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Associations of symptomatic and anatomical based severity of chronic rhinosinusitis with patients' anxiety and depression

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Abstract

Background Patients with chronic rhinosinusitis (CRS) have a high incidence rate of anxiety and depression. However, changes in anxiety and depression with different severities of CRS, and the effects of symptoms and anatomical factors on the anxiety and depression of CRS patients remain unclear.

Methods A total of 112 patients were enrolled in the study. The Sino-Nasal Outcome Test-20 (SNOT-20) score, Lund-Mackay scale and Lund-Kennedy scale were used to assess the severity of CRS, and the Generalized Anxiety Disorder-7 (GAD-7) and Patient Health Questionnaire-9 (PHQ-9) were used to evaluate anxiety and depression in patients.

Results In the univariate analysis, SNOT-20 scores, nasal symptom scores, facial/ear symptom scores and sleep scores are significantly positively correlated with patients' GAD-7 scores (all $P < 0.05$); the patients' SNOT-20 scores, nasal symptom scores, facial/ear symptom scores, sleep scores, and the higher side of the anterior ethmoid sinus and frontal sinus Lund-Mackay scores were significantly positively correlated with the patients' PHQ-9 scores (all $P < 0.05$). In a multivariate linear regression model, however, none of the covariates were found to be statistically associated with GAD-7. Another multivariate model indicated associations among the SNOT-20 sleep domain scores, the higher side of frontal sinus Lund-Mackay scores and PHQ-9 scores (both $P < 0.01$).

Conclusions Exacerbated nasal and facial/ear symptoms, sleep dysfunction increase patients' depression and anxiety. Lesions of the frontal sinus and anterior ethmoid sinus may be related to patients' depression. Treatment should be tailored to patients with these symptoms.

Key Words: Chronic Rhinosinusitis, Anxiety, Depression, Symptoms, Anatomical Factors

Introduction

Chronic rhinosinusitis (CRS) is one of the most prevalent clinical diseases, which is characterized by chronic inflammatory condition of sinonasal mucosa. At present, the prevalence rate of CRS varies in different regions: in western countries, the prevalence rate is between 3.4% and 16%^(1,2), while the average prevalence rate in China is about 8%⁽³⁾. CRS brings a huge economic burden to society and individuals. Previous reports suggest the direct cost of the treatment for CRS in American ranges from 3.9 billion to 12.5 billion US dollars annually⁽⁴⁾, some study also indicates the quality of life (QoL) of CRS patients was hugely reduced when compared to people without CRS⁽⁵⁾.

CRS is often accompanied by a variety of symptoms, including nasal symptoms (such as nasal congestion, runny nose, and decreased sense of smell), as well as extranasal symptoms (such as facial pain, sleep disorders, and cognitive dysfunction)^(6,7). In addition, studies⁽⁸⁻¹⁰⁾ have shown that patients with CRS have higher risks of psychological disorders than the general population. Anxiety and depression are the two most common psychological disorders affecting CRS patients. Another study suggested that the incidence rate of depression in CRS patients reached 25%⁽¹¹⁾. The existence of anxiety and depression will enhance the patient's perception of local symptoms of CRS (such as oropharynx and facial discomfort) and systemic symptoms (fatigue and decreased sexual function), which will increase the use of antibiotics and affect work and life. Anxiety and depression have a great impact on the patient's quality of life (QoL)⁽¹¹⁻¹³⁾, and bring certain challenges to the treatment of the disease⁽¹³⁻¹⁵⁾.

Therefore, it is beneficial to identify CRS patients with a potential risk of anxiety and depression, that may have a reduction in QoL. However, psychological factors were often ignored, which led to patients who show great pain or complaints of serious symptoms in patients with no corresponding objective findings clinically⁽¹⁶⁾. Another study⁽¹⁷⁾ suggested

that beyond the CRS symptom threshold, depressed mood could cause a reduction in health-related QoL. However, few studies have been carried out to evaluate the impact of the severity of CRS, symptoms and anatomical factors on patients' anxiety and depression.

Determining the association between the severity of CRS and anxiety and depression can help identify the potential anxiety and depression in patients. A better understanding of how symptoms and anatomical factors affect anxiety and depression can help with the precise diagnosis and treatment of CRS.

Methods

Study population and inclusion criteria

A prospective review was performed on 112 patients who met the diagnostic criteria for chronic sinusitis ⁽¹⁸⁾ and had not received treatment when admitted from January 2018 to January 2020. All diagnoses were made by professional ENT physicians. (Inclusion criteria: older than 18y of age, meet the diagnostic criteria for CRS; had not undergone any surgery or medical treatment; had no history of serious diseases such as cardio-cerebrovascular, liver, lung or kidney disease, hypertension, diabetes or tumors; and had no history of mental illness. Exclusion criteria: younger than 18y of age; had a history of surgery or long-term drug treatment; had a history of serious diseases such as cardio-cerebrovascular, liver, lung or kidney disease, hypertension, diabetes or tumors; had a history of mental illness, and could not or refused to cooperate). According to the Declaration of Helsinki, the study was also approved by the Medical Ethics Committee of Tongde Hospital of Zhejiang Province, written informed consent about the cases was obtained from all participants.

CRS severity evaluation

At the first visit, the patients were asked to complete the Nasal Sinus Outcome Test-20 (SNOT-20); the score was divided into nasal symptoms (0-18 points), facial/ear symptoms (0-12 points), sleep (0-12 Points) and emotional disorders (0-18 points) ^(12, 19); and a CT scan of the sinuses was performed, in which the Lund-Mackay CT score ⁽²⁰⁾ was used to evaluate the inflammation of the bilateral maxillary sinuses, anterior and posterior ethmoid sinuses, frontal sinuses, sphenoid sinuses, and ostiomeatal complexes (OMCs) (unilateral score range 0-12 points, 0-2 points for each item); and video endoscopy was performed, in which the Lund-Kennedy Nasal endoscopy score ⁽²⁰⁾ was used to evaluate patients' bilateral polyps, edema, rhinorrhea, scars and scabs (unilateral score range 0-10 points, each score 0-2 points). Symptoms, imaging and endoscopy were used to assess the severity of chronic rhinosinusitis in patients.

Anxiety and depression evaluation

The Generalized Anxiety Disorder-7 (GAD-7) Scale and the Patient Health Questionnaire-9 (PHQ-9): The GAD-7 has a high effectiveness, and it has great validity, and a strong correlation with the patient anxiety. It is simple to administer and has good credibility and validity ⁽²¹⁾. The score of each item is between 0 and 3, and the highest score is 21 points. The PHQ-9 is an effective and credible self-assessment scale for evaluating the severity of depression, and it has good sensitivity and specificity ⁽²²⁾. It was found in research that the PHQ-9 is suitable for longitudinal studies. Because of its high follow-up rate and self-report format, the PHQ-9 is widely used for simple diagnosis of depression and the evaluation of its severity ^(22, 23). The score of each item is between 0 and 3, and the highest score is 27 points.

Statistical analysis

Descriptive statistics for covariates were derived to characterize the patient cohort. Means and standard deviations are reported for covariates. Univariate linear analysis was performed to evaluate the association between each covariate and two outcomes, the GAD-7 and PHQ-9

scores. Univariate linear regression was applied for continuous covariates, and one-way Analysis of Variance (ANOVA) was used for categorical covariates.

Finally, multivariate linear regression analysis was carried out to identify covariates that were statistically significantly associated with GAD-7 and PHQ-9 score. All covariates mentioned previously were analyzed. Categorical variables, including sex, and all Lund-Mackay and Lund-Kennedy domain scores, were recoded to dummy variables in the model. Two final models were obtained with the use of a forward-selection algorithm, each of the GAD-7 and the PHQ-9 scores. The effect estimates and associated P-values for retained covariates in final models were all reported. All analyses were performed by R v3.2 (R core team, 2014).

Results

Baseline characteristics

A total of 112 patients who met the inclusion criteria were enrolled in the study. The basic characteristics of the whole cohort are shown in Table 1. No significant difference in age distribution between male and female patients was observed ($P=0.913$, median age male 41, female 40). No significant difference in GAD-7 scores ($P=0.518$) and PHQ-9 scores ($P=0.466$) between male and female patients was observed. And no significant difference in the presence of anxiety and depression was observed among CRS patients of different ages ($P>0.05$). That is, sex and age had no significant effect on the anxiety and depression of CRS patients.

Effect of CRS severity on anxiety and depression

Table 2 shows the scores of each scale for the entire cohort. Univariate analysis was performed to evaluate the association between the total score on the SNOT-20, the Lund-Mackay score and the Lund-Kennedy score on the side with the higher score and the patients' anxiety (GAD-7 score) and depression (PHQ-9 score). We found that the patients' total SNOT-20 score was positively correlated with their GAD-7 and PHQ-9 scores ($P<0.0001$ and

$P < 0.0001$, respectively) (Figure 1A), and their Lund-Mackay score and Lund-Kennedy score on the side with the higher score had no significant relationship with their GAD-7 and PHQ-9 scores ($P > 0.05$) (Table 3).

Effects of CRS symptoms on anxiety and depression

Table 3 shows the results of the linear correlation analysis of SNOT-20 domain scores for nasal symptoms, facial/ear symptoms and sleep and GAD-7 and PHQ-9 scores. We found that the patients' nasal symptoms (5.71 ± 3.7) ($P = 0.023$, $P = 0.037$), facial/ear symptoms (2.71 ± 2.7) ($P = 0.015$, $P < 0.0001$), and sleep (3.34 ± 3.18) ($P = 0.006$, $P < 0.0001$) were significantly positively correlated with their GAD-7 and PHQ-9 scores (Figure 1B,C,D).

Effects of anatomical factors on anxiety and depression

The number of sinuses involved had no significant effect on GAD-7 and PHQ-9 scores ($P = 0.706$ and $P = 0.252$, respectively); Among the maxillary sinus, anterior ethmoid sinus, posterior ethmoid sinus, frontal sinus, sphenoid sinus, and OMC, there was a significant difference in PHQ-9 scores with an anterior ethmoid sinus Lund-Mackay score of 0 and 2 (asymptomatic and severe inflammation) ($P = 0.025$), and the PHQ-9 scores of the patients with severe inflammation in frontal sinus (score=2) were significantly higher than those of patients with no inflammation (score=0) or mild inflammation (score=1) in the frontal sinus ($P = 0.028$, $P = 0.007$). Inflammation in other anatomical locations had no significant effect on GAD-7 and PHQ-9 scores (Figure 2 A, B). Edema, discharge and polyps had no significant impact on patients' anxiety and depression (Figure 2 A, B).

Multivariate linear regression analysis of anxiety and depression in CRS patients

GAD-7 and PHQ-9 scores were used as dependent variables in two different adjusted multivariate linear regression models controlling for age and sex. The stepwise forward model selection technique was applied to determine the final set of covariates in the two models. That is, the determination of the smallest number of covariates yielded a residual

sum of squares that converged to the residual sum of squares of the model with all covariates (Figure 3 A-D). For GAD-7 scores, age; the number of nasal sinus involved; SNOT-20 domain scores of nasal symptoms, facial/ear symptoms and sleep; Lund-Kennedy scores of discharge; and Lund-Mackay scores of the anterior ethmoid sinus, posterior ethmoid sinus, sphenoid sinus, frontal sinus, maxillary sinus and OMC were selected in the final model. Nevertheless, none of the covariates were significantly associated with GAD-7 scores.

For PHQ-9 scores, age; SNOT-20 domain scores of facial/ear symptoms and sleep; sex; and Lund-Mackay scores of the anterior ethmoid sinus, posterior ethmoid sinus and frontal sinus were included in the final model. Notably, the sleep domain score of the SNOT-20 ($\beta=0.33$, $P=0.0027$), and severe frontal sinus symptom ($\beta=2.3$, $P=0.0062$) both had significant relationships with PHQ-9 scores. The coefficient of the frontal sinus means that the average PHQ-9 score was 2.33 higher among patients with severe frontal sinus symptoms than among patients with no or mild symptoms.

Discussions

Recently, the interaction between CRS and psychological disorders (especially anxiety and depression) and quality of life (QoL) has received increasing attention⁽⁸⁻¹¹⁾. Earlier studies^(18, 24) suggested that anxiety, depression and the severity of somatic symptoms usually interact with each other, and the appearance of anxiety and depression is usually inconsistent with the objective assessment of the severity of CRS. The effects of symptoms on anxiety and depression are rarely reported, and no studies have reported the relationship between anatomical factors and anxiety and depression.

Our study found that the patients' nasal symptoms, facial/ear symptoms and sleep dysfunction were positively correlated with anxiety and depression, and we first report that severe lesions of the frontal sinus and anterior ethmoid sinus were positively correlated with

depression in CRS patients. Multivariate linear regression analysis confirmed the impact of severe frontal sinus inflammation and sleep dysfunction on depression.

In the analysis of the association between anatomical factors and anxiety and depression in CRS patients, the lesions of the frontal sinus and anterior ethmoid sinus were significantly related to the depression. The frontal sinus is located in the front of the brain, and the anterior ethmoid sinus is located in front of the brain, adjacent to the frontal lobe, which is the emotional part of the brain ⁽²⁵⁾. Therefore, we speculate that in CRS patients, there may be several explanations for the frontal sinus lesions of having an impact on anxiety and depression. First, the sensory nerve of the frontal sinus is innervated by the optic branch of the trigeminal nerve, which is densely distributed around the sinus ostium ⁽²⁶⁾. The frontal sinus drainage channel is long and narrow, and its lesions are likely to cause obstructions of the sinus ostium, so that it will form a "ball-valve mechanism", which increases the pressure in the sinus and exerts pressure on the frontal sinus wall and sinus ostium ^(27, 28). On the one hand, the pain and fullness caused by stress will affect the QoL of CRS patients and stimulate the patients' depression. On the other hand, we assume there are direct or indirect nerve conduction pathways on the frontal sinus mucosa that affect the frontal lobe and cause depression; second, the lesions of the frontal sinus often cause pneumosinus dilatans (PD) ⁽²⁹⁾, which refers to the overaerification of the frontal sinus, and the deformation of the bone and soft tissue around the sinus ^(27, 30). We assume that, on the one hand, the increase in frontal sinus volume may directly or indirectly exert pressure on the frontal lobe or reduce the local space of the cranial cavity of the frontal lobe, resulting in changes in the patient's mood. On the other hand, the discomfort caused by PD can reduce the patients' QoL ⁽³¹⁾, which can further aggravate the patients' depression. In addition, some studies have suggested that patients with PD have changes in hormones in the body that can cause depression ^(32, 33); therefore we assume that lesions in the frontal sinus can cause depression in the same way.

There are many heteromorphoses of the anterior ethmoid sinus that may affect the ventilation function of the nasal cavity and the drainage of the frontal sinus ⁽³⁴⁾. Disturbances in nasal ventilation causes a decrease in olfaction, which is related to depression ⁽³⁵⁾.

We also found that sleep disorders can cause anxiety and depression in CRS patients, which is consistent with the conclusions of many studies ^(6, 10, 12, 36, 37). Earlier studies have found that the proportion of CRS patients with sleep disorders can reach 60-75%, which is much higher than that of the normal population ^(6, 38, 39). The disturbance of CRS to patients' sleep is mainly manifests as difficulties inducing sleep, difficulties maintaining sleep, early morning awakening and excessive daytime sleepiness ⁽³⁹⁾. Nasal obstruction is the most important factor that causes a decline in sleep quality, which can be found in similar studies in patients with allergic rhinitis ⁽³⁹⁻⁴¹⁾. Sleep disorders can cause a decline in QoL, which can induce anxiety and depression ^(42, 43). Some studies also found that an increase in the severity of CRS is often accompanied by a corresponding increase in the level of certain cytokines in the body, such as IL-1 β and TNF- α , which often account for the occurrence of depression ^(42, 44, 45). Depression caused by the decline in sleep quality can also be seen in other diseases, such as rheumatoid arthritis ⁽⁴⁶⁾. Another study ⁽⁴⁷⁾ found that the risk of depression in CRS patients increased with the aggravation of sleep disorders, and in patients with a high risk of depression, headache and facial pain were also prevalent. Therefore, we consider that sleep disorders have a direct and more significant effect on patients' anxiety and depression. Therefore, in the future treatment, anti-insomnia treatment for CRS patients may simultaneously improve patients' anxiety and depression.

In our results, nasal symptoms and facial/ear symptoms also affected anxiety and depression in CRS patients, and there were many other studies had similar conclusions to ours ^(10, 36, 37, 48, 49). Nasal and facial/ear symptoms include discharge, olfactory dysfunction, running nose, headache and ear fullness. A previous study ⁽⁴⁹⁾ have found that olfactory dysfunction

seriously damages the patients' nasal-symptom-related QoL. Compared with the control group, CRS patients showed a higher level of psychological stress and depression. After olfactory function was improved, the patients' psychological state was also improved. And patients with nasal obstruction have a higher risk of depression, and that nasal obstruction can be used as a predictor of depression⁽⁴⁸⁾. A study used the SNOT-20 and Hospital Anxiety and Depression Scale (HADS) to evaluate patients' symptoms and anxiety and depression, and it also revealed that there was a significant correlation between nasal symptoms and depression. Facial/ear symptoms mainly affect the patients' sleep and cause the patients' physical symptoms, causing the patients' QoL to drop, thereby triggering the patient's emotional instability^(11, 12, 37). After surgery to improve patients' disease-specific symptoms, whether their anxiety and depression improve is still controversial^(14, 15, 43).

Limitations

This study has the following advantages. First, this is the first study to explore the correlation between anatomical factors and anxiety and depression. We first report the association of frontal sinus and anterior ethmoid sinus symptoms with depression. Second, we also confirmed the effect of CRS-related symptoms (sleep disorders, nasal and facial/ear symptoms) on anxiety and depression in previous studies. Third, for the study sample selection, CRS patients who were initially diagnosed were enrolled, which excludes the effects of drugs and surgical treatment on patients' anxiety and depression, and this study excluded the emotional effects of systemic diseases on CRS patients, which can be more credible. Our study enhances the understanding of CRS and provides new ideas for clinicians to conduct effective interventions for CRS patients.

Our study also has several limitations. First, our conclusions come from the findings of the single-center research, the sample size we included in the research is insufficient, and future study on multi-center and a large patient population is needed to verify the statistical results;

second, anxiety and depression are affected by many factors, that we have not fully considered; therefore, our results require further research to confirm; Third, our research does not elaborate on the specific physiological mechanism of anxiety and depression in CRS patients; therefore future research is needed to clarify the molecular regulatory mechanism behind this conclusion.

Conclusion

Exacerbated nasal and facial/ear symptoms and sleep dysfunction increased patients' depression and anxiety. The lesions of the frontal sinus and anterior ethmoid sinus may be related to patients' depression. As a result, treatment should be tailored to patients with these symptoms.

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Authors' contributions

Chenyang Lei participated in the design of the study. Chenyang Lei, Zeyu Sun and Xiandan Luo performed data collection and statistical analysis, Chenyang Lei and Zeyu Sun drafted the manuscript. All authors read and approved the final manuscript.

Competing interests

The authors declare that they have no competing interests.

Ethics approval and consent to participate

This study was approved by the Ethics Committee of Tongde Hospital of Zhejiang Province (No. 20180626), and informed consent was obtained from the patients.

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Declarations

Ethics approval and consent to participate

The study was also approved by the Medical Ethics Committee of Tongde Hospital of Zhejiang Province, written informed consent about the cases was obtained from all participants.

Consent for publication

Written informed consent for publication of their clinical details was obtained from the patient.

Availability of data and materials

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

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

CY Lei and GY Xiong participated in the design of the study. CY Lei, ZY Sun and XD Luo performed data collection and statistical analysis, JS Yao and ZY Sun drafted the manuscript. All authors read and reviewed the final manuscript.

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Figures

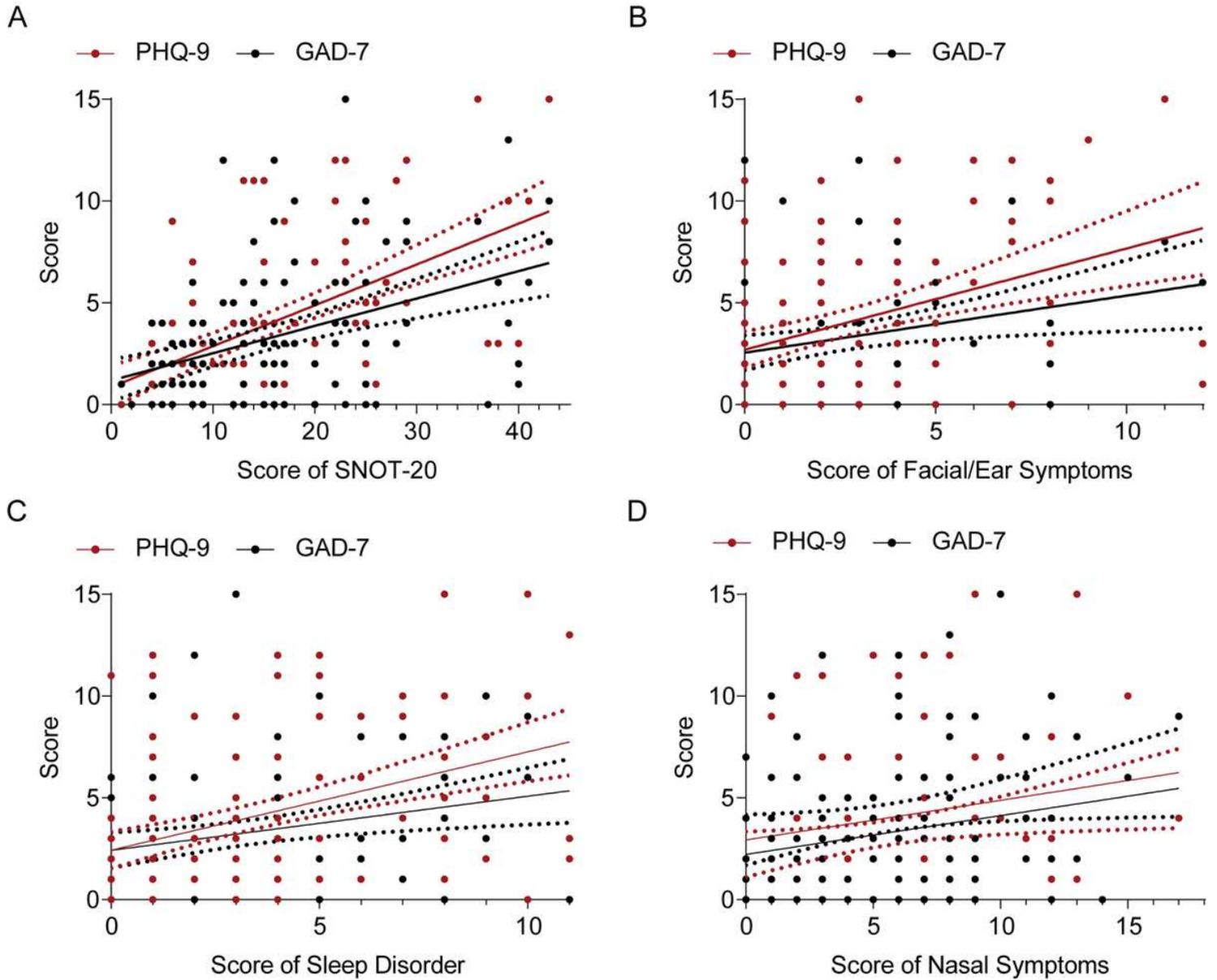
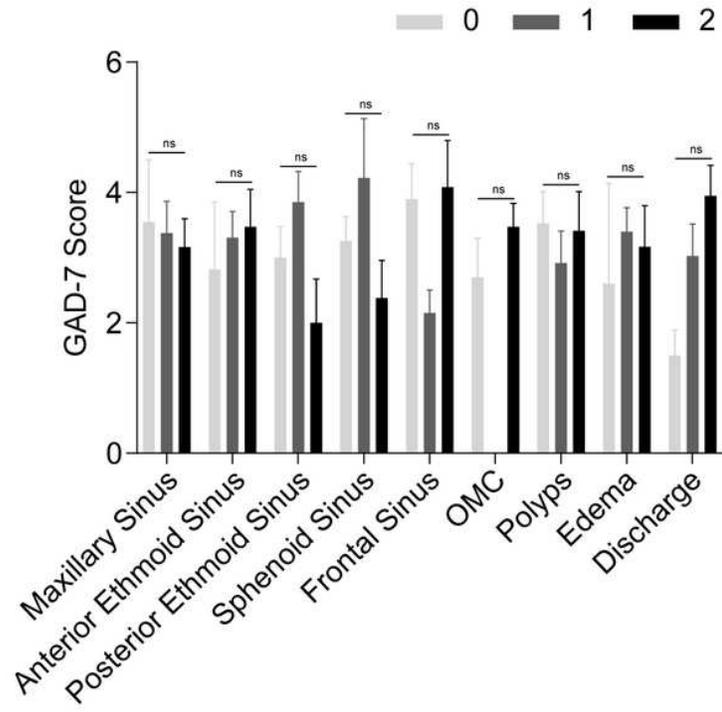
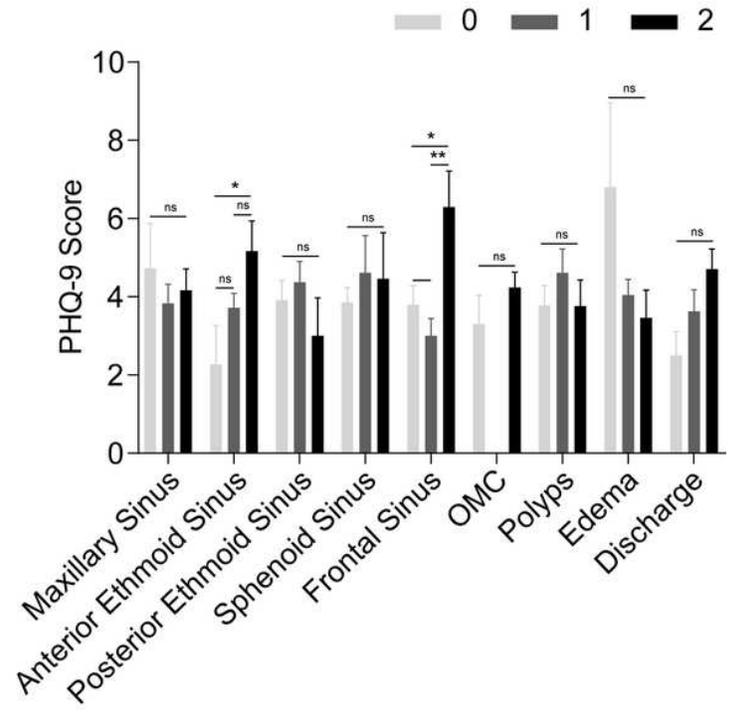


Figure 1

Effect of CRS severity on anxiety and depression

A**B****Figure 2**

Effects of anatomical factors on anxiety and depression

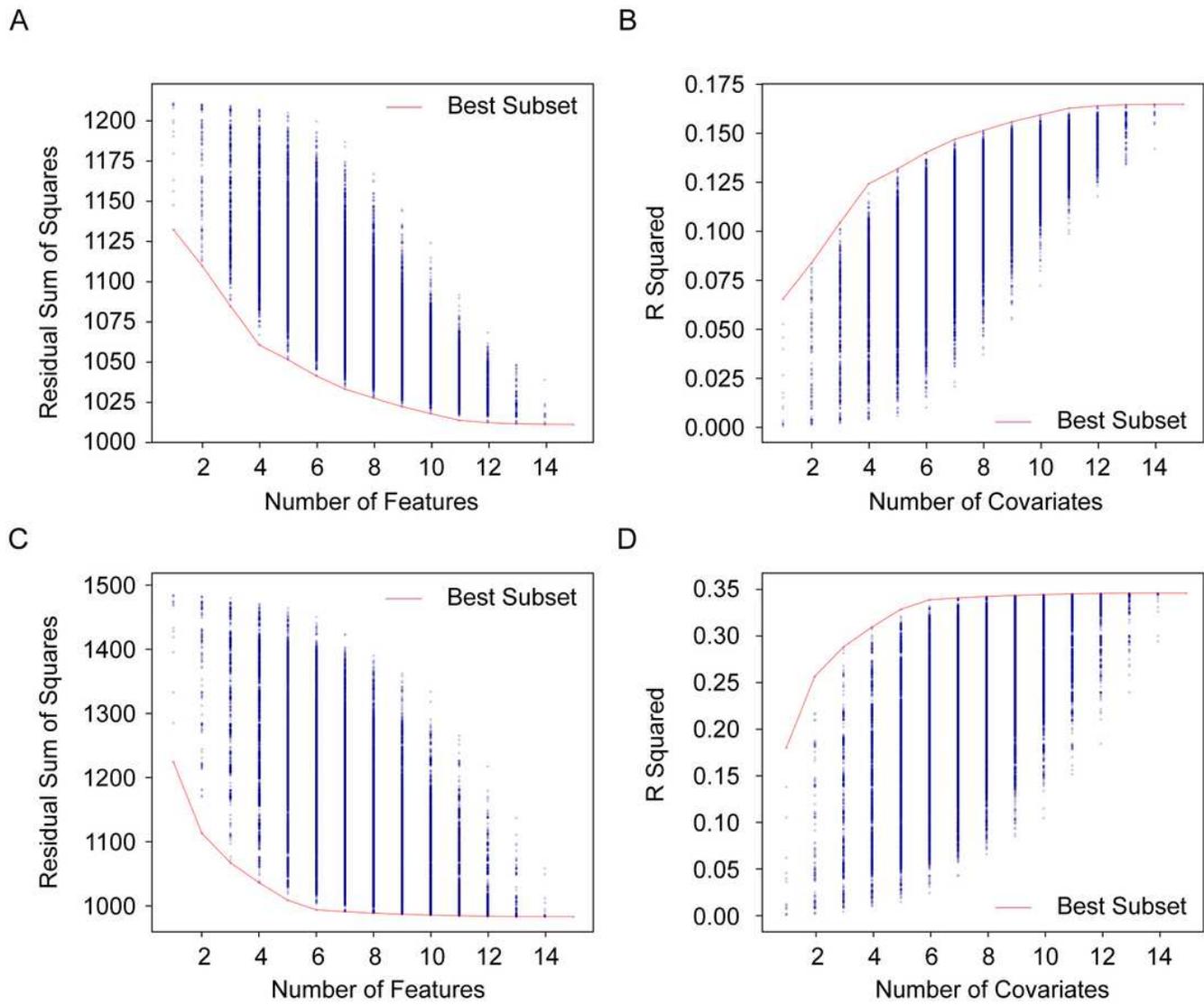


Figure 3

Multivariate linear regression analysis of anxiety and depression in CRS patients