600 g, n (%)	13 (18.6)	8 (34.8)	0.11
600-800 g, n (%)	38 (54.3)	9 (39.1)	0.16
800-1000 g, n (%)	19 (27.1)	6 (26.1)	0.92
Small for gestational age, n (%)	12 (17.1)	9 (39.1)	<0.05
Male, n (%)	39 (55.7)	12 (52.2)	0.77
1-min Apgar score	4.3±1.3	4.0±1.6	0.41
5-min Apgar score	7.0±1.1	6.7±1.5	0.29
Age at echocardiography, postnatal days	84.1±10.9	85.1±10.5	0.70
PMA at echocardiography, weeks	36.9±0.7	37.2±0.9	0.18
Maternal characteristics			
Maternal age, year	33.0±4.0	33.9±3.9	0.37
Multiple gestation, n (%)	24 (34.3)	10 (43.5)	0.43
Pregnancy induced hypertension, n (%)	8 (11.4)	4 (17.4)	0.48
Oligohydramnios, n (%)	19 (27.1)	10 (43.5)	0.14
In vitro fertilization, n (%)	21 (30.0)	9 (39.1)	0.42
Clinical chorioamnionitis, n (%)	38 (54.3)	13 (56.5)	0.85
Pathologic chorioamnionitis, n (%)	48 (68.6)	15 (65.2)	0.77
Cesarean section, n (%)	53 (75.7)	16 (69.6)	0.56
Gestational diabetes, n (%)	4 (5.7)	0 (0.0)	0.57
Complete antenatal steroid, n (%)	43 (61.4)	17 (73.9)	0.28
Duration of PPROM, day	4.9±9.3	5.9±10.2	0.69
PPROM duration ≥28 days, n (%)	1 (1.4)	3 (13.0)	<0.05
PPROM at <26+0 weeks, n (%)	9 (12.9)	3 (13.0)	1.00

PH, pulmonary hypertension; BPD, bronchopulmonary dysplasia, PPROM, Preterm premature rupture of membranes; PMA, post-menstrual age. Data are show as N (%) or mean±SD.

Supplemental Table 3. Main cause of death before 36 weeks PMA

	All (N=39)	No Early PH (N=18)	Early PH (N=21)	*P* value
IVH, n (%)	3 (7.7)	1 (5.6)	2 (9.5)	1.00
Pneumonia, n (%)	2 (5.1)	2 (11.1)	0 (0.0)	0.21
Pulmonary hypoplasia, n (%)	6 (10.3)	0 (0.0)	6 (28.6)	<0.05
Pneumothorax, n (%)	1 (2.6)	0 (0.0)	1 (4.8)	1.00
NEC, n (%)	12 (30.8)	6 (33.3)	6 (28.6)	0.75
Intestinal perforation, n (%)	2 (5.1)	2 (11.1)	0 (0.0)	0.21
Sepsis, n (%)	13 (33.3)	7 (38.9)	6 (28.6)	0.31

PMA, Post-menstrual age; PH, Pulmonary hypertension; IVH, Intraventricular hemorrhage; NEC, Necrotizing enterocolitis, Data are show as N (%)

Supplement Table 4. Neonatal morbidities and mortality among moderate to severe BPD

	No late PH (N=70)	Late PH (N=23)	*P* value
Early PH, n (%)	17 (24.3)	14 (60.9)	<0.05
IVH grade 3-4, n (%)	9 (12.9)	2 (8.7)	0.73
PDA >2mm (%) at early echocardiogram*	45 (64.3)	18 (78.3)	0.21
Enrollment for PDA RCT [23], (%)	23 (32.9)	8 (34.8)	0.87
NEC grade 2b-3, n (%)	7 (10.0)	2 (8.7%)	1.00
Invasive ventilator before 36 weeks PMA, day	43.7±23.3	51.4±22.1	0.17
Invasive ventilator before 36 weeks PMA >28 days, n (%)	46 (65.7)	21 (91.3)	<0.05
Early sepsis (<7 days), n (%)	2 (2.9)	1 (4.3)	1.00
Late sepsis (7 days ~ 36 weeks PMA), n (%)	13 (18.6)	8 (34.8)	0.11
ROP stage 3-4, n (%)	44 (62.5)	15 (65.2)	1.00
Periventricular leukomalacia, n (%)	7 (10.0)	5 (21.7)	0.16
Death after 36 weeks PMA, n (%)	4 (5.7)	5 (21.7)	<0.05

*PDA was managed using conventional nonintervention treatment (not to treat) with careful fluid management based on our unit policy [22]; BPD, bronchopulmonary dysplasia; PH, Pulmonary hypertension; IVH, Intraventricular hemorrhage; PDA, Patent ductus arteriosus; Randomized clinical study, NEC, Necrotizing enterocolitis; PMA, Post-menstrual age; ROP, Retinopathy of premature, Data are show as N (%) or mean±SD