

Online Data Supplement

Circulating 1,3-Beta-D-Glucan is Associated with Lung Function, Respiratory Symptoms, and Mediators of Matrix Degradation in Chronic Obstructive Pulmonary Disease

Matthew Gorgone, DO^{1*} Deepti Singhvi, MD^{1*} Seyed Mehdi Nouraei, MD¹ Malcolm Finkelman, PhD² Yonglong Zhang, PhD² Jiantao Pu, PhD³ Divay Chandra, MD¹ Yingze Zhang, PhD¹ Georgios D. Kitsios, MD, PhD^{1,4} Alison Morris, MD, MS^{1,4} Frank C. Sciurba, MD¹ Jessica Bon, MD, MS^{1,5}

*Authors contributed equally

¹ Division of Pulmonary, Allergy and Critical Care Medicine, Department of Medicine, University of Pittsburgh, Pittsburgh, Pennsylvania, United States

²Associates of Cape Cod Incorporated, East Falmouth, Massachusetts, United States

³Department of Radiology, University of Pittsburgh, Pittsburgh, Pennsylvania, United States

⁴Center for Medicine and the Microbiome, University of Pittsburgh, Pittsburgh, Pennsylvania, United States

⁵Veterans Affairs Pittsburgh Healthcare System, Pittsburgh, Pennsylvania, United States

**Table S1: Control Participant Characteristics
N = 50**

Age, median (IQR)	63.0 (60.0 – 69.0)
Female, n (%)	23 (46.0)
BMI, median (IQR)	28.7 (25.0 – 31.3)
Diabetes, n (%)	8 (16.1)
Current smoker, n (%)	26 (52.0)
Pack years, median (IQR)	40.5 (25.0 – 67.5)
ICS, n (%)	4 (8.0)
Oral steroid use in past 30 days, n (%)	8 (16.0)
Current oral steroid use, n (%)	5 (10.0)
FEV1pp , median (IQR)	93.2 (84.3 – 99.7)
FEV1/FVC, median (IQR)	75.2 (72.4 – 79.9)
DLCOpp, median (IQR)	78.5 (66.9 – 90.0)
SGRQ Total, median (IQR)	16.8 (8.1 – 25.8)
Visual Emphysema, n (%) ^a	
0 = none	28 (60.9)
1-2= trace/mild	16 (34.8)
3-5 = moderate/severe	2 (4.3)
Any prior exacerbations, n (%)	7 (14.0)
Any sputum production, n (%)	26 (52.0)

COPD = chronic obstructive pulmonary disease defined as post-bronchodilator FEV1/FVC ratio <0.7; IQR = interquartile range; ICS = current use of inhaled corticosteroids; FEV1pp = forced expiratory volume in the first second percent predicted; FEV1/FVC = forced expiratory volume in the first second/forced vital capacity; DLCOpp = diffusing capacity of the lung for carbon monoxide percent predicted; SGRQ = Saint George's Respiratory Questionnaire; ^an=46

Table S2: Baseline characteristics in COPD participants with High versus low 1,3-beta-d-glucal levels

	Low BDG N = 198	High BDG n = 49	p-value
Female (%)	99 (50)	20 (41)	0.27
Age (mean (SD))	64.2 (7.3)	60.9 (7.5)	0.0029
BMI (median (IQR))	26.1 (22.4 – 29.4)	26.4 (23.6 – 32.9)	0.11
Diabetes (%) ^a	32 (16.2)	8 (16.3)	0.930
Creatinine (median (IQR)) ^b	0.64 (0.47 – 0.85)	0.45 (0.31 – 0.58)	0.033
Current smoker (%)	37 (19)	5 (10)	0.20
Pack years (median (IQR)) ^c	50 (34 – 71)	55 (33 – 68)	0.90
ICS (%) ^a	129 (65)	37 (76)	0.23
Steroids (%) ^c	58 (29)	18 (37)	0.39
Current oral steroids (%) ^c	44 (22)	15 (31)	0.19

*COPD = post-Bronchodilator FEV1/FVC ratio <0.7

Steroids = Oral corticosteroid use in last 30 days, SD = Standard Deviation, IQR = Inter Quartile Range, ICS = Current use of inhaled corticosteroids. ^an=197 Low BDG; n=49 High BDG, ^bn=134 Low BDG; n=10 High BDG, ^cn=197 Low BDG; n=48 High BDG

Table S3: Clinical Outcomes in COPD Participants with High versus Low 1,3-beta-d-glucan Levels, Current Smokers Removed

	Low BDG N = 161	High BDG N = 44	p-value
FEV1pp, median (IQR)	30.2 (22.4 – 46.3)	25.7 (23.2 – 36.3)	0.072
FEV1/FVC, median (IQR)	36.8 (30.3 – 46.2)	30.7 (26.7 – 42.4)	0.037
GOLD Category, n (%)			0.051
1	12 (7.5)	0 (0)	
2	26 (16.1)	4 (9.1)	
3	43 (26.7)	9 (20.5)	
4	80 (49.7)	31 (70.4)	
SGRQ, median (IQR)	63 (44.6 – 74.4)	65 (59.4 – 74.1)	0.043
Any prior exacerbations, n (%)	87 (54.4)	32 (72.7)	0.038
Any sputum production, n (%)	77 (48.1)	30 (68.2)	0.026

BDG = 1,3-beta-d-glucan; IQR = interquartile range; FEV1pp = forced expiratory volume in the first second percent predicted; FEV1/FVC = forced expiratory volume in the first second/forced vital capacity; GOLD = Global initiative for Obstructive Lung Disease; SGRQ = Saint George's Respiratory Questionnaire

Table S4: Comparison of Matrix Metalloproteinase Levels Between Participants with High versus Low 1,3-beta-d-glucan Levels

	Low BDG N = 198	High BDG N = 49	p-value
MMP1 (pg/mL), median (IQR)	1879 (1318 – 3277)	2667 (1513 – 7029)	<0.001
MMP7 (pg/mL), median (IQR)	13098 (9662 – 18958)	10017 (7518 – 14224)	0.019
MMP9 (pg/mL), median (IQR)	36.3 (26.9 – 48.7)	32.8 (24.7 – 48.4)	0.54
TIMP1 (pg/mL), median (IQR)	67246 (56800 – 78941)	71410 (53899 – 84262)	0.12
TIMP2 (pg/mL), median (IQR)	65828 (58747 – 73834)	60363 (51429 – 67245)	0.040
TIMP4 (pg/mL), median (IQR)	1478 (1119 – 1876)	1306 (1000 – 1560)	0.18

MMP = Matrix metalloproteinase; TIMP = tissue inhibitors of metalloproteinases