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Abstract

Introduction: The relationship between esophageal and pulmonary diseases has been extensively studied, however, despite the increasing interest in understanding this bidirectional relationship, a lot remains to be elucidated. Given the significant morbidity and mortality often associated with some pulmonary disorders, an understanding of the pathophysiological mechanisms involved in this interaction is extremely important. This study further explores the relationship among various esophageal and pulmonary disorders.

Methods: This is a retrospective study of patients who underwent high resolution esophageal manometry (HREM) and pH studies at the Yale Gastrointestinal and Motility Lab between 2016 and 2019. Data was extracted from the electronic medical record after studies were reviewed by two motility specialists using the Chicago Classification v. 4.0. A total of 1078 patients were divided into five groups according to the presence of four pulmonary diagnoses: asthma (270); obstructive sleep apnea (OSA, 160); interstitial lung disease (ILD, 59); chronic obstructive pulmonary disease (COPD, 74); control (no pulmonary diagnosis, 565).

Results: The prevalence of ineffective esophageal motility (IEM) was significantly higher in ILD, asthma, and OSA patients compared to control (22.7, 18.5, 20.0 and 12.9%, respectively). Moreover, the incidence of absent contractility was four times greater in ILD patients than control patients. No statistical difference was found in frequency of motility disorders between COPD and control patients. Demeester score was higher in both OSA (36.1) and asthma (40.9) patients than in the control group (24.7) and proton pump inhibitor (PPI) was more effective in decreasing the score in these two groups.

Discussion: The prevalence of motility disorders is higher in patients with pulmonary diseases. Screening those populations with HREM and pH testing with impedance (when available) can promote bi-directional benefits and improve chronic cough management in this group.





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Esophageal Motility Disorders Frequency in Patients with Pulmonary Disorders: A Retrospective Study.

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Patient Demographics

Table 1.

	normal	asthma	OSA	ILD	COPD	
Age; mean ± SEM, yr	53.4 ± 0.7	53.1 ± 0.9	$56.6 \pm 0.9^*$	$62.4 \pm 2.2^{**}$	$64.6 \pm 1.4^{**}$	
n	(565)	(269)	(159)	(59)	(74)	
AI; mean ± SEM, kg/m ²	28.2 ± 0.3	$31.0 \pm 0.5^{**}$	$34.6 \pm 0.7^{**}$	29.1 ± 1.0	28.9 ± 0.8	
n	(543)	(270)	(157)	(59)	(74)	
emale frequency; n (%)	368 (65.1)	220 (81.5)**	120 (75.0)*	33 (55.9)	48 (65.8)	
tient's age and BMI were compared to the normal group using Student's t-test						

*p < 0.05; **p < 0.001. A chi-square test of independence was performed to examine the relation between gender and pulmonary diagnosis

Chicago Classification (v4) among patients with different pulmonary diagnosis

ble 2.	Pulmonary diagnosis frequency					
Chicago Classification	Normal (N= 565)	Asthma (N= 270)	OSA (N= 160)	ILD (N=59)	COPD (N= 74)	
EGJOO n %	83 14.69%	34 12.59%	19 11.88%	5 8.47%	12 16.22%	
Achalasia I n %	3 0.53%	0 0%	0 0%	0 0%	0 0%	
Achalasia II n %	31 5.49%	9 3.33%	4 2.50%	0 0%	4 5.41%	
Achalasia III n %	10 1.77%	3 1.11%	0 0%	1 1.69%	1 1.35%	
Absent contractility n %	19 3.36%	12 4.44%	6 3.75%	10 16.95% [*]	4 5.41%	
IEM n %	73 12.92%	50 18.52% [*]	32 20.00%*	14 23.73% [*]	13 17.57%	
Jackhammer n %	16 2.83%	9 3.33%	8 5.00%	2 3.39%	5 6.76%	
DES n %	9 1.59%	7 2.59%	5 3.13%	1 1.69%	0 0%	
Normal n %	321 56.81%	146 54.07%	86 53.75%	26 44.07%	35 47.30%	

Comparison between the groups were performed using Fischer's exact test.*p < 0.05



LES

Comparison of HREM Metrics among patients with different pulmonary diagnosis

Table 3.

NormalAsthmaOSAILDCOPDS pressure (IRP basai) n30.42 ± 0.9 (564)28.33 ± 1.1 (270)28.02 ± 1.5 (160)24.56 ± 2.0 (59)30.19 ± 1.9 (74)pressure (IRP residual) n11.17 ± 0.4 (564)9.64 ± 0.5 (267)9.24 ± 0.68 (160)9.02 ± 0.9 (59)11.94 ± 1.25 (74)DCI n2412 ± 288 (504)2130 ± 158 (240)2015 ± 213 (144)2060 ± 2.25 (45)2060 ± 2.25 (45)2060 ± 2.25 (45)Distal latency n7.01 ± 0.0 (379)6.88 ± 0.1 (185)6.38 ± 0.15 (102)7.03 ± 0.26 (37)7.11 ± 0.35 (47)DS pressure (basai) n6.66 ± 1.4 (565)6.12 ± 2.35 (270)6.14 ± 3.57 (160)7.03 ± 0.26 (160)4.04 ± 0.25 (160)S pressure (residual) n3.00 ± 0.5 (565)1.33 ± 0.38 (270)3.14 ± 0.45 (160)2.00 ± 0.45 (59)4.04 ± 0.45 (40)						
Spressure (IRP basal) 30.42 ± 0.96 28.33 ± 1.11 28.02 ± 1.55 24.56 ± 2.04 30.19 ± 1.90 n 1564 (270) (160) 9.02 ± 0.96 11.94 ± 1.25 pressure (IRP residual) 11.17± 0.44 9.64 ± 0.50° 9.24 ± 0.66° 9.02 ± 0.94 11.94 ± 1.25 DCI 2412 ± 288.9 2130 ± 158.5 2251 ± 217.5 260 ± 272.1 2542 ± 398.9 n (504) (240) (144) (45) 7.11 ± 0.34 DIstal latency 7.01 ± 0.09 6.88 ± 0.17 6.83 ± 0.15 7.03 ± 0.28 7.11 ± 0.34 N 6.66 ± 1.45 61.02 ± 2.13 61.14 ± 3.57 71.39 ± 7.52 54.69 ± 5.29* N 56.56 ± 1.45 (270) (160) 2.00 ± 0.63 4.04 ± 0.67 Spressure (residual) 3.00 ± 1.05 1.33 ± 0.38 3.14 ± 0.43 2.00 ± 0.63 4.04 ± 0.67 N 3.00 ± 1.05 (270) (160) (59) 4.04 ± 0.67		Normal	Asthma	OSA	ILD	COPD
n(564)(270)(160)(59)(74)pressure (IRP residual) n11.17±0.44 (564)9.64±0.50° (267)9.24±0.66° (160)9.02±0.94 (59)11.94±1.25 (74)DCI n2412±2880 (504)2130±1585 (240)2251±2175 (144)2060±2721 (45)2542±398.9 (70)Distal latency n7.01±0.09 (379)6.88±0.17 (185)6.83±0.15 (102)7.03±0.28 (37)7.11±0.34 (47)Distal latency n6.666±1.45 (565)61.02±2.13° (270)61.14±3.57 (160)71.39±7.52 (59)54.69±5.29° (74)Es pressure (pasal) n3.00±1.05 (565)1.33±0.38 (270)3.14±0.43 (160)2.00±0.63 (59)4.04±0.67 (74)	S pressure (IRP basal)	30.42 ± 0.96	28.33 ± 1.11	28.02 ± 1.55	24.56 ± 2.04	30.19 ± 1.90
pressure (IRP residual) n 11.17±0.44 (564) 9.64±0.50* (267) 9.24±0.66* (160) 9.02±0.94 (59) 11.94±1.25 (74) DCI n 2412±2880 (504) 2130±158.5 (240) 2251±217.5 (144) 2060±272.1 (45) 2542±398.9 (70) Distal latency n 7.01±0.09 (379) 6.88±0.17 (185) 6.83±0.15 (102) 7.03±0.28 (37) 7.11±0.34 (47) DES pressure (basal) n 66.66±1.45 (565) 61.02±2.13* (270) 61.14±3.57 (160) 7.03±7.52 (59) 54.69±5.29* (74) S pressure (residual) n 3.00±1.05 (565) 1.33±0.38 (270) 3.14±0.43 (160) 2.00±0.63 (59) 4.04±0.67 (74)	n	(564)	(270)	(160)	(59)	(74)
n (564) (267) (160) (59) (74) DCI 2412 ± 288.9 2130 ± 158.5 2251 ± 217.5 2060 ± 272.1 2542 ± 398.9 n (504) (240) (144) (45) 2542 ± 398.9 Distal latency 7.01 ± 0.09 6.88 ± 0.17 6.83 ± 0.15 7.03 ± 0.28 7.11 ± 0.34 N 66.66 ± 1.45 61.02 ± 2.13 61.14 ± 3.57 71.39 ± 7.52 64.69 ± 5.29* Spressure (basal) 30.0 ± 1.05 1.33 ± 0.38 3.14 ± 0.43 2.00 ± 0.63 4.04 ± 0.67 N 3.00 ± 1.05 (270) (160) (59) (74)	pressure (IRP residual)	11.17± 0.44	$9.64 \pm 0.50^{*}$	$9.24 \pm 0.66^{*}$	9.02 ± 0.94	11.94 ± 1.25
DCl n2412 ± 288.92130 ± 158.52251 ± 217.52060 ± 272.12542 ± 398.9n(504)(240)(144)(45)(70)Distal latency n7.01 ± 0.096.88 ± 0.176.83 ± 0.157.03 ± 0.287.11 ± 0.34JES pressure (basal) n66.66 ± 1.4561.02 ± 2.13*61.14 ± 3.5771.39 ± 7.5254.69 ± 5.29*S pressure (residual) n3.00 ± 1.051.33 ± 0.383.14 ± 0.432.00 ± 0.634.04 ± 0.67n(565)(270)(160)(160)(59)(74)	n	(564)	(267)	(160)	(59)	(74)
n(504)(240)(144)(45)(70)Distal latency n7.01 ± 0.09 (379)6.88 ± 0.17 (185)6.83 ± 0.15 (102)7.03 ± 0.28 (37)7.11 ± 0.34 (47)JES pressure (basal) n66.66 ± 1.45 (565)61.02 ± 2.13* (270)61.14 ± 3.57 (160)71.39 ± 7.52 (59)54.69 ± 5.29* (74)S pressure (residual) n3.00 ± 1.05 (565)1.33 ± 0.38 (270)3.14 ± 0.43 (160)2.00 ± 0.63 (59)4.04 ± 0.67 (74)	DCI	2412 ± 288.9	2130 ± 158.5	2251 ± 217.5	2060 ± 272.1	2542 ± 398.9
Distal latency n7.01±0.09 (379)6.88±0.17 (185)6.83±0.15 (102)7.03±0.28 (37)7.11±0.34 (47)JES pressure (basal) n66.66±1.45 (565)61.02±2.13* (270)61.14±3.57 (160)71.39±7.52 (59)54.69±5.29* (74)S pressure (residual) n3.00±1.05 (565)1.33±0.38 (270)3.14±0.43 (160)2.00±0.63 (59)4.04±0.67 (74)	n	(504)	(240)	(144)	(45)	(70)
n(379)(185)(102)(37)(47)JES pressure (basal) n66.66 ± 1.45 (565)61.02 ± 2.13* (270)61.14 ± 3.57 (160)71.39 ± 7.52 (59)54.69 ± 5.29* (74)S pressure (residual) n3.00 ± 1.05 (565)1.33 ± 0.38 (270)3.14 ± 0.43 (160)2.00 ± 0.63 (59)4.04 ± 0.67 (74)	Distal latency	7.01 ± 0.09	6.88 ± 0.17	6.83 ± 0.15	7.03 ± 0.28	7.11 ± 0.34
JES pressure (basal) n 66.66 ± 1.45 (565) $61.02 \pm 2.13^*$ (270) 61.14 ± 3.57 (160) 71.39 ± 7.52 (59) $54.69 \pm 5.29^*$ (74)S pressure (residual) n 3.00 ± 1.05 (565) 1.33 ± 0.38 (270) 3.14 ± 0.43 (160) 2.00 ± 0.63 (59) 4.04 ± 0.67 (74)	n	(379)	(185)	(102)	(37)	(47)
n(565)(270)(160)(59)(74)S pressure (residual)3.00 ± 1.051.33 ± 0.383.14 ± 0.432.00 ± 0.634.04 ± 0.67n(565)(270)(160)(59)(74)	JES pressure (basal)	66.66 ± 1.45	$61.02 \pm 2.13^*$	61.14 ± 3.57	71.39 ± 7.52	$54.69 \pm 5.29^*$
S pressure (residual) 3.00 ± 1.05 1.33 ± 0.38 3.14 ± 0.43 2.00 ± 0.63 4.04 ± 0.67 n(565)(270)(160)(59)(74)	n	(565)	(270)	(160)	(59)	(74)
n (565) (270) (160) (59) (74)	S pressure (residual)	3.00 ± 1.05	1.33 ± 0.38	3.14 ± 0.43	2.00 ± 0.63	4.04 ± 0.67
	n	(565)	(270)	(160)	(59)	(74)

The HREM parameters of the four pulmonary disease groups (asthma, OSA, ILD and COPD) were compared to the normal group using Student's t-test. *p < 0.05

PPI Effect among different pulmonary diagnosis



Figure 1. Different letters mean averages were significantly different. *p < 0.05



BMI effect on demeester score



Figure 2. BMI levels differences between normal demeester score group and abnormal demeester score were compared using Student's t-test.

Conclusions

- The IEM prevalence is higher in patients with asthma, OSA and ILD compared to patients without pulmonary diseases.
- ILD patients have higher prevalence of absent contractility compared to patients without pulmonary disorders.
- PPI seems to be more efficient in reducing the demeester score in patients with asthma and OSA compared to normal patients.
- Patients with elevated demeester score have higher BMI compared to the group with normal demeester score.
- More data is necessary to explore what pH studies parameters are different among the 5 pulmonary groups in patients with similar BMI.
- Screening these populations with HREM and pH testing with impedance (when available) can promote bi-directional benefits and improve chronic cough management in this group.
- Future studies can identify if the risk for esophageal motility disorders in patients with pulmonary diseases is dependent on the severity of the latter.