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SCIENTIFIC INVESTIGATIONS

Twenty-year follow-up of children with obstructive sleep apnea

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Study Objectives: Obstructive sleep apnea (OSA) in children is associated with acute metabolic, cardiovascular, and neurocognitive abnormalities. The long-term outcomes of childhood OSA into adulthood have not been established. We performed a 20-year follow-up of patients with polysomnography-documented OSA in childhood compared to a healthy control group to evaluate the long-term anthropometric, sleep, cognitive, and cardiovascular outcomes.

Methods: Children diagnosed with severe OSA between ages 1 and 17 years (mean, 4.87 ± 2.77) were prospectively contacted by telephone as young adults after approximately 20 years. Data collected included reported anthropometric information, educational level, health history, and Berlin questionnaire scores.

Results: Young adults with confirmed severe OSA in childhood had significantly higher adulthood body mass index (P = .038), fewer academic degrees (P < .001), and more snoring (P = .045) compared to control patients. The apnea-hypopnea index during childhood trended toward predicting cardiovascular outcomes and the results of the Berlin questionnaire in adulthood.

Conclusions: Adults with a history of severe childhood OSA have a high risk of snoring, elevated body mass index, and lower academic achievement in adulthood. Thus, children with severe OSA may be at increased risk of chronic diseases later in life. The intervening coronavirus disease 2019 (COVID-19) pandemic has introduced considerable additional neurobehavioral morbidity complicating the identification of the full long-term consequences of childhood OSA.

Keywords: children, obstructive sleep apnea, sleep-disordered breathing, COVID-19

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BRIEF SUMMARY

Current Knowledge/Study Rationale: Obstructive sleep apnea is a common cause of acute metabolic, cardiovascular, and neurocognitive sequelae in children. The long-term consequences of childhood obstructive sleep apnea into adulthood are unknown.

Study Impact: Adults with a history of severe childhood obstructive sleep apnea have a high risk of snoring, elevated body mass index, and lower academic achievement in adulthood. The apnea-hypopnea index during childhood trended toward predicting cardiovascular outcomes and the results of the Berlin questionnaire in adulthood.

INTRODUCTION

Obstructive sleep apnea (OSA) consists of a spectrum of abnormal breathing patterns during sleep characterized by a combination of snoring, increased upper airway resistance, electrocortical arousals, and/or gas exchange abnormalities.[1] The prevalence of OSA in children is 1%–4%.[2–4] The main risk factors for OSA in children are adenotonsillar hypertrophy,[5] obesity, craniofacial abnormalities,[6] and neuromuscular disease. OSA-associated morbidity includes elevated blood pressure, daytime sleepiness, learning problems, and growth failure.[1,7,8] There is a correlation between the severity of OSA and hypertension[9,10] and neurocognitive dysfunction.[11]

If untreated, pediatric OSA may lead to substantial morbidity that may not be completely reversible with available treatment.[12] Thus, the adverse consequences may not simply be confined to the child's immediate well-being and development but may continue to be detrimental to the patient's long-term health into adulthood.[13] Nevertheless, there is very little long-term outcome data on adults who experienced OSA in childhood. Therefore, the aim of the current study was to assess the predictive performance of the apnea-hypopnea index (AHI) evaluated during childhood in predicting health consequences in these children as adults after a 20-year follow-up.

METHODS

Study design and population

This was a case-control study with a prospective questionnaire to evaluate the clinical characteristics of adult patients who were diagnosed with severe OSA (AHI > 10 events/h) in childhood between 1996 and 2006. The study was conducted from January 2020–July 2020.

Data collection

Data collection was carried out in 3 phases. The first phase was to identify children with severe OSA diagnosed at the Sleep Disorders Laboratory, Department of Pediatrics, Insubria University, F. Del Ponte Hospital, Varese (Italy), between 1996 and 2006 (time zero; T0). The patients with OSA included in this study were otherwise typically developing children with no known genetic conditions, neurodevelopmental disorders, psychiatric disorders, or cardiac disease. The second phase was to administer a questionnaire to these patients as young adults in 2020 if they could be contacted (adult follow-up; T1). Finally, the third phase was to enroll young adults without a history of pediatric OSA as control patients.

Phase 1

At T0, the clinical data were collected from medical records including sex, age, height, weight, symptoms, parental history of OSA, exposure to passive smoke, and results of polysomnography (PSG).

Phase 2

At T1, an attempt was made to contact patients identified as having OSA as children using a telephone interview (∼20-year follow-up) to obtain age, height, weight, Berlin questionnaire results,[14] educational level (academic achievement), treatment (surgery), and cardiovascular complications (myocardial infarction or hypertension). The complete telephone questionnaire is available in **Appendices 1** and **2** in the supplemental material.

Phase 3

The control group participants were recruited from young adults in a family practice clinic in Lombardy, Italy. The inclusion criteria included the absence of symptoms of OSA in childhood and no previous PSG.

PSG

Overnight PSG was performed at T0 using a Healthdyne Technologies instrument (Alice 3, Marietta, GA). The channels recorded included nasal pressure (nasal cannulas), nasal flow (thermistor), chest/abdominal movement (inductive bands), pulse oximetry, electrocardiogram, and transcutaneous carbon dioxide. Sleep staging was based on data from electroencephalogram (channels: C4-M1, C3-M2, O1-M2, O2-M1, F4-M1, F3-M2), electrooculogram (ROC/M1, LOC/M2), and submental electromyogram. PSG also included audio/video recordings and a body position sensor. The sleep stage scoring criteria were derived from Kales and Rechtshaffen.[15] An obstructive apnea was defined as a decrease in the thermistor of at least 90% lasting at least 2 breaths. An obstructive hypopnea was defined as a reduction in the thermistor of 50%–90% associated with either a 3% oxygen desaturation or an electroencephalogram arousal. An oxygen desaturation was defined as a 3% drop in the baseline oxygen saturation. The AHI was defined as the total number of obstructive apneas and hypopneas divided by the total sleep time.

The Berlin questionnaire is divided into questions regarding snoring, daytime somnolence, hypertension, and body mass index (BMI). Scores from the snoring and daytime somnolence categories were considered positive if the responses indicated frequent symptoms (> 3–4 times/week), whereas hypertension was considered present if there was a history of hypertension, and the BMI was considered elevated if it was > 30 kg/m^2. Patients were scored as being at high risk for OSA if they had a positive score in 2 or more categories, and those who did not were scored as being at low risk.[16] Obesity was defined as a BMI > 2 standard deviations from the mean for age.

Statistical analysis

Data were presented as n (%) or mean (standard deviation). Differences of categorical variables were analyzed using the chi-square test. Quantitative variables were compared using the Kruskal-Wallis test. No missing values were observed. AHI was categorized based on tertiles as follows: first tertile 10 < AHI ≤ 13 events/h, second tertile 13 < AHI ≤ 20 events/h, third tertile AHI > 20 events/h.

The performance of AHI in predicting cardiovascular complications, Berlin questionnaire score ≥ 2, and obesity was assessed using a receiver operating characteristic (ROC) analysis.[17] Estimation of the area under the curve was performed using nonparametric ROC analysis and significance was tested using the method described by DeLong et al.[18] Moreover, to avoid overrating the test performance in the ROC analysis, we performed a 5-fold cross validation.[19] Analyses were performed using R 3.6.2 software (GNU General Public License, Boston, MA). A P value < .05 was considered statistically significant. In addition, a multiple-variable logistic mixed model was fitted to predict 2 positive values on the Berlin questionnaire using the predictor variables of BMI, sex, and AHI. Another multiple-variable logistic mixed model was fitted to predict hypertension using the predictor variables of BMI, sex, and AHI.

RESULTS

Characteristics of study population

There were 180 children from our hospital identified to have had severe OSA between 1996 and 2006, and 100 (55.5%) were successfully contacted and enrolled in the study. No differences were found between patients lost to follow-up and those who completed the study (**Table S1** in the supplemental material). At T0, the mean age at OSA diagnosis was 4.87 (± 2.77) years. At T1, the mean age at follow-up was 23.58 (± 4.04) years. **Table 1** presents the T0 baseline demographic, clinical, and polysomnographic information.

Table 2 reports the characteristics of the children with severe OSA at T0 categorized according the AHI tertiles. At T0, obesity was statistically significant higher in the third tertile (P = .023). No baseline symptoms were statistically significantly different between the AHI tertiles. Drowsiness and nocturnal anxiety trended higher in children with more severe OSA but did not reach statistical significance (P = .058 and P = .062, respectively).

Table 3 reports the characteristics of enrolled patients with OSA recruited by telephone interview at follow-up (T1). The Berlin questionnaire score (score ≥ 2; %) at T1 was

Table 1—Baseline characteristics of children with severe OSA at baseline (T0).

Characteristics	Number
Physical Characteristics	
n	100
Males, n (%)	51 (51.00)
Age, y, mean (SD)	4.87 (2.77)
Height, cm, mean (SD)	105.95 (16.70)
Weight, kg, mean (SD)	20.28 (14.69)
BMI, kg/m^2, mean (SD)	16.64 (4.59)
Obesity, n (%)	16 (16.00)
AHI, events/h, mean (SD)	19.91 (11.37)
Parental/caregiver risk and treatment	
Parental history of OSA, n (%)	26 (26.00)
Cigarette smoke exposure, n (%)	32 (32.00)
Tonsil and/or adenoid surgery, n (%)	90 (90.00)
Reported symptoms	
Nocturnal snoring, n (%)	96 (96.00)
Oral or mixed breath, n (%)	93 (93.00)
Apneas, n (%)	90 (90.00)
Nasal voice, n (%)	76 (76.00)
Rhinitis, n (%)	68 (68.00)
Nocturnal movements, n (%)	67 (67.00)
URI, n (%)	64 (64.00)
Nocturnal cough, n (%)	44 (44.00)
Nocturnal anxiety, n (%)	43 (43.00)
Irritability, n (%)	41 (41.00)
Feeling of suffocation, n (%)	39 (39.00)
Wheezing, n (%)	34 (34.34)
Enuresis, n (%)	30 (30.00)
Drowsiness, n (%)	25 (25.00)
Insomnia, n (%)	24 (24.00)
Diurnal headache, n (%)	22 (22.00)
Growth delay (height ≤ fifth percentile), n (%)	16 (16.00)
School problems, n (%)	7 (7.00)
Cyanosis, n (%)	5 (5.00)

AHI = apnea-hypopnea index, BMI = body mass index, OSA = obstructive sleep apnea, SD = standard deviation, T0 = baseline (time zero), URI = upper respiratory infection.

significantly higher in patients categorized in the third childhood AHI tertile (20.6%; $P = .003$). The cardiovascular complications trended higher with more severe OSA but did not reach statistical significance (14.7%; $P = .095$). All other follow-up variables at T1 were comparable among childhood AHI tertiles. There were no differences in outcomes based on treatment received. Of the 8 young adults with childhood OSA who had obesity at T1, only 1 was also obese at T0. Of the 17 patients with AHI ≥ 13 events/h who had drowsiness at T0, only 4 had drowsiness at T1.

Table 4 presents the demographic, anthropometric, symptom, treatment, and health outcomes of patients and control patients in adulthood at T1. Patients with confirmed severe OSA in childhood had significantly higher adulthood BMI ($P = .038$) and fewer academic degrees ($P < .001$). Among reported symptoms, nocturnal snoring was more frequent in adult patients ($P = .045$), particularly both slightly and louder snoring ($P < .001$) than in control patients. Regarding treatment, history of childhood surgery (adenotonsillectomy or adenoidectomy) was more frequent in patients than in control patients ($P < .005$). Surprisingly, nocturnal anxiety ($P < .001$), insomnia ($P < .025$), drowsiness ($P < .001$), and irritability ($P < .001$) were more commonly reported in control patients. Of the 16 patients who had growth delay at T0, only 1 developed obesity at T1. The academic achievements of these 16 children were significantly different from that of the remaining 84 children; in particular, children with growth delay more frequently had less academic experience (ie, less than 8 years of education; 68.75% vs 25.00%; $P = .002$).

ROC/regression analysis

The area under the curve and 95% confidence interval (CI) for the T0 AHI in predicting T1 cardiovascular complications, obesity, and Berlin questionnaire scores ≥ 2 are presented in **Figure 1**. Good predictive performances of AHI at T0 were found for Berlin questionnaire scores ≥ 2 (0.81; 95% CI, 0.71–0.91) and cardiovascular complications (0.725; 95% CI, 0.52–0.93) at the T1 20-year follow-up. The multiple-variable logistic mixed model to predict 2 positive values on Berlin questionnaire scores, accounting for BMI and sex, showed that the AHI yielded an odds ratio of 1.185 with a 95% CI of 1.029–1.365. The multiple-variable logistic mixed model to predict hypertension, accounting for BMI and sex, showed that the AHI yielded an odds ratio of 1.152 with a 95% CI of 0.999–1.333.

DISCUSSION

We observed that obesity was more common in children with more severe OSA at baseline (T0), as expected. At T1 follow-up (approximately 20 years later), children who had had the most severe OSA no longer had a higher BMI relative to children with more mild OSA, but did have a significantly higher Berlin questionnaire score, indicating more sleep-disordered breathing symptoms. Compared to control patients, patients with childhood OSA at follow-up had higher BMI, more snoring, and lower academic achievements. However, most children with OSA did not have obesity as young adults. The AHI at T0 trended toward predicting the T1 long-term follow-up report for both the Berlin questionnaire (score ≥ 2) and cardiovascular complications. Interestingly, control patients had more nocturnal anxiety, insomnia, drowsiness, and irritability, which we hypothesize to have occurred because they were recruited during the coronavirus disease 2019 (COVID-19) pandemic, whereas patients with childhood OSA were interviewed mostly prepandemic.

In our sample of enrolled children with OSA, a family history of sleep-disordered breathing was present in 26%, which

Table 2—Characteristics of the study sample at baseline (T0) stratified by AHI severity tertiles.

Characteristics	First Tertile AHI (10–13 events/h)	Second Tertile AHI (13–20 events/h)	Third Tertile AHI (> 20 events/h)	*P*
n	35	31	34	
Sex, male, n (%)	15 (42.86)	15 (48.39)	21 (61.76)	.274
Age, y, mean (SD)	4.60 (2.45)	4.87 (2.68)	5.15 (3.19)	.773
Height, cm, mean (SD)	105.46 (16.30)	105.61 (13.79)	106.76 (19.73)	.946
Weight, kg, mean (SD)	18.50 (10.16)	19.08 (10.66)	23.21 (20.59)	.771
BMI *z* score	–0.16 (1.40)	–0.13 (1.77)	0.66 (2.02)	.248
Obesity, n (%)	2 (5.71)	4 (12.90)	10 (29.41)	.023
Polysomnography				
Average SpO_2, mean (SD)	96.38 (1.50)	95.75 (1.76)	95.20 (2.41)	.016
Minimum SpO_2, mean (SD)	76.60 (7.77)	75.74 (7.24)	66.65 (10.74)	< .001
ODI, events/h, mean (SD)	105.63 (42.41)	127.77 (40.24)	222.85 (93.96)	< .001
AHI, events/h, mean (SD)	11.49 (1.13)	16.27 (1.88)	31.91 (12.14)	< .001
Parent/caregiver risk				
Parental OSA history, n (%)	11 (31.43)	10 (32.26)	5 (14.71)	.181
Parental smoking, n (%)	10 (28.57)	12 (38.71)	10 (29.41)	.627
Children's symptoms				
Oral/mixed breathing, n (%)	32 (91.43)	27 (87.10)	34 (100.00)	.114
Nocturnal snoring, n (%)	34 (97.14)	28 (90.32)	34 (100.00)	.126
Obstructive apneas, n (%)	34 (97.14)	27 (87.10)	29 (85.29)	.211
Nasal voice, n (%)	27 (77.14)	24 (77.42)	25 (73.53)	.917
Nocturnal movements, n (%)	22 (62.86)	19 (61.29)	26 (76.47)	.349
Rhinitis, n (%)	26 (74.29)	18 (58.06)	24 (70.59)	.342
URI, n (%)	24 (68.57)	19 (61.29)	21 (61.76)	.783
Nocturnal anxiety, n (%)	17 (48.57)	8 (25.81)	18 (52.94)	.062
Irritability, n (%)	11 (31.43)	14 (45.16)	16 (47.06)	.356
Wheezing, n (%)	13 (37.14)	8 (25.81)	13 (39.39)	.473
Drowsiness, n (%)	8 (22.86)	4 (12.90)	13 (38.24)	.058
Feeling of suffocation, n (%)	13 (37.14)	14 (45.16)	12 (35.29)	.690
Diurnal headache, n (%)	7 (20.00)	5 (16.13)	10 (29.41)	.408
Enuresis, n (%)	9 (25.71)	11 (35.48)	10 (29.41)	.685
Insomnia, n (%)	12 (34.29)	5 (16.13)	7 (20.59)	.192
Height ≤ fifth percentile, n (%)	5 (14.29)	5 (16.13)	6 (17.65)	.930
School problems, n (%)	1 (2.86)	2 (6.45)	4 (11.76)	.346
Cyanosis, n (%)	3 (8.57)	1 (3.23)	1 (2.94)	.485

AHI = apnea-hypopnea index, BMI = body mass index, ODI = oxygen desaturation index, OSA = obstructive sleep apnea, SD = standard deviation, SpO_2 = oxygen saturation, T0 = baseline (time zero), URI = upper respiratory infection.

did not differ among AHI tertiles. Family studies have shown that relatives of patients with OSA have a 2- to 4-fold increased risk of developing OSA compared with control patients because of genetic risk factors including obesity.[20] The prevalence of OSA ranges from 13%–55% in children with obesity.[21,22] In our study of children with severe OSA, 16% were obese, with a significantly higher number at 29.4% for patients in the third AHI tertile (AHI > 20 events/h). At follow-up, the percentage of patients with OSA with obesity decreased to 8%, but the average BMI at T1 was greater than that of the control patients. The incidence of snoring also decreased over time from 96% during childhood to 36% after a 20-year follow-up. It is not surprising to see such improvement; the AHI has also been reported to decrease after a 5%–10% weight loss.[23] However, despite the reduction in snoring and obesity in the highest AHI tertile over the study period, there was a persistence in increased sleep-related breathing disorders, as evidenced by the higher Berlin questionnaire scores.

The Berlin questionnaire is a widely used questionnaire for OSA and has been reported to have a high sensitivity and specificity for

Table 3—Characteristics of the study population after 20-year follow-up categorized according to AHI tertiles obtained at T0.

Characteristics	First Tertile AHI (10–13 events/h)	Second Tertile AHI (13–20 events/h)	Third Tertile AHI (> 20 events/h)	*P*
n	35	31	34	
Age, y, mean (SD)	23.63 (3.61)	23.45 (3.94)	23.65 (4.63)	.978
Height, cm, mean (SD)	169.54 (10.83)	170.77 (9.85)	171.3 (10.01)	.756
Weight, kg, mean (SD)	65.74 (10.83)	66.10 (15.20)	72.09 (16.42)	.128
BMI, kg/m^2, mean (SD)	22.93 (3.76)	22.88 (4.90)	24.39 (3.85)	.248
Obesity, n (%)	1 (2.86)	4 (12.90)	3 (8.82)	.316
Education	24 (68.57)	22 (70.97)	22 (64.71)	.861
Snoring, n (%)	11 (31.43)	9 (29.03)	17 (50.00)	.151
Your snoring is:				.256
Slightly louder than breathing, n (%)	8 (66.67)	3 (33.33)	6 (35.29)	
Louder than talking, n (%)	2 (16.67)	6 (66.67)	8 (47.06)	
As loud as talking, n (%)	2 (16.67)	0 (0.00)	3 (17.76)	
How often do you snore?				.124
1–2 times/wk, n (%)	3 (25.00)	4 (44.44)	4 (23.53)	
3–4 times/wk, n (%)	8 (66.67)	1 (11.11)	8 (47.06)	
Almost every day, n (%)	1 (8.33)	4 (44.44)	5 (29.41)	
Has your snoring ever bothered other people?	4 (33.33)	6 (66.67)	9 (52.94)	.302
Has anyone noticed that you stop breathing during sleep?				.558
1–2 times/wk, n (%)	2 (5.71)	3 (9.68)	4 (11.76)	
1–2 times/mo, n (%)	0 (0.00)	0 (0.00)	1 (2.94)	
3–4 times/wk, n (%)	0 (0.00)	0 (0.00)	1 (2.94)	
Rarely or never, n (%)	33 (94.29)	28 (90.32)	28 (82.35)	
Berlin questionnaire score ≥ 2, n (%)	0 (0.00)	1 (3.23)	7 (20.59)	.003
Treatments				
Adenotonsillectomy, n (%)	23 (65.71)	20 (64.52)	21 (61.76)	.941
Tonsillectomy, n (%)	1 (2.86)	1 (3.23)	4 (11.76)	.219
Adenoidectomy, n (%)	7 (20.00)	7 (22.58)	6 (17.65)	.884
No treatment, n (%)	4 (11.43)	3 (9.68)	3 (8.82)	.935
Cardiovascular sequelae, n (%)	1 (2.86)	1 (3.23)	5 (14.71)	.095

AHI = apnea-hypopnea index, BMI = body mass index, SD = standard deviation, T0 = baseline (time zero).

OSA in adults.[24] Interestingly, young adults with a history of very severe childhood OSA (third tertile; AHI > 20 events/h) had a significantly higher Berlin questionnaire score (20.6%, $P = .003$) compared with children with less severe OSA, along with control patients.

Childhood OSA is a strong risk factor for neurobehavioral problems, such as sleepiness, impaired attention, hyperactivity, learning disorders, memory impairment, poor academic performance, and depression.[11,25,26] Although excessive daytime sleepiness is frequently reported by adults with OSA, it occurs less frequently in children.[27] Calhoun et al[28] reported that excessive daytime sleepiness was mainly associated with obesity, asthma, anxiety/depression, and difficulty falling asleep, but not OSA. On the other hand, Liu et al[29] reported that daytime sleepiness mediated the relationship between OSA symptoms and depression, loneliness, and poor school performance in Chinese children. Children with parent-reported OSA symptoms may be at high risk for poor progress in reading, writing, and math[30,31] and experience unsatisfactory progress/learning problems.[31] In our data, children with OSA achieved a lower level of academic achievement compared to control patients.

In total, 90% of young adult patients reported having airway surgery after a diagnosis of OSA in childhood. Nevertheless, young adults with childhood OSA had worse sleep respiratory symptoms at night than adult control patients. Specifically, young adults with childhood OSA had more snoring (37% vs 23%; $P = .045$), more snoring that was louder than talking (44.7% vs 8.7%; $P = .013$), and more apneas ($P = .048$) compared to the control group. Previous work has also shown that children likely to manifest persistent OSA after surgical

Table 4—Demographics, physical characteristics, symptoms during sleep and daytime, treatment, and health complications of adult patients and control patients.

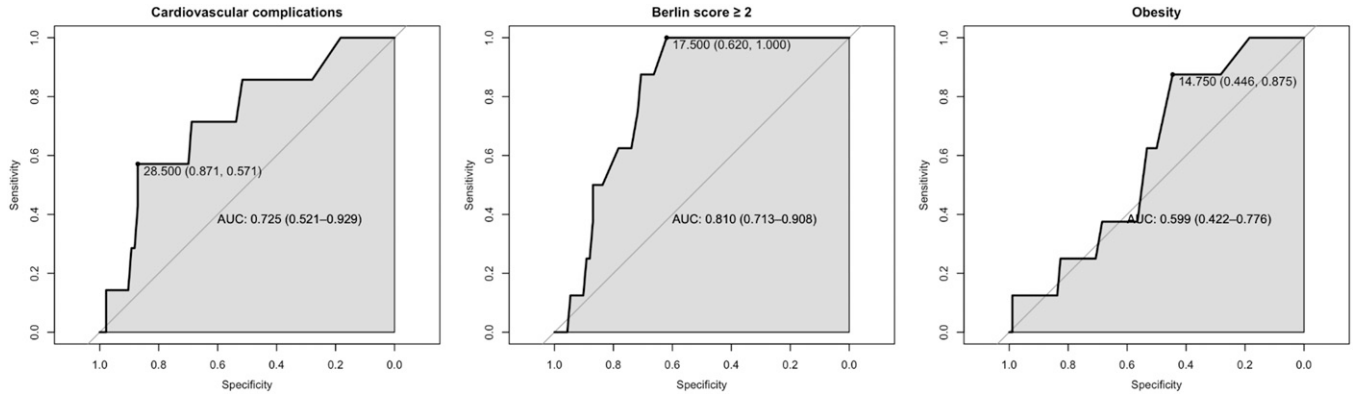
Characteristics	Patients	Control Patients	*P*
n	100	100	—
Age, y, mean (SD)	23.58 (4.04)	24.17 (3.88)	.337
Sex, male, n (%)	53 (53.00)	44 (44.00)	.258
Weight, kg, mean (SD)	68.01 (14.45)	65.22 (14.35)	.161
Height, cm, mean (SD)	170.54 (10.18)	171.00 (10.06)	.983
BMI, kg/m^2, mean (SD)	23.33 (4.19)	22.10 (3.28)	.038
Academic degree, n (%)			< .001
Primary school	1 (1.00)	0 (0.00)	
Middle school	31 (31.00)	8 (8.00)	
High school	47 (47.00)	60 (60.00)	
College degree	21 (21.00)	32 (32.00)	
Snoring, n (%)	37 (37.00)	23 (23.00)	.045
Your snoring is:			.013
Slightly louder than breathing	17 (44.74)	15 (65.22)	
As loud as talking	4 (10.53)	6 (26.09)	
Louder than talking	17 (44.74)	2 (8.70)	
How often do you snore?			< .001
Almost every day	10 (26.32)	4 (15.38)	
3–4 times/wk	17 (44.74)	6 (23.08)	
1–2 times/wk	11 (28.95)	5 (19.23)	
1–2 times/mo	0 (0.00)	6 (23.08)	
Never	0 (0.00)	5 (19.23)	
Snoring bothered other people?	19 (50.00)	13 (50.00)	> .99
Stop breathing during sleep?, n (%)			.048
1–2 times/wk	9 (9.00)	1 (1.00)	
1–2 times/mo	1 (1.00)	3 (3.00)	
3–4 times/wk	1 (1.00)	0 (0.00)	
Rarely or never	89 (89.00)	96 (96.00)	
Berlin questionnaire score ≥ 2, n (%)	8 (8.00)	2 (2.00)	.101
Nocturnal anxiety, n (%)	2 (2.00)	29 (29.00)	< .001
Insomnia, n (%)	19 (19.00)	34 (34.00)	.025
Drowsiness, n (%)	18 (18.00)	53 (53.00)	< .001
Irritability, n (%)	19 (19.00)	43 (43.00)	< .001
Adenotonsillectomy, n (%)	64 (64.00)	2 (2.00)	< .001
Tonsillectomy, n (%)	6 (6.00)	1 (1.00)	.124
Adenoidectomy, n (%)	20 (20.00)	5 (5.00)	.003
Hypercholesterolemia, n (%)	2 (2.00)	10 (10.00)	.037
Cardiovascular sequelae, n (%)	7 (7.00)	5 (5.00)	.766

BMI = body mass index, SD = standard deviation.

removal of enlarged upper airway lymphoid tissues include those with severe baseline OSA.[32]

Our finding that adult control patients experienced more nocturnal anxiety (29% vs 2%; $P < .001$), insomnia (34% vs 19%; $P = .025$), drowsiness (53% vs 18%; $P < .001$), and irritability (43% vs 19%; $P < .001$) compared to adults with childhood OSA was initially surprising. However, the patients with OSA were surveyed before the COVID-19 pandemic, whereas the control patients were interviewed during the pandemic, which severely affected Lombardy, Italy.[33] The consequences of the COVID-19 pandemic have included social isolation, reduced sleep quality, increased anxiety and mental stress, weight gain,

Figure 1—Receiver operating characteristic curves for AHI.



Performance of AHI severity during childhood in predicting cardiovascular complications, Berlin questionnaire score ≥ 2, and obesity at 20-year follow-up. AHI = apnea-hypopnea index, AUC = area under the curve.

and sleep deprivation.[34,35] Thus, there may be an overlap between the psychological consequences of OSA[36–38] and mental health problems secondary to the COVID-19 pandemic (depression and anxiety).[39] Similarly, a survey conducted among French adults showed an increased rate of sleep problems from 49% in 2017 to 74% after the lockdown (May 7–10, 2020), suggesting that the pandemic may have a long-lasting psychological impact.[40] During the first period of the COVID-19 pandemic, young people reported mental distress, particularly among females (78.09%) and students (66.82%).[41] Furthermore, a high percentage of respondents to a survey conducted during the pandemic presented with anxiety and anxiety-depressive disorders.[42]

Little long-term follow-up data have been presented regarding cardiovascular outcomes after pediatric OSA. Walter et al[43] reported that the parasympathetic activity derived from heart rate variability analysis decreased in children with OSA after resolution of their OSA but increased in children with persistent OSA after 3 years. Similarly, Chan et al[44] found that children with moderate-severe OSA early in life had an elevated nocturnal systolic blood pressure and less blood pressure dipping overnight after a 10-year follow-up. In the present study, the prognostic performance of AHI severity during childhood in predicting cardiovascular complications in adulthood was confirmed by ROC analysis. However, we found no differences in the frequency of cardiovascular complications between young adults with childhood OSA and control patients. Perhaps control patients recruited directly from a medical clinic are more likely than the general population to have had cardiovascular complications.

Limitations

This study was limited by the unfortunate occurrence of the COVID-19 pandemic during data collection. As a result of the pandemic lockdown, participants noted decreased physical activity (reported by 53% of the participants), increased sedentary time (reported by 63%), increased sleeping hours,[45] and increased snacking.[46] We cannot exclude the possibility that the increased incidence of hypercholesterolemia present in the control patients resulted from dysregulated nutrition and/or reduced physical activity during the initial period of the pandemic. Other limitations include the requirement that control patients accurately report their childhood OSA symptom status, that control patients were recruited from a family medicine practice and therefore may have been biased toward people with medical illnesses, and the lack of objective testing obtained at follow-up. We do not have specific socioeconomic or parental education data on the parents of the control group participants, and therefore the interpretation of academic performance between the groups is limited. The strength of the study is that it is the first study to document the long-term young-adult outcomes of severe childhood OSA.

CONCLUSIONS

Adults with a history of severe childhood OSA have a higher risk of having snoring, elevated BMI, and lower academic achievement in adulthood. An elevated childhood AHI is associated with both cardiovascular complications and a Berlin questionnaire score ≥ 2 in young adulthood. Thus, children with severe OSA may be at increased risk of chronic diseases later in life. The intervening COVID-19 pandemic has introduced considerable additional neurobehavioral morbidity, limiting the identification of the full long-term consequences of childhood OSA.

ABBREVIATIONS

AHI, apnea-hypopnea index
BMI, body mass index
CI, confidence interval
COVID-19, coronavirus disease 2019

OSA, obstructive sleep apnea
PSG, polysomnography
ROC, receiver operating characteristic
T0, baseline (time zero)
T1, 20-year follow-up

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DISCLOSURE STATEMENT

All authors have seen and approved the manuscript. Work for this study was performed at the Pediatric Sleep Disorders Center, Department of Pediatrics, F. Del Ponte Hospital, Insubria University, Varese, Italy. The authors report no conflicts of interest.