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The Impact of Diabetes Mellitus on Outcomes of Endoscopic Sinus Surgery: A nested case-control study

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Abstract

Background—Given the immune impairment associated with diabetes mellitus (DM), its impact on chronic rhinosinusitis (CRS) is a potentially relevant concern, yet it has not been well-studied. A single retrospective study reported worse post-operative quality of life outcomes in diabetic CRS patients. Our study evaluated the effect of comorbid DM on outcomes of endoscopic sinus surgery (ESS) using a prospective study design.

Methods—Using a multi-centered, prospective cohort of patients (n=437) undergoing ESS for recalcitrant CRS, a nested case-control comparison was performed between 20 DM adult patients (cases) and 20 non-diabetic patients (controls), matched 1:1 for age and Lund-Mackay CT scores. Outcome measures included 22-item Sinonasal Outcome Test (SNOT-22), Rhinosinusitis Disability Index (RSDI), Patient Health Questionnaire (PHQ-2), and Brief Smell Identification Test (BSIT).

Results—Mean follow-up was similar between cases (12.6[6.0] months) and controls (12.9[5.9] months; p=0.862). All preoperative scores were statistically equivalent between DM and non-DM cohorts. Both cohorts showed significant post-ESS improvement in SNOT-22 (p=0.001) and RSDI scores (p<0.001), and no significant change in PHQ-2 or BSIT scores. The magnitude of score changes was statistically equivalent between the two cohorts for all outcome measures with no

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differences in postoperative score changes between insulin-dependent diabetics and those managed by oral hypoglycemics or dietary restriction (p 0.444).

Conclusions—Diabetic CRS patients experience similar degrees of symptomatic benefit from ESS compared to controls. Insulin dependence does not appear to adversely affect surgical outcome but a larger cohort would better assess the effect of diabetes type and control on surgical outcomes in CRS.

MeSH Key Words

Diabetes mellitus; comorbidity; sinusitis; quality of life; outcome assessment; endoscopy

INTRODUCTION

Chronic rhinosinusitis (CRS) is one of the most common chronic diseases in the US.^{1–3} The benefit of endoscopic sinus surgery (ESS) in medically recalcitrant CRS has been well established in terms of symptoms, quality of life (QOL) scores and endoscopic findings after sinus surgery.^{4–7} Comorbidities in CRS such as asthma, allergy, acetylsalicylic acid (ASA) sensitivity, depression, and prior sinus surgery have been shown to adversely impact surgical outcomes.^{4,8–10} However the effect of diabetes mellitus (DM), one of the most common comorbidities in the US, is still not well known. The prevalence of diabetes in the US population is 8.3%, and in 2011 more than 220 million people worldwide were living with DM.^{11,12} One might predict that comorbid DM in CRS would be associated with more severe symptoms and worse surgical outcomes in CRS given the association of DM with impaired innate and adaptive immunity as well as compromised wound healing and organ failure.^{11,13}

A single previous retrospective study by Zhang et al. reported worse short-term postoperative QOL outcomes in CRS patients with DM with higher susceptibility to gram negative infections.¹⁴ The goal of our study was to evaluate the effect of comorbid DM on surgical outcomes in patients with CRS using a nested case-control study design drawn from a large prospective cohort. Our comparators were validated measures of clinical disease severity and disease-specific treatment outcome measures.

METHODS and MATERIALS

Study population

Adult patients (≥ 18 years of age) with an existing diagnosis of medically recalcitrant CRS were prospectively enrolled into an on-going, North American, multi-institutional, observational treatment outcomes investigation. Enrollment sites consisted of three academic rhinology practices, including Oregon Health & Science University (OHSU, Portland, OR, USA), the Medical University of South Carolina (MUSC, Charleston, SC, USA), and Stanford University (Stanford, CA, USA). The Institutional Review Board at each enrollment site provided approval and annual review of all study protocols and the informed consent process.

Inclusion criteria consisted of a current diagnosis of refractory CRS as determined by the 2007 Adult Sinusitis Guidelines endorsed by the American Academy of Otolaryngology – Head and Neck Surgery¹; previous treatment within the past year with at least a single course of broad spectrum or culture directed antibiotics (2 weeks duration) and either topical nasal corticosteroid sprays (3 weeks duration) or a 5-days trial of systemic corticosteroid therapy. Each patient enrolled was required to complete all study questionnaires and provide informed consent in English. Patients were ensured that study participation would in no way change the elected treatment course.

Surgical Intervention – Endoscopic Sinus Surgery

All study subjects failed medical therapy and selected endoscopic sinus surgery as the next treatment modality. The extent of sinus surgery was based on the extent of patient's disease and intraoperative judgment of the enrolling physician/surgeon. The specific procedures performed on each patient were recorded and included either unilateral or bilateral maxillary antrostomy, partial or total ethmoidectomy, sphenoidotomy, frontal sinusotomy, inferior turbinate reduction, septoplasty, and computer navigation.

Clinical Disease Severity Measures

Patient data from this cohort included age, gender, race, ethnicity, history of prior sinus surgery, nasal polyps, asthma, ASA sensitivity, current tobacco use (packs/day), alcohol consumption, depression, allergies (confirmed via skin prick or RAST testing), ciliary dysfunction/cystic fibrosis, comorbid diabetes, exacerbations of recurrent acute rhinosinusitis (RARS), immunodeficiency/immunosuppression, septal deviation, turbinate hypertrophy, and asthma/sinusitis related steroid dependency. Additional diabetic history was retrospectively collected from medical records including DM type and treatment, blood glucose levels, and HbA1c levels when available.

Objective baseline measures of disease included computed tomography (CT) and endoscopic scores which were recorded utilizing established scoring systems, the Lund-Kennedy endoscopy scoring system, where higher scores indicate worse disease severity (score range: 0–20) and the Lund-Mackay bilateral scoring system for CT, where higher scores again represent worse disease severity (score range: 0–24).

Disease-specific Treatment Outcome Measures

Study participants were asked to complete three QOL survey instruments: the 22-item Sinonasal Outcome Test (SNOT-22), the Rhinosinusitis Disability Index (RSDI), and the 2-item Patient Health Questionnaire (PHQ-2). The SNOT-22 is a validated, treatment outcome measure of chronic sinonasal conditions utilizing a Likert scale (0–5) scoring system. Higher total scores on the SNOT-22 suggest worse patient functioning and symptom severity (score range: 0–110).¹⁵ The RSDI is a 30-item, disease-specific survey that evaluates the impact of CRS on a patient's physical (score range: 0–44), functional (score range: 0–36), and emotional (score range: 0–40) sub-domains utilizing a Likert scale (0–4) scoring regimen.¹⁶ The PHQ-2 is an abridged version of the PHQ-9 instrument developed as a depression screening tool (score range: 0–6). A score of 3 or more is described as an optimal cut-point for a positive indication for depression.¹⁷ The PHQ-2 was included as a measure of

comorbid chronic illness, in addition to disease-specific outcomes measures, due to the known influence of depression on outcomes of CRS.^{18,19} The enrolling physician/surgeon at each location was blinded to all patient-based survey responses for the study duration.

Olfactory function was operationalized during preoperative and postoperative follow-up assessments using the Brief Smell Identification Test (BSIT).²⁰ The BSIT is a validated, 12-item quantitative test of olfactory impairment that utilizes 12 microencapsulated “scratch and sniff” odorant strips activated with a standard #2 pencil (score range: 0–12). Study participants are asked to identify specific odors out of four possible choices. Lower total scores indicate worse olfactory function. Male and female respondents can be categorized as having “normal” (BSIT ≥ 9) or “abnormal” (BSIT <9) olfaction determined in each participant based on young male and female adult norms.

Study participants were asked to complete all study survey instruments and BSIT olfactory evaluations preoperatively and at subsequent post-operative clinic visits. Participants with at least 6 months follow-up were included in final analyses while patients were considered lost to follow-up if they had not completed any survey evaluations within 18 months postoperatively. Additional endoscopic scores were collected if subjects underwent postoperative endoscopy exams during standard follow-up appointments

Nested Case-Control Selection

A nested case-control design was selected to evaluate differences in surgical outcomes given the relative rarity of DM within the population of subjects with CRS. Case subjects were identified as study participants with a confirmed diagnosis of either insulin-dependent or non-insulin-dependent comorbid DM. Control subjects were selected from the remaining cohort among study participants with CRS without a concurrent diagnosis of DM. Study cases were matched using a 1:1 ratio to controls based on age (± 3 years) and Lund-Mackay CT scores (± 4 units).

Exclusion Criteria

Study participants with a concurrent diagnosis of cystic fibrosis, autoimmune disease, immunosuppression or any type of immunodeficiency were excluded as potential confounding diagnoses. Participants were removed from final analyses if they did not complete baseline QOL evaluations, had not yet reached the 6-month follow-up appointment window, or were lost to follow-up.

Data Management and Statistical Analyses

De-identified data was collected and transferred from each enrollment site to the central coordinating site and entered into a secure, relational database (Microsoft Access, Microsoft Corp., Redmond, WA., USA) using standardized clinical research forms. Statistical analysis was completed using a commercially available statistical software package (SPSS v.22.0, IBM Corp., Armonk, NY, USA). Descriptive analysis of clinical disease severity measures, demographics, clinical characteristics, surgical procedures, and outcome measures was completed to evaluate assumptions of linearity, distribution, and normality. Mean values and [standard deviations] were reported when appropriate. Differences in preoperative

demographics, clinical characteristics, surgical procedures, and survey response scores between two independent groups were evaluated using the Mann-Whitney U tests or Pearson's chi-square (χ^2) or Fisher's exact testing where appropriate. Within group, mean differences over time (postoperative – preoperative scores) were compared using Wilcoxon Signed-Rank tests or two-sided matched pair t-tests for continuous measures or McNemar's χ^2 for paired sample frequencies. Statistical associations were determined at the 0.050 level of significance.

RESULTS

Final Study Cohorts

A total of 473 participants met eligibility and inclusion requirements and consented to endoscopic sinus surgery between March 2011 and April 2014. A total of 20 (4.2%) participants presented with comorbid DM across all three enrollment sites (OHSU, n=7; MUSC, n=8; Stanford, n=5) and were matched to 20 non-diabetic CRS controls with similar follow-up. Baseline demographics, clinical characteristics, and clinical disease severity measures were not significantly different between case and control subgroups (Table 1). Furthermore, the incidence of prior sinus surgery was identical in both case (55%) and control groups (55%).

Case study subjects with diabetes were found to have a mean preoperative blood glucose level of 138.5[49.4] mg/dL. (range: 75.0–258.0 mg/dL.). Preoperative hemoglobin A1C was available for 9/20 cases subjects with an average 7.0% (range: 5.3%–8.9%). A total of 5 case subjects were controlling their DM using strict dietary regimen, 10 cases were using oral medication, and 4 cases were using insulin supplementation, while one study subject used a combination of oral and insulin therapies.

Baseline SNOT-22, RSDI, and PHQ-2 scores were similar between study subjects with and without DM (Table 2). The extent of surgical procedure performed was statistically similar between case and control cohorts for all sinuses except the maxillary; maxillary antrostomy was performed more often in the CRS control group than in the DM group ($p=0.013$) (Table 3). Case subjects with DM were followed for an average of 12.6[6.0] months compared to 12.9[5.9] months for controls ($p=0.862$).

Postoperative Improvement in Clinical Disease Severity Measures

Changes in clinical disease severity measures were evaluated between the preoperative and most recent follow-up time points for the 20 case subjects with DM and 20 matched controls. Mean Lund-Kennedy endoscopy scores during follow up were available for 7 patients in the case subjects group with DM, however the difference was not significantly different over time (6.5[4.4] to 4.1[3.6]; $p=0.854$). Mean endoscopy scores were found to significantly improve from 6.9[4.5] to 4.2[2.9] for control subjects ($n=12$; $p=0.026$). The change in mean endoscopy scores during follow up was statistically similar between case and controls ($p=0.261$). Average olfactory BSIT scores were not found to change significantly after sinus surgery for either case (8.9[3.0] to 8.3[2.8]; $p=0.290$) or control (9.8[2.8] to 9.9[2.0]; $p=0.788$) subjects.

Postoperative Improvements in Symptom and Quality of Life Measures

Significant postoperative improvements were reported by both case and control subjects on the SNOT-22 survey total scores, RSDI total scores, as well as all three sub-domains of the RSDI (Table 4) while no significant changes in PHQ-2 scores were found for either group. The average magnitude of postoperative change for each patient-reported outcome measure was statistically similar between DM case subjects and matched controls ($p>0.134$; Table 5).

Within the case cohort, the type of DM did not affect the degree of postoperative improvement. Subjects who were insulin dependent ($n=5$) had similar degrees of improvement in patient reported outcome measures to those who were controlling blood glucose levels through oral hypoglycemic medication regimens and/or dietary restriction ($n=15$; $p=0.444$).

In addition, patients who had well controlled blood glucose preoperatively (fasting blood glucose ≤ 110 mg/L.) showed similar degree of improvement in patient reported outcome measures as those with poorly controlled blood glucose (fasting blood glucose >110 mg/L.) (SNOT-22, $p=0.393$; RSDI, $p=0.967$; PHQ-2, $p=0.699$). Data regarding the hemoglobin A1C levels were available only for 9 patients. We compared diabetic patients with good metabolic control (A1C level ≤ 6.5) to those with poor metabolic control (A1C level $>6.5\%$). The change in outcome scores was not statistically different for any of the patient reported outcome measures (SNOT-22, $p>0.999$; RSDI, $p=0.286$; PHQ-2, $p=0.410$).

DISCUSSION

Drawn from a large multi-centered prospective cohort, our nested case-control study suggests that diabetic patients with CRS experience similar symptomatic benefit from ESS compared to matched non-diabetic patients with CRS. Comorbid diabetes was a relatively rare condition in our study, with a prevalence of 4.2%, which is lower than the prevalence of diabetes in the general population (8.3%). A previously published series of diabetic patients with CRS by Zhang et al reported a prevalence of 5.0% which is also lower than the general prevalence of diabetes.¹⁴

After matching cases and controls for age and Lund-Mackay CT score, the groups showed very good comparability in other clinical dimensions. Cases and controls had similar preoperative degrees of QOL impairment, as measured by the SNOT-22 and RSDI instruments. Likewise, cases and controls showed no significant differences in endoscopy scores or olfactory function at baseline. There was also no difference in the frequency of prior surgery between cases and controls. Moreover, the overall extent of endoscopic sinus surgery performed was similar between cases and controls. Diabetic patients had similar QOL improvement after surgery as matched non-diabetic patients, and furthermore insulin dependence did not appear to adversely affect surgical outcome more so than other forms of diabetes.

To date, there has been only one previous study that has evaluated the impact of diabetes on surgical outcomes after ESS.¹⁴ Zhang et al. compared 19 CRS patients with comorbid DM to 357 patients without DM in a retrospective cohort study and concluded that DM was

associated with significantly worse short term outcomes after FESS at 6 months postoperatively. The authors found that DM patients had a lesser degree of improvement of SNOT-22 at 6 months postoperatively ($p=0.047$) but not at 1- and 3 months postoperatively. There are several important study differences which may explain the variation in reported findings in our investigation. First, not every patient in the Zhang study completed SNOT-22 evaluations at every follow-up time point, and patients with these missing dependent variables were still included using mixed-effects linear modeling. Secondly, Zhang et al. reported 6-month follow-up compared to the average 12-month follow-up in the current study. It is conceivable that both patients with and without comorbid DM experience worsening of symptoms between the 6 and 12-month follow-up time points, as measured by the SNOT-22 instrument. Lastly, the only comparable outcome measure employed by both studies was the SNOT-22, with no other subjective or objective measures that could be compared between each study.

The theoretical risk of poor surgical outcomes incurred by comorbid DM is quite accepted given the known negative impact of DM on wound healing established by numerous experimental and clinical studies.^{21–23} The effect of preoperative glycemic control on postoperative complications has also been well studied in many fields such as thoracic and cardiovascular surgery, neurosurgery and orthopedic surgery.^{24–26}

However, the actual risk may be lower than imagined. A Cochrane review studied the effect of intensive versus conventional glycemic control on surgical outcomes and post-operative complications in 12 randomized clinical trials encompassing 1403 diabetic patients.²⁷ This review found no significant differences between the two glycemic control strategies. However, heterogeneity was found in the inclusion criteria, the range of glucose levels considered to be “tight” control, and duration of follow-up.

There is evidence that when DM is poorly controlled, patients do experience a higher rate of complications. Guzman et al. studied 10,532 patients with uncontrolled DM undergoing cervical spine surgery and found that uncontrolled DM was associated with a significant increase in the prevalence of postoperative cardiac, respiratory, and genitourinary complications, pulmonary embolism and postoperative infection.²⁵ Furthermore, Humphers et al. and Han et al. reported in retrospective studies that elevated HbA1c level was an independent risk factor for postoperative complications in patients with diabetes undergoing orthopedic surgery.^{26,28} Indeed, the risk of systemic complications may be a deterrent for surgeons to offer elective sinus surgery to patients with advanced DM, irrespective of the potential for satisfactory healing at the surgical site.

Although no diabetic animal model has been established for studying sinus wound healing, the effect of glycemic control on tympanic membrane healing has been studied by Kaftan et al. in an animal model of induced diabetes.²⁹ Well controlled diabetic rats and poorly controlled diabetic rats both showed significant delay in mean healing period compared to controls. There was no difference between well compensated versus poorly compensated diabetic groups.

The wound healing milieu of the paranasal sinuses has unique characteristics that differentiate it from other wound healing models. These include the typically inflamed background of CRS, a functional ciliated epithelium and mucus blanket, and in many cases the presence of bacteria, whether pathogenic or native to the local environment. Given these considerations, one might assume that patients with impaired immunity would fare worse than normal hosts after ESS. However, this area has been studied in only a limited way³⁰, as the majority of studies published on CRS outcomes have excluded patients with immune dysfunction. Khalid et al. have shown that patients with immune dysfunction (either immunodeficiency or autoimmunity) who undergo ESS have similar improvements in both objective and QOL outcomes compared to controls. They conclude that patients with relatively milder forms of immune dysfunction may benefit from ESS and may be managed in an ambulatory setting.³¹ Similarly, it appears from our study that the immune impairments associated with DM may not be significant enough to offset the benefit of ESS.

The primary limitation of our study is the relatively small sample size. Despite being drawn from a large cohort, diabetic patients in our study appeared to be underrepresented among patients undergoing ESS. This was also seen in Zhang et al.¹⁴ There are several potential factors that could help to explain this disparity. First, given that DM can be associated with multiple illnesses requiring medical attention, it is possible that patients with DM disproportionately do not seek care for chronic rhinosinusitis because other medical issues prevail. Secondly, since this study considered only patients who underwent surgery, it is possible that patients with DM or their surgeons opted for medical management preferentially over surgery. There may have been selection bias against the sickest patients with DM who may have been too ill to pursue or be considered for elective surgery.

The disadvantage of a limited sample size in a nested case-control study also may have affected our ability to detect differences in outcome between treatment subgroups, such as patients with different forms of DM. Given the low prevalence of patients with DM among patients undergoing ESS, meaningful gains in sample size would require even larger cohorts than what has been possible with a multi-institutional prospective trial. A post hoc analysis was conducted to assess whether our study was powered enough to detect a minimally important difference in terms of the SNOT-22 score. Evaluating the mean difference between SNOT-22 improvement scores over time between two dependent, matched pairings was based on previously reported unequal standard deviation values for SNOT-22 score from patients with and without comorbid DM (18.0 and 23.0, respectively)¹⁴, an inherent within-patient correlation coefficient between pre-treatment and post-treatment scores of 0.500, 80% power ($1-\beta$), a conventional error probability of 0.050, and a two-tailed test approach. A total sample size of 38 (19 participants per group) was adequate to detect a mean difference of a 10.0 point magnitude improvement between matched pairing groups with and without comorbid diabetes mellitus.

Another relative shortcoming of our study is relatively limited data regarding the degree of hyperglycemic control achieved by patients. Because patients were enrolled from tertiary rhinology practices, information regarding the perioperative management of the patients' DM, usually through a remote local primary care physician, was often limited. Because the

multi-institutional cohort was not initially designed to collect data about diabetes metabolic control, data such as HbA1c levels were not available for all patients.

CONCLUSION

In this nested case-control study, diabetic patients with CRS present with similar QOL impairment, endoscopic scores and olfactory function when matched with non-diabetic controls of similar age and radiologic score. Diabetic patients with CRS experience similar degrees of symptomatic benefit from ESS compared to matched controls. Among diabetic patients, insulin dependence does not appear to adversely affect surgical outcome, but a larger cohort would better assess the effect of diabetes type and metabolic control on surgical outcomes in CRS.

References

1. Rosenfeld RM, Andes D, Bhattacharyya N, et al. Clinical practice guideline: adult sinusitis. *Otolaryngol Head Neck Surg.* 2007; 137(3 Suppl):S1–31. [PubMed: 17761281]
2. Benson V, Marano MA. Current estimates from the National Health Interview Survey, 1995. *Vital Health Stat* 10. 1998; (199):1–428. [PubMed: 9914773]
3. Cherry DK, Woodwell DA. National Ambulatory Medical Care Survey: 2000 summary. *Adv Data.* 2002; (328):1–32. [PubMed: 12661586]
4. Smith TL, Mendolia-Loffredo S, Loehrl TA, Sparapani R, Laud PW, Nattinger AB. Predictive factors and outcomes in endoscopic sinus surgery for chronic rhinosinusitis. *Laryngoscope.* 2005; 115(12):2199–205. [PubMed: 16369166]
5. Khalid AN, Quraishi SA, Kennedy DW. Long-term quality of life measures after functional endoscopic sinus surgery. *Am J Rhinol.* 2004; 18(3):131–6. [PubMed: 15283485]
6. Poetker DM, Smith TL. Adult chronic rhinosinusitis: surgical outcomes and the role of endoscopic sinus surgery. *Curr Opin Otolaryngol Head Neck Surg.* 2007; 15(1):6–9. [PubMed: 17211176]
7. Bhattacharyya N. Clinical outcomes after endoscopic sinus surgery. *Curr Opin Allergy Clin Immunol.* 2006; 6(3):167–71. [PubMed: 16670508]
8. Kennedy DW. Prognostic factors, outcomes and staging in ethmoid sinus surgery. *Laryngoscope.* 1992; 102(12 Pt 2 Suppl 57):1–18. [PubMed: 1453856]
9. Batra PS, Kern RC, Tripathi A, et al. Outcome analysis of endoscopic sinus surgery in patients with nasal polyps and asthma. *Laryngoscope.* 2003; 113(10):1703–6. [PubMed: 14520093]
10. Smith TL, Litvack JR, Hwang PH, et al. Determinants of outcomes of sinus surgery: a multi-institutional prospective cohort study. *Otolaryngol Head Neck Surg.* 2010; 142(1):55–63. [PubMed: 20096224]
11. Rammaert B, Lanternier F, Poiree S, Kania R, Lortholary O. Diabetes and mucormycosis: a complex interplay. *Diabetes Metab.* 2012; 38(3):193–204. [PubMed: 22386924]
12. Boronat M, Saavedra P, Lopez-Rios L, Riano M, Wagner AM, Novoa FJ. Differences in cardiovascular risk profile of diabetic subjects discordantly classified by diagnostic criteria based on glycated hemoglobin and oral glucose tolerance test. *Diabetes Care.* 2010; 33(12):2671–3. [PubMed: 20807875]
13. Association AD. Diagnosis and classification of diabetes mellitus. *Diabetes Care.* 2010; 33(Suppl 1):S62–9. [PubMed: 20042775]
14. Zhang Z, Adappa ND, Lautenbach E, et al. The effect of diabetes mellitus on chronic rhinosinusitis and sinus surgery outcome. *Int Forum Allergy Rhinol.* 2014; 4(4):315–20. [PubMed: 24415555]
15. Hopkins C, Gillett S, Slack R, Lund VJ, Browne JP. Psychometric validity of the 22-item Sinonasal Outcome Test. *Clin Otolaryngol.* 2009; 34(5):447–54. [PubMed: 19793277]
16. Benninger MS, Senior BA. The development of the Rhinosinusitis Disability Index. *Arch Otolaryngol Head Neck Surg.* 1997; 123(11):1175–9. [PubMed: 9366696]

17. Kroenke K, Spitzer RL, Williams JB. The Patient Health Questionnaire-2: validity of a two-item depression screener. *Med Care*. 2003; 41(11):1284–92. [PubMed: 14583691]
18. Mace J, Michael YL, Carlson NE, Litvack JR, Smith TL. Effects of depression on quality of life improvement after endoscopic sinus surgery. *Laryngoscope*. 2008; 118(3):528–534. [PubMed: 18043488]
19. Davis GE, Yueh B, Walker E, Katon W, Koepsell TD, Weymuller EA. Psychiatric distress amplifies symptoms after surgery for chronic rhinosinusitis. *Otolaryngol Head Neck Surg*. 2005; 132(2):189–196. [PubMed: 15692525]
20. Doty, R. The Brief Smell Identification Test Administration Manual. NJ: Sensonics Inc; 2001.
21. Goodson WH 3rd, Hung TK. Studies of wound healing in experimental diabetes mellitus. *J Surg Res*. 1977; 22(3):221–7. [PubMed: 14280]
22. Black E, Vibe-Petersen J, Jorgensen LN, et al. Decrease of collagen deposition in wound repair in type 1 diabetes independent of glycemic control. *Arch Surg*. 2003; 138(1):34–40. [PubMed: 12511146]
23. Blakytyn R, Jude E. The molecular biology of chronic wounds and delayed healing in diabetes. *Diabet Med*. 2006; 23(6):594–608. [PubMed: 16759300]
24. Desai SP, Henry LL, Holmes SD, Hunt SL, Martin CT, Hebsur S, et al. Strict versus liberal target range for perioperative glucose in patients undergoing coronary artery bypass grafting: a prospective randomized controlled trial. *J Thorac Cardiovasc Surg*. 2012; 143(2):318–25. [PubMed: 22137804]
25. Guzman JZ, Skovrlj B, Shin J, Hecht AC, Qureshi SA, Iatridis JC, et al. The impact of diabetes mellitus on patients undergoing degenerative cervical spine surgery. *Spine*. 2014; 39(20):1656–65. [PubMed: 24983933]
26. Humphers JM, Shibuya N, Fluhman BL, Jupiter D. The impact of glycosylated hemoglobin and diabetes mellitus on wound-healing complications and infection after foot and ankle surgery. *J Am Podiatr Med Assoc*. 2014; 104(4):320–9. [PubMed: 25076074]
27. Buchleitner AM, Martinez-Alonso M, Hernandez M, Sola I, Mauricio D. Perioperative glycaemic control for diabetic patients undergoing surgery. *Cochrane Database Syst Rev*. 2012; 9:Cd007315. [PubMed: 22972106]
28. Han HS, Kang SB. Relations between long-term glycemic control and postoperative wound and infectious complications after total knee arthroplasty in type 2 diabetics. *Clin Orthop Surg*. 2013; 5(2):118–23. [PubMed: 23730475]
29. Kaftan H, Reuther L, Miehe B, Hosemann W, Kloting I. Influence of glycemic control on tympanic membrane healing in diabetic rats. *Laryngoscope*. 2011; 121(4):823–7. [PubMed: 21305552]
30. Ryan MW. Diseases associated with chronic rhinosinusitis: what is the significance? *Curr Opin Otolaryngol Head Neck Surg*. 2008; 16(3):231–6. [PubMed: 18475077]
31. Khalid AN, Mace JC, Smith TL. Outcomes of sinus surgery in ambulatory patients with immune dysfunction. *Am J Rhinol Allergy*. 2010; 24(3):230–3. [PubMed: 20537292]

Table 1

Baseline characteristics for study patients with and without comorbid diabetes mellitus

Demographics:	Diabetes mellitus Case Subjects (n=20)		CRS Control Subjects (n=20)		p-value
	Mean [SD]	N (%)	Mean [SD]	N (%)	
Age (years)	59.6 [14.4]		59.4 [14.8]		0.968
Male		12 (60.0)		8 (40.0)	----
Female		8 (40.0)		12 (60.0)	0.206
White/Caucasian		14 (70.0)		19 (95.0)	0.091
Hispanic/Latino		1 (5.0)		0 (0.0)	>0.999
Clinical characteristics:					
Previous sinus surgery		11 (55.0)		11 (55.0)	>0.999
Nasal polypsis		4 (20.0)		6 (30.0)	0.716
Asthma		7 (35.0)		10 (50.0)	0.337
ASA sensitivity		0 (0.0)		2 (10.0)	0.487
Tobacco use/current smoker		3 (15.0)		0 (0.0)	0.231
Alcohol consumption		6 (30.0)		12 (60.0)	0.057
Depression		3 (15.0)		4 (20.0)	>0.999
Allergy		7 (35.0)		10 (50.0)	0.337
Septal deviation		6 (30.0)		9 (45.0)	0.327
Turbinate hypertrophy		0 (0.0)		4 (20.0)	0.106
Asthma/sinusitis steroid dependency		2 (10.0)		2 (10.0)	>0.999
Clinical disease severity measures:					
Lund Mackay computed tomography score	12.2 [6.8]		12.5 [6.4]		0.862
Lund Kennedy Endoscopy score	6.5 [4.4]		6.9 [4.5]		0.718
BSIT score	9.0 [2.8]		9.8 [2.8]		0.354
Abnormal olfaction (BSIT < 9)		6 (30.0)		4 (20.0)	0.716

Valid percentages are reported for variables with any missing data. CRS, chronic rhinosinusitis; SD, standard deviation; ASA, acetylsalicylic acid; CF, cystic fibrosis; RARS, recurrent acute rhinosinusitis; BSIT, Brief Smell Identification Test.

Table 2

Baseline symptom and quality of life scores for subjects with and without comorbid diabetes mellitus

Symptom & Quality of Life measures:	Diabetes mellitus Case Subjects (n=20)		CRS Control Subjects (n=20)		p-value
	Mean [SD]	N(%)	Mean [SD]	N (%)	
SNOT-22 Scores	46.6 [22.0]		51.4 [26.6]		0.698
Total RSDI Score	43.9 [24.5]		45.4 [28.2]		0.640
Physical subscale	18.1 [9.3]		17.6 [11.5]		>0.999
Functional subscale	13.6 [9.0]		15.3 [9.4]		0.583
Emotional subscale	12.2 [8.2]		12.6 [9.5]		0.698
PHQ-2 Scores	1.8 [1.8]		1.3 [1.8]		0.398
Positive indication for depression (3)		6 (30.0)		4 (20.0)	0.716

Valid percentages are reported for variables with any missing data. CRS, chronic rhinosinusitis; SD, standard deviation; SNOT-22, 22-item Sinonasal Outcome Test; RSDI, Rhinosinusitis Disability Index; PHQ-2, 2-item Patient Health Questionnaire.

Table 3

Extent of surgical procedures completed during endoscopic sinus surgery

	Diabetes mellitus Case Subjects (n=40 sides)	CRS Control Subjects (n=40 sides)	
Surgical procedures:	N(%)	N(%)	p-value
Maxillary antrostomy	32 (80.0)	39 (97.5)	0.013
Sphenoidotomy	19 (47.5)	26 (65.0)	0.115
Partial ethmoidectomy	6 (15.0)	7(17.5)	0.762
Total ethmoidectomy	27 (67.5)	31(77.5)	0.317
Middle turbinate resection	4 (10.0)	4 (10.0)	>0.999
Inferior turbinate reduction	4 (10.0)	3 (7.5)	0.692
Frontal sinusotomy (<i>Draf</i> 1)	4 (10.0)	1 (2.5)	0.359
Frontal sinusotomy (<i>Draf</i> 2a)	16 (40.0)	11 (27.5)	0.237
Frontal sinusotomy (<i>Draf</i> 2b)	6 (15.0)	8 (20.0)	0.556
Frontal sinusotomy (<i>Draf</i> 3)	1 (2.5)	0 (0)	>0.999

CRS, chronic rhinosinusitis; *Draf* 3 frontal sinusotomy are bilateral by definition.

Table 4

Comparison of preoperative and postoperative symptom and quality of life scores in subjects with and without comorbid diabetes mellitus

Symptom & Quality of Life measures:	Preoperative (n=20)		Postoperative (n=20)		p-value
	Mean [SD]	N (%)	Mean [SD]	N (%)	
Diabetes mellitus Case Subjects (n=20)					
SNOT-22 Scores	46.6 [22.0]		27.7 [19.3]		0.001
Total RSDI Score	43.9 [24.5]		25.2 [23.9]		<0.001
Physical subscale	18.1 [9.3]		8.4 [8.7]		0.001
Functional subscale	13.6 [9.0]		8.1 [9.6]		0.007
Emotional subscale	12.2 [8.2]		8.6 [9.4]		0.039
PHQ-2 Scores	1.8 [1.8]		1.4 [1.5]		0.063
Positive indication (3)		6 (30.0)		5 (25.0)	>0.999
CRS Control Subjects (n=20)					
SNOT-22 Scores	51.4 [26.6]		31.6 [27.8]		0.009
Total RSDI Score	45.4 [28.2]		23.8 [25.3]		0.007
Physical subscale	17.6 [11.5]		9.9 [11.5]		0.018
Functional subscale	15.3 [9.4]		6.4 [7.6]		0.005
Emotional subscale	12.6 [9.5]		7.5 [7.6]		0.038
PHQ-2 Scores	1.3 [1.8]		0.9 [1.1]		0.166
Positive indication for depression (3)		4 (20.0)		1 (5.0)	0.250

CRS, chronic rhinosinusitis; SD, standard deviation; SNOT-22, 22-item Sinonasal Outcome Test; RSDI, Rhinosinusitis Disability Index; PHQ-2, 2-item Patient Health Questionnaire.

Table 5

Comparison of change in symptom and QOL scores between subjects with and without comorbid diabetes mellitus

	Diabetes mellitus Case Subjects (n=20)	CRS Control Subjects (n=20)	
Symptom & Quality of Life measures :	Mean Change [SD]	Mean Change [SD]	p-value
SNOT-22 Scores	-18.9 [18.8]	-19.9 [30.6]	0.841
Total RSDI Score	-19.8 [20.3]	-21.7 [31.9]	0.771
Physical subscale	-10.2 [9.1]	-7.7 [13.1]	0.496
Functional subscale	-5.8 [8.1]	-9.0 [11.0]	0.134
Emotional subscale	-3.8 [7.8]	-5.1 [10.0]	0.749
PHQ-2 Scores	-0.5 [1.1]	-0.5 [1.5]	0.640
Endoscopy Scores	-2.1 [6.6]	-2.7 [3.6]	0.261

CRS, chronic rhinosinusitis; SD, standard deviation; SNOT-22, 22-item Sinonasal Outcome Test; RSDI, Rhinosinusitis Disability Index; PHQ-2, 2-item Patient Health Questionnaire.