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Effectiveness of Tonsillectomy vs Modified Uvulopalatopharyngoplasty in Patients With Tonsillar Hypertrophy and Obstructive Sleep Apnea
The TEAMUP Randomized Clinical Trial

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IMPORTANCE Modified uvulopalatopharyngoplasty (mUPPP) is a surgical treatment for selected adults with obstructive sleep apnea (OSA). Tonsillectomy (TE) alone is a less extensive alternative treatment.

OBJECTIVE To investigate whether mUPPP is more effective than TE alone in treating adult patients with tonsillar hypertrophy and moderate to severe OSA.

DESIGN, SETTING, AND PARTICIPANTS This blinded randomized clinical trial compared the effectiveness of mUPPP with TE alone before surgery and 6 months postsurgery in adults with tonsillar hypertrophy (sizes 2, 3, or 4 according to the Friedman staging) and moderate to severe OSA in a university hospital in Stockholm, Sweden. Participants underwent surgery from January 2016 to February 2021; the last postsurgery follow-up was completed in September 2021. Data analyses were performed from January to September 2022.

INTERVENTIONS mUPPP vs TE alone.

MAIN OUTCOMES AND MEASURES Between-group differences on the apnea-hypopnea index (AHI) and Epworth sleepiness scale (ESS).

RESULTS The study cohort comprised 93 patients (mean [SD] age, 41.6 [9.4] years; 80 [86%] men; race/ethnicity were not considered) with a mean (SD) body mass index of 29.0 (2.8), calculated as weight in kg divided by height in m^2. Of these, 90 participants (97%) completed the protocol (mUPPP, n = 45; TE, n = 45). The mean (SD) AHI score (number of events per hour [events/h]) for the mUPPP group decreased by 43%, from 51.0 (22.6) to 28.0 (20.0) events/h; and for the TE group, 56%, from 56.9 (25.1) to 24.7 (22.6) events/h. The mean between-group difference in AHI score was 9.2 events/h (95% CI, 0.5 to 17.9), with a small effect size (Cohen *d* = 0.44) in favor of TE. For ESS scores, the between-group difference was also small, only 1.1 (95% CI, −1.3 to 3.4; Cohen *d* = 0.21). Neither difference was considered to be clinically relevant.

CONCLUSIONS AND RELEVANCE This randomized clinical trial demonstrated that mUPPP was not more effective than TE alone in treating patients with tonsillar hypertrophy and moderate to severe OSA. However, there was a small difference in favor of TE. Because TE alone is less extensive, it could be considered as an alternative to mUPPP in this selected group of patients with OSA.

TRIAL REGISTRATION ClinicalTrials.gov Identifier: NCT02523248

Visual Abstract

Supplemental content

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Obstructive sleep apnea (OSA) is associated with several adverse health effects, such as increased mortality and morbidity in cardiovascular diseases[1,2] and vehicle crashes.[3] In addition, patients with OSA experience poor quality of life[4] and daytime sleepiness.[5] In a systematic review from 2017, the overall prevalence of OSA of any severity ranged from 9% to 38%.[6] A relative increase of 14% to 55% in OSA prevalence has occurred over the past few decades.[7]

The first line of treatment is nonsurgical, with continuous positive airway pressure (CPAP) or a mandibular retaining device (MRD). These approaches are often effective,[1,8] but adherence to treatment remains a challenge because many patients use them insufficiently or not at all.[9,10] For these patients, pharyngeal surgery may be an option, as recommended in a recent review by the American Academy of Sleep Medicine (AASM).[11]

A common surgical procedure for OSA is uvulopalatopharyngoplasty (UPPP).[12,13] Although different definitions exist, UPPP usually includes a tonsillectomy (TE) and a uvulopalatoplasty: suturing the palatal pillars and reducing the size of the uvula. Some early UPPP techniques extensively reduced the palatal tissues and were associated with significant adverse effects.[14] In addition, the evidence for effectiveness was of low quality. Consequently, a Cochrane review from 2005 did not recommend surgical treatment.[15] Since then, a modified UPPP technique (mUPPP), with a more conservative reduction of the uvula and soft palate,[16-18] has been used at Karolinska University Hospital (Stockholm, Sweden). In addition to this method, multiple palatal advancement techniques have been described since 2005, involving varying degrees of surgical dissection and invasiveness.[12,13,19]

Still, UPPP of any type is a painful procedure and not without risks. In recent years, the effectiveness of UPPP has been measured using polysomnographic studies (PSG) in 3 randomized clinical trials (RCTs) of patients with moderate to severe OSA; all intervention groups showed significant improvements compared with the untreated control groups.[16-18] The effect seems to persist in the long term, although to a lesser extent.[20]

In children, TE alone is the standard treatment for OSA and is often effective.[21] Also, previous RCTs of children have shown no additional beneficial effect when combined with a pharyngoplasty, a procedure similar to a mUPPP.[22,23] However, in adults, TE alone has traditionally not been considered an alternative for sleep apnea surgery, probably as tonsil hypertrophy is unusual in adults. In fact, TE alone is not mentioned as an option when discussing isolated surgery to treat adult OSA in the 2010 AASM practice guidelines[12] or in a 2020 review of the literature.[13] Still, a meta-analysis of 17 studies that evaluated TE alone as a treatment for OSA in patients with enlarged tonsils (sizes 2, 3, or 4) demonstrated a 65.2% reduction according to the apnea-hypopnea index (AHI).[24]

Because mUPPP is expected to widen the airways by suturing the palatal pillars and the palatopharyngeus muscle laterally and is performed in addition to a TE, we presumed it to be a more effective treatment than a TE alone. However, to our knowledge, no previous trial has compared the methods. Therefore, the present RCT aimed to compare the effectiveness of mUPPP with that of TE among a population of selected patients with medium to large tonsils (sizes 2, 3, or 4, per the Friedman scale[25]) and moderate to severe OSA—the hypothesis being that the results of mUPPP would be superior to those of TE alone.

Key Points

Question Is modified uvulopalatopharyngoplasty (mUPPP) more effective than tonsillectomy (TE) alone in treating adult patients with tonsillar hypertrophy and moderate to severe obstructive sleep apnea (OSA)?

Finding This randomized clinical trial of 93 patients with tonsillar hypertrophy and OSA demonstrated that mUPPP was not more effective than TE alone in treating patients with tonsillar hypertrophy and moderate to severe OSA. However, there was a small, not clinically meaningful difference in favor of TE.

Meaning The findings of this randomized clinical trial indicate that TE alone could be considered as an alternative to mUPPP among this selected group of patients with OSA.

Methods

The TEAMUP (Tonsillectomy and Modified Uvulopalatopharyngoplasty) RCT was reviewed and approved by the Swedish Regional Ethics Board (No. 2015/755-31/2). All participants provided written informed consent. The study followed the Consolidated Standards of Reporting Trials (CONSORT) reporting guidelines. The trial protocol is available in Supplement 1.

Trial Design and Participants

This trial was a single-enter RCT with 2 parallel groups and stratified randomization according to tonsil sizes. All patients and research members were blinded to study data and treatment allocation. Any patient with a suspected or established diagnosis of OSA who was referred to the Otorhinolaryngology Department (ORL) at the Karolinska University Hospital was considered for inclusion in the trial. Study inclusion was between January 2016 and February 2021, with the last follow-up PSG performed in September 2021.

Prospective study participants underwent a full night in-laboratory PSG, preceded or followed by a physical examination by an ORL resident or specialist, including a fiber endoscopy of the upper airway and a pharyngeal examination with Friedman staging of the tonsil size and tongue position.[25] All patients had failed or declined nonsurgical treatment (ie, a CPAP and/or MRD). Inclusion criteria were age, 30 to 65 years; AHI score, more than 15 events per hour (events/h); tonsil size, 2, 3, or 4 on the Friedman scale[25]; Friedman stages 1 to 2; and failure of nonsurgical treatment (CPAP or MRD). Exclusion criteria were: complicated or class 4 cardiovascular condition (per American Society of Anesthesiologists classification); complex psychiatric condition; neuromuscular disease; craniofacial deformity (eg, clinically severe retrognathia, syndrome

with craniofacial deformity); body mass index (BMI, calculated as weight in kilograms divided by height in meters squared) more than 34; previous pharyngeal surgery; night-shift work; and less than fluent knowledge of the Swedish language. Any patient who met the criteria was asked to consent to participate.

Randomization and Blinding

Participants were randomized before surgery. Stratified randomization was performed using 2 groups classified by tonsil size: group A, medium tonsil size (Friedman size 2); and group B, with large tonsil size (sizes 3 and 4). Randomized sealed envelopes with a ratio of 1:1 (mUPPP to TE) were compiled by an ORL statistician and 3 staff members who were not otherwise involved in the trial; the process was concealed from the researchers and anyone else involved in the trial. Five envelopes from each group were mixed to create a block of 10; they were kept in a secured location after surgery. All patients received a unique participant number and a stratification according to tonsil size. Final inclusion and randomization occurred immediately before surgery. The patients were not told which surgical procedure they had undergone, neither after surgery nor during follow-up visits. Treatment allocation was also blinded to the hospital staff, the personnel at the sleep laboratory, and the PSG scorer.

Polysomnography

Each patient was scheduled to undergo 2 PSGs: the first 1 month before surgery and the second 6 months after surgery. The PSG data were interpreted manually by a single certified scorer blinded to the treatment allocation. A total of 16 channels were recorded: electroencephalography (sensors C3-A2, O1-A2, O2-A1, and C4-A1), electrooculography (left and right), electromyography (chin and tibialis, left and right), oronasal thermistor and flowmetry, transcutaneous oxygen saturation, respiratory movements (abdomen and thorax), snoring, electrocardiography, pulse, and body position. The parameters were defined according to AASM 2012 (hypopnea is defined as a 30% drop in amplitude and 3% desaturation/arousal).[26] Noxturnal software, version 5.1 (Nox Medical) was used. The participants were awakened at 6:00 AM because the sleep laboratory shares its location with a daycare unit in the ORL at the Karolinska University Hospital.

Questionnaire and Satisfaction Survey

The Epworth Sleepiness Scale (ESS) is a self-administered questionnaire with 8 questions scored on a 4-point scale. The questionnaire evaluates the risk of falling asleep or dozing off during 8 common activities. The ESS score ranges from 0 to 24, and a higher score indicates higher average daytime sleepiness. We used the Swedish validated version.[27] The standard suggested criteria for interpretation were: normal, 0 to 10; mild, 11 and 12; moderate, 13 to 15, and severe, 16 to 24. The ESS was completed during preoperative and postoperative PSGs. The minimum clinically important improvement has been suggested[28] as between -2 and -3. In addition, at the postoperative PSG, the patients responded to a 1-question survey of whether they were satisfied with having had surgery (yes/no).

Adverse Events

Adverse events were evaluated through the electronic medical journal system in the health care region and were defined as any contact initiated by the patient. A serious adverse event (SAE) was defined according to good clinical practice as an event that results in death or is life threatening, requires inpatient hospitalization or prolongation of existing hospitalization, or results in persistent or significant disability or incapacity.

Intervention

Surgery was performed with general anesthesia, and a nasal tube was used for intubation. The surgical safety program included perioperative and postoperative tranexamic acid (5 days) and penicillin prophylaxis (3 days). Nonsteroid anti-inflammatory drugs, paracetamol, and oxycodone were administered for pain relief as needed. Patients with moderate OSA were monitored in a postoperative recovery room for 6 to 12 hours, and patients with severe OSA were monitored for 12 to 24 hours and were encouraged to use a CPAP (if available).

Modified UPPP

Local anesthesia without adrenaline was administered in the peritonsillar region and with adrenaline in the soft palate. Subsequently, an excision of the anterior tonsillar pillar of 2 to 3 mm was performed, followed by a TE, described in the next section. Absorbable monofilament single sutures (Monocryl 4-0, Johnson & Johnson) were used to lift the posterior pillar with the palatopharyngeal muscle to the anterior pillar, closing the tonsillar pillar. Finally, amputation of the uvula was performed, leaving approximately 1 cm. This surgical method has been described in detail by Browaldh and colleagues.[16]

Tonsillectomy

Local anesthesia without adrenaline was administered in the peritonsillar region. An extracapsular TE was performed using cold instruments with compression as the primary method for hemostasis, with bipolar diathermia as a complement when needed.

Outcomes

The primary outcome was the between-group difference in mean change in AHI scores from baseline to 6 months postsurgery as measured by PSG in patients who underwent TE vs mUPPP. Secondary outcomes were the difference in postoperative mean AHI score adjusted for clinically relevant baseline factors (eg, AHI score and BMI) and PSG data (ie, the respiratory disturbance index [RDI], the oxygen desaturation index [ODI], and the nadir oxygen saturation). Moreover, ESS scores, the satisfaction rate, supplementary surgery rate, and adverse events were evaluated. Subgroup analyses were performed for AHI scores with different tonsil sizes (Friedman scale, size 2 and sizes 3-4), Friedman stage (stages 1 and 2), and BMI (normal, <25; overweight, 25 to <30; and obese, 30 to 34).

Sample Size and Power Analysis

The original power analysis was based on results from a previous study.[16] A difference of 10 events/h in AHI was defined

Figure 1. CONSORT Flow Diagram of Patient Enrollment and Randomization

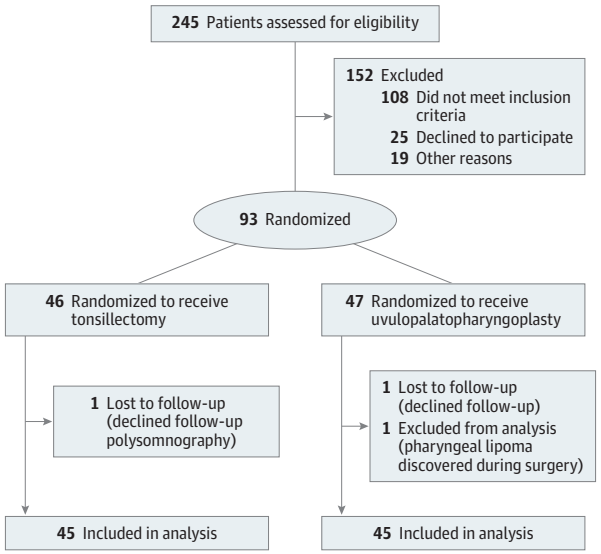


Table 1. Baseline Characteristics of Participants, by Surgical Method[a]

Characteristic	TE	mUPPP
Patients, No.	46	47
Age, mean (SD), y	41.5 (9.1)	41.8 (9.9)
Sex, No. (%)		
Men	40 (87)	40 (85)
Women	6 (13)	7 (15)
BMI, mean (SD)	29.1 (2.7)	28.9 (2.9)
Normal (<25), No. (%)	3 (6.5)	4 (8.5)
Overweight (25 to <30), No. (%)	21 (45.7)	22 (46.8)
Obese (≥30.0), No. (%)	22 (47.8)	21 (44.7)
Tonsil size (Friedman scale), No. (%)		
Median (IQR) size	3 (2-3)	3 (2-3)
2	14 (30.4)	16 (34.0)
3	26 (56.5)	23 (48.9)
4	6 (13.0)	8 (17.0)
3-4	32 (69.6)	31 (66.0)
Friedman stage, No. (%)		
Stage 1	29 (63.0)	24 (51.1)
Stage 2	17 (37.0)	23 (48.9)
AHI score, events/h (SD)	56.9 (25.1)	51.0 (22.6)
RDI score, events/h (SD)	59.0 (23.9)	51.9 (21.8)
ODI, events/h (SD)	48.7 (27.7)	43.9 (23.8)
ESS, mean (SD)	11.4 (4.2)	9.6 (6.1)

Abbreviations: AHI, apnea-hypopnea index; BMI, body mass index calculated as weight in kilograms divided by height in meters squared; ESS, Epworth sleepiness scale; mUPPP, modified uvulopalatopharyngoplasty; ODI, oxygen desaturation index; RDI, respiratory disturbance index; TE, tonsillectomy.

[a] No statistically significant between-group differences were found.

as a minimally clinically important between-group difference, along with an SD of 21, which generated a sample size of 70 patients per group with an 80% power and an α level of 5%.

Interim Analysis

Because of the generally slow inclusion after 5 years and a pause in OSA surgery and sleep research because of the COVID-19 pandemic, an interim analysis was performed in January 2021. At that point, we had complete data for 83 patients who had undergone both the preoperative and postoperative PSGs; for 5 patients, we had only the preoperative PSG data.

The interim analysis was performed by an independent statistician blinded to treatment allocation, and the analysis did not consider treatment effect. In the interim analysis, the SD was 20.7, indicating that 68 patients per group would be needed to obtain 80% power with a significance level of 5%. This finding was similar to the results of the original power analysis; however, it was considered unrealistic to include 50 more patients during the ongoing pandemic. Thus, it was decided that only patients already on the waiting list for a baseline PSG would be included. Thereafter, the study was terminated.

Statistical Analysis

The primary analysis was per the trial protocol, but intention-to-treat (ITT) analyses were also performed regarding the primary outcome of changes in AHI (additional details are available in Supplement 1). The missing variables were imputed to a change in AHI score with the same percentage change as the average change in the same group. In addition, a more conservative ITT was performed with the assumption of no change from baseline.

The PSG variables were parametric data, and parametric statistical tests (paired and unpaired *t* tests) were used to analyze differences within and between groups. The results were given as the mean (SDs or 95% CIs). Ordinal data were analyzed with nonparametric tests, such as the Wilcoxon signed-rank test within groups and the Mann-Whitney test between groups. The results were given as the median (IQR) or mean (SDs or 95% CIs).

The statistical inference was performed with effect sizes and 95% CIs using Cohen *d*, relating the magnitude of group difference to the SD. Cohen *d* is suggested to be interpreted as follows: small, less than 0.50; medium, 0.50 to 0.79; and large, 0.80 or more. The subgroup analyses were performed with the same statistical methods as the primary outcome.

Univariate linear regression models were used to determine confounding factors (AHI at baseline, BMI at baseline, change in BMI, age at baseline, sex, tonsil size [per Friedman scale[25]], Friedman stage, time in supine position at baseline, and change in time in supine position) or interaction terms (sex and tonsil size) that could affect the AHI score at follow-up. Variables considered significant ($P < .05$) in the univariate analysis were included in a forward stepwise linear multiple regression model. The findings were considered significant at $P < .05$. All data were analyzed using Stata, version 15.1 for Mac (StataCorp Inc) from January to September 2022.

Follow-Up Assessments

For each patient, a clinical evaluation was scheduled for approximately 3 months after surgery, and a follow-up assessment including a PSG, a questionnaire, and a survey was scheduled for 6 months after surgery. If the postoperative PSG showed severe OSA and the clinical evaluation indicated that the patient had undergone a TE (soft palate and pillars without scarring), the patient was offered supplementary uvulopalatoplasty.

Results

Of 245 patients screened for participation (**Figure 1**), 93 (mean [SD] age, 41.6 [9.4] years; 80 [86%] men and 13 [14%] women; race and ethnicity were not considered) were enrolled. This cohort had a mean (SD) BMI of 29.0 (2.8). Ninety patients (mUPPP, n = 45; TE, n = 45) completed the follow-up and were included in the final analysis per the trial protocol (available in Supplement 1). The dropout rate was 3% (3 participants of 93).

Baseline characteristics are listed in **Table 1**. There was a baseline mean between-group difference of 5.9 events/h in AHI, with higher values for the TE group. No statistically significant differences existed between the groups. Nineteen surgeons performed the procedures, and the median (IQR) number of procedures per surgeon was 3 (1-6). The mean (SD) time between preoperative PSG and surgery was 2.9 (2.8) months, and between surgery and postoperative PSG, it was 7.0 (3.1) months.

Primary Outcome

For the mUPPP group (n = 45 patients), the mean (SD) decrease in AHI score was 43%, from 51.0 (22.6) to 28.0 (20.0) events/h. For the TE group (n = 45 patients), the mean decrease in AHI was 56%, from 56.9 (25.1) to 24.7 (22.6) events/h. The unadjusted analysis showed a small between-group difference in favor of TE, with a mean of 9.2 events/h (95% CI, 0.5- 17.9; Cohen *d* = 0.44; **Table 2** and **Figure 2**).

Neither of the ITT analyses changed the results significantly compared with the per-protocol analysis. The ITT analyses (n = 93) with an imputed average change showed a mean of 9.6 events/h (95% CI, 1.1-18.2; Cohen *d* = 0.46) and the ITT analyses with an imputed no change from baseline showed a mean of 9.4 events/h (95% CI, 0.8-18.1; Cohen *d* = 0.45).

Secondary Outcomes

The regression model revealed that AHI and BMI at baseline were confounding factors, so they were adjusted for. The adjusted results showed a small mean postoperative difference in AHI of 6.4 events/h (95% CI, -0.6 to 13.5; Cohen *d* = -0.31) in favor of TE.

The RDI and AHI scores in a nonsupine position showed a medium between-group difference in favor of TE. The other PSG parameters (eg, ODI) showed a small between-group difference according to the Cohen *d* effect size (Table 2).

Seventy-eight patients (87%) responded to the ESS questionnaire. For the mUPPP group, the mean (SD) ESS score was

Table 2. Between-Group Differences of Tonsillectomy vs Uvulopalatopharyngoplasty, by Polysomnographic Data, BMI, and Epworth Sleepiness Scale at Baseline and Follow-up[a]

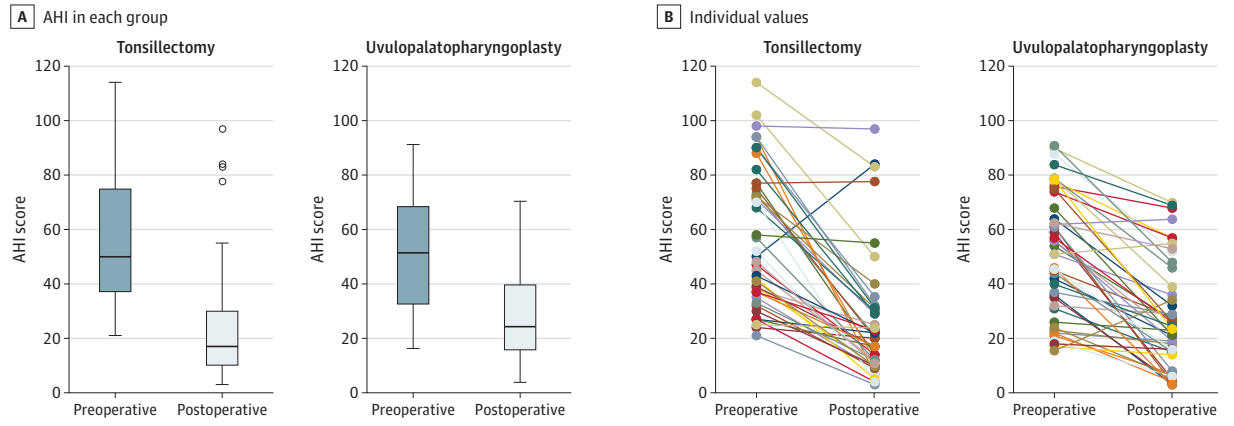
Outcome	TE, mean (SD)				mUPPP, mean (SD)				Between-group differences in change (95% CI)	Effect size[b]
	Pateients, No.	Baseline	Follow-up	Change (95% CI)	Patients, No.	Baseline	Follow-up	Change (95% CI)		
BMI	45	29.1 (2.8)	29.5 (3.2)	0.4 (-0.2 to 1.0)	45	28.9 (2.9)	29.9 (3.8)	1.0 (0.4 to 1.6)	0.6 (-0.2 to 1.4)	0.30
AHI (events/h)	45	56.9 (25.1)	24.7 (22.6)	-32.1 (-39.2 to -25.1)	45	51.0 (22.6)	28.0 (20.0)	-23.0 (-28.4 to -17.6)	9.2 (0.5 to 17.9)	0.44
AHI in supine (events/h)	41	73.7 (25.3)	41.4 (31.5)	-32.3 (-43.6 to -21.0)	41	67.0 (27.8)	47.4 (31.8)	-19.6 (-32.1 to -7.2)	12.7 (-3.9 to 29.3)	0.34
AHI in nonsupine (events/h)	41	46.5 (33.3)	13.5 (19.9)	-33.0 (-41.3 to -24.7)	43	42.1 (26.9)	21.1 (20.9)	-21.0 (-27.3 to -14.7)	12.0 (1.8 to 22.2)	0.51
Time in supine (%)	44	37.9 (28.4)	37.6 (30.6)	-0.3 (-10.0 to 9.4)	45	27.2 (27.6)	30.5 (29.4)	3.2 (-5.7 to 12.2)	3.5 (-9.4 to 16.5)	0.11
RERA (events/h)	45	2.7 (7.9)	2.1 (1.9)	-0.5 (-2.9 to 1.9)	45	1.4 (1.4)	2.5 (3.2)	1.1 (0.0 to 2.1)	1.6 (-1.0 to 4.2)	0.26
RDI (events/h)	45	58.5 (23.9)	26.8 (22.0)	-31.7 (-38.4 to -25.0)	45	51.9 (21.9)	30.6 (19.8)	-21.3 (-26.7 to -15.9)	10.3 (1.9 to 18.8)	0.51
ODI (events/h)	45	48.1 (27.7)	22.5 (23.7)	-25.7 (-33.8 to -17.5)	44	43.6 (24.2)	22.8 (15.9)	-20.8 (-26.4 to -15.2)	4.9 (-5.0 to 14.7)	0.21
Mean oxygen saturation (%)	45	92.2 (2.9)	92.7 (3.1)	0.5 (-0.5 to 1.5)	45	92.3 (2.3)	93.5 (1.2)	1.2 (0.5 to 1.9)	0.7 (-0.5 to 1.9)	0.24
Nadir of oxygen saturation (%)	45	77.9 (8.6)	83.7 (6.9)	5.8 (3.4 to 8.2)	45	77.4 (9.6)	83.2 (7.2)	5.7 (2.9 to 8.5)	-0.1 (-3.8 to 3.5)	-0.01
ESS score	38	11.4 (4.2)	7.2 (5.1)	-4.2 (-5.7 to -2.7)	40	9.1 (6.1)	5.8 (3.8)	-3.3 (-5.1 to -1.4)	1.1 (-1.3 to 3.4)	0.21

Abbreviations: AHI, apnea-hypopnea index score; BMI, body mass index calculated as weight in kilograms divided by height in meters squared; ESS, Epworth sleepiness scale; mUPPP, modified uvulopalatopharyngoplasty; ODI, oxygen desaturation index; RDI, respiratory disturbance index; RERA, respiratory effort related arousals; TE, tonsillectomy.

[a] Unless otherwise indicated, data are reported as mean (SD) values.

[b] Effect sizes were calculated using Cohen *d* relating the magnitude of group difference to the SD. Interpreted as small (<0.5), medium (0.5 to <0.8), and large (≥0.8).

Figure 2. Preoperative and Postoperative Apnea-Hypopnea Index (AHI) Scores in Each Study Group



A, Horizontal lines and boxes indicate the median and the first to third quartiles, respectively; whiskers, the 1.5 IQR; and circles, the outliers. B, The line graphs represent the individual values.

9.1 (6.1) at baseline and 5.8 (3.8) at 6 months (n = 40); and for the TE group, 11.4 (4.2) at baseline and 7.2 (5.1) at 6 months (n = 38). The mean between-group difference in the change in ESS scores was small, only 1.1 (95% CI, -1.3 to 3.4; Cohen *d* = 0.21). The subgroup analyses with different tonsil sizes according to the Friedman scale, Friedman stage, and BMI categories are presented in **Table 3**.

Seventy-four patients (82%; mUPPP, 84%; TE, 80%) responded to the surgery satisfaction question. In the mUPPP group, 34 (89%) patients responded *yes*, satisfied with the surgery; 4 responded *no*, not satisfied. In the TE group, 32 (89%) patients responded *yes*; 4 responded *no*.

All 90 patients were discharged the day after surgery without complications. One SAE occurred among the mUPPP group and 4 SAEs among the TE group, 2 of which occurred in a single patient. All SAEs required readmission to the hospital due to postoperative bleeding; however, no patient required additional treatment in the operating room. There were 6 nonserious adverse events among the UPPP group (all required a prescription for prolonged pain relief) and 8 among the TE group (4 prescriptions for prolonged pain relief, 2 consultations for a swollen uvula, and 2 prescriptions for an antibiotic prescription for a suspected infection). There were no deaths, and no patient was excluded from the study because of an adverse event.

Two patients with severe residual OSA (AHI, 31 and 50) underwent a supplementary uvulopalatoplasty. One patient had an additional PSG performed after the second surgery and experienced an improvement in AHI of 9 events/h (50 to 41).

Discussion

This RCT compared mUPPP with TE alone to treat moderate to severe OSA in patients with tonsillar hypertrophy, with the hypothesis that mUPPP is superior to TE alone in improving nocturnal respiration and daytime sleepiness. Although this study could not verify this hypothesis, the results showed a small difference in effect size in favor of TE. Because TE alone is also a more conservative procedure than mUPPP, TE could be considered an alternative to mUPPP in patients with tonsillar hypertrophy (sizes 2, 3, or 4).

There is no universally accepted minimal important change in AHI score. A difference of 10 events/h was defined before the start of the study as clinically meaningful, but lower values may also be of clinical importance. In addition, although the between-group difference in mean AHI was small according to the Cohen *d* effect size, the clinically significant difference of 10 events/h was within the confidence interval (95% CI, 0.5-17.9). Hence, a clinically relevant difference of more than 10 events/h in favor of TE could not be ruled out.

The mean percentage decrease in AHI in the TE group was 56% compared with 43% in the mUPPP group. However, the TE group had a higher preoperative mean AHI (ie, +5.9 events/h; 10% higher) than the mUPPP group, a potential bias for a larger percentage decrease in the TE group. This group difference in baseline was adjusted with regression analysis, as recommended by Clifton and colleagues.[29] When comparing the postoperative values adjusted for baseline AHI and baseline BMI, the between-group difference in AHI scores decreased to 6.4 events/h, a smaller difference but still in favor of TE according to the effect size. In addition, the RDI and AHI scores in nonsupine positions showed a medium effect size of between-group difference in favor of TE. Taken together, these results indicate that achieving a clinically more meaningful benefit from mUPPP instead TE alone would be unlikely.

The findings of this RCT were counterintuitive to what we expected: a more extensive surgery should be more effective than a less extensive surgery. There are several possible explanations. First, the study population was selected to have tonsillar hypertrophy (sizes 2, 3, and 4), with approximately two-thirds of the included patients having a tonsil size of 3 or 4. Given that both groups underwent TE, it would have had a similar widening effect on the throat. The subgroup analysis

demonstrated medium effect size group differences in AHI changes between size 2 tonsils, indicating that these patients benefited from TE alone. However, the trial was not powered for this analysis; therefore, interpretations should be made carefully.

Second, TE alone may cause scarring of the palate and pillars, and the added effect of the pharyngoplasty could be minor, comparatively. Our choice of a conservative mUPPP was to avoid unnecessary adverse effects, but a disadvantage was that it might not have been radical enough to be efficient. Arguably, at several international clinics, a pharyngoplasty includes more radical surgery. For example, a recent review of 15 studies of barbed reposition pharyngoplasty, including TE, showed a mean reduction in AHI scores of 65% to 93%,[30] far better than the results of the present study. However, given that the review also included studies with multilevel surgeries, it is difficult to compare the effectiveness and the adverse effects of the various techniques.

Third, several studies of patients with long-term snoring have suggested that damaged sensory and muscular nerve functioning in the palate and uvula are associated with increased severity of OSA.[31,32] Modified UPPP could be expected to cause more damage to the nerves of the palate and uvula than would TE alone, and therefore, may contribute to worsened OSA.

Finally, the results may have been skewed in favor of TE because there were more patients with Friedman stage I disease in the TE group. However, there was no statistically significant baseline difference between the groups in the Friedman stage, and it was not a confounding factor according to the regression analysis.

The mUPPP in the present study was not equally effective (43% reduction in AHI score) as it was in our previous RCT (a 60% reduction[16]) with the same method and with patients of similar baseline characteristics. This difference is difficult to explain because our method did not change. Sommer and colleagues[17] found a 54% reduction in AHI score after UPPP in an RCT using a method similar to the mUPPP used in the present trial.

Although the AHI is the most widely used parameter of OSA severity, it is not the only parameter. Alternative measures, such as the "hypoxic burden," reflected by the depth and duration of respiratory-related desaturations, seem to be better associated with mortality independent of other confounders.[33] The ODI and nadir oxygen saturation rates in the present study showed small or no between-group differences, similar to patient-related outcomes such as excessive daytime sleepiness and satisfaction rate.

Limitations and Strengths

The main limitation of this study was the small sample size and premature termination of the study, which reduced the number of included patients from 140 to 93—34% fewer patients than suggested in the original power analysis—which reduced the power from 80% to 63% based on the original assumptions in the SD and treatment difference. This reduction could have affected the likelihood of finding a larger between-group difference. However, because the group differ-

Table 3. Apnea-Hypopnea Index Scores at Baseline and Follow-up for Tonsillectomy (TE) vs Modified Uvulopalatopharyngoplasty (mUPPP), by Tonsil Size, Stage, and Weight Category

Outcome	TE, mean (SD)				mUPPP, mean (SD)				Between-group differences in change (95% CI)	Effect size[a]
	Patients, No.	AHI score, mean (SD)		Change (95% CI)	Patients, No.	AHI score, mean (SD)		Change (95% CI)		
		Baseline	Follow-up			Baseline	Follow-up			
Tonsil size, Friedman scale										
Size 2	13	51.8 (26.5)	24.0 (23.9)	-27.9 (-39.9 to -15.8)	16	52.0 (23.4)	35.0 (21.1)	-17.1 (-27.0 to -7.1)	10.8 (-3.9 to 25.6)	0.56
Size 3-4	32	59.0 (24.7)	25.1 (4.0)	-33.9 (-42.8 to -25.0)	29	50.5 (22.5)	24.2 (18.6)	-26.3 (-32.7 to -19.9)	7.6 (-3.3 to 18.5)	0.36
Stage per Friedman staging										
Stage 1	29	57.4 (23.9)	24.14 (23.1)	-33.3 (-23.7 to -42.8)	22	45.7 (21.3)	20.7 (17.1)	-25.0 (-16.7 to -33.3)	8.2 (-4.6 to 21.0)	0.36
Stage 2	16	55.9 (28.1)	25.9 (22.3)	30.1 (-19.3 to -40.8)	23	56.1 (23.0)	35.1 (20.3)	-21.0 (-13.6 to -28.4)	9.1 (-3.1 to 21.2)	0.49
Weight category by BMI										
Normal (<25)	3	54.0 (37.0)	8.0 (5.6)	-46.0 (-136.2 to 44.2)	4	31.8 (18.2)	8.5 (7.0)	-23.3 (-57.8 to 11.3)	22.8 (-33.1 to 78.6)	0.80
Overweight (25-29.9)	21	60.3 (22.9)	21.5 (12.7)	-38.7 (-46.3 to -31.1)	21	47.7 (23.6)	25.8 (21.5)	-21.9 (-29.7 to -14.2)	16.8 (6.3 to 27.3)	1.00
Obese (30-34)	21	54.0 (26.5)	30.4 (29.5)	-23.6 (-35.1 to -12.1)	20	58.3 (20.0)	34.3 (17.4)	-24.0 (-32.9 to -15.2)	-0.4 (-14.6 to 13.7)	-0.02

Abbreviation: BMI, body mass index calculated as weight in kilograms divided by height in meters squared.

[a] Effect sizes were calculated using Cohen *d* to relate the magnitude of group difference to the SD. Interpreted as small (<0.50), medium (0.50-0.79), and large (≥0.80).

ences favored TE, adding 47 more patients would not have changed our main conclusion that mUPPP was not more effective than TE alone.

Furthermore, the results cannot be generalized to the overall population of patients with OSA because we excluded patients with small (size 1) tonsils or no tonsils. This limitation is of clinical importance because most adults do not have tonsillar hypertrophy. Indeed, in a sample of individuals without OSA, only approximately 6% were considered to have large tonsils (ie, sizes 3 and 4).[34] Likewise, the findings of this study cannot be generalized to patients with severe obesity (BMI, ≥34), patients younger than 30 years or older than 65 years, or women because they were underrepresented (14%).

Another limitation was the lack of data from a preoperative drug-induced sleep endoscopy. Arguably, an endoscopy may have revealed that the pharynx was not the site of obstruction. However, there is still no international consensus on interpreting findings from drug-induced sleep endoscopy,[35] and there is a lack of correlation with surgical success.[36] Furthermore, the RCT design should compensate for uneven distribution.

A final limitation is the relatively short follow-up time of 6 months. For most patients, OSA is a lifelong condition; therefore, long-term effectiveness is important. There may be a difference when comparing the surgical methods over the long term; therefore, we have planned a 5-year follow-up for this cohort.

The strength of the present study is the RCT design, minimizing the risk of selection bias, confounding factors, and regression to the mean. A further strength is the in-laboratory PSG, the gold standard for investigating OSA. Additionally, only a single PSG scorer blinded to treatment allocation manually interpreted all of the PSG finding, limiting the interrater variability. The study also had a low dropout rate (3%).

Conclusions

This RCT did not confirm our hypothesis that mUPPP is more effective than TE alone in treating patients tonsillar hypertrophy and moderate to severe OSA to treat nocturnal respiration and daytime sleepiness. Instead, there was a small difference in favor of TE. Because TE alone is a less extensive procedure than mUPPP, TE could be considered an alternative for this selected group of patients with OSA; however, further studies, including long-term evaluations, are needed.

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Acquisition, analysis, or interpretation of data: All authors.
Drafting of the manuscript: Sundman, Friberg.
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