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The association of obstructive sleep apnea and left ventricular hypertrophy in obese and overweight children with history of elevated blood pressure

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Abstract

Obesity is a potent cardiovascular disease (CVD) risk factor and is associated with left ventricular hypertrophy (LVH). Obstructive sleep apnea (OSA) is common among individuals with obesity and is also associated with CVD risk. The authors sought to determine the association of OSA, a modifiable CVD risk factor, with LVH among overweight/obese youth with elevated blood pressure (EBP). This was a cross-sectional analysis of the baseline visit of 61 consecutive overweight/obese children with history of EBP who were evaluated in a pediatric obesity hypertension clinic. OSA was defined via sleep study or validated questionnaire. Children with and without OSA were compared using Fisher's exact tests, Student's *t* tests, and Wilcoxon rank sum test. Multivariable logistic regression evaluated the association between OSA and LVH. In this cohort, 71.7% of the children had LVH. Children with OSA were more likely to have LVH (85.7% vs 59.4%, $P = 0.047$). OSA was associated with 4.11 times greater odds of LVH (95% CI 1.15, 14.65; $P = 0.030$), remaining significant after adjustment for age, sex, race, and BMI *z*-score (after adjustment for hypertension, $P = 0.051$). A severe obstructive apnea-hypopnea index (AHI >10) was associated with 14 times greater odds of LVH (95% CI 1.14, 172.64, $P = 0.039$). OSA was significantly associated with LVH among overweight/obese youth with EBP, even after adjustment for age, sex, race, and BMI *z*-score. Those with the most severe OSA (AHI >10) had the greatest risk for LVH. Future studies exploring the impact of OSA treatment on CVD risk in children are needed.

1 | INTRODUCTION

Cardiovascular disease (CVD) remains the leading cause of mortality worldwide.[1] The increasing prevalence of obesity is thought to contribute to this statistic,[2] as obesity has known direct and indirect effects on CVD risk factor development and cardiovascular (CV) events.[3] In addition to causing hypertension, obesity is also associated with both structural and functional cardiac changes, including left ventricular hypertrophy (LVH) and impaired systolic and diastolic function.[4] LVH is an independent risk factor for future CVD and is an important intermediate outcome in the pediatric population as it can track into adulthood, where it causes arrhythmias and cardiac events.[5] As such, CVD prevention and treatment efforts target LVH and the risk

factors associated with its development, such as hypertension and obesity.

Obstructive sleep apnea (OSA) and sleep-disordered breathing are common among individuals with obesity.[6] Because OSA can both cause and exacerbate existing hypertension[4] and may also contribute to cardiac changes,[7] this extreme form of sleep-disordered breathing is a potential modifiable risk factor for CVD. In terms of a pathophysiologic mechanism, OSA may contribute to LVH through more severe obstructive events leading to greater oxygen deprivation and more nocturnal hypertension, resulting in cardiac remodeling.

With the inherent challenges to effective treatment of obesity, having another treatment target for CVD risk reduction has important clinical implications, particularly for those with obesity who are at increased CVD risk. We therefore sought to determine the association of OSA with left ventricular hypertrophy among a high-risk group: overweight and obese youth with elevated blood pressure. We further sought to determine whether the OSA severity, as defined by the obstructive apnea-hypopnea index (AHI), was predictive of LVH among these children and adolescents.

The definition of LVH in the pediatric population has been an area of recent debate in the literature. Among specialists who treat children with hypertension, there is "considerable variation in every step of the evaluation of pediatric LVH."[8] Much of the debate centers around how to properly account for the fact that children are actively growing, and whether or not an adult threshold for LVH can be appropriately applied to children. Because of this lack of consensus, we have included three definitions of LVH that have been used in the pediatric literature in our analyses.

2 | METHODS

2.1 | Study subjects and study design

This was a cross-sectional analysis of data obtained from the baseline visit of consecutive children evaluated in an urban pediatric obesity hypertension clinic between January 1, 2015, and January 1, 2018. The study population consists of overweight and obese patients with a history of elevated blood pressure who were referred for evaluation of hypertension. Informed consent and assent were obtained at the baseline visit for inclusion in the prospective patient registry. The Institutional Review Board at Johns Hopkins University School of Medicine approved this study.

2.2 | Data collection

2.2.1 | Anthropometric measurements

Height was measured with a stadiometer to the nearest 0.1 cm, and weight was measured (wearing light clothing) by a calibrated standing balance scale to the nearest 0.1 kg. Body mass index (BMI) was calculated as (kg/m^2). Height, weight, BMI percentiles, and *z*-scores were calculated using Centers for Disease Control and Prevention normative growth data.[9,10] Waist circumference was measured 1 cm above the patients' navel on exhale using a Gulick tape measure which applies known tension. Hip circumference was measured at the widest girth around the hip and buttocks in triplicate.

2.2.2 | Blood pressure measurements

After five minutes of rest, a single study physician (TMB) obtained three manual BP measurements with a calibrated aneroid sphygmomanometer, 30 seconds apart. BP cuffs were selected based on measured mid-arm circumference. The three BP measurements were averaged to provide one overall measurement for the baseline visit. In order to compare the degree of BP elevation among all patients, in comparison with the threshold for hypertension, BPs were indexed. A patient's average systolic BP was divided by the corresponding 95th percentile systolic BP for the patient's age, sex, and height.[11] This gives a systolic BP index (SBPi) such that SBPi ≥1 indicates a SBP above the threshold for hypertension, and each 0.1 increment above or below 1 represents a 10% increase or decrease from that threshold. The same calculation was carried out for each patient's average diastolic BP, yielding a diastolic BP index (DBPi). For participants 13 years of age and older, 130 mm Hg was used as the denominator for calculating SBPi and 80 mm Hg was used as the denominator for calculating DBPi, in accordance with current guidelines regarding the threshold for hypertension.[11]

2.2.3 | Definition of LVH

Standardized two-dimensional guided M-mode echocardiography done within 3 months of the baseline visit was used to determine left ventricular mass, which was calculated using the Devereux Equation[12]:

$$\begin{aligned}\text{LVM (g)} = 0.81\,[1.04\,(&\text{intraventricular septal thickness} + \\ &\text{posterior wall thickness} + \text{LV end - diastolic internal dimension})^3 \\ &-(\text{LV end diastolic internal dimention})^3] + 0.06\end{aligned}$$

Three of the included children had echocardiogram done 7-8 months from the baseline visit. The left ventricular mass index (LVMI) was then calculated as (LVM/height in meters$^{2.7}$). LVH was defined in three separate ways consistent with previous pediatric studies and clinical hypertension guidelines: as LVMI ≥38.6 g/m$^{2.7}$, as LVMI ≥95th percentile[11,13] or as LVMI ≥51 g/m$^{2.7}$. The definition of LVH as LVMI ≥38.6 g/m$^{2.7}$ is a widely used definition of LVH in pediatrics and corresponds to the 95th percentile of LVM distribution among 192 healthy children aged 6-17 in the early 1990s.[14] The fourth report selected the definition of LVH as LVMI ≥51 g/m$^{2.7}$, a value that has been associated with a 4-fold greater risk of cardiovascular disease in adults.[15] We chose to include all three definitions of LVH in our analyses for completeness, as the best

method for indexing LV mass in children remains an area of active investigation.[11]

2.2.4 | Definition of OSA

Obstructive sleep apnea was defined based on sleep study results when available within 12 months of the baseline visit (n = 21). In instances where there was no sleep study within this timeframe (n = 34), or there was an intervention to treat OSA after the sleep study (tonsillectomy and adenoidectomy or the use of CPAP with adherence, n = 6), then OSA was defined according to a validated sleep questionnaire.[16,17]

For those children with a sleep study that fell within the criteria above, the severity of the obstructive AHI was categorized as mild, moderate, or severe with 1.5≤ AHI ≤5 defined as mild, 5< AHI ≤10 defined as moderate, and AHI >10 defined as severe.[18]

The sleep studies involved full in-laboratory polysomnography, using RemLogic sleep software to collect data. Polysomnography included electroencephalography (EEG), submental and tibial electromyography (EMG), right and left electrooculography (EOG), electrocardiography (ECG), oxygen saturation (SaO_2), end-tidal CO_2, oximeter pulse waveform, audio- and videorecording, nasal airflow monitored with a pressure transducer, as well as thoracic and abdominal plethysmography. Identification and scoring of sleep stages, arousals, and respiratory events were performed in accordance with AASM standards.

2.3 | Statistical analysis

Clinical variables were compared between those with and without OSA at baseline visit. Categorical variables were compared using Fisher's exact tests, and continuous variables were compared using Student's *t* tests for normally distributed data and Wilcoxon rank sum test for non-normally distributed data.

Logistic regression was used to evaluate the association between OSA and LVH. To evaluate whether demographic variables or obesity

TABLE 1 Characteristics and cardiovascular disease risk factors stratified by obstructive sleep apnea (OSA)

Mean (SD), median (IQR), or N (%); n as indicated by footnotes	Overall (n = 61)	OSA (n = 28)	No OSA (n = 33)	*P*-value
Demographics				
Age (y) Ma, Age[a]	13.1 (3.8), 61	13.0 (3.8), 28	13.2 (3.9), 33	0.830
Male[b]	37 (60.7), 61	16 (57.1), 28	21 (63.6), 33	0.793
African American[b]	50 (82.0), 61	23 (82.1), 28	27 (81.8), 33	1.000
Measures of adiposity				
Weight (kg)[a]	100.0 (36.4), 61	105.2 (43.1), 28	95.7 (29.5), 33	0.327
Weight percentile[c]	100.0 (99.0, 100.0), 60	100.0 (99.8, 100.0), 28	100.0 (99.0, 100.0), 32	0.172
Weight *z*-score[a]	2.8 (0.6), 58	2.9 (0.6), 27	2.7 (0.6), 31	0.099
BMI (kg/m^2)[c]	36.3 (32.1, 42.5), 61	37.5 (32.6, 44.4), 28	35.8 (30.5, 40.6), 33	0.297
BMI *z*-score[c]	2.6 (2.4, 2.8), 58	2.7 (2.5, 2.9), 27	2.5 (2.3, 2.7), 31	0.018
Waist circumference (cm)[a]	110.8 (21.0), 55	113.9 (23.6), 27	107.8 (18.2), 28	0.290
Waist circumference *z*-score[a]	2.6 (0.6), 53	2.7 (0.5), 26	2.5 (0.6), 27	0.150
Hip circumference (cm)[a]	116.6 (18.6), 55	117.4 (19.9), 27	115.8 (17.6), 28	0.754
Hip circumference *z*-score[a]	3.6 (0.9), 53	3.6 (0.8), 26	3.5 (1.0), 27	0.622
Waist:Hip ratio[a]	0.9 (0.1), 55	1.0 (0.1), 27	0.9 (0.1), 28	0.061
Waist:Hip *z*-score[a]	1.7 (1.3), 53	2.1 (1.3), 26	1.4 (1.3), 27	0.064
CVD risk factors				
Systolic BP (mm Hg)[a]	122.3 (15.9), 61	124.3 (19.0), 28	120.6 (12.8), 33	0.377
Systolic BP index[a]	0.96 (0.09), 61	0.98 (0.11), 28	0.94 (0.08), 33	0.178
Diastolic BP (mm Hg)[a]	65.6 (11.3), 61	67.0 (13.4), 28	64.3 (9.2), 33	0.372
Diastolic BP index[a]	0.79 (0.12), 61	0.81 (0.14), 28	0.78 (0.11), 33	0.273
Hypertension[b]	33 (54.1), 61	17 (60.7), 28	16 (48.5), 33	0.441
LVMI ($g/m^{2.7}$)[c]	43.6 (38.1, 57.5), 60	48.5 (40.7, 60.4), 28	42.0 (36.6, 51.5), 32	0.047
LVH (LVMI ≥38.6 $g/m^{2.7}$)[b]	43 (71.7), 60	24 (85.7), 28	19 (59.4), 32	0.043
LVH (LVMI ≥95th percentile)[b]	40 (66.7), 60	22 (78.6), 28	18 (56.3), 32	0.100
LVH (LVMI ≥51 $g/m^{2.7}$)[b]	17 (28.3), 60	11 (39.3), 28	6 (18.8), 32	0.093

Abbreviations: BMI, body mass index; BP, blood pressure; LVH, left ventricular hypertrophy; LVMI, left ventricular mass index.
[a]Reporting mean (SD).
[b]Reporting N (%).
[c]Reporting median (IQR).

confounded this potential relationship, two multivariable regression models were conducted: one adjusting for age, sex, and race, and another further adjusting for BMI *z*-score. To evaluate whether BP mediated this potential relationship, a third multivariable regression model was conducted, further adjusting for the presence of hypertension.

Logistic regression was used to evaluate the association between OSA severity (AHI) and LVH among those participants that had undergone a sleep study within the criteria defined above.

A two-sided *P* value <0.05 was considered statistically significant. Statistical analyses were conducted using Stata 15 (StataCorp, LP). Data were managed using REDCap (Research Electronic Data Capture) hosted at Johns Hopkins University.

3 | RESULTS

Sixty-one patients were enrolled in the clinic registry and completed their baseline visit by January 2018. At baseline, the mean age of the children was 13.1 years (standard deviation [SD] 3.8) and 78% had class III obesity (defined as a BMI ≥140% of 95th percentile or ≥40 kg/m^2). Of these 61 children, 28 (46%) have OSA. Of these 28 children diagnosed with OSA, 16 were diagnosed by sleep study.

TABLE 2 Odds of LVH in children with OSA compared to those without OSA[a]

Model	Odds ratio	95% confidence interval	*P*-value
1			
LVH (LVMI ≥38.6 g/m$^{2.7}$)	4.11	1.15-14.65	0.030
LVH (LVMI ≥95th percentile)	2.85	0.91-8.93	0.072
LVH (LVMI ≥51 g/m$^{2.7}$)	2.80	0.87-9.01	0.083
2			
LVH (LVMI ≥38.6 g/m$^{2.7}$)	4.57	1.18-17.73	0.028
LVH (LVMI ≥95th percentile)	2.98	0.91-9.74	0.071
LVH (LVMI ≥51 g/m$^{2.7}$)	5.51	1.19-25.43	0.029
3			
LVH (LVMI ≥38.6 g/m$^{2.7}$)	4.39	1.02-19.00	0.048
LVH (LVMI ≥95th percentile)	2.54	0.72-8.95	0.148
LVH (LVMI ≥51 g/m$^{2.7}$)	3.07	0.51-18.42	0.221
4			
LVH (LVMI ≥38.6 g/m$^{2.7}$)	4.31	0.99-18.78	0.051
LVH (LVMI ≥95th percentile)	2.45	0.69-8.68	0.165
LVH (LVMI ≥51 g/m$^{2.7}$)	3.46	0.55-21.55	0.184

Note: Model 1: unadjusted.
Model 2: adjusting for age, sex, and race.
Model 3: adjusting for age, sex, race, and BMI *z*-score.
Model 4: adjusting for age, sex, race, BMI *z*-score, and HTN.
Abbreviations: HTN, hypertension; LVH, left ventricular hypertrophy; LVMI, left ventricular mass index.
[a]Among the 61 children who either underwent sleep study or completed a screening questionnaire.

3.1 | Association of OSA and LVH

Table 1 compares demographic and anthropometric characteristics and CVD risk factors between children with and without OSA. There were no statistically significant differences in age, sex, or race between the two groups. Most raw measures of adiposity, including weight, BMI, waist circumference, and hip circumference, were not significantly different between the two groups; however, those with OSA had a greater BMI *z*-score than those without OSA (2.7 vs 2.5, *P* = 0.018). Children with OSA had greater LVMI, with a median value of 48.5 g/m$^{2.7}$, compared to children without OSA, with a median value of 42.0 g/m$^{2.7}$ (*P* = 0.047). Children with OSA were more likely to have LVH defined as LVMI ≥38.6 g/m$^{2.7}$ than children without OSA (85.7% vs 59.4%, *P* = 0.047). While non-significant, a greater prevalence of children with OSA had LVH when defined as either LVMI ≥95th percentile or ≥51 g/m$^{2.7}$ than children without OSA (78.6% vs 56.3%, *P* = 0.10; 39.3% vs 18.8%, *P* = 0.093, respectively). Other CVD risk factors, including mean clinic BP (mm Hg or index) and presence of hypertension, while greater among those with OSA, were not statistically different between the two groups.

Table 2 displays the association of OSA with each definition of LVH. In an unadjusted logistic regression model, children with OSA have a 4.11 times greater odds of having LVH when defined as LVMI ≥38.6 g/m$^{2.7}$ (95% CI 1.15, 14.65; *P* = 0.030) compared to those without OSA. This association remains significant after adjustment for age, sex, race, and BMI *z*-score. This association also maintains near significance after further adjustment for hypertension (*P* = 0.051). While non-significant, OSA is also associated with a 2.8 times greater odds of LVH when defined as either LVMI ≥95th percentile (OR 2.85, 95% CI 0.91, 8.93, *P* = 0.072) or as LVMI ≥51 g/m$^{2.7}$ (OR 2.8, 95% CI 0.87, 9.01; *P* = 0.083). The association between OSA and LVH gains significance after adjustment for age, sex, and race (*P* = 0.029) when LVH is defined as LVMI ≥51 g/m$^{2.7}$.

3.2 | OSA severity and LVH

Table 3 displays the association of OSA severity as defined by the AHI with LVH among the 21 children with eligible sleep study data. With increasing AHI severity, the odds of LVH increased for each definition of LVH. In an unadjusted logistic regression model, severe obstructive AHI was associated with 14 times greater odds of LVH when defined as either LVMI ≥38.6 or LVMI 95th percentile (95% CI 1.14, 172.64, *P* = 0.039 for both), and 13.33 times greater odds of LVH defined as LVMI ≥51 g/m$^{2.7}$ (95% CI 1.07, 166.37; *P* = 0.044).

4 | DISCUSSION

In this cross-sectional analysis of overweight and obese youth with elevated blood pressure, we found that almost half of the cohort

TABLE 3 Odds of LVH in patients with mild, moderate, and severe obstructive AHI compared to those with obstructive AHI <1.5 among the 21 children who underwent a sleep study

	Odds ratio	95% confidence interval	*P*-value
Patients with mild obstructive AHI[a]			
LVH (LVMI ≥38.6 g/m$^{2.7}$)	10.00	0.78-128.77	0.077
LVH (LVMI ≥95th percentile)	4.00	0.45-35.79	0.215
LVH (LVMI ≥51 g/m$^{2.7}$)	1.60	0.08-31.77	0.758
Patients with moderate obstructive AHI[b]			
LVH (LVMI ≥38.6 g/m$^{2.7}$)	12.00	0.96-150.69	0.054
LVH (LVMI ≥95th percentile)	12.00	0.96-150.69	0.054
LVH (LVMI ≥51 g/m$^{2.7}$)	6.00	0.46-77.75	0.170
Patients with severe obstructive AHI[c]			
LVH (LVMI ≥38.6 g/m$^{2.7}$)	14.00	1.14-172.64	0.039
LVH (LVMI ≥95th percentile)	14.00	1.14-172.64	0.039
LVH (LVMI ≥51 g/m$^{2.7}$)	13.33	1.07-166.37	0.044

Abbreviations: AHI, apnea-hypopnea index; LVH, left ventricular hypertrophy; LVMI, left ventricular mass index.
[a]Mild obstructive AHI defined as 1.5≤ obstructive AHI ≤5.
[b]Moderate obstructive AHI defined as 5< obstructive AHI ≤10.
[c]Severe obstructive AHI defined as obstructive AHI >10.

had OSA. While striking, this high proportion is consistent with current estimates of OSA prevalence among obese youth.[19] In studies assessing the prevalence of OSA by polysomnography in obese children and adolescents, the prevalence of OSA has varied from 13% to 59%.[20] Previous epidemiological research has found that two important risk factors for sleep-disordered breathing in children are obesity and African American race.[21] These risk factors likely contribute to the high prevalence of OSA in this cohort made up of children from an obesity hypertension clinic, the majority of whom are African American.

Even more remarkable, greater than 70% of the cohort had LVH when defined as LVMI ≥38.6 g/m$^{2.7}$, two-thirds had LVH when defined as LVMI ≥95th percentile, and one-quarter had LVH when defined as LVMI ≥51 g/m$^{2.7}$, a cutoff associated with a 4-fold increase in CV morbidity and mortality in adults. These findings are well above published prevalence estimates for LVH among youth with hypertension,[11,15] which range from 8% to 41% depending on the definition used. Further, among these overweight and obese children with history of elevated blood pressure, OSA was a significant independent predictor of LVH when defined as LVMI ≥38.6 g/m$^{2.7}$ but the most severe form of OSA (severe AHI) was significantly associated with all three definitions of LVH. These findings suggest an important role of this CVD risk factor on intermediate outcomes in a pediatric population at great risk.

Obstructive sleep apnea screening is a recommended step in the evaluation of resistant hypertension. Diagnosis and treatment of OSA can decrease SBP and DBP by 10 mm Hg.[22] Nocturnal hypertension is more common among those with OSA, and hypertension is a known risk factor for LVH.[23] Therefore, identification of pediatric patients with OSA could allow for targeted interventions that have the added benefit of decreasing LVH and thus one's CVD risk.

Individuals with OSA have fragmented sleep, leading to symptoms such as daytime somnolence that may decrease physical activity. OSA can also alter the secretion of hormones that regulate hunger and metabolism, such as leptin and ghrelin.[19] Untreated OSA can therefore lead to dysregulated weight and an increased drive for carbohydrate-rich foods, hindering weight loss efforts and making CVD risk reduction even more challenging. Because of these hormonal and sleep changes that occur in OSA, it is possible that treatment of OSA would help in the effort to decrease BMI.

Further, both obesity and OSA promote inflammation with leptin as well as insulin resistance, factors that can contribute to LVH.[24,25] This may explain why, while OSA is typically thought to cause right heart disease, OSA was independently associated with cardiac remodeling of the left ventricle in our study. Other studies in different patient populations support our finding. Among adults with OSA diagnosed by sleep study, OSA was a significant independent predictor of LVH, even when controlling for hypertension.[26] In a non-obese, non-hypertensive, largely non-African American pediatric population, AHI was the sole independent predictor of LVMI and severe OSA (AHI >10) was associated with a 11.2 greater odds (95% CI 1.9-64) of LVH (LVMI ≥38.6 g/m$^{2.7}$) than less severe OSA (AHI <10).[27]

Our results show different strengths of association depending on the definition of LVH. This merits discussion in light of the lack of consensus in the pediatric literature regarding LVH. The association of OSA and LVH was the strongest and most consistent when LVH was defined as LVMI ≥38.6 g/m$^{2.7}$. Our goal in this study was not to argue for the best definition of LVH, but rather to investigate the association of OSA and LVH. However, our results suggest that the value of LVMI ≥38.6 g/m$^{2.7}$ may be a more sensitive marker for end-organ damage in the pediatric population, as compared to the value of 51 g/m$^{2.7}$ which has been associated with increased risk of adverse cardiovascular outcomes in adults.

The important role of sleep on CV health was emphasized in the most recent American Academy of Pediatrics' Clinical Practice Guideline for pediatric hypertension evaluation and management.[11] Adult studies have demonstrated the strong association of OSA and nocturnal hypoxia with CVD risk.[22,28] While studied less in children, recommendations address the need to screen for OSA both in hypertensive youth and in overweight and obese youth via standardized questionnaire as utilized in this study and via less-structured history taking and physical examination.

Additionally, 24-hour ambulatory blood pressure monitoring (ABPM) has been suggested as a tool to identify those with nocturnal

hypertension, an entity more common with OSA. 24-hour ABPM can also identify "non-dippers" and "reverse dipper," adverse CVD risk factors in adults that are also associated with OSA. In a study among hypertensive adults, those classified as "non-dippers" based on ABPM results were significantly more likely to have LVH compared to those with the expected dip in nighttime blood pressure.[29]

The universal treatment for obesity-related OSA is weight loss. However, this is a challenging endeavor with a long timeframe for success. Therefore, other treatment approaches such as continuous positive airway pressure (CPAP) and tonsillectomy and adenoidectomy should be considered while individuals work on this critical, but difficult to achieve,[30] factor, because effective OSA treatment reduces both daytime and nighttime blood pressures.[31] While our cross-sectional study cannot show causality, we are hopeful that based on these results future research will investigate the effective treatment of OSA as a potential means to reduce left ventricular mass index in obese children with elevated blood pressure.

Despite the promise of CVD risk reduction with OSA treatment, pediatric providers should recognize that there remain challenges to CPAP adherence among youth.[32,33] In fact, of the fourteen individuals prescribed CPAP in our study population, thirteen openly acknowledged not adhering to CPAP at home due to complaints of discomfort and difficult sleeping. Regular monitoring for adherence to CPAP and repeated emphasis of the importance of treatment are often required. Recognizing the impact these comorbid conditions have on CVD risk may help elevate the perceived importance of treatment for providers and families alike. Further, as we wait for clinical trials to confirm the efficacy of OSA treatment on LVH regression, these data may motivate youth and their families to be adherent to CPAP when OSA persists. As noted by Sawyer et al, successful interventions to increase CPAP adherence are "imperative to improve (the) health and functional outcomes in all persons with CPAP-treated OSA".[33]

Our study has several important limitations. First, our cohort size is small and from one urban pediatric obesity hypertension clinic, and thus may not be a general representation of all obese youth with elevated blood pressure. Moreover, despite a consistent strength of association between OSA and LVH across all models (OR 2.45-4.57), the sensitivity to detect statistically significant group differences may have been limited by this study's smaller sample size. Second, this is a cross-sectional analysis of data obtained from chart review; therefore, this study cannot establish causality. Thirdly, not all children had sleep studies completed, thus we utilized a validated sleep questionnaire to determine the presence/absence of OSA for some of these children. To determine how this classification scheme might have impacted our results, we conducted sensitivity analyses that included only the group of children who underwent a sleep study within the appropriate time frame. This showed that increasing severity of obstructive AHI was associated with LVH, with severe obstructive AHI (obstructive AHI >10) significantly associated with LVH regardless of how LVH was defined. These results were consistent with our overall study results and fit well with the physiologic plausibility of how OSA might contribute to LVH among obese children and adolescents with elevated blood pressure. That is, more severe obstructive events lead to greater oxygen deprivation, greater "non-dipping" of BP and more nocturnal hypertension, all of which results in cardiac remodeling designed to counterbalance these events. In addition to conducting sensitivity analyses of the 21 children who underwent sleep study, we examined how well the PSQ correlated with sleep study results in our cohort. Of the 21 children who underwent sleep study, 16 were diagnosed with OSA. Of these 16 children, three would have been misclassified as not having OSA by the PSQ. Of the five children who were found to not have OSA via sleep study, three would have been misclassified as having OSA by the PSQ. This reflects the use of the PSQ as an initial screening questionnaire, in that it may be over-estimating OSA in those children who do not in fact have OSA. However, we are reassured by the fact that more than 80% of the children who did have OSA diagnosed by sleep study would have been accurately reflected in the PSQ results.

5 | CONCLUSION

In summary, OSA was found to have a significant association with LVH among obese children and adolescents with history of elevated blood pressure. This cohort had a very high prevalence of LVH, likely a reflection of the extreme level of obesity among these children and adolescents. Those with the most severe form of OSA, with an AHI >10, had the greatest risk for pathologic cardiac remodeling. Although the study population is a small cohort from a single urban clinic, it provided data from a group of obese children and adolescents at increased CVD risk, with standardized anthropometric, BP, and echocardiography measurements. These data, as well as those from others, suggest that OSA may be an underappreciated CVD risk factor, and one that is treatable if identified. Therefore, screening for OSA should be a consistent part of the evaluation and care of patients with hypertension.

CONFLICT OF INTEREST

The authors have no conflicts of interest to disclose.

AUTHOR CONTRIBUTIONS

Each author has seen and approved the final version submitted for your review and takes full responsibility for its contents. All authors have participated in the content and design; analysis and interpretation of data; drafting or revising of the manuscript; have seen and approved the manuscript as submitted; and take full responsibility for the manuscript. I (CEH) personally wrote the first draft of the manuscript.

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