The efficacy of different training programs guided by cardiopulmonary exercise test goals for the treatment of male patients with chronic obstructive pulmonary disease

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Abstract
To explore the therapeutic effect of aerobic exercise nursing plans based on target heart rate in cardiopulmonary exercise tests on male patients with chronic obstructive pulmonary disease. This study recruited 90 male patients with chronic obstructive pulmonary disease who met specific screening criteria and were evenly divided into a control group and an experimental group based on a random number table. The control group received respiratory training based on the target heart rate in the cardiopulmonary exercise test, while the experimental group received aerobic exercise based on the target heart rate in the cardiopulmonary exercise test. Both groups received 12 weeks of exercise each. Cardiopulmonary function tests showed that peak oxygen consumption (peak VO2), anaerobic threshold (AT), forced expiratory volume in the first second (FEV1), forced vital capacity (FVC), and the FEV1/FVC ratio in the test group were significantly higher than those in the control group (p < 0.05); furthermore, the carbon dioxide ventilation equivalent (VE/VCO2) slope was significantly lower than that in the control group (p < 0.05). The 6MWT of the test group was significantly higher than that in the control group (p < 0.05). The CAT score, Borg score and scores related to the symptoms, activities, and impacts related to quality-of-life were significantly reduced after intervention (p < 0.05). Aerobic exercise based on cardiopulmonary exercise testing can improve the health status, quality of life and prognosis of COPD patients.

Keywords
COPD; Male; Cardiopulmonary exercise test; Aerobic exercise; Nursing effect

1. Introduction
Chronic obstructive pulmonary disease (COPD) is known as the “three highs” due to its high morbidity rate, mortality rate and socioeconomic impact. Previous studies estimated that by 2022, there would be close to 100 million COPD patients in China [1, 2]. Developing methods to prevent and control COPD has become very serious due to its listing as a major disease in the “Healthy China 2030 Action Plan” [3]. In addition to basic nutritional support and health education, the pulmonary rehabilitation program includes respiratory exercise training and aerobic exercise. These exercises include lip retraction breathing exercises and diaphragmatic breathing exercises, as well as training for coughing ability.

Aerobic exercise can also increase cardiopulmonary endurance, and therefore represents the core aspect of pulmonary rehabilitation. Heart rate is a more prevalent indicator of exercise intensity in clinical practice, and peak heart rate can acquire from exercise tests to predict the intensity of exercise. Currently, cardiopulmonary exercise tests are used internationally to determine the exercise intensity of patients; it has been discovered that peak oxygen uptake and anaerobic threshold cannot be easily controlled in a precise manner in daily rehabilitation exercises [4, 5]. Previous research demonstrated that there are more male patients with COPD than females at all ages, that exercise training improves muscle function and endurance, and that exercise rehabilitation under a cardiopulmonary exercise protocol can effectively improve cardiopulmonary function and exercise endurance in patients with chronic heart failure, thus reducing mortality and re-hospitalization rates [6, 7]. Given the high prevalence of COPD in male patients in China, the specific purpose of this study was to investigate the rehabilitative benefits of aerobic exercise training when directed by the target heart rate of a cardiopulmonary exercise test in male COPD patients.

2. Research subjects and research methods
2.1 General information

We recruited all male COPD patients who were hospitalized in multiple centers in our city between November 2020 and December 2022. The inclusion criteria were as follows: (1) male patients who met the diagnostic criteria for COPD [8]; (2) COPD grade I to II; (3) patients who had received uninterrupted drug therapy during the study period; (4) patients who were able to communicate normally and complete questionnaires independently; (5) patients with high levels of compliance, and (6) patients who understood the study, participated voluntarily and signed an informed consent form. The exclusion criteria were as follows: (1) unstable vital signs; (2) patients with severe liver and kidney diseases, such as organ failure or malignant tumors; (3) patients with coagulation disorders, acute and chronic infectious diseases or mental disorders, or other diseases that can reduce nursing cooperation; (4) patients with heart diseases such as unstable coronary artery disease or uncontrolled congestive heart failure with drug treatment; (5) pulmonary hypertension and patients with local or systemic diseases that are not suitable for exercise; (6) patients with other diseases that could affect exercise training and cannot complete training rehabilitation according to the study process, and (7) patients who did not want to join the study and refused to sign the informed consent form.

According to the screening criteria, 90 male patients were finally included in the study and were divided into control and test groups according to a random number table. General information for the two groups is shown in Table 1.

2.2 Research methods

Both groups of subjects were subjected to cardiopulmonary exercise testing. The testing protocol involved cleaning the skin of the patient’s thorax and back, connecting the electrocardiogram and helping the patient to fit a facemask without air leakage. Next, we adjusted the height of the seat and armrests according to the reagent height ratio of the subjects, connected blood pressure and blood oxygen saturation (SaO₂) detecting devices, and then trained the patient with a 2900 bicycle-type exercise cardiopulmonary tester (COSMED, Rome, Italy).

The patient was fitted with the testing equipment and instructed to still on the power bike and rest for 3 min; then the patient was asked to pedal without load at a rate of 60 r/min for 3 min to warm up. Then, the power of the bike was set according to the specific clinical situation; the patient was asked to maintain the incremental rate of 20–30 w/min and to reach the symptomatic limitation within 6–10 min of exercise to obtain maximum power. It was important to ensure that the exercise was terminated when the patient felt extreme respiratory distress, extreme lower limb fatigue, or when the SaO₂ was lower than 85%. Upon such termination, the patient’s arterial partial pressure of oxygen (PaO₂) was measured immediately, and the blood pressure, heart rate and other indicators were recorded during a 5–10 min sedentary recovery period after the end of training. The formula for calculating the target heart rate was as follows: target heart rate = 70% × (peak heart rate − quiet heart rate) + quiet heart rate [9]. Following the termination of exercise, patients were instructed to rest for half an hour during the slow and sedentary state. Patients in the control group followed a routine nursing program, including basic medication, disease propaganda, the prevention of adverse reactions, the development of dietary plans, and also given respiratory training based on the cardiopulmonary exercise test under the guidance of the target heart rate by blowing up balloons, candles and lip-contracting respiration; the specific routine was 10 min per training session, 3 times a week for a total of 12 weeks. Rehabilitation exercises were performed according to the clinical situation of each patient and their individual wishes, without excessive intervention and guidance from healthcare personnel. The experimental group also received the routine care provided to the control group but also implemented aerobic exercise training based on cardiopulmonary exercise tests under the guidance of the target heart rate. The aerobic exercise program was implemented as follows. The training mode involved pedaling a power bicycle; the training intensity involved different exercise loads corresponding to the anaerobic threshold of patient testing for personalized training, and an incremental load power program. At the beginning of the exercise, no load power or a lower constant load power was provided and the patient warmed up for 10 minutes. Then, the exercise load was slowly increased to 70% of the power at the anaerobic threshold, keeping the same incremental exercise load per minute; this was 20 w/min for males, and the total duration of the load power incremental test was maintained within 10 min. The patients maintained a uniform pedaling speed during the exercise process, with the rotational speed maintained at 55–65 r/min. The final speed before the end of the test was 55–65 r/min and for the last 2 min before the end of the test, the load power was reduced to zero. The patient was asked to continue to pedal slowly without load for 5 min; then, the test was ended. The training frequency was 30–45 min/times/d, 5 times/week, for a total of 12 weeks.

2.3 Observed indicators

2.3.1 Cardiopulmonary function

The exercise cardiopulmonary testing system was used before and after the intervention to assess each patient’s cardiopulmonary function indicators, including peak oxygen consumption (peak VO₂), as determined by an aerobic capacity curve, anaerobic threshold (AT), carbon dioxide ventilation equivalent slope (VE/VCO₂ slope), forced expiratory volume in the first second (FEV1), forced vital capacity (FVC), and the FEV1/FVC were also measured using a pulmonary function tester (PFT-B, Anhui Institute of Electronic Science, Hefei, China).

2.3.2 The 6 min walking distance, chronic obstructive pulmonary patient (COPD) self-assessment test and Borg dyspnea score

The 6-minute walking distance (6MWT), chronic obstructive pulmonary disease assessment test (CAT) score, and the Borg dyspnea score were determined and compared before and after the intervention. For the 6MWT, the patient was asked to walk back and forth along a flat-to-floor surface for a distance of 30 m in a quiet room over a 6 min period. It was important to advise each patient that shortness of breath or exhaustion may occur during the walking test. Thus, walking may be...
TABLE 1. A comparison of general information for the 90 subjects.

<table>
<thead>
<tr>
<th>Grouping</th>
<th>Number of cases</th>
<th>Mean age (yr) ± SD</th>
<th>Mean duration of illness (yr) ± SD</th>
<th>Height (cm) ± SD</th>
<th>BMI (kg/m²) ± SD</th>
<th>COPD Grade I</th>
<th>COPD Grade II</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>45</td>
<td>58.88 ± 5.58</td>
<td>5.90 ± 1.67</td>
<td>168.10 ± 7.25</td>
<td>24.08 ± 3.12</td>
<td>20 (44.44)</td>
<td>25 (55.56)</td>
</tr>
<tr>
<td>Test group</td>
<td>45</td>
<td>60.57 ± 6.46</td>
<td>6.37 ± 1.32</td>
<td>169.72 ± 8.78</td>
<td>25.03 ± 2.27</td>
<td>22 (48.89)</td>
<td>23 (51.11)</td>
</tr>
<tr>
<td>t value</td>
<td></td>
<td>1.331</td>
<td>1.462</td>
<td>0.958</td>
<td>1.652</td>
<td>0.179</td>
<td></td>
</tr>
<tr>
<td>p value</td>
<td></td>
<td>0.187</td>
<td>0.147</td>
<td>0.340</td>
<td>0.102</td>
<td>0.673</td>
<td></td>
</tr>
</tbody>
</table>

BMI: body mass index; COPD: chronic obstructive pulmonary disease.

slowed down or stopped so that the patient could take rest appropriately. Patients were able to stand against a wall while resting but needed to continue to walk as long as possible while able to do so. It was important that the patient should walk as long a distance as possible in 6 minutes, but not run or jog.

The CAT score divides symptoms using a scale of 1 to 8, with each scale using a six-point scale of 0 to 5; a higher score represents a higher degree of severity. The CAT score is a composite symptom score totaling 0 to 40 points, with 0 to 10 points representing a mild effect, 11 to 20 points representing a moderate effect, 21 to 30 points representing a severe effect, and 31 to 40 representing a very severe effect [10]. The Borg dyspnea rating scale is a vertical scale describing the intensity of dyspnea. This uses a 0 to 10 points scale and requires subjects to rate their overall feeling of respiratory discomfort, with 0 representing no dyspnea at all and 10 representing the maximum value of dyspnea or the most intense level experienced [11].

2.3.3 Quality-of-life

The quality-of-life of each patient was assessed and compared before and after intervention using the St. George’s Respiratory Questionnaire (SGRQ) [12], which incorporates symptoms (cough, sputum, croup, dyspnea), activity (physical function, household chores and amateur hobbies) and disease impact (the impact of disease on daily life, social function and emotional state). The questionnaire covers these three major areas (symptoms, activity and impact) with a total of 50 entries, and the final score was calculated using a weighted average method with scores ranging from 0 to 100, indicating no impact on life at all to extreme impact on life, respectively.

2.4 Statistical methods

All data obtained in this study were analyzed by IBM SPSS version 25 (IBM Corp., Armonk, NY, USA). Measurement data are expressed as mean ± standard deviation (mean ± SD) and were compared by independent sample t-tests. A paired t-test was used for comparisons before and after treatment within the same group, and p < 0.05 indicated that the differences were statistically significant.

3. Results

3.1 Cardiopulmonary function indices

There were no significant differences in cardiopulmonary function-related indicators between the two groups of subjects prior to intervention (p > 0.05). After the intervention, the peak VO₂, AT, FEV₁, FVC and FEV₁/FVC showed a tendency to increase to varying degrees within each of the two groups, while the VE/VCO₂ slope decreased to varying degrees. When compared between groups, the peak VO₂, AT, FEV₁, FVC and FEV₁/FVC in the experimental group were all significantly higher than those of the control group after the intervention; furthermore, the VE/VCO₂ slope was significantly lower in the intervention group than in the control group (p < 0.05) (Tables 2 and 3).

3.2 6MWT, CAT and Borg dyspnea scores

Data relating to the 6MWT, CAT score and Borg dyspnea score of the subjects in the two groups before intervention were not significant (p > 0.05). When compared with the pre-intervention period within the same group, the 6MWT results of the two groups of subjects showed an increasing trend but to differing degrees; the CAT and Borg scores showed a decreasing trend. The test group’s post-intervention 6MWT was significantly higher than that of the control group, and the CAT score and Borg score were significantly lower than those in the control group (p < 0.05) (Table 4).

3.3 Quality-of-life

Symptom score, activity score, impact score and total score were not significantly different in both groups prior to the intervention (p > 0.05). Compared with pre-intervention scores within the same group, scores for both groups decreased to different degrees after the intervention; symptom score, activity score, impact score and total score in the test group were significantly lower than those in the control group (p < 0.05) (Table 5).
### TABLE 2. A comparison of cardiopulmonary function indices between the two groups of subjects.

<table>
<thead>
<tr>
<th>Project</th>
<th>peak VO₂ (mL/min/kg)</th>
<th>t</th>
<th>p</th>
<th>AT (mL/min/kg)</th>
<th>t</th>
<th>p</th>
<th>VE/VCO₂ slope</th>
<th>t</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pre-intervention</td>
<td></td>
<td></td>
<td>After Intervention</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control group (n = 45)</td>
<td>17.98 ± 2.66</td>
<td>2.206</td>
<td>121</td>
<td>13.35 ± 2.25</td>
<td>4.606 &lt;0.001</td>
<td>34.54 ± 7.77</td>
<td>30.97 ± 2.97</td>
<td>4.262 &lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Test group (n = 45)</td>
<td>17.21 ± 3.49</td>
<td>0.014</td>
<td>5.171</td>
<td>15.01 ± 2.20</td>
<td>8.691 &lt;0.001</td>
<td>35.11 ± 4.68</td>
<td>28.97 ± 3.44</td>
<td>7.091 &lt;0.001</td>
<td></td>
</tr>
</tbody>
</table>

peak VO₂: peak oxygen consumption; AT: anaerobic threshold; VE/VCO₂: carbon dioxide ventilation equivalent.

### TABLE 3. A comparison of cardiopulmonary function indices between the two groups of subjects.

<table>
<thead>
<tr>
<th>Project</th>
<th>FEV1 (L)</th>
<th>t</th>
<th>p</th>
<th>FVC (L)</th>
<th>t</th>
<th>p</th>
<th>FEV1/FVC (%)</th>
<th>t</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pre-intervention</td>
<td></td>
<td></td>
<td>After Intervention</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control group (n = 45)</td>
<td>1.18 ± 0.17</td>
<td>15.011 &lt;0.001</td>
<td>1.15 ± 0.21</td>
<td>2.66 ± 0.46</td>
<td>20.032 &lt;0.001</td>
<td>62.69 ± 5.41</td>
<td>63.85 ± 3.27</td>
<td>0.944 0.348</td>
<td></td>
</tr>
<tr>
<td>Test group (n = 45)</td>
<td>1.18 ± 0.23</td>
<td>13.455 &lt;0.001</td>
<td>1.16 ± 0.23</td>
<td>3.31 ± 0.72</td>
<td>19.082 &lt;0.001</td>
<td>61.93 ± 5.18</td>
<td>69.54 ± 5.87</td>
<td>6.521 &lt;0.001</td>
<td></td>
</tr>
</tbody>
</table>

FEV1: forced expiratory volume in the first second; FVC: forced vital capacity.

### TABLE 4. A comparison of 6MWT, CAT and Borg dyspnea scores between the two groups of patients.

<table>
<thead>
<tr>
<th>Project</th>
<th>6MWD (m)</th>
<th>t</th>
<th>p</th>
<th>CAT score</th>
<th>t</th>
<th>p</th>
<th>Borg dyspnea score</th>
<th>t</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pre-intervention</td>
<td></td>
<td></td>
<td>After Intervention</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control group (n = 45)</td>
<td>295.89 ± 28.55</td>
<td>3.950 &lt;0.001</td>
<td>13.45 ± 3.83</td>
<td>12.14 ± 2.67</td>
<td>1.882 0.063</td>
<td>3.74 ± 1.35</td>
<td>3.32 ± 1.49</td>
<td>1.401 0.165</td>
<td></td>
</tr>
<tr>
<td>Test group (n = 45)</td>
<td>300.01 ± 33.29</td>
<td>9.152 &lt;0.001</td>
<td>13.46 ± 3.39</td>
<td>9.28 ± 2.79</td>
<td>6.387 &lt;0.001</td>
<td>3.88 ± 1.42</td>
<td>2.57 ± 1.40</td>
<td>4.407 &lt;0.001</td>
<td></td>
</tr>
</tbody>
</table>

6MWD: The 6-minute walking distance; CAT: chronic obstructive pulmonary disease assessment test.
TABLE 5. A comparison of quality-of-life between the two groups of subjects.

<table>
<thead>
<tr>
<th>Project</th>
<th>Symptom score</th>
<th>Activity score</th>
<th>Impact score</th>
<th>Total score</th>
<th>t</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pre-intervention</td>
<td>Post-intervention</td>
<td>Pre-intervention</td>
<td>Post-intervention</td>
<td>Pre-intervention</td>
<td>Post-intervention</td>
</tr>
<tr>
<td>Control group (n = 45)</td>
<td>28.15 ± 5.62</td>
<td>6.026</td>
<td>35.73 ± 6.91</td>
<td>9.201</td>
<td>&lt;0.001</td>
<td>23.24 ± 5.93</td>
</tr>
<tr>
<td>Test group (n = 45)</td>
<td>25.96 ± 6.43</td>
<td>9.730</td>
<td>32.82 ± 8.86</td>
<td>11.201</td>
<td>&lt;0.001</td>
<td>15.46 ± 5.44</td>
</tr>
<tr>
<td>t</td>
<td>1.721</td>
<td>1.738</td>
<td>0.119</td>
<td>0.224</td>
<td>11.206</td>
<td></td>
</tr>
<tr>
<td>p</td>
<td>0.089</td>
<td>0.086</td>
<td>0.906</td>
<td>0.823</td>
<td>&lt;0.001</td>
<td></td>
</tr>
</tbody>
</table>
4. Discussion

COPD is a disease characterized by persistent airflow limitation, often manifesting with chronic cough, sputum, shortness of breath or dyspnea, wheezing and chest tightness as the disease progresses; severe cases also experience a loss of appetite and weight loss [13]. COPD is a common and prevalent disease with a global prevalence of 9%–10% in people aged 40 years and older [3]. COPD is now the fourth most common cause of mortality among Chinese citizens, with prevalence rates of 8.6% in those aged 20 years and older and 13.7% in those aged 40 years and older [14, 15]. As a major chronic disease on the same scale as hypertension and diabetes mellitus, airflow limitation and airway obstruction are the most important pathophysiological changes. The cause of COPD remains unknown, although it is known that genetic factors, pulmonary growth and development, asthma, infection, long-term smoking and the inhalation of occupational dust or chemicals are closely related to the occurrence and progression of the disease [16]. Pulmonary rehabilitation is a multidisciplinary and comprehensive intervention based on evidence-based medicine for patients with symptoms and limitations in daily activities. Focusing on cardiopulmonary rehabilitation training for COPD patients is an important part of the treatment process, and paying attention to the specific cardiopulmonary function of patients is of great significance of us to improve and enhance their quality-of-life [17]. Traditional cardiopulmonary rehabilitation guidance is based on assessing the actual physiological condition of the patient, and care protocols are often developed in accordance with the experience of healthcare professionals, thus resulting in treatment outcomes that do not necessarily meet expectations and may be detrimental to the management of disease overall [18, 19].

For many years, the value of cardiopulmonary exercise testing as a pulmonary function diagnostic tool has been studied in clinical practice, primarily to reflect metabolic gas capacity during exercise with increasing load, maximum exercise capacity, and to reveal cardiopulmonary pathology, as well as the interaction and reserve capacity of the circulatory system following comprehensive analysis of specific test parameters to guide cardiopulmonary rehabilitation [20]. Over recent years, cardiopulmonary exercise tests have been used more widely in clinical practice, especially in the exercise rehabilitation of chronic diseases such as heart failure, metabolic syndrome and coronary artery disease [21–23]. Previous studies have shown that exercise protocols based on cardiopulmonary exercise can help patients rebuild their breathing patterns, improve the amplitude and range of diaphragmatic activity, strengthen the gas exchange capacity of the alveoli, and thus improve their cardiopulmonary function while clarifying the patient’s actual physiological condition and formulating individualized exercise prescriptions [24, 25]. It has been suggested that this type of protocol can also be used to develop exercise prescriptions for the pulmonary rehabilitation of COPD [26, 27]. On the basis of our results, we can now offer patients with personalized aerobic exercise prescriptions based on the target heart rate in the cardiopulmonary exercise test; this can be used as a guide to the effect of exercise rehabilitation in COPD. This is because the development of a personalized exercise prescription should match the current physiological function of each patient.

Our experimental outcomes demonstrated that after intervention, the level of improvement in cardiopulmonary function indices in the experimental group was significantly higher than that in the control group, thus demonstrating that aerobic exercise under the direction of the target heart rate of the cardiopulmonary exercise test significantly improved the cardiopulmonary function of patients. These outcomes were in line with earlier reports [28]. Our data further confirmed that individualized, rational and safe exercise patterns for specific patients can contribute to the improvement of cardiopulmonary function and that this may be related to the fact that specific exercise rehabilitation protocols can strengthen the patient’s respiratory strength, reduce oxygen consumption and improve respiratory efficacy [29]. The 6MWT, CAT and Borg scores are all reliable indicators for evaluating the effect of pulmonary rehabilitation in COPD. In this study, we compared the three scores under two different modes of care and found that the 6MWT in the test group was significantly higher than that in the control group. Furthermore, the CAT and Borg scores were significantly lower than that in the control group. These results indicated that the exercise rehabilitation program adopted by the test group was more helpful in terms of patient recovery; this may be related to the significant improvement of cardiopulmonary function and the improvement of exercise endurance, although the exact reasons for this need to be investigated further. In this study, we also assessed quality-of-life in the two groups of patients. We discovered that the three scores and the overall score in the test group were significantly higher than those of the control group, thus indicating that the quality-of-life for patients in the test group had been significantly improved and enhanced when compared to the control group.

This study has certain limitations that need to be acknowledged. For example, we only investigated the effect of the rehabilitation exercise program on the recovery of male patients with COPD. There may be significant differences in various indices, such as serological indices and exercise tolerance, between patients of different genders. Other limitations include the limited sample size of our study. Therefore, to further investigate the specific mechanisms underlying the rehabilitation program described herein, it is necessary to perform further research with a larger sample size.

5. Conclusions

In conclusion, the cardiopulmonary exercise test accompanied by target heart rate guidance provides an evidence-based protocol for the development of exercise rehabilitation programs for patients. Furthermore, this protocol can be scientifically evaluated and based on the actual physiological condition of an individual patient, thus allowing the development of a specific and personalized exercise program. Aerobic exercise programs based on the cardiopulmonary exercise test target heart rate can help to improve cardiopulmonary function, promote recovery and improve quality-of-life.
AVAILABILITY OF DATA AND MATERIALS
The authors declare that all data supporting the findings of this study are available within the paper and any raw data can be obtained from the corresponding author upon request.

AUTHOR CONTRIBUTIONS
HS, JFZ and FHQ—designed the study and carried them out; HS, JFZ, FHQ, YJD, JW and FT—supervised the data collection, analyzed the data, interpreted the data, prepared the manuscript for publication and reviewed the draft of the manuscript. All authors have read and approved the manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE
Ethical approval was obtained from the Ethics Committee of Affiliated Hangzhou First People’s Hospital (Approval no. 2018-129-01). Written informed consent was obtained from a legally authorized representative for anonymized patient information to be published in this article.

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CONFLICT OF INTEREST
The authors declare no conflict of interest.

REFERENCES


