

Supplementary Data

Peripheral blood eosinophils: a surrogate marker for airway eosinophilia in stable COPD

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Table S1: Summary of sensitivity and specificity for different percentage blood eosinophil cut points for detecting sputum eosinophilia (sputum eosinophil $\geq 3\%$)

Percentage Blood eosinophil count (%)	Sensitivity %	Specificity %	Correctly Classified %	LR+	LR-
≥ 0.56	97.78	6.25	35.46	1.0430	0.3556
≥ 0.79	97.78	7.29	36.17	1.0547	0.3048
≥ 1.08	97.78	8.33	36.88	1.0667	0.2667
≥ 1.11	97.78	9.38	37.59	1.0789	0.2370
≥ 1.14	97.78	10.42	38.30	1.0915	0.2133
≥ 1.15	97.78	11.46	39.01	1.1043	0.1939
≥ 1.16	97.78	12.50	39.72	1.1175	0.1778
≥ 1.19	97.78	13.54	40.43	1.1309	0.1641
≥ 1.22	97.78	14.58	41.13	1.1447	0.1524
≥ 1.23	97.78	15.63	41.84	1.1588	0.1422
≥ 1.25	97.78	17.71	43.26	1.1882	0.1255
≥ 1.32	97.78	18.75	43.97	1.2034	0.1185
≥ 1.33	97.78	20.83	45.39	1.2351	0.1067
≥ 1.35	97.78	22.92	46.81	1.2685	0.0970
≥ 1.37	97.78	26.04	48.94	1.3221	0.0853
≥ 1.39	97.78	27.08	49.65	1.3410	0.0821
≥ 1.41	97.78	28.13	50.35	1.3604	0.0790
≥ 1.47	97.78	29.17	51.06	1.3804	0.0762
≥ 1.50	97.78	31.25	52.48	1.4222	0.0711
≥ 1.54	97.78	32.29	53.19	1.4441	0.0688
≥ 1.56	97.78	33.33	53.90	1.4667	0.0667

≥ 1.61	97.78	38.54	57.45	1.5910	0.0577
≥ 1.64	97.78	39.58	58.16	1.6184	0.0561
≥ 1.70	93.33	40.63	57.45	1.5719	0.1641
≥ 1.72	93.33	41.67	58.16	1.6000	0.1600
≥ 1.75	91.11	41.67	57.45	1.5619	0.2133
≥ 1.79	91.11	42.71	58.16	1.5903	0.2081
≥ 1.85	91.11	43.75	58.87	1.6198	0.2032
≥ 1.89	91.11	44.79	59.57	1.6503	0.1984
≥ 1.92	91.11	45.83	60.28	1.6821	0.1939
≥ 1.94	91.11	46.88	60.99	1.7150	0.1896
≥ 2.04	91.11	47.92	61.70	1.7493	0.1855
≥ 2.06	91.11	48.96	62.41	1.7850	0.1816
≥ 2.08	91.11	50.00	63.12	1.8222	0.1778
≥ 2.11	91.11	51.04	63.83	1.8610	0.1741
≥ 2.13	88.89	52.08	63.83	1.8551	0.2133
≥ 2.17	88.89	53.13	64.54	1.8963	0.2092
≥ 2.20	88.89	54.17	65.25	1.9394	0.2051
≥ 2.30	86.67	56.25	65.96	1.9810	0.2370
≥ 2.31	86.67	57.29	66.67	2.0293	0.2327
≥ 2.41	86.67	58.33	67.38	2.0800	0.2286
≥ 2.47	86.67	59.38	68.09	2.1333	0.2246
≥ 2.53	86.67	61.46	69.50	2.2486	0.2169
≥ 2.54	86.67	62.50	70.21	2.3111	0.2133
≥ 2.63	86.67	63.54	70.92	2.3771	0.2098
≥ 2.70	86.67	64.58	71.63	2.4471	0.2065

≥ 2.78	82.22	66.67	71.63	2.4667	0.2667
≥ 2.82	80.00	66.67	70.92	2.4000	0.3000
≥ 2.86	80.00	67.71	71.63	2.4774	0.2954
≥ 2.90	80.00	69.79	73.05	2.6483	0.2866
≥ 2.94	77.78	69.79	72.34	2.5747	0.3184
≥ 2.97	73.33	69.79	70.92	2.4276	0.3821
≥ 3.06	73.33	70.83	71.63	2.5143	0.3765
≥ 3.13	73.33	71.88	72.34	2.6074	0.3710
≥ 3.17	73.33	72.92	73.05	2.7077	0.3657
≥ 3.19	73.33	73.96	73.76	2.8160	0.3606
≥ 3.23	71.11	73.96	73.05	2.7307	0.3906
≥ 3.28	68.89	75.00	73.05	2.7556	0.4148
≥ 3.30	68.89	76.04	73.76	2.8754	0.4091
≥ 3.37	66.67	76.04	73.05	2.7826	0.4384
≥ 3.39	64.44	76.04	72.34	2.6899	0.4676
≥ 3.53	64.44	77.08	73.05	2.8121	0.4613
≥ 3.57	64.44	78.13	73.76	2.9460	0.4551
≥ 3.66	64.44	79.17	74.47	3.0933	0.4491
≥ 3.67	64.44	84.38	78.01	4.1244	0.4214
≥ 3.70	62.22	84.38	77.30	3.9822	0.4477
≥ 3.75	60.00	84.38	76.60	3.8400	0.4741
≥ 3.81	60.00	85.42	77.30	4.1143	0.4683
≥ 3.85	57.78	85.42	76.60	3.9619	0.4943
≥ 3.90	55.56	87.50	77.30	4.4444	0.5079
≥ 3.92	55.56	88.54	78.01	4.8485	0.5020

≥ 3.95	51.11	88.54	76.60	4.4606	0.5522
≥ 4.00	48.89	88.54	75.89	4.2667	0.5773
≥ 4.04	44.44	90.63	75.89	4.7407	0.6130
≥ 4.08	42.22	90.63	75.18	4.5037	0.6375
≥ 4.12	42.22	91.67	75.89	5.0667	0.6303
≥ 4.21	40.00	91.67	75.18	4.8000	0.6545
≥ 4.23	37.78	91.67	74.47	4.5333	0.6788
≥ 4.29	35.56	91.67	73.76	4.2667	0.7030
≥ 4.41	33.33	91.67	73.05	4.0000	0.7273
≥ 4.48	31.11	91.67	72.34	3.7333	0.7515
≥ 4.76	28.89	91.67	71.63	3.4667	0.7758
≥ 4.82	28.89	92.71	72.34	3.9619	0.7670
≥ 4.84	28.89	93.75	73.05	4.6222	0.7585
≥ 5.05	26.67	93.75	72.34	4.2667	0.7822
≥ 5.08	26.67	94.79	73.05	5.1200	0.7736
≥ 5.19	24.44	94.79	72.34	4.6933	0.7971
≥ 5.71	20.00	94.79	70.92	3.8400	0.8440
≥ 5.80	17.78	94.79	70.21	3.4133	0.8674
≥ 6.06	15.56	94.79	69.50	2.9867	0.8908
≥ 6.25	15.56	95.83	70.21	3.7333	0.8812
≥ 6.32	13.33	95.83	69.50	3.2000	0.9043
≥ 6.58	13.33	96.88	70.21	4.2667	0.8946
≥ 6.76	13.33	97.92	70.92	6.4000	0.8851
≥ 6.86	11.11	97.92	70.21	5.3333	0.9078
≥ 7.89	8.89	97.92	69.50	4.2667	0.9305

≥ 9.07	6.67	97.92	68.79	3.2000	0.9532
≥ 9.09	6.67	98.96	69.50	6.4000	0.9432
≥ 11.46	4.44	98.96	68.79	4.2666	0.9656

Abbreviations: LR (+), positive likelihood ratio; LR (-), negative likelihood ratio.

Table S2: Summary of sensitivity and specificity for different ENR cut-off points for detecting sputum eosinophilia (sputum eosinophil ≥ 3%)

ENR	Sensitivity %	Specificity %	Correctly Classified %	LR (+)	LR (-)
≥ 0.0067	97.78	6.25	35.46	1.0430	0.3556
≥ 0.01	97.78	7.29	36.17	1.0547	0.3048
≥ 0.0116	97.78	8.33	36.88	1.0667	0.2667
≥ 0.0138	97.78	9.38	37.59	1.0789	0.2370
≥ 0.0144	97.78	10.42	38.30	1.0915	0.2133
≥ 0.0166	97.78	11.46	39.01	1.1043	0.1939
≥ 0.0172	97.78	12.50	39.72	1.1175	0.1778
≥ 0.0178	97.78	13.54	40.43	1.1309	0.1641
≥ 0.0188	97.78	15.63	41.84	1.1588	0.1422
≥ 0.0192	97.78	16.67	42.55	1.1733	0.1333
≥ 0.0196	97.78	18.75	43.97	1.2034	0.1185
≥ 0.0204	97.78	19.79	44.68	1.2190	0.1123
≥ 0.0208	97.78	21.88	46.10	1.2516	0.1016

≥ 0.0212	97.78	22.92	46.81	1.2685	0.0970
≥ 0.0227	97.78	27.08	49.65	1.3410	0.0821
≥ 0.0232	97.78	32.29	53.19	1.4441	0.0688
≥ 0.0238	97.78	34.38	54.61	1.4899	0.0646
≥ 0.0243	95.56	34.38	53.90	1.4561	0.1293
≥ 0.0250	95.56	37.50	56.03	1.5289	0.1185
≥ 0.0256	95.56	38.54	56.74	1.5548	0.1153
≥ 0.0260	93.33	42.71	58.87	1.6291	0.1561
≥ 0.0263	93.33	43.75	59.57	1.6593	0.1524
≥ 0.0270	93.33	45.83	60.99	1.7231	0.1455
≥ 0.0285	91.11	45.83	60.28	1.6821	0.1939
≥ 0.0289	91.11	46.88	60.99	1.7150	0.1896
≥ 0.0294	88.89	47.92	60.99	1.7067	0.2319
≥ 0.0307	88.89	48.96	61.70	1.7415	0.2270
≥ 0.0313	88.89	51.04	63.12	1.8156	0.2177
≥ 0.0322	88.89	52.08	63.83	1.8551	0.2133
≥ 0.0333	88.89	54.17	65.25	1.9394	0.2051
≥ 0.0344	88.89	55.21	65.96	1.9845	0.2013
≥ 0.0350	86.67	55.21	65.25	1.9349	0.2415
≥ 0.0357	86.67	56.25	65.96	1.9810	0.2370
≥ 0.0363	86.67	57.29	66.67	2.0293	0.2327
≥ 0.0370	84.44	57.29	65.96	1.9772	0.2715

≥ 0.0377	84.44	58.33	66.67	2.0267	0.2667
≥ 0.0384	84.44	59.38	67.38	2.0786	0.2620
≥ 0.0392	84.44	60.42	68.09	2.1333	0.2575
≥ 0.04	82.22	61.46	68.09	2.1333	0.2893
≥ 0.0425	80.00	62.50	68.09	2.1333	0.3200
≥ 0.0434	73.33	65.63	68.09	2.1333	0.4063
≥ 0.0444	73.33	66.67	68.79	2.2000	0.4000
≥ 0.0454	73.33	67.71	69.50	2.2710	0.3938
≥ 0.0480	71.11	69.79	70.21	2.3540	0.4139
≥ 0.0483	71.11	70.83	70.92	2.4381	0.4078
≥ 0.0491	71.11	71.88	71.63	2.5284	0.4019
≥ 0.05	71.11	72.92	72.34	2.6256	0.3962
≥ 0.0508	68.89	72.92	71.63	2.5436	0.4267
≥ 0.0512	66.67	72.92	70.92	2.4615	0.4571
≥ 0.0517	66.67	73.96	71.63	2.5600	0.4507
≥ 0.0526	66.67	75.00	72.34	2.6667	0.4444
≥ 0.0535	66.67	79.17	75.18	3.2000	0.4211
≥ 0.0540	64.44	80.21	75.18	3.2561	0.4433
≥ 0.0545	64.44	81.25	75.89	3.4370	0.4376
≥ 0.0549	64.44	82.29	76.60	3.6392	0.4321
≥ 0.0555	64.44	83.33	77.30	3.8667	0.4267
≥ 0.0566	64.44	84.38	78.01	4.1244	0.4214

≥0.0571	64.44	86.46	79.43	4.7590	0.4112
≥0.0576	60.00	86.46	78.01	4.4308	0.4627
≥0.06	60.00	87.50	78.72	4.8000	0.4571
≥0.0606	57.78	88.54	78.72	5.0424	0.4769
≥0.0612	55.56	89.58	78.72	5.3333	0.4961
≥0.0634	53.33	92.71	80.14	7.3143	0.5034
≥0.0652	51.11	92.71	79.43	7.0095	0.5273
≥0.0666	48.89	92.71	78.72	6.7048	0.5513
≥0.0681	46.67	92.71	78.01	6.4000	0.5753
≥0.0689	44.44	93.75	78.01	7.1111	0.5926
≥0.0694	42.22	93.75	77.30	6.7556	0.6163
≥0.07	42.22	94.79	78.01	8.1067	0.6095
≥0.0714	40.00	94.79	77.30	7.6800	0.6330
≥0.0735	35.56	94.79	75.89	6.8267	0.6799
≥0.0740	35.56	95.83	76.60	8.5333	0.6725
≥0.075	33.33	95.83	75.89	8.0000	0.6957
≥0.0754	28.89	95.83	74.47	6.9333	0.7420
≥0.0769	26.67	95.83	73.76	6.4000	0.7652
≥0.0816	24.44	95.83	73.05	5.8667	0.7884
≥0.0833	24.44	96.88	73.76	7.8222	0.7799
≥0.0938	22.22	96.88	73.05	7.1111	0.8029
≥0.0952	20.00	96.88	72.34	6.4000	0.8258

≥0.1	17.78	96.88	71.63	5.6889	0.8487
≥0.1016	15.56	97.92	71.63	7.4667	0.8624
≥0.1025	15.56	98.96	72.34	14.9333	0.8533
≥0.1052	13.33	98.96	71.63	12.7999	0.8758

Abbreviations: ENR, eosinophil/neutrophil ratio; LR (+), positive likelihood ratio; LR (-), negative likelihood ratio.

Table S3: Classification of participants by sputum and blood eosinophils at peripheral blood eosinophil cut-off point of $0.2 \times 10^9/L$

		Eosinophilic COPD by sputum eosinophils		Total
		Yes (≥3%)	No (< 3%)	
Eosinophilic COPD by PBE	Yes (≥ $0.2 \times 10^9/L$)	41 (91.1)	48 (50)	89
	No (< $0.2 \times 10^9/L$)	4 (8.9)	48 (50)	52
Total		45 (100)	96 (100)	141

Abbreviations: PBE, peripheral blood eosinophils. Data are expressed as number n (%).

Table S4: Classification of participants by sputum and blood eosinophils at peripheral blood eosinophil cut-off point of $0.4 \times 10^9/L$

		Eosinophilic COPD by sputum eosinophils		Total
		Yes ($\geq 3\%$)	No ($< 3\%$)	
Eosinophilic COPD by PBE	Yes ($\geq 0.4 \times 10^9/L$)	14 (31.1)	8 (8.3)	22
	No ($< 0.4 \times 10^9/L$)	31 (68.9)	88 (91.7)	119
Total		45 (100)	96 (100)	141

Abbreviations: PBE, peripheral blood eosinophils. Data are expressed as number n (%).

Table S5. Comparison of demographics, clinical characteristics and sputum cell counts between true positives (sputum eosinophil $\geq 3\%$ and peripheral blood eosinophils count $\geq 0.3 \times 10^9/L$) and false negatives (sputum eosinophil $\geq 3\%$ and peripheral blood eosinophils count $< 0.3 \times 10^9/L$).

Variable	True Positives (n=27)	False Negatives (n=18)	P-value
Demographics			
Age, years	70.8 (64.4, 75.0)	68.0 (62.5, 75.6)	0.61
Gender, male	20 (74)	10 (56)	0.22
BMI, kg/m^2	30 ± 6.5	29.5 ± 5.9	0.78
Post bronchodilator			
FEV ₁ , % predicted	61.1 ± 20.6	54.0 ± 15.3	0.22
Reversibility, L	0.028 (0.0, 0.154)	0.046 (0.018, 0.071)	0.83
Reversibility, %	2.78 (0.0, 15.44)	4.6 (1.8, 7.1)	0.83

CCI score	4.0 ± 0.2	3.4 ± 0.2	0.048
Frequent vs. Non-frequent exacerbators ^ϕ	13 vs. 14 (48.1 vs. 51.9)	9 vs. 9 (50 vs. 50)	0.99
SGRQ	42.5 (29.7, 59.0)	44.9 (39.8, 54.5)	0.41
BODEx	2 (1,3)	2 (1,5)	0.88
mMRC score ≥ 2	13 (48)	11 (61)	0.54
ICS or ICS/LABA combination use	25 (92.6)	16 (88.9)	1.00
ICS dose [¥] , µg/day	500 (160,500)	450 (250,500)	0.82
LAMA use	19 (70.4)	16(88.8)	0.27
Sputum cell counts			
Eosinophil (% count)	5.3 (4.3, 15.8)	6.6 (4.8, 9.3)	0.92
Neutrophil (% count)	45.3 (35, 67.5)	51 (33.5, 61.8)	0.75

Abbreviations: FEV₁, forced expiratory volume in 1 second; CCI, Charlson Comorbidity Index; BMI, body mass index; SGRQ, St. George Respiratory Questionnaire; BODEx, body mass index, airflow obstruction, dyspnoea, severe exacerbation; mMRC, modified Medical Research Council; ICS, inhaled corticosteroids; LABA, long-acting beta₂ agonist; LAMA, long-acting muscarinic antagonists; ^ϕFrequent exacerbators, ≥2 exacerbations in the previous year and non-frequent exacerbators <2 exacerbations in the previous year; [¥]ICS dose calculated as beclomethasone equivalents where 1µg of beclomethasone = 1µg budesonide = 0.5µg fluticasone. Data expressed as means ± standard deviation, median (IQR), or as number (%). Data are expressed as means ± SD, median (IQR), or as number n (%).