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ORIGINAL RESEARCH

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Incidence of frailty and construction of prediction model in elderly male patients with chronic obstructive pulmonary disease

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Abstract

The incidence of frailty was studied and prediction model was constructed for the elderly male patients with chronic obstructive pulmonary disease (COPD). Total of 266 elderly males having COPD were selected, and Fried Frailty Phenotype was employed to investigate their frailty status. According to the clinical experience, literature and reports; age, BMI (Body Mass Index), course and condition of COPD, laboratory findings, lung function, life quality, nutritional status and disease acceptance were designated as independent variables; and the incidence of frailty was taken as dependent variable. A binary logistic regression model was applied to analyze the factors affecting incidence of frailty, and a prediction model was constructed for the clinical screening of elderly male COPD patients at high frailty risk. The scores of 266 elderly male COPD patients investigated by frailty phenotype (FP) phenotype ranged from 0 to 5, and mean score was 1.83 $\pm$ 0.43. Total of 103 patients scored more than 3 among these patients. The frailty detection rate was 38.72%. Multi-factors logistic regression analysis suggested that age, hospitalization for acute exacerbation of COPD within a year, and interleukin 6 (IL-6) levels were the risk factors for incidence of frailty in elderly male COPD patients, while FEV1 (Forced Expiratory Volume in 1 second) and MNA-SF (Mini Nutritional Assessment Short-Form) levels were the protective factors. COPD frailty was higher in elderly men. Age, inflammatory response, lung function, disease control and nutritional status were the independent factors affecting incidence of frailty. Strengthening the screening for frailty in elderly patients and monitoring their inflammatory response, lung function, and nutritional status were significant in reducing incidence and improving prognosis.

Keywords

Elderly men; COPD; Frailty; Influencing factors; Prediction model

1. Introduction

COPD incidences are on the rise with developing economies, transportation, industrial activities and aging population. According to the China Pulmonary Health (CPH 2018), COPD prevalence rate in China is 8.6% with estimated 99.9 million people of COPD [1]. COPD morbidity among the adults of over 20 years is 8.6%, and 13.7% in over 40 years age. COPD morbidity is 27% among the old people. COPD prevalence rate increases with age. Men have higher prevalence rate than women of all age groups, which is linked to the factors like higher proportion of men smoke and work in dusty environments [2–4]. Frailty is a geriatric syndrome involving multidimensional clinical states, like physical, psychological and social. COPD patients have higher risks of exposure compared to the healthy elderly adults. Studies have shown that frailty risk in elderly COPD patients is twice that of non-COPD patients of same age [5, 6]. Moreover, frailty and COPD are mutually causal. The impaired skeletal muscle function and inflammatory response triggered by frailty further enhance the risk of acute exacerbation of COPD, which result in the progression or deterioration of disease [7–10]. Understanding the frailty status of elderly male COPD patients and analyzing its influencing factors are important in taking targeted measures and improving patients' prognosis. This research work is designed on this background approach.

2. Object and methods

2.1 Object

A prospective study was carried out. Elderly male COPD patients admitted in Affiliated Hospital of Guangdong Medical University from January 2021 to December 2022 were randomly selected. The flow chart of inclusion criteria and exclusion criteria is shown in Fig. 1.

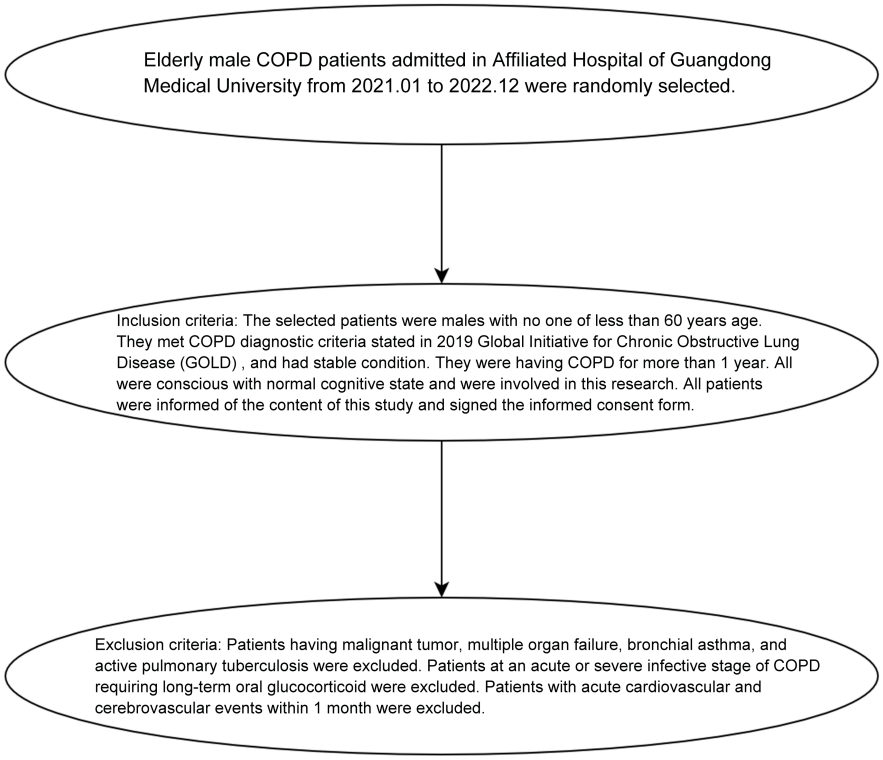

FIGURE 1. The flow chart of inclusion criteria and exclusion criteria. COPD: chronic obstructive pulmonary disease.

The multi-factor analysis required that, the medium effect size $f^2 = 0.15$, $\alpha = 0.05$, $1 - \beta = 0.90$. There were 24 independent variables. Thus, the required sample size calculated by G*Power 3.1.9.2 software (Share-Net Bangladesh, Germany) ranged from 120 to 360. Considering the actual situation, a total of 266 cases were included into this study.

2.2 Collect information and questionnaires

2.2.1 Basic information

Through their medical records, the general information and medical records of elderly male COPD patients selected for the study were collected regarding age, gender, height, weight, BMI, living (alone or otherwise), educational background, complications (diabetes, high blood pressure, coronary heart disease, hyperlipidaemia), smoker or non-smoker, COPD course (referring to the period of COPD symptoms first appearing in patients to the patients participating in study), home oxygen therapy or none, and hospitalization for acute COPD exacerbation within a year or not.

2.2.2 Lab tests

Five mL venous blood was collected from the objects in morning time after 12 hours of fasting and sent to laboratory for testing blood cells, nutritional indexes and inflammatory factors. Blood analyses also included white blood cell count (WBC), neutrophil count (NEUT), albumin (ALB), C-reactive protein (CRP), IL-6, *etc*. Five mL arterial blood was collected once the subjects stopped taking oxygen or 30 min after oxygen intake, and sent to laboratory within 10 min for blood gas analysis which included PaO_2/FiO_2 (partial pressure of oxygen/ Fraction of inspiration oxygen) and lactic acid (Lac).

2.2.3 Lung function tests

Stable elderly COPD patients were tested for lung functions with spirometer (MS-DIFFUTION, Jaeger, Wuppertal, Germany). Forced Vital Capacity (FVC), FEV1 and Forced Expiratory Volume in 1 second/Forced Vital Capacity (FEV1/FVC) were recorded.

2.2.4 GOLD stages

Patients were classified by the degree of airflow limitation and FEV1 levels according to the GOLD stages [11].

2.2.5 Dyspnea evaluation

Dyspnea severity was divided into 4 levels according to Modified Medical Research Council (mMRC) [12] Dyspnea Scale.

2.2.6 Living quality with COPD

COPD assessment test (CAT) [13] assessed patients' health against 8 questions such as cough, expectoration, chest distress, asthma, activity and sleep. Each question carried 5 points making 40 in total. Scores of 0 to 10 indicated mild impact of COPD onto the patient, 11 to 20 as moderate, 21 to 30 as severe, and 31 to 40 as very serious. The Cronbach's α value was 0.796.

2.2.7 Nutritional assessment

MNA-SF was adopted for interviewing patients. The scores were calculated. Assessment included 6 items, whether patients had weight changes, stress, acute diseases within 3 months, appetite, mental state, BMI and activities within 3 months. No less than 11 points indicated good nutritional condition, and less than 11 points indicated poor nutritional condition. Cronbach's α value was 0.843.

2.2.8 Diseases acceptance

AIS (Acceptance of Illness Scale) [14] assessed the patients' acceptance to diseases. Total scores ranged from 8 to 40 points. Patient with <20 points had poor acceptance, and *vice versa*.

2.2.9 Frailty assessment

Patients' frailty was assessed according to Chinese Experts Consensus on Assessment and Intervention for elderly patients with frailty issued in 2017 [15]. The scale evaluated 5 physical conditions including losses in weight, walking speed, grip strength, physical activities and the self-fatigue. Each question carried 1 point with total of 5. Patients with ≥3 points had frailty stage, 1–2 at pre-frailty stage, and 0 at no-frailty stage.

2.3 Quality control

The questionnaires were distributed by professionals and the patients were informed of the purpose and confidentiality of the survey. They were required to fill in the questionnaires according to their own situation in a quiet room.

2.4 Methods

In this study, patients of pre-frailty and no-frailty stages were considered as non-frailty group, while others as frailty group. General information, laboratory test results, dyspnea degree, lung function, life quality and nutritional status of the two groups were compared. Univariate analysis indicators were analyzed with binary logistic regression, and frailty was taken as the dependent variable. A model was then created to check the factors affecting frailty of elderly male COPD patients.

2.5 Statistics

SPSS 19.0 (Statistical Package for Social Sciences, IBM (International Business Machine), Armonk, NY USA) was employed for the data processing. Measurement data were expressed as ($\bar{x} \pm s$). Means of the two groups were compared by t test, and count data was expressed by using cases. The χ^2 test was employed to compare two groups for analyzing statistically significant variables ($p < 0.05$) through multivariate logistic regression analysis. Receiver operating curve (ROC) was drawn to evaluate the application value of COPD frailty prediction model in elderly men. $p < 0.05$ was statistically significant.

3. Results

3.1 Prevalence of frailty in elderly COPD men

Scores of 266 elderly male COPD patients ranged from 0 to 5 as investigated by FP phenotype, and mean score was 1.83 ± 0.43. Total of 103 patients scored >3. Frailty detection rate was 38.72%.

3.2 Single factor analysis affecting frailty in elderly male COPD patients

The single factor analysis revealed that age, hospitalization for acute exacerbation COPD within a year, the differences between patients in non-frailty and frailty groups were statistically significant ($p < 0.05$) for serum IL-6, CRP, PaO_2/FiO_2, FVC, FEV1, FEV1/FVC, GOLD stages of lung function, mMRC, CTA and MNA-SF levels. There was no significant difference ($p > 0.05$) regarding BMI, education level, and living alone (Table 1).

3.3 Multi-factors logistic regression analysis of frailty in elderly male COPD patients

The multi-factors logistic regression analysis suggested that age, hospitalization for acute exacerbation of COPD within a year, and IL-6 levels were the risk factors for frailty incidence in elderly male COPD patients, while FEV1 and MNA-SF levels were protective factors. Frailty prediction model in elderly male COPD patients was: $Y = 1/[1 + \exp(-\chi)]$, $\chi = -6.787 + 1.135 \times$ age $+ 1.325 \times$ hospitalization for acute exacerbation within a year $+ 0.698 \times$ IL-6 $- 0.578 \times$ FEV1 $- 0.869 \times$ MNA-SF. More details can be found in Table 2.

3.4 Application value of prediction model

According to ROC curve (Fig. 2), area under the curve (AUC) of prediction model for frailty was 0.712 in elderly male COPD patients, while the sensitivity and specificity of prediction were 0.68 and 0.675 respectively. Sensitivity, also termed as true positive rate, refers to the proportion of samples judged as positive. Specificity, known as true negative rate, is the proportion of samples being false positive.

The model was internally verified by the Bootstrap method and repeatedly sampled for 1000 times. The results showed that, this model had a good differentiation and calibration degree in predicting the risk of COPD fragility in elderly men. The C-index was 0.877 (95% CI 0.766–9.431), and the fragility incidence of the predicted model was highly consistent with that of the reality. The Brier score was 0.125. The internal validation data of 80 cases were used for external validation. The results showed that, this model had a good differentiation and calibration degree in predicting the risk of COPD fragility in elderly men. The C-index was 0.861 (95% CI 0.811–0.931), indicating that the predicted incidence of the predicated model was relatively consistent with that of the reality. The Brier scored was 0.143.

4. Discussions

American Geriatrics Society has proposed frailty as a non-specific state. Its symptoms caused by aging include declining physiological functions, diminished capacity towards external stress, and series of pathophysiological changes in nervous and endocrine systems [16–19]. The elderly with comorbid chronic diseases are more prone to frailty compared to healthy people of same age. Studies indicated that detection rates of frailty with COPD ranged 10.25% to 57% [20–22]. Frailty reduces patient ability to maintain stability and resist stress. It is, a precursor of disability. The current situation of frailty and analyzing its risk factors is imperative for reducing its incidence, improving life quality of elderly patients with chronic diseases, and minimizing burden on family and society. In this work, the frailty phenotype was employed to statistically compute frailty

TABLE 1. Single factor analysis affecting frailty in elderly male COPD patients (n = 266).

Factors	Group	Frailty (n = 103)	Non-Frailty (n = 163)	t/χ^2	p
Age					
	60–75 yr	43	103	11.720	0.001
	>75 yr	60	60		
BMI					
	Normal	46	65	0.594	0.441
	Underweight/Overweight/Obese	57	98		
Education level					
	Not more than primary school	76	114		
	Secondary school	18	28	1.096	0.578
	College graduate and above	9	21		
Living alone					
	Yes	33	47	0.308	0.579
	No	70	116		
Complications					
	Yes	87	134	0.229	0.632
	No	16	29		
Smoking					
	Yes	71	106	0.432	0.511
	No	32	57		
COPD Course					
	0–5 yr	30	54		
	6–10 yr	34	58	1.248	0.536
	>10 yr	39	51		
Home Oxygen Therapy					
	Yes	17	38	1.784	0.182
	No	86	125		
Hospitalization for acute exacerbation of COPD within a year					
	Yes	38	29	12.222	<0.001
	No	65	134		
WBC ($\times 10^9$/L)		6.13 ± 1.15	6.17 ± 1.03	0.295	0.768
NEUT (%)		62.36 ± 11.34	63.11 ± 12.25	0.500	0.617
IL-6 (pg/mL)		7.15 ± 1.15	3.23 ± 0.52	37.853	<0.001
CRP (mg/L)		3.34 ± 1.07	2.51 ± 0.27	9.448	<0.001
PaO_2/FiO_2		311.15 ± 26.69	346.58 ± 28.74	10.065	<0.001
ALB (g/L)		33.25 ± 3.79	34.08 ± 3.47	1.833	0.068
Hb (g/L)		142.05 ± 20.73	143.12 ± 22.41	0.390	0.697
FVC (%)		80.14 ± 7.48	87.59 ± 8.41	7.340	<0.001
FEV1 (%)		40.36 ± 4.58	48.74 ± 4.83	14.060	<0.001
FEV1/FVC (%)		50.36 ± 8.13	55.65 ± 7.94	5.244	<0.001

TABLE 1. Continued.

Factors	Group	Frailty (n = 103)	Non-Frailty (n = 163)	t/χ^2	p
GOLD stages of lung function					
	Stage 1	2	11	8.094	0.044
	Stage 2	35	74		
	Stage 3	56	67		
	Stage 4	10	11		
mMRC					
	Level 0–1	3	20	6.996	0.008
	Level 2–4	100	143		
CTA					
	≤10 points	20	63	10.876	<0.001
	>0 points	83	100		
MNA-SF					
	≥11 points	68	147	23.783	<0.001
	<11 points	35	16		
AIS					
	<20 points	50	74	0.251	0.616
	≥20 points	53	89		

BMI: Body Mass Index; COPD: chronic obstructive pulmonary disease; WBC: white blood cell count; NEUT: neutrophil count; IL: interleukin; CRP: C-reactive protein; PaO_2/FiO_2: (partial pressure of oxygen/Fraction of inspiration oxygen); ALB: albumin; Hb: hemoglobin; FVC: Forced Vital Capacity; FEV: Forced Expiratory Volume; GOLD: Global Initiative for Chronic Obstructive Lung Disease; mMRC: Modified Medical Research Council; CTA: COPD assessment test; MNA-SF: Mini Nutritional Assessment Short-Form; AIS: Acceptance of Illness Scale.

TABLE 2. Multi-factors logistic regression analysis.

Factors	β	SE	Wald χ^2 value	OR	p	95% CI
Age	1.135	0.378	9.016	3.111	0.003	1.483–6.527
Hospitalization for acute exacerbation of COPD within a year	1.325	0.569	5.423	3.762	0.020	1.233–11.476
IL-6	0.698	0.214	10.639	2.010	0.001	1.321–3.057
CRP	0.743	0.435	2.917	2.102	0.088	0.896–4.931
PaO_2/FiO_2	1.758	0.987	3.173	5.801	0.076	0.838–40.146
FVC	0.754	0.425	3.147	2.125	0.077	0.924–4.889
FEV1	−0.578	0.141	16.804	0.561	<0.001	0.426–0.740
FEV1/FVC	0.854	0.511	2.793	2.349	0.095	0.863–6.395
GOLD stages of lung function	1.474	0.854	2.979	4.367	0.085	0.819–23.286
mMRC	1.114	0.789	1.999	3.047	0.158	0.650–14.275
CTA	0.698	0.365	3.657	2.010	0.057	0.983–4.110
MNA-SF	−0.869	0.321	7.329	0.419	0.007	0.224–0.787

COPD: chronic obstructive pulmonary disease; IL: interleukin; CRP: C-reactive protein; FVC: Forced Vital Capacity; FEV: Forced Expiratory Volume; GOLD: Global Initiative for Chronic Obstructive Lung Disease; mMRC: Modified Medical Research Council; CTA: COPD assessment test; MNA-SF: Mini Nutritional Assessment Short-Form; PaO_2/FiO_2: Partial pressure of oxygen/Fraction of inspiration oxygen; SE: Standard error; OR: Odd ratio; CI: confidence interval.

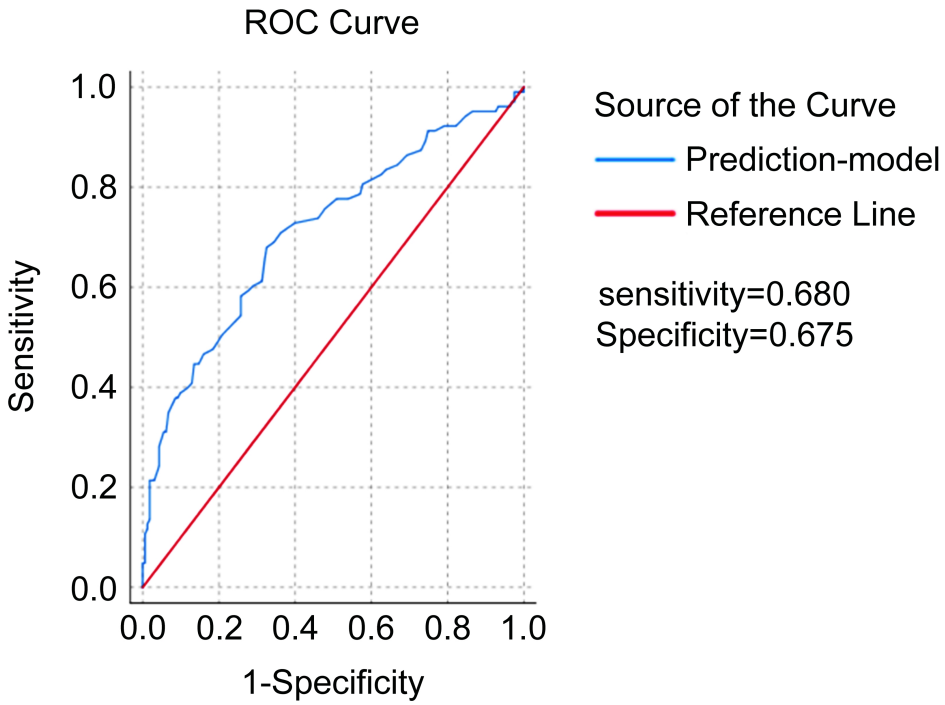

FIGURE 2. ROC Curve of the Prediction Model. ROC: Receiver operating curve.

incidence of elderly male COPD patients, and results depicted that frailty incidence was 38.72% which was almost like the previous results.

Authors analyzed the linked factors affecting frailty of elderly COPD patients and found that age, hospitalization for acute exacerbation of COPD within a year, serum inflammatory factor IL-6, CRP, lung function indexes FVC, FEV1, FEV1/FVC, lung function GOLD stages, mMRC, life quality (CTA) and nutritional index (NCS-AF) were correlated with frailty. Multivariate regression analysis proposed that age, hospitalization for acute exacerbation of COPD within a year, IL-6, FEV1 and MNA-SF were independently correlated to frailty.

Age was the main physiological cause of frailty. This study exhibited comparison of male COPD patients aged 60 to 75 years, wherein those of over 75 years had higher frailty incidence. Multivariate regression analysis suggested that frailty incidence in elderly men aged over 75 years was 3.111 times higher than those aged 60 to 75 years. It was thus recommended to screen male COPD patients of over 75 years age for the frailty and take in time targeted measures to reduce disability incidences [22, 23].

Inflammation was a common pathogenic factor of frailty and COPD [24, 25]. This study depicted that, for elderly male COPD patients, the serum inflammatory factors such as CRP and IL-6 levels were higher in frailty group than in non-frailty, indicating that frailty patients had severer inflammatory response. Multivariate regression model analysis proposed that IL-6 level was risk for frailty in elderly COPD male patients. IL-6 was a common inflammatory factor. Its increase meant that body had continuous inflammation. In addition, the increasing levels of IL-6 were associated with some frailty features such as weight loss, bone density reduction, and thrombocytosis [26]. It was thus suggested that proactive methods to control chronic inflammation in elderly male COPD patients could reduce the frailty risk to certain extent.

The frailty risk was also correlated to patient's status of lung functions and COPD severity. In this study, patients who had hospitalization for acute exacerbation of COPD within a year and decline in lung functions were at higher frailty risk. When patients suffered serious COPD and lung dysfunctions, the frailty risk was increased and they received higher inflammatory response caused by chronic hypoxia, serious cell apoptosis, muscle degradation and skeletal muscle dysfunction [27].

Patients' score in MNA-SF could be independent factor affecting frailty risk in elderly COPD patients. This study found that for elderly male COPD patients, the ones with malnutrition were prone to frailty. COPD was a chronic wasting disease. The respiratory muscles of patients worked harder, and resting energy expenditure was more than for normal people. The increasing frailty risk was linked to insufficient nutritional intake because of breathing difficulties, which resulted in losing muscle and fat, carried anemia and did lesser activities [28]. It was thus recommended to improve the nutritional management of COPD patients.

This study found that, according to the frailty prediction model for elderly male COPD patients based on multi-factors Logistic regression analysis, the AUC was 0.712, and the sensitivity and specificity were 0.68 and 0.675, respectively.

Multi-factors logistic regression analysis suggested that age, hospitalization for acute exacerbation of COPD within a year, and IL-6 levels were the risk factors for incidence of frailty in elderly male COPD patients, while FEV1 (Forced Expiratory Volume in 1 second) and MNA-SF (Mini Nutritional Assessment Short-Form) levels were the protective factors. Frailty prediction model in elderly male COPD patients was: $Y = 1/[1 + \exp(-\chi)]$, $\chi = -6.787 + 1.135 \times \text{age} + 1.325 \times$

hospitalization for acute exacerbation within a year + 0.698 × IL-6 − 0.578 × FEV1 − 0.869 × MNA-SF.

However, there are some limitations. This study is a single-center study with limited sample size. The result may not be so comprehensive. In order to ensure the reliability, it is necessary to increase the sample size and carry out multi-centers research.

5. Conclusions

This study investigated the frailty incidence and its risk factors in elderly male COPD patients and provided clinical measures for improving the frailty status, their life quality and prognosis. In conclusion, frailty in COPD was more common in elderly men. It was necessary to screen frailty in elderly patients, monitor inflammatory response, lung function and nutritional status to reduce incidence and improve patients' prognosis. Moreover, targeted measures were required in severe and persistent inflammatory reactions, decreased lung function and poor nutritional status to reduce the risks of elderly male patients with COPD having frailty.

AVAILABILITY OF DATA AND MATERIALS

The data presented in this study are available on reasonable request from the corresponding author.

AUTHOR CONTRIBUTIONS

KC and QJD—designed the study and carried it out; prepared the manuscript for publication and reviewed the manuscript draft. KC, QJD, YJG and KWZ—supervised data collection, analyzed and interpreted the data. All authors had read and approved the manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Ethical approval was obtained from Ethics Committee of Affiliated Hospital of Guangdong Medical University (Approval no. PJ2016114). Written informed consent was obtained from 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.

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