

Changes in the laryngopharyngeal reflux After UPPP for OSA: A Clinical Observational Study

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Abstract

Objectives. The study used re-flux symptom index (RSI) and Reflux Finding Score (RFS) questionnaire to estimate laryngopharyngeal reflux (LPR) change after uvulopalatopharyngoplasty (UPPP) for obstructive sleep apnea (OSA). **Design.** An observational, retrospective study. **Setting.** University, tertiary level hospital. **Participants.** 91 subjects were recruited and divided into three groups: control group (n=27), OSA mild to moderate group (n=29) and OSA severe group (n=35) according to polysomnography. All subjects completed preoperative RSI and RFS under electronic laryngoscope. 34 OSA patients with UPPP surgery completed postoperative polysomnography, again after 6-month follow-up. **Main outcome measures.** Polysomnography, RSI and RFS questionnaire. **Results.** RSI and RFS in OSA patients were higher than non-OSA patients. Severe OSA patients also had higher RSI and RFS than mild to moderate OSA. LPR symptoms had positive and L-SpO₂ had negative correlation with AHI and CT90. The mean RSI and RFS before UPPP surgery were 15.88 ± 4.85 and 13.18 ± 4.80 ; these number decreased to 9.53 ± 4.16 and 8.65 ± 4.87 after surgery ($P < 0.05$). In 25 successful-surgery patients, RSI and RFS scores and individual variables of RSI were downward after surgery. **Conclusion.** LPR symptoms are common among OSA patients, the coexistence of OSA and LPR cannot be ignored. Successful UPPP surgery as a treatment for OSA patients, potentially reduces laryngeal reflux symptoms and improves laryngoscope signs by alleviating sleep respiratory disorder.

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these number decreased to 9.53 ± 4.16 and 8.65 ± 4.87 after surgery ($P < 0.05$). In 25 successful-surgery patients, RSI and RFS scores and individual variables of RSI were downward after surgery.

Conclusion. LPR symptoms are common among OSA patients, the coexistence of OSA and LPR cannot be ignored. Successful UPPP surgery as a treatment for OSA patients, potentially reduces laryngeal reflux symptoms and improves laryngoscope signs by alleviating sleep respiratory disorder.

Key points:

- (1) The presence of laryngopharyngeal reflux (LPR) in obstructive sleep apnea (OSA) is very frequent.
- (2) Chronic upper airway inflammation is the result of many conditions, among which OSA and LPR are two reasons that cannot be ignored.
- (3) Uvulopalatopharyngoplasty is a useful treatment of OSA. It is still controversial that whether it improves LPR.
- (4) Reflux Symptom Index (RSI) and Reflux Finding Score (RFS) are more commonly used and useful in diagnosing LPR and quantifying the severity of LPR symptoms.
- (5) The present study revealed the coexistence of OSA and LPR is common. Successful UPPP surgery as a treatment for OSA patients can improve LPR.

Introduction

Obstructive sleep apnea (OSA) is a growing public health problem. About 2%–4% of middle-aged adults have OSA.¹ Middle-aged people suffer from sleep-disordered breathing with a high percentage of 83.² Repetitive collapse and reopening of the upper airway during sleep are two major characteristics of OSA, resulting in intermittent hypoxia (IH) and sleep fragmentation. IH correlates with systemic/airway inflammation and oxidative stress.³ The treatments of OSA include continuous positive airway pressure (CPAP) or surgery. Uvulopalatopharyngoplasty (UPPP) was first suggested by Fujita et al.⁴ If the obstruction site of OSA is located at the palatopharyngeal level, UPPP usually achieve an ideal outcome by eliminating redundant mucosal folds, hypertrophic tonsils and the excessively thickened and elongated soft palate.

Laryngeal mucosal inflammation and damage of laryngopharyngeal reflux (LPR) occurs when gastric acid flow back to the laryngopharynx, and is a common disease in otolaryngology⁵. Although 24-hour pH monitoring is the gold standard for diagnosing the presence of LPR, Reflux Symptom Index (RSI) and Reflux Finding Score (RFS) are more commonly used and useful in diagnosing LPR and quantifying the severity of LPR symptoms.^{5, 6}

Chronic upper airway inflammation is the result of many conditions, among which OSA and LPR are two reasons that cannot be ignored. The presence of LPR in OSA is very frequent: 20%–67% OSA patients coexist with LPR.⁷ In recent years, many studies have explored the association between OSA and LPR, but the correlation between them is still controversial. Some studies demonstrated that CPAP treatment significantly improved reflux symptoms in OSA patients.⁸ But few studies have been done about the effect of surgery treatment for OSA on reflux disease. The aim of this study was to evaluate the change in laryngeal reflux symptoms and signs after UPPP for OSA, based on patients' responses to the RSI and RFS questionnaire.

Methods

Procedure and participants

Adult participants were recruited between January 2016 to January 2017. Only male included to minimize gender confounder variance, particularly considering that OSA is more common in males. Of all 128 participants, 17 (13%) declined to participate and 20 (16%) were found to be ineligible (female, with CPAP or anti-reflux treatment) leaving 91 (71%) for the present study. The study included cases with newly diagnosed OSA (confirmed by PSG). Controls were selected without OSA (confirmed by PSG). Participants from OSA

were eligible for LPR if both RSI score >13 and RFS score >7. The study design has been described in **Figure 1**.

Approval by the Human Research Ethics Committee

The study was approved by the ethics committee of <Blinded for review>, and all participants gave written informed consent.

Assessment of OSA

All individuals with clinical suspicion underwent overnight polysomnography (PSG). They were asked if they had a specific set of symptoms indicating OSA: witnessed snoring; observed to have apneas; non-restful sleep; daytime sleepiness. Diagnosis of OSA was defined by standard criteria.⁹

The Epworth Sleepiness Scale (ESS) questionnaire, which is widely used for assessing daytime sleepiness, was also finished by the patients on the same visit. Demographic data including gender, age, BMI, AHI, minimum oxygen saturation and oxygen saturation <90% were also obtained.

Assessment of LPR

LPR was defined as both RSI score >13 and RFS score >7.

During the initial visit, all the patients filled out RSI questionnaire to evaluate the severity of LPR-related symptoms, which containing 9-item and 0-5 score: the higher the score, the more serious the problem.

The RFS⁵ is a useful tool to assess and follow-up LPR patients, which contains 8 items for judging severity of laryngoscopic findings. The laryngoscopy were reviewed by an otolaryngologist blinded to patient RSI and PSG information. They rated 8 items from 0 (normal) to 4 (severe problem) according to laryngoscopic findings.

UPPP surgery

UPPP significantly relieve airway obstruction at palate level. The individuals who underwent UPPP surgery must meet the following inclusion criteria: (1)Suffered from OSA and without serious psychiatric, cardiopulmonary, or neurological disease; (2)overnight PSG indicating AHI [?] 5 and BMI;40kg/m²; (3) Thickened and elongated soft palate and without severe nasal congestion; (4) Friedman stage I or II; (5) Unsuccessful CPAP treatment or reject CPAP treatment. Individuals and (6) No history of surgical therapy for OSA or anti-reflux treatment before or after surgery. Surgeon (LSS) performed UPPP surgery all the time. The successful UPPP was defined as post-operative AHI is reduced by at least 50% and ;20/h.¹⁰

Follow-up

All individuals were re-evaluated in our sleep disorder center during follow-up visits after 6 months of UPPP surgery. Polysomnography, RSI questionnaire and ESS questionnaire were obtained from each patient. The investigator (LSS) was not involved in the care of any of the patients.

Statistical analysis

Chi-square or Mann-Whitney U was used in different type of variables, and regression analysis was performed to show effect of different variables on outcome data by statistical analysis system (version 24.0; SPSS Inc., Chicago, IL). Significant was defined as *p*value;0.05.

Results

Population characteristics

The initial characteristics of 64 OSA cases (AHI[?]5 events/h) and 27 controls are presented in **Table 1**. No significant changes were found between the OSA and control group in sex (all male) age and BMI. Individuals with OSA had more AHI and lower nighttime SpO₂ (CT90 and L-SpO₂) in PSG. As anticipated, RSI and RFS score of OSA patients were higher than the controls.

Relationship between OSA and LPR

In 64 OSA patients, AHI and CT90 have a positive correlation with RSI and RFS, which means the degree of OSA is associated with the severity of LPR (**Figure 2A, 2B**). L-SpO₂ negatively correlate with RSI and RFS (**Figure 2C**). In addition, RSI and RFS scores of severe OSA were higher than mild to moderate OSA patients, so as the prevalence of LPR (**Table 2**).

Surgical outcome

Table 3 showed post-operative AHI, nighttime SpO₂ (CT90 and L-SpO₂) and ESS decreased, among 34 OSA patients after UPPP surgery. What's more, both RSI and RFS decreased after treatment for OSA.

The surgical success rate was 73.53% (25/34). In 25 successful-surgery patients, RSI and RFS were downward after surgery, and the prevalence of LPR changed just after successful UPPP surgery (**Table 4**).

Figure 3 showed except for hoarseness ($P=0.054$), all individual variables of postoperative RSI significantly improved ($P<0.05$). When we compared the pre- and post-surgery changes in individual variables of RSI to patients in successful or unsuccessful surgeries group, all variables of successful-postoperative RSI improved ($P<0.05$) except hoarseness and postnasal drip ($P=0.117$ and $P=0.052$, respectively), but all variables in the RSI showed no significant changes after unsuccessful surgery.

Discussion

This study investigated the effect of UPPP surgery for OSA on laryngeal reflux symptoms based on patient responses to the RSI and RFS questionnaire. We found (1) a close correlation between OSA and LPR: LPR are more prevalent in OSA patients than the general population and the degree of AHI and CT90 were positively and L-SpO₂ negatively related with LPR symptoms. (2) UPPP surgery, especially successful surgery significantly lowered not only in terms of the mean RSI and mean RFS scores but also individual variables of RSI.

The coexistence of OSA with LPR has been reported to have a prevalence of 20%–67%.^{11, 12} Although previous studies were unable to demonstrate a direct relationship between OSA and LPR, they did suggest a possible causative relationship between them.¹³ Our study indicated OSA patients had higher RSI and RFS than non-OSA patients. RSI and RFS of severe OSA patients were higher than mild to moderate OSA. The degree of AHI and CT90 were positively and L-SpO₂ negatively related with LPR symptoms. All these means the degree of OSA is associated with the severity of LPR and there is a close correlation between OSA and LPR. Interreaction of OSA and LPR can explain our results. OSA causes inflammatory injury, low intrathoracic pressure and leakage of lower esophageal sphincter; in turn, LPR (Acid reflux) results in esophagus, larynx, and pharynx mucosal injury and laryngopharyngeal symptoms.

Some studies report that anti-reflux therapy on OSA patients improve the symptoms and PSG parameters of OSA.¹⁴ At the same time, other studies report that CPAP can reduce GER events and improve nocturnal GER symptoms in OSA patients.^{10, 11} But few studies have reported the effect of OSA surgery on LPR.¹⁵ UPPP is not the first choice of treatment in most OSA patients compared to CPAP. If CPAP is refused or obstructive plane is definite, surgery can be considered for OSA, especially multilevel surgery. UPPP can achieve favorable result when airway obstruction only at the level behind palate, and our study included participants whose block plane in the oropharynx. The present study demonstrated post-operative AHI, nighttime SpO₂ (CT90 and L-SpO₂), RSI and RFS got a great improvement. Interestingly, the mean postoperative RSI and RFS in successful surgery group showed significant decrease, but there just one significant difference (mean RFS) occurred in unsuccessful group. We proposed successful UPPP surgery lowered RSI and RFS scores; unsuccessful surgery just improved RFS.

In the study, we supposed that effective UPPP could improve LPR symptoms and signs via three ways. Firstly, UPPP solves the problem of OSA-induced inflammatory injury via reducing airflow obstruction and increasing nocturnal blood oxygen saturation. Published studies have proposed that mouth breathing and snoring aggravates pharyngeal inflammation and LPR, and chronic intermittent hypoxia can lead to systemic

inflammation of the whole body and respiratory in OSA.¹⁶⁻¹⁸ Secondly, successful UPPP lowers OSA-induced esophageal change. It has been postulated that OSA causing lowering intrathoracic pressure and leakage of lower esophageal sphincter¹⁹: (1) when either apneas or hypopnea occur, OSA patient overcome the hypoxia by sleep breathing effort, which produce high transdiaphragmatic pressure and low intrathoracic pressure, exacerbating the lower esophageal sphincter(LES) pressure gradient and favoring acid reflux into esophagus, resulting in laryngeal mucosal injury.²⁰⁻²² (2) the inflammation that goes with OSA may make the patient prone to dysphagia by hypoxia-reoxygenation, promoting narrow the upper airway.¹⁷ Additionally, some studies have found that hypoxia inducible factor(HIF)-2 α may play an important role in reflux esophagitis, indicating that nocturnal low oxygen saturation may aggravate LPR symptoms.²³ (3) the OSA-induced airway resistance cause reflux events coexisting transient LES pressure relaxation.^{24, 25} Thirdly, LPR-induced inflammation cannot be ignored in the cycle between OSA and LPR. Previous studies have proposed that LPR results in esophagus, larynx, and pharynx mucosal injury and laryngopharyngeal symptoms, which promote: (1) tissue thickening and hypertrophy caused by chronic inflammation can directly cause narrow upper airway and (2) increased sensitivity of the laryngopharyngeal mucosa, inflammation-mediated tissue damage and sensory impairment contribute to upper respiratory collapse.¹³ UPPP improves LPR in two aspects mentioned above, which break the cycle between OSA and LPR.

Patients often have postoperative complaints after UPPP surgery, including pharyngeal pain, swallowing difficulty and lump sensation. Most symptoms are the same as listed on the RSI questionnaire and might result from scarification of surgical wound. But our study found most symptoms improved after UPPP. This unexpected finding likely benefited from UPPP which removes the upper airway obstruction.

Our study has limitations. Firstly, a more objective and easy measure to evaluate the effects of UPPP to LPR is needed to clarify our results and evaluate obstruction level. There are several reasons we chose RSI and RFS instead of 24-hour pH monitoring to diagnose LPR and evaluate the effect of UPPP. First of all, RSI and RFS are not only easy to operate for both patients and doctors, but also convenient for follow-up. Secondly, 24-hour pH monitoring is difficult for patients to accept leading to poor adherence. In addition, further discussion was focused on subjective sensation of upper respiratory tract after UPPP surgery. Secondly, OSA patients often complain similar symptoms (lump sensation, throat-clearing, difficulty swallowing) listed in the RSI questionnaire after surgery treatment, which are difficult to tell apart. Further study need compare every OSA patient pre-operative and post-operative changes of each items in RSI and RFS questionnaires. Thirdly, UPPP can solve IH or upper airway resistance of OSA. Future study with more cases is needed to explore whether IH or upper airway resistance improve LPR.

Conclusion

In summary, LPR symptoms are prevalent in OSA patients, the coexistence of OSA and LPR cannot be ignored. Successful UPPP surgery as a treatment for OSA patients, potentially reduces laryngeal reflux symptoms and improves laryngoscope signs by alleviating sleep respiratory disorder.

Data Availability Statement

The data supporting the findings of this study are available with request of the corresponding author.

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Table 1 Initial characteristics of participants

Characteristic	Controls (n=27)	OSA(n=64)	P value
Age (years)	43.85 $\pm$ 10.95	42.98 $\pm$ 10.21	0.718
BMI (kg/m2)	26.73 $\pm$ 3.74	27.19 $\pm$ 3.46	0.576
AHI (events/h)	3.00 $\pm$ 1.20	34.62 $\pm$ 14.8	<0.05
ESS	4.33 $\pm$ 1.88	11.31 $\pm$ 6.14	<0.05
L-SpO2 (%)	85.78 $\pm$ 3.70	70.16 $\pm$ 11.09	<0.05
CT90 (%)	1.14 $\pm$ 1.51	29.29 $\pm$ 21.75	<0.05
RSI	7.59 $\pm$ 4.70	13.70 $\pm$ 5.56	<0.05
>13	n=6	n=33	<0.05? _L ?
13	n=21	n=31	
RFS	6.04 $\pm$ 3.55	10.45 $\pm$ 5.03	<0.05
>7	n=8	n=43	<0.05? _L ?
7	n=19	n=21	

Data are presented as median $\pm$ SD. BMI: body mass index, AHI: apnea/hypopnea index, ESS: Epworth Sleepiness Scale (range 0-24), L-SpO2: lowest blood oxygen saturation during recording time, CT90%: percentage of recording time when oxygen saturation of arterial blood<90%, RSI: reflux symptom index, RFS: reflux finding score.

Table 2 Reflux symptom index and reflux finding score between mild-moderate OSA and severe OSA patients before UPPP

	Mild-moderate OSA (n=29)	Severe OSA (n=35)	P value
RSI	11.34 $\pm$ 5.40	15.66 $\pm$ 4.96	j0.05
>13	n=9	n=24	j0.05
[?]13	n=20	n=11	
RFS	7.07 $\pm$ 2.78	13.26 $\pm$ 4.75	j0.05
>7	n=14	n=29	j0.05
[?]7	n=15	n=6	

Data are presented as median $\pm$ SD. RSI: reflux symptom index, RFS: reflux finding score.

Table 3 Various factors before and after UPPP surgery

Characteristic	Before Surgery	After Surgery	<i>P</i> value
BMI (kg/m ²)	27.33±3.98	26.64±3.45	0.370
AHI (events/h)	46.73±8.00	19.94±11.30	¡0.05
ESS	15.15±5.29	9.59±3.89	¡0.05
L-SpO ₂ (%)	65.56±10.16	81.28±7.22	¡0.05
CT90 (%)	38.18±19.70	11.65±13.80	¡0.05
RSI	15.88±4.85	9.53±4.16	¡0.05
>13	n=24	n=6	¡0.05?;??
13	n=10	n=28	
RFS	13.18±4.80	8.65±4.87	¡0.05
>7	n=28	n=11	¡0.05?;??
7	n=6	n=23	

Data are presented as median ± SD. BMI: body mass index, AHI: apnea/hypopnea index, ESS: Epworth Sleepiness Scale (range 0-24), L-SpO₂: lowest blood oxygen saturation during recording time, CT90%: percentage of recording time when oxygen saturation of arterial blood<90%, RSI: reflux symptom index, RFS: reflux finding score.

Table 4 Changes between reflux symptom index and reflux finding score in patients with UPPP surgery

	Successful(n=25)	Successful(n=25)	Successful(n=25)	<i>P</i> value	Unsuccessful (n=9)	Unsuccessful (n=9)	<i>P</i>
	Before Surgery	After Surgery			Before Surgery	After Surgery	
RSI	16.04±4.48	8.60±3.50	<0.05	<0.05	15.44±6.06	12.11±4.94	<0.05
>13	n=18	n=3	<0.05	<0.05	n=6	n=3	0.3
13	n=7	n=22			n=3	n=6	
RFS	13.44±4.87	7.92±4.52	<0.05	<0.05	12.44±4.80	10.67±5.52	0.1
>7	n=22	n=7	<0.05	<0.05	n=6	n=4	0.3
7	n=3	n=18			n=3	n=5	

Data are presented as median ± SD. RSI: reflux symptom index, RFS: reflux finding score.

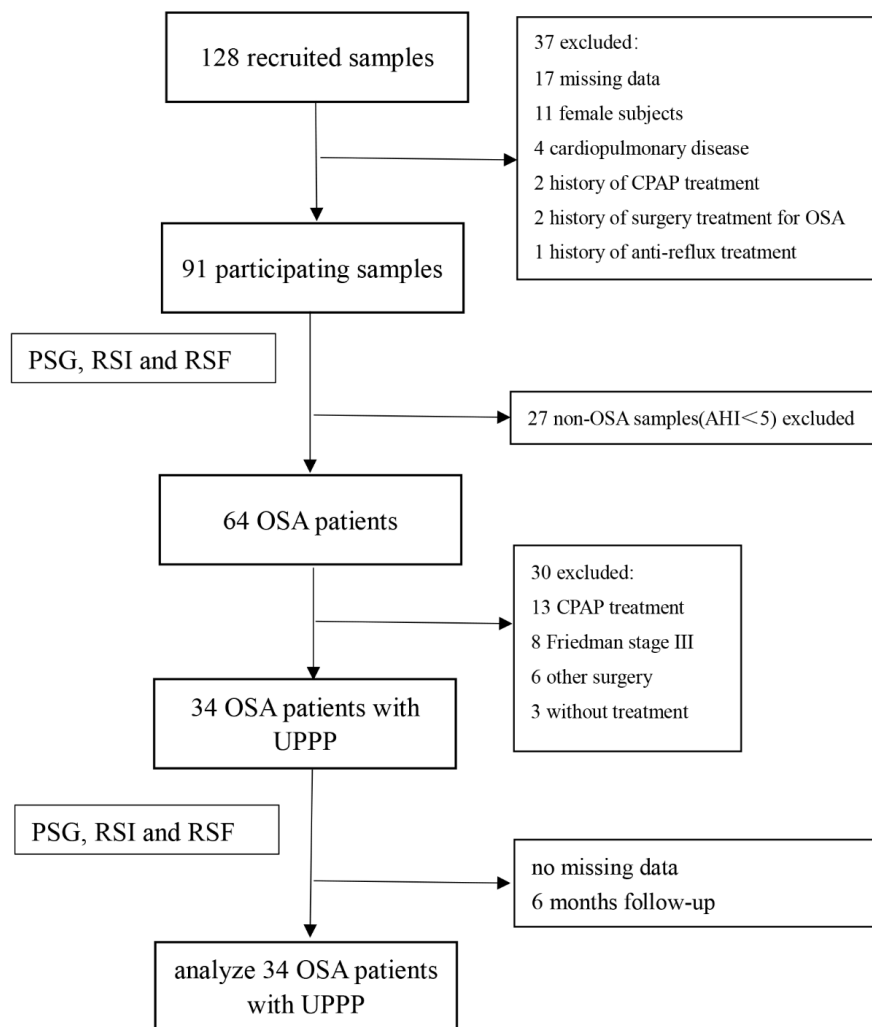


Figure 1 Flow diagram of participates. AHI: apnea hypopnea index; CPAP: continuous positive airway pressure; PSG: polysomnography; RSI: reflux symptom index, RFS: reflux finding score; UPPP: uvulopalatopharyngoplasty surgery.

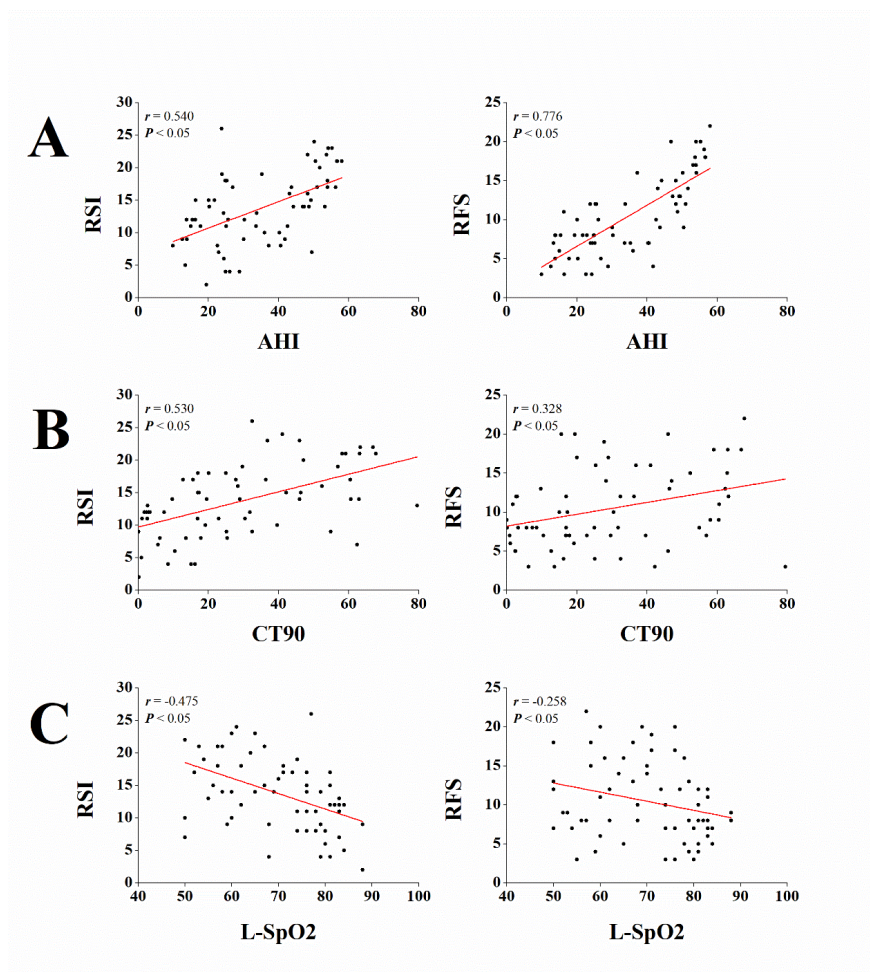


Figure 2 Correlation of LPR and sleep parameters. RSI and RFS scores were positively correlated with AHI (A) and CT90 (B), and negatively correlated with L-SpO2(C). RSI: reflux symptom index, RFS: reflux finding score. AHI: apnea hypopnea index; CT90: percentage of recording time when oxygen saturation of arterial blood < 90%; L-SpO2: lowest SpO2 during sleep.

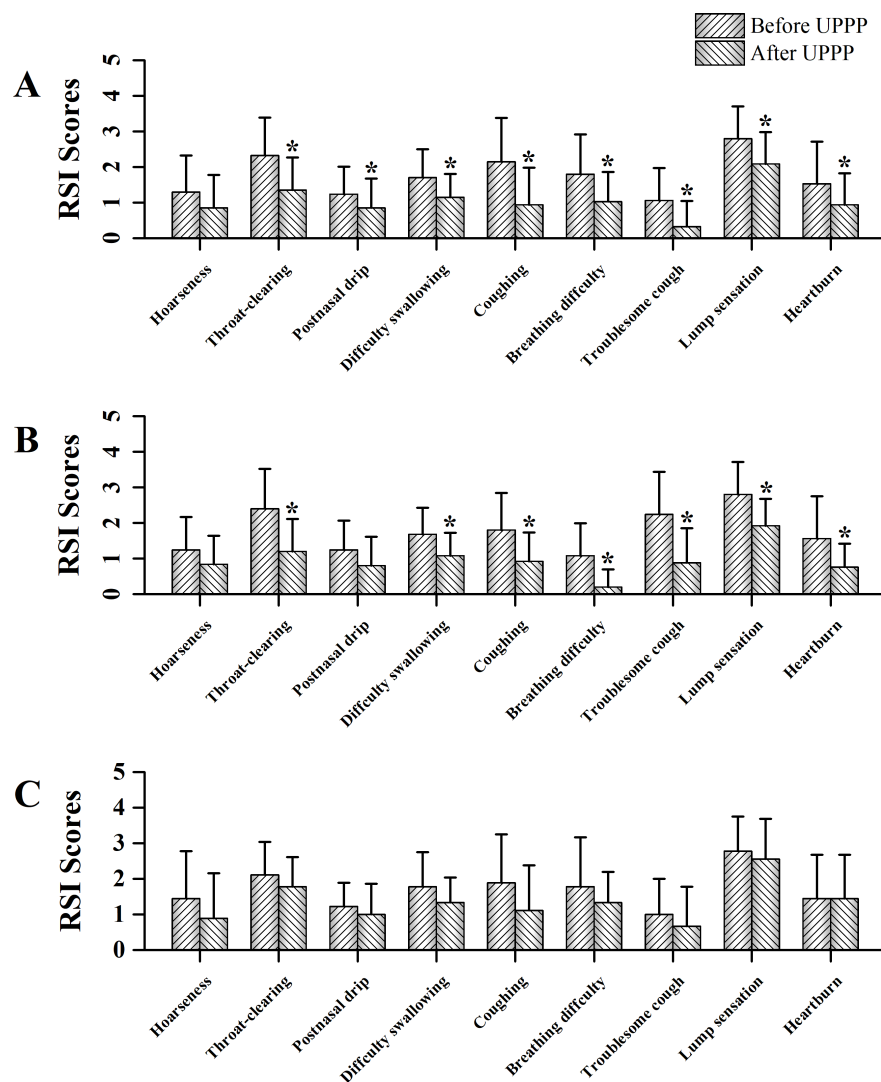


Figure 3 Reflux symptom index scores before and after UPPP surgery in different groups. (A) All individual variables (except hoarseness) in the RSI improved significantly after surgery. Except hoarseness and postnasal drip, all variables in the RSI improved significantly after successful surgery (B), but all variables in the RSI showed no significantly changes after unsuccessful surgery (C). * ? < 0.05 compared with before UPPP group.