

Impaired mucosal healing and infection associated with *Staphylococcus aureus* after endoscopic sinus surgery

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ABSTRACT

Background: Differentiating normal nasal discharge and postoperative crust from infection after endoscopic sinus surgery (ESS) can be difficult. We investigated whether bacteria cultured at operation was predictive for postoperative mucosal infection—defined as frank pus, thick mucus, and/or abnormal crusting seen on endoscopic examination associated with positive microbiology.

Methods: The records of 48 patients with chronic rhinosinusitis (CRS) with infection at the time of ESS were retrospectively reviewed. Results of intraoperative cultures were compared with those taken at the time of postoperative mucosal infection.

Results: Fourteen of 16 patients (87.5%) with intraoperative infection with *Staphylococcus aureus* progressed to postoperative mucosal infection with *S. aureus*, whereas patients who cultured “other” bacteria intraoperatively progressed to postoperative mucosal infection in 6/19 cases (31.6%), with *S. aureus* cultured in only 3/19 cases (15.8%; $p = 0.0001$).

Conclusion: *S. aureus* infection at ESS predicts for abnormal, *S. aureus*-associated mucosal healing and infection post-ESS. Although a prospective trial is warranted, these findings suggest a future role for aggressive anti-*S. aureus* therapy peri- and/or postoperatively in patients who culture positive for this organism to improve postsurgical outcomes.

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Key words: Endoscopic sinus surgery, nasal crusting, postoperative infections, sinus cavity infections, *Staphylococcus aureus*, surgical outcomes, wound healing

Postoperative infections after endoscopic sinus surgery (ESS) for chronic rhinosinusitis (CRS) are common, although the exact incidence is not well documented in the literature.^{1,2} The impact of such infections on the healing of the sinuses and the eventual outcome of surgery is also unknown. Nasal discharge is common and often subjectively discomforting post-ESS³ but differentiating normal postoperative crust and blood clot from an infection is often difficult and therefore treatment may not always be adequate.

The role of bacteria in CRS is known to be an important one, because even healthy, disease-free paranasal sinuses are no longer thought to be sterile.⁴ After ESS for CRS, multiple studies have also shown the presence of culture-proven bacterium in aerated sinuses with apparent healthy, healing mucosa. Coagulase-negative *Staphylococcus* and *Staphylococcus aureus* are the most common isolates in this setting.^{5,6}

Although coagulase-negative *Staphylococcus* is considered a skin and paranasal sinus contaminant with questionable pathogenicity,^{7,8} *S. aureus* in the postoperative period has a potentially more pathogenic role. Not only is it the most common isolate in acute exacerbations of CRS,⁹ *S. aureus* has also been shown to be the most common organism found at surgery for CRS,¹⁰ as well as the most common isolate in postoperative infection after ESS.¹ The exact role of *S. aureus*, especially pertaining to mucosal healing, in the perioperative and early postoperative periods still is to be fully documented in the literature.

To our knowledge, there has been no study specifically exploring the role of *S. aureus* infection after ESS, particularly during the early postoperative period. This study, therefore, was designed to determine the role of *S. aureus* during this time, specifically in patients with active infection at surgery.

MATERIALS AND METHODS

Study Design and Population

This was a retrospective chart review performed in the tertiary rhinology practice of the senior author (P.J.W.). Records of all patients undergoing ESS for CRS in an 18-month period between January 1, 2007 and June 31, 2008 were retrospectively reviewed. All patients met the American Academy of Otolaryngology–Head and Neck Surgery diagnostic criteria for CRS.¹¹ Patients were included in the study if, at operation, the presence of any potential infectious etiology (such as frank pus, submucosal abscesses, fungus, eosinophilic mucin, or abnormal thick mucus) was observed with the resultant microbiology result known.

Standard post-ESS management in these patients included 5 days of a broad-spectrum oral antibiotic (usually amoxicillin and clavulanic acid) and at least 2 months of nasal lavage with saline. Where polyps were found at the time of surgery, patients were given a 3-week tapered course of prednisolone postoperatively. Routine follow-up post-ESS was at 2 and 6 weeks. Surgeon and/or patient concern may have resulted in increased frequency of patient follow-up in some instances.

In our practice, swabs for microscopy, culture, and sensitivities are sent in all patients in whom evidence of potential infection is observed at surgery (as outlined previously in this article). Patients were not included in the overall analysis if there were no such signs of infection at surgery, even though swabs may have been sent for academic reasons in these cases.

Exclusion Criteria

Patients were excluded from the study if they were not followed up twice within the 90-day postoperative period by the operative surgeon.

Data Collection

Preoperative demographic data including age, sex, and medical history (including history of smoking, immunodeficiency, gastroesophageal reflux disease, asthma, and aspirin sensitivity) were recorded. A history of previous sinus surgery was noted, and results of

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allergy testing (skin-prick or modified radioallergosorbent testing) for each patient were also obtained.

Intraoperative records were analyzed specifically for the presence of frank pus, submucosal abscesses, fungus, eosinophilic mucin, or abnormal thick mucus. The subsequent microbiological results were obtained where these features of infection were observed.

All patients were examined endoscopically at each postoperative visit for the presence of frank pus, thick mucus, or abnormal crusting. Endoscopically guided cultures were obtained if any of these features were present. The combination of these abnormal endoscopic findings and a subsequent microbiology result showing at least one causal organism defined postoperative infection in this study. Thus, the diagnosis of postoperative mucosal infection was made objectively rather than subjectively, reflecting poor mucosal evolution postoperatively rather than overt symptomatology of sinus infection.

Data Analysis

Tests on count data were made using Fisher's exact test; tests on continuous data were made using Wilcoxon rank-sum test.

RESULTS

Demographic Data

One hundred forty-one consecutive procedures for CRS were performed during the study period. Ninety-four patients (52 men and 42 women; mean age, 50.0 years) met the follow-up criteria. A significant proportion of patients excluded (32/47 or 68.1%) were from interstate, their follow-up being performed by their referring ear, nose, and throat specialist rather than the operative surgeon.

Sixty-two of 94 (66.0%) procedures were revision sinus surgery, with 38/94 (40.4%) of patients having had two or more previous procedures, reflecting the tertiary referral nature of our practice. A breakdown of diagnosis classification is shown in Table 1.

Intraoperative Microbiology

Forty-eight of 94 patients (51.1%) had evidence of frank pus, submucosal abscesses, fungus, eosinophilic mucin, and/or abnormal thick mucus and had swabs sent for microbiology and, hence, were therefore included in the study. Multiple organisms were isolated in 6/48 cases (12.5%) and 13/48 cases (27.1%) were negative with no growth recorded. There were 41 bacterial isolates in total. As shown in Table 2, the predominant isolate was found to be *S. aureus*, present in 16/48 (33.3%) of patients.

Swabs for microscopy, culture, and sensitivities were not sent in 10/94 (10.6%) patients with documented evidence of infectious etiology at surgery; hence, resultant microbiology is unknown. Of these

Table 1 Diagnosis*

	n
AFS	4
AFS-like	6#
CRS with polyps	47§
CRS without polyps	24
Samter's triad	5¶
Unknown	8
Total	94

*Based on current rhinosinusitis consensus research definitions and clinical trial guidelines.¹²

#Negative for fungal elements, otherwise criteria for AFS met.

§Defined as polyps noted at endoscopic sinus surgery, regardless of site.

¶Aspirin sensitivity, asthma, and polyposis.

AFS = allergic fungal rhinosinusitis; CRS = chronic rhinosinusitis.

Table 2 Intraoperative bacteriology

	n
<i>Staphylococcus aureus</i>	16
<i>Pseudomonas</i>	7*
Coagulase negative staph/staph epidermis	4#
<i>Escherichia coli</i>	3§
<i>Proteus mirabilis</i>	2*
<i>Streptococcus pneumoniae</i>	2
<i>Moraxella</i>	1
<i>Haemophilus influenzae</i>	1§
<i>Corynebacterium</i>	1#
<i>Klebsiella</i>	1¶
<i>Streptococcus G</i>	1¶
<i>Citrobacter diversus</i>	1*
<i>Acinetobacter</i>	1
Total	41
No growth	13

*Includes a single episode where organism and *S. aureus* cultured together.

Includes a single episode where coagulase negative staph and *Corynebacterium* cultured together.

§ Includes a single episode where *E. coli* and *Haemophilus influenzae* cultured together.

¶ Includes a single episode where *Klebsiella* and *Streptococcus G* cultured together.

patients, 2/10 (20.0%) progressed to infection with *S. aureus*, 2/10 (20.0%) progressed to infection with "other" bacterium, and 6/10 (60.0%) had an unremarkable postoperative period. These patients were not included in further analysis.

Postoperative Microbiology

Of the 48 patients, 28 (58.3%) had evidence of abnormal mucosal healing (such as frank pus, thick mucus, or abnormal crusting), plus subsequent positive microbiology, at one or more postoperative visit. These patients, therefore, fit our definition of post-ESS mucosal infection. There were 37 episodes of post-ESS infection in total, with multiple organisms cultured in 5/37 episodes (13.5%) resulting in 42 isolates. Again, *S. aureus* was the most common isolate, present in 30/37 episodes (81.1%; Table 3).

Postoperative *S. aureus*

Fourteen of 16 patients (87.5%) of patients who had intraoperative infection with *S. aureus* progressed to postoperative infection with *S. aureus* (Table 4). Those without intraoperative *S. aureus* progressed to infection with *S. aureus* in 8/32 of cases (25.0%). This was a statistically significant difference ($p = 0.0001$). In contrast, patients who

Table 3 Bacteriology at postoperative mucosal infection

	n
<i>Staphylococcus aureus</i>	30
<i>Pseudomonas</i>	5
<i>Escherichia coli</i>	2*
Coagulase negative staph	1
<i>Staphylococcus intermedius</i>	1
<i>Haemophilus influenzae</i>	1#
Group G <i>Streptococcus</i>	1#
<i>Klebsiella</i>	1#
Total	42

*Includes two episodes where organism and *S. aureus* cultured together.

Includes a single episode where organism and *S. aureus* cultured together.

Table 4 Number of patients by intraoperative and postoperative mucosal infection

	Post-ESS Mucosal Healing			Total
	Complicated by <i>Staphylococcus aureus</i> * Infection	Complicated by "Other" Infection	Uncomplicated, Infection Free	
Intraoperative microbiology				
<i>S. aureus</i> *	14	0	2	16
Other	3	3	13	19
No growth	5	3	5	13
Total	22	6	20	48

*Note, where *S. aureus* was isolated in conjunction with another bacterium at a particular episode, this has been recorded as a *S. aureus* infection rather than an "other."

ESS = endoscopic sinus surgery.

cultured "other" bacterium intraoperatively showed good mucosal recovery, with mucosal infection in 6/19 cases (31.6%) and associated with *S. aureus* in only 3/19 cases (15.8%). There were no cases in which a patient who had intraoperative infection with *S. aureus* progressed unfavorably to postoperative mucosal infection with a different bacterium. Importantly, where *S. aureus* was cultured along with another bacterium, this was recorded as an *S. aureus* infection in keeping with the importance of this bacterium in this setting. The mean time to first episode of postoperative mucosal infection with *S. aureus* was 37.5 days (Table 5).

Postoperative Mucosal Infection in Patients without Infection at Surgery

Thirty-six of 94 (38.3%) patients had no evidence of infectious etiology at surgery; 5/36 (13.9%) progressed to postoperative mucosal infection with *S. aureus*, with 4/36 (11.1%) progressing to mucosal infection with "other" bacterium. Hence, 27/36 (75.0%) had good mucosal recovery with an unremarkable postoperative period.

DISCUSSION

In our series, 51.1% of patients undergoing ESS for CRS had signs of infection at the time of surgery, from which *S. aureus* was the most common bacterial isolate. This study has shown that in patients with *S. aureus* infection, the 90-day postoperative period is complicated by mucosal infection with *S. aureus* in 87.5% of cases.

Postoperative infection is common and is a major cause of postoperative morbidity, irrespective of procedure or surgical subspecialty.¹³ As a surgical procedure, ESS has a number of unique features that predispose to increased rates of postoperative infection. ESS involves removal of bone and mucosa to extirpate disease, improve aeration of the sinuses, and maximize the dimensions of the natural sinus ostia to facilitate mucociliary clearance.¹⁴ This results in a loss of the integrity

of the mucosal surface, reducing its physical protective effect and altering the innate immune functions of the mucosal layer. Additionally, during and after ESS, the surgical site is exposed to airborne pathogens as well as those from the skin and upper aerodigestive tract.

Despite the widespread use of ESS, there is surprisingly little literature on infection after this procedure. By including all patients with abnormal mucosal healing post-ESS (such as pus, thick mucus, or abnormal crusting as seen on endoscopic examination; positive microbiology was also required) in our definition of mucosal infection, we have captured many patients who may have otherwise been thought to have normal post-ESS nasal discharge. This definition is entirely subjective and quite different from that of acute bacterial sinusitis—a diagnostic picture traditionally used to describe infection post-sinus surgery.²

The role of *S. aureus* in the immediate postoperative period has not been fully explored. Bhattacharyya *et al.*¹ compared the bacteriology of asymptomatic patients post-ESS with subsequent bacteriology in the same patients if—and when—they later presented with acute infective exacerbations of CRS (mean follow-up, 14.5 months). This study showed that 75% of post-ESS infections had arisen *de novo*, suggesting a dynamic role for *S. aureus* in this setting.¹ However, the role of intraoperative bacteriology in these patients was not explored. In contrast, our study highlights the importance of *S. aureus* infection present at the time of surgery and the subsequent failure to clear this infection with our current postoperative treatment regime. Where there is *S. aureus* infection at operation, the 90-day postoperative period is more likely to be complicated by mucosal infection with *S. aureus* than be infection free ($p = 0.0001$). This suggests that postoperative infection with *S. aureus* is not the result of *de novo* infection, but rather the result of persistent *S. aureus* infection refractory to surgery.

By contrast, in those who culture an organism other than *S. aureus* from intraoperative infection, progression to postoperative mucosal

Table 5 Mean time in days post-operatively to first episode of mucosal infection

	Post-ESS Mucosal Healing			Time
	Complicated by <i>Staphylococcus aureus</i> Infection*	Complicated by "Other" Infection	Uncomplicated, Infection Free	
Intraoperative microbiology				
<i>S. aureus</i> *	38.4 (14–69)	—	NA	38.4 (14–69)
Other	34.0 (16–64)	42.7 (21–84)	NA	38.3 (16–84)
No growth	37.2 (17–63)	53.7 (33–72)	NA	43.4 (12–72)
Time	37.5 (14–69)	48.2 (21–84)	NA	

*Note, where *S. aureus* was isolated in conjunction with another bacterium at a particular episode, this has been recorded as a *S. aureus* infection rather than an "other."

ESS = endoscopic sinus surgery.

infection is less common (6/19 or 31.7%), with *de novo* *S. aureus* attributable in 50% of postoperative infections in this group. Mean time to first postoperative mucosal infection with *S. aureus* was 10.7 days less than for other infections (37.5 days versus 48.2 days, postoperatively). Although this result was not statistically significant ($p = 0.26$), this may be a reflection of the especially pathogenic nature of *S. aureus* during this period.

Interestingly, the patients in whom no organisms were cultured from intraoperative swabs, despite the presence of pus intraoperatively, did worse than the patients who grew other bacteria, progressing to postoperative mucosal infection in 8/13 (61.5%) of cases. The significance of this is unknown. However, this may support a role for biofilms in the pathogenesis of CRS.¹⁵ In this manner biofilm bacteria may be difficult to culture intraoperatively. However, they may be stressed or disrupted during the surgical procedure, resulting in a phenotypic shift and shedding of planktonic bacteria, which may then be cultured in the postoperative period.

In patients without infectious etiology at surgery, progression to postoperative mucosal infection occurred in 9/36 (25.0%), a rate less than one-half that observed in the study group (25.0% versus 51.1%; $p = 0.004$). This would further suggest that postoperative mucosal infection occurs as a result of surgically recalcitrant disease rather than *de novo* infection.

Thus, those patients who grow *S. aureus* on intraoperative culture are a particularly recalcitrant subset of patients. Additional research using the prospective collection of data with prior determined diagnostic criteria is warranted to confirm these results and further explore postoperative *S. aureus*-related mucosal infection. Nevertheless, the current results suggest that our treatment protocols are not sufficient to clear *S. aureus* infection in this group and that new, novel treatment approaches may be required for these patients. One such potential modality may be nasal lavage with mupirocin.¹⁶

CONCLUSION

The presence of *S. aureus* infection at ESS is seemingly a strong predictor for abnormal, *S. aureus*-mediated post-ESS mucosal healing and infection. Additional research using prospective data collection is required, although it appears that there may be a potential role for aggressive anti-*S. aureus* therapy peri- and/or postoperatively as an adjuvant therapy in addition to surgery to improve postsurgical outcomes in patients thought to be at high risk.

REFERENCES

1. Bhattacharyya N, Gopal HV, and Lee KH. Bacterial infection after endoscopic sinus surgery: A controlled prospective study. *Laryngoscope* 114:765–767, 2004.
2. Ragab SM, Lund VJ, and Scadding G. Evaluation of the medical and surgical treatment of chronic rhinosinusitis: A prospective, randomised, controlled trial. *Laryngoscope* 114:923–930, 2004.
3. Lee JY, and Byun JY. Relationship between the frequency of postoperative debridement and patient discomfort, healing period, surgical outcomes, and compliance after endoscopic sinus surgery. *Laryngoscope* 118:1868–1872, 2008.
4. Brook I. The role of bacteria in chronic rhinosinusitis. *Otolaryngol Clin North Am* 38:1171–1192, 2005.
5. Bhattacharyya N, and Gopal HV. The microbiology of the ethmoid sinus after endoscopic sinus surgery. *Ear Nose Throat J* 81:458–461, 2002.
6. Al-Shemari H, Abou-Hamad W, Libman M, et al. Bacteriology of the sinus cavities of asymptomatic individuals after endoscopic sinus surgery. *J Otolaryngol* 36:43–48, 2007.
7. Jiang RS, Hsu CY, and Jang JW. Bacteriology of the maxillary and ethmoid sinuses in chronic sinusitis. *J Laryngol Otol* 112:845–848, 1998.
8. Gordts F, Halewyck S, Pierard D, et al. Microbiology of the middle meatus: A comparison between normal adults and children. *J Laryngol Otol* 114:184–188, 2000.
9. Lin A, and Busaba NY. *Staphylococcus aureus* and endoscopic sinus surgery. *Curr Opin Otolaryngol Head Neck Surg* 14:19–22, 2006.
10. Kostamo K, Richardson M, Virolainen-Julkunen A, et al. Microbiology of chronic hyperplastic sinusitis. *Rhinology* 42:213–218, 2004.
11. Lanza DC, and Kennedy DW. Adult rhinosinusitis defined. *Otolaryngol Head Neck Surg* 117:S1–S7, 1997.
12. Meltzer EO, Hamilos DL, and Hadley JA. Rhinosinusitis: Establishing definitions for clinical research and patient care. *Otolaryngol Head Neck Surg* 131(suppl 6):S1–62, 2004.
13. Fry DE. The economic costs of surgical site infection. *Surg Infect (Larchmt)*. 3(suppl 1):S37–S43, 2003.
14. Messerklinger W (ed.). Endoscopic operation. In *Endoscopy of the Nose*. Munich: Urban and Schazenberg. 49–50, 1978.
15. Palmer J. Bacterial biofilms in chronic rhinosinusitis. *Curr Opin Otolaryngol Head Neck Surg* 14:19–22, 2006.
16. Uren B, Psaltis A, and Wormald PJ. Nasal lavage with mupirocin for the treatment of surgically recalcitrant chronic rhinosinusitis. *Laryngoscope* 118:1677–1680, 2008. □

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