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Outcome Prediction Model for Radiofrequency Uvulopalatopharyngoplasty with Tonsillectomy in Adult Obstructive Sleep Apnea: Retrospective Cohort Study

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Keywords
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Abstract
Introduction: Knowing an individualized outcome prediction is essential when counseling patients before surgery. We aim to identify predictors and build a model for the outcome of radiofrequency uvulopalatopharyngoplasty with tonsillectomy (rfUPPP + TE). ***Methods:*** All adult patients undergoing rfUPPP + TE for sleep-disordered breathing from 2015 to 2022 in our institution were included. Preoperative evaluations included detailed upper airway examinations and standardized questionnaires. Postoperative outcomes were measured through home sleep apnea testing and repeated questionnaires 3 months post-surgery. The primary endpoint was the postoperative apnea-hypopnea index (AHI) and the AHI responders using the Sher criteria. ***Results:*** We analyzed 247 patients with a mean age of 46 ± 11 years, predominantly male (88.7%), and a mean BMI of 29.0 kg/m^2. The mean AHI was reduced from 26.4 ± 18.6/h preoperatively to 16.2 ± 14.6/h postoperatively. Daytime sleepiness improved from 8.9 ± 48 to 4.0 ± 3.1 and snoring from 7.9 ± 2.1 to 3.3 ± 2.2. Multivariate analysis indicated that higher tonsil grades, preoperative AHI, and snoring levels were associated with a greater reduction in AHI. Age and body weight were negative predictors for AHI reduction. For AHI responders, according to Sher, tonsil grade was the only predictor in a multivariate analysis. The ROC curve of this simple model, with a corrected AUC of 0.625, compared favorably against two established models. ***Conclusion:*** Our study highlights that tonsil grade, preoperative AHI, snoring, and, to a smaller extent, age and weight are key determinants of AHI reduction, emphasizing the importance of preoperative evaluation. Despite the multifactorial nature of obstructive sleep apnea, preoperative evaluation can predict the outcome of rfUPPP + TE and guide surgical planning.

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Plain Language Summary

Soft palate surgery is the most frequently performed procedure for sleep-disordered breathing. Predicting individualized outcomes is essential in counseling patients on their expected results after surgery. In this retrospective analysis, we examined preoperatively available predictors, such as head and neck examination, sleep study, and questionnaires, in a cohort of 247 patients. The apnea-hypopnea index, a measure of sleep-disordered breathing severity, showed a greater reduction in patients with large tonsils, heavy self-reported snoring, and a higher preoperative apnea-hypopnea index. Higher age and body weight negatively impacted results after soft palate surgery. The study highlights the importance of preoperative evaluation, especially regarding tonsil grade and upper airway anatomy. Despite the multifactorial nature of obstructive sleep apnea, surgical outcomes can be predicted with careful assessment.

Introduction

Obstructive sleep apnea (OSA) is a common condition characterized by the recurrent narrowing or collapse of the upper airway during sleep, resulting in inspiratory airflow limitation or complete obstruction. It affects between 6 and 17% of the general adult population [1] and is associated with various adverse health outcomes, including cardiovascular disease and increased mortality [2]. While continuous positive airway pressure therapy is the primary treatment for OSA and is highly effective, 46–83% of patients do not adhere to this treatment option despite technological advancements [3].

Uvulopalatopharyngoplasty, with or without tonsillectomy, is the most commonly performed surgical procedure for treating OSA [4, 5]. Numerous studies and meta-analyses [4–8] have shown favorable treatment outcomes in reducing respiratory events and improving self-reported symptoms like daytime sleepiness and snoring. Other articles show less favorable outcomes, especially in the long term, and the effect on late complications of OSA is unclear. Therefore, the effectiveness of this palatal surgery in managing OSA is often questioned [5, 7, 9, 10] due to limited supporting evidence and possible morbidity of the surgical treatment. Additionally, comparing outcomes across studies is challenging due to various surgical techniques and the lack of precise characterization of patient cohorts, particularly regarding upper airway anatomy. Surgical treatment is associated with adverse outcomes, such as velopharyngeal insufficiency, swallowing difficulties, and taste disturbances. The risk of complications further increases the need for appropriate patient counseling [11].

The preoperative assessment of different clinical parameters is vital in determining the appropriate treatment for each patient. Estimating the expected outcome is crucial when counseling patients on different treatment options. There has yet to be a consensus among researchers regarding the predictors of success for uvulopalatopharyngoplasty with or without tonsillectomy. Several publications consider tonsil grade an essential factor [12–15]. Other indicators for outcome might be, for example, tongue position, body mass index, age, time below 90% oxygen saturation, preoperative apnea-hypopnea index (AHI), and vertical distance between mandible and hyoid [15–18]. Researchers such as Stuck et al. [5], Lai et al. [12], and Jara and Weaver [13] emphasize the importance of further research to identify additional outcome predictors. This knowledge is essential for improving treatment outcomes through better patient selection and preoperative counseling. This study aims to identify predictors of success for radiofrequency uvulopalatopharyngoplasty with tonsillectomy (rfUPPP + TE) and assign a numerical weight to each factor to estimate the outcomes regarding obstructive events.

Methods

Patients and Data

To find predictors of rfUPPP + TE, we conducted a retrospective analysis of all adult patients who underwent rfUPPP + TE for OSA at our institution from 2015 to 2022. Excluded were all patients under 18 years old, patients with central sleep apnea or relevant missing data, such as a follow-up sleep study, or those who declined the use of their data. Patients undergoing concomitant surgeries, except nasal surgery, were also excluded. This study has been approved by the local Ethics Committee (EKNZ 2021–02324), and the article follows the STROBE guidelines (online suppl. Document 1; for all online suppl. material, see https://doi.org/10.1159/000540222) [19]. All patients underwent a preoperative head and neck examination, which was reported on standardized forms and included basic anthropomorphic metrics and a detailed description of the upper airway anatomy with a specific focus on Friedman tongue position [20], pharyngeal webbing, uvula size, tonsil grade according to Brodsky [21, 22], and septal deviation. In the case of asymmetrical palatal tonsils, the higher-grade side was chosen. Standardized questionnaires such as the Epworth Sleepiness Scale (ESS) [23], Insomnia Severity Index (ISI) [24], and a visual analog scale from 0 to 10 for snoring intensity were used to assess patient-reported symptoms. Home sleep apnea testing was performed preoperatively and 3 months after the surgery to determine the outcome.

Surgery

All patients in the study underwent rfUPPP + TE in general anesthesia. If tonsils were present, an extracapsular cold-steel tonsillectomy was performed in all patients, irrespective of

Table 1. Patient characteristics are given as mean and standard deviation, median and interquartile range, or number and percentage

Parameter	Study cohort (n = 247)
Gender (female)	28 (11.3)
Age, years	46.0 (11.0)
Height, cm	176.9 (8.4)
Weight, kg	90.7 (14.9)
Body mass index, kg/m^2	29.0 (4.3)
Neck circumference, cm	41.7 (3.7)
AHI	
Preoperative	26.4 (18.6)
Postoperative	16.2 (14.6)
Reduction absolute	10.2 (16.7)
Reduction relative, %	45 (−7, 66)
Responder	103 (41.7)
ESS	
Preoperative	8.9 (4.8)
Postoperative	4.0 (3.1)
Reduction absolute	5.0 (4.6)
Reduction relative, %	60 (33, 81)
Responder	76 (60.8)
Snoring index (VAS 0–10)	
Preoperative	7.9 (2.1)
Postoperative	3.3 (2.2)
Reduction absolute	4.9 (2.6)
Reduction relative, %	67 (51, 80)
Responder	59 (56.7)

According to the Sher criteria, AHI responders were defined as a reduction ≥50% from baseline and a postoperative value ≤20/h. Analogously, responders on the ESS were defined as a reduction ≥50% from baseline and a postoperative value ≤10. For the visual analog scale, a reduction ≥50% from baseline and a postoperative value ≤3 was considered a response to treatment.

tonsil grade. During the tonsillectomy, the palatoglossal arch was conservatively resected for 2–3 mm. After the tonsillectomy, the palatopharyngeal arch was incised to release the soft palate. A radiofrequency UPPP was performed with a bipolar ablation probe with four to five radiofrequency applications per side. The radiofrequency was applied until the automated stop or tissue effect was observed.

Statistical Analysis

The primary endpoint was AHI, building upon previous analyses [15, 25]. The outcomes were assessed as postoperative AHI values and as AHI responders according to the Sher criteria [26]. These define responders by a postoperative AHI ≤20/h and a reduction ≥50% of the preoperative value.

Univariate Model Building

We followed the steps outlined by Steyerberg and Vergouwe [27] and the TRIPOD guidelines for model building [28]. We modeled the AHI reduction using linear regressions for each biologically plausible variable. Logistic models were fitted and evaluated separately for each possible predictor to assess responders.

Multivariate Model Building

For multivariate models, we multiply imputed missing values [29] with predictive mean matching for numerical data, logistic regression for binary data, and polytomous regression for unordered categorical data for 50 iterations. All parameters were selected using stepwise regression with backward elimination based on the stacked imputed data with pooling according to Rubin's rule. The multivariate logistic model was validated with bootstrapping to subtract model optimism and estimate the corrected performance. Statistical analysis was conducted using R version 4.3.1 (R Foundation for Statistical Computing, Vienna, Austria) with the consultation of the Clinical Trial Unit Bern. Descriptive statistics are given as mean and standard deviation or number and percentage.

Results

A total of 380 adult patients were assessed for inclusion. Fifty patients were excluded due to missing preoperative examinations, including assessments of tonsil grade, and 82 patients were lost to follow-up. One additional patient was excluded for undergoing concomitant tongue base surgery. A total of 247 patients met the inclusion criteria and were analyzed (online suppl. Fig. 1). Patient characteristics are given in Table 1. Tonsil size, according to Brodsky, was 0 in 7 (3%), 1 in 63 (26%), 2 in 123 (49%), 3 in 47 (19%), and 4 in 7 (3%) of patients [22]. The follow-up duration was 102 days (interquartile range 91–138). No significant changes to the BMI were found within the follow-up duration (29 ± 4.3 vs. 28.6 ± 4.2, p = 0.37). The mean AHI was reduced from 26.4 ± 18.6 to 16.2 ± 14.6 (p < 0.01). Based on the Sher criteria, 41.7% of the cohort (n = 103) was classified as responders. A similar significant reduction was found for daytime sleepiness on the ESS (p < 0.01) and snoring (p < 0.01, Table 1). A detailed comparison of the whole cohort of pre- and postoperative sleep studies and patient-reported outcomes is given in online supplemental Table 1. As a sensitivity analysis, we additionally compared patients with (n = 101) and without (n = 146) concomitant nasal surgery and found no differences between the groups (online suppl. Table 2).

Predictors for AHI Reduction

While the whole cohort showed a relevant reduction in AHI, the aim was to identify predictors for the reduction on an individual level. Therefore, the postoperative AHI

Table 2. Factors influencing the AHI reduction are modeled using univariate linear regressions for each parameter, and the estimated effect with a 95% CI is given

	Univariate analysis			Multivariate analysis		
	effect	95% CI	*p* value	effect	95% CI	*p* value
Age, years	0.03	−0.16–0.22	0.77	−0.16	−0.3–−0.01	0.03
Gender (female)	5.45	−1.13–12.04	0.1			
Neck circumference, cm	0.13	−0.46–0.72	0.66			
Height, cm	−0.4	−0.65–−0.14	<0.01			
Weight, kg	−0.12	−0.26–0.03	0.11	−0.18	−0.29–−0.07	<0.01
BMI, kg/m^2	0.11	−0.4–0.62	0.67			
ASA classification	2.89	−3.76–9.53	0.39			
Tonsil grade	5.64	3.17–8.1	<0.01	2.94	1.06–4.82	<0.01
Uvula grade	1.67	−3.94–7.28	0.56			
Webbing	0.02	−2.97–3.02	0.99			
Tongue grade	2.59	0–5.18	0.05			
Epiglottis configuration	6.5	0.06–12.94	0.05			
Snoring (VAS)	1.75	0.62–2.88	<0.01	1.03	0.17–1.88	0.02
ESS	0.65	0.19–1.1	0.01			
ISI	−0.18	−1.09–0.73	0.69			
Preoperative Sleep Study						
AHI, events/hour	0.59	0.51–0.68	<0.01	0.59	0.5–0.67	<0.01
Apnea index, events/hour	0.79	0.65–0.94	<0.01			
AHI central, events/hour	0.25	−0.6–1.1	0.56			
ODI, events/hour	0.39	0.28–0.51	<0.01			
AHI supine, events/hour	0.29	0.21–0.38	<0.01			
ODI supine, events/hour	0.25	0.15–0.35	<0.01			
Cartwright Index	−3.02	−4.81–−1.24	<0.01			
Mean oxygen saturation, %	−1.32	−2.56–−0.08	0.04			
Mean oxygen desaturation, %	−1.41	−2.23–−0.59	<0.01			
Time below 90% oxygen saturation, %	0.23	0.05–0.41	0.01			
Mean heart rate, beats per minute	0.19	−0.12–0.51	0.23			

A multivariate model was fitted for all parameters with backward stepwise parameter selection, for which the results are given analogously to the univariate model. AHI, apnea-hypopnea index, ODI, oxygen desaturation index, Cartwright Index, ratio of supine to non-supine apnea-hypopnea index.

was modeled using the preoperative AHI and all biologically plausible preoperative predictors, and the results are displayed in Table 2. A multivariate model was fitted to find relevant combinations of predictors, illustrated in Figure 1 and Table 2. Three variables were associated with larger AHI reduction: higher tonsil grade, higher preoperative AHI, and more patient-reported snoring. A negative correlation with AHI reduction was found for increased age and body weight. While several variables, such as gender, neck circumference, height, BMI, ASA (American Society of Anesthesiologists) score, and others, showed significant relationships in the univariate model, they were not retained in the multivariate model, suggesting that their individual effects are overshadowed when other variables are accounted for.

Predictors for AHI Responders

Table 3 shows the univariate analysis assessing potential determinants of postoperative AHI responders as defined by the Sher criteria. Tonsil grade was the strongest predictor of a positive outcome, showing an increase in odds ratio of 1.9 (95% CI 1.35–2.71, $p < 0.01$) per tonsil grade. The responder rate by tonsil grade 0–4 increased from 14% (1/7), 29% (18/63), 42% (51/123), and 57% (2/47) to 86% (6/7), respectively. Some evidence was found that mean heart rate increased responder odds, whereas age and uvula grade reduced the odds of being a responder. Other explored variables did not yield statistical significance regarding postoperative AHI response, notably BMI, preoperative AHI, tongue position, and neck circumference. In a subsequent multivariate analysis, only the tonsil grade emerged as a significant predictor of postoperative AHI response after 3 months.

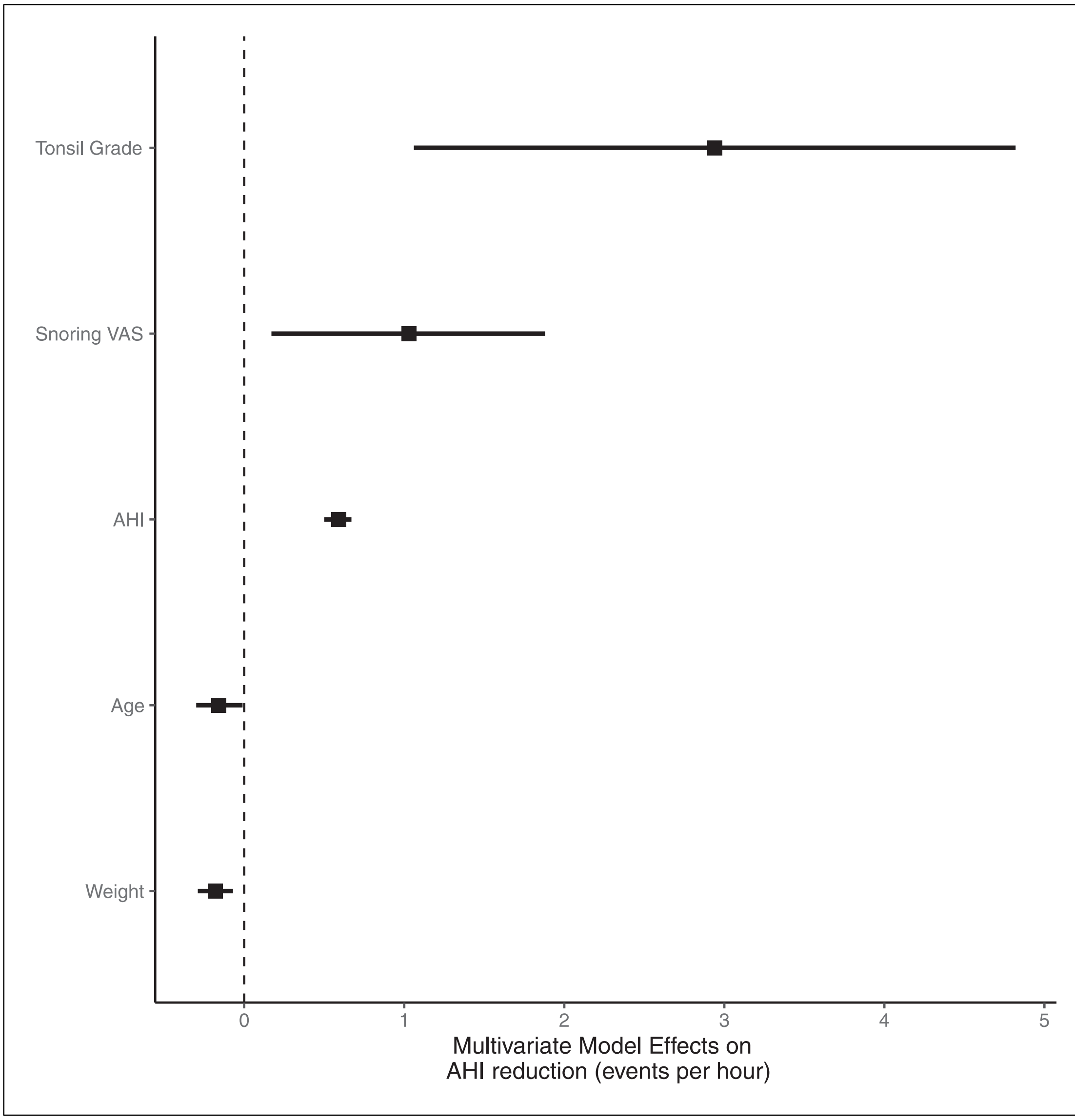

Fig. 1. Effects of different factors on AHI reduction are visualized in a forest plot with squares indicating the estimate and bars the 95% confidence intervals for a multivariate model.

Prediction models for AHI responders are provided as receiver operating characteristic curves in Figure 2. The figure shows three models: a simple model based on tonsil grade (solid line), a model proposed by Choi et al. [25] based on age, tongue grade, and tonsil grade (dotted line), and a model put forth by Friedman et al. [15] based on tongue and tonsil grade (short dashed line). The diagonal line of no discrimination is given as a long-dashed line. The model tonsil grade model yields a corrected AUC of 0.625. The larger the area under the curve of a model, the better it is at discriminating between responders and non-responders.

Discussion

Predictors in Our Study

Over the whole study population, we observed an improvement in respiratory events after rfUPPP + TE, showing the effectiveness of palatal surgery in treating OSA. We observed no changes in BMI in our cohort after surgery. Several predictors emerged for an individualized preoperative assessment of outcome. The multivariate model offers valuable insights into factors influencing AHI reduction, with tonsil grade, preoperative OSA severity, and patient-reported snoring being positive predictors. Less favorable

Table 3. Factors influencing the apnea-hypopnea responders are modeled using univariate logistic regressions, and the estimated effect with a 95% CI is given

	Univariate analysis			Multivariate analysis		
	effect	95% CI	*p* value	effect	95% CI	*p* value
Age, years	0.98	0.95–1	**0.05**			
Gender (female)	1.22	0.54–2.73	0.62			
Neck circumference, cm	0.99	0.92–1.08	0.88			
Height, cm	0.99	0.95–1.02	0.39			
Weight, kg	1	0.98–1.01	0.62			
BMI, kg/m^2	1	0.94–1.07	0.98			
ASA classification	1.29	0.53–3.27	0.58			
Tonsil grade	1.9	1.35–2.71	<**0.01**	1.9	0.135–2.71	<**0.01**
Uvula grade	0.48	0.24–0.94	**0.03**			
Webbing	1.03	0.71–1.49	0.87			
Tongue grade	1.01	0.73–1.4	0.95			
Epiglottis configuration	1.7	0.74–3.92	0.21			
Snoring (VAS)	1.1	0.95–1.29	0.2			
ESS	1.03	0.97–1.09	0.31			
ISI	0.91	0.81–1.02	0.11			
Preoperative Sleep Study						
AHI, events/hour	0.02	0–0.03	0.03			
Apnea index, events/hour	0.99	0.96–1.02	0.58			
AHI central, events/hour	0.99	0.94–1.03	0.62			
ODI, events/hour	0.99	0.89–1.1	0.86			
AHI supine, events/hour	0.01	−0.01–0.02	0.23			
ODI supine, events/hour	1.01	0.99–1.02	0.35			
Cartwright Index	0.9	0.66–1.15	0.44			
Mean oxygen saturation, %	1.04	0.88–1.23	0.66			
Mean oxygen desaturation, %	1	0.88–1.15	0.96			
Time below 90% oxygen saturation, %	1	0.97–1.02	0.83			
Mean heart rate, beats per minute	1.05	1–1.09	**0.03**			

No improvement was found by the multivariate model beyond the univariate model with tonsil grade as a predictor. AHI, apnea-hypopnea index, ODI, oxygen desaturation index, Cartwright Index, ratio of supine to non-supine apnea-hypopnea index.

outcomes were observed in older and heavier patients, suggesting that older and overweight individuals might have intrinsic physiological or anatomical changes that make them less receptive to the benefits of the surgery. Since the AHI reduction was about half of the preoperative AHI severity, patients with severe OSA are at greater risk for persistent OSA after surgery and will likely need additional treatment. Other factors like gender, neck circumference, and BMI showed relevant associations in the univariate but not in the multivariate model. These multiple factors point to the complex interplay of these variables. While these factors are relevant, their influence is moderated or even negated in the presence of stronger predictors. To predict AHI response based on the Sher criteria, tonsil grade showed the most robust association with the outcome. This simple model outperformed more complex models for AHI responders found in the literature.

However, it is imperative to note the large variability in response as reflected in the standard deviations. Additional variability might stem from the intramural part of the tonsils, which cannot be assessed on clinical examination but contributes to the volume change of a tonsillectomy. These factors underscore the necessity for personalized approaches, considering the variability in responses across different predictive factors.

Predictors in the Literature

Several studies in the literature investigate predictors for uvulopalatopharyngoplasty with or without tonsillectomy outcomes. To enhance patient selection, Friedman et al. [15] introduced an anatomical staging system that considers tongue position, palatal tonsil size, and BMI and found that this staging system can predict surgical success. Subsequently, other researchers

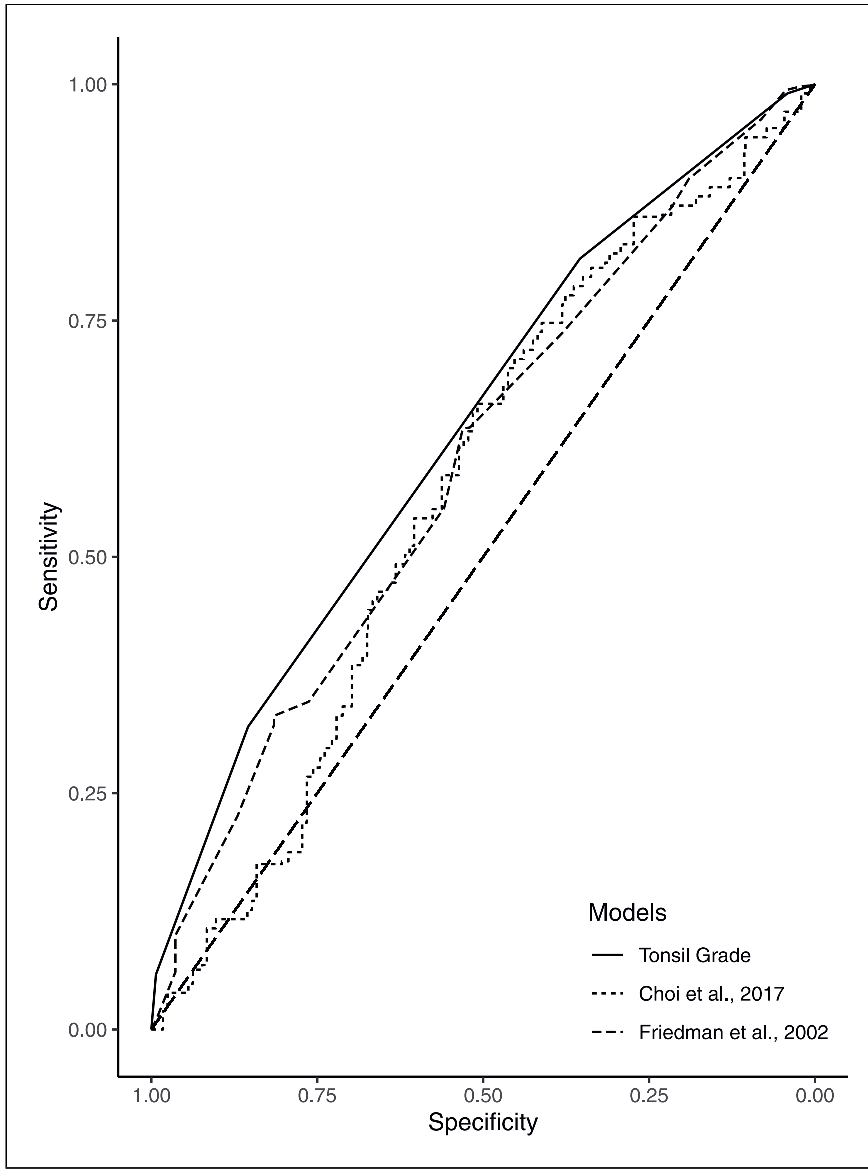

Fig. 2. Receiver operating characteristic curves comparing three prediction models for AHI responders: a simple model based on tonsil grade (solid line), a model proposed by Choi et al [25]. based on age, tongue grade, and tonsil grade (dotted line), and a model put forth by Friedman et al. [15] based on tongue and tonsil grade (short dashed line). The diagonal line of no discrimination is given as a long-dashed line. The model tonsil grade model yields a corrected AUC of 0.625. The larger the area under the curve of a model, the better it is at discriminating between responders and non-responders.

published studies investigating predictive factors and models with variable results.

Tonsil grade was a critical factor in determining the response to UPPP ± TE in multiple studies [16–18, 25]. A meta-analysis by Camacho et al. [30] demonstrated that TE alone is effective, especially for young patients with large tonsils. A large randomized trial found no benefit of an additional UPPP to tonsillectomy, raising further doubt about whether addressing the palate is necessary [8]. In our cohort, a simple model based on tonsil grade alone outperformed more complex models in predicting AHI responders. Based on these studies and our results, we believe that removing palatine tonsils is a critical factor in the success of palatal surgery. Since all patients in our study underwent combined tonsillectomy and palatal surgery, we cannot differentiate between the relative importance of each step on the outcome.

Several studies reported higher tongue positions as a negative predictor [15, 25, 31]. Age [16, 17, 25] showed a neutral or negative effect on outcomes. Interestingly, despite many studies examining the role of gender, this did not impact the outcome significantly. Similarly, BMI [16, 17] did not consistently predict outcomes in the studies, again underscoring the multifactorial nature of the disease and its response to treatment. Multiple studies found that OSA severity is not a predictive factor of outcomes in palatal surgery [17, 31]. However, a study by Zhang et al. [18] and our results suggest that the duration of oxygen saturation below 90% may be a negative predictor.

Additional investigations for patient selection, like the Müller maneuver or drug-induced sleep endoscopy, have been explored, revealing that multilevel collapse [32] and complete concentric collapse of the velum [33] are unfavorable. Some smaller studies have also linked specific cephalometric measurements, like the distance between the mandibula and hyoid [18], to positive palatal surgery outcomes.

UPPP surgery is also associated with a considerable rate of sequelae. Aggressive resection techniques have been modified to reduce morbidity while maintaining effectiveness. However, the adverse effects are still substantial, with 32% foreign body sensation, 17% difficulty swallowing, 8% taste disturbances, and 8% velopharyngeal insufficiency [11]. This further highlights the importance of preoperative counseling in appropriately setting patients' expectations. Our study aims to aid the informed decision by giving predictors for successful outcomes.

Limitations

The retrospective design leads to several limitations of our study. The cohort consisted mainly of middle-aged, moderately overweight males, which may limit the generalizability of our findings to other demographic groups. The non-randomized design leads to a possible self-selection of patients who elect to undergo surgery, which limits generalizability even though the same operating technique was used in all patients. Plentiful surgical techniques exist to address the soft palate. Conservative resective modifications and barbed suture UPPP are widely adopted. There is evidence that radiofrequency techniques are inferior to conventional UPPP [34], while other studies show equal or superior effectiveness [35]. We performed TE + rfUPPP, limiting the generalizability of our results to other surgical methods.

Further, the considerable variability in sleep apnea testing illustrates the difficulty of precisely quantifying sleep medicine outcomes due to factors such as night-to-night variability. While subjects were advised to follow their usual bedtime routines, confounding factors such as alcohol consumption, sleep medication use, nicotine intake, and caffeine consumption were not controlled during the sleep measurements, which could affect night-to-night variability [36]. Additionally, a considerable proportion of patients were lost to follow-up. This could introduce a negative bias as patients who experienced significant improvements may not have returned for the follow-up appointments. The follow-up duration was over 3 months, and long-term results are beyond the scope of this article.

Strengths and Future Research

The strengths of this study are the large cohort and the standardized surgical procedure, which was performed with the same technique in all patients. Tonsillectomy was performed irrespective of tonsil grade, resulting in a more homogeneous population than many other studies that do not consistently perform tonsillectomy. Further strengths are the detailed standardized upper airway anatomy examination and the systematic follow-up with home sleep apnea testing of patients undergoing rfUPPP + TE. Future research should prospectively confirm each predictor individually in an independent cohort.

Conclusion

Considering our research and the literature, it is evident that while numerous factors influence postoperative AHI outcomes, the tonsil grade consistently emerges as a paramount determinant. We further identified patient-reported snoring and preoperative AHI as a positive predictor for AHI reduction. Age and body weight are associated with a more minor AHI reduction. These findings underscore the importance of meticulous preoperative evaluation of tonsil grade and upper airway anatomy to enhance surgical outcomes. The importance of tonsil size indicates the importance of tonsillectomy on the postoperative outcome. Although the multifactorial nature of sleep apnea requires a holistic approach to patient assessment, our study reiterates the potential efficacy of surgical intervention, especially when tailored to individual patient profiles.

Statement of Ethics

This study protocol was reviewed and approved by Ethikkommission Nordwest- und Zentralschweiz, Approval No. 2021–02324. The need for informed consent was waived by the Ethikkommission Nordwest- und Zentralschweiz, Basel, Switzerland.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

S.T., K.T., M.C., and U.B. had the original idea and designed the study. S.T. and K.A. collected data. S.T. did the analysis. K.A. wrote the first draft. S.T., K.A., M.C., U.B., and K.T. revised the manuscript and wrote sections of the paper. The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

Data Availability Statement

The data that support the findings of this study are not publicly available due to their containing information that could compromise the privacy of research participants but are available from the corresponding author upon reasonable request.

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