Investigating the Correlation between LPR & Obesity

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Objectives: To determine whether Drug-Induced Sleep Endoscopy (DISE) findings of Laryngopharyngeal Reflux (LPR) correlate with obesity, gender, Epworth Sleepiness scale, and OSA severity.

Study design: Single center retrospective cohort study.

Methods: Patients greater than 18 years of age who underwent DISE by one surgeon at a tertiary care center from July 2016 to July 2022 were included. DISE findings, patient characteristics, demographics, polysomnogram(s), and Epworth Sleepiness Scale(s) were extracted. Fisher's exact test was used to compare categorical variables, and independent sample t-test was used to compare continuous variables. All statistical analyses were performed using IBM SPSS Statistics 28.

Results: The study included 178 patients (60.87 years ± 11.54; 31.24 BMI ± 6.21). 38 patients had LPR, and 103 patients had a BMI>30. LPR+ patients BMI was 33.11 ± 5.60, and LPR- patients BMI was 30.74 ± 6.28. There was a statistically significant relationship between obesity and LPR ($p = 0.005$). Additionally, obesity mild-moderately affected patients having LPR ($d = .404$). There was no statistically significant difference between LPR+ patients and ESS, AHI, and gender ($p = .395, .174, \& .302$ respectively).

Conclusion: DISE aids in the diagnosis and evaluation of Obstructive Sleep Apnea (OSA) by simulating natural sleep. Using this highly precise diagnostic procedure, our study shows a relationship between findings of LPR in obese patients with obesity playing a small-medium role. There was no difference between LPR and ESS, AHI, and gender.

Introduction: Obstructive Sleep Apnea (OSA) is characterized by episodes of complete or partial airway collapse, with an associated decrease in oxygen saturation or sleep arousal. OSA in the adult population is categorized into three different categories based on the Apnea-Hypopnea Index (AHI) events per hour. Mild OSA corresponds to an AHI 5 to less than 15. Additionally, moderate OSA corresponds to an AHI of 15 and less than 30, and severe OSA is an AHI greater than 30. Though population estimates vary significantly, the burden of moderate-to-severe OSA in the United States is thought to be somewhere between 3-17% of the population[1]. For patients with mild OSA, epidemiological estimates increase to 37-50%[2]. OSA correlates with high levels of comorbidities such as hypertension, diabetes, depression, anxiety, coronary artery disease, and myocardial infarction[3,4,5]. Hypersomnolence-induced traffic accidents are also a concern for those suffering from OSA. These patients suffer from a lack of restful sleep and severe daytime sleepiness[6]. OSA affects males at a higher rate than females, but postmenopausal females are at a higher risk compared to other females[4].

Continuous Positive Airway Pressure (CPAP) is still the gold standard medical treatment for OSA; however, adherence rates are relatively low, ranging between 30 and 60%[7]. Therefore, many patients seek alternatives, including surgical treatment. Due to this trend, Drug Induced Sleep Endoscopy (DISE) has become a highly utilized procedure to identify levels of collapse that ENT sleep surgeons can treat. DISE closely mimics what is occurring during normal sleep by

intravenous anesthetics such as midazolam and propofol. This procedure identifies the levels of collapse with great confidence[8]. However, there are concurrent DISE findings discovered incidentally during the procedure, of which the frequency, variety, and relationships between findings, have not been elucidated yet. One such concurrent finding is Laryngopharyngeal Reflux (LPR), which occurs when gastric contents irritate the vocal cords and can cause a sore throat[3]. The aim of this study was to determine whether DISE findings of LPR correlate with obesity and if so, what the effect of obesity is on causing LPR. We also desired to determine if the severity of sleep apnea in our cohort, as measured by AHI, was worsened in the LPR-positive group compared to the LPR-negative group. Secondary parameters included analysis of gender and Epworth Sleepiness Scale (ESS).

Methods: Patients greater than 18 years of age who underwent DISE by one surgeon at a tertiary care center from July 2016 to July 2022 were included. DISE findings, patient characteristics, demographics, polysomnogram(s), and Epworth Sleepiness Scale(s) were extracted. Fisher's exact test was used to compare categorical variables, such as LPR diagnosis and obesity, and independent sample t-test was used to compare continuous variables such as ESS, AHI, and BMI. All statistical analyses were performed using IBM SPSS Statistics 28.

Results: The study included 178 patients (60.87 years ± 11.54; 31.24 BMI ± 6.21). 38 patients (21.3%) had LPR, and 103 patients (57.9%) were obese. Mean LPR-positive patient BMI was 33.11 ± 5.60, and mean LPR-negative patient BMI was 30.74 ± 6.28. There was a statistically significant relationship between obesity and LPR diagnosis upon DISE ($p = 0.005$) using a one-tailed test and assuming equal variances, with a Chi-square value of 6.746. Additionally, an independent sample t-test generated an effect size of $d = 0.404$ via Cohen's d test, which

showed a small-to-medium effect size of obesity on developing LPR. When comparing LPR-positive and LPR-negative patients, we saw no statistically significant difference in ESS, with the mean score (scored from 0 to 24) increasing from 11.05 in our LPR-negative cohort to 11.32 in our LPR-positive cohort ($p = 0.395$). We also saw no statistically significant difference between AHI scores, with the mean score of events per hour increasing from 37.67 in our LPR-negative cohort to 41.43 in our LPR-positive cohort. There was also no statistically significant difference between genders ($p = 0.302$). For complete data, refer to Figures 1-6.

Discussion & Conclusion: LPR and obesity have been shown to have a relationship previously, where LPR is more severe in obese patients[9] but until this point, correlation between obesity and LPR diagnosis upon DISE in OSA patients had yet to be clarified. Also, by generating an effect size of $d = 0.404$ via Cohen's d test, this study was the first to show a small-medium effect size of obesity on LPR likelihood in OSA patients. A previous systematic review had found that rates of laryngopharyngeal reflux in OSA patients ranged from 30.6-89.2%[3], which is considerably different than the rate found in this study of 21.3%. The means of diagnosis and screening varied between studies where Reflux Symptom Index (RSI) was sometimes used as a non-procedural method of LPR diagnosis[3]. Further research would help to clarify the rate at which LPR occurs in the OSA population. Future work as an extension from this project would be analyzing the rate of occurrence of LPR with other concurrent findings and measures of obstruction, such as Lingual Tonsillar Hypertrophy, laryngomalacia, macroglossia, tracheomalacia, laryngeal polyps, vocal cord nodules, as well as their specific areas of collapse. Additionally, it would be of interest to determine if any significant differences between race or socioeconomic status existed in terms of LPR occurrence. Further data collection of patients

undergoing DISE as well as extending our statistical analyses on the existing cohort of patients would help improve both the power and the scope of our study.

Figure 1. Expected levels of LPR and Obesity within our cohort

LPR? (Y/N) * Obese? Crosstabulation

			Obese?		
			n	y	Total
LPR? (Y/N)	N	Count	66	74	140
		Expected Count	59.0	81.0	140.0
	Y	Count	9	29	38
		Expected Count	16.0	22.0	38.0
Total		Count	75	103	178
		Expected Count	75.0	103.0	178.0

Figure 2. Mean BMI comparison between LPR-positive and LPR-negative cohorts

	LPR? (Y/N)	N	Mean	Std. Deviation	Std. Error Mean
BMI	NoLPR	138	30.5847	6.09625	.51895
	YesLPR	38	33.1179	5.59587	.90777

Figure 3. Statistical significance of LPR and Obesity relationship

		Significance	
		One-Sided p	Two-Sided p
LPR? (Y/N)	Equal variances assumed	.005	.009
	Equal variances not assumed	.003	.006

Figure 4. Pre-operative AHI levels between LPR-positive and LPR-negative cohorts

Group Statistics

	LPR? (Y/N)	N	Mean	Std. Deviation	Std. Error Mean
pre-op PSG AHI (no CPAP)	YesLPR+	36	41.43	22.675	3.779
	NoLPR-	133	37.67	20.875	1.810

Figure 5. ESS levels between LPR-positive and LPR-negative cohorts

Group Statistics

	LPR? (Y/N)	N	Mean	Std. Deviation	Std. Error Mean
ESS	YesLPR+	37	11.32	5.391	.886
	NoLPR-	129	11.05	5.439	.479

Figure 6. Calculated effect size of obesity on LPR within our cohort

				95% Confidence Interval	
		Standardizer[a]	Point Estimate	Lower	Upper
LPR? (Y/N)	Cohen's d	.404	-.400	-.700	-.099
	Hedges' correction	.406	-.398	-.697	-.098
	Glass's delta	.452	-.357	-.658	-.055

d. References

1. Peppard PE, Young T, Barnet JH, Palta M, Hagen EW, Hla KM. “Increased prevalence of sleep-disordered breathing in adults.” *Am J Epidemiol*. 2013;177(9):1006-1014. doi:10.1093/aje/kws342

2. Franklin KA, Lindberg E. “Obstructive sleep apnea is a common disorder in the population-a review on the epidemiology of sleep apnea.” *J Thorac Dis*. 2015;7(8):1311-1322. doi:10.3978/j.issn.2072-1439.2015.06.11

3. Magliulo G, Iannella G, Polimeni A, De Vincentiis M, Meccariello G, Gulotta G, Pasquariello B, Montevecchi F, De Vito A, D'Agostino G, Gobbi R, Cammaroto G, Vicini C. “Laryngopharyngeal reflux in obstructive sleep apnoea patients: Literature review and meta-analysis.” Am J Otolaryngol. 2018 Nov-Dec;39(6):776-780. doi: 10.1016/j.amjoto.2018.09.006. Epub 2018 Sep 12. PMID: 30224217.

4. Pinto, J. A., Ribeiro, D. K., Cavallini, A. F., Duarte, C., & Freitas, G. S. (2016). “Comorbidities Associated with Obstructive Sleep Apnea: a Retrospective Study.” *International archives of otorhinolaryngology*, *20*(2), 145–150. https://doi.org/10.1055/s-0036-1579546

5. Mohananey et al., “Recognized Obstructive Sleep Apnea Is Associated With Improved In-Hospital Outcomes After ST Elevation Myocardial Infarction.”

6. Molnar M.Z., Mucsi I., Novak M., Szabo Z., Freire A.X., Huch K.M., A Arah O., Ma J.Z., Lu J.L., Sim J.J., et al. “Association of Incident Obstructive Sleep Apnea with Outcomes in a Large Cohort of US Veterans.” *Thorax.* 2015;70:888–895. doi: 10.1136/thoraxjnl-2015-206970.

7. Weaver TE, Sawyer AM. Adherence to continuous positive airway pressure treatment for obstructive sleep apnoea: implications for future interventions. Indian J Med Res. 2010 Feb;131:245-58. PMID: 20308750; PMCID: PMC2972705.

8. Stanley JJ. Drug-induced sleep endoscopy: techniques, interpretation and implications. Curr Opin Pulm Med. 2020 Nov;26(6):623-628. doi: 10.1097/MCP.0000000000000723. PMID: 32890018.

9. Lechien JR, Mouawad F, Bobin F, Bartaire E, Crevier-Buchman L, Saussez S. Review of management of laryngopharyngeal reflux disease. Eur Ann Otorhinolaryngol Head Neck Dis. 2021 Sep;138(4):257-267. doi: 10.1016/j.anorl.2020.11.002. Epub 2020 Nov 27. PMID: 33257265.