

# Neonatal nutritional risk and pulmonary function

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## Abstract

**Introduction:** The neonatal period is a critical initial stage of postnatal lung development and maturation. This study aimed to investigate the effects of the nutritional status on pulmonary function in late preterm and full-term neonates.

**Methods:** A total of 172 newborns were included in the study. Nutritional risk screening, weight measurement, assessment of albumin and caloric intake, and a pulmonary function examination were conducted on the 7th day after birth.

**Results:** There was a significant correlation between the nutritional risk and changes in body weight. Tidal volume (VT), minute ventilation (MV), VT per kg body weight (VT/kg), and MV per kg body weight (MV/kg) in the low nutritional risk group were significantly higher than those in the medium nutritional risk group (all  $P < .05$ ). Albumin and caloric intake in the low nutritional risk group were significantly higher than those in the medium nutritional risk group (both  $P < .01$ ). VT, VT/kg, MV, and MV/kg in the weight loss group were lower than those in the no weight loss group (all  $P < .05$ ).

**Conclusions:** Changes in neonatal weight mainly affect lung volume (VT, VT/kg, MV, and MV/kg), suggesting that an improvement in the neonatal nutritional status is important for the development of lung volume.

**Abbreviations:** MV = minute ventilation, MV/kg = MV per kg body weight, TEF50/TIF50 = ratio of the expiratory to inspiratory flow rate when exhaling and inhaling 50% of the tidal breath volume, TPTEF/TE = ratio of the time to peak tidal expiratory flow to total expiratory time, VPTEF/VE = ratio of volume to peak tidal expiratory flow to total expiratory volume, VT = tidal volume, VT/kg = VT per kg body weight.

**Keywords:** lung development, neonate, nutrition, weight

## 1. Introduction

Nutrition is the material basis for the growth and development of newborns and the maintenance of normal physiological function. Whether the nutritional status of the newborn affects the development of the respiratory system is unclear. Neonatal lung development includes the two aspects of volume development and airway resistance. These two aspects can be reflected by neonatal tidal breathing pulmonary function parameters. Previous studies have suggested that indicators of tidal breathing pulmonary function in the neonate include lung volume parameters (tidal volume [VT]; VT per kg body weight [VT/kg], minute ventilation [MV], and MV per kg body weight [MV/kg]) and indicators of airway obstruction (ratio of the time to peak tidal expiratory flow to total expiratory time [TPTEF/TE], ratio of volume to peak tidal expiratory flow to total expiratory volume [VPTEF/VE] and ratio of the expiratory to inspiratory flow rate

when exhaling and inhaling 50% of the tidal breath volume [TEF50/TIF50]).<sup>[1–3]</sup>

Nutritional risk refers to the risk that existing or potential nutritional and metabolic status affects the clinical outcome of disease or surgery. Nutritional risk is also the risk that existing or potential nutritional factors lead to adverse clinical outcomes in patients.<sup>[4]</sup> At present, commonly used screening tools for children's nutritional risk include the Screening Tool for Risk on Nutritional Status and Growth (STRONGkids), the Screening Tool for the Assessment of Pediatric Malnutrition, and the Pediatric Yorkhill Malnutrition Score. The STRONGkids was proposed by Hulst et al.<sup>[5]</sup> The STRONGkids is simple and easy to implement. This study aimed to investigate the effects of different nutritional risks and changes in weight on neonatal lung function. We used the tidal breathing pulmonary function test to determine neonatal lung development and adopted the STRONGkids as the nutritional risk screening tool.

XZ, JL, and BW contributed equally to this work.

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This study was approved by the Ethics Committee of the First Affiliated Hospital of Fujian Medical University (approval no. 2019-172).

The datasets generated during and/or analyzed during the current study are not publicly available, but are available from the corresponding author on reasonable request.

The authors declare that they have no potential conflicts of interest.

Our manuscript adheres to standards in this field for data availability. However, because of the confidentiality of patient information, the data in the manuscript are not available publicly. The authors can provide the data at any time if necessary.

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## 2. Materials and Methods

### 2.1. Study design and methods

This was an observational study. Late preterm and full-term neonates who were hospitalized in the Department of Neonatology of the First Affiliated Hospital of Fujian Medical University from May 2019 to June 2021 were selected as subjects. The measurement of body weight, neonatal nutritional risk screening, and a neonatal tidal breathing lung function examination were performed on the 7th day after birth. We routinely monitor neonates' growth and nutrition on the 7th day after birth. This procedure was as follows. At 7 AM on the 7th day, we measured and recorded the neonate's weight before feeding, and then serum albumin concentrations were detected by the bromocresol green method at a clinical laboratory of our hospital. Nutritional risk screening was performed at 9 AM, and a neonatal tidal pulmonary function test was performed between 3 and 5 PM. On the morning of the 8th day, the caloric intake of the newborn was calculated according to the amount of milk consumed on the previous day (i.e., the 7th day after birth). The caloric supply of 100 mL of breast milk or 100 mL of full-term formula milk was 67 kcal.<sup>[6]</sup> An example of this calculation is as follows: In a 2.5 kg, full-term infant who has ingested 400 mL of milk in the last 24 hours, the number of calories is calculated by 4 multiplied by 67 kcal/100 mL = 268 kcal. This amount is then divided by body weight, which equals 107.2 kcal/kg/d. By analyzing the correlation between the neonatal nutritional risk and changes in weight, the effects of different nutritional risks and changes in weight on neonatal pulmonary function were further determined. This study was carried out in accordance with the standards of the Declaration of Helsinki and the Ethics Committee of the First Affiliated Hospital of Fujian Medical University (approval no. 2019-172).

### 2.2. Inclusion and exclusion criteria

The inclusion criteria were a gestational age  $\geq 34$  weeks and  $< 42$  weeks, and no respiratory support after birth. The exclusion criteria were as follows: pulmonary infection, aspiration pneumonia, apnea, or wet lung; the application of pulmonary surfactant; the use of caffeine; congenital heart disease; various congenital malformations (including congenital diaphragmatic hernia, esophageal tracheal fistula, and esophageal atresia); neuromuscular disease; a smoking history of the mother; and a family history of bronchial asthma. Parents or guardians of all of the patients provided written informed consent at enrollment.

### 2.3. Questionnaire survey method

The purpose and significance of this study were explained to the parents of the patients, and a one-to-one general information questionnaire was provided to the parents of the patients after obtaining the informed consent of the parents.

### 2.4. Screening of neonatal nutritional risk

The STRONGkids, which was constructed by Hulst et al., was used for screening neonatal nutritional risk at 1 week after birth.<sup>[5]</sup> This tool evaluates subjective assessment (1 point), disease with high nutritional risk (2 points), nutrient intake and losses (1 point), and weight loss or slow weight gain (1 point). The score is calculated by adding the scores from the four aspects. Nutritional risk assessment criteria were as follows: a total score of 4–5 points was rated as high risk, 1–3 points as medium risk, and 0 points as low risk.

### 2.5. Weight measurement

The newborn's weight was measured by an electronic infant scale on the 7th day after birth before feeding at 7 AM and compared with the newborn's birth weight. Weight was divided into weight loss and no weight loss.

### 2.6. Pulmonary function examination of neonates

**2.6.1. Instruments.** After nutritional risk screening and weight measurement were completed, neonatal pulmonary function tests were performed. The Jaeger Masterscreen device (Jaeger Company, Germany) was used to examine tidal breathing pulmonary function, and the environmental temperature, humidity, and capacity were calibrated before initiating each test.<sup>[7–9]</sup>

**2.6.2. Measurement methods.** We measured the crown–heel length and removed nasal and mouth secretions. Each newborn was in a deep sleep and clothed in loose garments. They were laid flat on baby beds, with their heads at the midline and the neck slightly extended in a neutral position (Figure 1). Deep sleep is a state of regular breathing, with no eye movement, and no other motions. We selected the appropriate size of the facemask to cover the newborn's nose and mouth so that there was no leakage. The facemask was connected to a flow sensor, and the flow and volume signals of the subjects' tidal breathing were displayed on a screen in real-time. After smooth breathing, each newborn was subjected to 5 consecutive tests. Each test recorded 20 times tidal breathing. The data were automatically calculated after being transmitted to a computer through the flow sensor of the pulmonary function instrument.<sup>[10]</sup> This test was conducted between 3 and 5 PM by a pulmonary function test specialist.

**2.6.3. Measurement parameters.** On the basis of previous studies, the following parameters were assessed. One parameter was VT, which is the amount of air inhaled or exhaled each breath during calm breathing. VT/kg was used to correct the effect of body weight on tidal volume. Additionally, we assessed MV, which is the amount of air that is inhaled or exhaled from the lungs each minute. MV/kg was used to correct the effect of body weight on minute ventilation. Furthermore, TPTEF/TE,



**Figure 1.** Tidal breathing analysis in neonates using the MasterScreen system.

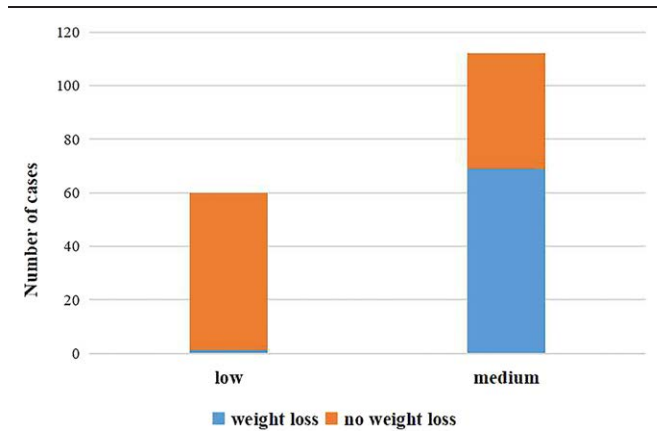


Figure 2. Neonatal nutritional risk and changes in weight.

which is the ratio of the time from exhalation to peak expiratory flow to the time of exhalation, and VPTEF/VE, which is the ratio of the volume of exhaled air to the tidal volume when peak expiratory flow is reached during exhalation, were assessed. We also assessed TEF50/TIF50, which is the ratio of expiratory flow when exhaled at 50% tidal volume to inspiratory flow when inhaled at 50% tidal volume.<sup>[3,9,11]</sup>

2.7. Statistical analysis

Measurement data are shown as mean ± standard deviation (SD). Percentiles are shown for quantitative variables and proportions are shown for all categorical data. Differences in means were tested for statistical significance with the independent-samples *t* test, and categorical data were compared with the  $\chi^2$  test. All statistical analyses were conducted with SPSS version 22.0 (IBM Corp., Armonk, NY, USA), and *P* < .05 was considered statistically significant.

3. Results

3.1. Basic information of the participants

A total of 172 newborns (102 boys and 70 girls) were included in the study. Among them, there were late preterm infants (*n* = 41, gestational age ≥ 34 and < 37 weeks [35.45 ± 1.14 weeks]; birth weight: 2.48 ± 0.45 kg) and full-term infants (*n* = 131; gestational age ≥ 37 and < 42 weeks [39.39 ± 1.03 weeks]; birth weight: 3.34 ± 0.44 kg). The disease spectrum included 22 cases of septicemia without respiratory function affected, 35 cases of neonatal hyperbilirubinemia, 12 cases of hypoglycemia, and 3 cases of hypocalcemia. The remaining high-risk neonates were admitted to hospital for observation because of high-risk factors, such as amniotic fluid opacity and a maternal history of diabetes. These patients with disease were included in our study because their disease status was mild, and their respiratory function was not affected. Additionally, on the 7th day after birth, most of these patients had recovered and were discharged in a healthy condition.

Table 1

Pulmonary function test results of newborns with different nutritional risks.

| Nutritional risks level | n   | VT, mL       | VT/body weight, mL/kg | MV, L       | MV/body weight, L/kg | VPTEF/VE, %  | TPTEF/TE, %  | TEF50/TIF50, % |
|-------------------------|-----|--------------|-----------------------|-------------|----------------------|--------------|--------------|----------------|
| Low                     | 60  | 24.85 ± 4.90 | 7.34 ± 1.39           | 1.54 ± 0.33 | 0.45 ± 0.09          | 34.21 ± 7.84 | 34.29 ± 9.56 | 101.55 ± 25.17 |
| Medium                  | 112 | 20.45 ± 3.99 | 6.84 ± 1.25           | 1.24 ± 0.28 | 0.42 ± 0.10          | 34.17 ± 5.74 | 34.54 ± 7.10 | 98.86 ± 22.60  |
| <i>t</i>                |     | 6.538        | 2.40                  | 6.32        | 2.47                 | 0.04         | -0.19        | 0.72           |
| <i>P</i>                |     | .000         | .018                  | .000        | .015                 | .971         | .850         | .476           |

All values are presented as mean ± standard deviation.

MV = minute ventilation, TPTEF/TE = ratio of time to peak tidal expiratory flow to total expiratory time, TEF50/TIF50 = ratio of the expiratory to the inspiratory flow rate when exhaling and inhaling 50% of the tidal breath volume, VPTEF/VE = volume to peak tidal expiratory flow to total expiratory volume, VT = tidal volume.

Table 2

Comparison of albumin and caloric intake in different nutritional risk groups.

| Nutritional risks level | Albumin (g/L) | Caloric intake (kcal/kg-d) |
|-------------------------|---------------|----------------------------|
| Low                     | 34.08 ± 4.86  | 102.26 ± 32.91             |
| Medium                  | 32.12 ± 3.77  | 76.82 ± 27.76              |
| <i>T</i>                | 2.92          | 5.36                       |
| <i>P</i>                | .004          | .000                       |

All values are presented as mean ± standard deviation.

3.2. Association between the neonatal nutritional risk and changes in weight

Among the 172 neonates, 60 were at low nutritional risk, of whom 1 (1.67%) had weight loss and 59 (98.33%) had no weight loss. One hundred twelve patients were at medium nutritional risk; among these 69 (61.61%) had weight loss and 43 (38.39%) had no weight loss. None of the neonates had a high nutritional risk (Figure 2). Correlation factor analysis between the nutritional risk and the changes in body weight showed that the correlation coefficient was -0.582 (*P* < .001), indicating that there was a significant negative correlation between these two factors.

3.3. Pulmonary function test in newborns with different nutritional risks

According to the results of the neonatal nutritional risk screening, the 172 neonates were divided into the low nutritional risk group and the medium nutritional risk group. The lung function test results of the two groups are shown in Table 1. VT, MV, VT/kg, and MV/kg in the low nutritional risk group were significantly higher than those in the medium nutritional risk group (all *P* < .05). There were no significant differences in indicators reflecting airway obstruction (VPTEF/VE, TPTEF/TE, and TEF50/TIF50) between the two groups.

3.4. Albumin and caloric intake in the different nutritional risk groups

Albumin concentrations and the caloric intake in the low nutritional risk group were significantly higher than those in the medium nutritional risk group (both *P* < .01, Table 2).

3.5. Pulmonary function test in newborns with different changes in body weight

The newborns' body weight at the examination was compared with that at birth. The pulmonary function test results of the group who lost weight and the group who did not lose weight are shown in Table 3. VT, VT/kg, MV, and MV/kg in the weight loss group were significantly lower than those in the no weight loss group (all *P* < .05). However, there were no significant differences in VPTEF/VE, TPTEF/TE, or TEF50/TIF50 between the two groups.

**Table 3**  
**Pulmonary function test results of newborns with different weight changes.**

| Weight Changes | n   | VT, mL     | VT/body weight, mL/kg | MV, L     | MV/body weight, L/kg | VPTEF/VE, % | TPTEF/TE, % | TEF50/TIF50, % |
|----------------|-----|------------|-----------------------|-----------|----------------------|-------------|-------------|----------------|
| Weight loss    | 70  | 20.84±4.08 | 6.70±1.16             | 1.28±0.29 | 0.41±0.09            | 34.99±5.73  | 35.66±6.95  | 100.25±21.71   |
| No weight loss | 102 | 22.77±5.11 | 7.22±1.38             | 1.40±0.35 | 0.44±0.09            | 33.63±7.00  | 33.62±8.61  | 99.49±24.74    |
| <i>t</i>       |     | -2.63      | -2.56                 | -2.35     | -2.04                | 1.35        | 1.65        | 0.207          |
| <i>P</i>       |     | .009       | .011                  | .020      | .043                 | .179        | .101        | .836           |

All values are presented as mean ± standard deviation.

MV = minute ventilation, TPTEF/TE = ratio of time to peak tidal expiratory flow to total expiratory time, TEF50/TIF50 = ratio of the expiratory to the inspiratory flow rate when exhaling and inhaling 50% of the tidal breath volume, VPTEF/VE = volume to peak tidal expiratory flow to total expiratory volume, VT = tidal volume.

#### 4. Discussion

In this study, we showed that an improvement in the neonatal nutritional status was important for the development of lung volume. Lung capacity-related parameters (VT, VT/kg, MV, and MV/kg) in the low nutritional risk group and the no weight loss group were significantly higher than those in the medium nutritional risk group and the weight loss group.

Lung development begins in utero and continues into early childhood.<sup>[12-14]</sup> The neonatal period is the initial stage of postnatal development, and it is important for lung development and maturity. The nutritional status early in life is critical for lung development. Studies have shown that extrauterine growth retardation is still common in neonates, indicating that newborns are at a high nutritional risk.<sup>[15,16]</sup> In recent years, studies have shown that an inadequate nutrition intake in the early period after birth is an important factor.<sup>[17]</sup> We adopted the STRONGkids as a nutritional risk screening tool. We found that among the 172 newborns, 112 (65.12%) had a medium nutritional risk. This finding suggested that doctors should pay attention to the nutritional problems of newborns.

Previous studies on patients with cystic fibrosis mostly focused on the effects of nutritional status on lung development and pulmonary function. Kilinc et al.<sup>[18]</sup> studied 143 patients with cystic fibrosis who were followed up for 2 years. They found that appropriate nutritional support could maintain or improve the respiratory function of children with cystic fibrosis. In newborns, the basic treatment of neonatal bronchopulmonary dysplasia (BPD) is also nutritional treatment. An increasing number of studies have confirmed that nutritional support is important for the prevention of BPD in premature infants. Ehrenkranz et al.<sup>[19]</sup> found that early after premature birth, especially 1 week after birth, nutritional support was negatively correlated with the incidence of BPD. Furthermore, with an increase of 1 kcal/kg/d in total energy, there was a 2% decrease in the incidence of BPD. The mechanism may be due to nutrition by adjusting the structure of the lungs and directly affecting the development of the lungs. Limiting nutrition can lead to early alveolar structure simplification, and affect the morphological, physiological, and biochemical function of the lungs.<sup>[20]</sup> Nutritional support therapy may be helpful to improve the lung function of premature infants with BPD.

At present, there is a lack of research on the effects of the nutritional status on lung development in late preterm and full-term infants without respiratory diseases. Our study ruled out confounding factors (e.g., a family history of bronchial asthma receiving respiratory support) that may have affected neonatal pulmonary function in this study.<sup>[21]</sup> We selected late preterm and full-term newborns whose respiratory function was not impaired after birth as the research subjects to determine the effect of the nutritional status on lung function in normal newborns.

In our study, the newborns' body weight at the examination was compared with that at birth. They were divided into two groups: those who lost weight and those who did not. Postnatal weight loss usually occurs between 1 and 5 days

after birth.<sup>[22]</sup> Our study showed that up to 59.30% of newborns still experienced weight loss on the 7th day after birth, although they had passed the physiological weight-loss period. Additionally, there was a significant correlation between neonatal nutritional risk and changes in weight. Furthermore, serum albumin concentrations and the caloric intake in the low nutritional risk group were significantly higher than those in the medium nutritional risk group. These findings indicated that the nutritional status of neonates in the low nutritional risk group was better than that in the medium nutritional risk group. Lung capacity-related parameters in the low nutritional risk group and no weight loss group were significantly higher than those in the medium nutritional risk group and the weight loss group, respectively. Hancox et al.<sup>[23]</sup> also assessed the relationship between birth weight, postnatal growth, and adult lung function in a cohort of 1037 children. They found that low birth weight and low weight gain in newborns were associated with decreased lung function in adults. Canoy et al.<sup>[24]</sup> conducted a longitudinal cohort study of 5390 full-term newborns and tracked them from the fetal stage to adulthood. They showed that adult forced expiratory volume in the first second and forced vital capacity increased linearly with an increase in birth weight, and an increase in infant weight was positively correlated with adult lung function. These previous findings are consistent with our findings. A difference between studies is that these previous studies were retrospective, and our study had the advantage of being conducted in the neonatal period.

This study has some limitations. One limitation is this was a single-center study, and because lung development can show variations according to different ethnic groups, our results need to be validated and compared with other ethnic groups. In the future, we plan to conduct a multicenter cohort study to investigate the effects of different nutritional patterns on neonatal lung development. Nevertheless, our study has some strengths. This is the first study to investigate the effects of nutritional status on pulmonary function among neonates. These findings provide new insights into the early development of a pulmonary function. A cohort study with a long-term follow-up of patients is required in the future.

#### 5. Conclusions

This study shows that neonatal weight gain is positively correlated with an improvement in neonatal lung function. Additionally, the effect of neonatal changes in weight on pulmonary function is mainly through lung capacity, indicating that an improvement in the neonatal nutritional status is important for the development of lung capacity.

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### Author contributions

XZ, JL, and BW designed the study and contributed to the concept and definition of intellectual content; XZ, SX, and HH performed a literature search, clinical studies, and experimental studies; FH, XZ, and BW analyzed the data; XZ and JL wrote the paper; XZ reviewed and edited the manuscript. All authors read and approved the manuscript.

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