Premiere Publications from The Triological Society

Read all three of our prestigious publications, each offering high-quality content to keep you informed with the latest developments in the field.

**THE LARYNGOSCOPE**

**FOUNDED IN 1896**

Editor-in-Chief: Samuel H. Selesnick, MD, FACS

The leading source for information in head and neck disorders.

[Laryngoscope.com](http://Laryngoscope.com)

**LARYNGOSCOPE INVESTIGATIVE OTOLARYNGOLOGY**

Editor-in-Chief: D. Bradley Welling, MD, PhD, FACS

Rapid dissemination of the science and practice of otolaryngology-head and neck surgery.

[InvestigativeOto.com](http://InvestigativeOto.com)

**ENT TODAY**

Editor-in-Chief: Alexander Chiu, MD

Must-have timely information that Otolaryngologist-head and neck surgeons can use in daily practice.

[Enttoday.org](http://Enttoday.org)
Pediatric Subperiosteal Abscess Secondary to Acute Sinusitis: A Systematic Review and Meta-analysis

Eelam A. Adil, MD, MBA; Molly E. Muir, BA; Kosuke Kawai, ScD; Natasha D. Dombrowski, BA; Michael J. Cunningham, MD

INTRODUCTION

Periorbital or orbital spread of infection is the most common complication of acute sinusitis and can result in the formation of a subperiosteal abscess (SPA).1 The ethmoid sinus is the most common infection source, attributable to the shared lamina papyracea.2 SPA accounts for 9% to 28% of orbital complications resulting from sinusitis.3,4 Among the different types of orbital complications, management of SPA is the most controversial, with some clinicians advocating medical management alone, others promoting early surgical intervention in addition to antibiotic therapy, and the most recent studies suggesting surgery in select cases after considering age, location of SPA, and abscess volume.3–8

OBJECTIVES/HYPOTHESIS: The surgical versus medical management of subperiosteal abscess can be controversial. The purpose of this study was to summarize current literature and provide pooled analyses to help direct management decisions.

STUDY DESIGN: Systematic review and meta-analysis.

METHODS: Patients <18 years old with subperiosteal abscess secondary to acute sinusitis were reviewed, and a meta-analysis was conducted. Studies including five or more patients written in English were the primary search focus.

RESULTS: Thirty-eight studies met inclusion criteria for the systematic review, and seven studies contained sufficient data for the meta-analysis. A total of 1,167 patients between the ages of 10 days and 18 years were included. Eleven sign/symptom categories were identified, with restricted ocular motility (n = 289, 45.9%), proptosis (n = 277, 44%), and fever (n = 223, 35.4%) being most frequent. Staphylococcus aureus was the most common pathogen isolated from cultures. Patients with abscess volume greater than the threshold specified in each individual study were over three times more likely to require surgical intervention compared to those with smaller abscess volume (pooled risk ratio [RR] = 3.61, 95% confidence interval [CI]: 2.40–5.44). Proptosis and gaze restriction also significantly predicted surgical intervention (pooled RR = 1.65: 95% CI: 1.29–2.12 for proptosis/pooled RR = 1.90: 95% CI: 1.20–3.00 for gaze restriction).

CONCLUSIONS: Approximately half of patients with a subperiosteal abscess undergo surgical drainage. Abscess volume appears to be the most significant predictive risk factor. Detailed data from future studies regarding radiologic and ophthalmologic parameters are needed to provide more definitive values predictive of which patients are likely to fail medical therapy.

KEY WORDS: Orbital complication, pediatric, sinus surgery, sinusitis, subperiosteal abscess.

LEVEL OF EVIDENCE: 2a

Laryngoscope, 130:2906–2912, 2020

Despite a prevalence decrease attributed to the introduction of the pneumococcal conjugate vaccine (PCV7) in 2000, orbital complications such as SPA accounted for 18,293 inpatient hospital days and $10 million in hospital charges in 2009.9 Given this significant healthcare burden and the potential morbidity of these infections, identifying the most efficient and effective management strategy for such orbital complications is highly desirable. There are currently no published clinical practice guidelines regarding management of these infections from the American Academy of Otolaryngology–Head and Neck Surgery or the American Academy of Ophthalmology. Previously identified surgical predictors include proptosis, gaze restriction, and abscess volume. Patient age ≥9 years has also been implicated to be a potential surgical indicator.10,11 Extensive research has been dedicated to this topic, but limited consensus regarding management has been reached. The purpose of the current study was to critically evaluate the literature regarding SPA. Our goals were to analyze trends with regard to microbiology, examine the use of adjuvant medical therapies, evaluate predictors for surgical intervention via meta-analysis, and identify gaps in the existing literature.

MATERIALS AND METHODS

This systematic review and meta-analysis was reported following the Preferred Reporting Items for Systematic Reviews...
Fig. 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram.

TABLE I. Presenting Signs and Symptoms Within Identified Studies.*

<table>
<thead>
<tr>
<th>Presenting Sign/Symptom</th>
<th>No. of Patients</th>
<th>Articles</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ophthalmoplegia/restricted ocular motility</td>
<td>289 (45.9%)</td>
<td>Rubin et al., 1989; Souliere et al., 1990; Arjmand et al., 1993; Manning, 1993; Deutsch et al., 1996; Sajjadian et al., 1999; Rahbar et al., 2001; Sobol et al., 2002; Brown et al., 2004; Ho et al., 2007; Yang et al., 2009; Gavriel et al., 2011; Kinis et al., 2013; Le et al., 2014; Tabarino et al., 2015; Wan et al., 2016; Nation et al., 2017; Coudert et al., 2018</td>
</tr>
<tr>
<td>Proptosis</td>
<td>277 (44.0%)</td>
<td>Rubin et al., 1989; Souliere et al., 1990; Manning, 1993; Arjmand et al., 1993; Deutsch et al., 1996; Kessler et al., 1998; Sajjadian et al., 1999; Rahbar et al., 2001; Sobol et al., 2002; Brown et al., 2004; Oxford &amp; McClay, 2006; Ho et al., 2007; Yang et al., 2009; Gavriel et al., 2011; Huang et al., 2011; Kinis et al., 2013; Wan et al., 2016; Sciarretta et al., 2017; Nation et al., 2017; Coudert et al., 2018</td>
</tr>
<tr>
<td>Fever</td>
<td>223 (35.4%)</td>
<td>Kessler et al., 1998; Sobol et al., 2002; Sinclair &amp; Berkowitz, 2007; Ho et al., 2007; Yang et al., 2009; Huang et al., 2011; Le et al., 2014; Wan et al., 2016; Sciarretta et al., 2017; Quintanilla-Dieck et al., 2017</td>
</tr>
<tr>
<td>Eyelid edema</td>
<td>160 (25.4%)</td>
<td>Arjmand et al., 1993; Sajjadian et al., 1999; Rahbar et al., 2001; Oxford &amp; McClay, 2006; Sinclair &amp; Berkowitz, 2007; Yang et al., 2009; Kinis et al., 2013; Wan et al., 2016; Sciarretta et al., 2017</td>
</tr>
<tr>
<td>Chemosis</td>
<td>136 (21.6%)</td>
<td>Souliere et al., 1990; Arjmand et al., 1993; Kessler et al., 1998; Sajjadian et al., 1999; Brown et al., 2004; Oxford &amp; McClay, 2006; Ho et al., 2007; Yang et al., 2009; Huang et al., 2011; Wan et al., 2016; Nation et al., 2017</td>
</tr>
<tr>
<td>Erythema</td>
<td>99 (15.7%)</td>
<td>Arjmand et al., 1993; Sajjadian et al., 1999; Rahbar et al., 2001; Oxford &amp; McClay, 2006; Kinis et al., 2013</td>
</tr>
<tr>
<td>Decreased visual acuity/visual loss</td>
<td>59 (9.4%)</td>
<td>Arjmand et al., 1993; Deutsch et al., 1996; Sobol et al., 2002; Oxford &amp; McClay, 2006; Sinclair &amp; Berkowitz, 2007; Ho et al., 2007; Huang et al., 2011; Tabarino et al., 2015</td>
</tr>
<tr>
<td>Diplopia</td>
<td>56 (8.9%)</td>
<td>Souliere et al., 1990; Arjmand et al., 1993; Huang et al., 2011; Coudert et al., 2018</td>
</tr>
<tr>
<td>Leukocytosis &gt;12</td>
<td>52 (8.3%)</td>
<td>Huang et al., 2011; Quintanilla-Dieck et al., 2017</td>
</tr>
<tr>
<td>Purulent rhinorrhea</td>
<td>18 (2.9%)</td>
<td>Manning, 1993; Sinclair &amp; Berkowitz, 2007; Huang et al., 2011; Tabarino et al., 2015</td>
</tr>
<tr>
<td>Headache</td>
<td>10 (1.6%)</td>
<td>Sajjadian et al., 1999; Wan et al., 2016</td>
</tr>
</tbody>
</table>

*No differentiation was made between medically versus surgically treated patients in this table. Symptoms were included only if they were mentioned in more than one article. Calculations were based on the 630 patients presented in the 24 publications that identified specific presenting symptoms and their percentage of occurrence.
and Meta-analyses (PRISMA) guideline. A PICO (population, intervention, control, outcome) question was developed to help focus the quantitative portion of the systematic review: In children less than 18 years of age with SPA secondary to acute sinusitis, what clinical signs are predictors of surgical intervention?

**Literature Search Strategy**

A comprehensive literature search of the PubMed, MEDLINE, and Google Scholar databases was conducted. Disease-specific (subperiosteal abscess, orbital complication, orbital abscess, acute sinusitis) and population-specific (pediatric) terms were used as search parameters (PubMed: “[subperiosteal abscess” or “orbital complication” or “orbital abscess” or “acute sinusitis)” and pediatric). All articles published before the August 28, 2019 search date identified by these terms and written in English were included. Additional sources were acquired from reference lists of published review articles. Abstracts and articles were then further reviewed as detailed below.

**Study Selection Criteria**

Article eligibility was determined by two independent review authors (E.A.A. and M.M.) to ensure consensus agreement. Articles were included if they presented pediatric (defined as <18 years old) data in randomized controlled trials, observational studies, or reviews. Case reports or series with less than five patients were excluded. Both retrospective and prospective studies were considered for inclusion. Studies including adult data only were excluded, but those that presented combined adult and pediatric data were considered for inclusion if the pediatric data were discernable from the remainder of the cohort. Studies that did not specify the type of orbital complication or studies reporting SPA secondary to causes other than acute sinusitis were excluded. Demographic data, presenting symptoms, diagnostic methods, microbiology, treatment, and outcome were extracted. The Newcastle-Ottawa Scale was used to assess the quality of included articles.

**Statistical Analysis**

DeRSimonian and Laird random effects models were utilized to evaluate prognostic factors for requiring surgical intervention. The logarithm of the crude risk ratio (RR) and the corresponding standard errors from individual studies were used to estimate the pooled RR. Heterogeneity between studies was assessed using the I² statistic. Publication bias was evaluated by visually inspecting funnel plots for potential asymmetry. All statistical analyses were conducted using Stata version 15.0 (StataCorp, College Station, TX) and R statistical software (R Foundation for Statistical Computing, Vienna, Austria).

**RESULTS**

The initial literature search produced 1,574 articles (Fig. 1). An additional 72 articles were identified through reference review. After all duplicates were removed, 1,249 publications remained for eligibility examination. Each article’s title and abstract were reviewed for inclusion and exclusion criteria. Studies were deemed eligible for full-text review if they included five or more pediatric
patients presenting with an SPA secondary to acute sinusitis. Of the initial 1,249 publications, 116 full-text articles were reviewed in their entirety. Thirty-eight studies meeting all inclusion criteria were included in the systematic review (see Supporting Information, Table S1). Quality assessment ratings ranged from 6–9 (see Supporting Information, Table S2). Seven studies contained sufficient data to be included in the meta-analysis (Fig. 1).

Demographics
The 38 studies included 1,167 patients between the ages of 10 days and 18 years presenting with SPA secondary to acute sinusitis over the course of 29 years (1989–2018). The mean age was 7.0 years based on the 936 patients for whom specific age data were available. Sixty-five percent were male, based on the 726 patients with denoted gender data. A surgical drainage procedure was performed in 616 (53.6%) patients. Of the 616 undergoing an initial surgical drainage procedure, 28 (4.9%) patients required a second surgical procedure. Two (0.35%) patients required a third surgical procedure. Mean length of hospitalization was 5.8 days for medically treated patients and 8.7 days for surgically managed patients. Eleven patients also had a reported intracranial complication with cerebral abscess being the most common.
**Presenting Signs/Symptoms**

Twenty-four publications identified their patients' presenting signs/symptoms as well as their rate of occurrence (Table I). Eleven sign/symptom categories were identified, with restricted ocular motility (n = 289, 45.9%) being the most common. Proptosis (n = 277, 44%) and fever (n = 223, 35.4%) were also frequent. Decreased visual acuity and diplopia were each described in less than 10% of patients.

**Microbiology**

Twenty studies included microbiology data, identifying both the culture results as well as the number of patients with each microorganism. There were 351 culture results in total. Figure 2 highlights the bacteriology trends from 1993 through 2018 for the five most common microorganisms: *Haemophilus influenzae*, *Streptococcus pneumoniae*, *Streptococcus anginosus*, *Staphylococcus aureus*, and anaerobic bacteria. For *S. aureus*, both methicillin-sensitive and methicillin-resistant strains were included. The category of anaerobic bacteria includes multiple species.

**Adjuvant Therapies**

Management of all SPA patients consisted of oral and/or intravenous (IV) antibiotics; the specific regimen varied greatly. In addition to antibiotic therapy, some authors described the use of adjuvant therapies; details, however, with respect to dosing, frequency, and duration were rare. One hundred six patients (14.1%) were solely medically managed and prescribed oxymetazoline nasal spray twice a day in addition to antibiotic therapy. Forty-four patients (4.1%), both medically and surgically managed, had a nasal regimen that involved some combination of oxymetazoline, saline, and a nasal steroid. Twenty-four patients (2.2%) were discharged after surgery with a 2-week nasal steroid spray regimen. No studies described the use of oral steroid therapy. Given the limited data regarding the use of adjuvant therapies, no conclusive statement can be made regarding the efficacy of their use in SPA treatment.

**Meta-analysis of Predictors of Surgical Intervention**

The authors of 10 publications identified significant predictors of surgical intervention in their patient populations (Table II). These predictors were determined via statistical analysis of possible risk factors present in patients who required surgical intervention in comparison to those receiving solely medical therapy. Abscess volume and proptosis measurements greater than a certain benchmark value were the two most common surgical predictors identified. Abscess location, specifically superiorly, was an additional frequent predictor.

Seven of these studies included sufficient data to be included in a meta-analysis (Fig. 3). Patients with larger abscess volume were over three times more likely to require surgical intervention compared to those with a smaller abscess volume (pooled RR = 3.61, 95% confidence interval [CI]: 2.40-5.44). Almost 83% (60/72) of patients with larger abscess volume required surgery, whereas 21% (28/133) of patients with smaller abscess volume required surgery. The cutoff point used for abscess volume varied from 0.5 mL\(^2\) and 0.67 mL\(^2\) to 1.25 mL\(^2\) and 3.8 mL\(^2\). Four other studies found surgically managed SPA had significantly larger mean abscess volume than medically managed SPA.\(^6\,8\,25\,28\) These four studies, however, were excluded from the meta-analysis because the number of cases meeting the threshold of abscess volume was not reported.

Proptosis (pooled RR = 1.65, 95% CI: 1.29-2.12) and gaze restriction (pooled RR = 1.90, 95% CI: 1.20-3.00) were also significant predictors requiring surgical intervention. Age ≥9 years was not associated with SPA requiring surgical intervention (pooled RR = 1.25, 95% CI: 0.90-1.73). There was no evidence of publication bias for all predictors examined (see Supporting Information, Fig. S1).

**DISCUSSION**

The objectives of this systematic review were to analyze trends with regard to microbiology, examine the use of adjuvant medical therapies, evaluate predictors for surgical intervention via meta-analysis, and identify gaps in the existing literature. Thirty-eight studies reporting 1,167 pediatric patients with SPA secondary to acute sinusitis were included in the study. Presenting signs and symptoms fell into 11 categories, with restricted ocular motility (n = 289, 45.9%), proptosis (n = 277, 44%), and fever (n = 223, 35.4%) being most frequent. Although all patients were treated with IV or oral antibiotics, there were significant gaps in the literature surrounding adjuvant therapies. Microbiology has changed over time, with the five most common microorganisms identified as *H. influenzae*, *S. pneumoniae*, *S. anginosus*, *S. aureus* (both methicillin sensitive and methicillin resistant), and anaerobic bacteria. Based on a meta-analysis of seven studies with sufficient data, large abscess volume, proptosis, and gaze restriction all significantly predicted surgical intervention.

**Microbiology Trends Over Time**

Over the 29 years assessed in this literature search, *S. aureus* was consistently the most common microorganism isolated in SPA patients. Because many of the studies included in this review did not differentiate between methicillin-resistant *S. aureus* (MRSA) and methicillin-sensitive *S. aureus*, it is difficult to assess from this cohort any change in the relative proportions of these *Staphylococcus* subtypes. However, one systematic review assessing the prevalence of MRSA in nonhospitalized sinusitis patients found from 2006 to 2012 the prevalence of MRSA among all positive cultures grew from 0% to 15.9%, and the prevalence of MRSA among cultures positive for *S. aureus* grew from 0% to 68.8%.\(^43\) Additionally, a comparative case series of patients with sinus-related SPA found MRSA was present in four of seven patients positive for *S. aureus* between 2002 and 2012.\(^42\) In contrast, no patients presented with MRSA between 1977
and 2002, pointing to a marked increase in MRSA prevalence over time.

Anaerobic bacteria were also commonly isolated in patients with SPA, consistently being reported in culture results from 1994 to 2018. This aligns with prior research finding no significant difference in the prevalence of anaerobic organisms over time. Anaerobic isolates have been reported to be uncommon in patients younger than 9 to 11 years. Such age discrepancy was not investigated in our study.

The prevalence of S. anginosus associated with SPA increased over the course of the study period, with two cases reported in the first half and 43 cases documented in the second half. This organism is particularly aggressive due to the production of extracellular enzymes, leading to tissue liquefaction and abscess formation. The increase in prevalence of S. anginosus may be a consequence of the introduction of the PCV7 in 2000 and the 13-valent version in 2010. The effectiveness of these vaccines in reducing macrolide-resistant invasive pneumococcal disease associated with S. pneumoniae could explain the relatively increased prevalence of other causative organisms. Given this documented increased prevalence of MRSA and S. anginosus–related infections, and correspondingly the specific therapy required to treat these organisms, obtaining middle meatus cultures in both medically and surgically treated SPA patients is strongly recommended.

**Predictors of Medical Failure**

Although many studies report successful resolution of SPA with medical management alone, surgical drainage of SPA is warranted in select patients with emergent ophthalmic issues or those who fail medical therapy. Identifying patients who will likely fail medical therapy is critical, because delayed surgical drainage can lead to prolonged hospital stays and further orbital or intracranial complications. A study published in 2000 expanded upon the prior work from this institution that aimed at defining which patients with SPA could be managed with IV antibiotic therapy alone. In this prospective, non-comparative case series, the authors defined nine criteria for surgical intervention including age >9 years, presence of frontal sinusitis, nonmedial location of SPA, large SPA, suspicion of anaerobic subperiosteal infection, recurrence of SPA after previous drainage, evidence of chronic sinusitis, acute optic nerve or retinal compromise, and/or infection of dental origin. When these guidelines were followed, only two of 29 (6.9%) patients failed medical management and later required SPA drainage. However, older age was not identified as a predictor for requiring surgical intervention in our meta-analysis (Fig. 3). Abscess volume is identified as the most significant factor associated with failure of medical therapy requiring surgical intervention. The minimum volume of concern greatly varied across individual studies, ranging from 0.5 mL to 3.8 mL. Two studies included in the meta-analysis documented an abscess volume <1 mL to be predictive of medical failure, indicating a relatively small volume abscess may require surgical intervention. Additionally, proptosis greater than 2 to 3 mm or gaze restriction may predict medical failure. Of critical importance is many of the studies included in this systematic review did not specifically define abscess volume, amount of proptosis, or degree of gaze restriction. Future SPA studies should be as detailed as possible in these three respects to maximize our understanding of the factors predisposing to medical failure.

**Limitations**

As the literature included in this review was published over a large timeframe, it is likely management trends have changed slightly over time. Therefore, this discussion of overall trends in medical management versus surgical treatment may be skewed by changes in practice. The evaluations included in this systematic review and meta-analysis may have been biased due to lack of comparability between surgical and nonsurgical patients with regard to patient characteristics (i.e., comorbidities), specific antibiotic treatment choice, and use of adjunctive therapy. In addition, surgeon preference certainly plays a role in determining when patients are deemed a medical failure. In spite of these limitations, pooling data for analysis is beneficial given the relatively small case series included within each study.

**CONCLUSION**

Management of SPA is a controversial topic, with approximately half of patients undergoing surgical drainage according to our analyses. S. aureus and anaerobic bacteria are the most common isolates noted in recent studies, and therefore, consideration should be given to empiric therapy with both MRSA and S. anginosus coverage until culture results are available. Orbital abscess volume appears to be the most significant risk factor for failing medical therapy, with more research necessary to determine a specific volume threshold for surgical intervention. Gaze restriction and proptosis are also common indicators of SPA requiring more objective documentation. Future research regarding pediatric SPA should be as detailed as possible regarding patient variables and treatment to enhance comparative analysis of results.

**BIBLIOGRAPHY**
