Original Article

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CT-Derived Deep Learning-Based Quantification of Body Composition Associated with Disease Severity in Chronic Obstructive Pulmonary Disease

CT 기반 딥러닝을 이용한 만성 폐쇄성 폐질환의 체성분 정량화와 질병 중증도

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Purpose Our study aimed to evaluate the association between automated quantified body composition on CT and pulmonary function or quantitative lung features in patients with chronic obstructive pulmonary disease (COPD).

Materials and Methods A total of 290 patients with COPD were enrolled in this study. The volume of muscle and subcutaneous fat, area of muscle and subcutaneous fat at T12, and bone attenuation at T12 were obtained from chest CT using a deep learning-based body segmentation algorithm. Parametric response mapping-derived emphysema (PRM^{emph}), PRM-derived functional small airway dis-

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ease (PRM^{fSAD}), and airway wall thickness (AWT)-Pi10 were quantitatively assessed. The association between body composition and outcomes was evaluated using Pearson's correlation analysis.

Results The volume and area of muscle and subcutaneous fat were negatively associated with PRM^{emph} and PRM^{fSAD} ($p < 0.05$). Bone density at T12 was negatively associated with PRM^{emph} (r = -0.1828, p = 0.002). The volume and area of subcutaneous fat and bone density at T12 were positively correlated with AWT-Pi10 (r = 0.1287, p = 0.030; r = 0.1668, p = 0.005; r = 0.1279, p = 0.031). However, muscle volume was negatively correlated with the AWT-Pi10 (r = -0.1966, p = 0.001). Muscle volume was significantly associated with pulmonary function ($p < 0.001$).

Conclusion Body composition, automatically assessed using chest CT, is associated with the phenotype and severity of COPD.

Index terms Multidetector Computed Tomography; Chronic Obstructive Pulmonary Disease; Deep Learning; Muscle

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a heterogeneous, multisystem disease characterized by airflow obstruction (1). Patients with COPD exhibit alterations in body composition, which is an important prognostic factor (1, 2). The prevalence of low muscle mass and reduced muscle function in patients with COPD is twice that in the healthy elderly population (1). COPD with skeletal muscle loss is associated with adverse clinical outcomes including decreased pulmonary function, diminished quality of life, and increased mortality (2-6). Additionally, osteoporosis is highly prevalent in patients with COPD and associated with an increased risk of osteoporotic fractures, which may result in increased morbidity and mortality (7). Body weight loss and muscle wasting are associated with the presence of osteoporosis in COPD patients, and systemic inflammation may be linked to both osteoporosis and muscle loss (8, 9).

Chest CT is routinely performed to detect lung cancer and evaluate the phenotype and severity of COPD and extrapulmonary abnormalities in patients with COPD. CT can accurately differentiate between fat, muscle, and bone using the specific attenuation of each tissue, and may allow for the assessment of alterations in body composition (10-12). Chest CT-derived markers of body composition—including the pectoralis muscle, erector spinae, adipose tissue, and bone density—are associated with disease severity and clinical outcomes in patients with COPD (11-15). However, investigators used a single axial slice of the CT scan for the quantitative assessment of body composition. In recent years, deep learning-based algorithms have shown potential in the automated quantification of body composition from CT images and can thus reduce the laborious work required for segmentation (16-18).

This study aimed to evaluate the association between the automated quantification of body composition and pulmonary function or quantitative lung features in patients with COPD.

MATERIALS AND METHODS

STUDY POPULATION

A total of 504 participants were selected from a Korean cohort (the Chronic Obstructive Pulmonary Disease in Dusty Areas cohort) between 2012 and 2017, which aimed to assess the clinical outcomes of participants residing near cement factories. All enrolled participants were assessed using medical interviews, spirometry, and chest CT. We excluded 214 participants with lung quantification error (n = 8), lobectomy (n = 4), lung disease (n = 10), severe lung parenchymal distortion (n = 30), forced expiratory volume in 1 s (FEV_1)/forced vital capacity (FVC) $\geq$ 0.7 (n = 160), and body composition quantification error (n = 3). Ultimately, 290 patients with COPD were enrolled in the study (Fig. 1).

This study was approved by our Institutional Review Board (IRB No. 2012-06-007) and all participants provided written informed consent.

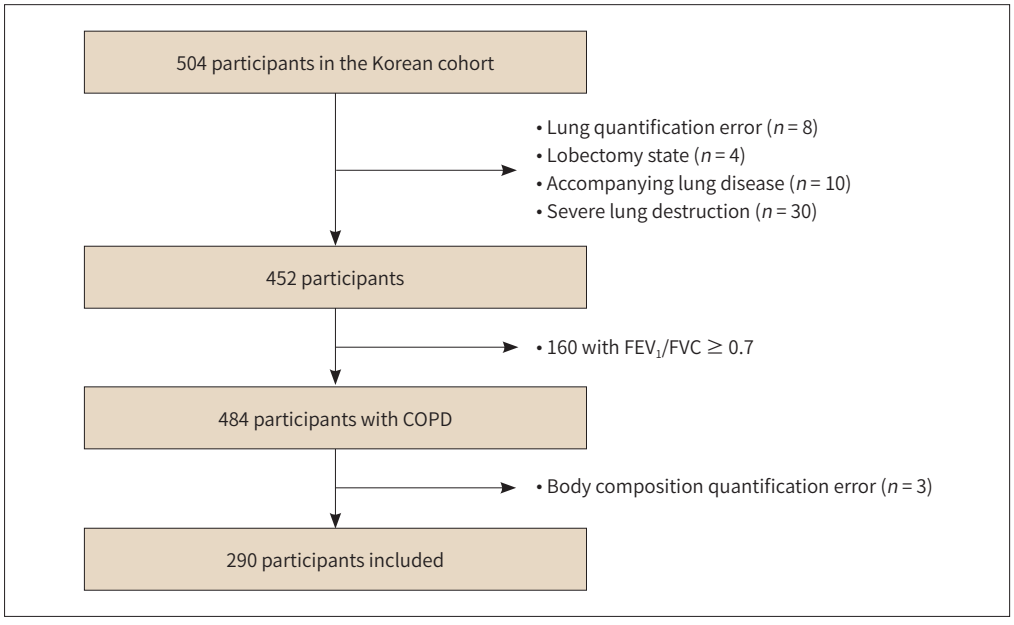
PULMONARY FUNCTION

Spirometry was performed before and after administrating 400 μg of salbutamol using EasyOne (NDD, Zurich, Switzerland) and pulmonary function measures selected according to the American Thoracic Society/European Respiratory Society criteria (19). The severity of airflow limitation was classified according to the 2017 Global Initiative for Chronic Obstructive Lung Disease (GOLD) grading system as grade 1 ($\geq$ 80%), grade 2 (50%–79%), grade 3 (30%-49%), or grade 4 (< 30%) (20).

CT ACQUISITION AND IMAGE ANALYSIS

All participants underwent thin-section unenhanced chest CT during full inspiration and

Fig. 1. The flowchart for study participants.



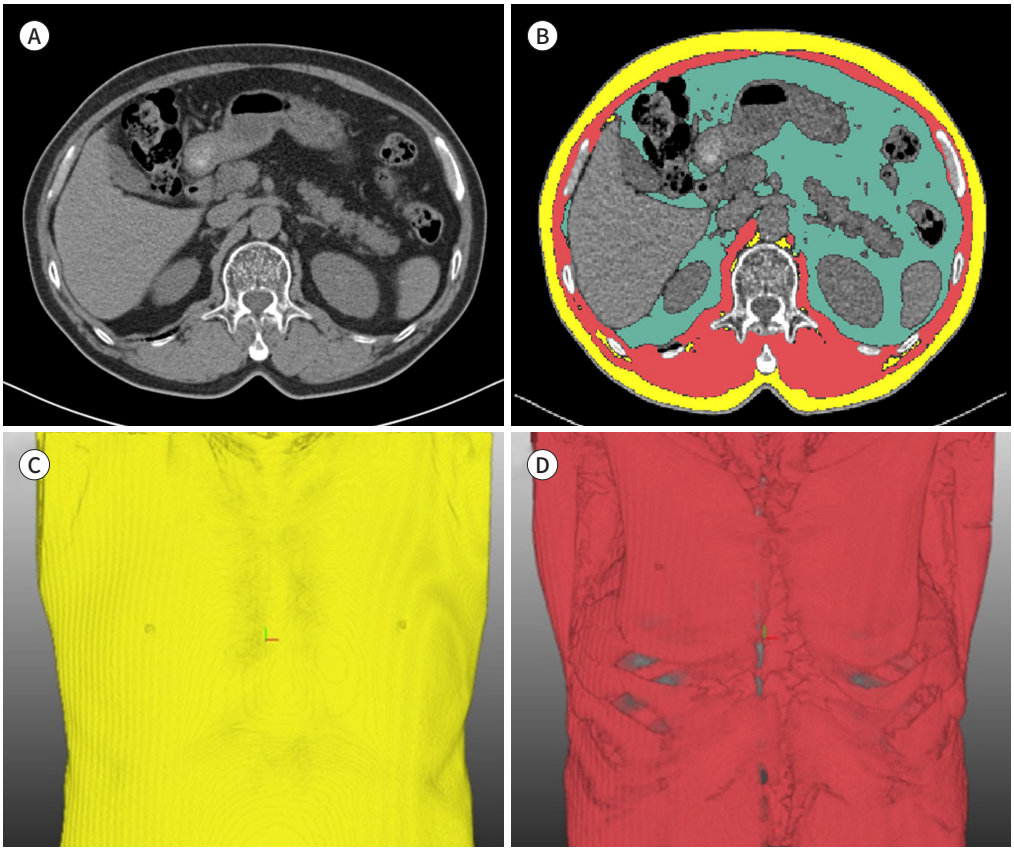
COPD = chronic obstructive pulmonary disease, FEV_1 = forced expiratory volume in 1 s, FVC = forced vital capacity

expiration in the supine position. CT images were acquired using a first-generation, dual-source CT scanner (Somatom Definition; Siemens Healthcare, Forchheim, Germany) in a caudocranial direction using the following parameters: 140 kVp, 100 mA, 0.9–1 beam pitch, and slice thickness of 0.6 mm. CT data were reconstructed using a soft convolution kernel (B30f).

Quantification of body composition on CT was automatically performed using a commercially available deep learning-based body composition analysis software platform (version 1.0.0.0; DeepCatch, Medical IP Co. Ltd, Seoul, Korea). The software measures the volume of subcutaneous fat and muscle, area of subcutaneous fat and muscle at the 12th thoracic vertebra (T12) level, and bone attenuation at the T12 level on chest CT (12). A thoracic radiologist confirmed the T12 levels (Fig. 2).

Lung segmentation and quantification of emphysema, functional small airway disease, and bronchial wall thickness were performed using the Aview® system (Coreline Soft Inc., Seoul, Korea). Parametric response mapping (PRM) analysis was classified into PRM^{fSAD} (> -950 Hounsfield unit [HU] at inspiration and ≤ -856 HU at expiration), or PRM^{emph} (≤ -950 HU at inspiration and ≤ -856 HU at expiration) (21, 22). The standardized airway wall thickness (AWT)-Pi10 was derived by plotting the square root of the airway wall area against the internal perimeter of each measured airway (21). CT images were classified into three sub-

Fig. 2. Automated quantification of body composition from chest CT.
A-D. CT measurement of muscle and subcutaneous fat at the 12th thoracic vertebra lower margin using fully automated body segmentation (red, muscle; yellow, subcutaneous fat, A, B) and volume measurement of subcutaneous fat (C) and muscle (D) using fully automated body segmentation.



types according to the PRM^{emph}: mild (PRM^{emph} < 5%), moderate (PRM^{emph} ≥ 5% and < 10%), and severe (PRM^{emph} ≥ 10%) emphysema.

STATISTICAL ANALYSIS

Parametric data are expressed as mean ± standard deviation, whereas nonparametric data area expressed as numbers and percentages. Pearson's correlation analysis was used to measure the association between body composition and quantitative CT variables or spirometry adjusted for age and sex. One-way ANOVA was used to analyze the differences in body composition among the subtypes adjusted for age and sex. Statistical significance was set at $p < 0.05$. Data analyses were performed using SAS version 9.3 (SAS Institute Inc., Cary, NC, USA).

RESULTS

Finally, we included 290 participants (236 male; mean age, 72.6 ± 7.3 years) in this study. The subtypes were divided into GOLD grades: 148 (51.0%) participants were GOLD grade 1, 119 (41.0%) participants were GOLD grade 2, and 23 (8.0%) participants were GOLD grades 3 or 4. With the subtypes divided according to PRM^{emph}, 165 participants (56.9%) had mild emphysema, 69 participants (23.8%) had moderate emphysema, and 56 participants (19.3%) had severe emphysema. The volume of muscle and subcutaneous fat on chest CT were measured from the supraclavicular fossa to the mid-kidneys. Detailed characteristics of the participants are presented in Table 1.

Table 1. Characteristics of the 290 Participants

Variables	Patients
Age	72.6 ± 7.3
Sex, male	236 (81.4)
Smoking	287
Current	76 (26.5)
Former	138 (48.1)
None	73 (25.4)
FVC, L	3.11 ± 0.8
FEV_1, L	1.84 ± 0.56
FVC/FEV_1	0.59 ± 0.09
Muscle volume, mm^3	3849760.1 ± 847590.2
Subcutaneous fat volume, mm^3	2798949.5 ± 1434847.4
Muscle area at the T12, mm^2	8685.8 ± 2033.1
Subcutaneous fat volume, mm^2	5973.4 ± 3611.8
Bone density at the T12, HU	240.0 ± 46.7
PRM^{emph}, %	6.4 ± 6.9
PRM^{fSAD}, %	28.5 ± 15.9
AWT-Pi10	4.7 ± 0.4

Data are shown as mean ± standard deviation or number (%) values.
AWT = airway wall thickness, emph = emphysema, FEV_1 = forced expiratory volume in 1 s, fSAD = functional small airway disease, FVC = forced vital capacity, HU = Hounsfield unit, PRM = parametric response mapping

Participants with greater muscle volume and area at T12 had significantly lower emphysema and lower PRM^{fSAD} (r = -0.1667, p = 0.005; r = -0.2511, p < 0.001; Table 2). As muscle volume increased, FVC and FEV_1 increased (r = 0.3999, p < 0.001; r = 0.3563, p < 0.001). The muscle area at T12 was not significantly correlated with pulmonary function (p > 0.05). Muscle volume was negatively correlated with the AWT-Pi10 (r = -0.1966, p = 0.001). As the subcutaneous fat volume and area at T12 increased, PRM^{emph} and PRM^{fSAD} decreased, and AWT-Pi10 increased. Subcutaneous fat volume positively correlated with FVC (r = 0.1259, p = 0.033). However, FEV_1/FVC was not associated with the volume and area of muscle or subcutaneous fat (p > 0.05). When the subtypes were divided according to PRM^{emph}, muscle and subcutaneous fat were significantly lower in the severe emphysema group (p < 0.05) (Table 3).

Bone density at T12 showed a weak negative correlation with PRM^{emph} (r = -0.1828, p = 0.002). As the bone density at T12 increased, AWT-Pi10 and FEV_1 increased (r = 0.1279, p = 0.031; r = 0.1275 and p = 0.031, respectively). However, PRM^{fSAD} and FEV_1/FVC were not associated with bone density (r = -0.0934, p = 0.115; r = 0.0922, p = 0.111). Body composition parameters were assessed according to the GOLD grades of the subjects. There were no significant

Table 2. Relationship between Body Composition and Pulmonary Function or CT Quantitative Features

	AWT-Pi10		PRM^{emph}		PRM^{fSAD}		FVC		FEV_1		FEV_1/FVC	
	r	*p*	*r*	*p*	*r*	*p*	*r*	*p*	*r*	*p*	*r*	*p*
Muscle volume	-0.1966	0.001	-0.1667	0.005	-0.2511	< 0.001	0.3999	< 0.001	0.3563	< 0.001	0.0890	0.133
SF volume	0.1287	0.030	-0.1849	0.002	-0.1965	0.001	0.1259	0.033	0.0618	0.297	-0.0447	0.451
Muscle area at T12	0.1046	0.077	-0.2923	< 0.001	-0.2577	< 0.001	0.1078	0.069	0.1022	0.084	0.0472	0.426
SF area at T12	0.1668	0.005	-0.1973	0.001	-0.1701	0.004	0.0452	0.447	0.0241	0.685	-0.0114	0.848
Bone density at T12	0.1279	0.031	-0.1828	0.002	-0.0934	0.115	0.0923	0.120	0.1275	0.031	0.0922	0.111

AWT = airway wall thickness, emph = emphysema, FEV_1 = forced expiratory volume in 1 s, fSAD = functional small airway disease, FVC = forced vital capacity, PRM = parametric response mapping, SF = subcutaneous fat

Table 3. Body Composition of the Three Emphysema Subtypes

	Mild (*n* = 165)	Moderate (*n* = 69)	Severe (*n* = 56)	*p*-Value
Muscle volume, mm^3	3869298.3 ± 924893.0	3838417.6 ± 760911.2	3806167.6 ± 710709.0	0.002
SF volume, mm^3	3078383.2 ± 1389467.2	2667636.1 ± 1455300.1	2137415.0 ± 1319573.9	0.013
Muscle area at T12, mm^2	9004.0 ± 1992.5	8382.7 ± 1949.6	8121.5 ± 2107.1	< 0.001
SF area at T12, mm^2	6766.8 ± 3625.4	5526.6 ± 3519.2	4185.9 ± 2941.3	0.015
Bone density at T12, HU	244.1 ± 48.1	237.8 ± 47.1	230.6 ± 40.8	0.007

HU = Hounsfield unit, SF = subcutaneous fat

Table 4. Body Composition in the Three Emphysema Subtypes according to Their GOLD Grade

	GOLD grade 1 (*n* = 148)	GOLD grade 2 (*n* = 119)	GOLD grade 3 & 4 (*n* = 23)	*p*-Value
Muscle volume, mm^3	3871048.7 ± 887464.3	3882595.8 ± 781425.1	3542883.3 ± 890070.3	0.008
SF volume, mm^3	2838672.5 ± 1197748.8	2850318.9 ± 1667305.0	2277560.1 ± 1496571.3	0.410
Muscle area at T12	8698.6 ± 1942.4	8805.4 ± 2086.1	7983.8 ± 2270.5	0.147
SF area at T12	6109.3 ± 3228.4	6017.8 ± 3982.3	4868.7 ± 3905.3	0.668
Bone density at T12, HU	243.5 ± 47.7	238.2 ± 46.1	226.8 ± 42.3	0.070

GOLD = Global Initiative for Chronic Obstructive Lung Disease, HU = Hounsfield unit, SF = subcutaneous fat

differences in muscle, subcutaneous fat, or bone density according to the GOLD grade, except for muscle volume ($p > 0.05$) (Table 4).

DISCUSSION

Changes in body composition are known prognostic factors in patients with COPD (1, 2). In this study, we identified the association between COPD manifestation and body composition parameters quantitatively measured by CT. Increased muscle volume in COPD patients is associated with increased lung function. Participants with lower muscle and subcutaneous fat exhibited severe emphysema and functional small airway disease. Participants with a larger subcutaneous area and volume had increased airway thickness. Increased bone density in patients was associated with increased airway thickness and decreased emphysema.

CT has become a widely used diagnostic modality, and body composition analysis using CT is required clinically (10). The clinical significance of CT-derived markers of body composition is well established in patients with chronic diseases including COPD (23). Approximately 22% of patients with COPD develop sarcopenia (1). Measurement of the cross-sectional area of the pectoralis muscle and erector spinae using CT provides a reproducible measure of muscle mass and associated with clinical outcomes in patients with COPD (7, 12). Recently, artificial intelligence has emerged as a promising tool for automatic volumetric quantification of body composition (23). In this study, we used a deep learning algorithm to assess the muscle, subcutaneous fat, and bone on chest CT. Our results are consistent with those of previous studies that reported that subjects with higher muscle mass tended to have better lung function and less emphysema (14, 24, 25). In addition, a negative association was observed between the muscles and functional small airways.

Obesity and adipose tissue depots, including those in the subcutaneous area, are associated with lower mortality in patients with COPD, a phenomenon known as the obesity paradox (11, 26, 27). We investigated the effects of subcutaneous fat deposits on COPD manifestations. Several studies indicate that abdominal and generalized obesity are negatively associated with pulmonary function (28, 29). Our findings show that subcutaneous fat volume is associated with FVC but not with FEV_1. One study found that epicardial adipose tissue is independently associated with AWT (30). In this study, subcutaneous fat area and volume were positively correlated with airway thickness. Diaz et al. (31) reported that the subcutaneous fat area is directly related to inflammatory biomarkers; thus, systemic inflammatory mediators are thought to play an important role in airway remodeling (30). Another study showed that increased air trapping and decreased subcutaneous adipose tissue were independently associated with impaired physical activity in symptomatic COPD patients (32). Our results also showed that emphysema and functional small airway disease decreased as subcutaneous fat increased.

Smoking negatively affects bone density, and the prevalence of osteoporosis is reported to be 4%–59% in patients with COPD (13, 33). Low BMI, muscle wasting, systemic inflammation, and physical inactivity are all associated with osteoporosis in COPD (8). Several studies have reported that the extent of emphysema is significantly correlated with reduced bone density, while increased AWT is associated with higher bone density (33-35). Our results were similar, finding that reduced bone density at T12 was correlated with severe emphysema and

decreased AWT. Jaramillo et al. (33) reported that GOLD grade 3 and 4 groups showed low bone density. In this study, as GOLD grade increased, bone density tended to decrease; however, the difference was not significant. Nevertheless, higher bone density is associated with higher FEV_1 in our study. The use of inhaled corticosteroids is associated with decreased bone density (36, 37). Another study did not determine an association between corticosteroids and osteoporosis (8). Our study did not demonstrate an association between corticosteroid use and bone density in patients with COPD.

Our study has several limitations. First, we automatically measured the volume of muscle and subcutaneous fat using CT and a deep learning algorithm on chest CT. The scan coverage of the chest CT was from the supraclavicular fossa to the mid-kidneys. However, there were slight differences in the chest CT scan range for each patient, which may have affected the volume measurements. Second, compared to previous studies, our study showed a relatively weak correlation between CT-derived body composition and quantitative CT variables. Most of the participants had mild-to-moderately severe COPD, so the number of patients with severe COPD was small. In addition, the small sample size of 290 patients with COPD enrolled in our study may have contributed to the weak correlation. Therefore, further studies including at larger population with varying COPD severities are necessary. The correlation between the cross-sectional area of the erector spinae muscles at the 12th thoracic vertebra and COPD is well established (12, 25). Therefore, we conducted a cross-sectional analysis at the T12 level. However, T12 may not reflect the total bone density because the lower thoracic vertebrae are relatively prone to fractures in old age, which can affect bone density. Third, we did not assess the physical activity or exercise capacity.

In conclusion, CT-derived body composition including muscle, subcutaneous fat, and bone density, was correlated with the phenotypes and severity of COPD. The quantification of body composition on chest CT is a useful imaging marker for the assessment of COPD.

Author Contributions

Conceptualization, B.S.H.; data curation, B.S.H., K.W.J., S.J.E.; formal analysis, B.S.H., S.J.E., L.M., L.E.J.; methodology, B.S.H., K.W.J., C.Y.K., Y.H.J.; writing—original draft, B.S.H., S.J.E.; and writing—review & editing, B.S.H., L.M., L.E.J., C.Y.K., Y.H.J., K.W.J.

Conflicts of Interest

The authors have no potential conflicts of interest to disclose.

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CT 기반 딥러닝을 이용한 만성 폐쇄성 폐질환의 체성분 정량화와 질병 중증도

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목적 만성폐쇄성폐질환의 CT에서 자동 정량 측정된 체성분과 폐기능 또는 정량적 변수들 사이의 연관성을 알아보고자 하였다.

대상과 방법 총 290명의 만성폐쇄성폐질환 환자를 대상으로 연구하였다. 흉부 CT에서 근육 및 피하지방 부피, T12 레벨에서 근육 및 피하지방 면적 및 골 감쇠를 딥러닝 기반 분할 알고리즘을 사용하여 획득하였다. Parametric response mapping-derived emphysema (이하 PRM^{emph}), PRM-derived functional small airway disease (이하 PRM^{fSAD}) 및 기도 벽 두께 (airway wall thickness; 이하 AWT)-Pi10을 정량적으로 평가하였다. Pearson 상관 분석을 사용하여 체성분과 결과 간의 연관성을 평가하였다.

결과 근육과 피하지방의 부피와 면적은 PRM^{emph}와 PRM^{fSAD}와 음의 상관관계를 보였다($p < 0.05$). T12에서의 골밀도는 PRM^{emph}와 음의 상관관계를 보였다($r = -0.1828$, $p = 0.002$). 피하지방의 부피와 면적과 T12에서의 골밀도는 AWT-Pi10과 양의 상관관계를 보였다($r = 0.1287$, $p = 0.030$; $r = 0.1668$, $p = 0.005$; $r = 0.1279$, $p = 0.031$). 반면에 근육 부피는 AWT-Pi10과 음의 상관관계를 보였다($r = -0.1966$, $p = 0.001$). 근육 부피는 폐기능과 의미 있는 연과성을 보였다($p < 0.001$).

결론 흉부 CT에서 정량적으로 평가된 체성분은 만성폐쇄성폐질환의 표현형 또는 중증도와 연관성을 보인다.

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