Data-driven Identification and Investigation of Comorbidity Profiles in Patients with Chronic Obstructive Pulmonary Disease: A Multicohort Study

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Introduction

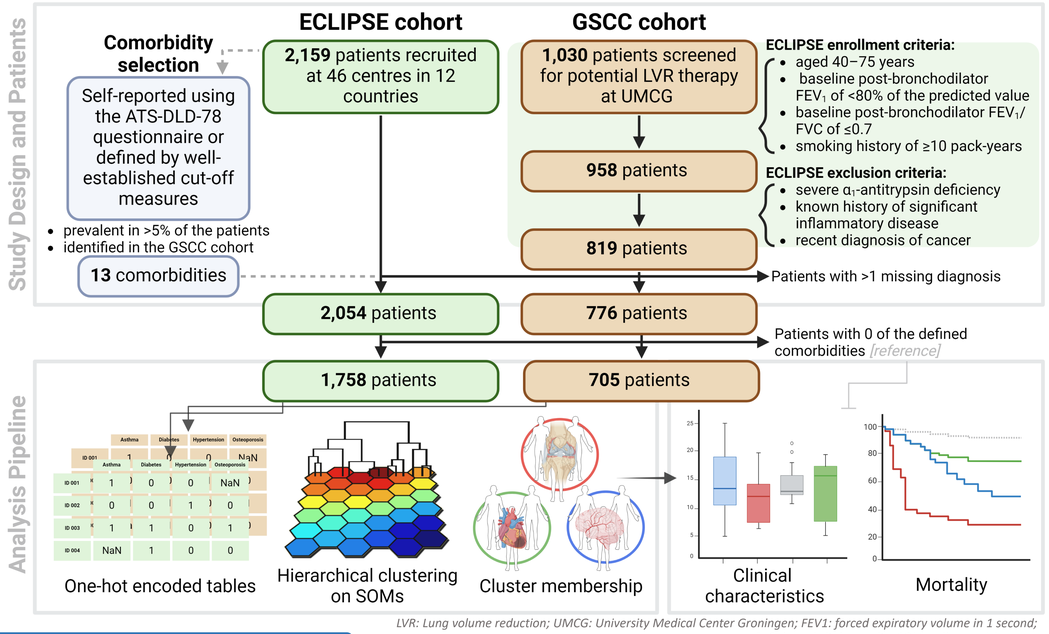
Comorbidities are common in chronic obstructive pulmonary disease (COPD), adversely affecting patients' quality of life and their disease trajectories. While previous studies have predominantly examined individual comorbidities, there has been limited exploration of their coexistence.

This study aimed to identify comorbidity clusters among real-world cohorts of COPD patients using machine learning techniques, and to investigate clinical characteristics and mortality within these clusters.

Methods

The analyses were based on data obtained from two sources:

The Evaluation of COPD Longitudinally to Identify Predictive Surrogate End-points (**ECLIPSE**; *NCT00292552*) study and the Groningen Severe COPD cohort (**GSCC**; *NCT04023409*)



LVR: Lung volume reduction; UMCG: University Medical Center Groningen; FEV1: forced expiratory volume in 1 second; FVC: forced vital capacity; SOM: self-organizing map

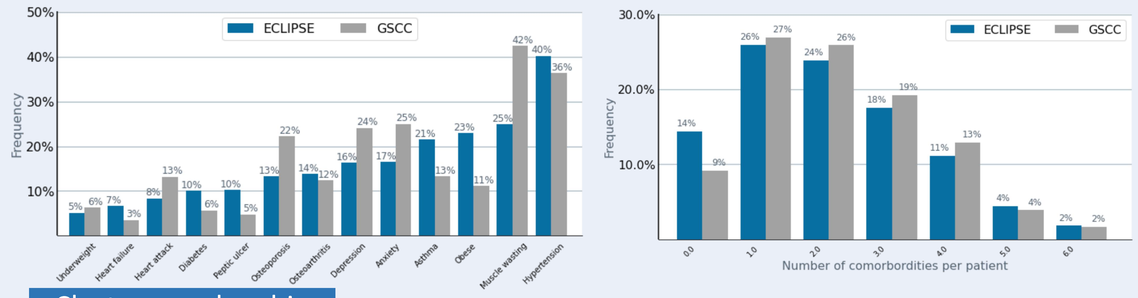
Baseline characteristics

	ECLIPSE *(n=2,054)*	GSCC *(n=776)*	P-value
Age, years	63.3 ± 7.1	61.4 ± 6.92	<0.001
Male, n (%)	1,337 (65.1)	266 (34.3)	<0.001
BMI, kg/m^2	26.5 ± 5.7	24.4 ± 4.3	<0.001
FFMI, kg/m^2	17.7 ± 3.4	15.6 ± 2.0	<0.001
Current smoker, n (%)	746 (36.3)	15 (1.9)	<0.001
FEV_1, % predicted	43.7 ± 14.9	29.6 ± 10.0	<0.001
FEV_1/FVC	0.45 ± 0.11	0.31 ± 0.07	<0.001
mMRC score	1.66 ± 1.1	2.63 ± 0.63	<0.001
SGRQ-C, total score	49.7 ± 20.4	58.9 ± 13.2	<0.001
GOLD stage E, n (%)	443 (22.0)	434 (58.9)	<0.001
AECOPD*	0.78 ± 0.98	2.3 ± 2.1	<0.001
Emphysema (-950HU)	17.7 ± 12.3	36.4 ± 8.24	<0.001

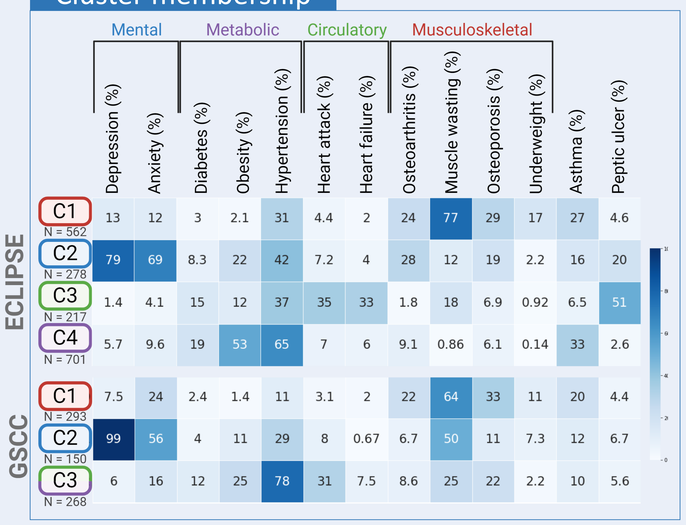
*BMI: body mass index; FFMI: fat-free mass index; FEV_1: forced expiratory volume in 1 second; FVC: forced vital capacity; mMRC: Modified Medical Research Council; SGRQ-C: St. George's Respiratory Questionnaire (COPD), GOLD: global initiative for chronic obstructive lung disease; AECOPD: acute exacerbation of COPD; HU: hounsfield units. *Average number of moderate exacerbations recorded in the 12 months prior to study entry.*
Summary statistics are expressed as mean ± standard deviation for continuous variables, while categorical variables are presented as total numbers and frequency distributions.

Results

Prevalence of Comorbidities



Cluster membership

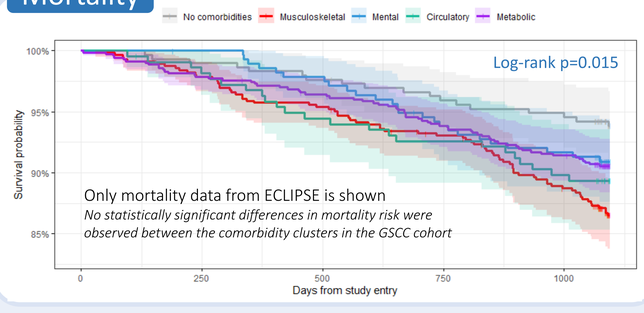


C1: Musculoskeletal
Females with lower BMI, FFMI and worse spirometry measures. More emphysema.

C2: Mental
Females and the youngest average age and above-average SGRQ-C scores.

C3/C4: Circulatory/Metabolic
Older males with above-average FFMI.

Mortality



	Univariate	Multivariate
C1	2.27 (1.36-3.80): p=0.002	2.50 (1.46-4.27): p<0.001
C2	1.50 (0.82-2.75): p=0.19	1.70 (0.92-3.13): p=0.09
C3	1.80 (0.97-3.33): p=0.06	1.60 (0.86-2.97): p=0.13
C4	1.58 (0.94-2.65): p=0.09	1.44 (0.83-2.47): p=0.19

Patients with no comorbidities were used as reference. Data are presented as hazard ratios with 95% confidence intervals and p-values. Multivariate mortality analyses are adjusted for age, sex, and BMI at baseline.

Conclusion

This study confirms **distinct comorbidity clusters** in two well-characterized cohorts of patients with COPD which can be linked to different patient subgroups. In a broad COPD patient population, comorbidity profiles could hold prognostic relevance. The findings of this study enhance the understanding of the comorbidity landscape in COPD and highlights **the importance of comorbidity assessment** in clinical management.

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Disclosures: LE, MAK, DJL, and JMBS are employed at Nordic Bioscience, and DJL, MAK, and JMBS are shareholders. CBN and JCY are employed at GSK.

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