ORIGINAL ARTICLE

The Change of Central Apnea Index after Adenotonsillectomy in Children: A Systematic Review and Meta-Analysis

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Background: Central sleep apnea has been reported in pediatric patients with obstructive sleep apnea (OSA). However, the effect of adenotonsillectomy (TA) on the presentation of the central apnea index (CAI) remains unclear.

Objective: To investigate the effect of TA on CAI in children with OSA through a systematic review and meta-analysis.

Materials and Methods: A systematic search was performed to identify original studies that compare the CAI obtained before and after TA from polysomnography (PSG) in children under 18 years of age. Non-original studies and full papers that were not available were excluded. Only relevant data were pooled for meta-analysis.

Results: Eleven studies with 689 participants were included. The mean age was 5.6±3.0 years and the mean BMI was 21.0±10.6 kg per m^2. Post-TA CAI decreased significantly from pre-TA CAI, with a mean difference (MD) of 0.70 events per hour (95% CI 0.25 to 1.15), especially in the non-Down syndrome subgroup with a MD of 0.75 events per hour (95% CI 0.24 to 1.26). Other parameters, including the apnea-hypopnea index and oxygen saturation, were also significantly improved after TA. However, there was no significant difference in CAI reduction between the subgroups of patients with and without TA, and those with and without obesity.

Conclusion: This meta-analysis revealed that pediatric patients with OSA who underwent TA had a significant reduction in CAI, particularly in patients without Down syndrome. The present study suggested that CAI should be considered an important PSG parameter in post-TA patients. A further well-controlled and long-term study considering the impact of pediatric OSA surgery on CAI is needed.

Keywords: Central sleep apnea; Obstructive sleep apnea; Adenoidectomy; Tonsillectomy; Adenotonsillectomy

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Obstructive sleep apnea (OSA), one of the most unfavorable conditions on the spectrum of sleep problems, can affect 2% to 4% of children(1-3). Its common clinical manifestations in pediatric patients include repetitive snoring, restless sleep, excessive daytime drowsiness, neurobehavioral abnormalities during the day, and mood disorders(4). If OSA was undiagnosed or mistreated, there is a higher risk of developmental problems, neurocognitive effects, and cardiovascular complications(5-7).

According to the American Academy of Sleep Medicine (AASM) scoring guidelines, a central apnea in children is defined as the absence of chest or abdominal movement coupled with a decrease in airflow of at least 90% from the pre-event baseline, lasting more than 20 seconds or at least the duration of two breaths during baseline breathing, associated with an arousal, or at least 3% oxygen desaturation(8). An average number of central apnea per hour of sleep is reported as a central apnea index (CAI). According to normative polysomnography (PSG) values using AASM standards, a CAI of a healthy child should be less than 0.4 events per hour(9-11). Underlying medical disorders, including brain defects such as Chiari malformation, Prader-Willi syndrome, Down syndrome, gastroesophageal reflux disease (GERD), obesity, and hypothyroidism, can be linked to this condition. However, CAI is frequently found to be higher in pediatric patients with OSA compared to

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healthy children[12,13] as shown by its prevalence of 14.9% to 16.9% using criteria of CAI of one or more event per hour[14,15], and prevalence of 3.3% to 5.4% using criteria of CAI of five or more events per hour[14,16]. During obstructive events, the hypercapnia and the hypoxemia trigger arousals. These arousals lead to hyperventilation, which drives CO_2 levels below the apneic threshold, resulting in central apnea[17,18]. This process is exacerbated by a high loop gain, which is observed in children with OSA[19].

Adenotonsillectomy (TA) is considered the first-line treatment of OSA in children. Post-TA, the decrease in central apnea occurs due to reduced airway obstruction, fewer arousals, and normalization of ventilatory control mechanisms[20]. However, the change in CAI following TA has been inconsistent and uncertain. Therefore, the objective of the present study was to determine the effect of TA on CAI in children with OSA.

Materials and Methods

This systematic review and meta-analysis were registered in PROSPERO on November 17, 2021, with registration number CRD42021285541. Using the registration number 068/2565, the Siriraj Institutional Review Board authorized the exemption. The following protocol had been written according to the Preferred Reporting Item for Systematic Review and Meta-analyses (PRISMA) and Meta-analyses of Observational Studies in Epidemiology (MOOSE) guidelines[21,22].

Eligibility criteria

The inclusion criteria for the present study were randomized controlled trials, cohort studies, retrospective studies, and case series that evaluated the effectiveness of adenoidectomy, tonsillectomy, or TA in children under the age of 18 years and reported relevant data on pre- and post-operative CAI from PSG. Included studies were restricted to the English language. Exclusion criteria were non-original studies such as review and letter to editors, and studies that full paper were not available.

Search strategy

A systematic search was done using OVID Medline, EMBASE database, and manual bibliographic search, including grey literature. The following PICO elements were used in the search strategy for the present study, children with OSA for patient, TA for intervention, preoperative and postoperative for comparation, and CAI for outcome. The search terms were "Sleep apnea", "Central sleep apnea", "Obstructive sleep apnea", "Adenoidectomy", "Tonsillectomy" and "Adenotonsillectomy" as keywords. The last search was performed on June 11, 2023. Duplicated records were removed.

Study selection and data extraction

The title and abstract screening were performed by two independent reviewers (SW, NK) who then decided which studies to include. The full text articles of relevant reports were reviewed according to the eligibility criteria by two independent reviewers (SW, NK). The final decision on study inclusion was made and disagreements were resolved by the third reviewer (AT). The data collection was then performed. The following characteristics of the included studies were extracted, year, nation, number of participants, mean age, gender, body mass index (BMI), comorbidities, tonsil or adenoid size, and complications. The preoperative and postoperative PSG parameters, including the apnea-hypopnea index (AHI), CAI, minimum oxygen saturation ($minSpO_2$), mean oxygen saturation ($meanSpO_2$), oxygen desaturation index (ODI), arousal index (AI), and duration of each sleep stage, were also retrieved. If there was insufficient information from the publications, the corresponding authors of each article were contacted for more data.

Assessment of risk of bias

The quality of the included studies was assessed by two independent reviewers (SW, NK). The risk of bias in retrospective study, cohort study, and case series was assessed according to the Risk of Bias Assessment Tool for Nonrandomized Studies (RoBANS) in six domains, which were selection of participants, confounding variable, intervention or exposure measurement, blinding of outcome assessment, incomplete outcome data, and selective outcome reporting[23]. Each domain was categorized as low, high, or unclear risk. Randomized control trials (RCT) were evaluated using the Cochrane risk-of-bias tool for randomized trials (RoB tool) in six domains, which were random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, and selective reporting[24]. Disagreements were resolved by the third reviewer (AT).

Data synthesis

For the meta-analysis, data were combined.

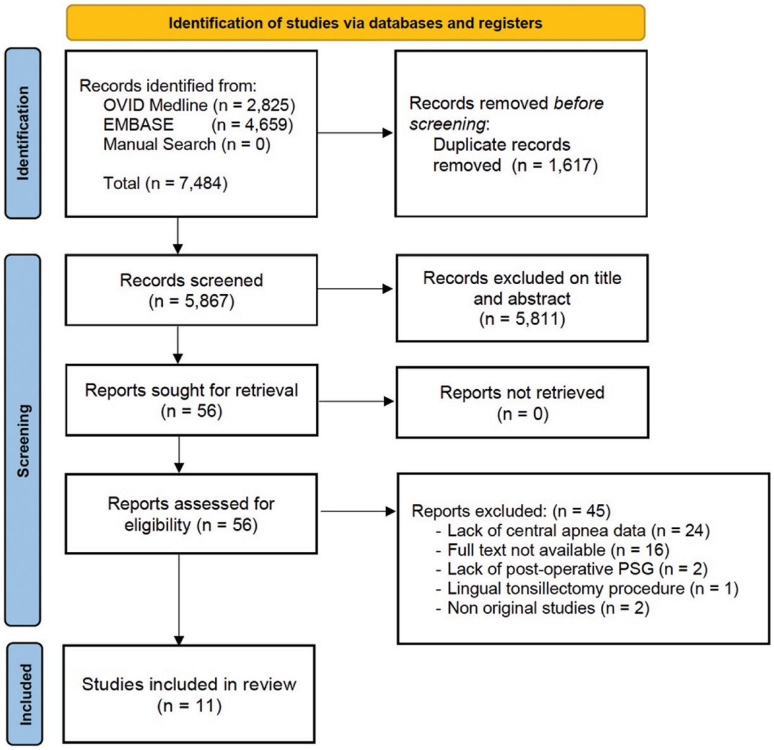

Figure 1. Flow diagram for study retrieval and selection.

The effect size of the continuous outcome data was reported as the mean difference (MD) or standard mean difference (SMD) with standard deviation (SD) and a 95% confidence interval (CI). In the absence of SD, the Cochrane Handbook for Systematic Reviews of Interventions recommended calculating standard errors, confidence intervals, t-values, and p-values[25]. Review Manager version 5.4 (the Nordic Cochrane Centre, the Cochrane Collaboration, Copenhagen, Denmark, 2020) was used for the statistical analysis. A random-effects model was applied. The Cochrane Q test and the I^2 statistic were used as measures of heterogeneity. An I^2 was interpreted with 0% to 40% as may not be important, 30% to 60% to represent moderate heterogeneity, 50% to 90% to represent substantial heterogeneity, and 90% to 100% for considerable heterogeneity. Subgroup analysis was performed to assess the potential effect of related factors such as syndrome and obesity. Publication bias was reported by funnel plot. Sensitivity analysis was performed to ensure that the effects were still significant.

Results

Study selection

The search results revealed 7,484 studies from Ovid Medline with 2,825, EMBASE with 4,659, and Manual search with 0. After 1,617 duplicates were eliminated, 5,867 studies' titles and abstracts were checked, and 56 studies had their full texts retrieved. For the following reasons, the remaining 45 articles were eliminated from the final analysis, lingual tonsillectomy procedure, lack of central apnea data, complete text not available, lack of postoperative PSG, and non-original studies. Thus, the final analysis included 11 studies for both qualitative and quantitative analysis. The overall agreement rate of the reviewers was 96% (Cohen's kappa correlation: 0.88). The study retrieval and selection process are illustrated in Figure 1.

Characteristics of the studies and participants

Six hundred eighty-nine participants from the eleven selected studies were included, each study sample ranging from 20 to 242 participants. The mean BMI was 21.0±10.6 kg per m², and the mean age was 5.6±3.0 years, with a range of 2.7 to 13.5 years. Detailed characteristics of the studies and participants are presented in Table 1. The included studies were published between 2008 and 2021. The studies were conducted in the United State[14,15,26-28], Japan[29], Belgium[30], Brazil[31],

Table 1. Summary of the characteristics of studies and participants

Authors	Year	Country	Study design	n	Age (year) mean±SD	Boy n (%)	BMI (kg/m^2) mean±SD	CAI (events/hour) mean±SD		AHI (events/hour) mean±SD		$minSpO_2$ (%) mean±SD		Follow up PSG (months)	Outcomes
								Pre-op.	Post-op.	Pre-op.	Post-op.	Pre-op.	Post-op.		
Arima, et al.[29]	2019	Japan	Retrospective	242	5.35±2.26	168 (69)	16.31±2.94	1.35±1.73	0.83±1.20	24.06±19.5	3.28±3.69	82.5±9.3	89.62±4.57	7.2±2.4	The surgical result for OSA children in Japan. Result: After surgery for OSA children was 40% with AHI <2 and 85% with AHI <5.
Baldassari, et al.[15]	2012	U.S.	Case series	15	5.63±5.23	10 (67)	NA	3.9±2.9	1.9±4.8	22.8±16.63	5.4±5.25	NA	NA	NA	Change in The CAI after TA for pediatric OSA. Result: 15 of 101 children had pre-op CAI >1 (range 1.1 to 11.1). There was significant improvement of CAI after TA (p=0.008).
Boudewyns, et al.[30]	2016	Belgium	Retrospective	41	2.7±2.38	NA	16.3±1.69	2.2±1.62	1.3±1.39	10.9±12.54	1.2±1.62	86.6±6	91±3.1	3 to 6	Prevalence of CSA in children with OSA and effect of TA on CSA. Result: 67%of 90 children with OSA had abnormal CAI and prevalence of CSA was 7.8%. After TA CAI decrease from 2.2 to 1.3/hour (p<0.001).
da Rocha, et al.[31]	2017	Brazil	Retrospective	27	6.7±3.6	15 (56)	NA	1.33±1.81	1.99±3.53	14.6±11.8	13.6±16.7	75±19	83±7	3.03 to 108.2	PSG parameters of DS with OSA after TA and therapeutic outcome Result: After TA, 29.6% of DS with OSA were resolved from OSA. The CAI was worse in heart disease patient. There were significant improvement of parent's complaints, arousal index and $minspO_2$.
De, et al.[27]	2017	U.S.	Prospective cohort	20	13.5±2.25	15 (75)	39.9±10.1	2.3±5.2	0.7±1.0	29.4±23.4	27.6±34.5	80.1±7.9	82.0±8.7	1st night after TA	Sleep architecture and breathing at the 1st night of TA in obese children with OSA. Result: 85% of 20 obese children undergoing TA are increase risk for residual OSA on the 1st night of surgery.
de la Chaux, et al.[32]	2008	Germany	Prospective cohort	20	4.1±2.0	NA	NA	0.3±0.8	0.3±0.6	14.9±8.7	1.1±1.6	71.7±11.1	91.2±3.5	3 to 12	PSG results after laser tonsillotomy with adenoidectomy in the Tx of OSA. Result: Laser tonsillotomy combination with adenoidectomy, the AHI decreased from 14.9 to 1.1/hour and the $minSpO_2$ increased 71% to 91%.
Del-Río Camacho, et al.[13]	2019	Spain	Retrospective	TA=66	4.84±0.71	NA	NA	2.63±0.87	1.26±1.35	NA	NA	NA	NA	6 to 12	Prevalence of CSA (CAI>5) and improvement of CAI after TA compared to no surgery. Result: 5.6% of 1279 PSG had CAI >5. After TA, CAI decreased by 1.37/hour compare in no surgery decreased by 0.8/hour.
				No TA =43		NA	NA	2.12±3.40	1.74±1.95	NA	NA	NA	NA		
Fehrm, et al.[33]	2020	Sweden	Randomized controlled trial	TA=29	3.25±0.66	15 (52)	BMI z score 0.2±1.4	1.7±1.6	NA	4.8±1.9	NA	89.6±3.7	NA	6	Benefit of TA compared with watchful waiting in 2 to 4 years children. Result: Small differences between the group changes in mean OAHI 1/hour. There were large improvement in quality of life after TA.
				No TA =31	3.08±0.92	19 (61)	BMI z score 0.2±1.1	2.1±2.2	NA	5.1±2.2	NA	88.0±5.5	NA		
Ingram, et al.[28]	2017	U.S.	Retrospective	75	5.1±3.6	41 (55)	NA	1.5±1.9	1.4±1.7	21.3±19.8	8.1±8.1	78.6±7.4	81.3±5.1	6	PSG outcomes of children with OSA after TA. Result: Children with DS and OSA who undergo TA experience improvements in both respiratory event frequency and gas exchange but 48% still have moderate to severe residual OSA.
Judd, et al.[14]	2021	U.S.	Retrospective	123	5.53±4.26	78 (63)	BMI percentile 92	2.1±2.23	0.42±0.82	21.32±17.85	3.81±4.27	88.5±7.69	86.0±10.25	0.59 to 11.89	Improvement in CSA following TA in children. Result: 17% of 123 patients had pre-op CAI >5/hour. CAI significant decreased following TA from 2.1% to 0.4%, p<0.001.
Thottam, et al.[26]	2015	U.S.	Case series	36	5.0±3.53	18 (50)	17.3±8.1	0.8±2.08	0.3±1.65	10.4±14.6	3.5±14.7	86±10.25	88±8.25	NA	Change of both CSA and OSA in children DS after TA. Result: 86.7% of severe OSA significant reduced AHI to moderate or mild (p<0.001), 66.7% of 15 patients of CAI >1 had resolution of CSA (p=0.004)

BMI=body mass index; CAI=central apnea index; AHI=apnea-hypopnea index; $minSpO_2$=minimum oxygen saturation; SD=standard deviation; TA=adenotonsillectomy; NA=not available data

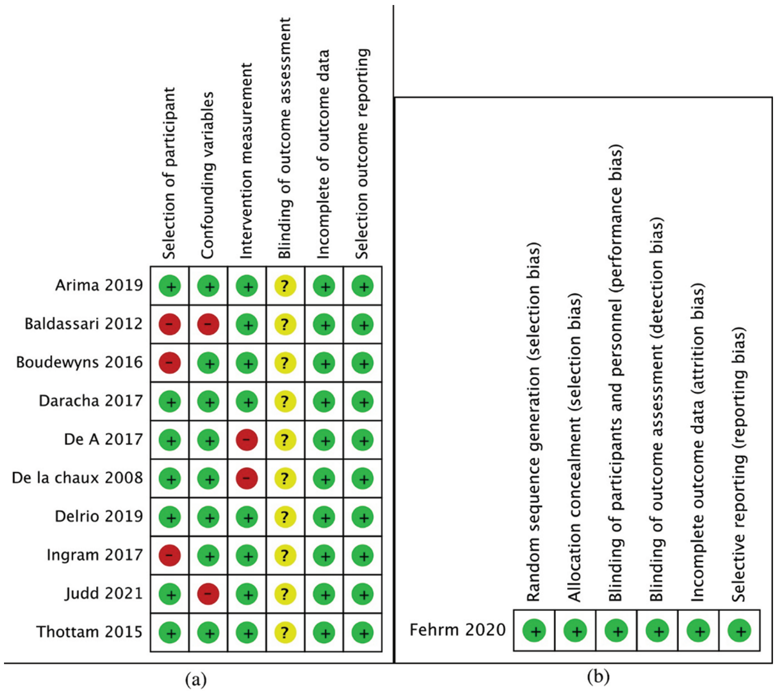

Figure 2. Risk of bias summary of the included studies. (a) non-randomized studies, (b) randomized studies.

Spain[13], Germany[32], and Sweden[33]. There were six retrospective studies[13,14,28-31], two prospective cohort studies[27,32], two case series[15,26], and one randomized control trial[33]. The postoperative evaluation of PSG ranged from 1 day to 108 months. According to the variations in CAI mean, funnel plots for the standard errors were produced. The result of the funnel plot's symmetry was done. Sensitivity analysis was performed considering the follow-up period on CAI, and the result remained unchanged. Subgroup analysis was performed in two subgroups of comorbidities: Down syndrome and obese patients. There was not enough data on other comorbidities such as ODI, AI, duration of each sleep stage, tonsil or adenoid size, and complication after TA for analysis.

Assessment of risk of bias

Assessments of risk of bias in included studies are presented in Figure 2. Ten non-randomized studies were evaluated using RoBANS. A low risk of bias was present in inadequate outcome data and selective outcome reporting. A high risk of bias was present in the participant selection, confounding variable, and intervention measurement domains, whereas the risk of bias in the blinding of the outcome assessment domain was unclear. Using the RoB tool, an RCT was evaluated and found to have a low risk of bias in the six domains.

Comparison I: pre-TA versus post-TA

Outcome 1. CAI

Eleven studies evaluated CAI at pre-and post-TA[13-15,26-33]. The number of patients for the outcome was 689. The meta-analysis revealed that the CAI after TA was statistically significantly lower than before TA for 0.70 events per hour (95% CI 0.25 to 1.15, $p<0.002$). There was substantial heterogeneity ($I^2=81\%$). The forest plot is shown in Figure 3.

1) CAI subgroup analysis: Down syndrome versus non-Down syndrome: A subgroup analysis was performed to compare Down syndrome versus non-Down syndrome. The meta-analysis revealed that the post-TA CAI was lower than the pre-TA CAI, with no statistically significant differences in the subgroup of patients with Down syndrome with MD at 0.14 events per hour (95% CI –0.32 to 0.60, $p=0.55$). However, CAI in post-TA was significantly decreased from pre-TA in the subgroup without Down syndrome with MD at 0.75 events per hour (95% CI 0.24 to 1.26, $p=0.004$). However, there was no significant difference between both groups ($p=0.08$). The forest plot is shown in Figure 4.

2) CAI subgroup analysis: obese versus non-obese group: A subgroup analysis was performed to compare obese versus non-obese groups. The meta-analysis showed that CAI after TA decreased from pre-TA in both groups. However, there were no

Study or Subgroup	Pre-TA Mean	Pre-TA SD	Pre-TA Total	Post-TA Mean	Post-TA SD	Post-TA Total	Weight	Mean Difference IV, Fixed, 95% CI
Arima 2019	1.35	1.73	242	0.83	1.73	242	29.3%	0.52 [0.21, 0.83]
Baldassari 2012	3.9	2.9	15	1.9	4.8	15	0.3%	2.00 [−0.84, 4.84]
Boudewyns 2016	2.2	1.62	41	1.3	1.39	41	6.5%	0.90 [0.25, 1.55]
Daracha 2017	1.33	1.81	27	1.99	3.53	27	1.2%	−0.66 [−2.16, 0.84]
De A 2017	2.3	5.2	20	0.7	1	20	0.5%	1.60 [−0.72, 3.92]
De la chaux 2008	0.3	0.8	20	0.3	0.6	20	14.5%	0.00 [−0.44, 0.44]
Delrio 2019	2.63	0.87	66	1.26	1.35	66	18.6%	1.37 [0.98, 1.76]
Fehrm 2020	1.7	1.6	24	1.2	3.55	24	1.1%	0.50 [−1.06, 2.06]
Ingram 2017	1.5	1.9	75	1.4	1.7	75	8.4%	0.10 [−0.48, 0.68]
Judd 2021	2.1	2.23	123	0.42	0.82	123	15.8%	1.68 [1.26, 2.10]
Thottam 2015	0.8	2.08	36	0.3	1.65	36	3.7%	0.50 [−0.37, 1.37]
Total (95% CI)			**689**			**689**	**100.0%**	**0.77 [0.60, 0.94]**

Heterogeneity: $Chi^2 = 52.18$, df = 10 ($P < 0.00001$); $I^2 = 81\%$
Test for overall effect: Z = 9.05 ($P < 0.00001$)

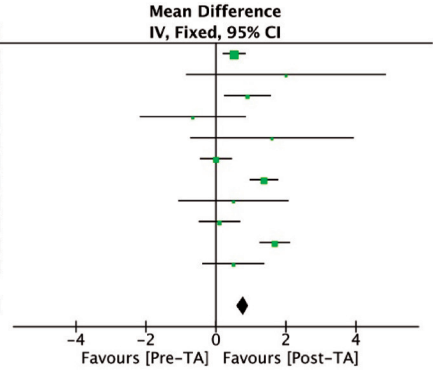

Figure 3. Forest plot of change in central apnea index after adenotonsillectomy.

TA=adenotonsillectomy; CAI=central apnea index; CI=confidence interval

Study or Subgroup	Pre-TA Mean	Pre-TA SD	Pre-TA Total	Post-TA Mean	Post-TA SD	Post-TA Total	Weight	Mean Difference IV, Random, 95% CI
1.2.2 Down syndrome								
Daracha 2017	1.33	1.81	27	1.99	3.53	27	5.4%	−0.66 [−2.16, 0.84]
Ingram 2017	1.5	1.9	75	1.4	1.7	75	13.7%	0.10 [−0.48, 0.68]
Thottam 2015	0.8	2.08	36	0.3	1.65	36	10.2%	0.50 [−0.37, 1.37]
Subtotal (95% CI)			**138**			**138**	**29.3%**	**0.14 [−0.32, 0.60]**
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 1.78$, df = 2 (P = 0.41); $I^2 = 0\%$								
Test for overall effect: Z = 0.60 (P = 0.55)								
1.2.3 non-Down syndrome								
Arima 2019	1.35	1.73	242	0.83	1.73	242	16.9%	0.52 [0.21, 0.83]
Baldassari 2012	3.9	2.9	15	1.9	4.8	15	1.9%	2.00 [−0.84, 4.84]
Boudewyns 2016	2.2	1.62	41	1.3	1.39	41	12.7%	0.90 [0.25, 1.55]
De A 2017	2.3	5.2	20	0.7	1	20	2.7%	1.60 [−0.72, 3.92]
De la chaux 2008	0.3	0.8	20	0.3	0.6	20	15.4%	0.00 [−0.44, 0.44]
Delrio 2019	2.63	0.87	66	1.26	1.35	66	16.0%	1.37 [0.98, 1.76]
Fehrm 2020	1.7	1.6	24	1.2	3.55	24	5.1%	0.50 [−1.06, 2.06]
Subtotal (95% CI)			**428**			**428**	**70.7%**	**0.75 [0.24, 1.26]**
Heterogeneity: $Tau^2 = 0.26$; $Chi^2 = 24.38$, df = 6 (P = 0.0004); $I^2 = 75\%$								
Test for overall effect: Z = 2.88 (P = 0.004)								
Total (95% CI)			**566**			**566**	**100.0%**	**0.56 [0.14, 0.97]**

Heterogeneity: $Tau^2 = 0.24$; $Chi^2 = 30.76$, df = 9 (P = 0.0003); $I^2 = 71\%$
Test for overall effect: Z = 2.64 (P = 0.008)
Test for subgroup differences: $Chi^2 = 3.05$, df = 1 (P = 0.08), $I^2 = 67.2\%$

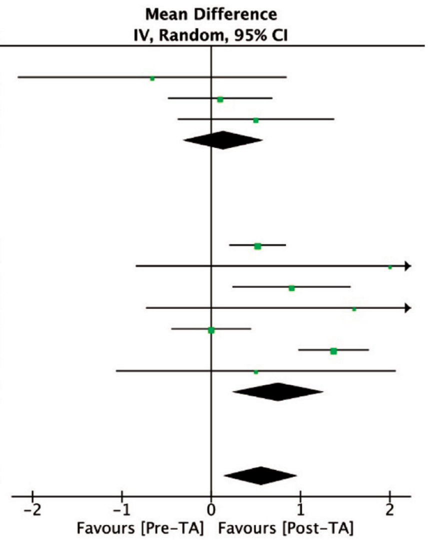

Figure 4. Forest plot of change in central apnea index after adenotonsillectomy in Down syndrome and non-Down syndrome subgroup analysis.
TA=adenotonsillectomy; CAI=central apnea index; CI=confidence interval

significant differences (p=0.35) between obese with MD at 1.6 (95% CI –0.72 to 3.92) and non-obese group with MD at 0.42 (95% CI –0.46 to 1.30).

Outcome 2. AHI

Nine studies with 599 patients evaluated AHI both before and after TA[14,15,26-32]. The meta-analysis showed that AHI after TA decreased significantly from before TA for 12.57 events per hour (95% CI, 8.50 to 16.64; P <0.001). There was substantial heterogeneity (I^2=84%). The forest plot is shown in Figure 5a.

Outcome 3. minSpO₂

Eight studies with 584 participants evaluated minSpO_2 before and after TA for the outcome[14,24-27,29-31]. The meta-analysis showed that minSpO_2 after TA increased significantly from pre-TA for 6.46% (95% CI –9.16 to –3.76, p<0.001). There was substantial heterogeneity (I^2=87%). The forest plot is shown in Figure 5b.

Outcome 4. meanSpO₂

Five studies with 393 patients evaluated meanSpO_2 at before and after TA for the outcome[15,28-30,32]. The meta-analysis showed that the meanSpO_2 after TA increased significantly from pre-TA by 1.31% (95% CI –2.16 to –0.46, p=0.003). There was substantial heterogeneity (I^2=78%). The forest plot is shown in Figure 5c.

Comparison II: TA versus no surgery

Outcome 1. CAI change from baseline

Two studies evaluated CAI changes between participants who underwent TA and those who did

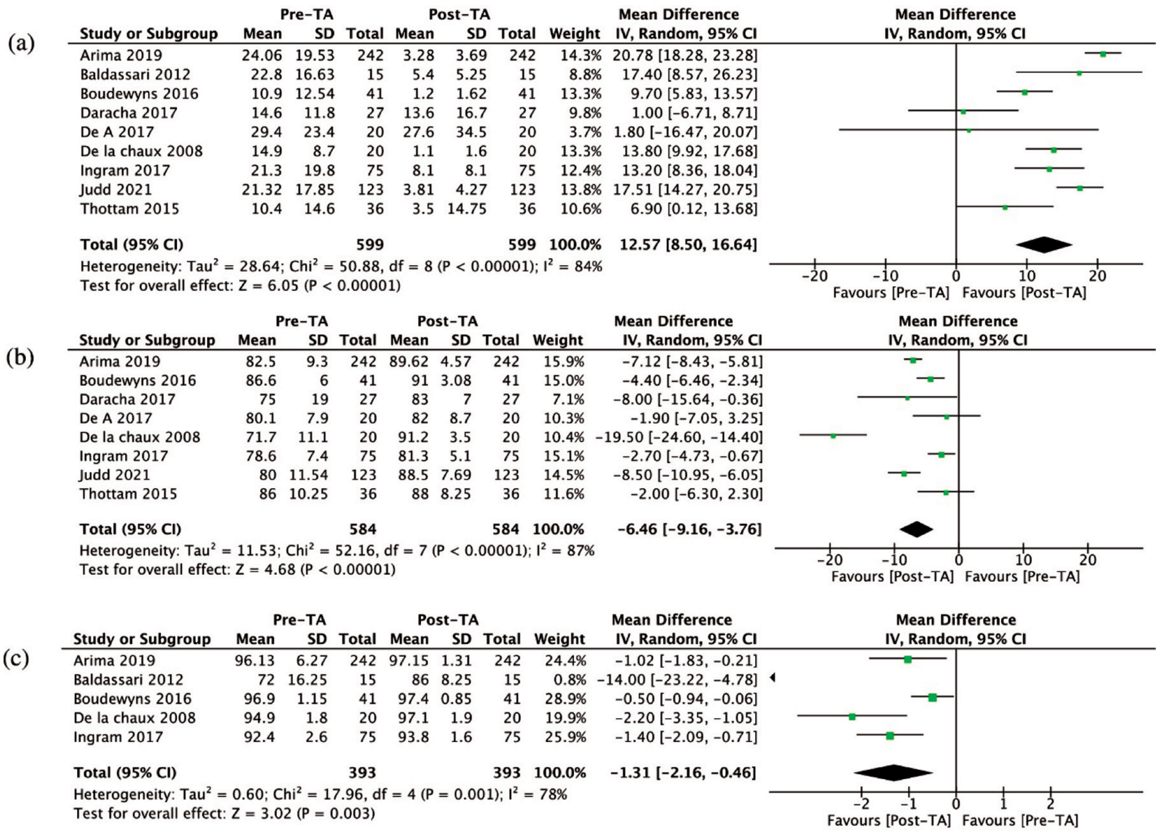

Figure 5. Forest plot of change in polysomnographic parameters after adenotonsillectomy. (a) apnea-hypopnea index, (b) minimum oxygen saturation, (c) mean oxygen saturation.

TA=adenotonsillectomy; CAI=central apnea index; CI=confidence interval

not undergo surgery[13,33]. Although the TA group had higher CAI changes than the non-surgery group, there were no significant differences with MD at –3.9 events per hour (95% CI –1.15 to 0.37, p=0.32).

Outcome 2. Postoperative CAI

Two studies compared children with OSA received TA with those who did not, to assess the postoperative CAI[13,33]. There was no significant difference in postoperative CAI between both groups with MD at –4.7 events per hour (95% CI –1.10 to 0.16, p=0.15).

Discussion

To the authors' knowledge, the present study is the first systematic review and meta-analysis to evaluate the effect of TA on the change in CAI in children with OSA. Numerous studies have looked at this problem as a secondary outcome, however, their findings are inconclusive. The present study results showed that CAI was significantly reduced in pediatric OSA who received TA. However, this was not shown in Down syndrome. CAI reduction did not show significant differences between the obese versus non-obese subgroup (p=0.35). The present study suggests that those without Down syndrome may experience more benefits of TA for the decrease in CAI. The findings of the present study were also consistent with the previous meta-analysis, which found that TA improved several sleep parameters in children with OSA, including AHI, meanSpO_2, and minSpO_2[34].

Physiological CSA commonly occurs during normal sleep, in various contexts, such as the onset of sleep and post-arousal. Most central apneas in healthy children are not scored in sleep studies[35]. However, central apneas lasting more than 20 seconds can impact oxygenation and heart rate similarly to obstructive events[35,36]. After obstructive episodes, arousal and hypercapnia may lead to hyperventilation and subsequent central apnea. Treatment of OSA with TA significantly reduces obstructive events and related central apneas, as seen in a study where

62% of patients with CAI of five or more events per hour had their CAI drop to less than one event per hour post-TA[14,20]. Therefore, prior to further investigation into the origin of CSA, the treatment of children who have both OSA and CSA should focus on obstructive disorders[20]. According to the study, CAI decreased by a statistically significant 0.70 events per hour in pediatric OSA patients who had TA, but the clinical importance of this reduction was unclear. Additionally, the study did not find a significant difference in CAI changes between TA recipients and non-recipients, due to the limited number of participants.

Children with Down syndrome often experience a variety of neurogenetic problems, increasing the risk of CSA and hypoventilation. Patients with Down syndrome and adenotonsillar hypertrophy can share an OSA and CSA pathophysiological mechanism[20]. TA is the first-line treatment for children with OSA that could reduce AHI by up to 51% in those with Down syndrome[37]. The present study result did not show a significant reduction in CAI with MD of 0.14 event per hour, after TA in Down syndrome. This may indicate that TA can only treat obstructive upper airway diseases, but not treat other conditions, including neuromuscular problems.

Obesity often increases the prevalence of obstructive apnea and central apnea associated with severe desaturation[38,39]. This could be explained by factors such as decreased intrathoracic volume, resulting in fewer oxygen reserves[40], altered ventilatory response to hypoxia and hypercapnia, hypoventilation caused by leptin resistance[41], and central apnea, followed by narrowing or collapse of the upper airway[42,43]. The previous meta-analysis showed that TA can improve AHI without complete resolution of OSA in obese children[44]. Neither the obese nor the non-obese groups in the present study had a statistically significant increase in CAI from pre-TA to post-TA. However, this comparison only covered a small number of individuals.

There were limitations to the present study. First, the majority of the included studies were observational studies with higher or uncertain risks of bias and lower levels of evidence. Second, there was high heterogeneity in all comparisons, including the postoperative PSG follow-up time that varied between studies. This can compromise the reliability of pooled results and hinder clear conclusions. Finally, there is a limitation in comparing the data concerning the CAI change after TA due to its small sample size. More long-term and well-controlled studies considering CAI in post-TA pediatric OSA are recommended.

Conclusion

The present meta-analysis revealed that pediatric patients with OSA who underwent TA had a significant reduction in CAI, particularly in patients without Down syndrome. The study suggests that CAI should be considered an important PSG parameter in post-TA patients. A further well-controlled and long-term study is recommended considering the impact of pediatric OSA surgery on CAI.

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Authors' contributions

SW: research design, article search and selection, risk of bias evaluation, data extraction and analysis, discussion, manuscript preparation, and approval of the manuscript. AT: research design, article selection, risk of bias evaluation, discussion, revision, conclusion, manuscript writing, and approval of the manuscript. NK: article search and selection, risk of bias evaluation, data extraction, and approval of the manuscript. WB: essential intellectual contribution, research design, data analysis, discussion, revision, conclusion, and approval of the manuscript.

Data availability

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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Conflicts of interest

The authors declare no conflict of interest.

References

1. Lumeng JC, Chervin RD. Epidemiology of pediatric obstructive sleep apnea. Proc Am Thorac Soc 2008;5:242-52.
2. Redline S, Tishler PV, Schluchter M, Aylor J, Clark K, Graham G. Risk factors for sleep-disordered breathing in children. Associations with obesity, race,

and respiratory problems. Am J Respir Crit Care Med 1999;159:1527-32.
3. Suen JS, Arnold JE, Brooks LJ. Adenotonsillectomy for treatment of obstructive sleep apnea in children. Arch Otolaryngol Head Neck Surg 1995;121:525-30.
4. Marcus CL, Brooks LJ, Draper KA, Gozal D, Halbower AC, Jones J, et al. Diagnosis and management of childhood obstructive sleep apnea syndrome. Pediatrics 2012;130:576-84.
5. Nieminen P, Löppönen T, Tolonen U, Lanning P, Knip M, Löppönen H. Growth and biochemical markers of growth in children with snoring and obstructive sleep apnea. Pediatrics 2002;109:e55.
6. Gozal D, Kheirandish-Gozal L, Bhattacharjee R, Spruyt K. Neurocognitive and endothelial dysfunction in children with obstructive sleep apnea. Pediatrics 2010;126:e1161-7.
7. Li AM, Au CT, Sung RY, Ho C, Ng PC, Fok TF, et al. Ambulatory blood pressure in children with obstructive sleep apnoea: a community based study. Thorax 2008;63:803-9.
8. Berry RB, Quan SF, Abreu AR, Bibbs MML, DelRosso, Harding SM, et al., The AASM manual for the scoring of sleep and associated events: rules, terminology and technical specifications, version 2.6. Darien, Illinois: American Academy of Sleep Medicine; 2020.
9. Beck SE, Marcus CL. Pediatric polysomnography. Sleep Med Clin 2009;4:393-406.
10. Traeger N, Schultz B, Pollock AN, Mason T, Marcus CL, Arens R. Polysomnographic values in children 2-9 years old: additional data and review of the literature. Pediatr Pulmonol 2005;40:22-30.
11. Uliel S, Tauman R, Greenfeld M, Sivan Y. Normal polysomnographic respiratory values in children and adolescents. Chest 2004;125:872-8.
12. Don DM, Geller KA, Koempel JA, Ward SD. Age specific differences in pediatric obstructive sleep apnea. Int J Pediatr Otorhinolaryngol 2009;73:1025-8.
13. Del-Río Camacho G, Medina Castillo L, Rodríguez-Catalán J, Soto Insuga V, Gómez García T. Central sleep apnea in children with obstructive sleep apnea syndrome and improvement following adenotonsillectomy. Pediatr Pulmonol 2019;54:1670-5.
14. Judd RT, Mokhlesi B, Shogan A, Baroody FM. Improvement in central sleep apnea following adenotonsillectomy in children. Laryngoscope 2022;132:478-84.
15. Baldassari CM, Kepchar J, Bryant L, Beydoun H, Choi S. Changes in central apnea index following pediatric adenotonsillectomy. Otolaryngol Head Neck Surg 2012;146:487-90.
16. Kritzinger FE, Al-Saleh S, Narang I. Descriptive analysis of central sleep apnea in childhood at a single center. Pediatr Pulmonol 2011;46:1023-30.
17. Katz ES, D'Ambrosio CM. Pathophysiology of pediatric obstructive sleep apnea. Proc Am Thorac Soc 2008;5:253-62.
18. White DP. Pathogenesis of obstructive and central sleep apnea. Am J Respir Crit Care Med 2005;172:1363-70.
19. Wellman A, Jordan AS, Malhotra A, Fogel RB, Katz ES, Schory K, et al. Ventilatory control and airway anatomy in obstructive sleep apnea. Am J Respir Crit Care Med 2004;170:1225-32.
20. McLaren AT, Bin-Hasan S, Narang I. Diagnosis, management and pathophysiology of central sleep apnea in children. Paediatr Respir Rev 2019;30:49-57.
21. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71.
22. Brooke BS, Schwartz TA, Pawlik TM. MOOSE reporting guidelines for meta-analyses of observational studies. JAMA Surg 2021;156:787-8.
23. Park J, Lee Y, Seo H, Jang B, Son H, Kim S, et al. Risk of Bias Assessment tool for Non-randomized Studies (RoBANS): Development and validation of a new instrument. Abstracts of the 19th Cochrane Colloquium 2011.19-22 Oct; Madrid, Spain.
24. Higgins JP, Altman DG, Gøtzsche PC, Jüni P, Moher D, Oxman AD, et al. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. BMJ 2011;343:d5928. doi: 10.1136/bmj.d5928.
25. Higgins JPT, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, Welch VA, editors. Cochrane handbook for systematic reviews of interventions, version 6.3 [Internet]. London: Cochrane; updated February 2022 [cited 2024 Nov 4]. Available from: https://training.cochrane.org/handbook/archive/v6.3.
26. Thottam PJ, Choi S, Simons JP, Kitsko DJ. Effect of adenotonsillectomy on central and obstructive sleep apnea in children with Down syndrome. Otolaryngol Head Neck Surg 2015;153:644-8.
27. De A, Waltuch T, Gonik NJ, Nguyen-Famulare N, Muzumdar H, Bent JP, et al. Sleep and breathing the first night after adenotonsillectomy in obese children with obstructive sleep apnea. J Clin Sleep Med 2017;13:805-11.
28. Ingram DG, Ruiz AG, Gao D, Friedman NR. Success of tonsillectomy for obstructive sleep apnea in children with Down syndrome. J Clin Sleep Med 2017;13:975-80.
29. Arima S, Koike S, Fujinaga M, Mihara T, Sato S, Suzuki M, et al. Normalization of breathing with adenotonsillectomy in Japanese pediatric OSA. Auris Nasus Larynx 2019;46:758-63.
30. Boudewyns A, Van de Heyning P, Verhulst S. Central apneas in children with obstructive sleep apnea syndrome: prevalence and effect of upper airway surgery. Sleep Med 2016;25:93-7.
31. da Rocha M, Ferraz RCM, Guo Chen V, Antonio Moreira G, Raimundo Fujita R. Clinical variables determining the success of adenotonsillectomy in children with Down syndrome. Int J Pediatr

Otorhinolaryngol 2017;102:148-53.
32. de la Chaux R, Klemens C, Patscheider M, Reichel O, Dreher A. Tonsillotomy in the treatment of obstructive sleep apnea syndrome in children: polysomnographic results. Int J Pediatr Otorhinolaryngol 2008;72:1411-7.
33. Fehrm J, Nerfeldt P, Browaldh N, Friberg D. Effectiveness of adenotonsillectomy vs watchful waiting in young children with mild to moderate obstructive sleep apnea: A randomized clinical trial. JAMA Otolaryngol Head Neck Surg 2020;146:647-54.
34. Lee CH, Hsu WC, Chang WH, Lin MT, Kang KT. Polysomnographic findings after adenotonsillectomy for obstructive sleep apnoea in obese and non-obese children: a systematic review and meta-analysis. Clin Otolaryngol 2016;41:498-510.
35. O'Driscoll DM, Foster AM, Ng ML, Yang JS, Bashir F, Wong S, et al. Central apnoeas have significant effects on blood pressure and heart rate in children. J Sleep Res 2009;18:415-21.
36. Tamanyan K, Weichard A, Biggs SN, Davey MJ, Nixon GM, Walter LM, et al. The impact of central and obstructive respiratory events on cerebral oxygenation in children with sleep disordered breathing. Sleep 2019;42. doi: 10.1093/sleep/zsz044.
37. Nation J, Brigger M. The efficacy of adenotonsillectomy for obstructive sleep apnea in children with Down syndrome: A systematic review. Otolaryngol Head Neck Surg 2017;157:401-8.
38. Verhulst SL, Schrauwen N, Haentjens D, Suys B, Rooman RP, Van Gaal L, et al. Sleep-disordered breathing in overweight and obese children and adolescents: prevalence, characteristics and the role of fat distribution. Arch Dis Child 2007;92:205-8.
39. Kohler M, Lushington K, Couper R, Martin J, van den Heuvel C, Pamula Y, et al. Obesity and risk of sleep related upper airway obstruction in Caucasian children. J Clin Sleep Med 2008;4:129-36.
40. Naimark A, Cherniack RM. Compliance of the respiratory system and its components in health and obesity. J Appl Physiol 1960;15:377-82.
41. O'Donnell C P, Schaub CD, Haines AS, Berkowitz DE, Tankersley CG, Schwartz AR, et al. Leptin prevents respiratory depression in obesity. Am J Respir Crit Care Med 1999;159:1477-84.
42. Pépin JL, Pajon A, Veale D, Ferretti G, Lévy P. Central sleep apnoea syndrome with upper airway collapse. Eur Respir J 1993;6:592-5.
43. Badr MS, Toiber F, Skatrud JB, Dempsey J. Pharyngeal narrowing/occlusion during central sleep apnea. J Appl Physiol (1985) 1995;78:1806-15.
44. Costa DJ, Mitchell R. Adenotonsillectomy for obstructive sleep apnea in obese children: a meta-analysis. Otolaryngol Head Neck Surg 2009;140:455-60.