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Culture-inappropriate antibiotic therapy decreases quality of life improvement after sinus surgery

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Abstract

Background—Despite their widespread use, antibiotics have not been shown to improve chronic rhinosinusitis (CRS) outcomes. We aimed to determine whether culture-inappropriate postoperative antibiotic therapy was associated with less quality of life (QOL) improvement following functional endoscopic sinus surgery (FESS).

Methods—This retrospective cohort study recruited 376 adult CRS patients undergoing FESS between 10/1/2007 to 12/31/2011. Patient demographics, comorbidities and medications were collected at baseline. Trimethoprim-sulfamethoxazole and clindamycin were administered for 2 weeks postoperatively. The antibiotic appropriateness was determined based on bacterial resistance profile of organisms identified during intraoperative culture. The QOL outcome was defined as change of 22 item Sinonasal Outcome Test scores from preoperative visit to 1-, 3- and 6-month post-FESS. Clinically significant difference was defined as at least ½ SD of baseline QOL score in the reference group. Mixed-effects regression models were performed.

Results—Seven percent of patients (n=27) had culture-inappropriate antibiotic therapy, and additional 5% (n=19) had culture-specific antibiotic adjustment. Compared to patients with culture-appropriate antibiotics, patients with culture-inappropriate antibiotics had significantly less improvement of QOL from baseline to postoperative 1-month and 3-month follow-up where the difference became clinically significant; patients with antibiotic adjustment had more QOL improvement from baseline to 1-month follow-up, but their QOL worsened at 3-month follow-up,

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and these changes were not clinically significant. However, all effects washed out at 6-month follow-up with no significant differences.

Conclusions—Culture-inappropriate postoperative antibiotic therapy decreased short-term QOL improvement to a clinically meaningful level after FESS. Culture guided selection of antibiotics may improve short-term FESS outcome.

Keywords

antibiotic therapy; quality of life; endoscopic sinus surgery; chronic rhinosininitis; culture; the 22-question Sinonasal Outcome Test

Introduction

Chronic rhinosinusitis (CRS) is one of the most common chronic diseases and represents a major public health problem. It affects 14% to 16% of the U.S. population.¹ CRS has a substantial negative health impact, adversely affecting mood, physical functioning, and social functioning.^{2,3} CRS is a heterogeneous multifactorial disease with multiple distinct components⁴, such as genetic, infectious, immune, anatomic, allergic, and inflammatory components⁴. However, the mainstay of medical therapy for CRS is the combination of long-term antibiotic therapy and nasal steroids⁵, and it is unclear whether culture-inappropriate antibiotic therapy makes a difference in treatment outcomes. Functional endoscopic sinus surgery (FESS) is indicated when maximum medical therapy fails,^{6,7} and empiric antibiotics are routinely administered during postoperative care of FESS. However, there are no clinical guidelines to support either preoperative or postoperative antibiotic use in CRS. Randomized clinical trials have shown conflicting results regarding the efficacy of utilizing empiric postoperative antibiotics in surgical outcomes.^{8,9} One potential explanation is that postoperative antibiotic therapy for CRS is typically empiric, which may not be culture appropriate.

CRS has been shown to have a greater impact on quality of life (QOL) of bodily pain and social functioning than angina, congestive heart failure and chronic obstructive pulmonary disease using global QOL scores.^{10,11} Thus, it is of considerable interest to assess the effect of culture-inappropriate antibiotic therapy on QOL outcome. As disease-specific QOL tools are often preferable to evaluate treatment effects¹², the aim of our study was to determine whether CRS patients with culture-inappropriate postoperative antibiotic therapy had decreased improvement of disease specific QOL after FESS compared to CRS patients with culture-appropriate therapy.

Methods

We conducted a retrospective cohort study. A cohort study can clearly demonstrate the appropriate temporal sequence between exposure and outcome. A retrospective cohort study is the first critical step to test an unknown hypothesis and is efficient to do when there is no evidence to support the needs of conducting expensive and time consuming prospective studies. In addition, it is unethical to assign culture-inappropriate antibiotics to patients in prospective studies. Given the fact that there are no clinical guidelines to support empiric

antibiotics in postoperative patients, if this retrospective study showed that CRS patients with culture-inappropriate postoperative antibiotic coverage had less postoperative QOL improvement as compared to patients with culture-appropriate therapy, the findings would support the need for a future randomized controlled trial to further testing the causality and support culture-appropriate antibiotic use in CRS by assigning patients to either culture-appropriate antibiotics or no postoperative antibiotics groups. This study was approved by the institutional review board of the University of Pennsylvania.

Study population

Adult CRS patients (18 years or older) who underwent FESS were enrolled from October, 1, 2007 to December, 31, 2011 at the Department of Otorhinolaryngology–Head and Neck Surgery, the University of Pennsylvania. CRS was diagnosed based on the objective and subjective guidelines set forth by the Sinus and Allergy Health Partnership¹³. Patients with cystic fibrosis, congenital or acquired immunodeficiency, congenital mucociliary, non-invasive fungal balls and invasive fungal disease, systemic vasculitis and granulomatous diseases, cocaine abuse, or neoplasia were excluded.^{6,7}

Exposure

Culture-inappropriate postoperative antibiotic therapy was defined as at least one organism identified in intraoperative culture resistant to or not covered by the initially prescribed postoperative antibiotics. In this study population, Trimethoprim-sulfamethoxazole (TMP-SMX), 800–160 mg twice daily, and clindamycin, 150 mg three times daily, were routinely prescribed for 14 days postoperatively. For patients who were sulfa allergic, levofloxacin, 500 mg daily for 14 days was substituted for TMP-SMX. If *Pseudomonas aeruginosa* was identified in intraoperative culture, TMP-SMX was replaced by Levofloxacin at 1 week postoperative visit. When patient culture results demonstrated susceptibilities to intravenous antibiotics only, adjustment was not made to avoid the risk of intravenous antibiotics in outpatient setting. Thus, the appropriateness of postoperative antibiotic therapy was categorized as culture-inappropriate, culture-appropriate after adjustment, culture-appropriate, and undetermined. The detailed definitions are listed in Table 1.

Each patient had endoscopically guided sinus culture taken from one of the diseased sinuses during FESS to avoid contaminant^{14–16}. An aerobic culture and an anaerobic culture (after May 2008) were collected from each patient. The aerobic cultures were collected with the BBL Culture Swab Collection & Transport System (Copan for Becton, Dickinson and Company, in Sparks MD), and the anaerobic cultures were collected with BD Eswab Collection & Transport System (Copan for Becton, Dickinson and Company, in Sparks MD). The samples were immediately sent to the hospital microbiology laboratory for standard microbiological speciation. For aerobes, sheep blood (5%), chocolate, and MacConkey agar plates were inoculated at 37°C aerobically (MacConkey) and under 5% carbon dioxide (blood and chocolate) and examined at 24 and 48 hours.¹⁷ Aerobes were identified using standard methods.¹⁷ For anaerobes, the samples were plated on a Brucella agar supplemented with 5% sheep blood, Vitamin K and Hemin. Plates were then incubated anaerobically for 4 days then examined after 24 hours, 48 hours and after 4 days. If it grew, then aero tolerance testing was done and if any grew anerobically, standard methods were

used to identify the anaerobes.¹⁸ The antibiotic susceptibility tests were performed based on the performance standards for antibiotic susceptibility testing published by the Clinical and Laboratory Standards Institute.¹⁹ However, in our clinical practice, antibiotic susceptibility tests were not routinely performed for coagulase-negative *staphylococci* (CNS), *Corynebacterium diphtheria*, *Streptococcus spp.* other than *Streptococcus pneumoniae*, *Moraxella catarrhalis*, *Haemophilus spp.* (only beta-Lactamase was tested), and anaerobes. Thus, the samples with these bacterial isolates were categorized as undetermined antibiotic appropriateness.

Outcome

Quality of life was measured by the disease-specific health related quality of life instrument, the 22-question Sinonasal Outcome Test (SNOT-22),^{20,21} before FESS, 1-month, 3-month and 6-month after FESS. The SNOT-22 contains 22 symptoms related items on sinonasal symptoms, sleep, emotional and psychosocial functioning, where each item is scored on a range of 0 to 5 depending on severity, thus giving a total score of 0 to 110. Higher scores represent worse QOL. A review assessing the reliability, validity, responsiveness and ease of use of 15 disease-specific QOL instruments for CRS concluded that the SNOT-22 was the most suitable for the evaluation of outcome.²⁰ Clinically significant change of SNOT-22 score was defined as difference of at least ½ SD of the baseline SNOT-22 score in the reference group,^{22,23} i.e. patients with culture-appropriate therapy. The primary outcome was defined as the continuous change of SNOT-22 scores from preoperative clinic visit to 1-month post-FESS follow-up visit, because this difference in SNOT-22 was more likely to reflect the direct effect of culture-inappropriate postoperative antibiotic therapy after adjusting for confounding factors. The secondary outcomes were the changes of SNOT-22 scores from preoperative clinic visit to postoperative clinic visits at 3- and 6-month follow-up. This is to explore the potential long-term effects of culture-inappropriate postoperative antibiotic therapy.

Potential confounders

The following potential confounders were collected during preoperative visit: age²⁴, sex^{25,26}, race, asthma^{24,27}, nasal polyps^{24, 27}, allergic rhinitis²⁸, obstructive sleep apnea, diabetes, smoking status²⁸, gastroesophageal reflux disease (GERD)²⁹, prior FESS history, and Samter's triad. Additionally, administered oral antibiotics, nasal steroids, oral steroids and any nasal rinse in the month prior to sample collection were recorded, and dichotomized into yes or no categories. We collected but did not adjust for postoperative use of steroids and nasal rinse, because every postoperative patient was on nasal rinse and nasal steroids, and all the patients with nasal polyps were on oral steroids, which was collinear with nasal polyps. All the potential confounders were tested as categorical variables except for age.

Statistical Analysis

The outcome data was natural log transformed if the assumption of normality was violated. We compared the exposure, patient characteristics and baseline SNOT-22 scores between patients with and without SNOT-22 scores at the last visit to examine if missing data depended on patient characteristics. The patient characteristics that differed significantly

were forced into the final multiple regression model to adjust for the difference. In the univariate analysis, one-way ANOVA test and Pearson's χ^2 test were used to compare patient's characteristics between exposure groups. We conducted our primary analysis using the linear mixed-effects regression model, with fixed effects for time modeled as a categorical variable, antibiotic therapy, and the interaction between the two in order to allow the effects of culture-inappropriate antibiotic therapy to vary over time. The model also included random effects for patient to account for the correlation between repeated measures per patient. Linear mixed effects regression models allow for data assumed to be missing at random. If a SNOT-22 score was missing at a certain time point, the rest of the scores from that same patient were still included in the mixed effects model. Potential confounding variables listed above were considered, and preoperative antibiotic use and prior FESS history were forced into the final model to adjust for their effects on intraoperative culture and/or postoperative QOL. A manual backward elimination was performed and potential confounders with $p < 0.05$ or changed the point estimate of primary association by 15% were retained in the final model. Both the unadjusted and the adjusted results from the linear mixed effects regression model were presented as coefficients and 95% confidence intervals (95% CIs). A value of $p < 0.05$ was considered statistically significant. Statistical analyses were conducted using STATA 11 (Stata Corp, College Station, Texas).

Results

The analyses included 376 CRS patients with preoperative SNOT-22 scores. As shown in table 2, the mean $\pm$ SD age of this study population was 48 ± 13 years old; 42.6% were female ($n=160$); 88.6% were white ($n=333$), 8.2% were black ($n=31$) and 3.2% were other races ($n=12$). For postoperative antibiotic therapy, 7.2% patients ($n=27$) had culture-inappropriate antibiotics, 5.0% patients ($n=19$) had culture-appropriate antibiotics after adjustment, 17.6% patients ($n=66$) had initially culture-appropriate antibiotics, and 70.2% patients ($n=264$) had determined appropriateness of postoperative antibiotics due to the lack of antibiotic susceptibility tests and anaerobic culture results in certain patients. In the univariate analysis, patients with culture-inappropriate antibiotics were significantly more likely to have prior FESS.

The prevalence of bacterial isolates is listed in Table 3. Most cultures were polymicrobial. The most common aerobic culture isolates was CNS ($n=217$), and 73 cultures grew CNS only. *S. aureus* ($n=104$), *P. aeruginosa* ($n=31$), *Enterobacteriaceae spp.* ($n=35$) and *S. pneumoniae* ($n=17$) were the most common organisms isolated. For the 224 anaerobic cultures after May, 2008, 54.9% were positive ($n=123$) and most of them were also positive for aerobic cultures. Only one culture grew anaerobes only. The most common anaerobic isolates were *Propionibacterium acne* ($n=82$) and *Peptostreptococcus spp.* ($n=24$).

Among the 376 patients with baseline SNOT-22 scores, 71.3% ($n=268$), 52.7% ($n=198$) and 49.7% ($n=187$) patients had 1-, 3- and 6- month postoperative follow-up SNOT-22 scores, respectively. Their pre-FESS and post-FESS 1-, 3- and 6- month mean SNOT-22 scores were 40 ± 22 , 20 ± 18 , 20 ± 18 and 21 ± 20 , respectively. There were no significant differences in patient characteristics, antibiotic therapy, and baseline SNOT-22 scores between patients with and without follow-up SNOT-22 scores. The $\frac{1}{2}$ SD of baseline

SNOT-22 score in culture-appropriate antibiotic therapy group, i.e. 11, was defined as the clinical meaningful change. Figure 1 shows the mean changes of SNOT-22 scores in patients stratified by the appropriateness of postoperative antibiotic therapy. Compared to patients with culture-appropriate antibiotic therapy, patients with inappropriate antibiotic therapy had less QOL improvement from baseline to 1-month follow-up and the difference was 7, non-clinically significant, but the difference increased to 11 from baseline to 3-month follow-up, clinically significant. In addition, after culture specific antibiotic adjustment, patients with the adjustment had more QOL improvement at 1-month follow-up and this difference, 10, was not clinically significant; however, these patients' QOL declined over time, and they had non-clinically significantly worse QOL improvement at 3-month follow-up, i.e. 6. None of the differences of QOL improvement were clinically significant at 6-month follow-up. In addition, there were no clinically significant QOL improvements between patients with undetermined and culture-appropriate antibiotic therapy from baseline to any follow-up time-points.

In the final covariate-adjusted linear mixed effects model, we evaluated the changes of log-transformed SNOT-22 scores, i.e. $\ln(\text{SNOT-22 score} + 1)$, over time by antibiotic therapy. Asthma and diabetes were significant confounders identified during the manual backward elimination and thus were adjusted in the final model along with preoperative antibiotic use and prior FESS. Table 4 shows the unadjusted and adjusted results. When keeping time and other covariates in the model constant, compared to patients with culture-appropriate postoperative antibiotic therapy, patients with culture-inappropriate postoperative antibiotic therapy had significantly less improvement of QOL from baseline to 1-month follow-up (adjusted-coefficient = 0.84, 95% CI, 0.19, 1.49, $p=0.012$). This difference was also significant at 3-month follow-up, but not at 6-month follow-up in the final model. Interestingly, compared to patients with culture-appropriate therapy, patients with culture specific antibiotic adjustment did not have significantly different improvement of QOL from baseline to 1-month follow-up (adjusted-coefficient = -0.01 , 95% CI, -0.57 , 0.55 , $p=0.972$), but had significantly less improvement of QOL from baseline to 3-month follow-up. Similar results were found in patients with undetermined appropriateness of postoperative antibiotic therapy. However, at 6-month follow-up, patients in all groups had similar SNOT-22 scores.

Discussion

To our knowledge, this appears to be the first study to evaluate the effect of culture-inappropriate antibiotic therapy in CRS. Our study showed that culture-inappropriate postoperative antibiotic therapy is associated with less QOL improvement during short-term follow-up after FESS. Compared to CRS patients with culture-appropriate postoperative antibiotic therapy, patients with culture-inappropriate antibiotic therapy had clinically significantly less QOL improvement at 3-month follow-up. The antibiotic adjustment based on culture results improved the QOL immediately at 1-month follow-up, but these resistant bacteria seemed to be associated with a rebound QOL decrease at 3-month follow-up, and these differences were not clinically significant. At 6-month postoperative follow-up, the differences of QOL improvement between any groups were washed away.

Our findings suggest it is important to adjust postoperative antibiotics based on intraoperative culture to facilitate recovery immediate after FESS. Due to the lack of guidelines for empiric antibiotic therapy in CRS,^{6,7} various groups of systemic antibiotics have been studied in the treatment of CRS, including penicillins^{30–32}, cephalosporins^{30,32}, quinolones³¹ and macrolides^{33,34}. A randomized control trial showed that amoxicillin/clavulante for 3 weeks did not improve symptom, endoscopic scores, and bacterial growth 3 weeks after FESS,⁸ while another randomized control trial showed the use of amoxicillin/clavulanate for 2 weeks in the postoperative period was able to improve the outcome in the early blood crust healing phase on postoperative days 5 and 12.⁹ However, the antibiotics used in these studied were not adjusted based on culture results, and the 2 clinical trials showed conflicting results. Our results provide evidence that culture-inappropriate antibiotic therapy does not provide clinical benefits, and should be avoided.

We found antibiotic adjustment based on culture results was associated with improved QOL at 1-month follow-up, but QOL worsened at the 3-month follow-up. However, none of these QOL changes were clinically significant. One potential explanation of the changes is that the presence of multidrug resistant bacteria itself may be associated with unfavorable outcomes of FESS for CRS. In addition, all patients had similar postoperative QOL at 6-month follow-up, despite of more significant QOL improvement in patients with culture-appropriate antibiotic therapy at 1- and 3-month follow-up. This may be because other potential treatments and health care the patients with undesirable outcomes obtained after 3-month postoperative follow-up.

Asthma and diabetes were the other 2 factors found to be associated with poor postoperative QOL improvement in our study. Asthma has been shown to be strongly associated with CRS severity on CT scans and revision FESS rates in previous studies.^{16,24,27,35} However, the association between diabetes and CRS has rarely been studied. Patients with diabetes are known to be liable to infections and postoperative infection.³⁶ Further studies are needed to explore whether diabetes put CRS patients in a negative prognostic category after FESS. Several other risk factors for CRS development and unfavorable treatment outcomes have been reported in other studies, such as include smoking status²⁸, nasal polyps^{24, 27}, allergic rhinitis²⁸, aspirin intolerance²⁵, and gastroesophageal reflux²⁹. CRS is accompanied by nasal polyps in about 19% to 36% of patients,^{25,37} and nasal polyps has been demonstrated to be associated with refractory CRS.^{24,27} The prevalence of allergic rhinitis was as high as 56% in CRS patients,²⁸ and allergic rhinitis is associated with the development of CRS and nasal polyps^{28,38}. Aspirin intolerance predicts poor outcomes measured by Lund-MacKay CT scores and QOL after FESS³⁹. All these factors were assessed in our study except for aspirin intolerance, which were studied as part of the Samter's triad, but none of them independently associated short-term QOL improvement after FESS for CRS. Our findings agreed with other studies that adjusted for potential risk factors via multiple regression models.⁴⁰

In our study, neither prior FESS history nor preoperative antibiotics were found to be significantly associated with postoperative QOL improvement. However, the majority of patients with culture-inappropriate postoperative antibiotic therapy had prior FESS, which suggests high bacterial resistance rates in patients with prior FESS. Kingdom et al. showed a

statistically significant higher incidence of resistance for CNS and *S. aureus* in patients undergoing revision FESS when compared with patients without prior surgery.⁴¹ Smith et al found patients undergoing primary surgery were significantly more likely to improve on the QOL measured by Rhinosinusitis Disability Index and the Chronic Sinusitis Survey after an average of 17.4 months postoperative follow-up.⁴⁰ In our study, to assess the direct effect of 2-week postoperative antibiotic therapy, the postoperative follow-up used is short-term, which may contribute to our negative findings of the association between prior FESS history and QOL improvement.

There are several limitations of our study. First, due to the complex nature of polymicrobial sinus infection, we were not able to determine the appropriateness of antibiotic therapy in patients who did not have antibiotic susceptibility test results for CNS, *C. diphtheria*, *Streptococcus spp.* other than *S. pneumoniae*, *M. catarrhalis*, *Haemophilus spp.*, or anaerobes. Thus, we categorized these patients as a separate undetermined group, and analyzed them separately in the covariate-adjusted linear mixed effects model. Second, anaerobic culture results were not available before May 2008. However, all the other factors remained the same and the same definitions of antibiotic therapy applied to both patients before and after May 2008. Third, even though most CRS patients who underwent FESS in our institute had intraoperative culture, baseline SNOT-22 scores were only available in approximately 55% of all CRS patients who underwent FESS in our institute during the same time period. In addition, not every patient completed all the postoperative follow-up SNOT-22 scores. We compared patient characteristics, and there were no significance between patients included versus not, as well as between patients with and without follow-up SNOT-22 scores. Furthermore, the mixed-effects model we chose for the analysis can provide unbiased estimate when the patients with missing follow-up data had similar characteristics as patients without missing follow-up data. If a SNOT-22 score was missing at a certain time point, the rest of the scores from that same patient were still included in the mixed effects model. Forth, we did not a control group without postoperative antibiotic therapy, and thus the baseline level of QOL improvement attributable to FESS alone cannot be determined. Finally, no objective postoperative outcome was available in this retrospective study, such as systematical endoscopic findings. However, subject complaints reflected by QOL scores were the main reason that CRS patients seek treatment.

Conclusions

Patients with culture-inappropriate postoperative antibiotic therapy had statistically significantly less improvement of QOL during short-term follow-up after FESS as compared to patients with culture-appropriate therapy. This difference was not clinically significant at 1-month follow-up, but became clinically significant at 3-month follow-up. Antibiotic adjustment based on culture results provided immediate non-clinically significant benefit in short-term QOL improvement at 1-month follow-up, but these patients' QOL declined over time. The efforts of culture-inappropriate postoperative antibiotic therapy seem to be washed away at 6-month follow-up with neither statistical nor clinical differences between groups. Despite the limitations, the knowledge gained in our study provides crucial information to guide postoperative antibiotic use in CRS patients. Future randomized clinical trials are needed to evaluate the effect of culture-appropriate antibiotic therapy on CRS prognosis.

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Figure 1.

Pre- and post-FESS change of mean SNOT-22 scores by appropriateness of antibiotic therapy

Table 1

Definitions of appropriateness of postoperative antibiotic therapy

2-week postoperative antibiotic therapy	Definition
Culture-inappropriate	At least one organism identified in intraoperative culture resistant to or not covered by the initially prescribed postoperative antibiotics, and antibiotics were not adjusted after culture results were available.
Culture-appropriate after adjustment	At least one organism identified in intraoperative culture resistant to or not covered by the initially prescribed postoperative antibiotics, but antibiotics were adjusted to culture-appropriate after culture results were available.
Culture-appropriate	All identified organisms had antibiotic susceptibility tests and were covered by the initially prescribed antibiotics.
Undetermined	The identified organisms with antibiotic susceptibility tests were covered by the initially prescribed antibiotics, but there were organisms isolated without antibiotic susceptibility tests or there were unknown results for anaerobic culture.

Table 2

The characteristics of CRS patients by antibiotic therapy (N=376)

Characteristics	Total	Antibiotic therapy		
		Culture-appropriate	Culture-appropriate after adjustment	Culture-inappropriate
n (col%)				Un-determined
Age (y ± SD)	48 ± 13	51 ± 15	49 ± 10	46 ± 17
Sex (Female)	159(42.5)	28(42.4)	10(52.6)	17(63.0)
Race				
White	330(89.4)	58(90.6)	17(89.5)	24(92.3)
Black	29(7.9)	3(4.7)	1(5.3)	1(3.8)
Other	10(2.7)	3(4.7)	1(5.3)	1(3.8)
Asthma	205(54.5)	29(43.9)	13(68.4)	17(63.0)
Polyps	226(60.1)	35(53.0)	14(73.7)	16(59.3)
Allergic rhinitis	248(66.0)	41(62.1)	14(73.7)	18(66.7)
Obstructive sleep apnea	17(4.5)	0(0)	0(0)	2(7.4)
Diabetes	26(6.9)	4(6.1)	4(21.1)	2(7.4)
Smoking				
Former smoker	75(19.9)	16(24.2)	4(21.1)	6(22.2)
Smoker	51(13.6)	7(10.6)	1(5.3)	1(3.7)
Gastroesophageal reflux disease	96(25.6)	11(16.7)	8(42.1)	5(19.2)
Samter's triad	30(8.0)	4(6.1)	2(10.5)	3(11.1)
Prior FESS	227(60.7)	36(54.5)	18(94.7)	21(80.8)
Steroid use				
Nasal	65(17.4)	12(18.2)	2(10.5)	2(7.4)
Oral	119(31.9)	22(33.3)	9(47.4)	9(33.3)
Both	31(8.3)	5(7.6)	2(10.5)	3(11.1)
Nasal rinse	131(35.1)	17(25.8)	8(42.1)	12(46.2)
Preoperative antibiotics	67(17.9)	8(12.1)	2(10.5)	5(18.5)
Total, n (row%)	376	66 (17.6)	19 (5.0)	27 (7.2)

Table 3

The aerobic and anaerobic bacteria isolated

Bacteria	No. of isolates
Aerobes (n=376)	356
<i>Staphylococcus aureus</i>	104
Coagulase-negative staphylococcus	217
<i>Corynebacterium spp.</i>	46
<i>Pseudomonas aeruginosa</i>	31
<i>Streptococcus pneumoniae</i>	17
Other Streptococcus	39
<i>Haemophilus influenzae</i>	11
Other <i>Haemophilus spp.</i>	7
<i>Moraxella catarrhalis</i>	7
Enterobacteriaceae spp	35
<i>Escherichia coli</i>	8
<i>Serratia spp.</i>	6
<i>Enterobacter spp.</i>	5
<i>Citrobacter spp.</i>	5
<i>Klebsiella spp.</i>	3
<i>Proteus mirabilis</i>	3
<i>Morganella morganii</i>	3
<i>Stenotrophomonas maltophilia</i>	1
<i>Pantoea spp.</i>	1
<i>Achromobacter spp.</i>	3
<i>Pseudomonas stutzeri</i>	1
Upper respiratory flora without further identification	26
Anaerobes (n=224)	123
<i>Propionibacterium acnes</i>	82
Non-sporulating gram-positive bacilli other than <i>P. acnes</i>	26
<i>Peptostreptococcus spp.</i>	24
<i>Fusobacterium nucleatum</i>	2
Gram negative bacilli or rods	4
Gram negative cocci	1
Mixed anaerobic flora	7
No growth	10

Table 4

Unadjusted and adjusted coefficients and 95% CIs from linear mixed effects regression models

Difference of natural log transformed SNOT-22 scores	Unadjusted			Adjusted		
	Coef.	95% CI	p-value	Coef.	95% CI	p-value
From baseline to 1-month follow-up						
Culture-appropriate		Reference			Reference	
Culture-appropriate after adjustment	−0.09	−0.63, 0.46	0.755	−0.01	−0.57, 0.55	0.964
Culture-inappropriate	0.71	0.22, 1.21	0.005	0.83	0.18, 1.49	0.013
Undetermined	−0.06	−0.38, 0.26	0.700	−0.03	−0.35, 0.29	0.836
From baseline to 3-month follow-up						
Culture-appropriate		Reference			Reference	
Culture-appropriate after adjustment	0.84	0.26, 1.43	0.004	0.87	0.28, 1.47	0.004
Culture-inappropriate	0.93	0.39, 1.47	0.001	1.06	0.38, 1.74	0.002
Undetermined	0.51	0.13, 0.89	0.009	0.52	0.15, 0.90	0.007
From baseline to 6-month follow-up						
Culture-appropriate		Reference			Reference	
Culture-appropriate after adjustment	0.15	−0.45, 0.76	0.620	0.19	−0.42, 0.81	0.537
Culture-inappropriate	0.30	−0.24, 0.85	0.275	0.56	−0.15, 1.27	0.123
Undetermined	−0.13	−0.49, 0.22	0.461	−0.14	−0.50, 0.21	0.431
From baseline to postoperative follow-up with versus without the covariates below[*]						
Asthma		NA		0.19	0.03, 0.35	0.021
Diabetes		NA		0.34	0.03, 0.64	0.031
Prior FESS		NA		0.07	−0.09, 0.24	0.396
Preoperative antibiotics		NA		0.11	−0.10, 0.32	0.308

* Their effects on QOL improvement were averaged across all postoperative follow-up time points.