

Neural Respiratory Drive Measured Using Surface Electromyography of Diaphragm as a Physiological Biomarker to Predict Hospitalization of Acute Exacerbation of Chronic Obstructive Pulmonary Disease Patients

Dan-Dan Zhang, Gan Lu, Xuan-Feng Zhu, Ling-Ling Zhang, Jia Gao, Li-Cheng Shi, Jian-Hua Gu, Jian-Nan Liu

Chronic Airway Disease Research Office, Department of Respiratory, Geriatric Hospital of Nanjing Medical University, Jiangsu Province Geriatric Hospital, Nanjing, Jiangsu 210024, China

Abstract

Background: Neural respiratory drive (NRD) using diaphragm electromyography through an invasive transesophageal multi-electrode catheter can be used as a feasible clinical physiological parameter in patients with chronic obstructive pulmonary disease (COPD) to provide useful information on the treatment response. However, it remains unknown whether the surface diaphragm electromyogram (EMGdi) could be used to identify the deterioration of clinical symptoms and to predict the necessity of hospitalization in acute exacerbation of COPD (AECOPD) patients.

Methods: COPD patients visiting the outpatient department due to acute exacerbation were enrolled in this study. All patients who were subjected to EMGdi and classical parameters such as spirometry parameters, arterial blood gas analysis, COPD assessment test (CAT) score, and the modified early warning score (MEWS) in outpatient department, would be treated effectively in the outpatient or inpatient settings according to the Global Initiative for Chronic Obstructive Lung Disease guideline. When the acute exacerbation of the patients was managed, all the examination above would be repeated.

Results: We compared the relationships of admission-to-discharge changes (Δ) in the normalized value of the EMGdi, including the change of the percentage of maximal EMGdi (Δ EMGdi%max) and the change of the ratio of minute ventilation to the percentage of maximal EMGdi (Δ VE/EMGdi%max) with the changes of classical parameters. There was a significant positive association between Δ EMGdi%max and Δ CAT, Δ PaCO₂, and Δ pH. The change (Δ) of EMGdi%max was negatively correlated with Δ PaO₂/FiO₂ in the course of the treatment of AECOPD. Compared with the classical parameters including forced expiratory volume in 1 s, MEWS, PaO₂/FiO₂, the EMGdi%max (odds ratio 1.143, 95% confidence interval 1.004–1.300) has a higher sensitivity when detecting the early exacerbation and enables to predict the admission of hospital in the whole cohort.

Conclusions: The changes of surface EMGdi parameters had a direct correlation with classical measures in the whole cohort of AECOPD. The measurement of NRD by surface EMGdi represents a practical physiological biomarker, which may be helpful in detecting patients who should be hospitalized timely.

Key words: Acute Exacerbation of Chronic Obstructive Pulmonary Disease; Neural Respiratory Drive; Surface Diaphragm Electromyography

INTRODUCTION

The morbidity and mortality associated with chronic obstructive pulmonary disease (COPD) exerts a considerable economic burden,^[1] a large proportion of which has been contributed by the occurrence of acute exacerbation of COPD (AECOPD),^[2] especially for the hospitalization of AECOPD.^[3] Therefore, it is essential to early identify COPD patients who are at-risk of acute exacerbation and determine whether hospitalization is necessary. Therefore,

Address for correspondence: Dr. Jian-Nan Liu, Chronic Airway Disease Research Office, Department of Respiratory, Geriatric Hospital of Nanjing Medical University, Jiangsu Province Geriatric Hospital, Nanjing, Jiangsu 210024, China
E-Mail: liujianan@163.com

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more physiological biomarkers are needed to instruct patients accurately during AECOPD to avoid the waste of medical resources. Recent studies showed that, as a non-invasive and more acceptable clinical operation, the diaphragm electromyography measurements using electrodes placed on the skin could reflect the state of neural respiratory drive (NRD), which may be helpful to detect patients who should be hospitalized timely.^[4]

The diaphragm is the most important respiratory muscle. Its activity is closely related to all respiratory diseases and is able to reflect the severity of the disease. In a stable stage, patients with COPD are characterized by impaired diaphragm function, which is known to alter the initial length of the diaphragm to reduce the extra inspiratory pressure generation.^[5] Moreover, in the acute exacerbation stage, the emergence of diaphragmatic fatigue is earlier than that of compensatory increase in chest wall, accessory respiratory muscle activity and respiratory failure,^[6,7] which is considered to be one of the most important pathophysiological mechanisms of AECOPD.

Recent studies showed NRD measured by diaphragm electromyogram (EMGdi) through an invasive transesophageal multi-electrode catheter reflects the balance between respiratory muscle load and capacity. The value of EMGdi could reveal the severity of stable COPD and predict the clinical change of AECOPD.^[4,8] However, whether the non-invasive surface EMGdi can be used as an objective biomarker to monitor the severity of AECOPD and to predict the requirement of hospitalization has not been reported previously.

METHODS

Ethical approval

The study protocol was approved by the Ethics Committee of the Geriatric Hospital of Nanjing Medical University. All participants signed written informed consent.

Patient recruitment

This study was performed at one teaching hospital. Patients with a physician diagnosis of AECOPD were enrolled within 6 h from admission to the outpatient respiratory medicine departments of Geriatric Hospital of Nanjing Medical University from July 2016 to June 2017. Inclusion criteria were (I) forced expiratory volume in 1 s (FEV_1)/forced vital capacity (FVC) <70% after bronchodilation, according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD); (II) severity is more than Stage 2, percentage of FEV_1 ($FEV_1\%$) predicted <80%; (III) experience acute exacerbation which was defined as an acute worsening of respiratory symptoms that result in additional therapy. Exclusion criteria were (I) history of oral corticosteroids within 1 week; (II) complications from other comorbidities, such as acute coronary syndrome, worsening congestive heart failure, pulmonary embolism; and (III) history of other respiratory, cardiovascular, neuromuscular, and

musculoskeletal diseases that could interfere with the exercise performance and inspiratory muscle activities.

Admission data

Demographic and anthropometric data were collected within 2 h after patients were enrolled in this study. FEV_1 , $FEV_1\%$, and FVC were measured using a pneumotachometer (3830, Hans-Rudolph, Shawnee, USA) or a handheld spirometer (Micro, CareFusion, Basingstoke, UK) according to international standards. Arterial samples for arterial blood gas analysis were collected through a heparinized needle and syringe system. The samples were processed as soon as possible on the ward-based blood gas analyzer (500, RAPID Point, Siemens, Germany). Symptoms were assessed using the COPD assessment test (CAT) score. Standard physiological observations (respiratory rate, heart rate, oxygen saturation, body temperature, and blood pressure) were collected, and an aggregate score derived from these was recorded as the modified early warning score (MEWS) score, according to local protocol.

Diaphragm electromyogram measurement

Surface EMGdi was measured with patients in a semi-recumbent or seated position, as previously described.^[9] After skin preparation, two pairs of recording electrodes (RED DOT, USA) were separately placed at the intersection point of the sixth and eighth intercostal space and the anterior axillary line. The distance between each recording electrodes was 3–5 cm, and the optimal position was determined by the greatest amplitude of EMGdi in electrode pairs 1 and 3. The reference electrode (No. 5) was placed in the left side edge of manubrium sterni, keep away from the recording electrodes.^[10] The EMGdi signals were band-pass filtered between 10 Hz and 2 kHz and amplified using signal amplifier (3808; Yinghui Medical Technology Co, Ltd, Guangzhou, China). The raw signal was converted to root mean square (RMS) with LabChart 7.5 software (Powerlab, AD Instruments Co, Australia) with the time constant of 100 ms. In order to avoid the influence of the electrocardiogram on EMGdi, RMS was measured from the segments between QRS complexes. The peak of RMS selected from five pairs of electrodes was measured on a breath-by-breath basis. The peak RMS EMGdi activity for each inspiration was averaged over 1 min of tidal breathing and normalized to a value of EMGdi obtained during a maximal inspiratory sniff maneuver, obtained before each measurement.^[11] A ratio of VE to RMS of EMGdimax ($VE/EMGdi\%max$) of each breath, which is used to assess respiratory efficiency,^[12,13] can reflect the neuromuscular uncoupling and correlate with disease severity.^[5]

Study protocol

Baseline $EMGdi\%max$, $VE/EMGdi\%max$, FEV_1 , $FEV_1\%$, FVC, CAT, MEWS, and arterial blood gas analysis were collected at the time of admission in this study. At the same time, treatment place either in the outpatient or inpatient setting and therapeutic regimen were decided by senior attending physician depending on the severity of this

exacerbation. The senior attending physicians, who were blinded to EMGdi data, were asked to provide an opinion regarding clinical improvement or deterioration between successive assessments. Medical fitness for admission, outpatient follow-up, hospitalization, and discharge was determined by the senior attending physician. Potential indications for hospitalization commonly used in clinical practice are incorporate with a marked increase in the intensity of symptoms such as sudden development of resting dyspnea, severe underlying COPD, and onset of new physical signs (e.g., cyanosis and peripheral edema). All of the treatments above were performed according to the GOLD guidelines. All the test items were completed within 6 h since the patients were identified at the expected stage of this study, acute exacerbation stage or adequately recovered stage, and at least 2 h after the last bronchodilator dose. Admission-to-discharge changes in EMGdi%max and VE/EMGdi%max were expressed as change of the percentage of maximal EMGdi (Δ EMGdi%max) and change of the ratio of minute ventilation to the percentage of maximal EMGdi (Δ VE/EMGdi%max), respectively.

Statistical analysis

Data were analyzed using independent or paired *t*-test where appropriate. Data that were not normally distributed, as defined by the Kolmogorov–Smirnov test, were transformed and then analyzed as parametric data. Relationships between EMGdi data and classical parameters were analyzed using regression analysis. Generalized linear mixed model analyses were used to assess the association between Δ EMGdi%max, Δ VE/EMGdi%max, and classical measure parameters with physician-defined fully recovered. Logistic regression and receiver-operator characteristic (ROC) analyses were used to identify and test the utility of predicting the necessity of hospitalization of acute exacerbation. Data analysis was conducted using SPSS software (IBM, USA). All data are presented as mean \pm standard deviation unless otherwise stated, with *P* < 0.05 considered as statistically significant.

RESULTS

Acute exacerbation and after adequate treated data

A total of 60 patients were enrolled in this study, of all of them, 22 patients were classified should be treated in hospital ward unit, and the other 38 patients were classified could be treated in outpatient department appropriately [Table 1]. None of the patients required invasive ventilator support, and none of them had transferred to the intensive care unit or death. Six (27%) hospital patients required noninvasive ventilator support following admission to hospital. The median length of follow-up time of outpatients was 6 (interquartile range [IQR] 5–8) days. Median length of hospital stay was 10 (IQR 7–14) days. Median interval from the date of need a hospitalization to the date of hospitalization was 0 (IQR 0–1) days.

Symptom scores and physiological data

Significant differences in FEV₁, FVC, FEV₁% predicted, CAT score, MEWS score, PaO₂/FiO₂, respiratory rate, EMGdi%max, and VE/EMGdi%max were observed between acute exacerbation stage and after adequate treatment stage both in inpatients group and outpatients group. However, differences of PaCO₂, SpO₂ only between those two stages above only exist in inpatients group. Moreover, FEV₁/FVC ratio, pH, temperature, and heart rate have no significant difference between those two stages both in inpatients group and outpatients group. There were also significant differences of FEV₁, FVC, FEV₁% predicted and CAT score in inpatients compared with these parameters of outpatients both at acute exacerbation stage and after adequate treatment. However, there were significant differences of MEWS score, PaO₂/FiO₂, PaCO₂, EMGdi%max, and VE/EMGdi%max only at acute exacerbation stage [Table 2].

Changes in surface diaphragm electromyogram of inpatients and outpatients at acute exacerbation stage and after adequate treatment

Surface EMGdi data are reported as RMS (mV), the amplitude of each electrode signal is -0.15 – 0.15 mV.

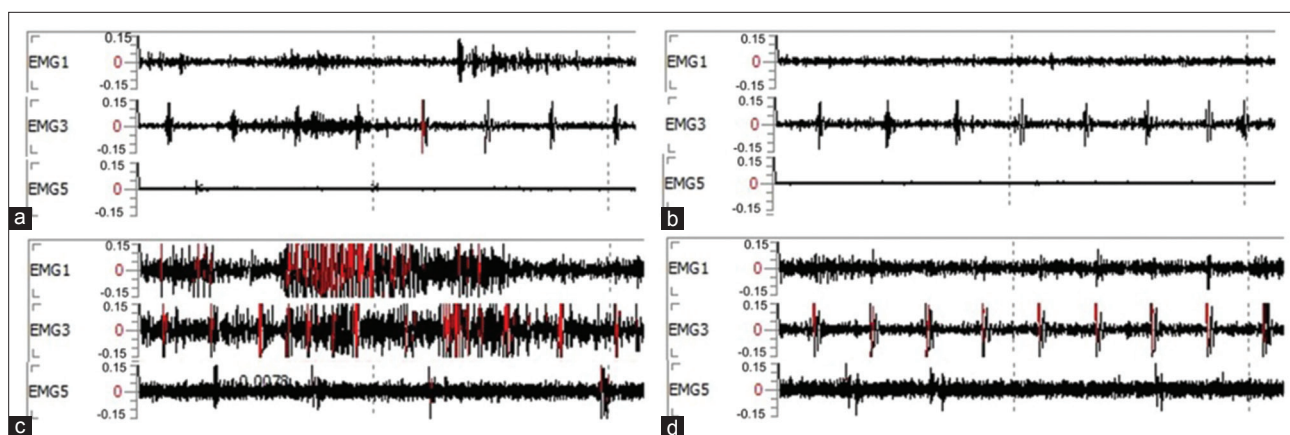


Figure 1: Representative trace of surface diaphragm electromyography in a patient who suffered acute exacerbation at the time of admission (a) and when was fully recovered after adequately treatment (b) in outpatient department. Representative trace of surface diaphragm electromyography at the time of hospitalization in a patient who should be treated in inpatient department due to acute exacerbation (c), and at the time of discharged after adequately treated (d).

Table 1: Baseline characteristics of patients with a physician diagnosis of acute exacerbation of COPD at admission to hospital

Characteristics	Inpatients	Outpatients	Statistical value	P
Anthropometrics and smoking history				
Subjects (n)	22	38		
Age (years)	72.5 ± 8.6	70.9 ± 8.2	0.745*	0.762
Height (m)	166.57 ± 5.65	169.17 ± 6.83	-0.117*	0.918
Weight (kg)	62.64 ± 12.57	63.78 ± 8.95	-0.273*	0.609
Smoking history (pack years)	36.85 ± 19.55	34.12 ± 10.54	0.607*	0.226
Male (%)	81	76		
Current exacerbation history				
Duration of symptoms (days)	3 (1–5)	4 (1–6)	12.71†	0.151
Systemic steroids before admission (%)	14	3		
Antibiotics before admission (%)	23	18		
Comorbidities				
Ischemic heart disease (%)	59	53		
Cerebrovascular disease (%)	50	39		
Hypertension (%)	77	84		
Diabetes mellitus (%)	32	29		
Disease severity				
GOLD stage 2 (%)	5	21		
GOLD stage 3 (%)	55	68		
GOLD stage 4 (%)	41	11		
Admission investigations arterial blood gases				
Routine laboratory tests				
Hs-CRP (mg/L)	67.5 ± 40.3	24.8 ± 10.1		
PCT (µg/L)	0.57 (0.02–1.66)	0.08 (0.02–0.13)		
Leukocytes (×10 ⁹ /L)	11.4 ± 8.2	6.9 ± 3.3		
Neutrophils (×10 ⁹ /L)	9.3 ± 5.8	6.2 ± 3.1		
Eosinophils (×10 ⁹ /L)	0.5 (0.1–0.9)	0.6 (0.2–1.0)		
Hemoglobin (g/L)	129 ± 19	132 ± 14		
Platelets (×10 ⁹ /L)	256 ± 79	252 ± 81		
Duration of treatment stay (days)	10 ± 4	7 ± 2		
pH	7.40 ± 0.05	7.38 ± 0.07		
Bicarbonate (mmol/L)	23.1 ± 4.1	25.1 ± 3.7		
Base excess (mmol/L)	1 (-3–5)	1 (-4–5)		
Lactate (mmol/L)	3.2 ± 2.1	2.3 ± 1.9		

Data were shown as mean±SD, range, or percentage. **t* values; † χ^2 value. COPD: Chronic obstructive pulmonary disease; GOLD: Global initiative for chronic obstructive lung disease; pH: pH value; PaCO₂: Arterial partial pressure of carbon dioxide; PaO₂: Arterial partial pressure of oxygen; Hs-CRP: Hypersensitive C-reactive protein; PCT: Procalcitonin; IQR: Interquartile range; SD: Standard deviation.

Representative trace of surface diaphragm electromyography in one patient who had suffered acute exacerbation and fully recovered after adequately treatment were shown in Figure 1.

Relationship between surface diaphragm electromyogram and classical physiological parameters

Acute exacerbation stage-to-discharge stage change (Δ) in EMGdi%max was correlated with Δ CAT score ($r = 0.372$, $P < 0.05$) and Δ PaCO₂ ($r = 0.279$, $P < 0.05$) and was inversely correlated with Δ PaO₂/FiO₂ ($r = -0.344$, $P < 0.05$) [Figure 2].

Predictors of surface diaphragm electromyogram and classical parameters in the early diagnosis of necessity of hospitalization

ROC analysis for the prediction of the early diagnosis of the necessity of hospitalization gave an area under the curve (AUC) of 0.8122 for EMGdi%max and AUC of

0.7560 for VE/EMGdi%max. By contrast, AUC for FEV₁, PaO₂/FiO₂, CAT, and MEWS was 0.6681, 0.8092, 0.9025, and 0.7333, respectively [Figure 3].

EMGdi%max at the time of admission to predict the necessity of hospitalization

A significant difference in PaO₂/FiO₂, CAT, MEWS, and EMGdi%max at the time of admission (first measurement within 6 h of admission) was demonstrated between patients who could be treated at outpatient department and those who should be hospitalized. However, FEV₁ and VE/EMGdi%max of admission did not predict hospitalization in the univariate logistic regression model [Table 3]. After adjustment for the previously identified potentially confounding variables, the EMGdi%max (odds ratio = 0.094, 95% confidence interval = 0.022, 0.166) remained give good prediction of hospitalization in the multiple logistic regression model.

Table 2: Physiological measurement parameters in patients at acute exacerbation stage and after adequate treatment

Parameters	Inpatients (n = 22)		Outpatients (n = 38)	
	Acute exacerbation stage	After adequate treatment	Acute exacerbation stage	After adequate treatment
Spirometry				
FEV ₁ (L) ^{†‡}	0.88 ± 0.42*	1.05 ± 0.45	1.22 ± 0.61*	1.35 ± 0.61
FVC (L) ^{†‡}	1.53 ± 0.44*	1.77 ± 0.47	2.09 ± 0.82*	2.30 ± 0.83
FEV ₁ % predicted (%) ^{†‡}	41.59 ± 14.70*	50.13 ± 14.70	54.72 ± 15.40*	62.59 ± 13.92
FEV ₁ /FVC ratio (%)	55.9 ± 14.4	56.0 ± 12.3	58.6 ± 15.6	59.3 ± 15.8
Symptom score				
CAT score ^{†‡}	25.73 ± 4.72*	16.3 ± 3.78	17.63 ± 4.41*	12.76 ± 3.44
MEWS score [†]	3.00 ± 0.87*	0.45 ± 0.59	2.24 ± 0.63*	0.24 ± 0.43
Arterial blood gas analysis				
pH	7.40 ± 0.05	7.37 ± 0.90	7.38 ± 0.08	7.38 ± 0.08
PaO ₂ /FiO ₂ [†] (mmHg)	251.58 ± 75.01*	362.55 ± 45.49 [†]	329.45 ± 41.70*	358.03 ± 49.07
PaCO ₂ [†] (mmHg)	51.29 ± 9.10*	44.33 ± 5.21	46.83 ± 7.48	46.65 ± 9.52
Routine observations				
SpO ₂ (%)	90.43 ± 4.32*	94.17 ± 2.25	94.17 ± 1.45	95.32 ± 2.01
Temperature (°C)	37.31 ± 1.93	36.92 ± 0.39	37.09 ± 1.08	36.85 ± 0.54
Heart rate (beats/min)	87.25 ± 7.36	74.28 ± 8.22	73.16 ± 6.45	72.11 ± 6.89
Respiratory rate (breaths/min)	28.34 ± 3.87*	18.43 ± 3.96	24.34 ± 4.82*	17.55 ± 4.32
EMGdi parameters				
EMGdi%max (%) [†]	29.57 ± 9.73*	17.47 ± 8.81	19.83 ± 11.19*	16.05 ± 12.06
VE/EMGdi%max (%) [†]	23.74 ± 4.86*	36.62 ± 10.34	30.06 ± 7.57*	40.38 ± 8.34

Values are expressed as mean ± SD. EMGdi: Electromyography of the diaphragm; MEWS: Medical early warning score; SpO₂: Transcutaneous oxygen saturation. After adequate treatment stage compared with acute exacerbation stage. **P*<0.05. Parameters of inpatients compared with parameters of outpatients at acute exacerbation stage; [†]*P*<0.05. Parameters of inpatients compared with parameters of outpatients after adequate treatment; [‡]*P*<0.05. pH: pH value; PaCO₂: Arterial partial pressure of carbon dioxide; PaO₂: Arterial partial pressure of oxygen; FVC: Forced vital capacity; FEV₁: The forced expiratory volume for 1 s; CAT: COPD Assessment Test; COPD: Chronic obstructive pulmonary disease; SD: Standard deviation; EMGdi: The surface diaphragm electromyogram; EMGdi%max: Percentage of maximal EMGdi; VE: Ventilation.

Table 3: Univariate logistic regression analysis for predictors of hospitalization

Items	OR	P	95% CI
FEV ₁	4.775	0.351	0.179 to 127.497
PaO ₂ /FiO ₂	0.957	0.012	0.925 to 0.990
CAT	1.453	0.045	1.009 to 2.093
MEWS	50.351	0.033	1.385 to 1830.950
EMGdi%max	1.143	0.044	1.004 to 1.300
VE/EMGdi%max (%)	0.944	0.508	0.796 to 1.120

FEV₁: The forced expiratory volume for 1 s; PaO₂/FiO₂: The PaO₂/fraction of inspired oxygen ratio; CAT score: Capability assessment toolkit score; MEWS: Modified early warning score; EMGdi%max: The percentage of maximal EMGdi; VE/EMGdi%max: The ratio of minute ventilation to the percentage of maximal EMGdi; OR: Odds ratio; CI: Confidence interval.

DISCUSSION

The NRD measured by surface diaphragm electromyography, as a noninvasive examination method, has been extensively adopted in clinical practice. The surface EMGdi may be a reproducible physiological biomarker in identifying patients who suffer from AECOPD and who should be treated in inpatient settings.

Critique of the method

Patient selection

Despite the limitation of a small sample size, the

demographics and baseline data of AECOPD patients recruited in outpatients group and in inpatients group conform to a normal distribution and have comparability in this study [Table 1].

Surface diaphragm electromyogram measurement

NRD has been widely used as a feasible clinical physiological parameter among patients with COPD. It can provide useful information on treatment response and risk of readmission.^[4] However, most of the previous studies of the NRD required the placement of an invasive esophageal electrode or used surface electromyography of accessory respiratory muscle, which limited the possibility of this technique from being widely used in the clinic.^[4,14]

Recently, studies have shown that the diaphragm electromyography examination using electrodes placed on the skin is correlated with the examination using esophageal electrodes.^[5] In this study, although the degree of variability with surface EMGdi of patients with COPD was greater than the degree of variability tested by esophageal electrodes.^[9] The inter-occasion correlation of surface EMGdi and invasive EMGdi for both stable COPD and AECOPD patients was larger than 80%, which is a level that has previously been used to indicate acceptable inter-test agreement for surface electromyography.^[9,15]

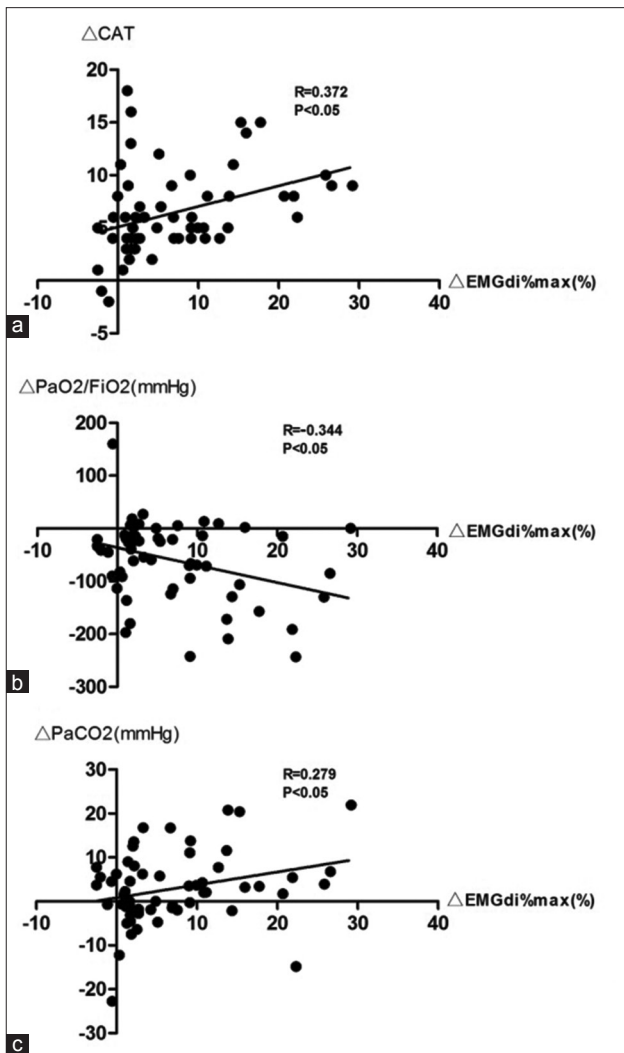


Figure 2: Relationship between changes of admission-to-discharge in EMGdi%max, and changes in CAT (a), PaO₂/FiO₂ (b), and PaCO₂ (c) (*n*=60). EMGdi%max: The percentage of maximal EMGdi; CAT score: Capability Assessment Toolkit score; PaO₂/FiO₂: The PaO₂/fraction of inspired oxygen ratio; PaCO₂: Arterial partial pressure of carbon dioxide.

Compared with the electromyography of the accessory respiratory muscle, EMGdi has its unique advantages. The diaphragm, as the most important respiratory muscle, plays a pivotal role in all breathing process, whereas the effect of the accessory respiratory muscle is only manifested significantly when patients suffer from dyspnea.^[16] Therefore, compared with accessory respiratory muscle, the electrical activity collection of diaphragm is not limited to the severity of the disease. EMGdi can be detected at any stage of COPD with a reliable sensitivity and specificity, and either in the upper costal breathing type or in the costo-diaphragmatic breathing type.^[17] Moreover, EMGdi is not easily disturbed by other respiratory muscles and will not be affected by electrode movement or lung volume change.^[18]

Definition of clinical change

Potential indications for hospital admission commonly used in clinical practice now are incorporate with marked increase

in intensity of symptoms such as the sudden development of resting dyspnea, severe underlying COPD, and onset of new physical signs (e.g., cyanosis and peripheral edema).^[19] These methods of assessment are neither simple nor convenient and may be affected by patients' own perception and doctors' experience, limiting the reliability of these instruments as objective evaluations for COPD exacerbation.^[20] Therefore, we use more established instruments such as spirometry, arterial blood gas analysis, CAT, and MEWS to complete the diagnosis of AECOPD in clinical practice and to instruct patients to be hospitalized timely. In this study, we found that placing electrodes at the position of diaphragm can reflect the state of NRD, and may be helpful in detecting early AECOPD, and predict the necessity of hospitalization. There is a crucial balance in respiratory mechanics between load and capacity. AECOPD causes a reduction in respiratory muscle capacity and an increase in load; thus, it disrupts the balance and triggers breathlessness and eventually respiratory failure. EMGdi could acutely detect this imbalance, further bringing NRD testing closer to the clinic.^[21-23] EMGdi, therefore, can be used as a supplement to the classical measure parameters such as lung function tests, FEV₁, exercise tolerance tests, and the BODE index in the assessment of AECOPD. This could lead to better COPD management and reduce acute exacerbation, which is the most common cause of repeated hospital admissions. Furthermore, it could lower down significant consumption of medical resources.^[5]

Significance of findings

The EMGdi%max, as a product of the mean peak inspiratory tidal EMGdi normalized to the maximal maneuver, reflects the activity of NRD, which is closely related to severity of COPD.^[24] In addition, there was also an index defined as the ratio of minute ventilation (VE) and EMGdi%max, which has been shown to reflect the efficiency of pulmonary VE driven by the respiratory center. When the ventilator response is limited by impaired pulmonary mechanics, VE/EMGdi%max related to disproportionally breathlessness variation,^[24,25] and expressed an increase with pulmonary disease improved, and also this index could get over the limitation of the variability of single VE parameter, evaluated the curative effect of different treatments more objectively.^[13,14]

In this study, we observed that patients who suffered from acute exacerbation showed an increase in EMGdi%max, incorporated with a decrease of VE/EMGdi%max, especially in the inpatients group. With patients responding to therapy and with their respiratory muscle unloading, we observed that there was a decline in EMGdi%max and an increase of VE/EMGdi%max. Our findings suggested that the surface EMGdi was a feasible tool for assessment of NRD in the AECOPD. In addition, our data also demonstrated that there was a direct correlation between the changes of EMGdi parameters and the changes of CAT, PaO₂/FiO₂, and PaCO₂, indicating that EMGdi is an effective measurement to track clinical changes of patients with AECOPD. In the course

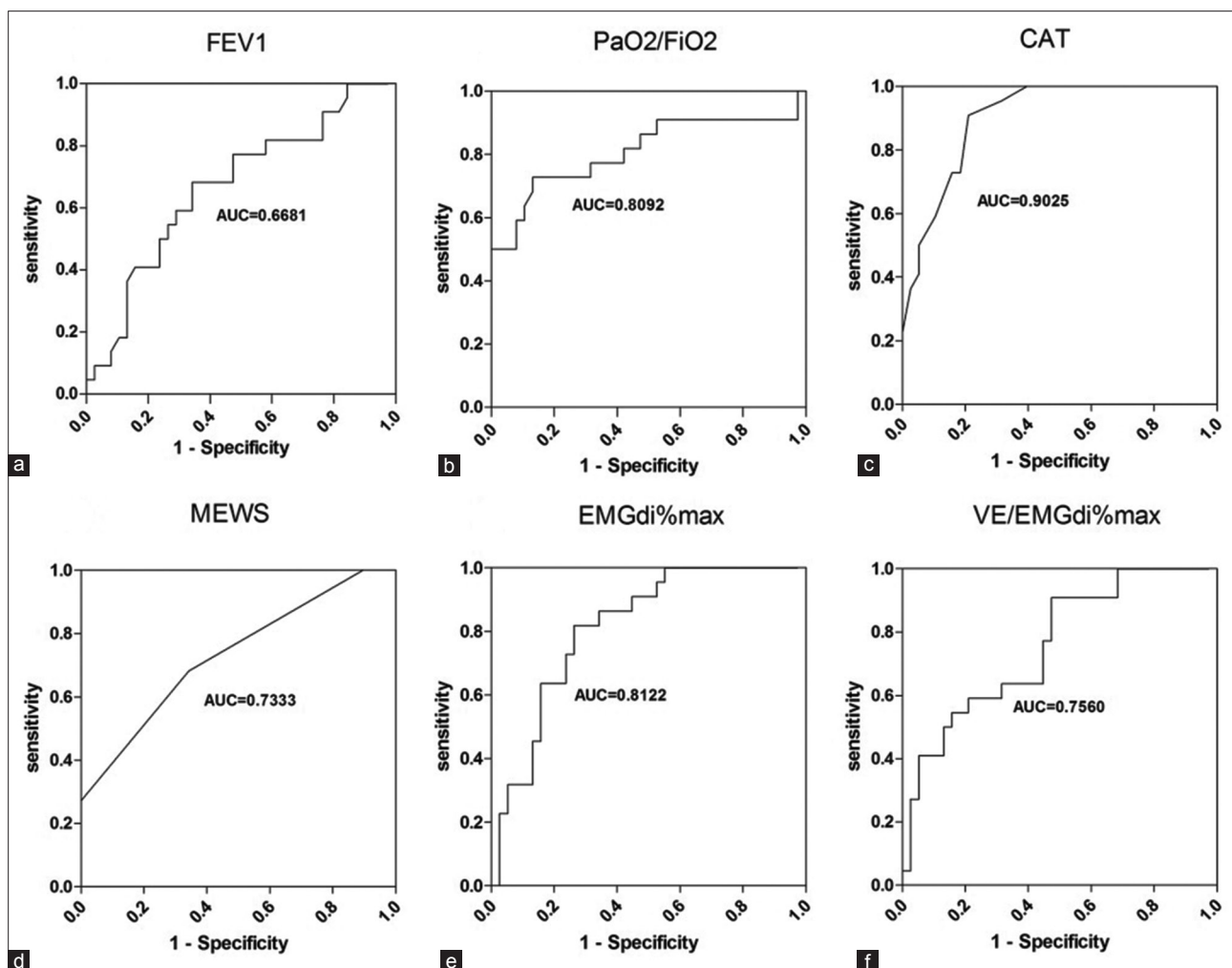


Figure 3: Receiver-operator curves for prediction of the early diagnosis of necessity of hospitalization for (a) FEV_1 , (b) PaO_2/FiO_2 , (c) CAT, (d) MEWS, (e) $EMGdi\%max$ and (f) $VE/EMGdi\%max$. ROC: Receiver-operator curve; AUC: Area under the receiver-operator curve; PaO_2/FiO_2 : The PaO_2 /fraction of inspired oxygen ratio; MEWS: Medical early warning score; FEV_1 : Forced expiratory volume in 1 s; $EMGdi\%max$: The percentage of maximal $EMGdi$.

of AECOPD treatment, the variation of $EMGdi\%max$ was positively correlated with ΔCAT and $\Delta PaCO_2$ but negatively correlated with $\Delta PaO_2/FiO_2$. The current data also supported the concept that the inpatient level of NRD at the time of admission was a key factor of reflecting the necessity of hospitalization. Although spirometry has been improved in recent years, the variabilities of FEV_1 and FVC as 17% and 15% respectively are still unavoidable in COPD patients.^[22] For example, arterial blood gas analysis has a rejection rate of 12.5% as its invasive characteristic and CAT may be affected by other complications such as chronic heart failure.^[26,27] Furthermore, surface electromyography of the diaphragm, as a non-invasive technique, can be more easily accepted by the patient, and may partly compensate for the shortcomings of other traditional indicators.

Naturally, our study has some limitations. First, because the study was conducted in a geriatric hospital, the majority of patients enrolled are the elderly. Second, since this study was only observational with a limited sample size, large-scale studies are expected to further validate our findings.

In conclusion, $EMGdi$ calculated as a product of $EMGdimax$ and $VE/EMGdimax$ has a reliable correlation with standard clinical physiological parameters in identifying patients with AECOPD, who need to be treated at inpatient department. Furthermore, NRD represented by surface electromyography of the diaphragm may be used as a physiological biomarker to instruct patients to be admitted hospital timely during AECOPD to avoid waste of medical resources.

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Conflicts of interest

There are no conflicts of interest.

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体表膈肌肌电反映的呼吸中枢驱动作为AECOPD患者住院治疗的预测指标的价值研究

摘要

背景: 大量研究表明经食道膈肌肌电检测系统反映的呼吸中枢驱动在COPD患者的治愈率、28天再住院率以及支气管扩张剂的应用效果方面具有关键的评估作用。近年来随着技术进步, 体表膈肌肌电技术在临床开始使用, 它既保留了经食道膈肌肌电的灵敏性、特异性, 也规避了侵入性操作的风险, 具有较高的患者接受度。但是, 表面膈肌肌电能否用于稳定期COPD患者临床症状恶化的识别以及预测AECOPD患者住院必要性尚未可知。

方法: 收集因COPD急性加重至门诊就诊的COPD患者60例。在门诊按照GOLD指南对患者进行评估分级, 其中22例患者评估为需要住院治疗组, 另38例评估为门诊治疗组。两组患者均在入组当日行体表膈肌肌电、肺功能、动脉血气分析等检查, 并予CAT、MEWS评分, 之后仍依据GOLD指南给患者制定治疗方案, 充分治疗并随访, 在每位患者被评定为病情稳定后重复入院当日的各项检测。

结果: 比较各参数在急性加重至稳定期之间差值的相关性, $\Delta\text{EMGdi}\%_{\text{max}}$ 与 ΔCAT 、 ΔPaCO_2 、 ΔpH 具有明显正相关, 与 $\Delta\text{PaO}_2/\text{FiO}_2$ 负相关。在评估患者住院治疗的必要性方面, $\text{EMGdi}\%_{\text{max}}$ 较 FEV_1 、MEWS、 $\text{PaO}_2/\text{FiO}_2$ 具有更高的灵敏性。 $\text{EMGdi}\%_{\text{max}}$ (OR 1.143, 95% CI 1.004 to 1.300)对AECOPD患者住院治疗必要性具有较好的预测价值。

结论: 在COPD急性加重至治疗稳定的过程中, 体表膈肌肌电参数的变化与肺功能、动脉血气分析、CAT评分、MEWS评分等指标有较好的一致性。体表膈肌肌电可以作为AECOPD患者住院治疗的预测指标。