INTRODUCTION

With the increasing use of sialendoscopy in the management of salivary gland obstructive disorders, the acquisition of disease-specific outcomes data is important. Currently, there is a paucity of detailed prospective and long-term evidence demonstrating the impact of sialendoscopic-assisted salivary duct surgery (SASDS) on chronic obstructive sialadenitis symptoms. Greater clarity pertaining to the specific positive prognostic factors for success and risk factors for refractory disease is needed to help improve patient counseling, identify appropriate candidates for surgical management, and highlight areas for management modification. Without the use of sialendoscopy, traditional approaches for the management of sialolithiasis include conservative measures (hydration, massage, and sialagogues) and surgical approaches such as open resection of palpable sialoliths without endoscopic confirmation of complete extirpation; marsupialization without endoscopic duct patency confirmation, thereby risking possible subsequent iatrogenic stenosis; blind distal duct dilation with the risk of unidentified duct perforation or false passage; and more frequent use of sialadenectomy with the inherent morbidity and risks. 1–4

Various symptom and outcome instruments and approaches have been employed to assess the efficacy of SASDS. 5–16 The recently developed Chronic Obstructive Sialadenitis Symptoms (COSS) questionnaire by our group has been used to measure the impact of treatments on sialadenitis-specific symptoms in a retrospective study and in a series of short-term (3-month follow-up) prospective studies. 17–21 Based on the current body of relevant literature, the long-term durability of symptom reduction...
following SASDS and risk factors for treatment failure remain unclear.

In this study, we aimed to prospectively assess symptoms of chronic obstructive sialadenitis prior to and 3 months and 1 year after SASDS in patients with sialolithiasis using the COSS questionnaire. With this data, we aim to elucidate whether short-term symptom severity improvements are also sustained at 1 year following SASDS. In cases of disease refractory to SASDS, we seek to identify potential risk factors for symptom persistence or recurrence. We also hope to determine whether open surgical approaches for sialolithiasis predispose to iatrogenic fibrosis and long-term obstructive salivary disease.

**MATERIALS AND METHODS**

**Subjects: Patients/Glands**

Following study approval by our institutional review board, we prospectively recruited all adult patients with chronic obstructive sialadenitis symptoms scheduled for SASDS at our medical center between 2015 and mid-2016. After obtaining informed consent, patients completed the COSS questionnaire at the following time points: just prior to SASDS (either during the clinic visits within a month of SASDS or in the preoperative area before surgery), at 3 months postoperatively, and at 1 year postoperatively. If patients had two or more symptomatic glands, they completed the first 10 questions of the questionnaire separately for each gland, generating gland-specific scores. For this particular study, we included all adult patients over 18 years old with confirmed or highly suspected sialolithiasis, excluding any subsequent sialadenectomy of the affected gland within 1 year of SASDS. We considered cases to have sialolithiasis if any sialoliths were found during sialendoscopy or if preoperative/intraoperative imaging indicated presence of sialoliths that could not be visualized during sialendoscopy but were still strongly suspected to be in the parenchyma of the glands by surgeon-performed ultrasound (SP-US) or computed tomography (CT).

All SASDS procedures were performed at our medical center by one of 2 surgeons (W.R.R. and J.L.C.) under general anesthesia or rarely under conscious sedation, as described in past articles by our group.17–21

**COSS Questionnaire**

The COSS questionnaire is a patient-reported symptom-assessment instrument comprised of 20 questions measuring sialadenitis-specific symptoms that has been used in prior sialendoscopy/chronic sialadenitis studies.17–21 The COSS questionnaire measures 10 gland-specific symptoms with possible impact on social functioning and 10 questions pertaining broadly to salivary function, oral function, and quality of life (Table I). The patients score each question on a scale of 0 to 10; the sum of the 20-item scores is then divided by 2 to determine the total COSS score on a scale of 0 to 100.

**Sialolithiasis Categories**

For submandibular duct cases, we defined distal sialolithiasis as being found from the buccal mucosa ostium to the anterior border of the masseter muscle, proximal as being found from the anterior border of the masseter to the first tributary of the parotid duct, and parenchymal sialolithiasis as being found more proximal to the first tributary and within the parenchyma of the glands.

**Database and Statistical Management**

Clinical, intraoperative, and COSS questionnaire data were entered into REDCap (Research Electronic Data Capture), a secure and encrypted database platform. We collected the following demographic and clinical variables: age, gender, race, smoking history, history of radioactive iodine (RAI), autoimmune conditions, duration of symptoms, and preoperative SP-US and/or CT imaging findings. For operative findings, we recorded the presence of the following: sialoliths (number and location), stenoses (partial or complete, location), sludge, and ducal wall inflammation. We recorded the following specific operative interventions: sialolith extraction technique, sialodochotomy (location), sialodochoplasty (location), secondary intention (in the case of many proximal/hilar submandibular duct open sialolithotomies), dilation (type and location), and stent placement.

Based on a retrospective study using the COSS questionnaire,17 we classified glands with complete symptom resolution as those with COSS scores of less than 10; partial resolution of symptoms with COSS scores between 10 and 25; and those with no resolution of symptoms as COSS score above 25. Univariate analyses were used to assess relative risk (RR) correlations between disease characteristics and the lack of complete resolution of symptoms (total COSS score > 10) at 1 year. For the sialolithiasis glands with refractory disease at 1 year (partial or no resolution or total COSS score > 10), we conducted a focused descriptive analysis of possible specific risk factors for failure.
Statistical analysis was performed using Stata statistical software version 15 (StataCorp LLC, College Station, TX). The paired t test and the Wilcoxon matched-pairs signed-ranks test were used to compare mean and median preoperative and postoperative scores, respectively. The Kruskal-Wallis equality-of-populations rank test was used in two or more independent sample comparisons for continuous variables that were not normally distributed. RR calculations were performed using log-binomial generalized linear regression models. For univariate analyses, we reported RR with 95% confidence intervals (CIs). Tukey box plot of COSS score distribution was performed; the box corresponds to the IQR and whiskers represent (Q1 – 1.5 × IQR) and (Q3 + 1.5 × IQR). Circular markers represent outliers. A two-sided P value of less than 0.05 was used to determine statistical significance.

RESULTS

Ninety-six adult patients underwent SASDS at our institution for symptomatic glands with chronic obstructive sialadenitis, consented to enrolling in the study, and completed the preoperative-SASDS and 1-year follow-up COSS questionnaire for 110 glands at the time of data analysis. Of these, 67 patients with 69 glands had evidence of sialolithiasis by preoperative/intraoperative imaging or as visualized during the procedure and a 1-year COSS score. Two patients had sialolithiasis in two glands each.

Table II shows the demographic and etiologic characteristics of our cohort, including duration of symptoms and gland type affected. In two glands out of 69 (3%), sialolithiasis was present concurrently with a known inflammatory condition: one with RAI exposure and one with systemic lupus erythematosus (SLE). Twenty-one of 69 (30.4%) sialolithiasis glands additionally had concurrent stenosis visualized during sialendoscopy.

Sixty-five (94%) of the sialolithiasis glands were visualized to have sialoliths during sialendoscopy. In four (6%) glands, one or more sialoliths were highly suspected on perioperative imaging but were unreachable by sialendoscopy due to the parenchymal location. In 10 out of 69 (14%) glands with sialolithiasis, at least one sialolith could not be surgically extracted, making them residual sialolithiasis cases in our analysis. Six of these 10 (60%) residual sialolith cases had one or more other sialoliths extracted during the SASDS. Of the 59 out of 69 (86%) fully extracted sialolithiasis cases, 38 (64%) had sialoliths within the proximal duct, whereas in 21 (36%) cases sialoliths were found distally. Eighteen cases (26%) had extraction by sialendoscopy alone for nonimpacted sialoliths. Forty-seven cases (68%) underwent extraction via an open/hybrid approach.

None of the 69 glands with sialolithiasis underwent subsequent sialadenectomy within 1 year of SASDS. One patient with a residual submandibular gland sialolith did undergo a sialadenectomy 1 year and 9 months after SASDS.

In Table III, we present the median COSS scores pre- and post-SASDS for the overall sialolithiasis cohort and the above-described subgroups. All sialolithiasis comparisons, cumulative and by subtype, showed statistically significant improvements after SASDS in the median COSS scores from preoperative to 3-months postoperative and from preoperative to 1-year postoperative (P < 0.05) (Table III). None of the median COSS scores in the various subgroups at 3-month and 1-year follow-up were significantly different from one another, suggesting general stability of all outcomes over time.

Because full extraction of sialoliths is a common event (59 cases, 86%), we highlight the stability of COSS scores at the 3-month and 1-year postoperative time points for this particular scenario (Fig. 1). For this subgroup, Figure 2 shows the changes from the preoperative to the 1 year after SASDS in each of the 20 individual symptoms that make up the COSS questionnaire. Compared to the preoperative scores, 18 out of the 20 symptoms had a statistically significant reduction in symptom score at 1-year post-SASDS. SASDS sialolith extraction appeared to have no effect on excess saliva and bloody exudate symptom scores for such cases.

Sialolithiasis cases with concurrently visualized stenosis had higher preoperative COSS scores than sialolithiasis cases without stenosis (40 vs. 27.3, respectively; P < 0.05); however, subsequent COSS scores at 3-months and 1-year post-SASDS were not statistically different, suggesting similar response to surgical treatment (Table III). Otherwise, there were no statistically significant differences in the median COSS scores between the sialolithiasis subtypes at each time point of COSS assessment (preoperative, 3-months, and 1-year post-SASDS).

Four out of 69 (5.7%) sialolithiasis glands underwent transfacial parotid sialolithotomy with full extraction, with mean COSS scores as follows: preoperative, 39.9 (range: 27–58); and 1-year postoperative, 1 (range: 0–3). Sixteen out of 69 (23%) sialolithiasis glands underwent posterior floor of mouth/proximal submandibular duct sialolithotomy with full extraction and without sialodochoplasty. These 16 cases had the following median COSS scores: preoperative, 21.3 (IQR: 4.5–44.3; range: 0–72); 3 months, 1.25 (IQR: 0–5.5; range: 0–16.5); and 1 year,
1.25 (IQR: 0–4.5; range: 0–14.5). The improvements for these cases between preoperative to 3-month and preoperative to 1-year follow-up were statistically significant (P = 0.005 and 0.0008, respectively). Furthermore, we found no statistically significant differences in 1-year post-SASDS scores between these 16 cases without sialodochoplasty and 19 cases that underwent submandibular duct sialolithotomy and sialodochoplasty.

We categorized post-SASDS COSS scores by previously described criteria by our group for complete, partial, and nonresolution of symptoms (Table IV). Notably, complete resolution of symptoms was achieved in 95% and 86% of glands with sialolithiasis at 3-months and 1-year post-SASDS, respectively. No significant differences between the proportions of glands achieving complete resolution of symptoms was found from 3 months to 1 year for each subgroup analyzed, further supporting durability of effect. On univariate analysis, there was no significant risk of partial or nonresolution of symptoms associated with location of sialoliths, presence or location of stenosis, type of gland, or extraction method at 1 year. However, patients with residual sialolithiasis were more likely to have partial or nonresolution of symptoms at 1 year than participants with fully extracted sialoliths (RR 3.9, 95% CI: 1.8–8.4; P = 0.001).

Of the four transoral parotid sialolithotomy (fully extracted) cases, all (4 out of 4, 100%) showed continued complete resolution of symptoms at 1 year after SASDS. Of the 16 posterior floor of mouth/proximal submandibular duct sialolithotomy without sialodochoplasty cases, 15 (93.75%) showed durability of complete resolution at 1 year after SASDS. Only one (6.25%) case had partial resolution at 3 months and 1 year.

We performed a detailed analysis for the 10 cases (14.5%) that were refractory, defined by scores in the range for partial resolution (8 cases) or nonresolution (2 cases), at 1-year post-SASDS. Given the small sample size, risk factors were not otherwise discernable with statistical significance, except for residual sialoliths having a higher RR than cases that underwent full sialolith extraction.
extraction. Potential contributory risk factors included intraparenchymal retained sialoliths based on radiologic assessment (unreachable by sialendoscopy) (3 cases), impacted retained sialendoscopically visualized sialolith (1 case), concurrent known inflammatory condition (RAI-S or SLE; 2 cases), extraction of a relatively large (2.5-cm) hilar sialolith (1 case), and concurrent partial or complete duct stenosis (3 cases). The two sialolithiasis cases with no resolution of symptoms both had concurrent stenosis, with one having known SLE. There were no surgical complications related to these 10 refractory cases.

Complications
Five out of 69 (7.2%) patients experienced one SASDS-related complication. The complications were as follows: 1) one laser-induced duct perforation; 2) one possible new infection that resolved with antibiotics; 3) two partial tongue hypoesthesias (one temporary and one persistent); and 4) one parotid sialocele after a transfacial sialolithotomy that underwent botulinum toxin injection to the gland parenchyma, resolving within 2 weeks. All complications except the persistent numbness were temporary, with resolution within a period of days to a few weeks. The persistent tongue hypoesthesia cases (side and tip but not dorsum or ventral aspect) has lasted for over 3 years after a 3-cm hilar submandibular duct sialolith open extraction. There were no cases of ranula, submandibular gland sialocele, or facial nerve weakness.

DISCUSSION
In this study, we use 1-year follow-up with the COSS questionnaire scores to demonstrate a meaningful symptom reduction and persistent effect of SASDS in a vast majority of sialolithiasis patients. Making the decision to proceed with SASDS for a patient with most subtypes of sialolithiasis can be encouraged by not only the high chance of symptom reduction and elimination but also by the safety demonstrated by this study cohort. The applicability and generalizability of this study is strengthened by the prospective nature of the assessment, the size of the cohort, and the high response rate of the COSS questionnaire completion at 1-year of follow-up. Our study helps improve our understanding of the benefits and limitations of SASDS by adding to the growing body of outcomes literature for chronic obstructive sialadenitis.1–12 The COSS
questionnaire is a possible tool for assessing symptom intensity and frequency over time in various patient cohorts.

Our results indicate that residual sialoliths in the parenchyma of the gland are not always symptomatic but may eventually become so. This could be due to the far upstream location of parenchymal sialoliths, which may not cause a degree of obstruction that is clinically relevant. Thus, in situations of retained parenchymal sialoliths, transparenchymal approaches for extraction and/or sialadenectomy may not be urgently required; instead, a trial of observation may be suitable in some patients. Parenchymal sialoliths, however, do have a reduced likelihood of endoscopic extraction and, with that, a reduced likelihood of complete symptom resolution.

Proximal sialoliths, when reachable and fully extracted during SASDS, have as favorable a symptom-reduction outcome as distal sialoliths, regardless of whether purely endoscopic means or open approaches are used. Given the findings that open/hybrid sialolithotomy techniques had statistically similar highly successful outcomes compared to endoscopic approaches, it is unlikely that carefully performed open approaches cause harmful obstructive ductal scarring in the long run. The patients that underwent proximal/hilar submandibular duct sialolithotomy without a subsequent sialodochoplasty, and those who underwent transfacial parotid duct sialolithotomy both demonstrated short-term and long-term dramatic COSS questionnaire symptom reductions.

With the sialolith extracted, concurrent stenosis (21 cases) does not appear to be a major risk factor for failure of symptom reduction. It may be that with the extraction of the sialolith, the nidus of inflammation has been removed. The sialolithotomy incision may dilate or bypass the stenotic region (via sialodochoplasty), thereby reducing the likelihood of recurrent symptomatic obstruction. Nonetheless, in at least three of the 10 cases with symptoms refractory to SASDS, concurrent stenosis was found intraoperatively making it a possible risk factor.

With respect to the individual symptoms in the COSS questionnaire, SASDS across all sialolithiasis subtypes appears to have the most dramatic response for periprandial swelling frequency and severity and significantly reduces social concerns and chewing dysfunction.

In this study, gland preservation was achieved for at least a year in all glands, a similar rate to other studies. However, in at least one case, gland excision was performed after 1 year.

Given the results of this study, we feel that the following management strategies for sialolithiasis are valid, as described in our previous studies. For all sialolithiasis cases, except for select isolated asymptomatic parenchymal sialoliths, an initial sialendoscopic evaluation of the duct system should be performed to assess the reachability and extractability of the sialolith(s) by endoscopic means. Sialendoscopy will also allow for an assessment of the possibility of concurrent stenosis and the presence of multiple sialoliths. In cases of moderately sized sialoliths (4–10 mm) that are impacted, endoscopic laser lithotripsy can be performed with endoscopic extraction of the fragments, although careful consideration needs to be made of the risks of ductal wall thermal damage and further blockage with liquefied sialolith sludge. Larger (> 4–7 mm) or impacted sialoliths may be extracted by open approaches via transoral or transfacial approaches, with careful attention to the lingual and facial nerves where present. Intraoperative SP-US can be particularly helpful for open localization approaches. The hilar submandibular duct can be left to heal on its own without sialodochoplasty. Other duct types and locations should be opened with a sialodochoplasty or repaired. Stenoses found in the process of sialolithotomy should be managed by dilation and or sialodochoplasty, if feasible. Unreachable sialoliths can be managed by observation or sialadenectomy, depending on the presence and severity of symptoms. In
general, we feel that for any nonparenchymal sialoliths, endoscopic or, if necessary, open sialolithotomy should be strongly considered. For any symptomatic parenchymal sialoliths, the following should be considered: endoscopic or, if necessary, open sialolithotomy; intraglandular botulinum toxin injection; or sialadenectomy. Observation for asymptomatic parenchymal sialoliths is reasonable, with the patient being advised of the slight risk of acute sialadenitis and the possibility with time of continued sialolith growth and the development of obstructive symptoms.

We acknowledge several limitations present within this study. Measuring sialadenitis-related symptoms can be challenging with any instrument given the intermittent and fluctuating nature of obstructive disease. Certain patients may have underreported their symptoms during lulls in inflammation. In the two patients who underwent two-gland SASDS, the less symptomatic glands may have skewed responses toward more severely affected glands. With several stratifications and subset analyses, the resultant small sample sizes may have inhibited our ability to find significant correlations of clinicopathologic and therapeutic factors with symptom change. Symptom reduction and resolution and the high gland-preservation rate may not continue with longer term follow-up beyond 1 year. This study reflects the technique and preferences of only a two-surgeon research team at a single institution. Thus, the generalizability of our study would be improved if similar results were seen in the context of a multi-institutional effort. Also, the COSS questionnaire is not yet validated. Refinement of the questions with a more detailed subanalysis of the 20 variables in a variety of normal and disease entities is required.

CONCLUSION

Based on this 1-year prospective study of patient-reported symptoms scores using the COSS questionnaire, SASDS is effective in patients with sialolithiasis in reducing and usually eliminating symptoms in both the short term (3 months) and the long term (1 year). SASDS is associated with a very high rate of salivary gland preservation for sialolithiasis. SASDS appears to be very safe with rare and minor surgical complications. Endoscopic and open approaches alone or in combination, whether for distal or proximal sialoliths, were similarly highly successful; this suggests that the development of subsequent ductal stenosis from iatrogenic scar is unlikely. Residual sialolithiasis is a risk factor for symptom persistence. Ultimately, however, given low rate of refractory disease in sialolithiasis patients after SASDS, the identification of other risk factors is challenging. Further investigation is needed on this topic. Validation and refinement of the COSS questionnaire and multi-institutional symptom-based outcomes studies are still needed to further evaluate the impact of SASDS.

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BIBLIOGRAPHY