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ORIGINAL RESEARCH

Serum Creatinine to Cystatin C Ratio is an Effective Indicator for Muscle Strength Decline in Men with Acute Exacerbation of Chronic Obstructive Pulmonary Disease

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Purpose: This study explored the value of the serum creatinine/cystatin C (Cr/CysC) ratio in diagnosing the reduction of muscle strength in men with acute exacerbation of chronic obstructive pulmonary disease (AECOPD).

Patients and Methods: In this study, we enrolled 72 male patients with AECOPD and 32 male patients with stable chronic obstructive pulmonary disease (COPD). We compared clinical characteristics between the AECOPD and stable COPD groups. Then, we subdivided AECOPD patients into normal muscle strength and low muscle strength groups; we compared the clinical characteristics between these two groups. We analyzed the relationships of serum creatinine (Cr), cystatin C (CysC), and Cr/CysC ratio with clinical characteristics in male AECOPD patients. We also investigated whether the Cr/CysC ratio could aid in the diagnosis of muscle strength decline via receiver operating characteristic curve and binary logistic regression analysis.

Results: We found that handgrip strength, Cr/CysC ratio, serum Cr, FEV_1, FVC, and FEV_1%pred were lower in AECOPD patients than in stable COPD patients. Among AECOPD patients, BMI, weight, FEV_1, FVC, FEV_1%pred, and Cr/CysC ratio were lower in the low muscle strength group than in the normal muscle strength group; there were more patients with ≥2 acute exacerbations within the past year in the low muscle strength group. The Cr/CysC ratio was correlated with handgrip strength, FEV_1, FVC, FEV_1%pred, BMI and weight. The area under curve for low handgrip strength was greater for the Cr/CysC ratio than for Cr. Binary logistic regression analysis showed that a Cr/CysC ratio <0.99 was a risk factor for decreased muscle strength in male patients with AECOPD.

Conclusion: The Cr/CysC ratio is a useful predictor of muscle strength decline in male AECOPD patients, while a low Cr/CysC ratio is a risk factor for muscle strength decline in male patients with AECOPD.

Keywords: muscle strength, AECOPD, male, Cr/CysC ratio, handgrip strength

Introduction

Chronic obstructive pulmonary disease (COPD) is a common chronic airway disease characterized by persistent respiratory symptoms and irreversible airflow limitation, which severely threatens human health.[1] In 2010, there were 384 million patients suffering from COPD worldwide, with an overall prevalence of 11.7%.[2] The prevalence of COPD is expected to gradually increase in the next 40 years; more than 5.4 million people are expected to die of COPD and related diseases each year by 2060.[3,4] Patients with COPD often exhibit comorbidities such as cardiovascular disease, osteoporosis, skeletal muscle disease, lung cancer, anxiety, and depression; these additional diseases have significant impacts on mortality, frequency of acute exacerbation, hospitalization rate, and quality of life in affected patients.[5]

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Sarcopenia is a common comorbidity of COPD with clinical features that include age-related loss of skeletal muscle mass and loss of muscle strength and/or reduced physical performance.[6] According to the most recent European Working Group on Sarcopenia in Older People, low muscle strength is a prerequisite for the diagnosis of sarcopenia; handgrip strength (HGS) measurement is a reliable alternative to complex muscle strength measurement methods, such as arm and leg strength measurement.[7] Studies have shown that malnutrition is one of the main factors for frequent exacerbations of COPD and increased risk of death, and it is also an important contributor to sarcopenia.[8,9] HGS is not only a simple method to screen for sarcopenia but also a useful tool for diagnosing malnutrition.[10] Current studies have shown that HGS is positively correlated with forced vital capacity (FVC) and forced expiratory volume in 1 second (FEV_1) in COPD patients and it can be used to assess the severity of patients.[11–13] Low HGS is associated with adverse events in patients with COPD; patients with low HGS also have worse quality of life, as well as increased risks of morbidity, mortality, and exacerbation.[14–16]

Serum creatinine (Cr) is mainly produced by creatine via slow and stable non-enzymatic cyclization; it is then released into the blood and excreted through the kidneys. However, creatine is mainly produced by the liver and transported to the muscles; 98% of the creatine pool is stored in the muscles. Thus, the serum Cr concentration is related to muscle mass; this concentration is easily affected by renal function.[17] Cystatin C (CysC) is a low molecular weight protein produced by all nucleated cells at a constant rate; it can be freely filtered by the glomerulus and reabsorbed, then catabolized in the proximal tubules. CysC concentration is mainly determined by the glomerular filtration rate, regardless of sex, age, and muscle mass.[18]

Based on the physiological characteristics of serum Cr and CysC, the serum Cr/CysC ratio has been used to evaluate sarcopenia.[19–21] Some studies have found that Cr/CysC ratio was a valuable indicator of muscle mass and was positively correlated with muscle mass.[22,23] Cr/CysC ratio can also assess muscle strength and has been shown to be associated with decreased muscle strength in terminal cancer patients, non-dialysis chronic kidney disease patients and elderly inpatients.[20,21,24] Cr/CysC ratio has shown a good correlation with HGS in patients with stable COPD.[25] In addition, because of differences in physical fitness between men and women, HGS is usually higher in men than in women,[26] and Cr/CysC ratio as an evaluation index of muscle strength corresponds to higher.[27] A cross-sectional study including 2339 participants aged ≥40 years found that HGS and Cr/CysC ratios were higher in men than in women;[27] moreover, the Cr/CysC ratio was positively correlated with HGS.[27] To our knowledge, there have been few studies of the Cr/CysC ratio in patients with COPD;[25,28,29] only one study has investigated the clinical value of Cr/CysC ratio in patients with acute exacerbation of chronic obstructive pulmonary disease (AECOPD).[28]

This study was performed to analyze the relationships of the Cr/CysC ratio with various clinical indicators and HGS in male AECOPD patients; it also explored the feasibility of the Cr/CysC ratio as an assessment of muscle strength decline in AECOPD patients.

Materials and Methods

Patient Population

This prospective study enrolled 72 male AECOPD patients and 32 male stable COPD patients who were treated in the Affiliated Hospital of Guangdong Medical University from November 2020 to October 2021. COPD and AECOPD were diagnosed in accordance with the Global Initiative for Chronic Obstructive Lung Disease 2020 (GLOD 2020) criteria.[1] AECOPD were defined as an acute worsening of respiratory symptoms that result in additional therapy.[1] Inclusion criteria included: (1) all patients met the diagnostic criteria for COPD defined by GOLD 2020: dyspnea, history of chronic cough or sputum production, and/or a history of exposure to factors for the disease, together with lung function tests showed forced expiratory volume in 1 second/forced vital capacity (FEV_1/FVC) <0.70 after inhalation of bronchodilator, (2) male sex, (3) consent to participate in the study, and (4) age ≥40 years. Exclusion criteria included inability to complete spirometry and/or the presence of the following conditions: chronic kidney disease or acute kidney injury, comorbid malignancy or history of treatment for malignancy, severe respiratory disease except COPD, and/or comorbidity that affected muscle status (eg, abnormal thyroid function, orthopedic disease, or severe neuromuscular disease). Our study complied with the Declaration of Helsinki Ethical Principles for Medical Research Involving Human Subjects.

The study protocol was approved by the Ethics Committee of the Affiliated Hospital of Guangdong Medical University (Approval number: PJ2017066; Date: 4th Sep 2017); all participants provided written informed consent.

Subgroups

According to the Asian Working Group for Sarcopenia (AWGS) 2019 guidelines, HGS < 28 kg in men is defined as low muscle strength.[6] In this study, the HGS was measured in all participants. Participants with HGS < 28 kg and ≥ 28 kg were included in the low muscle strength and normal muscle strength groups, respectively. All participants used an electronic handgrip dynamometer (CAMRYEH102, Xiangshan, Zhongshan, China) to perform strength measurements with their dominant hand. During the measurement, we first adjusted the dynamometer to an appropriate grip distance according to the size of the participants' hand; Then, the participants' body kept upright, feet were shoulder-width apart, elbows were fully extended, and the force was measured by squeezing with the dominant hand.[23] A total of three HGS measurements were taken, and the maximum HGS value was used for subsequent analyses.

Clinical and Laboratory Measurements and Spirometry

Data were collected regarding age, sex, course of disease, height, weight, body mass index (BMI), smoking history, and exacerbation history. Serum Cr was measured by the picric acid method, and urea nitrogen was measured by urease ultraviolet absorption spectrophotometry. Serum CysC was measured by latex enhanced immune turbidimetry and the assay details were as follows: Buffer-diluted serum samples were mixed with latex covalently bound antibodies to form stable antigen–antibody complexes, resulting in a certain degree of turbidity. By measuring the absorbance of the mixture and comparing it with the calibration solution under the same conditions, the concentration of CysC in the sample could be calculated. All measurements were conducted by our hospital's clinical laboratory. The COPD Assessment Test (CAT) was used to assess the impact of COPD on health status;[30] the modified Medical Research Council (mMRC) dyspnea scale was used to assess the degree of dyspnea.[31] We performed spirometry according to the guidelines for lung function tests formulated by the Chinese Thoracic Society. The procedures and diagnostic criteria in this guideline are not significantly different from the ATS/ERS guideline.[32]

Statistical Analysis

All statistical analyses were performed using SPSS software, version 22.0 (SPSS Inc., Chicago, IL, USA). The normalities of data distributions were assessed using the Kolmogorov–Smirnov test. Independent samples *t*-tests were used for the comparison of normally distributed continuous variables. The Mann–Whitney *U*-test was used for the comparison of non-normally distributed continuous variables. Categorical variables were compared using the two-sided Fisher's exact test or the chi-squared test. Correlations between continuous variables were assessed by Spearman correlation analysis. Receiver operating characteristic (ROC) curves were used to compare the efficacies of serum Cr and Cr/CysC ratios for predicting muscle strength decline in male AECOPD patients; they were also used to calculate the corresponding cut-off value. The risk factors in male AECOPD patients, combined with muscle strength decline, were analyzed via binary logistic regression; variance inflation factors (VIF) were computed as a collinearity diagnostic check. VIF < 10 indicates that there is no multicollinearity among the parameters, and that these parameters will be included in the binary logistic regression for statistics. Two-sided *P*-values <0.05 were considered to indicate statistical significance.

Results

Participant Characteristics

In total, 32 patients with stable COPD and 72 patients with AECOPD were enrolled in this study. No differences between groups were found in terms of age, height, weight, BMI and BMI stratification, smoking history, course of disease, ≥2 acute exacerbations within 1 year, FEV_1/FVC, CysC, or urea nitrogen (all $P > 0.05$). Compared with the stable COPD group, the AECOPD group had higher CAT and mMRC scores; it also had lower FEV_1, FVC, FEV_1%pred (percent of Forced Expiratory Volume in 1 second), HGS, Cr/CysC ratio, and serum Cr (all $P < 0.05$) (Table 1).

Table 1 Comparison of Characteristics Between Stable COPD and AECOPD Groups

Clinical Characteristics	Stable COPD Group (n = 32)	AECOPD Group (n = 72)	*P* value
Age (years)	65.13±9.67	68.25±7.70	0.081
Height (m)	1.65(1.62–1.69)	1.64(1.61–1.67)	0.260
Weight(kg)	55.27±7.78	53.70±9.05	0.398
BMI (kg/m^2)	20.50±2.98	20.08±3.38	0.544
Underweight[a] (n, %)	8(25.00%)	25(34.72%)	0.355
Normal weight[b] (n, %)	20(62.50%)	37(51.40%)	0.277
Overweight[c] (n, %)	4(12.50%)	10(13.90%)	0.612
Smoking history (Yes/No)	30/2	64/8	0.720
Course of disease (months)	48(36.00–114.00)	84(51–120)	0.055
Acute exacerbations ≥2 within one year (Yes/No)	9/23	26/46	0.504
HGS (kg)	34.00(27.80–35.40)	29.20(22.70–31.70)	<0.01
mMRC score	1.5(0.00–3.0)	2(2–3)	<0.01
CAT score	9.0(4.0–17)	19(14–22)	<0.01
FEV_1 (L)	1.23(0.78–1.53)	0.86(0.63–1.20)	<0.01
FVC (L)	2.50±0.74	2.03±0.62	<0.01
FEV_1/FVC	48.71±9.33	45.34±9.10	0.088
FEV_1%pred	45.93±16.88	36.51±15.29	<0.01
Cr (mg/dl)	0.94±0.19	0.81±0.14	<0.01
CysC (mg/L)	0.89±0.18	0.86±0.15	0.478
Cr/CysC ratio	1.08(0.91–1.23)	0.91(0.84–1.10)	<0.01
Urea nitrogen (μmol/L)	5.10(4.06–6.18)	5.14(4.36–6.20)	0.610

Notes: [a]Underweight (BMI<18.5 kg/m^2); [b]Normal weight (18.5 kg/m^2 ≤BMI< 24 kg/m^2); [c]Overweight (24 kg/m^2 ≤BMI< 28 kg/m^2).

Abbreviations: COPD, chronic obstructive pulmonary disease; AECOPD, acute exacerbation of chronic obstructive pulmonary disease; BMI, body mass index; HGS, handgrip strength; mMRC, modified British Medical Research Council; CAT, COPD Assessment Test; FEV_1, forced expiratory volume in 1 second; FVC, functional vital capacity; FEV_1/FVC, forced expiratory volume in 1 second /forced vital capacity; FEV_1%pred, percent of forced expiratory volume in 1 second; Cr, creatinine; CysC, cystatin C; Cr/CysC, creatinine/cystatin C.

Comparison of Clinical Characteristics Between Normal Muscle Strength and Low Muscle Strength Subgroups of AECOPD Patients

Based on the normal value of HGS in men, as defined by the AWGS 2019 guidelines, patients with AECOPD were divided into normal muscle strength and low muscle strength groups. No differences between the groups were found in terms of age, height, BMI stratification, course of disease, smoking history, CAT score, mMRC score, FEV_1/FVC, serum Cr, CysC, and urea nitrogen (all $P > 0.05$). BMI, weight, FEV_1, FVC, FEV_1%pred, HGS, and Cr/CysC ratio were lower in the low muscle strength group than in the normal muscle strength group; there was a greater proportion of patients with ≥2 acute exacerbations within 1 year ($P < 0.05$) (Table 2).

Correlations of Serum Cr, CysC, and Cr/CysC Ratio with Clinical Characteristics in Patients with AECOPD

The Cr/CysC ratio was positively correlated with BMI ($r = 0.469$, $P<0.01$), weight ($r = 0.469$, $P < 0.01$), HGS ($r = 0.388$, $P < 0.01$), FEV_1 ($r = 0.246$, $P = 0.037$), FVC ($r = 0.332$, $P < 0.01$), and FEV_1%pred ($r = 0.244$, $P = 0.039$). Serum CysC showed no correlations with the above indicators except weight ($r = -0.242$, $P = 0.041$), while Cr was positively correlated with only BMI, weight and FEV_1%pred ($r = 0.307$, $r = 0.241$, $r = 0.287$, respectively, $P<0.05$) (Table 3).

Sensitivity and Specificity of Serum Cr and Cr/CysC Ratio for Identifying Male AECOPD Patients with Decreased Muscle Strength

ROC curve analysis showed that Cr/CysC ratio at the cut-off of 0.99 yielded an area under the curve (AUC) of 0.731 for identifying male AECOPD patients with low muscle strength, with a sensitivity and specificity of 83.9% and 63.4%,

Table 2 Comparison of Clinical Characteristics Between Normal Muscle Strength and Low Muscle Strength Groups of AECOPD Patients

Clinical Characteristics	Normal Muscle Strength Group (n = 41)	Low Muscle Strength Group (n = 31)	*P* value
Age (years)	66.22(59.27–72.22)	69.04(64.51–75.96)	0.055
Height (m)	1.63±0.05	1.65±0.06	0.113
Weight (kg)	56.33±8.32	50.23±8.92	0.004
BMI (kg/m^2)	21.28±3.15	18.48±3.03	<0.01
Underweight[a] (n, %)	8(19.50%)	17(54.80%)	0.351
Normal weight[b] (n, %)	24(58.50%)	13(41.90%)	0.703
Overweight[c] (n, %)	9(22.00%)	1(3.20%)	0.862
Smoking history (Yes/No)	2/39	6/25	0.068
Course of disease (months)	73(48–120)	120(60–120)	0.228
Acute exacerbations ≥2 times within one year (Yes/No)	10/31	16/15	0.026
HGS (kg)	31.50(30.30–37.00)	22.30(20.40–24.70)	<0.01
mMRC score	2(1–3)	3(2–3)	0.067
CAT score	17.15±6.90	19.52±5.85	0.145
FEV_1 (L)	0.90(0.71–1.38)	0.77(0.52–1.06)	0.027
FVC (L)	2.19±0.67	1.81±0.47	<0.01
FEV_1/FVC	46.41±8.39	43.94±9.93	0.257
FEV_1%pred	39.93±16.46	32.00±12.44	0.028
Cr/CysC ratio	1.02(0.87–1.16)	0.85(0.80–0.92)	<0.01
Cr (mg/dl)	0.83±0.11	0.78±0.17	0.191
CysC (mg/L)	0.83±0.13	0.90±0.17	0.086
Urea nitrogen (μmol/L)	5.03(4.25–5.92)	5.45(4.50–6.33)	0.363

Notes: [a]Underweight (BMI<18.5 kg/m^2); [b]Normal weight (18.5 kg/m^2 ≤BMI< 24 kg/m^2); [c]Overweight (24 kg/m^2 ≤BMI< 28 kg/m^2).
Abbreviations: BMI, body mass index; HGS, handgrip strength; mMRC, modified British Medical Research Council; CAT, COPD Assessment Test; FEV_1, forced expiratory volume in 1 second; FVC, functional vital capacity; FEV_1/FVC, forced expiratory volume in 1 second/forced vital capacity; FEV_1% pred, percent of forced expiratory volume in 1 second; Cr/CysC, creatinine/cystatin C; Cr, creatinine; CysC, cystatin C.

Table 3 Relationships of Serum Cr, Cr/CysC Ratio, and CysC with Clinical Characteristics in Patients with AECOPD

	Cr/CysC Ratio		Cr		CysC	
	r value	*P* value	*r* value	*P* value	*r* value	*P* value
Weight (kg)	0.469	<0.01	0.241	0.042	−0.242	0.041
BMI (kg/m^2)	0.469	<0.01	0.307	<0.01	−0.188	0.113
HGS (kg)	0.388	<0.01	0.187	0.115	−0.172	0.148
FEV_1 (L)	0.246	0.037	0.201	0.091	−0.098	0.414
FVC (L)	0.332	<0.01	0.215	0.070	−0.147	0.217
FEV_1%pred	0.244	0.039	0.287	0.014	−0.039	0.742

Abbreviations: Cr/CysC, creatinine/cystatin C; Cr, creatinine; CysC, cystatin C; BMI, body mass index; HGS, handgrip strength; FEV_1, forced expiratory volume in 1 second; FVC, functional vital capacity; FEV_1% pred, percent of forced expiratory volume in 1 second.

respectively. The AUC for serum Cr was 0.605; the optimal sensitivity (41.9%) and specificity (85.4%) were obtained with a cut-off concentration of 0.73 mg/dL (Figure 1).

Analysis of Risk Factors for Muscle Strength Decline in Male Patients with AECOPD

Binary logistic regression analysis of the AECOPD group was performed with HGS as the dependent variable. In order to avoid the existence of collinearity in these variables interfering with the accuracy of the regression analysis, we performed collinearity diagnosis and found collinearity in BMI and weight, as well as FEV_1 and FEV_1%pred. Therefore, FVC, FEV_1 and weight were included in the binary logistic regression analysis as independent variables.

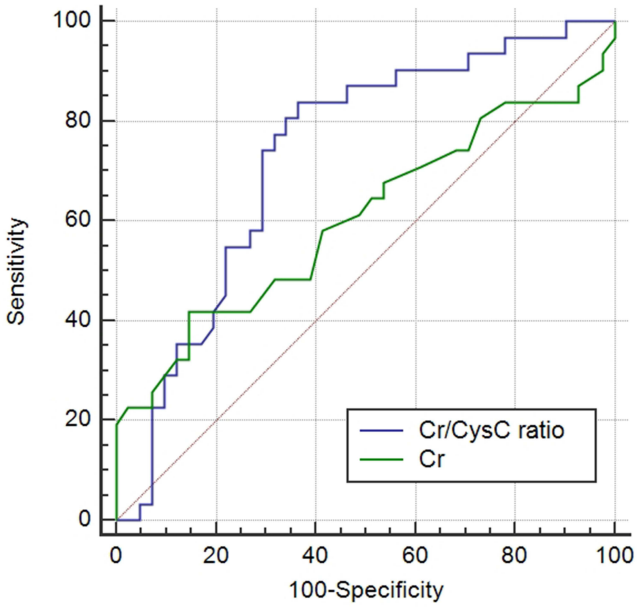

Figure 1 ROC curve analysis of Cr/CysC ratio and Cr for low muscle strength.
Abbreviations: Cr, creatinine; Cr/CysC, creatinine/cystatin C.

Cr/CysC ratio was dichotomized based on the appropriate cut-off value that was determined according to the ROC curve. The results showed that Cr/CysC ratio <0.99 (OR = 5.779, 95% CI: 1.671–19.982, $P<0.05$) was identified as a risk factor for low muscle strength in male patients with AECOPD (Table 4).

Discussion

The main causes of sarcopenia include satellite cell senescence, oxidative stress, chronic inflammation, and motor unit loss.[33] However, the causes of sarcopenia in patients with COPD are more complex; factors such as chronic hypoxia, malnutrition, long-term glucocorticoid use, and muscle waste should be considered.[34] The diagnosis of sarcopenia is inseparable from the measurement of muscle mass and muscle strength; low muscle strength is a key factor in the diagnosis of sarcopenia.[7] In recent years, there has been increasing focus on muscle strength, mainly because muscle strength is more reliable than muscle mass for predicting adverse events. In a 3-year follow-up of 498 patients, Schaap et al found that the incidence of recurrent falls was associated with low HGS; it was not associated with low muscle mass.[35] In a follow-up study with a mean interval of 4.9 years, HGS were strongly associated with mortality, while muscle mass measured by CT (Computer Tomography) or DXA (dual-energy X-ray absorptiometry) was not strongly associated with mortality.[36] Therefore, we presumed that HGS can adequately estimate muscle strength; we used HGS to detect muscle strength in this study.

In our study, we found that HGS in male patients with stable COPD was 34 kg, similar to the value of 31 kg reported by Hirai.[25] Moreover, HGS in AECOPD patients was 29.20 kg, lower than in stable COPD patients. In the study by Lee, the HGS in AECOPD patients was 25.3 kg, which was lower than the value in our study; this is presumably because the

Table 4 Analysis of Risk Factors for Low Muscle Strength in Male Patients with AECOPD

Factor	Regression Coefficient	Standard Error	Wald	*P*	OR	95% CI
Cr/CysC ratio	1.754	0.663	7.680	<0.05	5.779	1.671–19.982
Weight(kg)	−0.037	0.036	1.059	>0.05	0.964	0.898–1.034
FVC (L)	−0.630	1.134	0.309	>0.05	0.532	0.058–4.920
FEV_1 (L)	0.160	1.670	0.009	>0.05	1.173	0.044–30.970

Abbreviations: Cr/CysC, creatinine/cystatin C; FVC, functional vital capacity; FEV_1, forced expiratory volume in 1 second.

previous study included female patients.[37] A recent study has indicated that HGS is correlated with the Cr/CysC ratio, which could help identify low HGS.[27] Some reports have shown that Cr/CysC ratio is correlated with HGS in patients with non-dialysis chronic kidney disease or with liver disease.[21,38] However, few studies have explored the relationship between Cr/CysC ratio and HGS in patients with COPD. The Cr/CysC ratio has been significantly correlated with HGS in male stable COPD patients; it is more effective than other markers (eg, CysC, Cr, and albumin) for diagnosing sarcopenia.[25] Here, we compared the Cr/CysC ratio between stable COPD patients and AECOPD patients; we found that the Cr/CysC ratio was lower in AECOPD patients (1.08 vs 0.91). Similarly, the Cr/CysC ratio was lower in the low muscle strength group than in the normal muscle strength group (0.85 vs 1.02). These results suggested that the Cr/CysC ratio may be related to the condition of COPD and also to HGS in patients with AECOPD. Correlation analysis revealed that the Cr/CysC ratio was positively correlated with HGS in AECOPD patients, while Cr was not associated with HGS. This finding suggests that the Cr/CysC ratio can partially eliminate the influences of other factors on Cr or CysC, thereby improving the evaluation of muscle strength.

The roles of Cr/CysC in COPD are to assess sarcopenia and evaluate disease severity. The Cr/CysC ratio exhibits relationships with important clinical characteristics in COPD patients, such as FEV_1, 6-minute walk test results, and fat-free body mass index; it could also be used to predict hospitalization in COPD patients. Furthermore, the Cr/CysC ratio was lower in patients with COPD than in healthy controls; it was also lower in patients with mMRC score ≥2, patients with CAT score ≥10, and patients with a high risk of exacerbation.[29] A lower Cr/CysC ratio may be indicative of more severe dyspnea, a longer hospital stay, and worse lung function in AECOPD patients.[28] Our results were similar to previous findings that AECOPD patients had a lower Cr/CysC ratio, which was correlated with FEV_1, FVC, and FEV_1% pred. Additionally, patients with a lower Cr/CysC ratio had worse lung function.

Muscle strength is an important factor that affects lung function; there is a good correlation between HGS and respiratory muscle strength.[39,40] Because the Cr/CysC ratio is a useful index for evaluating muscle strength, it can be used to evaluate respiratory muscle conditions that severely restrict airflow and affect the risks of acute exacerbation, hospitalization, and death in COPD patients.[41–43] In this regard, the Cr/CysC ratio may be an important prognostic indicator.[24,44] Here, calculation using the ROC curve showed that the cut-off value of the Cr/CysC ratio for predicting decreased muscle strength in male AECOPD patients was 0.99, which is greater than the value reported by Hirai (0.71). This is presumably because our predicted target was muscle strength decline, whereas Hirai et al predicted sarcopenia (ie, low muscle mass + low muscle strength).[25] Multivariate binary logistic regression showed that a Cr/CysC ratio <0.99 was a risk factor for muscle strength decline in male AECOPD patients, which may provide insights for the diagnosis and treatment of sarcopenia patients.

Although our findings suggest that the Cr/CysC ratio can be used to predict whether patients with AECOPD exhibit comorbid muscle weakness, our study was conducted in a single center, and the sample size was limited. Therefore, further confirmatory studies are needed. Because of the higher COPD incidence in men, we only included male patients; thus, sex differences in the Cr/CysC ratio were not analyzed. We did not measure the muscle mass among participants in this study; accordingly, we could not evaluate the diagnostic value of the Cr/CysC ratio in male AECOPD patients with sarcopenia.

Conclusions

The findings in this study suggest that the Cr/CysC ratio is associated with HGS and lung function in male patients with AECOPD. When the Cr/CysC ratio was <0.99, it was a useful predictor of decreased muscle strength in male AECOPD patients. Moreover, a low Cr/CysC ratio is a risk factor for muscle strength decline in male patients with AECOPD.

Abbreviations

AECOPD, acute exacerbation of chronic obstructive pulmonary disease; COPD, chronic obstructive pulmonary disease; Cr, creatinine; CysC, cystatin C; Cr/CysC, creatinine/cystatin C; AUC, area under the curve; HGS, handgrip strength; BMI, body mass index; FEV_1, forced expiratory volume in 1 second; FVC, functional vital capacity; FEV_1% pred, percent of forced expiratory volume in 1 second; FEV_1/FVC, forced expiratory volume in 1 second /forced vital capacity; GOLD 2020, Global Initiative for Chronic Obstructive Lung Disease 2020; ROC, receiver operating

characteristic; CAT, COPD Assessment Test; mMRC, modified British Medical Research Council; AWGS, Asian Working Group for Sarcopenia.

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Disclosure

The authors declare no conflicts of interest in this work.

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