Correlation Between Rectus Femoris Muscle Cross-Sectional Area and Severity of Acute Exacerbations of Chronic Obstructive Pulmonary Disease

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ABSTRACT

Objective: To assess the correlation between rectus femoris muscle cross-sectional area (RFCSA) and the severity of acute exacerbations of chronic obstructive pulmonary disease (ECOPD).

Study Design: Observational study.

Place and Duration of the Study: Respiratory and Critical Care Medicine Ward, Suzhou Ninth Hospital affiliated to Soochow University, Suzhou, Jiangsu, China, from May 2021 to April 2024.

Methodology: Data of seventy-two ECOPD patients were collected regarding their gender, age, height, and weight. The patients' RFCSA, the Forced Expiratory Volume in 1 second predicted (FEV1% predicted), the COPD assessment test (CAT), and the modified Medical Research Council (mMRC) Dyspnoea Scale were determined. To analyse the data, the patients were divided into four groups, the groups were classified as: Mild group (the value of FEV1% predicted 80% or more), moderate group (the value of FEV1% predicted between 50% and 79%), severe group (the value of FEV1% predicted between 30% and 49%), and very severe group (the value of FEV1% predicted 30% or less).

Results: There were significant differences in RFCSA (H 41.80, p <0.001), FEV1% predicted (H 63.91, p <0.001), and CAT (H 24.50, p <0.001) among the four groups. RFCSA, FEV1% predicted, and CAT varied significantly among the groups. In ECOPD patients, RFCSA showed positive relationship with FEV1% predicted (r = 0.75, p <0.001). A strong negative correlation was obtained between RFCSA and CAT in ECOPD patients (r = -0.69, p <0.001).

Conclusion: RFCSA may be an indicator for evaluating the severity of ECOPD.

Key Words: *Rectal muscle cross-sectional area*, *Forced expiratory volume in 1 second predicted*, *Exacerbations of chronic obstructive pulmonary disease*, *COPD assessment test*, *Modified medical research council*.

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INTRODUCTION

Chronic obstructive pulmonary disease (COPD) presents as prolonged many respiratory symptoms, such as dyspnoea, cough, expectoration and/or exacerbations due to abnormalities of the airways (bronchitis, bronchiolitis), and/or alveoli (emphysema).[1-3] In China, Wang found that the disease causes persistent airflow obstruction and the incidence rate of COPD for individuals above 40 years is 13.7%.[4] In present, COPD is the 3rd most common non-infective disease after hypertension and diabetes.[5,6] It is associated with several pulmonary comorbidities such as lung cancer, bronchiectasis, and obstructive sleep apnoea.[7,8]

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The detrimental effects of COPD may extend beyond the lungs, impacting skeletal muscle healthy. Rectus femoris function is the most commonly observed complication in this context.[9] In COPD, rectus femoris dysfunction is associated with reduced exercise tolerance and functional performance. Fortunately, rectus femoris dysfunction can be assessed through a relatively simple and non-invasive test: Rectus femoris ultrasound.[10] ECOPD means that the exacerbation of chronic obstructive pulmonary disease, which is defined as an event characterised by increased dyspnoea and/or sputum and cough, that worsens in less than fourteen days.[11] It may be accompanied by tachypnoea and/ or tachycardia. It often happens with increased local and systemic inflammation caused by irritation, infection, or other insults to the airways. ECOPD is a major reason for hospitalisation and death among COPD patients.[12] So, how to assess ECOPD disease severity with a relatively easy and noninvasive method? In this paper, the correlation analysis between rectus femoris muscle cross-sectional area (RFCSA) and the severity of ECOPD disease was investigated, with the aim of providing a new assessment tool for ECOPD disease severity.

METHODOLOGY

Seventy-two ECOPD patients from the Department of Respiratory and Critical Care Medicine in the Suzhou Ninth Hospital Affiliated to Soochow University, Jiangsu, China, who were hospitalised from May 2021 to April 2024, were enrolled in the study. Patients were included in this study if they were aged above 40 years, were diagnosed by the GOLD (2023 report) criteria,[1] and they had a sudden exacerbation of respiratory manifestations including coughing, sputum production, or dyspnoea. The exclusion criteria were comorbidity with solid or haematologic neoplastic underlying disease, presence of other underlying lung diseases, combination of acute respiratory infectious diseases, existence of serious cardiovascular and cerebrovascular diseases, severe liver and renal insufficiency, and co-existence of neuromuscular system lesions or patients with severe cognitive impairment. All patients were enrolled voluntarily and signed an informed consent form and the study was approved by the Suzhou Ninth Hospitals Affiliated to Soochow University, China (Ethical Review Approval No: KYLW2023-050-01: Youth Research Fund of Suzhou Nine Hospitals Affiliated to Soochow University, Jiangsu, China, in 2021: Subject No. YK202116).

The cross-sectional area of the rectus femoris muscle was measured using the Siemens ACUSON Redwood digital colour Doppler ultrasound diagnostic instrument by an ultrasound specialist with 10 years of experience. The lung function was examined by a respiratory specialist with 10 years of experience using a Master Screen lung function analyzer. The COPD Assessment Test (CAT) and the modified Medical Research Council (mMRC) Dyspnoea Scale were collected by a dedicated personnel.

The data were analysed by SPSS version 26.0. To assess the significance of gender, Fisher's exact test was employed due to the small sample size or low expected frequency in certain categories. Data that followed a normal distribution were expressed as mean ± standard deviation ($\bar{x} \pm s$), and comparisons among multiple groups were conducted using the one-way ANOVA test. For detailed comparisons between two specific groups within the larger dataset, the Scheffe test was used. Data that did not follow a normal distribution were presented as median (P25, P75), with comparisons among multiple groups performed using the non-parametric Kruskal-Wallis H test, followed by pairwise comparisons using the Nemenyi test. To assess the relationship between the RFCSA and clinical indicators, Spearman's correlation coefficient was used. Throughout the analysis, a p-value less than 0.05 ($p \leq 0.05$) was considered statistically significant.

RESULTS

Seventy-two patients hospitalised for ECOPD in the sickroom of Suzhou Ninth Hospital Affiliated to Soochow University were included. The group consisted of 56 males and 16 females, aged from 52 to 86 years. Patients were divided into four groups based on the severity of their lung function as measured by a post-bronchodilator FEV1% predicted. Nine patients were placed in mild group (FEV1% predicted ≥80%), 25 patients in moderate group (50% ≤FEV1% predicted <79%), 27 patients in severe group (30% ≤FEV1% predicted <49%)), and 11 patients in very severe group (FEV1% predicted <30%). In the study, there were no significant differences in age or gender distribution between the groups. Table I provides a detailed breakdown of the patients' clinical characteristics.

There was no statistically significant difference in age ($p = 0.42$) and gender ($p = 0.78$, Fisher's exact test) between the groups.

The comparison of RFCSA, body mass index (BMI), FEV1% predicted, CAT, and mMRC are listed in Table II.

The analysis identified that RFCSA was associated with higher FEV1% predicted as shown by a positive correlation ($r = 0.75$, $p < 0.001$), and the positive correlation was strong. RFCSA was linked to fewer symptoms (lower CAT) with a significant negative correlation ($r = -0.69$, $p < 0.001$). Finally, no association was found between muscle size (RFCSA) and breathlessness (mMRC, $r = -0.09$, $p = 0.474$).

Table I: Gender and age in different groups.

Groups	Gender			Age (years)		
	Males	Females	Male-to-Female Ratio	Oldest	Youngest	Average age
Very severe	9	2	4.5:1	85	52	71.64 ± 9.41
Severe	22	5	4.4:1	85	71	72.70 ± 4.30
Moderate	19	6	3.17:1	85	63	73.80 ± 5.62
Mild	6	3	2:1	86	66	75.89 ± 6.92

Table II: Comparison of RFCSA, BMI, FEV1% predicted, CAT, and mMRC.

Groups	RFCSA	BMI	FEV1% predicted	CAT	mMRC
Very severe	4.05 (4.02 4.18)	19.50 ± 2.30	25.10 (21.50 27.50)	31.00 (30.00 32.00)	2.00 (2.00 3.00)
Severe	4.57 (4.24 4.89)	21.45 ± 3.88	35.30 (33.60 42.70)	28.00 (24.00 31.00)	2.00 (2.00 3.00)
Moderate	5.71 (4.98 5.81)	22.13 ± 3.34	60.80 (57.10 70.85)	24.00 (21.00 28.50)	2.00 (2.00 2.50)
Mild	6.35 (5.35 6.66)	23.27 ± 3.34	93.00 (83.35 98.60)	23.00 (20.00 23.00)	2.00 (2.00 2.00)
H/F	41.80	2.30	63.91	24.50	1.80
p-value	<0.001	0.09	<0.001	<0.001	0.61

Notes: The data of BMI were presented as mean ± standard deviation, and p-values were determined by the one-way ANOVA test, followed by the Scheffe test. The data of RFCSA, FEV1% predicted, CAT, and mMRC were presented as median (P25, P75), and p-values were determined by the non-parametric Kruskal-Wallis H test, followed by the Nemenyi test. Statistically significant p-values were defined as those below the 0.05 level.

DISCUSSION

COPD has many extrapulmonary complications, and the most commonly associated is skeletal muscle dysfunction, with quadriceps lesions being the most obvious.[13,14] Several studies have demonstrated that RFCSA can replace quadriceps muscle strength.[15] Herein, ultrasonography is employed to evaluate the RFCSA instead of quadriceps muscle strength, which serves as a more objective, reproducible, simple, and easy-to-use tool.

In the study, significant differences in RFCSA between the ECOPD groups were found, with a strong positive correlation between RFCSA and patients' FEV1% predicted value. This suggests that the lower muscle mass (RFCSA) is associated with more significant airflow obstruction (lower FEV1% predicted). Several factors drive the occurrence of muscle loss in ECOPD patients, including hypoxia, hypercapnia, acidosis, systemic inflammation, oxidative stress, malnutrition, and an imbalance between protein synthesis and breakdown.[16-19] The combination of these factors decreases stored glycogen in the muscle, oxygen delivery, and oxidative capacity of the myocytes, this leads to progressive muscle atrophy, and loss of muscle strength and mass. The results suggested that the RFCSA decreased in all ECOPD groups. The findings demonstrated the correlation between RFCSA and disease severity in the ECOPD patients was significantly negative. This suggests that RFCSA might serve as a biomarker of disease severity.

Notably, there were significant differences of CAT in ECOPD among the four disease groups. However, the mMRC did not show significant differences between all groups. One possible explanation is the limited sensitivity of the mMRC due to the simplicity of its categorisation system. This may hinder the detection of subtle variations in dyspnoea severity among patients excluding mild COPD patients. In contrast, the CAT incorporates a wider range of symptoms, allowing for a more nuanced assessment of ECOPD severity.[20] The study revealed a significant negative correlation between the CAT and RFCSA. This suggests that reduced RFCSA in ECOPD patients might be attributable to several factors. Early-stage ECOPD is known to trigger systemic inflammation and oxidative stress, both of which have been implicated in decreased physical activity levels. Additionally, hypoxia, carbon dioxide retention, and acidosis during ECOPD can decrease gastrointestinal motility and contribute to nutritional deficiencies. Combined, these factors can decrease activity levels and RFCSA expression. As the CAT increases, the RFCSA decreases, suggesting that RFCSA may be a robust biomarker for evaluating the severity of acute exacerbations of ECOPD based on clinical symptoms.

In this study, the major limitation is that the research results were derived from a single hospital. Additional studies are to be conducted across different hospitals to validate the results.

CONCLUSION

The severity of RFCSA varied among ECOPD patients. Patients with lower FEV1% predicted and higher CAT had smaller RFCSA. Therefore, RFCSA will be a useful biomarker for assessing the severity of ECOPD.

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ETHICAL APPROVAL:
This study was approved by the Suzhou Ninth Hospitals Affiliated to Soochow University (Ethical Review Approval No: KYLW2023-050-01).

PATIENTS' CONSENT:
All patients provided written informed consent.

COMPETING INTEREST:
The authors declared no conflict of interest.

AUTHORS' CONTRIBUTION:
WW, WS: Carried out the studies.
HB, FZ: Collected data.
WW, LD: Drafted the manuscript.
XH: Performed the statistical analysis and participated in designing.
WW, XH, WS: Contributed to acquisition, analysis, interpretation of data, and drafting of the manuscript.
All authors approved the final version of the manuscript to be published.

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