

Title: Effects of Asymptomatic Proximal and Distal Gastroesophageal Reflux on Asthma Severity

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ONLINE DATA SUPPLEMENT

Table E1

Cough by proximal or distal pH probe status

Mini-AQLQ cough response	Positive	Negative	P-value
N	160	144	
Bothered by cough (mean \pm SD) (1-7 \uparrow)*	4.4 \pm 1.8	4.8 \pm 1.8	0.06
Bothered by cough – ASUI (% of group)			0.41
Not at all	23	25	
Mild	43	49	
Moderate	29	24	
Severe	4	2	

*Lower score correspond to more bothered, e.g, 1= all the time, 7= None of the time

Cough by proximal pH probe status

Mini-AQLQ cough response	Positive	Negative	P-value
N	93	149	
Bothered by cough (1-7 \uparrow) mean \pm SD - QL	4.2 \pm 1.9	4.7 \pm 1.6	0.08
Bothered by cough – ASUI (% of group)			0.19
Not at all	22	22	
Mild	41	50	
Moderate	31	25	
Severe	6	2	

Table E2: Baseline AQLQ and SF36 responses by probe status

	pH probe result		P-value [†]
	Distal or proximal positive	Distal negative/ Proximal negative or not done	
Asthma QoL (↑) (score range: 1-7) – N (%)	160 (53)	144 (47)	
Total AQL mean ± SD	4.4 ± 1.3	4.8 ± 1.2	0.01
Symptoms	4.4 ± 1.4	4.8 ± 1.2	0.02
Activities	5.1 ± 1.4	5.5 ± 1.2	0.007
Emotional	4.4 ± 1.7	4.8 ± 1.6	0.05
Environment	3.7 ± 1.6	4.0 ± 1.7	0.17
SF-36 Quality of Life (↑) (score range: 0-100) – N	160	143	
Mean physical score ± SD	43 ± 10	45 ± 9	0.06
Mean emotional score ± SD	48 ± 11	49 ± 11	0.55
Physical functioning	65 ± 24	69 ± 24	0.11
Role physical	50 ± 42	62 ± 40	0.01
Bodily pain	66 ± 25	70 ± 23	0.15
General health	55 ± 22	56 ± 20	0.75
Vitality	50 ± 20	52 ± 20	0.45
Social functioning	72 ± 26	77 ± 25	0.17
Role emotional	67 ± 40	70 ± 40	0.48
Mental health	72 ± 20	74 ± 17	0.68

[†]P-values compare positive on distal or proximal probe result to negative distal result and negative or missing on proximal results based on Wilcoxon Rank Sum tests

Table E3: Acid exposure time in distal esophagus

	%Time with distal pH <4			P-value† Trend
	<5.5	5.5-10%	>10%	
pH Probe Classification – N (%)	199(65)	56 (18)	49 (16)	
Distal positive	10	96	100	
Proximal positive	27	65	59	
Demographic characteristics				
Mean age at randomization, yr ± SD	42 ± 14	41 ± 13	44 ± 12	0.48
Males (% of group)	30	32	37	0.38
Race or ethnic group (% of group)				
White	50	55	45	0.88
Black	38	34	45	
Hispanic	10	7	8	
Other	2	4	2	
Former smoker (% of group)	17	21	18	0.67
BMI	32 ± 9	33 ± 7	34 ± 8	0.19
Obese (BMI≥30)	49	61	57	0.15
Asthma Characteristics – N	160	93	81	
Mean age of asthma onset yr ± SD	17 ± 17	17 ± 17	14 ± 18	0.40
Use of inhaled short-acting beta-agonist (MDI/Neb) ≥ 2 times/week (% of group)	79	79	84	0.58
Unscheduled health care visit in past year (%)	58	75	55	0.72
Oral corticosteroids for asthma in past year (%)	47	64	43	0.82
Night awakenings due to asthma in past 2 weeks	13	14	20	0.18
Daily use of ICS (%)	100	100	100	
Mean ACS (↓) (score range: 0-6) ± SD	1.9 ± 0.8	1.9 ± 0.9	1.9 ± 0.9	0.57
Mean ASUI (↑) (score range: 0-1) ± SD	0.76 ± 0.16	0.71 ± 0.19	0.74 ± 0.18	0.26
Mean AQL (↑) (score range: 1-7) ± SD	4.7 ± 1.2	4.3 ± 1.2	4.7 ± 1.2	0.84

	%Time with distal pH <4			P-value† Trend
	<5.5	5.5-10%	>10%	
SF-36 Quality of Life (↑) (score range: 0-100) – N	198	124	49	
Mean physical score ± SD	44 ± 10	43 ± 10	43 ± 10	0.29
Mean emotional score ± SD	48 ± 11	46 ± 11	52 ± 9	0.20
Mean Pulmonary Function Measures - N	199	56	49	
Pre-BD FEV1 (%predicted ± SD) *	76 ± 14	77 ± 17	77 ± 14	0.61
Pre-BD FVC (%predicted ± SD) *	87 ± 13	88 ± 15	90 ± 13	0.33
FEV1 %change post-BD ± SD	11 ± 10	10 ± 11	10 ± 9	0.54
FVC %change post-BD ± SD	6 ± 7	5 ± 8	5 ± 9	0.60
Peak expiratory flow rate (%predicated ± SD)	80 ± 17	79 ± 19	77 ± 17	0.27
Methacholine contraindicated (% of group)	42	50	35	0.61
PC ₂₀ mg/mL - N	80	28	17	
mean ± SD	4.1 ± 4.9	3.2 ± 4.5	3.7 ± 4.1	0.53
GERD Symptom Assessment Scale - N	199	56	81	
Mean number of symptoms (0-15) ± SD	6.6 ± 3.5	7.4 ± 3.3	8 ± 4	0.03
Burning or acid taste (% of group)	53	59	61	0.23
Mean distress score (↓) (score range: 0-3) ± SD	0.55 ± 0.47	0.63 ± 0.50	0.70 ± 0.52	0.10
Other conditions - N	199	56	49	
Self-reported GERD (% of group)	10	16	31	0.0003
Eczema (% of group)	13	16	10	0.78
Sinusitis (% of group)	36	41	45	0.20
Rhinitis (% of group)	59	66	61	0.56
Food allergies (% of group)	19	23	18	0.83
Allergies worsen asthma (% of group)	77	77	80	0.72

KEY: ACS = Asthma Control Score. ASUI = Asthma Symptom Utility Index. AQL = Asthma Quality of Life. ↑ = higher score is better, ↓ = lower score is better, FEV₁ = Forced expiratory volume in 1 second, FVC = Forced vital capacity, BD = bronchodilator, SD = standard deviation, GERD = gastroesophageal reflux disease, SF-36 = RAND 36 item health survey.

*Predicted values for FEV1 and FVC are taken from: Hankinson JL, Odencrantz JR, Fedan KB. Spirometric reference values from a sample of the general U.S. population. Am J Respir Crit Care Med. 1999;159:179-87.

†P-values are for trend – Cochran-Armitage trend test of categorical variables and linear regression for continuous variables.

Table E4: Asthma outcomes in relation to acid exposure time in proximal esophagus

	%Time with distal pH <4			P-value† Trend
	<0.5	0.5-1.0%	>1.0%	
pH Probe Classification – N (%)	123(51)	51 (21)	68 (28)	
Distal positive	24	33	72	
Proximal positive	1	47	100	
Demographic characteristics				
Mean age at randomization, yr ± SD	42 ± 14	43 ± 11	44 ± 14	0.43
Males (% of group)	30	29	29	0.92
Race or ethnic group (% of group)				
White	50	41	53	0.63
Black	38	47	37	
Hispanic	11	10	6	
Other	2	2	4	
Former smoker (% of group)	17	20	19	0.70
BMI	32 ± 8	32 ± 9	33 ± 8	0.59
Obese (BMI≥30)	54	49	53	0.86
Asthma Characteristics – N	123	51	68	
Mean age of asthma onset yr ± SD	17 ± 18	14 ± 15	16 ± 18	0.67
Use of inhaled short-acting beta-agonist (MDI/Neb) ≥ 2 times/week (% of group)	81	80	76	0.44
Unscheduled health care visit in past year (%)	57	67	60	0.55
Oral corticosteroids for asthma in past year (%)	46	51	57	0.15
Night awakenings due to asthma in past 2 weeks	11	14	16	0.26
Daily use of ICS (%)	100	100	100	
Mean ACS (↓) (score range: 0-6) ± SD	1.8± 0.7	1.8 ± 0.9	1.9 ± 0.9	0.19
Mean ASUI (↑) (score range: 0-1) ± SD	0.76 ± 0.16	0.74 ± 0.18	0.73 ± 0.18	0.27
Mean AQL (↑) (score range: 1-7) ± SD	4.7 ± 1.2	4.6 ± 1.4	4.4 ± 1.3	0.15

	%Time with distal pH <4			P-value† Trend
	<0.5	0.5-1.0%	>1.0%	
SF-36 Quality of Life (↑) (score range: 0-100) – N	122	51	68	
Mean physical score ± SD	46 ± 10	44 ± 9	42 ± 9	0.02
Mean emotional score ± SD	48 ± 12	50 ± 10	46 ± 11	0.27
Mean Pulmonary Function Measures - N	123	51	68	
Pre-BD FEV1 (%predicted ± SD) *	77 ± 14	76 ± 15	77 ± 16	0.96
	88 ± 13	88 ± 12	87 ± 17	0.68
Pre-BD FVC (%predicted ± SD) *				
FEV1 %change post-BD ± SD	10 ± 10	10 ± 10	10 ± 10	0.55
FVC %change post-BD ± SD	6 ± 8	6 ± 7	4 ± 7	0.30
Peak expiratory flow rate (%predicated ± SD)	80 ± 17	80 ± 17	81 ± 20	0.67
Methacholine contraindicated (% of group)	52	61	60	0.23
PC ₂₀ mg/mL - N	57	19	28	0.85
mean ± SD	3.5 ± 4.6	5.1 ± 4.8	3.1 ± 4.2	
GERD Symptom Assessment Scale - N	123	56	81	
Mean number of symptoms (0-15) ± SD	6.8 ± 3.5	7.2 ± 3.7	7.1 ± 3.4	0.45
Burning or acid taste (% of group)	55	59	56	0.89
Mean distress score (↓) (score range: 0-3) ± SD	0.56 ± 0.41	0.67 ± 0.60	0.56 ± 0.38	0.67
Other conditions - N	123	51	68	
Self-reported GERD (% of group)	11	22	19	0.12
Eczema (% of group)	15	8	16	0.95
Sinusitis (% of group)	41	35	44	0.73
Rhinitis (% of group)	64	61	62	0.70
Food allergies (% of group)	20	20	19	0.95
Allergies worsen asthma (% of group)	76	78	82	0.28

KEY: ACS = Asthma Control Score. ASUI = Asthma Symptom Utility Index. AQL = Asthma Quality of Life. ↑ = higher score is better, ↓ = lower score is better, FEV₁ = Forced expiratory volume in 1 second, FVC = Forced vital capacity, BD = bronchodilator, SD = standard deviation, GERD = gastroesophageal reflux disease, SF-36 = RAND 36 item health survey.

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