



Body Composition and COPD: A New Perspective

Xin Wang ^{1,2}, Qianqian Liang^{1,2}, Zheng Li¹⁻⁴, Fengsen Li ¹⁻⁴

¹Department of Integrated Pulmonology, Fourth Clinical Medical College of Xinjiang Medical University, Urumqi, Xinjiang, People's Republic of China; ²Xinjiang National Clinical Research Base of Traditional Chinese Medicine, Urumqi, Xinjiang, People's Republic of China; ³Xinjiang Key Laboratory of Respiratory Disease Research, Urumqi, Xinjiang, People's Republic of China; ⁴Xinjiang Clinical Medical Research Center of Respiratory Obstructive Diseases, Urumqi, Xinjiang, People's Republic of China

Correspondence: Zheng Li; Fengsen Li, Tel +86-13999297797; +86-13999980996, Email peterli1129@hotmail.com; fengsen602@163.com

Abstract: The proportion of obese or overweight patients in COPD patients is increasing. Although BMI, WC and other easy to measure indicators have been proven to be related to the risk of COPD, they cannot accurately reflect the distribution and changes of body composition, ignoring the body composition (such as fat distribution, muscle content, water content, etc.), the relationship between it and disease risk may be missed. By analyzing the correlation between different body composition indexes and COPD patients, we can provide new research ideas for the prognosis judgment or intervention of COPD disease.

Keywords: obesity, COPD, body composition, BMI, waist circumference, waist-to-hip ratio, body fat rate, visceral fat, FFMI, extracellular water, intracellular water, phase angle

Introduction

COPD is a pulmonary dysfunction marked by morbidity or comorbidities of progressive irreversible airflow obstruction, chronic airway inflammation, and systemic consequences, marked by ongoing respiratory symptoms and airflow restriction. Typically brought on by anomalies in the alveoli or the airways brought on by prolonged exposure to harmful chemicals or particles.¹ Despite the fact that BMI is linked to the risk of dying from COPD, the obesity paradox has recently brought attention back to the link between obesity and COPD. Although the correlation has been shown, BMI is unable to capture the association between COPD and body composition. The impact of BMI, WC, FFMI, PhA, body fat percentage, visceral fat, and body water on COPD is covered in this article. The development of the research is outlined as follows.

BMI

The obesity paradox states that while a high BMI has a considerable protective effect on the prognosis of COPD, a low BMI level will hasten the decrease of lung function.^{2,3} Obesity is also strongly associated with a higher risk of death and prevalence.⁴ Overweight or obese individuals make up for 65% of COPD patients.⁵ For every 5kg/m² rise in BMI over the normal range [(22–25) kg/m²], the proportional increase in all-cause mortality is similarly larger, will increase 30% level of studies that correlate medical expenditures.^{6,7} In a study comparing BMI to GOLD scores,⁸ it was discovered that there was a U-shaped association between BMI and spending in GOLD grades 1–3, but in GOLD grade 4, health care spending reduced virtually linearly as BMI rose.

Low BMI raises the risk of exacerbations and lowers COPD survival rates.^{9,10} Furthermore, lower BMI has been linked to worsened COPD and increased mortality.¹¹ Low socioeconomic level, poor health, inadequate physical exercise, and recurring illnesses are all frequently linked to low BMI. The risk of COPD exacerbation and possibly death can be decreased by maintaining a normal body mass index.¹² Weaker respiratory muscles may increase the chance of COPD flare-ups and also decrease airway ventilation and load capacity.^{13,14} Increased body weight also increases the

respiratory muscles' effectiveness. It is being investigated in ECLIPSE (COPD Longitudinal Assessment to Determine Predictive Surrogate Endpoints),¹⁵ obese individuals have considerably higher serum levels of TNF- α , interleukin (IL)-6, leptin, and c-reactive protein (CRP), which was 3.3 times greater compared to patients of normal weight, and COPD participants are related with persistent systemic inflammation. Although BMI is frequently employed as a marker for determining the severity of a disease, BMI is unable to reflect the distribution of body fat, muscle, and other tissues, which will cause us to miss the association between fat distribution and illness risk. Future studies evaluating the association between obesity and mortality should go beyond BMI and take into account the distribution of body composition for the advancement of COPD. Relevant conclusions in the literature are shown in Table 1, and the literature from 2009 to 2020.

WHR

Indicators of abdominal fat content include WC, which is also used to predict the prognosis and course of numerous disorders.^{16–19} The faster the lung function declines, the higher the WC value.²⁰ Behrens et al observed that abdominal

Table 1 Conclusions Related to BMI

Author	Year	Study Design	Country, Latitude Degree	Parameters Under Study	Relevant Conclusion
R. Q. Graumam et al ⁴	2018	Cross-sectional study	Brazil	Gender, age, smoking history, BMI, bone densitometry (DXA), lung function, limb lean body mass (ALM), bone mass index (SMI), fat mass index (FMI), vertebral fracture, Baecke questionnaire, laboratory tests	In COPD, the prevalence of low BMI was significantly higher in GOLD 3 and 4 than in GOLD 1 and 2, with approximately 42.2% of men and 20.8% of women with COPD having low BMI compared with 14.3% and 3.2% of men and women in the control group ($p = 0.027$)
Lisa D. M. Verberne et al ⁵	2017	Cross-sectional study	Dutch	Age, sex, BMI, smoking, comorbidities, prescription drugs were associated	Obese patients had more comorbidities, and SABA prescriptions were significantly more frequent in overweight and obese patients than in normal-weight patients, and obese patients were significantly more likely to receive LAMA and LABA + ICS prescriptions
Florian Kirsch et al ⁸	2020	Prospective Studies	Germany	Age, sex, smoking status, income, BMI, lung function, medication use, health care expenditure, quality of life, Charlson index, Pulmonary emphysema, DMP interruption, corticosteroid DDDs	Patients with a BMI of 30 or just above had the lowest health care expenditures, underweight and obese patients had the highest health care expenditures, and overweight ($25 \leq \text{BMI} < 30$) and obesity ($30 \leq \text{BMI} < 35$) were associated with reduced mortality and improved health-related quality of life.
Paul Stoll et al ⁹	2016	Cross-sectional study	Japan	Age, sex, BMI, comorbidities, 5 and 8 year survival after discharge	Patients with BMI ≥ 25 kg/m ² had significantly higher 5-year and 8-year OS than patients with BMI < 25 kg/m ² . Overweight patients (BMI > 25 kg/m ²) hospitalized for acute exacerbation of COPD had lower all-cause in-hospital mortality compared with patients with BMI < 25 kg/m ² .

(Continued)

Table 1 (Continued).

Author	Year	Study Design	Country, Latitude Degree	Parameters Under Study	Relevant Conclusion
Lingyi Yang et al ¹⁰	2019	Prospective Studies	China	Lung function, mMRC score, 6-minute walk distance (6MWD), body weight, BMI, fat-free mass (FFM), fat mass (FM), lean-to-fat (LTF) ratio, skeletal muscle mass (SMM) and other body composite variables, annual number of exacerbations	In the subgroup of BMI < 25 kg/m ² , a low LTF ratio was significantly associated with a reduced risk of acute exacerbation of COPD (OR = 4.528; P < 0.05, the cumulative incidence of acute exacerbation of COPD was significantly increased (P = 0.014),
Eun Kyung Kim et al ¹¹	2020	Prospective Studies	Korea	Age, gender, smoking, BMI, Charlson's comorbidity score, pulmonary function, St George's respiratory questionnaire score, emphysema index, CT air retention index and airway size, BMI, number of acute exacerbations of COPD, mortality, 6-minute walk distance (6MWD), mMRC score, medication history, smoking status	During the annual follow-up period, a decrease in the BMI group was associated with a significant increase in mortality. In this cohort, a 5.9% increase in the BMI group was observed to be associated with lower mortality (p = 0.004), emphysema index (B = -0.080, p < 0.001), serum hemoglobin (B = 0.333, P < 0.001), p = 0.009), serum creatinine (B = 1.955, p = 0.032) and serum protein (B = 0.763, p = 0.021) were independent factors associated with BMI.
Hye Jung Park et al ¹²	2019	Prospective cohort study	Korea	Smoking, BMI, COPD incidence, COPD-free survival, and overall survival	Among never-smokers or light smokers, the incidence of COPD in the low BMI group (5.6–6.7%) was significantly higher than that in the other groups (2.8–4.7%). In subjects with smoking history ≥ 30 years, the incidence of COPD was higher in the low BMI group (20.1%) than in the other groups (8.4–12.4%). Compared with a low BMI, normal or above normal weight was significantly protective against developing COPD (hazard ratio, 0.609–0.739). Copd-free survival (HR 0.491–0.622) and overall survival (HR 0.440–0.585) were also better than those in patients with low BMI (both P < 0.0001).

Abbreviations: BMI, body mass index; COPD, chronic obstructive pulmonary disease; 6MWD, 6-minute walk distance; FFM, fat-free mass; FM, fat mass; LTF, lean-to-fat; SMM, skeletal muscle mass.

obesity, primarily evaluated by waist circumference,²¹ was positively related with an elevated risk of COPD. A prospective 10-year follow-up of 600 Italian women likewise revealed a substantial correlation between abdominal obesity, as measured by waist circumference, and COPD hospitalizations or risk of mortality.²⁰ According to sexual research,²² a larger waist size was associated with a lower forced vital capacity (P=0.008) and a higher FEV1/FVC ratio (P=0.031). As the waist circumference of COPD patients increases, the risk also increases.²⁰ By using WC measurement as an evaluation index of abdominal obesity, there is a strong correlation with COPD hospitalization, acute exacerbation, and risk of death.²⁰

The WHR, is a key marker for identifying central obesity,²³ and WHtR is also positively connected with the risk of developing COPD.²⁰ The typical apple-shaped body associated with high WHR is visceral fat,²⁴ which is easy to release

fatty acids into the blood and can result in elevated cholesterol, insulin resistance, and other symptoms.^{25–30} Additionally, the rise in WHR is correlated with elevated levels of serum adiponectin,³¹ free fatty acid levels,³² metabolic illness,³³ and systemic inflammation. Obesity-related chronic systemic inflammation may shorten telomeres and cause skin cells to age,³⁴ which in turn causes intra-alveolar inflammation and impacts lung function, particularly FEV1.³³ ADPN levels in individuals with COPD were positively connected with FEV1 and FVC and adversely correlated with disease severity.³² According to a cross-sectional study done in China,³⁵ FEV1 fell by 5.42 mL and 14.23 mL and FVC declined by 5.70 mL and 16.92 mL for every 1% rise in WHtR ($P < 0.05$).

WC and WHR are crucial markers for assessing the severity of metabolic and COPD disorders, but as measures for measuring body surface, they are unable to reveal the distribution of subcutaneous and VAT in abdominal fat and cannot sufficiently represent changes in body composition. As a result, more research on the mechanism of fat distribution on COPD is required. Relevant conclusions in the literature are shown in Table 2, and the literature is from 2014 to 2021.

Table 2 Conclusions Related to WHR

Author	Year	Study Design	Country, Latitude Degree	Parameters Under Study	Relevant Conclusion
Chunlong Li et al ¹⁶	2018	Cross-sectional study	China	Age, sex, education, occupations, tobacco use, alcohol consumption, physical activities, current diseases, medical treatment, inherited diseases, BMI, Smoking, alcohol consumption, physical activity, HOMA-IR, WHR, VAI, ZJU, APRI, FLI, HIS, TyG, Laboratory testso	The optimal cut-off point at WHR>0.50 yielded their high sensitivities (84.0% and 70.8%, respectively) with the maximum Youden index (0.476) in whole population. Similarly, the optimal cut-off points at WHR> 0.47 and WHR>0.53 resulted in reasonable sensitivity (75.5% and 72.8%, respectively) and specificity (63.8% and 53.4%, respectively) in lean and overweight/ obese population, respectively.
Ibrahim Mahmoud et al ¹⁷	2021	Cross-sectional study	Emirati	Sex, age, race, smoking habits, daily physical activity, anthropometric measurements and fingers (BMI, WC, WHR), Comorbidities, including hypertension, diabetes, dyslipidemia, assessed using systolic, diastolic blood pressure, fasting blood sample	Overweight/obesity identified by WC, WHR and BMI are predictors of hypertension, with ORs (95% CI) of 1.62 (1.35–1.96), 1.52 (1.27–1.83) and 1.44 (1.20–1.74), respectively.
Jiachen Li et al ²⁰	2020	Prospective cohort study	China	Age, sex, marital status, highest level of education), lifestyle (smoking, passive smoking, alcohol consumption, physical activity, diet, household air pollution) and medical history, height, weight, WC, hip circumference, WHR, WHtR, lung function, metabolic equivalent task hours (MET-h)	Overweight (BMI 24.0–<28.0 kg m ²) and obesity (BMI ≥28.0 kg m ²) were not associated with an increased risk after adjustment for waist circumference. A higher waist circumference (≥85 cm for males and ≥80 cm for females) was positively associated with COPD risk after adjustment for BMI, waist-to-hip ratio and waist-to-height ratio were positively related to COPD risk.
Gundula Behrens et al ²¹	2014	Cross-sectional study	America	Age, sex, race distribution, marital status, education, smoking, NIH-AARP diet, medical history, BMI, WC, Hip, WHR, physical activity, smoking, COPD incidence	For waist circumference, only underweight remained positively associated with COPD (relative risk [RR] 1.56, 95% confidence interval [CI] 1.15–2.11). Larger waist circumference (highest v. normal categories, adjusted RR 1.72, 95% CI 1.37–2.16) and higher waist-hip ratio (highest v. normal categories, adjusted RR 1.46, 95% CI 1.23–1.73) were also positively associated with COPD, hip circumference (highest v. normal categories, adjusted RR 0.78, 95% CI 0.62–0.98) and physical activity (≥ 5 v. 0 times/wk, adjusted RR 0.71, 95% CI 0.63–0.79) were inversely associated with COPD.

(Continued)

Table 2 (Continued).

Author	Year	Study Design	Country, Latitude Degree	Parameters Under Study	Relevant Conclusion
Ahmad Jayedi et al ²³	2020	A systematic review and dose-response meta-analysis of prospective cohort studies		Location, age range or mean age (years), sex, number of participants, waist circumference, hip circumference, thigh circumference, waist-to-hip ratio, waist-to-height ratio, waist-to-thigh ratio, body adiposity index, body shape index, BMI, All-cause mortality	The risk of all cause mortality did not change for a waist circumference of 60–80 cm (hazard ratio 1.01, 95% confidence interval 0.99 to 1.03) and then increased sharply and linearly ($P_{\text{nonlinearity}} < 0.001$, $n=23$). The analysis of men indicated a J shaped relation with the risk of all cause mortality, which was lowest at a waist circumference of 90 cm (hazard ratio 0.96, 95% confidence interval 0.94 to 0.98), and then increased sharply and linearly ($P_{\text{nonlinearity}} < 0.001$, $n=16$). Indices of central fatness including waist circumference, waist-to-hip ratio, waist-to-height ratio, waist-to-thigh ratio, body adiposity index, and A body shape index, independent of overall adiposity, were positively and significantly associated with a higher all cause mortality risk. Larger hip circumference and thigh circumference were associated with a lower risk.
Nina F. Caspersen et al ²²	2018	Cross-sectional study	Norwegian	Age, gender, height, smoking habits, weight, body mass index, waist-hip ratio, metabolic syndrome, obstructive sleep apnoea (OSA) and C-reactive protein, ADPN, lung function	The median (interquartile range) level of serum ADPN was 7.6 (5.4–10.4) mg/L. ADPN levels were positively associated with FVC % of predicted (beta 3.4 per SD adiponectin, $p < 0.001$) in univariate linear regression analysis, but the association was attenuated in multivariate analysis (standardized beta 0.03, $p = 0.573$)
Yu-En Hsu et al ³³	2021	Cross-sectional study	China	Ex, age, histories of diabetes mellitus, smoking, hypertension, asthma and emphysema or bronchitis, levels of total cholesterol, LDL-C, HDL-C, diet, lifestyle factors, LAP, BRI, CI, BAI, AVI, BMI, WHR, WHtR	The results showed that the participants with high BMI (per 1 kg/m ² ; coefficient β , 0.303; $p < 0.001$), high WHR (per 1%; β , 0.123; $p < 0.001$), high WHtR (per 1%; β , 0.190; $p < 0.001$), high LAP (per 10; β , 0.245; $p = 0.002$), high BRI (per 1; β , 0.565; $p < 0.001$), high CI (per 0.1; β , 0.694; $p = 0.005$), high BAI (per 1; β , 0.263; $p < 0.001$), and high AVI (per 1; β , 0.296; $p < 0.001$) were significantly associated with a high FEV1/FVC.
Heng He et al ³⁵	2020	Prospective cohort study	China	Gender, age, city, family income, occupational hazard exposure, lifestyles, height, weight, body mass index, smoking status, drinking status, education levels, BMI, WC, WHR, WHtR, lung function test, Plasma CRP Measurements	Abdominal obesity indices (WC, WHR and WHtR) and lung function parameters, including forced expiratory volume in 1 s (FEV1) and forced vital capacity (FVC) (all $P < 0.05$). Each 1-unit increase in WC was associated with a 3.39 mL decrease in FEV1 and a 3.96 mL decrease in FVC (all $P < 0.05$). Each 1% increase in WHR and WHtR was associated with a 5.42 mL and a 14.23 mL decrease in FEV1, and a 5.70 mL and a 16.92 mL decrease in FVC (all $P < 0.05$).

Abbreviations: HOMA-IR, homeostasis model assessment of insulin resistance; WHR, waist circumference-to-height ratio; VAI, visceral adiposity index; ZJU, Zhejiang University index; APRI, aspartate aminotransferase-to-platelet ratio index; FLI, fatty liver index; HIS, hepatic steatosis index; TyG, triglycerides and fasting blood glucose index; WC, waist circumference; WHtR, waist-to-Height Ratio; MET-h, metabolic equivalent task hours; BMI, body mass index; CRP, C-reactive protein; FEV1, Forced Expiratory Volume in the first second; FVC, Forced Vital Capacity; OSA, obstructive sleep apnoea; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; LAP, lipid accumulation product; BRI, body roundness index; CI, conicity index; BAI, body adiposity index; AVI, abdominal volume index.

BFP

Obesity is typically defined as a BMI of more than 30 kg/m², but this measurement does not take into account the distribution or composition of body fat. Due to the obesity paradox,² increasing numbers of studies have shown that determining obesity solely by BMI is incorrect, necessitating more research to identify the contributing components.

According to studies,³⁶ visceral fat, percentage trunk body fat, and projected FVC value in older women are all inversely connected with body fat percentage.

Body fat percentage, is the percentage of body fat in the total body weight that reflects the body's overall body fat content. The location of the deposition within the airway wall may affect the functional effect of airway adipose tissue on lung function.³⁷ A form of fat accumulation that affects lung function in addition to the direct impact of adipose tissue is increased airway wall thickness brought on by localized adipose tissue inflammation. Airway remodeling occurs when there is an excessive buildup of fat, thickening of the airway wall, or infiltration of inflammatory cells as a result of repeated airway injury and stimulation.^{38–40} Chest and abdominal fat buildup may lower lung function,⁴¹ which in turn causes the airway to widen and raise airway resistance. Anatomical evidence of mortality from asthma,³⁷ All subject groups had adipose tissue in their airways, however it was only discovered on the lateral side of the airway wall and was mostly located in medium and large airways. Rarely is adipose tissue seen in the tiny airways. However, more research is required to validate the link between body fat percentage and COPD, and additional fat distribution subdivision is required to investigate the impact of COPD patients. Relevant conclusions in the literature are shown in Table 3, and the literature time is from 2019 to 2020.

Visceral Fat

Human adipose tissue is made up primarily of SAT and VAT. In the human body, VAT primarily surrounds the organs and serves as support and protection. It can also be stored as energy. In recent years, it has been discovered that MetS worsens patients' inflammatory conditions^{42,43} and raises the risk of COPD exacerbation, which lowers FEV1 and FVC.⁴⁴ It is crucial to define the connection between fat distribution and disease since BMI, WC and body fat percentage cannot assess the distribution of body fat because different BMI groups have VAT and BMI values that are not equal.^{15,45} It's essential to establish a connection.

Table 3 Conclusions Related to BFR

Author	Year	Study Design	Country, Latitude Degree	Parameters Under Study	Relevant Conclusion
Ryosuke Kawabata et al ³⁶	2020	Cross-sectional study	Japan	Gender, age, smoking status, weight, FVC, FEV1, BFP, SMI, BMI, VFA, WC, WHR	In the older female group, there was a significantly negative correlation between the predicted FVC% and body composition index ($r = -0.139$, $p = 0.037$ for body fat percentage; $r = -0.138$, $p = 0.039$ for body fat percentage of the trunk; $r = -0.172$, $p = 0.010$ for VFA).
Ohn G. Elliot et al ³⁷	2019	Cross-sectional study	Australian	Gender, age, ever smoked, BMI, weight, age at onset of asthma, duration of asthma, years, corticosteroid use, airway size and the area of adipose tissue within the airway wall	While adipose tissue was identified in airways from all subject groups, it was limited to the outer airway wall and was observed predominantly in large to medium sized airways (>6mm Pbm). Adipose tissue area/Pbm was positively correlated with BMI in all case groups and all airway size groups
Gwen Skloot et al ⁴¹	2019	Cross-sectional study	America	Gender, age, weight, smoking status, BMI, lung function, allergy skin testing	The obese group was characterized by increased Mch reactivity, concentrated in small airways.

Abbreviations: BMI, body mass index; BFP, body fat percentage; WC, waist circumference; WHR, waist circumference-to-height ratio; FEV1, Forced Expiratory Volume in the first second; FVC, Forced Vital Capacity; SMI, skeletal muscle mass index; VFA, Visceral fat area.

One of the significant co-morbidities of COPD is metabolic illness.^{6,46} Stronger respiratory load and lung elastic resistance are needed to preserve muscles with the progression of COPD and the worsening of airway blockage, and the acute phase will More lactic acid and CO₂ are created, which lowers exercise tolerance and increases dyspnea. This process finally results in an excessive buildup of VAT.^{47–49} FEV₁ and FVC were inversely linked with excessive VAT buildup.^{50–52} When serum insulin levels are not right, extra blood glucose gets stored as fat.⁵³

VAT has an adverse effect on the lung because it squeezes the organs and lessens the diaphragm's capacity to collapse during breathing.⁵⁴ This results in decreased respiratory muscle activity⁵⁵ and respiratory limitation. Secondly, a series of inflammation-related factors such as leptin, adiponectin, TNF- α , IL-6, IL-8 etc. are produced by excessive adipose tissue,⁵⁶ which actively contribute to the body's inflammatory reaction process of the organism.^{50,57,58} The aberrant build up of VAT in COPD patients may worsen airway obstruction by decreasing lung compliance, impairing chest wall or diaphragm movement.⁵⁹

VAT that has accumulated abnormally has a metabolic activity that results in the production of numerous inflammatory mediators, such as TNF- α , interleukin (IL)-6, leptin, adiponectin, and others. This can support theories about ectopic fat accumulation and a poor prognosis,⁶⁰ and the release of inflammatory mediators into the blood brought on by VAT will worsen the condition of COPD patients.^{61,62}

Adiponectin and leptin are unique because adiponectin may protect endothelial cells from hyperglycemia, fatty acid, and lipid metabolism disorders through a variety of metabolic, vascular, and protective mechanisms,^{63,64} while lung epithelial cells can stimulate adiponectin to produce anti-inflammatory factors and inhibit inflammatory responses.⁶⁵

Leptin levels on average are inversely correlated with fat mass. Leptin levels that are higher can boost energy expenditure and decrease appetite. When you fast, your body will immediately transmit signals to use less energy.⁶⁶ According to certain research, serum leptin levels are not only inversely connected with FEV₁, but they may also serve as possible indicators of emphysema progression.⁶⁷ Numerous COPD mechanisms, including inflammation,⁶⁸ oxidative stress,⁶⁹ proteinase-antiproteinase imbalance,⁷⁰ and others, are influenced by leptin. But it's not clear what role it plays in the development of COPD, and more research is still needed. Relevant conclusions in the literature are shown in Table 4, and the literature time is from 2011 to 2022.

FFMI

FFMI, an indirect measure of muscle mass, is frequently used to define a condition in which there is abnormally low muscle mass together with impaired muscle strength or function,^{71–73} and FFMI is also a reliable indicator of COPD mortality.^{74,75} Patients with COPD who have abnormally low FFMI have detrimental effects on their ability to exercise, dyspnea, respiratory muscle function, and lung function. They also have a higher chance of dying and longer exacerbations.^{33,76,77} When determining a patient's prognosis for COPD, muscle mass is important.^{4,78} Skeletal muscle loss, muscular wasting, and physical function impairment are twice as common in COPD patients as in the general senior population. In addition to having a lower quality of life, the risk is 17 times more than average.^{79,80}

As the COPD worsens, the body's anaerobic glycolysis of glucose will rise, lactic acid will build up, and metabolic pathway modifications will be triggered, leading to aberrant skeletal muscle function and structure,^{49,81} poor standard of living.^{77,82} Some of the potential causes of muscle dysfunction and structural damage in COPD include muscle atrophy, muscle fiber type, changed metabolism and remodeling of the chest wall, malnutrition, airflow obstruction, and inflammation.^{78,79,83,84}

TNF- α , interleukin, and other pro-inflammatory factors may be released as a result of muscle atrophy and motor unit loss,⁸⁵ but their excessive release will exacerbate structural damage and raise levels of systemic inflammation.⁸⁶ Pro-inflammatory substances including TNF- α and interleukin will also be released due to the decline in protein synthesis and rise in protein breakdown.⁸⁷ In COPD patients, TNF- α The increase of will promote protein decomposition and reduce protein synthesis, and cause the reduction of muscle fibers and the loss of myosin heavy chain, which will directly induce the loss of skeletal muscle protein and reduce exercise endurance.⁸⁸ While activated NF-kB can inhibit the proteasome subunit (in the ubiquitin-proteasome pathway), this will eventually cause skeletal muscle atrophy by reducing the expression of the myoblast-determining protein 1 (MyoD). Therefore, it will affect the evolution and disease status of COPD by boosting the muscle content of COPD patients, avoiding the atrophy of muscle fibers and motor units, and

Table 4 Conclusions Related to VAT

Author	Year	Study Design	Country, Latitude Degree	Parameters Under Study	Relevant Conclusion
Isabelle K Vila et al ⁴²	2022	Randomized controlled trial	France	STING, cGAS, FADS2, delta-6 Desaturase, polyunsaturated fatty acids, interferon responses, cytosolic DNA	While revealing increased glucose uptake in the visceral adipose tissue (VAT), the brown adipose tissue (BAT), and a tendency ($p = 0.08$) in the subcutaneous adipose tissue (SAT), reflecting increased metabolic activity in adipose tissues.
Lucia Baila-Rueda et al ⁴³	2022	Cross-sectional study	Spain	Adipose tissue, 24S-hydroxycholesterol, 27-hydroxycholesterol, oxysterols and cholesterol, total cholesterol, triglycerides, and HDL cholesterol, Apolipoprotein A1, apolipoprotein B, lipoprotein (a), insulin, leptin, glucose, glycated hemoglobin (HbA1c), and high-sensitivity C-reactive protein (hs-CRP) were also measured	Women with higher BMI had lower HDL cholesterol ($P = 0.033$) and apolipoprotein A1 ($P = 0.043$) and higher insulin ($P = 0.037$), HOMA-IR ($P = 0.008$), and HbA1c ($P = 0.024$). An inverse correlation between visceral adipose tissue cholesterol concentration and serum total cholesterol (Spearman's coefficient -0.221).
Justin C Brown et al ⁴⁴	2018	Cross-sectional study	America	Age, height, weight, WC, thigh circumferences, apVAT, BMI, WC	apVAT accounted for more variance in biomarkers of inflammation than BMI ($R^2=3.8\%$; $P<0.001$), WC ($R^2=3.1\%$; $P<0.001$), and BMI+WC ($R^2=2.9\%$; $P<0.001$). apVAT accounted for more variance in biomarkers of lipid metabolism than BMI ($R^2=2.9-9.2\%$; $P<0.001$), WC ($R^2= 2.9-5.2\%$; $P<0.001$), and BMI+WC ($R^2=2.4-4.1\%$; $P = 0.01$).
Lin Ding et al ⁴⁵	2017	Cross-sectional study	China	Age, gender, smoking and drinking status, family history of CAD, educational attainment, height, weight, WC, BMI, physical activity, hypertension, dyslipidemia, and diabetes, VFA, γ -glutamyltranspeptidase (GGT), SAT, liver fat accumulation; subclinical coronary atherosclerosis, 75-goral glucose tolerance test (OGTT)	Most indicators of fat accumulation such as BMI, waist circumference, visceral fat areas, and GGT levels increased significantly with increasing coronary stenosis (all $P < 0.01$), except for subcutaneous fat areas which were similar among groups ($P = 0.487$). One-SD increase in BMI, waist circumference, log (visceral fat areas), and log (GGT levels) was associated with 10%, 3%, 66%, and 55% increase in risks of having $<50\%$ coronary stenosis, respectively.
Ryuko Furutate et al ⁴⁶	2011	Cross-sectional study	Japan	Weight, height, comorbidities, smoking status, WC, BMI. Fat-free mass (FFM) and fat mass (FM), FFMI, lung function, Arterial blood gases, mMRC, The 6-minute walk test, Analysis of emphysema, VFA, SAT, triglyceride, high-density lipoprotein (HDL)-cholesterol, fasting blood glucose	The COPD group ($n = 101$) had a higher smoking index than the control group ($n = 62$). The COPD group had a larger VFA than the control group. VFA was positively correlated with the MMRC scale score ($P = 0.013$, $Rho = 0.252$).
Paula Duarte de Oliveira et al ⁵⁰	2017	Prospective cohort study	Brazil	Gender, skin, birth weight, maternal smoking during pregnancy, schooling, family socioeconomic level, smoking at 30 years, self-reported wheezing in last year, any kind of corticosteroid use in the last 3 months, habitual physical activity, total fat mass, SAT and VAT thicknesses	Women had higher total fat mass compared to men (37.3 versus 24.5%); on the other hand, men had higher mean VAT than women (6.9 versus 4.9 cm). Concerning the spirometry, men had mean FEV1 and FVC 1.1 L and 1.3 L, respectively, higher than women.

Yide Wang et al ⁵²	2021	Cross-sectional study	China	Gender, age and education level, smoking status, medical history, lung function, BMI, Visceral adipose index (VAI)	Males having a significantly higher VAI than females: 13.17 ± 3.91 vs 7.58 ± 2.65 . The piecewise linear spline models indicated a significant threshold effect between lung function and VAI in the general population and the males population, showing an inverted U-shaped curve. But there was no significant association between VAI and lung function in females. FEV1% predicted and FVC% predicted increased with the increase of VAI (β 0.76; 95% CI 0.30, 1.21) and (β 0.50; 95% CI 0.06, 0.94) in males with $VAI \leq 14$, while FEV1% predicted and FVC% predicted decreased with the increase of VAI (β -1.17; 95% CI -1.90, -0.45) and (β -1.36; 95% CI - 2.08, - 0.64) in males with $VAI \geq 15$.
Alvar Agustí et al ⁵⁵	2012	Cohort studies	Spain	Lung function, smoking status, BMI, FFMI, 6 MWD, BODE index. Circulating WBC count, IL-6, IL-8 and TNF- α	On average the WBC count and levels of CRP, IL-6 and fibrinogen were significantly higher in COPD patients than in smokers with normal lung function and nonsmokers, whereas IL-8 and TNF- α values were higher in smokers without COPD. In patients with COPD, the WBC count and the serum levels of CRP, IL-6 and fibrinogen, but not those of IL-8 and TNF- α , tended to increase with the severity of airflow limitation.
Damien Viglino et al ⁵⁸	2020	Prospective study	Canada	Age, gender, smoking status, weight, height, WC, Pittsburgh Sleep Quality Index, hip circumferences, glucose, lipid profiles, lung function, VAT, Blood sample and biochemical analysis	Triglycerides, total/HDL cholesterol ratio and HOMA-IR were positively associated with the three indices of adiposity (BMI, waist-to-hip ratio and VAT area) in individuals with COPD and controls. (all regression lines with a $p < 0.05$). The COPD 2+ status was associated with a VAT area >75th percentile (OR = 2.27, CI 95% 1.00; 5.15, $p = 0.05$).

Abbreviations: STING, stimulator of interferon genes; cGAS, Cyclic GMP-AMP synthetase; FADS2, Polyclonal Antibody to Fatty Acid Desaturase 2; VAT,⁴² visceral adipose tissue; BAT, the brown adipose tissue; SAT,⁴² subcutaneous adipose tissue; HbA1c, glycated hemoglobin; hs-CRP, high-sensitivity C-reactive protein; BMI, body mass index; HDL, high-density lipoprotein; VAT,^{44,46} Visceral fat; WC, waist circumference; FFM, fat-free mass; FM, fat mass; FFMI, Fat-free mass index; SAT,⁴⁶ subcutaneous fat; VFA, Visceral fat area; 6 MWD, Six Minute Walk Distance; IL-6, interleukin 6; IL-8, interleukin 8; TNF- α , Tumor necrosis factor - α .

promoting protein synthesis. Nutritional support rehabilitation techniques will be a significant type of intervention for stable COPD. Relevant conclusions in the literature are shown in Table 5, and the literature period is from 2016 to 2021.

Body Water

ECW and ICW make up body water, and BIA may directly detect electrical resistance and reactance in the body, which represents the movement of fluid between the two compartments. Increased ECW/ICW has been linked to an increased risk of cardiovascular disease, stroke, myocardial infarction, and all-cause mortality in dialysis patients, according to studies.^{89–93} Although skeletal muscle accounts for a sizable amount of ICW, decreased ICW and a greater ECW/ICW ratio point to a reduction in skeletal muscle cells.^{94,95}

Low ICW values are also linked to an increased risk of death,⁹⁶ organ aging, and signs and symptoms of sarcopenia.^{97,98} ICW is favorably correlated with muscle mass markers such as serum creatinine and mid-upper arm muscular circumference and negatively correlated with inflammation. Since muscles and internal organs contain roughly 75% water, this can reveal an aberrant iso-water distribution status. In one investigation, pulmonary edema and pleural effusion in individuals with renal illness were linked to fluid overload and pulmonary capillary permeability; this association may explain why patients with end-stage renal disease have diminished lung function.⁹⁹

Increased ECW/ICW and lower extremity water are linked to exercise intolerance in COPD patients, and alterations in cellular hydration status may have an impact on how well their skeletal muscles use oxygen.¹⁰⁰ The ECW/ICW ratio is also negatively correlated with peak oxygen consumption in COPD patients. In COPD patients with sarcopenia,⁹⁹ and much more so in those with severe sarcopenia,¹⁰¹ the ECW/ICW ratio is elevated.

The systemic inflammation in COPD patients may be the source of the cellular hydration state, and the ECW/ICW ratio can indicate the cellular hydration status. Studies have revealed a negative correlation between the plasma total adiponectin level and the ICW value in COPD patients as well as the ECW/ICW ratio.⁹⁴ A positive association suggests that two points are mostly responsible for the modifications in cellular metabolism brought on by the decline in plasma adiponectin levels. One is the possibility that cell contraction could promote or prevent cell anabolic processes.⁹⁴ Skeletal muscle is the second type. Protein catabolism produced by decreased cellular hydration may lower creatine phosphate reserves in the skeletal muscle of COPD patients, and protein catabolism itself may be a crucial indicator of protein catabolism in a number of disorders.⁹⁵

Apoptosis, a morphological indicator of programmed cell death that may also be related to cell shrinkage, regulates cell volume.¹⁰² However, few research have examined how individuals with COPD are affected by their body fluid distribution and hydration status, and these connections have not yet been confirmed. Early diagnosis of body fluid issues can be used to inform clinical judgment at the earliest possible stage of the disease, so that COPD patients' illness condition can be improved as soon as possible. Relevant conclusions in the literature are shown in Table 6, and the literature period is from 1997 to 2021.

PhA

In BIA, PhA is a crucial measuring index that is now recognized as a crucial health indicator.¹⁰³ Although the biological significance of PhA is not fully understood, it is thought to be a marker of changes in soft tissue quantity and quality as well as cell membrane function (permeability, electrical properties).^{104,105} The value of the PhA is primarily determined by the size of the cell membrane capacitive reactance, which can assess the body's nutritional status, survival, and prognosis.^{103,106–109} It is a measure of cell health and integrity, intracellular and ECW distribution.^{110,111} Additionally, it can be used to evaluate the consistency and efficiency of cells. Condition, which can increase energy and physical performance, is the body part that is most metabolically active.¹¹²

PhA is strongly connected with fat mass, nutritional state, muscle function, mortality, and prognosis, according to studies.^{113–116} A low PhA was also associated with a higher risk of mortality.¹¹⁷ Men were more likely to have a low PhA than women (4.9 (1.0) vs 4.3 (0.9); $p < 0.001$),¹¹⁸ and it was inversely correlated with age and the severity of the disease ($r = 0.37$, $p < 0.001$),¹¹⁹ PhA has been discovered to be significantly higher in overweight people¹¹⁶ and recent research reveals that PhA and FEV1 are positively associated.¹¹⁹ However, research has showed that PhA levels drop after muscle damage, suggesting that changes in bodily fluids occur along with cell membrane failure. In general, high PhA indicates

Table 5 Conclusions Related to FFMI

Author	Year	Study Design	Country, Latitude Degree	Parameters Under Study	Relevant Conclusion
Afsane Ahmad et al ⁷²	2021	Cross-sectional study	Iran	Age, educational degree, job circumstances, smoking habits, type of tobacco used and age of onset, smoking status, medical history, researchers. Spirometry test, weight, weight loss%, dietary intake, gastrointestinal symptoms, functional capacity, respiratory stress, physical examination, calf circumference (CC), FFM, FFMI	The results of univariate analysis showed muscle mass (p=0.036), total protein (p=0.043), FFM (p=0.047), FFMI (p=0.007), SGA (p=0.029), right handgrip strength (p=0.004) and left hand grip strength (p=0.023) were associated with FEV1. In addition, the results of multivariate analysis demonstrated low values of FFMI (p=0.005) and right handgrip strength (p=0.042) were the main detrimental factors for FEV1. The results of multivariate analysis were confirmed by stepwise model.
Jamie R Chua et al ⁷³	2019	Cross-sectional study	Philippines	Demographic, BMI, health information, body composition, grip strength, six-minute walking distance, FEV1, FEV1/FVC, PIF, PEF, CAT	Sarcopenic COPD patients had statistically significant reduced peak inspiratory flow (r= -0.6074, P value 0.0001), peak expiratory flow (r= -0.3993, P value 0.0144), hand grip strength (r= -0.3751, P value 0.0007), and CAT score (r= -0.3751, P value 0.0157) compared to non-sarcopenic patients. Low FFMI had statistically significant reduction in PIF (r= -0.5791, P value 0.0002), PEF (r= -0.4475, P value 0.0055), and hand grip strength (r= -0.4560, P value 0.0027), however low CAT score (r= -0.3422, P value 0.0285).
M. FEKETE et al ⁷⁵	2021	Cross-sectional study	Hungary	Weight, BMI, FFM, Malnutrition Universal Screening Tool (MUST), body mass, body fat percentage, muscle percentage, water content, 6MWD, Spirometry, quality of life, the Saint George's Respiratory Questionnaire (SGRQ-C), mMRC, CAT	Respiratory distress was more frequent in patients with low FFMI compared to those with normal FFMI (FEV1ref%: 38.9 versus 48.6, P 5 0.023), FFMI was significantly correlated with FEV1 (r 5 0.370, P < 0.001) and 6MWD as well (r 5 0.531, P < 0.001), as shown in Table 6. We found a statistically significant relationship between CAT points and FFMI (r=5 0.4906, P 5=0.0003) and CAT points with SMMI (r=5 0.4532, P 5=0.0009).
Ester Marco et al ⁷⁶	2018	Prospective cohort study	Spain	Age, sex, smoking history, the Mini Nutritional Assessment Short Form (MNA-SF), BMI, FFMI, the number of admissions and days of stay during the follow up period, mMRC, 6 MWT, lung function, body composition	The total number of days spent in the hospital during this period was significantly higher in patients with malnutrition: median (P25, P75) of 18 (1, 53.5) days in malnourished patients, compared to in front of 9 (3, 20.5) days in patients without malnutrition (p ¼ 0.041).

(Continued)

Table 5 (Continued).

Author	Year	Study Design	Country, Latitude Degree	Parameters Under Study	Relevant Conclusion
HIANG PING CHAN et al ⁸⁰	2016	Prospective cohort study	Singapore	Gender, race, age, FEV1, FVC, BMI, airflow obstruction, St George's Respiratory Questionnaire and age (BOSA), 10-point index (BOSA index), all-cause mortality, SGRQ	Mortality increases with worse BOSA grades, and that race and gender did not affect mortality.
Paula Portal Teixeira et al ⁸²	2022	Prospective cohort study	Brazil	Age, gender, ethnicity, education levels, smoking habit and morbidity history, FFMI, calf circumference (CC), adductor muscle pollicis thickness (AMPT), C-reactive protein (CRP), mMRC	Low FFMI, and CC predicted malnutrition (low CC; OR = 4.6; 95% CI, 2.2–9.7 and low FFMI; OR = 8.8, 95% CI, 3.7–20.8).
Zinka Matkovic et al ⁸⁵	2017	Cross-sectional study	Spain	Age, sex, smoking history, treatment recorded, COPD exacerbations in the previous year, BMI, WC, hip, calf circumference (CC), WHR, mid-upper arm circumference (MUAC), triceps skin fold (TSF), mid-arm muscle circumference (MAMC)	Regarding nutritional status, patients with low exercise capacity had a lower LMI, FFMI, BMC, BMD ($p < 0.01$), and T-score ($p < 0.05$). Similar to patients with low exercise capacity, patients with low physical activity (7128 steps/day) were significantly older, had worse lung function, a higher CAT score and mMRC dyspnoea grade, more frequent exacerbations and worse health related quality of life. They also had a slower gait speed and shorter 6MWD ($p < 0.01$).

Abbreviations: CC, calf circumference; FFM, fat-free mass; FM, fat mass; FFMI, Fat-free mass index; FEV1, Forced Expiratory Volume in the first second; FVC, Forced Vital Capacity; PIF peak inspiratory flow; PEF, peak expiratory flow; BMI, body mass index; COPD, chronic obstructive pulmonary disease; MUST, Malnutrition Universal Screening Tool; 6 MWD, Six Minute Walk Distance; SGRQ-C, the Saint George's Respiratory Questionnaire; MNA-SF, the Mini Nutritional Assessment Short Form; AMPT, adductor muscle pollicis thickness; CRP, C-reactive protein; MUAC, mid-upper arm circumference; TSF, triceps skin fold; MAMC, mid-arm muscle circumference; LMI, lean mass index; BMC, bone mass content; BMD, bone mineral density.

Table 6 Conclusions Related to Body Water

Author	Year	Study Design	Country, Latitude Degree	Parameters Under Study	Relevant Conclusion
Takahiro Yoshikawa et al ⁹⁴	2012	Cross-sectional study	Japan	Age, plasma, high molecular weight (HMW), adiponectin. ICW, ECW, ECW/ICW ratio, physical examinations, anthropometric, measurements, BMI, assessment of lung function, blood sampling	Regarding the state of cellular hydration, the plasma levels of total adiponectin were inversely correlated with the ECW/ICW ratio and positively with ICW values in patients with COPD. TNF- α levels were closely correlated with total adiponectin levels in COPD patients ($r = 0.75$, $P < 0.001$).
E.M. Baarends et al ¹⁰⁰	1997	Cross-sectional study	Netherlands	Age, lung function, BMI, TBW, ECW, ICW, FFM, FM%, ECW/TBW	The transfer factor of the lung for carbon monoxide (TL, CO) intrathoracic gas volume (ITGV), maximal expiratory and inspiratory mouth pressure, forced expiratory volume in one second (FEV1), FFM-index (FFM/height ²), body mass index (weight/height ²) and ICW-index correlated strongly ($p < 0.01$) to peak oxygen consumption ($V \dot{O}_2$). The ratio ECW/ICW correlated only weakly, but significantly, with peak $V \dot{O}_2$ ($r = -0.25$, $p < 0.05$). The results of this study further more indicate that severe FFM depletion is related to a blunted tidal volume response to peak exercise, a decreased peak oxygen pulse and an early anaerobic metabolism in patients with COPD.
Francesca de Blasio et al ¹⁰¹	2017	Cross-sectional study	Italy	Age, height, weight, BMI, 4 m gait speed, lung function, FFM, FFMI, FM, SM, Albumin, C-reactive protein, 250kHz/5 kHz, Ph A, Albumin	The overall prevalence of malnutrition and sarcopenia was 19.8% and 24.0% respectively, increasing with disease severity. The prevalence of sarcopenia was significantly higher in patients with malnutrition (71.2% vs 12.3%; $p < 0.001$), especially in those with systemic inflammation (cachectic patients) (85.7% vs 61.3%; $p < 0.001$). Malnourished patients with sarcopenia had a significant reduction in BMI, fat-free mass and HGS compared to non-sarcopenic patients. Finally, impedance ratio significantly increased and phase angle decreased in patients with severe sarcopenia and in cachectic patients.
Roohi Chhabra et al ¹⁰²	2021	Prospective cohort study	British	Age, gender, Dialysis months, No BP meds, Clinical Frailty score, Davies grade, weight, BMI, TBW, ECW, ICW, FFM, FM%, ECW/TBW	More patients in the lower predialysis serum sodium cohort had diabetes, greater frailty scores, higher CRP, and higher ratios of both ECW/ICW and ECW/TBW, with lower serum creatinine, LMI and right arm lean mass, and muscle strength. ECW/TBW (0.409 ± 0.016 vs 0.402 ± 0.016 , $p < 0.01$), C reactive protein (CRP) (9 (4–6) vs 5 (2–12) g/L, $p < 0.05$), CFS (5 (4–6) vs 4 (3–6), $p < 0.05$) were higher.

Abbreviations: HMW, high molecular weight; ICW, intracellular water; ECW, extracellular water; BMI, body mass index; TBW, total body water; FFM, fat-free mass; FM, fat mass; SM, Skeletal Muscle; PhA, phase angle; LMI, lean mass index; CFS, Clinical Frailty score; CRP, C-reactive protein.

the integrity of the cell membrane, whereas low PhA suggests cell death or diminished function,¹²⁰ as well as inadequate nourishment and a poor prognosis for illness.¹⁰¹ Muscle deterioration and poor nutrition are frequent side effects of COPD. PhA has not yet been proven to be a reliable prognostic sign of the illness. Early diagnosis of the condition and muscle atrophy in these indications can offer trustworthy proof for the prognosis and treatment of COPD. Relevant conclusions in the literature are shown in [Table 7](#), and the literature period is from 2015 to 2022.

Table 7 Conclusions Related to PhA

Author	Year	Study Design	Country, Latitude Degree	Parameters Under Study	Relevant Conclusion
Giliane Belarmino et al ¹⁰⁷	2017	Prospective Study	Brazil	Age, weight, height, Severe ascites (%), Model for endstage liver disease score, Encephalopathy (%), BMI, Midarm muscle circumference (cm), IL-6/IL-10 ratio (pg/mL), Handgrip strength (kg), Albumin (g/dL)	Patients from the PA > 4.9° group were younger and had higher MAMC, albumin, and ND-HGS values and lower severe ascites and encephalopathy incidences, IL-6/IL-10 ratios, and CRP levels than did patients from the PA ≤ 4.9° group. The PA ≤ 4.9° group were significantly more likely to die, as demonstrated by Kaplan-Meier curves.
Büntzel J et al ¹⁰⁸	2019	Prospective Study	Germany	Gender, age, BMI, SD, PA, Median survival (mo)	Patients with a PA>5° showed a significantly better overall survival (p=0.016; Figure 1). Median survival in this group was 51.16 months (range=7.02–116.79 months), while median survival of malnourished patients was 13.84 months (range=0.69–125.19 months).
M. Dittmar I et al ¹¹²	2015	Cross-sectional study	British	Age, weight, height, BMI, Resistanc, PhA, the total body potassium measurement, 5, 50 and 100 kHz he resistance, reactance and phase angle at three frequencies	The phase angle at 100 kHz strongly correlated with total body potassium (r = 0.70, P = 0.001). The phase angle at 100kHz discriminated more strongly between patients with Type 2 diabetes and control subjects than did the phase angle at 50 kHz. Phase angle ratios better discriminated between patients and control subjects than phase angles alone (phase angle at 5 kHz/phase angle at 50 kHz ratio, P = 1.51 9 10 16; phase angle at 5kHz/phase angle at 100 kHz ratio, P = 2.13 9 10).
Laurence Genton et al ¹¹³	2016	Retrospective study	Switzerland	Age, weight, height, BMI, PhA, impedance, resistance, reactance, FFM, CIRS, Comorbidities, medication, lung function	When replacing sex-specific phase angle quartiles by sex-specific FFMI quartiles in models 1 and 2, the R2 (95% CI) decreased from 15.6 (11.4, 27.2) to 8.6 (3.8, 16.5) in women and from 21.5 (17.1, 29.2) to 14.2 (9.4, 20.2) in men. The addition of sex-specific FFMI quartiles to models 1 and 2 led to an R2 (95% CI) of 15.1 (11.7, 28.0) in women and 21.3 (17.4, 29.7) in men. Thus, the phase angle better predicts mortality than BIA-derived FFMI, and the addition of FFMI to phase angle does not improve the Cox regression models. Kaplan-Meier analyses 160 showed the higher risk of mortality with lower phase angle or 161 standardized phase angle quartiles

(Continued)

Table 7 (Continued).

Author	Year	Study Design	Country, Latitude Degree	Parameters Under Study	Relevant Conclusion
F de Blasio et al ¹¹⁸	2017	Cross-sectional study	Italy	Age, sex, height, weight, BMI, FEV1, Impedance, Bioimpedance index, PhA, Handgrip strength, FFMI, FM, FFM, BODE index	An inverse correlation between PhA and BODE index was observed both in males ($r = -0.343$, $P < 0.001$) and females ($r = -0.358$, $P < 0.01$), whereas a marked decline across GOLD stages was observed only in males (5.37 ± 0.89 , 5.00 ± 0.92 and 4.82 ± 0.99 degrees in stages I/II, III and IV, respectively). With respect to respiratory muscle strength, there was in both genders a significant association of MIP or MEP with BIA estimates of FFM, and also with PhA (for MEP only in males).
Nathalie Martínez-Luna et al ¹¹⁸	2022	Cross-sectional study	America	Age, sex, height, weight, diabetes, Hypertension, smoking status, Heart failure, Hospitalization previous year, BMI, lung function, Flmpedance, Bioimpedance index, PhA, Handgrip strength, FFMI, FM, FFM, SMMI, BODE index, Exercise tolerance	A linear regression adjusted model showed associations between body mass index, fat-free mass, skeletal muscle mass index, appendicular skeletal muscle mass index, and phase angle (PhA), and sarcopenia with FEV1 (%). As regards FVC (%), PhA and exercise tolerance had positive associations.

Abbreviations: BMI, body mass index; PA, prealbumin; PhA, phase angle; FFM, fat-free mass; FM, fat mass; FEV1, Forced Expiratory Volume in the first second; FVC, Forced Vital Capacity.

Conclusions and Prospects

Obesity and COPD are both major global health issues, and a higher percentage of patients with COPD are overweight or obese than previously assumed. Abnormal lipid metabolism can lower immunity, airway repair, and remodeling function in COPD patients, and excessive fat buildup can lead to metabolic abnormalities and exacerbate the inflammatory state. Using a single measure and ignoring body composition (such as fat distribution or muscle content), lacking the assessment of fat distribution, visceral fat index and inflammation level related to fat metabolism may miss the association between these factors and increased disease risk. The relationship between the composition, structure, and distribution of the body and COPD is further employed to assess the outcome and prognosis of the disease in comparison to BMI, WHR, and other readily accessible measuring indicators. Finding out how changes in body composition impact the disease process of COPD, as well as further elucidating the association between body composition and COPD, may help researchers come up with new ideas for the diagnosis, treatment, prognosis, and outcome of COPD, whether it will develop into a novel research procedure for the treatment of COPD, whether it may alleviate clinical symptoms and stop disease progression by controlling the body composition structure of COPD patients.

Abbreviations

COPD, Chronic obstructive pulmonary disease; BMI, body mass index; WC, Waist Circumference; WHR, Waist-to-hip Ratio; WHtR, Waist-to-height Ratio; BFP, Body Fat Percentage; ADPN, circulating adiponectin; SAT, subcutaneous fat; VAT, visceral fat; MetS, metabolic syndrome; FFMI, Fat-free mass index; TNF- α , Tumor necrosis factor - α ; ECW, extracellular water; ICW, intracellular water; BIA, bioelectrical impedance analysis; PhA, phase angle; 6 MWD, Six Minute Walk Distance; IL-6, Interleukin 6; IL-8, Interleukin 8.

Acknowledgments

We thank all those who participated in the data collection and revision of the article.

Funding

This study is supported by National Natural Science Foundation of China (82060803), Xinjiang Medical University Graduate Innovation and Entrepreneurship Project (CXCY2022027) and Urumqi Science and Technology Talents Project (2019).

Disclosure

The authors declare that there is no conflict of interests regarding the publication of this paper.

References

- Muneswarao J, Verma AK, Hassali MA. Global initiative for chronic obstructive lung disease (GOLD) 2018 report: highlighting an incorrect information. *Pulm Pharmacol Ther*. 2017;2017:S1094553917303139.
- Jahangir E, Schutter AD, Lavie CJ. Low weight and overweightness in older adults: risk and clinical management. *Prog Cardiovasc Dis*. 2014;57(2):127–133. doi:10.1016/j.pcad.2014.01.001
- Yang L, Drake BF, Colditz GA. Obesity and other cancers. *J Clin Oncol*. 2016;34(35):4231–4237. doi:10.1200/JCO.2016.68.4837
- Graumam RQ, Pinheiro MM, Nery LE, Castro C. Increased rate of osteoporosis, low lean mass, and fragility fractures in COPD patients: association with disease severity. *Osteoporos Int*. 2018;2018:1.
- Verberne L, Leemrijse CJ, Swinkels I, Dijk CV, Bakker DD, Nielen M. Overweight in patients with chronic obstructive pulmonary disease needs more attention: a cross-sectional study in general practice. *Npj Prim Care Respir Med*. 2017;27(1):63.
- Wouters E. Obesity and metabolic abnormalities in chronic obstructive pulmonary disease. *Ann Am Thorac Soc*. 2017;14(Supplement_5):S389–S394.
- Huang L, Luo FM. Research progress on the relationship between obesity and pulmonary function in chronic obstructive pulmonary disease. *Chin J Tuberc Respir Med*. 2019;2019(11):862–864.
- Kirsch F, Schramm A, Kurz C, Schwarzkopf L, Leidl R. Effect of BMI on health care expenditures stratified by COPD GOLD severity grades: results from the LQ-DMP study. *Respir Med*. 2020;175:14.
- Stoll P, Foerster S, Virchow JC, Lommatzsch M. Overweight is a predictor of long-term survival in hospitalised patients with exacerbations of COPD. *Respir Med*. 2016;2016:59–62.
- Yang L, Zhu Y, Huang JA, Jin J, Zhang X. A low lean-to-fat ratio reduces the risk of acute exacerbation of chronic obstructive pulmonary disease in patients with a normal or low body mass index. *Med Sci Monit*. 2019;25:5229–5236. doi:10.12659/MSM.914783
- Kim EK, Singh D, Park JH, Park YB, Kim S-I. Impact of body mass index change on the prognosis of chronic obstructive pulmonary disease. *Respiration*. 2020;99(11):1–11. doi:10.1159/000511022
- Park HJ, Cho JH, Kim HJ, Park J-Y, Lee HS, Byun MK. The effect of low body mass index on the development of chronic obstructive pulmonary disease and mortality. *J Intern Med*. 2019;286(5):5. doi:10.1111/joim.12949
- Varga JT. Smoking and pulmonary complications: respiratory prehabilitation. *J Thorac Dis*. 2019;11(S5):S639–S644. doi:10.21037/jtd.2018.12.11
- Avã GL, Rozgonyi Z, Pvdã S, Varga JT. A mellkassebészeti mütéti teherbíró képesség megítélése, perioperatív légzésrehabilitáció[Risk stratification before thoracic surgery, perioperative pulmonary rehabilitation]. *Orv Hetil*. 2017;2017:1989–1997. Hungarian.
- Martin M, Almeras N, Després J-P, et al. Ectopic fat accumulation in patients with COPD: an ECLIPSE substudy. *Int J Chron Obstruct Pulm Dis*. 2017;12:451–460. doi:10.2147/COPD.S124750
- Li C, Guo P, Zhang R, et al. Both WHR and FLI as better algorithms for both lean and overweight/obese NAFLD in a Chinese population. *J Clin Gastroenterol*. 2018;53:1.
- Mahmoud I, Sulaiman N. Significance and agreement between obesity anthropometric measurements and indices in adults: a population-based study from the United Arab Emirates. *BMC Public Health*. 2021;2021:1.
- Green HD, Beaumont RN, Wood AR, Hamilton B, Jones SE. Genetic evidence that higher central adiposity causes gastro-oesophageal reflux disease: a Mendelian randomization study. *Int J Epidemiol*. 2020;49(4):4. doi:10.1093/ije/dyaa082
- Berntsson J, Eberhard J, Nodin B, Leandersson K, Larsson AH, Jirstrom K. Pre-diagnostic anthropometry, sex, and risk of colorectal cancer according to tumor immune cell composition. *Oncol Immunology*. 2019;8(12):1664275. doi:10.1080/2162402X.2019.1664275
- Li J, Zhu L, Wei Y, et al. Association between adiposity measures and COPD risk in Chinese adults. *Eur Respir J*. 2020;55(4):1901899. doi:10.1183/13993003.01899-2019
- Behrens G, Matthews CE, Moore SC, Hollenbeck AR, Leitzmann MF. Body size and physical activity in relation to incidence of chronic obstructive pulmonary disease. *CMAJ*. 2014;186(12):E457. doi:10.1503/cmaj.140025
- Vatrella A, Calabrese C, Mattiello A, et al. Abdominal adiposity is an early marker of pulmonary function impairment: findings from a Mediterranean Italian female cohort. *Nutr Metab Cardiovasc Dis*. 2016;26(7):643–648. doi:10.1016/j.numecd.2015.12.013
- Jayedi A, Soltani S, Zargar MS, Khan TA, Shab-Bidar S. Central fatness and risk of all cause mortality: systematic review and dose-response meta-analysis of 72 prospective cohort studies. *BMJ*. 2020;370:1.
- Stefan N, Schick F, Ring H-U. Causes, characteristics, and consequences of metabolically unhealthy normal weight in humans. *Cell Metab*. 2017;26(2):292–300. doi:10.1016/j.cmet.2017.07.008
- Emdin CA, Khera AV, Natarajan P, et al. Genetic association of waist-to-hip ratio with cardiometabolic traits, type 2 diabetes, and coronary heart disease. *JAMA*. 2017;317(6):626–634. doi:10.1001/jama.2016.21042
- Streng KW, Voors AA, Hillege HL, et al. Waist-to-hip ratio and mortality in heart failure. *Eur J Heart Fail*. 2018;20(9):9. doi:10.1002/ejhf.1244
- Xuan DU, Khemayanto H, Bi-Min S. Abdominal obesity and gastroesophageal cancer risk: systematic review and meta-analysis of prospective studies. *Biosci Rep*. 2017;37:3.

28. Pang Y, Kartsonaki C, Guo Y, et al. Central adiposity in relation to risk of liver cancer in Chinese adults: a prospective study of 0.5 million people. *Int J Cancer*. 2019;2019:1.
29. Xue R, Li Q, Geng Y, Wang H, Zhang S. Abdominal obesity and risk of cardiovascular disease: a dose-response meta-analysis of 31 prospective studies. *Br J Nutr*. 2021;2021:1–31.
30. Marchioro J, Gazzotti MR, Moreira GL, et al. Anthropometric status of individuals with COPD in the city of São Paulo, Brazil, over time - analysis of a population-based study. *J Bras Pneumol*. 2019;45(6):e20170157. doi:10.1590/1806-3713/e20170157
31. Brooks GC, Blaha MJ, Blumenthal RS. Relation of C-reactive protein to abdominal adiposity. *Am J Cardiol*. 2010;106(1):56–61. doi:10.1016/j.amjcard.2010.02.017
32. Caspersen NF, Røsjø H, Flyvbjerg A. The association between circulating adiponectin levels, lung function and adiposity in subjects from the general population; data from the Akershus sleep apnea project. *BMC Pulm Med*. 2018;18(1):54. doi:10.1186/s12890-018-0618-4
33. Hsu Y-E, Chen S-C, Geng J-H, Wu D-W, Wu P-Y, Huang J-C. Obesity-related indices are associated with longitudinal changes in lung function: a large Taiwanese population follow-up study. *Nutrients*. 2021;13(11):11. doi:10.3390/nu13114055
34. Urban MH, Ay L, Funk G-C, et al. Insulinresistenz bei Patienten mit COPD möglicherweise an vaskulärer Dysfunktion beteiligt. *Wien Klin Wochenschr*. 2014;126(3–4):106–112. doi:10.1007/s00508-013-0478-0
35. He H, Wang B, Zhou M, et al. Systemic inflammation mediates the associations between abdominal obesity indices and lung function decline in a Chinese general population. *Diabetes Metab Syndr Obes*. 2020;2020:1.
36. Kawabata R, Soma Y, Kudo Y, et al. Relationships between body composition and pulmonary function in a community-dwelling population in Japan. *PLoS One*. 2020;15(11):e0242308. doi:10.1371/journal.pone.0242308
37. Elliot JG, Donovan GM, Wang KCW, Green FHY, James AL, Noble PB. Fatty airways: implications for obstructive disease. *Eur Respir J*. 2019;54(6):6. doi:10.1183/13993003.00857-2019
38. Liu Y, Wei L, He C, Chen R, Meng L. Lipoxin A4 inhibits ovalbumin-induced airway inflammation and airway remodeling in a mouse model of asthma. *Chem Biol Interact*. 2021;349:109660. doi:10.1016/j.cbi.2021.109660
39. Hirota N, Martin JG. Mechanisms of airway remodeling. *Chest*. 2013;144(3):1026–1032. doi:10.1378/chest.12-3073
40. Karakioulaki M, Papakonstantinou E, Stolz D. Extracellular matrix remodeling in COPD. *Eur Respir Rev*. 2020;29(158):190124.
41. Skloot G, Schechter C, Desai A, Toggias A. Impaired response to deep inspiration in obesity. *J Appl Physiol*. 2011;82(3):726–734.
42. Vila IK, Chamma H, Steer A, et al. STING orchestrates the crosstalk between polyunsaturated fatty acid metabolism and inflammatory responses. *Cell Metab*. 2022;34(1):125–139.e128.
43. Lucia BR, Ana C, Itziar LM, et al. Association of cholesterol and oxysterols in adipose tissue with obesity and metabolic syndrome traits. *J Clin Endocrinol Metab*. 2022;2022(9):9.
44. Brown JC, Harhay MO, Harhay MN. Anthropometrically predicted visceral adipose tissue and blood-based biomarkers: a cross-sectional analysis. *Eur J Nutr*. 2016;2016:1.
45. Ding L, Peng K, Lin L, et al. The impact of fat distribution on subclinical coronary atherosclerosis in middle-aged Chinese adults. *Int J Cardiol*. 2017;235:118–123.
46. Furutate R, Ishii T, Wakabayashi R, et al. Excessive visceral fat accumulation in advanced chronic obstructive pulmonary disease. *Int J Chron Obstruct Pulmon Dis*. 2011;6:423–430.
47. Ogawa E, Nakano Y, Ohara T, et al. Body mass index in male patients with COPD: correlation with low attenuation areas on CT. *Thorax*. 2009;64(1):20–25.
48. Ferté JB, Boyer FC, Taiar R, Pineau C, Barbe C, Rapin A. Impact of resistance training on the 6-minute walk test in individuals with chronic obstructive pulmonary disease: a systematic review and meta-analysis. *Ann Phys Rehabil Med*. 2022;65(3):101582.
49. Yan XJ, Li FS, Xu D, et al. Study on the content of skeletal muscle in patients with chronic obstructive pulmonary disease with different viscera deficiency in stable stage. *World Sci Technol*. 2018;20(2):4.
50. de Oliveira PD, Wehrmeister FC, Horta BL, et al. Visceral and subcutaneous abdominal adiposity and pulmonary function in 30-year-old adults: a cross-sectional analysis nested in a birth cohort. *BMC Pulm Med*. 2017;17(1):157.
51. Choe EK, Kang HY, Lee Y, Choi SH, Kim HJ, Kim JS. The longitudinal association between changes in lung function and changes in abdominal visceral obesity in Korean non-smokers. *PLoS One*. 2018;13(2):e0193516.
52. Wang Y, Li Z, Li F. Nonlinear relationship between visceral adiposity index and lung function: a population-based study. *Respir Res*. 2021;22(1):161.
53. Singh S, Bodas M, Bhatraju NK, et al. Hyperinsulinemia adversely affects lung structure and function. *Am J Physiol Lung Cell Mol Physiol*. 2016;310(9):L837–845.
54. Taniguchi A, Tsuge M, Miyahara N, Tsukahara H. Reactive oxygen species and antioxidative defense in chronic obstructive pulmonary disease. *Antioxidants*. 2021;10:10.
55. Agustí A, Edwards LD, Rennard SI, et al. Persistent systemic inflammation is associated with poor clinical outcomes in COPD: a novel phenotype. *PLoS One*. 2012;7(5):e37483.
56. van den Borst B, Gosker HR, Wesseling G, et al. Low-grade adipose tissue inflammation in patients with mild-to-moderate chronic obstructive pulmonary disease. *Am J Clin Nutr*. 2011;94(6):1504–1512.
57. Choe EK, Kang HY, Lee Y, Choi SH, Kim HJ, Kim JS. Longitudinal associations between abdominal obesity and lung function using a linear mixed model. *PLoS One*. 2018;13(2):e0193516.
58. Moualla M, Qualls C, Arynchyn A, et al. Rapid decline in lung function is temporally associated with greater metabolically active adiposity in a longitudinal study of healthy adults. *Thorax*. 2017;72(12):1113–1120.
59. Viglino D, Martin M, Piché ME, et al. Metabolic profiles among COPD and controls in the CanCOLD population-based cohort. *PLoS One*. 2020;15(4):e0231072.
60. Soler-Catalua JJ, Jose J, Catalua S. Severe acute exacerbations and mortality in patients with chronic obstructive pulmonary disease institution at which the work was carried out: licence. *Thorax*. 2005;60(11):925–931.
61. Wynn TA, Chawla A, Pollard JW. Macrophage biology in development, homeostasis and disease. *Nature*. 2013;496(7446):445–455.
62. Escors D. *Differentiation of Murine Myeloid-Derived Suppressor Cells*. Springer International Publishing; 2016.

63. Cheng K, Lam K, Wang Y, et al. Erratum. Adiponectin-induced endothelial nitric oxide synthase activation and nitric oxide production are mediated by APPL1 in endothelial cells. *Diabetes*. 2016;65(10):3218.
64. Stern JH, Rutkowski JM, Scherer PE. Adiponectin, leptin, and fatty acids in the maintenance of metabolic homeostasis through adipose tissue crosstalk. *Cell Metab*. 2016;23(5):770–784.
65. Carolan BJ, Kim YI, Williams AA, et al. The association of adiponectin with computed tomography phenotypes in chronic obstructive pulmonary disease. *Am J Respir Crit Care Med*. 2013;188(5):561–566.
66. Jeffrey F. Starvation in the midst of plenty: reflections on the history and biology of insulin and leptin. *Endocr Rev*. 2018;2018:1.
67. Oh YM, Jeong BH, Woo SY, et al. Association of plasma adipokines with chronic obstructive pulmonary disease severity and progression. *Ann Am Thorac Soc*. 2015;12(7):1005.
68. Cho Y, Song M, Kim T, Ryu J. Identification of novel cytokine biomarkers of hexanal exposure associated with pulmonary toxicity. *Environ Pollut*. 2017;229:810–817.
69. Nikolaus N, Gatterer H, Faulhaber M, Bartscher M, Pramsöhler S, Pesta D. Hypoxia, oxidative stress and fat. *Biomolecules*. 2015;5(2):1143–1150.
70. Franciosi AN, Carroll TP, McElvaney NG. Pitfalls and caveats in α 1-antitrypsin deficiency testing: a guide for clinicians. *Lancet Respir Med*. 2019;7:12.
71. Singer JP, Lederer DJ, Baldwin MR. Frailty in Pulmonary and critical care medicine. *Ann Am Thorac Soc*. 2016;2016:1.
72. Ahmadi A, Mazloom Z, Eftekhari MH, et al. Muscle mass and function are related to respiratory function in chronic obstructive pulmonary disease. *Med J Islam Repub Iran*. 2021;2021:1.
73. Chua JR, Albay AB Jr, Tee ML. Body composition of Filipino Chronic Obstructive Pulmonary Disease (COPD) patients in relation to their lung function, exercise capacity and quality of life. *Int J Chron Obstruct Pulmon Dis*. 2019;14:2759–2765.
74. Luo Y, Zhou L, Li Y, et al. Fat-free mass index for evaluating the nutritional status and disease severity in COPD. *Respir Care*. 2016;61(5):680–688.
75. Fekete M, Fazekas-Pongor V, Balazs P, et al. Effect of malnutrition and body composition on the quality of life of COPD patients. *Physiol Int*. 2021;108:2.
76. Marco E, Sánchez-Rodríguez D, Dávalos-Yerovi VN, et al. Malnutrition according to ESPEN consensus predicts hospitalizations and long-term mortality in rehabilitation patients with stable chronic obstructive pulmonary disease. *Clin Nutr*. 2018;38:1.
77. McDonald M, Diaz AA, Rutten E, Lutz S, Washko GR. Chest computed tomography-derived low fat-free mass index and mortality in COPD. *Eur Respir J*. 2017;50(6):1701134.
78. Barreiro E, Sznajder JI, Nader GA, Budinger G. Muscle dysfunction in patients with lung diseases: a growing epidemic. *Am J Respir Crit Care Med*. 2016;191(6):616–619.
79. Barreiro E. 10. Chronic obstructive pulmonary disease and oxidative damage. *Protein Carbonyl*. 2017;2017:5.
80. Chan HP, Mukhopadhyay A, Chong PLP, et al. Role of BMI, airflow obstruction, St George's Respiratory Questionnaire and age index in prognostication of Asian COPD. *Respirology*. 2016;2016:45.
81. Liao WH, Chen JW, Chen X, Lin L, Chen R. Impact of resistance training in subjects with COPD: a systematic review and meta-analysis. *Respir Care*. 2015;60(8):1130.
82. Teixeira PP, Kowalski VH, Valduga K, Araújo B, Silva FM. Low muscle mass is a predictor of malnutrition and prolonged hospital stay in patients with acute exacerbation of COPD: a longitudinal study. *J Parenter Enteral Nutr*. 2020;2020:6.
83. Bian AL, Hu HY, Rong YD, Wang J, Wang JX, Zhou XZ. A study on relationship between elderly sarcopenia and inflammatory factors IL-6 and TNF- α . *Eur J Med Res*. 2017;22(1):25.
84. Lieskovska J, Guo D, Derman E. IL-6-overexpression brings about growth impairment potentially through a GH receptor defect. *Growth Horm IGF Res*. 2002;12(6):388–398.
85. Matkovic Z, Cvetko D, Rahelic D, et al. Nutritional status of patients with chronic obstructive pulmonary disease in relation to their physical performance. *Copd*. 2017;14(6):626–634.
86. Li MJ, Zhang XR, Gao YP. Inflammation and sarcopenia. *Chin J Osteopor Bone Mineral Dis*. 2020;13(4):7.
87. Jaitovich A, Barreiro E. Skeletal Muscle dysfunction in chronic obstructive pulmonary disease. what we know and can do for our patients. *Am J Respir Crit Care Med*. 2018;198(2):175–186.
88. Webster JM, Kempen L, Hardy RS, Langen R. Inflammation and skeletal muscle wasting during cachexia. *Front Physiol*. 2020;11:597675.
89. Liu MH, Wang CH, Huang YY, et al. Edema index established by a segmental multifrequency bioelectrical impedance analysis provides prognostic value in acute heart failure. *J Cardiovasc Med*. 2012;13(5):299–306.
90. Minasian AG, Van DE, Dekhuijzen PN, et al. Pulmonary function impairment in patients with chronic heart failure: lower limit of normal versus conventional cutoff values. *Heart Lung*. 2014;43(4):311–316.
91. Wang Y, Gu Z. Effect of bioimpedance-defined overhydration parameters on mortality and cardiovascular events in patients undergoing dialysis: a systematic review and meta-analysis. *J Int Med Res*. 2021;49(9):3000605211031063.
92. Katharina D, Sheila L, Susan G, Lucas JR. The association between decreased hand grip strength and hip fracture in older people: a systematic review. *Exp Gerontol*. 2018;111:1–9.
93. Zhang XS, Liu YH, Zhang Y, et al. Handgrip strength as a predictor of nutritional status in Chinese elderly inpatients at hospital admission. *Biomed Environ Sci*. 2017;11:24–32.
94. Hiroshi K, Takahiro Y. Association of plasma adiponectin levels with cellular hydration state measured using bioelectrical impedance analysis in patients with COPD. *Int J Chron Obstruct Pulmon Dis*. 2012;2012:515–521.
95. Mamoto T, Fujiwara H, Toyama Y, Hirata K, Yoshikawa J, Fujimoto S. Relationship between exercise performance and water distribution measured by new bioelectrical impedance analysis in patients with chronic obstructive pulmonary disease. *Clin Physiol Funct Imaging*. 2003;23:4.
96. Ohashi Y, Joki N, Yamazaki K, Kawamura T, Sakai K. Changes in the fluid volume balance between intra- and extracellular water in a sample of Japanese adults aged 15–88 years old: a cross-sectional study. *Am J Physiol Renal Physiol*. 2017;314(312):ajrenal.00477.02017.
97. Umehara T, Kaneguchi A, Kawakami W, Katayama N, Kito N. Association of muscle mass and quality with hand grip strength in elderly patients with heart failure. *Heart Vessels*. 2022;37(8):1380–1386.

98. Hioka A, Akazawa N, Okawa N, Nagahiro S. Increased whole-body extracellular to intracellular water ratio in community-dwelling elderly women is associated with decreased handgrip strength and gait speed. *Nutrition*. 2021;86:111175.
99. Orea-Tejeda A, Gómez-Martínez M, González-Islas D, et al. The impact of hydration status and fluid distribution on pulmonary function in COPD patients. *Sci Rep*. 2022;12(1):1216.
100. Baarends EM, Schols AM, Mostert R, Wouters EF. Peak exercise response in relation to tissue depletion in patients with chronic obstructive pulmonary disease. *Eur Respir J*. 1997;10(12):2807–2813. doi:10.1183/09031936.97.10122807
101. de Blasio F, Di Gregorio A, de Blasio F, Bianco A, Bellofiore B, Scalfi L. Malnutrition and sarcopenia assessment in patients with chronic obstructive pulmonary disease according to international diagnostic criteria, and evaluation of raw BIA variables. *Respir Med*. 2018;134:1–5. doi:10.1016/j.rmed.2017.11.006
102. Chhabra R, Davenport A. Prehemodialysis hyponatremia and extracellular water: is it simply too much water? *Ther Apher Dial*. 2022;26(1):154–161. doi:10.1111/1744-9987.13685
103. Lukaski HC, Kyle UG, Kondrup J. Assessment of adult malnutrition and prognosis with bioelectrical impedance analysis: phase angle and impedance ratio. *Curr Opin Clin Nutr Metab Care*. 2017;20(5):330. doi:10.1097/MCO.0000000000000387
104. Giorgi A, Vicini M, Pollastri L, Lombardi E, Magni E. Bioimpedance patterns and bioelectrical impedance vector analysis (BIVA) of road cyclists. *J Sports Sci*. 2018;36(22):1–6. doi:10.1080/02640414.2018.1470597
105. Camina Martín MA, de Mateo Silleras B, Nescolarde Selva L, Barrera Ortega S, Domínguez Rodríguez L, Redondo Del Río MP. Bioimpedance vector analysis and conventional bioimpedance to assess body composition in older adults with dementia. *Nutrition*. 2015;31(1):155–159. doi:10.1016/j.nut.2014.06.006
106. Kim S, Shin J, Hwang C. Predicting clinical outcomes using phase angle assessed by bioimpedance analysis in maintenance haemodialysis patients. *Nephrology*. 2016;21(Suppl.2):99.
107. Belarmino G, Gonzalez MC, Torrinhas RS, et al. Phase angle obtained by bioelectrical impedance analysis independently predicts mortality in patients with cirrhosis. *World J Hepatol*. 2017;9(7):401–408. doi:10.4254/wjh.v9.i7.401
108. Büntzel J, Micke O, Kisters K, Büntzel J, Mücke MR. Malnutrition and survival – bioimpedance data in head neck cancer patients. *In Vivo*. 2019;33(3):979–982. doi:10.21873/invivo.11567
109. Pereira MME, Queiroz M, De Albuquerque NMC, et al. The prognostic role of phase angle in advanced cancer patients: a systematic review. *Nutr Clin Pract*. 2018;33(6):813–824. doi:10.1002/ncp.10100
110. Earthman CP. Body composition tools for assessment of adult malnutrition at the bedside. *JPEN J Parenter Enteral Nutr*. 2015;39(7):787–822. doi:10.1177/0148607115595227
111. Mulasi U, Kuchnia AJ, Cole AJ, Earthman CP. Bioimpedance at the bedside: current applications, limitations, and opportunities. *Nutr Clin Pract*. 2015;30(2):180–193. doi:10.1177/0884533614568155
112. Dittmar M, Reber H, Kahaly GJ. Bioimpedance phase angle indicates catabolism in Type 2 diabetes. *Diabet Med*. 2015;32(9):1177–1185. doi:10.1111/dme.12710
113. Genton L, Norman K, Spoerri A, et al. Bioimpedance-derived phase angle and mortality among older people. *Rejuvenation Res*. 2017;20(2):118–124. doi:10.1089/rej.2016.1879
114. Gomes TLN, Soares JDP, Borges TC, Pichard C, Pimentel GD. Phase angle is not associated with fatigue in cancer patients: the hydration impact. *Eur J Clin Nutr*. 2020;74(9):1–5. doi:10.1038/s41430-020-0597-4
115. Custódio Martins P, De Lima TR, Silva AM, Santos Silva DA. Association of phase angle with muscle strength and aerobic fitness in different populations: a systematic review. *Nutrition*. 2022;93:111489. doi:10.1016/j.nut.2021.111489
116. Zanella PB, Àvila CC, Chaves FC, et al. Phase angle evaluation of lung disease patients and its relationship with nutritional and functional parameters. *J Am Coll Nutr*. 2021;40(6):529–534. doi:10.1080/07315724.2020.1801535
117. Maddocks M, Kon SSC, Jones SE, et al. Bioelectrical impedance phase angle relates to function, disease severity and prognosis in stable chronic obstructive pulmonary disease. *Clin Nutr*. 2015;34(6):1245–1250. doi:10.1016/j.clnu.2014.12.020
118. de Blasio F, Santaniello MG, de Blasio F, et al. Raw BIA variables are predictors of muscle strength in patients with chronic obstructive pulmonary disease. *Eur J Clin Nutr*. 2017;71(11):1336–1340. doi:10.1038/ejcn.2017.147
119. Martínez-Luna N, Orea-Tejeda A, González-Islas D, et al. Association between body composition, sarcopenia and pulmonary function in chronic obstructive pulmonary disease. *BMC Pulm Med*. 2022;22(1):106. doi:10.1186/s12890-022-01907-1
120. Norman K, Stobäus N, Pirlich M, Bösby-Westphal A. Bioelectrical phase angle and impedance vector analysis – clinical relevance and applicability of impedance parameters. *Clin Nutr*. 2012;31(6):854–861. doi:10.1016/j.clnu.2012.05.008

Publish your work in this journal

The International Journal of COPD is an international, peer-reviewed journal of therapeutics and pharmacology focusing on concise rapid reporting of clinical studies and reviews in COPD. Special focus is given to the pathophysiological processes underlying the disease, intervention programs, patient focused education, and self management protocols. This journal is indexed on PubMed Central, MedLine and CAS. The manuscript management system is completely online and includes a very quick and fair peer-review system, which is all easy to use. Visit <http://www.dovepress.com/testimonials.php> to read real quotes from published authors.

Submit your manuscript here: <https://www.dovepress.com/international-journal-of-chronic-obstructive-pulmonary-disease-journal>