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Extrasinus Complications From Odontogenic Sinusitis: A Systematic Review

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Abstract

Objective. Odontogenic sinusitis (ODS) can cause infectious orbital, intracranial, and osseous complications. Diagnosis and management of complicated ODS have not been discussed in recent sinusitis guidelines. The purpose of this systematic review was to describe epidemiological and clinical features, as well as management strategies of complicated ODS.

Data Sources. PubMed, EMBASE, and Cochrane Library.

Review Methods. A systematic review was performed to describe various features of complicated ODS. All complicated ODS studies were included in qualitative analysis, but studies were only included in quantitative analysis if they reported specific patient-level data.

Results. Of 1126 studies identified, 75 studies with 110 complicated ODS cases were included in qualitative analysis, and 47 studies with 62 orbital and intracranial complications were included in quantitative analyses. About 70% of complicated ODS cases were orbital complications. Only 23% of complicated ODS studies were published in otolaryngology journals. Regarding ODS-related orbital and intracranial complications, about 80% occurred in adults, and 75% were male. Complicated ODS occurred most commonly from apical periodontitis of maxillary molars. There were no relationships between sinusitis extent and orbital or intracranial complications. High rates of anaerobic and α-hemolytic streptococcal bacteria were identified in complicated ODS. Management generally included systemic antibiotics covering aerobic and anaerobic bacteria, and surgical interventions were generally performed to address both the complications (orbital and/or intracranial) and possible infectious sources (dentition and sinuses).

Conclusion. ODS should be considered in all patients with infectious extrasinus complications. Multidisciplinary management between otolaryngologists, dental specialists, ophthalmologists, and neurosurgeons should be considered to optimize outcomes.

Keywords

odontogenic sinusitis, acute sinusitis, sinusitis complications, orbital cellulitis, brain abscess

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Extrasinus spread of bacterial rhinosinusitis can cause orbital, intracranial, and osseous complications and may occur in 3% to 20% of patients hospitalized for acute bacterial rhinosinusitis.[1] These complications can occur from acute rhinosinusitis (ARS) or chronic rhinosinusitis (CRS)[2] and tend to be associated with ARS in pediatric patients and CRS in adults. Among complication types, 60% to 80% are orbital, 15% to 20% are intracranial, and 3% to 10% are osseous. Orbital and osseous complications are more common in children, whereas intracranial complications occur at any age but have a predilection for adolescents or young adults. Males have also generally been affected more frequently by complicated rhinosinusitis.[1]

Orbital complications include preseptal cellulitis or abscess, postseptal (orbital) cellulitis, subperiosteal abscess, orbital abscess (intraconal), and cavernous sinus thrombosis.[1,3] Intracranial complications include meningitis, cerebritis, abscesses (epidural, subdural, or intraparenchymal), or cerebral venous sinus thrombosis.[1] Osseous complications refer to sinus wall osteomyelitis that can cause subcutaneous subperiosteal abscess, sinocutaneous fistula, or orbital or intracranial spread.[1]

Odontogenic sinusitis (ODS) refers to bacterial maxillary sinusitis, with or without extension to other paranasal sinuses, secondary to either adjacent infectious maxillary dental pathology or following complications from dental procedures.[4,5] Potential dental pathologies causing ODS include apical periodontitis with or without periapical lesions (endodontic infection), marginal periodontitis (periodontal infection), oroantral communication or fistula, or dental treatment–related maxillary sinus foreign bodies.[6-8] Studies have shown that ODS could account for 25% to 40% of all chronic

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maxillary sinusitis[9,10] and 45% to 75% of unilateral maxillary sinus opacification on computed tomography (CT).[11-14]

Despite its relatively high prevalence, ODS has received significantly less attention in the literature compared to rhinosinusitis.[15] While ODS diagnosis and management have been discussed in recent review or consensus articles,[4-6] these have mainly focused on uncomplicated ODS. Complicated ODS with extrasinus spread has been described but only in case reports or small series. The purpose of this systematic review was to describe epidemiological and clinical features, as well as management strategies of complicated ODS.

Materials and Methods

A systematic review was conducted according to Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) methodology.[16] Institutional review board exemption was granted.

Search Strategy

PubMed, EMBASE, and Cochrane Library literature searches were performed from January 1900 through September 2020. Complete search strategies are shown in Supplementary Table S1 (in the online version of the article).

Eligibility Criteria

To be included, studies had to demonstrate patients with extrasinus infectious complications, maxillary dental pathology, and at least maxillary sinusitis ipsilateral to the dental pathology. Two separate sets of study inclusion criteria were used—one for inclusion into qualitative analysis and one for quantitative analysis.

For qualitative analysis, some variables were analyzed at the patient level and some at the study level. At the patient level, the total number of published complicated ODS cases, frequencies of complication types, and published cases per decade were analyzed. At the study level, journal types and evidence levels were analyzed.[17] Studies were excluded if abstracts were non-English or unavailable and if there was no maxillary sinusitis, no bacterial sinusitis (eg, fungal sinusitis, neoplasia), or no odontogenic source.

For quantitative analysis, only ODS-related orbital and intracranial complication studies were included and were required to report the following patient-level variables (primary outcome measures): age, sex, extrasinus complication types, disease laterality, sinusitis extent, and causative dental pathology. Studies were excluded if full-text articles were non-English or unavailable and if clinical data could not be determined.

Study Selection

Abstracts or articles from initial search results were screened by 2 authors independently (A.J.C., R.T.D.) to determine whether studies reported extrasinus complications due to bacterial ODS from maxillary odontogenic sources. Any conflicts were resolved by the senior author (J.R.C.). Screened abstracts or articles that represented complicated ODS underwent full-text review independently by two authors (A.C., J.R.C.) to collect data for qualitative and quantitative analyses. Results were compared between authors for accuracy, and discrepancies were resolved by the senior author (J.R.C.).

Data Extraction

In addition to variables for qualitative analysis and primary outcome variables for quantitative analysis, the following secondary outcome measures were analyzed on quantitative analysis, when available: orbital and intracranial abscess locations, timing of causative dental procedures, tooth type, symptom durations, presence of dental pain, body temperature and presence of fever ($\geq$38°C),[18] white blood cell count and presence of leukocytosis (>11,000/mL),[19] presence of ophthalmoplegia and visual acuity loss, neurological deficits, and bacterial cultures (individual species and cumulative frequencies of anaerobes and α-hemolytic streptococci). In addition, preoperative and postoperative antibiotic types, durations, and routes of administration; the use of monotherapy or polytherapy; and aerobic vs anaerobic coverage[20,21] were also reported. Last, types of dental, sinus, orbital, and intracranial interventions; times to interventions; and ophthalmologic and neurologic outcomes were reported for orbital and intracranial complications, respectively.

Assessment of Quality and Bias of Individual Studies

The National Heart, Blood, and Lung Institute Study Quality Assessment Tool for Case Series was used to evaluate quality and bias of case series,[22] but only 7 series met inclusion criteria for assessment. Supplementary Table S2 (in the online version of the article) shows the questions and rating system used in this assessment. Note that 91% of included studies were case reports, which increase bias and decrease quality but cannot be graded by validated assessment tools.

Statistical Analysis

Statistical analyses were performed using SAS v9.4 (SAS Institute). Continuous data were described as means and standard deviations or medians and interquartile ranges. Nominal data were described with percentages and counts. Due to the small sample sizes and inherent bias from included studies, statistical comparisons between study variables were not performed.

Results

Figure 1 shows the systematic review flow diagram. Of the 1126 studies identified, 777 abstracts or articles were screened after duplicates were removed. After applying exclusions, 75 studies with 110 cases of ODS-related orbital, intracranial, and osseous complications were included for qualitative analysis. Of those, 47 studies with 62 cases of ODS-related orbital and intracranial complications were included for quantitative analysis, but no osseous complications were included. Supplementary Table S3 (in the online version of the article) shows studies included in qualitative and quantitative analyses, with study years, sample sizes, and complication types. Supplementary Table S4 (in the online version of the article) shows

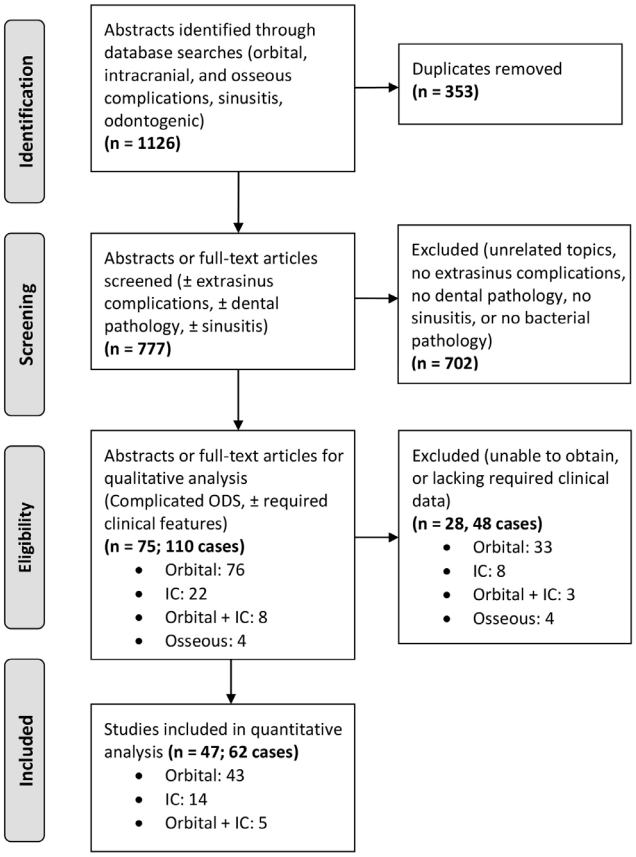

Figure 1. Study selection diagram showing inclusions and exclusions for the complicated odontogenic sinusitis (ODS) systematic review. IC, intracranial.

specific reasons for exclusion from qualitative and quantitative analyses.

Qualitative Analysis

Frequencies of different complication types from the 110 complicated ODS cases were as follows: 69% orbital, 19% intracranial, 8% orbital plus intracranial, and 4% osseous (**Figure 1**). Roughly equal proportions of all ODS complications were published per decade in the past 30 years: 2010s (28%), 2000s (24%), and 1990s (30%). Significantly fewer ODS complications were published in the 1980s (16%) and 1970s (2%). **Figure 2** shows frequencies of journal types having published ODS complications, with 40% being published in dental journals and 23% in otolaryngology journals. Of the 75 studies on complicated ODS, 91% were level 5 evidence (case reports) and 9% were level 4 (case series).

Quantitative Analysis: Primary Outcome Measures

Of the 62 patients with orbital and intracranial complications, 81% were adults and 74% were male. Mean age was 31.7 ± 16.5 years, with mean age being 37.0 ± 13.6 for adults and 9.7 ± 4.0 for pediatrics. Across sexes and ages, orbital complications were more common than intracranial complications (**Table 1**).

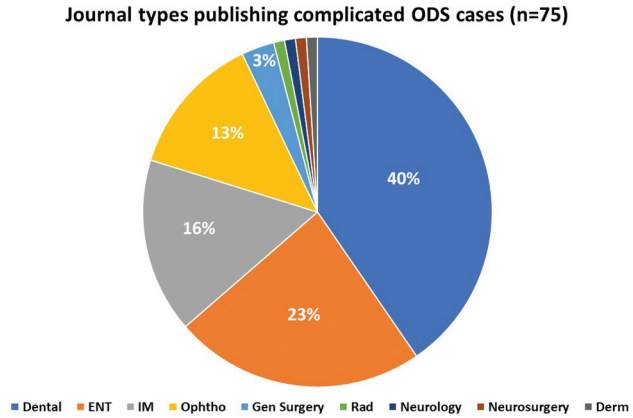

Figure 2. Percentages of journal specialty types having published complicated odontogenic sinusitis (ODS) studies. Derm, dermatology; ENT, ear, nose, throat (otolaryngology); Gen Surgery, general surgery; IM, internal medicine; Ophtho, ophthalmology; Rad, radiology.

Table 1. Reported Frequencies of Odontogenic Sinusitis-Related Orbital and Intracranial Complications in Males and Females and in Adult and Pediatric Patients.

Characteristic	Orbital complications, % (No./total No.)	Intracranial complications, % (No./total No.)
Male (n = 46)	73.9 (34/46)	34.8 (16/46)
Female (n = 16)	87.5 (14/16)	18.8 (3/16)
Adult (n = 50)	76.0 (38/50)	32.0(16/50)
Pediatrics (n = 12)	83.3 (10/12)	25.0 (3/12)

Table 2 shows the frequencies of different orbital and intracranial complication types, as well as abscess locations. Note there were 5 cases of concurrent orbital and intracranial complications. Among orbital complications, nearly 70% were due to pre- or postseptal abscesses, with 46% overall being subperiosteal. Subperiosteal and orbital abscesses were located medially or inferiorly most commonly (62%) but occurred in all locations, and 2 abscesses occurred within the optic nerve. Postseptal orbital cellulitis represented 29% of orbital complications. Regarding intracranial complications, only abscesses met inclusion criteria (42% subdural, 42% intraparenchymal, 16% epidural). Intracranial abscesses occurred most in the frontal region (47%) and affected temporal and parietal regions equally (24% each). There was also 1 optic chiasm abscess.

All orbital and intracranial complications occurred unilaterally with roughly equal proportions on each side (55% right), and 97% occurred ipsilateral to the dental pathology and sinusitis. Two cases of unilateral ODS with pansinusitis spread to the contralateral sphenoid sinus, causing extrasinus complications contralateral to the causative dental pathology.[23,24]

Table 2. Reported Frequencies of Different Types of Orbital and Intracranial Complications Due to Odontogenic Sinusitis and Locations of Orbital and Intracranial Abscesses.

Characteristic	Frequency, % (No.)[a]
Orbital complications (n = 48)	
Preseptal cellulitis	0
Preseptal abscess	2.1 (1)
Postseptal cellulitis	29.2 (14)
Subperiosteal abscess	45.8 (22)
Orbital abscess	16.7 (8)
Intraoptic nerve abscess	4.2 (2)
Cavernous sinus thrombosis	2.1 (1)
Orbital abscess locations (n = 37)	
Medial	40.5 (15)
Inferior	21.6 (8)
Diffuse	10.8 (4)
Intraconal only	10.8 (4)
Superior	5.4 (2)
Lateral	5.4 (2)
Intraoptic nerve	5.4 (2)
Intracranial complications (n = 19)	
Meningitis	0
Subdural abscess	42.1 (8)
Intraparenchymal abscess	42.1 (8)
Epidural abscess	15.8 (3)
Intracranial abscess locations (n = 17)	
Frontal	47.1 (8)
Temporal	23.5 (4)
Parietal	23.5 (4)
Optic chiasm	5.9 (1)

[a]Cases of concurrent orbital and intracranial complications were included in these analyses.

Table 3. Reported Dental Pathologies Causing Odontogenic Sinusitis With Orbital and Intracranial Complications (n = 62).

Dental pathology	Frequency, % (No.)
Primary pathology	
Apical periodontitis	62.9 (39)
Dentigerous cyst	1.6 (1)
Following dental procedures	
Extraction with no OAC/OAF	16.1 (10)
Root canal therapy	6.4 (4)
Foreign body	4.8 (3)
Extraction with OAC/OAF	3.2 (2)
Other OAF	1.6 (1)
Repaired OAF	1.6 (1)
Procedure for dental caries	1.6 (1)

Abbreviations: OAC, oroantral communication; OAF, oroantral fistula.

Table 3 shows the frequencies of different dental pathologies leading to complicated ODS. Apical periodontitis caused 63% of cases. ODS complications followed dental procedures in about 35% of cases. Dental extractions without oroantral communication or fistula caused 16% of cases overall and represented 45% of ODS complications from dental procedures. When dental procedures preceded extrasinus complications, median time to admission was 7 days (interquartile range, 3-14 days). Molars were the causative dentition in 80% of cases, followed by premolars (12%), incisors (5%), and canines (3%).

Table 4. Extent of Sinus Opacification on Computed Tomography for Intracranial and Orbital Complications Due to Odontogenic Sinusitis.

Sinuses opacified	Intracranial complications (n = 14), % (No.)[a]	Orbital complications (n = 43), % (No.)[a]
Maxillary only	36.7 (5)	18.6 (8)
Maxillary + ethmoid	42.9 (6)	46.5 (20)
Maxillary + ethmoid + frontal	21.4 (3)	32.5 (14)
Pansinusitis	0 (0)	2.3 (1)
Pansinusitis + contralateral sphenoid	7.1 (1)	0 (0)

[a]Note that the 5 cases of both orbital and intracranial complications were not included in this analysis.

Table 4 shows the frequencies of different extents of sinus opacification on CT as they occurred in orbital and intracranial complications, and there were roughly equivalent degrees of sinus opacification between both complication types.

Quantitative Analysis: Secondary Outcome Measures

Symptoms were reported in 53 of 62 cases and included a variety of dental, sinonasal, orbital, and neurologic symptoms. Dental pain was reported in 37% of patients (20/53), and 80% of dental pain occurred with endodontic disease (14 periapical abscesses, 2 prior root canals). When symptom durations were reported (n = 43), patients always presented acutely after a mean of 5.1 ± 4.3 days.

Mean body temperature for 21 patients was 38.5 ± 0.8°C, and 68% had fever. Mean white blood cell (WBC) count for 24 patients was 17,700 ± 5800 cells/mm^3, and 88% presented with leukocytosis.

Table 5 shows bacterial culture results from 52 cases. No growth occurred in 5.8% of cases. Anaerobes were reported in nearly 90% of cases and α-hemolytic streptococci in nearly 40% of cases. Cultures were reported from different sources in the following frequencies: sinus (65%), orbit (37%), brain (21%), face (2%), and tooth (2%).

Regarding preoperative antimicrobial characteristics, 37 cases received a median of 1 day of intravenous antibiotics, with 97% having aerobic and 70% aerobic plus anaerobic coverage. Polytherapy was used in 54% of cases preoperatively. Postoperatively, 33 cases received a median of 14 days of antibiotics (combination of intravenous and oral), with 97% having both aerobic and anaerobic coverage and nearly 80%

Table 5. Individual Cultured Bacteria From Different Anatomic Sites in Reported Odontogenic Sinusitis-Related Orbital and Intracranial Complications (n = 52).

Bacteria	Frequency, % (No.)
Anaerobes (obligate)	
Anaerobes	88.5 (46)
Peptostreptococcus spp.	23.1 (12)
Fusobacterium spp.	19.2 (10)
Prevotella spp.	19.2 (10)
Bacteroides spp.	5.8 (3)
Propionibacterium acnes	5.8 (3)
Mixed anaerobic flora	5.8 (3)
Actinomyces spp.	3.8 (2)
Veillonella parvula	3.8 (2)
Porphyromonas spp.	1.9 (1)
Aerobes (gram positive)	
α-Hemolytic streptococci	38.5 (20)
α-Hemolytic streptococcus (nontyped)	13.5 (7)
Microaerophilic streptococcus	9.6 (5)
Streptococcus intermedius	5.8 (3)
Streptococcus anginosus	3.8 (2)
Streptococcus constellatus	1.9 (1)
Streptococcus oralis	1.9 (1)
Streptococcus group F	1.9 (1)
MSSA	13.5 (7)
β-Hemolytic *Streptococcus*	9.6 (5)
Streptococcus group C	1.9 (1)
Streptococcus group A	1.9 (1)
Streptococcus pneumoniae	1.9 (1)
Micrococcus	1.9 (1)
MRSA	1.9 (1)
Staphylococcus lugdunensis	1.9 (1)
Corynebacterium spp.	1.9 (1)
Coagulase-negative staphylococcus	21.2 (11)
Aerobes (gram negative)	
Enterobacter spp.	3.8 (2)
Haemophilus parainfluenza	1.9 (1)
Nonspeciated	
Upper respiratory flora	3.8 (2)
Gram-positive cocci	3.8 (2)
Gram-negative rods	1.9 (1)

Abbreviations: MSSA, methicillin-sensitive *Staphylococcus aureus*; MRSA, methicillin-resistant *Staphylococcus aureus*.

receiving polytherapy for the treatment duration. A wide variety of agents were reported both preoperatively and postoperatively, without clear preferences for specific antibiotics.

Table 6 shows the different types of orbital, intracranial, sinus, and dental interventions performed for complicated ODS and mean times to interventions. There was variability in the sequence of orbital, intracranial, sinus, and dental treatments, although on average, they occurred in close proximity to one another within 1 to 2 days after admission. No interventions were performed in 13% to 25% of reported cases.

Table 6. Orbital, Intracranial, Sinus, and Dental Interventions Reported to Treat Orbital and Intracranial Complications From Odontogenic Sinusitis.

Treatments	Frequency, % (No.)
Orbital interventions (n = 45)	
Decompression	13.3 (6)
I&D	66.7 (30)
No intervention	22.2 (10)
Intracranial interventions (n = 12)	
Craniotomy	66.7 (8)
Burr hole	8.3 (1)
No intervention	25.0 (3)
Sinus interventions (n = 60)	
ESS	50.0 (30)
Caldwell-Luc	25.0 (15)
Other external	15.0 (9)
No intervention	18.3 (11)
Dental interventions (n = 39)	
Extraction	82.1 (32)
I&D of apical abscess	5.1 (2)
No intervention	12.8 (5)

Abbreviations: ESS, endoscopic sinus surgery; I&D, incision and drainage.

Table 7 shows rates of ophthalmoplegia and vision loss at presentation and after intervention. For all orbital complications, 85% of patients presented with ophthalmoplegia (41/48), and 69% presented with vision loss (33/48). After interventions, 86% of ophthalmoplegia improved (31/36), while only 50% of vision loss improved (16/32). The frequencies of ophthalmoplegia and vision loss at presentation, as well as their improvements, were equivalent between patients with postseptal orbital cellulitis and orbital abscesses (subperiosteal, orbital, and intraoptic nerve abscesses). Of the 25 patients with reported acuity levels, none of the 14 patients presenting with light perception or worse recovered vision. The 11 patients whose acuity was better than light perception all had improved vision. Of interest, those with improved vision underwent orbital intervention 1.1 ± 1.7 days after presentation (n = 9), as opposed to patients with no vision improvement who underwent intervention at 2.4 ± 3.4 days (n = 11).

Regarding intracranial complications, neurologic symptoms were only reported for 10 patients: altered mental status (n = 6), hemiparesis (n = 4), and no deficits (n = 2). Of the 10 patients who underwent intracranial interventions, 8 ''improved,'' but no specific outcome measures were reported.

Mean hospital length of stay was 15 ± 13.2 days. There was 1 death reported in a patient with combined orbital and intracranial complications.

Discussion

The incidence of complicated ODS is unknown, as prior publications on rhinosinusitis-related extrasinus complications have generally not reported the frequencies of odontogenic

Table 7. Reported Frequencies of Ophthalmoplegia and Vision Loss at Presentation and Their Improvements After Interventions.

Variable	All orbital complications, % (No./total No.)	Postseptal orbital cellulitis, % (No./total No.)	Orbital abscesses,[a] % (No./total No.)
Ophthalmoplegia at presentation	85.4 (41/48)	92.9 (13/14)	86.7 (26/30)
Ophthalmoplegia improved	86.1 (31/36)	100 (11/11)	87.0 (20/23)
Vision loss at presentation	68.8 (33/48)	78.6 (11/14)	66.7 (20/30)
Vision loss improved	50.0 (16/32)	45.5 (5/11)	57.9 (11/19)

[a]Subperiosteal, orbital, and intraoptic nerve abscesses.

sources. ODS has also not been discussed as a cause of extrasinus complications of sinusitis in recent international sinusitis guidelines.[1,25] There are multiple reasons for this underrepresentation of ODS as a cause of extrasinus complications. First, there has been an overall paucity of ODS publications in the sinusitis literature,[15] and only recently has international consensus been reached on diagnosing ODS.[4] In addition, as demonstrated in this review, only 23% of complicated ODS studies have been published in the otolaryngology literature. Taken together, these factors make it possible that ODS has been underrecognized as a cause of complicated sinusitis.

There have also been some interesting trends in the literature supporting the notion of complicated ODS being underrepresented. First, rhinosinusitis complications are frequently unilateral,[2,26-28] and studies on rhinosinusitis-related orbital[26,29-34] and intracranial[35-37] complications have often reported high rates of odontogenic bacteria in sinus cultures. However, these studies have typically not reported the presence of ODS. As ODS is one of the most common causes of unilateral sinus disease,[13] and certain odontogenic bacteria are more common in ODS than in rhinosinusitis,[38,39] prior rhinosinusitis complication studies could have overlooked ODS as a cause of extrasinus complications. Future studies on sinusitis complications should consider the frequency with which complications stem from odontogenic sources.

Clinical Features

When comparing complicated ODS and rhinosinusitis, extrasinus complication types have been reported in similar frequencies: orbital > intracranial > osseous. Complicated ODS affected all ages and sexes in this review. Similar to rhinosinusitis, complicated ODS affected males more commonly. Contrary to rhinosinusitis, complicated ODS occurred more in adults for both orbital and intracranial complications, whereas rhinosinusitis-related orbital complications occur more in pediatrics. Patterns of sinus involvement were also different in complicated ODS. For rhinosinusitis, the ethmoid sinus has been implicated more for orbital complications and the frontal sinus for intracranial complications.[1] However, the current review showed no clear predilection of sinusitis extent in ODS-related orbital or intracranial complications. Larger studies will be necessary to corroborate this relationship.

This study also showed other interesting similarities and differences between complicated and uncomplicated ODS. Regarding similarities, multiple uncomplicated ODS studies have shown higher rates of certain anaerobic and α-hemolytic streptococcal species in sinus cultures.[6,38-40] These prior studies typically included patients with chronic symptoms, but the current review showed very similar microbiology in patients with acute presentations. Similarly, Brook[41] demonstrated no significant differences in sinus cultures between ODS patients with acute vs chronic symptoms, and therefore ODS microbiology may be stable over time. Last, the frequencies of maxillary, ethmoid, and frontal sinus involvement for complicated ODS cases (21%, 74%, 29%) were similar to uncomplicated ODS in the previously mentioned ODS review study (31%, 69%, 41%),[6] suggesting similar sinus involvement regardless of symptom chronicity or extrasinus spread.

Regarding differences between complicated and uncomplicated ODS, a recent review article analyzed 22 studies with 1680 patients with uncomplicated ODS and showed a mean age of 51 years, no sex predilection, and a median symptom duration of 6 months.[6] Based on the current review, patients with complicated ODS were younger with a mean age in their 30s, similar to another complicated ODS literature review.[42] Complicated ODS also demonstrated a male predilection and acute symptom presentations averaging less than 7 days. Last, while 60% of complicated ODS patients did not have dental pain, 70% of those with dental pain had periapical abscesses. This would imply patients had symptomatic apical periodontitis with acute apical abscesses. This is unique from uncomplicated ODS due to endodontic disease, which usually results from asymptomatic apical periodontitis with or without chronic apical abscesses.[6]

Pathophysiology

Based on the 110 complicated ODS cases from this review and the recent ODS literature review of 1680 uncomplicated ODS cases (which excluded series with <20 patients),[6] complicated ODS represents roughly 7% or less of published ODS cases. What might account for extrasinus spread in these cases? While it is possible that dental procedures predispose patients to infectious spread, they represented far fewer dental causes in this review compared to apical periodontitis, so spread cannot be explained by physical manipulation of the dentition alone. Does age contribute? Younger adults were

affected more than in uncomplicated ODS, so perhaps younger age is a risk, but more studies are necessary to understand this association. Could immune status account for extrasinus spread? While possible, reviewed studies rarely reported immune status of patients, so future studies are again necessary.

There are multiple potential paths of extrasinus spread in ODS. Dental infections can spread from teeth into the sinus mucosa or lumen, then submucosally via thrombophlebitis or direct extension outside the sinuses. Infection can also spread from teeth hematogenously through veins in the maxillary alveolar marrow spaces, or submucosally through oral or facial veins, and eventually to the face, pterygoid plexus, orbit, brain, or systemically.[42] While it may be intuitive that the sinuses are the avenue through which ODS causes extrasinus complications, it is not so straightforward. There have been at least 69 reports of isolated dental pathology causing extrasinus complications without sinusitis (see Suppl. Table S2 in the online version of the article). The current review also showed no clear relationship between sinusitis extent and intracranial or orbital complications, which could lend support to some complicated ODS cases resulting from thrombophlebitic spread directly from dentition, causing both sinusitis and extrasinus complications separately. However, until infectious spread in complicated ODS is better understood, both the sinuses and dentition should be considered possible infectious sources requiring treatment.

With regard to ODS-related orbital complications, one concerning trend compared to nonodontogenic complications has been a high rate of permanent vision loss. Prior studies on nonodontogenic orbital complications have reported permanent vision loss in 0% to 12% of patients.[43-46] Regarding odontogenic orbital complications, Youssef et al[42] performed a literature review of 24 patients with odontogenic orbital cellulitis. Similar to the current review, they found that only 54% of patients presenting with vision loss experienced vision improvement, and patients presenting with light perception or worse never recovered vision. However, due to small sample sizes and limitations of analyzing case reports or series, statistical analyses were limited in the Youssef et al[42] and the current review for determining prognostic variables for vision outcomes. Future studies are needed to determine features portending better or worse vision outcomes in these cases.

Based on the literature, explanations for higher rates of vision loss in complicated ODS are speculative. One possible explanation could be higher rates of orbital abscesses in complicated ODS.[47] Patt and Manning[45] reported only a 2.5% incidence of blindness in 159 rhinosinusitis-related orbital complications, and all 4 patients had abscesses. Erickson and Lee[44] showed a 10% rate of vision loss in 30 patients with a 57% incidence of orbital abscesses. The current review showed a 50% rate of vision loss with a 67% orbital abscess incidence, but there were similar rates of vision loss between orbital cellulitis and abscesses. More investigation is needed to understand the mechanisms behind vision loss in complicated ODS. To facilitate this understanding, future studies should report best-corrected visual acuity, pupillary exam and afferent pupillary defect presence, intraocular pressures, proptosis, color vision assessment, and fundoscopy (optic nerve and retinal changes).

Intracranial spread from ODS or dental sources is particularly perturbing, and the reasons for such spread are speculative. While direct extension from ethmoid or frontal sinusitis would seem plausible, this review showed that sinusitis extent in ODS-related intracranial complications was relatively equal between the different sinuses (**Table 4**). Brook[37] also reported 8 intracranial abscesses from ODS; 3 of 8 patients had maxillary sinusitis alone, and none had frontal sinusitis. These reports, coupled with the numerous reports of isolated dental infections causing intracranial abscesses, suggest that hematogenous spread is important in the pathophysiology of ODS-related intracranial complications. Future studies would be beneficial in determining the propensity for hematogenous infectious spread from maxillary dentition compared to sinuses, as well as the most likely vascular routes of such intracranial spread. In addition, studies comparing microbiology and other clinical features between cases of hematogenous vs direct spread would be beneficial.

Despite intracranial complications causing potentially serious sequelae and mortality rates of 0% to 19%,[1] there were significantly fewer publications on ODS-related intracranial complications. In addition, many did not report clinical features or outcome measures. Future studies require more complete and consistent data reporting.

Diagnosis and Management

Clinicians should consider dentition as a possible source of all extrasinus complications. They should assess for maxillary dental pathology on sinus CT and inquire about prior dental pathology or dental procedures. When dental pathology is considered, patients should be evaluated by dental specialists for dental testing, examination, and imaging as needed.[4,6]

When managing extrasinus complications, one must address the extrasinus complications as well as infectious sources. For rhinosinusitis, it has been recommended that unless patients meet emergency surgery criteria, patients should receive 48 hours of intravenous antibiotics with close monitoring for deterioration. If patients do not improve after 48 hours, surgery is warranted.[1] Based on current understanding of complicated ODS, both the dentition and sinuses could be infectious sources, and therefore treating both the sinuses and dentition should be considered, in addition to the orbital and/or intracranial complications. Additional treatment considerations for complicated ODS are antimicrobial coverage, how the teeth and sinuses are treated, and the timing of different interventions.

Regarding antibiotic use for suspected or confirmed complicated ODS, clinicians should administer antibiotics with aerobic and anaerobic coverage. The current review showed that preoperatively, antibiotics only covered anaerobes in 70% of cases, compared to 97% postoperatively, suggesting perhaps odontogenic sources were not always suspected before surgery. Postoperatively, antibiotics were prescribed on average for 2 weeks, with polytherapy in nearly 80% of cases. Surgeons should try to obtain cultures sterilely from as

many sources as possible to optimize antibiotic selection, but polytherapy will often be required due to the likelihood of anaerobic infection.[21]

For dental treatment in complicated ODS, 82% of patients with treatable dental pathology underwent extraction, and 13% had no intervention during hospital admissions. While root canal therapy could theoretically be offered to patients with apical periodontitis, endodontic therapy may not be available in hospital settings. One question that arises is, do all patients with complicated ODS require dental treatment emergently, or could it be performed in the outpatient setting after treating the extrasinus complications and sinusitis? Also, could tooth-preserving root canal therapy be considered? Another question pertains to the timing of dental treatment in patients with complicated ODS with no emergent surgical indications. Should these patients be managed with antimicrobial therapy alone or antimicrobial therapy plus early dental extraction? In the current study, dental treatment was generally performed around the same time as other interventions, but larger series across more centers are necessary to determine optimal type and timing of dental treatment for complicated ODS.

Regarding sinus treatment for complicated ODS, only 50% of cases in the literature were treated with endoscopic sinus surgery (ESS), with external approaches being performed in 40% of cases. This was likely due to a substantial number of patients being managed by oral surgeons without otolaryngologists. A recent consensus statement on ODS management reported that for complicated ODS, all diseased sinuses should be addressed to minimize further extrasinus spread.[5] As ESS offers significantly lower morbidity compared to external maxillary, ethmoid, and frontal sinus surgery, ESS should be considered in all complicated ODS cases.

While the exact sequence of different treatments was variable, average times to each intervention type were similar, occurring 1 to 2 days after admission. Until more evidence accumulates, it is prudent to address the emergent complications first. If logistically feasible, both the sinuses and dentition should be addressed concurrently or soon after orbital or intracranial interventions, as there have been reports of delayed ESS leading to recurrent intracranial infection.[1] It will be important in future studies to determine the optimal timing of different treatments for complicated ODS.

For orbital complications, improved vision outcomes were noted in patients who presented with visual acuity loss better than light perception and in those who underwent orbital interventions earlier, although the effect of surgical timing could not be analyzed statistically. A larger sample size would be necessary to assess the effect of time to surgery for vision recovery while controlling for orbital complication type and preoperative acuity levels. Until more is understood about vision loss in complicated ODS, based on the current review and the Youssef et al[42] review, orbital intervention should be considered for subperiosteal and orbital abscesses, as well as in patients with vision loss, especially in patients with visual acuity better than light perception, as they may obtain more improvement.

Limitations

One limitation of this study was that all reviewed studies were either case reports or series, introducing publication bias. Due to publication bias, small overall sample size, and variability in the reporting of some clinical variables, results from this study must be viewed with caution. However, this literature-based review demonstrated common clinical features and treatment strategies for complicated ODS. These findings can be explored in future studies, ideally through prospective series and cohort designs, since randomized trials will likely not be feasible.

Another limitation was that osseous complications from ODS were excluded from quantitative analysis. This was due to the scarcity of ODS-related osseous complication studies, as only 4 cases have been documented.[48-51] Interestingly, a recent retrospective series of 17 frontal osteomyelitis cases showed that about 50% had dental pathology and sinusitis ipsilateral to both the dental and frontal disease on CT. While dental pathology was not confirmed by dental evaluation, it is plausible that a significant proportion of those cases were from ODS.[52]

A final limitation was that studies only reported acute presentations of complicated ODS, but it would be important to know if patients had symptomatic or asymptomatic ODS prior to extrasinus spread. Future studies should consider this as it could help guide outpatient ODS monitoring, especially in asymptomatic patients.

Conclusions

Complicated ODS generally presents unilaterally, most often in adult men in their 30s, and most commonly from apical periodontitis of maxillary molars. ODS should be considered in all patients with infectious extrasinus complications. When ODS is suspected, dental specialists should be consulted to assess for dental pathology. Treatment requires multidisciplinary collaboration to address orbital and intracranial complications, as well as possible dental and sinus infectious sources.

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Author Contributions

John R. Craig, study concept and design, data acquisition, analysis and interpretation of data, drafting of manuscript, critical revision of manuscript; **Atif J. Cheema**, data acquisition, manuscript drafting, critical revision of manuscript; **Raven T. Dunn**, data acquisition, critical revision of manuscript; **Swapna Vemuri**, analysis and interpretation of data, critical revision of manuscript; **Edward L. Peterson**, analysis and interpretation of data, drafting of manuscript, critical revision of manuscript.

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Supplemental Material

Additional supporting information is available in the online version of the article.

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