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SKUP³ RCT; Continuous Study: Changes in Sleepiness and Quality of Life After Modified UPPP

Nanna Browaldh, MD, PhD; Johan Bring, PhD; Danielle Friberg, MD, PhD

Objectives/Hypothesis: Our previous study showed that modified uvulopalatopharyngoplasty (UPPP), including tonsillectomy, significantly improved nocturnal respiration in obstructive sleep apnea syndrome (OSAS) patients. This is a continuous study of changes in daytime sleepiness and quality of life.

Study Design: Prospective randomized controlled trial (RCT), two parallel arms.

Methods: Sixty-five patients with apnea-hypopnea index ≥ 15 , body mass index < 36 , Epworth Sleepiness Scale (ESS) ≥ 8 , Friedman stage I or II, failing nonsurgical treatment. The intervention group ($n = 32$) underwent surgery, and the controls ($n = 33$) had no treatment. At baseline and the 7-month follow-up, polysomnography, questionnaires, and vigilance tests were implemented.

Results: All patients answered the questionnaires, and 48 took the vigilance test. Epworth Sleepiness Scale decreased significantly in the intervention group, from a mean (standard deviation) of 12.5(3.2) to 6.8(3.9), but nonsignificantly in the control group, from 12.9(3.1) to 12.5(3.9), a significant group difference ($P < 0.001$). The physical and mental component score on the Short Form-36 questionnaire increased significantly in the intervention group, from a mean 47.8(8.3) to 51.2(8.8) and from 42.1(10.6) to 48.1(9.7), respectively, but with nonsignificant changes in the controls: 49.0(9.0) to 48.3(9.1) and 41.0(10.2) to 42.7(11.5), significant group differences ($P = 0.007$, $P = 0.031$), respectively. The sleep latency/vigilance test showed a significant mean increase in the intervention group of 7(12.4) minutes and a decrease in the controls of 2.2(10.6), a significant group difference ($P = 0.011$). There were significant correlations between changes in subjective outcomes and nocturnal respiration.

Conclusion: This RCT shows that modified UPPP was effective in improving daytime sleepiness and quality of life in OSAS patients. It strengthens the body of evidence on the potential effect of surgery offered to selected patients.

Key Words: Obstructive sleep apnea syndrome, Short Form-36, quality of life, uvulopalatopharyngoplasty, randomized controlled trial, sleepiness.

Level of Evidence: 1b.

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INTRODUCTION

Obstructive sleep apnea syndrome (OSAS) involves an intermittent pharyngeal breathing obstruction during sleep. Among different etiologies, examples of anatomical factors contributing to the upper airway narrowing are macroglossia, excessive mucosa in the soft palate and pharyngeal walls, hypertrophied tonsils, nasal obstruction, and deformity of the facial skeleton. The prevalence of OSAS in adults between 30 and 70 years of age was recently estimated to be approximately 14% in males and 5% in females.¹ Obstructive sleep apnea syndrome is associated with increased morbidity and mortality.^{2–4} There is

also an increased risk of poor sleep and quality of life, excessive daytime sleepiness, and traffic accidents.⁵

Uvulopalatopharyngoplasty (UPPP)⁶ was the predominant treatment for OSAS before continuous positive airway pressure (CPAP) devices became widely available. Since then, the main treatment for OSAS has been CPAP, but an increasing number of patients are also treated with a mandibular retaining device (MRD). When properly used by the patient, CPAP is a successful treatment for sleep apnea. Continuous positive airway pressure has also shown improvement regarding subjective parameters such as the Epworth Sleepiness Scale (ESS).⁷ Compared to placebo, both CPAP and MRDs have been shown to significantly improve subjective sleepiness measured by the ESS, but their impact on objective sleepiness measured by a maintenance of wakefulness test (MWT) is inconsistent.^{8,9} Additionally, there are studies showing that, despite normalization of the apnea-hypopnea index (AHI), improvement is varying in subjective and objective sleepiness as well as in quality of life.^{10,11}

The surgical techniques for UPPP have varied with more or less extensive resections of the tonsillar pillars, soft palate, and uvula, as well as use of the hot (laser) or cold knife with or without tonsillectomy. Also, the role of UPPP has been questioned because of side effects, complications, and a lack of efficacy in treating OSAS.

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Fig. 1. Flow of participants.

Single center (June, 2007–May, 2011).

*Patients from the second center (n = 4) who deviated from the study protocol were excluded in the per protocol analysis but included in the intention-to-treat analyses.

AHI = apnea-hypopnea index; ESS = Epworth Sleepiness Scale; SF-36 = Short Form-36 questionnaire.

Therefore, randomized controlled trials (RCTs) have been called for.¹² In a recently published Sleep Apnea Karolinska UPPP (SKUP³) RCT, our group has shown by polysomnography (PSG) that respiratory events during sleep were significantly reduced in selected OSAS patients treated with a conservative cold-knife technique (modified UPPP), compared to no treatment for 6 months.¹³ The aim of this continuing study was to investigate the efficacy of modified UPPP in terms of changes in daytime sleepiness and quality of life, as measured with questionnaires and vigilance tests.

MATERIALS AND METHODS

The two parallel cohorts in this single-center prospective RCT have been presented in detail previously¹³ and are briefly described below in this continuous report.

Participants

All OSAS patients referred to the Oto-Rhino-Laryngology Department of the Karolinska University Hospital in Huddinge, Stockholm, Sweden, from June 2007 to May 2011 for UPPP were

eligible candidates for the study. The patients underwent a first full-night in-lab PSG procedure. The morning after, they filled out questionnaires and underwent a vigilance test.

The inclusion criteria were: 1) males and females > 18 years of age; 2) AHI ≥ 15 events/hour of sleep (from PSG; see below); 3) ESS score ≥ 8 ; 4) marked daytime sleepiness three times a week or more; 5) body mass index (BMI) < 36 kg/m²; 6) Friedman stage I or II¹⁴; and 7) having tried and failed or withholding of CPAP and MRD treatments, and no use of these treatments during the last 3 months. Patients with Friedman stage I and BMI < 30 kg/m² were not required to have failed CPAP/MRD treatment before inclusion.

The exclusion criteria were: 1) serious psychiatric, cardiopulmonary, or neurological disease—or an American Society of Anesthesiologists classification of > 3; 2) patients who decline surgery; 3) insufficient knowledge of Swedish; 4) night-shift workers; 5) patients who could be dangerous in traffic according to responses in our nonstandardized questionnaire; 6) severe nasal congestion (could be included after topical nasal treatment); 7) previous tonsillectomy; 8) Friedman stage III; and 9) severe clinical worsening of OSAS during the study.

All participants in this study gave their informed consent and were recruited from a single center (Fig. 1).

TABLE I.
Baseline Characteristics in Each Group.

Characteristic	n =	Intervention	n =	Control
Age	32	41.5 (11.5)	33	42.9 (11.7)
BMI (kg/m ²)	32	28.2 (2.9)	33	27.7 (3.3)
AHI (events/h sleep)	32	53.3 (19.7)	33	52.6 (21.7)
Nadir of oxygen saturation (%)	32	79.9 (5.3)	33	81.0 (6.6)
Arousal index (events/h sleep)	32	64.0 (16.2)	33	60.3 (22.7)
ESS	32	12.5 (3.2)	33	12.9 (3.1)
SF-36 PF	32	83.7 (19.2)	33	87.0 (18.4)
SF-36 PR	32	69.5 (36.3)	33	75.8 (39.3)
SF-36 BP	32	78.3 (27.1)	32	80.9 (23.0)
SF-36 GH	32	61.3 (24.1)	33	59.8 (23.9)
SF-36 VT	32	42.8 (22.0)	33	42.3 (21.9)
SF-36 SF	32	74.2 (23.3)	33	77.3 (22.4)
SF-36 RE	32	77.1 (36.6)	33	81.8 (34.5)
SF-36 MH	32	71.8 (19.3)	33	66.1 (18.8)
SF-36 PCS	32	47.3 (8.6)	32	49.2 (8.9)
SF-36 MCS	32	42.5 (10.7)	32	41.2 (10.1)
Sleep latency (minutes)	27	30.7 (11.1)	29	33.6 (9.0)

The above data are the mean (SD).

AHI = apnea-hypopnea index; BMI = body mass index; BP = bodily pain; ESS = Epworth Sleepiness Scale; GH = general health; MH = mental health; MCS = mental component summary; n = number of patients; PCS = physical component summary; PF = physical functioning; PR = role physical; RE = role emotional; SD = standard deviation; SF = social functioning; VT = vitality.

Intervention

The patients were randomized to receive either modified UPPP within 1 month (intervention group) or no treatment at all for 7 months (control group). The patients in the control group received delayed surgery. Our method was a modification of the method initially described by Fujita,⁶ but with only minor resections of the soft palate and uvula using the cold steel technique, including tonsillectomy,¹³ in order to avoid scarring and unwanted side effects.

Hypothesis

Modified UPPP significantly reduces daytime sleepiness and improves the quality of life compared to expectancy.

Outcomes

Outcomes were scheduled for measurement 6 months after intervention and control and consisted of changes in 1) the validated ESS questionnaire⁷; 2) a self-reported quality of life instrument, the Short Form-36 questionnaire (SF-36)¹⁵; and 3) sleep latency from a vigilance test measured using a modified OSLER test¹⁶; plus other outcomes from correlation tests between changes in 4) subjective (ESS and SF-36 questionnaires) and 5) objective findings (vigilance test, as well as AHI from PSG data).

Epworth Sleepiness Scale

The ESS is an eight-item questionnaire concerning the propensity to fall asleep in different situations in daily life.⁷ It has been translated into Swedish. The items are presented in scales of 0–24: an ESS score of 8–10 is mild sleepiness; 11 to 15 is moderate sleepiness; 16 to 20 is severe sleepiness; and 21 to 24 is excessive sleepiness.¹⁷

Health Survey SF-36

A standardized Swedish manual for SF-36 was used. The health survey SF-36 covers eight domains of health-related quality of life (HRQOL) measurements for evaluation of the previous four weeks. The domains are: physical functioning (PF), role physical (RP), bodily pain (BP), general health (GH), vitality (VT), social functioning (SF), role emotional (RE), and mental health (MH). Scores from each subscale range from 0 to 100, and a higher score indicates a better HRQOL.¹⁵ The SF-36s Mental Component Summary (MCS) and Physical Component Summary (PCS) were also evaluated. These summary scores range from 0 to 100 and replicate the results from the eight domains of the SF-36. Mental Component Summary and PCS are dependent on the scores for the eight domains, which are weighted following a special template. A mean score of 50 (standard deviation [SD] 10) demonstrates a representative sample of the population in the United States.¹⁸ The Swedish version of the SF-36 has been validated for the Swedish population.^{18,19} Normative data from Sweden, broken down by sociodemographic variables, have shown to be consistent with those of the United States.¹⁹

Vigilance Test

The Oxford sleep resistance (OSLER) test is a vigilance test. It has been shown to discriminate normal sleep subjects from OSAS patients and is performed in a dark room, isolated from external noise.¹⁶ The original test is performed 4 x 40 minutes during 1 day, and the patient is asked to remain awake and respond to an illuminated light every 3 seconds. When the patient fails to respond for 21 seconds, the test is ended and it is understood that the patient is asleep. The standard analysis of the OSLER test is the determination of sleep latency. In the present study, the patients performed the test once (modified OSLER) the morning directly after the in-lab PSG. The patients

TABLE II.
Results From Evaluations With Questionnaires and Vigilance Test at Baseline and Follow-up in Each Group, Also Within and Between-Groups Comparisons in the Available Data Analysis.

	n =	Intervention Group		Within Group	n =	Control Group		Within Group	Between Groups
		Baseline	Follow-up	Comparison <i>P</i>		Baseline	Follow-up	Comparison <i>P</i>	Comparison <i>P</i>
BMI (kg/m ²)	32	28.2 (2.9)	28.2 (3.1)	0.77	33	27.7 (3.3)	28.1 (3.7)	0.17	0.25
ESS	32	12.5 (3.2)	6.8 (3.9)	< 0.001	33	12.9 (3.1)	12.5 (3.9)	0.50	< 0.001
SF-36 PF	32	83.7 (19.2)	88.5 (15.9)	0.094	33	87.0 (18.4)	87.4 (16.7)	0.96	0.16
SF-36 RP	31	68.5 (36.5)	83.1 (34.4)	0.033	33	75.8 (39.3)	81.1 (31.9)	0.39	0.13
SF-36 BP	32	78.3 (27.1)	84.1 (23.4)	0.090	32	80.9 (23.0)	80.6 (25.9)	0.94	0.18
SF-36 GH	32	61.3 (24.1)	71.7 (24.0)	0.001	32	59.0 (23.7)	58.0 (25.6)	0.67	0.004
SF-36 VT	32	42.8 (22.0)	63.9 (23.0)	< 0.001	32	41.4 (21.7)	42.8 (24.3)	0.68	< 0.001
SF-36 SF	32	74.2 (23.3)	87.5 (20.6)	0.005	33	77.3 (22.4)	69.7 (29.8)	0.12	0.003
SF-36 RE	31	76.3 (36.7)	87.1 (29.4)	0.059	33	81.8 (34.5)	89.9 (27.0)	0.09	0.75
SF-36 MH	32	71.8 (19.3)	77.8 (17.8)	0.009	32	65.4 (18.6)	70.4 (19.7)	0.17	0.49
SF-36 PCS	31	47.8 (8.3)	51.2 (8.8)	0.009	31	49.0 (9.0)	48.3 (9.1)	0.37	0.007
SF-36 MCS	31	42.1 (10.6)	48.1 (9.7)	< 0.001	31	41.0 (10.2)	42.7 (11.5)	0.39	0.031
Sleep latency (minutes)	22	31.7 (10.8)	38.7 (5.1)	0.013	26	35.0 (8.0)	32.8 (10.9)	0.40	0.011

Data are the mean (SD) and *P* values from the Wilcoxon signed-rank test for within-group comparisons.

P values from independent samples between-group comparisons, Mann-Whitney *U* tests. Significant differences, *P* < 0.05, are shown in bold type.

BMI = body mass index; BP = bodily pain; ESS = Epworth Sleepiness Scale; GH = general health; MH = mental health; MCS = mental component summary; n = number of patients; PCS = physical component summary; PF = physical functioning; RE = role emotional; RP = role physical; SD = standard deviation; SF-36 = Short Form-36 questionnaire; SF = social functioning; VT = vitality.

were not allowed to exercise or to consume caffeine, theine, or alcohol before the test.

Sample Size

The sample size was chosen to obtain 90% power, with α level of 5%, and resulted in 64 patients. The sample size calculation was based on the night-to-night variability of the oxygen desaturation index values in patients with OSAS,²⁰ and also from one of our previous studies on patients with OSAS undergoing UPPP.²¹

Randomization

The patients were randomized using sealed envelopes. The envelopes were distributed in a predetermined order that was concealed from the researchers. Sixty-five randomized patients followed the study protocol and fulfilled all criteria (see Fig. 1). Altogether, 71 patients were randomized. After randomization, six patients (4 in the intervention group and 2 in the control group) were excluded due to deviation from the study protocol.¹³ Four of these patients were from a second center, which was excluded in this single-center study.

Statistical Analysis

The available data (i.e., complete data, per protocol) analysis for ESS, sleep latency, and follow-up time are presented as the median and range in the text and as the mean and SD in tables. All other parameters are expressed as the mean and SD.

Changes within groups are calculated by subtracting the outcomes at the first registration in connection with PSG 1 (baseline) from those in PSG 2 (follow-up). Because of the nature of the questionnaire parameters and the skew distribution of the vigilance, nonparametric statistical analyses were chosen: *P* values from the Wilcoxon signed-rank (WSR) test for within-group comparisons, and *P* values from independent samples between

group comparisons, the Mann-Whitney *U* tests. For correlations between changes in ESS, SF-36, vigilance, and AHI, the non-parametric Spearman's rank correlation test was used.

All statistical calculations were performed using Statistica 10.0 (StatSoft, Inc., Tulsa, OK) or R 2.15, and the significant level was determined to be *P* < 0.05.

Sensitivity Analysis

Intention-to-treat (ITT) analyses were performed for all 71 randomized patients, including the six excluded patients (Fig. 1). Both ESS and SF-36 were completed by 32 of 36 patients in the intervention group and by 33 of 35 in the control. The vigilance test was completed by 22 of 36 and by 26 of 35 patients, respectively. The missing variables were imputed to no change from baseline.

Nonparametric tests were used, as above. Paired and unpaired *t* tests were also performed to investigate whether the results changed with parametric statistical methods.

RESULTS

For the 65 included patients (59 men and 6 women), the median time between baseline and follow-up was 7.2 months (range 4.8–14.6) for the intervention group and 6.7 months (4.8–8.5) for the control group.

See Table I for baseline characteristics of the two groups. There were no significant changes in BMI between baseline and follow-up in either group (Table II).

Changes in the Epworth Sleepiness Scale

All 65 participants completed all ESS questionnaires; there were no dropouts, and the results were analyzed in the available data analysis (per protocol) (Table II). The median ESS score had significantly

Fig. 2. Results for (A) ESS, (B) eight SF-36 domains, and (C) SF-36 component summary for the intervention and control groups, respectively. (A) Box plots and lines showing the ESS on two different polysomnography recordings (before and after) in the intervention group (grey) and the control group (white). Boxes represent the median and 25% and 75% values, whiskers the nonoutlier range, and dots the outliers. *P* values represent the changes within groups, Wilcoxon signed-rank test. (B) Box plots showing the changes in SF-36 domains between two different polysomnography recordings (after minus before) in the intervention group (grey) and the control group (white). The domains are: physical functioning, role physical, bodily pain, general health, vitality, social functioning, role emotional, and mental health. (C) Box plots showing the changes in SF-36s MCS and PCS between two different polysomnography recordings in the intervention group (grey) and the control group (white). BP = bodily pain; ESS = Epworth Sleepiness Scale; GH = general health; MH = mental health; PF = physical functioning; RE = role emotional; RP = role physical; SF = social functioning; SF-36 = Short Form-36 questionnaire; VT = vitality.

decreased from 12 (range 8–21) to 6 (2–16) ($P < 0.001$) in the intervention group, a mean reduction of 5.7 (3.9). The corresponding change for the control group was nonsignificant, from a median of 13 (8–18) to 12 (5–21), with a significant difference between the groups ($P < 0.001$) (Fig. 2). The ITT analysis did not change results markedly.

Changes in SF-36

Sixty-five participants completed the questionnaires. Three patients failed to respond to one, two, or three domains, respectively. In the intervention group, all domains showed improvements, which were statistically significant for RP, GH, VT, SF, and MH—as well as

TABLE III.
Correlations Between Changes in ESS, Sleep Latency, SF-36, and AHI, Respectively, in the Available Data Analysis.

	Change in ESS	Change in SF-36 GH	Change in SF-36 VT	Change in SF-36 SF	Change in SF-36 RE	Change in SF-36 PCS	Change in SF-36 MCS	Change in Sleep Latency
Change in ESS	n = 65 1	n = 64 -0.17	n = 64 -0.56***	n = 65 -0.50***	n = 64 0.19	n = 62 -0.12	n = 62 -0.30*	n = 48 0.47***
AHI	0.39**	-0.33**	-0.30*	-0.29*	-0.01	-0.26*	-0.18	-0.25
sleep latency (n=48)	0.47***	0.27	0.38**	0.41**	-0.33*	0.31*	0.03	1

Spearman's rank correlation test was used. R values are presented. Significant correlations ($P < 0.05$) are shown in bold type.

** $P < 0.05$, *** $P < 0.01$, **** $P < 0.001$.

AHI = apnea-hypopnea index; ESS = Epworth Sleepiness Scale; GH = general health; MCS = mental component summary; n = number of patients; PCS = physical component summary; RE = role emotional; SF-36 = Short Form-36 questionnaire; SF = social functioning; VT = vitality.

MCS and PCS. Significant changes between the two groups were seen in GH, VT, SF, MCS, and PCS (Table II) (Fig. 2).

Changes in Vigilance

In the vigilance tests, only 48 of 65 patients had complete data (baseline and follow-up), with a dropout rate of 26% (Table II). In the available data analysis, the median sleep latency in the intervention group was significantly changed from 38.4 minutes (range 11–40) to 40 (16–40) ($P = 0.013$), a median difference of 1.6 minutes and a mean reduction of 7 (12.4) minutes. Before intervention, nine out of 22 patients (41%) passed the vigilance test. At follow-up, however, 20 of 22 patients (91%) passed the 40-minute test. In the control group, the median sleep latency remained unchanged, with 40 minutes (15.5–40) at baseline and 40 minutes (3.65–40) at follow-up. Also in the control group, 16 of the 26 patients (62%) passed the vigilance test at baseline and 15 of 26 (58%) passed it at follow-up. The difference in sleep latency between the two groups was statistically significant.

Correlation Tests

There were significant weak to moderate correlations between changes in ESS and changes in AHI; SF-36 domains SF, VT, and MCS; and sleep latency (Table III). In addition, there were significant correlations between changes in ESS, VT, and SF and sleep latency, respectively. Reversibly, there was a significant negative weak correlation between RE and sleep latency ($R = -0.33$, $P = 0.024$).

Sensitivity Analysis

The ITT analysis for all 71 randomized patients also showed significant differences within and between groups for ESS, SF-36, and vigilance test, respectively. T tests showed no differences in significance compared to the nonparametric results presented in Table II.

DISCUSSION

This RCT shows that treatment with modified UPPP significantly reduced self-reported symptoms of

daytime sleepiness and improved the quality of life, as well as of objectively measured vigilance, compared to no treatment in OSAS patients.

In our previous SKUP³ study, we found that AHI and other respiratory parameters were significantly reduced in the intervention group, compared to the controls.¹³ In the present study, we were also able to show that the improvements in daytime sleepiness, both self-reported and according to the vigilance test, as well as in the quality of life, had a similar pattern. These results strengthen the body of evidence on the effect of surgery that could be offered to selected patients. Significant but modest correlations were seen between changes in subjective and objective outcomes, also with nocturnal respiration.

In our RCT, the median ESS score was halved from 12 to 6 in the intervention group, and this result is identical to those from a 1-year follow-up of 158 OSAS patients in a study from our group.²¹ Furthermore, in our 15-year follow-up of another study of 50 OSAS patients, the median ESS score after UPPP was 6.²² These findings are also similar to those in other studies investigating the effects of UPPP; for example, the one by Yaremchuk et al.²³ and the multicenter study by Weaver et al.²⁴ The fact that this RCT (level 1 evidence) found similar outcomes suggests that the results from previous case series are reasonably accurate, because this RCT validates the results of these previous case series studies. Our results regarding the effect of UPPP are also similar to those in another RCT, which compared therapeutic CPAP with subtherapeutic CPAP in OSAS patients. Those results from ESS, SF-36 domains, and vigilance measured with MWT also showed significant differences between groups, in favor of CPAP.²⁵ However, another RCT showed that, although CPAP and MRD seem to improve ESS and the quality of life, no improvement in objective sleepiness measured with an MWT for CPAP or an MRD was seen compared to placebo.⁸ A meta-analysis including patients with severe OSAS showed that CPAP therapy improved the mean sleep latency by only 1 minute compared to placebo.⁹ Our vigilance test was not an MWT, only a modified Osler test, which showed a significant mean improvement of 7 minutes in sleep latency after UPPP.

Many studies show that OSAS has significant adverse effects on patients' quality of life, but also that CPAP treatment can improve it, especially the SF-36 scores RP, GH, VT, and SF.^{25–27} Compared to the general Swedish population, our patients had lower subscale scores on the SF-36, especially on RP, GH, VT, and SF; however, they increased to normal or less subnormal values for the present age group after UPPP.²⁸ Our finding that three SF-36 domains—GH, VT and SF—all showed highly significant differences between groups in favor of modified UPPP is important. According to a study by Stewart et al.,²⁹ 9-point differences in physical functioning or health perception are comparable to the effect of having back problems or myocardial infarction. The results in the present study should therefore be considered to be not only statistically significant but also clinically significant.

The polysomnographic results from our previous study showed that the mean AHI changed significantly in the 32 patients undergoing UPPP, with a delta mean (SD) of –32 (25), but nonsignificantly in the 33 patients in the expectancy group, with a delta mean (SD) of –6 (17).¹³ These delta AHI values were used in the correlation tests in the present study, which showed modest but statistically significant correlations. This was not demonstrated in another RCT of patients undergoing radio-frequency reduction of the palate and tongue base or sham surgery.¹⁰ However, their effect of treatment was lower than in the present study. Still, it cannot be excluded that the outcome from the questionnaires may be influenced by the placebo effect of surgery. However, the objective vigilance test and PSG are less sensitive to placebo, and these investigations showed the same pattern as in the questionnaires.

Strengths and Weaknesses

The strengths of the present study include the randomized controlled design, but also the investigation of the OSAS patients with in-laboratory PSG and the use of objective vigilance tests. Also, the PSG recordings were performed the night before the vigilance test and could assess sleep quality. In addition, our results from subjective and objective symptoms of daytime sleepiness and from PSG are concordant. Furthermore, our main results were verified by both parametric and nonparametric statistical methods.

There are several limitations in this study. Firstly, the power analysis was made based on calculations from our original study¹³ concerning improvement in nocturnal respiration and not on the secondary outcomes in this study. However, the original study showed the same halving of ESS as in this RCT, which strengthens the results. Furthermore, there has been a demand for the subjective outcomes in SKUP.^{3,30} A second limitation is that the surgical group was only compared with expectancy. It would have been useful to compare with placebo surgery and/or nonsurgical treatment also. However, it would be unethical to perform placebo surgery under general anesthesia in patients with moderate-to-severe OSAS. Furthermore, our patients were already noncom-

pliant with nonsurgical treatments. A third limitation is the missing data and dropouts for the vigilance test in both groups, and also the fact that six patients were excluded after randomization. On the other hand, these patients were allocated to separate groups, and sensitivity analyses were performed that did not affect the results. A fourth weakness is that the MWT test, which is the gold standard, was not used; instead, the modified OSLER was used. However, MWT tests are resource- and time-demanding and our patients did not receive any financial compensation, which explains a high dropout rate and why we were only able to perform the vigilance test once per day. Nevertheless, another study showed that the OSLER test four times daily produces reproducible and stable results over time in OSAS patients.³¹ To sum up, the results from the vigilance tests have to be interpreted with caution, although we cannot ignore the fact that our results are consistent.

Generalizability

Many patients with OSAS had serious comorbid illnesses and were excluded from the present study, as well as those with BMI > 36 and Friedman stage III. Compared to the general adult OSAS population in Sweden, and also to OSAS patients having CPAP treatment, our study population was 10 to 15 years younger and had a lower BMI.^{32,33} Additionally, there were few women in the study. Consequently, these results do not address all patients seen in general clinical practice.

CONCLUSION

This RCT shows that modified UPPP significantly improved daytime sleepiness and quality of life, compared to controls, in selected OSAS patients. Several significant but modest correlations were seen between changes in daytime sleepiness, quality of life, and nocturnal respiration, respectively. These results strengthen the body of evidence for modified UPPP, which could be offered to selected OSAS patients.

Acknowledgment

The study was first rejected by the Swedish Regional Ethics Committee (2007/449-31/3). After an appeal, it was approved by the Central Ethics Committee (Ö21-2007).

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