Correlation between pulmonary function and the software-based quantification of the degree of emphysema and airway wall thickening in patients with COPD

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Background

- The previous studies revealed that the radiological findings show morphological phenotypes in accordance with the presence or absence of emphysema and airway wall thickening (AWT) in patients with chronic obstructive pulmonary disease(COPD).
  [Respirology 11: 731-740, Respir Med 100:1742-1752].
- Recently, the degree of airway disease and emphysema evaluated using the software-based quantification on chest high-resolution computed tomography (HRCT) are independently associated with aspects of the pathophysiology in patients with COPD. Using these indices, patients with COPD can be divided into four phenotypes: the airway-dominant phenotype, the emphysema-dominant phenotype, the mixed phenotype (airway and emphysema), and the normal by CT phenotype.
- There continues to be a lack of information on the correlation between the morphological phenotypes and clinical characteristics such as pulmonary function, including respiratory impedance, and health-related quality of life in patients with COPD.

Subjects & Methods

- A total of 134 stable patients with COPD whose GOLD stage is stage Ⅱ or more had been enrolled in the outpatient clinic of the Shinshu University Hospital from April 2012 to October 2016.
- All the patients underwent chest high-resolution computed tomography (HRCT) and pulmonary function tests, including respiratory impedance measurements by means of the forced oscillation technique (FOT) which assess the oscillatory flow resistance of the respiratory system. Health-related quality of life was evaluated using the St. George's Respiratory Questionnaire（SGRQ）and the COPD assessment test (CAT), and exercise tolerance was evaluated using the 6-minute walking test in some patients.
- The degree of emphysema and AWT were measured using software-based quantification, and presented as values of low attenuation volume (LAV) and AWT-Pi10, respectively. AWT-Pi10 is a standardized airway wall thickness at an internal perimeter of 10 mm. We used the ZioCube® software for measurement of WA% and AWT-Pi10. Also, we used the LungVision® software for measurement of %LAV.
- In advance, we defined upper limits of "normal" for the CT measurements of LAV% and WA% as the mean +2SD for these measurements in 20 non-COPD smokers. As a result, the upper limits of WA% is 69.6%, and the upper limits of %LAV is 3.0%. Based on these cut-offs, as previously reported [Chest 122(6 suppl): 271S-5S], the patients with COPD were divided into four groups as follows:
  1) normal by CT phenotype (NCT; low LAV% and low WA%)
  2) airway-dominant phenotype (AD; low LAV% and high WA%)
  3) emphysema-dominant phenotype (ED; high LAV% and low WA%)
  4) mixed phenotype (Mixed; high LAV% and high WA%)

Results

Figure 1. Correlation between WA% and LAV% in patients. Horizontal line shows the mean +2SD of LAV% of the asymptomatic smokers. Vertical line shows the mean +2SD of WA% of the asymptomatic smokers.

WA%, percentage of airway wall area; LAV, low attenuation volume; normal by CT phenotype:, NCT; airway dominant phenotype; AD, emphysema dominant phenotype; ED, mixed phenotype: Mixed.

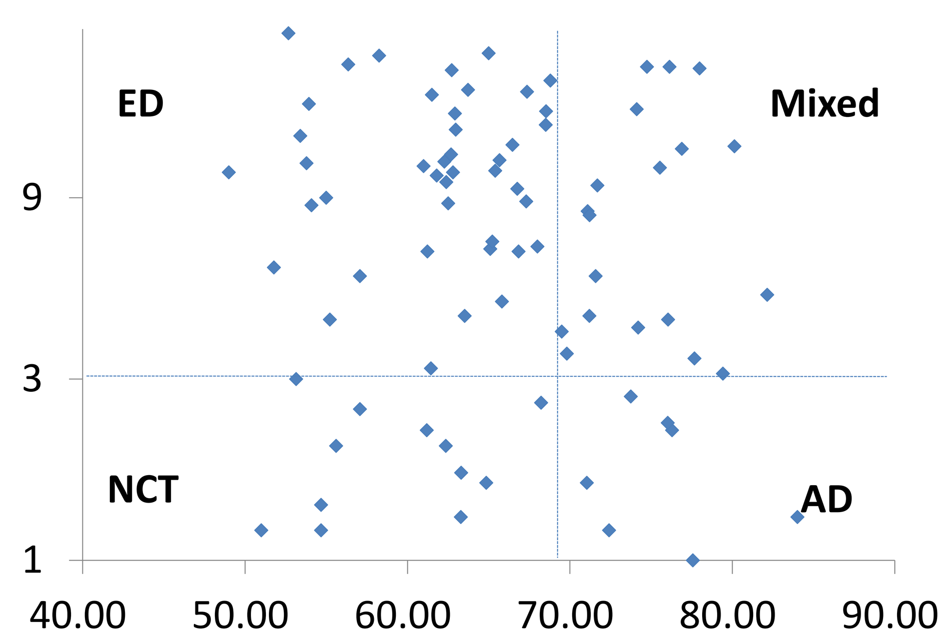
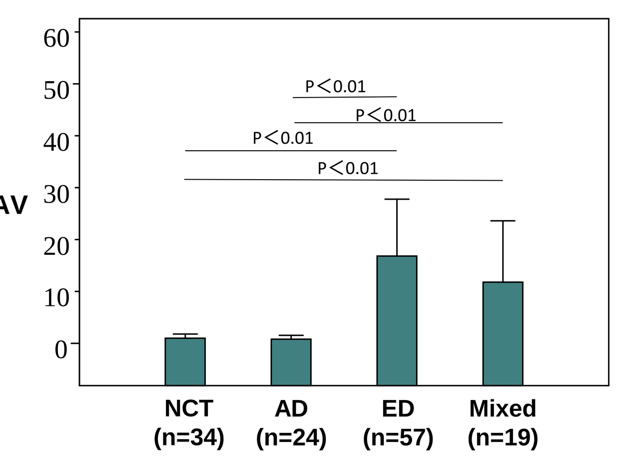
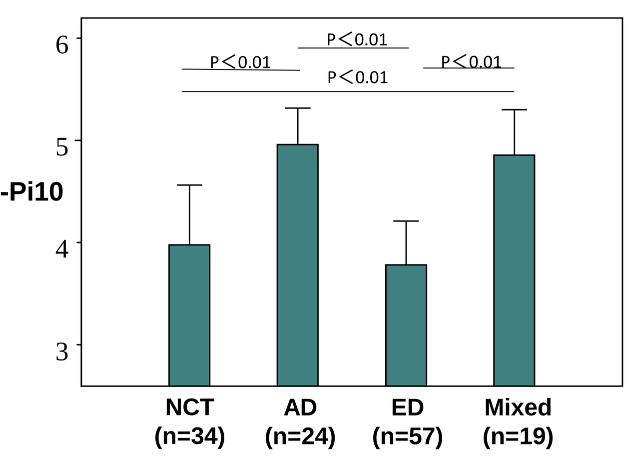


Table 1. Clinical characteristics and pulmonary function in the four groups .
** p<0.01, * p<0.05 vs. NCT phenotype; †† p<0.01, † p<0.05 vs. ED phenotype; ‡‡ p<0.01, ‡ p<0.05 vs. AD phenotype

	NCT (n=34)	AD (n=24)	ED (n=57)	Mixed (n=19)
Age, years old	71.4±9.7	73.3±7.33	72.3±6.5	75.0±6.9
Gender				
Male, n (%)	34(100.0)	24(100.0)	53(93.0)	18(95.0)
Female, n (%)	0(0.0)	0(0.0)	4(7.0)	1(5.0)
Smoking Index, pack-years	54.6±28.0	63.5±38.0	60.6±22.0	64.1±37.0
Body mass index, kg/m^2	23.0±2.8	24.7±3.7	20.5±2.6**‡‡	22.0±3.5
Chest HRCT findings				
AWTPi10	3.98±0.59	4.96±0.36**	3.78±0.43‡‡	4.85±0.44**††
WA%(%)	60.77±5.86	75.93±3.63**	61.41±5.76‡‡	75.50±3.89**††
LAV(%)	0.99±0.79	0.80±0.74	16.81±10.97**‡‡	11.79±11.84**‡‡
Pulmonary function data				
VC, %predicted	90.74±14.73	86.21±10.62	95.31±15.24	93.18±17.58
FVC, % predicted	87.62±14.12	83.63±10.54	95.45±17.85‡‡	85.86±19.48
FEV_1, % predicted	67.26±12.54	60.89±12.28	57.85±15.08*	51.77±14.13**
FEV_1/FVC, %	61.55±5.76	58.13±9.62	48.43±9.69**‡‡	47.97±9.86**‡‡
PEFR, % predicted	72.75±19.95	63.09±14.12	57.05±17.47**	55.72±15.62*
MMF, % predicted	24.95±7.09	21.78±8.98	18.70±7.72**	15.59±6.49**
FRC, % predicted	91.01±14.24	92.95±21.25	108.23±25.97**‡	107.06±20.86*
RV, % predicted	132.76±22.83	135.6±34.11	163.34±52.06**‡	162.79±36.61*
TLC, % predicted	105.19±12.64	101.78±10.40	117.91±19.43**‡	115.11±16.11
DLco, % predicted	72.72±16.90	72.90±18.02	51.93±23.51**‡‡	55.76±22.34*
DLco/VA, % predicted	4.22±1.06	4.38±1.16	2.67±0.92**‡‡	2.97±1.17**‡‡
delta N_2, %N_2/L	3.09±1.79	3.25±1.71	4.82±3.63*	3.59±1.80





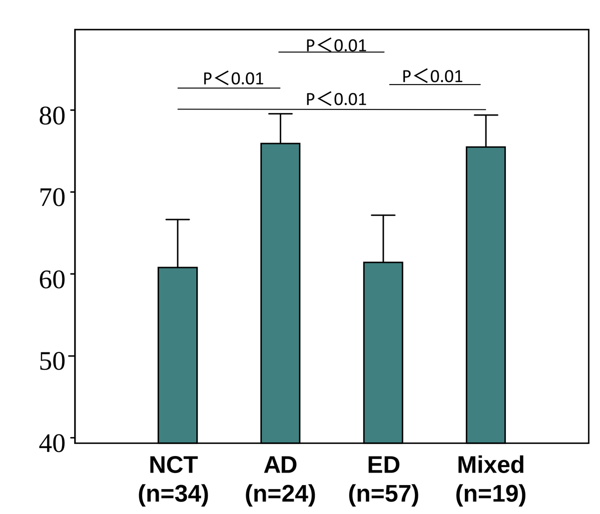


Table2. Respiratory impedance in the four groups.
** p<0.01, * p<0.05 vs. NCT phenotype; †† p<0.01, † p<0.05 vs. ED phenotype; ‡‡ p<0.01, ‡ p<0.05 vs. AD phenotype

	NCT (n=34)	AD (n=24)	ED (n=57)	Mixed (n=19)
Whole-breath				
R5(cmH_2O/L/s)	3.03±1.40	4.36±1.58**	3.19±1.06‡‡	4.22±0.81**††
R20(cmH_2O/L/s)	2.41±0.98	3.46±1.43*	2.46±0.75	3.16±0.58
R5-R20(cmH_2O/L/s)	0.67±0.49	0.90±0.92	0.74±0.51	1.06±0.35
X5(cmH_2O/L/s)	-1.02±0.97	-2.10±1.24**	-1.13±0.99‡‡	-2.31±1.58**††
Fres(Hz)	11.98±4.86	16.45±5.21*	13.50±5.81‡	18.46±5.51**††
ALX(cmH2O/L/s Hz)	6.81±8.68	16.49±12.28**	8.65±9.79‡	20.10±18.57**†
Expiratory phase				
R5(cmH_2O/L/s)	3.28±1.54	4.83±1.95*	3.56±1.23	4.60±0.94**†
R20(cmH_2O/L/s)	2.50±1.02	3.70±1.77*	2.65±0.86	3.33±0.64**†
R5-R20(cmH_2O/L/s)	0.78±0.63	1.13±0.93	0.91±0.55	1.27±0.48
X5(cmH_2O/L/s)	-1.26±1.42	-2.92±2.05**	-1.48±1.51‡‡	-3.30±2.67**††
Fres(Hz)	13.17±5.73	18.82±6.30**	15.00±7.05	21.19±6.93**††
ALX(cmH2O/L/s Hz)	9.02±13.14	24.59±20.40**	12.48±15.54‡	31.23±32.43**†
Inspiratory phase				
R5(cmH_2O/L/s)	2.79±1.32	3.88±1.35*	2.82±0.99‡‡	3.84±0.82**††
R20(cmH_2O/L/s)	2.31±0.96	3.21±1.15**	2.27±0.69‡‡	2.99±0.63*††
R5-R20(cmH_2O/L/s)	0.48±0.49	0.66±0.98	0.55±0.53	0.85±0.28*
X5(cmH_2O/L/s)	-0.76±0.63	-1.28±0.70**	-0.77±0.54‡‡	-1.30±0.65*††
Fres(Hz)	10.78±4.39	14.07±4.88*	11.99±4.89	15.71±4.37**†
ALX(cmH2O/L/s Hz)	4.34±5.26	8.38±6.86*	4.74±4.74‡	8.97±5.94*†
Differences between inspiratory and expiratory phases				
R5(cmH_2O/L/s)	0.49±0.58	0.96±1.13	0.74±0.70	0.76±0.71
R20(cmH_2O/L/s)	0.20±0.36	0.49±0.83	0.38±0.38	0.34±0.51
R5-R20(cmH_2O/L/s)	0.29±0.30	0.47±0.51	0.37±0.37	0.42±0.37
X5(cmH_2O/L/s)	-0.52±1.05	-1.64±1.80*	-0.72±1.10	-2.00±2.27**††
Fres(Hz)	2.38±3.15	4.75±4.30	3.01±3.47	5.48±3.57*†
ALX(cmH2O/L/s Hz)	4.81±10.12	16.22±17.99**	7.39±11.87	22.26±28.20**†

Table 3. Health-related quality of life and exercise tolerance in the four groups.
CAT, COPD Assessment Test; SGRQ, St. George's Respiratory Questionnaire
** p<0.01, * p<0.05 vs. NCT phenotype

	NCT	AD	ED	Mixed
CAT				
n	28	22	50	17
Cough	0.43±0.92	0.86±1.13	1.06±1.38	1.41±1.46*
Phlegm	0.29±0.76	0.55±1.10	0.98±1.39*	1.12±1.27
Chest tightness	0.25±0.65	0.59±1.01	0.55±1.04	1.00±1.06*
Breathlessness going up hills/stairs	0.54±1.23	1.50±1.63	1.42±1.74	2.63±1.67**
Activity limitations at home	0.04±0.19	0.05±0.21	0.34±0.92	0.18±0.53
Confidence leaving home	0.25±0.80	0.23±0.61	0.44±1.18	0.29±0.77
Sleep	0.29±0.76	0.27±0.77	0.30±0.86	0.29±0.59
Energy	0.54±0.96	0.73±1.20	0.64±1.10	0.65±1.11
Total score	2.61±4.56	4.77±4.50	5.72±7.52	7.41±4.49*
SGRQ				
n	10	9	34	13
Symptom	18.36±13.10	25.85±23.04	29.24±22.12	36.21±17.52
Activity	9.43±10.87	12.51±14.11	34.66±24.34**	33.41±22.55
Impact	1.92±3.29	8.35±7.63	15.05±19.39	10.38±10.29
Total score	7.07±5.44	12.36±9.54	23.70±19.63*	21.98±11.16*
6-minute walking test				
n	9	6	21	5
6-minute walking distance, m	441.9±106.0	348.5±126.8	425.4±124.7	481.4±154.7
pre SpO2, %	96.1±1.1	96.3±1.6	94.9±2.1	94.4±1.8
post SpO2, %	93.7±3.8	94.8±2.1	89.7±6.4	87.0±4.7
delta SpO2, %	2.4±3.6	1.5±1.9	5.3±5.4	7.0±3.7

Summary of Results

- **Clinical characteristics**
  BMI was significantly lower in the ED phenotypes than in the NCT and the AD phenotypes.
- **Pulmonary function and respiratory impedance**
  FEV1, %FEV1, RV, %RV, FRC,%FRC were significantly lower in the ED and the mixed phenotypes than in the NCT phenotype.
  DLCO, %DLCO, DLCO/VA were significantly lower in the ED and the mixed phenotypes than in the NCT and the AD phenotypes.

  R5 (whole-breath, inspiratory and expiratory phases), Fres (whole-breath, inspiratory and expiratory phases), ALX (whole-breath, inspiratory and expiratory phases) were significantly higher in the AD and the mixed phenotypes than in the NCT phenotype. X5 (whole-breath, inspiratory and expiratory phases) was significantly lower in the AD and the mixed phenotypes than in the NCT phenotype.

  There were no significant differences in respiratory impedance between the ED phenotype and the NCT phenotype.
- **Health-related quality of life**
  The total score of the CAT was significantly higher in the mixed phenotype than in the NCT phenotype.
  The total score of SGRQ was significantly higher in the ED and the mixed phenotypes than in the NCT phenotype.

Discussion

- The morphological phenotypes, which is classified according to the software-based quantification of the degree of emphysema and airway wall thickening, show several clinical characteristics in patients with COPD, as previously described [Chest 2002 122(6Suppl) :271S-5S].
- The parameters of lung hyperinflation and ventilation heterogeneity were significantly higher, and the parameters of airflow limitation and diffusion capacity of the lung were significantly lower in the ED and the mixed phenotypes. In addition, the total score of the SGRQ was significantly higher in these phenotypes**.** Our findings suggest that **health-related quality of life is associated with the degree of emphysema as well as these pulmonary function parameters.**
- The respiratory impedance measurements by means of the FOT may help to analyze airway mechanics and to identify abnormalities of the airways in patients with COPD [Inter Med 49: 23-30, 2010]. We found that the parameters of respiratory resistance such as R5 and R20 were significantly higher in the AD and mixed phenotypes who had airway wall thickening.
- The larger within-breath changes of X5 to more negative may represent easy collapsibility of small airways in expiration of tidal breath in patients with COPD [Inter Med 49: 23-30, 2010]. We found that the differences between inspiratory and expiratory phases of X5 had significantly less negative values in the AD and the mixed phenotypes.
- Our findings suggest that **the respiratory impedance measurements by means of the FOT reflect the degree of airway disease, and detect airway remodeling in patients with COPD.**

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