Treatment outcomes of obstructive sleep apnoea in obese community-dwelling children: the NANOS study

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ABSTRACT The first line of treatment of obstructive sleep apnoea syndrome (OSAS) in children consists of adenotonsillectomy (T&A). The aim of the present study was to evaluate treatment outcomes of OSAS among obese children recruited from the community.

A cross-sectional, prospective, multicentre study of Spanish obese children aged 3–14 years, with four groups available for follow-up: group 1: non-OSAS with no treatment; group 2: dietary treatment; group 3: surgical treatment; and group 4: continuous positive airway pressure treatment.

117 obese children (60 boys, 57 girls) with a mean age of 11.3±2.9 years completed the initial (T_0) and follow-up (T_1) assessments. Their mean body mass index (BMI) at T_1 was 27.6±4.7 kg·m^{-2}, corresponding to a BMI Z-score of 1.34±0.59. Mean respiratory disturbance index (RDI) at follow-up was 3.3±3.9 events·h^{-1}. Among group 1 children, 21.2% had an RDI $\geqslant$3 events·h^{-1} at T_1, the latter being present in 50% of group 2, and 43.5% in group 3. In the binary logistic regression model, age emerged as a significant risk factor for residual OSAS (odds ratio 1.49, 95% confidence interval 1.01–2.23; $p<0.05$) in obese children surgically treated, and RDI at T_0 as well as an increase in BMI emerged as significant risk factors for persistent OSAS in obese children with dietary treatment (OR 1.82, 95% CI 1.09–3.02 ($p<0.03$) and OR 8.71, 95% CI 1.24–61.17 ($p=0.03$)).

Age, RDI at diagnosis and obesity are risk factors for relatively unfavourable OSAS treatment outcomes at follow-up.

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Introduction

Sleep disordered breathing (SDB) is a highly prevalent condition potentially leading to intermittent hypoxaemia, hypercapnia and disrupted sleep. SDB and, more specifically, obstructive sleep apnoea syndrome (OSAS), have been associated with a large array of neurocognitive, behaviuoral, cardiovascular and metabolic adverse consequences that are particularly prominent in obese children [1–5].

Adenotonsillar hypertrophy emerges as the most important condition associated with OSAS, even among obese children [6–12]. It is widely accepted that the first line of treatment for OSAS consists of surgical removal of upper airway adenoids and tonsils (T&A). However, persistence of abnormal polysomnographic findings after T&A is frequent, being reported in 20–60% of cases, and with obese children constituting a particularly important risk group for residual OSAS [13–22]. However, despite the high rates of obesity in children in both developed and developing countries [23, 24], the overall evidence regarding T&A outcomes in obese children is scarce.

We conducted the present two-phase study with the aim to assess the contributions of obesity and adenotonsillar hypertrophy to paediatric OSAS. A previous report specifically focussed on the prevalence and risk factors of OSAS in obese children recruited from the community [12]. In the initial study, we found that the prevalence of OSAS in obese children was high, ranging from 21.5 to 39.5% depending on the cut-off and the polysomnographically obtained respiratory disturbance used [12]. In the present study, we examined the treatment outcomes of OSAS among obese children recruited from the community [12].

Subjects and methods

A detailed description of the methods pertaining to this cross-sectional, prospective multicentre study has been published previously [12]. Briefly, inclusion criteria were ages between 3 and 14 years, body mass index (BMI) >95th percentile for age and sex, and informed consent from parents or legal caretakers with assent being obtained from children older than 12 years. The study was approved by the local human subject committees of the institutions of the various participating cities in which paediatric sleep laboratories were available. To guarantee the confidentiality of the data, coding of all data was performed, such that personal information was not available to the investigator-based network. Exclusion criteria were failure to fulfil inclusion criteria, and presence of known genetic syndromes or any chronic debilitating disease.

In Spain, the National Health System includes a programme of "well-child visits" from birth to 14 years of age, in which systematic assessments of physical and mental development are conducted at pre-determined ages, and include among many other items, including measurement of height and weight. Based on this initial well-child assessment, obesity in the cohort was defined as the presence of a BMI corresponding to >95th percentile for age and sex using national reference values [25, 26].

Decisions on the need for treatment during the first phase of the study were reached by strictly following the Spanish consensus criteria, using a respiratory disturbance index (RDI) $\geqslant$3 events·h^{-1} total sleep time (TST) as the cut-off criterion for treatment of OSAS [14]. Based on the severity of OSAS, four groups were accordingly available for follow-up.

Group 1: no polysomnographic evidence of OSAS (*i.e.* children with RDI <3 events·h^{-1} TST). No treatment was administered. A random sample of 52 children who had an RDI <3 events·h^{-1} TST was selected for the present follow-up study.

Group 2: mild OSAS. Children with RDI $\geqslant$3 events·h^{-1} TST (but <10 events·h^{-1} TST) and/or presence of obstructive hypoventilation without significant adenotonsillar hypertrophy (0–2 grade of tonsillar hypertrophy and/or adenoid hypertrophy <25%). The treatment for this group consisted of supervised dietary modification by a nutritionist.

Group 3: moderate–severe OSAS. Children with RDI $\geqslant$3 events·h^{-1} TST, and apnoea–hypopnoea index (AHI) $\geqslant$10 events·h^{-1} TST, and/or presence of obstructive hypoventilation with significant adenotonsillar hypertrophy (3–4 grade of tonsillar hypertrophy and/or adenoid hypertrophy >25%) as confirmed by nasopharyngoscopy. The treatment approach was surgical T&A.

Group 4: moderate–severe OSAS. Children with RDI $\geqslant$3 events·h^{-1} TST and AHI $\geqslant$10 events·h^{-1} TST, and/or presence of obstructive hypoventilation without nasopharyngoscopic adenotonsillar hypertrophy. The treatment approach was continuous positive airway pressure (CPAP) treatment *via* a nasal mask.

65 of the 98 children who were diagnosed with OSAS using the criterion of an RDI $\geqslant$3 events·h^{-1} TST in the first phase of the study completed the specific treatment and follow-up protocol. However, 33 children failed to appear for their scheduled follow-up clinical visits and assessments despite multiple telephone or mailed reminders. No differences in age, sex and BMI z-score were present between the adherent and lost to follow-up groups.

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All participants underwent assessment of their medical and sleep history, filled out a questionnaire about snoring and an abbreviated version of the Pediatric Sleep Questionnaire (PSQ) [27], and were subjected to a comprehensive physical examination that also included craniofacial evaluation by visual inspection, as well as an otolaryngology assessment that included an awake nasopharyngoscopy under topical sedation, followed by an overnight sleep study in the laboratory using standard techniques. Methodological details have been published previously [12].

An overnight polysomnographic study was performed in the laboratory using standard techniques in the presence of one of the caretakers throughout the study. Children arrived accompanied by one of their parents to the sleep laboratory at approximately 19:30–20:00 h, and a lights-off routine was implemented at 21:00 h with discontinuation of the sleep recordings at 08:00 h. After removal of movement and technical artefacts, the studies were scored according to standard criteria as defined by the by the American Academy of Sleep Medicine (AASM) [28]. The proportion of time spent in each sleep stage was expressed as percentage of TST. Apnoea index and AHI were defined as the number of apneas, and the number of apnoeas and hypopneas per hour of TST, respectively. The AHI, obstructive AHI (OAHI), and the respiratory disturbance index (RDI) were also calculated. Furthermore, the flow limitation index was calculated based on all events in which flow limitation was identified [28]. The sleep respiratory disturbance index (SRDI) includes all types of index of respiratory events used in the analysis.

T&A was performed under general anaesthesia, and if severe OSAS was present, children were admitted to the inpatient paediatric unit for postoperative cardiorespiratory monitoring. Adenoidectomy was performed by curettage and haemostasis by compression or coagulation and tonsillectomy was performed by cold dissection and haemostasis by ligation and bipolar coagulation. In those children who required CPAP treatment, the pressure was adjusted by conventional titration as delineated by the AASM guidelines [29].

Data analysis

Data are presented as mean±SD. Descriptive statistics, Chi-squared analyses for trends, and odd ratios as well as 95% confidence intervals were calculated. Comparisons of polysomnographic and demographic characteristics before and after treatment were conducted with paired sample t-tests, or analysis of variance followed by *post hoc* comparisons, with p-values adjusted for unequal variances when appropriate after assessment using the Levene's test for equality of variances, or Chi-squared analyses with the Fisher exact test for dichotomous outcomes. Correlations were performed with the use of linear regression, followed by calculation of Pearson correlation coefficients. To examine potential predictors for unsuccessful treatment (*i.e.* RDI >3 events·h^{-1} TST after treatment), we performed a general lineal model and logistic regression analysis. A two-tailed $p<0.05$ was considered as achieving statistical significance. All analyses were conducted with the use of SPSS software (version 22.0; SPPS Inc., Chicago, IL, USA).

Results

A total of 117 obese children (60 boys, 57 girls) aged 10.3±2.9 and 11.3±2.9 years at baseline (T_0) and follow-up (T_1), completed the initial and follow-up assessments within 11.8±4.1 months. Their mean BMI at follow-up was 27.6±4.7 kg·m^{-2}, corresponding to a BMI z-score of 1.34±0.59 (table 1).

TABLE 1 Anthropometric characteristics of the study cohort (n=117)

	Anthropometric measures	
	T_0	T_1
Sex		
Male	60 (51.3)	
Female	57 (48.7)	
Age years	10.35±2.89	11.32±2.85
Weight kg	59.90±21.01	65.25±21.72
Height m	1.46±0.18	1.51±0.17
BMI kg·m^{-2}	27.06±4.05	27.63±4.7
BMI percentile	96.84±0.54	95.26±6.73
Neck circumference cm	33.82±3.72	33.82±3.42
Waist circumference/hip circumference ratio	0.90±0.07	0.88±0.07
Systolic blood pressure mmHg	103.2±14.3	105.9±12.4
Diastolic blood pressure mmHG	62.0±10.7	63.1±9.4

Data are presented as n (%) or mean±SD. BMI: body mass index; T_0: baseline; T_1: follow-up.

Initial findings: T0

The mean abbreviated PSQ score was 4.56±3.82. Based on such a questionnaire, there was a 19.7% prevalence of OSAS. Nasopharyngoscopic assessments showed that 60.7% of the children had no evidence of choanal obstruction from enlarged adenoids, and that 31.6% had grade 0 tonsillar hypertrophy. Craniofacial evaluations revealed that 2.6% of the children had retrognathia with 18.1% having dental malocclusion.

For the whole cohort, the mean RDI at T1 was 3.3±3.9 events·h^{-1} TST, with a mean obstructive RDI (ORDI) of 3.0±3.7 events·h^{-1} TST and a mean obstructive AHI (OAHI) of 1.6±2.5 events·h^{-1} TST. Mean nadir arterial oxygen saturation S_{aO_2} was 90.7%±3.5%, and the total time spent with S_{aO_2}<90% (T90%) was 0.2%±0.9% of TST; 52 children had no evidence of OSA (group 1), with 36 children being allocated to group 2, 23 children in group 3 (T&A) and six children in group 4 (CPAP treatment) (table 2).

Follow-up findings: T1

Using an SRDI ⩾3 events·h^{-1} TST, the prevalence of OSAS was 17.1–34.2% depending on OAHI, ORDI or RDI as the selected respiratory disturbance index. Based on a classification of OSAS as mild (SRDI ⩾3 and <5 events·h^{-1} TST), moderate (SRDI ⩾5 and <10 events·h^{-1} TST) or severe (SRDI >10 events·h^{-1} TST), severe OSAS was present in 3.4–8.5% of the children (table 3).

Using an RDI ⩾3 events·h^{-1} TST on polysomnography (PSG) at follow-up for the presence of OSAS: Among subjects included in group 1 (non-OSAS, RDI <3 events·h^{-1} TST at T0), 41 (78.8%) of children remained with an RDI <3 events·h^{-1} TST at T1 (non-OSAS) at follow-up, while 11 (21.2%) had an RDI ⩾3 events·h^{-1} TST at T1 (incident cases). Among group 2 (mild OSAS who received dietary treatment at T0), 18 (50%) remained with an RDI ⩾ 3 events·h^{-1} TST at T1 (persistent cases) and 18 (50%) had an RDI <3/h TST at T1 (remission cases). In Group 3 (moderate-severe OSAS who received surgical treatment) 10 (43.5%) remained with an RDI ⩾3 events·h^{-1} TST at T1 (residual cases), while 13 (56.5%) had RDI<3 events·h^{-1} TST at T1 (resolved cases). In group 4 (moderate–severe OSA who received CPAP treatment) one (16.6%) remained with an RDI ⩾3 events·h^{-1} TST at T1 (residual cases), while five (83.3%) had RDI <3 events·h^{-1} TST at T1 (controlled cases).

The residual OSAS were 30.4, 13.1 and 7.2% for OAHI ⩾1, OAH1 ⩾3 and OAHI ⩾5, respectively. Table 4 shows incidence, persistence and residual OSAS based on the different cut-off criteria used (RDI ⩾3, OAHI ⩾3, OAHI ⩾1) on PSG for diagnosis of OSAS.

General linear model approaches were used to assess differences between study groups. Statistically significant differences in the distribution of RDI and AHI between groups were observed (p<0.001), but not in BMI and age (p=0.104 and p>0.05, respectively). After adjusting for age and BMI, age was significantly associated with T0–T1 RDI changes (p<0.05) and AHI changes (p<0.05).

To examine potential predictors in development or persistence of OSAS at T1, a general linear model approach was used. Comparing the incident group (n=11) and the non-OSA group that were originally included in group 1, there were no significant differences in age and BMI, but significant differences in the degree of tonsillar hypertrophy emerged, with proportion of children with grade 3–4 tonsillar hypertrophy in the incident cases being higher (27.3%) than among those who remained free of OSAS (2.4%, p<0.05; table 5). Comparisons of group 2 subjects with persistent OSAS (n=18) to those without evidence of OSAS at T1 (remission cases), the BMI in the remission cases decreased, while BMI increased in the group with persistent OSAS (change in BMI from T0 to T1: −0.33±2.83 and 0.36±2.05 kg·m^{-2}, respectively). The degree of tonsillar hypertrophy was not statistically significant between those with remission compared to those with persistent OSAS (p>0.05; table 5). In group 3, the residual group (n=10) and the resolved cases (n=13), revealed no significant differences in either age or BMI. However, the risk of residual OSAS increased with increasing age and BMI (table 5).

A statistically significant association between BMI change from T0 to T1 (BMI1−BMI0) and parallel RDI changes emerged (r=0.269; p=0.003) for the whole cohort, and was present in group 2 (r=0.362, p=0.03) and group 3 (r=0.661; p<0.001).

In the binary logistic regression model, in group 1 (non-OSAS) and group 2 (mild OSAS with dietary treatment), using OSAS a dichotomous outcome variables, sex, age, RDI at T0, BMI1−BMI0, retrognathia, tonsillar hypertrophy and adenoid hypertrophy (>25%) as a co-variables, the odds ratio for tonsillar hypertrophy was 4.37 (p=0.291) in group 1. In group 2, RDI at T0 and BMI1−BMI0 emerged as a significant risk factors for OSAS persistent (OR 1.82, 95% CI 1.09–3.02 (p<0.03) and OR 8.71, 95% CI 1.24–61.17 (p=0.03)) respectively.

In the binary logistic regression model using OSAS as a dichotomous outcome variable, and sex, age, RDI at T0, BMI1−BMI0 and retrognathia as co-variables, we found that age emerged as a significant risk factor for residual OSAS (OR 1.49, 95% CI 1.01–2.23, p=0.047) in group 3, surgically treated. Although not statistically significant, the OR for BMI change was 2.93 (p=0.523) and 8.57 (p=0.268) for retrognathia.

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TABLE 2 Polysomnographic measures at baseline (T_0) and follow-up (T_1) in 117 obese children in the four groups studied

	Group 1 (non-OSA)	Group 2 (mild OSA, dietary treatment)	Group 3 (moderate–severe OSA treated surgically)	Group 4 (moderate–severe OSA treated with CPAP)
Participants n	52	36	23	6
Respiratory measures				
Respiratory events n				
T_0	9.56±5.32	51.44±32.37	131.13±130.60	173.0±115.15
T_1	14.60±18.69[¶]	28.14±27.89[#]	24.39±24.71[#]	16.50±34.07[¶]
Central apnoeas n				
T_0	0.62±1.10	3.29±10.04	6.0±10.72	1.17±1.47
T_1	0.94±3.84	2.11±6.03	0.91±1.70[¶]	4.17±5.49
Obstructive apnoeas n				
T_0	0.65±1.62	4.89±9.37	37.13±64.40	35.33±76.35
T_1	2.04±5.45	3.47±5.85	1.00±2.31[¶]	1.17±2.40
Mixed apnoeas n				
T_0	0.02±0.14	0.42±1.10	3.17±10.08	0.83±1.33
T_1	0.62±3.64	0.64±1.58	0.09±0.42	0.0±0.0
Hypopnoeas n				
T_0	2.96±3.51	16.39±19.32	53.74±70.76	120.67±107.22
T_1	5.00±8.61	9.44±14.07[¶]	8.70±16.39[¶]	10.83±25.56
Flow-limited events n				
T_0	5.60±4.70	26.53±19.56	30.17±37.99	14.83±15.54
T_1	6.17±11.28	12.75±16.50[¶]	13.00±15.68[¶]	0.50±0.84[¶]
RDI events·h^{-1} TST				
T_0	1.48±0.83	8.57±8.35	18.92±20.15	30.10±18.33
T_1	2.24±2.93	4.70±4.91[#]	3.60±3.50[#]	2.80±5.83[¶]
REMS RDI events·h^{-1} TST				
T_0	1.74±2.12	6.07±6.11	21.14±30.85	36.99±33.66
T_1	1.57±2.80	3.69±4.31[¶]	6.42±12.29[¶]	1.92±1.27[¶]
NREMS RDI events·h^{-1} TST				
T_0	1.17±1.09	6.03±5.68	16.15±20.30	27.67±17.40
T_1	2.02±3.14	4.14±5.10[¶]	3.10±3.54[¶]	1.53±3.26[¶]
ORDI events·h^{-1} TST				
T_0	1.34±0.85	7.98±4.91	17.88±19.06	29.29±18.28
T_1	2.06±2.83	4.34±4.48[#]	3.33±3.60[#]	2.10±4.92[¶]
Central AHI events·h^{-1} TST				
T_0	0.09±0.18	0.59±2.03	0.85±1.55	0.19±0.17
T_1	0.15±0.64	0.35±0.90	0.12±0.22[¶]	0.69±0.94
OAHI events·h^{-1} TST				
T_0	0.57±0.60	3.57±3.90	13.54±19.77	27.36±18.89
T_1	1.16±1.82[¶]	2.25±2.99[¶]	1.38±2.38[#]	2.05±4.77[¶,+]
Apnoea index events·h^{-1} TST				
T_0	0.20±0.32	1.40±2.82	6.74±12.64	6.34±13.25
T_1	0.55±1.32	1.02±1.64	0.28±0.43[¶]	0.88±1.34
Hypopnoea index events·h^{-1} TST				
T_0	0.47±0.57	2.70±3.01	7.62±10.16	21.19±18.54
T_1	0.76±1.37	1.58±2.60	1.22±2.25[¶]	1.86±4.36[¶,+]
Flow limited index events·h^{-1} TST				
T_0	0.86±0.72	4.36±3.26	4.08±4.85	2.62±2.29
T_1	0.93±1.68	2.07±2.81[¶]	1.89±2.11[¶]	0.07±0.14[¶,+]
Baseline S_{aO_2}				
T_0	98.27±1.43	97.60±1.83	98.48±1.24	99.17±1.16
T_1	97.96±1.01	97.54±1.36	98.35±0.94	99.17±0.41
Mean S_{aO_2}				
T_0	96.50±1.49	96.08±1.64	95.91±2.64	96.17±1.16
T_1	96.31±1.18	96.17±1.36	96.57±1.30	97.00±1.09
Nadir S_{aO_2}				
T_0	91.29±3.63	90.44±3.02	86.86±10.96	87.50±3.61
T_1	91.06±3.10	90.31±3.95	90.27±3.73[¶]	93.00±1.55[¶,+]
T90%				
T_0	1.31±5.13	3.27±14.70	2.54±10.25	0.28±0.36
T_1	0.23±1.28	0.28±0.68	0.09±0.34	0.00±0.00

Continued

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TABLE 2 Continued

	Group 1 (non-OSA)	Group 2 (mild OSA, dietary treatment)	Group 3 (moderate–severe OSA treated surgically)	Group 4 (moderate–severe OSA treated with CPAP)
ODI				
T_0	0.18±0.50	1.95±4.00	6.84±21.60	19.88±19.25
T_1	0.24±0.56	1.57±2.67	0.94±2.38	0.42±0.57[¶,+]
Peak P_{ETCO_2} mmHg				
T_0	47.10±4.65	47.76±5.55	47.95±5.44	46.33±4.03
T_1	47.15±5.11	44.26±5.45	47.84±5.38	50.00±3.69
P_{ETCO_2} >50 mmHg %TST				
T_0	2.79±6.62	4.30±11.34	10.01±22.11	1.82±4.45
T_1	7.90±14.03[¶]	3.06±7.82	3.80±9.11	3.32±7.98
Mean heart rate beats·min^{-1}				
T_0	77.44±10.09	80.89±16.06	85.76±11.92	83.50±8.26
T_1	75.10±10.45[¶]	77.03±17.58[¶]	76.05±12.37[#]	76.67±8.82[¶,+]
Sleep measures				
Sleep efficiency %				
T_0	79.99±10.02	78.89±10.61	84.75±8.27	69.76±21.61
T_1	81.54±9.89	79.74±16.55	83.11±11.36	81.86±13.69
NREMS latency mins				
T_0	34.80±24.07	31.83±23.27	24.13±19.58	46.42±26.29
T_1	33.04±29.40	31.77±33.45	35.59±36.35	15.75±22.63
REMS latency mins				
T_0	123.72±54.33	123.31±79.70	127.98±75.81	222.30±74.64
T_1	137.30±68.28	150.39±80.90	126.13±48.35	158.00±60.68
Awake %TST				
T_0	22.63±13.68	22.76±18.82	15.52±11.16	23.00±23.56
T_1	24.48±16.38	19.60±20.56	18.10±15.17	14.70±10.06
N1 %				
T_0	11.82±8.00	11.29±10.70	12.02±7.80	14.25±5.90
T_1	12.58±8.13	9.82±8.97	11.29±6.85	9.19±5.80
N2 %				
T_0	43.04±8.16	43.03±9.93	42.50±12.30	40.41±11.04
T_1	42.67±8.75	41.79±12.77	43.32±11.61	46.31±8.23
N3 %				
T_0	25.95±10.85	29.21±12.17	27.70±23.85	36.02±16.13
T_1	24.91±9.78[¶]	31.20±13.69[¶]	26.68±20.57	33.91±12.23
REMS %				
T_0	19.19±6.24	16.47±5.93	18.25±6.57	9.30±4.99
T_1	19.85±5.14	17.18±6.11	20.71±7.33	12.97±3.87
Arousal index				
T_0	9.44±7.50	16.85±10.99	13.73±19.24	25.72±14.67
T_1	10.30±7.63	12.64±6.74[¶]	12.83±7.07	9.72±4.39[¶,+]
PLM index				
T_0	0.22±0.87	1.45±3.22	1.00±3.33	7.10±8.07
T_1	0.15±0.64	1.31±3.82	1.24±4.46	1.00±1.41

Data are presented as mean±SD. OSA: obstructive sleep apnoea; CPAP: continuous positive airway pressure; RDI: respiratory disturbance index; TST: total sleep time; REMS: rapid eye movement sleep; NREMS: non-REMS; ORDI: obstructive RDI; AHI: apnoea–hypopnea index; OAHI: obstructive AHI; S_{aO_2}: arterial oxygen saturation; T90%: total time spent with S_{aO_2} <90%; ODI: oxygen desaturation index; P_{ETCO_2}: end tidal carbon dioxide tension; N1-N3: NREM sleep stages; PLM: periodic leg movements during sleep. [#]: mean difference p<0.001; [¶]: mean difference p<0.05; [+]: measures obtained while subjects were receiving CPAP.

When we used a general lineal model for repeated measures, only in group 3 did surgically treated age >11 years (p=0.033), retrognathia (p=0.026) and neck circumference (p=0.002) emerged as significant risk factors for residual OSAS.

Discussion

This study prospectively assessed the outcomes of OSAS in a community-based cohort of children in whom obesity was diagnosed by their primary care physicians. We previously described the high prevalence of both snoring and OSAS in obese "healthy" children [12]. Here we found that, in obese

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TABLE 3 Prevalence and severity of OSAS based on different cut-off criteria in 117 obese children at baseline (T_0) and follow-up (T_1)

Diagnostic criterion	Prevalence (95% CI)		Severity-based prevalence					
			Mild OSAS (⩾3 and <5 events·h^{-1} TST)		Moderate OSAS (⩾5 and <10 events·h^{-1} TST)		Severe OSAS (⩾10 events·h^{-1} TST)	
	T_0	T_1	T_0	T_1	T_0	T_1	T_0	T_1
Participants n	248	117	117	117	117	117	117	117
OSAS (RDI ⩾3 events·h^{-1} TST)	39.5% (33.4–45.6%)	40 (34.2%) (25.2%–43.2%)	12 (10.3)	16 (13.7)	22 (18.8)	14 (12)	31 (26.5)	10 (8.5)
OSAS (ORDI ⩾3 events·h^{-1} TST)	35.9% (29.9–41.9%)	38 (32.5%) (23.6%–41.4%)	17 (14.5)	15 (12.8)	18 (15.4)	14 (12)	30 (25.6)	9 (7.7)
OSAS (OAHI ⩾3 events·h^{-1} TST)	21.5% (16.3–26.6%)	20 (17.1%) (9.8%–24.3%)	14 (12)	11 (9.4)	10 (8.5)	5 (4.3)	15 (12.8)	4 (3.4)
OSAS (OAHI >1 event·h^{-1} TST)	46.6% (40.6–53%)	44 (37.6%) (28.4%–46.8%)						

Data are presented as n (%) (95% CI) or n (%), unless otherwise stated. OSAS: obstructive sleep apnoea syndrome; TST: total sleep time; RDI: respiratory disturbance index; ORDI: obstructive respiratory disturbance index; OAHI: obstructive apnoea–hypopnoea index.

TABLE 4 Incidence, persistence and residual OSAS based on different cut-off criteria in 117 obese children

	Groups for follow-up (T_0-T_1) n=117							
	Non–OSAS		Mild OSAS treated by diet		Moderate-severe OSAS treated surgically		Moderate-severe OSAS treated with CPAP	
Groups at T_1 Diagnostic criteria	**Non-OSAS**	**Incident cases**	**Remission cases**	**Persistent cases**	**Resolved cases**	**Residual cases**	**Resolved cases**	**Residual cases**
RDI ⩾3	41 (78.84)	11 (21.15)	18 (50)	18 (50)	13 (56.5)	10 (43.5)	5 (83.3)	1 (16.6)
OAHI ⩾3	45 (86.5)	7 (13.5)	27 (75)	9 (25)	20 (86.9)	3 (13.1)	5 (83.3)	1 (16.6)
OAHI ⩾1	33 (70.2)	14 (29.8)	19 (46.3)	22 (53.6)	16 (69.6)	7 (30.4)	5 (83.3)	1 (16.6)

Data are presented as n (%). OSAS: obstructive sleep apnoea syndrome; CPAP: continuous positive airway pressure; RDI: respiratory disturbance index; OAHI: obstructive apnoea–hypopnoea index. For RDI ⩾3 and OAHI ⩾3, number of subjects per group were non-OSAS: 52 (44.4%); mild OSAS treated by diet: 36 (30.8%); moderate-severe OSAS treated surgically: 23 (19.7%); and moderate-severe OSAS treated with CPAP: 6 (5.1%). For OAHI ⩾1, number of subjects per group were non-OSAS: 47 (40.2%); mild OSAS treated by diet: 41 (35%); moderate-severe OSAS treated surgically: 23 (19.7%); and moderate-severe OSAS treated with CPAP: 6 (5.1%).

TABLE 5 Characteristics of the variables included in the general linear model

	RDI		AHI		BMI		BMI_1-BMI_0	Age at T_1 years	TH %
	T_0	T_1	T_0	T_1	T_0	T_1			
Non-OSAS									
Non-OSAS n=41	1.40±0.79	0.92±0.75	0.52±0.52	0.39±0.42	25.79±3.24	26.16±3.99	0.37±2.38	10.93±2.73	2.4
Incident cases n=11	1.80±0.91	7.15±2.79	0.79±0.83	4.06±2.12	27.96±4.02	28.35±5.37	0.39±2.04	11.59±2.64	27.3
Mild OSAS									
Remission cases n=18	5.97±2.19	1.71±0.89	2.62±1.63	0.60±0.64	27.84±4.04	27.50±5.02	−0.33±2.82	12.18±2.36	0
Persistent cases n=18	11.18±6.29	7.69±5.47	4.53±5.17	3.91±3.50	27.94±3.02	28.30±4.00	0.36±2.05	12.20±2.24	11.1
Moderate–severe OSAS treated surgically									
Resolved cases n=13	20.57±24.21	1.22±0.87	13.99±23.98	0.43±0.55	26.22±5.19	26.42±3.07	0.19±3.81	9.69±3.62	0
Residual cases n=10	16.76±14.23	6.70±3.18	12.95±13.70	2.63±3.24	25.92±3.87	27.75±4.96	1.83±1.45	10.91±3.67	0
Moderate–severe OSAS treated with CPAP									
Resolved cases n=5	28.12±19.77	0.42±0.18	24.87±19.99	0.10±0.17	33.31±3.55	35.21±3.90	1.90±1.74	11.82±2.25	0
Residual cases n=1	40.00	14.70	39.83	11.79	40.12	39.37	−0.75	16.75	0

OSAS: obstructive sleep apnoea syndrome; CPAP: continuous positive airway pressure; RDI: respiratory disturbance index; AHI: apnoea–hypopnoea index; BMI: body mass index; TH: tonsillar hypertrophy; T_0: baseline; T_1: follow-up.

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children with OSAS treated by adenotonsillectomy, there was a high percentage of residual OSAS, and that in a group of obese children with OSAS without adenotonsillar hypertrophy treated with nutritional interventions, there was a high percentage of persistent OSAS. Furthermore, obese children without OSAS during the initial assessment showed a high risk of developing OSAS at follow-up. Finally, we also identified a portion of obese children with OSAS who presented no evidence of adenotonsillar hypertrophy and were therefore best managed with CPAP.

Some methodological issues deserve comment. First, the prospectively designed recruitment of this cohort was based on the initial diagnosis of obesity during routine well-child visits, thereby preventing any potential *a priori* selection bias. Therefore, none of these children had been previously evaluated for snoring or were clinically suspected or treated for OSAS**.** As in the previous study [12], we used previously established consensus guidelines in Spain using a RDI $\geqslant$3 events·h^{-1} TST as the cut-off criterion for treatment of OSAS [14], and such an approach resulted in an OSAS prevalence of 34.2%. However, even if we apply alternative criteria (*e.g.* ORDI $\geqslant$3 events·h^{-1} TST, OAHI $\geqslant$3 events·h^{-1} TST, or AHI > 1 events·h^{-1} TST), the prevalence would still be very high (*i.e.* 17.1% to 37.6% for AHI >1 event·h^{-1} TST) [13, 14]. As shown in table 3, we also examined the distribution of OSAS and the effects of treatment according to other widely accepted severity cut-off values.

The treatment of choice for OSAS in children is adenotonsillectomy; however, many studies show that in obese children the success rate of surgery (expressed as a post-operative OAHI <1 event·h^{-1} TST or <5 events·h^{-1} TST) is lower [30–36]. In a meta-analysis, 49% of obese children had a postoperative AHI<5 events·h^{-1} TST, 25% of children had an AHI <2 events·h^{-1} TST and only 12% of children had a postoperative AHI <1 event·h^{-1} TST [21]. In a retrospective multicentre study of 578 children that included approximately 50% obese children, T&A resulted in a significant reduction of AHI, but complete resolution of OSA was recorded in only 27.2%, using a post-T&A AHI cut-off of <1 event·h^{-1} TST [33]. In this particular study, age (< or $\geqslant$7 years) and BMI Z-score emerged as the two principal factors contributing to post-T&A AHI outcomes [33]. An earlier prospective study carried out in 110 children revealed that only 25% had normalisation of their postoperative PSG, and that pre-T&A AHI and obesity were the major outcome determinants [30]. In another series, obese children had an OR of 3.7 (95% CI 1.3–10.8) for residual OSAS [35]. In the only randomised controlled trial to date, normalisation of polysomnographic findings was observed in a large proportion of children in the early adenotonsillectomy group when compared with the watchful waiting group (79 *versus* 46%), but occurred less frequently in obese children [34]. Similarly unfavourable treatment outcomes of adenotonsillectomy (postoperative OAHI <1 event·h^{-1} TST in 22.7–25% of cases) have been reported previously in a study of both lean and obese children with OSAS [37].

In our study, 43.5% of children treated by T&A had residual OSAS defined as a postsurgical RDI $\geqslant$3 events·h^{-1} TST, even if we apply alternative criteria (*e.g.* AHI $\geqslant$3 events·h^{-1} TST, or AHI >1 event·h^{-1} TST or AHI >5 events·h^{-1} TST), the residual OSAS would still be high (*i.e.* 7.2–43.5%) (table 5). Our study is therefore consistent with previous studies, showing that although T&A yields significant improvements in respiratory abnormalities in children with OSAS, it is less likely to normalise PSG findings in obese children. Interestingly, the severity of OSAS did not seem affect the response to T&A, contrary to previous reports [36].

A potential opportunity for intervention that may improve overall T&A outcomes in obese children with OSAS is the implementation of concurrent dietary modifications aiming at preventing the excessive accelerated weight gain observed in this group [38–40]. There are few studies evaluating the effect of weight loss as a treatment modality for OSAS in obese children. In a study of 61 obese children undergoing an intensive supervised weight-loss programme, despite a higher median relative decrease in BMI Z-score in OSAS compared with obese children without OSAS, 38% of the children with OSAS still had significant OSAS despite losing weight [7]. However, this study also showed that weight loss is effective in improving or resolving OSAS. In our study, group 2 consisting of children with mild OSAS treated with diet, we observed improvements in respiratory parameters, with half of the children in this group showing resolution of OSAS, albeit with the other half continuing to suffer from OSAS.

Comprehensive analysis of the potential factors associated with the presence, persistence or resolution of OSAS in our cohort led to identification of two significant factors, namely tonsillar hypertrophy and BMI, in addition to age. Notwithstanding, it is apparent that weight accrual in obese patients with OSAS is clearly associated with incidence, persistence or residual OSAS, while weight reductions are associated with improvement in polysomnographic parameters, as evidenced by the significant correlations between changes in BMI and concomitant changes in RDI. In addition, children with residual OSAS show greater weight gain with respect to children without residual OSAS after adenotonsillectomy; therefore, more stringent dietary control in children with OSAS and obesity is necessary.

Retrognathia and dental malocclusion were included in the analyses as potential factors associated with residual OSAS. Retrognathia was a significant risk factor of residual OSAS in the general lineal model for repeated measures (p=0.026). However, only 2.6% of the children included in this study had evidence of retrognathia, which might explain why this risk factor did not achieve statistical significance. Nonetheless, we believe that craniofacial factors need to be evaluated in the context of residual OSAS and, if present, be followed by orthodontic therapy [13, 14].

As indicated above, a limitation of this study is the relatively small sample size in each of the subgroups studied and their potential for inducing a beta 2 error. However, we should also remark that our total follow-up sample consisted of 117 obese children, *i.e.* the largest obese cohort studied thus far in a prospective fashion. We should also consider that the duration of follow-up was somewhat shorter than ideal, whereby recurrence or *de novo* incidence of OSAS may occur over longer periods of time. Thus, it is possible that the overall frequency of OSAS after treatment may be even greater at 2 or 5 years follow-up. Another possible limitation is the lack of follow-up in 33 children. However as indicated above, no differences in age, sex and BMI Z-score were present between the adherent and lost to follow-up groups. Based on our present findings, we surmise that a greater influence of adenotonsillar hypertrophy appears to be present in younger children in whom obesity operates as an OSAS risk enhancer, while the presence of obesity takes over as the major determinant in older children.

In summary, in addition to the high prevalence of OSAS and the relatively unfavourable OSAS outcomes involved in its treatment and follow-up, current findings place obesity in children as a major public health problem, particularly when considering the potentially serious adverse consequences when obesity and OSAS are concurrently present. These findings also indicate the need to develop effective tools that will enable objective and accurate prediction of the response to treatment of obese children with OSAS [41–45], and the identification of those at risk for developing OSAS with end-organ damage.

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