USING ECHOCARDIOGRAPHY TO INVESTIGATE THE EXPRESSION OF NT-PROBNP IN PREMATURE INFANTS WITH PATENT DUCTUS ARTERIOSUS

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ABSTRACT:

BACKGROUND: This study aimed to evaluate the relationship between PDA, serum NT-proBNP levels at 2–3 and 8–9 days of life, and BPD/death in very preterm infants. Patent ductus arteriosus (PDA) is a common complication in very preterm infants. It is known that there is an association between PDA and development of bronchopulmonary dysplasia (BPD) or death before the postmenstrual age (PMA) of 36 weeks. However, this association remains one of the most contentious aspects of the problem.

METHODS: Ninety premature infants were chosen as the subjects of the study between February 2019 and March 2020, including 52 in the non-PDA group and 38 in the PDA group (26 sPDA cases and 12 cases with asymptomatic PDA, or asPDA). On the third day following delivery, the general data about these babies was documented, including their gender, delivery technique, maternal infection, and blood NT-proBNP level. Under the guidance of an artificial intelligence convolutional neural network, they were screened using echocardiographic indicators (AI-CNN). The specificity and sensitivity of sPDA as well as the relationship between serum sPDA NT-proBNP expression and echocardiographic markers were ascertained by displaying the Receiver Operating Characteristic (ROC) curves.

RESULTS: The median size of PDA in the first 3 days of life was significantly smaller in infants who survived without BPD. At the same time, echocardiographic signs of hsPDA were significantly more often found in infants who died or developed BPD. There were no statistically significant differences between the groups in the frequency of pharmacological treatment and requirements for the second course of treatment. However, pharmacological treatment of hsPDA did not significantly reduce the incidence of BPD in infants who did not receive treatment, $p > 0.05$). At the same time, longer persistence of hsPDA did not increase the risk of death or future BPD development ($rs = 0.16$, $p = 0.47$).

CONCLUSION: The expression level of serum NT-proBNP on the 3rd day after birth was closely related to the diameter of ductus arteriosus and progress of LA/AO, which had clinical value for early diagnosis of PDA. However, the sample size of included PIs was small, which would lead to some errors or a bias compared to the actual situations. In the future, the sample size would be increased for in-depth research.

KEYWORDS: Echocardiography, NT-proBNP and Symptomatic PDA

Introduction:

Approximately half of preterm newborns born before 28 weeks of pregnancy have patent ductus arteriosus (PDA). PDA has been linked to an increased chance of developing bronchopulmonary dysplasia (BPD) and/or dying before 36 weeks of postmenstrual age (PMA). However, the risk is determined by the size of the PDA shunt rather than by the existence or absence of PDA. Increased pulmonary blood flow and altered pulmonary fluid filtration rate from a significant left-to-right PDA shunt can result in pulmonary edema, elevated pulmonary pressure, and structural alterations that may aid in the development of BPD. Plasma N-terminal pro-brain natriuretic peptide (NT-proBNP) possesses the physiological properties of diuresis, natriuretic excretion, vasodilation, and decreased peripheral vascular resistance.[1] It can also reflect left ventricular load and pulmonary blood volume. It is highly significant in the prediction of sPDA and has the ability to control variations in peripheral blood cell levels. Many studies have found variations between the

PDA and NT-proBNP research results. These differences can be attributed to differing detection techniques and observation populations. Convolutional neural networks (AI-CNNs) were used in this study to optimize echocardiography and enhance image resolution in order to investigate and analyze the left atrium/aorta (LA/AO) correlation ratio and provide a reference value for the early detection of PDA in clinical settings.[2,3]

METHODS:
Ninety-one PIs (six PDA and twenty-two non-PDA infants) who were born at our hospital were included as research subjects. Out of the 38 PDA babies, 12 were cases of asymptomatic PDA (asPDA) and 26 were cases of sPDA. The hospital's ethics committee had to provide its clearance before the experiment could proceed. Forms for informed consent had been signed by the parents of the newborns included. Infants having a gestational age of [28 weeks, 34 weeks] and a body weight of [1 kg, 1.5 kg] who were admitted to the hospital within 24 hours of delivery met the inclusion criteria. Infants with septicemia or issues with liver and renal function after one week of birth, as well as those whose information was lacking, were among the exclusion criteria.

Measurement of NT-proBNP amounts in the serum
Blood samples were taken twice during the first 24 to 72 hours of life, or before ibuprofen/paracetamol was administered, and after the second course of treatment concluded, or on the eighth or ninth day of life if expectant management was employed. For the first and second blood samples, the median [IQR] age was two and eight days, respectively. Serum was extracted as soon as possible after each blood collection, frozen, and kept at minus 25 °C. Following the manufacturer's instructions, serum NT-proBNP concentrations were determined using the electrochemiluminescence immunoassay technique (Elecsys proBNP II test; Roche Diagnostics, Germany). The 5–35,000 pg/mL measurement limits were available.[4]

Echocardiography technology based on AI-CNN
Like humans, CNN gains knowledge through local observation, and its neurons are able to use both local and global learning strategies. One can learn about the characteristics of other locations by utilizing the data that the network gathers from nearby areas. The size of the convolution kernel, which is independent of other pixels, is the only restriction on the output of convolution values. The input layer pre-processes the data information that is imported into the picture segmentation function layer.[5] Information about the imported data is extracted by the convolution layer in order to extract features. The size of the output feature map will be $(N-m+2k)/v+1$ if the input is N, the convolution kernel is m, the step size is v, and the edge zero-fill value is k. The excitation layer performs nonlinear mapping analysis on the convolution layer's output using the sigmoid and RELU activation functions. To lower the number of overfittings, the pooling layer compresses the image data and parameters. The fully-connected layer: toward the end of CNN, all neurons in neighbouring layers are connected by weights. The classification layer: the data information is categorized using the logistic regression and Softmax regression classification methods.[6]

STATISTICS ANALYSIS
The study employed traditional methods of descriptive, comparative, correlation, and logistic regression analysis using the $\chi 2$, Mann-Whitney, and Wilcoxon criteria, as well as adjusted odds ratios (aOR). Nonparametric data is represented by the median [IQR]. To assess the correlation between nonparametric variables, the Spearman's rank correlation coefficient (rS) was employed. Consideration was given to all values if p was less than 0.05.

RESULTS
Ninety PIs were included, with 38 infants in the PDA group and 52 infants in the non-PDA group. The GA, delivery methods, gender, birth weight, maternal infection during pregnancy, premature rupture of membranes, and positive pressure ventilation of PIs were compared.

More patients with hemoptysis and hoarseness in pulmonary tuberculosis combined with lung cancer group than in the pulmonary tuberculosis group ($P<0.05$), and other symptoms were not significantly different ($P>0.05$).

Table 1: General information about PDA patients and infants without PDA

Data characteristics		PDA	Non-PDA	t/χ^2	P
Gender	Male	22	25	0.211	0.789
	Female	17	26		
Delivery methods	Cesarean section	19	27	0.014	0.868
	Spontaneous delivery	20	24		
GA (weeks)		32.8±1.2	33.9±1.1	0.133	0.869
Birth weight (g)		1,515±296	1,610±212	1.068	0.291
Maternal infection		1	4	1.514	0.264
Premature rupture of fetal membrane		4	10	0.631	0.501
Positive pressure ventilation		12	14	1.497	0.257

The median size of PDA in the first 3 days of life was significantly smaller in infants who survived without BPD. At the same time, echocardiographic signs of hsPDA were significantly more often found in infants who died or developed BPD. There were no statistically significant differences between the groups in the frequency of pharmacological treatment and requirements for the second course of treatment. However, pharmacological treatment of hsPDA did not significantly reduce the incidence of BPD in infants who did not receive treatment, p > 0.05). At the same time, longer persistence of hsPDA did not increase the risk of death or future BPD development (rs = 0.16, p = 0.47).

DISCUSSION:

hsPDA is a common complication in very preterm infants born at < 32 weeks of gestation. It is known that a large left-to-right PDA shunt significantly increases the risk of developing BPD or death. The results of this study showed that infants who died or developed BPD significantly more often had hsPDA than babies who survived without BPD. Our data confirmed the results of a recent meta-analysis, according to which in five out of nine studies the hsPDA or PDA was significantly more likely diagnosed in infants who developed BPD. According to our results, death or BPD occurred significantly more often in infants with lower gestational age, birth weight, and the condition of such infants after birth was more compromised, as evidenced by significantly lower Apgar scores, the need for intubation and MV in delivery room as well as by the significantly higher SNAPPE-II scores on the first day of NICU hospitalization.[7,8]

Studies have shown that NT-ProBNP has a sensitivity of 0.90 (95% CI: 0.79-0.96) and a specificity of 0.84 (96% CI: 0.77-0.90) for

diagnosing hsPDA in preterm infants 72 hours after the birth of the newborn. Results of different diagnostic methods are quite different, which may also be related to the different diagnostic instruments and diagnostic methods. The results of this study showed that at 72 hours after birth, serum NT-proBNP expression in PI with sPDA was positively correlated with the diameter of the ductus arteriosus (r = 0.462, P < 0.001), and it was positively correlated with the ratio of left atrium/aorta (LA/AO) (r = 0.573, P < 0.001), but was not correlated with LVEF.[9]

Our study also has some limitations, primarily due to its non-blinding design, specific approach to treatment (early administration based only on the PDA size), relatively small number of patients, and proportion of the most immature infants. Prospects for further research are to study the possibility of using serum NT-proBNP concentrations in the first days of life to form a risk group and targeted testing of potential preventive interventions.[10]

CONCLUSION

Regardless of later death or development of BPD, the serum NT-proBNP values at 2–3 days of life were higher in very preterm infants with hsPDA, and at 8–9 days of life – in babies with persistent PDA. The expression level of serum NT-proBNP on the 3rd day after birth was closely related to the diameter of ductus arteriosus and progress of LA/AO, which had clinical value for early diagnosis of PDA. However, the sample size of included PIs was small, which would lead to some errors or a bias compared to the actual situations. In the future, the sample size would be increased for in-depth research. hsPDA was significantly more often diagnosed in infants who later developed BPD or died, however,

pharmacological treatment of hsPDA did not reliably reduce the incidence of BPD or death.

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