

Prognostic value of different scoring models in patients with multiple organ dysfunction syndrome associated with acute COPD exacerbation

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Background and objective: Chronic obstructive pulmonary disease (COPD) represents an increasing healthcare concern as a leading cause of morbidity and mortality worldwide. Our objective was to predict the outcome of COPD patients associated with multiple organ dysfunction syndrome (MODS) by scoring models.

Methods: A retrospective study was performed on severe COPD patients within 24 hours of the onset of MODS. The Acute Physiology and Chronic Health Evaluation (APACHE) II, APACHE III, Multiple Organ Dysfunction Score (MODS), Simplified Acute Physiology Score II (SAPS II), and Sepsis-related Organ Failure Assessment (SOFA) scores were calculated for patients.

Results: A total of 153 elderly patients were recruited. Compared to 30-day survivors, the number of failing organs and all of the scoring models were significantly higher in 30-day non-survivors. The SOFA showed the highest sensitivity and area under the curve (AUC) for predicting the prognosis of patients with MODS induced by acute exacerbation of COPD. The results of logistic regression indicated that factors that were correlated with the prognosis of COPD included the exacerbation history, SOFA score, number of failing organs, and duration of ICU stay. The value of exacerbation frequency for predicting the outcome of COPD was excellent (AUC: 0.892), with a sensitivity of 0.851 and a specificity of 0.797.

Conclusions: The SOFA score, determined at the onset of MODS in elderly patients with COPD, was a reliable predictor of the prognosis. The exacerbation frequency, number of failing organs, and the SOFA score were risk factors of a poor prognosis, and the exacerbation frequency could also effectively predict the outcome of COPD.

Keywords: Acute exacerbation (AE); chronic obstructive pulmonary disease (COPD); multiple organ dysfunction syndrome (MODS); prognosis

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Introduction

Chronic obstructive pulmonary disease (COPD) is a prevalent disease and a major cause of morbidity in elderly patients worldwide (1,2). Severe exacerbation of COPD has been associated with increased mortality (3), which has been

attributed to complex underlying diseases that are more likely to progress into multiple organ dysfunction syndrome (MODS) due to their association with inflammatory mediators (4). In 2008, COPD was the fourth leading cause of death in urban areas and the third leading cause in rural

areas in China (5). Results are consistent with the American epidemic, and what is worse, COPD will be the third leading cause of death by 2020 in America (6). It has been reported that the total expense of COPD was \$1,963.8 per patient, which accounted for 40% of the average family's total income (\$4,849.8) in China in 2006 (5). Presently, COPD has aroused considerable concern in the medical and scientific communities due to its poor prognosis and the growing, substantial burden the disease imposes on healthcare systems (7).

The MODS is characterized by more than one organ system failing, especially during critical illness (8). Therefore, it is important to assess the severity and predict outcomes of elderly COPD patients (age ≥ 60 years old) with MODS to improve the therapeutic treatments and prognosis of this disease.

Scoring models have been widely utilised in the intensive care unit (ICU) setting and provide physicians with objective information to help inform decisions related to the treatment and prognosis of COPD. In the present study, we compare the predictive value of different scoring models for critically ill patients with COPD, including the Acute Physiology and Chronic Health Evaluation scores [APACHE II (9) and APACHE III (10)], Multiple Organ Dysfunction Score (MODS) (11), Simplified Acute Physiology Score II (SAPS II) (12), and Sepsis-related Organ Failure Assessment (SOFA) Score (13), which have been evaluated and validated in many centres and are widely used by most ICUs to predict clinical outcomes.

Methods

Patient recruitment

We performed a retrospective analysis of 153 patients, aged 60 years or older (<http://www.who.int>), who were admitted to the Respiratory ICU and Emergency ICU of the Chinese People's Liberation Army (PLA) General Hospital between January 2008 and June 2012.

Patients who met the following conditions were included in the study: (I) on admission to the hospital, a diagnosis of acute exacerbation (AE) of COPD (AECOPD), without any organ dysfunction, was made based on clinical symptoms and the GOLD guidelines (14); (II) the patient developed MODS during hospitalisation, the definition of which was proposed by the American College of Chest Physicians/Society of Critical Care Medicine (ACCP/SCCM) (15); and (III) the patient's prognosis was clear based on

30-day outcome (survivors or non-survivors). Patients with the following conditions were excluded from this study: (I) acute respiratory distress syndrome; (II) massive pulmonary embolism; (III) heart failure or cancer; or (IV) respiratory failure due to reasons other than COPD.

All of the patients signed written informed consent forms. The present study was approved by the Clinical Ethics Committee of the Chinese PLA General Hospital.

Definition of acute exacerbation (AE) of COPD

AECOPD is an acute event characterised by an increase in the severity of the patient's respiratory symptoms (increased sputum volume, acutely worsening dyspnea, and the presence of purulent sputum) that is beyond normal day-to-day variations, and leads to a change in treatment (14,16,17).

Data extraction

The starting point of this study was the day when a patient developed MODS associated with the AECOPD described at the time of hospitalisation. Clinical data from 153 elderly patients were collected and analysed retrospectively, including basic information (e.g., age, gender, and co-morbid diseases), exacerbation history in the preceding year, the number of failing organs, important vital signs (e.g., body temperature, breathing rate, heart rate, and blood pressure) laboratory tests (e.g., blood tests such as white blood cell and platelet counts), blood biochemistry (e.g., bilirubin, creatinine, and electrolytes) within 24 hours of the onset of MODS, duration of the ICU stay, and the 30-day outcome. The APACHE II, APACHE III, MODS, SAPS II and SOFA scores were calculated.

Statistical analysis

The SPSS Statistics 17.0 software (SPSS Inc. Chicago, Illinois, USA) for Windows was used for data analysis. Data were expressed as the mean $\pm$ standard deviation (SD) (normal distribution) or as the median (interquartile range for non-normal distributions) for continuous variables and as percentages for categorical variables. Student's *t*-test was used to compare normally distributed data between two groups. An analysis of variance was employed to compare multiple groups, and the Kruskal-Wallis rank sum test was used to compare two groups with non-normal data. The qualitative results were evaluated using the chi-square test. The predictive values of the scoring systems were analysed

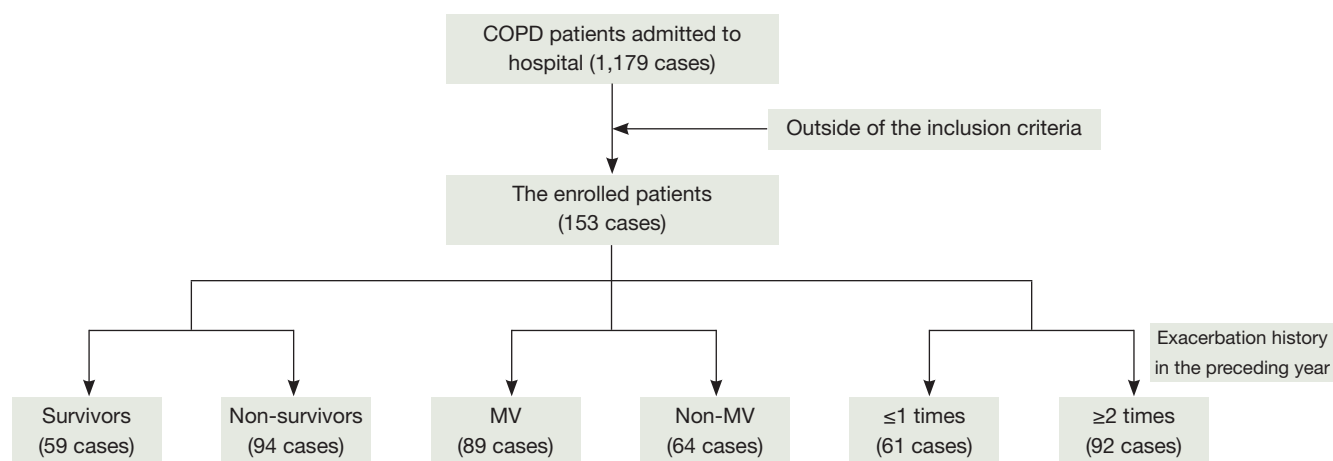


Figure 1 Flow chart of patient enrolment in this study. COPD, chronic obstructive pulmonary disease.

using a receiver operating characteristic (ROC) curve, and the sensitivity, specificity, area under the curve (AUC) and 95% confidence intervals (95% CI) of each scoring system were calculated. Logistic regression analysis was used to analyse the related factors affecting the prognosis of these patients. A P value <0.05 on a two-sided test was considered statistically significant.

Results

One hundred fifty-three patients with COPD complicated by MODS were enrolled in the study (*Figure 1*), with a mean age of 77 ± 10 years (range, 60-101 years). Ninety-five patients (62.1%) were males, and 89 patients (58.2%) required mechanical ventilation. Based on the 30-day outcome, these patients were divided into two groups: a 30-day survival group (59 cases) and a 30-day non-survival group (94 cases). The overall mortality rate was 61.4%.

Table 1 lists the general characteristics of the patients' conditions. The number of failing organs in the non-survival group was significantly higher than in the survival group ($P < 0.001$). There were statistically significant differences in urine output, serum blood urea nitrogen (BUN), and serum creatinine between the survivors and non-survivors ($P < 0.05$). All of the objective scoring models in survivors, including the APACHE II, APACHE III, MODS, SAPS II and SOFA scores, were significantly lower than those of the non-survivors ($P < 0.001$). However, the length of the ICU stay in the survival group was longer than that of the non-survival group.

The power of each scoring system (APACHE II, APACHE III, MODS, SAPS II and SOFA) for predicting

the outcome for the overall study population is shown in *Table 2* and *Figure 2*. The sensitivity (0.936) and the AUC (0.875) of the SOFA score at a cut-off point of 6.5 was remarkably higher than those of the other scoring models, but the specificity of the SOFA score (0.695) was inferior to that of the APACHE II score (0.865), which was the most accurate model.

These five scoring models were also used to assess the prognosis of patients requiring mechanical ventilation, and the ROC curves of these assessments are depicted in *Table 3* and *Figure 3*. The sensitivity (0.902) and the AUC (0.890) of the SOFA score at a cut-off point of 7.5 was remarkably higher than those of the other scoring models, but the specificity of the SOFA score (0.786) was inferior to that of the APACHE II score (0.893), which was the most accurate model. The combined prognostic value for patients of the two scoring models (APACHE II and SOFA) was not significantly improved (*Table 3*).

To determine the factors related to the prognosis, logistic regression analysis was performed. Four indicators were associated with the prognosis of elderly patients with MODS associated with the AE of COPD: the exacerbation history, SOFA scores, number of failing organs, and length of the ICU stay, and the odds ratio (OR) values were 5.910, 1.387, 3.617 and 0.927, respectively (*Table 4*).

Table 4 shows that the exacerbation history is a high-risk factor for a poor prognosis of COPD. A ROC curve was employed to assess the prognosis of the patients studied in relation to their exacerbation history. The results showed that the AUC of the exacerbation history was 0.892, with a sensitivity of 0.851 and a specificity of 0.797 at a cut-off point

Table 1 Demographic and biochemical data of the enrolled patients

Characteristics	Outcomes of patients (n=153)		P value
	Survivors (n=59)	Non-survivors (n=94)	
Age (years)	77±10	76±9	0.422
Gender (No., %)			0.367
Male	34 (22.2)	61 (39.9)	
Female	25 (16.3)	33 (21.6)	
Number of failing organs*	3 [2, 3]	4 [3, 5]	<0.001
Acute renal failure (%)	5 (3.3)	41 (26.8)	
Vital signs and laboratory tests			
Body temperature (°C)	37.3±1.3	37.7±1.8	0.067
Heart rate (beats/min)	105±31	113±31	0.131
Mean arterial pressure (mmHg)	82±26	79±22	0.401
Urine output (mL/24 hours)*	1,983±1,189	1,472±1,273	0.014
WBC count (10 ⁹ /L)	11.6±6.2	14.8±6.1	0.148
Platelet count (10 ⁹ /L)	151±69	117±75	0.069
Serum albumin (g/L)	30.5±6.8	30.8±9.5	0.824
Serum glucose (mmol/L)	9.5±4.5	10.1±4.8	0.464
Serum BUN (mmol/L)*	14.2±11.1	20.6±13.8	0.003
Serum creatinine (μmol/L)*	80.0 (60.3, 113.0)	127.0 (89.0, 215.5)	<0.001
Scoring systems			
APACHE II*	19±7	28±8	<0.001
APACHE III*	71±29	101±29	<0.001
MODS*	6±3	9±3	<0.001
SAPS II*	44±16	62±17	<0.001
SOFA	6±3	12±4	<0.001
Mechanical ventilation (No.)	32	57	0.435
Length of ICU stay (days)*	17±11	13±7	0.013

Quantitative data with a normal distribution are presented as the mean ± SD. Quantitative data with a non-normal distribution are presented as the mean (25th and 75th percentiles). Qualitative data are presented as n (%). *, represents the comparison between survivors and non-survivors, P<0.05. WBC counts, white blood cell counts; BUN, blood urea nitrogen; ICU, intensive care unit; APACHE, Acute Physiology and Chronic Health Evaluation; MODS, multiple organ dysfunction syndrome; SAPS, Simplified Acute Physiology Score II; SOFA, Sepsis-related Organ Failure Assessment; SD, standard deviation.

Table 2 Prognostic values of each scoring model for the enrolled patients

Scoring models	Cut-off	Se	Sp	Youden index	AUC	95% CI
APACHE II	25.5	0.617	0.865	0.481	0.789	0.714-0.863
APACHE III	86.0	0.649	0.797	0.446	0.775	0.699-0.851
MODS	6.5	0.777	0.678	0.455	0.739	0.656-0.823
SAPS II	53.5	0.681	0.814	0.494	0.802	0.729-0.875
SOFA	6.5	0.936	0.695	0.631	0.875	0.817-0.932

Se, sensitivity; Sp, specificity; ROC curve, receiver operating characteristic curve; APACHE, the acute Physiology and Chronic Health Evaluation; MODS, multiple organ dysfunction syndrome; SAPS, Simplified Acute Physiology Score II; SOFA, Sepsis-related Organ Failure Assessment; AUC, area under the curve; 95% CI, 95% confidence interval.

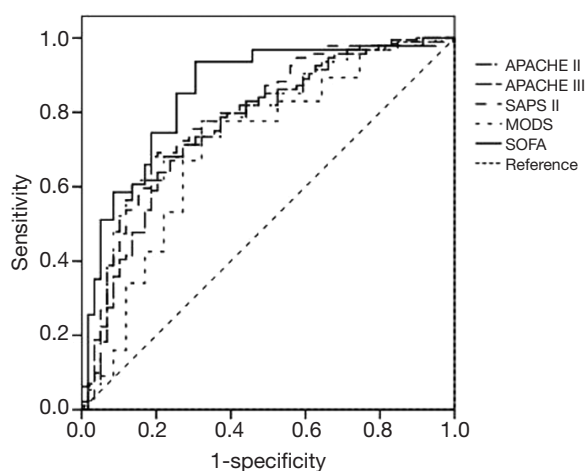


Figure 2 The ROC curves of the scoring systems for predicting the prognosis of enrolled patients (n=153). MODS, multiple organ dysfunction syndrome; SOFA, Sepsis-related Organ Failure Assessment; APACHE, the acute Physiology and Chronic Health Evaluation; SAPS, Simplified Acute Physiology Score II; ROC, receiver operating characteristic.

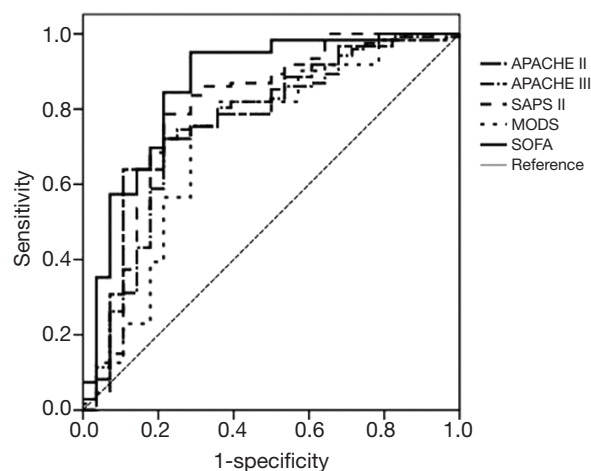


Figure 3 The ROC curves of the scoring systems for predicting the prognosis of enrolled patients requiring mechanical ventilation (n=89). ROC, receiver operating characteristic; SOFA, Sepsis-related Organ Failure Assessment.

Table 3 Prognostic values of each scoring model for the enrolled patients requiring mechanical ventilation

Scoring models	Cut-off	Se	Sp	Youden index	AUC	95% CI
APACHE II	25.5	0.689	0.893	0.581	0.800	0.699-0.904
APACHE III	86.0	0.689	0.821	0.510	0.773	0.663-0.883
MODS	7.5	0.754	0.714	0.468	0.759	0.643-0.876
SAPS II	53.0	0.770	0.821	0.592	0.813	0.704-0.923
SOFA	7.5	0.902	0.786	0.687	0.890	0.813-0.967
Combined diagnosis	0.548	0.934	0.786	0.720	0.890	0.803-0.967

Se, sensitivity; Sp, specificity; ROC curve, receiver operating characteristic curve; APACHE, the acute Physiology and Chronic Health Evaluation; MODS, multiple organ dysfunction syndrome; SAPS, Simplified Acute Physiology Score II; SOFA, Sepsis-related Organ Failure Assessment; AUC, area under the curve; 95% CI, 95% confidence interval.

Table 4 Factors related to the prognosis of patients with MODS associated with acute COPD exacerbation using logistic regression analysis

Variable	B	Se	Wald	df	P value	OR	95% CI
Exacerbation history in the preceding year	1.777	0.354	25.163	1	0.000	5.910	2.952-11.832
SOFA	0.327	0.068	23.165	1	0.000	1.387	1.214-1.585
Number of failing organs	1.339	0.315	18.041	1	0.000	3.617	2.057-7.077
Length of ICU stay	-0.076	0.035	4.756	1	0.029	0.927	0.865-0.992

MODS, multiple organ dysfunction syndrome; COPD, chronic obstructive pulmonary disease; SOFA, Sepsis-related Organ Failure Assessment; ICU, intensive care unit; Se, sensitivity; Sp, specificity.

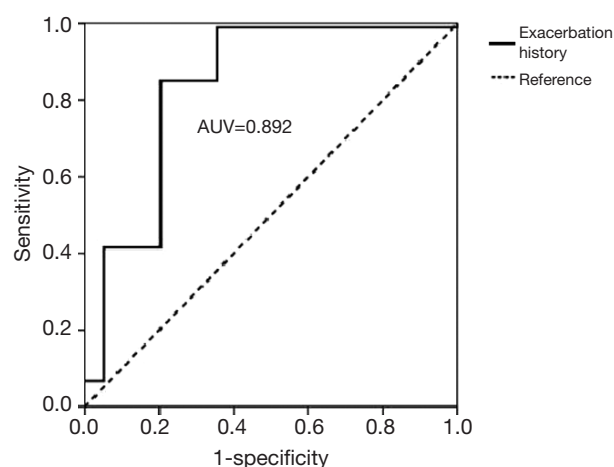


Figure 4 The ROC curve of the SOFA score for predicting the outcome of enrolled patients based on exacerbation frequency. ROC, receiver operating characteristic; SOFA, Sepsis-related Organ Failure Assessment.

of 2 (Figure 4). SOFA scores were increased in parallel with the fit of the frequency of exacerbation, with significant differences between two groups (≤ 1 times group and ≥ 2 times group) ($P < 0.001$). A more frequent exacerbation history corresponded to higher scores and a worse prognosis (Figure 5).

Discussion

In this retrospective study, one third of the patients were women suffering from COPD, and the proportion is gradually increasing. Some published studies have indicated that smoking increases the risk of COPD (18,19), and passive smoke exposure is also a risk factor (20-22), particularly for Chinese rural women. Cooking mainly depends on biomass fuels, including straw and firewood in rural areas, and the exhaust gases, which contain sulphur dioxide and other harmful substances, are likely to increase the pathogenesis of COPD (23).

Compared with the survival group, the number of failing organs in our study was remarkably higher in the non-survival group. The results of logistic regression analysis showed that the number of failing organs was a risk factor for a poor prognosis of elderly COPD patients with MODS. A previous study indicated that a higher number of failing organs was associated with a higher prognostic assessment score and corresponded to a higher mortality rate in 197 patients with MODS (24). The length of the ICU stay in non-survivors

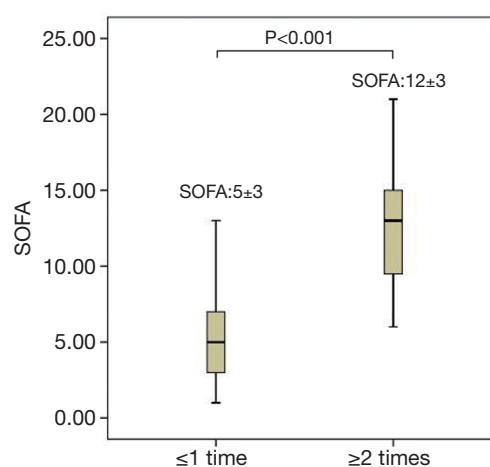


Figure 5 The difference in SOFA scores between different levels of exacerbation frequency in the preceding year before admission to the hospital in patients with COPD. SOFA, Sepsis-related Organ Failure Assessment; COPD, chronic obstructive pulmonary disease.

was less than that of survivors and was an advantageous factor for predicting the prognosis in the present study. The above results indicated that longer positive treatment corresponded to a better prognosis for this critical illness.

Age was not an independent factor for prognosis and showed no significant difference between survivors and non-survivors. However, age is a component of APACHE scores, and it was reported that age was a prognostic factor in the supporting study (25). Study of larger sample sizes may be needed to reconcile our results.

The scoring models showed a better performance compared to the severity of illness systems. The present study is most likely the first report to determine that the SOFA and SAPS II scores show very good discrimination ($AUC > 0.80$) for predicting the prognosis of elderly patients suffering from MODS associated with COPD compared with APACHE II, APACHE III and MODS scores. Additionally, the SOFA scoring system may be more appropriate to use in predicting outcomes due to its high sensitivity, excellent predictive value, simplicity and ease of assessment. The SOFA was the only one of the five scoring models to be retained in the multivariable analysis as an independent risk factor for 30-day mortality, and some previous studies had demonstrated that the SOFA score reliably predicted long-term outcomes in patients with trauma (26) or acute myocardial infarction (AMI) (27). Consequently, the SOFA score could be a good predictor for short-term as well as long-term outcomes.

The SOFA score also increased in parallel with the fit of exacerbation frequency, which was associated with mortality. The exacerbation history was an outstanding risk factor for a poor 30-day prognosis of patients with MODS caused by COPD in our study. Published studies verify that the frequency of COPD exacerbation in the preceding year is risk factor for mortality (28,29). In our study, we also assessed the prognosis of COPD through the number of previous acute onsets of COPD, and then drew the conclusion that the exacerbation history performs well in predicting the outcome of severe COPD patients (AUC: 0.892), with a sensitivity of 0.851 and a specificity of 0.797 at a cut-off point of 2, using the ROC curve.

Our study has two major limitations. First, this is a retrospective study, and some useful indicators were missed, such as the 6-min walk test, the COPD Assessment Test (CAT) and the Modified British Medical Research Council (mMRC) questionnaire, which also can predict outcomes of COPD patients. In addition, the data collected from one centre can lead to results that are not generalisable. However, these research results are important because they can guide the design of a prospective and observational study which could validate the conclusions of this study, and can allow the clinical significance of these findings to be further explored.

Conclusions

In summary, this study showed that SOFA scores determined at the onset of MODS in elderly patients with COPD were a reliable predictor of the prognosis. The exacerbation history, number of failing organs, and the SOFA score were risk factors of a poor prognosis, and the exacerbation history could also make an effective prediction of the outcome of COPD. It would be useful to combine the assessment scores with the other elements (number of exacerbations, etc.) to develop a new prediction model that would be more accurate, specifically for COPD. We suggest that a multi-centre prospective study with a larger sample size would be useful to evaluate the efficacy of these scoring models in predicting outcomes for elderly patients with MODS associated with AECOPD.

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Authors' contributions: All authors are fully responsible for the presented analysis and conclusions drawn in the manuscript. Dr. Xiao: conceived the idea, designed and initiated the study, performed statistical analysis, drafted the manuscript, and approved the final version; Dr. Guo: designed and initiated the study, collected the data, and approved the final version; Dr. Su and Dr. Li: conceived the idea, designed and initiated the study, and approved the final version; Dr. Xie: conceived the idea, designed and initiated the study, amended and commented on the manuscript, and approved the final version.

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